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David H Barlow, Todd J Farchione, Jacqueline R Bullis, Matthew W Gallagher, Heather Murray-Latin, Shannon Sauer-Zavala, Kate H Bentley, Johanna Thompson-Hollands, Laren R Conklin, James F Boswell, Amantia Ametaj, Jenna R Carl, Hannah T Boettcher, Clair Cassiello-Robbins. 2017. "The Unified Protocol for Transdiagnostic Treatment of Emotional Disorders Compared With Diagnosis-Specific Protocols for Anxiety Disorders A Randomized Clinical Trial." JAMA PSYCHIATRY, Volume 74, Issue 9, pp. 875 - 884 (10). <https://doi.org/10.1001/jamapsychiatry.2017>
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A Randomized Equivalence Evaluation of the Unified Protocol for Transdiagnostic
Treatment of Emotional Disorders Compared to Diagnosis-Specific CBT for Anxiety
Disorders

David H. Barlow, Ph.D.^a

Todd J. Farchione, Ph.D.^a

Jacqueline R. Bullis, Ph.D.^{a,b}

Matthew W. Gallagher, Ph.D.^{a,c}

Heather Murray-Latin, Ph.D.^a

Shannon Sauer-Zavala, Ph.D.^a

Kate H. Bentley, M.A.^a

Johanna Thompson-Hollands, Ph.D.^{a,d}

Laren R. Conklin, Ph.D.^{a,e}

James F. Boswell, Ph.D.^{a,f}

Amantia Ametaj, M.A.^a

Jenna R. Carl, Ph.D.^{a,g}

Hannah T. Boettcher, M.A.^a

Clair Cassiello-Robbins, M.A.^a

^aCenter for Anxiety and Related Disorders, Boston University, Boston, Massachusetts

^bDivision of Depression and Anxiety Disorders, McLean Hospital/Harvard Medical School, Cambridge, Massachusetts

^cDepartment of Psychology/Texas Institute for Measurement, Evaluation and Statistics, University of Houston, Houston, Texas

^dNational Center for PTSD at VA Boston Healthcare System, Boston, Massachusetts

^eDepartment of Behavioral Health, Chalmers P. Wylie VA Ambulatory Care Center, Columbus, Ohio

^fDepartment of Psychology, University at Albany, SUNY Albany, New York

^gBig Health Ltd, San Francisco, California

Corresponding author: David H. Barlow, Ph.D., Center for Anxiety and Related Disorders, Boston University, 648 Beacon Street 6th Fl, Boston, MA 02215; Email: dhbarlow@bu.edu; Phone: 617-353-9610; Fax: 617-353-9609

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KEY POINTS

Question: Is a single transdiagnostic psychological treatment, the Unified Protocol (UP), at least as effective as various well-established single-disorder protocols (SDPs) in the treatment of various anxiety disorders?

Findings: In this randomized controlled equivalence trial of 223 adults, treatment with the UP produced reductions in symptom severity for four different anxiety disorders that were statistically equivalent to SDPs both at acute outcome and at 6-month follow-up.

Meaning: The UP, a transdiagnostic intervention consisting of five core modules, may produce effects comparable to SDPs targeting individual disorders, thereby facilitating dissemination and increasing access to these treatments.

ABSTRACT

Importance: Transdiagnostic interventions have been developed to address barriers to the dissemination of evidence-based psychological treatments (EBPTs), but only a few preliminary studies have compared these approaches to existing EBPTs.

Objective: To determine whether the Unified Protocol (UP) is at least as efficacious as single-disorder protocols (SDPs) in the treatment of anxiety disorders.

Design: From May 2011 to March 2015, 223 patients were randomly assigned by principal diagnosis to the UP, a SDP, or a waitlist control (WLC) condition. Patients received up to 16 sessions of the UP or a SDP over 16-21 weeks. Outcomes were assessed at baseline, posttreatment, and 6-month follow-up. Analysis in this equivalence trial was based on intention to treat.

Setting: Outpatient treatment center.

Participants: Patients with a principal diagnosis of panic disorder with or without agoraphobia, generalized anxiety disorder, obsessive-compulsive disorder, or social anxiety disorder were eligible for the study. Exclusions included conditions requiring treatment prioritization or a prior course of cognitive-behavior therapy.

Interventions: UP or SDPs.

Main Outcomes and Measures: Blind evaluations of principal diagnosis clinical severity rating (CSR) were used to evaluate an a priori hypothesis of equivalence between the UP and SDPs.

Results: Among the 223 patients (124 women [56%]; 99 men [44%]; mean [SD] age, 31.1 [11.0] years), 88 were randomized to the UP, 91 to a SDP, and 44 to the WLC condition. Patients were more likely to complete treatment with the UP than SDPs (odds

ratio, 3.11; 95% CI, 1.44 to 6.74). Both UP (Cohen's d , -0.93; 95% CI, -1.29 to -0.57) and SDPs (Cohen's d , -1.08; 95% CI, -1.43 to -0.73) were superior to WLC at acute outcome. Reductions in CSR from baseline to posttreatment (b, 0.25; 95% CI, -0.26 to 0.75) and 6-month follow-up (b, 0.16; 95% CI, -0.39 to 0.70) indicated statistical equivalence between the UP and SDPs.

Conclusions and Relevance: The UP produces symptom reduction equivalent to gold standard EBPTs for anxiety disorders with less attrition. Thus, it may be possible to utilize one protocol instead of multiple SDPs to more efficiently treat the most commonly occurring anxiety and depressive disorders.

