Published in final edited form as:
Depress Anxiety. 2013 November ; 30(11): 1099–1106. doi:10.1002/da.22149.

Trajectories of Change in Anxiety Severity and Impairment During and After Treatment with Evidence-Based Treatment for Multiple Anxiety Disorders in Primary Care

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Abstract

Background—Coordinated Anxiety Learning and Management (CALM) is a model for delivering evidence-based treatment for anxiety disorders in primary care. Compared to usual care, CALM produced greater improvement in anxiety symptoms. However, mean estimates can obscure heterogeneity in treatment response. This study aimed to identify (1) clusters of participants with similar patterns of change in anxiety severity and impairment (trajectory groups); and (2) characteristics that predict trajectory group membership.

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Disclosures

All authors have received research support from the National Institutes of Health. In addition, M. Stein, MD, has received financial support for consultancy from Care Management Technologies; for his role as Co-Editor in Chief for UpToDate Psychiatry and Deputy Editor for Depression and Anxiety; and for expert testimony unrelated to the reported work. M. Craske, PhD, has received book royalties. P. Roy-Byrne, MD, has received financial support for his role as Co-Editor in Chief for UpToDate Psychiatry, Journal Watch Psychiatry, and Depression and Anxiety. He has also obtained payment for expert testimony from various law firms; for a lecture for the Arizona Psychiatric Society; and he owns stock/stock options from Valant Medical Solutions.

Methods—The CALM randomized controlled effectiveness trial was conducted in 17 primary care clinics in 4 US cities in 2006–2009. 1,004 English- or Spanish-speaking patients age 18–75 with panic, generalized anxiety, social anxiety, and/or posttraumatic stress disorder participated. The Overall Anxiety Severity and Impairment Scale was administered repeatedly to 482 participants randomized to CALM treatment. Group-based trajectory modeling was applied to identify trajectory groups and multinomial logit to predict trajectory group membership.

Results—Two predicted trajectories, representing about two-thirds of participants, were below the cut-off for clinically significant anxiety a couple of months after treatment initiation. The predicted trajectory for the majority of remaining participants was below by nine months. A small group of participants did not show consistent improvement. Being sicker at baseline, not working, and reporting less social support were associated with less favorable trajectories.

Conclusions—There is heterogeneity in patient response to anxiety treatment. Adverse circumstances appear to hamper treatment response. To what extent anxiety symptoms improve insufficiently because adverse patient circumstances contribute to suboptimal treatment delivery, suboptimal treatment adherence, or suboptimal treatment response requires further investigation.

Clinical Trial Registration—clinicaltrials.gov Identifier: NCT00347269

Keywords

Anxiety/anxiety disorders; CBT/cognitive behavior therapy; primary care; treatment; life events/ stress

INTRODUCTION

CALM, a flexible model for delivering evidence-based treatment for anxiety disorders in primary care clinics, resulted in greater improvement in anxiety symptoms than usual care according to mean estimates at baseline, 6, 12, and 18 months [1; 2]. In randomized controlled trials mean estimates from few points in time are commonly used to assess treatment. Yet a small number of measurements separated by months may be insufficient to gauge treatment impact, particularly in mental health where response to medications and therapy often evolve over time [3; 4]. Also, overall means obscure whether some patients respond quickly, others take longer, do not improve sufficiently, or get worse (treatment response heterogeneity). Thus, to understand treatment impact better, it is useful to identify: (a) ways in which patients respond to treatment over time; (b) groups of patients who respond similarly; and (c) whether groups can be described. Such information can inform efforts to optimize treatment, including tailoring treatment to individual patients [5].

Extant information about trajectory groups in mental health stems primarily from pharmacotherapy depression trials [3; 6–9]. All studies reported heterogeneous response trajectories. Depending on sample size and follow-up time, up to four separate trajectory groups emerged, including patients who responded early, patients who took longer to respond, patients who responded more, and patients who responded only minimally if at all. The latter group comprised 10% to 20% of study participants and typically participants sicker at baseline. Results from three studies of depressed patients treated with cognitive behavioral therapy (CBT) or with CBT and antidepressants are less consistent. Similar to pharmacotherapy trials, almost a quarter of participants who completed 6 sessions of internet-based CBT did not get better, and patients sicker at baseline were less likely to improve [10]. However, all participants improved in the other CBT-only [11] and the CBT-pharmacotherapy study [9]. Moreover, in the former study, patients with more severe baseline major depressive disorder improved more. In a randomized controlled pharmacotherapy trial of patients with recent-onset psychosis treated for twelve weeks [12],

all participants improved over the following two years. There were five distinct ways in which patients progressed and patients sicker at baseline showed poorer response.

