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J Consult Clin Psychol. Author manuscript; available in PMC 2015 April 01.

Published in final edited form as:
J Consult Clin Psychol. 2014 April ; 82(2): 212–224. doi:10.1037/a0035458.

Predictors and Moderators of Treatment Response in Childhood Anxiety Disorders: Results from the CAMS Trial

Scott N. Compton[1,§], **Tara S. Peris**[2], **Daniel Almirall**[3], **Boris Birmaher**[4], **Joel Sherrill**[5], **Phillip C. Kendall**[6], **John S. March**[1], **Elizabeth A. Gosch**[7], **Golda S. Ginsburg**[8], **Moira A. Rynn**[9], **John C. Piacentini**[2], **James T. McCracken**[2], **Courtney P. Keeton**[8], **Cynthia M. Suveg**[10], **Sasha G. Aschenbrand**[9], **Dara Sakolsky**[4], **Satish Iyengar**[4], **John T. Walkup**[11], and **Anne Marie Albano**[9]

[1]Department of Psychiatry and Behavioral Sciences, Duke University Medical Center

[2]Semel Institute for Neuroscience and Human Behavior, University of California at Los Angeles

[3]Survey Research Center, Institute for Social Research, University of Michigan

[4]Western Psychiatric Institute and Clinic, University of Pittsburgh Medical Center

[5]Division of Services and Intervention Research, National Institute of Mental

[6]Department of Psychology, Temple University

[7]Department of Psychology, Philadelphia College of Osteopathic Medicine

[8]Division of Child and Adolescent Psychiatry, The Johns Hopkins Hospital

[9]Department of Child Psychiatry, Columbia University Medical Center

[10]Department of Psychology, University of Georgia

[11]Division of Child and Adolescent Psychiatry, Weill Cornell Medical College

Abstract

Objective—To examine predictors and moderators of treatment outcomes among 488 youth ages 7-17 years (50% female; 74% ≤ 12 years) with DSM-IV diagnoses of separation anxiety disorder, social phobia, or generalized anxiety disorder who were randomly assigned to receive either cognitive behavior therapy (CBT), sertraline (SRT), their combination (COMB), or medication management with pill placebo (PBO) in the Child/Adolescent Anxiety Multimodal Study (CAMS).

Method—Six classes of predictor and moderator variables (22 variables) were identified from the literature and examined using continuous (Pediatric Anxiety Ratings Scale; PARS) and categorical (Clinical Global Impression Scale-Improvement; CGI-I) outcome measures.

Results—Three baseline variables predicted better outcomes (independent of treatment condition) on the PARS, including low anxiety severity (as measured by parents and independent evaluators) and caregiver strain. No baseline variables were found to predict week 12 responder

[§]Corresponding author: Scott N. Compton, Duke University Medical Center, Department of Psychiatry and Behavioral Sciences, DUMC Box 3527, Durham, NC 27710. scompton@duke.edu.

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status (CGI-I). Participant's principal diagnosis moderated treatment outcomes, but only on the PARS. No baseline variables were found to moderate treatment outcomes on week 12 responder status (CGI-I).

Discussion—Overall, anxious children responded favorably to CAMS treatments. However, having more severe and impairing anxiety, greater caregiver strain, and a principal diagnosis of social phobia were associated with less favorable outcomes. Clinical implications of these findings are discussed.

Keywords

childhood; adolescent; anxiety disorders; predictors; moderators; sertraline; cognitive behavioral therapy

Predictors and Moderators of Treatment Outcome for Child and Adolescent Anxiety

Childhood anxiety disorders are among the most common mental health conditions affecting youth, and they are associated with persistent difficulties and long-term impairment into adulthood (Costello, Egger, & Angold, 2005; Ezpeleta, Keeler, Alaatin, Costello, & Angold, 2001; Goldstein, Olfson, Wickramaratne, & Wolk, 2006; Kessler, Berglund, Demler, Jin, & Walters, 2005; Wittchen, Stein, & Kessler, 1999). Randomized controlled trials (RCT) for pediatric anxiety disorders suggest that both cognitive behavioral therapy (CBT) and selective serotonin reuptake inhibitor medications (SSRIs) are effective in decreasing anxiety symptoms, functional impairment (see Compton et al., 2004; Ipser, Stein, Hawkridge, & Hoppe, 2009; James, Soler, & Weatherall, 2005; Silverman, Pina, & Viswesvaran, 2008; Walkup, Labellarte, & Ginsburg, 2002), and, in some cases, comorbid diagnoses (Barrett, 1998; Barrett, Dadds, & Rapee, 1996; Beidel et al., 2007; Kendall, 1994; Kendall et al., 1997; Silverman, Kurtines, Ginsburg, Weems, Lumpkin, et al., 1999; Silverman, Kurtines, Ginsburg, Weems, Rabian, et al., 1999; Silverman et al., 2008; Walkup et al., 2008). Despite these encouraging findings, not all youngsters are responsive (e.g., CBT or SSRIs) with 40-50% non-response rates. Moreover, there are limited data that clinicians can use to guide treatment decisions regarding which patients might benefit most and which might benefit least from currently available empirically supported treatments.

Identifying predictors and moderators of treatment outcome is key to individualizing treatment (Kazdin, 2007). In the context of RCTs, predictors can be baseline characteristics of participants that are related to post-treatment outcomes in a consistent way (i.e., both in terms of magnitude and direction) regardless of which treatment the participant received. Kramer et al. (2002) refer to these as *non-specific predictors* to connote the understanding that the predictive relationship is not specific to one treatment or another. Non-specific predictors are useful in identifying, at baseline, refractory subgroups of individuals who require new or refined interventions. Moderators can also be baseline characteristics of participants that are associated with post-treatment outcomes. However, for moderators, the association differs in magnitude or direction (or both) depending on the specific treatment. That is, moderators specify for whom an assigned treatment is likely to be more or less effective. Such information is highly useful for matching individuals to specific treatments.

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Further, because both predictors and moderators are correlates of primary outcomes, they can be helpful in the design of future RCTs by identifying potential stratification variables (Kernan, Viscoli, Makuch, Brass, & Horwitz, 1999).

The Child/Adolescent Anxiety Multimodal Study (CAMS) is the largest RCT of anxious children and adolescents to date. CAMS evaluated the relative efficacy of CBT (Coping cat program), medication (sertraline; SRT), their combination (COMB), and pill placebo (PBO) in 488 youth between the ages of 7 and 17 who met DSM-IV diagnostic criteria for one or more of the following disorders: separation anxiety disorder (SAD), social phobia (SoP), or generalized anxiety disorder (GAD) (see Compton et al., 2010 for study design and rationale). In terms of mean outcomes after 12 weeks of acute treatment, CAMS found a clear ordering of outcomes with COMB treatment superior to both mono-therapies and PBO, and the two mono-therapies superior to PBO. CBT and SRT were not significantly different from each other (Walkup et al., 2008). These findings, as well as results from other RCTs, support the conclusion that each treatment is effective for youth suffering from anxiety disorders, with evidence suggesting that COMB treatment is more effective than mono-therapies.

CAMS, with an N of 488 and a heterogeneous sample, is well suited to explore predictors and moderators of outcome. In addition, CAMS collected data in key domains relevant to potential predictor and moderator analyses using psychometrically sound measures, multiple informants, and independent evaluators (IEs) blind to treatment condition. Finally, unlike other trials, CAMS involved randomization to more than one empirically supported treatment.