Trial Registration: [clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT01243606) identifier: NCT01243606

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INTRODUCTION

Despite the development of robust evidence-based psychological treatments (EBPTs) for anxiety, mood, and related “emotional” disorders (J. R. Bullis et al., unpublished data), the public health impact of these interventions has been limited.¹⁻⁴ Two of the foremost barriers to widespread dissemination and implementation of EBPTs are the burden associated with training clinicians to competently administer different manual-based interventions for each individual anxiety, depressive, or related disorder (single-disorder protocols; SDPs) and the criticism that these protocols lack external validity.⁵⁻⁷ For this reason, in a recent report the Institute of Medicine (IOM; now the National Academy of Medicine) recommended increased emphasis on further development, dissemination, and implementation of EBPTs. One approach is to develop interventions applicable to several related disorders (transdiagnostic^{8,9}) based on theory or empirical grounds^{10,11} and initial results have been promising¹²⁻¹⁶. The Unified Protocol for Transdiagnostic Treatment of Emotional Disorders (UP)¹⁷ is an emotion-focused, cognitive-behavioral intervention consisting of five core modules or components that target temperamental characteristics, particularly neuroticism and resulting emotion dysregulation, underlying all anxiety, depressive, and related disorders.^{18,19} By addressing shared mechanisms associated with neuroticism, specifically negative evaluation and avoidance of intense emotional experience²⁰, this approach could simplify training efforts while also addressing concerns about generalizability to routine care settings by simultaneously accommodating comorbid emotional disorders. Such an approach may increase access to EBPTs for the most common psychiatric disorders.

After developing preliminary support for the efficacy of the UP for the treatment of anxiety and comorbid depressive disorders,^{21,22} it was important to determine the relative efficacy of this approach compared to well-established SDPs, which are currently first line treatments in extant clinical practice guidelines.^{23,24} We hypothesized that the UP would be at least as efficacious as SDPs at acute outcome and at six months following treatment when delivered to a heterogeneous group of patients with principal anxiety disorders and diverse comorbidities.

STUDY DESIGN

Participants

A sample of 223 patients was recruited from treatment-seeking individuals at the Center for Anxiety and Related Disorders at Boston University (CARD). The study was approved by the institutional review board of Boston University and written informed consent was obtained prior to any research activity. Recruitment was designed to be broadly inclusive. Individuals were eligible for the study if they were 1) assigned a principal (most interfering and severe) diagnosis of panic disorder with or without agoraphobia (PD/A), generalized anxiety disorder (GAD), obsessive-compulsive disorder (OCD), or social anxiety disorder (SAD); 2) 18 years or older; and 3) fluent in English. Following long-standing procedures in our clinical trials, individuals taking psychotropic medications at the time of enrollment were required to be stable on the same dose for at least six weeks prior to enrolling in the study, and were requested to maintain these medications and dosages during treatment.

Exclusion criteria consisted primarily of conditions that required prioritization for immediate or simultaneous treatment: specifically, a current diagnosis of bipolar disorder, schizophrenia, schizoaffective disorder, or organic mental disorder; current high suicide risk; or recent (within three months) history of substance use disorder, with the exception of nicotine (1 patient), marijuana (0 patients), and caffeine (0 patients). Individuals were also excluded if they had received at least eight sessions of cognitive-behavioral therapy (CBT) within the past five years. Anyone receiving non-CBT psychotherapy focused on an emotional disorder agreed to discontinue that treatment.

Procedures

Figure 1 depicts the study design and summarizes patient flow. The study consisted of two phases: 1) a 16-session acute treatment (12 sessions for patients with a principal diagnosis of PD/A) or 16-week waitlist control (WLC) phase; and 2) a 6-month follow-up phase (WLC patients were not included in the follow-up phase of the study). The acute treatment phase was limited to a maximum of 21 weeks (16 weeks for PD/A). If patients were unable to complete the full course of treatment during the specified treatment window, treatment was terminated and follow-up assessments were conducted.

Randomization and Blinding

Patients were randomized by principal diagnosis (PD/A, GAD, OCD, and SAD) using a computerized block randomization with a 2:2:1 allocation ratio to UP, SDP, and WLC study conditions, respectively. The project coordinator was unaware of these assignments until after each patient was deemed eligible for the study and consented. Patients were unaware of study hypotheses and were instructed not to reveal their randomization status to raters prior to each assessment. To further protect blinding, raters were located separately from therapists and a new rater was assigned in the event of an accidental unblinding.

Interventions

Number and length of treatment sessions were based on each SDP's recommended dose of treatment as described below. Treatment dosage for the UP was matched to each principal diagnosis' corresponding SDP so that there were no differences between the active treatment conditions in the amount of treatment patients received.

Single-Disorder Protocols

The SDPs included: Managing Social Anxiety: A Cognitive-Behavioral Therapy Approach – 2nd edition (MSA-II);^{25,26} Mastery of Your Anxiety and Panic – 4th edition (MAP-IV);^{27,28} Mastery of Your Anxiety and Worry – 2nd edition (MAW-II);^{29,30} and Treating Your OCD with Exposure and Response (Ritual) Prevention Therapy – 2nd edition.³¹⁻³³ As recommended by the protocol developers, patients with a principal diagnosis of SAD, GAD, or OCD received 16 sessions of treatment and patients with a principal diagnosis of PD/A received 12 sessions. Treatment sessions were approximately 50-60 minutes except for patients with a principal diagnosis of OCD, for whom treatment sessions were 80-90 minutes.

