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RESEARCH ARTICLE

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Prior histories of posttraumatic stress disorder and major depression and their onset and course in the three months after a motor vehicle collision in the AURORA study

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Abstract

Background: A better understanding of the extent to which prior occurrences of posttraumatic stress disorder (PTSD) and major depressive episode (MDE) predict psychopathological reactions to subsequent traumas might be useful in targeting posttraumatic preventive interventions.

Methods: Data come from 1306 patients presenting to 29 U.S. emergency departments (EDs) after a motor vehicle collision (MVC) in the advancing understanding of recovery after trauma study. Patients completed self-reports in the ED and 2-weeks, 8-weeks, and 3-months post-MVC. Associations of pre-MVC probable

PTSD and probable MDE histories with subsequent 3-months post-MVC probable PTSD and probable MDE were examined along with mediation through intervening peritraumatic, 2-, and 8-week disorders.

Results: 27.6% of patients had 3-month post-MVC probable PTSD and/or MDE. Pre-MVC lifetime histories of these disorders were not only significant (relative risk = 2.6–7.4) but were dominant (63.1% population attributable risk proportion [PARP]) predictors of this 3-month outcome, with 46.6% prevalence of the outcome among patients with pre-MVC disorder histories versus 9.9% among those without such histories. The associations of pre-MVC lifetime disorders with the 3-month outcome were mediated largely by 2- and 8-week probable PTSD and MDE (PARP decreasing to 22.8% with controls for these intervening disorders). Decomposition showed that pre-MVC lifetime histories predicted both onset and persistence of these intervening disorders as well as the higher conditional prevalence of the 3-month outcome in the presence of these intervening disorders.

Conclusions: Assessments of pre-MVC PTSD and MDE histories and follow-ups at 2 and 8 weeks could help target early interventions for psychopathological reactions to MVCs.

KEYWORDS

major depression, motor vehicle collision, posttraumatic stress disorder, trauma

1 | INTRODUCTION

Although it is known that prior history of posttraumatic stress disorder (PTSD; Beliveau et al., 2019; Breslau et al., 2008; Kessler et al., 2018) and major depressive episode (MDE; Bedaso et al., 2020; Heron-Delaney et al., 2013) both strongly predict adjustment after subsequent traumas (Ikin et al., 2010; Pozzato et al., 2020) and are highly comorbid (Kenardy et al., 2018), a better understanding of these associations is needed to inform early intervention targeting. Are these histories important because they are associated with peritraumatic symptoms that can be assessed in the immediate aftermath of a subsequent trauma? Or are they also (or instead) associated with PTSD and MDE present several weeks later, persistence of these disorders, and/or delayed onset of these disorders several months later? The current report presents initial data on these questions from the Advancing Understanding of RecOvery afteR traumA (AURORA) study, a longitudinal study of posttraumatic psychopathology among patients presenting to an emergency department (ED) in the immediate aftermath of a traumatic experience (McLean et al., 2020). We focus on motor vehicle collision (MVC), as most AURORA patients presented with MVCs and the number of patients with other individual traumas is currently too small for comparative analysis. Previous AURORA reports examined PTSD and MDE separately in a smaller MVC sample (Joormann et al., 2020; Kessler et al., 2020), documenting that history of PTSD predicts post-MVC PTSD, and history of MDE predicts post-MVC MDE. The sample in these reports was too small, though, to consider joint histories of PTSD-MDE as we do in the current report.

2 | MATERIALS AND METHODS

2.1 | Sample

AURORA enrollment began in September 2017. Patients had to be age 18–75, to present at one of 29 urban U.S. EDs within 72 h of trauma, to speak and read English, to be oriented to time-space, physically able to use a smartphone, and possess a smartphone for >1 year. We excluded patients with a solid organ injury Grade >1, significant hemorrhage, or need for a chest tube or operation with general anesthesia. For the current report, we also required completion of a 3-month assessment before March 30, 2020 (Figure S1). We initially excluded patients likely to be admitted but subsequently included those admitted for no more than 24 h (as of April 4, 2018) and then no more than 72 h (as of December 11, 2018).

After providing written informed consent, patients received an interviewer-administered assessment, self-report questionnaire, and biological sample collections in the ED (McLean et al., 2020). Subsequent 2-week, 8-week, and 3-month surveys were sent by text or e-mail for self-completion or telephone interview. Patients were reimbursed $60 for the ED assessment and $40 for each follow-up. These procedures were approved by each participating institutional review board. A total of 1306 patients met all criteria, provided informed consent, and completed both the baseline ED assessment and the 3-month follow-up. We retained the subset of these patients who failed to complete either the 2-week (n = 55), 8-week (n = 72), or

both ($n = 22$) surveys, imputing these missing values and using appropriate analysis methods described below to deal with these imputations.

2.2 | Measures

2.2.1 | Sociodemographics

ED interviews assessed patient age, gender, race–ethnicity, marital status, education, family income, and employment status.

2.2.2 | MVC characteristics

Patient self-reported MVC characteristics included: role in the MVC (driver alone, driver with passengers, and passenger); collision with moving vehicle versus stationary object; the amount of vehicle damage, mode of transport to the ED (ambulance, other direct, and non-direct), number of other passengers injured in a vehicle, anyone injured outside the vehicle, whether the patient hit their head or suffered a concussion (defined by self-reported loss of consciousness, amnesia, or disorientation (McLean et al., 2009), the severity of injury (abbreviated injury scale; Loftis et al., 2018), and admission versus discharge from the ED. We also obtained patient self-ratings on a 0–10 visual response scale of global pain and 20 other somatic symptoms currently and in the prior 30 days (Farrar et al., 2001). The 20-item scale was adapted from prior scales (King et al., 1995; Pennebaker & Watson, 1991; Cronbach's $\alpha = .85$). A difference score was calculated for this scale and standardized to a within-sample mean/variance of 0/1.

2.2.3 | Peritraumatic distress and dissociation

Peritraumatic distress and dissociation were assessed in the ED with eight items from the peritraumatic distress inventory (Brunet et al., 2001) and the five-item revised Michigan critical events perception scale (Michaels et al., 1999), both standardized to mean/variance 0/1 (Cronbach's $\alpha = .80–.77$).

