A Systematic Review and Meta-Analysis of the Unified Protocol as a Transdiagnostic Emotion Regulation Based Intervention

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Current approaches towards understanding, diagnosing, and treating psychopathology in clinical practice typically occur through disorder specific conceptualisations of mental illness. Whilst this approach has demonstrated substantial clinical utility across a range of mental disorders (Barlow, 2014), the validity of discrete diagnostic classifications has been questioned, in light of the high symptom overlap present between disorders, and the high rates of diagnostic comorbidity present in clinical populations (Brown, Campbell, Lehman, Grisham, & Mancill, 2001; Clark & Taylor, 2009; Norton, 2006; Watkins, 2015). In addition, prior research suggests reduced treatment efficacy towards primary (Coplan, Aaronson, Panthangi, & Kim, 2015) and secondary diagnoses (Allen, Ehrenreich, & Barlow, 2005; Tsao, Mystkowski, Zucker, & Craske, 2005), for individuals presenting with comorbid presentations. Whilst existing disorder specific interventions such as CBT have demonstrated clinical utility across a range of internalising psychopathologies (see Hofmann, Asnaani, Vonk, Sawyer, & Fang, 2012), it may also be the case that disorder specific interventions have reduced clinical utility, within individuals who present to treatment, with comorbid diagnoses.

In response to this issue, clinical research and practice has increasingly turned to transdiagnostic approaches to psychological intervention. Transdiagnostic approaches are thought to arise from three different orientations to treatment development (Sauer-Zavala et al., 2017). The first involves the universal application of therapeutic principles across multiple disorders whereby, for instance, similar cognitive therapy approaches might be applied across multiple disorders. In contrast, a "modular" approach involves clinicians choosing from a collection of strategies to generate a treatment which can be applied across disorders (Sauer-Zavala et al. p. 130). Finally, the "shared mechanisms" approach implies that there are common underlying mechanisms which should drive the development of interventions (Suaer-Zavala et al. p.130). While different in their approach to treatment

development, each of these transdiagnostic approaches may allow treatment to be delivered through one single protocol, increasing the efficiency and efficacy of treatment (Newby et al., 2015; Sauer-Zavala et al., 2017). Although existing literature poses a range of potential mechanistically transdiagnostic factors, emotion regulation (ER) has continued to receive increased empirical support across internalising disorders.

Internalising psychopathology refers to the structural classification of disorders containing underlying dimensions of fear and distress, and reflects high negative affectivity (for review, see Krueger & Markon, 2006). Whilst typically characterised across anxiety and depression, more recent factor analyses research has extended this classification to include borderline personality disorder (Eaton et al., 2011; James & Taylor, 2008), and eating disorders (Forbush et al., 2010; Mitchell, Wolf, Reardon, & Miller, 2014). ER, which broadly refers to the ability to modulate or alter the intensity and duration of emotional states (Gross & Thompson, 2007), has been implicated across models of internalising psychopathology. These include major depressive disorder (Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008), generalised anxiety disorder (Mennin, Holoway, Fresco, Moore, & Heimberg, 2007), social anxiety disorder (Kashdan & Breen, 2008), somatoform disorders (Waller & Scheidt, 2006), borderline personality disorder (Schulze et al., 2011), and eating disorders (Wild et al., 2007).

As a putative mechanism of change in therapy, ER has been implicated across treatment modalities, as whilst Cognitive Behavioural Therapy (CBT; Beck, 1976) indirectly targets ER based processes, more recent third-wave psychological interventions such as Dialectical Behaviour Therapy (DBT; Linehan, 1993), Acceptance Commitment Therapy (ACT; Hayes, Strosahl, & Wilson, 1999), and mindfulness based interventions (Chambers, Gullone, & Allen, 2009) directly target ER as a component of treatment. In a recent systematic review analysing the involvement of ER across treatment, Sloan and colleagues (2017) identified ER across intervention modalities and disorder presentations, indicating that

ER is involved as a transdiagnostic factor both in the expression and treatment of psychopathology. However, many of the studies included in this review did not evaluate individuals presenting with comorbid presentations. This presents a limitation across research systematically reviewing single disorder treatment programs, as much of the real world clinical population presents with a variety of comorbid disorders, and as a result, many of these studies suffer from reduced ecological validity and clinical applicability (Ollendick, Jarrett, Grills-Taquechel, Hovey, & Wolff, 2008; Riosa, McArthur, & Preyde, 2011; Sloan et al., 2017). Thus, the current review aimed to examine the transdiagnostic role of ER as a treatment process, by evaluating the treatment efficacy of an ER based transdiagnostic intervention program; The Unified Protocol for Emotional Disorders (UP; Ellard, Fairholme, Boisseau, Farchione, & Barlow, 2010).

The UP is a manualised ER-based transdiagnostic intervention program which focuses on addressing core emotion dysregulation across psychopathology to effect changes in a broad range of outcomes, including positive and negative affect. The UP holds particular appeal as a transdiagnostic approach given that it could be described as a "shared mechanisms" approach and is thus derived from underlying theories of psychopathology, in contrast to universal principles, which, although derived from theory, also rely on pre-existing knowledge of how therapy should be conducted (Sauer-Zavala et al., 2017). Each of the five core modules aims to address different aspects of ER, for instance, the module focusing on cognitive flexibility fosters the development of cognitive reappraisal skills in contexts of high emotion and the tolerance-related modules allow the development of tolerance-skills, as opposed to unhelpful avoidance behaviours in emotion charged situations. There is also a module focused on psychoeducation and awareness of responding and coping, which is important for fostering emotional awareness as a foundation for improved ER, as well as two additional modules: 1) motivational interviewing/enhancement, 2) review and

relapse prevention modules, however these are considered to be only indirectly related to ER. In line with the framework of Gross' (1998) process model, which describes ER as a set of strategies that aim to alter an emotional experience, the UP takes a cognitive behavioural approach towards developing adaptive ER skills (i.e. reappraisal, acceptance), and reducing maladaptive ER skills (i.e. suppression, avoidance). This is consistent with research implicating heightened patterns of maladaptive ER strategy engagement, and reduced adaptive ER strategy engagement, with the onset and maintenance of psychopathology (Aldao & Nolen-Hoeksema, 2012; Aldao, Nolen-Hoeksema, & Schweizer, 2010; Gross & Jazaieri, 2014).

In addition, in line with Gratz and Roemer's (2004) multidimensional model, the UP also builds towards core competencies of healthy ER, including an awareness and acceptance of emotional experiences, the ability to flexibly modulate the intensity and duration of emotional experiences, and a willingness to experience emotions within everyday life. This model is supported by research implicating deficits in these areas with heightened symptomology across internalising disorders (Sloan et al., 2017), and these deficits were greater within treatment seeking populations compared to healthy controls (Lavender et al., 2015). As such, UP aims to reduce psychopathological expression, by shifting patterns in key ER based skills. Beyond psychopathology, the UP is also assumed to lead to improvements in overall functioning and quality of life (Ellard et al., 2010). The UP currently has empirical support across a range of internalising clinical presentations, including depression (Boswell, Anderson, & Barlow, 2014), anxiety disorders (Farchione et al., 2012), chronic pain (Allen et al., 2012), borderline personality disorder (Lopez et al., 2015), as well as across a range of anxiety based comorbidities (de Ornelas Maia, Sanford, Boettcher, Nardi, & Barlow, 2017; Hague, Scott, & Kellett, 2015; Laposa, Mancuso, Abraham, & Loli-Dano, 2017; Reinholt et al., 2017; Sauer-Zavala, Bentley, & Wilner, 2016) and is perhaps the most researched,

accessible and established of the various transdiagnostic approaches. While other transdiagnostic treatment approaches have also been developed, these other approaches have for the most part been restricted to the domain of anxiety disorders (e.g., Norton 2006; Schmidt et al., 2012) or are yet to attain the substantial transdiagnostic evidence base of the UP (e.g., Gros, 2014) and no other transdiagnostic approach places such central importance on difficulties in emotion regulation as a driver of psychopathology. Whilst existing research has qualitatively examined the UP as a transdiagnostic intervention (see Norton & Paulus, 2016) there are currently no quantitative meta-analytic reviews analysing these effects.

