Delivery of Evidence-Based Treatment for Multiple Anxiety Disorders in Primary Care: A Randomized Controlled Trial

Dr Peter Roy-Byrne, MD, **Dr Michelle G. Craske, PhD**, **Dr Greer Sullivan, MD, MSPH**, **Dr Raphael D. Rose, PhD**, **Dr Mark J. Edlund, MD, PhD**, **Dr Ariel J. Lang, PhD**, **Dr Alexander Bystritsky, MD**, **Dr Stacy Shaw Welch, PhD**, **Dr Denise A. Chavira, PhD**, **Dr Daniela Golinelli, PhD**, **Dr Laura Campbell-Sills, PhD**, **Dr Cathy D. Sherbourne, PhD**, and **Dr Murray B. Stein, MD, MPH**

Department of Psychiatry and Behavioral Sciences, University of Washington School of Medicine and Harborview Center for Healthcare Improvement for Addictions, Mental Illness, and Medically Vulnerable Populations (CHAMMP), Seattle, Washington (Drs Roy-Byrne and Welch); Departments of Psychology (Drs Craske and Rose) and Psychiatry and Biobehavioral Sciences, David Geffen School of Medicine (Dr Bystritsky), University of California, Los Angeles, California; Department of Psychiatry (Drs Sullivan and Edlund) and VA South Central Mental Illness Research, Education, and Clinical Center (Dr Sullivan), University of Arkansas for Medical Sciences, Little Rock, Arkansas; Departments of Psychiatry (Drs Lang, Chavira, Campbell-Sills, and Stein) and Family and Preventive Medicine (Dr Stein), University of California, San Diego, California, and VA San Diego Health Care System Center of Excellence for Stress and Mental Health (Dr Lang); and RAND Corporation, Santa Monica, California (Drs Sullivan, Golinelli, and Sherbourne)

Abstract

Context—Improving the quality of mental health care requires moving clinical interventions from controlled research settings into "real world" practice settings. While such advances have been made for depression, little work has been done for anxiety disorders.

Objective—To determine whether a flexible treatment-delivery model for multiple primary care anxiety disorders (panic, generalized anxiety, social anxiety, and/or posttraumatic stress disorders) would be superior to usual care.

Design, Setting, and Participants—Randomized controlled effectiveness trial of CALM ("Coordinated Anxiety Learning and Management") compared to usual care (UC) in 17 primary care

clinics in 4 US cities. Between June 2006 and April 2008, 1004 patients with anxiety disorders (with or without major depression), age 18–75, English- or Spanish-speaking, enrolled and subsequently received treatment for 3–12 months. Blinded follow-up assessments at 6, 12, and 18 months after baseline were completed in October 2009.

Intervention(s)—CALM allowed choice of cognitive behavioral therapy (CBT), medication, or both; included real-time web-based outcomes monitoring to optimize treatment decisions and a computer-assisted program to optimize delivery of CBT by non-expert care managers who also assisted primary care providers in promoting adherence and optimizing medications.

Main Outcome Measure(s)—12-item Brief Symptom Inventory (anxiety and somatic symptoms) score. Secondary outcomes: Proportion of responders ($\geq$ 50% reduction from pre-treatment BSI-12 score) and remitters (total BSI-12 score < 6).

Results—Significantly greater improvement for CALM than UC in global anxiety symptoms: BSI-12 group differences of −2.49 (95% CI, −3.59 to −1.40), −2.63 (95% CI, −3.73 to −1.54), and −1.63 (95% CI, −2.73 to −0.53) at 6, 12, and 18 months, respectively. At 12 months, response and remission rates (CALM vs. UC) were 63.66% (58.95–68.37) vs. 44.68% (39.76–49.59), and 51.49% (46.60–56.38) vs. 33.28% (28.62–37.93), with a number needed to treat (NNT) of 5.27 (4.18–7.13) for response and 5.5 (4.32–7.55) for remission.

Conclusions—For patients with anxiety disorders treated in primary care clinics, a collaborative care intervention, compared to usual care, resulted in greater improvement in anxiety symptoms, functional disability, and quality of care over 18 months.

Improving the quality of mental health care requires continued efforts to move evidence-based treatments of proven efficacy into "real world" practice settings with wide variability in patient characteristics and provider skill.[1] The effectiveness of one approach, "collaborative care", is well established for primary care depression[2–5] but has been infrequently studied for anxiety disorders,[6, 7] despite their common occurrence in primary care.[8] The multiplicity of anxiety disorders, and the fact that anxious patients are less likely to seek[9] and harder to engage[10] in treatment, likely are contributing factors. Furthermore, whereas effective treatment for both anxiety and depressive disorders relies in part on pharmacotherapy, psychosocial treatments such as cognitive behavioral therapy (CBT) are important for anxious patients. Not only do they strongly prefer psychological treatment over medications,[10, 11] but CBT may have advantages over pharmacotherapy in terms of maintaining clinical improvements over time.[12, 13]

In response to primary care provider preferences for interventions that have the capacity to address a range of common mental disorders rather than just one, we designed a flexible treatment delivery model, CALM ("Coordinated Anxiety Learning and Management"),[14] and compared its effectiveness to care as usual. CALM addresses the four most common anxiety disorders–panic disorder (PD), generalized anxiety disorder (GAD), social anxiety disorder (SAD) and posttraumatic stress disorder (PTSD)–even when they co-occur with depression. CALM optimizes treatment engagement by allowing choice of treatment modality[15] (pharmacotherapy and/or CBT) and provision of additional treatment when needed.[2] A web-based outcomes system is used to facilitate measurement-based care[16] and a computer-assisted program helps guide non-expert care managers in delivering evidence-based CBT.[17] In this way, CALM seeks to accommodate the complexity of real-world clinical settings, while maximizing fidelity to the evidence-base in the context of a broad range of patients, providers, practice settings, and payers.