Two studies have examined treatment response heterogeneity in anxiety disorders and both used effectiveness designs. One delivered PTSD treatment for very disabled Vietnam combat veterans in a specialty inpatient setting [5]. Over the course of 24 months, two veteran groups improved moderately, but a very small group got worse before returning to baseline values. The second study focused on patients with GAD who completed a six-session internet CBT course [10]. One group of participants improved and another did not get better. As in depression studies, the latter group comprised about 20% of study participants and participants who were sicker at baseline. Effectiveness studies provide greater external validity than clinical trials because their samples are more representative of all patients and don't remove participants for failing to adhere to strict treatment protocols. Such studies also deliver treatment in a flexible real-world manner by allowing session numbers and treatment length to vary and by not necessarily delivering treatment by "experts". Compared to prior anxiety effectiveness studies, CALM treated patients with multiple anxiety disorders, offered choice of treatment modality, and included patients from a broader demographic group.

The CALM study administered the Overall Anxiety Severity and Impairment Scale (OASIS) [13–16] repeatedly to participants randomized to CALM treatment. We used these scores to identify clusters of participants with similar trajectories of change in anxiety severity and impairment. In addition, we aimed to identify whether participant characteristics predict trajectory group membership. To address these aims, we applied group-based trajectory modeling [17; 18].

MATERIALS AND METHODS

Clinical Trial Overview

CALM is a prospective, longitudinal, randomized controlled effectiveness trial of a collaborative care intervention (CALM treatment) compared to usual care treatment (UC) conducted under naturalistic conditions. All participants gave written informed consent for the study, which was approved by the institutional review boards of the RAND Corporation, University of Arkansas, University of California at San Diego and Los Angeles, and University of Washington.

The study, its methods, and treatment are described in detail in [1; 19]. Briefly, between 2006 and 2008, CALM enrolled 1,004 English- or Spanish-speaking primary care patients between 18 and 75 years old from 17 clinics in 4 US cities. Participants had to meet *DSM-IV* criteria for at least one of panic disorder, generalized anxiety disorder, social anxiety disorder, or posttraumatic stress disorder and score at least 8 on the OASIS. Of 503 participants randomized to CALM treatment, 482 had at least one intervention contact. Their data were used for the analyses reported here.

CALM treatment

The CALM treatment model offered participants 10–12 weeks of CBT, anti-anxiety medication, or both and followed patient preference for treatment. Participants with persistent symptoms could receive more of the same treatment or the alternative modality up to 3 more times at 3-month intervals. After treatment completion, participants entered into continued care and received monthly follow-up telephone calls to reinforce CBT skills, medication adherence, or both. The model included real-time, web-based clinical outcome monitoring [20] and a computer-assisted program optimized CBT delivery by non-expert

care managers [21]. These specially trained clinicians also assisted with treatment adherence and optimizing medications. Psychiatrists provided consultation regarding the likelihood of benefit from more treatment [19].

Measures

Anxiety severity and impairment—We assessed temporal change in anxiety severity and impairment with the OASIS [13–16] administered by care managers during contact with study participants. This 5-item self-report instrument of anxiety-related severity and impairment with established concurrent and discriminant validity can be used for any anxiety disorder. It addresses anxiety frequency and severity, level of avoidance, work/school/home interference, and social interference with a 5-level Likert scale.

Trajectory group membership characteristics—In addition to identifying distinct anxiety trajectory groups, we examined participant characteristics to distinguish trajectory group membership. Based on earlier findings [22–26], we hypothesized higher odds of membership in less favorable anxiety trajectory groups for patients sicker at baseline and for patients experiencing socioeconomic adversity. In contrast, patients with more social support would have lower odds.

The following baseline measures were available to address illness severity: number of anxiety conditions experienced, comorbid major depressive disorder, and number of major chronic medical conditions (collected with the Medical Outcomes Study [MOS] Checklist). Available measures of socioeconomic adversity included not working, no health insurance coverage, age, education, being female, and born outside the US. Married or living with a partner and extent of social support were available to proxy social support. Extent of social support came from MOS Social Support Survey items reflecting instrumental and psychological support [27] We combined the four items by calculating a mean score for each study participant after analyses of Cronbach's alpha (0.825) indicated high internal consistency and factor analysis suggested unidimensionality of the four items. Factors one and two had eigenvalues of 2.64 and 0.56; and factor one accounted for 65.9% of total variance versus 13.9% for factor two.

