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Review

A systematic review of Unified Protocol applications with adult populations: Facilitating widespread dissemination via adaptability

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HIGHLIGHTS

- This systematic review reports on 77 studies using the Unified Protocol.
- The Unified Protocol (UP) has been applied to a wide range of presenting problems.
- Most studies used UP to treat anxiety, depressive, or obsessive-compulsive disorders.
- The Unified Protocol has been tested in 11 countries and with numerous adaptations.
- Results suggest adaptations typically achieved their intended results.

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ABSTRACT

The Unified Protocol for Transdiagnostic Treatment of Emotional Disorders (UP) was designed to be a flexible, evidence-based intervention that could treat a wide range of emotional disorders. The purpose of this systematic review is to summarize (1) the range of presenting problems to which the UP has been applied with adult patients, and (2) the settings in which the protocol has been used, as well as any modifications made to it. Using PRISMA guidelines, we conducted a literature search of PsychInfo, PubMed, Proquest Dissertations and Theses, and Web of Science. The 77 studies included in this review indicated the UP has been applied to a wide range of presenting problems including anxiety, depressive, bipolar, traumatic-stressor, substance use, eating, borderline personality, insomnia, and physical health disorders. Additionally, the UP has been applied to non-diagnosable problems such as non-suicidal self-injury, subclinical presentations, and sexual minority stress. The strongest base of evidence for the UP is among Caucasian females in the United States with anxiety-related or depressive disorders. Numerous adaptions of the UP were present in the literature. Overall, results suggest the UP can be flexibly applied to a range of diagnostic presentations. However, many studies reviewed were preliminary and further research is needed.

Anxiety, depressive, and related disorders (e.g., obsessive-compulsive disorder [OCD], trauma and stressor-related disorders) are among the most frequently occurring psychiatric conditions, with past-year prevalence rates of up to 19.1% in the United States (Harvard Medical School, 2007). These disorders are likely to co-occur, with lifetime comorbidity estimates as high as 76% (Brown, Campbell, Lehman, Grisham, & Mancill, 2001). To account for these high rates of co-morbidity, research has identified a number of shared features including overlap in diagnostic criteria (Brown & Barlow, 2009) and common neurobiological mechanisms (e.g., hyperexcitability of limbic structures and limited inhibitory control by cortical structures; Etkin & Wager, 2007; Mayberg et al., 1999; Porto et al., 2009; Shin & Liberzon, 2010). Additionally, Barlow and colleagues have described a functional model to account for the development and maintenance of the full range of these common conditions (Barlow, Ellard, Sauer-Zavala, Bullis, & Carl, 2014; Barlow, Sauer-Zavala, Carl, Bullis, & Ellard, 2014). In this model, anxiety, depressive, and related disorders are referred to as emotional disorders (Bullis, Boettcher, Sauer-Zavala, Farchione, &

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Barlow, 2019) to highlight the causal role dysregulated emotions play for these diagnoses. Specifically, emotional disorders are characterized by: 1) frequent and intense negative emotions, 2) aversive reactions to these emotional experiences, including the perception of emotions as unacceptable or uncontrollable, and 3) engagement in avoidant regulation strategies to escape or suppress the experience of strong emotions (Sauer-Zavala & Barlow, 2014).

Despite ample evidence for common psychopathological mechanisms across the range of emotional disorders, at least 51 separate treatments for these conditions have been described that have amassed, at minimum, modest research support (American Psychological Association, Division 12, 2019). The proliferation of treatment manuals designed to target single diagnoses represents a barrier to the dissemination of empirically-supported interventions (McHugh, Murray, & Barlow, 2009). Specifically, a separate manual for each *Diagnostic and Statistical Manual* (*DSM; e.g., American Psychiatric Association [APA], 2013*) disorder creates a training burden for clinicians in routine practice who must receive costly and time-consuming training in multiple approaches to meet the needs of complex caseloads. Additionally, disorder-specific interventions typically do not address real-world patient presentations that, as described earlier, are characterized by a high degree of comorbidity.

In response to these issues, the Unified Protocol for Transdiagnostic Treatment of Emotional Disorders (UP; Barlow, Allen, & Choate, 2004; Barlow et al., 2011; Barlow et al., 2018; Barlow et al., 2018; Wilamowska et al., 2010) was developed to treat the range of psychiatric disorders characterized by the functional model described previously. The UP explicitly targets shared mechanisms (i.e., aversive, avoidant reactions to strong emotional experiences) via eight treatment modules that focus on: 1) setting goals and increasing motivation for treatment, 2) psychoeducation on the adaptive nature of emotional experiences, 3) mindful emotion awareness (i.e., mindfulness), 4) cognitive flexibility (i.e., developing more balanced, alternative thoughts), 5) changing the action tendencies associated with strong emotions, 6) interoceptive exposures, 7) emotion exposures, and 8) relapse prevention (described in detail in Payne, Ellard, Farchione, Fairholme, & Barlow, 2014). The modules are designed to facilitate patients' adoption of a willing, approach-oriented stance toward emotional experiences; increasing acceptance of emotions reduces reliance on avoidant coping that has been shown to paradoxically increase the frequency/intensity of emotions (Campbell-Sills, Barlow, Brown, & Hofmann, 2006), as well as to exacerbate disorder symptoms (e.g., Purdon, 2004). Thus, by targeting shared mechanisms, the UP offers practical advantages over single-disorder protocols, most notably the ability to facilitate more efficient treatment for a wide range of presenting problems.

There is promising emerging evidence to support the UP's efficacy in addressing emotional disorders. For example, in early open- and wait-list-controlled trials conducted by its developers, the UP demonstrated large reductions in anxiety symptoms (Ellard, Fairholme, Boisseau, Farchione, & Barlow, 2010; Farchione et al., 2012). Additionally, results from a recent, large equivalence trial suggest that the UP is associated with comparable symptom improvement for primary anxiety-related disorders as single-disorder protocols designed explicitly for that condition (Barlow et al., 2017). Moreover, a recent meta-analysis (Sakiris & Berle, 2019) of the UP found moderate to large effect sizes for improvement in depression and anxiety (respectively) when the UP was compared to TAU, waitlist, and medication. The researchers also indicated the UP led to moderate increases in adaptive emotion regulation strategies and decreases in maladaptive strategies.

1. Transdiagnostic mechanism-based interventions have greater potential for adaptability

There are several qualities of the UP that make this intervention particularly adaptable from setting to setting, increasing the likelihood of its widespread dissemination. Indeed, clinicians in routine practice prefer flexible treatments (i.e., those that provide the clinician with the ability to choose the order of skills presented and the amount of time spent teaching each skill) which allow for the execution of principles of change individually tailored to each patient (Addis & Krasnow, 2000; McHugh et al., 2009; Persons, 2006), and may be more likely to use an empirically-based intervention if it can be readily adapted.

First, the UP can be used to intervene on *any* emotion causing distress and interference in an individual's life, allowing it to be tailored to a wide variety of presenting problems. By utilizing an emotion-focused functional model (instead of a diagnosis-specific model) to determine whether a patient can benefit from the UP, this treatment can more easily be applied beyond anxiety-related and depressive disorders. For instance, individuals with eating disorders, borderline personality disorder, insomnia, and substance use disorders may display aversive, avoidant reactions to frequently occurring negative emotions (see Bullis et al., 2019), underscoring the transdiagnostic and adaptable nature of the UP. Second, there is evidence to suggest the UP can be applied to presenting problems that are not diagnoses as defined in the *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; *DSM-5*, American Psychiatric Association [APA], 2013), including non-suicidal self-injury (NSSI; Bentley, Nock, & Barlow, 2014), suicidal thoughts and behaviors (Bentley et al., 2017), and dysregulated anger (Cassiello-Robbins & Barlow, 2016).

Adding further to its adaptability, modular treatments, like the UP, are designed to be flexible with regard to both the order in which skills are delivered as well as the amount of time spent on a given treatment component, providing an opportunity for treatment personalization (Chorpita & Weisz, 2009). Chorpita, Daleiden, and Weisz (2005) describe modular treatments as comprising modules that are self-contained and do not rely on each other in order to produce their intended effects. These treatments thus differ from integrated treatments that are cumulative and need to be delivered in a specific sequence. Modular treatments have demonstrated steeper trajectories of improvement compared to traditional manualized treatment suggesting this approach improves treatment efficiency (Weisz et al., 2012). The UP was originally described as modular in that time spent focusing on a given skill could be shortened or extended based on the needs of the patient (Wilamowska et al., 2010), although in its standard presentation, the UP is an integrated treatment in which each module builds on the one before it. More recent examinations of the UP have begun to test its modularity with regard to Chorpita et al.'s (2005) definition. Indeed, emerging evidence suggests the UP modules can be presented independently from one another (Sauer-Zavala et al., 2017) and re-ordered based on individual patient characteristics (Sauer-Zavala, Cassiello-Robbins, Ametaj, Wilner, & Pagan, 2019), paving the way for additional adaptations tailored to unique delivery settings.

1.1. Present study

The purpose of this systematic review is to summarize the ways in which the UP has been flexibly applied by reviewing (1) the full range of presenting problems it has been used to address, as well as (2) the settings in which the protocol has been used, including any modifications that were made. This study extends the previous meta-analysis by Sakiris and Berle (2019) which focused more narrowly on the UP's effect on anxiety-related and depressive symptoms, emotion regulation, and affect; though the attention to these outcomes is understandable given the constraints of calculating meta-analytic statistics (i.e., the need to include studies with enough appropriate data to compute effect sizes), this approach neglects the wide range of presenting problems beyond anxiety and depression to which the UP has been applied. Additionally, previous reviews have not highlighted the diversity in protocol modifications that have been executed with the UP. A qualitative description of the ways in which the protocol has been modified and the success of such adaptations will further clarify the flexibility of this treatment.

2. Method

This review was conducted in accordance with the standard set by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Moher, Liberati, Tetzlaff, & Altman, 2009).

2.1. Inclusion and exclusion criteria

The present review included studies that met the following criteria: 1) a treatment study that 2) reported using any modification of Barlow and colleagues' Unified Protocol (e.g., the full protocol, UP modules, UP skills, UP-based treatment), and 3) included original data, 4) on adult patients, and was available in 5) full text and 6) in English. Because the UP was originally designed as an adult treatment and developed relatively independently from the child and adolescent versions of the UP (Ehrenreich-May et al., 2018), and there are distinct developmental considerations present in clinical research treatments for children and adolescents (e.g., explicit caregiver involvement; outcome ratings by children vs. parents; differences in childhood and adult experiences of disorders), this review focused on applications of the UP to adults in order to allow for streamlined conclusions regarding adult populations. Studies derived from the same treatment trials but with non-overlapping, original data were included. Studies were excluded if they did not meet all inclusion criteria.

2.2. Search strategy, article selection, and data extraction

A comprehensive literature review of four databases (PsychInfo, PubMed, Proquest Dissertations and Theses, and Web of Science) was conducted from the earliest inclusive dates until March 17, 2019. An additional literature review from March 17, 2019 until August 26, 2019 was conducted to identify relevant studies published while this review was in preparation. The search strategy included permutations of terms related to the UP (Unified Protocol for Transdiagnostic Treatment of Emotional Disorders, Unified Protocol) and terms relevant to intervention studies (clinical trial, effectiveness, evaluation, open trial, randomized, single case experimental design, treatment, therapy, intervention, empirical study, pilot). Additionally, the first author (CCR) reviewed the reference section of coded articles to identify potential articles the original search may have missed. Additional details regarding the literature search are available from the first author upon request.

The first three authors (CCR, MWS, JWT) participated in study selection and data extraction. One coder independently reviewed and determined each study's eligibility based on title and then abstract. Once relevant articles were identified, two coders reviewed the full text of each article to determine its eligibility for this review. Coders had 95.82% agreement on which articles were eligible after reviewing the full text. After identifying relevant articles, two coders independently extracted data from each study; discrepancies were resolved through discussion. The total agreement between coders was 87.57% for data extraction. The first author (CCR) also coded each study for information regarding fidelity ratings and training procedures relevant to the UP to assess the quality of each study. Twenty percent of the articles were chosen at random by the second author (MWS) and double coded. Agreement for study quality coding was 99%.

3. Results

3.1. Description of included studies

Fig. 1 presents the study selection process. The initial search yielded a total of 7244 unique publications. After examining titles and abstracts, 263 articles were considered for further review. After reviewing the full text of these articles, 76 were determined to be eligible for the current review and are presented in Appendix A. All references included in the results section of this paper (and Appendix A) are available in Appendix C. Because one article (Ellard et al., 2010) included two studies, 77 studies are reported in this review. All included studies are presented in Appendix A, which is organized hierarchically by 1) principal diagnosis examined and 2) alphabetically by author. All studies were published after 2010 and over half of the studies were published between 2017 and 2019. Throughout the results we will use k to denote the number of studies and n_{UP} to denote the number of patients who received the UP across indicated studies.

Of the studies reviewed, 31 were randomized controlled trials (RCTs), 21 were open trials, 14 used a single case experimental design (SCED), nine were case studies, two were implementation studies, and two were case series. Over half of studies (k = 50) did not have an active psychosocial treatment as the comparison condition. However, in the RCTs reviewed, the comparison conditions included waitlist (k = 14), treatment as usual (k = 2), and active psychosocial treatments (k = 17). Active psychosocial comparison treatments included extant evidence-based treatments for the target disorder(s), standard treatment provided prior to implementation of the UP, an altered version of the UP, and supportive counseling.

With regard to reported fidelity assessments and training procedures (Appendix B), 20 studies (25.97%) either used data from another trial (i.e., secondary analyses), were the original treatment development studies, or were internet-delivered treatment and thus these metrics were not applicable. Of the remaining 57 studies, 12 (21.05%) reported adherence ratings with all but one study (Bentley, Sauer-Zavala, Stevens, & Washburn, 2018) reporting excellent adherence and/or adherence over 80% adherence to the UP across rated sessions. Additionally, 13 studies (22.81%) reported that adherence ratings were conducted and/or that adherence was monitored in ongoing supervision but did not provide any data about treatment adherence; the remaining studies (k = 32) either provided no information about adherence ratings or only indicated the UP Therapist Guide was followed but did not indicate how adherence was ensured. Of the 59 studies that were not treatment development studies, internet-delivered, or secondary analyses, 25 (42.37%) indicated therapists received UP-specific training (e.g., attended a workshop, received certification in UP delivery from the treatment developers). The remaining studies (k = 34) did not report UP-specific therapist training procedures.

3.2. Settings and modality

Results indicated the UP has been implemented in several countries, most commonly in the United States (k = 46). It has also been tested in Iran (k = 15), Spain (k = 4), Sweden (k = 3) Brazil (k = 2), the United Kingdom (k = 2), Canada (k = 1), Denmark (k = 1), Hong Kong (k = 1), Saudi Arabia (k = 1), and Japan (k = 1). Of note, this result describes the number of studies published in English that report the use of the UP; it does not indicate how many UP studies may be published in non-English languages. Overall, results from these studies indicate the treatment was able to achieve its intended effects in countries outside the one in which it was developed (the United States).