Unified Protocol

The UP contains strategies similar to those in the SDPs including cognitive reappraisal and exposure, but the focus is on reactions to emotion experience itself, such as autonomic arousal rather than situational factors, e.g. crowds.^{17, 34} The UP consists of five core treatment modules: a) mindful emotion awareness; b) cognitive flexibility; c) identifying and preventing patterns of emotion avoidance; d) increasing awareness and tolerance of emotion-related physical sensations; and e) interoceptive and situational emotion-focused exposures. The five core modules are preceded by a module focused on enhancing motivation as well as an introductory module on the adaptive nature of emotions that provides a framework for understanding emotional experiences.

Therapists and Treatment Integrity

Therapists for the study included doctoral students in clinical psychology with two to four years of experience, postdoctoral fellows with five to six years of experience,

and licensed psychologists with ten or more years of experience. Each therapist administered both types of treatment in approximately equal proportions. Initial training and certification in the treatment protocols utilized procedures employed in clinical trials at CARD over the last 20 years.³⁵ Twenty percent of treatment sessions were randomly selected and rated for adherence and competence by an external team of expert raters associated with development of the specific treatments using standardized adherence ratings approved by the respective protocol developers. Treatment fidelity scores were good to excellent (mean: UP = 4.44; SDPs = 4.09 out of 5).

Assessments and Instruments

Patients were assessed for current DSM diagnoses using the Anxiety Disorders Interview Schedule (ADIS^{36, 37}), a semi-structured clinical interview that focuses on DSM diagnoses of anxiety, mood, somatic symptom, and substance use disorders, with screening for other disorders. Diagnoses are assigned a dimensional clinical severity rating (CSR) on a scale from 0 (no symptoms) to 8 (extremely severe symptoms), with a rating of 4 or above (definitely disturbing/disabling) representing the clinical threshold for DSM diagnostic criteria.¹ The ADIS CSR was assessed by study evaluators blinded to condition allocation, and served as the primary outcome for the power analysis and a priori specification of the equivalence margin. To maintain interrater reliability throughout the trial, a study evaluator was randomly selected each month to rate an audiotaped assessment conducted by another evaluator; rated assessments were equally

¹ Due to the introduction of DSM-5 partway through the trial, 168 patients (75%) were assigned diagnoses based on DSM-IV criteria and 55 patients (25%) were assigned diagnoses based on DSM-5 criteria. To standardize clinical severity ratings across these phases, an additional rating was assigned to overall PD/A symptoms for those patients diagnosed according to DSM-5, despite the separation of panic disorder and agoraphobia in DSM-5.

distributed across principal diagnoses and time points. Using criteria specified in Brown et al.,³⁸ interrater agreement was 98% for principal diagnosis ADIS CSR.

Clinical response was assessed using the clinician-rated Clinical Global Impression Severity (CGI-S) and Improvement Scales (CGI-I).³⁹ General symptoms of anxiety and depression were assessed using the clinician-rated Hamilton Anxiety Rating Scale⁴⁰ and the Hamilton Rating Scale for Depression⁴¹ in accordance with the Structured Interview Guide for the Hamilton Anxiety and Depression Rating Scale (SIGH-A and SIGH-D).^{42,43} Self-reported outcomes included the Overall Anxiety Severity and Impairment Scale (OASIS)⁴⁴ and Overall Depression Severity and Impairment Scale (ODSIS).⁴⁵ In addition, self-reported interference in the areas of work, home management, private leisure, social leisure, and family relationships was assessed with the Work and Social Adjustment Scale (WSAS).^{46,47} Additional clinician-rated measures were used to assess diagnosis-specific symptom outcomes and these results are presented in eTables 1-3. Patients were assessed at baseline, following every four treatment sessions (i.e., after sessions 4, 8, 12), posttreatment (i.e., after session 16), and at 6-month follow-up.

Sample Size Calculation

Power calculations were performed using SAS PROC POWER⁴⁸ for the primary aims of 1) evaluating equivalence of the UP and SDPs, and 2) evaluating the efficacy of the UP and SDPs relative to a benchmark WLC, and were based on conventional target values of power = 0.80 and alpha = 0.05. Using an allocation ratio of 2:1 for active treatment to WLC groups, results of the power calculations indicated that a sample size

of 91 per active treatment group provided adequate power for the analyses of both equivalence and superiority.

Statistical Analysis

All analyses were conducted with Mplus 7.2⁴⁹ on the intent-to-treat sample that included all randomized patients (i.e., 88 patients for the UP, 91 for the SDP, and 44 for the WLC conditions, respectively). Missing data were accommodated using multiple imputation (10000 imputed datasets) and robust maximum likelihood methods under a missing at random assumption. Between-condition effect sizes (Cohen's *d*) were calculated for each condition comparison using the imputed data.

The principal hypothesis of equivalence was evaluated using slope difference scores from latent growth models (LGM) with treatment condition as a predictor of slope. The intercept was centered on the baseline assessment, the intermediate slope loadings were freely estimated, and the final slope loading was fixed at 1.0. Slopes therefore represented total change from baseline to post-treatment (or follow-up) and could reflect nonlinear trajectories of change. Model fit was evaluated based on the confirmatory fit index (CFI; ≥ 0.90). The equivalence margin of 0.75 ADIS CSR units was selected based on available meta-analytic reviews of CBT outcome studies⁵⁰ and recommendations for selecting a priori equivalence limits.⁵¹ A priori calculations determined that the 0.75 ADIS CSR margin corresponded with changes of 0.61 and 0.64 units at posttreatment on the SIGH-A and SIGH-D, respectively, and was selected as this difference or less would not represent a clinically meaningful difference between two treatments that would lead us to prefer one over the other. If the entire confidence interval for the observed mean difference between the UP and SDPs falls within the zone of equivalence (-0.75, +0.75),

the two treatments would be determined equivalent. To minimize inflation of type I error, comparisons among conditions were based primarily on the interpretation of confidence intervals and effect sizes.