Data Analysis

Trajectory Groups—We applied group-based trajectory modeling (GBTM) to examine whether different groups of CALM participants experienced similar patterns of change in anxiety severity and impairment [17]. GBTM attempts to identify distinct clusters of individuals who follow similar trajectories of change over time. It assigns individuals probabilistically to groups, with probabilities summing to 1 for each person. As such, and as Nagin [28] has emphasized, groups identified by GBTM should be considered statistical "approximations of a more complex reality", not groups literally distinct from each other. GBTM requires specifying functional forms of trajectory shapes with polynomial functions. We started with a cubic specification to accommodate that OASIS scores may decline steadily, increase before going down, or decrease before increasing again. We estimated GBT models with SAS procedure *proc traj* [29; 30], after preparing data with SAS version 9.3 (SAS Institute, Cary, NC, USA).

OASIS scores were not collected on the same day for each person nor was the same number of scores collected per person. Between baseline and the end of the study, a total of 6,700 scores were recorded (mean per person: 13.9; min: 1; max: 36). To reduce noise in the data, we created weekly OASIS scores from the day-based measures. Week 1 started on the day after baseline, week 2 on day 8 after baseline etc. If more than one OASIS score was available for a participant during a week, the scores were averaged. Within one year after

baseline, the average number of weeks with at least one score was 12.9 (min: 1; max: 34). Thus, not every participant had an OASIS score for each week during follow-up. *proc traj* uses all available data, regardless of whether participants have the same number of observations.

A central decision in GBTM is determining how many groups best represent the heterogeneity of trajectories in the sample. The Bayesian Information Criterion (BIC) [31], which is based on the likelihood function and accounts for the number of parameters in a model, is commonly used to select the number of groups estimated by GBTM [28; 32]. According to this criterion, the GBTM with the smallest absolute BIC value is chosen. Nagin and Odgers (2010) recommend the following additional criteria to assess model adequacy (p. 118):

1. "Obtaining for each trajectory group a close correspondence between the estimated probability of group membership and the proportion of the sample assigned to each group based on the posterior probability of group membership,
2. Ensuring that the average of the posterior probabilities of group membership for individuals assigned to each group exceeds a minimum threshold of 0.7,
3. Establishing that the odds of correct classification based on the posterior probabilities of group membership exceed a minimum threshold of 5,
4. Observing reasonably tight confidence intervals around group membership probabilities."

Probability of Trajectory Group Membership—GBTM estimates simultaneously (a) parameters that describe the trajectory of each group and (b) the relationship of individual-level characteristics to the probability of group membership. GBTM specifies the latter as a multinomial logit model. We first estimated univariate associations between characteristics and group membership probabilities. Variables significant at $p < .05$ were then included in a multivariate multinomial logit model to identify measures associated with group membership.

RESULTS

The majority of the sample consisted of women (70%), had more than 12 years of education (80%), and represented a broad age range and diverse race/ethnicity (Table 1). At baseline, the sample was quite ill: the average number of anxiety disorders was almost two and close to two-thirds had comorbid major depressive disorder. In addition, the average number of major chronic medical conditions was over two. The baseline OASIS score ranged from 8 to 20. About half of the sample (51.5%) had a baseline OASIS score of 12 or higher and 20% had a score of at least 15.

Trajectory Groups

BIC values for trajectory groups with cubic shapes are presented in Table 2. Based on their results, the 7-group trajectory model has the smallest absolute BIC value. However, some groups in the 7-group model have very few members and, thus, trajectory shapes with wide and overlapping confidence intervals. The models with 5 or 6 groups also include groups with fewer than ten members. Therefore, we selected the 4-group solution for further examination.

In the cubic 4-group model, denoted (3,3,3,3), trajectory shape parameter estimates are significant for linear, quadratic, and cubic terms for 3 of the groups, but suggest a constant, or 0-order, trajectory for the remaining group. BIC values for the (3,3,3,0) group model are −15,983.83 (n=482) and −16,005.75 (n=6,355), both lower than the corresponding BIC values for the cubic 4-group model. Thus, we assessed model adequacy with the recommended diagnostic criteria [17] for the (3,3,3,0) group model.

According to Table 3, the (3,3,3,0) model fits the data well. The estimated probability of group membership (column 1) and the proportion of the sample assigned to each group (column 3) are almost identical; the average posterior probability of assignment (column 4) and the odds of correct classification (column 5) exceed the recommended thresholds of 0.7 and 5 for each group; and the confidence intervals for group membership probabilities are not large.