With regard to treatment settings, the UP has been primarily tested in outpatient settings (k = 69). It has also been evaluated in hospital settings (e.g., inpatient, crisis stabilization units; k = 3) and a residential treatment facility for eating disorders (k = 2). Interestingly, three studies utilized an internet-delivered version of the UP, and one study offered a choice of internet-delivered or outpatient treatment. The internet-delivered adaptations of the UP reported small or non-significant treatment effects. Overall, the results from these studies indicate the UP has been able to achieve its intended effects in

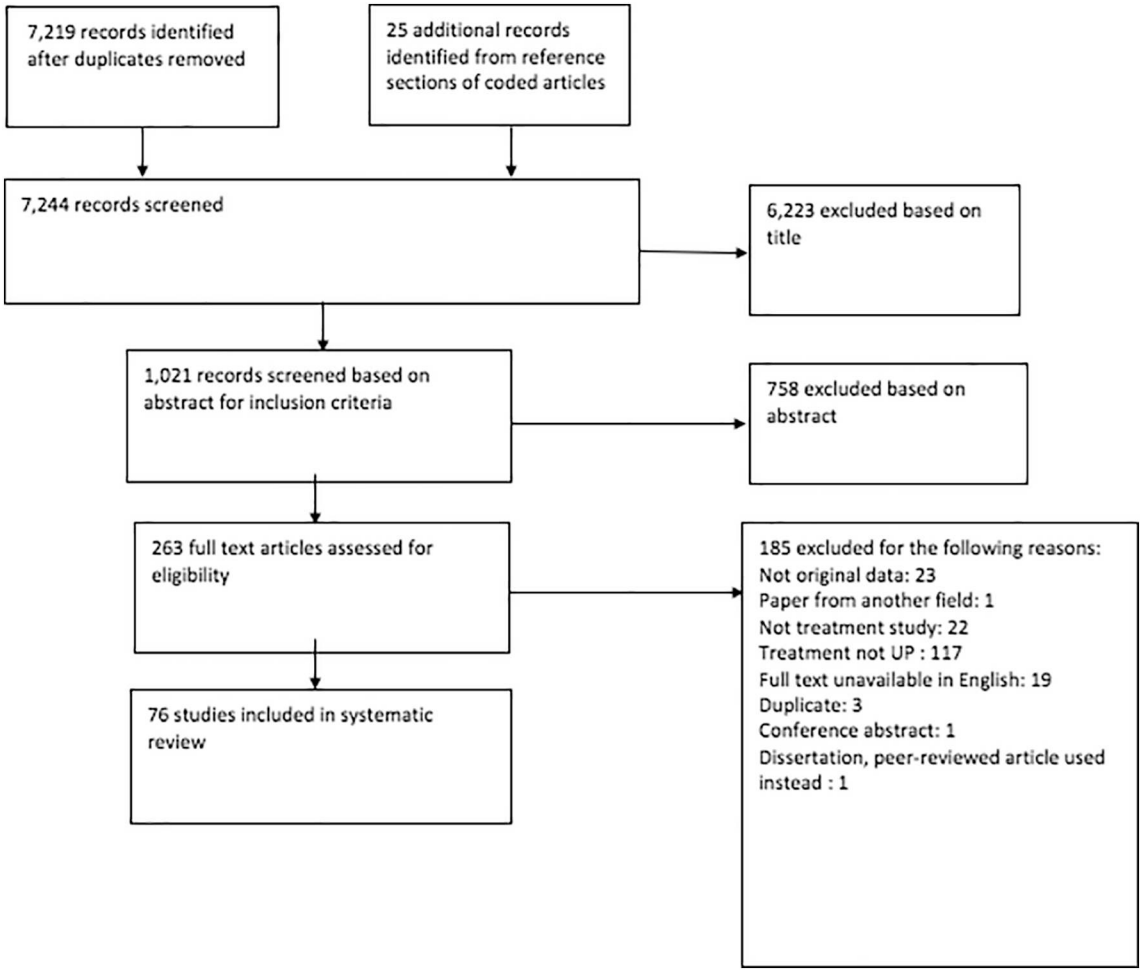

Fig. 1. Flow diagram of literature search.

outpatient settings and when holistically incorporated into a residential treatment facility. However, the UP has demonstrated similar effects as TAU conditions when not holistically incorporated into hospital and internet-delivered settings.

Finally, treatment was commonly delivered individually (k = 59), although group delivery was also noted (k = 17), and one study did not specify this mode of delivery. Both individual and group delivery formats of the UP tended to lead to improvements in the targeted symptoms, suggesting the feasibility of adapting the UP to different numbers of patients.

3.3. Modifications to the UP

Twenty-six studies (34%) reported UP delivery was not modified from the manual. Seven of these papers were derived from Farchione et al., 2012 and six were derived from Barlow et al., 2017; thus, these 13 papers do not represent independent studies in which the UP was delivered without modification. The majority of studies reviewed made at least some modification to the UP (k = 51; 66%).

The alterations made to the UP protocol varied widely from study to study. Some modifications such as changing session duration/frequency, translating the manual into another language, or incorporating examples relevant to a certain condition (e.g., NSSI or insomnia), might be considered relatively minor as they involve little alteration to treatment content.

Larger alterations to the protocol included reordering or omitting modules (Sauer-Zavala et al., 2017; Sauer-Zavala et al., 2019), incorporating content from other evidence-based treatments (e.g., behavioral activation, Farchione et al., 2017; dialectical behavior therapy, Gonzáles-Robles et al., 2019), and incorporating UP theory with other models of understanding behavior (e.g., minority stress experience; Pachankis et al., 2015; Parsons et al., 2017). Studies making these types of alterations often grounded their treatment in the UP and continued to work in the UP framework while rearranging the protocol or adding supplementary material. Overall, the results of these studies suggest modifications to the treatment were largely acceptable and feasible to patients and therapists and resulted in efficacious outcomes (i.e., symptom reduction).

Perhaps the largest scale modifications occurred when the UP was applied to unique treatment settings such as residential treatment facilities (Thompson-Brenner et al., 2018a, 2018b), hospitals (Bentley et al., 2018), and community mental health clinics (Sauer-Zavala et al., 2019). For example, for settings in which patients are present for most or all of the day, UP exercises were expanded and varied to ensure patients at different levels of care could benefit, while all staff members (e.g., nutritionists, nurses) were also trained to be familiar with UP concepts to use them clinically. For settings in which reading was an anticipated barrier to treatment, the length and complexity of the protocol was reduced (e.g., Castro-Camacho et al., 2018). While some

studies noted an improvement in outcomes after implementation (Thompson-Brenner et al., 2018a; 2018b) others did not (Bentley et al., 2018). Further, the acceptability and feasibility of UP implementation was mixed. Two studies suggested successful implementation in a residential treatment facility for eating disorders (Thompson-Brenner et al., 2018a; 2018b). On the other hand, Bentley et al. (2018) noted clinician fidelity to the protocol was variable after its implementation in a hospital setting. Additionally, Sauer-Zavala et al. (2019) noted patients with opioid use disorders in a community mental health clinic for the homeless sometimes refused to participate in UP sessions. Such findings suggest that, although the UP is often acceptable to patients and clinicians, this is not uniformly the case.

3.4. Patient characteristics

Appendix A reports the majority demographics present in each study sample. Sixty studies examined predominantly female samples while six used exclusively male samples. The remaining studies did not list the demographics of the UP group specifically. Of note, four of the six studies with a majority of male patients were case studies. In 25 studies, the majority of patients identified as Caucasian and in only three studies was the majority of the sample African-American. These results suggest the majority of patients treated with the UP in research studies have been Caucasian and female.

Overall, the studies reviewed examined diagnostically heterogeneous samples, with the full range of emotional disorders represented (anxiety, depressive, bipolar, eating, borderline personality, somatic symptom, trauma-related, and insomnia). The most common diagnoses present in the study samples were anxiety disorders (79%) and depressive disorders (69%). Twenty-six studies (34%) included patients with post-traumatic stress disorder (PTSD). Five studies included patients with bipolar disorders and five studied patients with borderline personality disorder (BPD). Interestingly, some presentations that might not be immediately considered emotional disorders, such as substance use disorders (k = 3), impulse control disorder (k = 1), attention deficit hyperactivity disorder (k = 3), were also present in the study samples, albeit to a much lesser extent.

In line with the functional model of emotional disorders, the UP was also applied to presenting problems not classified as diagnoses in *DSM-5*. Two studies specifically included patients engaging in NSSI (Bentley et al. 2017a, 2017c) and one study looked at the effects of the UP on anger (Cassiello-Robbins et al., 2018), although dysregulated anger was not an inclusion criterion for the sample. Two studies applied the UP to compulsive, risky sexual behavior. Additionally, five studies applied this protocol to address the emotional sequelae present with medical disorders (chronic pain [k = 2], irritable bowel syndrome [k = 1], infertility [k = 1], and Parkinson's disease [k = 1]). Finally, studies applied the UP to subclinical presentations of anxiety/depression (k = 2) and paranoia (k = 1). In the following sections, we review the evidence supporting the use of the UP with different disorders.

3.4.1. Primary anxiety-related disorders with/without comorbid depressive disorder

The majority of studies reviewed (k = 33) focused on patients with a primary diagnosis of an anxiety-related disorder. Of note, while obsessive-compulsive and related disorders are no longer considered anxiety disorders in *DSM-5*, they are included in this section as they were classified as anxiety disorders in *DSM-IV*, when a number of these studies were conducted. Given the large number of studies present for this class of disorders, we will first review studies that delivered the UP with no modifications and then those that modified the protocol in some way.

3.4.1.1. Studies using standard UP.

One case study described a patient who achieved responder status without high-end state functioning regarding OCD and panic disorder with agoraphobia diagnoses. This patient also reported improvements in anxiety, depressive, and panic symptoms, time spent on obsessions and compulsions, and interpersonal relationships (Boisseau et al., 2010). Through five open trials conducted in three countries (US, Japan, Spain; n_{UP} = 61), the UP demonstrated preliminary efficacy in treating anxiety disorders with or without comorbid mood disorders, in both individual and group formats (Bullis et al., 2015; Ellard et al., 2010; Ito et al., 2016; Osma et al., 2015).

The UP has also demonstrated significant improvements in anxiety-related and depressive symptoms compared to waitlist in the United States and Iran (Farchione et al., 2012; Khakpoor, Baytmar, & Saed, 2019; Mohajerin, Bakhtiyar, Olesnycky, Dolatshahi, & Motabi, 2019; Zemestani, Imani, Ottaviani, 2017). Farchione et al. (2012) indicated the UP led to greater improvements in diagnostic severity and functioning compared to waitlist (e.g., delayed treatment). Additional analyses of the data from this trial indicated that, compared to waitlist, the UP led to medium-to-large improvements in negative affect, work/social adjustment, positive affect, and self-esteem, with smaller relative improvements in quality of life, intolerance of uncertainty, neuroticism/behavioral inhibition, and extraversion/behavioral activation (Boswell et al., 2013b; Carl et al., 2014; Gallagher et al., 2013). When all patients who completed the UP (either immediately or delayed) in the Farchione et al. (2012) trial were considered (n = 37), improvements in diagnostic severity, work/social adjustment, and positive affect were generally maintained 18 months post-treatment, while patients reported some regression in anxiety-related and depressive symptoms and negative affect (Bullis et al., 2014). Beyond anxiety-related and depressive symptoms, the UP led to decreases in anxiety sensitivity that were associated with lower post-treatment clinical severity (Boswell et al., 2013a) and lower likelihood thought-action fusion but no change in moral thought-action fusion (Thompson-Hollands et al., 2013). With regard to moderators of outcomes, higher baseline symptom severity generally predicted less change in anxiety-related and depressive symptoms across treatment; however, among patients exhibiting higher readiness to change, greater baseline symptom severity predicted greater change in anxiety-related and depressive symptoms (Boswell et al., 2012). Although the UP was rated as more credible than typical CBT, patients had similar expectancies of improvement in the UP as in typical CBT, and neither credibility nor expectancy was related to treatment outcomes (Thompson-Hollands et al., 2014). One study specifically examined patients with primary body dysmorphic disorder (BDD; Khakpoor et al., 2019) and reported the UP led to greater decreases in BDD and depressive symptoms, appearance anxiety, emotion dysregulation, and delusional beliefs than waitlist, which were generally maintained at 3-month follow-up.

Finally, the UP has been compared to other active treatments. In the largest RCT in the United States to date, Barlow et al. (2017) compared the UP to four single-disorder CBT protocols (SDPs) and waitlist. Compared to SDPs, the UP led to similar improvements in diagnostic severity, anxiety-related and depressive symptoms, work/social adjustment, hope, quality of life, savoring beliefs, positive affect, and number of comorbid disorders (Barlow et al., 2017; Gallagher et al., 2019; Steele et al., 2018; Wilner Tirpak et al., 2019). The UP led to greater improvements on all these measures compared to waitlist control. A similar percentage of patients no longer met criteria for their primary diagnosis in the UP (63.6%) and SDP (57.1%) conditions at the end of treatment, and these gains tended to be maintained at 6-month follow-up (Barlow et al., 2017; Wilner et al., 2018). In a subsample of patients from this study, the UP led to small, nonsignificant decreases in anger while SDPs led to moderate, nonsignificant increases in anger

(Cassiello-Robbins et al., 2018). At a mechanistic level, the working alliance mediated the effect of pre-treatment expectancies and changes in anxiety-related symptoms in SDPs but not in the UP (Sauer-Zavala et al., 2018a). Lotfi et al. (2014) also compared the UP to SDPs and found the UP led to greater decreases in anxiety symptoms, but similar improvements in depressive symptoms and quality of life.

Among patients with anxiety or depressive disorders in Brazil, the UP led to significantly larger decreases in anxiety and depressive symptoms than a medication-only condition (de Ornelas Maia, Nardi, & Cardoso, 2015). In Spain, a study compared standard UP to the UP with an additional four-module component on the regulation of positive affect. The treatments led to similar pre- to post-treatment improvements in anxiety and depressive symptoms, positive and negative affect, and quality of life, which were generally maintained at 3-month follow-up (González-Robles et al., 2019). Further, 58–67% of patients no longer met criteria for any mental disorder at post-treatment, similar to Ellard et al., 2010.

3.4.1.2. Studies using modified UP. An internet-delivered UP was provided to pregnant women with a primary fear of giving birth in Sweden (n_{UP} = 127) compared to treatment-as-usual (TAU; Rondung et al., 2018). Although patients in TAU reported lower fear of birth at post-treatment, patients in the UP reported lower fear of birth at 1-year follow-up. It is noteworthy that patients only spent an average of 40 min on the UP (time spent on TAU was unavailable).