We hypothesized that CALM would be superior to usual care (UC) in reducing psychic and somatic symptoms of anxiety and in improving global measures of functioning, health-related

quality of life, and quality of care delivered. We expected small to moderate effect sizes similar to those found in previous collaborative care studies for depression.

METHODS

Setting, Subjects, and Design

Between June 2006 and April 2008, 1004 primary care patients with PD, GAD, SAD, and/or PTSD were enrolled in the CALM study. A total of 17 clinics in Little Rock, LA County, San Diego and Seattle, serving > 35,000 patients with > 780,000 annual visits, were purposively selected based on a number of considerations, including provider interest, space availability, size and diversity of the patient population, and insurance mix. Primary care providers (120 internists and 28 family physicians) referred all potential subjects, facilitated by an optional five question anxiety screener.[18] To determine eligibility, referred subjects met with a specially trained clinician, the Anxiety Clinical Specialist (ACS). The 14 ACS (11 female, 3 male) included 6 social workers, 5 RNs, 2 master's level psychologists and 1 PHD psychologist. Eight had some mental health experience, 4 were familiar with but had no formal training with CBT, and 7 had some psychopharmacology experience.

Eligible subjects were patients at participating clinics, 18–75 years old, who met DSM-IV criteria for one or more of PD, GAD, SAD, or PTSD (based on the Mini International Neuropsychiatric Interview[19] administered by the ACSs after formal training and diagnostic reliability testing), and scored at least 8 (moderate anxiety symptoms on a scale ranging from 0–20) on the Overall Anxiety Severity and Impairment Scale (OASIS), validated as clinically significant in a separate analysis.[20] Co-occurring major depression was permitted. Persons unlikely to benefit from CALM (ie, unstable medical conditions, marked cognitive impairment, active suicidal intent or plan, psychosis, bipolar I disorder, substance abuse of dependence except for alcohol and marijuana abuse) were excluded. Subjects already receiving ongoing CBT or medication from a psychiatrist (N = 7) were excluded, as were persons who could not speak English or Spanish (N = 2). All subjects gave informed, written consent for the study, which was approved by each institution's Institutional Review Board.

After a baseline interview (see below) subjects were randomized to CALM or UC, using an automated computer program at RAND, where all post-eligibility assessments were conducted by phone. Randomization was stratified by clinic and presence of co-morbid major depression, using a permuted block design. Block size was masked to all clinical site study members. The CONSORT diagram describes patient flow from eligibility screening through consent and randomization (Figure 1).

Intervention (CALM)/Usual Care (UC)

CALM used a web-based monitoring system,[16] modeled on the IMPACT intervention,[2] with newly developed anxiety content, and a computer-assisted CBT program.[17] ACSs received six half days of didactics, which focused on mastering the CBT program, plus motivational interviewing (modified for anxiety concerns) to enhance engagement, outreach strategies for ethno-racial and impoverished minorities, and a medication algorithm for anxiety.[21] CBT training also included role-playing, and required successful completion of two training patients over several months.

CALM patients initially received their preferred treatment, either medication, CBT, or both, over 10 to 12 weeks. Since the effects of CBT delivered for one disorder are known to generalize to co-morbid disorders,[22] patients with multiple anxiety disorders were asked to choose the most disabling or distressing disorder to focus on with the expectation that their co-morbid disorders would also improve. The CBT program, a "repackaging" based on already validated

CBT treatments,[23] included 5 generic modules (education, self-monitoring, hierarchy development, breathing training, relapse prevention) and 3 modules (cognitive restructuring, exposure to internal and external stimuli) tailored to the four specific anxiety disorders. CBT was administered by the ACS (typically in 6 to 8 weekly sessions), while medication was prescribed. A local study psychiatrist provided single session medication management training to providers using a simple algorithm, as needed consultation by phone or e-mail, and very rarely, a face to face assessment for complex or treatment refractory patients. The algorithm emphasized first line use of SSRI or SNRI antidepressants, dose optimization, side effect monitoring, followed by second and third step combinations of two antidepressants or an antidepressant and benzodiazepine for refractory patients.[21] For medication management, the ACS provided adherence monitoring, counseling to avoid alcohol and optimize sleep hygiene and behavioral activity, and relayed medication suggestions from the supervising psychiatrist to the PCP.

The ACS tracked patient outcomes on a web-based system by entering scores for the OASIS and a 3-item version of the Patient Health Questionnaire-9 (PHQ-9), and examining graphical progress over time. The goal was either clinical remission, defined as an OASIS < 5 = "mild", sufficient improvement such that the patient did not want further treatment, or improvement with residual symptoms or other emergent problems requiring a non-protocol psychotherapy (ie, DBT, family or dynamic psychotherapy). Symptomatic patients thought to benefit from additional treatment with CBT or medication could receive more of the same modality ("stepping up") or the alternative modality ("stepping over"), for up to three more steps of treatment. After treatment completion, patients were entered into "continued care" and received monthly follow-up phone calls to reinforce CBT skills and/or medication adherence. ACSs interacted regularly with PCPs in person and over the phone. PCPs remained the clinician of record and prescribed all medications. All ACSs received weekly supervision from a psychiatrist and psychologist.