To place results from the present analyses within the context of the broader treatment literature on pediatric anxiety disorders, we reviewed peer-reviewed psychosocial and medication studies for all DSM-IV pediatric anxiety disorders (ages 6-18) published between 1980 and 2010 that included either predictor analyses or moderator analyses. Studies were identified from previous literature reviews (Compton, Burns, Egger, & Robertson, 2002; Ginsburg, Kingery, Drake, & Grados, 2008; Ollendick & King, 2000; Silverman et al., 2008; Walkup et al., 2002) and by conducting Medline and PsycINFO searches using the following search terms: treatment outcome study, clinical trial, controlled clinical trial, anxiety, anxiety disorder, separation anxiety, anxiety neurosis, generalized anxiety disorder, obsessive-compulsive disorder, panic disorder, phobias, post-traumatic stress disorder, social anxiety, school refusal, and selective mutism.

This search identified 98 RCTs (53 psychosocial; 45 medication trials). With respect to predictors, 28 (28.6%) studies reported a formal predictor analysis, 17 (17.3%) of which found one or more significant findings. As in Table 1, findings from the predictor analyses were mixed. Among the significant findings, higher baseline symptom severity and poorer family functioning were consistent predictors of poorer outcome. With respect to moderator analyses, 16 (16.3%) studies reported a formal moderator analysis, but only 5 (5.1%) found significant results. However, these findings were also mixed with some studies showing that gender, type of anxiety disorder, severity of principal anxiety disorder, and comorbidities moderating the effect of treatments. In general, there are few consistent findings across

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studies. Small sample sizes (e.g., under 100) have been the norm, and findings, when present, often do not remain consistent across measures or informants. This variability limits the strength of the conclusions and underscores the need for further work.

Based on the literature, as well as recommendations about the domains that should be included when conducting predictor and moderator analysis in pediatric RCTs (Burns, Hoagwood, & Mrazek, 1999; Jensen, Hoagwood, & Petti, 1996), the present study evaluated 22 potential predictors and moderators of CAMS outcomes in the following domains: demographic characteristics, measures of severity, principal anxiety disorder and psychiatric comorbidity, parental and family psychopathology, psychosocial factors, and treatment expectancy.

Method

Participants

CAMS enrolled 488 children and adolescents between the ages of 7 and 17 across six study sites (see Compton et al., 2010; Walkup et al., 2008). As noted earlier, to be eligible for the study youth had to meet DSM-IV-TR (American Psychiatric Association, 2000) criteria for one or more of the following anxiety disorders: SAD, SoP, or GAD. Exclusion criteria included major depressive disorder (MDD), bipolar disorder, pervasive developmental disorder, and schizophrenia or schizoaffective disorder. Eligible participants were randomly assigned to one of the four treatment conditions and underwent 12 weeks of acute treatment: COMB (n=140), SRT (n=133), CBT (n=139), or PBO (n=76). Assessments were conducted at baseline, and weeks 4, 8, and 12 by IEs who were blind to study condition.

Of the total participants, 49.6% were female, 78.9% were Caucasian, 74.2% were 12 years of age or younger, 74.9% were rated as markedly to severely ill on the baseline Clinician Global Impressions-Severity rating scale (CGI-S; Guy, 1976), and 55.4% were recruited through advertisements and other forms of outreach (for details, see Kendall et al., 2010)

Description of Moderator and Predictor Variables Assessed in CAMS

Demographic Characteristics

Age and Gender: Age at baseline, in years, was dichotomized developmentally into preadolescents (7-12 years) and adolescents (13-17 years). Age was examined as a continuous variable and the results did not change. Gender was recorded at baseline.

Socioeconomic Status (SES): Hollingshead's two-factor index of social position classified the family SES (Hollingshead, 1957). The two-factor index combines ratings of parental occupation on a 1-9 scale (1=low occupational prestige using 1970 Census occupational codes) and education level on a 1-7 scale (1=less than 7th grade education). In generating a summary score, occupation is given a weight of 5 and education a weight of 3. Among families in which data was present on both father and mother (63.5% of the sample), each individual score was calculated and then averaged. The resulting total scores were collapsed into an ordinal scale of 1 and 5 (1=low SES). SES was further dichotomized into High SES (Scores 4-5; 78.9%) and Low SES (Scores 1-3; 21.1%).

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Race: Parents classified their children into one of the following categories: White, African American, Asian, Native Hawaiian or Other Pacific Islander, American Indian or Alaskan Native, or Other. As the majority of participants were white, race was dichotomized into two categories: majority (white; 78.9%) and minority (collapsing all other categories; 21.1%).

Hispanic Origin: Parents indicated whether their child was of Hispanic origin (e.g., Spanish, Hispanic, or Latino; 12.1%) or not (87.9%).

Referral Source: Referral sources were categorized: (1) advertisements or other forms of outreach (i.e., presentations to parent groups; 55.7%) or (2) referral by a physician or other mental health provider (44.3%). This variable was examined based on prior data suggested that participants recruited to RCTs via advertisements (relative to referral) show more favorable outcomes (Brent et al., 1998).

Measures of Symptom Severity

Duration of Anxiety Disorder: Maximum duration (in months) of a participant's anxiety disorder was calculated by identifying the anxiety disorder with the earliest onset. This date of onset was then subtracted from the date of study entry. The disorder used in this calculation did not have to the participant's principal disorder identified at baseline.

Severity of Symptoms from Three Sources: A principal component analysis (PCA) was conducted on a set of measures that assessed symptom severity from the perspective of the child, parent, and IE. The PCA reduced the number of questionnaires to the principal components that account for most of the observed variance. Following a brief description of the PCA[1] each measure is described.

The principal axis method was used to extract components, which was followed by a varimax (orthogonal) rotation. Three components displayed eigenvalues greater than 1, and the scree test also suggested that the first three components were clinically meaningful and resulted in a simple structure. The three components (accounting for 67% of the variance) were retained for rotation. In interpreting the rotated factor pattern, all child symptom reports loaded onto the first component, which was labeled *Global Child Anxiety Severity Rating* component, all parent symptom reports loaded on the second component, which was labeled *Global Parent Anxiety Severity Rating* component, and finally all IE measures loaded onto the third component, which was labeled *Global IE Anxiety Severity Rating* component.

The following child-report and parent-report questionnaires were included in the PCA:

- *Multidimensional Anxiety Scale for Children* (MASC; March, Parker, Sullivan, Stallings, & et al., 1997). The MASC measures anxiety symptoms from the perspective of the child and parent. Higher scores suggest greater impairment and severity. The MASC total score from the child and parent was used in the PCA. The MASC has been shown to have acceptable internal consistency ($\alpha = .87$) in

[1]Additional details regarding the PCA are available by request from the first author.

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clinical samples (Rynn et al., 2006) and has normative data on the child version. With respect to predictive validity, MASC scores do well predicting to ADIS-identified specific anxiety disorders (Villabo, Gere, Torgersen, March, & Kendall, 2012).