Thus, the current systematic review and meta-analysis aimed to review published studies on the UP, in order to determine the degree to which the UP, as an ER focused intervention, leads to reductions across psychopathological outcomes. This will not only provide insight into the transdiagnostic efficacy of the UP as a manualised intervention, but will also help to determine whether ER and positive and negative affectivity show the expected improvements associated with the UP, which would be consistent with, though not conclusive of, its hypothesised role as a shared mechanism in psychopathology. In regards to the scope of research that will be considered in this current study, in line with the purpose of the UP, analysis will focus on internalising disorders (Ellard et al., 2010). Hence, our primary aim was to determine whether the UP is similarly efficacious across a range of internalizing disorders, regardless of the mode of administration or outcome measure used. In order to assess the assumption that these psychopathology related changes are associated with changes in ER and validate our primary research question, the secondary aim of the study was to evaluate the degree to which UP intervention leads to ER related changes, as indicated by measures reflecting changes in adaptive and maladaptive ER strategies. This will allow the current review to confirm a key prerequisite for the possibility that difficulties in ER act in a mechanism way in contributing to psychopathology, that is, an association between changes

in ER and changes in symptoms following the UP. Similarly, to the extent that positive and negative affectivity are thought to be key targets for the UP, we also sought to confirm that these variables also showed increases and decreases respectively, as predicted by the approach. A third aim of the current study was to evaluate secondary gains brought by the UP, which may provide insight as to the degree to which ER related effects translate to benefits such as reductions in functional impairment and improvements to quality of life.

Method

The review protocol was pre-registered in PROSPERO (CRD42018103874).

Search Strategy

To identify studies for possible inclusion, we conducted a comprehensive systematic search of electronic databases 'PsycInfo', 'Pubmed', 'Medline', 'Embase', and 'Cumulative Index of Nursing and Allied Health Literature' (CINAHL). The search strategy consisted of the following search terms;

(i) The keyword "Unified Protocol" was used to specifically obtain studies relating to the intervention of interest

(ii) The keywords "Affective Disorder*" or "Depressive Disorder*", or "Anxiety Disorder*", or "Major Depressive Disorder", or "Social Anxiety Disorder", or "Obsessive Compulsive Disorder", or "Panic Disorder", or "Post Traumatic Stress Disorder", or "Generalised Anxiety Disorder", were used, in order to obtain studies specifically targeting internalising psychopathology. Alternative phrases, words and spelling used, can be found in Supplementary Table 1.

(iii) The keywords "Treatment", or "Treatment Outcomes", or "Treatment Effectiveness", or "Treatment Evaluation", or "Treatment Efficacy", or "Experimental Design", or "Empirical Study", or "Clinical Trial", or

"Intervention" were utilised, in order to obtain studies with appropriate outcome data.

Inclusion/exclusion criteria

Studies were included in the current review if:

(i) Participants were over the age of 18, and diagnosed with at least one internalising disorder, or comorbid internalising disorders..

(ii) At least one validated self-report or clinician rated measure of internalising psychopathology was reported, with sufficient data for Hedges *g* effect size calculation for baseline verses post-treatment and/or follow-up data.

(iii) Experimental research design, including randomised control trials, quasi-experimental design, case series design, or other similar research designs specifically examining the UP, regardless of administration format.

(iv) A diagnosis was confirmed by structured or semi-structured diagnostic interview.

Studies were excluded from the current review, if they were; a) not published between the years 2010 and 2018, b) did not provide sufficient data relevant to internalising psychopathology outcome data, c) did not provide sufficient data to calculate effect sizes (e.g., pre- and post-treatment means, SDs and sample sizes in the case of calculating standardized mean differences), and d) if they did not confirm that all participants met the criteria for a mental disorder when assessed with a structured or semi-structured diagnostic interview.

Identification and Screening Process

Initial screening of studies involved removal of studies based on inclusion/exclusion criteria, through evaluation of titles and abstracts. Remaining studies (k= 110) were reviewed

by a secondary rater, and inclusion/exclusion criteria were again applied. Secondary rating demonstrated 94% agreement, and strong inter-rater reliability (Cohen's Kappa= 0.81). Disagreements were mostly due to excluding criteria not being apparent in the titles/abstracts, and disagreements were resolved by discussion and mutual agreement on inclusion status.

Data Extraction and Management

Data extraction involved the collection of study characteristics, such as author names, sample details, study design, disorder presentations, psychopathology measures, and ER measures. Data was then transferred to the Comprehensive Meta-Analysis (version 3.3.070, Biostat, Inc.) software package, with relevant raw data (i.e., means, standard deviations, Cohen's *d*, etc.), automatically transformed and standardised into Hedges g effect size data, for both uncontrolled (within study effects) and controlled (between study UP verses control group) data. Given that many studies reported multiple measures which loaded onto a single effect size construct (i.e., multiple psychopathology and emotion regulation measures), one single measure was selected, in order to maintain the assumption of independence for meta-analyses (Lipsey & Wilson, 2001). Measures were selected based on the following criteria; a) clinician rated structured/semi-structured interviews of clinical severity were prioritised over self-report measures in order to establish greater reliability and validity of clinical severity, b) stronger psychometric properties were prioritised over measures with weaker psychometric properties, so as to maintain reliability and validity of measurement, c) measures which were included in a greater number of studies among our final sample of papers were prioritised over measures which were not already included in the analysis, in order to reduce measure error variability, and maintain consistency between included measures.

Outcomes Variables

The primary research question evaluating the treatment efficacy of the UP was operationalised using Hedges g effect size statistics for mean differences in symptom severity measures. The secondary research question evaluating the UP efficacy for ER change was operationalised by grouping adaptive and maladaptive ER engagement measures separately. The third research question evaluating secondary benefits to UP intervention was operationalised by grouping measures which were not directly related to the two aims above. For each of the above aims, Hedges *g* effect size data representing mean differences between baseline, post-intervention, and follow-up time points were generated for baseline verses follow-up data within the UP (i.e., uncontrolled effect), and between UP and control groups (i.e., controlled effect). Effect sizes were interpreted in accordance to Cohen's (1977) recommendation, as small (< 0.2), medium (0.5), and large (> 0.8).

Statistical Analyses

A random effects model was used to calculate each Hedges g effect size and associated 95% confidence interval, as each study included in this analysis is assumed to be independent of one another, and thus variation in the true effect size is assumed to not be consistent or fixed. The Q-statistic and associated significance test was used to calculate heterogeneity between psychopathology constructs, and between each respective adaptive and maladaptive ER measure. The I^2 statistic was used to evaluate the proportion of heterogeneity within each pooled effect size estimate, to measure the dispersion of effects. I^2 values were interpreted as the following; low (25%), moderate (50%), and high (75%) (Higgins, Thomson, Deeks, & Altman, 2003). A moderator analysis was also conducted via a meta-regression procedure, in order to examine sources of significant heterogeneity between psychopathology variables. Moderator variables were study design (RCT, quasi-experimental, treatment response studies), study duration, and the categorical variable of administration format (i.e., face-to-face, group, online).