UC patients continued to be treated by their physician in the usual manner with no intervention, ie, with medication, counseling (7 of 17 clinics had limited in-clinic mental health resources, usually a single provider with limited familiarity with evidence based psychotherapy[24]) or referral to a mental health specialist. After the eligibility diagnostic interview, the only contact UC patients had with study personnel was for assessment by phone.

Assessments

The assessment battery was administered at baseline, 6, 12, and 18 months via centralized phone survey by the RAND Survey Research Group who were blinded to treatment assignment. The last subject was assessed in October 2009. Because prior studies indicated outcome differences by ethno-racial groupings,[3] race-ethnicity data was obtained by subject self-report using standard classification. The primary outcome was a generic measure of two key components of all anxiety disorders, psychic and somatic anxiety: the Brief Symptom Inventory subscales for anxiety and somatization (total 12 items, BSI-12[25]). *Response* was defined as a $\geq 50\%$ reduction on the BSI-12, or meeting the definition of remission, and *remission* was defined as a face-valid per item score of < 0.5 (between "none" and "mild", total BSI-12 score < 6) consistent with previous analyses using the BSI for depression outcomes.[26] Secondary measures included PHQ-8 depression,[27] anxiety sensitivity (ASI),[28] and functional status (Sheehan Disability[29], the CDC Healthy Days Measure of restricted activity days,[30] and SF-12v2[31]). Quality of care was measured by patient self-report of psychotropic medication type, dose, and adherence, and number and consistency of CBT elements occurring in reported psychotherapy sessions.[32] More detailed information on CALM patients' number and type (CBT vs. medication/care management) of sessions was extracted from the web-based management system.

Analysis

During the proposal phase, we had assumed an attrition rate of 28% at month 18. Therefore, we had anticipated needing a sample size of 1040 to detect effect sizes of 0.3 standard deviations with at least 80% power. Although the enrolled sample size (N = 1004) was marginally smaller than projected, subject attrition was lower (20% at month 18), yielding a larger than anticipated sample size at the follow-up time points.

We compared demographics and baseline anxiety and depression disorders rates by intervention group using t-tests and chi-square tests for continuous and categorical variables respectively. To estimate the intervention effect over time we jointly modeled the outcomes at the four assessment times (baseline and 3 follow-ups at 6, 12 and 18 months) by time, intervention, the interaction of time and intervention, and site. Time was treated as a categorical variable. To avoid restrictive assumptions, the covariance of the outcomes at the four 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.[33] This approach correctly handles the additional uncertainty arising from missing data and uses all available data to obtain unbiased estimates for model parameters.[34] This is an efficient way for conducting an intent-to-treat analysis since it includes all the subjects with a baseline assessment. For cross-sectional analyses (such as those assessing the percentage of responders at the 3 follow-up times), we used attrition weights to correctly account for those subjects that missed one or more follow-up assessments[35] The statistical software used was SAS version 9. All *P* values were 2-tailed and are adjusted using Hochberg's[36] correction method to account for multiple comparisons.

RESULTS

Sample Selection, Attrition, and Description

Figure 1 depicts study subject flow and reasons for non-eligibility. Two-thirds of referred patients (1062/1620 [66%]) were eligible for the study, a majority of these (1036/1062 [98%]) consented to participate, and a majority (1004/1036 [97%]) were randomized. Over 80% of subjects were assessed at each evaluation window and study retention was high and similar in both study arms. Table 1 shows that the sample was 70% female, ethnically diverse (44% non-white), and broad in age range. It was a fairly ill group with over half having at least two chronic medical conditions and at least two anxiety disorders, and two-thirds with co-morbid major depression. CALM and UC were comparable on all these dimensions.

Intervention (CALM) Participation

After the baseline assessment, 482 of 503 (95%) subjects randomized to CALM had at least one intervention contact. Over the course of the year, subjects had 7.0 +/− 4.1 (Median = 8) CBT visits (1% [35/3,386] by phone, < 1% [11/3,386] focused on depression) and 2.24 +/− 3.57 (Median = 1) medication/care management visits (43% [462/1,078] by phone). Of the 482 subjects, 166 (34%) had only CBT visits, 43 (9%) had only medication/care management visits, and 273 (57%) had some of both. Visits for 218 (45%) subjects were confined to the first three months and 424 (88%) subjects had all visits by 6 months. A small proportion of subjects (69/482 [14%]) also had an in-person visit with the study psychiatrist.

Quality of Care

Table 2 depicts self-reported Quality of Care received at baseline, 6, 12 and 18 months for the two groups, using progressively more stringent definitions of care quality. At both 6 (54.83 % [95% CI, 51.00–58.66] vs 9.98 % [95% CI, 6.08–13.88]) and 12 (21.64 % [95% CI, 18.19–25.09] vs 9.31 % [95% CI, 5.83–12.79]) month assessments, significantly more CALM

subjects received psychotherapy with at least 3 of 6 CBT elements (eg, exposure, relaxation, cognitive restructuring, homework) usually or always delivered. At 6 months only, significantly more CALM subjects either took medication of appropriate[21] type, dose and duration (≥ 2 months) or had an appropriate change in medication (dose increase or medication switch/addition) if they were already on medication: 25.35% (95% CI, 21.28–29.43%) vs. 17.11% (95% CI, 13.51–20.70). Rates of overall psychotropic use did not differ between CALM and UC over time.