Figure 1 displays observed mean OASIS scores (solid lines) and the corresponding predicted OASIS trajectories (dashed lines) with their 95% confidence intervals (dotted lines) for the (3,3,3,0) model. None of the confidence intervals for the 4 groups overlap which is an indication that the 4-group result identified distinct aspects of the distribution of trajectories in the population [17]. In this 4-group model, OASIS scores improved for three groups over time. Group 1 (red line) improved relatively quickly. Less than one month after baseline, it reached the OASIS cut-off score of 8, which is used as an indicator of clinically significant anxiety. OASIS scores continued to drop until about week 20 and then stayed low. Group 1, which represents 27.6% of the sample, was least anxious at baseline (average OASIS score = 10.5). A second and largest group (light blue line; 40.1% of sample; average OASIS score = 11.8) took a little longer to reach below the OASIS cut-off for clinically significant anxiety (about 2 months), but continued to improve steadily and remained well below the score afterwards. OASIS scores for a third group (green line; 28.7% of sample) also improved continuously according to its predicted trajectory. However, the OASIS score did not reach the 8-point cut-off until around week 33 and barely improved thereafter. Group 3 started with an average OASIS score of 13.3. Finally, for a small fourth group (dark blue line; 3.7% of sample) OASIS scores did not appear to improve consistently. At baseline, this group had the highest average OASIS score (15.4). There was a statistically significant difference in average baseline OASIS scores across groups ($p<.0001$).

Trajectory Group Membership: Univariate and Multivariate Associations

Univariate estimates in Table 4 suggest being sicker at baseline was a risk factor associated with following the two less favorable trajectories (Groups 3 and 4), where being sick was measured with the number of anxiety disorders, the presence of comorbid major depressive disorder, and the number of major chronic medical conditions. Not working at baseline was also a risk factor associated with these two groups. In contrast, reporting more social support and being married or living with a partner were associated with less risk of following Group 3 and 4 trajectories.

In multivariate analyses, the number of anxiety disorders endorsed by a patient remained a significantly associated risk factor and the extent of social support persisted as a protective factor. Not working at baseline continued to be a risk factor associated with Group 4 membership.

DISCUSSION

The current analysis is the first to examine heterogeneity in how anxiety severity and impairment symptoms progress after treatment begins among patients with a range of anxiety disorders. The analysis used data from the first randomized controlled effectiveness

trial of an evidence-based collaborative care treatment model for multiple anxiety disorders in primary care settings. The results suggest that anxiety symptom trajectories are not uniform. About two-thirds of participants were predicted to belong to one of two trajectory groups. For both groups, the predicted trajectories indicated clinically significant recovery from anxiety within a couple of months after the start of treatment and relatively little change thereafter. One group attained the recovery cut-off more quickly, but for both groups the predicted trajectories stayed below the cut-off score during the remaining study period. Finding a "response" for two-thirds of participants is broadly consistent with results from depression trajectory studies [6–8].

The phenomenon of "sudden gains", that is, a rapid, large decrease in symptoms between consecutive treatment sessions has received considerable attention [33]. A recent meta-analysis concluded that sudden gains are associated with short- and long-term improvements in anxiety symptoms, especially for patients receiving CBT [34]. The trajectory of the group that improved fastest could be considered consistent with experiencing such gains. Over 90% of patients in this group participated in CBT, but 44% were also treated with medications.

The predicted anxiety trajectory for the majority of remaining participants (Group 3) showed improvement, but did not reach the clinically significant cut-off until nine months after treatment began. Finally, no sustained improvement was apparent for a small, fourth group. This latter group is smaller than groups found not responding in most extant studies of depression or anxiety trajectory groups [7; 8; 10]. Exceptions are [5] and [6], who each identified a small group of patients whose symptoms got worse. At baseline, the symptoms of both groups from prior studies were less severe. In contrast, the current group without improvement had worse baseline symptom scores. Moreover, current participants who were not working at baseline and who reported less social support were less likely to follow a favorable trajectory, consistent with earlier studies on depression and anxiety trajectories.

Several study limitations should be noted. One, data to examine changes in anxiety symptoms were available for up to one year after randomization. Yet studies of collaborative care for depression indicate that clinical benefits continue beyond 12 months [35]. Two, as an effectiveness study, CALM was not designed with group-based trajectory modeling in mind. Data measuring anxiety symptoms were therefore not available for the entire year at equal intervals for every study participant. OASIS scores were available for an average of 13 weeks ($p=0.669$ for mean difference between groups) and the mean length of contact from baseline to last contact was 266 days ($p=0.124$ for mean difference between groups). If participants with fewer data were more or less likely to improve than participants with more data, our results may not represent all symptom trajectory groups. Related to this limitation is the possibility that trajectory groups may be better represented with shapes other than polynomials and with differing lengths of follow-up. Group-based trajectory modeling is not amenable to modeling either. Three, the predicted trajectory group that did not improve was too small to examine associations between group membership and more than a few baseline characteristics. Four, data measuring anxiety severity and impairment were not available for the usual care group. It is therefore not possible to compare predicted trajectories of patients receiving evidence-based care with those who did not receive such care. Lastly, the methods to determine the optimal number of trajectory groups leave room for interpretation. Thus, future studies need to confirm that the number of groups and trajectory shapes identified here are generalizable to other patients, settings, and treatment approaches for patients with anxiety disorders.

