## Washington University School of Medicine

## Digital Commons@Becker

2020-Current year OA Pubs

**Open Access Publications** 

1-10-2023

# Childhood adversities and risk of posttraumatic stress disorder and major depression following a motor vehicle collision in adulthood

H N Ziobrowski Harvard Medical School S L House Washington University School of Medicine in St. Louis Washington University School of Medicine in St. Louis et al.

Follow this and additional works at: https://digitalcommons.wustl.edu/oa\_4



Part of the Medicine and Health Sciences Commons

## Please let us know how this document benefits you.

## **Recommended Citation**

Ziobrowski, H N; House, S L; Barch, D M; and et al., "Childhood adversities and risk of posttraumatic stress disorder and major depression following a motor vehicle collision in adulthood." Epidemiology and Psychiatric Sciences. 32, e1 (2023).

https://digitalcommons.wustl.edu/oa\_4/1185

This Open Access Publication is brought to you for free and open access by the Open Access Publications at Digital Commons@Becker. It has been accepted for inclusion in 2020-Current year OA Pubs by an authorized administrator of Digital Commons@Becker. For more information, please contact vanam@wustl.edu.

## Epidemiology and Psychiatric Sciences

#### cambridge.org/eps

## **Original Article**

Cite this article: Ziobrowski HN et al (2023). Childhood adversities and risk of posttraumatic stress disorder and major depression following a motor vehicle collision in adulthood. *Epidemiology and Psychiatric Sciences* 32, e1, 1–11. https://doi.org/10.1017/S2045796022000798

Received: 13 July 2022 Revised: 2 December 2022 Accepted: 18 December 2022

#### **Keywords:**

Depression; mental health; post traumatic stress disorder; Trauma

#### **Author for correspondence:**

Ronald C. Kessler, E-mail: kessler@hcp.med.harvard.edu

© The Author(s), 2023. Published by Cambridge University Press. This is an Open Access article, distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives licence (http://creativecommons.org/licenses/by-nc-nd/4.0), which permits non-commercial re-use, distribution, and reproduction in any medium, provided that no alterations are made and the original article is properly cited. The written permission of Cambridge University Press must be obtained prior to any commercial use and/or adaptation of the article.



## Childhood adversities and risk of posttraumatic stress disorder and major depression following a motor vehicle collision in adulthood

- H. N. Ziobrowski<sup>1</sup>, B. Holt-Gosselin<sup>2,3</sup>, M. V. Petukhova<sup>1</sup>, A. J. King<sup>1</sup>, S. Lee<sup>1</sup>,
- S. L. House<sup>4</sup>, F. L. Beaudoin<sup>5</sup>, X. An<sup>6</sup>, J. S. Stevens<sup>7</sup>, D. Zeng<sup>8</sup>, T. C. Neylan<sup>9</sup>,
- G. D. Clifford<sup>10,11</sup>, S. D. Linnstaedt<sup>6</sup>, L. T. Germine<sup>12,13,14</sup>, K. A. Bollen<sup>15</sup>,
- S. L. Rauch<sup>12,14,16</sup>, J. P. Haran<sup>17</sup>, A. B. Storrow<sup>18</sup>, C. Lewandowski<sup>19</sup>, P. I. Musey<sup>20</sup>,
- P. L. Hendry<sup>21</sup>, S. Sheikh<sup>21</sup>, C. W. Jones<sup>22</sup>, B. E. Punches<sup>23,24</sup>, M. C. Kurz<sup>25,26,27</sup>,
- R. A. Swor<sup>28</sup>, L. A. Hudak<sup>29</sup>, J. L. Pascual<sup>30,31</sup>, M. J. Seamon<sup>31,32</sup>, E. Harris<sup>33</sup>,
- C. Pearson<sup>34</sup>, R. C. Merchant<sup>35</sup>, R. M. Domeier<sup>36</sup>, N. K. Rathlev<sup>37</sup>, B. J. O'Neil<sup>38</sup>,
- P. Sergot $^{39}$ , L. D. Sanchez $^{35,40}$ , S. E. Bruce $^{41}$ , M. W. Miller $^{42,43}$ , R. H. Pietrzak $^{44,45}$ ,
- J. Joormann<sup>2</sup>, D. M. Barch<sup>46</sup>, D. A. Pizzagalli<sup>14,47</sup>, S. E. Harte<sup>48,49</sup>,
- J. M. Elliott<sup>50,51,52</sup>, K. J. Ressler<sup>14,47</sup>, S. A. McLean<sup>53,54</sup>, K. C. Koenen<sup>55</sup> and
- R. C. Kessler<sup>1</sup> (D)

<sup>1</sup>Department of Health Care Policy, Harvard Medical School, Boston, MA, USA; <sup>2</sup>Department of Psychology, Yale University, New Haven, CT, USA; <sup>3</sup>Interdepartmental Neuroscience Graduate Program, Yale School of Medicine, New Haven, CT, USA; <sup>4</sup>Department of Emergency Medicine, Washington University School of Medicine, St. Louis, MO, USA; <sup>5</sup>Department of Emergency Medicine & Department of Health Services, Policy, and Practice, The Alpert Medical School of Brown University, Rhode Island Hospital and The Miriam Hospital, Providence, RI, USA; <sup>6</sup>Department of Anesthesiology, Institute for Trauma Recovery, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; <sup>7</sup>Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, GA, USA; <sup>8</sup>Department of Biostatistics, Gillings School of Global Public Health, University of North Carolina, Chapel Hill, NC, USA; <sup>9</sup>Departments of Psychiatry and Neurology, University of California San Francisco, San Francisco, CA, USA; <sup>10</sup>Department of Biomedical Informatics, Emory University School of Medicine, Atlanta, GA, USA; <sup>11</sup>Department of Biomedical Engineering, Georgia Institute of Technology and Emory University, Atlanta, GA, USA; <sup>12</sup>Institute for Technology in Psychiatry, McLean Hospital, Belmont, MA, USA; <sup>13</sup>The Many Brains Project, Belmont, MA, USA; 14Department of Psychiatry, Harvard Medical School, Boston, MA, USA; 15Department of Psychology and Neuroscience & Department of Sociology, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; <sup>16</sup>Department of Psychiatry, McLean Hospital, Belmont, MA, USA; <sup>17</sup>Department of Emergency Medicine, University of Massachusetts Chan Medical School, Worcester, MA, USA; <sup>18</sup>Department of Emergency Medicine, Vanderbilt University Medical Center, Nashville, TN, USA; <sup>19</sup>Department of Emergency Medicine, Henry Ford Health System, Detroit, MI, USA; <sup>20</sup>Department of Emergency Medicine, Indiana University School of Medicine, Indianapolis, IN, USA; <sup>21</sup>Department of Emergency Medicine, University of Florida College of Medicine -Jacksonville, Jacksonville, FL, USA; <sup>22</sup>Department of Emergency Medicine, Cooper Medical School of Rowan University, Camden, NJ, USA; <sup>23</sup>Department of Emergency Medicine, Ohio State University College of Medicine, Columbus, OH, USA; <sup>24</sup>Ohio State University College of Nursing, Columbus, OH, USA; <sup>25</sup>Department of Emergency Medicine, University of Alabama School of Medicine, Birmingham, AL, USA; <sup>26</sup>Department of Surgery, Division of Acute Care Surgery, University of Alabama School of Medicine, Birmingham, AL, USA; <sup>27</sup>Center for Injury Science, University of Alabama at Birmingham, Birmingham, AL, USA; <sup>28</sup>Department of Emergency Medicine, Oakland University William Beaumont School of Medicine, Rochester, MI, USA; <sup>29</sup>Department of Emergency Medicine, Emory University School of Medicine, Atlanta, GA, USA; 30 Department of Surgery, Department of Neurosurgery, University of Pennsylvania, Philadelphia, PA, USA; <sup>31</sup>Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA; <sup>32</sup>Department of Surgery, Division of Traumatology, Surgical Critical Care and Emergency Surgery, University of Pennsylvania, Philadelphia, PA, USA; <sup>33</sup>Department of Emergency Medicine, Einstein Medical Center, Philadelphia, PA, USA; 34Department of Emergency Medicine, Wayne State University, Ascension St. John Hospital, Detroit, MI, USA; <sup>35</sup>Department of Emergency Medicine, Brigham and Women's Hospital, Boston, MA, USA; <sup>36</sup>Department of Emergency Medicine, Saint Joseph Mercy Hospital, Ypsilanti, MI, USA; <sup>37</sup>Department of Emergency Medicine, University of Massachusetts Medical School-Baystate, Springfield, MA, USA; <sup>38</sup>Department of Emergency Medicine, Wayne State University, Detroit Receiving Hospital, Detroit, MI, USA; <sup>39</sup>Department of Emergency Medicine, McGovern Medical School at UTHealth, Houston, TX, USA; 40 Department of Emergency Medicine, Harvard Medical School, Boston, MA, USA; <sup>41</sup>Department of Psychological Sciences, University of Missouri – St. Louis, St. Louis, MO, USA; <sup>42</sup>National Center for PTSD, Behavioral Science Division, VA Boston Healthcare System, Boston, MA, USA; <sup>43</sup>Department of Psychiatry, Boston University School of Medicine, Boston, MA, USA; <sup>44</sup>National Center for PTSD, Clinical Neurosciences Division, VA Connecticut Healthcare System, West Haven, CT, USA; 45Department of Psychiatry, Yale School of Medicine, New Haven, CT, USA; <sup>46</sup>Department of Psychological & Brain Sciences, Washington University in St. Louis, St. Louis, MO, USA; 47 Division of Depression and Anxiety, McLean Hospital, Belmont, MA, USA; <sup>48</sup>Department of Anesthesiology, University of Michigan Medical School, Ann Arbor, MI, USA; <sup>49</sup>Department of Internal Medicine-Rheumatology, University of Michigan Medical School, Ann Arbor, MI, USA; <sup>50</sup>Kolling Institute, University of Sydney, St Leonards, New South Wales, Australia; <sup>51</sup>Faculty of Medicine and

