ORIGINAL ARTICLE

# Disorder-Specific Impact of Coordinated Anxiety Learning and Management Treatment for Anxiety Disorders in Primary Care

*Michelle G. Craske, PhD; Murray B. Stein, MD, MPH; Greer Sullivan, MD; Cathy Sherbourne, PhD; Alexander Bystritsky, MD; Raphael D. Rose, PhD; Ariel J. Lang, PhD; Stacy Welch, PhD; Laura Campbell-Sills, PhD; Daniela Golinelli, PhD; Peter Roy-Byrne, MD*

**Context:** Anxiety disorders commonly present in primary care, where evidence-based mental health treatments often are unavailable or suboptimally delivered.

**Objective:** To compare evidence-based treatment for anxiety disorders with usual care (UC) in primary care for principal and comorbid generalized anxiety disorder (GAD), panic disorder (PD), social anxiety disorder (SAD), and posttraumatic stress disorder (PTSD).

**Design:** A randomized controlled trial comparing the Coordinated Anxiety Learning and Management (CALM) intervention with UC at baseline and at 6-, 12-, and 18-month follow-up assessments.

**Setting:** Seventeen US primary care clinics.

**Patients:** Referred primary care sample, 1004 patients, with principal *DSM-IV* diagnoses of GAD (n=549), PD (n=262), SAD (n=132), or PTSD (n=61) (mean [SD] age, 43.7 [13.7] years; 70.9% were female). Eighty percent of the participants completed 18-month follow-up.

**Interventions:** CALM (cognitive behavior therapy and pharmacotherapy recommendations) and UC.

**Main Outcome Measures:** Generalized Anxiety Disorder Severity Scale, Panic Disorder Severity–Self-report Scale, Social Phobia Inventory, and PTSD Checklist–Civilian Version scores.

**Results:** CALM was superior to UC for principal GAD at 6-month (−1.61; 95% confidence interval [CI], −2.42 to −0.79), 12-month (−2.34; −3.22 to −1.45), and 18-month (−2.37; −3.24 to −1.50), PD at 6-month (−2.00; −3.55 to −0.44) and 12-month (−2.71; −4.29 to −1.14), and SAD at 6-month (−7.05; −12.11 to −2.00) outcomes. CALM was superior to UC for comorbid SAD at 6-month (−4.26; 95% CI, −7.96 to −0.56), 12-month (−8.12, −11.84 to −4.40), and 18- month (−6.23, −9.90 to −2.55) outcomes. Effect sizes favored CALM but were not statistically significant for other comorbid disorders.

**Conclusions:** CALM (cognitive behavior therapy and pharmacotherapy medication recommendations) is more effective than is UC for principal anxiety disorders and, to a lesser extent, comorbid anxiety disorders that present in primary care.

*Arch Gen Psychiatry. 2011;68(4):378-388*

Anxiety disorders are common, costly, and debilitating.[1-4] Although effective evidence-based psychosocial (ie, cognitive behavior therapy [CBT]) and pharmacologic treatments for anxiety disorders exist, these treatments often are unavailable (ie, CBT) or are suboptimally provided (ie, pharmacotherapy). Because most persons with anxiety disorders present for treatment in primary care,[5-8] we conducted a randomized controlled trial of a collaborative care intervention (ITV) designed to improve evidence-based treatment for anxiety disorders common in primary care. In addition to comparing disorder-specific outcomes between the ITV and usual care (UC) during 18-month follow-up, we aimed to evaluate treatment effects at the level of the individuals in the study, who most often have a constellation of disorders and symptoms rather than a single anxiety disorder.

To implement evidence-based treatments in primary care, innovative approaches were required to overcome the limitations of current models of provision. For example, CBT has evolved into specific applications for specific anxiety disorders, yet separate, uniquely tailored CBT manuals for each principal anxiety disorder are unlikely to be implemented in most treatment settings and especially in primary care. To provide treatment for

**Author Affiliations** are listed at the end of this article.



©2011 American Medical Association. All rights reserved.
Downloaded From: http://jamanetwork.com/ on 05/22/2013

multiple anxiety disorders, we created a model of CBT that addresses the 4 most common anxiety disorders in primary care settings (panic disorder [PD] with or without agoraphobia, generalized anxiety disorder [GAD], social anxiety disorder [SAD], and posttraumatic stress disorder [PTSD])[5] in 1 program. Furthermore, given the relative dearth of highly trained mental health providers available in primary care settings, we designed the CBT program to be used by persons with minimal or no training in mental health. Specifically, we developed a computerized program to guide the mental health provider (and the patient), thereby reducing the amount of expertise and training needed. Computer-assisted programs have been used in training in CBT[9,10] and in self-directed CBT,[11] but they have not been used for ongoing assistance of the mental health provider in the provision of CBT.

The approach to providing pharmacotherapy was also modified to suit the needs of primary care settings. That is, because it is well known that provision of pharmacotherapy in primary care is often of suboptimal quality,[12] we used a "collaborative care model"[13] in which patients remained under the care of their primary care physician while psychiatrists' advice for pharmacotherapy optimization was relayed to primary care physicians by health care managers, or anxiety clinical specialists (ACSs). Patients in the ITV arm had the option of choosing CBT, pharmacotherapy, or both, and ACSs were responsible not only for providing CBT but also for assisting primary care providers in managing medications.

We presented data elsewhere[14] showing that Coordinated Anxiety Learning and Management (CALM) was superior to UC using general outcome measures of anxiety that span disorders rather than disorder-specific measures. The purpose of this study was to address disorder-specific outcomes for each participant's constellation of anxiety disorders. Most individuals with an anxiety disorder meet the diagnostic criteria for at least 1 other diagnosis, most commonly another anxiety or mood disorder, in community-based or population-based samples[1,15] and in samples drawn from treatment settings.[16] Evidence-based treatment efficacy studies, including pharmacotherapy and psychotherapy studies, typically select participants on the basis of a principal disorder, often operationalized as the disorder that is most troubling to the individual or associated with the most distress or interference with functioning. Evaluation of outcome based solely on improvement in this principal disorder means that treatment effects are estimated from only 1 feature, albeit the most pressing, of the entire symptom constellation in each individual. This approach is at variance with the demands of real-world clinical practice, where individual persons with co-occurring disorders, rather than the specific individual disorders, must be treated. To address this issue, we evaluated outcomes not only for the principal disorder but also for comorbid disorders.

Our approach in the CALM ITV was to target the principal anxiety disorder. Because previous research has indicated that adequate CBT of a principal anxiety disorder simultaneously improves rates of comorbid disorders,[17-22] we hypothesized that the CALM ITV would benefit comorbid disorders as well. Previous studies compared CBT with no-treatment comparisons in restricted samples and limited their assessment of comorbidity to diagnostic assignment. The present study investigated the effects of targeted CBT on comorbidity in a generalizable sample relative to a UC comparison using sensitive dimensional measures of comorbid anxiety disorder symptom severity.

## METHODS

### DESIGN

This randomized controlled effectiveness trial compared the CALM ITV with UC in 17 primary care clinics in 4 US cities (Seattle, Washington; San Diego, California; Los Angeles, California; and Little Rock, Arkansas). A total of 1004 patients with anxiety disorders (with or without major depression) were randomized, and those randomized to ITV received treatment for up to 12 months. Blinded assessments occurred 6, 12, and 18 months after baseline.

### PARTICIPANTS

Between June 1, 2006, and April 1, 2008, a total of 1004 primary care patients with PD with or without agoraphobia, GAD, SAD, or PTSD were enrolled. The participating research institutions were the University of Washington, the University of California at Los Angeles, the University of California at San Diego, the University of Arkansas for Medical Sciences, and the RAND Corp (an assessment site only).[23]

#### Recruitment

Primary care providers (PCPs) and clinic nursing staff directly referred potential participants. At some sites, a 5-question anxiety screener, the Overall Anxiety Severity and Impairment Scale,[24] was used to identify potential participants. A trained study clinician, the ACS, functioned as the main care manager/interventionist and as the diagnostician who met with referred participants to determine eligibility. All the participants gave written informed consent to participate in this study, which was approved by each institution's institutional review board.

#### Inclusion Criteria

An eligible participant had to be a patient at a participating clinic, be 18 to 75 years old, meet *DSM-IV* criteria for 1 or more of GAD, PD, SAD, or PTSD (based on the Mini-International Neuropsychiatric Interview)[25] administered by the ACS after formal training and diagnostic reliability testing), and score at least 8 (moderate and clinically significant anxiety symptoms on a scale ranging from 0-20) on the Overall Anxiety Severity and Impairment Scale.[24] On the Mini-International Neuropsychiatric Interview, participants indicated which of the disorders for which they met diagnostic criteria was currently "most troubling" to them, and this became their principal anxiety disorder; other assigned diagnoses became their comorbid anxiety disorders.

