Original Research

Journal of Interpersonal Violence
2022, Vol. 37(13-14) NP11460–NP11489

DOI: 10.1177/0886260520978195
journals.sagepub.com/home/jiv
SAGE

Predicting Posttraumatic Stress Disorder Among Survivors of Recent Interpersonal Violence

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Abstract

A substantial minority of women who experience interpersonal violence will develop posttraumatic stress disorder (PTSD). One critical challenge for preventing PTSD is predicting whose acute posttraumatic stress symptoms will worsen to a clinically significant degree. This 6-month longitudinal study adopted multilevel modeling and exploratory machine learning (ML) methods to predict PTSD onset in 58 young women, ages 18 to 30, who experienced an incident of physical and/or sexual assault in the three months prior to baseline assessment. Women completed baseline assessments of theory-driven cognitive and neurobiological predictors and interview-based measures of PTSD diagnostic status and symptom severity at 1-, 3-, and 6-month follow-ups. Higher levels of self-blame, generalized anxiety disorder severity, childhood trauma exposure, and impairment across multiple domains were associated with a pattern of high and stable

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posttraumatic stress symptom severity over time. Predictive performance for PTSD onset was similarly strong for a gradient boosting machine learning model including all predictors and a logistic regression model including only baseline posttraumatic stress symptom severity. The present findings provide directions for future work on PTSD prediction among interpersonal violence survivors that could enhance early risk detection and potentially inform targeted prevention programs.

Keywords
PTSD, prediction, interpersonal violence, women, longitudinal, assault

Traumatic events that are deliberately caused by other people such as physical or sexual assault are referred to as interpersonal violence and are associated with greater risk for developing posttraumatic stress disorder (PTSD) compared to non-interpersonal traumatic events such as accidents (Ozer et al., 2003; Shalev et al., 2019). Interpersonal violence has received less attention in prospective research compared to other types of traumatic events despite being a common risk factor associated with elevated risk for PTSD (Morris & Rao, 2013). Young women are more likely to experience interpersonal violence (Coker et al., 2016) and twice as likely to develop PTSD during their lifetimes (Kilpatrick et al., 2013) compared to their male counterparts. Fortunately, resilience is the norm: although many survivors will exhibit elevated posttraumatic stress symptoms in the days and weeks following interpersonal violence, most will recover without a need for treatment (McNally, 2003; Santiago et al., 2013). However, waiting for individuals to develop PTSD before intervening can be costly: one in five survivors of interpersonal violence will develop PTSD (Breslau et al., 1998) and the economic burden of PTSD to society is substantial (Wang et al., 2016). Efforts to prevent PTSD in recent trauma survivors have shown promise (Kearns et al., 2015) but must address two key questions: who is at greatest risk for developing PTSD following violence exposure, and what factors contribute to this increased risk?

Given the well-established heterogeneity in posttraumatic stress symptom presentations and course (Bonanno & Mancini, 2012; Galatzer-Levy & Bryant, 2013), it is perhaps not surprising that a range of biopsychosocial factors (genetic, neurobiological, cognitive, sociodemographic, environmental) have been implicated in risk for PTSD (Brewin et al., 2000; Morris & Rao, 2013; Ozer et al., 2003; Yehuda, 2009; Zoladz & Diamond, 2013). Theoretical models of PTSD have emphasized the role of cognitive appraisals and coping strategies (Ehlers & Clark, 2000; Ehring et al., 2008; Foa et

al., 1989), stress response-driven alterations in memory consolidation and retrieval processes (de Quervain et al., 2009; Pitman et al., 1993; Yehuda et al., 1998), executive function (Aupperle et al., 2012), and contextual-processing deficits (Liberzon & Abelson, 2016) in risk for PTSD onset and maintenance. Many of these biopsychosocial factors exert statistically significant but small-to-moderate effects on the development of PTSD.