Outcomes

Table 3 examines trajectories of adjusted means over time for the primary BSI-12 outcome, and for all secondary outcomes. BSI-12 scores were significantly lower for CALM subjects at 6 (Δ 2.49 points [95% CI, −3.59 to −1.40], P <.001), 12 (Δ 2.63 points [95% CI, −3.73 to −1.54], P <.001) and 18 months (Δ 1.63 points [95% CI, −2.73 to −0.53], P =.05), with effects sizes of 0.30 (0.43–0.17), 0.31 (0.44–0.18), and 0.18 (−.30–0.06). Outcomes for intervention patients were significantly better for all other measures except physical health and satisfaction with medical care. Effect sizes were small to medium depending on the measure, and were greatest at 12 months. There were no significant differences in intervention effect over time by site, and all four disorders showed significant effects on the main BSI-12 outcome (eTable 1 [http://www.jama.com]).

Table 4 shows that a significantly (P < .001) higher proportion of CALM subjects responded and remitted, respectively. Response (including remission) rates at 6, 12, and 18 months were 57.46% (52.84–62.08), 63.66% (58.95–68.37), 64.64% (59.95–69.32) vs. 36.80% (32.21–41.39), 44.68% (39.76–49.59), 51.47% (46.49–56.45) (CALM vs. UC); remission rates 45.40% (38.78–48.03), 51.49% (46.60–56.38), 51.06% (46.16–55.96) vs. 27.49% (23.25–31.72), 33.28% (28.62–37.93), 36.77% (31.99–41.55). The number needed to treat (defined as 1/difference between intervention and control response or remission) at 12 months was 5.27 (4.18–7.13) for response and 5.5 (4.32–7.55) for remission.

COMMENT

These findings document the feasibility, acceptability (or satisfaction), and clinical effectiveness of a care delivery model designed to treat persons with any of four common anxiety disorders across 17 primary care clinics varying in patient characteristics, payer types, and organization. The model utilized both real time outcomes monitoring and a computer-guided, modular CBT program which assured a high degree of fidelity in CBT application. Even though different anxiety disorders (with or without depression) were targeted with this single intervention, effect sizes were similar to those obtained in previous anxiety effectiveness studies that had focused solely on panic disorder and/or generalized anxiety disorder.[6, 7] Importantly, the number needed to treat (NNT) was well within the range for treatments in medicine that are generally considered to be efficacious,[37, 38] and beneficial effects of the intervention persisted for at least one year after clinical visits had ceased, suggesting a longer term effect.

This study has a number of limitations. It was designed to test delivery of a blended package of treatments known to be evidence-based and we cannot determine which components of the blended intervention (eg, preference, CBT, medication, web-outcomes monitoring) accounted for the results. Subjects, a third of whom had failed at least one course of pharmacotherapy, were relatively well-educated and were referred to the study, all of which may have enhanced CBT engagement and response. We relied on self-report, rather than review of medical records, to assess amount and quality of treatment and used a relatively lean assessment battery intended to cover more domains while minimizing subject burden. The participating clinics had a higher

than usual amount of in-house mental health resources in usual care, though this may have led to an underestimate of the benefit of CALM vs UC.

The positive outcomes as a whole may have been mediated by higher rates of quality CBT at 6 and 12 months and higher quality medication treatment at 6 months. This improved quality of care was facilitated by real-time outcomes monitoring, which allowed for adjustment of type and amount of delivered treatment, and a computer-guided modular CBT program, which assured high fidelity when delivered by non-experts, though the relative contribution of each to improved outcomes cannot be determined. The high rate of selection of CBT treatment by patients confirms previous findings[11, 39] that anxious patients prefer psychosocial treatment approaches. Also the persistence of anxiety despite pharmacologic treatment in over half the sample at baseline may have further reinforced this preference. Because the intervention devoted most of its training resources to the CBT program, it is possible that the medication management component could be further improved with more focus on this modality.

The flexibility of treatment (eg, variation in number and type of sessions, and in criteria for continuing further treatment, use of both phone and in person contact), the targeting of multiple disorders, and the clinical effectiveness across a range of patients and clinics, suggest that the CALM treatment delivery model should be broadly applicable in primary care. However, implementation of this model will require reimbursement mechanisms for care management that are not currently available. In this vein, forthcoming analyses about the cost of CALM will be needed to help payers decide whether to support its uptake in clinical settings. Furthermore, the in-house model used by CALM would be less feasible for small or rurally-located practices, which might require a more centrally located care manager and perhaps internet or telephone delivery in order to serve multiple small and/or remote practices. Nonetheless, the success of the model tested here demonstrates that addressing multiple common mental disorders in the context of one delivery model is feasible and effective and could serve as a template for the development of unified approaches to management of the multiple psychiatric co-morbidities that are the rule, rather than the exception, in both the general population[40] and in clinical practice.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Appendix

Scientific Advisory Board: 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, Seattle); Lisa V. Rubenstein, MD, MSPH, FACP (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, Los Angeles; and RAND Corporation, Santa Monica, California); 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, Los Angeles; Department of Health Services, UCLA School of Public Health; and RAND Corporation, Santa Monica, California). These board members received compensation for their consultation.

