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Predictors of remission from Generalized Anxiety Disorder and Major Depressive Disorder

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Abstract

Background—The predictors of onset of major depressive disorder (MDD) and generalized anxiety disorder (GAD) are well-characterized. However the factors that predict remission from these conditions are less clear, and the study of this area is further complicated by differing definitions of remission.

Methods—Data come from the National Comorbidity Survey - Replication, and analysis was limited to respondents with a lifetime history of GAD (n=621) or MDD (n=1,299) assessed by the Composite International Diagnostic Interview. Predictors of remission included demographic factors, adverse childhood events, family history, and clinical characteristics. Multiple definitions of remission were explored to account for residual symptoms.

Results—Half (54.4%) of respondents with MDD and 41.1% of respondents with GAD experienced full remission. Older age and higher socioeconomic status were positively related to remission in a dose-response manner for both disorders. Adverse childhood experiences and family history of anxious/depressive symptoms were negatively associated with remission from MDD. Comorbid GAD was inversely associated with remission from MDD (Odds ratio (OR): 0.62, 95% Confidence interval (CI): 0.44-0.88), but comorbid MDD did not impact remission from GAD (OR: 0.93, 95% CI: 0.64-1.35). With the exception of the influence of comorbidity, these associations were robust across definitions of remission.

Limitations—Cross-sectional analysis and retrospective recall of onset of MDD/GAD.

Conclusions—Many individuals with MDD or GAD will experience full remission. Some predictors appear to have a general association with remission from both disorders, while others are uniquely associated with remission from MDD.

Introduction

Major Depressive Disorder (MDD) and Generalized Anxiety Disorder (GAD) are among the most common forms of mental illness and are major sources of disease burden and disability

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in the United States and globally.^{1,2} These two conditions often co-occur;³ Brown et al⁴ estimated the concurrent and lifetime comorbidity of MDD in GAD at 26% and 64%, respectively, and the concurrent and lifetime comorbidity of GAD in MDD at 5% and 9%. High levels of comorbidity have also been reported by other investigators.^{5,6,7} Using longitudinal data from the original National Comorbidity Survey, Kessler et al found that although each disorder is associated with increased risk of the other over an extended period of time, the strongest risk is for near-simultaneous onset of both disorders.⁸ The factors underlying this comorbidity likely reflect elements related to measurement (i.e., shared or similar symptomology), shared risk factors, and underlying shared liability to both disorders.^{9,10,11} For example, there is emerging evidence suggesting that “mixed” anxiety-depression may be a distinct disorder,¹² as well as the potential for a positive feedback relationship between these conditions, whereby comorbidity worsens the prognosis of both conditions.^{13,14,15} Family studies have suggested that parental history of MDD is associated with an increased risk of both MDD and a variety of anxiety disorders in offspring,¹⁶ further supporting the idea of a shared genetic liability.

Variation in the way remission is defined complicates study of this subject.^{17,18} Often, even if individuals no longer meet diagnostic criteria for MDD or GAD, they still experience residual symptoms,^{19,20} which can negatively impact their quality-of-life and may indicate an increased risk of recurrence.^{21,22,23} Despite these issues of measurement, remission does occur. GAD, which requires symptoms to be present for at least 6 months, is often considered to be chronic; however studies suggest that 46% of female and 56% of male cases experience remission.²⁴ Similarly, using data from the Baltimore Epidemiologic Catchment Area Study in which participants were followed for 23 years, and defining remission as at least one episode-free year, Eaton et al. found that approximately 50% of individuals who experience a single Major Depressive Episode will not experience another, and that approximately 85% of those with a new onset of depression eventually experienced remission from the initial episode.²⁵