Several single-case experimental design studies (SCEDs) have also been conducted with modified versions of the UP for people with anxiety-related and comorbid mood disorders. Among patients with generalized anxiety disorder (GAD), mantra-based meditation was added to standard UP after 1 or 3 weeks of treatment (Cooney Roxbury, 2017). All patients remitted from GAD at post-treatment. Standard UP led to similar improvements in worry, anxiety, sleep impairment, work/social adjustment, negative affect, self-compassion, and mindfulness, whereas UP + mantra meditation led to steeper improvements in depressive symptoms, quality of life, emotion dysregulation, and positive affect. Among patients randomized to receive the UP modules in a personalized order prioritizing their relative strengths or weaknesses, those whose order of UP modules prioritized their strengths exhibited earlier improvements in anxiety and depressive symptoms and experiential avoidance (Sauer-Zavala et al., 2019). Brake et al. (2016) asked patients with an anxiety disorder (n = 7) to complete exposure exercises while engaging in UP mindfulness skills or avoidance strategies. They found that UP mindfulness skills were associated with higher overall distress but greater intra-exposure declines in distress than avoidance strategies.

Finally, one case series reported on one patient completing standard UP with behavioral activation strategies incorporated (Boswell et al., 2017). The patient reported decreases in anxiety and depressive symptoms, worry, and stress.

3.4.1.3. Summary. Taken together, these results suggest that the UP is an efficacious treatment for people with anxiety-related disorder(s) and comorbid mood disorder(s). Specifically, the UP has led to improvements in diagnostic severity, anxiety-related and depressive symptoms, quality of life, work/social adjustment, hope, positive affect, and comorbid diagnoses that are similar to SDPs and greater than waitlist. Some evidence supports unique effects of the UP on anxiety symptoms, anxiety sensitivity, intolerance of uncertainty, likelihood thought-action fusion, and anger, although these effects are either smaller sized or reported in smaller samples. There is some evidence the UP has been effectively implemented cross-culturally in Spain, Japan, Iran, and Brazil with similar results as in American studies. Based on the preliminary evidence here, the UP may be successfully modified by prioritizing patient strengths early in treatment, incorporating behavioral activation principles, and adding a dedicated mantra meditation component. However, if delivered as an online intervention, practitioners may need to supplement the UP with further support to increase patient engagement.

3.4.2. Primary depressive disorder

Two RCTs and three case studies of the UP in an unmodified or group form have been conducted among patients with a primary depressive disorder. The RCTs, which took place in the UK and Iran, compared the UP to waitlist control (Marnoch, 2014) or English-language training (Bameshgi et al., 2019). Both studies indicated the UP led to improvements in anxiety and depression compared to waitlist. Additionally, Bameshgi et al. (2019), who recruited patients with depression and marital problems, noted improvements in three relationship communication patterns: mutual avoidance, mutually constructive communication, and demanding/withdrawing behaviors. In an open trial of a UP group for depressive disorders in Brazil, patients reported large improvements from pre- to post-treatment in depression and anxiety symptoms, quality of life, physical health and sexuality, and social relationships (de Ornelas Maia, Braga, Nunes, Nardi, & Silva, 2013). Two case studies and a SCED with one patient reported improvements in symptoms of depression and anxiety from pre- to post-treatment (Boswell, Anderson, & Barlow, 2014; Hague, Scott, & Kellett, 2015; Osma, Sánchez-Gómez, & Peris-Baquero, 2018). These studies took place in the United States, UK, and Spain. Of note, one study reported continued gains or improvement over 12-month follow-up on symptoms of depression, positive and negative affect, and quality of life, but not anxiety symptoms (Osma et al., 2018). Another study noted the return of GAD at 3-month follow-up (Hague et al., 2015).

3.4.2.1. Studies using modified UP. Three case studies with relatively minor modifications to the UP have been conducted. A woman in the United States with major depressive disorder (MDD) received the UP, modified to include aspects of behavioral activation (e.g., values identification, activity scheduling; Farchione, Boswell, & Wilner, 2017). This treatment led to improvements in depressive and anxiety symptoms, neuroticism/behavioral inhibition, extraversion/behavioral activation, negative and positive affect, and interpersonal problems. A woman in the United States with MDD and GAD received the UP, modified to include assertiveness training and grief processing (Donahue, Hormes, Gordis, & Anderson, 2019). The UP led to improvements in depressive symptoms to minimal levels, although anxiety symptoms remained in the clinical range. Finally, a woman in Colombia with MDD, PTSD, GAD, and panic disorder (PD) received the UP, adapted to better match her cultural context (e.g., including an orientation session, focusing on difficulties functioning instead of diagnoses; Castro-Camacho et al., 2019). She experienced full reductions in depressive, anxiety, and PTSD symptoms, as well as headaches, sleep difficulties, and uncomfortable physical sensations, which were generally maintained over 3-month and 2-year follow-up.

The UP has also been modified to treat suicidal thoughts and behaviors among inpatients with MDD and anxiety disorders (Bentley et al., 2017). In this study, the UP was shortened to five sessions focusing on core modules. Compared to TAU, UP + TAU led to similar improvements in depressive and anxiety symptoms, hopelessness, and overall psychopathology from pre- to post-treatment. These gains were partially reversed at 1- and 6-month follow-up.

3.4.2.2. Summary. The UP has been studied relatively infrequently (k = 10) among patients with a primary depressive disorder

(n_{UP} = 59). Among these studies, the UP appears to reliably lead to reductions in depressive symptoms and improvements in quality of life. However, the UP may be less efficacious at reducing or maintaining reductions in comorbid anxiety symptoms among these patients. The UP also appears to demonstrate good preliminary efficacy cross-culturally and for older patients, specifically. Finally, the UP may be either supplemented with additional modules or simplified to five core daily modules, depending on the setting and population, and still achieve promising outcomes.

3.4.3. Mixed emotional and related disorders

Several studies recruited patient samples with an array of diagnoses. Specifically, one RCT, three open trials, one pre-post implementation study, and two SCEDs have been conducted on the UP for patients with mixed emotional and related disorders. The RCT, conducted in Hong Kong, included patients with depressive, anxiety, adjustment, eating, and/or insomnia disorders randomized to receive a 15-week modified version of group UP (n = 54) or a CBT group. UP modifications included re-ordering of some modules, teaching distress tolerance skills from dialectical behavior therapy (DBT), and including an individual session after the group sessions. The UP group led to greater improvements in depressive and anxiety symptoms, and clinical severity at post-treatment but not positive or negative affect. The UP also led to greater improvements in stress and work/social adjustment by 9-month follow-up (Ling, 2018).

Three open trials (n_{UP} = 516) took place in the US (with a Veteran sample), Iran, and Denmark (Alatiq et al., 2019; Reinholt et al., 2016; Varkovitsky, Sherrill, & Reger, 2018). These studies included patients with PTSD, depressive disorders, sleep-wake disorders, substance use disorders, anxiety disorders, bipolar disorder, schizophrenia, OCD, panic disorder, social anxiety disorder, conversion disorder, specific phobia, complicated grief, somatic, eating, personality, and attention deficit/hyperactivity disorders. Two studies delivered the UP in group format (Reinholt et al., 2016; Varkovitsky, et al., 2018). Alatiq et al. (2019) made modifications to the UP including cultural adaptations in style and examples used and structural modifications (e.g., including a greater reliance on case formulation to determine the timing of module components). Overall, these studies indicated the UP led to improvements in symptoms of depression and anxiety, as well as emotion regulation (Varkovitsky et al., 2018), functioning, and quality of life (Alatiq et al., 2019; Reinholt et al., 2016).

In a pre-post implementation study in the United States, the UP was adapted for an inpatient setting to be delivered over 7 days and to incorporate explicit emotion-induction exercises (Bentley et al., 2018). Patients were diagnosed with mood, anxiety, substance use, somatic, and/or eating disorders. While the UP was generally viewed as acceptable, the Mindful Emotion Awareness module was rated as the most acceptable and the Motivation Enhancement module was viewed as least acceptable. The UP led to similar improvements in depression and anxiety symptoms, suicidality, and emotion dysregulation as the pre-UP TAU.

One SCED study examined the effects of the UP modified to incorporate skills targeting repetitive negative thinking and reported large improvements in clinical severity, depression, and anxiety (Akbari et al., 2015). Finally, in a SCED conducted in the United States, patients with an emotional disorder received 4 weeks of a single UP module. Each module demonstrated both specific effects on its intended outcome (e.g., Mindful Emotion Awareness module predicting changes in mindfulness) and general effects (e.g., Mindful Emotion Awareness module predicting changes in cognitive flexibility, behavioral approach, and emotional acceptance; Sauer-Zavala et al., 2017).

3.4.3.1. Summary. These results (k = 7) suggest the UP is generally efficacious for outpatients with a range of emotional and related disorders and that the UP can be delivered in group settings to patients with a variety of diagnostic presentations. Additionally, results suggest the UP may be modified for group settings and produce greater improvements than other CBT groups on depressive and anxiety symptoms and clinical severity. The UP may be applied to Veterans and cross-cultural samples with good efficacy, although more research is needed to strengthen this conclusion. The UP may produce similar improvements as TAU among inpatients. Finally, the modules of the UP have demonstrated some specificity regarding their psychological effects, although more research is needed to determine how specifically UP modules impact their putative mechanisms of action.

3.4.4. Bipolar disorder with comorbid anxiety disorder(s)

One RCT and one case series have been conducted in the United States on the UP for bipolar disorder (Ellard et al., 2012; 2017). In the RCT, patients with bipolar I or II were randomized to either standard individual UP with psychiatric TAU (n = 8) or psychiatric TAU alone (Ellard et al., 2017). In both studies, patients reported improvements in symptoms of depression and anxiety and, in the RCT, patients improved significantly compared to TAU.

3.4.4.1. Summary. These results suggest the UP shows promise for the treatment of bipolar disorder with comorbid anxiety disorder(s). However, while the UP appears to contribute to reductions in anxiety and depressive symptoms, its effects on manic symptoms are less robust. Given the small sample sizes (n_{UP} = 16), more research is needed to draw stronger conclusions.

3.4.5. Substance use disorders

One open trial of the UP for primary substance use disorder has been conducted at a health center specifically designed to service homeless individuals and their families (Sauer-Zavala et al., 2019). The UP was modified to focus on its five core modules, which providers could deliver in any order. All patients (n = 6) were diagnosed with opioid use disorder and MDD, with other diagnoses including stimulant use disorder (cocaine, unspecified), sedative use disorder, GAD, and PTSD. Patients reported medium-to-large improvements in anxiety and small worsening of depressive symptoms. Additionally, among patients with comorbid anxiety and alcohol use disorders in the United States, the UP was provided with venlafaxine or placebo and compared to a relaxation condition with venlafaxine or placebo. The UP + placebo group reported a greater decrease in the percentage of heavy drinking days compared to the relaxation + placebo group (Ciraulo et al., 2013).

3.4.5.1. Summary. Across studies, these preliminary results (n_{UP} = 51) suggest some benefits of the UP for emotional conditions among those with substance use disorders. However, more research in controlled settings is needed to draw stronger, more generalizable conclusions about these effects and any effects on substance use behaviors.

3.4.6. Eating disorders

Two large-scale implementation studies (n_{UP} = 409) have been conducted incorporating the UP into a residential eating disorders treatment facility. The UP was modified in several ways to better match this setting (e.g., designing modules to be delivered independently of each other; incorporating eating disorders examples; incorporating more active patient exercises; Thompson-Brenner et al., 2018a). Providers also defined phases of treatment for patients (i.e., early, middle, late) with assessments to determine when patients would move between phases. An initial subset of patients demonstrated small-to-medium sized pre- to post-treatment improvements in experiential

avoidance, mindfulness, and anxiety sensitivity. The UP also led to medium-sized improvement in eating disorder symptoms compared to treatment provided before UP implementation (Thompson-Brenner et al., 2018a). Among a larger sample of patients completing the UP at this site, the UP led to greater pre- to post-treatment improvements in experiential avoidance, mindfulness, and anxiety sensitivity but not depressive or eating disorder symptoms than treatment implemented before the UP. However, at 6-month follow-up, the UP led to greater pre- to post-treatment improvements in experiential avoidance and depressive and eating disorder symptoms but not mindfulness or anxiety sensitivity (Thompson-Brenner et al., 2018b).

3.4.6.1. Summary. These results suggest the UP can be successfully modified and implemented for the treatment of eating disorders in a residential facility. While the UP appears to outperform treatment provided prior to UP implementation, further research comparing the UP to other leading eating disorder treatments such as cognitive behavior therapy-enhanced (CBT-E; Fairburn, 2008) is needed.

3.4.7. Borderline personality disorder (BPD)

Four SCEDs have been conducted testing the UP for BPD, with three of these studies occurring in the United States. In the most recent SCED, half the patients with BPD and comorbid disorders reported reliable decreases in anxiety and depressive symptoms. One quarter of patients reported no change in anxiety and depressive symptoms, while one quarter reported an increase in these symptoms. Five patients no longer met criteria for BPD at post-treatment (Lopez et al., 2019). Similarly, in a second study, half the patients with BPD and comorbid disorders reported lower BPD features during treatment than at baseline. Three patients reported no difference in BPD features between treatment and baseline, and one patient reported elevated BPD features during treatment compared to baseline. Five patients no longer met criteria for BPD at post-treatment (Lopez et al., 2015). In a third SCED, three of five patients with BPD and comorbid disorders reported large reductions in BPD features, anxiety and depressive symptoms, and emotion dysregulation. One patient reported little change in these measures, and one patient reported no change or a small increase in these measures (Sauer-Zavala, Bentley, & Wilner, 2016). Lastly, in a study in Iran, all patients with BPD and comorbid disorders reported some reductions in emotion dysregulation and BPD features from baseline to post-treatment and follow-up (Mohammadi et al., 2018).

3.4.7.1. Summary. Overall, these results (n_{UP} = 27) suggest that the UP is shows promise for treating BPD features, emotion dysregulation, and comorbid symptoms of anxiety and depression, with about half of patients in each study exhibiting improvements on these measures. Of note, 12–25% of patients in each study also appear to deteriorate in the UP compared to baseline. Future research with larger samples and prognostic indicators of improvement and deterioration is warranted.

3.4.8. Non-suicidal self-injury (NSSI)

Two studies have been conducted on the UP for NSSI: a case study and a SCED study, both in the United States. In the case study, an 18-year-old female patient with NSSI and social anxiety disorder completed 16 weeks of the UP (Bentley, 2017a). By the end of treatment, she had refrained from any NSSI for 5 months, maintained low depressive and anxiety symptoms, and reported reductions in, but clinically high levels of, GAD symptoms and social anxiety. In the SCED study, patients with NSSI and other emotional disorders engaged in two UP modules: Mindful Emotion Awareness and Cognitive Reappraisal and Flexibility (Bentley, Nock, Sauer-Zavala, Gorman, & Barlow, 2017c). Mindful Emotion Awareness led to clinically meaningful reductions in NSSI for 3 of 5 patients, while Cognitive Flexibility led to clinically meaningful reductions in NSSI for 2 of 5 patients. Four of seven patients who completed exit interviews reported the cessation of NSSI since the start of the study.

