Experiencing core symptoms of anxiety and unipolar mood disorders in late adolescence predicts disorder onset in early adulthood

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Abstract:

Background Identification of youth at risk for anxiety and unipolar mood disorders (UMDs) can improve public health by targeting those who may warrant early or preventive intervention. This study examined whether endorsing core features of anxiety and UMDs predicted onset of later anxiety and UMDs across the next 7–9 years, and whether having subthreshold or subclinical manifestations of these disorders similarly predicted onset.

Methods Data from this study come from the Youth Emotion Project (YEP), a two-site investigation of common and specific risk factors for emotional disorders. Endorsement of core features of a disorder and subclinical or subthreshold anxiety and UMD diagnoses were determined using data from the Structured Clinical Interview for DSM-IV (SCID) at the baseline assessment. Participants completed annual SCIDs over the course of the next 7–9 years (depending on cohort).

Results Endorsement of panic attacks, obsessions and/or compulsions, and depression and/or anhedonia predicted onset of panic disorder, obsessive compulsive disorder, and major depressive disorder, respectively. When including all anxiety disorders in a model, only the presence of panic attacks uniquely predicted anxiety disorder onset. The presence of subclinical or subthreshold panic disorder, obsessive compulsive disorder, and social phobia at baseline predicted the full onset of these disorders over the follow-up period.

Conclusions Experiencing some symptoms of anxiety and UMDs in the absence of meeting diagnostic criteria is indicative of risk for later onsets of clinically significant DSM manifestations of these disorders. These individuals should be identified and targeted for prevention programs.

Keywords: anxiety | anxiety disorders | depression | generalized anxiety disorder | measurement | psychometrics | panic attacks | agoraphobia | OCD | obsessive compulsive disorder

Article:

Anxiety and mood disorders are prevalent,1 disabling,2-4 and costly to society.5-7 Identifying adolescents at risk for these disorders could offset their public health burden through universal screening and early intervention. Although theory-driven methods for identifying underlying psychological, biological, and environmental risk factors are essential for elucidating pathways, by which these disorders develop8 another approach for identifying those at risk for anxiety and mood disorders is to use self-reported symptom endorsement that can be directly and easily captured in a variety of settings by self-report or interviewers with relatively limited mental health training.

Identifying individuals who may be in a prodromal stage of disorder development may assist with early prevention and intervention. These individuals may endorse core features of a disorder (in the absence of meeting criteria for the disorder); or they may have a subthreshold disorder (i.e., not meeting all diagnostic criteria needed for the disorder), a subclinical disorder (i.e., not experiencing clinically significant distress or interference), or both. Indeed, individuals who have onsets of anxiety and UMDs are more likely to have had some symptoms prior to their disorder onsets than to be asymptomatic prior to their disorder onset.9 One study found that endorsement of depressed mood and "feeling nervous" predicted onset of depression and panic disorder, respectively, 1 year later,10 and another found that core features of unipolar depression (i.e., depressed mood and anhedonia) predicted onset of UMDs.11 These findings highlight the potential impact that early detection and intervention could have in preventing onset of the full disorder, especially given the significantly increased risk of anxiety and UMD onset during adolescence. Aside from these few studies, no other research to our knowledge has assessed whether symptom endorsement or the presence of subclinical diagnoses predict later disorder development; thus, more prospective research is needed in this area.

This study had two aims: (1) to assess whether the presence of core features of anxiety and UMDs, as measured by the screening items on a structured diagnostic interview, serve as a risk factors for the later onset of those disorders or other disorders, and (2) to examine whether the presence of subclinical and subthreshold diagnoses, as determined through the same structured diagnostic interview, are predictive of later full disorder onset. Because these diagnostic predictors come closer to a full diagnosis than a simple one or two item screener, one might presume that the latter predictors would predict later disorder onset, whereas the former predictors may be insufficient for detecting risk. However, endorsement of just the core features of a disorder may be sufficient in predicting later onsets. This is an empirical question we aimed to test in this study.

Data come from the Youth Emotion Project (YEP), a two-site investigation of common and specific risk factors for anxiety and UMDs. Participants completed a diagnostic assessment at baseline and annually over the next 7–9 years (depending on cohort). We hypothesized that endorsement of a core feature of a disorder (as measured by the screening items on the diagnostic assessment) and the presence of a subthreshold or subclinical diagnosis of a particular disorder

would predict the subsequent development of that disorder. Based on research showing that panic attacks are associated with a variety of other anxiety disorders12-14 and predict onset of major depressive episode,14, 15 we hypothesized that panic attacks would predict onset of anxiety disorders. We had no other hypotheses.