- Screen for Child Anxiety Related Emotional Disorders (SCARED; Birmaher et al., 1997). The SCARED is a child- and parent-measure of the presence of child anxiety symptoms. Higher scores indicate greater impairment and severity. The SCARED total score from the child and parent was used in the PCA. The internal consistency of the SCARED total score was $\alpha = .94$ (Muris, Mayer, Bartelds, Tierney, & Bogie, 2001);
- *Mood and Feelings Questionnaire* (MFQ; Angold et al., 1995). The MFQ assesses depressive symptoms from both the perspective of the child and parent. The MFQ total score was used in the PCA with higher scores indicating greater depressive symptom impairment and severity. The MFQ total score has shown internal consistency of .75 to .78, alphas (Costello, Benjamin, Angold, & Silver, 1991; Wood, Kroll, Moore, & Harrington, 1995).
- *Child Anxiety Impact Scale* (CAIS; Langley, Bergman, McCracken, & Piacentini, 2004). The CAIS evaluates participant anxiety related to impairment in school, social, and family functioning. Higher scores suggest higher levels of impairment. The CAIS total score has good internal consistency, with $\alpha = .87$ (Langley et al., 2004).
- *Physical Symptom Checklist* (PSC; TADS Study Team, 2004). The PSC was completed by the participant (no parent report) and was used to assess general health problems, including somatic and central nervous system symptoms. The PSC total score was used in the PCA. Analysis of the baseline PSC in the CAMS sample revealed that it possess excellent internal consistency, with $\alpha = .91$.

The following IE measures were also included in the PCA:

- Anxiety Disorder Interview Schedule Clinician Severity Rating (ADIS-CSR; Albano & Silverman, 1996; Silverman & Albano, unpublished manuscript). The ADIS-CSR is a single rating (from of 0 to 8) completed by the IE to summarize the overall severity of each disorder for which the participant met DSM-IV criteria. Higher scores suggest greater severity. The intraclass correlation coefficient (as discussed in Shrout & Fleiss, 1979) for the inter-rater reliability between the CAMS IEs and CAMS quality assurance (QA) raters on a random sample of 141 doubly rated assessments for each CSR diagnosis (ratings that focused on one or more of the three target anxiety disorders) was .88 for SAD, .85 for SoP, and .82 for GAD, respectively.
- *Clinical Global Impression Scale-Severity* (CGI-S; Guy, 1976). The CGI-S is a single IE rated item (range of 1 to 7) indicating the global severity of each participant's anxiety disorder(s). Higher scores suggest greater severity. Although widely used as an outcome measure in psychopharmacology trials, few studies of its psychometric properties have been published. However, in CAMS, the

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consistency of the IE ratings of the CGI-S with the PARS total score for the same participant revealed a correlation of .78 suggesting both measures tap overall anxiety severity.

- *Children's Global Assessment Scale* (CGAS; Shaffer et al., 1983). The CGAS is a single item (0 to 100) IE estimate of overall symptom severity and functional impairment. Lower scores indicate greater functional impairment (for the PCA and ease of interpretation, the CGAS was reversed scored). The intralcass coefficient for retest reliability was .83 (Bird, Canino, Rubio-Stipec, & Ribera, 1987).

Measures of Anxiety Disorder(s) and Psychiatric Comorbidity

Principal Anxiety Disorder: ADIS-CSR scores determined a participant's principal (primary) anxiety disorder. For those who met criteria for more than one target anxiety disorder, the highest ADIS-CSR score determined their principal disorder. When participants met criteria for two or more target anxiety disorders with the same ADIS-CSR score, data from the child SCARED or, when necessary, the parent SCARED were used. For example, if a participant met criteria for SAD and GAD each with an ADIS-CSR of 6, the SAD and GAD subscale scores on the SCARED were used (whichever subscale was highest, suggesting greater symptom severity, determined the principal disorder). In the unlikely event, this first step did not resolve the tie (i.e., child SCARED subscales were the same), the parent SCARED was used in a similar manner to break the tie. Of the participants at baseline, 74.6% of the principal diagnoses were determined by relying only on ADIS-CSR ratings. Remaining ties were broken using SAD, SoP and GAD subscales on the child and parent SCARED, 23.2% and 2.2% respectively.

Any Externalizing Disorder: If the participant met DSM-IV criteria on the ADIS-C/P for oppositional defiant disorder, conduct disorder, or attention-deficit hyperactivity disorder, then he or she received a 1 on this variable, 0 otherwise.

Parental and Family Psychopathology

The State-Trait Anxiety Inventory-A-Trait Scale (STAI-A-Trait; Spielberger, 1983): The STAI-A-Trait is a self-report measure of adult anxiety. The total score measures long-standing “trait anxiety” as opposed to “state anxiety” (higher scores indicate higher levels). Studies show that the STAI-A-Trait has internal consistency of > .86 (Gros, Antony, Simms, & McCabe, 2007; Gros, Simms, & Antony, 2010). The STAI-A-Trait has predictive validity in two situations (Kendall, 1978).

The Brief Symptom Inventory (BSI; Derogatis, 1993): The BSI is a dimensional measure of symptoms of parent psychopathology. The BSI Global Severity Index (BSI-GSI) provides a single score of current psychological distress and symptoms (higher values greater severity. The BSI-CSI has internal consistency $\alpha = .90$ (Derogatis & Melisaratos, 1983).

Family Mental Health Treatment History: Family history of mental health treatment was collected at baseline via an interview conducted by the site project coordinators. Data from first-degree biological relatives were included in the current analysis. A variable was created

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to indicate whether a biological parent or sibling was currently receiving mental health services or had received mental health services in the past or not.

For each of the parental measures mentioned above, 87% of the primary reporters were mothers, 9% were fathers, and 4% were other caretakers or relatives (e.g., grandparent).

Psychosocial Factors

The Brief Family Assessment Measure-III (BFAM-III; Skinner, Steinhauer, & Santa-Barbara, 1995): The BFAM-III was used to obtain a multi-rater assessment of family functioning from the perspective of children and their parents. The BFAM-III General Scale, tapping overall perceived family health, was used. Higher scores suggest greater levels of perceived family dysfunction. The BFAM-III has acceptable internal consistency, with alphas ranging from .60 to .80 (Skinner, Steinhauer, & Sitarenios, 2000).

The Caregiver Strain Questionnaire (CSQ; Brannan, Heflinger, & Bickman, 1997): The CSQ, completed by parents, indicates the impact of caring for a child with emotional problems. The CSQ assesses the following domains: disruption of family life and relationships, demands on time, negative mental and physical health effects on any family member, financial strain, sacrifice, disruption of social/community life, worry and guilt, fatigue and strain, and embarrassment. The CSQ total score was used with higher scores indicating greater amounts of caregiver strain. The CSQ has sound psychometric properties among families of children with emotional problems, with $\alpha = .70$ (Brannan et al., 1997; Khanna et al., 2011).

Treatment Expectancy

Pretreatment Expectancy: Prior to randomization, treatment expectancy was assessed by asking each child and parent to indicate how much improvement they expected under each of the three active treatments (COMB, SRT, CBT). Possible ratings were 1 (very much improvement) to 7 (very much worse). Treatment expectancy ratings for the treatment to which the child was randomly assigned were used in the current analyses. Expectations for improvement with SRT were also used for those participants assigned to PBO.