Publication Bias

In order to address the possibility of publication bias in the analysis, funnel plots with an index of study size plotted against effect size were produced, and visual assessment of symmetry was conducted (Rothstein, 2007). In line with recommendations based on the Cochrane Handbook for Systematic Reviews of Interventions, funnel plots for constructs with fewer than ten studies were not included, and fail-safe N statistics were not calculated due to unreliability (Sterne et al., 2011). Rather, analysis via through Duval and Tweedle's Trim and Fill procedure allowed us to evaluate effect size estimates, after adjusting for potential publication bias (Duval & Tweedie 2000a, 2000b). Differences in study quality were also qualitatively assessed via the Joanna Briggs Institute (JBI) appraisal tool (Tufanaru, Munn, Aromataris, Campbell, & Hopp, 2017).

Results

Study Extraction and Study Characteristics

From the initial 214 studies collected via the identification process, 15 studies were retained, and included into the analysis. A flow diagram of the screening process is presented in Figure 1. Of the 15 studies retained, a total of 1244 participants were measured from baseline to post-intervention across randomised control experimental designs (33%; e.g., Barlow et al., 2017), treatment response studies (33%; Bullis, et al., 2015), treatment response case series studies (21%; e.g., Ellard et al., 2012), and quasi-experimental designs (13%; e.g., De Ornelas Maia, Nardi & Cardoso, 2015). Sample sizes ranged from 3 to 616. The administration of the UP across these studies involved face-to-face (67%), group (27%), and online (6%) intervention, across an average of 15 sessions (*SD*= 3.2; range 12-20). From the total 15 studies included in the analysis, 47% included at least one measure of ER, and approximately 46% included a control reference group, comprised of treatment as usual

(14%), waitlist control (57%), and medication only (29%) comparison groups. For the majority of the included studies, clinical diagnosis was established via the The Anxiety Disorders Interview Schedule for DSM-IV: Lifetime Version (ADIS-IV-L; DiNardo, Brown, & Barlow, 1994) (40%), The Mini-International Neuropsychiatric Interview (M.I.N.I.; Lecrubier et al., 1997) (33%), The Structured Clinical Interview for DSM-IV (SCID-I/II/IV; First, Spitzer, Gibbon, & Williams, 1996) (20%), or other semi-structured psychiatric interviews (6%) (i.e. Thompson-Brenner et al., 2018). A summary of characteristics for each included study can be found in Table 1.

Primary Research Question: UP Treatment Efficacy across Internalising Psychopathology

A summary of uncontrolled effects across psychopathology measures for baseline verses post-intervention and follow-up can be found in Table 2, and the controlled effect can be found in Table 3. Each table also contains forest plots indicating effect size estimates, and corresponding 95% confidence intervals. Forest plots for each psychopathology construct can be found in Supplementary Tables 2(a) to 2(d). For the uncontrolled studies (Table 2), there was a range of between 2 and 12 studies, depending on disorder type, reporting baseline to post-treatment results, and between 3 and 5, for baseline to six-month follow-up. For controlled studies (Table 3), there were five studies within each disorder grouping reporting baseline to post-treatment results. No study contributed more than one sample for the present analyses. Table 4 also includes three to five studies examining adaptive and maladaptive ER, and two studies at six-month follow-up time points.

Uncontrolled effects. Baseline to post-intervention effect sizes across measures of psychopathology were generally in the large effect size range, with efficacy being strongest within obsessive compulsive disorder, and weakest within depression. The global psychopathology effect, which is a measure of global psychopathology symptom severity,

was also in the large effect range at baseline verses post-treatment. Across disorders, the efficacy of the UP continued to reduce psychopathological severity at six-month follow-up, with the greatest follow-up symptom improvement occurring for panic disorder with agoraphobia (g_{diff} = -.44), and the weakest follow-up improvement occurring for social anxiety disorder (g_{diff} = -.02). Significant heterogeneity was evident within all symptom domain groups except BPD, generalized anxiety disorder (GAD), panic disorder with agoraphobia (PDA), posttraumatic stress disorder (PTSD) and global psychopathology (p's>0.05) for the baseline to posttreatment comparisons and for all comparisons except GAD, PDA, PTSD, social anxiety disorder (SAD) and global psychopathology (for all baseline to 6mth comparisons).

Controlled effects. At post-intervention, the UP had significantly greater treatment efficacy compared to TAU, waitlist, and medication control groups, and this effect was moderate and large for depression and anxiety, respectively. Significant heterogeneity *not* was evident within all symptom domain groups except anxiety and depression (p's>0.05) for the baseline to posttreatment comparisons and there was no heterogeneity evident for any baseline to 6mth controlled comparisons.

Meta-regression. A meta-regression was conducted to examine possible moderating effects for heterogeneity for the controlled effect for anxiety and depression respectively at baseline verses post-intervention. A model accounting for administration format, and study duration was not significant for anxiety (Q=0.55, df=3, p=0.91) or depression symptoms (Q=0.74, df=3, p=0.86). Caution however is warranted in interpreting this effect, due to low study sample size and the small number of studies included in each regression. Scatterplots for each moderator variable on psychopathology outcomes can be found in Supplementary Figures 2(a) to 2(d).

Secondary Research Question: UP Treatment Efficacy on Emotion Regulation and Positive and Negative Affect

A summary of the random effects model for uncontrolled adaptive and maladaptive ER effects across baseline verses post-intervention and follow-up, can be found in Table 4. Each table also contains forest plots indicating effect size estimates, and corresponding 95% confidence intervals. Forest plots for adaptive and maladaptive ER effect sizes can be found in Supplementary Tables 3(a) to 3(d). A comparison to control group was not conducted, due to low study sample size (k=1).

Adaptive ER. Adaptive ER measures comprised of the Southampton Mindfulness Questionnaire (SMQ; Chadwick et al., 2008) and the Emotion Regulation Questionnaire – Reappraisal Subscale (ERQ-R; Gross & John, 2003). At post-intervention, the UP led to significant moderate increases in adaptive ER engagement, and this effect was no longer significant at six-month follow-up. There was significant heterogeneity found between adaptive ER measures at baseline verses post-intervention (Q= 7.75, df= 2, p= .02), and no significant heterogeneity at baseline verses six-month follow-up (Q= .29, df= 1, p= .59). A meta-regression was not conducted to examine this heterogeneity, due to the low number of studies included in the analysis.

Maladaptive ER. Maladaptive ER measures included the Multidimensional Experiential Avoidance Questionnaire (MEAQ; Gámez, Chmielewski, Kotov, Ruggero & Watson, 2011), the Emotion Regulation Questionnaire – Suppression Subscale (ERQ-S; Gross & John, 2003), and the Difficulties in Emotion Regulation Scale (DERS; Gratz & Roemer, 2004). At post-intervention, the UP significantly and moderately decreased maladaptive ER strategies, however retention of treatment effects at six-month follow-up were unable to be calculated, due to the low number of studies included in the analysis (k= 1).

There was significant heterogeneity found between maladaptive ER measures at baseline verses post-intervention (Q= 16.88, *df*= 5, *p*= .05). Given the small number of studies reporting maladaptive ER outcomes, we conducted two separate meta-regression analyses with intervention duration the sole predictor in the first analysis and treatment delivery format entered as the sole predictor in the second analysis. Neither duration of intervention nor delivery format (individual face-to-face vs group treatment vs online) accounted for this heterogeneity (*p*'s>0.05). We note that there appeared to be pronounced variation in the baseline to post-intervention effect sizes depending on the outcome measure used, with moderate to large reductions in MEAQ (g=-0.76, CI=-0.91, -0.61, p<0.01 and -1.03, CI=-1.73,-.33, p<0.01) and DERS (g=-1.00, CI=-1.89, -0.11, p=.03 & g=-1.35, CI=-2.23, -0.47, p<0.01), but only negligible reductions in ERQ-S (g=-0.02, CI=-0.66, 0.62, p=0.95).