To compare the UP and SDPs on other outcomes and to evaluate the UP and SDPs relative to the WLC, a 95% CI of between-condition effect sizes from LGM was utilized. Treatment response rates were evaluated by comparing the percentage of individuals in each condition who no longer met diagnostic criteria for their principal diagnosis (i.e., ADIS CSR ≤ 3) and by calculating the relative risk (RR) effect size with 95% CI. As an exploratory analysis, the percentage of individuals who no longer met diagnostic criteria for any emotional disorder (i.e., principal or comorbid) was also examined in each condition.

RESULTS

Sample Characteristics

Table 1 contains demographic and baseline diagnostic characteristics of patients within and across conditions. Most patients met criteria for at least one comorbid diagnosis (188 [84.3]) and the mean (SD) number of comorbid diagnoses was 2.29 (1.80). There were no differences in clinical severity or prevalence of comorbid disorders. The only demographic difference at baseline was that the WLC condition had a higher rate of married patients than the UP or SDP conditions ($\chi^2 = 10.97, p = .002$).

Treatment Credibility and Attrition

There were no statistically significant differences in patients' ratings of perceived credibility or expectancy between the UP and SDP conditions, as measured by ratings on the Credibility/ Expectancy Questionnaire.⁵² Patients in the UP condition (87.5%) were more likely to be classified as treatment completers (i.e., $\geq 75\%$ of sessions completed) than patients in the SDP condition (69.2%; odds ratio, 3.11; 95% CI, 1.44 to 6.74).

Equivalence

Slope difference scores and between-condition effect sizes for all outcomes from the LGM are presented in Table 2. Results of the LGM for principal diagnosis CSR were used to examine the primary research question of statistical equivalence of the UP and SDPs. The estimate of the UP vs SDPs effect on the slope of change in principal diagnosis CSR from baseline to posttreatment was 0.25 (95% CI, -0.26 to 0.75); from baseline to follow-up was 0.16 (95% CI, -0.39 to 0.70). The confidence intervals for the changes in CSR fell entirely within the pre-specified 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 both posttreatment and 6-month follow-up (Figure 2). The effect size (Cohen's *d*) difference for the slope of change in principal diagnosis from baseline to posttreatment was 0.15 (95% CI, -0.16 to 0.46); from baseline to follow-up was 0.10 (95% CI, -0.24 to 0.44).

Additional Clinician-Rated and Self-Reported Outcomes

The imputed means and between-condition effect sizes for the primary outcome, as well as other additional outcomes of interest are reported in Table 3. Consistent with hypotheses, the UP and SDPs each demonstrated superior effects to the WLC on both clinician-rated and self-reported outcomes of anxiety and depression based on the confidence intervals of the effect sizes. Effect sizes for comparisons of the UP vs SDPs at posttreatment and follow-up for all clinical outcomes were generally small and statistically non-significant; these findings were consistent across both the LGM-derived slope difference scores (Table 2) and effect sizes (Table 3). Change score means and within-condition effect sizes are reported in eTable 4.

Treatment Response and Remission

At posttreatment, 64% of patients in the UP condition no longer met diagnostic criteria for their principal diagnosis, compared to 57% and 27% in the SDP and WLC conditions, respectively. For the UP and SDP conditions, these percentages increased to 71% and 62%, respectively, at 6-month follow-up. The UP (RR = 2.38; 95% CI, 1.42 to 3.98) and SDP (RR = 2.15; 95% CI, 1.27 to 3.61) conditions were both associated with a significantly greater proportion of patients no longer meeting diagnostic criteria for their principal diagnosis than in the WLC condition.

As an exploratory analysis, we also examined the proportion of individuals who no longer met diagnostic criteria for any emotional disorder following treatment. At posttreatment, 62% of individuals in the UP condition no longer met diagnostic criteria for any emotional disorder, compared to 47% and 13% in the SDP and WLC conditions, respectively. These percentages decreased slightly to 57% and 41% for the UP and SDP conditions at 6-month follow-up.

DISCUSSION

Results indicated treatment equivalence of the UP and four different SDPs on changes in principal diagnosis severity at both posttreatment and 6-month follow-up, with the UP evidencing significantly less attrition than the SDPs possibly due to the inclusion of strategies for enhancing motivation. Treatment with both the UP and SDPs was consistently associated with improved outcomes relative to WLC on clinician-rated and self-reported outcomes. Also, relative to the WLC, patients receiving either the UP or SDPs had a greater chance of no longer meeting criteria for their principal diagnosis at posttreatment.

These findings provide support for the utility of a parsimonious, mechanism-focused transdiagnostic approach consisting of five core modules for addressing the most commonly occurring mental disorders. The present study also demonstrates that patients with diverse diagnoses view a transdiagnostic approach to be as credible as SDPs, which is an important consideration given the increasing emphasis on patient preferences in the implementation of EBPTs⁵³ and the finding that patients generally prefer psychosocial treatment options to other approaches.⁵⁴

Clinical trials are commonly criticized for failing to replicate the comorbidity and clinical complexity that clinicians encounter in real-world settings.⁵⁵⁻⁵⁷ However, inclusion criteria for this trial were liberal, including the full range of comorbid disorders thus allowing for significant heterogeneity among patients and, consequently, greater generalizability of results. Over 50% of patients were on psychotropic medications and approximately 30% were receiving non-CBT psychotherapy at the intake which was discontinued if the focus was on anxiety. In addition, most patients had received some

form of previous treatment that failed to provide significant or lasting symptom remission.