METHODS

PARTICIPANTS

High school juniors were recruited from two schools in suburban Chicago and suburban Los Angeles. Students were screened by completing the Neuroticism subscale from the revised Eysenck Personality Questionnaire (EPQ-R-N).16 Recruitment oversampled participants high in neuroticism (i.e., top third) to increase the likelihood of new anxiety and UMD onsets.17, 18 Six hundred and twenty-seven participants (68.9% female; mean age at baseline = 16.9 years, SD = 0.39) completed the baseline assessment, consisting of 58.7% high, 23.1% medium, and 18.2% low EPQ-R-N scorers. The sample was 48.2% Caucasian, 15.3% Hispanic, 13.1% African-American, 4.3% Asian-American, 0.6% Native American/Pacific Islander/Alaskan Native, 13.1% multiracial, and 5.4% who identified with another racial/ethnic group. Details of screening and recruitment are described elsewhere.8

MEAURES

Structured Clinical Interview for DSM-IV, nonpatient edition (SCID-I/NP).19

The SCID was used to assess for DSM-IV disorders. At each assessment, the SCID screening questions were used to identify which diagnostic sections should be administered. Endorsement of a screening item was operationalized as reporting that the symptom was experienced at the subthreshold (2) or threshold (3) levels. In the case of major depressive episode, endorsement of the major depressive episode screener was operationalized as a 2 or 3 on at least one of the two depression screening items on the SCID (i.e., endorsing depressed mood and/or anhedonia at subthreshold or threshold levels). Table 1 shows each SCID screening item used in the analyses.

Interviewers completed the sections for which the screener item was positively endorsed even if participants were not endorsing all required criteria within that section at a threshold level. When participants met threshold for some, but not all, diagnostic criteria for a disorder, a “not otherwise specified” (NOS) diagnosis was given (i.e., a subthreshold disorder). Interviewers rated the clinical severity of each current diagnosis (including NOS) in the past month using the Di Nardo and Barlow20 0–8 clinician severity rating (CSR) scale. Scores of 1 and 2 indicate that at least some symptoms have been present in the past month but symptom severity, impairment and distress are subclinical. A score of 3 indicates symptoms may be clinically significant. A score of 4 or above indicates that symptoms associated with clinically significant severity, distress, or impairment has been present in the past month. Due to concerns about retrospective recall of clinical severity, impairment and distress, past diagnoses (i.e., those that occurred during the interview period but not in the last month) were considered either a “clinical case” (coded as a 4), a “possible” case (coded as a 3), or “no case” (coded as a 0). In these analyses, subclinical diagnoses were defined as those with a CSR or 2 or 3 (see Section “Statistical Analysis”).

Table 1. Screening items in the SCID

Disorder Assessed	Item
Panic	Have you ever had an anxiety or panic attack, when you suddenly felt frightened or anxious or suddenly developed a lot of physical symptoms?
Social anxiety	Have there ever been times, in social situations including at school where you might have been observed or evaluated by others or when you were meeting new people, when you were fearful, anxious, or nervous?
Obsessive compulsive	Have you ever been bothered by thoughts that did not make any sense and kept coming back to you even when you tried not to have them? (Thoughts like hurting someone even though you really don not want to or being contaminated by germs or dirt?) And was there ever anything that you had to do over and over again and could not resist doing, like washing your hands again and again, counting up to a certain number, or checking something several times to make sure that you had done it right?
Generalized anxiety	In the last 6 months, have you been continually worried or anxious about a number of different things other than worry about panic, being embarrassed in social situations, contaminated by germs, etc.?
PTSD*	Did you ever think about [the trauma] when you did not want to, or did thoughts about [the trauma] come to you suddenly when you did not want them to?
Major depressive disorder	In the last month, has there been a time when you were feeling depressed or down most of the day nearly every day, or did you lose interest or pleasure in things you usually enjoyed?

*Item only asked if participants endorsed experiencing a traumatic event at any point in their lives, after being read a list of common traumatic events.