Positive and Negative Affect. The lower section of Table 4 summarises the results for positive and negative affect respectively. The uncontrolled studies of negative affect indicated reductions in negative affect at both post treatment and six month follow-up. For positive affect, there were significant reductions by post treatment, although improvement was not evident by six-month follow-up.Forest plots for positive and negative affect effect sizes can be found in Supplementary Tables 3(e) to 3(h).

Third Research Question: Secondary Treatment Effects

A summary of the random effects model for the controlled baseline verses post-intervention and follow-up effect sizes for functional impairment and quality of life can be found in Table 5. Each table also contains forest plots indicating effect size estimates, and corresponding 95% confidence intervals. Forest plots for each secondary measure can be found in Supplementary Tables 4(a) to 4(c).

Uncontrolled effects. There were significant and moderate to large effect sizes obtained across additional clinical measures. These included reductions in functional impairment and increases in quality of life. These therapeutic benefits were retained across time up to the six-month follow-up, for each respective construct quality of life (g=0.21, p=0.10).

Controlled effects. Due to the low number of studies available for comparison with control groups, functional impairment was the only construct that was included in the analysis. Compared to control, UP intervention had significantly and moderately reduced functional impairment at baseline verses post-intervention (*k = 4, g*= -.70, CI= -.95, -.46, SE= .13, *p*< .001), but insufficient studies available for baseline to six-month follow-up comparisons.

Publication Bias

Funnel plots generated across for anxiety and depression baseline to post-intervention can be found in Supplementary Figures 1(a) and 1(b).

Psychopathology measures. Duval and Tweedle's Trim and Fill procedure did not indicate corrections for publication bias across each respective uncontrolled baseline to post-intervention psychopathology measure, except for GAD, which indicated an adjusted effect size estimate from *g*= -0.97 to *g*= -0.86 (one study removed) and OCD, which changed from g=-1.23 to g=-1.03 (one study removed). Together, this suggested an unlikely or minimal publication bias effect.

ER measures. For uncontrolled studies of adaptive ER strategy measures from baseline to post-intervention, Duval and Tweedle's Trim and Fill procedure indicated an adjusted effect size estimate from *g*= .57 to *g*= .51 (one study removed). There was no

adjustment indicated for maladptive ER strategies. This collectively suggested unlikely or minimal publication bias effect, across both adaptive and maladaptive ER measures.

Risk of Bias Assessment

In order to comprehensively review the scope of UP research, the current study included research with different levels of quality. The majority of research maintained a high standard of reporting, with minor flaws in reporting specific randomisation and sampling procedures. There were no substantial discrepancies in quality between included studies. More detailed results for the JBI critical appraisal tool can be found in Supplementary Material 1.

Discussion

In the present meta-analytic review, we evaluated the transdiagnostic treatment efficacy of the UP across internalising disorders, as well as the degree of change in ER strategy engagement, in order to gain insight into the clinical applicability of ER as a shared mechanisms factor within psychological intervention. Across a total of 15 studies and a clinical sample of 1244 participants, baseline to post-intervention UP effects demonstrated large effect size reductions across measures of generalised anxiety disorder, obsessive compulsive disorder, panic disorder with/without agoraphobia, social anxiety disorder, post-traumatic stress disorder, and borderline personality disorder. Furthermore, these large symptom reductions were found to remain stable across a 6-month time-period. In addition, compared to inactive control conditions, the UP demonstrated moderate and large effect size reductions across measures of depression and anxiety, respectively. However, the relative benefit of these effects at 6-month follow-up are unclear, as analysis was limited to evaluating only a single study. Nonetheless, results of the current analysis support the transdiagnostic efficacy of the UP across internalising disorders, however further research is

required to determine whether these treatments are more beneficial than control conditions at 6-month follow-up.

Methodological limitations of the primary studies, including a wide range of relatively generic CBT protocols used for single intervention approaches, as well as relatively few manualized interventions, precluded us from making inferences about the outcomes from the UP when compared with disorder-specific protocols. However, effect sizes obtained in our review were comparable to those of previous meta-analyses evaluating the treatment efficacy of CBT, whereby large uncontrolled effects, and moderate to large controlled effects, were reported across anxiety and depression measures (Butler, Chapman, Forman, & Beck, 2006; Hofmann & Smits, 2008; Tolin, 2010; Stewart & Chambless, 2009). It is important to note that the conceptual foundations of the UP regarding extinction learning via avoidance reduction and building cognitive flexibility via identifying and altering maladaptive cognitions, are rooted in CBT practice, however are adapted to explicitly focus on the functional nature of emotions and the cognitive-behavioural reactions against emotional experiences (Ellard et al., 2010). Thus, the similarity in effect sizes obtained between meta-analyses may indicate that shifting key CBT based processes towards a dialogue of emotion focused language, emphasising emotional experiences and patterns of cognitive and behavioural responses to emotion, may provide comparable treatment benefits to standard CBT.

In addition, compared to single disorder interventions which directly target ER within treatment, current effect size estimates for anxiety and depression were larger than those previously reported by mindfulness based interventions (Khoury et al., 2013), were greater in reducing depressive symptom severity compared to DBT (Panos, Jackson, Hasan, & Panos, 2014), and was marginally less efficacious for global psychopathology effect size estimates compared to ACT (A-tjak et al., 2015; Hofmann, Sawyer, Witt, & Oh, 2010; Öst, 2014). This

may also indicate comparable efficacy to other prominent third-wave emotion focused interventions. Further randomised control trial studies evaluating the efficacy between treatment modalities is thus required to further evaluate these relationships.

Comparability of outcomes aside, a potential advantage of the UP when compared with standard CBT approaches which do explicitly emphasise emotion regulation skills (e.g., Andrews, Creamer, Crino, Hunt, Lampe, & Page, 2002; Greenberger & Padesky, 1995) is that the UP may have additive value in providing clients with broader, transdiagnostic skills in this regard. This has previously been identified as a limitation to standard CBT approaches (Coplan et al., 2015; Newby et al., 2015). Unfortunately, we were not able to examine the extent of such benefits in the present review, but further studies might aim to compare the outcomes of UP compared to standard CBT for secondary or co-occurring symptoms.

The secondary aim of the study was to evaluate a key assumption underlying our primary research question, namely, to what extent the UP leads to change across measures of adaptive and maladaptive ER strategy engagement. Results revealed that for measures of adaptive ER strategy engagement, significant moderate effect size improvements were evident for the mindfulness-related skills of awareness and acceptance of emotions, and cognitive reappraisal of negative emotions, at post-intervention. Unfortunately, only two of the included studies reported a 6-month follow up. For these studies, improvements appeared to be attenuated at 6-month follow-up and only small to moderate in magnitude. Additional follow-up studies will confirm whether ER skills can be developed and maintained following treatment in line with the stated objectives of the approach.

Similarly, UP interventions also led to significant moderate effect size reductions in maladaptive ER strategies of experiential avoidance of emotions, suppression of emotional experiences, and difficulties in employing emotion based skills, at post-intervention.