Treatment Assignment Reaction: Child and parent reactions to their randomly assigned treatment condition were recorded at the time of randomization. Scores ranged from 1 (extremely disappointed) to 5 (extremely pleased).

Outcome Measures

Consistent with the CAMS outcomes paper (Walkup et al., 2008), two measures (one continuous, one binary) were analyzed separately. The PARS was the continuous outcome and week 12 response rates based on the CGI-I was the binary outcome. Both measures were administered by IEs, blind to participant's treatment condition.

The PARS total score was computed by summing six items assessing anxiety severity, frequency, distress, avoidance, and interference during the previous week. PARS total scores can range between 0 to 30 with higher scores indicating greater impairment and severity.

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The PARS has internal consistency (α = .64) inter-rater reliability (*r* = .97), retest reliability (*r* = .55), and correlates significantly with several validity indicators (RUPP Anxiety Study Group, 2002).

IE ratings on the CGI-I determined responder status. Treatment responders were those who received a CGI-I score of 1 (very much improved) or 2 (much improved) at the 12-week assessment point; if CGI-I ≥ 3, the child was classified as a non-responder. The CGI-I is related to self-report and clinician-administered measures of improved symptomatology and improved functional impairment (Zaider, Heimberg, Fresco, Schneier, & Liebowitz, 2003).

Data Processing and Statistical Method

Missing Data—Of the 488 participants, 48 (10%) did not complete the post-treatment assessment. To manage missing values multiple imputation was employed (Little & Rubin, 2002; Rubin, 1996), using a sequential regression multivariate imputation algorithm as implemented in the IVEware (Raghunathan, Solenberger, & Van Hoewyk, 2002) package for SAS. The imputation model included all baseline demographic characteristics, total scores on all parent and child self-report measures at each assessment point, IE measures of clinical outcome at each assessment point, study site, and treatment condition. Twenty (20) imputed data sets were generated, and the results of identical analyses on each imputed data set were combined using conventional guidelines (Little & Rubin, 2002).

Statistical Models—To investigate potential moderators of treatment using the PARS as the outcome, separate longitudinal regression models were fit for each candidate moderator. Each regression model included dummy indicators for time (assessment visit, dummy coded with baseline as referent), treatment condition (dummy coded with PBO as referent), candidate moderator, and all two-way and three-way interaction terms. To adjust for possible site differences, dummy indicators for site were included. Residual error terms were assumed to follow a mean-zero, normal distribution with a compound symmetry covariance structure to capture the within person correlation over time. Models were fit using SAS PROC MIXED with the REPEATED statement. All continuous candidate moderators were grand mean centered. A candidate variable was considered a moderator if the multivariate three-way interaction term (time × treatment × moderator) was statistically significant. To enhance interpretation of significant moderators, fitted models were used to generate standardized effect size (ES) estimates at 12 weeks posttreatment for each pairwise between-treatment comparison. For categorical moderators this was done at different levels of the moderator (Aiken & West, 1991).

For the binary outcome (week 12 responder status based on the CGI-I), separate logistic regression models (one per candidate moderator) were used. These models were fit using SAS GENMOD with a logistic link function. Each logistic regression model included site (dummy coded), treatment condition (dummy coded with PBO as referent), candidate moderator, and all two-way interaction terms between the dummy coded treatment conditions and candidate moderator. For these models, a candidate moderator was considered to be significant if the multivariate two-way interaction terms (treatment × moderator) were statistically significant.

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Non-specific predictors are baseline measures that are not moderators, but still correlate with outcome (Kramer et al., 2002).[2] Therefore, to evaluate candidate non-specific predictors, we focused on models where the baseline measure was not found to moderate treatment effects. In these models, any candidate baseline variable that had a significant main effect was classified as a non-specific predictor.

All randomized patients were included in all analyses (intent-to-treat). A two-step procedure (Mehrotra & Heyse, 2004) adjusted results for multiple comparisons. First, candidate predictors and moderators were grouped into six subsets based on similar functional characteristics (i.e., demographic variables, measures of severity, etc). Second, an adaptive Benjamini-Hochberg false discovery rate (Benjamini & Hochberg, 1995, 2000) was used to adjust results for multiple comparisons within each subset. Candidate predictors and moderators with a corrected p-value of $\leq .05$ (two-sided) were considered significant. Following a significant moderator, we focus on the interpretation of ES estimates if the outcome was the PARS or differences in rates of response if the outcome was CGI-I responder status.

Results

Overall

Results of the predictor and moderator analyses are in Table 2. Of the 22 candidate variables evaluated, 3 (14%) emerged as predictors in models where the PARS at week 12 was the outcome and none were identified as predictors in models where the CGI-I responder status at week 12 was the outcome. Regarding moderators, 1 (4%) variable was found to moderate the relationship between treatment and outcome in models where the PARS was the outcome.[3] No candidate variables were found to moderate treatment outcomes on CGI-I responder status at 12 weeks post-treatment. Details are presented below.

Relationship Among Candidate Variables

Pearson correlations among the candidate predictors/moderators are in Table 3. As expected, significant correlations were found among principal diagnoses, child reports of anxiety severity, and parent reports of parent psychopathology and measures of child anxiety severity and functional impairment.

Predictors

Predictors of Week 12 PARS Total Score—Significant predictors of the PARS week 12 outcomes are summarized in Table 2. Among the demographic characteristics, parental and family psychopathology and treatment expectancy domains, no specific candidate variables predicted week 12 PARS outcomes after adjusting for multiple comparisons. However, two measures of baseline symptoms severity and one psychosocial factor significantly predicted week 12 PARS outcomes in the absence of moderation. That is, higher overall symptom severity at baseline (as measured by the *Global Parent Anxiety*

[2]To clarify, according to Kraemer et al. (2002), a moderator is a treatment specific predictor. A baseline measure cannot be both a moderator (treatment specific predictor) and a non-specific predictor. A baseline measure, however, may be neither.
[3]We examined age and gender as potential moderators of the reported findings but they were nonsignificant.

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Severity Index and *Global IE Anxiety Severity Index*) was associated with higher week 12 PARS scores across treatment conditions, p=.02 and p<.01, respectively. The *Global Child Anxiety Severity Index* did not predict week 12 PARS outcomes. Participants whose parents reported higher levels of baseline caregiver strain also had significantly higher week 12 PARS scores (p=.04).

Predictors of Week 12 CGI-I Response Rates—None of the candidate predictors were associated with week 12 response rates.

Moderators

Moderators of PARS Outcomes—For each covariate (putative moderator), Table 2 presents the results of the multivariate test of the null hypothesis that the covariate does not moderate any of the pairwise treatment effects on PARS outcomes at week 12 (the 4th assessment visit). This is the hypothesis test that the following 3 three-way interactions are zero: *I(visit = 4) × I(COMB) × moderator*, *I(visit = 4) × I(SRT) × moderator*, and *I(visit = 4) × I(CBT) × moderator*, where *I(visit = 4)* is a binary indicator for the 4th assessment visit that took place at week 12 (with baseline visit, as referent) and *I(COMB)*, *I(SRT)*, *I(CBT)* are binary indicators for COMB, SRT, CBT treatment conditions (with PBO, as referent), respectively. To facilitate the interpretation of the results, Table 3 also presents significant pairwise between-treatment ES estimates (with 95% confidence intervals) within each level of the putative moderator. A negative ES estimate indicates that participants in the treatment condition listed first had better outcomes on average than those in the comparison treatment condition listed second. For example, an ES of −0.80 in the comparison between COMB vs. SRT indicates that participants who received COMB scored 0.80 standard units lower, on average, than those who received SRT. A positive ES estimate indicates the opposite. As in Table 2, and presented in more detail in Table 3, only one variable was found to moderate the effects of treatment on the PARS: a participant's principal baseline anxiety diagnosis (p<.04).