Interviews were conducted at the baseline assessment and then every 10–18 months over the subsequent 9 years. Because participants were recruited in cohorts over 3 years, participants could complete between seven and nine follow-up interviews. Interviewers had at least a bachelor's degree and received extensive training and supervision. SCIDs were presented at diagnostic consensus meetings led by doctoral-level supervisors. Reliability of DSM diagnoses was assessed by having trained interviewers listen to a random selection of assessments (at least 10% at each time point) conducted at both sites. Agreement across raters was 93% for anxiety disorders and 95% for UMDs.

PROCEDURE

Participants completed annual SCID interviews over the phone or in person. Participants were contacted annually, even if they did not complete an interview for the previous year. Out of 627 participants who completed a baseline assessment, 496 (79.1%) completed the first follow-up assessment, 420 (67.0%) completed the second, 422 (67.3%) completed the third and fourth, 423 (67.5%) completed the fifth, 425 (67.8%) completed the sixth, 378 (60.3%) completed the seventh, 271 (43.2%) completed the eighth, and 138 (22.0%) completed the ninth.1 Because participants may have missed assessments and resumed later, and because most participants missed at least one assessment, it was not possible to examine clinical differences between “dropouts” and “completers.”2

STATISTICAL ANALYSES

Variables

Four sets of variables were created for each anxiety disorder and depression: (1) met DSM-IV-TR diagnosis at baseline, (2) had DSM-IV-TR onset of disorder during the follow-up period, (3) met criteria for subthreshold/subclinical disorder at baseline (see below), and (4) endorsed SCID screening item at baseline. Variables were dichotomous yes (1)/no (0) indicating the presence or absence of the diagnosis or endorsement of a screening item. DSM-IV-TR diagnoses at baseline were operationalized as diagnoses with a current or lifetime (i.e., prior to baseline) DSM-IV-TR diagnosis with a CSR ≥ 4. Disorder onsets were operationalized as DSM-IV-TR diagnoses with a CSR ≥ 4 within the7–9 years of follow-up after baseline.

Subthreshold and subclinical diagnoses assessed at baseline were included together in one composite variable that included current (at baseline) and past (lifetime history) subthreshold and subclinical diagnoses. Subclinical/subthreshold diagnoses were operationalized as the presence of a disorder that was either a DSM manifestation with a subclinical CSR (i.e., CSR of 2 or 3), or an NOS manifestation with a clinically significant CSR (i.e., CSR ≥ 4). We termed this variable the "subthreshold/subclinical composite." Cases with CSRs ≤ 1 (e.g., panic disorder with CSR = 1) and cases that were both NOS manifestations and subclinical CSRs (e.g., anxiety disorder NOS with a CSR = 2) were considered insufficiently symptomatic and were coded as not having a subclinical/suthreshold diagnosis at baseline.

Simple Models

Logistic regression analyses were conducted in Stata v.12 to test whether endorsement of each screening item and each subclinical/subthreshold composite was associated with a significant increase in the probability of subsequent onset of its associated disorder. First, endorsement of the core symptom in question (e.g., panic attacks) were entered as the independent variables, and the onsets for the disorder linked to that particular screener item (e.g., panic disorder) were entered as the dependent variables, excluding participants with that DSM-IV-TR diagnosis at baseline (e.g., had panic disorder at baseline). Next, the subthreshold/subclinical composites were entered as the independent variables, and the clinically significant onset for the disorder linked to that particular subclinical/subthreshold diagnosis was entered as the dependent variable, excluding participants with that DSM-IV-TR diagnosis at baseline. Analyses were conducted separately for each DSM-IV-TR anxiety disorder (social anxiety disorder, generalized anxiety disorder [GAD], panic disorder, obsessive compulsive disorder, and posttraumatic stress disorder). Participants who met criteria for any past or current anxiety disorder at baseline were excluded from analyses. Individuals with baseline UMDs were not excluded from the analyses predicting anxiety disorders in order to maximize power. There was a relatively high prevalence of baseline UMDs (N = 129) and low prevalence of most anxiety disorder onsets (see Table 2).

Parallel models were conducted with baseline major depressive disorder subclinical/subthreshold composite and screener item (i.e., depressed mood and/or anhedonia) as predictors in independent analyses with UMD onset as the dependent variable. Participants with a diagnosis of a UMD at baseline were excluded from these analyses.