Unfortunately however, the lack studies reporting follow-up data precluded the current analysis from evaluating whether these benefits were retained across time. Further research may examine whether some ER skills show persisting greater persistence of benefit from the UP than others. Nonetheless, the current state of the literature supports the assumption that, overall, the UP leads to significant changes in ER. This is highlighted by change across the core competencies of the protocol regarding adaptive ER improvements in the awareness, acceptance, willingness and cognitive flexibility towards emotional experiences. Likewise, reductions in maladaptive ER engagement in emotional avoidance, emotional suppression, and difficulties associated with ER strategy use were also evident.

There were moderate to large improvements in the frequency of positive and negative affect experienced across the post-intervention and follow-up intervals. Considering that increased frequency of negative affect experienced has been associated with maintaining factors of psychopathology such as impaired cognitive processing, reduced coping, increased social withdrawal, and reduced behavioural repertoire (Fredrickson, 2001; Fredrickson & Branigan, 2005; Watson, Clark, & Tellegen, 1998), it may also be the case that improvements in negative affectivity indirectly relate to reductions in symptom severity across internalising diagnoses, as demonstrated by our primary research question.

In regards to the third aim of the study, regarding secondary benefits occurring as a consequence of UP intervention, results indicated that there were large improvements in functional impairment and quality of lifeCompared to control groups, large reductions in functional impairment were evident at the post-intervention and six-month follow-up time points. These results not only highlight secondary benefits of the UP intervention, but also contribute to the existing body of literature implicating ER interventions with improvements in quality of life and daily functioning (see DeVibe et al., 2017).

Our review provides detailed information regarding the effectiveness of the UP as a transdiagnostic intervention. However, our conclusions need to be tempered by a number of limitations. First, we need to be hesitant in drawing inferences regarding the relative effect compared to other treatment modalities, due to the lack of research comparing these effects within the field. The current study was also unable to draw causal inferences between ER change and reductions in psychopathology severity, as the relative lack of research which reported ER related outcomes in the context of psychopathology outcomes, constrained our ability to conduct a structured mediational analysis (Fritz & MacKinnon, 2007). Thus, further verification of the assumption that the UP is related to ER change is required, especially given that our study did not require the presence of validated ER measures for inclusion. Thus, it is recommended that future UP research include measures of changes in ER. Ideally, this should also involve comparisons of changes in ER between treatment conditions so as to better identify underlying mechanisms of change, and how this may differ between interventions. An alternative possibility: that changes in ER might in fact follow from changes in psychological symptoms, should also be explored. Second, the studies included in this review which reported ER measures did not analyse important modifying factors implicated in the effectiveness of ER interventions, such as the context (Eftekhari, Zoellner, & Vigil, 2009; Gratz, Weiss, & Tull, 2015), and the interaction between co-occurring ER processes (Aldao & Nolen-Hoeksema, 2010, 2012; John & Gross, 2007). For instance, while re-appraisal may be helpful when a person fails an exam, it might not be as helpful in a different context, such as when a person is grieving the loss of a loved one. Further, multiple ER strategies may at times be deployed simultaneously and interact with each other in either compounding or subduing emotional states (Aldao & Nolen-Hoeksema, 2010; Aldao & Nolen-Hoeksema, 2012; John & Gross, 2007). Conceivably, the primary diagnosis or constellations of comorbidity in a person may also be important moderators, however the

variable reporting practices in the primary studies precluded a formal analysis of this possibility. Thus, we are unable to speculate on contextual factors or the complexity of interdependent ER processes on the basis of this review. The scope of our review was also limited to studies where participants met diagnostic criteria for an internalising disorder. Further research should aim to ascertain whether similar outcomes are achieved for sub-clinical populations. Finally, we were unable to determine whether particular participant diagnoses were associated with outcomes from the UP as primary studies often included a mix of disorder categories in their samples, precluding us from conducting the requisite analyses.

The above limitations notwithstanding, the current review was the first to systematically evaluate the UP as a transdiagnostic ER based intervention. It adds to the growing body of literature examining transdiagnostic processes underlying clinical interventions. Our extensive review, conducted across internalising disorders, derived from gold standard clinician-rated measures, across both controlled and uncontrolled studies provides confidence that the UP is an efficacious protocol with transdiagnostic value and apparent stability of gains across time. For clinicians, the UP thus appears to be a flexible and valuable approach for clients presenting with a range of internalising psychopathologies. Whilst improvements in ER skills appear to coincide with symptom reductions when the UP is applied, further research is required to continue examining relationships between these effects.

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Figure 1. Overview of the Screening Process

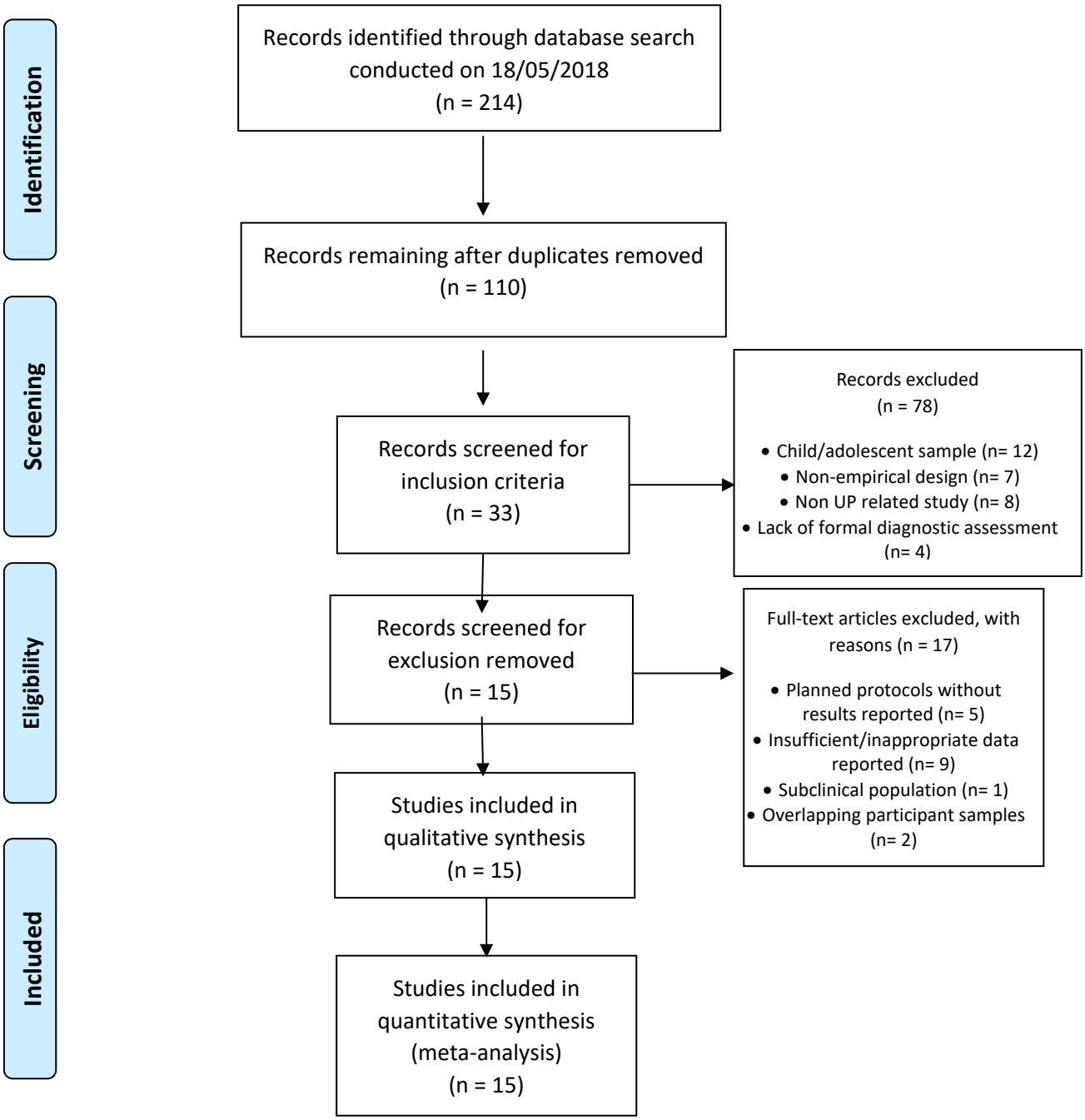


Table 1. Characteristics of Studies Included in the Meta-Analysis Evaluating the Transdiagnostic Effect of the Unified Protocol.