IMPLICATIONS FOR PRACTICE

The finding that anxious patients improve to different degrees and at different paces will resonate with clinicians treating such patients, as many may find these four trajectories of response familiar. With an increasing emphasis on measurement-based care, clinicians are more likely to have patient-specific, longitudinal outcome measures available when they see patients. However, it is not at all well described how outcome measurements should be used to optimize care beyond giving “more” or perhaps different treatment to patients who are not improving, have not reached a predetermined threshold, or have plateaued with current treatment. Thus, efforts to develop treatments specific to subgroups of anxious patients are urgently needed.

The findings presented above suggest some interesting additional points. First, it appears that there are two distinct trajectories that ultimately arrive at a similar endpoint. A higher proportion of patients opted for CBT-only treatment (48% vs. 37%) in the group that improved more quickly and fewer patients interrupted or suspended treatment (11% vs. 17%). The proportion using medication-only was the same (8%). However, these findings may be confounded by illness severity rather than reflect treatment approach. Second, if there was urgency to obtain a quicker response, for example for patients with significant functional impact of anxiety symptoms, it would be most helpful to be able to identify group membership a priori. Unfortunately, the current findings regarding predictors of group membership are similar to those in other extant analyses in that they do not yet provide clinically useful information. Predictive information with sensitivities and specificities applicable to clinical practice will be necessary to incorporate results from studies such as this into clinical practice.

FUTURE RESEARCH

Baer and colleagues recently posited that the role of environmental social conditions in which patients experience anxiety symptoms tends to get overlooked or underestimated [36]. The current findings, that adverse circumstances may impede response to treatment, suggest focusing future efforts on understanding to what extent a patient’s environment contributes to experiencing symptoms of anxiety, to treatment compliance, treatment response, and the ability to provide optimal care. Anxiety symptoms may, for instance, improve if environmental deficits, such as food insecurity or parenting stress, are addressed. Similarly, future treatments may want to broaden their focus from delivering optimal care in the health care system per se and enlist a patient’s social network to encourage patients to seek care or to support treatment compliance. Such approaches are consistent with applying knowledge about individuals’ environmental and social factors to develop personalized interventions as proposed in the National Institute of Mental Health Strategic Plan [37].

Acknowledgments

This work was supported by the following grants from the National Institute of Mental Health (NIMH): U01 MH057858 and K24 MH065324 (Dr. Roy-Byrne); U01 MH058915 (Dr. Craske); U01 MH070022 (Dr. Sullivan); U01 MH070018 (Dr. Sherbourne); and U01 MH057835 and K24 MH64122 (Dr. Stein).

References

1. Roy-Byrne P, Craske MG, Sullivan G, et al. Delivery of evidence-based treatment for multiple anxiety disorders in primary care: a randomized controlled trial. JAMA. 2010; 303(19):1921–1928. [PubMed: 20483968]