2.2.4 | Probable PTSD

The PTSD checklist for the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5) (PCL-5; Michaels et al., 1999) was administered in the ED for the 30 days before the trauma, at 2 weeks for the 2 weeks since the trauma and at 8 weeks and 3 months for the prior 30 days (Cronbach's $\alpha = .96$). A conservative 38+ threshold (Zuromski et al., 2019) was used to define probable threshold PTSD and 31–37 to define probable subthreshold PTSD (Bovin et al., 2016; Zuromski et al., 2019). Lifetime PTSD before the MVC was assessed in the 8-week survey with the PCL-5 (PTSD checklist for DSM-5) using the same thresholds. The lifetime assessment asked about the worst month of symptoms because of "any highly stressful experience that ever happened to you," whereas the post-MVS assessments asked about symptoms "either because of the event that brought you into the ED or any other highly stressful experience that ever happened to you."

2.2.5 | Probable MDE

Depression in the prior 30 days was assessed in the ED, 8-week, and 3-month surveys using the patient-reported outcomes measurement information system (PROMIS) depression short-form 8b (Cella et al., 2010; Cronbach's $\alpha = .95$). Scores were converted to a T-score based on PROMIS norms (PROMIS Cooperative Group, 2021). The same scale with a 2-week recall period was used in the 2-week survey. On the basis of the conservative assumption of a 5% MDE point prevalence in the general population (Brody et al., 2018), the PROMIS scale diagnostic threshold was set at 1.5 standard deviations above the general population mean to define probable threshold MDE and in the range, 1–1.5 standard deviations above the general population mean to define probable subthreshold MDE. The self-report version of the composite international diagnostic interview (Kessler & Ustün, 2004) was used in the 8-week survey to assess pre-MVC probable lifetime DSM-5 MDE.

2.2.6 | Role impairment

Although not used as an outcome, we examined associations between a modified version of the Sheehan disability scale (Leon et al., 1997) administered at 3-months with the 3-month prevalence of probable PTSD and MDE. This was done to examine the comparative severity of PTSD-alone, MDE-alone, and comorbid PTSD-MDE for purposes of determining which of these to include in our composite dependent variable.

2.3 | Analysis methods

We used multiple imputations (MIs) implemented with SAS PROC MI (SAS Institute Inc., 2017) in 30 MI replicate samples to correct for missing 2-week and/or 8-week surveys. Standard MI procedures were used to calculate standard errors (Rubin, 1987). Modified Poisson regression (Knol et al., 2012) was used to estimate associations, relative-risk (RR), and 95% confidence intervals of sociodemographic variables and MVC characteristics with a dichotomous outcome coded 1 for patients with 3-month post-MVC probable PTSD and/or MDE and 0 otherwise. We then sequentially added additional predictors, including pre-MVC histories of these disorders, peritraumatic symptoms assessed in the ED, 2-week disorders, and 8-week disorders. Analyses were carried out initially without taking into consideration clustering

across the 29 EDs and then replicated to focus on pooled within-ED associations.

Given the exploratory nature of the investigation and a large number of coefficients, we used a false discovery rate (FDR) correction to protect against false positives (Benjamini & Yekutieli, 2001). We indirectly assessed mediating effects by calculating population attributable risk proportions (PARPs) of the 3-month outcome associated with pre-MVC histories of either probable PTSD or MDE both with and without controls for mediators. PARP can be interpreted as the proportion of outcome cases associated with one or more risk factors as determined by calculating estimated values of the outcome in a prediction model in which the risk factors are all assumed to be absent (Bieler et al., 2010). We also examined interactions of pre-MVC histories of probable PTSD and/or MDE with 2-week and 8-week disorders in predicting the 3-month outcome. Statistical significance was consistently evaluated using .05-level two-sided MI-adjusted tests. Computer code is available from the senior author on request.

3 | RESULTS

3.1 | Effects of MI

Comparison of MI means with observed means in subsamples having valid data showed that MI estimates are consistent with observed data (Table S1).

3.2 | Associations of 3-month probable PTSD and MDE with role impairment

Prevalence of 3-months post-MVC probable disorders was 26.0% PTSD, 12.3% MDE, 27.6% either, 15.5% PTSD-alone, 1.6% MDE-alone, and 10.6% comorbid PTSD-MDE (Table 1). Even though MDE-alone was rare, mean days out of role was significantly higher among patients with MDE-alone than PTSD-alone (8.9 vs. 4.0 days, $F_1 = 9.6$, $p = .001$) and a higher proportion of patients with 3-month MDE-alone than PTSD-alone had severe role impairment (38.1% vs. 24.3%, $F_1 = 1.9$, $p = .172$; Table S2). These results led us to retain 3-month probable MDE-alone in the outcome, which we defined as 3-month probable PTSD and/or MDE. However, as predictors of MDE-alone might be different from those of PTSD, we also carried out final model sensitivity analyses to distinguish the predictors of 3-month probable PTSD versus 3-month probable MDE.

TABLE 1 Prevalence of 3-month probable PTSD, MDE, and their comorbidity ($n = 1306$)[a]

	%	SE
Either PTSD or MDE	27.6	(1.2)
PTSD (with or without MDE)	26.0	(1.2)
MDE (with or without PTSD)	12.3	(0.9)
Both PTSD and MDE	10.6	(0.8)
PTSD-alone[b]	15.5	(1.0)
MDE-alone[b]	1.6	(0.3)

Abbreviations: MDE, major depressive episode; PTSD, posttraumatic stress disorder; SE, standard error.

[a]To reduce redundancy, each survey-based assessment of probable PTSD and MDE is referred to in the table and subsequent footnotes as "PTSD" and "MDE."

[b]PTSD-alone indicates a diagnosis of PTSD and no diagnosis of MDE, MDE-alone indicates a diagnosis of MDE and no diagnosis of PTSD.

3.3 | Pre-MVC histories of probable PTSD and MDE predicting the 3-month outcome

No sociodemographic variables significantly predicted 3-month probable PTSD and/or MDE (Table S3), but three MVC characteristics were significant: vehicle damage, concussion, and severe pain (univariable RRs = 1.4–1.7; Table 2). All three remained significant in multivariable analysis (Model 1; RR = 1.4–1.8). Controlling these MVC characteristics, pre-MVC probable PTSD and MDE were also significant predictors of the 3-month outcome (Model 2; RR = 1.4–3.6) when we distinguished between probable PTSD and MDE present in the 30-days before the MVC (20.5% and 6.2% of patients, respectively) and lifetime disorders not present in the 30-days before the MVC (23.3% and 18.4% of patients, respectively). Joint associations among these predictors were significantly nonadditive ($F_4 = 5.7$, $p = .033$). The highest unadjusted nonadditive RR was pre-MVC lifetime comorbid probable PTSD and MDE with at least one of these two disorders present in the 30-days before the MVC (RR = 7.4). Less pronounced, but still statistically significant, RRs were found for lifetime history of both disorders without either in the past 30-days (RR = 4.5), lifetime probable PTSD-alone with or without 30-day prevalence (RR = 4.1), and lifetime probable MDE-alone with or without 30-day prevalence (RR = 2.6). These RRs were slightly attenuated when controlling for MVC characteristics (Model 3), but combined PARP (SE) for all pre-MVC disorder variables controlling MVC characteristics was still 63.1% (3.3). This means 3-month outcome prevalence would be reduced by 63.1% if we could block the causal forces linking pre-MVC PTSD-MDE to the outcome. Results were unchanged when we examined pooled within-ED associations (Table S4, Model 2), whereas between-ED variation in the outcome was nonsignificant ($F_{28} = 0.6$, $p = .98$) and when 3-month probable PTSD was the outcome (Table S4, Model 3).