#### Exclusion Criteria

Participants with unstable or life-threatening medical conditions, marked cognitive impairment, active suicidal intent or plan, psychosis, or bipolar I disorder were excluded from the



©2011 American Medical Association. All rights reserved.
Downloaded From: http://jamanetwork.com/ on 05/22/2013

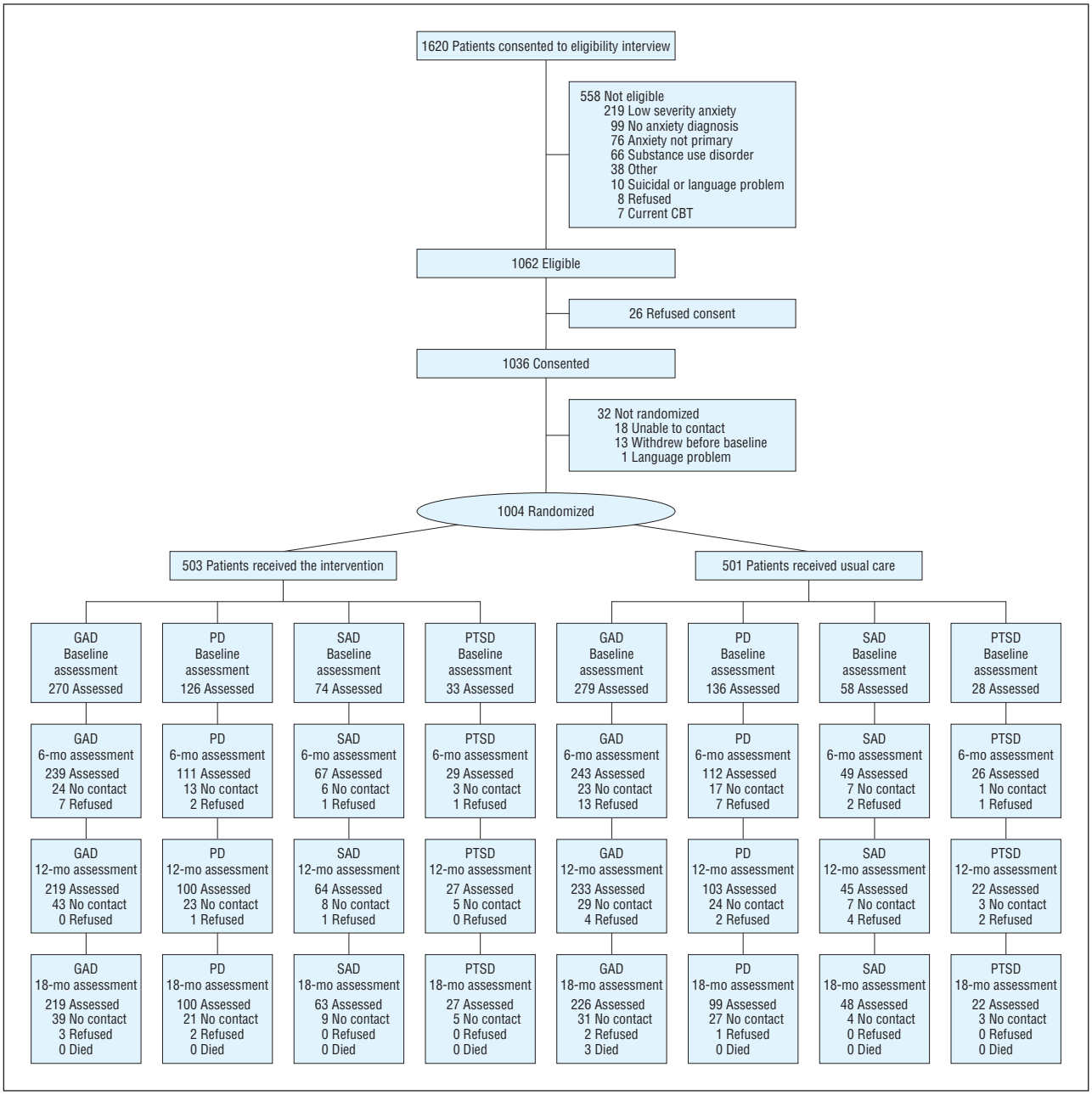


**Figure 1.** Consort diagram. CBT indicates cognitive behavior therapy; GAD, generalized anxiety disorder; PD, panic disorder; PTSD, posttraumatic stress disorder; and SAD, social anxiety disorder.

study. Alcohol and marijuana abuse (but not dependence) was permitted, but other drug abuse or dependence was exclusionary. Participants already receiving ongoing CBT (n=7) were excluded, as were those who could not speak English or Spanish (n=2).

## RANDOMIZATION

After baseline assessment, participants were randomized using stratified (by clinic and presence of comorbid major depression) permuted block randomization to receive ITV or UC by an automated program at RAND. Block size was masked to all clinical site study members. The consort diagram describes patient flow from referral, through eligibility screening, consent, and randomization for each principal anxiety disorder group (**Figure 1**).

## CALM ITV

The ITV participants received a treatment involving pharmacotherapy, computer-assisted CBT, or both, depending on their preference.

### Cognitive Behavior Therapy

The CBT program (called *CALM Tools for Living,* English and Spanish versions) contained 8 modules. The cognitive restructuring and 2 exposure modules were tailored to each of the 4 anxiety disorders through branching mechanisms, whereas the remaining modules (ie, self-monitoring, psychoeducation, fear hierarchy, breathing retraining, and relapse prevention) were mostly generic.[26] Participants selected their most distressing and dis-



©2011 American Medical Association. All rights reserved.
Downloaded From: http://jamanetwork.com/ on 05/22/2013

abling of the 4 anxiety disorders as the primary target in the first CBT session (this corresponded with the principal anxiety disorder designated in the Mini-International Neuropsychiatric Interview in most cases [74%-89% across disorders]).[1] Then, some CBT modules were tailored to the principal disorder (eg, exposure to trauma reminders for PTSD vs interoceptive exposure for PD), whereas the content of other modules was the same regardless of the principal disorder (eg, breathing retraining).

The ACS and the participant viewed the program together on the screen. Throughout, the program provided prompts to ACSs to engage in specific tasks, such as helping participants establish a fear hierarchy, demonstrating breathing skills, practicing cognitive skills, conducting interoceptive exposure, or designing in vivo exposure assignments. Occasionally, the ACS used additional strategies, such as behavioral activation and cognitive restructuring for depressed mood and motivational enhancement strategies, to maintain patient engagement.

### Medication

For participants who selected medication management only or combined with CBT, the ACS provided (56% in person and 43% by telephone) adherence monitoring and counseling to avoid alcohol and caffeine and to optimize sleep hygiene and behavioral activity and relayed feedback to PCPs about medication from the supervising psychiatrist. Medication was prescribed by the PCP. Medication consultation was available from a local study psychiatrist who provided single-session medication management training to PCPs using a simple algorithm.[12] The same algorithm was applied across all 4 anxiety disorders and emphasized first-line use of selective serotonin reuptake inhibitor or serotonin noradrenaline reuptake inhibitor antidepressants, with the goal of increasing the dose to the maximum tolerable dose. Lack of response prompted substitution of a different antidepressant. Suboptimal improvement prompted addition of another antidepressant or a benzodiazepine (in select cases, except PTSD). More elaborate interventions were considered after consultation with the expert study psychiatrist.

### Collaborative Care

The ACSs interacted regularly with PCPs in person and over the telephone. The PCPs remained the clinician of record and prescribed all medications. Psychiatrist consultation to PCPs was readily available by telephone, and more complex or treatment refractory cases could be seen by the psychiatrist for in-person consultation.

### Web-Based Tracking

The ACS tracked participant outcomes using a Web-based tracking system[14] that allowed for real-time monitoring of recruitment, enrollment, diagnoses, ineligibility, patient contact information, and continuous and session symptom assessments using the Overall Anxiety Severity and Impairment Scale[24] and a 3-item version of the Patient Health Questionnaire 9, assessing depressed mood, loss of interest, and fatigue.[27]

### Treatment Steps

The treatment goal was clinical remission (defined as an Overall Anxiety Severity and Impairment Scale score less than 5 ["mild"]), sufficient improvement such that the participant did not want further treatment, or improvement with residual symptoms or problems that required a different kind of treatment not offered in the protocol. After the first 10 to 12 weeks, symptomatic participants could receive more of the same modality (CBT or medication) or the alternative modality for up to 3 more steps (ie, another 10-12 weeks) of treatment. After completion of acute treatment, participants were entered into "continued care" and received monthly follow-up telephone calls to reinforce CBT skills and medication adherence for up to a year from study enrollment.