A primary goal of a moderator analysis is to provide empirical evidence to inform decision-making (i.e., to help clinicians decide which treatments, among a defined set of treatments, offers the highest probability of benefiting a patient with a specific baseline characteristic). In other words, moderator analyses can bring personalized treatments into better focus. Applied to the current context, moderator analysis can shed light onto which treatment (among those evaluated in CAMS) might confer the best outcomes for a child or adolescent with a certain baseline principal disorder.

Table 4 displays the results of pairwise comparisons between the 4 treatments evaluated in CAMS. Differences are expressed in terms of ES estimates. When interpreting the results, we relied loosely on Cohen's guidelines for interpreting ES estimates: namely, ES between 0.00-0.20 where considered small and suggest little practical advantage of one treatment over another, ES estimates between 0.21-0.60 were considered moderate and suggest modest practical advantage of one treatment over another, and ES estimates greater than 0.61 were considered large and suggest high practical advantage of one treatment over another.

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Diagnosis of Principal SAD: Participants with a principal diagnosis of SAD and treated with COMB had the most favorable outcomes on the PARS when compared to each of the other treatments, with ES estimates in the "large" range relative to SRT (0.98), CBT (0.91), and PBO (1.04). ES estimates between the remaining three treatment conditions (SRT, CBT, and PBO) were considerably smaller, suggesting that, based on the PARS, there is no clear advantage of one treatment over another. For heuristic purposes, the ordering of treatments that best describes outcomes for participants with a principal diagnosis of SAD is: COMB > SRT = CBT = PBO.

Diagnosis of Principal SoP: The overall pattern of pairwise comparisons among participants with a principal diagnosis of SoP suggests that, on the PARS, the two SRT-containing treatment conditions led to better treatment outcomes than did CBT or PBO. The magnitude of the ES differences, however, is in the *medium* range (COMB vs. CBT = 0.44, COMB vs. PBO = 0.59, SRT vs. CBT = 0.28, SRT vs. PBO = 0.43). ES estimates between COMB and SRT were in the *small* range (0.16), suggesting no clear advantage of COMB over SRT on the PARS. Likewise, the ES between CBT and PBO was also in the *small* range (0.13). For heuristic purposes, the ordering of treatments that best describes outcomes for participants with a principal diagnosis of SoP is: COMB = SRT > CBT = PBO.

Diagnosis of Principal GAD: The overall pattern of pairwise comparisons among participants with a principal diagnosis of GAD suggest that the two CBT-containing treatment conditions led to better outcomes. COMB treatment was again superior to the other treatments with ES estimates on the PARS in the *medium* range relative to SRT and CBT (0.69, 0.48, respectively) and in the *large* range relative to PBO (1.06). CBT showed a modest advantage over SRT and PBO, with ES estimates in the low end of the moderate range relative to SRT (0.21) and in the high end of the medium range relative to PBO (0.58). Finally, SRT alone conferred a moderate advantage relative to PBO, with a *medium* ES estimate of 0.37. For heuristic purposes, the ordering of treatments that best describes outcomes for participants with a principal diagnosis of GAD is: COMB > CBT > SRT > PBO.

Table 5 presents the model-based means and standard errors of the PARS at week 12. The means display the same pattern of results as found in the analyses of the ES estimates.

Moderators of post-treatment CGI-I Response Rates—Table 2 present the results of the multivariate tests of the null hypothesis that the covariate does not moderate any of the pairwise treatment effects when the outcome is treatment response status at week 12 (i.e., treatment responder or treatment non-responder). This is the hypothesis test that the 3 two-way interactions are zero: *I(COMB)* × *moderator*, *I(SRT)* × *moderator*, and *I(CBT)* × *moderator*, where *I(COMB), I(SRT), I(CBT)* are binary indicators for COMB, SRT, and CBT treatment conditions (with PBO, as referent), respectively. None of the candidate variables were found to moderate outcomes on week 12 treatment response rates.

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Discussion

The present study examined predictors and moderators of treatment outcome among anxious children and adolescents receiving CBT (Coping cat program), medication (sertraline), their combination, or pill placebo. With respect to predictors, within our sample of moderately severe cases, the most robust finding—across multiple measures and outcomes—was that youth with lower levels of baseline symptom severity and less caregiver strain had better outcomes independent of the type of treatment received. The clinical implications of these results suggest that higher levels of baseline symptom severity (at least as measured by IE and parent report) and caregiver strain are associated with smaller improvements by the end of 12 weeks of acute treatment. Moreover, findings linking severity of baseline symptoms and functional impairment to poorer treatment response are in keeping with the broader literature and suggest that very severe anxious children and adolescents may require interventions that are: (1) longer or more intensive, (2) added to or sequenced differently, or (3) different from those currently evaluated. Research that addresses how best to effectively treat those youth who are predicted to benefit less from currently available empirically supported treatments is much needed.

With regard to general demographics, no common demographic characteristics were found to predict treatment response on either (a) the PARS at Week 12 or (b) Week 12 response rates. Current research findings show a mixed picture with respect to demographic variables (such as age and gender). Unlike other childhood mental health conditions, such as attention deficit/hyperactive disorder (ADHD), there is little evidence to suggest that demographic factors (non-clinical characteristics) reliably predict treatment response. Although not clear why, perhaps this was due to the fact that CAMS, unlike the majority of previous trials in anxious populations, evaluated three state-of-the-art treatments and used a comparison (pill placebo) that carried with it many important non-specific treatment effects (e.g., regular visits with a caring professional, encouragement, etc). A parsimonious conclusion that can be drawn from the CAMS findings is that current evidence-based treatments are robust and can be used with confidence to treat anxious children and adolescents with a wide range of demographic characteristics, with the combination of CBT and SSRI medication (e.g., COMB) treatment associated with the greatest benefit.

Our results suggest that outcomes may vary based upon a child's principal, and by definition most impairing, anxiety disorder. These suggestions require further study. Analyses found that a child's principal anxiety disorder was a moderator of Week 12 PARS outcomes. It was not found to moderate or predict Week 12 CGI treatment response rates. Specifically, similarly to the results of the primary outcomes, the current moderator analyses suggest COMB treatment was associated with better outcomes overall across all diagnoses, with the greatest evidence for its added benefit among children and adolescents with a principal diagnosis of SAD. Among the two monotherapies (e.g., SRT-alone and CBT-alone), children and adolescents with SoP showed only slightly better outcomes with SRT than with CBT, whereas those diagnosed with GAD showed somewhat more favorable outcomes with CBT than SRT. The suggestion that medication may be particularly beneficial in children and adolescents with a principal disorder of social phobia is consistent with at least one prior study (Birmaher et al., 2003). It is worth noting, however, that individual CBT for SoP, as

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implemented in CAMS, did not routinely include exposure tasks with age-matched peers which has been shown to be highly effective by some (e.g., Silverman et al, 2008) and therefore may be less ecologically valid. For example, CBT delivered in peer groups that allow for naturalistic exposure and skills practice might be especially well suited for youth with a principal diagnosis of SoP (Manassis, Avery, Butalia, & Mendlowitz, 2004).

