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The Unified Protocol compared with diagnosis-specific protocols for anxiety disorders: 12-month follow-up from a randomized clinical trial

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Abstract

Objective: To examine whether the Unified Protocol (UP) remains equivalent to single-disorder protocols (SDPs) in the treatment of anxiety disorders at 12-month follow-up.

Method: We report results from the 12-month follow-up of a recent randomized equivalence trial [1]. Data are from 179 participants (55.31% female sex, 83.24% White, average age 30.66) who met criteria for a principal anxiety disorder and were randomized to either the UP or SDP conditions. Consistent with the parent trial, the primary outcome was principal diagnosis clinician severity rating (CSR) from the Anxiety Disorder Interview Schedule (ADIS). Secondary outcomes included anxiety, depression, and impairment. Missing data were accommodated using multiple imputation (10,000 imputed data sets) under a missing at random assumption. Equivalence between the UP and SDPs was tested using slope difference scores from latent growth models and 95% confidence interval of between-condition effect sizes.

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Results: The results indicated that the UP and SDP conditions remained equivalent with regard to principal diagnosis clinician severity rating at 12-month follow-up. In addition, there were no significant differences between conditions on secondary outcomes at 12-month follow-up.

Conclusions: The UP continues to yield outcomes comparable to SDPs at 12-month follow-up, and therefore provides a single intervention that can be used to treat the most commonly occurring psychiatric disorders with durable effects.

Keywords

transdiagnostic; unified protocol; cognitive-behavioral treatment; anxiety disorders

Introduction

The Unified Protocol (UP) is a transdiagnostic treatment with five core modules targeting neuroticism, the temperament at the core of emotional disorders. Emotional disorders are disorders that are characterized by: frequent and intense negative emotions, aversive reactions to emotions, and subsequent attempts to decrease or avoid emotions [2]. By targeting shared mechanisms, the UP has the potential to simplify training efforts and increase access to evidence-based psychological treatments for these disorders. Prior research has demonstrated the maintained effects of the UP compared to waitlist conditions [3–5]. In a recent randomized equivalence trial, we found that the UP was as effective as single-disorder protocols (SDPs) for heterogeneous anxiety disorders and that the effects were maintained out to 6-month follow-up [1]. In the current study, we report results from the 12-month follow-up of this trial examining equivalence between the UP and SDPs. To our knowledge, this is the first published report of 12-month follow-up data comparing the UP to an active comparison condition.

Method

The study was approved by the Institutional Review Board at Boston University. See the parent trial for additional demographic data, methodological details, and outcomes out to 6-month follow-up [1] ([clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT01243606) Identifier: NCT01243606). Participants who met criteria for a principal diagnosis of panic disorder with or without agoraphobia, generalized anxiety disorder, obsessive-compulsive disorder, or social anxiety disorder were randomized by principal diagnosis to the UP, SDP, or waitlist control condition (2:2:1 allocation ratio to UP, SDP, and waitlist, respectively). Participants randomized to the UP condition received the UP [6]. Participants randomized to the SDP condition received the SDP that matched their principal diagnosis. The SDP protocols were: *Mastery of Your Anxiety and Panic*, fourth edition [7]; *Mastery of Your Anxiety and Worry*, second edition [8]; *Treating Your Obsessive-Compulsive Disorder With Exposure and Response (Ritual) Prevention Therapy*, second edition [9]; and *Managing Social Anxiety: A Cognitive-Behavioral Therapy Approach*, second edition [10]. Consistent with the parent trial, we examined equivalence on the primary outcome of principal diagnosis clinician severity rating (CSR) from the Anxiety Disorder Interview Schedule (ADIS), along with secondary outcomes. Analyses were conducted using Mplus 8.0 on the intent to treat sample (all participants randomized to UP or SDP, N=179¹ [55.31% female sex, 83.24% identified as White, average age 30.66]).

Missing data were accommodated using multiple imputation (10,000 imputed data sets) under a missing at random assumption. Analyses paralleled those reported in the parent trial but focused on the 12-month follow-up instead of the 6-month follow-up. Equivalence on CSR and between condition differences in secondary outcomes was tested using slope difference scores from latent growth models (LGMs) and 95% CI of between-condition effect sizes (Cohen's *d*).

Results

The estimate of the UP vs. SDPs effect on the slope of change in principal diagnosis CSR from baseline to the 12-month follow-up was 0.13 (95% CI, -0.37 to 0.62). The CIs for changes in CSR fell entirely within the prespecified equivalence criteria of ± 0.75 CSR units and therefore support the hypothesis of statistical equivalence of the UP vs. SDPs when collapsing across diagnoses at 12-month follow-up (Figure 1). The effect size difference for the slope of change in principal diagnosis from baseline to the 12-month follow-up was small ($d=0.09$; 95% CI, -0.25 to 0.42; Table 1).

Effect sizes for comparisons of the UP vs. SDPs at the 12-month follow-up for all secondary outcomes were generally small in magnitude and statistically nonsignificant; these findings were consistent across both the LGM-derived slope difference scores and effect sizes (Table 1).

At the 12-month follow-up, 60 of 88 UP patients (68.6%) were estimated to no longer meet diagnostic criteria for their principal diagnosis, compared with 62 of 91 SDP patients (68.2%; relative risk, 1.00; 95% CI, 0.82-1.22). Furthermore, at 12-month follow-up, 42 of 71 UP patients (59.2%) no longer met diagnostic criteria for any emotional disorder compared with 34 of 66 SDP patients (51.5%; relative risk, 1.15; 95% CI, 0.85-1.56).