## ANXIETY CLINICAL SPECIALIST

The 14 ACSs (6 social workers, 5 registered nurses, 2 master's-level psychologists, and 1 doctoral-level psychologist) had some patient care experience (although only 8 had previous mental health care experience) and some exposure to primary care settings but did not have expertise in anxiety management or CBT.[23] All the ACSs were located in the participating primary care clinics.

The ACS training involved 3 full days of didactic presentations about the CBT program, motivational interviewing, evidence-based medications for anxiety, the medication algorithm, and common pitfalls that contribute to medication nonadherence. The CBT training additionally included recommended readings, a detailed content manual,[2] in-person or telephone-administered role-plays, successful completion of 2 training patients, and demonstrated proficiency as evaluated by expert psychologists.[3] Throughout the study, ACSs received ongoing group telephone supervision for approximately 1 hour per week from an expert psychologist and psychiatrist for diagnostic, CBT, and medication management issues.

## USUAL CARE

Participants in the UC group continued to be treated by their physician with medication, whatever counseling they were able to provide, or referral to a mental health specialist.[23] Their only contact with study personnel was for assessment.[14]

## MEASURES

The assessment battery was administered at baseline and at 6, 12, and 18 months via a centralized telephone survey by the RAND survey research group, blinded to group assignment.

### Disorder-Specific Measures

Disorder-specific scales were administered for every anxiety disorder assigned at baseline assessment. Each scale possesses good to excellent psychometric properties. For PD, the 7-item (0-4 scale) Panic Disorder Severity Scale–Self-report (PDSS-SR)[28] was used. For GAD, the 6-item (0-4 scale) Generalized Anxiety Disorder Severity Scale (GADSS)[29-31] was used. For SAD, the 17-item (0-4 scale) Social Phobia Inventory (SPIN)[32] was used. For PTSD, the 17-item (1-5 scale) PTSD Checklist–Civilian Version (PCL-C)[33,34] was used. Criteria for response and remission were consistent across disorders to facilitate comparisons. Given that published rates range from 30% to 50%,[35] "response" was defined as a reduction of 40% or more on each scale or meeting the definition of remission. For "remission," published definitions for cutoff scores were used where available (PDSS-SR: $\leq 7$; SPIN: $\leq 18$) and a similar strategy (ie, indicating no more than mild severity averaged across items) was used to derive cutoff scores for the remaining scales (PCL-C: $\leq 34$; GADSS: $\leq 6$).

### CBT Integrity

For the CALM CBT program, digital recordings of each ACS session at each site (n=259) were randomly selected for ad-



©2011 American Medical Association. All rights reserved.
Downloaded From: http://jamanetwork.com/ on 05/22/2013

**Table 1. Baseline Characteristics of 1004 Study Patients by Principal Anxiety Disorder**

| Characteristic | GAD (n=549) | | | PD (n=262) | | | SAD (n=132) | | | PTSD (n=61) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | ITV (n=270) | UC (n=279) | *P* Value | ITV (n=126) | UC (n=136) | *P* Value | ITV (n=74) | UC (n=58) | *P* Value | ITV (n=33) | UC (n=28) | *P* Value |
| Women, % | 71.48 | 73.48 | .60 | 71.43 | 65.44 | .30 | 64.86 | 67.24 | .78 | 84.85 | 78.57 | .53 |
| Age, mean, y | 43.99 | 46.02 | .37 | 40.60 | 38.75 | .24 | 39.81 | 42.09 | .35 | 47.45 | 47.32 | .97 |
| Education, % | | | | | | | | | | | | |
| <High school | 5.56 | 6.47 | | 6.35 | 2.96 | | 5.41 | 3.45 | | 6.06 | 7.14 | |
| 12 y | 15.19 | 17.99 | .58 | 15.87 | 8.89 | .09 | 13.51 | 32.76 | .04 | 21.21 | 21.43 | .99 |
| >12 y | 79.26 | 75.54 | | 77.78 | 88.15 | | 81.08 | 63.79 | | 72.73 | 71.43 | |
| Ethnicity, % | | | | | | | | | | | | |
| Hispanic | 23.33 | 15.77 | | 14.29 | 25.74 | | 20.27 | 20.69 | | 24.24 | 3.57 | |
| Black | 8.52 | 13.26 | .04 | 15.08 | 11.76 | .04 | 4.05 | 6.90 | .88 | 18.18 | 28.57 | .16 |
| White | 55.19 | 60.57 | | 54.76 | 55.15 | | 63.51 | 58.62 | | 42.42 | 39.29 | |
| Other | 12.96 | 10.39 | | 15.87 | 7.35 | | 12.16 | 13.79 | | 15.15 | 28.57 | |
| No. of chronic medical conditions, % | | | | | | | | | | | | |
| 0 | 21.56 | 15.77 | | 22.22 | 24.26 | | 25.68 | 25.86 | | 12.12 | 3.57 | |
| 1 | 20.07 | 20.77 | .20 | 22.22 | 24.26 | .80 | 28.38 | 24.14 | .85 | 15.15 | 28.57 | .29 |
| 2 | 58.36 | 64.16 | | 55.56 | 51.47 | | 45.95 | 50.00 | | 72.73 | 67.86 | |
| Anxiety disorder, % | | | | | | | | | | | | |
| Panic | 27.04 | 27.60 | .88 | 100.00 | 100.00 | .23 | 29.73 | 25.86 | .62 | 42.42 | 42.86 | .97 |
| GAD | 100.00 | 100.00 | .90 | 53.97 | 39.71 | .02 | 50.00 | 36.21 | .11 | 45.45 | 42.86 | .84 |
| Social phobia | 29.63 | 31.54 | .63 | 34.13 | 27.21 | .23 | 100.00 | 100.00 | .11 | 39.39 | 42.86 | .78 |
| PTSD | 12.22 | 12.54 | .91 | 15.08 | 11.76 | .43 | 9.46 | 17.24 | .19 | 100.00 | 100.00 | .97 |
| Major depressive disorder, % | 67.41 | 66.67 | .85 | 63.49 | 55.88 | .21 | 52.70 | 55.17 | .78 | 87.88 | 85.71 | .80 |
| No. of anxiety disorders, % | | | | | | | | | | | | |
| 1 | 46.30 | 46.95 | .88 | 32.54 | 43.38 | .07 | 35.14 | 43.10 | .35 | 27.27 | 17.86 | .39 |
| 2 | 39.63 | 37.28 | .57 | 38.10 | 38.24 | .98 | 43.24 | 36.21 | .41 | 30.30 | 46.43 | .20 |
| 3 | 12.96 | 12.90 | .98 | 23.02 | 14.71 | .09 | 18.92 | 18.97 | >.99 | 30.30 | 25.00 | .65 |
| 4 | 1.11 | 2.87 | .16 | 6.35 | 3.68 | .33 | 2.70 | 1.72 | .71 | 12.12 | 10.71 | .86 |

Abbreviations: GAD, generalized anxiety disorder; ITV, intervention; PD, panic disorder; PTSD, posttraumatic stress disorder; SAD, social anxiety disorder; UC, usual care.

herence and competency monitoring using a set of 1- to 7-point Likert scales (higher scores represent better performance) completed by 2 PhD-level independent raters who initially demonstrated interrater reliability. Ratings were made of adherence to the content of each module and overall therapist competency (an adherence manual is available on request from Dr Craske).

## STATISTICAL ANALYSIS

All statistical analyses were performed at RAND Corp. We compared demographics and other baseline characteristics between the ITV and UC groups using *t* tests for continuous variables and $\chi^2$ tests for categorical variables. To estimate the ITV effect over time for each principal anxiety disorder and each comorbid anxiety disorder group separately, we jointly modeled the outcomes using a repeated-measures analysis across the 4 assessments (baseline and follow-up at 6, 12, and 18 months) by time, intervention, the interaction of time × intervention, site, and patient characteristics found to be unbalanced ($P<.1$) between ITV and control at baseline (**Table 1**). Time was treated as a categorical variable. To avoid restrictive assumptions, the covariance of the outcomes at the 4 assessment times was left unstructured. We fitted the proposed model using a restricted maximum likelihood approach, which produces valid estimates under the missing-at-random assumption.[36] This approach correctly handles the additional uncertainty arising from missing data and uses all available data to obtain unbiased estimates for model parameters.[37] This is an efficient way of conducting an intention-to-treat analysis because it includes all participants with a baseline assessment: 94 participants (9.4%) completed baseline only, 63 (6.3%) completed baseline and 1 follow-up, 112 (11.2%) completed baseline and 2 follow-ups, and 735 (73.2%) completed baseline and all 3 follow-up assessments. For cross-sectional analyses (such as percentage of responders at the 3 follow-up times), we used attrition weights to correctly account for participants who missed 1 or more follow-up assessments.[38] The statistical software used was SAS version 9 (SAS Institute Inc, Cary, North Carolina). All *P* values were 2-tailed and were adjusted within outcome measures using the Hochberg[39] correction method to account for multiple comparisons.