Authors	Sample details	Study design	Disorder presentations	Psychopathology measures	Emotion regulation measures	Secondary measures
Barlow et al., 2017	223 outpatient adults	RCT experimental design - 16 session face-to-face UP intervention vs. WLC*, with 6MFU	Primary Diagnoses: GAD, OCD, PD, PDA, SAD	ADIS-IV-L CSR, CGI-S, PDSS-SR, SIGH-D	N/A	WSAS
Bullis et al., 2015	11 treatment seeking adults recruited via a Boston University psychology clinic	Treatment response study - 12 session group based UP intervention	Primary Diagnoses: Dysthymia, SAD, Anxiety NOS, Comorbid Diagnoses: SAD, GAD, , SP, ADHD, MDD, PTSD, Depression NOS, Anxiety NOS, Alcohol abuse, Trichotillomania,	OASIS, ODSIS	MEAQ	PANAS, WSAS, Q-LES-Q
de Ornelas Maia, Braga, Nunes, Nardi, & Silva, 2013	16 Brazilian adults recruited via public health service	Treatment response study - 12 session group based UP intervention	Primary Diagnoses: MDD Comorbid Diagnoses: GAD, PD, SAD, PTSD	BAI, BDI	N/A	ASEX, WHO-QoL
de Ornelas Maia, Nardi, & Cardoso, 2015	48 treatment-seeking Brazilian adults	Quasi-experimental design – 12 session group UP + medication TAU vs. medication TAU	Primary Diagnoses: MDD, Anxiety Comorbid Diagnoses: Anxiety	BAI, BDI	N/A	N/A

Table.1 *(continued)*

Authors	Sample details	Study design	Disorder presentations	Psychopathology measures	Emotion regulation measures	Secondary measures
Ellard et al., 2017	29 adults recruited via a Massachusetts Clinic	RCT experimental design – 18 session face-to-face UP intervention vs. TAU	Primary Diagnoses: BD Comorbid Diagnoses: GAD, SAD, PD, SAD	ACS, HAM-D-17, HAM-A	DERS	LIFE-RIFT, ACS
Ellard, Deckersbach, Sylvia, Nierenberg, & Barlow, 2012	3 treatment seeking adults	Treatment response case series – 15 session face-to-face UP intervention	Primary Diagnoses: BD Comorbid Diagnoses: PTSD, PDA, SAD, PTSD, GAD, ADHD, substance dependence	BAI, CGI-S, HAM-D-17	N/A	N/A
Ellard, Fairholme, Boisseau, Farchione, & Barlow, 2010	18 (study 1) and 15 (study 2) treatment seeking adults recruited via a Boston University psychology clinic. Independent samples obtained across studies.	Two treatment response pilot studies – 17-18 session face-to-face UP intervention, with 6MFU	Primary Diagnoses: GAD, SAD, OCD, PDA, Co-principal Diagnoses: GAD/PD, GAD/SAD Comorbid Diagnoses: GAD, SAD, PDA, MDD, SP, Hypochondriasis, Anxiety Disorder NOS, Dysthymia	ADIS-IV-L CSR-DEP, CSR-GAD, CSR-OCD, CSR-PDA, CSR-SAD, SIGH-D	N/A	PANAS, WSAS

Table.1 *(continued)*

Authors	Sample details	Study design	Disorder presentations	Psychopathology measures	Emotion regulation measures	Secondary measures
Farchione et al., 2012	37 treatment seeking adults via a Boston University psychology clinic	RCT experimental design – 18 session face-to-face UP intervention vs. WLC	Primary Diagnoses: GAD, SAD, 0CD. PDA, anxiety NOS, PTSD, Co-principal Diagnoses: GAD/SAD, OCD/PDA Comorbid Diagnoses: MDD, dysthymia, Depression NOS	ADIS-IV-L CSR, CSR-GAD, CSR-OCD, CSR-PDA, CSR-SAD, PDSS-SR, SIGH-D	N/A	PANAS, WSAS
Ito et al., 2016	17 treatment seeking Japanese adults	RCT experimental design – 18 session face-to-face UP intervention vs. WLC, with 3MFU	Primary Diagnoses: MDD, SAD, PTSD, anxiety NOS Comorbid Diagnoses: Anxiety disorders	CGI-S, CGI-GAF, GRID-HAMD, SIGH-A	ERQ	EQ-5D, PANAS, SDS

Table.1 *(continued)*

Authors	Sample details	Study design	Disorder presentations	Psychopathology measures	Emotion regulation measures	Secondary measures
Mohammadi, Bakhtiari, Arani, Dolatshahi, Habibi, 2018	6 Iranian adults referred for clinical trial	Multiple baseline experimental case series – 16-20 session face-to-face UP intervention	Primary Diagnosis: BPD Comorbid Diagnoses: MDD, anxiety disorder	BPI	DERS	N/A
Reinholt et al, 2017	47 Danish outpatient adults	Treatment response study - 15 session group based UP intervention	Primary Diagnoses: PD, PDA, SAD, GAD Comorbid Diagnoses: PDA, SAD, GAD, SP, MDD, dysthymia, ADHD, SDD, APD, OCD, ED NOS, PTSD	BDI-II, CGI-S, HAM-A	N/A	PANAS, WHO-5
Sauer-Zavala, Bentley, & Wilner, 2016	5 treatment seeking adults	Treatment response case series – 16-20 face-to-face session UP intervention	Primary Diagnoses: BPD Comorbid Diagnoses: GAD, MDD, SAD	DASS-A , DASS-D, , ZAN-BDP	DERS	N/A
Thompson-Brenner, Boswell, Espel-Huynh, Brooks, & Lowe, 2018	616 female cross-site ED hospital inpatients	Quasi-experimental design -face-to-face UP intervention vs. WLC	Primary Diagnoses: ED Comorbid Diagnoses: Depressive and anxiety disorders	ASI, CES-D, EDE-Q	MEAQ, SMQ	BMI

Table.1 *(continued)*

Authors	Sample details	Study design	Disorder presentations	Psychopathology measures	Emotion regulation measures	Secondary measures
Tulbure, Rusu, Sava, Salagean, & Farchione, 2018	105 treatment seeking Romanian adults	Treatment response study - 10 week online based UP intervention, with 6MFU	Primary Diagnoses: GAD, SAD, MDD, PD/A, PTSD, SP, OCD Comorbid Diagnoses: GAD, SAD, MDD, PDA, SP, OCD	BAI, BDI-II, OASIS, PCL-5, PDSS-SR, PSWQ, SPIN, YBOCS	ERQ	WSAS, QOLI, APS-R

