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Derivation and validation of risk prediction for posttraumatic stress symptoms following trauma exposure

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Abstract

Background. Posttraumatic stress symptoms (PTSS) are common following traumatic stress exposure (TSE). Identification of individuals with PTSS risk in the early aftermath of TSE is important to enable targeted administration of preventive interventions. In this study, we used baseline survey data from two prospective cohort studies to identify the most influential predictors of substantial PTSS.

Methods. Self-identifying black and white American women and men ($n = 1546$) presenting to one of 16 emergency departments (EDs) within 24 h of motor vehicle collision (MVC) TSE were enrolled. Individuals with substantial PTSS (⩾33, Impact of Events Scale – Revised) 6 months after MVC were identified via follow-up questionnaire. Sociodemographic, pain, general health, event, and psychological/cognitive characteristics were collected in the ED and used in prediction modeling. Ensemble learning methods and Monte Carlo cross-validation were used for feature selection and to determine prediction accuracy. External validation was performed on a hold-out sample (30% of total sample).

Results. Twenty-five percent ($n = 394$) of individuals reported PTSS 6 months following MVC. Regularized linear regression was the top performing learning method. The top 30 factors together showed good reliability in predicting PTSS in the external sample (Area under the curve = 0.79 ± 0.002). Top predictors included acute pain severity, recovery expectations, socioeconomic status, self-reported race, and psychological symptoms.

Conclusions. These analyses add to a growing literature indicating that influential predictors of PTSS can be identified and risk for future PTSS estimated from characteristics easily available/assessable at the time of ED presentation following TSE.

Introduction

Exposure to traumatic events is common in life (Eastel et al., 2019; Kilpatrick et al., 2013). While most individuals recover following trauma exposure, a substantial subset develops adverse posttraumatic neuropsychiatric sequelae such as posttraumatic stress symptoms (PTSS). PTSS can cause tremendous suffering, functional impairment, disability, and high health care costs (Bleich & Solomon, 2004; Dobie et al., 2004; Gaskin & Richard, 2012; Haskell et al., 2010; Kessler, 2000; Lew et al., 2009; McNally & Frueh, 2013; Outcalt et al.,

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2015; Stewart, Ricci, Chee, Hahn, & Morganstein, 2003; Surís & Lind, 2008). Even though individuals who develop PTSS often present for emergency care or other health care in the immediate/early aftermath of an inciting event, no risk prediction tools are in regular use and the development of such tools is still at an early stage. Continued development of such tools is valuable because preventive interventions delivered in the early aftermath of trauma might be the most efficacious (Fritz et al., 2015; Kearns, Ressler, Zatzick, & Rothbaum, 2012; Litz, Gray, Bryant, & Adler, 2002; Shalev et al., 2016).

A number of high-quality studies have successfully identified survey or biological characteristics that predict PTSS, either as individual predictors or sets of items identified via ensemble machine learning-based methodologies (Freedman, Brandes, Peri, & Shalev, 1999; Galatzer-Levy, Karstoft, Statnikov, & Shalev, 2014; Karstoft, Statnikov, Andersen, Madsen, & Galatzer-Levy, 2015b; Kessler et al., 2014; Kleim, Ehlers, & Glucksman, 2007; Linnstaedt et al., 2019a; Linnstaedt, Zannas, McLean, Koenen, & Ressler, 2019b; Powers et al., 2014; Rosellini, Dussaillant, Zubizarreta, Kessler, & Rose, 2018; Schultebraucks et al., 2020; Shalev et al., 2019; Symes, Maddoux, McFarlane, & Pennings, 2016; Ziobrowski et al., 2021). Identified characteristics have generally come from sociodemographic (Galatzer-Levy et al., 2014; Karstoft, Galatzer-Levy, Statnikov, Li, & Shalev, 2015a; Kessler et al., 2014; Powers et al., 2014), prior trauma (Karstoft et al., 2015b; Kessler et al., 2014; Symes et al., 2016), blood biomarker (Linnstaedt et al., 2019a, 2019b; Schultebraucks et al., 2020), and psychological or cognitive domains (Freedman et al., 1999; Galatzer-Levy et al., 2014; Karstoft et al., 2015a, 2015b; Kleim et al., 2007; Powers et al., 2014; Symes et al., 2016). Specifically, examples of previously identified predictors of PTSS include feelings of worthlessness, peritraumatic stress, nightmares, worrying, racing heart, blood cell counts, gender, and preexisting depression (Galatzer-Levy et al., 2014; Karstoft et al., 2015b; Kessler et al., 2014; Powers et al., 2014; Schultebraucks et al., 2020; Ziobrowski et al., 2021). The continued development and exposition of predictive factors and tools is important for several reasons. First, an array of tools is needed because the optimal tool may vary greatly depending on the timing related to trauma, trauma type, patient population, type of intervention (e.g. affecting optimal sensitivity/specificity trade-off), time/resources available to administer the tool, and types of screening questions that can be asked (e.g. even if highly predictive within a tool, childhood trauma history might be a viable assessment in a therapist's office but not an emergency or primary care waiting room). In addition, different datasets invariably contain information regarding different types of patient characteristics, and therefore the evaluation of the most influential predictors using a variety of large, high-quality datasets allows the continued surfacing of promising predictors and tools.