Analyses were conducted to evaluate the degree to which ITV was more effective than UC for each principal anxiety disorder: GAD (n=549), PD (n=262), SAD (n=132), and PSTD (n=61). We additionally analyzed the degree to which ITV was more effective than UC for each comorbid anxiety disorder, after excluding participants for whom the disorder in question was the principal anxiety disorder, resulting in the following cell sizes: GAD, n=207; PD, n=213; SAD, n=273; and PTSD, n=120. For the principal anxiety disorder analyses, we computed the effect sizes (as defined by Cohen)[40] at all waves and compared them across disorders using a *t* test.



©2011 American Medical Association. All rights reserved.
Downloaded From: http://jamanetwork.com/ on 05/22/2013

**Table 2. Adjusted Mean Disorder-Specific Outcome Scores by Principal Anxiety Disorder[a]**

| Type of Anxiety Disorder | Intervention Group | Usual Care Group | Difference | *P* Value[b] | Effect Size Difference |
|---|---|---|---|---|---|
| GADSS score (n = 548, 481, 452, and 444[c]) | | | | | |
| Baseline | 13.36 (12.91 to 13.80) | 13.72 (13.28 to 14.16) | −0.36 (−0.99 to 0.27) | .26 | −0.08 (−0.21 to 0.06) |
| 6 mo | 8.85 (8.27 to 9.43) | 10.46 (9.89 to 11.03) | −1.61 (−2.42 to −0.79) | <.001 | −0.33 (−0.50 to −0.16) |
| 12 mo | 7.66 (7.03 to 8.29) | 9.99 (9.38 to 10.61) | −2.34 (−3.22 to −1.45) | <.001 | −0.51 (−0.70 to −0.32) |
| 18 mo | 7.27 (6.66 to 7.89) | 9.64 (9.04 to 10.25) | −2.37 (−3.24 to −1.50) | <.001 | −0.64 (−0.87 to −0.40) |
| PDSS-SR score (n = 262, 223, 203, and 199[c]) | | | | | |
| Baseline | 13.83 (12.88 to 14.78) | 13.76 (12.85 to 14.68) | 0.07 (−1.26 to 1.40) | .92 | 0.01 (−0.20 to 0.22) |
| 6 mo | 6.05 (4.96 to 7.14) | 8.05 (6.97 to 9.14) | −2.00 (−3.55 to −0.44) | .04 | −0.35 (−0.62 to −0.08) |
| 12 mo | 5.64 (4.53 to 6.75) | 8.35 (7.26 to 9.44) | −2.71 (−4.29 to −1.14) | .003 | −0.46 (−0.73 to −0.19) |
| 18 mo | 6.13 (4.91 to 7.35) | 7.37 (6.15 to 8.59) | −1.24 (−2.98 to 0.50) | .32 | −0.23 (−0.56 to 0.09) |
| SPIN score (n = 132, 116, 109, and 111[c]) | | | | | |
| Baseline | 40.94 (38.05 to 43.83) | 41.84 (38.55 to 45.13) | −0.90 (−5.34 to 3.55) | .69 | −0.06 (−0.39 to 0.26) |
| 6 mo | 27.42 (24.18 to 30.66) | 34.48 (30.69 to 38.26) | −7.05 (−12.11 to −2.00) | .03 | −0.53 (−0.91 to −0.15) |
| 12 mo | 25.34 (22.13 to 28.55) | 31.05 (27.26 to 34.83) | −5.71 (−10.74 to −0.68) | .08 | −0.42 (−0.80 to −0.05) |
| 18 mo | 24.28 (20.90 to 27.65) | 28.74 (24.84 to 32.65) | −4.46 (−9.70 to 0.77) | .19 | −0.36 (−0.78 to 0.06) |
| PCL-C score (n = 61, 55, 49, and 49[c]) | | | | | |
| Baseline | 57.15 (52.86 to 61.43) | 56.90 (52.25 to 61.56) | 0.24 (−6.24 to 6.72) | .94 | 0.01 (−0.36 to 0.39) |
| 6 mo | 41.79 (35.17 to 48.41) | 46.84 (39.79 to 53.89) | −5.05 (−14.82 to 4.72) | .61 | −0.29 (−0.85 to 0.27) |
| 12 mo | 40.31 (33.71 to 46.91) | 48.01 (40.84 to 55.19) | −7.70 (−17.55 to 2.15) | .49 | −0.43 (−0.99 to 0.12) |
| 18 mo | 40.40 (33.95 to 46.85) | 46.07 (39.08 to 53.07) | −5.67 (−15.29 to 3.95) | .61 | −0.48 (−1.30 to 0.33) |

Abbreviations: GADSS, Generalized Anxiety Disorder Severity Scale; PCL-C, PTSD Checklist–Civilian Version; PDSS-SR, Panic Disorder Severity Scale–Self-report; SPIN, Social Phobia Inventory.

[a] Data are given as adjusted mean (95% confidence interval).The models control for site, education, ethnicity, and number of comorbid anxiety disorders. The model for the PDSS-SR also controls for the presence of comorbid GAD. Intervention × time effects based on the Wald test were significant at $P = .007$ for the PDSS-SR and at $P < .001$ for the GADSS.

[b] All the *P* values come from the longitudinal models (eg, given the estimates of the longitudinal model, we obtained the predicted means at the 4 time points by group and tested their difference at every time point using the correct *t* test).

[c] Values indicate the number of patients at each time point.

## RESULTS

### SAMPLE SELECTION, ATTRITION, AND DESCRIPTION

Figure 1 depicts study participant flow and reasons for ineligibility. Two-thirds of referred participants (1062 of 1620 [65.6%]) were eligible for the study, most of whom (1036 of 1062 [97.6%]) consented to participate, and most of whom (1004 of 1036 [96.9%]) were randomized. Study retention was high. Specifically, nonresponse rates ("no contact" and "cumulative refusals") ranged from 9.8% to 14.9% across all 4 principal anxiety disorders at 6 months, from 17.4% to 22.5% at 12 months, and from 15.9% to 24.0% at 18 months. Most demographic characteristics were similar across the ITV and UC groups in each principal anxiety disorder group (Table 1). There was some imbalance (at $P < .10$) in educational achievement, ethnicity, number of comorbid anxiety disorders, and GAD for PD only, which were used as covariates in the analyses. The sample was approximately 70% female, with somewhat lower rates for SAD and slightly higher rates for PTSD. The mean age was late 30s to late 40s, slightly older in the PTSD group. Most participants (64%-88%) had more than 12 years of education. The sample was ethnically diverse (36%-60% nonwhite). Many participants (46%-73%) had at least 2 chronic medical conditions (self-reported), and most (53%-82%) had more than 1 anxiety disorder and major depressive disorder (53%-88%). Those with PTSD had more physical and mental health comorbidities compared with the other groups.

### CALM PARTICIPATION

During the 1-year ITV, rates of CBT only (32%-43%), medication management only (3%-11%), and CBT plus medication (46%-65%) were similar across the 4 principal anxiety disorder groups, as were the percentage of visits dedicated to CBT vs medication management ($\chi^2_3 = 2.9$, $P = .41$). Participants who chose CBT were encouraged to complete 6 to 8 CBT sessions over 10 to 12 weeks, but flexibility was permitted. The mean number of CBT visits (6.7-8.2) and medication visits (2.1-2.9) and the percentage who completed all visits by 3 months (35%-52%) and by 6 months (85%-92%) were similar across the 4 groups.

### CBT INTEGRITY

Mean (SD) ACS adherence to the CALM CBT protocol was 5.0 (1.3) (on a 7-point scale), with no differences across the 4 principal anxiety disorder groups ($F_{3,258} = 0.62$, $P = .60$). Similarly, mean (SD) ACS competency was 5.3 (1.4) (on a 7-point scale), with no differences across the 4 principal anxiety disorder groups ($F_{3,258} = 2.2$, $P = .08$).