3.4.8.1. Summary. Together, these preliminary results suggest the UP, and specifically Mindful Emotion Awareness and Cognitive Flexibility modules, may contribute to reductions in NSSI. Larger-scale trials are much needed in this area, as these conclusions are based on 11 patients. However, these results also emphasize the ability of individual UP modules to lead to psychological improvements.

3.4.9. Insomnia disorder

Two studies have been conducted on the UP for insomnia disorder: a case study and a SCED study, both in Iran (Doos Ali Vand, Gharraee, Asgharnejad Farid, Ghaleh Bandi, & Habibi,

2018a; Doos Ali Vand, Gharraee, Asgharnejad Farid, Ghaleh Bandi, & Habibi, 2018b). Both studies reported improvements in sleep-related variables (e.g., onset latency, quality, beliefs) and the SCED study also indicated improvements in emotion dysregulation, anxiety sensitivity, and neuroticism.

3.4.9.1. Summary. The results of these studies (n_{UP} = 7) provide preliminary evidence the UP can be modified to include content related to sleep quality and that the delivery of such a modified protocol can lead to improvements in sleep and emotional outcomes. Further research is necessary for this population in order to draw stronger conclusions about these effects.

3.4.10. Subclinical symptoms

All applications of the UP to subclinical populations have involved UP groups with some modifications to the standard protocol. One RCT compared a UP group to a transdiagnostic cognitive therapy group based on Beck's model of emotional disorders, two RCTs compared a UP group to waitlist control, and one open trial of a UP group has been conducted. In Iran, patients with depression and anxiety symptoms were randomized to eight sessions of either UP or transdiagnostic cognitive therapy (Mohammadi, Birashk, & Gharaie, 2013). The UP led to greater decreases in anxiety than cognitive therapy and similar improvements in depression, stress, and work/social adjustment. In the United States, Bentley et al. (2017b) randomized undergraduate university students with elevated, but not clinical levels of, anxiety or depressive symptoms to engage in a 2-h workshop teaching five core UP principles (n = 45) or an assessment-only control condition. Students reported some improvements in neuroticism, quality of life, and experiential avoidance that were not significantly different from the assessment-only group. Participants rated the workshop as highly acceptable and satisfying. In Iran, female patients with subclinical paranoia were randomized to 10 sessions of either UP or waitlist control (Amirpour et al., 2018). The UP led to greater improvements in the intensity of paranoid thoughts and work/social adjustment than waitlist. In Canada, patients with “clinically significant” symptoms (determined by a psychiatric consultation) of social anxiety disorder, GAD, or panic disorder with/without agoraphobia received the UP modified to include exposure sessions earlier in treatment and to explicitly include imaginal exposures. Patients reported medium-to-large improvements in anxiety, depressive, and panic disorder symptoms, worry, and positive and negative affect. They reported small-to-medium improvements in social anxiety symptoms (Laposa et al., 2017).

3.4.10.1. Summary. Overall, these results (k = 4; n_{UP} = 97) provide preliminary support for the efficacy of UP groups for subclinical anxiety, depression, and paranoia. UP groups appear acceptable to this population and may produce greater changes in anxiety symptoms

than cognitive therapy groups. Given the relatively small sample sizes, more research is needed to draw stronger conclusions.

3.4.11. Physical health and neurological complaints

The UP has been applied to a range of physical health complaints including irritable bowel syndrome (IBS), chronic pain, psychosomatic complaints, infertility, and Parkinson's disease.

3.4.11.1. Irritable bowel syndrome. One RCT and one open trial of the UP have been conducted for patients with IBS, both in Iran (Johari-Fard & Ghafourpour, 2015; Mohsenabadi, Zanjani, Shabani, & Arj, 2018). Both studies reported decreases in IBS symptoms and improvements in quality of life. Additionally, the RCT indicated UP treatment was associated with greater improvement in IBS, depression, and anxiety symptoms, stress, frequency of cognitive reappraisal, and greater reductions in the frequency of expressive suppression compared to waitlist. Together, these findings (n_{UP} = 47) suggest the UP may be efficacious at reducing both IBS and emotional symptoms, although more research is needed to generalize these results.

3.4.11.2. Chronic pain. Two SCED studies using a guided internet-delivered version of the UP have been conducted for patients with chronic pain and emotional disorders, both in Sweden (Lorenz & Stranberg 2015; Wurm et al., 2017). Overall, the results of these studies (n_{UP} = 14) suggested an internet-delivered version of the UP may not be efficacious for treating chronic pain and that the UP may not reliably lead to improved depressive or anxiety symptoms in this population. The preliminary conclusions are based on only two studies and more research is needed to confirm or refute this observation.

3.4.11.3. Psychosomatic complaints. With regard to psychosomatic complaints, an open trial of group UP (n_{UP} = 20) for psychosomatic complaints (related to digestion and skin) in Iran, yielded significant improvements in all areas of emotion dysregulation except impulsivity and acting with awareness, putting things into perspective, and catastrophizing (Mazaheri et al., 2013). These results suggest the UP is a promising treatment for emotional aspects of psychosomatic complaints, although it is unclear from this study the degree to which the UP addresses psychosomatic complaints directly. Additional research can shed light on the extent to which the UP improves psychosomatic complaints and support the ability of this treatment to target the emotional aspects of this condition.

3.4.11.4. Infertility. One RCT in Iran examined the effects of the UP compared to 8 sessions of Mindfulness-Based Stress Reduction (MBSR), or waitlist (n_{UP} = 15; Mousavi et al., 2019) as treatment for patients with infertility. Patients reported greater decreases in anxiety and depressive symptoms in both the UP and MBSR conditions. However, it is unclear from the reported results if there were any significant differences between the UP and MBSR on these outcomes. These preliminary results suggest the UP delivered in a group format may be similarly effective in reducing anxiety and depressive symptoms among women with infertility and elevated emotional symptoms; however, more research is needed to replicate and confirm these findings.

3.4.11.5. Parkinson's disease. Finally, a SCED study in the United States applied 12 sessions of the UP (either in person or through videoconference) to patients with mild to moderate idiopathic Parkinson's Disease and a comorbid anxiety disorder (n_{UP} = 9). An optional information session for family members was offered at mid-treatment. Overall, these preliminary results indicated improvement in anxiety and depressive symptoms compared to baseline (Reynolds, Saint-Hilaire, Thomas, Barlow, & Cronin-Golomb, 2019) and additional research is needed to further support the utility of the UP in addressing emotional symptoms associated with Parkinson's disease.

3.4.11.6. Summary. Across these physical health and neurological complaints, the UP appears relatively efficacious at reducing anxiety and depressive symptoms (k = 7). The UP may also be efficacious at reducing IBS symptoms. Additionally, the UP may be as effective as MBSR for treating these symptoms among those with infertility. However, these results do not support the conclusion that the UP is efficacious at addressing chronic pain conditions. These studies exploring the efficacy of the UP for treating emotional sequelae associated with physical health and neurological complaints are preliminary in nature and more research is needed to replicate, confirm, and further clarify their results.

3.4.12. Sexual minority stress

The UP has been applied to gay and bisexual men in two studies, an open trial and an RCT, in the United States. In the open trial and RCT, patients engaged in 10 individual sessions of a version of ESTEEM, a modification of the UP designed to address the effects of sexual minority stress on HIV-related stressors, sexual compulsivity, substance use, and HIV transmission risk behaviors (Pachankis, Hatzenbuehler, Rendina, Safren, & Parsons, 2015; Parsons et al., 2017).

3.4.12.1. Summary. Together, the results of these studies (n_{UP} = 43) suggested the UP can be effectively modified to treat aspects of sexual minority stress and contribute to more frequent safe sex behaviors. ESTEEM may also impact patients' depressive and anxiety symptoms among those who are relatively elevated on these symptoms at the start of treatment. Given all patients in these trials were men, future researchers may extend these findings to a broader range of sexual orientations and gender identities.

4. Discussion

The purpose of this systematic literature review was to examine the ways in which the Unified Protocol (UP) has been studied in treatment research across adult patient populations and modified in different settings. While the UP is designed to treat the full range of emotional disorders (i.e., disorders characterized by aversive responses to emotions and avoidance-based emotion regulation strategies), no researchers to date have systematically examined the empirical evidence for this claim. Indeed, preliminary data from clinician reports suggest a primary hesitation to implementing the UP in their practice is the perceived inability to tailor the treatment to varying patient presentations (Cassiello-Robbins, Ametaj, Boettcher, Conklin, & Sauer-Zavala, 2015). The studies reviewed here demonstrate the UP has been applied to the full range of emotional disorders (anxiety, mood, eating, insomnia, bipolar, obsessive-compulsive, traumatic and stressor-related), typically with efficacious outcomes (i.e., symptom reduction and reduced avoidance). The strongest base of evidence appears to be for the efficacy of the UP in anxiety-related and depressive disorders. Additionally, while fewer studies utilized the UP for patients with eating disorders, these studies recruited relatively large samples, providing stronger evidence for the use of the UP with this patient population as well. Smaller studies provided more preliminary support for using the UP with other emotional disorders.

Two studies tested the effects of the UP on substance use. The

characterization of substance use disorders as emotional disorder is unclear. While aspects of substance use disorder presentations often fit the model of emotional disorders (e.g., substance use to provide relief from uncomfortable emotions), other presentations do not (e.g., substance use to enhance positive affect; McHugh & Goodman, 2019). In this review, studies that reported on substance-use outcomes showed mixed findings, with one indicating a reduction in heavy drinking days (Ciraulo et al., 2013) and the other noting a non-significant reduction in club drug use (Parsons et al., 2017). Such results support McHugh and Goodman's (2019) observations that the heterogeneity of presentations in this class of disorders might require different treatment strategies. While the UP may be one such treatment, other treatments should be explored as well.

Further, results from this review indicated the UP has been applied to patients who either did not meet the diagnostic threshold for a disorder (e.g., subclinical anxiety, depression, paranoia) or presented with problems not currently defined as diagnoses in *DSM-5* (e.g., NSSI, dysregulated anger, compulsive sexual behavior). Results suggested the UP predominantly led to desired outcomes for these patients. The ability of the UP to target these problems is a strength of the treatment. Since it is not confined to a single diagnosis and its associated symptoms, the UP framework is able to parsimoniously address a variety of presenting concerns. This being said, the evidence supporting the application of the UP to these presentations and disorders remains preliminary as there were only a few studies for a given presentation and many were open trials, case studies, or SCEDs consisting of relatively small samples. These studies thus require replication to confirm the generalizability of their results. One direction for future research with the UP will be to continue evaluating its efficacy for patient presentations beyond those with anxiety-related, depressive, and eating disorders. Further, given the preliminary nature of many studies reviewed, trials comparing the UP to other active psychosocial treatments for these conditions are also needed.

Additionally, results suggested the UP has predominantly been tested among patients who identify as female and Caucasian. This focus on female patients is not surprising as many emotional disorders (e.g., depression, anxiety-related, borderline personality, eating disorders) are more common in female populations (Kessler, Chiu, Demler, & Walters, 2005), and data suggest women seek treatment at higher rates than men (Möller-Leimkühler, 2002). Similarly, at least in the United States where the majority of the studies reviewed were conducted, Caucasian individuals typically receive mental health treatment at higher rates than other racial/ethnic groups (e.g., Shao, Richie, & Bailey, 2016), which may help explain why the majority of studies reviewed treated samples that were primarily Caucasian. Another direction for future research is to continue evaluating the UP in more diverse samples. Interestingly, some studies specifically provided the UP to patients from marginalized communities (e.g., gay and bisexual patients, patients with HIV). In these studies, however, the UP was adapted to focus on minority stress experiences. Research as to whether treatments need to be modified for minority populations remains mixed (Carter, Mitchell, & Sbrocco, 2012; Horrell, 2008). While no study reviewed here suggested differential outcomes or attrition based on gender, race, or ethnicity, it should be noted that none of these studies explicitly reported tests of this hypothesis. Whether an unmodified version of the UP is acceptable and effective for patients who identify as minorities (i.e., non-white, non-heterosexual) is an area for future research. Focus groups and assessment specifically of the acceptability of the UP with minority patients may be very valuable.

Relatedly, the literature reviewed here noted a number of cultural adaptions for use of the UP outside the United States. An important limitation when considering these results is that this review only examined studies published in English. It is possible that more studies describing the implementation of the UP are available in other languages and were not reviewed here. Overall, results of the English-language studies indicated these adaptations were generally efficacious regarding symptom reduction. However, these studies were mostly preliminary in nature and further research will be needed to confirm the utility of these cultural adaptions as well as the effectiveness of the UP in additional countries. For example, the majority of the non-US countries examined were first world countries. Whether the UP is useful in developing countries or countries characterized by high levels of poverty, as well as what modifications to the treatment might be needed to make it accessible in such counties, remains to be seen. Studies integrating the UP with the Common Elements Treatment Approach (CETA; Murray et al., 2014), a transdiagnostic treatment often specifically implemented in developing countries, may be especially useful for such questions.

An additional goal of this review was to examine modifications made to the UP. Some amount of flexibility has been incorporated as a noted strength in the UP from the start (e.g., tailoring the length of a given module to the needs of the patient; Sauer-Zavala et al., 2019). The literature reviewed here suggests the modifications being made to the treatment in research studies extends beyond the amount of time spent on specific treatment skills. The alterations made to the UP across studies were quite heterogeneous and included translation into another language, adding relevant examples, incorporating elements of other treatments (e.g., behavioral activation) or theories (e.g., minority stress model), and adaptations to unique treatment settings (e.g., residential treatment centers, hospitals, community mental health centers). Another notable adaption was the use of the UP as a group treatment. The current manual predominantly provides direction for delivering the UP as an individual treatment, although there is some information about group delivery as well. However, providers may be able to reach more patients delivering the UP in a group format. Indeed, in some countries a group intervention is the first line of treatment offered. The fact that group treatments consistently led to reductions in anxiety and depressive symptoms in the studies reviewed here suggests the UP can be successfully adapted to this modality.

When and how the UP should be adapted is a question of interest. Although some adaptations are clearly necessary (e.g., translation to a native language), adaptations that incorporate other treatment elements, reorder or omit skills, or make large structural changes to the treatment (i.e., division into phases) pose particularly complex questions regarding the “core” ingredients, active mechanisms, and/or “spirit” of the UP. For instance, at a content level, modifications to the UP that include other treatment elements should be tested against standard UP (e.g., Cooney Roxbury, 2017) to characterize the unique effect of added elements above and beyond standard UP. Second, at a structural and delivery level, modifications such as the ordering of UP modules based on baseline characteristics (Sauer-Zavala et al., 2019) or shared decision-making with the patient (Joosten et al., 2008) should be systematically tested to determine best practices for treatment personalization and optimization. Given that patients in community clinics attend fewer than five sessions, on average (Hansen, Lambert, & Forman, 2002; Wolitzky-Taylor, Zimmerman, Arch, De Guzman, & Lagoasino, 2015), it is important to prioritize the most useful skills for patients to improve the chances they receive maximum benefit from the sessions they do attend. However, these changes represent a deviation from the manual as written. Adaptations that involve reordering treatment skills will likely need to demonstrate more rapid (e.g., Weisz et al., 2012) or durable improvements in symptoms to be considered an evidence-based alternative to the standard treatment manual. Further, the UP manual describes the early modules as “foundational” and

evidence supporting the acceptability of delivering this content at a different point in treatment would also be needed. Indeed, Sauer-Zavala et al. (2019) noted that 33% of patients in a SCED study that involved re-ordering modules indicated they would prefer to receive psychoeducation first. Thus, more research is needed to identify any modules that should always be delivered at certain points in treatment and to describe how to best order modules to improve patient outcomes. Finally, at the level of dissemination and implementation, our review suggests the UP needs to be adapted to the needs of a setting in order to be implemented successfully. The studies reviewed here provide examples of barriers and facilitators to implementing the UP in a new institution. The relatively few examples described in the literature highlight the need for more systematic tests and descriptions of such research.