In the current study, we sought to contribute the continued development and exposition of predictive factors and tools for PTSS by identifying the optimal set of survey items that, at the time of emergency department (ED) evaluation after motor vehicle collision (MVC) trauma, predict substantial PTSS at 6 months. We utilized data from two longitudinal studies of MVC survivors [$n = 776$ Black Americans (Linnstaedt et al., 2016) and $n = 770$ White Americans (Platts-Mills et al., 2011)] that were performed by a common research team, with nearly identical methods and high follow-up rates (Linnstaedt et al., 2016; Platts-Mills et al., 2011). Available candidate predictors assessed in the ED included sociodemographic, trauma, reported pre-MVC health status, and peritraumatic pain and psychological symptom domains. The optimal set of predictors was derived using ensemble learning methods and validation was performed using data from a hold-out subsample of ED sites.

Methods

Cohorts

Data used in the current study were collected as part of two longitudinal cohort studies of MVC trauma survivors. These two studies enrolled individuals at one of 16 ED sites in the immediate aftermath of MVC and followed study participants over the course of 1 year. MVC trauma is one of the most common civilian traumatic stress exposures in industrialized nations, and similar to other forms of trauma, adverse posttraumatic neuropsychiatric sequelae are common (McLean et al., 2019). The first of the two studies enrolled only self-reporting White American individuals (June 2011 and June 2014) and the second study enrolled only self-reporting Black American individuals (between July 2012 and July 2015). These two racial groups were enrolled separately to avoid population stratification effects in each individual cohort. Both sister studies shared the common goal of understanding recovery *v.* development of adverse posttraumatic neuropsychiatric sequelae following trauma exposure. They have been described thoroughly previously (Linnstaedt et al., 2016; Platts-Mills et al., 2011) and details are provided below. The studies were approved by Institutional Review Boards (IRBs) at all collaborating institutions and all participants provided written informed consent after receiving a complete description of the study. Trained research assistants at each ED site used web-based screeners and questionnaires to determine eligibility and perform assessments (described below).

Study design and population

Study design

We adopted a study design that leveraged the multiple study sites enrolling participants in the two studies. This study design is illustrated in Fig. 1 and is described in the 'Site split study design' section. In brief, enrollment sites were grouped into three geographic regions in each cohort [cohort 1: $n = 361$, 361, and 54, for geographic regions 1 (Michigan study sites), 2 (Northeastern US study sites), and 3 (Southeastern US study sites), respectively; cohort 2: $n = 304$, 152, and 314 for geographic regions 1, 2, and 3]. Participant data were then partitioned into training (70% of the data) and test sets (30% of data, data from different study sites than training data). The training dataset had equal numbers of participants from each cohort and equal representation from each geographical region while, to increase rigor, the test dataset included participant data that were shuffled randomly (i.e. potential non-equal race, sex, age, etc., representation). Two hundred permutations of these training and test sets were used to determine external validation metrics. Within the training set, feature selection was performed using 100 rounds of Monte Carlo cross-validation that identified the top 30 variables based on average rankings across internal validation metrics. The selection of 30 variables was determined via the one standard error rule (Chan, Pristach, Welte, & Russell, 1993). This rule indicated that the most parsimonious subset of variables with the least error (up to one standard error) is 30 variables (online Supplementary Fig. S2; mean error and standard error for 30 variables: 0.17 ± 0.003). These 30 variables were then used to assess AUC,