©2011 American Medical Association. All rights reserved.
Downloaded From: http://jamanetwork.com/ on 05/22/2013

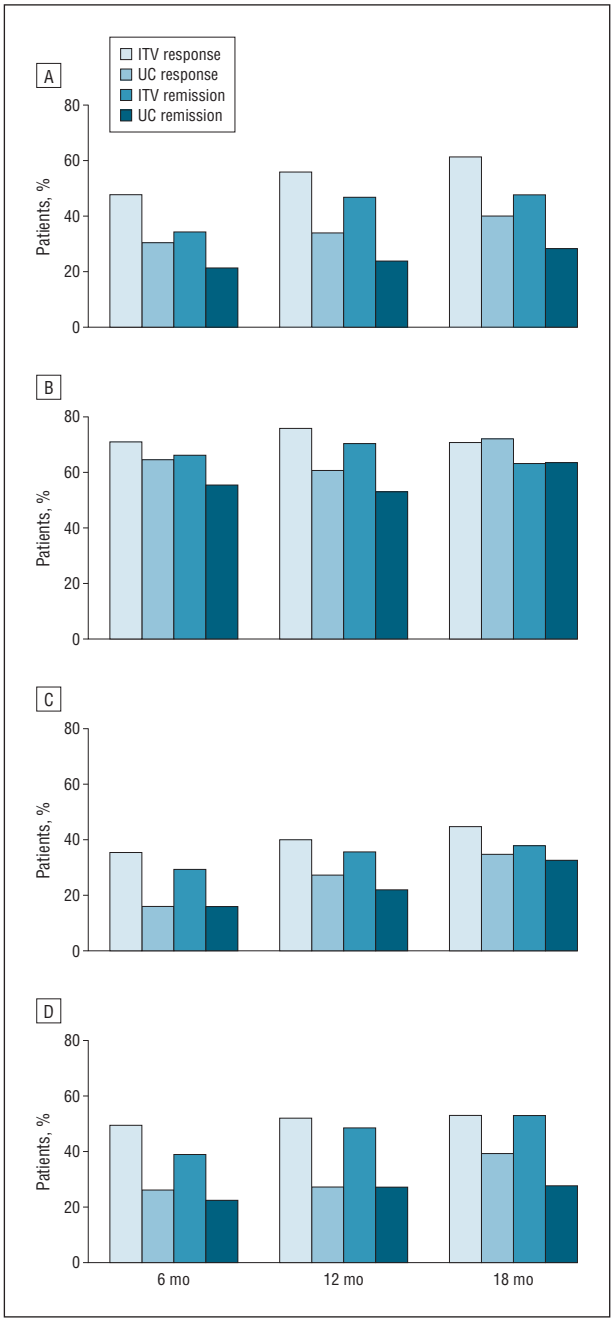


**Figure 2.** Response and remission rates of the intervention (ITV) and usual care (UC) groups for the principal anxiety disorders of generalized anxiety disorder (A), panic disorder (B), social anxiety disorder (C), and posttraumatic stress disorder (D). Response was defined as a reduction of 40% or more on each scale used. Remission was defined by using cutoff scores when available (PDSS-SR [Panic Disorder Severity Scale–Self-report]: ≤7; SPIN: ≤18) or an indication of no more than mild severity averaged across items (PCL-C [PTSD Checklist–Civilian version]: ≤34; and GADSS: ≤6).

## OUTCOMES

### Principal Anxiety Disorder

**Table 2** examines trajectories of adjusted mean scores over time for disorder-specific measures (GADSS, PDSS-SR, SPIN, and PCL-C) for each group. For GAD, GADSS scores were significantly lower in the ITV group than in the UC group at 6 months (effect size [ES], –0.33), 12 months (ES, –0.51), and 18 months (ES, –0.64). For PD, PDSS-SR scores were significantly lower in the ITV group than in the UC group at 6 months (ES, –35) and 12 months (ES, –0.46). For SAD, SPIN scores were significantly lower in the ITV group than in the UC group at 6 months (ES, –0.53). For PTSD, PCL-C scores were not significantly different between the ITV and UC groups at any follow-up assessment, although ESs were of similar magnitude to those of the other disorders: –0.29 at 6 months, –0.43 at 12 months, and –0.48 at 18 months. Effect sizes did not differ significantly across the 4 groups at any of the follow-up assessments with 1 exception: the ES for GAD was significantly larger than that for PD at the 18-month assessment ($P<.02$).

Response and remission rates are given in **Figure 2**. For GAD, response rates were significantly greater in the ITV group than in the UC group at 6 months (number needed to treat [NNT], 5.8; 95% confidence interval [CI], 4.2-9.2; $P<.001$), 12 months (4.6; 3.5-6.5; $P<.001$), and 18 months (4.7; 3.6-6.9; $P<.001$). The same pattern occurred for GAD remission rates at 6 months (NNT, 7.7; 95% CI, 5.1-15.4; $P<.01$), 12 months (4.4; 3.4-6.1; $P<.001$), and 18 months (5.2; 3.8-7.9; $P<.001$).

For PD, response rates were not significantly greater in the ITV group than in the UC group, although remission rates were significantly greater in the ITV group than in the UC group at 12 months (NNT, 5.7; 95% CI, 3.7-13.3; $P<.03$). For SAD, the response rates differed at 6 months (NNT, 5.1; 95% CI, 3.1-15.6; $P<.04$), although remission rates did not differ at any assessment. Finally, neither response nor remission rates to ITV vs UC differed significantly for PTSD, although they were numerically comparable with rates for GAD at 6 and 12 months.

### Comorbid Anxiety Disorders

**Table 3** examines trajectories of adjusted mean scores over time for disorder-specific measures (GADSS, PDSS-SR, SPIN, and PCL-C) for each comorbid anxiety disorder group. There was some imbalance (at $P<.10$) in age, ethnicity, and number of chronic medical conditions, which were used as covariates in the analyses. Although ESs always favored ITV, scores on the disorder-specific measures did not differ significantly between the ITV and UC groups at any follow-up assessment for GAD (ESs, –0.18 to –0.24), PD (ESs, –0.21 to –0.33), and PTSD (ESs, –0.18 to –0.33). Only for SAD were there significant differences, favoring ITV, at 6, 12, and 18 months (ESs, –0.29 to –0.55).

## COMMENT

The primary goals of this study were to evaluate the relative effectiveness of CBT and psychotropic medication recommendations compared with UC for each of 4 anxiety disorders when each presented as a principal anxiety disorder and the degree to which treatment effects extended beyond the principal disorder to symptoms of comorbid anxiety disorders. The ESs indicated that the ITV was superior to UC at 1 or more time points in the treatment of each principal anxiety disorder, although effects were not statistically significant for PTSD. Also, ESs indicated that the ITV was superior to UC for co-



©2011 American Medical Association. All rights reserved.
Downloaded From: http://jamanetwork.com/ on 05/22/2013