Adapting the UP in these ways raises the question of when the UP stops being the UP. This is a question that is currently unanswered as there are no clear guidelines delineating when the treatment can no longer be called the UP. A number of suggestions could be considered: for example, a treatment that utilizes the UP framework and case conceptualization may be considered the UP. Alternatively, a treatment could be called the UP if it uses all eight modules, regardless of the order in which they are delivered. However, these suggestions are not based on empirical evidence. One possible direction for future research is to conduct dismantling studies to identify which elements are crucial to success of the UP. Such research would lend insight into the active mechanisms involved in the UP and could be used to more clearly distinguish UP and UP-based treatments (i.e., those that include these crucial elements) from non-UP treatments (i.e., those that omit these crucial elements).

One potential risk in adapting the UP in multiple ways is that doing so will reduplicate the problem of single-disorder protocols (SDPs) by creating multiple domain-specific UP adaptations. A primary appeal of the UP, and other transdiagnostic treatments such as process-based CBT (Hofmann & Hayes, 2019), is that it is a single treatment applicable to many clinical presentations. This approach has the benefit of reducing training burden because trainees can learn one treatment that is likely to benefit heterogeneous patients on their caseload. Modifying the UP for specific patient presentations or adding elements from other treatments to it could potentially proliferate into multiple UPs that are essentially SDPs. Therefore, modifications to the UP need to be carefully considered. As previously mentioned, research justifying the need for modified versions of the UP by demonstrating their relative superiority to standard delivery can provide insight into the necessity and utility of proposed modifications.

The results reported and considerations raised here should be viewed in the context of the study's limitations. First, the heterogeneity of modifications to the UP makes it difficult to draw strong conclusions about their efficacy or to systematically evaluate each type of modification. Second, the outcomes assessed differed widely across studies. Even studies assessing similar outcomes (e.g., anxiety symptoms) used different measures. Because of the heterogeneity in these outcome measures, meta-analytic statistics could not be computed. Therefore, effect sizes describing the magnitude of the effects of the UP for various presenting problems are not available. A recent meta-analysis provides effect sizes for some measures (e.g., anxiety, depression, positive affect, negative affect, emotion regulation functional impairment, quality of life; Sakiris & Berle, 2019). However, other outcomes such as those related to insomnia, eating disorder symptoms, NSSI, etc., were not included in that meta-analysis. Third, the majority of studies did not provide data regarding treatment adherence or therapist training procedures, making it difficult to assess the quality of the included studies. Future treatment studies would benefit from including this information. Fourth, this study only examined the UP as applied to adults. Adolescent and child versions of the UP are published (Ehrenreich-May et al., 2018) and future researchers may systematically evaluate those as well. Fifth, our search was limited to English-language articles reporting on the UP or its adaptations. This search limitation may have led to biased conclusions regarding the cross-cultural efficacy of the UP. Sixth, when conducting a systematic review, the “file drawer problem” is always of concern. That is, it is not possible to know how many studies were conducted but not reported (Rosenthal, 1979). Therefore, it is possible studies with conflicting results that would change the interpretations offered here exist, but have not been published. Finally, it is possible the studies reviewed here engaged in flexible practices with regard to data collection, analysis, and reporting that could have artificially improved their chances of finding significant results (Simmons, Nelson, & Simonsohn, 2011). Such practices would also artificially strengthen the conclusions drawn in this study.

Despite these limitations, the results of this review have clinical implications. The studies reviewed indicated the UP is generally efficacious across diagnostic presentations, global borders, and healthcare settings. While the strongest base of evidence for the UP is among Caucasian females in the United States with anxiety-related or depressive disorders, many preliminary studies point to benefits of the UP beyond this population. This observation suggests the UP can be an effective treatment for a wide range of patient presentations, making it a potentially efficient and disseminable treatment. Additionally, this treatment might be positively perceived by patients who would find a consistent approach to understanding their symptoms (across diagnostic categories) easier to understand. While many results were preliminary and require further replication, the breadth of presenting problems treated successfully (i.e., leading to symptom reduction), as well as the numerous ways in which the UP was adapted and still produced favorable outcomes for patients, suggests it can be a flexibly applied tool in many clinical settings. Given the high demands often placed on clinicians to provide evidence-based treatment to a heterogeneous caseload, the UP could be a helpful treatment in which to train clinicians to reduce training burden. Training clinicians in one protocol that can be used for a range of diagnostic presentations may be helpful in making evidence-based treatments more appealing and practical while still allowing the flexibility that data suggest therapists prefer, thereby reducing the science to practice gap.

Overall, this systematic review is meant to synthesize and consolidate the broad literature on the UP since its publication in 2010. The results presented here are promising and more research focused on dissemination and implementation of this protocol will further advance our knowledge of its utility in a wide range of clinical settings.

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Contributors

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Declaration of competing interest

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Appendix A. Description of included studies

Article	Study type	Country	UP sample characteristics	Diagnoses	Tx modality/ setting	Modifications to UP	Length of Tx/ Session Frequency	Comparison Condition(s)	Description of primary findings
Primary anxiety disorder with/without comorbid depressive disorder									
Barlow et al. (2017)	RCT	USA	*n* = 88 Age: 31.1 (11.0) 83% Caucasian 54.5% Female	GAD, OCD, PD/A, SOC, SP, MDD	Individual/ Outpt	None	16 sessions/1 × per week	SDPs, WLC	UP and SDPs led to similar reductions in clinician-rated diagnostic severity at post-tx and 6mFU (both greater than WLC). UP had fewer dropouts than but similar pre-tx credibility as SDPs.
Boisseau et al. (2010)	Case Study	USA	*n* = 1 Age: 23 100% Caucasian 100% Male	OCD, PDA, GAD	Individual/ Outpt	Included body scan exercise[3] followed by emotion-induction exercise to facilitate nonjudgmental, present-focused awareness. Pt completed Texas Safety Maneuvers Scale[4] and Checklist of Emotional Avoidance Strategies before behavior module (module 5).	12–18 sessions/1 × per week	N/A	UP led to 60% reduction in time spent on obsessions and compulsions. Pt met responder status on all diagnoses.
Boswell et al. (2012)[1]	Open trial*	USA	*n* = 37 Age: 29.76 (9.54) 94.5% Caucasian 59.5% Female	AnxNOS, GAD, OCD, PDA, SOC, PTSD	Individual/ Outpt	None	18 sessions/1 × per week	N/A	Initial sx severity predicted less change, but higher severity was associated with greater dep and anx change when readiness to change was also higher
Boswell et al. (2013a)[1]	Open Trial*	USA	*n* = 54 Age: 30.00 (9.05) 90.7% Cauasian 57.4% Female	AG, AnxNOS, GAD, OCD, PD, SOC, SP, PTSD, MDD	Individual/ Outpt	None	18 sessions/1 × per week	N/A	Anx sensitivity decreased over tx, particularly between sessions 8–18. Greater reductions in anx sensitivity associated with greater reductions in clinical severity scores from pre- to post-tx and pre-tx to 6mFU.
Boswell et al. (2013b)[1]	RCT	USA	n = 26 Age: N/A	GAD, SOC, PDA, OCD, PTSD, Anx NOS, MDD, DYS, DDNOS, SP	Individual/ Outpt	None	18 sessions/1 × per week	WLC	UP led to significant decrease in intolerance of uncertainty (IU). IU change not significant in WLC.
Boswell et al. (2017)	Case study	USA	*n* = 1 Age: 35 100% African American 100% Male	GAD	Individual/ Outpt	UP "supplemented with GAD-specific CBT protocol,"[5] including relaxation methods and self-controlled desensitization	40 sessions/1 × per week	N/A	UP led to decreases in anx, dep, GAD, and stress scores from intake to termination to below clinical thresholds/into normal ranges.
Brake et al. (2016)	SCED	USA	*n* = 7 Age: 31.14 (12.28) 86% Caucasian 43% Female	GAD, PDA, SOC	Individual/ Outpt	UP mindfulness and exposure modules: initially imaginal exposures only, then interoceptive and in vivos were added to achieve sufficient emotion activation	12 sessions/2 × per week	Avoidance strategy	Mindfulness module associated with greater distress (SUDS), less change in anx, and similar changes in experiential avoidance compared to the use of avoidance strategies.
Bullis et al. (2014)	RCT	USA	*n* = 15 Age: 32.27 (10.42) 100% Caucasian 60% Female	GAD, OCD, PDA SOC, DD, PTSD	Individual/ Outpt	None	18 sessions/1 × per week	N/A	Significant and large reduction in severity of principal dx, number of dx's, & impairment from pre-tx to 24mFU. 66% met responder status, 60% met high end state functioning at 24mFU.
Bullis et al. (2015)	Open trial	USA	*n* = 11 Age: 44.55(16.79) 90.9% Caucasian 63.6% Female	AG, AnxNOS, GAD, OCD, PDA, SOC, SP, DDNOS, DYS, MDD, Alcohol Abuse, ADHD, trichotillomania, PTSD	Group/Outpt	2-h sessions with 5–6 participants per group.	12 sessions/1 × per week	N/A	UP led to large decreases in anx, experiential avoidance, & functional impairment. UP led to moderate decreases in dep. 6/11 pts. described sx as mild at post-tx (compared to 1/11 at pre-tx).

Carl et al. (2014)[1]	RCT	USA	n = 26 Age: N/A Ethnicity: N/A 59.5% Female	AnxNOS, GAD, OCD, PDA, SOC, DDNOS, DYS,MDD, PTSD	Individual/ Outpt	None	Max 18 sessions/1× per week	WLC	Small effects of the UP on neuroticism/ behavioral inhibition and extraversion/ behavioral activation compared to WLC at post-tx.
Cassiello-Robbins et al. (2018)[2]	RCT	USA	n = 14 Age: N/A 94.2% Caucasian 48.6% Female	GAD, OCD, PD, SOC, PTSD	Individual/ Outpt	None	16 sessions/1× per week	SDPs	UP led to small, nonsignificant, decrease in anger from pre- to post-tx. UP group had significantly lower anger scores than SDP at post-tx.
Cooney Roxbury (2017)	SCED	USA	n = 6 Age: 32.83 (15.46) 83.33% Caucasian 83.33% Female	GAD, PDA, SP, MDD	Individual/ Outpt	Train pts. to complete mantra- based meditation in either first 2 sessions or sessions 3 and 4	14 sessions/1× per week	14 session UP without mantra meditation training	Mantra condition led to better overall outcomes at post-tx: steeper decreases in emotion regulation difficulties after learning the mantra, and steeper improvements in quality of life and positive affect.
de Ornelas Maia et al. (2015)	RCT	Brazil	n = 24 100% Brazilian 81.3% Female	GAD, PD, SOC, MDD, PTSD	Group/Outpt	Group format, 2 h sessions	12 sessions	psychiatric med management	UP led to large decreases in anx and dep compared to med management.
Ellard et al. (2010) Study 1	Open Trial	USA	n = 18 Age: 30.0 (10.54) 94.4% Caucasian 58.8% Female	GAD, OCD, PD/A, SOC, SP, PTSD, DYS, MDD, Hypochondriasis, Impulse Control Disorder NOS	Individual/ Outpt	None	15 sessions/1× per week	N/A	For primary dx: 56% met responder status and 33% met high end-state functioning at post-tx. For secondary dx: 71% met responder status and 50% met high end-state functioning.
Ellard et al. (2010) Study 2	Open Trial	USA	n = 15 Age: 29.73 (7.11) 80% Caucasian 53.3% Female	AnxNOS, GAD, OCD, PD/A, SOC, SP, DYS, MDD, Hypochondriasis	Individual/ Outpt	Modified to increase pt. awareness of the interaction of each component of the 3-component model of emotions in the context of present-moment experience. Emotion awareness moved from session 6 to session 3, added optional booster sessions.	Up to 18 sessions/1× per week	N/A	For primary dx: 73% met responder status and 60% met high end-state functioning at post-tx. 85% met responder status at 6mFU. For secondary dx, 64% met responder status and 64% met high end-state functioning at post-tx.
Farchione et al. (-2012)	RCT	USA	n = 26 Age: N/A Ethnicity: N/A 59.5% Female	GAD, SOC, OCD, PDA, AnxNOS, PTSD, MDD, DYS, DDNOS	Individual/ Outpt	None	Up to 18 sessions/1× per week	WLC	UP led to large reductions compared to WLC on dx severity, overall anx, some dep measures, and overall functioning. UP led to more pts. not meeting criteria for dx's at post-tx than WLC. Tx gains generally maintained at 6mFU.
Gallagher et al. (-2013)[1]	Open Trial*	USA	n = 37 Age: 29.75 94.6% Caucasian 59.46% Female	GAD, SOC, PDA, OCD, PD, AnxNOS, PTSD	Individual/ Outpt	None	18 sessions/1× per week	Delayed tx (WLC)	UP led to significant increases in self-esteem compared to WLC. In pooled sample UP led to moderate (non-significant) increases in nearly all other quality of life metrics compared to WLC.
Gallagher et al. (-2019)[2]	RCT	USA	n = 88 83.4% Caucasian	GAD, SOC, PDA, OCD	Individual/ Outpt	None	16 sessions/1× per week	SDPs, WLC	UP led to moderate-to-large (significant) improvements in hope over the course of tx, similar in size to SDPs, and larger than WLC. UP led to slightly smaller (non-significant) increases in hope than SDPs.
Gonzales-Robles et al. (2019)	RCT	Spain	n = 12 Age: 27.75 (10.91) 100% Spanish 79.2% Female	GAD, MDD, AG, PD, SOC, DYS	Individual/ Outpt	Translated into Spanish; clinical examples adjusted for cultural relevance; included elements of DBT emotion awareness (mindfulness skills).	14 sessions/1× per week	Transdiagnostic protocol + positive affectivity regulation component	Transdiagnostic protocol led to large improvements in positive affect, negative affect, dep, anx, and quality of life. No significant between-group differences at post-tx or 3mFU. A similar proportion of both conditions (7 or 8 of 12) no longer met diagnostic criteria at post-tx or 3mFU.

