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Efficacy of the unified protocol for adolescents (UP-A): A systematic review of randomized controlled trials

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ABSTRACT

Objective: The Unified Protocol for Transdiagnostic Treatment of Emotional Disorders in Adolescents (UP-A) is a cognitive-behavioral therapy (CBT) approach designed to address shared etiological mechanisms underlying emotional disorders. This study aimed to conduct a systematic review of randomized controlled trials (RCTs) evaluating the efficacy of the UP-A for both the treatment and prevention of emotional disorders. **Method:** Six electronic databases (Scopus, PsycINFO, EBSCO, Google Scholar, PubMed, and Medline) were systematically searched for RCTs examining the effectiveness of the UP-A in adolescent populations. Eligible studies were screened, and methodological characteristics and key findings were analyzed. **Results:** Eleven RCTs, comprising a total of 1,002 participants, were conducted between 2017 and 2025. The included studies involved adolescents with diagnosed emotional disorders or related symptoms, as well as other mental disorders. Various delivery formats (individual, group, digital, and telehealth), settings (clinical and school-based), and purpose (treatment or prevention) were represented. Both within-group and between-group improvements favored the UP-A condition, particularly when compared to waitlist control groups. Positive outcomes extended to transdiagnostic etiological factors, including negative affect, anxiety sensitivity, intolerance of uncertainty, and emotion regulation strategies. **Conclusions:** This systematic review provides evidence supporting the UP-A as an effective intervention for emotional disorders and related transdiagnostic mechanisms across diverse formats and settings.

Keywords: Transdiagnostic; anxiety; depression; emotional disorders; treatment; prevention; sistematic review.

Eficacia del protocolo unificado para adolescentes (UP-A): Revisión sistemática de ensayos controlados aleatorizados

RESUMEN

Objetivo: El Protocolo Unificado para el Tratamiento Transdiagnóstico de los Trastornos Emocionales en Adolescentes (UP-A) es una intervención basada en la terapia cognitivo-conductual (TCC), diseñada para abordar los mecanismos etiológicos compartidos que subyacen a los trastornos emocionales. El objetivo de este estudio fue realizar una revisión sistemática de ensayos clínicos controlados aleatorizados (ECAs) que examinaran la eficacia del UP-A para el tratamiento o prevención de los trastornos emocionales. **Método:** Se realizó una búsqueda sistemática en seis bases de datos electrónicas (Scopus, PsycINFO, EBSCO, Google Scholar, PubMed y Medline) de ECAs que evaluaran la efectividad del UP-A en poblaciones adolescentes. Se seleccionaron los estudios elegibles, y se analizaron las características metodológicas y los hallazgos principales. **Resultados:** Se identificaron once ECAs, con un total de 1.002 participantes, realizados entre 2017 y 2025. Los estudios incluidos involucraron adolescentes con trastornos emocionales diagnosticados o con síntomas relacionados, así como también otros trastornos mentales.

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Se contemplan diversos formatos de aplicación (individual, grupal, digital y telemática), contextos (clínico y escolar) y objetivos (tratamiento o prevención). Las mejoras intra e intergrupos favorecieron la condición UP-A, especialmente en comparación con los grupos de lista de espera. Los resultados positivos también se observaron en factores etiológicos transdiagnósticos, incluyendo el afecto negativo, la sensibilidad a la ansiedad, la intolerancia a la incertidumbre, y las estrategias de regulación emocional. **Conclusiones:** Esta revisión sistemática aporta evidencia que respalda al UP-A como una intervención eficaz para los trastornos emocionales y los mecanismos transdiagnósticos relacionados, aplicada en diversos formatos y contextos.

Palabras clave: Transdiagnostico; ansiedad; depresión; trastornos emocionales; tratamiento; prevención; revisión sistemática.

Introduction

Emotional disorders are highly prevalent in adolescents. According to the systematic review and meta-analysis conducted by Sacco et al. (2022), the prevalence of emotional disorders among children and adolescents is high, with estimated rates of 7.9% for anxiety disorders, 2.5% for attention-deficit/hyperactivity disorder (ADHD), and 1.7% for depression. Point prevalence rates for anxiety disorders in children and adolescents generally exceed 7%, while depressive disorders tend to show rates around 3% (Ghandour et al., 2019).

Although prevalence rates reported by different meta-analyses on mental disorders in children and adolescents vary considerably across studies (differences may stem from a wide range of factors, such as diagnostic criteria, participant demographics, assessment methods, etc.), a consistent finding is that anxiety disorders tend to be the most common. In contrast, attention-deficit/hyperactivity disorder (ADHD) and depression typically show lower prevalence rates (see Sandín et al., 2018). As said by these authors, the estimated lifetime, annual, and current prevalence rates for anxiety disorders (including post-traumatic stress disorder and obsessive-compulsive disorder) in children and adolescents are 21.1%, 13.9%, and 7.5%, respectively. These figures are based on the reports from the National Comorbidity Survey (NCS) and published sources up to 2015. Contrary to expectations, Sandín et al. (2018) indicated minimal differences in anxiety disorder prevalence based on age (i.e., children vs. adolescents). Regarding anxiety disorders, Canals et al. (2019) found that the prevalence of any anxiety disorder among Spanish children and adolescents is 11.8%. Although depression rates are lower than those for anxiety, they are still considerable, ranging from 3.4% for depressive disorders to 12% for subclinical depressive symptoms (Canals et al., 2018; Pámias et al., 2016).

A sustained increase in emotional problems has been suggested in the current generation compared to previous ones (Borg et al., 2025), which may be associated, at least in part, with the effects of COVID-19 (Orgilés et al., 2021; Sandín, 2022; Sandín et al., 2020c, 2021). The meta-analysis conducted by Racine et al. (2021) revealed that the prevalence rates of depressive and anxiety symptoms among children and adolescents during the COVID-19 pandemic were 25.2% and 20.5%, respectively; these pooled estimates, which increased over time, represent approximately double the rates observed prior to the pandemic. In Spain, hospital admissions of adolescents due to mental disorders have risen from 3.9% in the year 2000 to 9.5% in 2021 (Soriano et al., 2025). This substantial increase highlights that the growing adolescent mental health crisis is also affecting Spain. Although hospitalization data do not directly reflect prevalence in the general population, they do suggest a rise in the occurrence of mental health problems.

Emotional disorders are also highly comorbid during adolescence, meaning that individuals diagnosed with one emotional disorder frequently present with additional emotional disorders. Research indicates that comorbidity between anxiety and depression in adolescents is particularly high, with estimates reaching up to 75% (Cummings et al., 2014). Similarly, Ghandour et al. (2019) reported that 73.8% of children and adolescents (ages 3-17) diagnosed with a depressive disorder also had a concurrent diagnosis of an anxiety disorder, while 32.3% of those diagnosed with anxiety also met criteria for depression. Although comorbid mental disorders are most commonly reported among individuals with current depression (Ghandour et al., 2019), both anxiety and depression are highly impairing and have been identified as leading contributors to the non-fatal disease burden among adolescents (Klaufus et al., 2022).

A major limitation of disorder-specific cognitive-behavioral therapy (CBT) is its inability to adequately address the high rates of comorbidity among emotional disorders. Despite the substantial overlap between emotional disorders, particularly anxiety and depressive

disorders, most psychological treatments continue to target specific diagnoses. Disorder-specific CBT has demonstrated strong efficacy across a wide range of mental health conditions and is considered the treatment of choice for emotional disorders (Moriana & Martínez, 2011). However, one of the main drawbacks of traditional CBT is its limited capacity to address comorbidity. Additionally, it has led to an excessive proliferation of intervention protocols. Separate protocols are required not only for anxiety and depression but also for individual disorders within each category. For example, numerous internationally accepted protocols exist for the treatment of specific anxiety disorders, including generalized anxiety disorder and panic disorder. While this approach may allow for in-depth focus on specific disorders, it presents significant challenges for implementation, particularly in clinical settings where logistical barriers may arise.

The transdiagnostic approach offers an innovative framework for treating emotional disorders (see Craske, 2012; Sandín et al., 2012). This perspective is based on the premise that the high comorbidity among emotional disorders stems from shared etiological factors, either causal or maintaining, which operate across hierarchical transdiagnostic levels. These include temperament traits (e.g., negative affect or neuroticism), clinical traits (e.g., anxiety sensitivity), and emotion regulation strategies (e.g., emotional avoidance) (Bullis et al., 2011; Sandín et al., 2020a). Transdiagnostic CBT (T-CBT) focuses on modifying these shared processes rather than targeting mechanisms specific to individual disorders. Importantly, T-CBT is a flexible treatment modality. Its transdiagnostic nature is defined not by its format in which it is delivery, but by its focus on addressing core etiopathogenic processes (specifically, vulnerability and maintenance factors) that are shared across multiple disorders (Sandín et al., 2020a).

The Unified Protocol for the Transdiagnostic Treatment of Emotional Disorders was developed by Ehrenreich-May et al. (2017, 2018) to implement T-CBT for emotional disorders in children and adolescents. It is derived from the original Unified Protocol (UP) created by Barlow et al. (2011) and includes two age-specific versions: the UP-C for children (ages 6–12) and the UP-A for adolescents (ages 12–18). These protocols are designed to be applicable to youth presenting with a wide range of emotional problems or disorders, without focusing on any particular diagnosis.