Current findings should be interpreted in light of study limitations. CAMS was designed to detect the main effects and predictor and moderator analyses were secondary, and should be considered within a hypothesis-generating context. Although CAMS evaluated a large, well-characterized, diverse sample, variability on some potential predictors/moderators was constrained (e.g., youth with comorbid depression were excluded as were children with severe cognitive limitations). Indeed, the range of socio-demographic, clinical, and contextual variables that have been suggested as potential predictors and moderators (e.g., Kendall, Hudson, Gosch, Flannery-Schroeder, & Suveg, 2008) and the data analytic challenges (e.g., limited samples and corresponding power) common to all moderator analyses of randomized clinical trials suggest the need for alternative approaches for conducting such analyses.

Limitations notwithstanding, the present investigation marks a comprehensive examination of moderators and predictors of treatment outcome for pediatric anxiety. The presence of only a few significant moderators is encouraging to the extent that it suggests that current evidenced-based treatments for pediatric anxiety disorders are effective across a diverse range of children and adolescents. Future studies are needed to examine the identified predictor and moderator variables more closely in the service of refining and tailoring treatments for this population.

Acknowledgments

Funding for this research project was supported by the following grants from NIMH: U01 MH64092 to Dr. Albano; U01 MH64003 to Dr. Birmaher; U01 MH064003 to Dr. Compton; U01 MH63747 to Dr. Kendall; U01 MH64107 to Dr. March; U01 MH64088 to Dr. Piacentini; and U01 MH064089 to Dr. Walkup. Sertraline and matching placebo were supplied free of charge by Pfizer, Inc.

Dr. Compton has received research support from Shire Pharmaceuticals and the National Institutes of Health. Dr. Birmaher is an author of and receives royalties from publications by Random House, Inc. and Lippincott Williams & Wilkins. Dr. Sherrill's participation was done as part of his duties as a NIH employee, and views within this article represent those of the authors and are not intended to represent the position of NIMH, NIH, or DHHS. Dr. Kendall is an author of and receives royalties from publications of materials for treating childhood anxiety. Dr. March has served on the advisory board for Lilly, Pfizer, BMS, and Shire. He has served as a consultant for BMS, Lilly, Pfizer, J&J, Shire, Travena, Translation Venture Partners, Alkermes, Vivus, and Avenir. He received study drug for an NIMH-funded study from Eli Lilly Pharmaceuticals and from Pfizer Pharmaceuticals. He is an equity holder in MedAvante. He receives royalties from MultiHealth Systems, OUP, and Guilford Press. He has received research support from Pfizer Pharmaceuticals and the National Institutes of Health. He has served on the DSMB for Lilly, Pfizer, and NIDA. Dr. Rynn has received research support from NIMH, NICHD, Eli Lilly, Pfizer, Inc., Merck, and Shire. She has served as a consultant for Shire. She receives royalties from APPI Press and writing fees from Oxford Press. Dr. Piacentini has received research support from Pfizer Pharmaceuticals. Dr. McCracken is a consultant for Roche, BioMarin, and PharmaNet, and has research contracts with Roche, Seaside Therapeutics, and Otsuka. Dr. Sakolsky receives funding from NIH and NARSAD, and honorarium from AACAP for teaching. Dr. Walkup is a consultant for Shire Pharmaceuticals and receives free medication and placebo from Lily, Pfizer, and Abbott for NIH funded studies. He receives honoraria from TSA and royalties from Guilford Press and Oxford Press. Dr. Albano is an author of and receives royalties for the Anxiety Disorders Interview Schedule from Oxford University Press.

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Table 1

Variables Examined as Potential Predictors/Moderators of CAMS Acute Treatment Outcomes and Findings from Previous Published Predictor and Moderator Analyses in Pediatric Anxiety

	Results from Previous Studies	
Category/CAMS Variable	**Previous Moderator**	**Previous Predictor**
Demographics		
Gender	1	2, 3
Age	1	4-8
Race		
SES		
Referral Source		
IQ		
Severity Markers		
Duration of episode		
Type of anxiety diagnosis		
Severity of primary diagnosis	9	6, 10-13
Functional impairment		11, 12, 14
Comorbidity		
Type of anxiety disorder	10	3, 9
Other internalizing disorder(s)		7, 15, 16
Externalizing disorder(s)		12, 17, 18
Number of comorbid disorders		
Tic disorder	19	
Family		
Parental/Family Psychopathology	12	7, 10, 16
Family functioning		13
Negative life events since treatment		18

Note: Previous studies are listed by order of appearance in table. A full citation can be found in the reference section: 1. Barrett et al. (1996); 2. Mendlowitz et al. (1999); 3. Ost et al. (2001); 4. Dummit et al. (1996); 5. Riddle et al. (2001); 6. Last et al. (1998); 7. Southam-Gerow et al. (2001); 8. Leonard et al. (1990); 9. Manassis et al. (2002); 10. Birmaher et al. (2003); 11. Piacentini et al. (2002); 12. Garcia et al. (2010); 13. Barrett et al. (2005); 14. Merlo et al. (2009); 15. Geller et al. (2003); 16. Berman et al. (2000); 17. Wever et al. (1997); 18. Kendall et al. (2004); 19. March et al. (2007). CAMS = Child/Adolescent Anxiety Multimodal Study

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Table 2

Baseline Predictors and Moderators of Acute Treatment Outcomes in CAMS (22)