Note: Measures include only those selected for analysis. See methods section for selection criteria.
Treatments: TAU= treatment as usual RCT = randomised control trial, WLC = waitlist control, UP = unified protocol.
Participants: ADHD = attention deficit hyperactivity disorder, APD= Avoidant Personality Disorder, BD = bipolar disorder, BPD = borderline personality disorder, ED = eating disorder, GAD= generalised anxiety disorder, MDD = major depressive disorder, NOS = not otherwise specified, OCD = obsessive compulsive disorder, PD = panic disorder, PDA = panic disorder with agoraphobia, PTSD = posttraumatic stress disorder, SAD = social anxiety disorder, SP = specific phobia.
Measures: ACS = Affective Control Scale, ADIS-IV CSR = Anxiety Disorders Interview Schedule for DSM-IV Clinical Severity Rating, APS-R = Almost Perfect Scale-Revised, ASEX = Arizona Sexual Experiences Scale, BAI = Beck Anxiety Inventory, BDI-II = Beck Depression Inventory-II, BPI = Borderline Personality Inventory, CGI-GAF = Clinical Global Impression – Global Assessment of Functioning, CGI-S = Clinical Global Impression- Severity Scale, DERS = Difficulties in Emotion Regulation Scale, ERQ= Emotion Regulation Questionnaire, GRID-HAMD = GRID-Hamilton Depression Rating Scale, HAM-A = Hamilton Anxiety Rating Scale, HAM-D-17 = Hamilton Depression Rating Scale - 17-item version, MEAQ = Multidimensional Experiential Avoidance Questionnaire, OASIS = Overall Anxiety Severity and Impairment Scale, ODSIS = Overall Depression Severity and Impairment Scale, PANAS = Positive and Negative Affect Schedule, PCL-5 = Posttraumatic Stress Disorder Checklist for DSM-5, PDSS-SR = Panic Disorder Severity Scale–Self-Report Version, PSWQ = Penn State Worry Questionnaire, Q-LES-Q = Quality of Life Enjoyment and Satisfaction Questionnaire, QOLI = Quality of Life Inventory, SDS = Sheehan Disability Scale, SIGH-A =Structured Interview Guide for the Hamilton Anxiety Scale, SIGH-D = Structured Interview Guide for the Hamilton Depression Scale, SMQ = Southampton Mindfulness Questionnaire , SPIN = Social Phobia Inventory, WHO-5 = World Health Organisation- Five Well-Being Index, WHO-QoL = World Health Organisation – Quality of Life Scale, WSAS = Work and Social Adjustment Scale, YBOCS = Yale Brown Obsessive Compulsive Scale.
Comparison: 3mfu = three-month follow-up, 6mfu = six-month follow-up. 12mfu = twelve-month follow-up, 18mfu = eighteen-month follow-up.
* Comparisons to single disorder protocols from this study were not included in this analysis, in order to retain consistency across inactive/passive TAU conditions.

Table 2. Uncontrolled Effect of the Unified Protocol across Internalising Disorders, and 95% Confidence Intervals.

Symptom domain	Comparison	*k*	Hedges *g* (Lower CI, Upper CI)	Variance	Std. Error	*Z*-value	*p*-Value	I^2	Summary Effect Size Forest Plot*
Anxiety	Baseline vs. post treatment	12	-.99 (-1.30, -.68)	.03	.16	-6.24	<.001	85.54	
	Baseline vs. 6mfu	5	-1.25 (-1.80, -.69)	.08	.28	-4.40	<.001	92.47	
Depression	Baseline vs. post treatment	12	-.92 (-1.21, -.64)	.02	.14	-6.43	<.001	80.00	
	Baseline vs. 6mfu	5	-1.07 (-1.56, -.58)	.06	.25	-4.27	<.001	90.19	
GAD	Baseline vs. post treatment	5	-.97 (-1.23, -.70)	.02	.14	-7.11	<.001	12.53	
	Baseline vs. 6mfu	3	-1.18 (-1.48, -.89)	.02	.15	-7.82	<.001	0	
OCD	Baseline vs. post treatment	5	-1.23 (-1.91, -.55)	.12	.35	-3.56	<.001	80.19	
	Baseline vs. 6mfu	3	-1.60 (-2.85, -.35)	.41	.64	-2.52	.012	89.77	

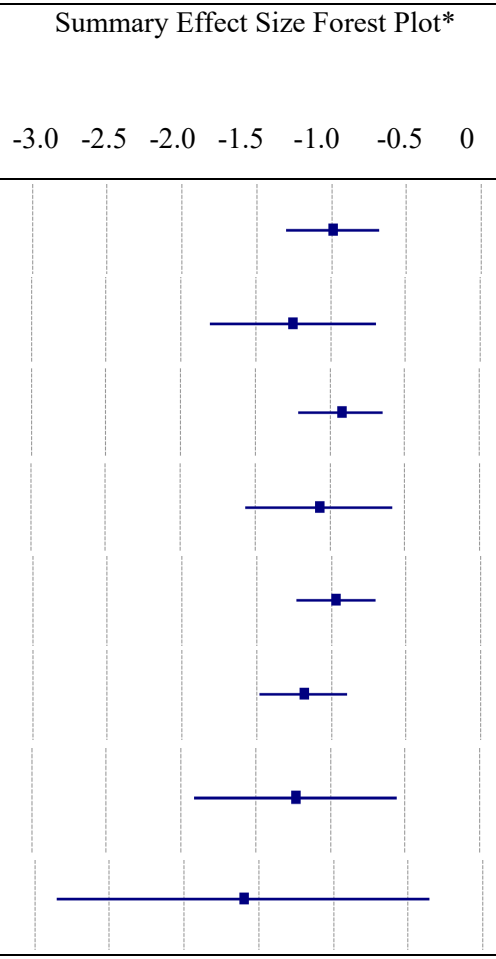
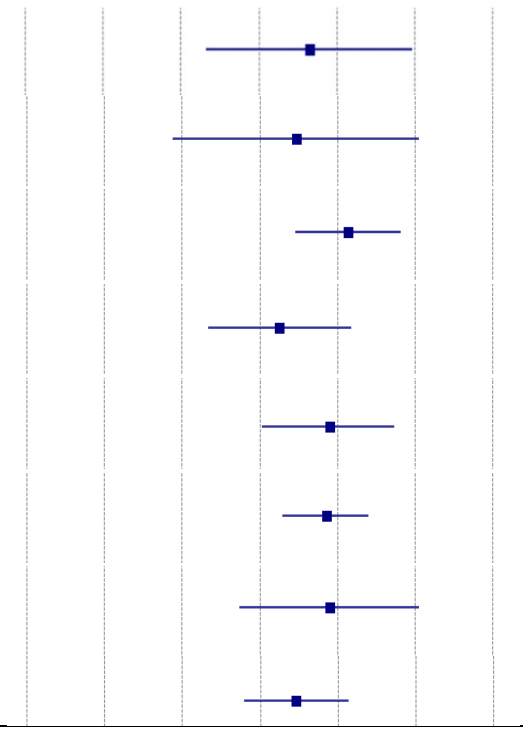