**Table 3. Adjusted Mean Disorder-Specific Outcome Scores by Comorbid Anxiety Disorders[a]**

| Type of Comorbid Anxiety Disorder | Intervention Group | Usual Care Group | Difference | *P* Value[b] | Effect Size Difference |
|---|---|---|---|---|---|
| GADSS score (n = 207, 171, 159, and 162[c]) | | | | | |
| Baseline | 14.72 (14.06 to 15.38) | 14.78 (14.00 to 15.56) | −0.06 (−1.08 to 0.97) | .91 | −0.01 (−0.22 to 0.20) |
| 6 mo | 9.74 (8.80 to 10.69) | 10.91 (9.76 to 12.07) | −1.17 (−2.67 to 0.33) | .39 | −0.24 (−0.54 to 0.07) |
| 12 mo | 9.18 (8.23 to 10.14) | 10.37 (9.17 to 11.56) | −1.18 (−2.71 to 0.35) | .39 | −0.24 (−0.55 to 0.07) |
| 18 mo | 8.92 (7.95 to 9.88) | 9.59 (8.40 to 10.78) | −0.67 (−2.20 to 0.86) | .78 | −0.18 (−0.60 to 0.24) |
| PDSS-SR score (n = 213, 185, 165, and 162[c]) | | | | | |
| Baseline | 12.73 (11.58 to 13.88) | 13.22 (12.05 to 14.38) | −0.49 (−2.14 to 1.17) | .56 | −0.09 (−0.38 to 0.21) |
| 6 mo | 6.84 (5.64 to 8.05) | 8.46 (7.22 to 9.70) | −1.62 (−3.37 to 0.13) | .21 | −0.25 (−0.52 to 0.02) |
| 12 mo | 5.45 (4.11 to 6.79) | 7.41 (6.04 to 8.78) | −1.96 (−3.90 to −0.02) | .19 | −0.33 (−0.65 to 0.00) |
| 18 mo | 4.73 (3.54 to 5.91) | 5.97 (4.76 to 7.18) | −1.24 (−2.97 to 0.48) | .31 | −0.21 (−0.50 to 0.08) |
| SPIN score (n = 271, 236, 207, and 203[c]) | | | | | |
| Baseline | 37.31 (35.10 to 39.52) | 36.26 (34.06 to 38.46) | 1.05 (−2.08 to 4.18) | .51 | 0.07 (−0.15 to 0.29) |
| 6 mo | 25.29 (22.67 to 27.92) | 29.55 (26.97 to 32.14) | −4.26 (−7.96 to −0.56) | .048 | −0.29 (−0.55 to −0.04) |
| 12 mo | 21.14 (18.50 to 23.78) | 29.26 (26.66 to 31.86) | −8.12 (−11.84 to −4.40) | <.001 | −0.55 (−0.80 to −0.30) |
| 18 mo | 20.35 (17.73 to 22.96) | 26.57 (24.01 to 29.13) | −6.23 (−9.90 to −2.55) | .003 | −0.48 (−0.77 to −0.20) |
| PCL-C score (n = 120, 102, 91, and 92[c]) | | | | | |
| Baseline | 55.27 (51.87 to 58.67) | 55.48 (52.21 to 58.75) | −0.21 (−5.03 to 4.61) | .93 | −0.01 (−0.30 to 0.28) |
| 6 mo | 41.97 (37.78 to 46.15) | 47.64 (43.46 to 51.83) | −5.67 (−11.69 to 0.34) | .26 | −0.33 (−0.68 to 0.02) |
| 12 mo | 41.00 (36.14 to 45.87) | 45.19 (40.35 to 50.04) | −4.19 (−11.14 to 2.76) | .71 | −0.28 (−0.73 to 0.18) |
| 18 mo | 40.07 (35.33 to 44.82) | 42.32 (37.58 to 47.06) | −2.24 (−9.04 to 4.55) | .93 | −0.18 (−0.71 to 0.36) |

Abbreviations: GADSS, Generalized Anxiety Disorder Severity Scale; PCL-C, PTSD Checklist–Civilian Version; PDSS-SR, Panic Disorder Severity Scale–Self-report; SPIN, Social Phobia Inventory.

[a] Data are given as adjusted mean (95% confidence interval). The models control for site, age, ethnicity, and number of chronic medical conditions. Intervention × time effects based on the Wald test were significant for the SPIN at $P < .001$.

[b] All the *P* values come from the longitudinal models (eg, given the estimates of the longitudinal model we obtained the predicted means at the 4 time points by intervention group and tested their difference at every time point using the correct *t* test).

[c] Values indicate the number of patients at each time point.

morbid anxiety symptoms, although the only comorbid anxiety to statistically significantly benefit from the ITV over and above UC was SAD.

The sample was ethnically diverse, medically ill, and highly comorbid for anxiety disorders and major depressive disorder. GAD was the most common principal anxiety disorder (55%), followed by PD (26%), then SAD (13%), and PTSD (6%). Retention in the study and participation in the CALM ITV were relatively similar across the 4 anxiety disorders. Also, most of each anxiety disorder group selected CBT with or without medication. Furthermore, nonexpert clinicians (ACSs) were equally successful in adhering to and competently applying CBT across the anxiety disorders when guided by the computerized program. That they were equally capable with PTSD compared with the other disorders highlights the value of the computer-guided program because it is often generally assumed that PTSD is more difficult than other anxiety disorders for inexperienced therapists. Because most ITV participants completed their treatment by 6 months, the 12- and 18-month follow-up assessments largely assessed sustainability of treatment effects.

For principal anxiety disorder outcomes, ITV was statistically superior to UC at 6 months for GAD, PD, and SAD; at 12 months for GAD and PD; and at 18 months for GAD. For PTSD, the results were nonsignificant at each follow-up time point. However, the statistical significance for PTSD comparisons was mitigated by the relatively small sample size, as the ESs for PTSD were actually equivalent to those for the other principal anxiety disorders, including GAD.

The ESs for differences between the ITV and UC groups were low to moderate. However, they are in the range of ESs for differences between CBT and other active treatments (such as psychodynamic, interpersonal, and supportive therapies) for anxiety disorders ($d = 0.43$).[41] Effectiveness trials typically yield lower ESs even with the same treatment protocol because they tolerate more "noise" in attempting to recreate the real world. Furthermore, our comparison was made more stringent by the fact that many participants in the UC group received active CBT or medication treatment; that is, as described in a previous article,[14] mental health services received were assessed at 6-, 12-, and 18-month follow-up time points in the ITV and UC groups, and 27% to 34% of the UC group reported receiving CBT with at least 3 elements, and 36% to 42% reported any appropriate antianxiety medication at an appropriate dose for at least 2 months. The active nature of UC in this study likely contributed to the low to moderate between-group ESs, the pattern of mostly continued improvement in the UC group over time, and the lack of differences between ITV and UC for the PD and SAD groups at 18 months. Concurrently, these ESs likely represent what would be achieved in real-world practice, where therapeutic alternatives must realistically be compared with other therapeutic options that patients might pursue.



©2011 American Medical Association. All rights reserved.
Downloaded From: http://jamanetwork.com/ on 05/22/2013

Nevertheless, the ESs indicated that the evidence-based ITV tailored to primary care was more effective than was UC for each principal anxiety disorder, at least to 12 months after study enrollment. The results with GAD were the strongest statistically and for ESs, which is particularly important because GAD is among the most commonly presenting anxiety disorders in primary care.[5,42] The GAD effects were confirmed when analyzing response and remission rates, where ITV was significantly superior to UC at each time point.

This is the first study, to our knowledge, to evaluate differences between ITV and UC on comorbid disorder outcomes in a generalizable sample and using dimensional measures of comorbidity. Measures of comorbid symptom severity typically improved over time. Also, the ESs of differences between ITV and UC (eg, 0.24-0.55) indicated that comorbidity decreased more in the ITV group than in the UC group at 6 and 12 months. However, only in the case of SAD in CALM did the changes statistically significantly exceed improvements in UC. Conceivably, study participation itself served as an effective treatment for comorbid SAD because regular contact with study personnel and particularly the ACS probably functioned as exposure therapy to social situations. Also, statistical significance between ITV and UC for GAD, PTSD, and PD symptoms may have been mitigated by sample size or an overall improvement in comorbid symptoms due to either nonspecific treatment effects shared between ITV and UC or the passage of time alone. By relying on no-treatment control comparisons, previous studies of CBT[17,18,20-22,26] were unable to attribute the effects on comorbidity specifically to CBT vs treatment in general. Overall, the present comorbidity findings are promising and encourage further investigation.

Because this study was designed to compare the CALM ITV with UC while mimicking real-world conditions, these data have some limitations. For example, independent diagnostic assessments were not made at each follow-up. The disorder-specific symptom scales may have been differentially sensitive to change, thus rendering comparisons across disorders problematic. Furthermore, the design does not permit dismantling of the degree to which ITV effects were attributable to specific components of the CALM ITV, such as CBT and psychotropic medications.

In summary, the CALM ITV had a greater positive impact on symptoms of principal anxiety disorders relative to UC in this primary care sample. In addition, the CALM ITV tended to have a greater positive impact on all comorbid symptoms, but the effects were statistically significant only for comorbid social anxiety symptoms. Although the overall improvement in comorbid symptoms is good news for clinical practice, future research may address whether sequential treatment initially targeting a principal anxiety disorder followed by targeting comorbid disorders yields even stronger benefits for comorbid symptoms. An alternative option of simultaneous delivery of more than 1 targeted CBT program has not been supported in the treatment of comorbid anxiety disorders[26] or comorbid anxiety and substance use disorders,[43] although unified CBT protocols[44] may prove more effective. These are questions for future research.

**Submitted for Publication:** August 6, 2010; final revision received October 28, 2010; accepted November 26, 2010.

**Author Affiliations:** Departments of Psychology (Drs Craske and Rose) and Psychiatry and Biobehavioral Sciences (Dr Bystritsky), University of California at Los Angeles; Departments of Psychiatry and Family and Preventive Medicine, University of California at San Diego (Drs Stein, Lang, and Campbell-Sills); South Central VA Mental Illness Research Education and Clinical Center, North Little Rock, Arkansas (Dr Sullivan); University of Arkansas for Medical Sciences, Little Rock (Dr Sullivan); RAND Corp, Santa Monica, California (Drs Sherbourne and Golinelli); and Center for Healthcare Improvement for Addictions, Mental Illness, and Medically Vulnerable Populations, University of Washington at Harborview Medical Center, Seattle (Drs Welch and Roy-Byrne).