Category/Variable (Measure)	Week 12 PARS		Week 12 Responder Status	
	Predictor *t* (raw and adjusted *p*-values)	Moderator *F* (raw and adjusted *p*-values)	Predictor *t* (raw and adjusted *p*-values)	Moderator *F* (raw and adjusted *p*-values)
Demographic Characteristics (6)				
Age (Preadolescent/Adolescent)	0.26 (.79; .79)	1.09 (.35; .78)	−0.67 (.50; .78)	0.14 (.94; .94)
Gender	2.08 (.04; .23)	0.36 (.78; .78)	−0.56 (.58; .78)	0.35 (.79; .94)
SES (Higher/Lower)	−0.96 (.34; .79)	0.79 (.50; .78)	−0.63 (.53; .78)	1.41 (.24; .94)
Race (Majority/Minority)	−0.79 (.43; .79)	0.41 (.75; .78)	0.37 (.71; .78)	0.19 (.91; .94)
Hispanic (Hispanic/Non-Hispanic)	1.16 (.24; .79)	1.72 (.16; .78)	1.24 (.22; .78)	1.19 (.31; .94)
Referral Source (Outreach/Referral)	0.67 (.50; .79)	0.71 (.54; .78)	0.28 (.77; .78)	0.20 (.90; .94)
Symptom Severity (4)				
Max Duration of Anxiety Disorder(s)	−1.17 (.24; .40)	0.08 (.97; .97)	−1.69 (.09; .36)	0.42 (.74; .74)
Global Child Anxiety Severity Index	−0.85 (.40; .40)	0.55 (.65; .97)	−0.19 (.85; .85)	0.48 (.70; .74)
Global Parent Anxiety Severity Index	**−2.65 (<.01; .02)***	0.79 (.50; .97)	−0.98 (.33; .85)	0.71 (.54; .74)
Global IE Anxiety Severity Index	**−5.28 (<.01; <.01)***	1.12 (.34; .97)	−0.44 (.66; .85)	0.87 (.45; .74)
Principal Anxiety Disorder(s) and Psychiatric Comorbidity (2)				
Principal Diagnosis	−2.22 (.03; .05)	**2.48 (.02; .04)***	0.56 (.73; .97)	0.58 (.75; .75)
Any Externalizing Disorder	−0.13 (.90; .89)	1.39 (.24; .24)	−0.04 (.97; .97)	1.84 (.14; .28)
Parental and Family Psychopathology (3)				
Parent Anxiety Symptoms (STAI-A-Trait)	−0.89 (.38; .64)	2.73 (.04; .13)	−0.60 (.55; .80)	2.67 (.05; .14)
Parent Current Level of Distress (BSI-GSI)	−0.47 (.64; .64)	2.23 (.08; .17)	−0.87 (.39; .80)	1.13 (.34; .67)
Family Mental Health Treatment History	−1.29 (.20; .60)	0.01 (.99; 1.0)	0.25 (.80; .80)	0.13 (.94; .94)
Psychosocial Factors (3)				
Family Functioning Child Report (BFAM-III-C)	−0.10 (.92; .92)	0.55 (.65; .66)	0.10 (.92; .92)	0.16 (.92; .92)
Family Functioning Parent Report (BFAM-III-P)	0.18 (.86; .92)	1.05 (.37; .66)	0.23 (.82; .92)	0.16 (.92; .92)
Caregiver Strain Questionnaire (CSQ)	**−2.54 (.01; .04)***	0.53 (.66; .66)	−0.93 (.35; .92)	0.57 (.63; .92)
Treatment Expectancy (4)				
Pre-Treatment Expectancy-C	1.10 (.27; .51)	0.63 (.57; .60)	−0.73 (.47; .87)	0.21 (.89; .89)
Pre-Treatment Expectancy-P	0.66 (.51; .51)	1.11 (.34; .60)	0.17 (.87; .87)	0.90 (.44; .89)
Treatment Assignment Reaction-C	−1.35 (.18; .51)	1.89 (.13; .60)	−1.20 (.23; .87)	1.16 (.32; .89)
Treatment Assignment Reaction-P	−1.27 (.21; .51)	0.80 (.49; .60)	−0.74 (.46; .87)	1.49 (.22; .89)

**p < .15

Adjusted *p*-values were those obtained by using the false discovery rate (FDR) correction procedure as implemented in SAS PROC MULTTEST version 9.3 TS Level 1M1.

*p < .05

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Table 3

Correlations and Corresponding p-values (in parentheses) Among Candidate Predictors/Moderators

	Gender	Age (binary)	SES	Race	Hispanic	Referral Source	Duration of Disorder	Anxiety Severity Child	Anxiety Severity Parent	Anxiety Severity IE	SoP	GAD	SAD	Any Internalizing Disorder	STAI-A-Trait	BSI-GSI	Family Mental Health Treatment	CSQ	BFAM-III-C	BFAM-III-P	PTE-C	PTE-P	TAR-C	TAR-P
Gender	—	.03 *(.53)*	−.07 *(.12)*	−.06 *(.18)*	**.15 *(<.01)***	.02 *(.70)*	−.04 *(.36)*	−.02 *(.61)*	**−.10 *(.03)***	−.03 *(.45)*	−.04 *(.38)*	.02 *(.60)*	.02 *(.66)*	.07 *(.12)*	<.01 *(.91)*	.01 *(.85)*	.05 *(.29)*	−.05 *(.25)*	.06 *(.20)*	.02 *(.71)*	−.08 *(.08)*	.01 *(.73)*	−.06 *(.17)*	−.03 *(.52)*
Age *(binary)*		—	**−.10 *(.04)***	−.04 *(.35)*	**.09 *(.04)***	.03 *(.50)*	**.30 *(<.01)***	**.21 *(<.01)***	−.04 *(.39)*	**.09 *(.05)***	**.17 *(<.01)***	.03 *(.45)*	**−.23 *(<.01)***	−.04 *(.37)*	−.03 *(.51)*	−.03 *(.47)*	−.02 *(.68)*	−.05 *(.28)*	.08 *(.07)*	**.10 *(.03)***	−.02 *(.59)*	.08 *(.08)*	.04 *(.43)*	<.01 *(.98)*
SES			—	<.01 *(.94)*	**−.19 *(<.01)***	**−.12 *(.01)***	.06 *(.22)*	**−.11 *(.02)***	.01 *(.80)*	−.03 *(.52)*	−.08 *(.08)*	.07 *(.14)*	.02 *(.71)*	−.03 *(.57)*	−.04 *(.37)*	−.08 *(.07)*	−.01 *(.83)*	.01 *(.75)*	−.09 *(.06)*	**−.12 *(<.01)***	.03 *(.53)*	−.03 *(.52)*	.07 *(.14)*	.02 *(.60)*
Race				—	**−.32 *(<.01)***	−.05 *(.23)*	.08 *(.07)*	−.09 *(.06)*	.04 *(.36)*	−.01 *(.90)*	**−.09 *(.05)***	**.09 *(.05)***	<.01 *(.91)*	−.04 *(.39)*	.04 *(.38)*	<.01 *(.99)*	**.14 *(<.01)***	.08 *(.07)*	**−.13 *(<.01)***	−.05 *(.25)*	<.01 *(.99)*	−.07 *(.14)*	−.02 *(.72)*	.08 *(.09)*
Hispanic					—	**.10 *(.03)***	**−.13 *(<.01)***	**.13 *(<.01)***	−.08 *(.09)*	−.08 *(.07)*	.06 *(.17)*	−.03 *(.49)*	−.04 *(.42)*	.08 *(.07)*	.04 *(.40)*	.04 *(.40)*	**−.10 *(.03)***	−.06 *(.21)*	**.17 *(<.01)***	.07 *(.11)*	−.01 *(.82)*	.07 *(.13)*	.07 *(.15)*	.03 *(.46)*
Referral Source						—	−.05 *(.33)*	.06 *(.18)*	−.03 *(.55)*	−.06 *(.18)*	−.08 *(.08)*	**.10 *(.03)***	−.02 *(.64)*	.04 *(.33)*	**.11 *(.01)***	.07 *(.15)*	−.02 *(.73)*	−.01 *(.76)*	.05 *(.28)*	.08 *(.07)*	−.02 *(.70)*	−.03 *(.50)*	.04 *(.41)*	−.01 *(.83)*
Duration of Disorder							—	.03 *(.48)*	.03 *(.57)*	**.18 *(<.01)***	**.17 *(<.01)***	**−.11 *(.01)***	−.07 *(.13)*	−.05 *(.24)*	**−.17 *(<.01)***	**−.11 *(.02)***	.03 *(.55)*	**−.08 *(.01)***	**−.12 *(<.01)***	**−.10 *(.02)***	.05 *(.27)*	−.02 *(.70)*	−.01 *(.88)*	−.01 *(.76)*
Anxiety Severity Child								—	.00 *(1.0)*	.00 *(1.0)*	.01 *(.83)*	.08 *(.07)*	−.10 *(.02)*	−.03 *(.57)*	.04 *(.34)*	.03 *(.51)*	−.01 *(.87)*	−.06 *(.20)*	**.24 *(<.01)***	.06 *(.16)*	−.03 *(.57)*	.01 *(.77)*	**.11 *(.02)***	.07 *(.14)*
Anxiety Severity Parent									—	.00 *(1.0)*	−.07 *(.11)*	<.01 *(.92)*	.08 *(.08)*	**.16 *(<.01)***	**.33 *(<.01)***	**.44 *(<.01)***	.06 *(.23)*	**.87 *(<.01)***	.04 *(.34)*	**.16 *(<.01)***	−.04 *(.39)*	−.08 *(.07)*	.05 *(.29)*	.06 *(.16)*
Anxiety Severity IE										—	.04 *(.33)*	−.05 *(.31)*	<.01 *(.97)*	−.04 *(.41)*	**−.10 *(.02)***	**−.11 *(.01)***	−.02 *(.65)*	.07 *(.14)*	−.02 *(.64)*	−.04 *(.36)*	<.01 *(.93)*	−.04 *(.34)*	−.02 *(.60)*	.05 *(.32)*
SoP											—	**−.63 *(<.01)***	**−.45 *(<.01)***	−.05 *(.25)*	<.01 *(.91)*	−.06 *(.16)*	−.03 *(.51)*	**−.12 *(.01)***	.06 *(.21)*	.03 *(.49)*	.08 *(.06)*	.05 *(.23)*	−.04 *(.33)*	.05 *(.28)*
GAD												—	**−.41 *(<.01)***	.01 *(.74)*	<.01 *(.93)*	.03 *(.57)*	.04 *(.37)*	−.02 *(.70)*	.02 *(.71)*	<.01 *(.91)*	**−.14 *(<.01)***	−.01 *(.85)*	.05 *(.27)*	−.03 *(.49)*
SAD													—	.04 *(.33)*	<.01 *(.98)*	.05 *(.31)*	−.01 *(.80)*	**.16 *(<.01)***	−.09 *(.06)*	−.04 *(.34)*	.06 *(.17)*	−.05 *(.24)*	−.01 *(.89)*	−.02 *(.64)*
Any Externalizing Disorder														—	**.12 *(<.01)***	**.10 *(.02)***	.01 *(.84)*	**.21 *(<.01)***	.06 *(.17)*	**.11 *(.01)***	−.02 *(.74)*	<.01 *(.95)*	−.01 *(.82)*	−.02 *(.74)*
STAI-A-Trait															—	**.86 *(<.01)***	**.14 *(<.01)***	**.32 *(<.01)***	**.11 *(.01)***	**.48 *(<.01)***	−.05 *(.24)*	.03 *(.51)*	**.08 *(.01)***	.05 *(.28)*
BSI-GSI																—	.05 *(.23)*	**.42 *(<.01)***	.06 *(.17)*	**.37 *(<.01)***	<.01 *(.93)*	.03 *(.48)*	**.12 *(.01)***	.05 *(.29)*
Family Mental Health Treatment																	—	.06 *(.25)*	−.04 *(.47)*	.01 *(.75)*	−.03 *(.58)*	−.04 *(.50)*	−.05 *(.32)*	.02 *(.67)*
CSQ																		—	.05 *(.24)*	**.18 *(<.01)***	<.01 *(.93)*	.02 *(.64)*	.05 *(.28)*	.03 *(.53)*
BFAM-III-C																			—	**.26 *(<.01)***	.04 *(.40)*	.07 *(.12)*	.04 *(.36)*	.01 *(.82)*
BFAM-III-P																				—	.01 *(.88)*	.04 *(.41)*	.05 *(.31)*	<.01 *(.96)*
PTE-C																					—	**.19 *(<.01)***	**−.30 *(<.01)***	**−.18 *(<.01)***
PTE-P																						—	**−.13 *(<.01)***	**−.49 *(<.01)***
TAR-C																							—	**.32 *(<.01)***
TAR-P																								—