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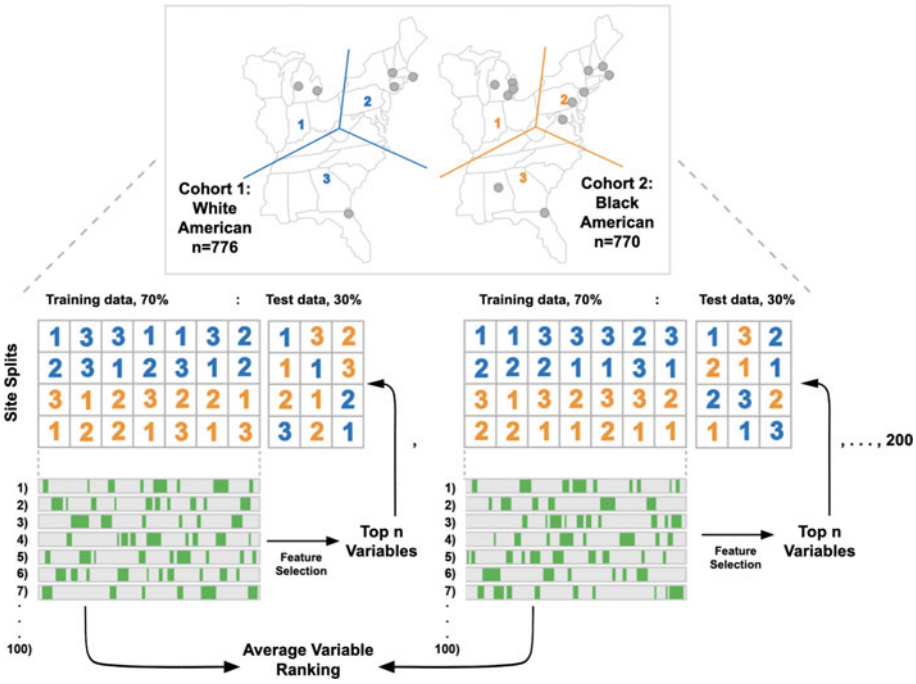

Fig. 1. Schematic of the study design employed in the current study to achieve rigorous training and test sets for machine learning algorithms. Participant data were derived from two longitudinal studies of motor vehicle collision trauma survivors. Enrollment occurred across 16 emergency department (ED) sites in the Eastern United States (gray dots top panel). Geographic locations of these ED enrollment sites were grouped into three broad areas as defined by blue numbers for cohort 1, the White America cohort (Platts-Mills et al., 2011) and orange numbers for cohort 2, the Black American cohort (Linnstaedt et al., 2016). Participant data from each of these three geographic locations were then used to generate 'site splits' for training datasets (70% of the combined Black and White cohorts) and test datasets (30% of the combined cohort). As shown in the middle panel, training datasets were balanced across races and geographic locations. Within each training data site split, 100 rounds of Monte Carlo cross-validation were performed (represented by gray and green bars, bottom panel) to estimate variable selection probabilities and conduct feature selection. Using this methodology, average variable rankings were calculated, and the top variables were used for external validation within test datasets that were not constrained for race, sex, or geographic locations.

accuracy, sensitivity, specificity, negative predictive values (NPVs), and positive predictive values (PPVs) in the hold out test dataset.

Motor vehicle collision study, cohort 1

The details of the first of our two MVC studies have been reported previously (Platts-Mills et al., 2011). In brief, individuals ⩾18 and ⩽65 years of age presenting to one of eight EDs in four no-fault insurance states (i.e. states that restrict ones right to seek compensation for pain or suffering that is associated with MVC: Michigan, Massachusetts, New York, and Florida) within 24 h of MVC and who did not have fracture other than finger or toe, other injury requiring hospital admission, were enrolled between June 2011 and June 2014. Additionally, to be enrolled, patients had to provide a telephone number for follow-up contact. Patients who were not alert and oriented per the treating clinician were excluded, as were pregnant patients, prisoners, patients unable to read and understand English, substantial soft tissue injury, passengers on a bus, or patients taking opioids above a total daily dose of 30 mg of oral morphine or equivalent. In addition, enrollment was limited to self-identifying non-Hispanic White Americans. Informed consent was obtained from all participants and IRB approval was obtained at all study sites.

Motor vehicle collision study, cohort 2

The details of the second of our two MVC studies have also been reported previously (Linnstaedt et al., 2016). This prospective longitudinal study enrolled self-identifying Black American individuals ⩾18 and ⩽65 years of age who presented within 24 h of MVC to one of 11 EDs in six states/districts (Michigan, Pennsylvania, Florida, Alabama, Massachusetts, and Washington DC) between July 2012 and July 2015. In brief, individuals who did not have a fracture or other injury requiring hospital admission were screened for eligibility. Patients who were not alert and oriented were excluded, as were patients who did not self-identify as Black American, were pregnant, prisoners, unable to read and understand English, or taking opioids above a total daily dose of 30 mg of oral morphine or equivalent. Furthermore, only non-Hispanic Black Americans were enrolled in the study. The study was approved by the IRB of all participating hospitals. Each participant provided written informed consent before enrollment.

Assessments collected at the time of trauma exposure (i.e. potential predictors)

All variables included as potential predictors are presented in online Supplementary Table S1. Descriptions of these assessments are provided in online Supplementary Methods.