Table 2. *(continued)*

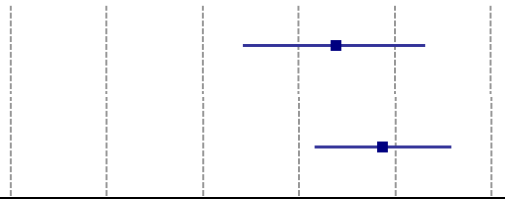
Symptom domain	Comparison	*k*	Hedges *g* (Lower CI, Upper CI)	Variance	Std. Error	*Z*-value	*p*-Value	I^2	Summary Effect Size Forest Plot*
PD	Baseline vs. post treatment	3	-1.17 (-1.84, -.51)	.12	.34	-3.45	<.001	76.02	
	Baseline vs. 6mfu	3	-1.26 (-2.06, -.47)	.17	.41	-5.87	<.001	82.95	
PDA	Baseline vs. post treatment	4	-.93 (-1.27, -.59)	.03	.17	-5.38	<.001	0	
	Baseline vs. 6mfu	2	-1.37 (-1.83, -.91)	.06	.23	-5.87	<.001	0	
SAD	Baseline vs. post treatment	5	-1.05 (-1.48, -.63)	.05	.22	-4.84	<.001	64.59	
	Baseline vs. 6mfu	3	-1.07 (-1.35, -.80)	.02	.14	-7.53	<.001	5.85	
BPD	Baseline vs. post treatment	2	-1.05 (-1.63, -.47)	.09	.30	-3.54	<.001	0	
GPE**	Baseline vs. post treatment	4	-1.27 (-1.60, -.93)	.03	.17	-7.43	<.001	56.17	



Note: Symptom domains and comparison points were not reported if they contained less than two studies in analysis.
Disorders: GAD= Generalised Anxiety Disorder, PD = Panic Disorder, PDA = Panic Disorder with Agoraphobia, SAD= Social Anxiety Disorder, PTSD = Post Traumatic Stress Disorder, BPD = Borderline Personality Disorder, GPE= Global Psychopathology Effect.
Comparison: 6mfu = six-month follow-up.
k = number of individual studies included in each summary effect size.
* Summary effect size forest plot comprises of Hedges g effect size statistic and corresponding 95% confidence interval, and does not reflect a separate meta-analysis conducted.
** Global psychopathology is a measure of Clinical Global Impressions – Severity Scale (Guy, 1976), which is a measure of global psychopathology symptom severity.

Table 3. Controlled Effect of the Unified Protocol across Internalising Disorders, and 95% Confidence Intervals.

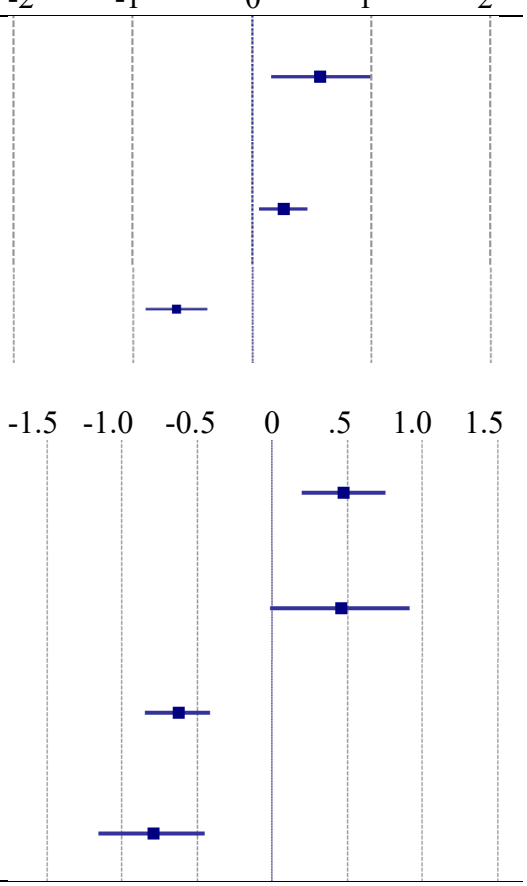
Symptom domain	Comparison	*k*	Hedges *g* (Lower CI, Upper CI)	Variance	Std. Error	*Z*-value	*p*-Value	I^2	Summary Effect Size Forest Plot*
Anxiety	Baseline vs. post treatment	5	-.81 (-1.29, -.34)	.06	.24	-3.37	.001	84.11	
Depression	Baseline vs. post treatment	5	-.57 (-.92, -.21)	.03	.18	-3.14	.002	71.94	



Note: Disorders and comparison points were not reported if they contained less than two studies in analysis. .
k = number of individual studies included in each summary effect size.
* Summary effect size forest plot comprises of Hedges g effect size statistic and corresponding 95% confidence interval, and does not reflect a separate meta-analysis conducted.

Table 4. Uncontrolled Effect of the Unified Protocol across Emotion Regulation Strategies and Positive and Negative Affect, with 95% Confidence Intervals.

Measure Type	Comparison	*k*	Hedges *g* (Lower CI, Upper CI)	Variance	Std. Error	*Z*-value	*p*-Value	I^2	Summary Effect Size Forest Plot*
Adaptive ER	Baseline vs. post treatment	3	.57 (.16, .99)	.05	.21	2.69	.01	74.18	
	Baseline vs. 6mfu	2	.26 (.06, .47)	.01	.10	2.51	.012	0	
Maladaptive ER	Baseline vs. post treatment	6	-.65 (-.98, -.33)	.03	.17	-3.95	<.001	70.38	
Positive Affect	Baseline vs. post treatment	5	.48 (.20, .76)	.02	.14	3.38	<.001	0	
	Baseline vs. 6mfu	2	.46 (-.01, .92)	.06	.24	1.94	.053	0	
Negative Affect	Baseline vs. post treatment	5	-.62 (-.84, -.41)	.01	.11	-5.67	<.001	0	
	Baseline vs. 6mfu	2	-.79 (-1.15, -.44)	.03	.18	-4.34	<.001	0	

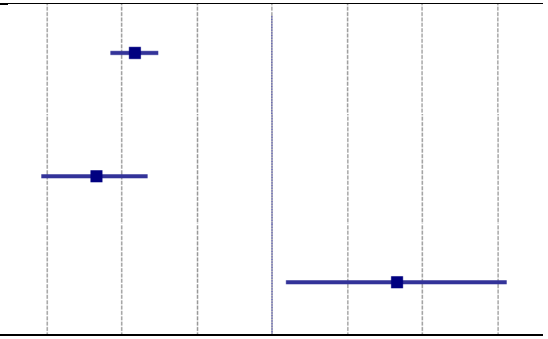


Note: Comparison points were not reported if they contained less than two studies in analysis. A comparison between the UP and control could not be made, due to all comparison points having less than two studies involved in analysis.
Comparison: 6mfu = six-month follow-up. ER = Emotion regulation.

k = number of individual studies included in each summary effect size.
* Summary effect size forest plot comprises of Hedges g effect size statistic and corresponding 95% confidence interval, and does not reflect a separate meta-analysis conducted.

Table 5. Uncontrolled Effect of the Unified Protocol for Secondary Treatment Effects, and 95% Confidence Intervals.

Construct	Comparison	*k*	Hedges *g* (Lower CI, Upper CI)	Variance	Std. Error	*Z*-value	*p*-Value	I^2	Summary Effect Size Forest Plot*
Functional Impairment	Baseline vs. post treatment	7	-.91 (-1.07, -.75)	.01	.08	-11.24	<.001	0	
	Baseline vs. 6mfu	4	-1.17 (-1.53, -0.82)	.03	.18	-6.47	<.001	65.07	
Quality of Life	Baseline vs. post treatment	4	.83 (.10, 1.57)	.14	.38	2.22	.027	0	



Note: Constructs and comparison points were excluded if they contained less than two studies in analysis. Excluded constructs include; Affect Appraisal, Hopelessness, Perfectionism, Sexual Dysfunction, Subjective Wellbeing, and Suicidal Ideation.
Comparison: 6mfu = six-month follow-up.
k = number of individual studies included in each summary effect size.
* Summary effect size forest plot comprises of summary effect size statistic and corresponding 95% confidence interval, and does not reflect a separate meta-analysis conducted.