Results from this trial should be interpreted in the context of several limitations. Patients in both groups were generally well-educated, and somewhat less depressed than comparable samples which may have augmented their ability to benefit from treatment, although prior studies have failed to observe consistent effects of education level on treatment outcome in anxiety disorders.⁵⁸ More importantly, the UP was developed at CARD (as were three of the four SDPs), and thus it is possible these results may not fully generalize to other clinical settings.

Nevertheless, utilizing a single protocol designed to target temperamental factors underlying the development and maintenance of the full range of emotional disorders has implications for bridging the science-to-service gap. Training providers in the delivery of one protocol that can simultaneously target commonly comorbid disorders may be more efficient and cost effective, as providers are adhering to core strategies that can be flexibly applied to a range of emotional experiences. Thus, a transdiagnostic approach, such as the UP, may decrease known barriers of receiving an EBPT delivered with fidelity, at an adequate dose, in a cost- and time-efficient manner.

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Study concept and design: Barlow, Farchione, Murray-Latin, Thompson-Hollands, Carl

Acquisition, analysis, or interpretation of the data: All authors

Drafting of the manuscript: Barlow, Farchione, Bullis, Gallagher, Murray-Latin, Bentley

Critical revision of the manuscript for important intellectual content: Barlow, Farchione, Bullis

Statistical analysis: Gallagher

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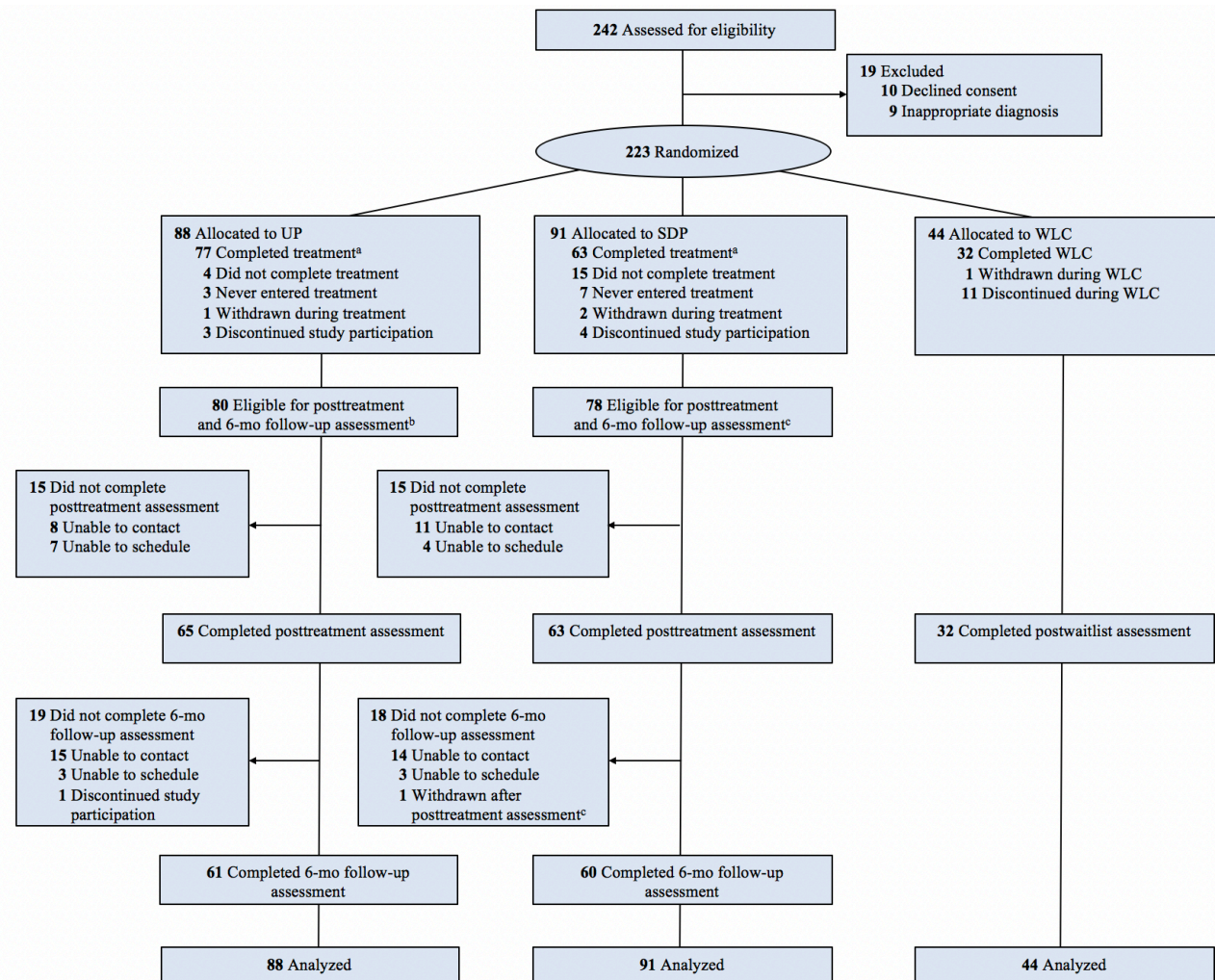
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Figure 1. Recruitment Flow Diagram for Unified Protocol (UP) Single-Disorder Protocol (SDP), and Waitlist Control (WLC) Conditions.