Table 2. Frequency of each disorder within each variable during the 7–9 years of follow-up

Disorder	Baseline clinically significant DSM diagnoses	Endorsed screening item	Subthreshold/ Subclinical	Number of clinically significant DSM onsets
Social anxiety	58	55	44	71
Generalized anxiety	17	26	22	30
Panic	7	14	6	15
Obsessive compulsive	17	11	12	14
Posttraumatic stress	5	13	11	14
Mood disorder	129	135	27	194

Note: Above frequencies for screening item endorsement and subclinical/subthreshold cases were calculated before excluding T1 cases of the disorder.

Comprehensive Models

A model excluding anyone with baseline anxiety or UMDs was conducted including all anxiety and major depressive disorder screening items as predictors of any anxiety disorder (i.e., any of the anxiety disorders collapsed together). An identical model was run with the subclinical/subthreshold composite items as predictors.

RESULTS

Table 2 presents the number of onsets over the follow-up period for each of the disorders predicted, after excluding those who had anxiety disorders at baseline (for the prediction of anxiety disorder) and UMDs at baseline (for the prediction of major depressive disorder). Figure 1 presents the onsets for each disorder by timepoint.

ANXIETY SYMPTOMS AS PREDICTORS OF ANXIETY DISORDER ONSET

Panic Disorder

Endorsement of panic attacks (i.e., panic disorder screening item; OR = 6.29, P < .01, CI = 2.14–18.50) and the panic subclinical/subthreshold composite (OR = 11.58, P < .05, CI = 1.21–110.85) significantly predicted the onset of later panic disorder (with or without agoraphobia).

Obsessive Compulsive Disorder (OCD)

Endorsement of obsessions or compulsions in the screener item (OR = 3.87, P < .05 CI = 1.11–13.54) and the obsessions/compulsions subclinical/subthreshold composite (OR = 27.70, P < .01 CI = 6.17–124.05) were associated with later onset of OCD.

Posttraumatic Stress Disorder (PTSD)

Endorsement of re-experiencing symptoms after a trauma (i.e., the PTSD screener item) was not significantly associated with later PTSD onset (OR = 2.73, P = .08, CI = 0.90–8.26). There was insufficient variability in the PTSD subclinical/subthreshold composite for the model to run.

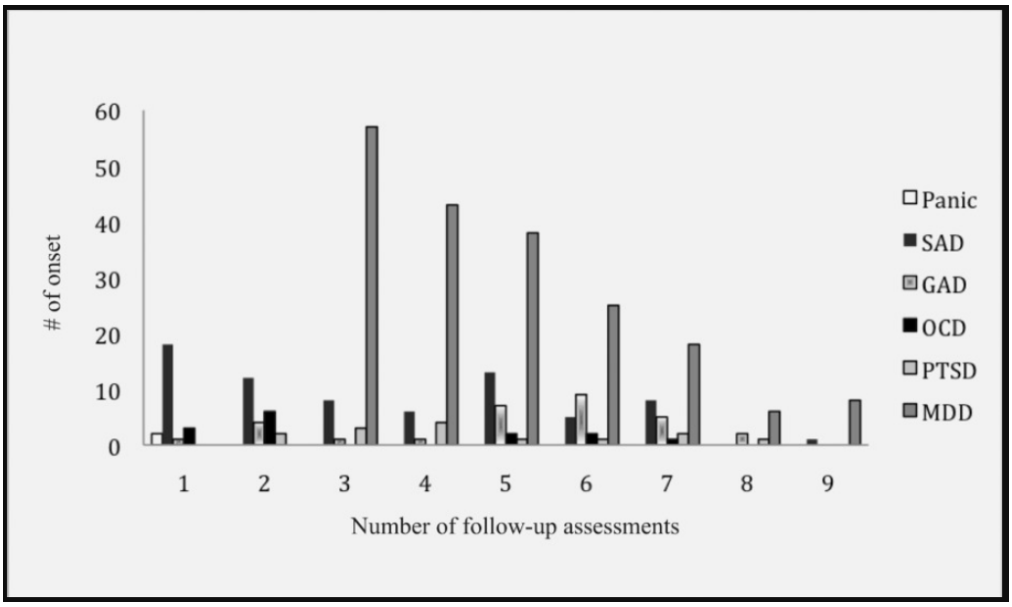

Fig. 1. Number of Onsets by Timepoint; GAD, generalized anxiety disorder; SAD, social anxiety disorder; OCD, obsessive-compulsive disorder; PTSD, posttraumatic stress disorder; MDD, major depressive disorder.