Data cleaning, imputation, and variable reduction

The two MVC cohort datasets were cleaned and imputed separately and then merged into a final dataset. Cleaning, variable reduction, and imputation steps were adapted from previously published protocols (Kuhn & Johnson, 2013; Stekhoven & Bühlmann, 2012) and are summarized in online Supplementary Fig. S1. Briefly, we first removed variables with >10% missingness, and participants with >50% missing data. This resulted in a total of 966 variables in cohort 1 and 958 variables in cohort 2 (of these variables, >97% of them contained less than 5% missing data). We then used missForest, a random forest-based non-parametric method, to impute variables with missing values. Compared to other methods like MICE that individually fit data types, missForest can leverage all available data during imputation. Without imputation, many variables would be removed, thus harming data quality (e.g. there could be potential overconfidence in results and induced bias). Using these complete data, we then scaled continuous covariates [(0,1) range], removed variables with zero or low variance (i.e. those variables in which the fraction of unique values over the sample size was 10% and the ratio of the frequency of the most prevalent value to the frequency of the

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second most prevalent value was 19), and removed one of any pair of variables in high correlation with each other (i.e. $|r| > 0.75$) (e.g. number of alcoholic drinks consumed per week was correlated with alcohol consumed per day, therefore one of these variables was removed). Finally, variables not present in both cohorts (i.e. because a questionnaire was used in one cohort but not the other) were removed. A total of 160 variables remained and are provided in online Supplementary Table S1. All cleaning steps were performed using RStudio (version 4.0.0).

Site split study design

Instead of using our two datasets as separate discovery and validation datasets and given the nearly identical study design of the two studies and that they were comprised of self-identifying Blacks and Whites, respectively, we opted to combine them into one large final dataset and then hold out a subset of study sites as external validation sites (test data), with the rest of the sites used as our training data. This enabled us to include self-identified race as a candidate predictor, increasing generalizability of the study. Further, we opted to not evaluate using only one train-test (or hold out) split, but instead evaluate test performance over several train-test splits. In this way, we can better assess the generalizability of the models rather than rely on a single, potentially sensitive estimate.

To generate our train-test splits, we generated all possible combinations of study site splits that could fulfill a 70:30 split between internal training and external test data. Within the training data, we constrained the possible combinations of study sites by three metrics: ratio of self-identifying Black Americans to self-identifying White Americans was between 0.45 and 0.55, the ratio of women to men was between 0.45 and 0.55 and every training set had to have at least one study site from each major geographical location (defined as Michigan area, Northern east coast, and Southern east coast). These constraints resulted in 605 different combinations of possible training sets. Due to computational costs of running our machine learning pipelines on all 605 combinations, we randomly selected 200 of these splits on which to evaluate performance.

Machine learning methods

K-nearest neighbors

K-nearest neighbors is a non-parametric supervised learning method for classification. Given a new input to classify, it looks for the majority class among the k-nearest data points in the training set, and chooses that majority class as the output (Kramer, 2013). It has been applied extensively in medical research (Ali, Neagu, & Trundle, 2019; Gallego, Pertusa, & Calvo-Zaragoza, 2018; Li et al., 2012; Shouman, Turner, & Stocker, 2012; Xing & Bei, 2020; Zhuang, Cai, Wang, Zhang, & Zheng, 2020).

Regularized regression

Regularized regression is least squares regression with either an L1 penalty (lasso regression), L2 penalty (ridge regression), or a combination of both (Elastic Net). Using regression allows for interpretable models, making it popular in the biomedical community, while still allowing for robust performance via regularization (Austin, Pan, & Shen, 2013; de Vlaming & Groenen, 2015; Kessler et al., 2017; Lund et al., 2019; Marafino, Boscardin, & Dudley, 2015; Odgers, Tellis, Hall, & Dumontier, 2016; Parker et al., 2009; Pavlou, Ambler, Seaman, De Iorio, & Omar, 2016; Privé, Aschard, & Blum, 2019).

Random forest

Random forest is an ensemble non-parametric method that aggregates over several decision trees to make predictions. Random forests are popular for its ability to model complex and non-linear interactions of effects. Random forests have also proven successful in the biomedical community (Antoniadi, Galvin, Heverin, Hardiman, & Mooney, 2021; Bayramli et al., 2021; Chen & Ishwaran, 2012; Hu & Steingrimsson, 2018; Kim, Yoo, Oh, & Kim, 2013; Wongvibulsin, Wu, & Zeger, 2019).

Support vector machines

Support vector machine (SVM) for classification works by finding the optimal 'separating hyperplane' among the classes. Radial kernels were explored for our prediction task, but linear SVMs were the most performant. SVMs have also shown success in biomedical classification (Byun & Lee, 2002; Georgoulas, Stylios, & Groumpos, 2006; Kim et al., 2013; Mittag et al., 2012; Yokota, Endo, & Ohe, 2017).