Health, University of Sydney, Northern Sydney Local Health District, New South Wales, Australia; <sup>52</sup>Physical Therapy & Human Movement Sciences, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA; <sup>53</sup>Department of Emergency Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; <sup>54</sup>Department of Psychiatry, Institute for Trauma Recovery, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA and <sup>55</sup>Department of Epidemiology, Harvard T.H. Chan School of Public Health, Harvard University, Boston, MA, USA

#### Abstract

Aims. Childhood adversities (CAs) predict heightened risks of posttraumatic stress disorder (PTSD) and major depressive episode (MDE) among people exposed to adult traumatic events. Identifying which CAs put individuals at greatest risk for these adverse posttraumatic neuropsychiatric sequelae (APNS) is important for targeting prevention interventions.

**Methods.** Data came from n = 999 patients ages 18–75 presenting to 29 U.S. emergency departments after a motor vehicle collision (MVC) and followed for 3 months, the amount of time traditionally used to define chronic PTSD, in the Advancing Understanding of Recovery After Trauma (AURORA) study. Six CA types were self-reported at baseline: physical abuse, sexual abuse, emotional abuse, physical neglect, emotional neglect and bullying. Both dichotomous measures of ever experiencing each CA type and numeric measures of exposure frequency were included in the analysis. Risk ratios (RRs) of these CA measures as well as complex interactions among these measures were examined as predictors of APNS 3 months post-MVC. APNS was defined as meeting self-reported criteria for either PTSD based on the PTSD Checklist for DSM-5 and/or MDE based on the PROMIS Depression Short-Form 8b. We controlled for pre-MVC lifetime histories of PTSD and MDE. We also examined mediating effects through peritraumatic symptoms assessed in the emergency department and PTSD and MDE assessed in 2-week and 8-week follow-up surveys. Analyses were carried out with robust Poisson regression models.

**Results.** Most participants (90.9%) reported at least rarely having experienced some CA. Ever experiencing each CA other than emotional neglect was univariably associated with 3-month APNS (RRs = 1.31-1.60). Each CA frequency was also univariably associated with 3-month APNS (RRs = 1.65-2.45). In multivariable models, joint associations of CAs with 3-month APNS were additive, with frequency of emotional abuse (RR = 2.03; 95% CI = 1.43-2.87) and bullying (RR = 1.44; 95% CI = 0.99-2.10) being the strongest predictors. Control variable analyses found that these associations were largely explained by pre-MVC histories of PTSD and MDE.

**Conclusions.** Although individuals who experience frequent emotional abuse and bullying in childhood have a heightened risk of experiencing APNS after an adult MVC, these associations are largely mediated by prior histories of PTSD and MDE.

#### Introduction

Most people experience a traumatic event at some time in their life (Kessler *et al.*, 2017). About one in four of these people develop an adverse posttraumatic neuropsychiatric sequelae (APNS) such as posttraumatic stress disorder (PTSD) or major depression (Kessler *et al.*, 2017). These APNS are associated with substantial psychological (Nichter *et al.*, 2019b), physical (Nichter *et al.*, 2019a) and economic (Atwoli *et al.*, 2015;

Greenberg *et al.*, 2015) burdens. Identifying risk factors could help prevent some of these APNS from occurring by targeting high-risk people experiencing traumas for preventive interventions.

Childhood adversities (CAs) are risk factors for APNS (McLaughlin et al., 2017). Nearly half of all U.S. children experience CAs (Green et al., 2010; Kessler et al., 2010). CAs predict numerous adult psychiatric disorders (Kessler et al., 2010). However, few longitudinal studies have examined CAs predicting APNS after a discrete adult traumatic event. Two recent studies did this, though, and found that CAs predicted increased risk of PTSD in the months following ED presentation with a traumatic event (Gould et al., 2021; Xie et al., 2022). These associations were found in one of the studies to be mediated by immediate stress responses (Gould et al., 2021) and in the other to be mediated by changes in thalamus nuclei volumes (Xie et al., 2022). We are aware of only one longitudinal study that examined the association of CAs with depression following trauma exposure (Wilson-Genderson et al., 2021). That association was significant and positive, but mediation was not examined.

In addition to their small number, prior longitudinal studies of CAs predicting APNS can be faulted for examining only total CA frequency scores (Gould et al., 2021; Xie et al., 2022) or a count of CA types (Wilson-Genderson et al., 2021). These approaches implicitly assume that each CA type confers the same risk for APNS. However, previous research in other populations suggests that CA types differ in their associations with adult APNS (McLaughlin et al., 2017). Specifically, non-longitudinal research found that childhood neglect and sexual abuse were most strongly associated with adult PTSD (McLaughlin et al., 2017). A related issue is that CA types often co-occur, raising the possibility not considered in previous research that interactions exist among different CA types in predicting adult APNS (Ziobrowski et al., 2020).

To address these limitations of previous research, we analysed data from a large prospective study of adults presenting at EDs following motor vehicle collision (MVC) to determine whether patient-reported CA history predicted APNS three months later, the amount of time traditionally used to define chronic PTSD (Feder et al., 2021). We first compared the association of ever experiencing each of six CA types with the outcome. We then investigated whether differential CA frequencies were important. We then used machine learning methods to determine whether interactions existed among the different CA types predicting APNS. Finally, we examined the extent to which the joint associations of the different CA types with 3-month APNS were explained by pre-MVC histories of PTSD and depression and mediated by more proximal associations with peritraumatic symptoms, 2-week PTSD and depression, and 8-week PTSD and depression. These possible mediation effects are important to understand to determine useful time windows for preventive interventions after trauma exposure.

#### **Methods**

### Sample

Data came from the Advancing Understanding of Recovery After Trauma (AURORA) study, an observational study of patients ages 18–75 presenting at 29 urban U.S. EDs within 72 h of trauma. Enrolment began September 2017. We focused on participants whose trauma was a MVC, by far the most common trauma

type in AURORA, and who completed all 2-week, 8-week and 3-month follow-up assessments by January 31, 2020. Other inclusion criteria were being able to speak and read English, oriented to time and place, able to comprehend the enrolment protocol, and in possession of a smartphone for >1 year. The roughly 5% of patients who were admitted to the hospital rather than released to home were initially excluded from the sample based on concerns that they would not be able to participate in prospective assessments. However, this restriction was subsequently relaxed to include patients who completed the ED assessment and were admitted for no more than 24 h (as of April 4, 2018) and then no more than 72 h (as of December 11, 2018). Patients with a solid organ injury Grade >1, significant haemorrhage or need for a chest tube or operation with general anaesthesia were excluded throughout because they were for the most part unable to complete the baseline assessment.

As described in detail elsewhere (McLean et al., 2020), after providing written informed consent, participants completed both an interviewer-administered assessment and a self-report questionnaire (SAQ) in the ED. Follow-up self-administered questionnaires were then completed 2-weeks, 8-weeks and 3-months post-MVC. The ED assessments took approximately 1 h to complete. Each follow-up SAQ took approximately 30 min to complete. All procedures were approved by the Institutional Review Boards of the participating institutions. Of the 2096 participants who presented after an MVC and completed the baseline assessment, 999 completed all three follow-up assessments (online Supplementary Fig. S1). This report focuses on these 999 participants.

#### Measures

#### Controls

We included two types of control variables in the analysis: sociodemographics and MVC characteristics. The socio-demographics assessed included age, race-ethnicity, sex, marital history, education and income. However, only the first three of these were used as controls in multivariable models, as the others might have been influenced by CAs and thus more likely to be mediators than confounders. A previous AURORA investigation found that three MVC characteristics predicted 3-month PTSD and/or major depressive episode (MDE), the two types of APNS considered here: any vehicle damage, concussion and severe pain reported in the ED (Joormann et al., 2022). Vehicle damage was reported by the patient in the ED. Concussion was assessed in the ED based on evidence of loss of consciousness, amnesia or disorientation (McLean et al., 2009). Self-rated global pain was reported on a 0-10 visual response scale (Farrar et al., 2001). Patients in the top 40% were categorised as having severe pain based on prior analyses documenting that this dichotomisation best captures the association of the 0-10 pain scale with the 3-months outcome (described below) (Joormann et al., 2022).