Both protocols emphasize emotion and emotion regulation, targeting core mechanisms shared across emotional disorders. Their primary goal is to reduce frequent and intense emotional responses to stress, as well as maladaptive reactions to those emotional responses, including fear, anxiety, sadness, anger, and associated emotional distress.

The UP-A integrates empirically supported cognitive-behavioral strategies through specific modules aimed at: (a) enhancing awareness and understanding of emotional experiences, (b) increasing cognitive flexibility and problem-solving skills, (c) identifying and preventing emotional avoidance and maladaptive emotion-driven behaviors, (d) fostering nonjudgmental present-focused mindfulness, (e) promoting engagement in positive behaviors, and (f) encouraging exposure to both interoceptive and situational emotional triggers. Treatment manuals are available in both the original English versions (Ehrenreich-May et al., 2017, 2018) and Spanish adaptations (Ehrenreich-May et al., 2020, 2022).

Following initial validation studies, primarily case studies and open trials, some randomized controlled trials (RCTs) have been conducted internationally. These studies have demonstrated the efficacy of the UP-A in reducing symptoms associated with emotional disorders (primarily anxiety and depression) and transdiagnostic etiological factors, both in adolescents diagnosed with emotional disorders and in those at risk (i.e., exhibiting elevated symptoms of anxiety and depression). Additionally, preliminary evidence suggests that the UP-A may be effective in treating other emotional problems, such as post-traumatic stress disorder, and in individuals with severe mental health conditions. Although some meta-analyses have examined the efficacy of T-CBT protocols, including those targeting adults (UP), children (UP-C), and adolescents (UP-A) (Carlucci et al., 2021; García-Escalera et al., 2016), most of the existing literature has focused on adult populations (Longley & Gleiser, 2023; Sakiris & Berle, 2019). Despite the UP-A being translated into more than ten languages, including Spanish, Portuguese, Farsi, Japanese, and Chinese (Roberts et al., 2025), no specific systematic review of its efficacy has yet been published.

The aim of the present study was to conduct a systematic review of the efficacy of RCTs conducted using the UP-A as an evidence-based treatment. While the program primarily targets anxiety and depression, this review also explores its potential clinical utility for other psychological problems. A second objective was to assess whether the UP-A produces beneficial effects across different levels of transdiagnostic etiological constructs (Sandín et al., 2020a), including first-level hierarchical traits such as temperament (e.g., negative affect/neuroticism), clinical traits (e.g.,

anxiety sensitivity), and emotion regulation strategies (e.g., emotional avoidance). It is expected that the findings will be consistent with those reported in adult populations. This systematic review aims to fill a critical gap in the literature and was conducted in accordance with PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses), following the recommendations of Shamseer et al. (2015) and the Cochrane Handbook (Higgins & Green, 2011).

Method

Search strategy

The search and selection of articles were conducted between January and March 2025 using the following electronic databases: Scopus, PsycINFO, EBSCO, Google Scholar, PubMed, and Medline. The primary search equation used was: (prevention OR treatment OR intervention) AND ("unified protocol") AND (adolescent OR teenagers). Additional searches were performed using the terms: ("unified protocol") AND (adolescent). All randomized controlled trials (RCTs) applying the UP-A manual (whether in its original form or with cultural or structural adaptations) were considered. In addition to database searches, references cited in previously published meta-analyses and systematic reviews on the efficacy of transdiagnostic treatments for emotional disorders were examined (e.g., Carlucci et al., 2021; Etchemendy et al., 2024; García-Escalera et al., 2016; Walder et al., 2025).

Inclusion and exclusion criteria

The following inclusion criteria were applied:

(1) Articles reporting original research data on the efficacy or clinical utility of the UP-A.
(2) Articles published in English or Spanish.
(3) Studies must be randomized controlled trials (RCTs).
(4) Participants must be adolescents (ages 12–18).
(5) Adaptations of the UP-A were accepted if the core modular structure was preserved (e.g., self-administered online formats, telehealth delivery, group applications, cultural adaptations).
(6) Research outcomes must be clearly described and aligned with the study objectives.
(7) Studies focused on either treatment or prevention were included (i.e., prevention interventions with healthy adolescents were also considered).

Studies were excluded if they consisted of:

(1) Open trials.
(2) Case studies or single-subject designs.
(3) Systematic reviews or meta-analyses.
(4) Any other type of theoretical review or non-empirical study.

Study selection process

Search results from each database were imported into the Zotero reference management software, where duplicate entries were removed. Zotero was also used to examine key characteristics of the retrieved references. An initial screening was conducted by reviewing titles and abstracts to exclude studies that did not meet the inclusion and exclusion criteria. A second screening involved full-text review of the preselected articles, further excluding those that failed to meet the criteria. The final set of articles included in the review was determined through this process. Initial screening was conducted by IR and subsequently reviewed by the remaining authors, with any discrepancies resolved through consensus.

Data extraction, coding, and synthesis

Data extraction was initially conducted by IR and subsequently reviewed, corrected and completed by the remaining authors. For each included study, the following variables were recorded: (a) authors, year of publication, and country; (b) participant characteristics, population type, study design, intervention format (individual, group, in-person, telehealth, digital), treatment duration, follow-up period, and attrition; (c) diagnostic interview (if applicable) and outcome variables (assessment instruments); (d) risk of methodological bias; and (e) main findings, including effect sizes when reported.

Risk of bias was independently assessed by all authors and resolved through consensus following discussion in cases of disagreement. The evaluation followed the RoB 2 criteria from the Cochrane Risk of Bias Tool for Randomized Trials (Sterne et al., 2019). The RoB 2 framework includes the following domains for assessing RCTs:

R Bias arising from the randomization process
D Bias due to deviations from intended interventions
Mi Bias due to missing outcome data
Me Bias in measurement of the outcome
S Bias in selection of the reported result

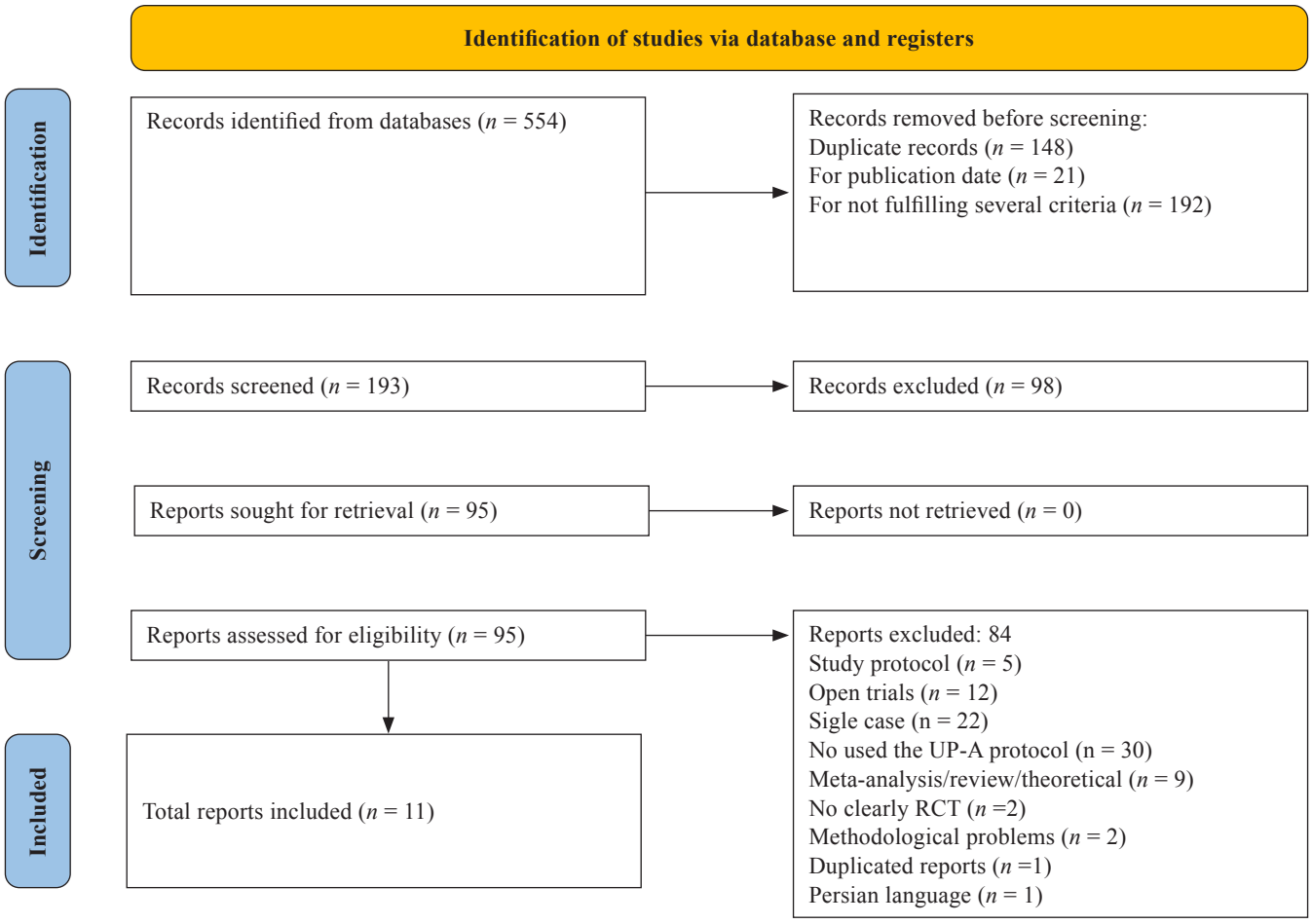

Figure 1. PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analyses) flow diagram, depicting the screening processes.