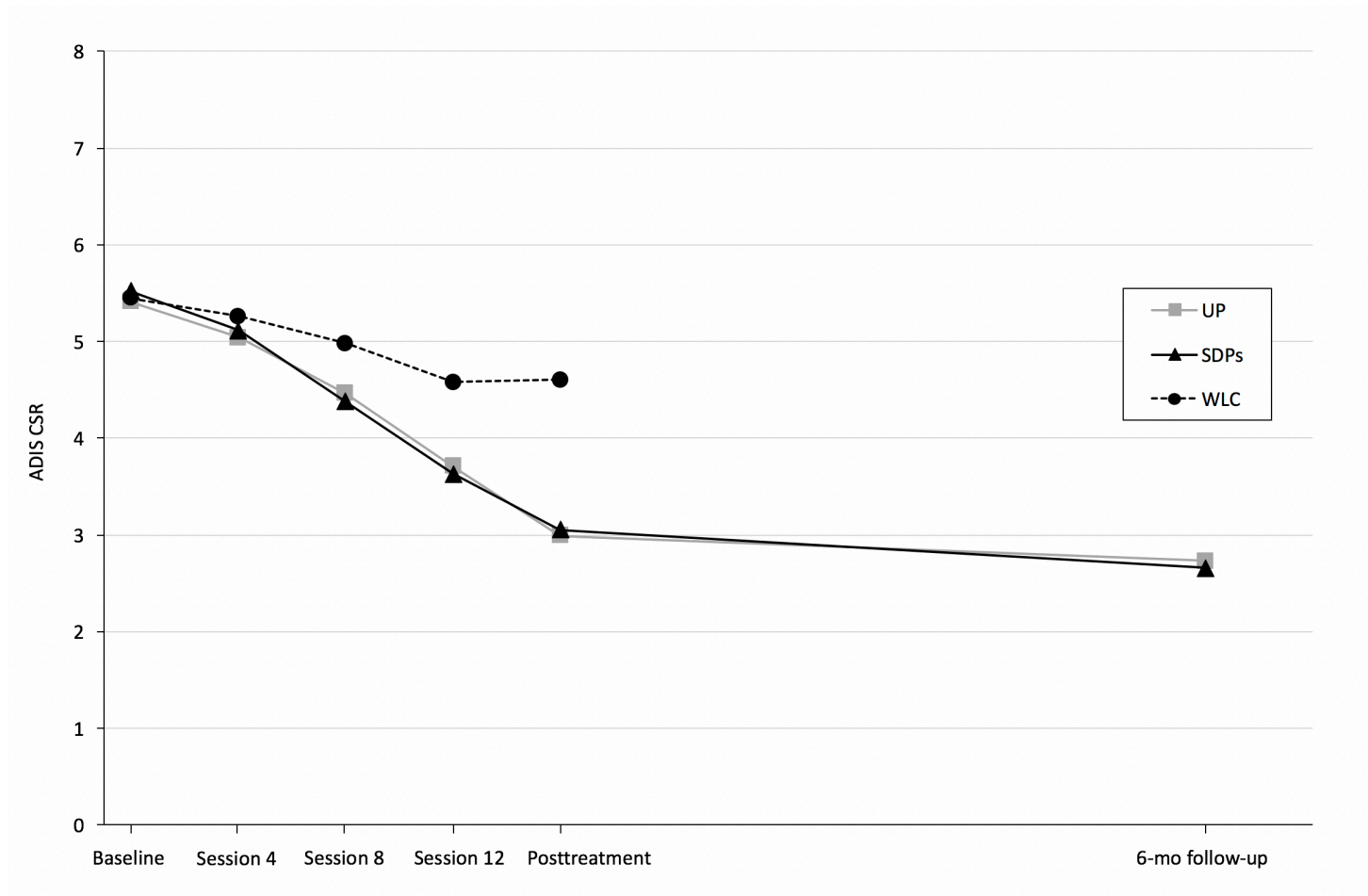
Abbreviations: UP, Unified Protocol; SDP, Single-Disorder Protocol; WLC, waitlist control.

^aCompleted treatment indicates that the patient attended at least 75% of allotted number of sessions (i.e., 9 of 12 for PD/A and 12 of 16 for other principal diagnoses).

^bOne patient with principal PD/A completed 12 sessions but was withdrawn prior to the posttreatment assessment (i.e., completed treatment, but was not eligible for posttreatment assessment).

^cOne patient was withdrawn from the study after completing the posttreatment assessment, but prior to 6-month follow-up, so was no longer eligible for 6-month follow-up; however, this individual is included in the “eligible for posttreatment and 6-month follow-up” classification ($n = 78$).

Figure 2. Model-Based Estimates of the Principal Diagnosis ADIS CSR Score Trajectories from Baseline to 6-Month Follow-Up.



Abbreviations: UP, Unified Protocol; SDP, Single-Disorder Protocol; WLC, waitlist control; ADIS CSR, clinical severity rating for principal diagnosis obtained from Anxiety Disorder Interview Schedule.

Table 1. Baseline Demographic and Diagnostic Characteristics by Condition.

