Psychological Medicine

cambridge.org/psm

Predictors of depressive symptom trajectories in a prospective follow-up of late adolescents

William Coryell[1], James Mills[1], Lilian Dindo[2] and Chadi A. Calarge[2]

[1]Department of Psychiatry, University of Iowa Carver College of Medicine, Iowa City, IA, USA and [2]Department of Psychiatry, Baylor University, Baylor College of Medicine, Houston, TX, USA

Original Article

Cite this article: Coryell W, Mills J, Dindo L, Calarge CA (2020). Predictors of depressive symptom trajectories in a prospective follow-up of late adolescents. *Psychological Medicine* **50**, 2283–2288. https://doi.org/10.1017/S0033291719002551

Received: 30 January 2019
Revised: 20 August 2019
Accepted: 30 August 2019
First published online: 2 October 2019

Key words:
Adolescents; childhood adversity; depressive symptoms; follow-up; trajectory

Author for correspondence:
William Coryell,
E-mail: William-coryell@uiowa.edu

Abstract

Background. Group-based trajectory modeling holds promise for the study of prognostic indicators in the mood disorders because the courses that the individuals with these disorders follow are so highly variable. However, trajectory analyses of major depressive disorder have so far not included some of the more robust predictors of mood disorder outcome, nor have they described interactions between these predictors.

Methods. A group of 186 individuals aged 15–20 years with past or current depressive symptoms, who had recently begun taking a serotonin reuptake inhibitors antidepressant, underwent extensive baseline evaluations and were then followed for up to 2 years. Trajectory analyses used weekly ratings of depressive symptoms and the resulting groups were compared by the risk factors of sex, psychiatric comorbidity, negative emotionality, and childhood adversity.

Results. A three-group solution provided the best statistical fit to the 2-year symptom trajectory. Negative emotionality and childhood adversity, though correlated, independently predicted membership in higher-morbidity groups. Female sex and comorbidity with generalized anxiety disorder (GAD) were also significantly more likely in the trajectory groups with higher symptom levels. However, the presence of GAD, rather than female sex, was the most important determinant of group membership. Negative emotionality was predictive of group membership only among women.

Conclusions. Trajectory analyses indicated that week-to-week variations in depressive symptoms across individuals could best be condensed into low, remitting and persistent symptom patterns. Female sex, anxiety symptoms, negative emotionality and childhood adversity were each independently associated with trajectories of higher morbidity but negative emotionality may be prognostically important only among women.

Introduction

The 1-year prevalence of depressive disorders in US adults is around 10% (Kessler *et al.*, 2003) and account for the most years lived with the disability of any illness (Üstün *et al.*, 2004). While depressive disorders result in substantial impairment over time for many individuals, some have only a few, discrete episodes. Numerous prospective studies have sought to categorize diverse courses of illness and to identify their clinical and biological correlates.

The metrics used to classify courses of illness have included likelihoods of, or times to, recovery, remission, and relapse, as well as morbidity indices derived from averages of symptom levels over a period of observation. However, none of these measures adequately captures temporal trends. One individual might recover within a few weeks and then relapse into a chronic episode, and another might recover many months after an episode's onset but then remain well for an extended period. The individuals, in either case, might differ markedly in average symptom levels as reflected in a morbidity index, but such a number would not adequately describe the disparate courses over time.

Such problems are, of course, not unique to mood disorders and, in aggregate, these concerns account for an increasing interest in trajectory analyses (Nagin and Odgers, 2010). Such approaches provide person-centered perspectives that identify subgroups based on common patterns in longitudinal observations (Shore *et al.*, 2018). Trajectory analyses of mood disorders in adolescents are particularly important because this age group encompasses the years of onset for a substantial proportion of individuals who experience mood disorders.

A recent meta-analysis of trajectory studies described 20 prospective follow-up studies with identified trajectories that ranged in number from three to eleven (Shore *et al.*, 2018). To summarize the findings of risks factors that distinguished between trajectories, the authors subsumed the symptom patterns in these studies into three groups they labeled as 'low,' 'moderate,' and 'high or increasing'. Female sex was consistently associated with the highest symptom trajectory. At least four studies found low SES, substance abuse, or a 'negative parental relationship' to also be significantly more characteristic of the highest symptom trajectory.