Each domain was assessed separately, considering its potential impact on study outcomes. For each domain, one of the following ratings was assigned: + (low risk of bias), ? (some concerns), or – (high risk of bias).

Effect sizes were recorded when explicitly reported in the articles. In most cases, Cohen's *d* was used. One study reported effect sizes using partial eta squared (η^2_p). Effect size magnitudes were classified as follows: small: $d = 0.20–0.49$, $\eta^2_p = .01$; moderate: $d = 0.50–0.79$, $\eta^2_p = .06$; and large: $d \geq 0.80$, $\eta^2_p = .14$

Results

Figure 1 shows the screening process conducted in accordance with the PRISMA guidelines for systematic reviews. A total of 11 randomized controlled trials (RCTs) were selected, comprising 1,002 participants, and published between 2017 and 2025. The main characteristics of the reviewed studies are summarized in Table 1. Below, we highlight and discuss several of these key features.

Sample characteristics

The reviewed RCTs were conducted in three countries: Spain (4 studies), Iran (4 studies), and the United States (3 studies). Sample sizes ranged from 40 to 196 participants ($M = 91.08$, $SD = 52.13$). The studies included diverse populations: adolescents diagnosed with anxiety and depressive disorders (4 studies), adolescents with post-traumatic stress disorder (PTSD) and general emotional disorders (1 study), adolescents with psychotic disorders (1 study), adolescents with borderline personality disorder (BPD) (1 study), adolescents with subclinical emotional symptoms, primarily anxiety and depression (2 studies), and non-clinical populations for universal prevention purposes (2 studies).

Intervention characteristics

All interventions were based on the UP-A treatment manuals (Ehrenreich-May et al., 2017, 2018). Six studies employed active control groups, while five used waitlist control groups (WLC). Several studies adapted the protocol for different formats, including individual and group delivery (either in-person or via telehealth), cultural adaptations, applications to mental disorders beyond anxiety and depression (e.g., PTSD, BPD, psychosis), universal prevention contexts, and self-administered online format. Treatment duration typically ranged from 9 to 16 weeks, with sessions held weekly and lasting approximately one hour. All studies included follow-up assessments, most commonly at 3 and 6 months, with the longest follow-up extending to 36 months.

Attrition rates varied widely across studies but were generally comparable between experimental and control groups within each study. Notably, attrition appeared to be influenced by the country in which the study was conducted. The highest attrition rates were observed in studies conducted in the United States, while studies conducted in Spain showed approximately half or lower attrition rates compared to the U.S. studies. Iranian studies reported negligible attrition, with most studies showing no participant dropout.

Assessment of outcome variables

Most studies employed mixed assessment methods, including self-report instruments completed by adolescents and/or their parents, as well as clinician-administered measures. The most frequently used tool was the Revised Child Anxiety and Depression Scale–30 (RCADS-30; an abbreviated form of the RCADS), which allows for the evaluation of anxiety symptoms, major depressive disorder symptoms, and obsessive-compulsive symptoms (three key domains in emotional disorders). The RCADS-30 can be completed by both adolescents and their parents.

Other commonly used instruments included the Strengths and Difficulties Questionnaire (SDQ) for assessing emotional and behavioral problems, and the Difficulties in Emotion Regulation Scale (DERS) for evaluating emotion dysregulation. The most widely used clinician-rated measure was the Clinical Global Impression (CGI) scale, particularly the severity subscale. Most studies also employed structured clinical interviews, with the ADIS-5-C/P and the MINI-KID being the most frequently used.

Risk of bias assessment

Table 1 presents the risk of bias ratings assigned to each study across the five RoB 2 domains. Notably, none of the studies were entirely free from bias. However, most studies demonstrated low risk of bias in the randomization process domain.

Efficacy of the UP-A

Although findings regarding the efficacy of the UP-A for emotional disorders were heterogeneous, they were generally promising. Overall, the results suggest a significant therapeutic effect associated with the UP-A intervention, regardless of delivery format (individual vs. group, in-person vs. telehealth, or digital self-administered) and type of control group (waitlist vs. active control). Table 1 summarizes the main outcomes reported in each study, including effect sizes where available.

The first RCT (Ehrenreich-May et al., 2017), conducted with clinically diagnosed patients, found that UP-A was more effective than a waitlist control in reducing clinician-rated symptom severity and parent-reported internalizing symptoms, with large effect sizes ranging from 1.04 to 1.98. Surprisingly, no significant differences were found in adolescent self-report measures. In contrast, the recent RCT by Ehrenreich-May et al. (2025) reported that, based on multivariate analyses, the largest differences between experimental and control groups were observed in adolescent self-reported outcomes, although the effect sizes were small ($d = 0.21$ for UP-A+ and $d = 0.22$ for TAU+). No significant differences were found between the UP-A+ and TAU+ groups, suggesting the potential relevance of measurement-based care (MBC) as an adjunctive or enhancing component of treatment. However, the lack of significant differences between these two groups remains noteworthy.

Two RCTs conducted with adolescents diagnosed with anxiety and depressive disorders (Espinosa et al., 2024; Zemestani et al., 2023) provide strong support for the efficacy of the UP-A in treating these conditions. Espinosa et al. (2024) found that an online self-applied adaptation of the UP-A (iUP-A), delivered via the AMtE platform (Sandín et al., 2019), demonstrated comparable efficacy to the individually delivered UP-A via telehealth (i.e., a virtual face-to-face). As expected, no differences were found between the two treatment conditions. Clinician-rated global symptom severity showed similar effect sizes (Cohen'*d*) over time in both groups, ranging from 1.22 to 1.87 for iUP-A and 1.54 to 1.70 for UP-A. Both delivered formats were effective

Table 1. Characteristics of the studies (randomized controlled trials) included in the systematic review

Study (country)	Participants (age range, % female)	Groups and sample size	Treatment format	Treatment duration (weeks)	Follow-up after treatment (months)	Attrition (%) Post/ follow-up	Diagnostic interviews	Outcome variables	Risk of bias (RoB2) R D Mi Me S	Main results
Ehrenreich-May et al., 2017 (USA)	Anxiety/ depressive disorders (12-17yr, 56.9%)	UP-A: 27 WLC: 24	Individual (in-person)	16	3/6	26/63/59.2 33.3	ADIS-IV-C/P	RCADS, CSR, CGI-S/I, ALIS.	+ ? + ? ?	All participants (both UP-A and WLC groups) improved significantly on all outcomes during treatment (RCADS, CSR, CGI-S/I and ALIS) (*d*s = 1.90 to 3.23), but the clinician rated outcomes showed greater improvement. However, adolescents in the UP-A condition exhibited significantly lower symptom levels at post-treatment than those in WLC group across all outcomes (*d*s = 0.77 to 1.84). Treatment × time interaction was significant for clinician-rated measures (CSR, CGI-S), and parent-rated internalizing symptoms (RCADS) (*d*s = 1.04 to 1.98), but not for self-reported RCADS and ALIS. The study did not provide separate data regarding anxiety and depression outcomes.
Ehrenreich-May et al., 2025 (USA)	Anxiety/ depressive disorders (12-18yr, 65.3%)	UP-A+: 68 TAU+: 60 TAU: 68	Individual (in-person)	16	3	26/38 28.3/25 20.6/23.5	ADIS-5-C/P	SCARED, CGI-S/I, CGAS, MFQ, SDQ, YOQ.	+ ? + + ?	Adolescents in all groups showed improvement in emotional disorder symptoms over time. Multivariate analyses indicated that the cluster of self-reported symptoms, including anxiety (SCARED), depression (MFQ), emotions/behaviors/social functioning (SDQ) and psychiatric symptoms (YOQ), decreased faster in both UP-A+ (*d* = 0.21) and TAU+ (*d* = 0.22) conditions compared to TAU. No significant differences were observed between UP-A+ and TAU+. Additionally, no group differences were found in the outcome variables assessed by caregivers (SCARED, MFQ, SDQ, YOQ) or independent evaluators (CGI-S, CGAS).