3.4 | Peritraumatic symptoms and 2-week disorders predicting the 3-month outcome

We next examined mediation through peritraumatic symptoms assessed in the ED and 2-week disorders (Table 3). Although both peritraumatic distress (RR = 1.3) and peritraumatic dissociation (RR = 1.6) were significant predictors of the 3-month outcome in univariable models, both

TABLE 2 Associations of MVC characteristics and pre-MVC lifetime histories of probable PTSD and MDE with 3-month probable PTSD and/or MDE (n = 1306)[a]

			Univariable models		Model 1[b]		Model 2[c]		Model 3[d,e]	
	%	SE	RR	(95% CI)	RR	(95% CI)	RR	(95% CI)	RR	(95% CI)
I. MVC characteristics[f]										
Any vehicle damage	93.5	(0.7)	1.7*	(1.1–2.8)	1.8*	(1.1–3.1)	1.4	(0.8–2.4)	1.4	(0.8–2.4)
Concussion	27.0	(1.2)	1.4*	(1.2–1.7)	1.4*	(1.1–1.7)	1.2	(1.0–1.5)	1.2	(0.9–1.5)
Severe pain reported in the ED[g]	41.0	(1.4)	1.7*	(1.4–2.1)	1.7*	(1.3–2.0)	1.4*	(1.1–1.8)	1.4*	(1.2–1.8)
F_3			–		12.8*		5.0*		5.1*	
II. Pre-MVC history of PTSD and/or MDE										
A. Pre-MVC history of PTSD										
30-day	20.5	(1.1)	4.9*	(3.7–6.5)	–	–	3.6*	(2.7–4.8)	–	–
Lifetime but not 30-day	23.3	(1.2)	3.8*	(2.9–5.1)	–	–	3.2*	(2.3–4.4)	–	–
F_2			68.7*		–	–	38.9*		–	–
B. Pre-MVC history of MDE										
30-day	6.2	(0.7)	3.7*	(2.7–4.9)	–	–	1.9*	(1.4–2.6)	–	–
Lifetime but not 30-day	18.4	(0.2)	2.3*	(1.8–2.9)	–	–	1.4*	(1.1–1.8)	–	–
F_2			47.7*		–		8.9*		–	
F_4			–		–		35.4*		–	
C. Joint pre-MVC histories of PTSD and MDE										
Both lifetime and ≥1 30-day	9.5	(0.8)	7.4*	(5.3–10.2)	–	–	–	–	6.6*	(4.8–9.2)
Both lifetime and neither 30-day	10.4	(0.8)	4.5*	(3.1–6.5)	–	–	–	–	4.4*	(3.1–6.3)
PTSD-alone: lifetime (with or without 30-day)[h]	23.7	(0.9)	4.1*	(3.0–5.6)	–	–	–	–	3.8*	(2.8–5.2)
MDE-alone: lifetime (with or without 30-day)[h]	4.7	(1.0)	2.6*	(1.4–4.6)	–	–	–	–	2.5*	(1.4–4.5)
F_4			38.9*		–		–		34.3*	
Total model $F_{3,7,7}$			–		12.8*		25.4*		24.7*	

Note: Estimates reflect multiply-imputed data (30 imputations).

Abbreviations: CI, confidence interval; ED, emergency department; MDE, major depressive episode; MVC, motor vehicle collision; PTSD, posttraumatic stress disorder; RR, relative risk.

[a]To reduce redundancy, each survey-based assessment of probable PTSD and MDE is referred to in the table and subsequent footnotes as "PTSD" and "MDE." Based on modified Poisson regression models with robust variance estimates.

[b]An interaction term for the joint occurrence of two or more MVC characteristics was nonsignificant (F_1 = 0.1, p = .73).

[c]Interactions between the two PTSD terms and the two MDE terms were significant (F_4 = 5.7, p = .033). Inspection showed that RRs were very similar for patients with pre-MVC histories of both PTSD and MDE in the presence of either PTSD-alone, MDE-alone, or both disorders in the 30 days before the MVC, leading us to collapse those three cells in further analyses. The RR was considerably lower among patients with pre-MVC histories of both PTSD and MDE in the absence of either disorder in the 30 days before the MVC. Patients with a pre-MVC history of PTSD but not MDE had a somewhat lower RR, which was comparable in the presence versus absence of prevalence in the 30 days before the MVC. The RR was lower still among patients with a pre-MVC history of MDE but not PTSD, again with comparable RRs in the presence versus absence of prevalence in the 30 days before the MVC. The four dummy predictor variables defining these combinations captured the significant component of the associations between joint pre-MVC histories of PTSD and MDE with 3-month PTSD or MDE (F_4 = 24.0, p < .001). The remainder of the joint association was nonsignificant (F_4 = 0.4, p = .84).

[d]Combined PARP (SE) for all four pre-MVC variables controlling MVC characteristics was 63.1% (3.3), which means that 3-month outcome prevalence would be reduced by 63.1% if we could block the causal forces linking these pre-MVC disorders to the outcome.

[e]See Table S4 for a re-estimation of the results in the current table controlling for between-ED variation in the outcome. As shown there, this variation was nonsignificant (F_{28} = 0.6, p = .98) and the results reported in the current table were unchanged when we examined pooled within-ED associations.

[f]See Table S3 for the derivation of the final functional form for three MVC characteristics.

[g]Although the linear pain score was significant, further analysis showed its association with the outcome to be nonlinear and to be well-captured by a dummy variable for a score in the top 40% of the patients with pain on the observed distribution on the pain severity rating scale.

[h]PTSD-alone indicates a diagnosis of PTSD and no diagnosis of MDE, and MDE-alone indicates a diagnosis of MDE and no diagnosis of PTSD.