**Correspondence:** Michelle G. Craske, PhD, Department of Psychology, University of California at Los Angeles, 405 Hilgard Ave, Los Angeles, CA 90095-1563 (craske@psych.ucla.edu).

**Author Contributions:** Dr Craske had full access to the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Financial Disclosure:** Dr Roy-Byrne is a member of the editorial boards of *UpToDate Psychiatry Version* (editor in chief [EIC]), *Depression and Anxiety* (EIC), and *Journal Watch for Psychiatry* (EIC).

**Funding/Support:** This work was supported by grants U01 MH058915 (Dr Craske), U01 MH057835 (Dr Stein), K24 MH64122 (Dr Stein), UO1 MH057858 (Dr Sullivan), U01 MH070018 (Dr Sherbourne), U01 MH070022 (Dr Roy-Byrne), and K24 MH065324 (Dr Roy-Byrne) from the National Institute of Mental Health.

**Role of the Sponsor:** The National Institute of Mental Health (as part of the U01 mechanism) was responsible for monitoring the operations and conduct of the study and for reviewing and approving the manuscript.

**Scientific Advisory Board to the CALM Project:** Frank Verlain deGruy III, MD, MSFM (Department of Family Medicine, University of Colorado Denver School of Medicine, Aurora); Wayne Katon, MD, and Jürgen Unützer, MD, MPH, MA (Department of Psychiatry and Behavioral Sciences, University of Washington School of Medicine); Lisa V. Rubenstein, MD, MSPH (Department of Medicine, David Geffen School of Medicine and VA Greater Los Angeles Center of Excellence for the Study of Healthcare Provider Behavior, University of California at Los Angeles; and RAND Corp); and Kenneth Wells, MD, MPH (Jane and Terry Semel Institute for Neuroscience and Human Behavior and Department of Psychiatry and Biobehavioral Sciences, David Geffen School of Medicine, University of California at Los Angeles; and Department of Health Services, University of California at Los Angeles School of Public Health; and RAND Corp). These board members received compensation for their consultation.

**Ethnic Advisory Board to the CALM Project:** Peter J. Guarnaccia, PhD (Department of Human Ecology and the Institute for Health, Health Care Policy and Aging Research, Rutgers University, New Brunswick, New Jer-



©2011 American Medical Association. All rights reserved.
Downloaded From: http://jamanetwork.com/ on 05/22/2013

sey); Maga Jackson-Triche, MD, MSHS (VA Northern California Health Care System and University of California Davis School of Medicine, Sacramento); Jeanne Miranda, PhD (Department of Psychiatry and Biobehavioral Sciences, University of California at Los Angeles); and David T. Takeuchi, PhD (School of Social Work and Department of Sociology, University of Washington). These board members received compensation for their consultation.

**Anxiety Clinical Specialists to the CALM Project:** Skye M. Adams, LMSW, and Sandy Sanders, MSW, LCSW (University of Arkansas for Medical Sciences); Michelle Behrooznia, MA, Shadha Hami Cissell, MSW, and Michele S. Smith, PhD (University of California, San Diego); Cindy Chumley (High Desert Medical Group, Lancaster, California); Laura Constantinides, RN (Southern California Permanente Medical Group, San Diego County); Margie Fort, MSW, LICSW, Alice S. Friedman, MSN, ARNP, Kelly H. Koo, MS, Molly Roston, MSW, and Jodi Rubinstein, LICSW (University of Washington); James W. Miller, MA, CRC (Desert Medical Group, Palm Springs, California); and Angelica Ruiz, CCRC (Desert Oasis Healthcare, Palm Desert, California). These individuals were compensated for their work on the project.

**Supervising Psychiatrists to the CALM Project:** C. Winston Brown, MD, Mohit Chopra, MD, and Dan-Vy Mui, MD (University of Arkansas for Medical Sciences); James W. Gaudet, MD (Southern California Permanente Medical Group, San Diego County); Stuart Levine, MD, MHA (University of California at Los Angeles, and HealthCare Partners, Torrance, California); R. Christopher Searles, MD (University of California, San Diego); and Jason P. Veitengruber, MD (University of Washington at Harborview Medical Center). These individuals were compensated for their work on the project.

**Primary Care Clinic Champions to the CALM Project:** Lee C. Abel, MD (Little Rock Diagnostic Clinic); Basil Abramowitz, MD, and Stacey Coleman, DO (Sharp Rees Stealy, San Diego County); Lisa D. Chew, MD, MPH, and Robert Crittendon, MD (Harborview Medical Center, Seattle); Matthew G. Deneke, MD (University of Arkansas for Medical Sciences); Anne M. Eacker, MD (University of Washington Medical Center Roosevelt, Seattle); Erwin Guzman, MD (Southern California Permanente Medical Group, San Diego County); Ralph Joseph, MD (St Vincent's Family Clinic, Little Rock); Gene A. Kallenberg, MD (University of California, San Diego); Richard Kovar, MD, and Carrie Rubenstein, MD (Country Doctor Community Health Centers, Seattle); T. Putnam "Putter" Scott, MD (Neighborcare Health, Seattle); and Ivan Womboldt, CRCC (Desert Medical Group, Palm Springs, California). These individuals were compensated for work on this project either directly or via administrative fee payments to their clinics.

**RAND Survey Research Group to the CALM Project:** Barbara Levitan, BA (RAND Corp). Ms Levitan was compensated for her work on this project.

**Translators:** Velma Barrios, MA (University of California at Los Angeles); and Avelina Martinez, MAT, ATA-Certified Translator from English into Spanish (Austin, Texas). These individuals were compensated for their work on this project.

**Proficiency Raters to the CALM Project:** Laura B. Allen, PhD, and Ancy E. Cherian, PhD (University of California at Los Angeles). These individuals were compensated for their work on this project.

**Analysis:** Bernadette Benjamin, MS (RAND Corp); Jutta M. Joesch, PhD, and Imara I. West, MPH (University of Washington). These individuals were compensated for their work on the project.

**Programming of Web-Based Outcomes System:** Youlim Choi, MS (University of Washington). Mr Choi was compensated for his work on this project.

**Programming of Computer CBT Program:** Vivid Concept LLC (http://www.vividconcept.com).

**Study Coordinators to the CALM Project:** Kristin Bumgardner, BS (University of Washington) (central coordination of overall study); Daniel Dickson, BA, Daniel Glenn, BA, and Michael E. J. Reding, MA (University of California at Los Angeles); Christina Reaves, MPH (University of Arkansas for Medical Sciences). These individuals were compensated for their work on the project.

**National Institute of Mental Health:** Matthew V. Rudorfer, MD (Adult Treatment and Preventive Interventions Research Branch, Division of Services and Intervention Research), and Elizabeth Zachariah, MS (Clinical Trials Operations and Biostatistics Unit, Division of Services and Intervention Research).

## REFERENCES


1. Kessler RC, Chiu WT, Demler O, Merikangas KR, Walters EE. Prevalence, severity, and comorbidity of 12-month *DSM-IV* disorders in the National Comorbidity Survey Replication [published correction appears in *Arch Gen Psychiatry*. 2005;62(7):709]. *Arch Gen Psychiatry*. 2005;62(6):617-627.
2. Saarni SI, Suvisaari J, Sintonen H, Pirkola S, Koskinen S, Aromaa A, Lönnqvist J. Impact of psychiatric disorders on health-related quality of life: general population survey. *Br J Psychiatry*. 2007;190:326-332.
3. Sareen J, Jacobi F, Cox BJ, Belik SL, Clara I, Stein MB. Disability and poor quality of life associated with comorbid anxiety disorders and physical conditions. *Arch Intern Med*. 2006;166(19):2109-2116.
4. Stein MB, Roy-Byrne PP, Craske MG, Bystritsky A, Sullivan G, Pyne JM, Katon W, Sherbourne CD. Functional impact and health utility of anxiety disorders in primary care outpatients. *Med Care*. 2005;43(12):1164-1170.
5. Kroenke K, Spitzer RL, Williams JB, Monahan PO, Löwe B. Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. *Ann Intern Med*. 2007;146(5):317-325.
6. Fernández A, Haro JM, Martinez-Alonso M, Demyttenaere K, Brugha TS, Autonell J, de Girolamo G, Bernert S, Lépine JP, Alonso J. Treatment adequacy for anxiety and depressive disorders in six European countries. *Br J Psychiatry*. 2007;190(2):172-173.
7. Weisberg RB, Dyck I, Culpepper L, Keller MB. Psychiatric treatment in primary care patients with anxiety disorders: a comparison of care received from primary care providers and psychiatrists. *Am J Psychiatry*. 2007;164(2):276-282.
8. Wang PS, Lane M, Olfson M, Pincus HA, Wells KB, Kessler RC. Twelve-month use of mental health services in the United States: results from the National Comorbidity Survey Replication. *Arch Gen Psychiatry*. 2005;62(6):629-640.
9. Carroll KM, Rounsaville BJ. A vision of the next generation of behavioral therapies research in the addictions. *Addiction*. 2007;102(6):850-869.
10. Gega L, Norman IJ, Marks IM. Computer-aided vs. tutor-delivered teaching of exposure therapy for phobia/panic: randomized controlled trial with pre-registration nursing students. *Int J Nurs Stud*. 2007;44(3):397-405.
11. Spek V, Cuijpers P, Nyklícek I, Riper H, Keyzer J, Pop V. Internet-based cognitive behaviour therapy for symptoms of depression and anxiety: a meta-analysis. *Psychol Med*. 2007;37(3):319-328.
12. Roy-Byrne P, Veitengruber JP, Bystritsky A, Edlund MJ, Sullivan G, Craske MG, Welch SS, Rose R, Stein MB. Brief intervention for anxiety in primary care patients. *J Am Board Fam Med*. 2009;22(2):175-186.
13. Wagner EH, Glasgow RE, Davis C, Bonomi AE, Provost L, McCulloch D, Carver P,