Variable	No. (%)			
	Total (N = 223)	Condition		
		UP (n = 88)	SDP (n = 91)	WLC (n = 44)
Age, mean (SD), y	31.1 (11.0)	31.0 (11.6)	30.4 (10.0)	32.7 (11.9)
Female sex	124 (55.6)	48 (54.5)	51 (56.0)	25 (56.8)
Hispanic	17 (7.6)	3 (3.4)	12 (13.2)	2 (4.5)
Race				
White	186 (83.4)	73 (83.0)	76 (83.5)	37 (84.1)
Asian	16 (7.2)	6 (6.8)	6 (6.6)	4 (9.1)
African American	15 (6.7)	8 (9.1)	5 (5.5)	2 (4.5)
Other	6 (2.6)	1 (1.1)	4 (4.4)	1 (2.3)
Married	47 (21.1)	14 (15.9)	15 (16.5)	18 (40.9) ^a
College degree or greater	149 (66.8)	50 (56.8)	63 (69.2)	36 (81.8)
Current psychotropic medication	121 (54.3)	47 (53.4)	53 (58.2)	21 (47.7)
Current psychotherapy	65 (29.1)	32 (36.4)	22 (24.2)	11 (25.0)
Previous psychiatric hospitalization	32 (14.3)	11 (12.5)	15 (16.5)	6 (13.6)
Principal diagnosis				
OCD	44 (19.7)	18 (20.5)	17 (18.7)	9 (20.5)
GAD	62 (27.8)	22 (25.0)	27 (29.7)	13 (29.5)
P/DA	59 (26.5)	25 (28.4)	22 (24.2)	12 (27.3)
SAD	58 (26.0)	23 (26.1)	25 (27.5)	10 (22.7)
Comorbid diagnoses ^b				
Any	188 (84.3)	72 (81.8)	78 (85.7)	38 (86.4)
OCD	15 (6.7)	3 (3.4)	10 (11.0)	2 (4.5)
GAD	40 (17.9)	11 (12.5)	20 (22.0)	9 (20.5)
P/DA	12 (5.2)	3 (3.4)	5 (5.5)	4 (9.1)
SAD	55 (24.7)	23 (26.1)	20 (22.0)	12 (27.3)
MDD	31 (13.9)	12 (13.6)	9 (9.9)	10 (22.7)
SP	36 (16.1)	15 (17.0)	14 (15.4)	7 (15.9)

Abbreviations: UP, Unified Protocol; SDP, single-disorder protocol; WLC, waitlist control; OCD, obsessive-compulsive disorder; GAD, generalized anxiety disorder; P/DA, panic disorder with or without agoraphobia; SAD, social anxiety disorder; MDD, major depressive disorder; SP, specific phobia.

^aSignificantly different using 2-tailed *t* test at $p < .05$.

^bComorbid diagnoses that were present in less than 20 cases are not listed separately in the table but are included in the “any” comorbid disorder category and the number of comorbid disorders.

Table 2. Slope Difference Scores and Between-Condition Effect Sizes from Growth Curve Models.

Outcome and Visit	Slope Difference Score, Mean (95% CI) ^a			Effect Size, Cohen's <i>d</i> (95% CI) ^a		
	UP vs WLC	SDP vs WLC	UP vs SDP	UP vs WLC	SDP vs WLC	UP vs SDP
Primary Clinician-Rated Outcome						
ADIS CSR						
Posttreatment	-1.51 (-2.14 to -0.87)	-1.75 (-2.40 to -1.10)	0.25 (-0.26 to 0.75)	-0.93 (-1.29 to -0.57)	-1.08 (-1.43 to -0.73)	0.15 (-0.16 to 0.46)
6-mo Follow-up			0.16 (-0.39 to 0.70)			0.10 (-0.24 to 0.44)
Additional Clinician-Rated Outcomes						
CGI-S						
Posttreatment	-1.47 (-1.96 to -0.98)	-1.40 (-1.90 to -0.91)	-0.07 (-0.46 to 0.32)	-1.36 (-1.76 to -0.97)	-1.30 (-1.70 to -0.90)	-0.06 (-0.43 to 0.30)
6-mo Follow-up			-0.05 (-0.45 to 0.36)			-0.05 (-0.45 to 0.36)
CGI-I						
Posttreatment	-1.20 (-1.67 to -0.73)	-1.06 (-1.53 to -0.59)	-0.14 (-0.50 to 0.22)	-1.54 (-2.18 to -0.90)	-1.36 (-2.01 to -0.71)	-0.18 (-0.64 to 0.28)
6-mo Follow-up			-0.07 (-0.41 to 0.26)			-0.06 (-0.31 to 0.20)
SIGH-A						
Posttreatment	-4.90 (-7.91 to -1.88)	-6.86 (-9.83 to -3.89)	1.96 (-0.41 to 4.34)	-0.86 (-1.37 to -0.36)	-1.21 (-1.68 to -0.74)	0.35 (-0.07 to 0.76)
6-mo Follow-up			2.09 (-0.37 to 4.55)			0.35 (-0.05 to 0.74)
SIGH-D						
Posttreatment	-3.59 (-6.09 to -1.09)	-3.53 (-6.01 to -1.04)	-0.06 (-2.05 to 1.92)	-1.20 (-2.16 to -0.24)	-1.18 (-2.12 to -0.23)	-0.02 (-0.68 to 0.64)
6-mo Follow-up			0.07 (-1.86 to 2.01)			0.02 (-0.46 to 0.50)
Self-Reported Outcomes						
OASIS						
Posttreatment	-4.25 (-5.68 to -2.82)	-4.47 (-5.92 to -3.02)	0.22 (-0.96 to 1.40)	-1.39 (-1.82 to -0.95)	-1.46 (-1.90 to -1.02)	0.07 (-0.31 to 0.46)
6-mo Follow-up			0.37 (-0.81 to 1.55)			0.13 (-0.28 to 0.54)
ODSIS						
Posttreatment	-1.69 (-3.19 to -0.18)	-0.68 (-2.18 to 0.82)	-1.01 (-2.19 to 0.17)	-0.73 (-1.35 to -0.10)	-0.29 (-0.93 to 0.34)	-0.44 (-0.94 to 0.07)
6-mo Follow-up			-0.55 (-1.77 to 0.67)			-0.20 (-0.65 to 0.25)
WSAS						
Posttreatment	-6.63 (-9.47 to -3.79)	-6.22 (-9.07 to -3.38)	-0.41 (-2.65 to 1.83)	-1.16 (-1.60 to 0.72)	-1.09 (-1.54 to -0.64)	-0.07 (-0.46 to 0.32)
6-mo Follow-up			-0.47 (-2.77 to 1.84)			-0.08 (-0.50 to 0.33)

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

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

Slope difference scores and between-condition effect sizes for diagnosis-specific outcomes are reported in eTable 4.