SoP = primary diagnosis of social phobia; GAD = primary diagnosis of generalized anxiety disorder; SAD = primary diagnosis of separation anxiety disorder; STAI-A-Trait = The State-Trait Anxiety Inventory-A-Trait Scale; BSI-GSI = Brief Symptom Inventory-Global Severity Index; CSG = Caregiver Strain Questionnaire; BFAM-III-C = Brief Family Assessment Measure-III-Child Report; BFAM-III-P = Brief Family Assessment Measure-III-Parent Report; PTE-C = Pretreatment Expectancy-Child Report; PTE-P = Pretreatment Expectancy-Parent Report; TAR-C = Treatment Assignment Reaction-Child; TAR-P = Treatment Assignment Reaction-Parent

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Table 4

CAMS Moderator of Week 12 Treatment Outcomes

Moderator	Subgroup	Week 12 PARS Pairwise Effect Size (ES) Difference (95% Confidence Intervals)‡						F (p-value)†
		COMB vs. SRT	COMB vs. CBT	COMB vs. PBO	SRT vs. CBT	SRT vs. PBO	CBT vs. PBO	
Primary Anxiety Disorder	SAD	−0.98 (−1.40, −0.55)	−0.91 (−1.31, −0.51)	−1.04 (−1.53, −0.55)	0.07 (−0.32, 0.46)	−0.06 (−0.53, 0.40)	−0.13 (−0.58, 0.32)	2.48 (0.04)
	SoP	−0.16 (−0.48, 0.16)	−0.44 (−0.73, −0.16)	−0.59 (−1.02, −0.16)	−0.28 (−0.59, 0.02)	−0.43 (−0.87, 0.01)	−0.15 (−0.57, 0.28)	
	GAD	−0.69 (−0.96, −0.42)	−0.48 (−0.76, −0.19)	−1.06 (−1.40, −0.72)	0.21 (−0.09, 0.51)	−0.37 (−0.72, −0.02)	−0.58 (−0.94, −0.22)	

CAMS = Child/Adolescent Anxiety Multimodal Study.

†This is a model-based omnibus test of the null hypothesis of no treatment effect moderation; that is, a test of the null hypothesis that, for all pairwise comparisons simultaneously, the average between treatment groups difference do not differ by level of the moderator.

‡The standardized effect size (ES) estimate, along with the 95% confidence interval, is reported for each between-group pairwise comparisons. A standard ES estimate is defined as the average between treatment groups difference in the 12-month outcome scaled by the standard deviation of the outcome. Values of 0.2, 0.5, or 0.8 are generally regarded as small, medium, or large (Cohen, 1988).

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Table 5

Model Estimated Mean Week 12 PARS Total Scores for Significant Moderator

	COMB M (SE)	SRT M (SE)	CBT M (SE)	PBO M (SE)
Principal Diagnosis				
SAD (n=111; 22.7%)	4.2 (1.1)	10.6 (1.0)	10.2 (0.9)	11.0 (1.3)
SoP (n=200; 41.0%)	8.6 (0.7)	9.7 (0.8)	11.5 (0.7)	12.5 (1.3)
GAD (n=177; 36.3%)	6.2 (0.8)	10.8 (0.9)	9.4 (0.8)	13.2 (1.2)