Ito et al. (2016)	Open trial	Japan	n = 17 Age: 35.18 (10.80) 100% Japanese 59% Female	MDD, SOC, PD, PTSD, Anx NOS	Individual/ Outpt	UP materials translated into Japanese; 50–90 min sessions as needed; more visual illustrations included in pt. workbook	23 sessions/1× per week	N/A	UP led to large improvements in anx, dep, & global functioning and medium-to-large improvements in positive affect and reappraisal frequency during tx and FU. 11.8% dropout. High adherence to UP by providers.
Khakpoor et al. (-2019)	RCT	Iran	n = 26 Age: 24.27 (2.65) 100% Iranian 72.7% Female	OCD; GAD; SOC; PD; MDD	Individual/ Outpt	None	20 sessions/1× per week	WLC	UP led to large, significant improvements in dep, anx, difficulties in emotion regulation, intolerance of uncertainty (IU), and psychological flexibility compared to WLC. Gains generally maintained over 2mFU. Changes in difficulties in emotion regulation, IU, and psychological flexibility were associated with changes in dep and anx.
Lotfi et al. (2014)	RCT	Iran	n = 11 Age: 33.9 (7.5) 100% Iranian 63.63% Female	GAD, SOC, PD/A, ANX-NOS, MDD	Individual/ Outpt	None	8 sessions/1× per week	SDP	UP led to greater reductions in anxiety (large and significant effect) but similar improvements in depressive sx and quality of life as SDPs.
Mohajerin et al. (-2019)	RCT	Iran	n = 64 Age: 28.71 (6.82) 100% Iranian 51.6% Female	BDD, GAD, MDD, SOC, OCD, excoriation	Individual/ Outpt	Psychoeducation delivered first; explicit focus of how UP content applies to BDD symptoms	14 sessions/1× per week	watchful waiting (weekly 30 min calls to check on sx; supportive listening; pts. seeing psychiatrists allowed to continue)	UP led to greater improvement in BDD sx than watchful waiting. No patients in UP group met criteria for BDD at end of tx, & gains were maintained at 3mFU
Osma et al. (2015)	Open Trial	Spain	n = 11 Age: 43.87 (12.66) 100% Caucasian 90.91% Female	OCD, MDD, Anx NOS, DDNOS, PDA	Group/Outpt	UP materials translated into Spanish; 2-h sessions	10 sessions/1× per week	N/A	6/8 pts. did not meet dx criteria at post-tx and 6/6 pts. (who could be contacted) did not meet dx criteria at 12mFU. High treatment retention (8/11).
Rondung et al. (2-018)	RCT	Sweden	n = 127 Age: N/A 100% Female	depression, anxiety, eating disorder, bipolar disorder, other non-specified psychiatric disorder, fear of birth	Internet/ Hospital	Self-help version with downloadable content; no interoceptive exposure module; de-emphasized cognitive flexibility and emphasized cognitive diffusion	8 modules + one postpartum module/1× per week	Counseling by midwives	Fear of birth did not differ between groups at post-tx. At 1 year postpartum, guided ICBT led to significantly lower levels of fear of birth. Of those assigned to guided ICBT, 81% started tx, 47% moved on to the second module, and 10% finished more than 4 modules.
Sauer-Zavala et al. (2019)	SCED	USA	n = 12 Age: 29.83 (7.03) 100% Caucasian 50% Female	MDD, SP, SOC, GAD, OCD, PDD, OST	Individual/ Outpt	Modules used were psychoeducation, mindful emotion awareness, cognitive flexibility, countering emotional behaviors, and interoceptive exposure	10 sessions/1× per week	Starting treatment with relative skill strengths or weaknesses	Reordering UP modules was acceptable/feasible. Both groups had similar outcomes at post-tx. Those in the strength condition demonstrated sx improvement more quickly.
Sauer-Zavala et al. (2018)[2]	RCT	USA	N/A	OCD, GAD, PD/A, SOC	Individual/ Outpt	None	16 sessions/1× per week	SDPs	Working alliance mediated the relation between expectancy and change in anx when tx conditions were collapsed and for the SDPs alone, but not for UP.
Steele et al. (2018)[2]	RCT	USA	n = 88 Age: N/A	SAD, PD, OCD, GAD, AG, DEP	Individual/ Outpt	None	16 sessions/1× per week	Single disorder protocols (MAP, MAW, TOCD, MSA)	UP led to similar decreases in comorbid disorders as SDPs. UP led to similar decreases in comorbid dep, GAD, and SOC sx as SDPs.
Thompson-Hollands et al. (2013)[1,6]	Open Trial*	USA	n = 37 Age: 29.67 (9.43) 97% Caucasian 58% Female	GAD, SOC, OCD, PDA, Anx NOS, PTSD, MDD, DYS, DD NOS, SP, Tourrettes	Individual/ Outpt	None	18 sessions/1× per week	Delayed tx	UP led to decreased likelihood thought-action fusion scores but not moral thought-action fusion scores. Results did not differ by dx.

Thompson-Hollands et al. (2014)[1]	Open Trial*	USA	n = 37 Age: 29.67 (9.43) 94.6% Caucasian 59.5% Female	SOC; OCD; PDA; GAD; AnxNOS; PTSD; MDD; DYS; DDNOS	Individual/ Outpt	None	18 sessions/1× per week	None	Mean UP credibility rating was higher than usual CBT credibility ratings, expectancy was similar to that of other UP and CBT studies. Neither baseline credibility nor expectancy were related to post-tx or 6mFU dep or anx sx, or work & social adjustment.
Tirpak et al. (2019)[2]	RCT	USA	n = 88	PD, GAD, SOC, OCD	Individual/ Outpt	None	16 sessions/1× per week	SDP, WLC	UP led to similar improvements in quality of life, savoring beliefs, and positive affect as SDPs. Both UP and SDPs outperformed waitlist on these measures (small-to-medium, significant effects).
Wilner et al. (2018)[2]	RCT	USA	n = 88 Age: 31.0 (11.60) 83.0% Caucasian 54.5% Female	OCD, GAD, PD, PD/A, SOC, MDD, Specific phobia, and others not listed	Individual/ Outpt	None	16 sessions/1× per week	SDPs, WLC	Both UP and SDPs led to greater quality of life than the WLC at post-tx. Reductions in clinical severity rating from baseline to end of tx and from baseline to 6mFU indicated statistical equivalence between UP and SDPs.
Zemestani et al. (-2017)	RCT	Iran	n = 20 Age: 23.20 (3.90) 100% Iranian 65% Female	GAD; SOC; PD; Mood Disorder (not Bipolar I or II)	Individual/ Outpt	90-min sessions	14 sessions/1× per week	WLC	UP led to greater improvements in dep, anx, expressive suppression, & cognitive reappraisal than WLC and was maintained at 3mFU.
Primary depressive disorder									
Bameshgi et al. (-2019)	RCT	Iran	n = 17 Age: 32.66 (9.39) 100% Iranian 100% Female	marital problems, depression	Individual/ Outpt	None	12 sessions/1× per week	English-language training	UP led to medium-to-large improvements in dep syx, avoidant, constructive, and demanding/withdrawing communication patterns compared to the English-language training group.
Bentley et al. (2017d)	RCT	USA	n = 5 Age: N/A 50% African American 16.7% Female	MDD, polysubstance abuse	Individual/ Hospital (crisis stabilization unit)	Delivered in 5 sessions; written to 8th grade reading level; added examples of self-injurious behaviors and substance use	5 sessions/1-2× per day	TAU	UP: 4/5 participants completed all sessions and scored 100% on skills acquisition questionnaire at EoT. No large or consistent differences between UP+TAU and TAU on suicidal outcomes at EoT, 1mFU, or 6mFU.
Boswell et al. (2014)	Case Study	USA	n = 1 Age: 64 100% Caucasian 100% Female	GAD, MDD	Individual/ Outpt	None	22 sessions/1× per week	N/A	Clinically significant decreases in anx and dep pre/post tx. Changes in mindfulness associated with, and temporally preceded changes in anx and dep. Changes in reappraisal temporally preceded changes in dep.
Castro-Camacho et al. (2019)	Case Study	Colombia	n = 1 Age: 50 100% Afro-Colombian 100% Female	MDD, PTSD, GAD, PD	Individual/ Outpt	Addition of Session 0 to orient pt. to treatment; replaced references to disorders in the manual to emotional difficulties and their impact on functioning; emphasized examples from pt.'s experience over abstract concepts; simplified and incorporated more graphic material in workbook; combined mindfulness exercises into one.	12 sessions/1× per week	N/A	UP led to improvements in anxiety, depressive, & PTSD sx as well as quality of life from clinical levels pre-tx to minimal levels at post-tx. These gains were maintained at 3mFU and 2yFU.
de Ornelas Maia et al. (2013)	Open Trial	Brazil	n = 16 Age: 35.62 (12.09) 100% Brazilian 87.5% Female	MDD, GAD, PD, SOC, PTSD	Group	2-h sessions; focus on psychoeducation, cognitive flexibility, countering emotional behaviors, & exposure (interoceptive and situational)	12 sessions/N/A	N/A	UP lead to significant improvements in anx, dep, quality of life, social relationships, and sexuality.
Donahue et al. (2019)	Case Study	USA	n = 1 Age: 25 100% African American 100% Female	MDD, GAD, with panic attacks	Individual/ Outpt	additional time on psychoeducation and alliance building, addition of assertiveness training and grief processing	20 sessions/1× per week	N/A	Reductions in dep sx from clinically significant to non-interfering. Reliable reductions in anx sx that remained in clinical range.

Farchione et al. (-2017)	Case Study	USA	n = 1 Age: 21 100% Caucasian 100% Female	MDD	Individual/ Outpt	Incorporated behavioral activation principles into UP using Valued Living Questionnaire[7] to assess valued life domains and relevant goals. Mixing module order to match pt.'s presenting problems	14 sessions/1× per week	N/A	UP led to decreases in dep and anx scores below clinical levels. Behavioral inhibition and negative affect scores decreased to within 1 SD of typical tx outcomes. Behavioral activation and positive affect scores increased to within 1 SD of typical tx outcomes.
Hague et al. (2015)	SCED	UK	n = 1 Age: 67 100% Caucasian 100% Female	MDD, GAD	Individual/ Outpt	Slower-paced sessions; domiciliary visits when pt.'s husband could not drive her to tx.	8 sessions/1× per week	N/A	UP led to clinically significant decreases in anx and dep during tx. Anx, but not dep, scores returned to low clinical levels at 3mFU. UP led to significant improvement from baseline to end of tx on daily structure, mood, confidence, & worry.
Marnoch et al. (2014)	RCT	UK	n = 7 Age: 76.71 (7.25) 57.1% Female	MDD, GAD, SOC, Mixed anx & dep, AG, PD	Individual/ Outpt	2-page UP workbook summaries written for pts. who did not tolerate the full readings; American phrasings and spellings changed to British; vignettes and examples changed to appeal to older audience and include more dep examples; cautionary statement included in session 9 re: health concerns with interoceptive exposures; location of sessions varied to accommodate pts./caregivers; tape recorders and larger font handouts provided as needed; family members/caregivers involved where necessary to facilitate homework planning and implementation	12 sessions/1× per week for first 10 sessions; bi-weekly for the last 2	Delayed tx	UP led to reduced dep scores but not anx or general distress compared to WLC.
Osma et al. (2018)	Case Study	Spain	n = 1 Age: 47 100% Spanish 100% Male	MDD, schizoid and depressive personality disorder traits	Individual/ Outpt	None	20 sessions/3 sessions of evaluation & tx planning, 9 weekly sessions, then 8 biweekly sessions	N/A	Absence of MDD at post-tx and 12mFU, increase in positive affect and decrease in negative affect at post-tx. At 12mFU positive affect returned to pre-tx levels and negative affect decreased significantly. Reduced schizoid and dep PD traits at post and FU. Pt indicated satisfaction with tx.
Mixed emotional and related disorders									
Akbari et al. (2015)	SCED	Iran	n = 3 age: 21.67 (1.53) 100% Iranian 66.7% female	DYS, OCD, GAD	Individual/ Outpt	Incorporation of skills targeting repetitive negative thinking, including attention training, detached mindfulness, and challenging metacognitive beliefs about repetitive negative thinking.	12 sessions/1× per week	N/A	Intervention led to large-sized improvements in clinical severity, dep, anx, negative affect, positive affect, work and social adjustment, repetitive negative thinking, worry, and obsessions and compulsions. Gains maintained at 1mFU.
Alatiq et al. (2019)	Open Trial	Saudi Arabia	n = 198 age: 32.2 (10.1) 100% Saudi Arabian 67.7% female	Depression, Anxiety, OCD, PD, SOC, PTSD, conversion, SP, complicated grief	Individual/ Outpt	Incorporation of UP and Norton's (2012) tx[8], case formulation driven, therapist could choose from tx elements based on presenting problem. Cultural adaptations (e.g., linking mindfulness to spiritual/religious practices).	5.3 sessions on average (SD = 4.7)/1× per week	N/A	Transdiagnostic CBT (T-CBT) led to small-to-medium sized improvements in dep, generalized anx, and functional impairment. T-CBT led to 67% of participants demonstrating clinical improvement, 15% of participants demonstrating no change, and 1% of participants worsening.
Bentley et al. (2018)	Other Implementation	USA	n = 61 Age: 34.10 (13.60) 75.2% Caucasian 51.7% Female	Anx disorders, bipolar disorder, perinatal DD, Unipolar DD, unspecified mood disorders, AUDs, somatic disorders, ED, adjustment disorder	Group/ Hospital	Developed 7 day schedule for all patients to receive all modules within first 2 days on the unit; developed 20 exposure exercises to be conducted on inpt unit	5-8 days/1× per day	Patient outcomes on inpatient unit prior to UP implementation	Patients improved significantly and similarly before and after UP implementation on dep, suicidal ideation, anx, and emotion regulation. Patients generally reported high UP acceptability. Clinician protocol fidelity was variable in the month after UP implementation.