Table 3. Means and Between-Condition Effect Sizes of Outcomes.

Outcome and Visit	Mean (SD)			Effect Size, Hedges g (95% CI) ^a		
	UP (n = 88)	SDP (n = 91)	WLC (n = 44)	UP vs WLC	SDP vs WLC	UP vs SDP
Primary Clinician-Rated Outcome						
ADIS CSR						
Baseline	5.41 (0.76)	5.52 (0.80)	5.45 (0.69)	-0.05 (-0.41 to 0.31)	0.09 (-0.27 to 0.45)	-0.14 (-0.43 to 0.16)
Posttreatment	2.99 (1.84)	3.05 (2.02)	4.60 (1.61)	-0.91 (-1.29 to -0.53)	-0.81 (-1.19 to -0.44)	-0.03 (-0.32 to 0.26)
6-mo Follow-up	2.73 (1.71)	2.66 (2.06)				0.03 (-0.26 to 0.33)
Additional Clinician-Rated Outcomes						
CGI-S						
Baseline	4.60 (0.90)	4.74 (0.98)	4.61 (0.71)	-0.01 (-0.38 to 0.35)	0.13 (-0.23 to 0.49)	-0.14 (-0.44 to 0.15)
Posttreatment	3.11 (1.34)	3.15 (1.49)	4.25 (1.15)	-0.89 (-1.26 to -0.51)	-0.79 (-1.16 to -0.42)	-0.03 (-0.32 to 0.26)
6-mo Follow-up	3.01 (1.41)	3.01 (1.35)				0.00 (-0.29 to 0.29)
CGI-I						
Session 1	3.49 (0.67)	3.49 (0.78)	3.74 (0.97)	-0.31 (-0.68 to 0.05)	-0.30 (-0.66 to 0.06)	0.01 (-0.28 to 0.30)
Posttreatment	2.22 (1.15)	2.39 (1.32)	3.38 (0.98)	-1.05 (-1.43 to -0.67)	-0.81 (-1.18 to -0.43)	-0.14 (-0.43 to 0.16)
6-mo Follow-up	2.30 (1.45)	2.21 (1.24)				0.07 (-0.22 to 0.36)
SIGH-A						
Baseline	17.06 (8.50)	17.01 (9.51)	16.77 (8.44)	0.03 (-0.33 to 0.40)	0.03 (-0.33 to 0.39)	0.01 (-0.29 to 0.30)
Posttreatment	10.38 (8.07)	8.94 (8.08)	14.63 (7.80)	-0.53 (-0.90 to -0.16)	-0.71 (-1.08 to -0.34)	0.18 (-0.12 to 0.47)
6-mo Follow-up	9.94 (7.94)	8.95 (8.49)				0.12 (-0.17 to 0.41)
SIGH-D						
Baseline	11.55 (7.02)	11.49 (6.30)	11.82 (6.32)	-0.04 (-0.40 to 0.32)	-0.05 (-0.41 to 0.31)	0.01 (-0.28 to 0.30)
Posttreatment	7.21 (6.12)	7.20 (7.10)	10.76 (6.20)	-0.57 (-0.94 to -0.21)	-0.52 (-0.88 to -0.15)	0.00 (-0.29 to 0.29)
6-mo Follow-up	7.57 (6.79)	6.87 (7.04)				0.10 (-0.19 to 0.39)
Self-Reported Outcomes						
OASIS						
Baseline	9.68 (3.81)	10.37 (6.30)	9.62 (3.77)	0.02 (-0.35 to 0.38)	0.13 (-0.23 to 0.49)	-0.13 (-0.42 to 0.16)
Posttreatment	4.70 (3.18)	4.98 (4.24)	7.91 (4.10)	-0.91 (-1.29 to -0.53)	-0.70 (-1.07 to -0.33)	-0.07 (-0.37 to 0.22)
6-mo Follow-up	4.86 (4.03)	4.78 (3.88)				0.02 (-0.27 to 0.31)
ODSIS						
Baseline	5.38 (5.14)	5.28 (4.69)	6.09 (5.00)	-0.14 (-0.50 to 0.22)	-0.17 (-0.53 to 0.19)	0.02 (-0.27 to 0.31)

Posttreatment	2.95 (3.82)	3.11 (4.17)	4.88 (5.09)	-0.45 (-0.81 to -0.08)	-0.39 (-0.76 to -0.03)	-0.04 (-0.33 to 0.25)
6-mo Follow-up	3.49 (4.39)	2.65 (3.88)				0.20 (-0.09 to 0.49)
WSAS						
Baseline	15.09 (7.36)	15.04 (6.38)	15.55 (6.89)	-0.06 (-0.42 to 0.30)	-0.08 (-0.44 to 0.28)	0.01 (-0.29 to 0.30)
Posttreatment	7.63 (7.61)	7.75 (7.67)	13.58 (7.52)	-0.78 (-1.15 to -0.41)	-0.76 (-1.13 to -0.39)	-0.02 (-0.31 to 0.28)
6-mo Follow-up	6.85 (7.07)	6.59 (7.95)				0.03 (-0.26 to 0.33)

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

^aNegative effect sizes indicate that the treatment listed first was associated with lower levels of the outcome and positive effect sizes indicate that the treatment listed first was associated with higher levels of the outcome.

Means and between-condition effect sizes for diagnosis-specific outcomes are reported in eTable 2.