Social Phobia

Endorsement of being anxious in social situations (i.e., the social anxiety screener item) did not significantly predict social phobia onset (OR = 1.66, P = .08, CI = 0.95–2.89), but the social anxiety subclinical/subthreshold composite was a significant predictor of later social phobia (OR = 3.24, P < .01, CI = 1.45–7.00).

Generalized Anxiety Disorder

Neither endorsement of excessive and uncontrollable worry for at least six months (i.e., the GAD screener item; OR = 1.98, P = .09, CI = 0.89–4.38) nor the generalized anxiety subclinical/subthreshold composite (OR = 3.41, P = .06, CI = 0.95–12.27) significantly predicted GAD over the follow-up period.

SYMPTOMS OF ANXIETY AND DEPRESSION AS PREDICTORS OF LATER ANXIETY DISORDER ONSET

A comprehensive model predicting any anxiety disorder onset was conducted with all of the anxiety disorder and major depressive disorder screening items as predictors in a model. Only endorsement of the panic screening item uniquely predicted the onset of any anxiety disorder (OR = 2.66, P < .05, CI = 1.27–5.59). None of the other anxiety disorder screening items were uniquely associated with greater odds of developing an anxiety disorder over the follow-up period (all Ps > .10).

MAJOR DEPRESSIVE DISORDER SYMPTOMS AS PREDICTORS OF UMD ONSET

Simple Model

Endorsement of depressed mood and/or anhedonia (i.e., depression screening item) was significantly associated with later onset of a UMD (OR = 2.52, P < .01, CI = 1.59–4.01), whereas the subclinical/subthreshold depression composite was not (OR = 1.46, P = .40, CI = 0.61–3.53).

Comprehensive Model

When including all anxiety and major depressive disorder screening items (and excluding participants with any baseline anxiety or UMD), depressed mood and/or anhedonia remained a significant predictor of later UMD onset (OR = 2.13, P < .01, CI = 1.23–3.71), and endorsement of panic attacks approached significance in predicting UMD onset (OR = 1.86, P = .05, CI = 0.10–3.47). None of the other core features of the disorders made a significant unique contribution to the model predicting UMD onset (all Ps > .18).

DISCUSSION

These data suggest that those who present with a core feature of panic disorder (i.e., panic attacks), OCD (i.e., compulsions), or major depressive disorder (i.e., depressed mood and/or anhedonia) should be the target of further monitoring, assessment, and preventive interventions. Analyses examining whether subclinical or subthreshold manifestations of disorders predicted later clinically significant DSM manifestations of the disorders indicated that subclinical/subthreshold panic disorder, OCD, and social phobia predicted later clinically significant onsets of those disorders. These findings highlight the dimensional nature of psychopathology and indicate that some symptomology (i.e., core features of some anxiety and UMDs, some symptoms of anxiety disorders with clinically significant distress or impairment, and all symptoms of some anxiety disorders without clinically significant distress or impairment) are risk markers for the later development of the full disorder. This suggests that preventive interventions may be warranted for these individuals.

Consistent with hypothesis, endorsement of panic attacks, in the absence of any baseline anxiety disorder, was associated with increased odds of developing panic disorder over the follow-up period. Similarly, the presence of subclinical or subthreshold panic disorder at baseline predicted a full, clinically significant panic disorder diagnosis over the follow-up. These findings are consistent with a growing body of literature showing that individuals who experience panic attacks are more likely to develop panic disorder later compared to controls who have no panic attacks.14, 21 Still, it is worth pointing out that the prevalence of panic attacks in the general population is considerably higher than that of panic disorder22, 23 and occasional panic attacks are observed in a sizeable percentage of nondisordered samples.24-26 Thus, there are still a significant number of individuals with panic attacks who will not develop panic disorder. This suggests that there likely are to be certain mediating (e.g., cognitive misappraisals of panic attacks, panic-related apprehension leading to behavioral avoidance) and moderating (e.g., neuroticism or anxiety sensitivity) risk (and protective) factors to explain who, among those who experience panic attacks, is most likely to go on to develop panic disorder.