*Significant at the .05 level, two-sided test.

became nonsignificant when controlling pre-MVC histories (Model 2). Two-week probable threshold PTSD-alone (RR = 3.4), subthreshold PTSD (RR = 2.5), and threshold MDE (RR = 1.6), in comparison, were all significant when added to the model (Model 3). The joint associations of these 2-week disorders with the outcome were nonadditive ($F_4 = 4.2$, $p = .046$), with the highest RR (Model 4) associated with having comorbid 2-week disorders (threshold or subthreshold; RR = 5.0) followed by having either probable threshold or subthreshold PTSD-alone (RR = 3.6) or MDE-alone (RR = 3.7).

Severe pain reported in the ED (the only significant MVC predictor in the final Table 2 model) remained significant when we adjusted for peritraumatic symptoms and 2-week disorders (RR = 1.4 in Models 1–2 vs. RR = 1.3 in Models 3–4). The associations of pre-MVC probable PTSD and MDE with the 3-month outcome, in comparison, were reduced substantially by these controls (Model 4), as indicated by PARP (SE) of the four pre-MVC history variables decreasing from 63.1% (3.3) to 46.8% (4.1). Results were unchanged when we examined pooled within-ED associations and when 3-month probable PTSD was the outcome (Table S5, Models 2–3).

3.5 | 2-week and 8-week disorders predicting the 3-month outcome

We next examined mediation through 8-week disorders. All four RRs of 8-week probable threshold and subthreshold PTSD and MDE were

TABLE 3 Associations of MVC characteristics, pre-MVC lifetime histories of probable PTSD and MDE, peritraumatic symptoms, and 2-week disorders with 3-month probable PTSD and/or MDE ($n = 1306$)[a]

			Model 1		Model 2[b]		Model 3[c]		Model 4[d,e]	
	%	SE	RR	(95% CI)	RR	(95% CI)	RR	(95% CI)	RR	(95% CI)
I. MVC characteristics										
Severe pain in ED[f]	41.0	(1.4)	1.4*	(1.2–1.8)	1.4*	(1.1–1.7)	1.3*	(1.0–1.6)	1.3*	(1.1–1.6)
II. Joint pre-MVC histories of PTSD and/or MDE										
Both lifetime and ≥1 30-day	9.5	(0.8)	6.9*	(5.0–9.6)	6.3*	(4.5–8.8)	2.9*	(2.0–4.2)	3.2*	(2.2–4.6)
Both lifetime and neither 30-day	10.4	(0.8)	4.5*	(3.1–6.4)	4.3*	(3.0–6.2)	2.6*	(1.8–3.8)	2.7*	(1.9–4.0)
PTSD-alone: Lifetime (with or without 30-day)[g]	23.7	(0.9)	3.9*	(2.9–5.4)	3.7*	(2.7–5.1)	2.4*	(1.7–3.3)	2.4*	(1.8–3.4)
MDE-alone: Lifetime (with or without 30-day)[g]	4.7	(1.0)	2.6*	(1.5–4.7)	2.6*	(1.4–4.6)	2.1*	(1.2–3.6)	2.1*	(1.2–3.7)
F_4			36.2*		30.1*		9.7*		11.7*	
III. Peritraumatic symptomatology[h]										
Peritraumatic distress	0.0	(1.0)	–	–	1.1[i]	(0.9–1.2)	–	–	–	–
Peritraumatic dissociation[i]	0.0	(1.0)	–	–	1.0[i]	(0.9–1.2)	–	–	–	–
F_2			–		–		–		–	
IV. 2-week PTSD and/or MDE										
a. PTSD[j]										
PTSD	37.4	(1.3)	–	–	–	–	3.4*	(2.3–4.9)	–	–
Subthreshold PTSD	12.4	(0.9)	–	–	–	–	2.5*	(1.7–3.9)	–	–
F_2			–		–		21.0*		–	
b. MDE										
MDE	13.9	(1.0)	–	–	–	–	1.6*	(1.1–2.2)	–	–
Subthreshold MDE	16.8	(1.0)	–	–	–	–	1.3	(0.9–1.7)	–	–
F_2			–		–		4.1*		–	
F_4			–		–		20.7*		–	
c. Joint 2-week PTSD and/or MDE										
Both (threshold or subthreshold)	29.0	(0.7)	–	–	–	–	–	–	5.0*	(3.5–7.2)
PTSD-alone (threshold or subthreshold)[g]	21.1	(0.9)	–	–	–	–	–	–	3.6*	(2.5–5.3)
MDE-alone (threshold or subthreshold)[g]	2.1	(0.4)	–	–	–	–	–	–	3.7*	(1.8–7.8)

TABLE 3 (Continued)

	%	SE	Model 1 RR	(95% CI)	Model 2[b] RR	(95% CI)	Model 3[c] RR	(95% CI)	Model 4[d,e] RR	(95% CI)
F_3			–		–		–		25.5*	
Total model $F_{5,7,9,8}$			33.6*		24.8*		25.7*		26.9*	

Note: Estimates reflect multiply-imputed data (30 imputations).

Abbreviations: AURORA, advancing understanding of recovery after trauma; CI, confidence interval; DSM-5, diagnostic and statistical manual of mental disorders, fifth edition; ED, emergency department; MDE, major depressive episode; MVC, motor vehicle collision; PARP, population attributable risk proportion; PCL-5, PTSD checklist for DSM-5; PTSD, posttraumatic stress disorder; RR, relative risk.

[a]To reduce redundancy, each survey-based assessment of probable PTSD and MDE is referred to in the table and subsequent footnotes as "PTSD" and "MDE." Based on modified Poisson regression models with robust variance estimates.

[b]An interaction between peritraumatic stress and peritraumatic dissociation was not significant ($F_1 = 0.7$, $p = .41$).

[c]Interactions between the two PTSD terms and the two MDE terms at 2 weeks were significant ($F_4 = 4.2$, $p = .046$). Inspection showed that RRs were very similar for patients with 2-week PTSD-alone (i.e., no MDE) and for those with 2-week MDE-alone (i.e., no PTSD), leading us to collapse the joint association into separate cells for either threshold or subthreshold. The distinction between threshold and subthreshold was nonsignificant both for PTSD ($F_1 = 1.2$, $p = .28$) and MDE ($F_1 = 1.0$, $p = .35$). However, RRs were considerably larger among patients with 2-week histories with overlapping PTSD and MDE diagnoses, so a third cell was created for these patients. The three dummy predictor variables defining these combinations, which left patients without any diagnosis as the reference category, captured the significant component of the associations between joint 2-week histories of PTSD and MDE with the outcome ($F_3 = 9.1$, $p < .001$). The remainder of the joint association was nonsignificant ($F_5 = 1.5$, $p = .17$).

[d]The combined PARP (SE) for all four pre-MVC variables controlling MVC characteristics fell from 63.1% (3.3) in Table 2 to 46.8% (4.1) in Table 3.