Neural networks

Neural networks are mathematical models inspired by the brain. Information is transmitted across the network by taking a linear combination of inputs (with weights, as in regression analysis) and applying non-linear functions. This design allows for powerful approximations (Bishop, 1995; Cybenko, 1989). Here, we used a simplified version of published methods, i.e. a single-layer neural network within an ensemble, to guard against overfitting.

SuperLearner

SuperLearner is an ensemble method that finds the optimal weighting among methods of interest; the authors showed that asymptotically, it is as optimal as the best possible prediction algorithm tested (Gruber et al., 2020; Petersen et al., 2015; Polley & Van Der Laan, 2010; Torquati et al., 2022; Wyss et al., 2018). SuperLearner has been employed in a variety of biomedical applications.

Feature selection and assessment of model performance

For a given study site split (which specifies a train and test dataset), we built machine learning models to perform binary classification of PTSS. We compared the performance of regularized logistic regression (Brennstuhl, Tarquinio, & Montel, 2015; Maddoux, McFarlane, Symes, Fredland, & Feder, 2018), random forests (Nash, Ponto, Townsend, Nelson, & Bretz, 2013), linear SVM (Defrin et al., 2008), and SuperLearner (Creamer, Bell, & Failla, 2003) [where an ensemble of these methods, with k-nearest neighbors (Johansen, Wahl, Eilertsen, & Weisaeth, 2007) and single-layer neural network (Zlomuzica, Preusser, Schneider, & Margraf, 2015), was used]. In our pipeline, we considered the number of top covariates to use in the model, k, as a hyperparameter to cross-validate on with model-specific hyperparameters, α. These parameters are selected in a nested CV-like approach using the training data. For a fixed k, α is selected by evaluating several α_i (from a grid), using Monte Carlo cross-validation. Then, the final (k, α) hyperparameter is selected using the one-standard error rule. To determine the top k covariates, we implemented stability selection from Shah and Samsworth (Kind & Buckingham, 2018), which utilizes several rounds of

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Monte Carlo cross-validation in order to robustly estimate the probability of variable selection. In our procedure, if the support of covariate i was non-zero according to Lasso, then i was considered a signal variable. Once the relevant model hyperparameters were chosen from the training set, we trained the model then calculated the mean and standard error for a variety of performance metrics on the test set. The pipeline was repeated for each machine learning method considered.

Results

Participants

Participants included in the current study were only those participants who completed 6-month follow-up questionnaires assessing PTSS outcomes (i.e. $n = 1546$). These individuals comprise >85% of enrolled individuals (88% of enrolled individuals in cohort 1 and 83% of enrolled individuals in cohort 2). Baseline characteristics of participants are shown in Table 1, and a comparison of individuals included in the current study analyses *v.* those individuals who were lost to follow-up is shown in online Supplementary Table S2. In both cohort 1 and cohort 2, most individuals were female and in their mid-30s. Education levels were higher in cohort 1, with 39% ($n = 303/776$) having received college or post-college education. This contrasts with cohort 2, where only 18% ($n = 140/770$) had college or post-college education. Collision characteristics were similar between the two groups. BMI was slightly higher in cohort 2. Twenty-five percent ($n = 394/1547$) of all participants reported PTSS 6 months following MVC (15% of White Americans and 36% of Black Americans).

Table 1. Baseline characteristics of study participants from two longitudinal studies of motor vehicle collision trauma survivors ($n = 1546$)

	Cohort 1: self-identifying White American individuals		Cohort 2: self-identifying Black American individuals	
	n or mean	% or S.D.	*n* or mean	% or S.D.
Participants, *n*	776	–	770	–
Females, *n* and %	485	62.50%	495	64.29%
Age, years, mean, and S.D.	36.30	13.48	35.53	12.70
Education, *n* and %				
HS or less	169	21.78%	305	39.87%
Some college	304	39.18%	325	42.20%
College	199	25.64%	110	14.29%
Post-college	104	13.80%	30	3.90%
Collision characteristics, *n* and %				
Driver	673	86.73%	542	70.39%
Airbag deployed	216	27.84%	228	29.61%
Front end	355	45.75%	339	44.03%
Severe vehicle damage	405	52.19%	412	53.51%
BMI, mean, and S.D.	27.76	6.37	30.03	7.59

S.D., standard deviation; HS, high school; BMI, body mass index.

Feature selection and internal validation

Variable importance, determined by calculating mean variable selection probability from 200 randomly selected internal site splits, was used to rank the top 30 predictors of substantial PTSS 6 months after MVC (Fig. 2). The most influential predictors of substantial PTSS included acute pain, psychological, and somatic symptoms, self-reported race, and cognitions and expectations regarding symptoms/recovery. As shown in Table 2, average AUCs for internal validation ranged from 0.83 ± 0.003 (random forest, SVM, SuperLearner) to 0.85 ± 0.002 (regularized regression). Additionally, the top 30 variables were included in a linear regression model to determine the direction of effect of each predictor. Regression coefficients from these linear regression models are presented in online Supplementary Table S3.