2. Craske MG, Stein MB, Sullivan G, et al. Disorder specific impact of CALM treatment for anxiety disorders in primary care. Archives of General Psychiatry. 2011; 68(4):378–388. [PubMed: 21464362]
3. Uher R, Muthén B, Souery D, et al. Trajectories of change in depression severity during treatment with antidepressants. Psychological Medicine. 2010; 40:1367–1377. [PubMed: 19863842]
4. Muthén, B.; Brown, HC.; Hunter, AM., et al. General approaches to analysis of course. In: ESP; MKK; Katherine, O., editors. Causality and Psychopathology: Finding the determinants of disorders and their cures. New York: Oxford University Press; 2010. p. 159-178.
5. Elliott P, Biddle D, Hawthorne G, et al. Patterns of treatment response in chronic posttraumatic stress disorder: An application of latent growth mixture modeling. Journal of Traumatic Stress. 2005; 18(4):303–311. [PubMed: 16281227]
6. Uher R, Mors O, Rietschel M, et al. Early and delayed onset of response to antidepressants in individual trajectories of change during treatment of major depression: a secondary analysis of data from the Genome-based Therapeutics for Depression (GENDEP) study. Journal of Clinical Psychiatry. 2011; 72(11):1478–1483. [PubMed: 22127194]
7. Gueorguieva R, Mallinckrodt C, Krystal JH. Trajectories of depression severity in clinical trials of Duloxetine: Insights into antidepressant and placebo responses. Archives of General Psychiatry. 2011; 68(12):1227–1237. [PubMed: 22147842]
8. Kuchibhatla MN, Fillenbaum GG. Trajectory classes of depression in a randomized depression trial of heart failure patients: A reanalysis of the SADHART-CHF trial. The American Journal of Geriatric Pharmacotherapy. 2011; 9(6):483–494. [PubMed: 22035643]
9. Stulz N, Thase ME, Klein DN, et al. Differential effects of treatments for chronic depression: A latent growth model reanalysis. Journal of Consulting and Clinical Psychology. 2010; 78(3):409–419. [PubMed: 20515216]
10. Sunderland M, Wong N, Hilvert-Bruce Z, Andrews G. Investigating trajectories of change in psychological distress amongst patients with depression and generalised anxiety disorder treated with internet cognitive behavioural therapy. Behaviour Research and Therapy. 2012; 50:374–380. [PubMed: 22498311]
11. Cuijpers P, van Lier PAC, van Straten A, Donker M. Examining differential effects of psychological treatment of depressive disorder: An application of trajectory analyses. Journal of Affective Disorders. 2005; 89:137–146. [PubMed: 16274750]
12. Levine SZ, Rabinowitz J, Case M, Ascher-Svanum H. Treatment Response Trajectories and Their Antecedents in Recent-Onset Psychosis: A 2-Year Prospective Study. Journal of Clinical Psychopharmacology. 2010; 30(4):446–449. [PubMed: 20631562]
13. Campbell-Sills L, Norman SB, Craske MG, et al. Validation of a brief measure of anxiety-related severity and impairment: the Overall Anxiety Severity and Impairment Scale (OASIS). Journal of Affective Disorders. 2009; 112(1–3):92–101. [PubMed: 18486238]
14. Norman SB, Cissell SH, Means-Christensen AJ, Stein MB. Development and validation of an Overall Anxiety Severity And Impairment Scale (OASIS). Depression and Anxiety. 2006; 23(4): 245–249. [PubMed: 16688739]
15. Norman SB, Allard CB, Trim RS, et al. Psychometrics of the Overall Anxiety Severity and Impairment Scale (OASIS) in a sample of women with and without trauma histories. Archives of Women's Mental Health. 2013; 16(2):123–129.
16. Norman SB, Campbell-Sills L, Hitchock CA, et al. Psychometrics of a brief measure of anxiety to detect severity and impairment: the Overall Anxiety Severity and Impairment Scale (OASIS). Journal of Psychiatric Research. 2011; 45(2):262–268. [PubMed: 20609450]
17. Nagin DS, Odgers CL. Group-based trajectory modeling in clinical research. Annual Review of Clinical Psychology. 2010; 6:109–138.
18. Peer JE, Spaulding WD. Heterogeneity in recovery of psychosocial functioning during psychiatric rehabilitation: an exploratory study using latent growth mixture modeling. Schizophrenia Research. 2007; 93(1–3):186–193. [PubMed: 17448644]
19. Sullivan G, Craske MG, Sherbourne CD, et al. Design of the Coordinated Anxiety Learning and Management (CALM) study: innovations in collaborative care for anxiety disorders. General Hospital Psychiatry. 2007; 29(5):379–387. [PubMed: 17888803]

20. Unützer J, Choi Y, Cook IA, Oishi S. A web-based data management system to improve care for depression in a multicenter clinical trial. Psychiatric Services. 2002; 53(6):671–673. 678. [PubMed: 12045303]
21. Craske MG, Rose RD, Lang AJ, et al. Computer-assisted delivery of cognitive behavioral therapy for anxiety disorders in primary-care settings. Depression and Anxiety. 2009; 26(3):235–242. [PubMed: 19212970]
22. Carter GC, Cantrell RA, Zarotsky V, et al. Comprehensive review of factors implicated in the heterogeneity of response in depression. Depression and Anxiety. 2012; 29(4):340–354. [PubMed: 22511365]
23. Roy-Byrne P, Sherbourne C, Miranda J, et al. Poverty and response to treatment among panic disorder patients in primary care. Am J Psychiatry. 2006; 163(8):1419–25. [PubMed: 16877656]
24. Chavira DA, Stein MB, Golinelli D, et al. Predictors of clinical improvement in a randomized effectiveness trial for primary care patients with panic disorder. Journal of Nervous and Mental Disease. 2009; 197:715–721. [PubMed: 19829198]
25. Durham RC, Allan T, Hackett CA. On predicting improvement and relapse in generalized anxiety disorder following psychotherapy. British Journal of Clinical Psychology. 1997; 36(Pt 1):101–119. [PubMed: 9051282]
26. Rodriguez BF, Weisberg RB, Pagano ME, et al. Characteristics and predictors of full and partial recovery from generalized anxiety disorder in primary care patients. The Journal of Nervous and Mental Disease. 2006; 194(2):91–97. [PubMed: 16477186]
27. Sherbourne CD, Stewart AL. The MOS Social Support Survey. Social Science and Medicine. 1991; 32(6):705–714. [PubMed: 2035047]
28. Nagin, DS. Group-based modeling of development. Cambridge, Massachusetts: Harvard University Press; 2005.
29. Jones BL, Nagin DS. Advances in group-based trajectory modeling and an SAS procedure for estimating them. Sociological Methods & Research. 2007; 35(4):542–571.
30. Jones BL, Nagin DS, Roeder K. A SAS procedure based on mixture models for estimating developmental trajectories. Sociological Methods & Research. 2001; 29(3):374–393.
31. Neath AA, Cavanaugh JE. The Bayesian information criterion: background, derivation, and applications. WIREs Computational Statistics. 2012; 4:199–203.
32. Chi FW, Weisner CM. Nine-Year psychiatric trajectories and substance use outcomes: An application of the group-based modeling approach. Evaluation Review. 2008; 32(1):39–58. [PubMed: 18198170]
33. Doane LS, Feeny NC, Zoellner LA. A preliminary investigation of sudden gains in exposure therapy for PTSD. Behaviour Research and Therapy. 2010; 48(6):555–560. [PubMed: 20304385]
34. Aderka IM, Nickerson A, Bøe HJ, Hofmann SG. Sudden gains during psychological treatments of anxiety and depression: A meta-analysis. Journal of Consulting and Clinical Psychology. 2012; 80(1):93–101. [PubMed: 22122290]
35. Simon GE, Ludman E, Rutter CM. Incremental benefit and cost of telephone care management and telephone psychotherapy for depression in primary care. Archives of General Psychiatry. 2009; 66(10):1081–1089. [PubMed: 19805698]
36. Baer JC, Kim M, Wilkenfeld B. Is it Generalized Anxiety Disorder or poverty? An examination of poor mothers and their children. Child and Adolescent Social Work Journal. 2012; 29(4):345–355.
37. NIMH. Services USDoHH, Health NIo. National Institute of Mental Health Strategic Plan. 2008.