©2011 American Medical Association. All rights reserved.
Downloaded From: http://jamanetwork.com/ on 05/22/2013

Sixta C. Quality improvement in chronic illness care: a collaborative approach. *Jt Comm J Qual Improv*. 2001;27(2):63-80.
14. Roy-Byrne P, Craske MG, Sullivan G, Rose RD, Edlund MJ, Lang AJ, Bystritsky A, Welch SS, Chavira DA, Golinelli D, Campbell-Sills L, Sherbourne CD, Stein MB. Delivery of evidence-based treatment for multiple anxiety disorders in primary care: a randomized controlled trial. *JAMA*. 2010;303(19):1921-1928.
15. Jacobi F, Wittchen H-U, Holting C, Höfler M, Pfister H, Müller N, Lieb R. Prevalence, co-morbidity and correlates of mental disorders in the general population: results from the German Health Interview and Examination Survey (GHS). *Psychol Med*. 2004;34(4):597-611.
16. Brown TA, Chorpita BF, Barlow DH. Structural relationships among dimensions of the *DSM-IV* anxiety and mood disorders and dimensions of negative affect, positive affect, and autonomic arousal. *J Abnorm Psychol*. 1998;107(2):179-192.
17. Borkovec TD, Abel JL, Newman H. Effects of psychotherapy on comorbid conditions in generalized anxiety disorder. *J Consult Clin Psychol*. 1995;63(3):479-483.
18. Brown TA, Barlow DH. Long-term outcome in cognitive-behavioral treatment of panic disorder: clinical predictors and alternative strategies for assessment. *J Consult Clin Psychol*. 1995;63(5):754-765.
19. Craske MG, Farchione TJ, Allen LB, Barrios V, Stoyanova M, Rose R. Cognitive behavioral therapy for panic disorder and comorbidity: more of the same or less of more? *Behav Res Ther*. 2007;45(6):1095-1109.
20. Stanley MA, Beck JG, Glasco JD. Treatment of generalized anxiety in older adults: a preliminary comparison of cognitive-behavioral and supportive approaches. *Behav Ther*. 1996;27(4):565-581.
21. Tsao JCI, Lewin MR, Craske MG. The effects of cognitive-behavior therapy for panic disorder on comorbid conditions. *J Anxiety Disord*. 1998;12(4):357-371.
22. Tsao JCI, Mystkowski JL, Zucker BG, Craske MG. Effects of cognitive-behavioral therapy for panic disorder on comorbid conditions: replication and extension. *Behav Ther*. 2002;33(4):493-509.
23. Sullivan G, Craske MG, Sherbourne C, Edlund MJ, Rose RD, Golinelli D, Chavira DA, Bystritsky A, Stein MB, Roy-Byrne PP. Design of the Coordinated Anxiety Learning and Management (CALM) study: innovations in collaborative care for anxiety disorders. *Gen Hosp Psychiatry*. 2007;29(5):379-387.
24. Campbell-Sills L, Norman SB, Craske MG, Sullivan G, Lang AJ, Chavira DA, Bystritsky A, Sherbourne C, Roy-Byrne P, Stein MB. Validation of a brief measure of anxiety-related severity and impairment: the Overall Anxiety Severity and Impairment Scale (OASIS). *J Affect Disord*. 2009;112(1-3):92-101.
25. Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, Hergueta T, Baker R, Dunbar GC. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for *DSM-IV* and *ICD-10*. *J Clin Psychiatry*. 1998;59(Suppl 20):22-33.
26. Craske MG, Rose RD, Lang A, Welch SS, Campbell-Sills L, Sullivan G, Sherbourne C, Bystritsky A, Stein MB, Roy-Byrne PP. Computer-assisted delivery of cognitive behavioral therapy for anxiety disorders in primary-care settings. *Depress Anxiety*. 2009;26(3):235-242.
27. Kroenke K, Spitzer RL, Williams JBW. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med*. 2001;16(9):606-613.
28. Houck PR, Spiegel DA, Shear MK, Rucci P. Reliability of the self-report version of the Panic Disorder Severity Scale. *Depress Anxiety*. 2002;15(4):183-185.
29. Andreescu C, Belnap BH, Rollman BL, Houck P, Ciliberti C, Mazumdar S, Shear MK, Lenze EJ. Generalized Anxiety Disorder Severity Scale validation in older adults. *Am J Geriatr Psychiatry*. 2008;16(10):813-818.
30. Weiss BJ, Calleo J, Rhoades HM, Novy DM, Kunik ME, Lenze EJ, Stanley MA. The utility of the Generalized Anxiety Disorder Severity Scale (GADSS) with older adults in primary care. *Depress Anxiety*. 2009;26(1):E10-E15.
31. Shear K, Belnap BH, Mazumdar S, Houck P, Rollman BL. Generalized Anxiety Disorder Severity Scale (GADSS): a preliminary validation study. *Depress Anxiety*. 2006;23(2):77-82.
32. Connor KM, Davidson JRT, Churchill LE, Sherwood A, Foa E, Weisler RH. Psychometric properties of the Social Phobia Inventory (SPIN): new self-rating scale. *Br J Psychiatry*. 2000;176:379-386.
33. Weathers PL, Furlong MJ, Solorzano D. Mail survey research in counseling psychology: current practice and suggested guidelines. *J Couns Psychol*. 1993;40(2):238-244.
34. Ruggiero KJ, Del Ben K, Scotti JR, Rabalais AE. Psychometric properties of the PTSD Checklist-Civilian Version. *J Trauma Stress*. 2003;16(5):495-502.
35. Ravindran LN, Stein MB. The pharmacologic treatment of anxiety disorders: a review of progress. *J Clin Psychiatry*. 2010;71(7):839-854.
36. Littell RC, Milliken GA, Stroup WW, Wolfinger RD. *SAS System for Mixed Models*. Cary, NC: SAS Publications; 1996.
37. Little RJA, Rubin DB. *Statistical Analysis With Missing Data*. New York, NY: John Wiley & Sons Inc; 1987.
38. Brick JM, Kalton G. Handling missing data in survey research. *Stat Methods Med Res*. 1996;5(3):215-238.
39. Hochberg Y. A sharper Bonferroni procedure for multiple tests of significance. *Biometnika*. 1988;75(4):800-802.
40. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. 2nd ed. Hillsdale, NJ: Erlbaum; 1988.
41. Tolin DF. Is cognitive-behavioral therapy more effective than other therapies? a meta-analytic review. *Clin Psychol Rev*. 2010;30(6):710-720.
42. Weisberg RB. Overview of generalized anxiety disorder: epidemiology, presentation, and course. *J Clin Psychiatry*. 2009;70(Suppl 2):4-9.
43. Randall CL, Thomas S, Thevos AK. Concurrent alcoholism and social anxiety disorder: a first step toward developing effective treatments. *Alcohol Clin Exp Res*. 2001;25(2):210-220.
44. Barlow DH, Allen LB, Choate ML. Toward a unified treatment for emotional disorders. *Behav Ther*. 2004;35(2):205-230.



©2011 American Medical Association. All rights reserved.
Downloaded From: http://jamanetwork.com/ on 05/22/2013