While there is a large body of research on the predictors of onset of MDD and GAD, including work on shared predictors of these conditions, predictors of remission are less frequently studied. Eaton et al. found that recurrence of depression following remission was predicted by female gender and younger age at onset.²⁵ Longitudinal studies using the National Epidemiologic Survey on Alcohol and Related Concerns have reported that psychiatric comorbidity, younger age at onset, and childhood maltreatment are associated with reduced likelihood of remission from MDD.^{26,27} Other investigations report that remission from MDD is positively associated with social support and negatively associated with adverse childhood experiences.^{28,29} There are fewer studies of remission from GAD; however, comorbid psychiatric disorders have been associated with lower likelihood of remission¹³ and higher likelihood of recurrence.¹⁴ As with MDD, adverse experiences in childhood are associated with greater persistence of anxiety disorders.²⁹ In a longitudinal study of the predictors of persistence of GAD and MDD (defined as meeting diagnostic criteria for each disorder at both the baseline interview and at follow-up) in the original National Comorbidity Survey Follow-up, childhood adverse experiences were significantly predictive of persistence for both disorders, and persistence for MDD (but not GAD) was associated with family history of mental illness.⁸ However, by defining persistence solely as

continuing to meet diagnostic criteria this study could not examine how other definitions of remission influence these relationships.

Although extant research has identified several factors of relevance to remission, the majority of existing studies conceptualize remission or persistence by examining whether individuals continue to meet diagnostic criteria, and do not account for subclinical or residual symptoms. The purpose of this study was to investigate the unique and shared factors related to remission from MDD and GAD in a large, community-based sample while exploring multiple definitions of remission to examine how robust our inferences are to these different measurement schemas.

Methods

Sample

Data come from the National Comorbidity Survey Replication (NCS-R),³⁰ a nationally-representative, cross-sectional survey. This survey used detailed in-person interviews to examine the prevalence of mental disorders and associated factors.³¹ The total NCS-R sample included 9,282 adults and further details of survey design and methodology are documented elsewhere.³² The present analysis was limited to respondents who: (a) met Diagnostic and Statistical Manual for Mental Disorders (DSM-IV) criteria for lifetime history of GAD or MDD, (b) had onset of disorder more than one year prior to interview (in order for it to be possible for them to meet our definition of remission), and (c) had complete data for all model variables. The final analytic sample size for GAD was 621 (82.6% of those with a lifetime history of GAD), and the analytic sample size for MDD was 1,299 (82.3% of those with a lifetime history of MDD). Descriptive statistics of those excluded from the samples, and a detailed breakdown of the reasons for exclusion, can be found in eTables 1 and 2.

The NCS-R was approved by the University of Michigan and all participants provided informed consent. This analysis used only publicly-available data from the Collaborative Psychiatric Epidemiologic Surveys available at <http://www.icpsr.umich.edu/icpsrweb/ICPSR/studies/20240>.

Measures

Lifetime history of MDD and GAD

Lifetime history of psychiatric disorder was assessed using the World Mental Health Survey Initiative adaptation of the Composite International Diagnostic Interview (WMH-CIDI),³³ a structured interview based on the clinical criteria for each psychiatric disorder as specified in the DSM-IV, designed to be administered by trained lay interviewers. This version of the CIDI was designed to address several methodological challenges faced by structured interview instruments, and performs well in comparisons with the Structured Clinical Interview for the DSM-IV (SCID), a clinician-administered semi-structured interview.³⁴ Lifetime history of MDD was defined as meeting the DSM-IV criteria for MDD with hierarchy. The DSM-IV hierarchy for MDD excludes depressive symptoms that are better explained by a psychotic disorder or bipolar disorder, but does not exclude anxiety disorders.

Lifetime history of GAD was defined as meeting the DSM-IV criteria for GAD without hierarchy. The DSM-IV hierarchy for GAD includes a requirement for the exclusion of anxiety symptoms that occur during an episode of depression. Since one of the main exposures under study in this paper is MDD/GAD comorbidity, it was necessary to omit the hierarchy for GAD in order to accurately assess experience of both MDD and GAD symptoms.

Remission status

Remission was operationalized in two ways, *Full remission* and *Diagnostic remission*. *Full remission* was defined as both (a) not meeting DSM-IV criteria in the 12-months prior to interview and (b) not reporting major residual affective or anxiety symptoms at the time of interview. Residual symptoms were assessed using two screening questions that broadly addressed disorder-related symptomatology, “How often did you feel nervous?” and “How often did you feel depressed?” Both questions refer to the respondent’s worst month in the past year, and were rated on a scale of “all of the time”, “most of the time”, “some of the time”, “a little of the time”, or “none of the time”, with answers of “all” or “most” of the time classified as positive for residual symptoms. *Diagnostic remission* was defined as not meeting DSM-IV criteria within the past 12-months, regardless of whether the respondent endorsed major residual symptoms within the past year. This is the inverse of the definition of “persistence” used in the NCS-R, which is defined as having both a lifetime and a 12-month diagnosis of the same disorder.³¹