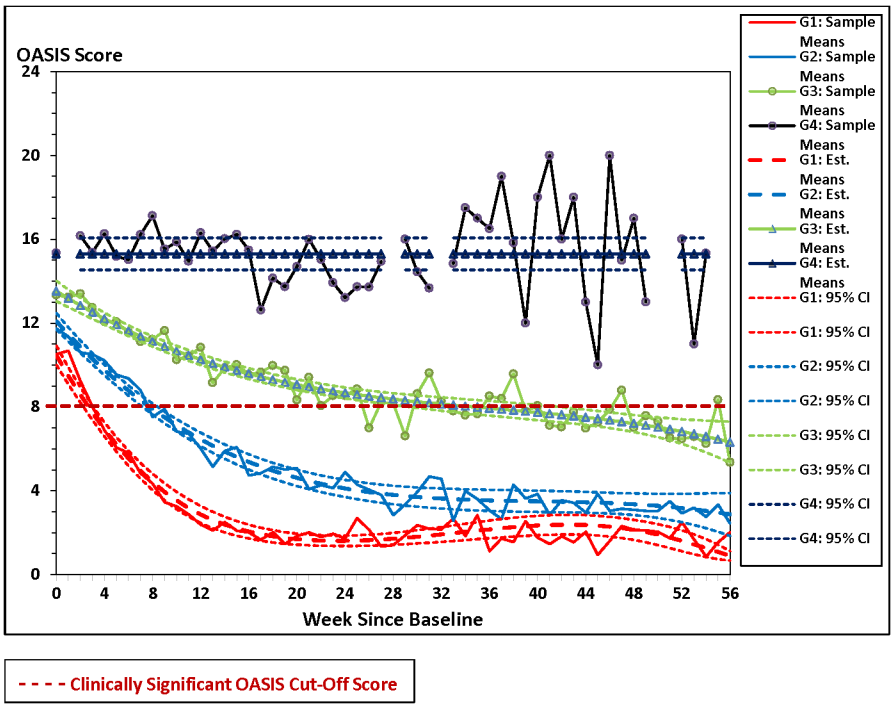

Figure 1. OASIS Trajectories for Study Participants Randomized to CALM Treatment [a]

[a] Solid lines represent mean observed OASIS scores; dashed lines represent predicted OASIS trajectories; and dotted lines 95% confidence intervals.