[e]See Table S5 for a re-estimation of the results in the current table controlling for between-ED variation in the outcome. As shown there, this variation was nonsignificant ($F_{28} = 0.5$, $p = .98$) and the results reported in the current table were unchanged when we examined pooled within-ED associations.

[f]Although the linear pain score was significant, further analysis showed its association with the outcome to be nonlinear and to be well-captured by a dummy variable for a score in the top 40% of the observed distribution of patients with pain on the pain severity rating scale.

[g]PTSD-alone indicates a diagnosis of PTSD and no diagnosis of MDE. MDE-alone indicates a diagnosis of MDE and no diagnosis of PTSD.

[h]Both peritraumatic distress (RR = 1.3, 95% CI = 1.2–1.5, $p < .001$) and peritraumatic dissociation (RR = 1.6, 95% CI = 1.3–2.0, $p < .001$) were significant in univariable models, both became nonsignificant when controls were introduced for pre-MVC PTSD-MDE (Model 2).

[i]This variable is continuous and standardized to a mean of 0 and a standard deviation of 1.

[j]An earlier AURORA report used a PCL-5 modification to assess 2-week DSM-5 acute stress disorder criterion B rather than 2-week PTSD (Kessler et al., 2020), but we instead used criteria for 2-week PTSD here to allow parallel analysis across all 3 follow-up assessments.

*Significant at the .05 level, two-sided test.

significant predictors of the 3-month outcome (RR = 1.4–4.3) in an additive model (Table S6, Model 1). However, joint associations were significantly nonadditive and inspection led us to collapse the 8-week probable threshold and subthreshold MDE into a single category because the RRs were the same ($F_1 = 0.1$, $p = .89$), resulting in significant interactions between the two terms for probable PTSD and the single composite MDE term ($F_2 = 5.4$, $p = .005$). The cross-classification of 8-week probable PTSD and MDE resulted in five statistically significant dummy predictor variables (Table S6, Model 2). The highest RRs were associated with comorbid 8-week probable threshold PTSD and either probable threshold or subthreshold 8-week MDE (RR = 7.5) followed by probable PTSD-alone (RR = 6.3), probable subthreshold PTSD either with (RR = 4.7) or without (RR = 3.0) 8-week probable MDE, and 8-week probable MDE-alone (RR = 3.9). The FDR correction for the possibility of false positives in estimating so many coefficients found that the great majority remained significant. Results were unchanged when we examined pooled within-ED associations and when 3-month probable PTSD was the outcome (Table S7, Models 2–3). We also investigated whether any of these associations were different when we distinguished between 3-month probable PTSD-alone and 3-month probable MDE (Table S7, Model 4). The only significant predictor was the dummy variable for having a pre-MVC history of both and pre-MVC 30-day prevalence of at least one of these disorders (RR = 0.5).

A marginally significant interaction was found between 2- and 8-week disorders after collapsing several extremely small cells that prevented the full interaction model from being estimated ($F_{12} = 1.8$, $p = .049$). Inspection showed this interaction was due entirely to a significantly reduced RR among patients with no threshold or subthreshold disorders at either 2- or 8-weeks ($F_1 = 11.5$, $p < .001$). No other interaction was significant ($F_{11} = 0.8$, $p = .60$). The subsequent model (Table 4, Model 1) consequently included only a single interaction for having at least one 2- or 8-week threshold or subthreshold disorder (RR = 4.0). Adding this interaction to the additive model led to substantial attenuation of the coefficients for 8-week disorders (RR = 1.8–4.8 compared to RR = 3.0–7.5 in Table S6, Model 2). The associations of pre-MVC lifetime PTSD and MDE with the 3-month outcome were also attenuated compared to the model controlling only 2-week disorders (RR = 1.4–1.7 in Table S6, Model 2, $F_4 = 2.5$, $p = .05$, vs. RR = 2.1–3.2 in Table 3, Model 4, $F_4 = 11.7$, $p < .001$). However, these coefficients remained largely significant after FDR correction even though PARP (SE) of pre-MVC probable PTSD and MDE further decreased from 46.8% (4.1) to 22.8% (4.4). Results were unchanged when we examined pooled within-ED associations and

TABLE 4 Associations of MVC characteristics, pre-MVC lifetime histories of probable PTSD and MDE, 2-week disorders, and 8-week disorders with 3-month probable PTSD and/or MDE ($n = 1306$)[a]

			Model 1[b,c] ($n = 1306$)		Model 2a ($n = 634$)		Model 2b ($n = 672$)		Model 2c ($n = 1306$)[d]			
									Main effects		Interactions	
	%	SE	RR	(95% CI)	RR	(95% CI)	RR	(95% CI)	RR	(95% CI)	RR	(95% CI)
I. MVC characteristics												
Severe pain in ED[e]	41.0	1.4	1.2	(1.0–1.5)	1.1	(0.9–1.5)	1.4	(0.9–2.4)	1.4	(0.9–2.4)	0.8	(0.5–1.4)
II. Joint pre-MVC histories of PTSD and/or MDE												
Either or both life disorders (with or without 30-day)	48.5	1.4							1.8	(0.4–8.0)		
Both lifetime and ≥1 30-day	9.5	0.8	1.7**	(1.2–2.4)	1.3	(0.7–2.3)	–	–	1.3	(0.7–2.3)	–	–
Both lifetime and neither 30-day	10.4	0.8	1.5**	(1.0–2.2)	1.1	(0.6–1.9)	–	–	1.1	(0.6–1.9)	–	–
PTSD-alone: Lifetime (with or without 30-day)[f]	23.9	0.9	1.5**	(1.1–2.1)	1.1	(0.6–1.9)	–	–	1.1	(0.7–1.9)	–	–
MDE-alone: Lifetime (with or without 30-day)[f]	4.7	1.0	1.4	(0.8–2.4)	1.0	–	–	–	1.0	–	–	–
F_4			2.3		0.5				0.7			
III. Joint 2-week PTSD and/or MDE												
Both (threshold or subthreshold)	29.0	0.7	1.6*	(1.1–2.3)	1.5	(1.0–2.3)	1.8	(0.7–4.6)	1.7	(0.7–4.3)	0.9	(0.3–2.4)
PTSD-alone (threshold or subthreshold)[f]	21.1	0.9	1.4	(0.9–2.1)	1.2	(0.7–2.0)	2.2	(0.9–5.3)	2.1	(0.9–5.1)	0.6	(0.2–1.6)
MDE-alone (threshold or subthreshold)[f]	2.1	0.4	1.8	(0.8–3.9)	1.4	(0.5–3.6)	4.0	(0.9–18.1)	4.0	(0.9–18.3)	0.3	(0.1–2.1)
F_3			1.9		1.4		1.5		1.5		0.9	
IV. Joint 8-week PTSD and/or MDE[g]												
PTSD and threshold or subthreshold MDE	22.0	1.1	4.8**	(3.1–7.6)	2.9**	(1.8–4.7)	19.9**	(6.8–58.8)	20.0**	(6.8–59.2)	0.1**	(0.0–0.5)
PTSD-alone[f]	8.9	0.8	4.0**	(2.4–6.5)	2.5**	(1.4–4.3)	12.0**	(4.0–36.4)	11.5**	(3.8–34.7)	0.2*	(0.1–0.7)
Subthreshold PTSD and threshold or subthreshold MDE	2.8	0.5	3.0*	(1.6–5.9)	1.7	(0.8–3.6)	14.4**	(3.1–67.6)	14.6**	(3.1–68.4)	0.1*	(0.0–0.6)
Subthreshold PTSD-alone[f]	9.1	0.8	1.8*	(1.0–3.3)	1.3	(0.6–2.6)	4.1*	(1.2–14.8)	4.1*	(1.1–14.8)	0.3	(0.1–1.4)
MDE-alone (threshold or subthreshold)[f]	3.8	0.5	2.4**	(1.2–4.7)	1.3	(0.6–2.8)	8.1**	(2.0–33.7)	8.3**	(2.0–34.4)	0.1*	(0.0–0.8)
F_5			11.6*		5.6*		7.0*		7.0*		2.4*	
V. Joint 2- or 8-week PTSD and/or MDE[h]												
Any 2-week or 8-week threshold or subthreshold disorder	61.2	1.4	4.0**	(1.7–9.4)	6.0**	(1.7–22.0)	1.1	(0.2–5.3)	1.1	(0.2–5.2)	5.3	(0.7–40.1)