Predictors of remission

Potential predictors of remission were selected in two categories: (1) factors known to be associated with risk of developing MDD or GAD which may then also influence disease persistence, and (2) factors relating to the clinical characteristics of each disorder. Factors selected on the basis of an existing association with risk of MDD or GAD included adverse early-life experiences and family history of depressive or anxious symptoms. Adverse childhood experiences (ACE) were operationalized as a summary count of events including parental death, parental divorce, other separation from caregiver, parental domestic violence, physical abuse, neglect, severe economic hardship, and parental criminality, each recorded dichotomously. The summary score ranged from zero to eight. Family history of depressive or anxious symptoms was assessed based on respondent report of parents’ behavior. Due to the shared genetic liability between MDD and GAD, parental history of either anxious or depressive symptoms was used for both disorders, rather than only parental history of symptoms that mirrored the respondent’s diagnosis. Factors relating to the clinical characteristics included age at onset of disorder (categorized as under 12, 12-17, 18-29 (reference group), 30-44, and 45+), a lifetime history of comorbid GAD (included in the MDD models), and a lifetime history of comorbid MDD (included in the GAD models).

Demographic covariates

A set of demographic covariates was selected based on theoretical potential to act as confounders of the relationships between the exposures and outcomes under study. These included age at interview (categorized as 18-29 (reference group), 30-44, 45-64, or 65+), gender, and socioeconomic status (SES). SES was indexed by household income-to-poverty

ratio (IPR), which is calculated by dividing household income by the Census poverty threshold for the respondent's household size.³⁵ The IPR was categorized as less than twice the poverty threshold (reference group), 2 to 3 times the poverty threshold, 4 to 5 times the poverty threshold, or 6 or more times the poverty threshold. Race/ethnicity and education were explored as potential covariates but preliminary analyses indicated they did not improve model fit or significantly influence the estimates of the other predictors.

Statistical Analysis

Initially, we used bivariate logistic regression to examine the characteristics of respondents who experienced full remission from MDD and/or GAD as compared to those who did not. Next, we fit a model that adjusted for demographic characteristics (age, gender, and IPR) for each disorder. Separate models were then constructed to test the addition of each of the main exposure variables to this demographic-adjusted model. A Bonferroni adjustment was applied to account for multiple comparisons, reflecting the fact that this analytic approach produces four models per outcome.

The initial analysis was conducted using the outcome of *Full remission*. Two sensitivity analyses were conducted by repeating this analytic strategy. The first used the *Diagnostic remission* categorization in which all individuals who no longer met DSM criteria were classified as remitted, regardless of residual symptoms (described above). The second sensitivity analysis examined the effect of applying the DSM-IV exclusion hierarchy rule when identifying cases of GAD (i.e., this hierarchy excludes cases of GAD that occur during an episode of another disorder such as major depression, and as a result, applying this hierarchy rule reclassified some (n=117) comorbid MDD-GAD cases as MDD-only). Results from these sensitivity analyses were compared to the main analysis to assess the degree to which these changes in the categorization impacted the inferences about predictors of remission.

All analyses were conducted using survey procedures in SAS 9.4 to account for complex sampling design. Forest plots to illustrate the adjusted relative odds and 95% confidence intervals of predictors of remission were constructed using R 3.1.1 with the forestplot package, and the proportional Venn diagram was created using The GIMP 2.8.8. All p-values refer to two-tailed tests, all confidence intervals are 95% confidence intervals except where otherwise noted due to multiple comparisons, and a Bonferroni-adjusted alpha of 0.0125 was used to assess statistical significance for the main exposure models.

Results

Figure 1 illustrates the number of cases and comorbidity between MDD and GAD and the probability of remission for each disorder under different classification schema. Half (54.4%) of respondents with a history of MDD and 41.1% of respondents with a history of GAD were in *Full remission* at the time of interview. Although 53.1% of the comorbid MDD/GAD group was in *Full remission* from at least one disorder, only 30.9% of this group was in *Full remission* from both disorders.