CAMBRIDGE UNIVERSITY PRESS

Notably, this meta-analysis did not examine childhood trauma. Yet, childhood trauma is firmly established as a risk factor for later development of depressive disorders, particularly those characterized by early-onset, chronicity, and treatment resistance (Barnhofer *et al.*, 2014; Nelson *et al.*, 2017). Childhood trauma increases the likelihood of anxiety disorders to at least the same degree as it does of depressive disorders (Li *et al.*, 2016) and is also associated with high levels of neuroticism (Hengartner *et al.*, 2015). Both anxiety disorders (Coryell *et al.*, 2009, 2012; Newman *et al.*, 2013) and neuroticism (Coryell *et al.*, 2017) are, in turn, well-established risk factors for symptom persistence in depressive disorders. However, efforts to describe interactions between anxiety disorders and neuroticism on the course of depressive illness are scarce and we are aware of no studies that do so using trajectory analysis.

In consideration of these issues, we sought to answer the following questions. If clear trajectory groupings emerge as predicted, will childhood adversity be associated with trajectories of higher depressive morbidity? If so, will correlations between measures of childhood adversity and neuroticism, or between childhood adversity and anxiety disorder, account for its prognostic effects on depressive morbidity? Does anxiety disorder mediate the relationship between neuroticism and membership in higher morbidity trajectory groups? Finally, do higher degrees of neuroticism, or rates of anxiety disorder, account for relationships between female sex and trajectory grouping. Evidence for the primacy of one risk factor over another can serve to more productively shape approaches to prognostic formulations and to shift the focus of research toward more fundamental etiological mechanisms.

Methods

Participants

As part of a study designed to examine the effects of selective serotonin reuptake inhibitors (SSRIs) on bone metabolism in adolescents and emerging adults, individuals 15–20 years of age were recruited from inpatient and outpatient settings, and through e-mail solicitations, to comprise two groups (Calarge *et al.*, 2014, 2017). Those in one were taking no psychotropic medications and those in the other had begun taking an SSRI within the previous month. Treatment with psychotropics, other than SSRIs, during the 2 years prior to study entry resulted in exclusion, with the exception of the use of benzodiazepines, trazodone, α_2-agonists, or stable doses of psychostimulants. Also excluded were individuals with an eating disorder, substance dependence, pregnancy, significant medical or surgical history, chronic use of medications potentially affecting bone metabolism, or with plans to move out of state within a year. As the presence of a mood disorder was not a requirement for inclusion in the parent study for either group, the current analyses restricted participants to those who had ever met criteria for a major depressive disorder (MDD) or who endorsed depressive clinically significant symptoms at study entry, including those who were naive to psychotropic medications (n = 186). The local Institutional Review Board approved the study and adult participants provided written informed consent. The parent/guardian of minor participants provided written informed consent while the minors gave written assent to the study.

Procedures

Experienced research coordinators collected demographic and clinical data in an initial interview that included the NIMH Diagnostic Interview Schedule for Children (DISC-IV) (Shaffer *et al.*, 2000) as well as an unstructured interview by a child psychiatrist (CAC). Consensus diagnoses were generated based on the structured interview, an unstructured assessment, and information from self-completed symptom rating scales. Parents of minors were also interviewed.

The intake assessment included the Early Trauma Inventory-Self Report (ETISR) (Bremner *et al.*, 2007). This is a 19-item questionnaire that covers general adverse life events that occurred before the age of 18 and that includes scores for physical, sexual, and emotional abuse, as well as a total score. Participants also completed the Multidimensional Personality Questionnaire (MPQ) (Patrick *et al.*, 2002) at their first follow-up visit. This is a factor-analytically derived inventory of personality that generates 11 primary scales. These loads, in turn, on three higher-order factors: positive emotionality (wellbeing, social potency, social closeness, and achievement), negative emotionality (stress reaction, alienation, and aggression), and constraint (control, harm avoidance, and traditionalism). The negative emotionality measure has been shown to strongly correlate with the NEO Personality Inventory dimension of neuroticism (McCrae and Costa, 1987; Church, 1994). Some attrition occurred between the first visit and the first follow-up so the number of individuals with MPQ data is smaller.

Face-to-face visits occurred at 4-month intervals over the subsequent 2 years. The symptom status of the disorder considered to be primary at the initial evaluation was also monitored with monthly telephone calls to the participants. Interviewers guided individuals to identify any change points in levels of psychopathology that had taken place since the last interview. Participants then quantified the number of symptoms present between those change points and results were recorded according to conventions in the A-LIFE (Calarge *et al.*, 2014), a modification of the Longitudinal Interval Follow-up Evaluation (LIFE) (Keller *et al.*, 1987) that includes additional disorders more commonly seen in youth. This yielded symptom level ratings during each week of follow-up interval on a scale of 1–6. The time period for this coverage included the 4 months preceding the initial face-to-face interview.