TABLE 4 (Continued)

	%	SE	Model 1[b,c] (*n* = 1306) RR	(95% CI)	Model 2a (*n* = 634) RR	(95% CI)	Model 2b (*n* = 672) RR	(95% CI)	Model 2c (*n* = 1306)[d] Main effects RR	(95% CI)	Interactions RR	(95% CI)
F_1			9.8*		7.5*		0.0		0.0		2.7	
Total model $F_{14,13,10,14,10}$			15.8*		5.7*		9.4*		7.9*		1.4	

Note: Estimates reflect multiply-imputed data (30 imputations).

Abbreviations: CI, confidence interval; ED, emergency department; MDE, major depressive episode; MVC, motor vehicle collision; PARP, population attributable risk proportion; PTSD, posttraumatic stress disorder; RR, relative risk.

[a]To reduce redundancy, each survey-based assessment of probable PTSD and MDE is referred to in the table and subsequent footnotes as "PTSD" and "MDE." Based on modified Poisson regression models with robust variance estimates.

[b]The combined PARP (SE) for all four pre-MVC variables controlling MVC characteristics fell from 46.8% (4.1) in Table 3 to 22.8 (4.4) in Table 4.

[c]See Table S7 for a re-estimation of the results in the current table controlling for between-ED variation in the outcome. As shown there, this variation was nonsignificant ($F_{28} = 0.3$, $p = .99$) and the results reported in the current table were unchanged when we examined pooled within-ED associations.

[d]See Table S8 for a re-estimation of the results in the current table controlling for between-ED variation in the outcome. As shown there, this variation was nonsignificant ($F_{28} = 0.3$, $p = .99$) and the results reported in the current table were unchanged when we examined pooled within-ED associations.

[e]Although the linear pain score was significant, further analysis showed its association with the outcome to be nonlinear and to be well-captured by a dummy variable for a score in the top 40% of the observed distribution of patients with pain on the pain severity rating scale.

[f]PTSD-alone indicates a diagnosis of PTSD and no diagnosis of MDE, and MDE-alone indicates a diagnosis of MDE and no diagnosis of PTSD.

[g]Before testing for interactions between 8-week disorders, the RRs for 8-week threshold and subthreshold MDE were collapsed into a single composite category because the individual RRs were not significantly different from each other (1.4 vs. 1.4; $F_1 = 0.1$, $p = .89$). Interactions between the two PTSD terms and one composite MDE term (i.e., for either threshold or subthreshold MDE) at 8 weeks were significant ($F_2 = 5.4$, $p = .005$). A joint 8-week cross-classification of the three-category PTSD measure with the two-category MDE measure was created, which left five dummy predictor variables defining the five possible combinations of 8-week comorbidity versus a sixth category of patients without any 8-week diagnosis.

[h]The interaction between 2- and 8-week disorders was significant after collapsing several extremely small cells that prevented the full interaction model to be estimated ($F_{12} = 1.8$, $p = .049$). However, inspection showed that this interaction was due entirely to the significantly lower relative-risk than in the additive model among patients with the conjunction of no 2-week disorders and no 8-week disorders ($F_1 = 11.5$, $p < .001$). None of the remaining interaction terms was significant either individually or as a set ($F_{11} = 0.8$, $p = .60$). As a result, the final model included only the single interaction term for the conjunction of having any 2-week disorder and any 8-week disorder.

*Significant at the .05 level, two-sided test.

**Significance at the .05 level, two-sided test when correcting for the false discovery rate.

when 3-month probable PTSD was the outcome (Table S8, Models 2–3).

Some insight into the mediating effects of 2-week and 8-week disorders can be obtained by estimating subgroup models separately for patients with (Table 4, Model 2a) and without (Model 2b) pre-MVC lifetime disorders. Among patients without such histories, none of the 2-week disorder profiles ($F_3 = 1.5$, $p = .21$) but all the 8-week disorder profiles (RR = 4.1–19.9) significantly predicted the 3-month outcome, with the latter coefficients significantly higher than among patients with pre-MVC histories ($F_5 = 2.4$, $p = .029$). Having at least one 2- and/or 8-week threshold or subthreshold disorder, in comparison, was not a significant predictor (RR = 1.1, $F_1 = 0.0$, $p = .86$).

Among patients with pre-MVC lifetime disorders, in comparison, neither pre-MVC lifetime disorder profiles ($F_4 = 0.5$, $p = .67$) nor 2-week disorder profiles ($F_3 = 1.4$, $p = .26$) predicted the 3-month outcome and the only significant 8-week profiles were those associated with probable threshold PTSD (with or without threshold or subthreshold MDE; RR = 2.5–2.9). The much more important predictor among these patients was a dummy variable for having any 2- or 8-week threshold or subthreshold disorder (RR = 6.0), which, as noted above, was not significant among patients without a pre-MVC history of these disorders.