Table 1 shows descriptive characteristics of the analytic sample stratified by *Full remission* status. Of the 1,299 respondents with a lifetime history of MDD, 783 (60.0%) met criteria for *Diagnostic remission* in the 12-months prior to interview. However, 76 (9.7%) of the respondents in *Diagnostic remission* still regularly experienced residual symptoms of depression. Similarly, of the 621 respondents with a lifetime history diagnosis of GAD, 311 (50.1%) met criteria for *Diagnostic remission* in the 12 months prior to interview. However, 56 (18.0%) of those in *Diagnostic remission* still regularly experienced residual symptoms of anxiety in the 12-months prior to interview.

Figure 2 illustrates the results of the logistic regression model predictors for *Full remission* from MDD, with a Bonferroni correction applied to the confidence intervals of the main exposures to account for multiple comparisons. Factors associated with higher odds of remission included older age (e.g., those aged 65+ had 3.62 times the relative odds of remission from MDD compared to those 18-29) and higher IPR, which showed a dose-response relationship. Factors inversely associated with odds of remission were adverse childhood experiences, parental history of anxious/depressive symptoms, and earlier onset of disorder. Under this definition of remission, lifetime comorbidity of GAD was associated with lower likelihood of remission from MDD (Odds Ratio (OR): 0.62; 95% Confidence Interval (CI): 0.44 - 0.88).

Figure 3 shows the results of the logistic regression model predicting full remission from GAD. In contrast to MDD, only older age and increasing IPR were significantly related to remission from GAD. Lifetime comorbidity of MDD was not significantly related to remission from GAD (OR: 0.93; 95% CI: 0.64 - 1.35).

Sensitivity analyses

The first sensitivity analysis applied the *Diagnostic* definition of remission. Descriptive characteristics of the sample using this definition of remission are shown in eTable 3, and the analytic results are shown in Table 2. Most results of this analysis were similar to the *Full remission* analysis, however some associations, while substantively unchanged, were no longer statistically significant (e.g., the dose-response relationship between IPR and remission was less apparent). Notably, comorbid GAD was no longer significantly inversely associated with remission from MDD under this classification schema (OR: 0.74 95% CI: 0.48-1.14).

The second sensitivity analysis applied the DSM-IV hierarchy rule when identifying cases of GAD. Descriptive characteristics of the sample using this case definition are shown in eTable 4, and results of this sensitivity analysis are shown in Table 2. Most of the substantive results were unchanged, but again comorbid GAD was no longer significantly inversely associated with remission from MDD under this case definition (OR: 0.71 95% CI: 0.46-1.10).

Discussion

This study is among the first and largest to our knowledge to examine the predictors of remission from MDD and GAD while accounting for residual symptoms in the definition of

recovery. In this community sample of adults with a history of MDD and/or GAD, 54.4% and 41.1%, respectively, of respondents were in *Full remission* with a duration of at least one year the time of interview. Adverse childhood experiences, family history of anxious/depressive symptoms, earlier age of disorder onset, and comorbid GAD were inversely related to *Full remission* from MDD. However, none of these factors were associated with remission from GAD. Additionally, older age and higher socioeconomic status were positively associated with remission from both disorders. While many of the predictors of remission were consistent across the three classification schemas examined here, the inferred importance of comorbidity between MDD and GAD is dependent on the specific operationalization of remission.

It is worth noting that many of the predictors associated with lower likelihood of remission have also been previously identified as factors influencing response to treatment^{36,37,38,39} and as risk factors for the development of MDD and/or GAD. Adverse childhood experiences^{40,41} and family history of anxious or depressive symptomology¹⁶ have both been associated with increased likelihood of developing MDD, and in this study are also found to be associated with lower likelihood of remission. Similarly, the incidence of most psychiatric disorders is inversely associated with socioeconomic status.^{42,43} If these factors play a causal role in the development of psychopathology, these findings suggest that they continue to exert a negative influence after the development of a disorder through negatively impacting the likelihood of remission. Alternately, these factors may be related to development and remission of MDD and GAD through a non-causal pathway, perhaps by influencing disease severity which is correlated with persistence.⁴⁴ As a final possibility, many existing studies of risk factors for psychiatric disorders are cross-sectional, which would lead to over-representation of chronic cases among the respondents who currently meet diagnostic criteria; as a result factors associated predominantly with illness duration may appear to have an association with incidence.