Study (country)	Participants (age range, % female)	Groups and sample size	Treatment format	Treatment duration (weeks)	Follow-up after treatment (months)	Attrition (%) Post/ follow-up	Diagnostic interviews	Outcome variables	Risk of bias (RoB2) R D Mi Me S	Main results
Espinosa et al., 2024 (Spain)	Anxiety/ depressive disorders (12-18yr, 78.3%)	iUP-A (AMtE): 28 UP-A: 30	Digital (self-applied) Individual (telehealth)	8 11-17	3	14.3/21.4 13.3/23.3	MINI-KID	RCADS-30, CGI-S, PANASN, CASI, EASI-A.	+ ? + ? +	As expected, no significant differences were found between UP-A and iUP-A. Both active treatments had a significant effect over time in: (a) self-reported anxiety and depressive disorder symptoms (RCADS-30 total score and subscales of MDD, PD, SP and GAD), with effect sizes (*d*s) ranging from 0.20 to 0.64 for iUP-A and 0.52 to 0.88 for UP-A. (b) clinician rated global severity (CGI-S), *d*s = 1.22/1.87 for iUP-A and 1.54/1.70 for UP-A. (c) self-reported measures of transdiagnostic etiological factors, including negative affect (PANASN-NA; *d*s = 0.20/0.77 for iUP-A and 0.67/0.63 for UP-A), anxiety sensitivity (CASI; *d*s = 0.33/0.59 for iUP-A and 0.74/0.72 for UP-A), and emotional avoidance (EASI; *d*s = 0.69/0.65 for UP-A). The authors conclude that, overall, both forms of the UP-A (digital self-administered and telehealth face-to-face) demonstrated comparable efficacy in treating emotional and transdiagnostic variables.
García-Escalera et al., 2020a (Spain)	Universal prevention (12-17yr, 54.3%)	UP-A: 90 WLC: 61	Group (in-person)	9	3	11.6/18.9 6.5/21.3	na	RCADS-30, EBAE-10, SDQ, SWLSN, KIDSCREEN-10, SES.	+ - + - ?	Over time, self-report measures of life satisfaction (SWLSN; *d* = 0.17) and self-esteem (SES; *d* = 0.17) showed significant increases in both groups, while self-perceived school adjustment (EBAE; *d* = 0.18) declined only in the control group. No further differences were observed between the groups across the remaining outcome variables.
García-Escalera et al., 2020b (Spain)	Universal prevention (12-17yr, 54.3%)	UP-A: 90 WLC: 61	Group (in-person)	9	3	11.6/18.9 6.5/21.3	na	RCADS-30, CDN, EAN.	+ - + - ?	Unexpectedly, self-reported outcome measures of anxiety and depressive disorder symptoms (RCADS-30 total score and some subscales) showed significant reductions across all participants, with effect sizes ranging from 0.18 to 0.32. However, time-related decreases in depression (CDN) were observed only among participants in the UP-A group who had elevated RCADS-30 scores (*d*s = 0.96/0.88). No such improvements were found in the control group.

Study (country)	Participants (age range, % female)	Groups and sample size	Treatment format	Treatment duration (weeks)	Follow-up after treatment (months)	Attrition (%) Post/ follow-up	Diagnostic interviews	Outcome variables	Risk of bias (RoB2) R D Mi Me S	Main results
García-López et al. 2024 (Spain)	High anxiety/ depression and emotional problems (12-18yr, 53%)	UP-A: 37 ACC (UTalk): 31	Group (telehealth)	8+1	6/7	2.7/24.3/2.7 9.7/9.7/9.7	ADIS-5-C/P	RCADS-30, SDQ, CD-RISC-10, KIDSCREEN-10, WAM-C/A, DERS.	+ + + ? ?	Participants in the UP-A condition showed significant improvements from pre-treatment to 6-month follow-up across nearly all outcome variables: RCADS-30 (d = 0.60), GAD (d = 0.61), PD (d = 0.48), MDD (d = 0.53), SAD (d = 0.40), OCD (d = 0.60), SDQ (self/parent report; ds = 0.65-0.75), WAM (d = 0.57), DERS (d = 0.43), and CD-RISC (d = 0.71), with the exception of SP and KIDSCREEN-10. Participants in the UTalk condition showed significant improvements on RCADS-30 (d = 0.37), PD (d = 0.46), OCD (d = 0.50), SDQ (parent-report; d = 0.67), DERS (d = 0.74), and CD-RISC (d = 0.66). At one month following a booster session (7-month follow-up), the UP-A group showed additional gains on RCADS-30, SDQ (self-report) and CD-RISC, compared to the 6-month follow-up. Between-group comparisons at 6 months revealed significant differences favoring the UP-A group only for SDQ (self-report; d = 0.24) and DERS (d = 0.13). However, at 7 months (post-booster), these differences extended to RCADS-30, PD, SAD, SDQ (self- and parent-report), WAM, KIDSCREEN, and CD-RISC, with effect sizes ranging from 0.24 to 0.67.
Javadi et al., 2024 (Iran)	Subclinical symptoms of emotional disorders (12-17yr, 30%)	UP-A: 20 WLC: 20	Individual (WhatsApp based video-calls)	6	3	0/0 0/0	K-SADS-PL	DASS-21, AAQ-2.	+ - + ? ?	Only participants in the UP-A condition showed significant improvements from pre-treatment to post-treatment. These changes were observed for both DASS-21 (anxiety, d = 0.84; depression, d = 0.60; stress, d = 1.02) and AAQ-2 (psychological flexibility, d = 0.69). Treatment gains were maintained at the 3-month follow-up (ds = 0.59 to 1.42). Significant differences favoring the UP-A group, compared to the WLC, were found for all outcome variables at post-treatment (ds = 0.71 to 1.37) and at the 3-month follow-up (ds = 1.04 to 1.38).

Study (country)	Participants (age range, % female)	Groups and sample size	Treatment format	Treatment duration (weeks)	Follow-up after treatment (months)	Attrition (%) Post/ follow-up	Diagnostic interviews	Outcome variables	Risk of bias (RoB2) R D Mi Me S	Main results
Mohajerin et al., 2023 (Iran)	PTSD and comorbid emotional disorder (12-17yr, 55%)	UP-A: 46 TF-CBT: 47	Individual (in-person) Individual Family (in-person)	12	3/6/9	0/0/0/0 0/0/0/0	SCID-5	CPSS-5-SR, CDI, YAM-5, OSI, STAXI-2 C/A, DERS.	+ + + ? ?	Both treatments resulted in reductions in PTSD symptoms and emotional disorder symptoms (anxiety, depression, anger) compared with baseline assessments. Significant differences between the UP-A and TF-CBT (trauma focused CBT) were observed in the reduction at post-treatment of PTSD, depression, and anxiety symptoms, as well as self-harm, with notable improvements in emotion regulation and anger control (*d*s ranged from 0.12 to 0.74). Participants in the UP-A condition exhibited significantly fewer indicators of PTSD (*d*s = 0.91 to 1.49), depression (*d*s = 0.02 to 0.98), anxiety (ds = 0.82 to 2.18), emotion dysregulation (*d*s = 0.78 to 1.15), self-harm (*d*s = 0.53 to 1.73), and anger expression (including internal and external expression, and anger control; *d*s = 0.18 to 0.78) across the follow-up periods.
Mohajerin et al., 2025 (Iran)	Borderline personality disorders (11-17yr, 67%)	UP-A: 46 MBT-A: 45	Individual (in-person)	12	6/12/18/ 24/36	0/0/0/0/0/0 0/0/0/0/0/0	SCID-5 SCID-5-PD	BSL-23, DSHI, DERS, STAXI-2, UPPS-P	+ ? + ? ?	Both primary and secondary outcomes significantly decreased following treatment with both MBT-A (a diagnosis-specific intervention) and UP-A, with remission levels progressively declining up to 36 months of follow-up for both conditions. However, compared to MBT-A, UP-A was more effective in reducing the severity of borderline symptoms (BSL-23; *d*s ranged from 0.64 to 1.12), emotional dysregulation (DERS; *d*s ranged from 0.65 to 0.95), and negative urgency (*d*s ranged from 0.42 to 077).
Weintraub et al., 2025 (USA)	Mood and psychotic spectrum diagnoses (13-17yr, 65%)	AppUP-A: 30 UP-A: 30	Group (telehealth) Mobile app (in experimental group)	9	3	16.7/20 20/20	MINI-KID, SIPS	CGAS, CGI, CDRS, YMRS, PQ-B, BSI, KINDL	+ ? - + ?	Both treatments were associated with significant improvements in global psychosocial functioning (CGAS; η^2_p = .65), overall global clinical improvements (CGI; η^2_p = .18) and quality of life (KINDL; η^2_p = .23–.31), and reductions in symptoms of depression (CDRS; η^2_p = .59), (hypo)mania (YMRS; η^2_p = .26), psychosis (PQ-B; η^2_p = .21) and overall psychopathological symptom severity (BSI; η^2_p = .26). The adjunctive app could slightly improve CGAS, CGI and mood.

Study (country)	Participants (age range, % female)	Groups and sample size	Treatment format	Treatment duration (weeks)	Follow-up after treatment (months)	Attrition (%) Post/ follow-up	Diagnostic interviews	Outcome variables	Risk of bias (RoB2) R D Mi Me S	Main results
Zemestani et al., 2023 (Iran)	Anxiety disorders and comorbid anxiety disorder symptoms (15-17yr, 43.3%)	UP-A: 30 WLC: 30	Group (in-person)	9	1	3.3/6.7 10/13.3	ADIS-5-C/P	YAM-5, ERQ-CA, IUSC.	+ ? - ? ?	Significant (between-group) improvements at post-treatment and follow-up favoring the UP-A condition, compared with the WLC, were found for anxiety disorder symptoms (YAM-5; *d*s ranged from 1.82 to 2.61), emotion regulation (ERQ-CA) reappraisal (*d*s = 1.30/1.07) and suppression (*d*s = 1.11/1.07), and intolerance of uncertainty (IUSC; *d*s = 1.66/1.54). Likewise, significant changes were observed over time for the UP-A group on all outcomes: YAM-5, *d*s = 2.06 to 2.76; ERQ-CA reappraisal, *d*s = 1.14/104; ERQ-CA suppression, *d*s = 1.27/1.12; and IUSC total, *d*s = 2.11/1.86).