The incremental elevation in RR among patients with versus without a pre-MVC lifetime history of either disorder after adjusting for the intervening 2- and 8-week disorders was a nonsignificant RR = 1.8 ($F_1 = 0.6$, $p = .43$; Table 4, Model 2c). When we removed the 2- and 8-week disorders from the model, in comparison, this coefficient increased to RR = 4.2 (3.1–5.5, $F_1 = 8.1$, $p = .004$). Consistent with the PARP estimates, this means that most of the gross association between pre-MVC lifetime history and the 3-month outcome is mediated through the 2- and 8-week disorders.

A better understanding of this complex set of specifications can be obtained by examining the conditional prevalence of the 3-month outcome in subsamples of patients with and without pre-MVC lifetime histories stratified by the joint prevalence of 2- and 8-week probable PTSD and MDE (Table 5). The higher risk of the 3-month outcome among patients with than without pre-MVC histories can be seen in four different ways: (1) a significantly higher probability of having 2-week disorders (71.0% vs. 34.2%, $F_1 = 81.5$, $p < .001$); (2) a significantly higher probability of disorder persistence at 8 weeks among patients with 2-week disorders (82.6% vs. 49.4%, $F_1 = 25.2$, $p < .001$); (3) a significantly higher probability of delayed disorder onset by 8 weeks among 2-week noncases (39.4% vs. 11.2%, $F_1 = 39.5$, $p < .001$); and (4) higher prevalence of the 3-month outcome within each of the three subsamples of patients with

TABLE 5 Distribution and prevalence of 3-month Probable PTSD and/or MDE in subgroups defined by pre-MVC lifetime history stratified by joint 2- and 8-week disorders[a]

	Pre-MVC lifetime PTSD and/or MDE														
	Yes (n = 630)					No (n = 676)					Total (n = 1306)				
	Distribution		Outcome prevalence			Distribution		Outcome prevalence			Distribution		Outcome prevalence		
	%	SE	%	SE	n[b]	%	SE	%	SE	n[c]	%	SE	%	SE	n[b]
Joint 2- and 8-week disorders[c]															
2-week	71.0**	(1.9)	59.2**	(2.4)	447	34.2	(1.9)	23.1	(2.9)	231	52.0	(1.4)	46.9	(1.9)	679
8-week	69.9**	(1.9)	61.6**	(2.4)	441	24.3	(1.7)	34.3	(3.9)	164	46.3	(1.4)	54.2	(2.0)	605
Either 2- or 8-week	82.4**	(1.6)	55.9**	(2.2)	520	41.6	(1.9)	21.7	(2.6)	281	61.3	(1.4)	43.9	(1.8)	801
Both 2- and 8-week	58.5**	(2.0)	66.6**	(2.5)	369	16.9	(1.5)	42.7	(4.8)	114	37.0	(1.4)	61.0	(2.2)	483
Neither 2- nor 8- week	17.6	(1.6)	2.9	(1.6)	111	58.4	(1.9)	1.6	(0.6)	395	38.7	(1.4)	1.9	(0.6)	505
2-week only	12.5**	(1.4)	24.4**	(4.9)	79	17.3	(1.5)	3.9	(1.9)	117	15.0	(1.0)	12.1	(2.4)	196
8-week only	11.4*	(1.3)	36.0*	(5.8)	7.2	7.4	(1.0)	15.2	(5.3)	50	9.3	(0.8)	27.5	(4.1)	122
8-week, among 2-week (persistence)	82.6	(1.9)	66.6*	(2.5)	369	49.4	(3.4)	42.7	(4.8)	114	71.1	(1.8)	61.0	(2.2)	483
8-week, among no 2-week (late onset)	39.4**	(3.8)	36.0*	(5.8)	72	11.2	(1.6)	15.2	(5.3)	50	19.4	(1.6)	27.5	(4.1)	122
Total			46.6**	(2.0)	630	–	–	9.9	(1.2)	676	–	–	27.6	(1.2)	1306

Abbreviations: PTSD, posttraumatic stress disorder; MDE, major depressive episode; MVC, motor vehicle collision.

[a]To reduce redundancy, each survey-based assessment of probable PTSD and MDE is referred to in the table and subsequent footnotes as "PTSD" and "MDE." Estimates based on multiply-imputed data (30 imputations) and frequencies may not always sum to 100.

[b]Denominator n's.

[c]2- and 8-week disorders are defined as any threshold or subthreshold PTSD or MDE.

*Significantly different from the subgroup with no pre-MVC lifetime history.

**Denotes significance after correction for the false discovery rate.

intervening 2- and/or 8-week disorders (i.e., those with both 2- and 8-week disorders [66.6% vs. 42.7%, $F_1 = 7.6$, $p = .006$], only 2-week disorders [24.4% vs. 3.9%, $F_1 = 11.4$, $p < .001$], and only 8-weeks disorders [36.0% vs. 15.2%, $F_1 = 4.0$, $p = .045$]). These differences resulted in a significantly higher prevalence of the outcome among patients with any 2- or 8-week disorder (55.9% vs. 21.7%, $F_1 = 41.8$, $p < .001$), and a nonsignificant difference in prevalence among patients with no 2- or 8-week disorder (2.9% vs. 1.6%, $F_1 = 0.7$, $p = .40$), leading to a significantly higher 46.6% prevalence of the 3-month outcome among patients with pre-MVC lifetime histories than 9.9% among patients without such histories ($F_1 = 120.5$, $p < .001$).

4 | DISCUSSION

Pre-MVC histories of probable PTSD and MDE are much higher in the AURORA sample than in the general population (Bromet et al., 2011; Koenen et al., 2017). This could be due to these lifetime disorders predicting either (i) increased risk of experiencing an MVC, (ii) increased probability of seeking ED treatment after an MVC, and/or (iii) increased probability of agreeing to participate in the AURORA study. Possibility (iii) was the only one we could study in AURORA, but this information was not collected. However, we have now modified the AURORA data collection design going forward based on this high prevalence to obtain reports about pre-trauma histories from a probability subsample of patients who decline to participate in AURORA.

We also found that pre-MVC histories were strong predictors of the 3-month outcome. This is broadly consistent with previous research showing that histories of PTSD (Beliveau et al., 2019; Breslau et al., 2008; Kessler et al., 2018) and more general psychopathology (Bedaso et al., 2020; Heron-Delaney et al., 2013) strongly predict posttraumatic adjustment. We also found that these associations were mediated by 2- and 8-week disorders and that significant interaction existed between pre-MVC histories and the mediators due to pre-MVC histories predicting onset and persistence of these intervening disorders as well as the higher conditional prevalence of the 3-month outcome in the presence of these intervening disorders.