Statistical methods

Participants' weekly MDD symptom levels from the A-LIFE were analyzed using group-based trajectory modeling (GBTM), a statistical method used to find clusters of individuals following similar patterns of symptom change over time (Nagin and Odgers, 2010). The GBTM approach was chosen because it is designed to identify subgroup trajectories across time in a manner that is easy to summarize and understand. GBTM models with three and four groups were generated using the censored normal distribution and the polynomial function of time (linear, quadratic, or cubic) that best fit the data. In each model, individuals were assigned to the group where the GBTM-determined probability of membership was highest. The choice of best-fitting model was informed by model fit indices (Akaike, 1974) and ultimately made by maximizing the number of non-redundant MDD patterns. The GBTM analysis was conducted using PROC TRAJ in SAS 9.4 (Jones *et al.*, 2001).

Baseline characteristics of the three trajectory groups were then compared using c^2 tests for categorical variables and ANOVA models for continuous variables. Group differences for ETISR (from baseline) and MPQ (from the first follow-up visit) scores

https://doi.org/10.1017/S0033291719002551 Published online by Cambridge University Press

Table 1. Baseline demographic and clinical characteristics of the participants divided into three trajectory groups

	Low	Remitting	Persistent
	n = 58	*n* = 69	*n* = 59
Female sex, *n* (%)[a]	32 (55.2)	43 (62.3)	50 (84.7)
Age, years, mean (s.d.)	18.9 (1.6)	18.9 (1.7)	19.1 (1.5)
SSRI, *n* (%)[b]	22 (37.9)	57 (82.6)	43 (72.9)
History of suicide attempt, *n* (%)	5 (13.5)	11 (22.4)	9 (20.9)
Lifetime diagnoses, *n* (%)			
MDD[c]	49 (84.5)	68 (98.6)	57 (96.6)
GAD[d]	10 (17.2)	27 (39.1)	29 (49.2)
Alcohol use disorder	5 (8.6)	9 (13.0)	7 (11.9)
Cannabis use disorder	6 (10.3)	9 (13.0)	7 (11.9)
Social phobia	15 (25.9)	20 (29.0)	24 (40.7)
ADHD	6 (10.3)	8 (11.6)	8 (13.6)
Mean (s.d.) scores			
Beck depression inventory[e]	6.7 (6.7)	17.6 (9.8)	18.6 (10.7)
Beck anxiety inventory[f]	6.7 (7.2)	12.4 (10.4)	12.8 (7.7)
Inventory of depressive symptomatology[g]	10.0 (7.0)	20.6 (9.0)	21.5 (10.4)

SSRI, selective serotonin reuptake inhibitor use at study entry; GAD, generalized anxiety disorder; ADHD, attention deficit hyperactivity disorder.
[a]$\chi^2 = 12.8$, $p = 0.002$; 2 < 3, $\chi^2 = 0.0$, $p = 0.005$; 1 < 3, $\chi^2 = 12.2$, $p = 0.000$.
[b]$\chi^2 = 29.9$, $p = 0.000$; 1 < 2, $\chi^2 = 28.6$, $p = 0.000$; 1 < 3, $\chi^2 = 13.0$, $p = 0.000$.
[c]$\chi^2 = 11.7$, $p = 0.003$; 1 < 2, $\chi^2 = 8.6$, $p = 0.004$.
[d]$\chi^2 = 13.6$, $p = 0.001$; 1 < 2, $\chi^2 = 5.6$, $p = 0.014$; 1 < 3, $\chi^2 = 13.0$, $p = 0.000$.
[e]$F = 30.4$, $p = 0.000$; Bonferroni: 1 < 2, $p = 0.000$; 1 < 3, $p = 0.000$.
[f]$F = 9.1$, $p = 0.000$; Bonferroni: 1 < 2, $p = 0.001$; 1 < 3, $p = 0.001$.
[g]$F = 31.0$, $p = 0.000$; Bonferroni: 1 < 2, $p = 0.000$; 1 < 3, $p = 0.000$.

Table 2. Measures of temperament and childhood adversity for the participants divided into three trajectory groups, mean (s.d.)