AAQ-2 = Acceptance and Action Questionnaire
ACC = Active Control Group
ADIS-5-C/P = Anxiety Disorders Interview Schedule for DSM-5, Child and Parent Versions
ADIS-IV-C/P = Anxiety Disorders Interview Schedule for DSM-IV, Child and Parent Versions
ALIS = Adolescent Life Interference Scale
AMtE = Aprende a Manejar tus Emociones *[Learn to Manage Your Emotions]*
AppUP-A = Mobile application-enhanced Unified Protocol condition
BSI = Brief Symptom Inventory
BSL-23 = Borderline Symptom List-23
d = Cohen's effect size
CASI = Childhood Anxiety Sensitivity Index
CDI = Children's Depression Inventory
CDN = Cuestionario de Depresión para Niños y Adolescentes *[Depression Questionnaire for Children and Adolescents]*
CD-RISC-10 = 10-Item Connor-Davidson Resilience Scale
CDRS = Children's Depression Rating Scale, Revised
CGAS = Clinical Global Assessment Scale
CGI-S/I = Clinical Global Impression Scale—Severity / Improvement
CPSS-5-SR = Child PTSD Symptom Scale—Self-Report Version for DSM-5
CSR = Clinician Severity Rating
DASS-21 = Depression Anxiety Stress Scale
DERS = Difficulties in Emotion Regulation Scale
DSHI = Deliberate Self-Harm Inventory
EAN = Escala de Ansiedad para Niños y Adolescentes *[Anxiety Scale for Children and Adolescents]*
EASI-A = Emotional Avoidance Strategy Inventory for Adolescents
EBAE-10 = Escala Breve de Ajuste Escolar *[Brief School Adjustment Scale]*
ERQ-CA = Emotion Regulation Questionnaire-Children and Adolescents
iUP-A = Self-administered UP-A online using the AMtE app
GAD = Generalized anxiety disorder
IUSC = Intolerance of Uncertainty Scale for Children
KIDSCREEN-10 Index = Quality of life scale for children and adolescents
KINDL = Assess quality of life in children and adolescents
K-SADS-PL = Kiddie Schedule for Affective Disorders and Schizophrenia for School Children-Present and Lifetime
MBT-A = Mentalization-Based Treatment for Adolescents
MFQ = Mood and Feelings Questionnaire
MINI-KID = Mini International Neuropsychiatric Interview for Children and Adolescents
MDD = Major depressive disorder
Na = Not applicable
OCD = Obsessive-compulsive disorder
OSI = Ottawa Self-Injury Inventory
PANASN = Escalas PANAS para Niños y Adolescentes *[PANAS scales for Children and Adolescents]*
PD = panic disorder
PQ-B = Prodromal Questionnaire Brief
PTSD = posttraumatic stress disorder
RCADS-30 = Revised Child Anxiety and Depression Scale–30 (subscales: MDD, PD, SP, SAD, GAD, and OCD)
RoB 2 = Cochran Risk of Bias, version 2. It includes the following domains: R = Bias arising from the randomization process, D = Bias due to deviations from intended interventions, Mi = Bias due to missing outcome data, Me = Bias in measurement of the outcome, S = Bias in selection of the reported result [+ = low risk of bias, ? = some concerns, - = high risk of bias]
SAD = Separation anxiety disorder
SCARED = Screen for Child Anxiety Related Emotional Disorders
SCID-5 = Structured Clinical Interview for DSM-5 Disorders
SCID-5 = Structured Clinical Interview for DSM-5 Disorders
SCID-5-PD = Structured Clinical Interview for DSM-5 Personality Disorders
SDQ = Strengths and Difficulties Questionnaire
SES = Self-Esteem Scale
SIPS = Structured Interview for Prodromal States
SP = Social phobia
STAI-C = State-Trait Anxiety Inventory for Children
STAXI-2 = State-Trait Anger Expression Inventory–2
STAXI-2-C/A = State-Trait Anger Expression Inventory–2 for Children and Adolescents
SWLSN = Satisfaction with Life Scale for Children and Adolescents
TAU = Treatment as usual
TAU+ = TAU plus measurement-based care (MBC). MBP is the ongoing use of assessment to track treatment processes and outcomes to inform clinical care; it includes the administration of the YOQ weekly on a tablet or computer during therapy sessions
TF-CBT = Trauma-focused CBT
UP-A = Unified Protocols for Transdiagnostic Treatment of Emotional Disorders in Children and Adolescents
UP-A+ = UP-A plus measurement-based care (MBC). MBP es the ongoing use of assessment to track treatment processes and outcomes to inform clinical care; it includes the administration of the YOQ weekly on a tablet or computer during therapy sessions
UPPS-P: Impulsive Behavior Scale (subscales: Negative urgency, Premeditation, Perseverance, Sensation Seeking and Positive urgency)
UTalk = A program of prevention of social anxiety and depression
WLC = Waitlist control
YAM-5 = Youth Anxiety Measure for DSM-5
YMRS = Young Mania Rating Scale
YOQ = Youth Outcome Questionnaire.

in reducing self-reported emotional symptoms over time (from pre- to post-treatment and follow-up), including general emotional symptoms (RCADS: d = 0.39/0.64 for iUP-A; d = 0.88/0.84 for UP-A), major depressive disorder symptoms (MDD; d = 0.44/0.62 for iUP-A; d = 0.81/0.54 for UP-A), and specific anxiety symptoms including GAD, SP, and PD (d = 0.20 to 0.57 for iUP-A; d = 0.52 to 0.77 for UP-A).

Zemestani et al. (2023) reported that UP-A was significantly more effective than waitlist control (WLC) in reducing anxiety symptoms at post-treatment and follow up (d = 1.82 to 2.61, M = 2.13). Significant improvements were found for the UP-A group, both at post-treatment (d = 2.10 to 2.46, M = 2.25) and follow-up (d = 2.06 to 2.76, M = 2.31).

Both studies also demonstrated that UP-A/iUP-A effectively reduced transdiagnostic risk factors, including negative affect, anxiety sensitivity, and emotional avoidance (Espinosa et al., 2024), as well as emotional suppression, intolerance of uncertainty, and increased cognitive reappraisal (Zemestani et al., 2023) (see Table 1 for a description of the effect sizes). Improvements over time (Cohen's d) for these outcomes ranged from 0,20 to 1.66 (M = 1.10).

Two additional RCTs (García-López et al., 2024; Javadi et al., 2024) examined the efficacy of UP-A in adolescents with elevated emotional symptoms. Javadi et al. (2024) found that UP-A was clearly superior to WLC across all outcome variables, including anxiety, depression, stress, and the transdiagnostic factor of psychological flexibility (ds ranged from 0.59 to 1.42, M = 0.82). Only participants in the UP-A group showed significant post-treatment improvements, which were maintained at 3-month follow-up (ds ranged from 0,71 to 1.38, M = 1.15).

García-López et al. (2024) assessed a broad range of outcomes, including anxiety and depression symptoms, emotional and behavioral problems, transdiagnostic risk factors, resilience, and health-related quality of life. The study compared UP-A with the UTalk program (a protocol designed for the prevention of social anxiety and depression in adolescents). While UTalk showed significant efficacy between pre-treatment and 6-month follow-up for several outcomes, UP-A led to improvements in nearly all outcome variables, except for social phobia symptoms and quality of life (ds for the UP-A condition ranged from 0.43 to 0.75, M = 0.56). At the 6-month follow-up, significant between-group differences favoring UP-A were found only for self-reported SDQ scores and emotion regulation difficulties. However, after a booster session one month later, group differences extended to additional outcomes, including symptoms of anxiety, panic disorder, separation anxiety, parent-reported SDQ, as well as other secondary relevant variables. The authors highlight the usefulness of delivering booster sessions to help maintain treatment gains of the UP-A, although only three variables (RCADS-30, self-reported SDQ, and CD-RISC) showed significant improvement between the 6-month follow-up and the post-booster assessment (one month after the booster session).

Three RCTs focused on other disorders, based on the hypothesis that anxiety and depression are central to many mental disorders. These included post-traumatic stress disorder (PTSD) (Mohajerin et al., 2023), borderline personality disorder (BPD) (Mohajerin et al., 2025), and psychotic disorders (Weintraub et al., 2025). Mohajerin et al. (2023) demonstrated that UP-A could be successfully applied to PTSD. Compared to trauma-focused CBT (TF-CBT, a treatment of choice for PTSD; Rueda-Flores et al., 2025), UP-A was more effective in reducing PTSD symptoms as well as comorbid symptoms of anxiety, depression, and anger. In a subsequent study, Mohajerin et al. (2025) extended the application of UP-A to adolescents with BPD. Based on its transdiagnostic nature, the authors hypothesized that UP-A would be non-inferior to mentalization-based therapy for adolescents (MBT-A). Interestingly, even though MBT-A is a treatment of choice for BPD (González & Crespo, 2022), the UP-A not only met this criterion but outperformed MBT-A in reducing borderline symptoms, emotional dysregulation, and impulsivity. However, Mohajerin et al. (2025) observed that the remission levels progressively declined over a 36-month follow-up period. Perhaps booster sessions delivered over time, similar to those reported by García-López et al. (2024), could help mitigate this loss.

In a recent RCT, Weintraub et al. (2025) compared the efficacy of group-based UP-A delivered with mobile app support (AppUP-A) versus standard group-based UP-A in adolescents with mood or psychotic spectrum disorders, alongside their parents. The primary finding was that UP-A, with or without app support, was effective in reducing symptomatology associated with depressive spectrum disorder, psychotic spectrum syndrome, and bipolar spectrum disorder. Improvements were observed in psychosocial functioning, depression, hypomania, and overall psychopathological severity. It appears that the use of the app only slightly improves mood, psychosocial functioning and overall clinical severity.