Two other predictors examined in this study, age at onset and comorbidity between MDD and GAD, only apply in situations where a psychiatric disorder is already present. Although these factors cannot be associated with the risk of developing a psychiatric disorder, they may be markers of other traits which do have such an association. Younger age at onset was associated with lower likelihood of remission from MDD, and earlier age of onset has been associated with higher genetic vulnerability to depression in prior studies.⁴⁵ Similarly, comorbid GAD among those with MDD was associated with lower likelihood of remission, and this co-occurrence is associated with greater disease severity.¹⁵ However, comorbid MDD was not associated with the likelihood of remission from GAD. Because GAD is a comparatively rare comorbidity in MDD cases, its presence may be a stronger indicator of disease severity or liability in this population than MDD is for GAD cases.

Among the 320 individuals with a lifetime history of both MDD and GAD, the largest group (46.9%) had not remitted from either disorder and the second-largest group (30.9%) had remitted from both disorders. Remission from only one disorder or the other appeared to be fairly rare. There are several potential interpretations of this pattern. One possibility is that factors associated with remission are associated with general psychosocial functioning, and that when circumstances exist to produce remission from one comorbid disorder, they are

also likely to produce remission from the other disorder. The concept of mixed anxiety and depression as a distinct disorder could also apply here,¹² with anxious and depressive symptoms developing and remitting together as shared manifestations of an underlying process. A third possibility is that the presence of one disorder exacerbates the other and decreases the likelihood of remission, such that when one disorder does remit, the likelihood of the other remitting increases. A rigorous examination of these explanations requires longitudinal data.

These findings are broadly consistent with prior work on persistence of mood and anxiety disorders over time.⁸ While conceptually persistence is the inverse of remission (i.e., cases not in remission at follow-up would be persistent) as our findings illustrate the way remission (and therefore persistence) is defined has an impact. Kessler et al. also reported a differential effect of comorbidity, with comorbid GAD predicting the persistence of MDD, but comorbid MDD not predicting persistence of GAD. They also reported that the period of greatest risk for developing MDD was at the time of onset of GAD (and vice versa) and that this risk declined over time. The decay in the strength of the association over time suggests that GAD is not merely a marker of the severity of MDD, and this relationship might instead be explained by shared causal or contributory factors.⁸

In both sensitivity analyses, factors that related to remission were broadly the same, but the effect sizes tended to become weaker and confidence intervals tended to become wider. This suggests that these alternate classification schemas (i.e., relying solely on diagnostic criteria to determine remission status, and applying the DSM hierarchy rules for identifying cases of GAD) can result in misclassifications that obscure (or create) between-group differences and may bias results. The classification of individuals with residual symptoms is an important consideration in both research and clinical applications, as these individuals may have a different disease course than fully-remitted individuals.^{21,22} Other outcomes, such as return to normal functioning and the experience positive states such as self-confidence and optimism, may also be important in defining remission.⁴⁶ The classification of individuals with symptoms of both MDD and GAD is also an important challenge: although the DSM-IV states that individuals whose GAD symptoms occur only during episodes of MDD should be excluded from diagnosis with GAD, the clinical characteristics of these cases are more similar to GAD/MDD comorbid cases than with MDD-only cases.⁴⁷

It is of particular interest that the finding that GAD was associated with lower odds of remission from MDD was not replicated in either sensitivity analysis. The *Diagnostic remission* analysis, in which individuals with residual symptoms were re-classified as “remitted,” would result in a reduction in power to detect factors associated with true remission (through misclassification) if residual symptoms are indeed representative of an ongoing (although milder) disease state. Alternately, it is possible that comorbidity itself might also be associated with report of residual symptoms (i.e., individuals in remission from one disorder might experience symptoms from the other disorder which may be reported as residual symptoms). In the second sensitivity analysis, in which the DSM exclusion hierarchy was applied in ascertaining cases of GAD, a large number of people previously classified as comorbid cases were re-classified as MDD-only. If the presence of GAD symptoms impacts the likelihood of remission from MDD, such re-classification of

individuals would also reduce the ability to detect this effect. Therefore, rather than representing a “failure to replicate” across these schemas, we interpret these results as indicative that these alternate classification strategies are less accurate reflections of underlying between-group differences, and thus reducing the ability to detect such differences.