Discussion

Consistent with the acute treatment and 6-month follow-up outcomes [1], reduction in principal disorder severity remained equivalent between the UP and SDPs at 12-month follow-up. Moreover, no statistically or clinically significant differences were found in secondary outcomes, nor in the proportion of patients who no longer met diagnostic criteria. These results indicate that the UP remains as effective as SDPs at 12-month follow-up. Transdiagnostic treatments like the UP may confer additional benefits related to attrition [1], training of therapists, and implementation, and therefore may facilitate increased access to evidence-based care that promotes enduring recovery.

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¹Participants randomized to the waitlist control condition in the parent trial did not complete follow-up assessments and therefore are not included.

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Figure 1.

Model-Based Estimates of the Principal Diagnosis ADIS CSR Score Trajectories from Baseline to 12-Month Follow-up

Abbreviations: ADIS CSR, clinical severity rating for principal diagnosis obtained from Anxiety Disorder Interview Schedule; SDP, single-disorder protocol; UP, Unified Protocol for Transdiagnostic Treatment of Emotional Disorders.

Figure 2.
Recruitment Flow Diagram

SDP indicates single-disorder protocol; UP, Unified Protocol for Transdiagnostic Treatment of Emotional Disorders; and WLC, waitlist control.

^a*Completed treatment* indicates that the patient attended at least 75% of the allotted number of sessions (ie, 9 of 12 for patients with panic disorder with or without agoraphobia and 12 of 16 for patients with other principal diagnoses).

^bOne patient with principal panic disorder with or without agoraphobia completed 12 sessions but was withdrawn before posttreatment assessment (ie, completed treatment, but was not eligible for posttreatment or follow-up assessment).

^cOne patient discontinued study participation at 6-month follow-up, and therefore was no longer eligible for the 12-month follow-up; however, this individual is included in the “eligible for posttreatment and follow-up assessments” classification (n = 80).

^dOne patient was withdrawn from the study after completing the posttreatment assessment, but before the 6-month follow-up, so was no longer eligible for the 6- or 12-month follow-

up; however, this individual is included in the “eligible for posttreatment and follow-up assessments” classification (n = 78).

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Table 1.

Means, Between-Condition Effect Sizes at 12-Month Follow-Up, Slope Difference Scores and Between-Condition Effect Sizes from Growth Curve Models

Outcome	Means and Between-Condition Effect Sizes			Slope Difference Scores and Between-Condition Effect Sizes from Growth Curve Models	
	UP Mean (95%CI)	SDP Mean (95%CI)	UP vs SDP, <i>g</i> (95%CI)	Slope Difference Score, Mean (95%CI) ^a	Effect Size, Cohen <i>d</i> (95%CI) ^a
Primary Clinician-Rated Outcome					
ADIS CSR	2.77 (2.43:3.11)	2.68 (2.32:3.04)	0.05 (−0.24:0.35)	0.13 (−0.37:0.62)	0.09 (−0.25:0.42)
Additional Clinician-Rated Outcomes					
SIGH-A	9.23 (7.72:10.74)	9.31 (7.41:11.2)	−0.01 (−0.30:0.28)	1.41 (−0.91:3.72)	0.26 (−0.17:0.69)
SIGH-D	6.69 (5.53:7.84)	6.71 (5.45:7.97)	0.00 (−0.30:0.29)	−0.22 (−2.17:1.73)	−0.06 (−0.58:0.46)
CGI-S	3.04 (2.75:3.34)	3.19 (2.91:3.47)	−0.10 (−0.40:0.19)	0.01 (−0.34:0.35)	0.01 (−0.36:0.37)
Self-reported Outcomes					
OASIS	5.19 (4.48:5.91)	5.27 (4.49:6.05)	−0.02 (−0.31:0.27)	0.37 (−0.71:1.44)	0.14 (−0.26:0.53)
ODSIS	3.19 (2.36:4.03)	3.19 (2.40:3.98)	0.00 (−0.29:0.29)	−0.37 (−1.49:0.75)	−0.15 (−0.60:0.30)
WSAS	6.61 (5.29:7.92)	7.72 (6.41:9.04)	−0.18 (−0.47:0.12)	−0.31 (−2.44:1.82)	−0.06 (−0.48:0.36)

Abbreviations: ADIS CSR, clinical severity rating for principal diagnosis obtained from Anxiety Disorder Interview Schedule; SDP, single-disorder protocol; UP, Unified Protocol for Transdiagnostic Treatment of Emotional Disorders; SIGH-A, Structured Interview Guide for Hamilton Anxiety Scale; SIGH-D, Structured Interview Guide for Hamilton Depression Scale; CGI-S, Clinical Global Impression-Severity Scale; CGI-I, Clinical Global Impression-Improvement Scale; OASIS, Overall Anxiety Severity and Impairment Scale; ODSIS, Overall Depression Severity and Impairment Scale; WSAS, Work and Social Adjustment Scale.

Note: Clinical Global Impression-Improvement Scale (CGI-I) scores were also examined, but these LGMs yielded poor fit statistics, and therefore are not reported. However, there were no significant differences between conditions on either CGI scale using either between condition effect sizes or LGMs.

^aNegative slope difference scores and effect sizes indicate that the treatment condition listed first was associated with a greater decrease/level in the outcome. Positive slope difference scores and effect sizes indicate that the treatment condition listed first was associated with a lesser decrease/level or a greater increase in the outcome.