MPQ Temperament	Low	Remitting	Persistent
Scores, *n*	55	56	51
Positive emotionality[a]	74.8 (13.9)	72.4 (12.7)	64.7 (14.4)
Negative emotionality[b]	34.4 (15.0)	40.9 (14.5)	44.0 (17.0)
Constraint	71.8 (13.8)	72.9 (13.2)	74.9 (14.6)
ETISR scores, *n*	55	62	54
General	1.9 (1.6)	2.0 (1.9)	2.4 (2.1)
Physical[c]	0.6 (0.6)	1.2 (1.5)	1.4 (1.4)
Emotional[d]	0.9 (1.3)	1.2 (1.5)	1.6 (1.6)
Sexual	0.3 (1.0)	0.4 (1.0)	0.4 (1.1)
Total[e]	3.7 (3.6)	4.8 (3.8)	5.9 (4.4)

MPQ, Multidimensional personality questionnaire from the first follow-up visit; ETISR, early trauma inventory – self-report from the baseline visit.
[a]$F = 7.9$, $p = 0.001$; Bonferroni: 1 < 3, $p = 0.001$; 2 < 3, $p = 0.012$.
[b]$F = 5.3$, $p = 0.006$; Bonferroni: 1 < 3, $p = 0.005$.
[c]$F = 4.0$, $p = 0.019$; Bonferroni: 1 < 3, $p = 0.021$.
[d]$F = 3.4$, $p = 0.037$; Bonferroni: 1 < 3, $p = 0.032$.
[e]$F = 4.1$, $p = 0.019$; Bonferroni: 1 < 3, $p = 0.015$.

were also examined using ANOVA models. Stepwise statistical comparisons across the three trajectory groups were followed by those pairwise comparisons that reached significance (Tables 1 and 2). A non-significant ($p = 0.133$) test of parallel lines justified the use of ordinal logistic regression model to assess the relationship of the GTBM groups with multiple predictors (sex, total ETISR, negative emotionality, and GAD) and all possible 2-way interaction effects.

Results

The sample of participants with past or present evidence of a depressive disorder ($n = 186$) is described in Table 1. Of these, 126 (67.7%) completed the full 2 years of follow-up. None of the variables listed in Table 1 differed significantly between those who did and those who did not complete the 2 years though a trend emerged for higher baseline IDS scores among non-completers: mean (s.d.) values for completers and non-completers were 16.6 (10.6) and 19.8 (9.4), respectively ($p = 0.052$).

A three-group trajectory model with a cubic function of time was chosen as the final model. Although this model did not have the lowest AIC value (three-group quadratic AIC = 28 388, three-group cubic AIC = 28 349; four-group quadratic AIC = 27 667, four-group cubic AIC = 27 585), it did have three distinct patterns of depressive symptoms over time (Fig. 1). The four-group model had two very similar patterns of remission, suggesting redundancy in the four-group solution. For the three-group model, symptom levels in the first group began at a relatively low level and declined somewhat over time. The second group began at high symptom levels but then decreased markedly such that the depression ratings resembled those of the first group by the end of follow-up. This pattern is consistent with a remitting depressive episode. The last group began at a high symptom level and showed a minimal decline over time, suggestive of a chronic, persistent course. Accordingly, we assigned the descriptors of 'Low,' 'Remitting,' and 'Persistent' to the three groups. The average probability of membership was >0.99 in each group.

The proportion of females and of individuals with generalized anxiety disorder (GAD) increased in a stepwise fashion across the groups with increasing morbidity (Table 1). Negative emotionality, the three symptom severity measures, and each of the ETISR childhood adversity scores showed equivalent stepwise increases across the three groups (Table 2). Positive emotionality decreased progressively across the groups while constraint did not vary significantly.

To simplify subsequent analyses, we selected the total ETISR score to represent childhood adversity and focused on negative emotionality from among the three measures of temperament. The two anxiety measures, the Beck Anxiety Inventory (BAI) score and the presence or absence of a GAD diagnosis, were both significantly associated with trajectory grouping in a logistic regression analysis but the association with GAD (OR 3.39, $\chi^2 = 14.2$, $p = 0.000$) was more robust than the BAI score (OR 1.05, $\chi^2 = 7.9$, $p = 0.005$). The presence of GAD was therefore used to represent anxiety morbidity in subsequent analyses.

The total ETISR score was significantly correlated with negative emotionality (Pearson's $r = 0.36$, $p = 0.000$). The introduction of negative emotionality to the logistic regression reduced the OR for

https://doi.org/10.1017/S0033291719002551 Published online by Cambridge University Press