Ethnic Advisory Board: Peter J. Guarnaccia, PhD (Department of Human Ecology and the Institute for Health, Health Care Policy and Aging Research, Rutgers University, New Brunswick, New Jersey); 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, Los Angeles); David T. Takeuchi, PhD (School of Social Work and Department of Sociology, University of Washington, Seattle). These board members received compensation for their consultation.

Additional Contributions:

Anxiety Clinical Specialists: Skye M. Adams, LMSW, and Sandy Sanders, MSW, LCSW (University of Arkansas for Medical Sciences, Little Rock); 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, Seattle); James W. Miller, MA, CRC (Desert Medical Group, Palm Springs, California); Angelica Ruiz, CCRC (Desert Oasis Healthcare, Palm Desert, California). These individuals were compensated for their work on the project.

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

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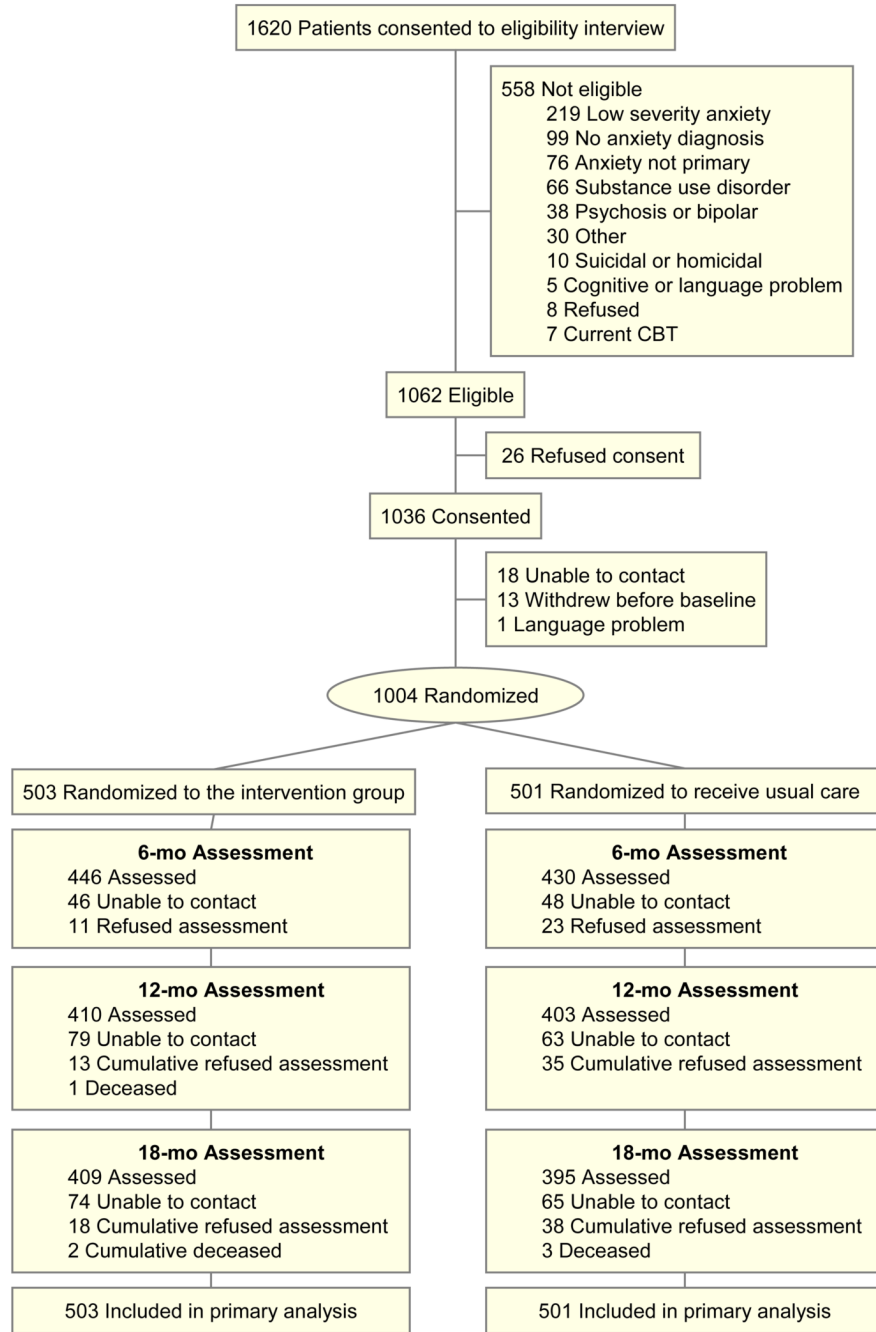
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Supervision: Roy-Byrne, Craske, Sullivan, Rose, Edlund, Lang, Bystritsky, Welch, Chavira, Campbell-Sills, Sherbourne, Stein.