#### CAS

In the 2-week survey, participants reported how often they experienced 6 types of CAs during their childhoods on a five-point scale ranging from never (0) to very often (4). Physical abuse, sexual abuse, emotional abuse, physical neglect and emotional neglect were assessed with items from the Childhood Trauma Questionnaire (Bernstein *et al.*, 2003). The physical abuse items asked participants how often people in their family hit them 'so hard that it left marks and bruises' and how often

they were 'physically abused' (Cronbach's  $\alpha = 0.90$ ). Sexual abuse was assessed by asking how often someone tried to make them 'do sexual things or watch sexual things,' how often someone 'molested' them, and how often they were 'sexually abused' (Cronbach's  $\alpha = 0.95$ ). Emotional abuse was assessed by asking how often people in their family 'said hurtful or insulting things' to them and how often they were 'emotionally abused' (Cronbach's  $\alpha = 0.84$ ). Physical neglect was assessed by asking how often someone 'took care of and protected' them and how often there was someone to take them to the doctor if they needed it (Cronbach's  $\alpha = 0.87$ ). Emotional neglect was assessed by asking how often there was someone that helped them feel important or special and how often they felt loved (Cronbach's  $\alpha = 0.93$ ). Bullying was assessed using two questions from the screening questionnaire for the Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II; First et al., 1997): how often other kids called them names or said mean things about them; and how often other kids threatened to hit or hurt them (Cronbach's  $\alpha = 0.80$ ). In each of these cases, respondents were asked how often these CAs occurred 'during your childhood,' with no age range used to define 'childhood.' Nor were separate questions asked about frequencies at different parts of childhood.

0-4 responses to questions within CA types were summed and responses to the neglect questions were reversed because they were expressed in positive terms, leading to high scale scores representing high CA frequency. Participants with a score of 1+ for a CA type were categorised as having experienced that type. A standardised score was then created by subtracting 1 from the total score for each CA type and dividing by the range so that each scale had a standard range between 0 and 1. As some scales were based on items that differed in level of abstraction (e.g., the physical abuse scale included an abstract question about frequency of being 'physically abused' and a more concrete question about frequency of being 'hit so hard that it left marks and bruises'), responses to the concrete question were, in effect, double counted because they were presumably included when the respondent reported frequency of the more general category. This was less than ideal from a psychometric perspective but was inherent in the scales used in the study.

### 3-month APNS

The APNS outcome was defined as meeting criteria for either PTSD or MDE in the 3-month survey. This outcome was determined based on evidence presented previously that 90 + % of respondents who met criteria for either 3-month PTSD or MDE had PTSD, that a great many significant predictors were found for having PTSD and/or MDE, but that we were unable to find significant predictors either of (i) depression without PTSD in the total sample or (ii) comorbid MDE in the subsample of respondents with PTSD (Joormann *et al.*, 2022).

PTSD was assessed with the PTSD Checklist for DSM-5 (PCL-5; Blevins *et al.*, 2015) (Cronbach's  $\alpha$  = 0.96). A 30-day recall period was used in administration in the ED, 8-week, and 3-month surveys, whereas a 2-week recall period was used in the 2-week survey. In the latter cases, participants were asked about symptoms occurring 'either because of the event that brought you into the ED or any other highly stressful experience that ever happened to you.' The decision to administer the scale in this way rather than ask separately about symptoms due to the focal trauma was part of a more general strategy of minimising question repetition to reduce respondent burden. There was also the concern that prior research found many patients with a history of multiple

trauma exposures unable to sort out the trauma(s) causing their PTSD symptoms (Karam *et al.*, 2014). Lifetime PTSD prior to the MVC was assessed using the same scale. In each case, a conservative PCL-5 38 + threshold (Zuromski *et al.*, 2019) was used to define probable PTSD (Zuromski *et al.*, 2019).

MDE in the past 30 days was assessed in the ED, 8-week, and 3-month survey with the Patient-Reported Outcomes Measurement Information System (PROMIS) Depression Short-Form 8b (Cella *et al.*, 2010; Cronbach's  $\alpha$  = 0.95). MDE with a 2-week recall period was assessed with the same scale in the 2-week survey. *T*-score transformation of scores was done based on PROMIS norms (PROMIS Cooperative Group, 2021). Based on the conservative assumption of a 5% MDE point prevalence in the general population, we set the diagnostic threshold to be 1.5 standard deviations above the general population mean to define MDE and in the range of 1.0–1.5 standard deviations above the general population mean to define subthreshold MDE. Lifetime MDE prior to the MVC was assessed with the self-report version of the Composite International Diagnostic Interview (Kessler and Üstün, 2004).

#### Mediation through intervening APNS

As noted in the introduction, we examined effects of pre-MVC lifetime histories of PTSD and MDE in explaining the associations of CAs with 3-month APNS. We also examined mediation effects through peritraumatic distress and dissociation (in the ED) and PTSD and MDE in the 2-week and 8-week surveys. Peritraumatic distress and dissociation were found in previous research to predict APNS (Thomas *et al.*, 2012; Lebois *et al.*, 2022). Peritraumatic distress was assessed with eight items from the Peritraumatic Distress Inventory (PDI; Brunet *et al.*, 2001). Peritraumatic dissociation was assessed with the five-item revised Michigan Critical Events Perception Scale (CEPS; Michaels *et al.*, 1999). The restriction of the PDI assessment to only 8 PDI items was part of a more general strategy of truncating long baseline scales using rational item selection to reduce respondent burden.

## Analysis methods

An inverse probability of response weight that adjusted for differences in baseline characteristics between participants in the final analysis sample v. baseline participants who did not complete all follow-up surveys (Mansournia and Altman, 2016) was used to adjust for loss to follow-up. Analysis began by comparing the distributions of socio-demographics, MVC characteristics, and CAs among participants with and without 3-month APNS in this weighted sample. We then estimated Poisson regression models with robust standard errors (Zou, 2004) to estimate risk ratios (RRs; Knol et al., 2012) for 3-month APNS. All models adjusted for age, race-ethnicity, sex, any vehicle damage, concussion, and severe pain reported in the ED. In Model A, the CA predictor was either a dummy variable for any occurrence (even if rarely) of the CA or the continuous variable for frequency of occurrence. Model B included both these variables in the same model. Model C included all 12 CA variables (i.e., the 6 pairs of ever v. never dichotomies and continuous frequency variables). We estimated this combined model in a 70% training sample and calculated area under the receiver operating characteristic curve (AUC) in the remaining 30% test sample.

Because CAs often co-occur (Ziobrowski et al., 2020) and were all positively correlated in our sample (online Supplementary Table S1), we ran an XGBoost machine learning model (Chen

and Guestrin, 2016) to search for interactions in predicting 3-month APNS. This model was estimated in the same 70% training sample as mentioned above and model accuracy was evaluated in the remaining 30% test sample. We then added the predicted probabilities from this XGBoost model to Model C and compared the test sample AUC to that of Model C.

Given that the most complete CA model included a substantial number of highly correlated measures, we estimated a lasso (least absolute shrinkage and selection operator) penalised regression model to generate the smallest subset of CA variables that captured the joint predictive associations among the many CA variables with 3-month APNS. The lasso model was estimated in the 70% training sample and evaluated in the 30% test sample. In Model D, we included only the CA variables that were selected by the lasso model and again calculated the model's AUC in the 30% test sample.

Once the final specification was estimated in Model D, we sequentially added pre-MVC histories of PTSD and MDE, peritraumatic symptoms assessed in the ED, 2-week PTSD and MDE, and 8-week PTSD and MDE to the model to investigate how much these controls explained the overall associations of CAs with 3-month APNS. In doing this, we built on our previously published derivation of functional forms of these control variables in predicting 3-month APNS (Joormann *et al.*, 2022). We calculated the AUCs of the sequential models in the 30% test sample.

The XGBoost models were estimated in R, version 4.0.5 (R Core Team, 2021). All other analyses were conducted using SAS statistical software, version 9.4 (SAS Institute Inc., 2013).

#### Results

#### Sample characteristics and outcome prevalence

Most respondents were female (68.0%) and non-Hispanic Black (52.6%) (Table 1). 24.0% were ages 18–24, 31.9% 25–34, 28.0% 35–49 and 16.1% ages 50+. Most (90.9%) respondents reported having had at least one CA. The most common CA was bullying (79.1%) followed by emotional abuse (65.4%) and emotional neglect (51.4%). Childhood sexual abuse was the least common CA (36.9%). Prevalence other than for emotional neglect was higher among participants with than without 3-month APNS. Fewer than 50% of respondents who ever experienced a CA reported frequency in the higher two of the four positive response categories (22.6–41.4%; Table 2).