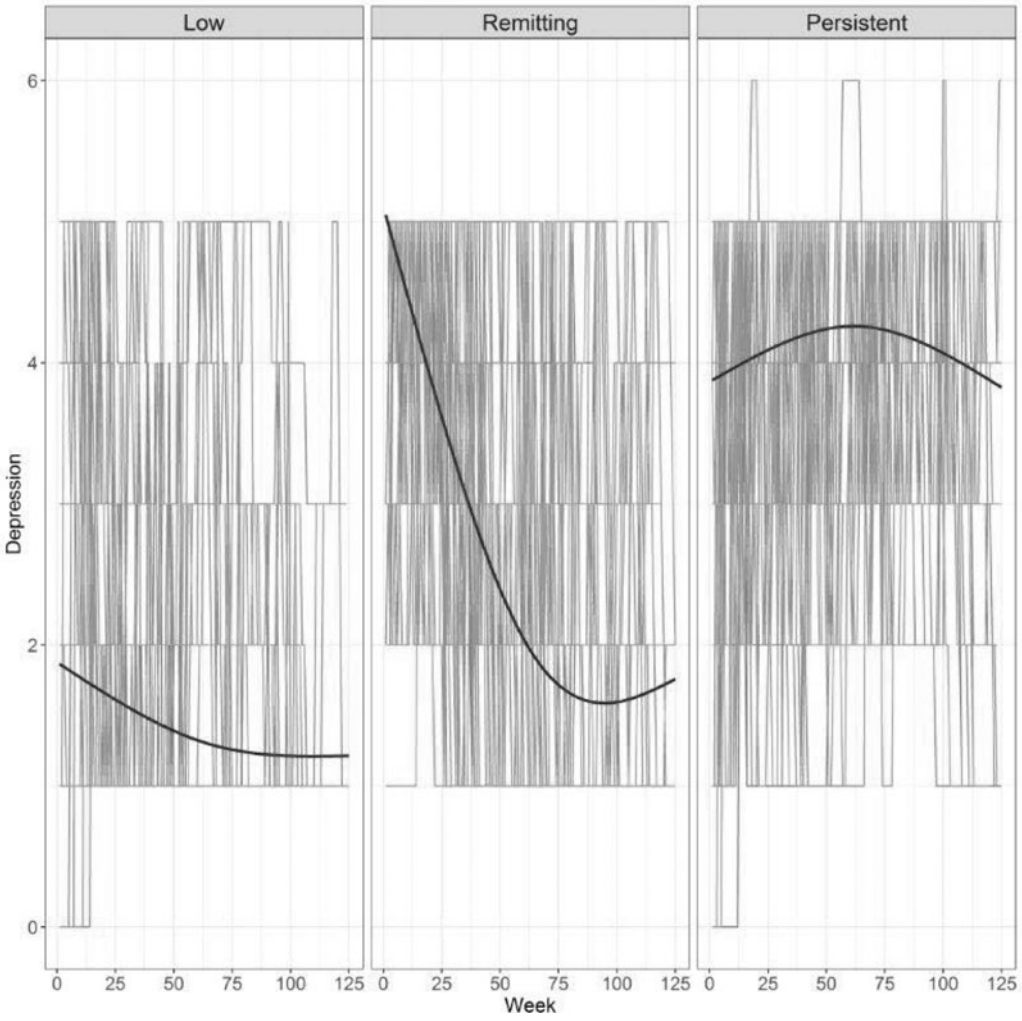

Fig. 1. Two-year depressive symptom trajectories.

ETISR from 1.11 (χ^2 = 6.8, p = 0.009) to 1.03 (χ^2 = 3.8, p = 0.052) and negative emotionality remained significantly predictive (OR 1.03, χ^2 = 6.0, p = 0.015). In contrast, the ETISR score did not differ between individuals with and without GAD. The introduction of GAD to the model had little effect on the relationship of ETISR scores to trajectory grouping (OR 1.11, χ^2 = 6.6, p = 0.010) and GAD status remained highly predictive (OR 3.65, χ^2 = 15.6, p = 0.000).

Females and males had mean (S.D.) negative emotionality scores of 37.0 (16.6) and 35.2 (16.9) (p = 0.316, Mann–Whitney U) and inclusion of negative emotionality in the logistic model had little effect on the relationship of sex to trajectory. Values for sex were OR 2.38 (χ^2 = 7.0, p = 0.008) and for negative emotionality were OR 1.03 (χ^2 = 7.7, p = 0.005). Similarly, the ETISR score did not differ by sex (p = 0.410) and both sex (OR 2.68, χ^2 = 9.0, p = 0.003) and ETISR score (OR 1.12, χ^2 = 7.6, p = 0.006) were significantly associated with trajectory grouping when tested together.

GAD was more prevalent among females (47/132 or 35.6%) than among males (17/89, 19.1%) (χ^2 = 7.0, df = 1, p = 0.006). Both GAD and sex were nevertheless significantly related to trajectory when tested together. Values for sex were OR 2.25 (χ^2 = 0.6 p = 0.014) and for GAD were OR 3.30 (χ^2 = 13.7, p = 0.000).