Table 1

Baseline Characteristics of Participants Randomized to CALM Treatment With ≥ 1 Intervention Contact (n=482)

Characteristic at Baseline	%	n
Female	70.33%	339
Education Level		
■< 12 years	4.77%	23
■12 years	15.56%	75
■> 12 years	79.67%	384
Married or Living Together	54.15%	261
Race/Ethnicity		
■Black	9.96%	48
■Hispanic	19.29%	93
■White	56.64%	273
■Other	14.11%	68
Foreign Born	15.21%	73
Not Working	28.33%	136
No Health Insurance	15.63%	75
Anxiety Disorder		
■Generalized Anxiety Disorder	77.39%	373
■Panic Disorder	46.67%	224
■Posttraumatic Stress Disorder	17.63%	85
■Social Anxiety Disorder	42.53%	205
Major Depressive Disorder	64.73%	312
	Mean	**SD**
OASIS Score	11.99	2.80
Age in years	43.43	13.26
Number of Anxiety Disorders	1.84	0.83
Number of Major Chronic Medical Conditions	2.23	1.94
Social Support Index	3.12	1.07

Table 2

BIC Values by OASIS Trajectory Group Model

Number of Trajectory Groups	Trajectory Shape	BIC[a] (n=482)	BIC[a] (n=6,355)
1	cubic	−17,602.77	−17,609.22
2	cubic	−16,450.17	−16,463.07
3	cubic	−16,182.45	−16,201.80
4	cubic	−15,991.82	−16,017.61
5	cubic	−15,997.54	−16,029.77
6	cubic	−15,976.67	−16,015.35
7	cubic	−15,871.13	−15,916.26
8	cubic	−15,882.43	−15,934.01
9	cubic	−15,907.73	−15,965.76

[a]BIC is the Bayesian Information Criterion.

Table 3

Adequacy of 4-Group OASIS Trajectory Model

Trajectory Group	Group Membership Probability (1)	95% CI Group Membership Probability (2)	Proportion Classified to Group i (3)	Average Posterior Probability of Assignment (4)	Odds of Correct Classification (5)	Number Assigned to Group (6)
1 (cubic)	0.276	0.223, 0.329	0.276	0.910	26.53	133
2 (cubic)	0.401	0.345, 0.457	0.402	0.888	11.81	194
3 (cubic)	0.287	0.241, 0.332	0.290	0.910	25.18	140
4 (constant)	0.037	0.017, 0.056	0.031	0.965	717.64	15

Table 4

Predictors of OASIS Trajectory Group Membership: Univariate Multinomial Logit Estimates[a]

	Trajectory Group 2		Trajectory Group 3		Trajectory Group 4	
Baseline Characteristic	**Coefficient Estimate** [b]	**SE**	**Coefficient Estimate** [b]	**SE**	**Coefficient Estimate** [b]	**SE**
Age (years)	−0.006	0.01	−0.02 +	0.01	0.01	0.02
Female	−0.16	0.28	0.03	0.29	0.08	0.63
Education Level						
■≤ 12 years	−0.68 *	0.35	−0.06	0.30	−0.60	0.78
■> 12 years	omitted category					
Married or Living Together	−0.18	0.27	−0.88 **	0.27	−1.14 +	0.62
Social Support Index	−0.42 **	0.13	−0.60 **	0.13	−1.03 **	0.29
Not Working	0.05	0.30	0.52 +	0.29	2.91 **	0.78
No Health Insurance	0.26	0.41	0.94 *	0.38	−0.06	0.82
Number of Anxiety Disorders	0.41 *	0.18	0.88 **	0.17	1.12 **	0.33
Major Depressive Disorder	0.03	0.26	0.72 *	0.28	2.51 *	1.07
Number of Major Chronic Medical Conditions	0.11	0.08	0.22 **	0.07	0.29 *	0.13

[a] Trajectory Group 1 is the comparison group.

[b] The coefficient estimates correspond to the parameters of a multinomial logit function.

+ p < .10

* p < .05

** p < .01

Table 5

Predictors of OASIS Trajectory Group Membership: Multivariate Multinomial Logit Estimates[a]

	Trajectory Group 2		Trajectory Group 3		Trajectory Group 4	
Baseline Characteristic	**Coefficient Estimate** [b]	**SE**	**Coefficient Estimate** [b]	**SE**	**Coefficient Estimate** [b]	**SE**
Married or Living Together	0.13	0.28	−0.56 +	0.31	0.10	0.64
Social Support Index	−0.48 **	0.15	−0.42 **	0.15	−0.84 **	0.33
Not Working	−0.003	0.33	0.37	0.34	1.98 **	0.69
No Health Insurance	0.14	0.42	0.80 *	0.39	−0.23	0.87
Number of Anxiety Disorders	0.45 *	0.19	0.82 **	0.19	0.98 **	0.33
Major Depressive Disorder	−0.21	0.28	0.21	0.31	1.99 +	1.08
Number of Major Chronic Medical Conditions	0.07	0.09	0.13	0.08	0.03	0.13
Constant	0.97	0.61	−0.64	0.67	−3.80 *	1.56
BIC	−15,801 (n = 478)				−15,850.35 (n = 6,282)	

[a] Trajectory Group 1 is the comparison group.

[b] The coefficient estimates correspond to the parameters of a multinomial logit function.

+ p < .10

* p < .05

** p < .01