External validation and model performance

Following selection of the top 30 variables, we then used our hold out sample (30% of the full dataset) to assess performance via external validation procedures. We found that regularized regression methods showed the strongest performance, with an average AUC of 0.79 ± 0.002 (Table 2 and Fig. 3).

Discussion

Findings from this study add to a growing body of literature (Freedman et al., 1999; Galatzer-Levy et al., 2014; Karstoft et al., 2015a, 2015b; Kessler et al., 2014; Kleim et al., 2007; Linnstaedt et al., 2019a, 2019b; Powers et al., 2014; Rosellini et al., 2018; Schultebraucks et al., 2020; Shalev et al., 2019; Symes et al., 2016; Ziobrowski et al., 2021) indicating that characteristics obtainable in the early aftermath of trauma exposure identify vulnerability to substantial persistent PTSS. The 30 characteristics identified in these datasets together showed good internal ($AUC = 0.85 \pm 0.002$) and external validated prediction accuracy ($AUC = 0.79 \pm 0.002$) for substantial PTSS at 6-month follow-up. Influential predictive domains in these datasets included peritraumatic pain and psychological symptoms, expectations of recovery and cognitions about pain, self-identified race, neighborhood socioeconomic status (Area Deprivation Index), and other sociodemographic characteristics.

The individual predictive characteristics identified in this study provide new insights for potential highly influential predictive factors for the development of substantial chronic PTSS. First, it remains poorly appreciated that peritraumatic pain and somatic symptoms are highly predictive for PTSS. The fact that few studies have evaluated such factors for inclusion in predictive tools for PTSS is consistent with the traditionally siloed approach to the study of adverse posttraumatic neuropsychiatric sequelae such as PTSS, pain, somatic symptoms, and depression, despite the fact that these outcomes are highly co-morbid and that vulnerability to these disorders is shared (Feinberg et al., 2017; McLean, Clauw, Abelson, & Liberzon, 2005; McLean et al., 2019; Short et al., 2022). This literature, and our study findings, supports the inclusion of peritraumatic pain and somatic symptoms in future studies interested in identifying/validating characteristics that individually or collectively best predict substantial

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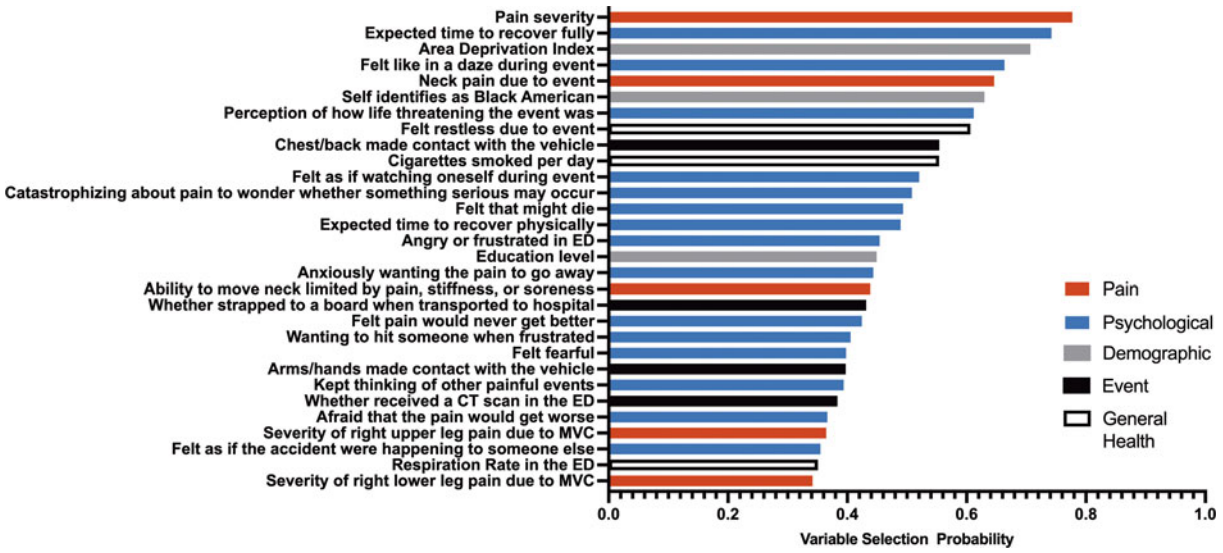

Fig. 2. The top 30 characteristics that predict 6-month posttraumatic stress symptom (PTSS) outcomes following motor vehicle collision (MVC) trauma exposure. These data were collected via patient self-report in the early peritraumatic period during emergency department (ED) assessment and enrollment into the two current longitudinal studies. Variables are listed in order of the most predictive (top, predictive probability = 0.78) to the least predictive (bottom, predictive probability = 0.34). For ease of interpretation, predictor characteristics were grouped into the broad category of pain (red), psychological symptoms (blue), sociodemographic characteristics (gray), details about the MVC event (black), and general health of the participant (white).