Additionally, García-Escalera et al. (2017) adapted the UP-A for universal prevention in school settings. In two studies (García-Escalera et al., 2020a, 2020b),

compared the UP-A with a waitlist control group to assess its preventive efficacy for anxiety, depression, and other emotional disorder-related variables in adolescents. In García-Escalera et al. (2020b), contrary to expectations, both groups showed similar reductions over time in anxiety and depression symptoms. However, a key finding was that adolescents with high baseline symptomatology (RCADS-30) experienced significantly greater reductions in the UP-A group, suggesting a potential indicated prevention effect. In García-Escalera et al. (2020a), both the UPA and WLC groups showed similar improvements over time in selfesteem and life satisfaction, while school adjustment declined in the WLC group. No significant changes were observed in other variables, such as quality of life and emotional/behavioral problems.

Discussion

To our knowledge, this is the first systematic review specifically dedicated to examining the efficacy of the unified protocol for adolescents (UP-A). Overall, the UP-A appears to yield effects comparable to those observed with the adult version (UP), although the evidence is less consistent. Despite variability in outcomes, the reviewed RCTs provide empirical support for the hypothesis that UP-A is effective in treating emotional disorders and related problems, particularly anxiety and depressive disorders.

Efficacy has been demonstrated through multiple sources of data, including self-reported, parent-reported, and clinician-rated measures of anxiety and depression symptom severity, as well as reductions in diagnostic frequency based on structured clinical interviews. Importantly, UP-A has shown superior outcomes regardless of whether the control group was passive (e.g., waitlist) or active (e.g., treatment-as-usual), with improvements observed immediately after the treatment and sustained at 3- and 6-month follow-ups. Some studies also report efficacy at longer-term follow-ups.

The effectiveness of the UP-A appears to be independent of delivery format (individual, face-to-face, group-based, telehealth, or online self-administered), setting and purpose (clinical treatment or indicated prevention). This flexibility underscores the clinical utility of the protocol across diverse populations and contexts.

Regarding anxiety, depression, and combined emotional symptoms, the reviewed studies generally indicate significant improvements in favor of the UP-A compared to control conditions, whether active or passive. Although effect sizes vary across studies (a common finding in systematic reviews and meta-analyses), most fall within the moderate to large range, both for baseline to post-treatment and for baseline to follow-up, and across separate and combined symptom domains (e.g., RCADS total scores). While some RCTs reported symptom reductions in both experimental and control groups (an expected outcome in some studies), most studies using waitlist controls showed no significant changes during post-treatment and follow-up in the control condition.

The effect sizes for anxiety, depression, and combined scores are comparable to those reported in meta-analyses of the adult UP protocol. For example, Carlucci et al. (2021) reported Hedges' *g* values ranging from 0.08 to 1.36 (overall = 0.45) for UP vs. control groups on self-reported anxiety, depression, and combined measures. Longley and Gleiser (2023) found effect sizes of $g = 0.26$ to 1.81 (overall = 0.80) for anxiety and $g = 0.07$ to 2.19 (overall = 0.97) for depression from baseline to post-treatment. From baseline to follow-up (2–6 months), moderate gains were observed: $g = 0.61$ for anxiety and $g = 0.68$ for depression. These findings suggest that the UP-A may offer comparable benefits to its adult counterpart, reinforcing its potential as a transdiagnostic, evidence-based intervention for adolescents.

An important line of development in research based on the UP-A has involved examining the efficacy of this protocol in modifying risk factors underlying emotional disorders corresponding to different hierarchical levels (Sandín et al., 2020a; Sandín & García-Escalera, 2025). In 6 of the 11 reviewed studies, the UP-A's ability to improve transdiagnostic outcome variables was investigated, including negative affect, anxiety sensitivity, and emotional avoidance (Espinosa et al., 2024), intolerance of uncertainty (Zemestani et al., 2023), and various emotion regulation-related variables, such as emotional dysregulation, psychological flexibility, emotional suppression, and reappraisal (García-López et al., 2024; Javadi et al., 2024; Mohajerin et al., 2023, 2025; Zemestani et al., 2023). Overall, effect sizes for transdiagnostic outcome variables ranged from moderate to large (see Table 1).

An emerging line of research, previously emphasized by Cassiello-Robbins et al. (2020), concerns the potential of the UP, due to its transdiagnostic nature, to address a broad range of emotional problems and disorders beyond anxiety and depression. As these authors note, the UP has been applied to a wide variety of psychological problems in addition to anxiety and depression, including eating disorders, insomnia, bipolar disorder, personality disorders, obsessive-compulsive disorder, PTSD, and stress-related disorders. In connection with this new research way, the efficacy of the UP-A has been tested in three RCTs not primarily focused on anxiety

or depression, but on other mental disorders, including PTSD (Mohajerin et al., 2023), borderline personality disorder (BPD) (Mohajerin et al., 2025), and psychotic disorders (Weintraub et al., 2025). These studies show that the UP-A, in addition to effectively reducing comorbid emotional symptoms (e.g., anxiety and depression), also significantly reduces symptomatology associated with the primary disorders (e.g., specific symptoms of PTSD or BPD), sometimes even more effectively than related disorder-specific treatments.

A key feature of the UP-A, as with its predecessor the UP, is its high versatility, making it an ideal treatment for application across various disorders and contexts, including both healthcare and educational settings (Sandín & García-Escalera, 2025), for both prevention and treatment. A particularly relevant recent development concerns the application of the UP-A in internet-based format. The meta-analysis by García-Escalera et al. (2016) is the most comprehensive to date on the efficacy of transdiagnostic treatments for anxiety and depression, examining the effectiveness of various protocols (including the UP and UP-A) across different formats (individual, group, internet, etc.) and contexts (clinical and educational settings; prevention and treatment), both in the adult population and in children and adolescents, and including both controlled and uncontrolled trials. One tentative conclusion of this meta-analysis was that internet-delivered transdiagnostic interventions were as effective, or even more effective, than face-to-face formats (individual or group). This new treatment method has recently garnered significant interest (Kolaas et al., 2024; Walder et al., 2025) and offers important advantages over traditional formats, such as facilitating access to evidence-based CBT in rural populations, economically disadvantaged groups, and ethnic minorities. It may also reduce or eliminate the stigma associated with psychiatric treatment and generally improve access to care across diverse populations (Andersson & Titov, 2014).

Of the 11 reviewed RCTs, only the one conducted by Espinosa et al. (2024) employed a digital adaptation of the UP-A (i.e., the iUP-A) administered via the AMtE platform (Sandín et al., 2019), delivered as a self-applied internet-based intervention. To the best of our knowledge, this is the first RCT to examine the efficacy of the iUP-A, and the first to compare an internet-based UP-A with the standard in-person or virtual face-to-face UP-A. Results of this study are consistent with evidence provided in the recent meta-analysis on the efficacy of online transdiagnostic treatments in adult populations (Kolaas et al., 2024). They also align with findings from two previous open field pioneering online studies that examined the efficacy of the iUP-A in samples of adolescents with anxiety and depressive disorders (Sandín et al., 2020b) and in adolescents with elevated levels of anxiety and depression (Schmitt et al., 2022).

Nonetheless, four of the evaluated RCTs utilized internet-based formats, although in the form of virtual face-to-face delivery (i.e., telehealth, videoconferencing, video calls), adapted either to clinical settings (Espinosa et al., 2024; Weintraub et al., 2025) or educational contexts (García-López et al., 2024; Javadi et al., 2024). Undoubtedly, adaptations of the UP-A for internet-based delivery, whether self-applied via websites or through telehealth formats, are expected to undergo significant development in the coming years.

Results of this systematic review are highly promising, suggesting that the UP-A is an effective transdiagnostic protocol for treating and preventing (indicated prevention) anxiety and depressive disorders or problems. Its efficacy may also extend to a wide range of other emotional and non-emotional disorders, including psychotic disorders. The evidence also suggests that the UP-A is highly flexible, capable of being applied and adapted to various formats and contexts, such as individual or group treatment, in-person or virtual delivery, and self-applied internet-based formats. It also appears suitable for both clinical settings and school-based interventions, an aspect that has already been extensively demonstrated with the UP (Cassiello-Robbins et al., 2020).

This review has several limitations that warrant a cautious interpretation of the findings. First, the number of reviewed RCTs is relatively small. Second, many of the assessment instruments used were self-report measures. Third, group comparisons were generally based on relatively small sample sizes. Fourth, many participants were recruited through advertisements or schools, with few recruited from clinical settings. Fifth, based on risk of bias assessments, many studies exhibited some bias in treatment delivery blinding and/or outcome variable assessment.

Future RCTs should aim to replicate the reported efficacy of the UP by including participants from clinical and educational settings, thereby testing whether the UP-A is effective in treating and preventing a broad spectrum of emotional and other psychological disorders. A key challenge will be to demonstrate more comprehensively its effectiveness in improving transdiagnostic variables corresponding to different hierarchical levels (Sandín et al., 2020a), quality of life, and positive factors.

Conflicts of interest

The authors have no conflicts of interest to disclose.