Ling (2018)	RCT	Hong Kong	n = 54 Age: 40.41 (10.96) 100% Chinese 74.1% Female	MDD, DYS, GAD, PD, AG, SOC, OCD, SPEC, Adjustment disorder, PTSD, Hypochondriasis, insomnia, ED	Group/Outpt	Added gratitude exercises; cultural adaptations; expansion of cognitive traps from 2 to 4; emotion awareness module delivered after cognitive; included distress tolerance in interoceptive exposure	15 sessions + one 45-min individual session + three 90-min booster sessions/1× per week	TAU	UP led to greater improvements in dep, anx, stress, psychosocial impairment in functioning, & clinical severity compared to TAU from pre-to post-tx. UP led to similar improvements as TAU in positive affect, negative affect, & total number of diagnoses from pre- to post-tx. UP led to significantly lower clinical severity and fewer dxs at 9mFU.
Reinholt et al. (2-016)	Open Trial	Denmark	n = 47 Age: 34.10 (9.92) 100% Danish 76.6% Female	PD, SOC, GAD, AG, SP, MDD, DYS, ADHD, SSD, avoidant personality disorder, OCD, unspecified ED, PTSD	Group/Outpt	UP materials translated into Danish; group sessions were 150 min each, with 7–9 participants and 2 therapists per group.	15 sessions/1× per week	N/A	UP led to large (significant) improvements in clinician-rated global symptom severity and anx; medium (significant) improvements in well-being, negative affect, and positive affect; & small (significant) improvements in self-reported anx, dep, self-reported global symptom severity, phobias. 85% completed tx.
Sauer-Zavala et al. (2017)	SCED	USA	n = 8 Age: 27.00 (10.49) 75% Caucasian 75% Female	GAD, SOC, OCD, SSD, AG, OSAD, PDD, SP, Other specified eating disorder, BDD, PTSD	Individual/ Outpt	Each pt. received 4 sessions of one module: psychoeducation, mindful emotion awareness, cognitive flexibility, or countering emotional behaviors	4 sessions/1× per week	N/A	UP modules in isolation led to reliable change in relevant skill domain for 5/8 pts.; 2/8 pts. did not show reliable change; 1 pt. showed nonsignificant deterioration. Emotion awareness and cognitive flexibility produced change specific to the associated skills, psychoeducation and countering emotional behaviors produced broader change across skill domains.
Varkovitzky et al. (2018)	Open Trial	USA	n = 52 Age: 46.65 (12.50) 65.4% Caucasian 17.3% Female	PTSD, MDD, sleep-wake disorder, SUD, anxiety, disorder, bipolar disorder, schizophrenia	Group/Outpt	90-min group sessions	16 sessions/1× per week	N/A	UP led to significant pre–post reductions in emotion regulation difficulty, dep, and PTSD sx severity, comparable to other PTSD group tx with veteran participants[9]. Reductions in emotion regulation difficulties predicted lower PTSD and dep sx severity at end of tx.
Bipolar disorder with comorbid anxiety disorder(s)									
Ellard et al. (2012)	Case Series	USA	n = 3 Age: 45.33 (20.11) 100% Caucasian 33.33% Female	Bipolar I, PTSD, SUD, PDA, SOC, OCD, GAD, ADHD	Individual/ Outpt	None	15 sessions/1× per week	N/A	33% dropout in the UP. Reductions in dep, anx, mania sx, and overall impairment for all participants (subclinical for 66% tx completers).
Ellard et al. (2017)	RCT	USA	n = 13[10] Age: 43.08 (13.84) 84.62% Caua-sian 53.9% Female	Bipolar I or II, GAD, PD, SOC	Individual/ Outpt	None	18 sessions/1× per week	psychiatric med management	UP led to large and significant decreases in anx and dep compared to med management, and small (non-significant) decreases in manic sx and life-interfering sx compared to med management.
Substance use disorders									
Ciraulo et al. (20-13)	RCT	USA	n = 45 Age: N/A 86.7% Caucasian 22.22% Female	GAD, PD, SOC, alcohol dependence, alcohol abuse	Individual/ Outpt	None	11 sessions/1× per week	Progressive muscle relaxation + placebo, progressive muscle relaxation + venlafaxine	UP led to a greater decrease in percent days of heavy drinking compared to the progressive muscle relaxation-placebo group. UP led to similar changes in anx, dep, and alcohol craving as all other groups pre- to post-tx and pre-tx to 6mFU.

Sauer-Zavala et al. (2019)	Open Trial	USA	n = 6 Age: 52.00 (3.37) 66.67% Caucasian 16.67% Female	Opioid use disorder, MDD, GAD, PTSD, Cocaine use disorder, Unspecified stimulant use disorder, Sedative use disorder	Individual/ Outpt	Five module adaptation: motivation, psychoed, mindful emotion awareness, cognitive flexibility, countering emotional behaviors. Modules presented in any order	8 sessions/1× per week or bi-weekly	N/A	UP led to non-significant reductions in dep and anx. Therapists and pts. indicated tx was acceptable. Therapists showed good knowledge of UP concepts. 3/6 pts. completed all 5 skills. UP content was covered in 85.3% of sessions due to crisis management or pt. refusal to participate in sessions.
Eating disorders									
Thompson-Brenner et al. (2018a)	Other Implementation	USA	n = 285 Age: N/A	AN, BN, EDNOS, OSFED, MDD, "anxiety disorders"	Individual, Group/ Residential Tx Facility	3 phases of tx with UP modules incorporated (moving from phase to phase based on clinical judgment); tx focused on eating, body, shape, & weight concerns (e.g., mirror exposures for body concerns); meal support and nutritional counseling offered	M = 27.13 SD = 10.41/N/A	Eclectic treatment provided prior to UP implementation	UP led to greater pre- to post-tx improvements in experiential avoidance, mindfulness, and anx sensitivity than eclectic treatment. UP led to similar pre- to post-tx improvements in dep and eating sx's. UP led to greater pre- to 6mFU improvements in experiential avoidance, dep and eating sx than eclectic treatment. UP led to similar pre- to 6mFU improvements in mindfulness and anx sensitivity. 64.5% of UP pts. achieved clinically significant improvement while 34.9% of eclectic treatment pts. did.
Thompson-Brenner et al. (2018b)	RCT	USA	n = 124	Eating disorders	Group/ Residential Tx Facility	Intensive tx administered in programs with varying lengths of stay; tx administered despite medical instability; training all levels of staff in UP; incorporation of groups for special concerns (e.g., SUD); adequate emphasis on the relational therapy principles integral to the identity of Renfrew; adaptation of tx rationale and principles to all activities and disciplines (e.g., nutrition)		Pre-implementaion of UP	UP led to improvements in experiential avoidance, mindfulness, and anx sensitivity. UP led to greater decreases in eating disorder sx than previous treatment period.
Borderline personality disorder									
Lopez et al. (2015)	SCED	USA	n = 8 Age: 40.00 (12.09) 87.5% Caucasian 100% Female	BPD; PD; SP; MDD; PTSD; SOC; GAD; DYS; OCD; PDA	Individual/ Outpt	Exposures that targeted BPD symptoms were prioritized over all other diagnoses.	16 sessions/1× per week	N/A	6/8 no longer met criteria for BPD at 1mFU. 3/8 showed clear pre/post reductions in sx. 2/8 also achieved reliable change. At 1mFU, 2/8 showed further improvement, 1/8 showed slight improvement, 5/8 worsened.
Lopez et al. (2019)	SCED	USA	n = 8 Age: 40 (12.09) 87.5% Caucasian 100% Female	PD, BPD, SP, DYS, MDD, PTSD, SOC, OCD, PD/A, GAD	Individual/ Outpt	None	16 sessions/1× per week	N/A	UP led to improvements in dep sx for 3/8 pts. but no change or worsening of sxs for 5/8 pts. UP led to improvements in anx sx for 2/8 pts. UP led to improvements in overall stress for 3/8 pts.
Mohammadi et al. (2018)	SCED	Iran	n = 6 Age: 22.67 (2.07) 100% Iranian 83.3% Female	BPD; MDD	Individual/ Outpt	Mindfulness not delivered; tx length tailored to each pt	20 sessions/1× per week	N/A	UP led to 68% reduction in BPD sx at post-tx, falling to 34% reduction at 1mFU. UP led to 25% reduction in emotion dysregulation at post-tx and 16% reduction at 1mFU. All

									participants remitted from MDD at post-tx, although 2 relapsed by 1mFU.
Sauer-Zavala et al. (2016)	Case Series	USA	*n* = 5 Age: 29.20 (7.53) 80% Caucasian 80% Female	BPD; GAD; MDD; SOC	Individual/ Outpt	Transitions between modules delayed at times due to participants' life circumstances.	20 sessions/1× per week	N/A	UP led to reductions in BPD, dep, and anx for 4/5 pts.
Non-suicidal self-injury									
Bentley et al. (2017c)	SCED	USA	*n* = 10 Age: 21.30 (3.68) 60% Caucasian 90% Female	GAD, OCD, OSAD, SOC, MDD, PDD(GAD), PDD (MDD), PTSD, BPD, NSSI disorder	Individual/ Outpt	Two modules (mindful emotion awareness & cognitive flexibility) delivered for 4 sessions each; NSSI examples added, references to other UP modules removed from workbook	8 sessions/1× per week	N/A	A similar number of patients showed reductions in NSSI in response to mindfulness (3/5) or reappraisal (2/5). The addition of reappraisal to mindfulness led to decreases in NSSI for 1 patient.
Bentley (2017a)	Case Study	USA	*n* = 1 Age: 18 100% Hispanic 100% Female	GAD, SOC, NSSI disorder	Individual/ Outpt	4 weeks of mindfulness followed by a 4-week assessment period, then 12 sessions to cover the remaining UP skills.	16 sessions/1× per week	N/A	UP led to no NSSI for 5 months. Small decreases in SOC and GAD, remaining in clinical range.
Insomnia disorder									
Doos Ali Vand et-al. (2018a)	Case Study	Iran	*n* = 1 Age: 32 100% Iranian 100% Male	GAD, MDD, chronic insomnia	Individual/ Outpt	Adapted UP concepts for insomnia based on book chapter describing application of UP for pt. with insomnia disorder[11]	14 sessions/1× per week	N/A	UP led to subclinical insomnia at post-tx and remission of insomnia at FU.
Doos Ali Vand et-al. (2018b)	SCED	Iran	*n* = 6 Age: 38.67 (10.84) 100% Iranian 66.67% Female	Insomnia Disorder; OCD; MDD; SOC; GAD; PD; SP	Individual/ Outpt	Content adapted for insomnia based on Bullis & Sauer-Zavala's chapter on the UP for insomnia[11]	14 sessions/1× per week	N/A	Reliable change for all pts. on anx sensitivity, emotion regulation, and sleep related cognitions at post-tx and 1mFU.
Subclinical symptoms									
Amirpour et al. (2018)	RCT	Iran	*n* = 15 Age: 26.40 100% Iranian 100% Female	Subclinical paranoia	Group/Outpt	Session content (text and audio files) reviewed between groups	10 sessions/2× per week	WLC	UP led to significant reduction in paranoid thoughts compared to WLC
Bentley et al. (2017b)	RCT	USA	*n* = 45 Age: N/A	Subclinical dep and anx	Group/Outpt	2 h session, with PowerPoint slides, didactic verbal material, media clips, & discussion. Modules covered: functional nature of emotions, mindful emotion awareness, cognitive flexibility, & emotion avoidance/alternative action.	1 session	Assessment Only	High acceptability & satisfaction (82% reported "very" or "extremely" acceptable; 69% reported "very" or "extremely" satisfied). 66% randomized to UP workshop attended. Skill use unrelated to 1mFU outcomes. Reminders did not influence skill use during 1mFU. Neuroticism, experiential avoidance, & quality of life improved significantly in the workshop condition (small effect size). UP workshop outperformed assessment on 1mFU increases in quality of life.
	RCT	Iran		None (subclinical)	Group/Outpt	2-h sessions			

Mohammadi et al. (2013)			*n* = 17 Age: 22.88 (1.62) 100% Iranian 75.8% Female				8 sessions/1 × per week	Cognitive therapy group	Transdiagnostic tx led to significant reductions in anx. Both groups led to improvements in dep, stress, and work/social adjustment.
Laposa et al. (2017)	Open Trial	Canada	*n* = 26 Age: 34.46(11.01) 92% Cauasian 62% Female	"clinically significant symptoms" of SOC, worry, PD/A (not diagnoses)	Group/Outpt	2 weeks spent on motivation; reordered modules (motivation, psychoeducation, interoceptive exposure, emotion exposure, mindful emotion awareness, cognitive flexibility, countering emotional behaviors, relapse prevention); 2-h groups.	14 sessions/1 × per week	N/A	UP led to large improvements in anx, worry, & PD scores; medium improvements in dep, positive affect, and negative affect; and small improvements in SOC scores.
Physical health and neurological complaints									
Johari-Fard & Ghafourpour (2015)	Open Trial	Iran	*n* = 15 100% Iranian 100% Female	Irritable bowl syndrome (IBS; non- mental health)	Group/Outpt	2 h groups	12 sessions/1 × per week	N/A	UP associated with reduced IBS severity and increased quality of life. Results maintained at 1mFU.
Lorenz & Stranberg (2015)	SCED	Sweden	*n* = 9 Age: 56.3 100% Swedish 66.67% Female	chronic pain, MDD, SOC, GAD, AG	Individual/ Internet	Therapists checked pt. progress online and called with feedback; shortened psychoeducational texts; added pain-related examples and pain exposure	10 sessions/1 × per week	N/A	No consistent change in pain intensity or dysfunction ratings across tx. 1/9 improved in dep sx, 2/9 remained unchanged, 2/9 deteriorated. 3/9 remained unchanged on anx, 2/9 deteriorated. 2/9 pts. completed tx and reported being "mainly satisfied."
Mazaheri et al. (2013)	Open Trial	Iran	*n* = 20 Age: 40.3 (11.64) 100% Iranian 55% Female	psychosomatic complaints (digestion and skin) and "emotional problems"	Group/Outpt	2 h sessions, additional information about emotion identification and naming, recognition of traumatic emotions, overcoming obstacles to positive emotions, problem solving, acceptance, no interoceptives	12 sessions/1 × per week	N/A	Modified UP (ECBT) led to significant improvements in overall emotion dysregulation (specifically, non-acceptance, difficulties pursuing goals, access to emotion regulation strategies, and clarity of emotions) and two cognitive strategies: putting things into perspective and catastrophizing.
Mohsenabadi et al. (2018)	RCT	Iran	*n* = 32 Age: 31.20 (4.70) 100% Iranian 63% Female	Irritable Bowel Syndrome	Individual/ Outpt	2-h sessions	12 sessions/1 × per week	WLC, could receive medication as usual	UP led to improved dep, anx, stress, symptom severity, expressive suppression, & cognitive reappraisal compared to WLC. Cognitive reappraisal and expressive suppression mediated the effect of tx on all outcomes. UP group had significant reductions in GI sx, but WLC did not.
Mousavi et al. (2019)	RCT	Iran	*n* = 15 Age: 20–44 100% Iranian 100% Female	Infertility (non-mental health)	Group/Outpt	2 h groups	10 sessions/1 × per week	WLC, Mindfulness based stress reduction (MBSR)	UP led to numerically greater improvements in anx and dep sx from pre- to post-tx and remaining stable through 3mFU compared to MBSR and significantly greater improvements in anx and dep sx compared to WLC.
Reynolds et al. (2019)	SCED	USA	*n* = 9 Age: 61.22 (13.12) 55.56% Female	(non-MH: mild-to-moderate idiopathic Parkinson's Disease), GAD, PD, DYS, Other Specified ANX, SOC, AG, MDD	Individual/ Outpt or Internet	optional 20–30 min informational session for partner or family member via internet or phone, tx delivered by internet for some pts	12 sessions/1 × per week	N/A	UP led to significant treatment response in anx and dep for 7/9 pts. 2/9 pts. who had elevated fears of falling at intake saw reductions over tx. 2/9 saw reductions in apathy by post-tx, 2/9 saw reductions by 6wFU, 1/9 saw increases. Pts rated the UP as very acceptable and were very satisfied. Pts participating online reported feeling natural, present with therapist, & absorbed in the sessions.