At 3 months post-MVC, a weighted 26.9% of respondents had APNS (i.e., PTSD and/or MDE), including 25.3% with PTSD and 11.6% with MDE (Table 3). This is about one-fourth lower than the 37.0% of respondents who had APNS in the 2-week assessment and 32.1% in the 8-week assessment. Conditional probabilities of APNS persistence to 3-months from 2-weeks (54.2%) and 8-weeks (65.4%) were considerably higher than conditional probabilities of later onset through 3-months given absence of APNS at 2-weeks (10.8%) or 8-weeks (8.7%).

#### Associations of CAs with 3-month APNS

Except for the emotional neglect dichotomy, each CA variable was univariably associated significantly with 3-month APNS, (RR = 1.3-2.4) (Table 4, Model A). In Model B, frequencies but not dichotomies of physical abuse, emotional abuse, emotional neglect and bullying were significant predictors (RRs from 1.8 to

Table 1. Distribution of socio-demographics, motor vehicle collision characteristics and childhood adversities

	Total sample ( <i>n</i> = 999)		3-mon	nts without th APNS 724)	Participa 3-mont ( <i>n</i> =		
	%	(n)	%	(n)	%	(n)	$\chi^2$
Socio-demographics							
Female	68.0	(713)	66.3	(505)	72.8	(208)	3.8
Age							0.8
50+	16.1	(190)	16.5	(142)	14.9	(48)	
35-49	28.0	(295)	27.5	(209)	29.3	(86)	
25-34	31.9	(295)	31.6	(211)	32.9	(84)	
18-24	24.0	(219)	24.4	(162)	22.9	(57)	
Race-ethnicity							2.8
Non-Hispanic White	32.3	(323)	32.0	(231)	33.2	(92)	
Non-Hispanic Black	52.6	(534)	53.1	(391)	51.3	(143)	
Hispanic	10.7	(100)	10.1	(68)	12.4	(32)	
Other	4.4	(42)	4.9	(34)	3.0	(8)	
Marital history							0.1
Married or cohabitating	41.4	(417)	41.2	(301)	41.9	(116)	
Previously married	13.0	(144)	12.9	(104)	13.3	(40)	
Never married	45.6	(438)	45.9	(319)	44.8	(119)	
Education							4.0
Less than high school	11.4	(113)	11.0	(77)	12.7	(36)	
High school grad	25.8	(247)	26.6	(183)	23.6	(64)	
Less than college	42.8	(427)	41.4	(300)	46.6	(127)	
College or more	20.0	(212)	21.1	(164)	17.1	(48)	
Income							9.2*
Greater than \$35 000	36.6	(358)	39.3	(281)	29.3	(77)	
\$ 19 000-\$ 35 000	31.9	(320)	31.2	(227)	33.8	(93)	
Less than \$ 19 000	31.6	(321)	29.6	(216)	37.0	(105)	
MVC characteristics							
Any vehicle damage	92.8	(927)	92.0	(666)	94.9	(261)	2.5
Concussion	27.8	(270)	25.1	(175)	35.3	(95)	10.2
Severe pain in the ED	40.4	(405)	34.3	(250)	57.0	(155)	42.2
Childhood adversities							
Any adversity	90.9	(905)	89.7	(646)	94.1	(259)	4.4*
Any physical abuse	42.6	(433)	39.7	(291)	50.4	(142)	9.2*
Any sexual abuse	36.9	(377)	32.0	(237)	50.3	(140)	28.2
Any emotional abuse	65.4	(654)	61.8	(447)	75.3	(207)	15.9
Any physical neglect	45.4	(442)	42.6	(295)	53.2	(147)	9.0*
Any emotional neglect	51.4	(501)	49.9	(348)	55.5	(153)	2.5
Any bullying	79.1	(798)	77.2	(567)	84.3	(231)	6.0*

APNS, adverse posttraumatic neuropsychiatric sequelae, defined as meeting criteria for posttraumatic stress disorder and/or major depressive episode; ED, emergency department; MVC, motor vehicle collision. Note: %'s and  $\chi^2$ 's are weighted.

<sup>\*</sup>Significant at the 0.05 level, two-sided test.

**Table 2.** Frequency of individual childhood adversity items (n = 999)

	Never		Rarely		Sometimes		Often		Very Often	
	%	(n)	%	(n)	%	(n)	%	(n)	%	(n)
Physical abuse										
Hit so hard left bruises	61.1	(603)	14.9	(150)	14.1	(144)	5.1	(53)	4.8	(49)
Physically abused	67.5	(671)	11.2	(111)	11.4	(115)	4.2	(43)	5.7	(59)
Sexual abuse										
Sexual things	68.2	(673)	9.8	(100)	11.7	(117)	5.8	(62)	4.5	(47)
Molested	68.9	(676)	10.9	(112)	9.5	(97)	5.4	(58)	5.3	(56)
Sexually abused	70.6	(695)	10.2	(105)	8.2	(84)	5.1	(53)	5.9	(62)
Emotional abuse										
Insults	40.4	(400)	20.3	(203)	20.9	(204)	9.9	(102)	8.5	(90)
Emotionally abused	49.7	(492)	11.2	(107)	18.4	(181)	8.9	(92)	11.9	(127)
Physical neglect										
Cared and protected	4.8	(44)	6.7	(69)	13.8	(138)	16.0	(153)	58.7	(595)
Taken to doctor	3.8	(34)	4.8	(48)	10.8	(104)	16.1	(156)	64.6	(657)
Emotional neglect										
Felt special	5.6	(54)	10.0	(101)	14.7	(144)	17.0	(164)	52.8	(536)
Felt loved	4.3	(41)	8.9	(91)	17.0	(165)	15.8	(150)	54.0	(552)
Bullying										
Called names	23.0	(222)	19.5	(193)	27.5	(278)	13.7	(138)	16.3	(168)
Kids threatened to hurt	39.3	(383)	23.7	(243)	23.4	(234)	7.4	(75)	6.3	(64)

Note: %'s are weighted.

2.4), indicating that RR of rarely  $\nu$ . never experiencing these CAs was the same as the RRs of higher pairs of response categories. Experiencing any sexual abuse but not frequency, in comparison, was associated with increased risk of 3-month APNS (RR = 1.4).

When all CA variables were included in the same model (Model C), only emotional abuse frequency remained statistically significant (RR = 2.1). The AUC for this model was 0.631 (Standard Error [s.e.] = 0.039) in the test sample. The XGBoost model that contained all CA variables had a lower AUC (0.624 [s.e. = 0.040]). The AUC of the model that combined XGBoost predicted probabilities to Model C was only minimally higher (0.640 [s.e. = 0.038]; online Supplementary Fig. S2), indicating that interactions among CAs are not of great importance in predicting 3-month APNS.

Based on this last result, we estimated a lasso model for CA measures (both dichotomies and continuous frequency measures) and controls (Model D). Only three CA variables were selected by that model: frequencies of emotional abuse (RR = 2.1) and bullying (RR = 1.5) and the dichotomy for any physical abuse (RR = 0.7). AUC was 0.679 (s.e. = 0.036). The RRs of the two frequency variables were somewhat smaller than their univariable associations. The RR of physical abuse, in comparison, was opposite its univariable association. Based on this inconsistency, we judged this predictor to be an aberration and excluded it from the final additive prediction model. The RRs for frequency of emotional abuse (RR = 2.0) and bullying (RR = 1.4) in that model were close to their values in Model D, but bullying was no longer statistically significant. AUC was 0.640 (s.e. = 0.038).

Controlling for pre-MVC, peritraumatic, 2-week and 8-week disorders

The RR for emotional abuse frequency was substantially attenuated in the final model when adjusting for pre-MVC histories of PTSD and MDE (Table 5) and the RR for bullying frequency became close to the null. AUC substantially increased to 0.763 (s.e. = 0.029). Further sequential adjustment for peritraumatic symptoms, 2-week PTSD and MDE and 8-week PTSD and MDE continued to weaken the associations of emotional abuse and bullying with the outcome. AUC of the final model was 0.875 (s.e. = 0.021).

### **Discussion**

CA prevalence in AURORA was much higher than in national general population surveys (Green *et al.*, 2010; Centers for Disease Control and Prevention, 2020). This might be because patients who come to EDs after MVCs without serious injuries and/or who agree to be in studies like AURORA have high CA prevalence. Consistent with this possibility, a prior AURORA report noted that pre-MVC lifetime PTSD and MDE were substantially higher than in general population surveys (Joormann *et al.*, 2022). Although we have no way to investigate causes, it is noteworthy that prior research has shown that people who experience MVCs have high prevalence of substance problems (Bogstrand *et al.*, 2012) and that people who choose to go to EDs after traumas are more likely than those who do not to have preexisting mental health problems (Krieg *et al.*, 2016).