Table 3. Risk factors for trajectory group membership: ordinal logistic regression

	OR (95% CI)	χ^2	p
Sex	2.23 (1.1–4.4)	5.5	0.019
Negative emotionality	1.03 (1.01–1.05)	6.6	0.010
Total ETISR score	1.09 (1.00–1.18)	4.1	0.044
GAD	3.65 (1.9–7.02)	15.2	0.000

When included together in the logistic regression model, each of these four variables was significantly related to trajectory groupings (Table 3). The presence of a GAD diagnosis was by far the variable most robustly associated with higher morbidity. Of the six possible interaction effects between these four variables only the sex by negative emotionality interaction effect was significant (χ^2 = 5.8, p = 0.016). Further exploration revealed that the relationship between negative emotionality and trajectory grouping existed for females but not for males.

Specifically, for females, mean (S.D.) negative emotionality scores were 31.5 (15.4), 42.6 (16.1) and 44.9 (15.9) across the three trajectory groups (F = 6.9, p = 0.002). In contrast, for

https://doi.org/10.1017/S0033291719002551 Published online by Cambridge University Press

males, the corresponding mean (S.D.) values were 37.8 (15.4), 38.0 (11.2) and 38.5 (23.5), respectively ($F = 1.3$, $p = 0.994$).

Discussion

This analysis applied group-based trajectory modeling to 2 years of weekly depressive symptom ratings collected from individuals in late adolescence who had lifetime histories of major depressive episodes. A three-group model offered the best statistical fit to the diverse temporal fluctuations seen across individuals and conformed to labels of 'low,' 'remitting,' and 'persistent'. The results thus resemble the three groups described by Shore *et al.* (2018) from their meta-analysis of trajectory studies as 'low,' 'moderate,' and 'high or worsening'.

Though the results of trajectory analyses are likely to vary by the sampling methods used to identify the individuals being studied, the similarities in the number, in the qualities of the resulting groups, and in the robustness with which sex was associated with increasing depressive morbidity provides some indication that these results are generalizable.

The analysis sought to quantify the prognostic import of four risk factors that were selected a priori and to test the extent to which each was independently related to trajectory group membership. The proportions of females and of individuals with GAD increased in step-wise fashion across 'low,' 'remitting,' and 'persistent' trajectory groups. Mean scores for childhood adversity (ETISR) and for negative emotionality likewise increased across these three groups. ETISR and negative emotionality were positively correlated and the latter appeared to be the more important predictor of poorer outcomes. Otherwise, female sex, negative emotionality, and the presence of GAD were each independently associated with trajectory groupings of increasing morbidity.

The most consistent finding among studies of depressive symptom trajectories is the association of female sex with higher levels of morbidity (Shore *et al.*, 2018). The present results are in full accord with the predicted pattern in showing a progressively higher percent of women across the three groups. The likelihood of GAD comorbidity also increased across trajectory groups in order of increasing depressive symptom morbidity (Brown *et al.*, 1998). Though a trend emerged for higher rates of GAD among females this did not account for the higher morbidity they experienced. Nor did the three other risk factors tested appear to account for the higher levels of morbidity among females. A novel finding in this report is that the presence of GAD was a stronger predictor of high morbidity group membership than was female sex while controlling for negative emotionality and childhood adversity.

Twin studies show that genetic diatheses for GAD and MDD overlap substantially (Kendler *et al.*, 1992) and this may account for the observation that GAD is the most likely of the DSM disorders to co-exist, either sequentially or concurrently, with MDD (Moffitt *et al.*, 2007). Both GAD and MDD are associated with disability but the disability is substantially higher when the two disorders occur together (Kessler *et al.*, 2002). The importance of GAD to the persistence of MDD symptoms over time helps to explain observations that the prognosis of mood disorders worsens progressively with increasing levels of anxiety symptoms, whatever the quality of those symptoms (Coryell *et al.*, 2009, 2012). However, most earlier studies of the prognostic importance of anxiety to mood disorder outcome used either an anxiety diagnosis or a measure of those anxiety symptoms present at the time of interview. They did not test whether diagnosis or a cross-sectional measure was more important for prognosis. The findings described here suggest that the diagnosis of GAD is the stronger predictor of morbidity, perhaps because it requires a persistence of symptoms of at least 6 months.

Of six possible interaction effects between the four risk factors tested in this analysis, only the one between sex and NE was significant. This personality measure was robustly associated with trajectories of higher symptom morbidity in women but had little relation to these groupings in men. These results are consistent with findings from a large twin study in which neuroticism was over 30% more potent as a risk factor for the development of MDD in women than it was in men (Kendler and Gardner, 2014). Also in support of these results are those of a large-community-based study in which the inclusion of neuroticism in a regression model substantially reduced the relationship between female sex and the diagnosis of major depression (Goodwin and Gotlib, 2004).