References

Andersson, G., & Titov, N. (2014). Advantages and limitations of internet-based interventions for common mental disorders. *World Psychiatry, 13*, 4–11. https://doi.org/10.1002/WPS.20083

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

Borg, M., Heffer, T., & Willoughby, T. (2025). Generational Shifts in Adolescent Mental Health: A Longitudinal Time-Lag Study. *Journal of Youth and Adolescence, 54,* 837-848. https://doi.org/10.1007/s10964-024-02095-3.

Bullis, J. R., Boettcher, H., Sauer-Zavala, S., Farchione, T. J., & Barlow, D. H. (2019). What is an emotional disorder? A transdiagnostic mechanistic definition with implications for assessment, treatment, and prevention. *Clinical Psychology: Science and Practice, 26*(2), e12278. https://doi.org/10.1037/h0101755

Canals, J., Hernández-Martínez, C., Sáez-Carles, M., & Arija-Val, V. (2018). Prevalence of DSM-5 depressive disorders and comorbidity in Spanish early adolescents: Has there been an increase in the last 20 years*? Psychiatry Research, 268*, 328-334. https://doi.org/10.1016/j.psychres.2018.07.023.

Canals, J., Voltas, N., Hernández-Martínez, C., Cosi, S., & Arija, V. (2019). Prevalence of DSM-5 anxiety disorders, comorbidity, and persistence of symptoms in Spanish early adolescents. *European Child & Adolescent Psychiatry 28*, 131–143. https://doi.org/10.1007/s00787-018-1207-z

Carlucci, L., Saggino, A., & Balsamo, M. (2021). On the efficacy of the unified protocol for transdiagnostic treatment of emotional disorders: A systematic review and meta-analysis. *Clinical Psychology Review*, *87*, 101999. https://doi.org/10.1016/j.cpr.2021.101999

Cassiello-Robbins, C., Southward, M. W., Tirpak, J. W., & Sauer-Zavala, S. (2020). A systematic review of Unified Protocol applications with adult populations: Facilitating widespread dissemination via adaptability. *Clinical Psychology Review, 78*, Article 101852. https://doi.org/10.1016/j.cpr.2020.101852

Craske, M. G. (2012). Transdiagnostic treatment for anxiety and depression. *Depression and Anxiety, 29*(9), 749–753. https://doi.org/10.1002/da.21992

Cummings, C. M., Caporino, N. E., & Kendall, P. C. (2014). Comorbidity of anxiety and depression in children and adolescents: 20 years after. *Psychological Bulletin, 140*(3), 816–845. https://doi.org/10.1037/a0034733

* Ehrenreich-May, J., Jensen-Doss, A., Milgram, L., Rosenfield, D., Shaw, A. M., LoCurto, J., Nanda Robinson, M., Caron, E. B., Lee, P., & Ginsburg, G. S. (2025). A randomized controlled effectiveness trial of transdiagnostic treatment and measurement-based care for adolescents with emotional disorders in community clinics. *Journal of Consulting and Clinical Psychology, 93*(3), 144–160. https://doi.org/10.1037/ccp0000947

Ehrenreich-May, J., Kennedy, S. M., Sherman, J. A., Bilek, E. L., Bennett, S. M., & Barlow, D. H. (2018). *Unified protocols for transdiagnostic treatment of emotional disorders in adolescents: Workbook.* Oxford University Press.

Ehrenreich-May, J., Kennedy, S. M., Sherman, J. A., Bennett, S. M., & Barlow, D. H. (2020). *Protocolo Unificado para el Tratamiento Transdiagnóstico de los Trastornos Emocionales en Adolescentes: Manual del Paciente.* Translated and adapted into Spanish by Bonifacio Sandín and Julia García-Escalera (original English version, 2018). Pirámide.

Ehrenreich-May, J., Kennedy, S. M., Sherman, J. A., Bilek, E. L., Buzzella, B. A., Bennett, S. M., & Barlow, D. H. (2017a). *Unified protocols for transdiagnostic treatment of emotional disorders in children and adolescents: Therapist guide.* Oxford University Press.

Ehrenreich-May, J., Kennedy, S. M., Sherman, J. A., Bilek, E. L., Buzzella, B. A., Bennett, S. M, & Barlow, D. H. (2022). *Protocolo unificado para el tratamiento transdiagnóstico de los trastornos emocionales en niños y adolescentes: Manual del terapeuta.* Translated and adapted into Spanish by Bonifacio Sandín and Julia García-Escalera (original English version, 2017). Pirámide.

* Ehrenreich-May, J., Rosenfield, D., Queen, A. H., Kennedy, S. M., Remmes, C. S., & Barlow, D. H. (2017b). An initial waitlist-controlled trial of the unified protocol for the treatment of emotional disorders in adolescents. *Journal of Anxiety Disorders, 46*, 46-55. https://doi.org/10.1016/j.janxdis.2016.10.006

* Espinosa, V., Valiente, R. M., García-Escalera, J., Chorot, P., Arnáez, S., Schmitt, J. C., & Sandín, B. (2024). Efficacy of a transdiagnostic internet-based program for adolescents with emotional disorders: A randomized controlled trial. *Behaviour Research and Therapy, 179,* 104560. https://doi.org/10.1016/j.brat.2024.104560

Etchemendy, E., Rasal, P., & Fernández-Álvarez, J. (2024). Abordajes transdiagnósticos en los trastornos emocionales a nivel iberoamericano: Una revisión crítica. *Revista de Psicoterapia*, *35*(127), 25–38. https://doi.org/10.5944/rdp.v35i127.39801

García-Escalera, J., Chorot, P., Valiente, R. M., Reales, J. M., & Sandín, B. (2016). Efficacy of transdiagnostic cognitive-behavioral therapy for anxiety and depression in adults, children and adolescents: A meta-analysis. *Revista de Psicopatología y Psicología Clínica*, *21*(3), 147-175. https://doi.org/10.5944/RPPC.VOL.21.NUM.3.2016.17811

García-Escalera, J., Valiente, R. M., Chorot, P., Ehrenreich-May, J., Kennedy, S. M., & Sandín, B. (2017). 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. *JMIR Research Protocols*, *6*(8), e149. https://doi.org/10.2196/resprot.7934

* García-Escalera, J., Valiente, R. M., Sandín, B., Ehrenreich-May, J., & Chorot, P. (2020a). Los efectos de un programa de prevención de la ansiedad y la depresión para adolescentes en variables educativas y de bienestar. *Revista de Psicodidáctica*, *25*(2), 143-149. https://doi.org/10.1016/j.psicod.2020.05.001

* García-Escalera, J., Valiente, R. M., Sandín, B., Ehrenreich-May, J., Prieto, A., & Chorot, P. (2020b). 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

wait-list-controlled trial. *Behavior Therapy, 51*(3), 461-473. https://doi.org/10.1016/j.beth.2019.08.003

* García-López, L., Jiménez-Vázquez, D., Muela-Martínez, J., Piqueras, J. A., Espinosa-Fernández, L., Canals-Sans, J., Vivas-Fernández, M., Morales-Hidalgo, P., Díaz-Castela, M., Rivera, M., & Ehrenreich-May, J. (2024). Effectiveness of a transdiagnostic indicated preventive intervention for adolescents at high risk for anxiety and depressive disorders. *Current Psychology, 43*(17), 15484-15498. https://doi.org/10.1007/s12144-023-05421-3

Ghandour, R. M., Sherman, L. J., Vladutiu, C. J., Ali, M. M., Lynch, S. E., Bitsko, R. H., & Blumberg, S. J. (2019). Prevalence and treatment of depression, anxiety, and conduct problems in US children. *The Journal of Pediatrics*, *206*, 256-267.

González, E., & Crespo, M. (2022). Systematic review of the relationship between post-traumatic symptomatology and suicidal behavior. *Revista de Psicopatología y Psicología Clínica*, *27*(1), 73–90. https://doi.org/10.5944/rppc.27757

* Javadi, V., Ahmadi, F., Ebrahimi, L. S., Dadashi, M., & Mousavi, S. E. (2024). Internet-based UP-A intervention on treatment of stress, anxiety, depression, and psychological flexibility among adolescents with sub-clinical diagnosis of emotional disorders during the COVID-19 pandemic: a clinical trial. *BMC Psychology, 12*(1). https://doi.org/10.1186/s40359-024-01735-4

Higgins, J., & Green, S. (2011). *Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0*. The Cochrane Collaboration.