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1620 Patients consented to eligibility interview

558 Not eligible
  219 Low severity anxiety
  99 No anxiety diagnosis
  76 Anxiety not primary
  66 Substance use disorder
  38 Psychosis or bipolar
  30 Other
  10 Suicidal or homicidal
  5 Cognitive or language problem
  8 Refused
  7 Current CBT

1062 Eligible

26 Refused consent

1036 Consented

18 Unable to contact
13 Withdrew before baseline
1 Language problem

1004 Randomized

503 Randomized to the intervention group

501 Randomized to receive usual care

6-mo Assessment
446 Assessed
46 Unable to contact
11 Refused assessment

6-mo Assessment
430 Assessed
48 Unable to contact
23 Refused assessment

12-mo Assessment
410 Assessed
79 Unable to contact
13 Cumulative refused assessment
1 Deceased

12-mo Assessment
403 Assessed
63 Unable to contact
35 Cumulative refused assessment

18-mo Assessment
409 Assessed
74 Unable to contact
18 Cumulative refused assessment
2 Cumulative deceased

18-mo Assessment
395 Assessed
65 Unable to contact
38 Cumulative refused assessment
3 Deceased

503 Included in primary analysis

501 Included in primary analysis

Figure 1. Flowchart of Participants
Non-response was related to younger age, less education, higher BSI-12 and OASIS scores at 6 months; younger age, higher BSI-12, Sheehan Disability and OASIS scores, higher rate of panic, and higher rate among Hispanics at 12 months; and younger age, higher BSI-12 and OASIS scores, lower preference for current health state, higher rate of panic, and higher rate among Hispanics at 18 months.

Table 1

Baseline Patient Characteristics[a]

	All (n = 1004)	Intervention[b] (n = 503)	Usual Care[b] (n = 501)
Age, mean (SD), y	43.47 (13.44)	43.3 (13.2)	43.7 (13.7)
Women	714 (71.12)	359 (71.4)	355 (70.9)
Education < High school	55 (5.49)	29 (5.77)	26 (5.21)
12 y	165 (16.47)	78 (15.5)	87 (17.4)
> 12 y	782 (78.04)	396 (78.7)	386 (77.4)
Ethnicity Hispanic	196 (19.52)	104 (20.7)	92 (18.4)
African American	116 (11.55)	51 (10.1)	65 (13.0)
White	568 (56.57)	279 (55.5)	289 (57.7)
Other	124 (12.35)	69 (13.7)	55 (11.0)
No. of chronic medical conditions 0	202 (20.14)	109 (21.7)	93 (18.6)
1	219 (21.83)	108 (21.5)	111 (22.2)
≥ 2	582 (58.03)	285 (56.8)	297 (59.3)
Anxiety disorder[c] Panic	475 (47.31)	235 (46.7)	240 (47.9)
Generalized anxiety	756 (75.30)	390 (77.5)	366 (73.1)
Social phobia	405 (40.34)	210 (41.8)	195 (38.9)
Posttraumatic stress	181 (18.03)	92 (18.3)	89 (17.8)
Major depressive disorder	648 (64.54)	330 (65.6)	318 (63.5)
Type of health insurance[c] Medicaid	101 (10.08)	47 (9.4)	54 (10.8)
Medicare	124 (12.38)	60 (12.0)	64 (12.8)
Other government insurance[d]	35 (3.49)	16 (3.2)	19 (3.79)
Private insurance	749 (74.75)	372 (74.3)	377 (75.3)
No insurance	141 (14.07)	77 (15.4)	64 (12.8)

[a]Data are reported as No. (%) unless otherwise indicated.

[b]There are no significant differences in any of the baseline characteristics between intervention and usual care patients.

[c]Because patients could have more than one, Ns may total more than 1004.

[d]Includes Veterans' Administration benefits, TRICARE, county programs, or other government insurance not otherwise specified.

Table 2

Anxiety Care[a]

	Intervention	Usual Care	*P* Value
Any Psychotropic Medication			
Baseline	64.4 (60.2–68.6)	62.1 (57.9–66.3)	0.94
6 months	69.9 (65.7–74.1)	68.3 (64.1–72.5)	0.94
12 months	66.3 (61.9–70.8)	64.0 (59.5–68.4)	0.94
18 months	61.4 (56.9–66.0)	61.2 (56.5–65.8)	0.94
Any Appropriate[b] Anti-Anxiety Medication at Appropriate Dose for ≥ 2 Months			
Baseline	29.0 (25.0–33.0)	30.6 (26.6–34.7)	0.94
6 months	46.4 (41.9–51.0)	41.5 (36.9–46.1)	0.94
12 months	42.1 (37.5–46.7)	36.0 (31.4–40.6)	0.94
18 months	40.8 (36.3–45.4)	37.5 (32.8–42.1)	0.94
Medication Change During First 6 Months[c,e]			
6 months	25.4 (21.3–29.4)	17.1 (13.5–20.7)	0.05
Medication Change During Second 6 Months[d,e]			
12 months	13.1 (9.73–16.5)	12.1 (8.80–15.3)	0.94
Any Counseling			
Baseline	45.9 (41.6–50.3)	46.7 (42.3–51.1)	0.94
6 months	88.1 (84.2–92.0)	51.0 (47.1–55.0)	<.001
12 months	58.4 (53.7–63.2)	46.3 (41.5–51.1)	0.01
18 months	39.1 (34.4–43.8)	42.6 (37.8–47.4)	0.94
Counseling with ≥ 3 CBT Elements[f]			
Baseline	20.5 (16.9–24.1)	22.0 (18.4–25.5)	0.94
6 months	82.1 (78.2–86.1)	33.6 (29.6–37.7)	<.001
12 months	49.1 (44.5–53.6)	26.6 (22.1–31.2)	<.001
18 months	26.2 (22.0–30.5)	27.7 (23.4–32.1)	0.94
Counseling with ≥ 3 CBT Elements[f] Delivered Consistently[g]			
Baseline	4.37 (2.56–6.19)	4.59 (2.78–6.41)	0.94
6 months	54.8 (51.0–58.7)	9.98 (6.08–13.9)	<.001
12 months	21.6 (18.2–25.1)	9.31 (5.83–12.8)	<.001

	Intervention	Usual Care	*P* Value
18 months	9.91 (7.07–12.8)	8.91 (6.02–11.8)	0.94

Abbreviation: CBT, cognitive behavioral therapy.