An earlier publication from this cohort assessed the relationships between mean symptom levels over the first year of follow-up and baseline measures of erythrocyte concentrations of eicosapentaenoic acid (EPA), an omega-3 essential fatty acid, negative emotionality, and childhood adversity (Coryell *et al.*, 2017).

Both EPA concentrations and ETISR emotional adversity scores were independently predictive of morbidity during follow-up but both exerted these effects largely through their influence on NE. In the current analysis, both ETISR scores and NE were again predictive of depressive morbidity, this time expressed as depressive symptom trajectories assumed over a 2-year prospective follow-up. With this new measure of depressive chronicity, however, NE and childhood adversity, though significantly correlated with each other, were independently related to trajectory groupings that reflected higher symptom levels.

Weaknesses attached to these analyses include the fact that they were secondary in nature. Participants were recruited to examine the effects of recently initiated SSRI treatment on bone density in a late adolescent population. The study was not powered by design to test the hypothesis addressed here. In particular, additional interactions between risk factors for high morbidity trajectories might have manifested had the sample been larger. The age range of the participants was also quite limited and the sample was heavily skewed toward college students, a reflection of the study's setting. This, in turn, limited the range of socioeconomic status and, possibly, childhood adversity. Findings may not generalize well to other sociodemographic groups. The follow-up length was also relatively short and in that the large majority of the studies listed in the Shore *et al.* (2018) were longer. A longer follow-up may have captured morbidity patterns more typical of individuals' lifetime illness.

Among the study's strengths is the breadth of baseline assessments. These extended well beyond that was necessary to test the original hypotheses. The surveillance intensity of the prospective follow-up comprised another strength. Few follow-up studies have employed thrice-yearly, in-person visits supplemented with intervening telephone assessments of the disorder considered primary at intake. Finally, this analysis went beyond the simple identification of risk factors for poorer outcomes to focus on the degree to which prognostically important factors operated independently or through their associations with other predictors and on whether interactions existed between them. The finding that anxiety co-morbidity, in the form of a GAD diagnosis was the most robust of the prognostic factors identified and this underscores the importance of further efforts to identify the genetic and phy substrates of co-existing anxiety and depressive symptomatology.

https://doi.org/10.1017/S0033291719002551 Published online by Cambridge University Press

Similarly, the observation that negative emotionality was of prognostic importance only in women has some support in the literature but needs replication before it is widely accepted.

Acknowledgements. This research received support from the National Center for Advancing Translational Sciences (2UL1TR000442-06) and the National Institute of Mental Health (R01MH090072).

Conflict of interest. None.

References

Akaike H (1974) A new look at the statistical model identification. *IEEE Transactions on Automatic Control* **19**, 716–723.

Barnhofer T, Brennan K, Crane C, Duggan D and Williams JMG (2014) A comparison of vulnerability factors in patients with persistent and remitting lifetime symptom course of depression. *Journal of Affective Disorders* **152**, 155–161.

Bremner JD, Bolus R and Mayer EA (2007) Psychometric properties of the early trauma inventory–self report. *The Journal of Nervous and Mental Disease* **195**, 211.

Brown TA, Chorpita BF and Barlow DH (1998) Structural relationships among dimensions of the DSM-IV anxiety and mood disorders and dimensions of negative affect, positive affect, and autonomic arousal. *Journal of Abnormal Psychology* **107**, 179.

Calarge CA, Butcher BD, Burns TL, Coryell WH, Schlechte JA and Zemel BS (2014) Major depressive disorder and bone mass in adolescents and young adults. *Journal of Bone and Mineral Research* **29**, 2230–2237.

Calarge CA, Mills JA, Janz KF, Burns TL, Schlechte JA, Coryell WH and Zemel BS (2017) The effect of depression, generalized anxiety, and selective serotonin reuptake inhibitors on change in bone metabolism in adolescents and emerging adults. *Journal of Bone and Mineral Research* **32**, 2367–2374.

Church AT (1994) Relating the Tellegen and five-factor models of personality structure. *Journal of Personality and Social Psychology* **67**, 898.

Coryell W, Solomon DA, Fiedorowicz JG, Endicott J, Schettler PJ and Judd LL (2009) Anxiety and outcome in bipolar disorder. *American Journal of Psychiatry* **166**, 1238–1243.

Coryell W, Fiedorowicz JG, Solomon D, Leon AC, Rice JP and Keller MB (2012) Effects of anxiety on the long-term course of depressive disorders. *The British Journal of Psychiatry* **200**, 210–215.