Klaufus, L., Verlinden, E., van der Wal, M., Cuijpers, P., Chinapaw, M., & Smit, F. (2022). Adolescent anxiety and depression: Burden of disease study in 53,894 secondary school pupils in The Netherlands. *BMC Psychiatry, 22*(1), 225. https://doi.org/10.1186/s12888-022-03868-5

Kolaas, K., Berman, A. H., Hedman-Lagerl¨of, E., Lindsäter, E., Hybelius, J., & Axelsson, E. (2024). Internet-delivered transdiagnostic psychological treatments for individuals with depression, anxiety or both: A systematic review with meta-analysis of randomised controlled trials. *BMJ Open, 14*(4), Articlee075796.https://doi.org/10.1136/bmjopen-2023-075796

Longley, S. L., & Gleiser, T. S. (2023). Efficacy of the Unified Protocol: A systematic review and meta-analysis of randomized controlled trials. *Clinical Psychology: Science and Practice, 30*(2), 208–221. https://doi.org/10.1037/cps0000141

* Mohajerin, B., Lynn, S. J., & Cassiello-Robbins, C. (2023). Unified protocol vs trauma-focused cognitive behavioral therapy among adolescents with PTSD. *Behavior Therapy, 54*(5), 823-838. https://doi.org/10.1016/j.beth.2023.03.003

* Mohajerin, B., Gallagher, M. W., & Howard, R. (2025). Unified protocol vs mentalization-based therapy for adolescents with borderline personality disorder: A randomized controlled trial. *Clinical Psychology & Psychotherapy, 32*(1), e70033. https://doi.org/10.1002/cpp.70033

Moriana, J. A., & Martínez, V. A. (2011). La psicología basada en la evidencia y el diseño y evaluación de tratamientos psicológicos eficaces. *Revista de Psicopatología y Psicología Clínica*, *16*(2), 81–100. https://doi.org/10.5944/rppc.vol.16.num.2.2011.10353

Orgilés, M., Espada, J. P., Delvecchio, E., Francisco, R., Mazzeschi, C., Pedro, M., & Morales, A. (2021). Anxiety and depressive symptoms in children and adolescents during COVID-19 pandemic: A transcultural approach. *Psicothema*, *33*(1), 125-130. https://doi.org/10.7334/psicothema2020.287

Pàmias, M., Puntí, J., Cebria, A., Parra, I., Garcia-Pares, G., Escayola, A., Laredo, A., Pujol, S., Pérez-Solá, V., & Palao, D. (2016). Prevalence of major depressive disorder among Spanish adolescents. *Journal of Public Health and Epidemiology*, *8*, 278-285. https://doi.org/10.5897/JPHE2015.0712.

Racine, N., McArthur, B. A., Cooke, J. E., Eirich, R., Zhu, J., & Madigan, S. (2021). Global prevalence of depressive and anxiety symptoms in children and adolescents during COVID-19: A meta-analysis. *JAMA Pediatrics, 175*(11), 1142–1150. https://doi.org/ 10.1001/JAMAPEDIATRICS.2021.2482

Roberts, A. G., Taylor-Cavelier, S., Diaz, K. I., Codd, E., Hawks, J. L., & Kennedy, S. M. (2025). Unified protocols for transdiagnostic treatment of emotional disorders in children and adolescents: Background, evidence base, and adaptations. *Advances in Psychiatry and Behavioral Health*, 5(1), 47-58. https://doi.org/10.1016/j.ypsc.2025.02.004

Rueda-Flores, E., Delgado-Pardo, G., Villegas-Navas, M. V., & Lanzarote-Fernández, M. D. (2025). Analysis of the efficacy of psychological treatments for early onset borderline personality disorder: An umbrella review. *Revista de Psicopatología y Psicología Clínica*, *30*(1), 75–94. https://doi.org/10.5944/rppc.39847

Sacco, R., Camilleri, N., & Eberhardt, J., Umla-Runge, K. & Newbury-Birch, D. (2022). A systematic review and meta-analysis on the prevalence of mental disorders among children and adolescents in Europe. *European Child & Adolescent Psychiatry. 33*(9). 2877-2894. https://doi.org/10.1007/s00787-022-02131-2

Sakiris, N., & Berle, D. (2019). A systematic review and meta-analysis of the Unified Protocol as a transdiagnostic emotion regulation-based intervention. *Clinical Psychology Review, 72*, Article 101751. https://doi.org/10.1016/j.cpr.2019.101751

Sandín, B. (2022). The impact of the COVID-19 pandemic on mental health in the adult population. In F. F. Tezanos (Ed.), *Cambios sociales en tiempos de pandemia* (pp. 923-951). Centro de Investigaciones Sociológicas (CIS).

Sandín, B., Chorot, P., y Valiente, R. M. (2012). Transdiagnóstico: Nueva frontera en psicología clínica. *Revista de Psicopatología y Psicología Clínica, 17*(3), 185–203. https://doi.org/10.5944/rppc.vol.17.num.3.2012.11839

Sandín, B., Chorot, P., & Valiente, R. M. (2018). Trastornos de ansiedad en niños y adolescentes *[Anxiety disorders in children and adolescents]*. In J. C. Arango-Lasprilla, I. Romero, N. Hewitt-Ramírez, & W. Rodríguez (Eds.), *Trastornos psicológicos y neuropsicológicos en la infancia y la adolescencia* (pp. 117-159). Manual Moderno.

Sandín, B., Chorot, P., & Valiente, R. M. (2020a). Psicopatología de la ansiedad y trastornos de ansiedad: Hacia un enfoque transdiagnóstico *[Psychopathology of anxiety: Toward a transdiagnostic model]*. In A. Belloch, B. Sandín y F. Ramos (Eds.), *Manual de Psicopatología* (Vol. 2, pp. 3-38). McGraw-Hill.

Sandín, B., Espinosa, V., Valiente, R. M., García-Escalera, J., Schmitt, J. C., Arnáez, S., & Chorot, P. (2021). Effects of coronavirus fears on anxiety and depressive disorder

symptoms in clinical and subclinical adolescents: The role of negative affect, intolerance of uncertainty and emotion regulation strategies. *Frontiers in Psychology, 12*, Article 716528. https://doi.org/10.3389/fpsyg.2021.716528

Sandín, B., & García-Escalera, J. (2025). Modelos transdiagnósticos para los trastornos emocionales en niños y adolescentes *[Transdiagnostic models for emotional disorders in children and adolescents]*. In E. Fonseca-Pedrero y S. Al-Halabí Díaz (Eds.), *Salud mental en contextos educativos* (409-450). Pirámide.

Sandín, B., García-Escalera, J., Valiente, R. M., Espinosa, V., & Chorot, P. (2020b). Clinical utility of an internet-delivered version of the unified protocol for transdiagnostic treatment of emotional disorders in adolescents (iUP-A): A pilot open trial. *International Journal of Environmental Research and Public Health*, *17*(22), 8306. https://doi.org/10.3390/ijerph17228306

Sandín, B., Valiente, R. M., García-Escalera, J., Campagne, D. M., & Chorot, P. (2020c). Psychological impact of the COVID-19 pandemic: Negative and positive effects in Spanish population during the mandatory national quarantine. *Revista de Psicopatología y Psicología Clínica*, *25*(1), 1e-21e. https://doi.org/10.5944/rppc.28107

Sandín, B., Valiente, R. M., García-Escalera, J., Pineda, D., Espinosa, V., Magaz, A. M., & Chorot, P. (2019). Protocolo unificado para el tratamiento transdiagnóstico de los trastornos emocionales en adolescentes a través de internet (iUP-A): Aplicación web y protocolo de un ensayo controlado aleatorizado *[Internet-delivered unified protocol for transdiagnostic treatment of emotional disorders in adolescents (iUP-A): Web application and study protocol for a randomized controlled trial]*. *Revista de Psicopatología y Psicología Clínica*, *24*(3), 197-215. http://doi.org/10.5944/rppc.26460

Schmitt, J. C., Valiente, R. M., García-Escalera, J., Arnáez, S., Espinosa, V., Sandín, B., & Chorot, P. (2022). Prevention of depression and anxiety in subclinical adolescents: Effects of a transdiagnostic internet-delivered CBT program. *International Journal of Environmental Research and Public Health*, *19*(9), 5365. https://doi.org/10.3390/ijerph19095365

Shamseer, L., Moher, D., Clarke, M., Ghersi, D., Liberati, A., Petticrew, M., Shekelle, P., & Stewart, L. A. (2015). Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: Elaboration and explanation. *BMJ*, 349. https://doi.org/10.1136/bmj.g7647

Soriano, V., Ramos, J. M., López-Ibor, M. I., Chiclana-Actis, C., Faraco, M., González-Cabrera, J., González-Fraile, E., Mestre-Bach, G., Pinargote, H., Corpas, M., Gallego, L., Corral, O., & Blasco-Fontecilla, H. (2025). Hospital admissions in adolescents with mental disorders in Spain over the last two decades: A mental health crisis? *European Child & Adolescent Psychiatry, 34*(3), 1125–1134. https://doi.org/10.1007/s00787-024-02543-2

Sterne, J. A., Savović, J., Page, M. J., Elbers, R. G., Blencowe, N. S., Boutron, I., ... & Higgins, J. P. (2019). RoB 2: A revised tool for assessing risk of bias in randomised trials. *BMJ*, *366*. https://doi.org/10.1136/bmj.l4898

Walder, N., Frey, A., Berger, T., & Schmidt, S. J. (2025). Digital mental health interventions for the prevention and treatment of social anxiety disorder in children, adolescents, and young adults: Systematic review and meta-analysis of randomized controlled trials. *Journal of Medical Internet Research*, *27*, e67067. https://doi.org/10.2196/67067

* Weintraub, M. J., Ichinose, M. C., Zinberg, J. L., Salimian, A., Brown, R. D., Morgan-Fleming, G., Gamarra, J. M., Tran, T., & Miklowitz, D. J. (2025). Effects of a multi-family app-enhanced cognitive behavioral therapy delivered via telehealth for parents of adolescents with mood or psychotic spectrum disorders. *Behavior Therapy*. https://doi.org/10.1016/j.beth.2025.02.002

*Zemestani, M., Ezzati, S., Nasiri, F., Gallagher, M. W., Barlow, D. H., & Kendall, P. C. (2024). A culturally adapted unified protocol for transdiagnostic treatment of anxiety disorders in adolescents (UP-A): A randomized waitlist-controlled trial. *Psychological Medicine*, *54*(2), 385 -398. https://doi.org/10.1017/s0033291723001903