[a] Data are presented as percentage (95% confidence interval). All time effects were significant at *P* <.001 in all models including four time points. Intervention × time effects based on the WALD test were significant at *P* <.001 for all three counseling models.

[b] Defined as medication of appropriate type, dose and duration (≥2 months) or had an appropriate change (dose increase or medication switch/addition) if they were already on medication.

[c] Medication change calculated based on 430 control and 446 intervention patients who responded at 6 months, weighted for non-response.

[d] Medication change calculated based on 391 control and 397 intervention patients who responded at 6 and 12 months, weighted for non-response.

[e] The *P* values for medication change come from a χ^2 test on data weighted for attrition. All other *P* values come from the longitudinal models (eg, given the estimates of the longitudinal model we obtained the predicted means at the four time points by intervention group and tested their difference at every time point using the correct t-test).

[f] Defined as receiving psychotherapy with at least 3 of 6 CBT elements (eg, exposure, relaxation, cognitive restructuring, homework).

[g] Defined as receiving psychotherapy with at least 3 of 6 CBT elements usually or always delivered.

Table 3

Adjusted Means for Anxiety Outcomes[a]

	Intervention[b]	Usual Care[b]	Difference (95% CI)	P Value	Effect Size
Brief Symptom Inventory (BSI-12) Score					
Baseline	16.38 (15.60 to 17.17)	16.24 (15.46 to 17.03)	0.14 (−0.97 to 1.25)	0.90	0.02 (−0.14 to 0.18)
6 months	9.19 (8.42 to 9.95)	11.68 (10.90 to 12.46)	−2.49 (−3.59 to −1.40)	<0.001	−0.30 (−0.43 to −0.17)
12 months	8.22 (7.45 to 8.99)	10.85 (10.07 to 11.63)	−2.63 (−3.73 to −1.54)	<0.001	−0.31 (−0.44 to −0.18)
18 months	8.21 (7.43 to 8.98)	9.84 (9.05 to 10.62)	−1.63 (−2.73 to −0.53)	0.05	−0.18 (−0.30 to −0.06)
Anxiety Sensitivity Index (ASI) Score					
Baseline	29.57 (28.37 to 30.78)	29.89 (28.68 to 31.10)	−0.32 (−2.03 to 1.39)	0.90	−0.02 (−0.13 to 0.08)
6 months	19.69 (18.41 to 20.96)	24.00 (22.71 to 25.29)	−4.31 (−6.13 to −2.50)	<0.001	−0.31 (−0.44 to −0.18)
12 months	17.37 (16.10 to 18.64)	22.11 (20.83 to 23.40)	−4.74 (−6.55 to −2.93)	<0.001	−0.34 (−0.47 to −0.21)
18 months	16.80 (15.52 to 18.08)	20.37 (19.08 to 21.67)	−3.57 (−5.39 to −1.76)	0.002	−0.26 (−0.39 to −0.13)
Depression (PHQ-8) Score					
Baseline	12.60 (12.07 to 13.12)	12.47 (11.94 to 12.99)	0.13 (−0.61 to 0.87)	0.90	0.02 (−0.09 to 0.13)
6 months	7.48 (6.93 to 8.02)	9.05 (8.49 to 9.60)	−1.57 (−2.35 to −0.79)	0.002	−0.25 (−0.37 to −0.12)
12 months	6.64 (6.07 to 7.22)	8.87 (8.28 to 9.45)	−2.22 (−3.05 to −1.40)	<0.001	−0.37 (−0.51 to −0.23)
18 months	6.47 (5.92 to 7.03)	7.92 (7.36 to 8.49)	−1.45 (−2.24 to −0.66)	0.006	−0.24 (−0.37 to −0.11)
Sheehan Disability Score					
Baseline	16.77 (16.14 to 17.40)	17.15 (16.51 to 17.78)	−0.38 (−1.27 to 0.52)	0.90	−0.05 (−0.17 to 0.07)
6 months	9.14 (8.42 to 9.86)	11.63 (10.89 to 12.36)	−2.49 (−3.52 to −1.46)	<0.001	−0.32 (−0.46 to −0.19)
12 months	8.24 (7.50 to 8.97)	11.69 (10.94 to 12.43)	−3.45 (−4.49 to −2.40)	<0.001	−0.44 (−0.59 to −0.32)
18 months	8.37 (7.62 to 9.12)	10.89 (10.13 to 11.65)	−2.52 (−3.59 to −1.45)	<0.001	−0.35 (−0.47 to −0.19)
Physical Health Composite Score (SF-12v2)					