Table 2. Prediction of 6-month posttraumatic stress symptoms (PTSS) using demographic and questionnaire data collected in the emergency department following motor vehicle collision trauma ($n = 1546$)

	AUC	Accuracy	PPV	NPV	Sensitivity (true Pos)	Specificity (true Neg)
Regularized regression						
Training	0.86 ± 0.001	0.78 ± 0.001	0.79 ± 0.003	0.78 ± 0.003	0.78 ± 0.003	0.78 ± 0.003
Internal	0.85 ± 0.002	0.76 ± 0.003	0.77 ± 0.004	0.76 ± 0.004	0.75 ± 0.006	0.77 ± 0.006
External	0.79 ± 0.002	0.70 ± 0.003	0.44 ± 0.004	0.88 ± 0.001	0.72 ± 0.006	0.69 ± 0.005
Random forest						
Training	0.99 ± 0.001	0.97 ± 0.002	0.98 ± 0.002	0.96 ± 0.003	0.97 ± 0.002	0.97 ± 0.002
Internal	0.83 ± 0.003	0.75 ± 0.003	0.74 ± 0.003	0.77 ± 0.004	0.70 ± 0.006	0.80 ± 0.005
External	0.78 ± 0.002	0.68 ± 0.003	0.42 ± 0.003	0.89 ± 0.001	0.75 ± 0.005	0.65 ± 0.004
SVM[a]						
Training	0.86 ± 0.002	0.78 ± 0.002	0.79 ± 0.003	0.77 ± 0.003	0.78 ± 0.003	0.78 ± 0.003
Internal	0.83 ± 0.003	0.75 ± 0.003	0.77 ± 0.004	0.74 ± 0.004	0.75 ± 0.006	0.75 ± 0.006
External	0.77 ± 0.002	0.69 ± 0.003	0.43 ± 0.004	0.87 ± 0.002	0.69 ± 0.006	0.68 ± 0.005
SuperLearner						
Training	0.95 ± 0.003	0.89 ± 0.005	0.90 ± 0.005	0.88 ± 0.005	0.89 ± 0.004	0.89 ± 0.004
Internal	0.83 ± 0.003	0.75 ± 0.003	0.76 ± 0.004	0.74 ± 0.004	0.75 ± 0.005	0.75 ± 0.005
External	0.77 ± 0.002	0.69 ± 0.003	0.44 ± 0.004	0.87 ± 0.001	0.70 ± 0.005	0.69 ± 0.004

Results presented are the average metrics calculated based on 200 stratified splits of the two cohorts into discovery and validation subsets (70% training and 30% test) based on enrollment study site (mean ± s.e.) as diagrammed in Fig. 1.
[a]Linear support vector machines.

chronic PTSS. In addition, this finding suggests the potential value of acute pain treatment to reduce the development of substantial PTSS, which has been identified in several studies (Holbrook, Galarneau, Dye, Quinn, & Dougherty, 2010; Saxe et al., 2001).

Interestingly, an individual's expectations of recovery – expected time to recover fully, and to recovery physically – were also among the most powerful predictive factors. This finding has several implications. First, expectations of recovery are simple to assess and should be considered when trying to develop

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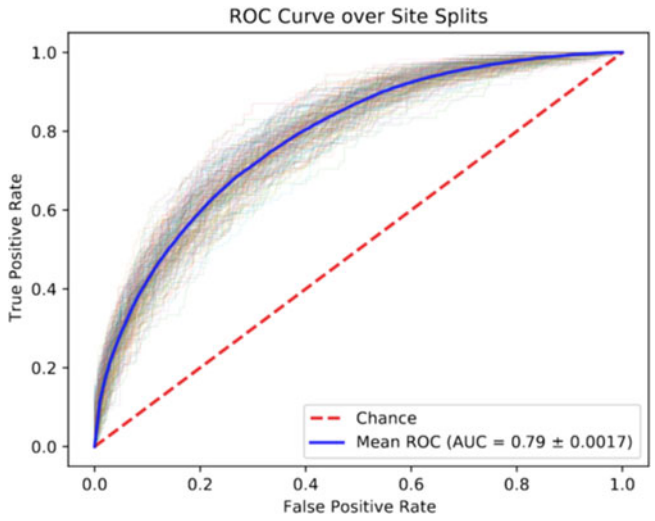