**Table 3.** Associations of childhood adversities with 3-month APNS (n = 999)

	M	Model A <sup>a</sup>		odel B <sup>b</sup>	Mo	Model C <sup>c</sup>		Model D <sup>d</sup>		
	RR	(95% CI)	RR	(95% CI)	RR	(95% CI)	RR	(95% CI)		
Physical abuse										
Any	1.3*	(1.1-1.6)	1.0	(0.7-1.3)	0.7	(0.5-1.0)	0.7*	(0.6-1.0)		
Frequency	2.0*	(1.5-2.6)	2.0*	(1.3-2.9)	1.0	(0.6-1.6)	-	-		
Sexual abuse										
Any	1.6*	(1.3-2.0)	1.4*	(1.1-1.9)	1.3	(1.0-1.7)	1.3	(1.0-1.7)		
Frequency	2.0*	(1.5-2.6)	1.3	(0.9-2.0)	0.9	(0.6-1.4)	1.0	(0.6-1.5)		
Emotional abuse										
Any	1.5*	(1.2-1.9)	1.0	(0.7-1.4)	1.0	(0.7-1.4)	-	-		
Frequency	2.4*	(1.9-3.2)	2.4*	(1.7-3.4)	2.1*	(1.3-3.5)	2.1*	(1.3-3.2)		
Physical neglect										
Any	1.4*	(1.1-1.7)	1.2	(0.9–1.5)	1.3	(0.9-1.8)	-	-		
Frequency	1.8*	(1.3-2.6)	1.5	(1.0-2.4)	1.3	(0.7-2.4)	1.2	(0.8-1.8)		
Emotional neglect										
Any	1.2	(0.9-1.4)	0.9	(0.7–1.2)	0.7	(0.5-1.0)	-	-		
Frequency	1.6*	(1.2-2.3)	1.8*	(1.2-2.9)	0.9	(0.5-1.8)	-	-		
Bullying										
Any	1.4*	(1.0-1.9)	1.0	(0.7-1.4)	1.0	(0.7-1.4)	-	-		
Frequency	2.2*	(1.6-3.0)	2.2*	(1.6-3.2)	1.5	(1.0-2.3)	1.5*	(1.0-2.2)		
AUC (s.e.)					0.631 (0.0	39)	0.632 (0.0	39)		

APNS, adverse posttraumatic neuropsychiatric sequelae, defined as meeting criteria for posttraumatic stress disorder and/or major depressive episode; CI, confidence interval; RR, risk ratio; s.e., standard error.

**Table 4.** Prevalence of PTSD, MDE and APNS in 2-week, 8-week and 3-month assessments (n = 999)

	PT	SD	M	DE	APNS (PTSD or MDE)		
	%	(s.E.)	%	(s.E.)	%	(s.e.)	
2-week	36.2	(1.6)	12.8	(1.1)	37.0	(1.6)	
8-week	31.1	(1.5)	12.2	(1.1)	32.1	(1.5)	
3-month							
Total	25.3	(1.4)	11.6	(1.0)	26.9	(1.4)	
2-week yes	52.5	(2.7)	47.1	(4.5)	54.2	(2.7)	
2-week no	9.9	(1.2)	6.4	(0.8)	10.8	(1.3)	
8-week yes	64.9	(2.9)	55.3	(4.7)	65.4	(2.9)	
8-week no	7.5	(1.0)	5.5	(0.8)	8.7	(1.1)	

PTSD, posttraumatic stress disorder; MDE, major depressive episode; APNS, adverse posttraumatic neuropsychiatric sequelae, defined as meeting criteria either for PTSD and/or MDE.

Note: %'s are weighted.

Both substance problems and mental disorders, as noted above, are associated with CAs (Petruccelli et al., 2019).

Although we found that most CAs had univariable associations with 3-month APNS, multivariable analyses revealed two important refinements. First, XGBoost showed that interactions among CAs did not meaningfully improve prediction accuracy. Second, lasso showed that two of the six continuous CA measures captured most of the significant linear-additive associations of all CA measures with 3-month APNS. Dichotomous CA measures were generally not important.

In interpreting the second of these results, it is important to recognise that the lasso is designed to provide a parsimonious characterisation of joint additive associations of highly intercorrelated predictors (Freijeiro-González *et al.*, 2021). This means that the variables selected are not necessarily the most important causally but explain the most variance in the outcome. It is noteworthy in this regard that emotional abuse, the CA selected as most important by lasso, had the highest RR in the univariable frequency models and a comparatively high prevalence. Prior research has shown that emotionally abused children are often also bullied by peers (Holt *et al.*, 2008; Martín-Babarro *et al.*, 2021). This is consistent

<sup>&</sup>lt;sup>a</sup>Models included only one childhood adversity variable (any or frequency) and controlled for age, race, sex, any vehicle damage, concussion and severe pain reported in the emergency department.

<sup>&</sup>lt;sup>b</sup>Models included variables for any and frequency of one childhood adversity and controlled for age, race, sex, any vehicle damage, concussion and severe pain reported in the emergency department.

<sup>&#</sup>x27;Models included all childhood adversity variables and controlled for age, race, sex, any vehicle damage, concussion and severe pain reported in the emergency department.

<sup>&</sup>lt;sup>d</sup>Models included childhood adversity variables that were identified by a lasso model and controlled for age, race, sex, any vehicle damage, concussion and severe pain reported in the emergency department.

Note: Risk ratios were estimated using Poisson regression models with robust standard errors.

<sup>\*</sup>Significant at the 0.05 level, two-sided test.

**Table 5.** Associations of frequency of emotional abuse and frequency of bullying with 3-month APNS adjusting for pre-MVC PTSD and MDE histories, peritraumatic symptoms and 2-week and 8-week post-MVC PTSD and MDE (n = 999)

	Frequency of emotional abuse		Frequency of bullying			
	RR	(95% CI)	RR	(95% CI)	AUC	(s.E.)
Final model <sup>a</sup>	2.0*	(1.4-2.9)	1.4	(1.0-2.1)	0.641	(0.038)
Adjusting for pre-MVC PTSD and MDE histories <sup>b</sup>	1.4*	(1.0-1.9)	1.1	(0.8-1.5)	0.763	(0.029)
Adjusting for pre-MVC PTSD and MDE histories and peritraumatic symptoms <sup>c</sup>	1.3	(1.0-1.8)	1.1	(0.8-1.5)	0.768	(0.029)
Adjusting for pre-MVC PTSD and MDE histories, peritraumatic symptoms and 2-week disorders <sup>d</sup>	1.2	(0.9-1.6)	0.9	(0.7-1.3)	0.785	(0.029)
Adjusting for pre-MVC PTSD and MDE histories, peritraumatic symptoms, 2-week disorders and 8-week disorders <sup>e</sup>	1.1	(0.9–1.5)	1.0	(0.7-1.3)	0.875	(0.021)
Adjusting for pre-MVC PTSD and MDE histories, peritraumatic symptoms and any 2-week or 8-week disorders <sup>f</sup>	1.1	(0.9–1.5)	1.0	(0.7-1.3)	0.838	(0.022)

APNS, adverse posttraumatic neuropsychiatric sequelae, defined as meeting criteria for posttraumatic stress disorder and/or major depressive episode; CI, confidence interval; MDE, major depressive episode; MVC, motor vehicle collision; PTSD, posttraumatic stress disorder; RR, risk ratio; s.E., standard error.

with the high correlation in AURORA between emotional abuse and bullying (online Supplementary Table S1). Indeed, 3 of the 4 highest correlations among CA measures involved emotional abuse, which is consistent with the lasso model selecting emotional abuse as the CA type most important in characterising overall CA exposure. Although the variables selected by the lasso model are not necessarily causal, our findings on emotional abuse align with previous research that found emotional abuse to be more strongly associated with internalising and externalising psychopathology than physical and sexual abuse (Heleniak *et al.*, 2016). Furthermore, compared with physical and sexual abuse, childhood emotional abuse has been found to be more strongly associated with emotional dysregulation including emotional sensitivity and arousal (Heleniak *et al.*, 2016), which are risk factors for APNS.

Once a parsimonious CA model was determined, the control variable analysis extended prior prospective studies of mediators (Gould et al., 2021; Xie et al., 2022) to document even more distal associations: specifically, to show that pre-trauma lifetime histories of PTSD and MDE explained most of the gross associations between CAs and 3-month APNS in AURORA. This raises the possibility that a meaningful proportion of the APNS found among patients presenting at EDs after MVCs are associated with chronic-recurrent APNS prior to the MVCs. If so, we would expect that longer-term prospective studies following the AURORA cohort over many years would find high rates of APNS recurrence associated with subsequent traumas.