	Intervention[b]	Usual Care[b]	Difference (95% CI)	P Value	Effect Size
Baseline	49.02 (48.02 to 50.02)	49.32 (48.32 to 50.32)	−0.30 (−1.71 to 1.11)	0.90	−0.03 (−0.17 to 0.11)
6 months	47.81 (46.79 to 48.83)	47.23 (46.20 to 48.25)	0.59 (−0.86 to 2.03)	0.90	0.05 (−0.07 to 0.17)
12 months	47.72 (46.68 to 48.77)	47.82 (46.77 to 48.87)	−0.10 (−1.58 to 1.38)	0.90	−0.01 (−0.16 to 0.14)
18 months	48.22 (47.18 to 49.26)	47.35 (46.30 to 48.40)	0.87 (−0.61 to 2.35)	0.90	0.08 (−0.05 to 0.22)
Mental Health Composite Score (SF-12v2)					
Baseline	31.64 (30.76 to 32.51)	32.06 (31.19 to 32.94)	−0.43 (−1.66 to 0.81)	0.90	−0.04 (−0.15 to 0.07)
6 months	43.98 (42.94 to 45.01)	39.99 (38.93 to 41.04)	3.99 (2.52 to 5.47)	<0.001	0.34 (0.21 to 0.47)
12 months	45.65 (44.54 to 46.76)	40.29 (39.17 to 41.41)	5.36 (3.78 to 6.93)	<0.001	0.47 (0.33 to 0.61)
18 months	45.64 (44.57 to 46.71)	41.75 (40.67 to 42.84)	3.89 (2.37 to 5.42)	<0.001	0.39 (0.24 to 0.54)
Healthy Days Score					
Baseline	11.46 (10.60 to 12.32)	11.16 (10.30 to 12.03)	0.30 (−0.92 to 1.52)	0.90	0.04 (−0.12 to 0.20)
6 months	5.74 (4.96 to 6.51)	7.81 (7.02 to 8.60)	−2.07 (−3.18 to −0.97)	0.005	−0.24 (−0.37 to −0.11)
12 months	5.77 (4.95 to 6.58)	7.51 (6.68 to 8.33)	−1.74 (−2.90 to −0.58)	0.05	−0.21 (−0.35 to −0.07)
18 months	5.06 (4.28 to 5.84)	6.94 (6.15 to 7.73)	−1.88 (−3.00 to −0.77)	0.02	−0.19 (−0.30 to −0.08)
Satisfaction with Overall Health Care Score					
Baseline	3.68 (3.59 to 3.77)	3.75 (3.66 to 3.84)	−0.07 (−0.20 to 0.06)	0.90	−0.06 (−0.17 to 0.05)
6 months	4.17 (4.07 to 4.26)	3.75 (3.66 to 3.85)	0.41 (0.28 to 0.55)	<0.001	0.40 (0.27 to 0.54)
12 months	4.03 (3.93 to 4.13)	3.80 (3.70 to 3.90)	0.22 (0.08 to 0.37)	0.03	0.22 (0.08 to 0.37)
18 months	3.88 (3.77 to 3.98)	3.79 (3.68 to 3.89)	0.09 (−0.06 to 0.24)	0.90	0.09 (−0.06 to 0.24)
Satisfaction with Mental Health Care Score					
Baseline	3.23 (3.14 to 3.33)	3.27 (3.17 to 3.36)	−0.03 (−0.17 to 0.10)	0.90	−0.03 (−0.17 to 0.10)
6 months	4.16 (4.06 to 4.26)	3.38 (3.28 to 3.49)	0.77 (0.63 to 0.92)	<0.001	0.72 (0.59 to 0.86)
12 months	3.88 (3.78 to 3.99)	3.36 (3.26 to 3.47)	0.52 (0.37 to 0.67)	<0.001	0.48 (0.34 to 0.62)

	Intervention[b]	Usual Care[b]	Difference (95% CI)	P Value	Effect Size
18 months	3.66 (3.55 to 3.77)	3.40 (3.29 to 3.51)	0.26 (0.10 to 0.41)	0.02	0.24 (0.09 to 0.38)

Abbreviations: CI, confidence interval; PHQ-8, Patient Health Questionnaire; SF-12v2, SF-12v2 Health Survey.

[a] All time effects were significant at $P < .001$ in all models. Intervention × time effects based on the WALD test were significant at $P < .001$ in all models for all outcomes except for the Physical Health Composite Score. All P values come from the longitudinal models (eg, given the estimates of the longitudinal model we obtained the predicted means at the four time points by intervention group and tested their difference at every time point using the correct t-test).

[b] Data are presented as adjusted mean (95% confidence interval).

Table 4

Proportion Achieving Response and Remission From Baseline BSI-12 Score[a]

	Intervention	Usual Care	NNT (95% CI)	*P* Value
Response[b]				
6 months	289/503 (57.46)	185/501 (36.80)	4.84 (3.93–6.29)	<0.001
12 months	320/503 (63.66)	224/501 (44.68)	5.27 (4.18–5.27)	<0.001
18 months	325/503 (64.64)	258/501 (51.47)	7.59 (5.51–12.22)	<0.001
Remission[c]				
6 months	218/503 (43.40)	138/501 (27.49)	6.28 (4.83–9.98)	<0.001
12 months	259/503 (51.49)	167/501 (33.28)	5.5 (4.32–7.55)	<0.001
18 months	257/503 (51.06)	184/501 (36.77)	7.0 (5.19–10.75)	<0.001

Abbreviations: BSI-12, Brief Symptom Inventory; CI, confidence interval; NNT, number needed to treat.

[a]Data presented as proportion (percentage) weighted for non-response at each follow-up.

[b]Response defined as ≥ 50% reduction on the BSI-12, with all those in remission considered to have responded.

[c]Remission defined as a per item BSI-12 score of <0.5 (total score <6).