Strengths and Limitations

Findings should be interpreted in light of study limitations. The main limitation is the use of cross-sectional data to investigate an event like remission that necessarily occurs over time. As a result our study focused on remission status at time of interview, but did not examine longitudinal factors such as number of episodes or past periods of remission. Furthermore, although it is possible to use 12-month vs. lifetime diagnoses to reconstruct disease history, other data on factors like socioeconomic status represent only a single point in time, and therefore changes in these factors cannot be associated with the outcome as they could be with longitudinal data. The cross-sectional data also introduces the possibility of recall bias. We also note that while psychiatric medications or psychotherapy may contribute to remission, exploratory analyses showed these were confounded by disease severity (i.e., confounding by indication, with more severe cases both more likely to receive treatment and less likely to remit),^{48,49,50} and thus we did not examine them as predictors of remission in this study; only randomized controlled trials are appropriate for assessing the impact of treatment on remission. However it is worth noting that other factors, such as socioeconomic status, may exert some of their influence on remission by way of their impact on access to treatment. Although disease severity has a known association with likelihood of remission,^{27,36} it was not examined in the current study as it is likely to be subject to differential recall bias (with individuals still in episode likely to report greater symptom severity than remitted individuals). However, although severity itself was not examined, our focus on MDD-GAD comorbidity may represent one dimension of severity.³ In examining comorbidity, this study looked only at the comorbidity between MDD and GAD due to the shared genetic liability between the two disorders^{9,10,16} and the potential for mixed MDD-GAD to be a distinct condition as theorized by other authors.¹² Because the statistical design of this study required a penalty for multiple comparisons, we elected not to examine other comorbidities, which would have resulted in a decline in statistical power. However, future research would benefit from a broader incorporation of comorbid conditions. Individuals were excluded from the study if they were missing data on one or more model variables, as shown in eTables 1 and 2 such individuals were more likely to be non-white, of lower socioeconomic status, and to have a family history of depressive/anxious symptoms. This study also has a number of strengths, including the large, population-based sample, the use of diagnostic instruments to assess history of psychopathology, and comprehensive assessment of predictors of remission. Our sensitivity analysis shows the results to be robust across a variety of outcome classification schemes of remission, which most prior studies have not addressed.

In conclusion, these findings deepen our understanding of factors related remission from two of the most common psychiatric disorders in the general population, and illustrate the importance of considering residual symptoms when studying remission.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Approximately 54.4% of adults with a history of MDD, 43.2% with a history of GAD, and 30.9% with comorbid MDD-GAD experienced remission
- Shared predictors of greater likelihood of remission from MDD and GAD were older age and higher socioeconomic status
- Childhood adversity, family history of anxious or depressive symptomology, and childhood onset were negatively associated with remission from MDD.
- Comorbid GAD was associated with lower likelihood of remission from MDD, but comorbid MDD did not impact likelihood of remission from GAD
- Findings remained broadly consistent across multiple definitions of remission

Figure 1.
Proportional Venn diagram of comorbidity and full remission

Figure 2. Predictors of full remission from MDD

Total N=1299, Remitted N=707.

Values are odds ratio and 95% confidence intervals.

Note: Each main exposure was fit in a separate model, all controlling for age, gender, and income-to-poverty ratio.

Figure 3. Predictors of full remission from GAD

Total N=621, Remitted N=255.

Values are odds ratios and 95% confidence intervals.

Each main exposure was fit in a separate model, all controlling for age, gender, and income-to-poverty ratio.