#### Limitations

The study has several limitations. First, our sample was confined to urban EDs and patients who agreed to participate in a long-

term prospective study. Findings might not generalise to other settings or segments of the population. Our sample was also limited to participants who were either discharged to home or admitted for only short hospitalisations. We also excluded patients with serious injuries that made it impossible to participate in the baseline assessment. However, as more than 95% of patients who present to the ED after an MVC are discharged to home (McLean et al., 2020), this exclusion is much less noteworthy than that most eligible patients failed to consent or to complete all follow-up assessments. Second, CAs were of necessity retrospectively self-reported. Subjective CA reports are known to be more predictive of psychopathology than objective measures (Danese and Widom, 2020), raising the possibility of systematic recall bias. This bias might have been exacerbated by CAs being assessed in the 2-week follow-up SAQ. Third, the AURORA study did not assess all CA types. Fourth, the PTSD and MDE measures came from self-report scales rather than clinical interviews. Fifth, the PTSD assessment did not specify that the MVC was the trauma causing symptoms, raising the possibility that other prior or subsequent traumatic events accounted for at least some of the PTSD. Sixth, other types of psychopathology were not considered. Substance use disorder is one of these that might be of special importance given the important role of substance use in MVCs.

#### Conclusions

Within the context of these limitations, we advanced prior CA-APNS research in several ways. First, we found that frequency measures are for the most part more important than dichotomous ever  $\nu$ . never measures of CA exposure in predicting 3-month APNS. Second, we found that interactive associations among

<sup>&</sup>lt;sup>a</sup>Models included frequency of emotional abuse and frequency of bullying and controlled for age, race, sex, any vehicle damage, concussion and severe pain reported in the emergency department.

bModels included frequency of emotional abuse and frequency of bullying and controlled for age, race, sex, any vehicle damage, concussion, severe pain reported in the emergency department, and pre-MVC lifetime histories of PTSD and MDE.

<sup>&</sup>lt;sup>c</sup>Models included frequency of emotional abuse and frequency of bullying and controlled for age, race, sex, any vehicle damage, concussion, severe pain reported in the emergency department, pre-MVC histories of PTSD and MDE, and peritraumatic distress and dissociation.

dModels included frequency of emotional abuse and frequency of bullying and controlled for age, race, sex, any vehicle damage, concussion, severe pain reported in the emergency department, pre-MVC histories of PTSD and MDE, peritraumatic distress and dissociation and 2-week disorders.

eModels included frequency of emotional abuse and frequency of bullying and controlled for age, race, sex, any vehicle damage, concussion, severe pain reported in the emergency department, pre-MVC histories of PTSD and MDE, peritraumatic distress and dissociation, 2-week disorders and 8-week disorders.

fModels included frequency of emotional abuse and frequency of bullying and controlled for age, race, sex, any vehicle damage, concussion, severe pain reported in the emergency department, pre-MVC histories of PTSD and MDE, peritraumatic distress and dissociation, 2-week disorders, 8-week disorders and interactions between 2-week and 8-week disorders. *Note*: Risk ratios were estimated using Poisson regression models with robust standard errors.

<sup>\*</sup>Significant at the 0.05 level, two-sided test.

CAs do not improve importantly on a linear-additive model of joint CA predictive associations, although the same might not be true for associations of CAs with other psychiatric disorders in other populations (e.g., Husky *et al.*, 2022). Third, we documented that the associations of CAs with 3-month APNS were largely explained by pre-MVC histories of PTSD and MDE, raising the intriguing possibility that many patients in studies of acute APNS might actually have chronic-recurrent pre-trauma APNS histories. Other recent epidemiological studies have pointed to the same possibility (Liu *et al.*, 2017; Kessler *et al.*, 2018). If this is the case, longer-term prospective studies will be needed to trace out important long-term causal pathways.

Overall, our findings suggest that people who frequently experienced emotional abuse and bullying may be at especially high risk of developing APNS after an MVC. Screening for these CAs in the ED could help identify individuals who need preventive services, and this information may also be helpful for treating patients who develop APNS following MVC who may have problems with emotional regulation.

Supplementary material. The supplementary material for this article can be found at  $\frac{https://doi.org/10.1017/S2045796022000798}{https://doi.org/10.1017/S2045796022000798}$ 

Financial support. The investigators wish to thank the trauma survivors participating in the AURORA Study. Their time and effort during a challenging period of their lives make our efforts to improve recovery for future trauma survivors possible. This project was supported by NIMH under U01MH110925, the U.S. Army MRMC, One Mind and The Mayday Fund. The content is solely responsibility of the authors and does not necessarily represent the official views of any of the funders. Support for title page creation and format was provided by AuthorArranger, a tool developed at the National Cancer Institute. Data and/or research tools used in the preparation of this manuscript were obtained from the National Institute of Mental Health (NIMH) Data Archive (NDA). NDA is a collaborative informatics system created by the National Institutes of Health to provide a national resource to support and accelerate research in mental health. Dataset identifier(s): NIMH Data Archive Digital Object Identifier (DOI) 10.15154/1526529. This manuscript reflects the views of the authors and may not reflect the opinions or views of the NIH or of the Submitters submitting original data to NDA. Dr Pizzagalli was partially supported by R01 MH095809.

Conflict of interest. Dr Neylan has received research support from NIH, VA and Rainwater Charitable Foundation and consulting income from Jazz Pharmaceuticals. In the last three years Dr Clifford has received research funding from the NSF, NIH and LifeBell AI, and unrestricted donations from AliveCor Inc, Amazon Research, the Center for Discovery, the Gates Foundation, Google, the Gordon and Betty Moore Foundation, MathWorks, Microsoft Research, Nextsense Inc, One Mind Foundation, Otsuka US, the Rett Research Foundation and Samsung Research. Dr Clifford has financial interest in AliveCor Inc and Nextsense Inc. He also is the CTO of MindChild Medical and CSO of LifeBell AI and has ownership in both companies. These relationships are unconnected to the current work. Dr Rauch reports grants from NIH during the conduct of the study; personal fees from SOBP (Society of Biological Psychiatry) paid role as secretary, other from Oxford University Press royalties, other from APP (American Psychiatric Publishing Inc.) royalties, other from VA (Veterans Administration) per diem for oversight committee, and other from Community Psychiatry/Mindpath Health paid board service, including equity outside the submitted work; other from National Association of Behavioral Healthcare for paid Board service; and Leadership roles on Board or Council for SOBP, ADAA (Anxiety and Depression Association of America), and NNDC (National Network of Depression Centers). Dr Sheikh has received funding from the Florida Medical Malpractice Joint Underwriter's Association Dr Alvin E. Smith Safety of Healthcare Services Grant; Allergan Foundation; the NIH/NIA-funded Jacksonville Aging Studies Center (JAX-ASCENT; R33AG05654); and the Substance Abuse and Mental Health Services Administration (1H79TI083101-01); and the Florida Blue Foundation. Dr Jones has no

competing interests related to this work, though he has been an investigator on studies funded by AstraZeneca, Vapotherm, Abbott, and Ophirex. Dr Joormann receives consulting payments from Janssen Pharmaceuticals. Dr Barch has received function from the NIMH, NIDA, and the American Foundation for Suicide Prevention and consults for Boehringer-Ingelheim. Over the past 3 years, Dr Pizzagalli has received consulting fees from Albright Stonebridge Group, Boehringer Ingelheim, Compass Pathways, Concert Pharmaceuticals, Engrail Therapeutics, Neumora Therapeutics (former BlackThorn Therapeutics), Neurocrine Biosciences, Neuroscience Software, Otsuka Pharmaceuticals and Takeda Pharmaceuticals; honoraria from the Psychonomic Society (for editorial work) and Alkermes and research funding from NIMH, Dana Foundation, Brain and Behavior Research Foundation and Millennium Pharmaceuticals. In addition, he has received stock options from Neumora Therapeutics (former BlackThorn Therapeutics), Compass Pathways, Engrail Therapeutics and Neuroscience Software. Dr Harte has no competing interests related to this work, though in the last three years he has received research funding from Aptinyx and Arbor Medical Innovations and consulting payments from Aptinyx, Heron Therapeutics and Eli Lilly. Dr Elliott reports support from the National Institutes of Health (NIH) through Grant Numbers R01HD079076 & R03HD094577: Eunice Kennedy Shriver National Institute of Child Health & Human Development; National Center for Medical Rehabilitation Research. He also reports funding from New South Wales Health, Spinal Cord Injury Award (2020-2025) and consulting fees (< \$15 000 per annum) from Orofacial Therapeutics, LLC. Dr Ressler has performed scientific consultation for Bioxcel, Bionomics, Acer, Takeda and Jazz Pharma; serves on Scientific Advisory Boards for Sage and the Brain Research Foundation, and he has received sponsored research support from Takeda, Brainsway and Alto Neuroscience. Dr Koenen's research has been supported by the Robert Wood Johnson Foundation, the Kaiser Family Foundation, the Harvard Center on the Developing Child, Stanley Center for Psychiatric Research at the Broad Institute of MIT and Harvard, the National Institutes of Health, One Mind, the Anonymous Foundation and Cohen Veterans Bioscience. She has been a paid consultant for Baker Hostetler, Discovery Vitality and the Department of Justice. She has been a paid external reviewer for the Chan Zuckerberg Foundation, the University of Cape Town and Capita Ireland. She has had paid speaking engagements in the last three years with the American Psychological Association, European Central Bank. Sigmund Freud University - Milan, Cambridge Health Alliance and Coverys. She receives royalties from Guilford Press and Oxford University Press. In the past 3 years, Dr Kessler was a consultant for Cambridge Health Alliance, Canandaigua VA Medical Center, Holmusk, Partners Healthcare, Inc., RallyPoint Networks, Inc. and Sage Therapeutics. He has stock options in Cerebral Inc., Mirah, PYM and Roga Sciences.