Wurm et al. (2017)[9]	SCED	Sweden	n = 5 Age: 46.40 (9.29) 100% Swedish 60% Female	chronic pain, GAD, SOC, DYS, AG	Individual/ Internet	Internet-delivered; systematic telephone support; content tailored to pt.'s goals (e.g., exposure exercises); shortened psychoeducational texts; reduced number of exercises; added pain-related psychoeducation and examples.	10 sessions/Self-guided	N/A	Reductions in sx were small and did not always reach significance. Feasibility and satisfaction were high.
Sexual minority stress									
Pachankis et al. (2015)[6]	RCT	USA	n = 32 Age: 26.19 (4.26) 52.4% Caucasian 100% Male All pts. identified as gay or bisexual.	N/A	Individual/ Outpt	Modules adapted to identify minority stress experiences, address reactions to minority stress by focusing on avoidance reactions (including substance use and condomless anal sex acts), attributing distress to minority stress instead of personal failings, practicing assertiveness skills for coping with minority stress safely.	10 sessions/1 × per week	WLC	Tx led to greater improvements in alcohol use, sexual compulsivity, condom use, self-efficacy, number of condomless anal sex acts with casual partners, and sexual orientation concealment compared to WLC. Tx led to similar improvements in dep, anx, number of days of heavy drinking, gay-related stress, rejection sensitivity, internalized homophobia, rumination, emotion dysregulation, social support, and assertiveness as WLC. Using pooled data, tx led to significant improvements in all measures except number of days of heavy drinking, sexual orientation concealment, and emotion dysregulation.
Parsons et al. (2017)	Open Trial	USA	n = 11 Age: 34.40 (9.60) 45.5% Black 100% Male All pts. HIV+.	N/A	Individual/ Outpt	Modules adapted to identify minority stress experiences, address reactions to minority stress by focusing on avoidance reactions (including substance use and condomless anal sex acts), attributing distress to minority stress instead of personal failure, confronting minority stress in safe contexts.	10 sessions/1 × per week	N/A	Tx led to large, significant reductions in dep, generalized anx, & OCD sx from pre-tx to 3mFU. Tx led to medium-to-large (non-significant) reductions in emotion dysregulation, anx-related functional impairment, & condomless anal sex with casual male partners. Tx led to small-to-medium (non-significant) reductions in sexual compulsivity, dep-related functional impairment, number of new male partners, drug use problems, and club drug use.

Note. The sample characteristics column reports the majority race/ethnicity and gender of the study sample. Number of sessions refers to the maximum number of sessions allowed in a protocol. Citations in footnotes are available in Appendix C.

Open Trial* = trial was originally a RCT using delayed treatment as the comparison condition. However, analyses reported in this paper pooled all participants who received treatment.

RCT = randomized controlled trial; SCED = single case experimental design; mFU = month follow-up; anx = anxiety; dep = depression; sx = symptom; EoT = end of treatment; ADHD = attention deficit hyperactivity disorder; AG = agoraphobia; AN = anorexia nervosa; AnxNOS = anxiety disorder not otherwise specified; AUD = alcohol use disorder; BN = bulimia nervosa; BPD = borderline personality disorder; DD = depressive disorder; DDNOS = depressive disorder not otherwise specified; DYS = dysthymia; ED = eating disorder; EDNOS = eating disorder not otherwise specified; GAD = generalized anxiety disorder; MDD = major depressive disorder; NSSI = non-suicidal self-injury; OSAD = other specified anxiety disorder; OCD = obsessive compulsive disorder; OSFED = other specified feeding and eating disorder; OST = other specified trauma related disorder; PD/A = panic disorder/with or without agoraphobia; PDD = persistent depressive disorder; PTSD = post-traumatic stress disorder; SOC = social anxiety disorder; SP = specific phobia; SSD = somatic symptom disorder; SUD = substance use disorder; Outpt = outpatient; SDP = single disorder protocol; WLC = waitlist control.

[1] Data derived from Farchione et al. (2012) trial.
[2] Data derived from Barlow et al. (2017) trial.
[3] Segal, Williams, & Teasdate (2002).
[4] Kamphuis & Telch (1998).
[5] Newman and Borkovec (2002).
[6] The demographics presented in this paper differ from the study from which they were derived.
[7] Wilson & Groom (2002).
[8] Norton (2012).
[9] Sloan, Feinstein, Gallagher, Beck, & Keane (2013).

[10] Results are based on $n = 8$ who completed treatment but the demographics available in the paper describe the $n = 13$ who were randomized to treatment.
[11] Bullis & Sauer-Zavala (2017).

Appendix B. Description of fidelity ratings and therapist training procedures in included studies

Article	Fidelity assessment	UP training procedures
Primary anxiety disorder with/without comorbid depressive disorder		
Barlow et al. (2017)	20% of sessions rated for adherence and competence using standardized criteria[3]; adherence scores excellent: $M = 4.44$ (out of 5)	All therapists received certification[4] in UP
Boisseau et al. (2010)	Not described	Not described
Boswell et al. (2012)[1]	N/A[5]	N/A
Boswell et al. (2013a)[1]	N/A	N/A
Boswell et al. (2013b)[1]	N/A	N/A
Boswell et al. (2017)	Not described	Not described
Brake et al. (2016)	Weekly meetings to monitor clinician adherence	Not described
Bullis et al. (2014)	N/A	N/A
Bullis et al. (2015)	Treatment adherence monitored during weekly supervision with licensed psychologist certified in UP	At least one group leader received certification in the UP from a UP treatment developer
Carl et al. (2014)[1]	N/A	N/A
Cassiello-Robbins et al. (2018)[2]	N/A	N/A
Cooney Roxbury (2017)	Not systematically assessed	Treatment session outlines created following the Therapist Adherence Rating Scale for the UP (TARS-UP) provided by the director of the Unified Protocol Institute
de Ornelas Maia et al. (2015)	Not described	Not described
Ellard et al. (2010) Study 1	Treatment adherence monitored during weekly supervision and manual development meetings	Training provided via supervision by senior team member
Ellard et al. (2010) Study 2	Treatment adherence monitored during weekly supervision and manual development meetings	Training provided via supervision by senior team member
Farchione et al. (2012)	Treatment adherence monitored during weekly supervision but not systematically assessed	All therapists were directly involved in developing the treatment protocol
Gallagher et al. (2013)[1]	N/A	N/A
Gallagher et al. (2019)[2]	N/A	N/A
Gonzales-Robles et al. (2019)	Therapists and patients provided with treatment manual; ongoing discussion in supervision about protocol adherence; adherence not systematically assessed	No UP-specific training described
Ito et al. (2016)	Treatment adherence monitored in weekly group supervision. One completed and one ongoing case were confirmed adherent by the UP developer (David H. Barlow). Principal investigator reviewed 34% of sessions via audiotape using the TARS-UP and reported 92% adherence	All sessions were conducted by clinical psychologists trained by the two clinical psychologists who translated the original UP therapist guide and workbook into Japanese. Therapists participated in 14 h of UP workshops, didactic training, direct observation of UP sessions, listening to audiotaped sessions, and weekly group supervision.
Khakpoor et al. (2019)	Sessions audiotaped and randomly inspected by supervisor. Treatment adherence discussed in weekly supervision. Supervisor indicated the therapist was adherent. No data provided	Therapists received training in CBT and transdiagnostic treatment. No UP-specific training described
Lotfi et al. (2014)	Not described	Not described
Mohajerin et al. (2019)	Sessions were recorded and rated for adherence. No data provided.	Treatment delivered by a therapist trained to administer the UP in a 16-h workshop
Osma et al. (2015)	Not described	The primary therapist was trained in CBT protocols for emotional disorders. No UP-specific training described
Rondung et al. (2018)	N/A	N/A
Sauer-Zavala et al. (2019)	Sessions audiotaped and rated for adherence using a modified version of the TARS-UP that reflected the changes made to the UP for this study. Average adherence across all sessions was excellent (Therapist 1: 93.35%; Therapist 2: 84.39%)	Therapists attended UP workshop and had ongoing consultation calls with a UP developer
Sauer-Zavala et al. (2018)[2]	N/A	N/A
Steele et al. (2018)[2]	N/A	N/A
Thompson-Hollands et al. (2013)[1]	N/A	N/A
Thompson-Hollands et al. (2014)[1]	N/A	N/A
Tirpak et al. (2019)[2]	N/A	N/A
Wilner et al. (2018)[2]	N/A	N/A
		No UP-specific training described

Zemestani et al. (-2017)	Adherence discussed in weekly supervision sessions. No adherence data provided	
Primary depressive disorder		
Bameshgi et al. (-2019)	Not described	Not described
Bentley et al. (20-17d)	Not described	Therapists received formal training and certification in the UP
Boswell et al. (20-14)	Sessions audiotaped and verified for adherence and competence by UP certified therapist. No data provided	Therapist was research certified in the UP
Castro-Camacho et al. (2019)	Not described	Therapists participated in a training workshop conducted by one of the UP developers and passed an evaluation testing knowledge of protocol content, theoretical foundation, and methodology
de Ornelas Maia et al. (2013)	Explicitly stated adherence was not monitored	Not described
Donahue et al. (2-019)	Not described	Not described
Farchione et al. (-2017)	Not described	Not described
Hague et al. (201-5)	Not described	Not described
Marnoch et al. (2-014)	12 sessions randomly selected rated for adherence using a checklist created for the study and were rated as 'fully adherent' by (1) completing weekly and homework review, (2) implementing the appropriate core exercise, and (3) setting related homework tasks	All therapists trained in administering the UP via a training DVD and UP Therapist Guide
Osma et al. (2018)	Not described	Therapist received certification from the Unified Protocol Institute
Mixed emotional and related disorders		
Akbari et al. (201-5)	Adherence monitored during weekly supervision and sessions were audiotaped to rate adherence. No data provided	No UP-specific training described
Alatiq et al. (2019)	At least 3 audiotapes from each therapist were rated using the Cognitive Therapy Rating Scale (CTRS)	All therapists received 1 week of intensive training in the protocol
Bentley et al. (20-18)	Sessions audiotaped and rated for adherence. Average clinician adherence rating for the six rated group sessions was 73.3%	One trainer, a licensed clinical psychologist with 18 years of CBT experience, was certified as a UP supervisor by audio-recorded group sessions, which were rated for adherence and competence by UP experts. This trainer provided UP training to other staff
Ling (2018)	Adherence monitored during weekly supervision meetings. No data provided	Therapists completed a training session and received all treatment materials before the treatment
Reinholt et al. (2-016)	Adherence monitored during supervision every other week conducted by a licensed psychologist certified in the UP. No data provided	No UP-specific training described
Sauer-Zavala et al. (2017)	Sessions audiotaped and 20% rated for adherence and competence. Average competence: 4.77 (out of 5). No rated sessions included extraneous content outside the assigned UP module	Study therapists were certified experts in the provision of the UP
Varkovitzky et al. (2018)	Not described	At least one group leader was trained in the UP via a workshop conducted by UP developers
Bipolar disorder with comorbid anxiety disorder(s)		
Ellard et al. (2012)	Not described	Not described
Ellard et al. (2017)	Not described	Treatment sessions conducted by a co-developer of the UP fully certified in the treatment
Substance use disorders		
Ciraulo et al. (20-13)	Not described	Not described
Sauer-Zavala et al. (2019)	Sessions were audiotaped and 20% rated for adherence and competence using standardized criteria. Average adherence: 4.45 (out of 5). A non-UP intervention strategy was delivered in one instance	Therapists were certified in the provision of the UP
Eating disorders		
Thompson-Brenner et al. (201-8a)	Recordings of groups were rated using adherence scales developed for the implementation of the UP in this setting. Average adherence was 88.17 (SD = 17.46, range = 40–100%)	All therapists received training from UP experts that included: introductory didactic, review of treatment manual, 28 h of didactic and experiential training, and one-on-one coach as needed. Review of session recordings in supervision
Thompson-Brenner et al. (201-8b)	N/A – described in Thompson-Brenner et al. (2018a)	N/A – described in Thompson-Brenner et al. (2018a)
Borderline personality disorder		
Lopez et al. (2015)	Not described	No UP-specific training described
Lopez et al. (2019)	Sessions audiotaped and 20% rated for adherence and competence using standardized criteria. 81% adherent and 85% quality	Not described
Mohammadi et al. (2018)	Not described	No UP-specific training described
Sauer-Zavala et al. (2016)	None	Therapists received formal training and certification in the UP
Non-suicidal self-injury		
Bentley et al. (20-17c)	Sessions audiotaped and 20% rated for adherence and competence using standardized criteria. Adherence ratings were all 100% and the mean overall session rating was 4.8 (out of 5)	The therapist received formal training and certification in the UP
Bentley (2017a)	Not described	Not described
Insomnia disorder		
	Not described	Not described

Doos Ali Vand et-al. (2018a)		
Doos Ali Vand et-al. (2018b)	Therapy sessions delivered according to UP manual. No data provided	No UP-specific training described
Subclinical symptoms		
Amirpour et al. (-2018)	Not described	No UP-specific training described
Bentley et al. (20-17b)	During Wave 2 workshops, but not Wave 1, group leaders rated adherence to each module	Workshops were developed by advanced doctoral students and research faculty with formal training and certification in the UP
Mohammadi et al. (2013)	Not described	Not described
Laposa et al. (20-17)	Treatment followed UP Therapist Guide. No data provided	Therapists read the UP Therapist Manual and watched the UP clinical demonstrations DVD. At least one group leader had run at least one UP group prior to this study
Physical health and neurological complaints		
Johari-Fard & Ghafourpour (2-015)	Not described	Not described
Lorenz & Stranberg (2015)	N/A	N/A
Mazaheri et al. (2-013)	Not described	No UP-specific training described
Mohsenabadi et al. (2018)	Adherence was monitored weekly, using standardized criteria, by a supervisor certified in the UP	No UP-specific training described
Mousavi et al. (2-019)	Not described	Not described
Reynolds et al. (2-019)	Sessions were audio or video taped and 12 were randomly chosen and rated for adherence by a certified UP trainer. All adherence ratings were above 85% with modal adherence of 100%	Not described
Wurm et al. (201-7)	N/A	N/A
Sexual minority stress		
Pachankis et al. (-2015)	All sessions were video recorded and 23.5% were rated for adherence using a checklist created for the study. Average adherence was 84.6% for the content described in the treatment manual	No UP-specific training described
Parsons et al. (20-17)	Not described	Not described

Note.

[1] Data derived from Farchione et al. (2012) trial.

[2] Data derived from Barlow et al. (2017) trial.

[3] Standardized adherence rating criteria have been developed and are available from the UP developers (David H. Barlow).

[4] Certification refers to the process in which therapists complete a full course of the UP with one patient in which all sessions are audiotaped and rated for adherence by a UP expert. In order to be certified, all UP modules must achieve a rating of 80% or greater adherence.

[5] N/A is used for studies that include data derived from another trial. For all other studies "Not described" is used to indicate the paper did not provide information about fidelity assessments and/or UP-related training procedures.

Appendix C. References only included in Results and Appendix A

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