Our findings highlight the importance of MDE in posttraumatic psychopathology. Probable 3-month MDE, although uncommon in the absence of 3-month probable PTSD, occurred among roughly half

of 3-month PTSD cases and was associated with much more role impairment than PTSD-alone. In addition, pre-MVC lifetime comorbid probable PTSD-MDE was both the strongest predictor of the 3-month outcome in univariable analyses and had the highest mediator RRs at both 2 and 8 weeks. These results are consistent with prior research showing that comorbid MDE is a strong predictor of PTSD persistence and severity (Pozzato et al., 2020; Schindel-Allon et al., 2010).

Our failure to find that peritraumatic symptoms were important predictors might seem inconsistent with prior research (Bronner et al., 2009; Vance et al., 2018; van der Velden & Wittmann, 2008), but we found gross associations (i.e., when we did not control for prior lifetime PTSD or MDE) similar to those in previous research. It was only when we controlled for pre-MVC lifetime histories that peritraumatic symptoms became nonsignificant, raising the possibility that peritraumatic distress dissociation might be markers of more characterological risk factors. Future research in this area should consequently include baseline assessments of prior lifetime PTSD and MDE.

In addition to showing the importance of pre-MVC diagnosis in the prediction of posttrauma adjustment, the mediation findings provide important symptom trajectory information. Specifically, we found that 2- and 8-week symptoms were highly predictive of 3-month outcomes, especially in high-risk participants with a history of pretrauma disorders. Conversely, our analyses showed that if participants did not show an onset of disorder by 8 weeks, they were unlikely to receive a 3-month diagnosis even if they were in this high-risk group. These findings are important for early identification and intervention and emphasize the importance of close monitoring of symptoms in the first weeks posttrauma. In particular, a regular follow-up around 2-weeks posttrauma should be easy to implement and could become part of routine medical follow-ups. Indeed, recent studies have pointed to the promise of easy-to-implement mobile health assessments and interventions in the first 30-days posttrauma (Price et al., 2017; Price et al., 2018) using a combination of active and passive strategies. Obtaining fine-grained trajectory information would help optimize the implementation of these novel assessments and interventions such as in a stepped-care approach (Ho et al., 2016).

The study has several limitations. First, the majority of people who experience trauma do not come to an ED, and many of those that came declined to participate in AURORA. This means that our results cannot be assumed to apply to the larger population. Second, PTSD and MDE were assessed by self-report rather than diagnostic interviews. Third, many statistical tests were conducted, increasing the risk of type I errors even with FDR corrections. Fourth, we focused on MVC because other traumas were too uncommon individually to be included with controls, limiting the generalizability of results. However, we will address this limitation as the AURORA sample size grows. Fifth, we were unable to carry out a full disaggregation to determine if (i) 3-month outcomes represented new onsets or continuations of pre-existing episodes or (ii) the significant predictors apply to episode onset, persistence, or both among new cases. Such analyses would require the nine coefficients in the first two columns of Table 5 to be estimated separately within each of eight logically possible subgroups defined by the cross-classification of a lifetime and recent pre-MVC probable PTSD and MDE. We attempted this but the coefficients were too unstable for interpretation. Once the full AURORA sample (which will be about three times the size of the current sample) is available, though, this disaggregation will become possible. We will also follow patients for 12 months rather than only the 3 months considered here, allowing an investigation of delayed-onset cases, which previous research shows to be common (Bryant et al., 2020; Lowe et al., 2020). Sixth, we only examined a subset of the survey predictors and none of the biomarkers available in the AURORA dataset in this early report. Most notable among the omitted predictors are measures of prior lifetime trauma exposure, which occurred definitionally among patients with prior PTSD, and which future research might show to account for the predictive associations of prior PTSD with our 3-month outcome.

Despite these limitations, our results suggest strongly that pre-MVC histories of PTSD and/or MDE are strong predictors of 3-month posttraumatic psychopathological responses and that these associations are largely mediated through intermediate disorders in ways that could have important implications for early interventions.

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CONFLICT OF INTERESTS

Dr. Jutta Joorman has served as a consultant for Janssen Pharmaceuticals. In the last 3 years, Dr. Gari D. Clifford has received research funding from the National Science Foundation, the National Institute of Health, and LifeBell AI; he has received unrestricted donations from AliveCor, Amazon Research, the Center for Discovery, the Gordon and Betty Moore Foundation, MathWorks, Microsoft Research, the Gates Foundation, Google, One Mind Foundation, and Samsung Research; he has a financial interest in AliveCor, and has received unrestricted funding from the company; he is the chief technology officer of MindChild Medical and chief security officer of LifeBell AI, and has ownership in both companies. In the past 3 years, Dr. Laura T. Germine has served on the Scientific Advisory Board of Sage Bionetworks, for which she received a small honorarium. Dr. Scott L. Rauch has a paid role as secretary of Society of Biological Psychiatry; he has received royalties from Oxford University Press and from American Psychiatric Publishing Inc.; has paid board service from Community Psychiatry, including equity outside the submitted work; and he has served as the board of director for Anxiety and Depression Association of America, and National Network of

Depression Centers. Dr. Christopher W. Jones has been an investigator on studies funded by Hologic Inc., Janssen, AstraZeneca, and Vapotherm. Over the past 3 years, Dr. Diego A. Pizzagalli has received consulting fees from BlackThorn Therapeutics, Boehringer Ingelheim, Compass Pathway, Concert Pharmaceuticals, Engrail Therapeutics, Otsuka Pharmaceuticals, and Takeda Pharmaceuticals; he has one honorarium from Alkermes; he has received research funding from Millennium Pharmaceuticals; and he has received stock options from BlackThorn Therapeutics. Dr. Steven E. Harte has received personal fees from the National Institute of Health/the University of North Carolina at Chapel Hill, Aptinyx, Heron Therapeutics, Memorial Sloan Cancer Center, and Eli Lilly; he has received grants from Aptinyx and Arbor Medical Innovations; and he reports membership to Arbor Medical Innovations. Dr. James M. Elliot has received grants from the National Institutes of Health. In the past 3 years, Dr. Ronald C. Kessler has served as a consultant for Datastat, Inc., Holmusk, RallyPoint Networks, Inc., and Sage Therapeutics and he has stock options in Mirah, PYM, and Roga Sciences. All other authors declare that there are no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data supporting this study's findings will eventually be openly available at the NIMH National Data Archive at https://nda.nih.gov/edit_collection.html?id=2526, reference number 2526.

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