**Ethical standards.** The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Availability of data and materials. The data that support the findings of this study will eventually be openly available at the NIMH National Data Archive at <a href="https://nda.nih.gov/edit\_collection.html?id=2526">https://nda.nih.gov/edit\_collection.html?id=2526</a>, reference number 2526.

#### References

Atwoli L, Stein DJ, Koenen KC and McLaughlin KA (2015) Epidemiology of posttraumatic stress disorder: prevalence, correlates and consequences. *Current Opinion in Psychiatry* **28**, 307–311.

Bernstein DP, Stein JA, Newcomb MD, Walker E, Pogge D, Ahluvalia T, Stokes J, Handelsman L, Medrano M, Desmond D and Zule W (2003)

Development and validation of a brief screening version of the Childhood Trauma Questionnaire. Child Abuse & Neglect 27, 169–190.

Blevins CA, Weathers FW, Davis MT, Witte TK and Domino JL (2015) The posttraumatic stress disorder checklist for DSM-5 (PCL-5): development and initial psychometric evaluation. *Journal of Traumatic Stress* 28, 489–498.

Bogstrand ST, Gjerde H, Normann PT, Rossow I and Ekeberg Ø (2012)
Alcohol, psychoactive substances and non-fatal road traffic accidents − a case-control study. BMC Public Health 12, 734.

Brunet A, Weiss DS, Metzler TJ, Best SR, Neylan TC, Rogers C, Fagan J and Marmar CR (2001) The peritraumatic distress inventory: a proposed measure of PTSD criterion A2. The American Journal of Psychiatry 158, 1480–1485.

- Cella D, Riley W, Stone A, Rothrock N, Reeve B, Yount S, Amtmann D, Bode R, Buysse D, Choi S, Cook K, DeVellis R, DeWalt D, Fries JF, Gershon R, Hahn EA, Lai J-S, Pilkonis P, Revicki D, Rose M, Weinfurt K and Hays R (2010) The Patient-Reported Outcomes Measurement Information System (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005–2008. *Journal of Clinical Epidemiology* 63, 1179–1194.
- Centers for Disease Control and Prevention (2020) BRFSS ACE Data.

  Available at <a href="https://www.cdc.gov/violenceprevention/aces/ace-brfss.html">https://www.cdc.gov/violenceprevention/aces/ace-brfss.html</a> (Accessed 14 November 2022).
- Chen T and Guestrin C (2016) XGBoost: A scalable tree boosting system.
  Proceedings of the 22nd ACM SIGKDD International Conference on Knowledge Discovery and Data Mining. Available at https://dl.acm.org/doi/pdf/10.1145/2939672.2939785 (Accessed 12 November 2022).
- Danese A and Widom CS (2020) Objective and subjective experiences of child maltreatment and their relationships with psychopathology. *Nature Human Behaviour* 4, 811–818.
- Farrar JT, Young Jr JP, LaMoreaux L, Werth JL and Poole MR (2001)
  Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. *Pain* 94, 149–158.
- Feder A, Costi S, Rutter SB, Collins AB, Govindarajulu U, Jha MK, Horn SR, Kautz M, Corniquel M, Collins KA, Bevilacqua L, Glasgow AM, Brallier J, Pietrzak RH, Murrough JW and Charney DS (2021) A randomized controlled trial of repeated ketamine administration for chronic post-traumatic stress disorder. American Journal of Psychiatry 178, 193–202.
- First MB, Gibbon M, Spitzer RL, Williams JBW and Benjamin LS (1997)

  Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II). Washington, DC: American Psychiatric Press, Inc.
- Freijeiro-González L, Febrero-Bande M and González-Manteiga W (2021)
  A critical review of LASSO and its derivatives for variable selection under dependence among covariates. *International Statistical Review* 90, 118–145.
- Gould F, Harvey PD, Hodgins G, Jones MT, Michopoulos V, Maples-Keller J, Rothbaum BO, Rothbaum AO, Ressler KJ and Nemeroff CB (2021) Prior trauma-related experiences predict the development of posttraumatic stress disorder after a new traumatic event. *Depression and Anxiety* 38, 40–47.
- Green JG, McLaughlin KA, Berglund PA, Gruber MJ, Sampson NA, Zaslavsky AM and Kessler RC (2010) Childhood adversities and adult psychiatric disorders in the national comorbidity survey replication I: associations with first onset of DSM-IV disorders. Archives of General Psychiatry 67, 113–123.
- Greenberg PE, Fournier AA, Sisitsky T, Pike CT and Kessler RC (2015) The economic burden of adults with major depressive disorder in the United States (2005 and 2010). *Journal of Clinical Psychiatry* 76, 155–162.
- Heleniak C, Jenness JL, Stoep AV, McCauley E and McLaughlin KA (2016) Childhood maltreatment exposure and disruptions in emotion regulation: a transdiagnostic pathway to adolescent internalizing and externalizing psychopathology. *Cognitive Therapy and Research* 40, 394–415.
- Holt MK, Kaufman Kantor G and Finkelhor D (2008) Parent/child concordance about bullying involvement and family characteristics related to bullying and peer victimization. *Journal of School Violence* 8, 42–63.
- Husky MM, Sadikova E, Lee S, Alonso J, Auerbach RP, Bantjes J, Bruffaerts R, Cuijpers P, Ebert DD, Garcia RG, Hasking P, Mak A, McLafferty M, Sampson NA, Stein DJ and Kessler RC (2022) Childhood adversities and mental disorders in first-year college students: results from the World Mental Health International College Student Initiative. Psychological Medicine, (published online ahead of print 11 January). Available at https://www.cambridge.org/core/journals/psychological-medicine/article/abs/childhood-adversities-and-mental-disorders-in-firstyear-college-students-results-from-the-world-mental-health-international-college-student-initiative/EC6458AF6455F977 9EA6492EB1283F6422D6952 (Accessed 12 November 2022).
- Joormann J, Ziobrowski HN, King AJ, Gildea SM, Lee S, Sampson NA, House SL, Beaudoin FL, An X, Stevens JS, Zeng D, Neylan TC, Clifford GD, Linnstaedt SD, Germine LT, Bollen KA, Rauch SL, Haran JP, Storrow AB, Musey Jr PI, Hendry PL, Sheikh S, Jones CW, Punches BE, McGrath ME, Hudak LA, Pascual JL, Seamon MJ, Chang