Fig. 3. ROC curves showing the mean (blue line) and standard error (gray lines) associated with 200 iterations of external validation in the current study. These data represent the most performative methodology, i.e. regularized regression, and indicates an AUC of 0.79 ± 0.002 for top variables predicting 6-month posttraumatic stress symptoms following motor vehicle collision trauma.

predictive tools for use in acute post-traumatic settings. Second, while expectations of time to physical recovery are no doubt influenced by individual circumstance (e.g. age 80 *v.* 18), self-efficacy (i.e. belief in one's capacity to implement behaviors necessary to attain an outcome) is an important driver of recovery expectations and is associated with more rapid fear extinction (Zlomuzica et al., 2015). Secondary preventive cognitive-behavioral interventions targeting self-efficacy (Nash et al., 2013) could improve outcomes for at-risk individuals.

To our knowledge, this study is the first to identify neighborhood socioeconomic status (SES) as a leading peritraumatic predictor of substantial PTSS symptoms. These findings are consistent with increasing appreciation that neighborhood SES has wide-ranging effects on health [e.g. via influences on stress system function (Do et al., 2011; Karb, Elliott, Dowd, & Morenoff, 2012), diet (Shahar, Shai, Vardi, Shahar, & Fraser, 2005), and educational and employment opportunities (Saifi & Mehmood, 2011; Vergunst et al., 2019)]. Because of its protean influences on health status and barriers to health improvement, neighborhood SES has been proposed as valuable to include in the medical record (Adler & Stead, 2015). Such inclusion would facilitate the examination of neighborhood SES as a predictor of adverse health outcomes and as a potential use in bedside clinical decision tools.

In contrast to neighborhood SES, Black *v.* White self-identified race has been identified as an important peritraumatic predictor of substantial PTSS in previous studies (Alegría et al., 2013). That this construct is a top predictor of PTSS underscores the need to include diverse racial and ethnic groups in future longitudinal studies assessing predictors of PTSS. It also highlights the need to identify racial/ethnic specific predictors [e.g. those related to discrimination (Brooks Holliday et al., 2020) and identity with one's race (Khaylis, Waelde, & Bruce, 2007)], as they might contribute substantial predictive power for identifying adverse outcomes of trauma in specific racial groups.

Strengths of this study include the inclusion of self-identified Black and White women and men, focus on a single homogeneous type of trauma exposure, identical study design between the two studies from which participant data were derived, high follow-up rates, and a diverse set of variables included as potential predictors in our models. Several limitations should also be noted when interpreting study results. First, self-identifying racial groups besides self-identifying Black and White Americans were not included. Therefore, the generalizability of our findings to other self-identifying racial groups is currently unknown. Second, despite the inclusion of a diverse set of predictors into the pool of candidate predictors, certain characteristics that have been shown to predict PTSS previously, such as previous trauma exposure (Adams et al., 2014; Ehring, Razik, & Emmelkamp, 2011; Karstoft et al., 2015b; Kessler et al., 2014), were not included. This is because these data were not collected from self-identifying White participants (those individuals in cohort 1). Third, despite high follow-up rates in both studies (though lower in the Black American cohort), bias could have been introduced via statistically significant differences in sex, age, and education of those who followed up *v.* those who were lost to follow-up. Fourth, while NPVs were high in all learning methods assessed, PPVs were low. This discrepancy could be due to the low prevalence (25%) of PTSS in this cohort, as low outcome prevalence often favors NPV (Steinberg, Fine, & Chappell, 2009). While low PPVs are not ideal, in the case of predicting PTSS, one could argue that testing positive while truly negative is less detrimental to treatment decisions than testing negative when truly positive.

Future studies should continue to refine optimal, parsimonious sets of PTSS predictors, leveraging data from studies performed to date. Optimal sets of PTSS predictors will very likely differ based on trauma type, assessment timing in relation to trauma exposure, setting, and/or patient population, and may include biological characteristics and/or utilizing tiering/targeting methods (e.g. utilize additional information only in individuals who cannot be risk stratified using a briefer set of predictors). Ultimately, the goal of this prediction work is to identify individual and collective predictors of PTSS and other adverse posttraumatic neuropsychiatric sequelae, both to gain understanding of potential risk factors and to aide in the development of decision support tools. Such tools will differ according to the factors influencing optimal predictors (e.g. trauma type, time from trauma, setting), and the optimal cut-off for such tools will also differ depending on the risks/benefits of the specific clinical decision the tool is intended to aide (e.g. risks/benefits of a specific secondary preventive intervention).

In conclusion, we identified promising individual predictors and a set of characteristics that effectively stratify individuals for risk of substantial PTSS 6 months following MVC. If further validated, these predictors could improve clinical efforts to identify vulnerable individuals at the time of ED presentation for secondary preventative interventions.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S003329172200191X

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