Table 1
Sample characteristics for Generalized Anxiety Disorder and Major Depressive Disorder,
stratified by Full Remission status

		GAD sample (n=621)		MDD sample (n=1299)	
		Unremitted (n=366)	Full remission (n=255)	Unremitted (n=592)	Full remission (n=707)
Demographic					
Age (mean, SE)		43.9 (0.8)	46.8 (1.0)	40.6 (0.8)	45.7 (0.6)
Gender					
	Male	102 (31.8%)	76 (34.0%)	186 (35.3%)	235 (36.8%)
	Female	264 (68.2%)	179 (66.0%)	406 (64.7%)	472 (63.1%)
Race					
	White	290 (80.7%)	210 (83.3%)	453 (77.8%)	565 (81.9%)
	Black	31 (6.9%)	15 (5.5%)	52 (7.2%)	50 (6.5%)
	Hispanic	26 (7.8%)	14 (5.6%)	45 (8.3%)	58 (8.1%)
	Other	19 (4.7%)	16 (5.7%)	42 (6.7%)	34 (3.6%)
IPR					
	< 2x poverty	99 (26.9%)	33 (12.6%)	157 (26.1%)	90 (13.7%)
	2-3x poverty	102 (27.4%)	76 (29.0%)	167 (29.5%)	177 (23.8%)
	4-5x poverty	87 (23.8%)	67 (26.6%)	123 (19.4%)	168 (23.3%)
	6+x poverty	78 (21.9%)	79 (31.7%)	145 (25.0%)	272 (39.3%)
Main exposures					
No. of ACEs (mean, SE)		1.2 (0.1)	1.0 (0.1)	1.2 (0.1)	0.8 (0.1)
Family history					
	Yes	196 (54.3%)	148 (59.8%)	317 (53.4%)	291 (42.2%)
	No	170 (45.6%)	107 (40.2%)	275 (46.6%)	416 (57.8%)
Age at onset					
	< 12	47 (12.3%)	18 (6.8%)	67 (10.3%)	39 (5.0%)
	12-17	71 (19.8%)	37 (13.7%)	164 (28.7%)	133 (19.8%)
	18-29	120 (33.8%)	89 (35.3%)	173 (27.8%)	223 (30.2%)
	30-44	83 (21.5%)	82 (33.2%)	121 (22.3%)	227 (32.3%)
	45+	45 (12.7%)	29 (11.1%)	67 (11.0%)	85 (12.7%)
GAD/MDD comorbid					
	Yes	195 (53.4%)	125 (52.2%)	176 (29.2%)	144 (21.0%)
	No	171 (46.6%)	130 (47.8%)	416 (70.8%)	563 (79.0%)

Note: Values are unweighted N's (weighted %) for categorical variables, and weighted mean (weighted SE) for continuous variables.

IPR: Income-to-poverty ratio. ACE: Adverse childhood experiences.

Table 2
Sensitivity analyses of correlates of remission under alternate operationalizations of remission

	Sensitivity analysis 1: Relative odds of “Diagnostic” remission		Sensitivity analysis 2: Relative odds of remission using GAD with hierarchy	
	GAD Odds Ratio (95% CI)	MDD Odds Ratio (95% CI)	GAD Odds Ratio (95% CI)	MDD Odds Ratio (95% CI)
No. of ACEs	0.98 (0.82-1.16)	0.87 (0.76-0.99)	0.96 (0.78-1.18)	0.80 (0.67-0.95)
Family history (ref=No)				
Yes	1.63 (0.95-2.45)	0.66 (0.46-0.95)	1.13 (0.74-1.72)	0.57 (0.46-0.71)
Age-at-onset (ref= 18-29)				
< 12	0.76 (0.32-1.84)	0.44 (0.23-0.82)	0.61 (0.21-1.79)	0.45 (0.24-0.84)
12-17	0.81 (0.41-1.61)	0.74 (0.48-1.14)	0.70 (0.31-1.56)	0.68 (0.44-1.06)
30-44	1.52 (0.84-2.76)	1.13 (0.66-1.94)	0.98 (0.48-1.99)	1.10 (0.56-2.15)
45+	0.78 (0.33-1.82)	0.62 (0.35-1.12)	1.03 (0.34-3.11)	0.64 (0.33-1.25)
Comorbid MDD/GAD (ref=No)				
Yes	1.04 (0.65-1.67)	0.74 (0.48-1.14)	0.81 (0.48-1.38)	0.71 (0.46-1.10)

Note: Each main exposure was fit in a separate model, all controlling for age, gender, and income:poverty ratio. Confidence intervals are 98.75% confidence intervals due to Bonferroni adjustment to account for multiple comparisons.