Coryell WH, Langbehn DR, Norris AW, Yao J-R, Dindo LN and Calarge CA (2017) Polyunsaturated fatty acid composition and childhood adversity: independent correlates of depressive symptom persistence. *Psychiatry Research* **256**, 305–311.

Goodwin RD and Gotlib IH (2004) Gender differences in depression: the role of personality factors. *Psychiatry Research* **126**, 135–142.

Hengartner MP, Cohen LJ, Rodgers S, Müller M, Roessler W and Ajdacic-Gross V (2015) Association between childhood maltreatment and normal adult personality traits: exploration of an understudied field. *Journal of Personality Disorders* **29**, 1–14.

Jones BL, Nagin DS and Roeder K (2001) A SAS procedure based on mixture models for estimating developmental trajectories. *Sociological Methods & Research* **29**, 374–393.

Keller MB, Lavori PW, Friedman B, Nielsen E, Endicott J, Mcdonald-Scott P and Andreasen NC (1987) The longitudinal interval follow-up evaluation: a comprehensive method for assessing outcome in prospective longitudinal studies. *Archives of General Psychiatry* **44**, 540–548.

Kendler KS and Gardner CO (2014) Sex differences in the pathways to major depression: a study of opposite-sex twin pairs. *American Journal of Psychiatry* **171**, 426–435.

Kendler KS, Neale MC, Kessler RC, Heath AC and Eaves LJ (1992) Major depression and generalized anxiety disorder: same genes, (partly) different environments? *Archives of General Psychiatry* **49**, 716–722.

Kessler RC, Berglund PA, Dewit DJ, Bedirhan Üstün T, Wang PS and Wittchen HU (2002) Distinguishing generalized anxiety disorder from major depression: prevalence and impairment from current pure and comorbid disorders in the US and Ontario. *International Journal of Methods in Psychiatric Research* **11**, 99–111.

Kessler RC, Berglund P, Demler O, Jin R, Koretz D, Merikangas KR, Rush AJ, Walters EE and Wang PS (2003) The epidemiology of major depressive disorder: results from the national comorbidity survey replication (NCS-R). *JAMA* **289**, 3095–3105.

Li M, D'arcy C and Meng X (2016) Maltreatment in childhood substantially increases the risk of adult depression and anxiety in prospective cohort studies: systematic review, meta-analysis, and proportional attributable fractions. *Psychological Medicine* **46**, 717–730.

McCrae RR and Costa PT (1987) Validation of the five-factor model of personality across instruments and observers. *Journal of Personality and Social Psychology* **52**, 81.

Moffitt TE, Caspi A, Harrington H, Milne BJ, Melchior M, Goldberg D and Poulton R (2007) Generalized anxiety disorder and depression: childhood risk factors in a birth cohort followed to age 32. *Psychological Medicine* **37**, 441–452.

Nagin DS and Odgers CL (2010) Group-based trajectory modeling in clinical research. *Annual Review of Clinical Psychology* **6**, 109–138.

Nelson J, Klumparendt A, Doebler P and Ehring T (2017) Childhood maltreatment and characteristics of adult depression: meta-analysis. *The British Journal of Psychiatry* **210**, 96–104.

Newman MG, Llera SJ, Erickson TM, Przeworski A and Castonguay LG (2013) Worry and generalized anxiety disorder: a review and theoretical synthesis of evidence on nature, etiology, mechanisms, and treatment. *Annual Review of Clinical Psychology* **9**, 275–297.

Patrick CJ, Curtin JJ and Tellegen A (2002) Development and validation of a brief form of the multidimensional personality questionnaire. *Psychological Assessment* **14**, 150.

Shaffer D, Fisher P, Lucas CP, Dulcan MK and Schwab-Stone ME (2000) NIMH diagnostic interview schedule for children version IV (NIMH DISC-IV): description, differences from previous versions, and reliability of some common diagnoses. *Journal of the American Academy of Child & Adolescent Psychiatry* **39**, 28–38.

Shore L, Toumbourou JW, Lewis AJ and Kremer P (2018) Longitudinal trajectories of child and adolescent depressive symptoms and their predictors – a systematic review and meta-analysis. *Child and Adolescent Mental Health* **23**, 107–120.

Üstün TB, Ayuso-Mateos JL, Chatterji S, Mathers C and Murray CJ (2004) Global burden of depressive disorders in the year 2000. *The British Journal of Psychiatry* **184**, 386–392.

https://doi.org/10.1017/S0033291719002551 Published online by Cambridge University Press