- AM, Pearson C, Peak DA, Domeier RM, Rathlev NK, O'Neil BJ, Sanchez LD, Bruce SE, Miller MW, Pietrzak RH, Barch DM, Pizzagalli DA, Harte SE, Elliott JM, Koenen KC, McLean SA and Kessler RC (2022) 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. *Depression and Anxiety* 39, 56–70.
- Karam EG, Friedman MJ, Hill ED, Kessler RC, McLaughlin KA, Petukhova M, Sampson L, Shahly V, Angermeyer MC, Bromet EJ, de Girolamo G, de Graaf R, Demyttenaere K, Ferry F, Florescu SE, Haro JM, He Y, Karam AN, Kawakami N, Kovess-Masfety V, Medina-Mora ME, Browne MA, Posada-Villa JA, Shalev AY, Stein DJ, Viana MC, Zarkov Z and Koenen KC (2014) Cumulative traumas and risk thresholds: 12-month PTSD in the World Mental Health (WMH) surveys. Depression and Anxiety 31, 130-142.
- Kessler RC and Üstün TB (2004) The World Mental Health (WMH) survey initiative version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI). International Journal of Methods in Psychiatric Research 13, 93–121.
- Kessler RC, McLaughlin KA, Green JG, Gruber MJ, Sampson NA, Zaslavsky AM, Aguilar-Gaxiola S, Alhamzawi AO, Alonso J, Angermeyer M, Benjet C, Bromet E, Chatterji S, de Girolamo G, Demyttenaere K, Fayyad J, Florescu S, Gal G, Gureje O, Haro JM, Hu CY, Karam EG, Kawakami N, Lee S, Lépine JP, Ormel J, Posada-Villa J, Sagar R, Tsang A, Ustün TB, Vassilev S, Viana MC and Williams DR (2010) Childhood adversities and adult psychopathology in the WHO World Mental Health Surveys. British Journal of Psychiatry 197, 378–385.
- Kessler RC, Aguilar-Gaxiola S, Alonso J, Benjet C, Bromet EJ, Cardoso G, Degenhardt L, de Girolamo G, Dinolova RV, Ferry F, Florescu S, Gureje O, Haro JM, Huang Y, Karam EG, Kawakami N, Lee S, Lepine J-P, Levinson D, Navarro-Mateu F, Pennell B-E, Piazza M, Posada-Villa J, Scott KM, Stein DJ, Ten Have M, Torres Y, Viana MC, Petukhova MV, Sampson NA, Zaslavsky AM and Koenen KC (2017) Trauma and PTSD in the WHO World Mental Health Surveys. European Journal of Psychotraumatology 8, 1353383.
- Kessler RC, Aguilar-Gaxiola S, Alonso J, Bromet EJ, Gureje O, Karam EG, Koenen KC, Lee S, Liu H, Pennell BE, Petukhova MV, Sampson NA, Shahly V, Stein DJ, Atwoli L, Borges G, Bunting B, de Girolamo G, Gluzman SF, Haro JM, Hinkov H, Kawakami N, Kovess-Masfety V, Navarro-Mateu F, Posada-Villa J, Scott KM, Shalev AY, Ten Have M, Torres Y, Viana MC and Zaslavsky AM (2018) The associations of earlier trauma exposures and history of mental disorders with PTSD after subsequent traumas. Molecular Psychiatry 23, 1892–1899.
- Knol MJ, Le Cessie S, Algra A, Vandenbroucke JP and Groenwold RH (2012) Overestimation of risk ratios by odds ratios in trials and cohort studies: alternatives to logistic regression. *Canadian Medical Association Journal* 184, 895–899.
- Krieg C, Hudon C, Chouinard MC and Dufour I (2016) Individual predictors of frequent emergency department use: a scoping review. BMC Health Services Research 16, 594.
- Lebois LAM, Harnett NG, van Rooij SJH, Ely TD, Jovanovic T, Bruce SE, House SL, Ravichandran C, Dumornay NM, Finegold KE, Hill SB, Merker JB, Phillips KA, Beaudoin FL, An X, Neylan TC, Clifford GD, Linnstaedt SD, Germine LT, Rauch SL, Haran JP, Storrow AB, Lewandowski C, Musey Jr PI, Hendry PL, Sheikh S, Jones CW, Punches BE, Swor RA, McGrath ME, Hudak LA, Pascual JL, Seamon MJ, Datner EM, Chang AM, Pearson C, Domeier RM, Rathlev NK, O'Neil BJ, Sergot P, Sanchez LD, Miller MW, Pietrzak RH, Joormann J, Barch DM, Pizzagalli DA, Sheridan JF, Smoller JW, Luna B, Harte SE, Elliott JM, Kessler RC, Koenen KC, McLean SA, Stevens JS and Ressler KJ (2022) Persistent dissociation and its neural correlates in predicting outcomes after trauma exposure. American Journal of Psychiatry 179, 661–672
- Liu H, Petukhova MV, Sampson NA, Aguilar-Gaxiola S, Alonso J, Andrade LH, Bromet EJ, de Girolamo G, Haro JM, Hinkov H, Kawakami N, Koenen KC, Kovess-Masfety V, Lee S, Medina-Mora ME, Navarro-Mateu F, O'Neill S, Piazza M, Posada-Villa J, Scott KM, Shahly V, Stein DJ, Ten Have M, Torres Y, Gureje O, Zaslavsky AM

- and Kessler RC (2017) Association of DSM-IV posttraumatic stress disorder with traumatic experience type and history in the World Health Organization World Mental Health surveys. *JAMA Psychiatry* 74, 270–281
- Mansournia MA and Altman DG (2016) Inverse probability weighting. British Medical Journal 352, i189.
- Martín-Babarro J, Toldos MP, Paredes-Becerra L, Abregu-Crespo R, Fernández-Sánchez J and Díaz-Caneja CM (2021) Association of different forms of child maltreatment with peer victimization in Mexican children and adolescents. Frontiers in Psychology 12, 662121.
- McLaughlin KA, Koenen KC, Bromet EJ, Karam EG, Liu H, Petukhova M, Ruscio AM, Sampson NA, Stein DJ, Aguilar-Gaxiola S, Alonso J, Borges G, Demyttenaere K, Dinolova RV, Ferry F, Florescu S, de Girolamo G, Gureje O, Kawakami N, Lee S, Navarro-Mateu F, Piazza M, Pennell BE, Posada-Villa J, Ten Have M, Viana MC and Kessler RC (2017) Childhood adversities and post-traumatic stress disorder: evidence for stress sensitisation in the World Mental Health Surveys. British Journal of Psychiatry 211, 280–288.
- McLean SA, Kirsch NL, Tan-Schriner CU, Sen A, Frederiksen S, Harris RE, Maixner W and Maio RF (2009) Health status, not head injury, predicts concussion symptoms after minor injury. American Journal of Emergency Medicine 27, 182–190.
- McLean SA, Ressler K, Koenen KC, Neylan T, Germine L, Jovanovic T, Clifford GD, Zeng D, An X, Linnstaedt S, Beaudoin F, House S, Bollen KA, Musey P, Hendry P, Jones CW, Lewandowski C, Swor R, Datner E, Mohiuddin K, Stevens JS, Storrow A, Kurz MC, McGrath ME, Fermann GJ, Hudak LA, Gentile N, Chang AM, Peak DA, Pascual JL, Seamon MJ, Sergot P, Peacock WF, Diercks D, Sanchez LD, Rathlev N, Domeier R, Haran JP, Pearson C, Murty VP, Insel TR, Dagum P, Onnela JP, Bruce SE, Gaynes BN, Joormann J, Miller MW, Pietrzak RH, Buysse DJ, Pizzagalli DA, Rauch SL, Harte SE, Young LJ, Barch DM, Lebois LAM, van Rooij SJH, Luna B, Smoller JW, Dougherty RF, Pace TWW, Binder E, Sheridan JF, Elliott JM, Basu A, Fromer M, Parlikar T, Zaslavsky AM and Kessler R (2020) The AURORA study: a longitudinal, multimodal library of brain biology and function after traumatic stress exposure. Molecular Psychiatry 25, 283–296.
- Michaels AJ, Michaels CE, Moon CH, Smith JS, Zimmerman MA, Taheri PA and Peterson C (1999) Posttraumatic stress disorder after injury: impact

- on general health outcome and early risk assessment. The Journal of Trauma: Injury, Infection, and Critical Care 47, 460-466.
- Nichter B, Norman S, Haller M and Pietrzak RH (2019a) Physical health burden of PTSD, depression, and their comorbidity in the U.S. veteran population: morbidity, functioning, and disability. *Journal of Psychosomatic Research* 124, 109744.
- Nichter B, Norman S, Haller M and Pietrzak RH (2019b) Psychological burden of PTSD, depression, and their comorbidity in the U.S. veteran population: suicidality, functioning, and service utilization. *Journal of Affective Disorders* **256**, 633–640.
- Petruccelli K, Davis J and Berman T (2019) Adverse childhood experiences and associated health outcomes: a systematic review and meta-analysis. Child Abuse & Neglect 97, 104127.
- PROMIS Cooperative Group (2021) PROMIS: Interpret Scores. Available at https://www.healthmeasures.net/score-and-interpret/interpret-scores/promis (Accessed 12 June 2022).
- R Core Team (2021) R: A language and environment for statistical computing (version 4.0.5). Available at https://www.R-project.org/ (Accessed 22 May 2022). SAS Institute Inc (2013) SAS\* Software, 9.4 Edn. Cary, NC: SAS Institute Inc.
- **Thomas É, Saumier D and Brunet A** (2012) Peritraumatic distress and the course of posttraumatic stress disorder symptoms: a meta-analysis. *Canadian Journal of Psychiatry* **57**, 122–129.
- Wilson-Genderson M, Heid AR, Cartwright F and Pruchno R (2021) Adverse childhood experiences, adult trauma, and depressive symptom trajectories. Aging & Mental Health 26, 2170–2178.
- Xie H, Huffman N, Shih CH, Cotton AS, Buehler M, Brickman KR, Wall JT and Wang X (2022) Adverse childhood experiences associate with early post-trauma thalamus and thalamic nuclei volumes and PTSD development in adulthood. *Psychiatry Research: Neuroimaging* 319, 111421.
- Ziobrowski HN, Buka SL, Austin SB, Sullivan AJ, Horton NJ, Simone M and Field AE (2020) Using latent class analysis to empirically classify maltreatment according to the developmental timing, duration, and co-occurrence of abuse types. Child Abuse & Neglect 107, 104574.
- Zou G (2004) A modified Poisson regression approach to prospective studies with binary data. *American Journal of Epidemiology* **159**, 702–706.
- Zuromski KL, Ustun B, Hwang I, Keane TM, Marx BP, Stein MB, Ursano RJ and Kessler RC (2019) Developing an optimal short-form of the PTSD Checklist for DSM-5 (PCL-5). *Depression and Anxiety* **36**, 790–800.