Consistent with hypothesis, endorsement of obsessions, and/or compulsions at baseline was significantly associated with OCD onset, as was the presence of sublinical or subthreshold OCD. Given the large confidence intervals and low number of OCD onsets, these findings should be considered tentative. However, if replicated, these findings suggest that obsessions and compulsions, even if not clinically significant, may be useful for determining whether someone is at risk for developing OCD.

Our results show that endorsement of the core features or subthreshold/subclinical features of PTSD and GAD did not predict later onset of these disorders. Similarly, endorsement of anxiety in social situations did not significantly predict later onset of social anxiety disorder in this sample, although subthreshold/subclinical case status did predict onset of social anxiety disorder. We interpret these findings with caution so as not to accept the null hypothesis. Samples with greater numbers of onsets for these disorders may be needed to ensure sufficient statistical power. Indeed, most nonsignificant odds ratios were in the expected direction with P-values in the P = .06 to P = .09 range. Possibly, participants in this sample who endorsed these screening items at baseline continued to have symptoms of these disorders but never met the threshold or clinical severity for a DSM-IV diagnosis.

When including all anxiety disorder screening items into a model predicting anxiety disorder onset, only panic attacks uniquely predicted anxiety disorder onset, above and beyond other predictors. This finding may be explained by the ubiquity of panic attacks across the anxiety disorders.1, 24 Thus, consistent with previous literature,12, 15, 27 a history of panic attacks appears to be a consistent and robust risk factor not only for panic disorder but for other anxiety disorders as well. The convergence of this body of literature has led to the inclusion of panic attacks as a specifier across DSM5 disorders.28

Finally, endorsement of depressed mood and/or anhedonia predicted later onset of UMDs. This is consistent with literature showing that subclinical depression symptoms predict later onset of a full major depressive episode.11, 29 This finding is noteworthy given that participants only had to endorse the depressed mood or anhedonia at a subthreshold level to screen positively for major depressive episode. This low threshold suggests that even mild-to-moderate symptoms of depression or anhedonia may be predictive of later UMDs. However, inconsistent with hypothesis and previous literature, the presence of a subclinical or subthreshold UMD at baseline did not predict later onsets. Because participants were excluded from these analyses if they already had a UMD onset by baseline (over 20% of the sample), it is possible that these analyses only represented a subgroup of individuals whose clinically significant UMDs had a later onset.

Despite the study's strengths, including a prospective design and large sample, there are limitations. First, some anxiety disorders (particularly social anxiety disorder) had an earlier average age of onset than the average age of our sample at the outset of our study, so our findings with regard to social anxiety disorder risk are limited to those who have a later age of onset than the average in the general population. Relatedly, it is worth noting the relatively high prevalence of a UMD at baseline in this sample, which may be attributed to the oversampling of those high in neuroticism. Still, this baseline prevalence points to the need for earlier screening and detection in childhood. Second, our analyses do not account for the role of stressful life events throughout the follow-up period. This is particularly important for the prediction of PTSD, as individuals who had not yet experienced traumatic events at baseline may have experienced trauma during the follow-up period, which would then put them at elevated risk of PTSD. Third, as would be expected based on epidemiological data,1 there were relatively few onsets for some of the anxiety disorders, which likely limited our power to detect effects. Although our sample was large, even larger samples are

needed. Finally, as would be expected in a 10-year longitudinal study, we had a number of participants who missed at least one, and often multiple assessments. Although some participants missed occasional assessments and resumed them later, others discontinued their participation in the study at some point in the follow-up. It is possible that dropout may be related to psychopathology, thus leading to a possible underestimation of occurrence of anxiety and mood disorders.

Taken together, these findings indicate that early detection through screening for the presence of some symptomology of anxiety and mood disorders can help to identify individuals at risk for the development of these disorders, and may be important to monitor and address through preventive interventions.

Notes:

1 Note that the eighth follow-up assessment was only available for Cohorts 1 and 2 (and a few participants from Cohort 3), and the ninth follow-up assessment was only available for Cohort 1 (and a few participants from Cohort 2). Thus, the lower percentages of total participants completing those assessments was expected.

2 However, there were no differences in prevalence of anxiety and mood disorders between those who completed only a baseline assessment and those who completed at least one follow-up (all ps ranging from .07–.99).

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