One approach to PTSD prediction is to assess risk factors that are present before, during, or immediately after the traumatic event, in order to learn more about their individual contributions to the prediction of posttraumatic stress symptom trajectories. For example, a stepwise logistic regression approach to predicting PTSD in a prospective study of recently traumatized individuals first tested clinical, psychological, and biological factors in isolation; multivariate models then examined the relative influence of those variables found to be significant in minimally adjusted models (Gandubert et al., 2016). General linear models consistently identify psychological (e.g., peritraumatic distress and dissociation, perceived life threat, prior trauma exposure, depression), biological (e.g., norepinephrine, heart rate), and social (e.g., social support, family psychiatric history) predictors of PTSD (Brewin et al., 2000; Morris et al., 2016; Ozer et al., 2003). These models are well-suited for testing limited numbers of theory-driven predictors to examine their unique influence on PTSD; however, they cannot simultaneously investigate the diverse array of factors that reflect the complexity and symptom heterogeneity of PTSD.

A second approach that addresses shortcomings of traditional statistical approaches for PTSD prediction is machine learning (ML), which identifies patterns from data in order to enhance predictive performance (Hastie et al., 2005). These algorithms can handle large, complex data structures with heterogeneous distributions, and, as such, are better-suited to PTSD prediction than general linear models (Galatzer-Levy et al., 2018). ML approaches have recently identified a host of sociodemographic, mental health, medical, psychosocial, and trauma features that contribute to PTSD prediction following military deployment (Karstoft, Statnikov, et al., 2015) and emergency hospitalization (Galatzer-Levy et al., 2014; Galatzer-Levy et al., 2017; Karstoft, Galatzer-Levy, et al., 2015; Papini et al., 2018); performance metrics for these models suggest fair-to-good predictive accuracy. Among the most commonly selected predictive features for PTSD in these ML models are acute posttraumatic stress symptom severity, depressive symptoms, age, injury severity, nightmares, prior trauma exposure, acute pain, and time spent in the emergency room.

The primary goal of the study was to evaluate biopsychosocial factors following interpersonal violence that contribute to risk for PTSD. A multilevel

modeling approach was used to examine relations between theory-driven baseline predictors and trajectories of posttraumatic stress symptom severity over time. A secondary goal was to accurately identify interpersonal trauma survivors at high risk for developing PTSD from a broad array of theory-driven cognitive and neurobiological factors assessed at baseline. An exploratory ML approach was used to determine the most relevant predictors for developing PTSD over a 6-month follow-up period. These complementary statistical approaches strike a balance between interpretability (i.e., *how are predictors associated with PTSD?*) and accuracy (i.e., *how well does a set of predictors correctly classify those who develop PTSD?*): whereas multilevel models facilitate mechanistic interpretations of relations between independent predictors and posttraumatic stress symptom severity, ML maximizes predictive accuracy at the cost of interpretability (Galatzer-Levy et al., 2017).

Method

Participants

Participants were young adult women ($n = 58$), ages 18 to 30, who had experienced an incident of interpersonal violence (i.e., physical and/or sexual assault, mugging) within three months (i.e., past 90 days) of their baseline assessment. Recruitment occurred through online advertisements and research participant registries, local agencies coordinating services for survivors of domestic violence and sexual assault, and through a team of nurse practitioners providing medical legal exams to rape survivors in a local hospital. Screening for interpersonal violence meeting Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV), criterion A was first conducted over the phone and then confirmed at baseline using the Life Events Checklist (LEC) (Gray et al., 2004). Screening and assessment measures were based on DSM-IV because data collection was initiated prior to the introduction of DSM-5 criteria and creation of validated DSM-5 assessment materials. Exclusion criteria included: current or past bipolar or psychotic disorder; current substance use disorder; current major depressive disorder (MDD) or PTSD resulting from a traumatic event that occurred prior to the three-month window (to ensure that predictive models were focused on symptoms/diagnoses emerging from the index trauma); serious health conditions known to influence hypothalamic-pituitary-adrenal (HPA) activity; pregnancy; and current use of prescription or non-prescription drugs known to affect HPA activity.

Research assessments were performed at baseline, and 1-, 3-, and 6-month follow-up periods. Predictors were assessed at baseline only through questionnaires administered via a secure web-based Research Electronic Data Capture

(REDCap) platform (Harris et al., 2009), two days of at-home saliva collection (for cortisol and alpha-amylase assays), and a social-evaluative stress task. Psychiatric outcomes (i.e., PTSD diagnostic status and symptom severity) were measured at baseline and all follow-up assessments using a semi-structured diagnostic interview. The present article reports data on potential baseline predictors and PTSD symptoms/diagnoses assessed over the 6-month follow-up period. All participants provided written informed consent, and study procedures were approved by the institutional review board.

Baseline Predictive Measures

A list of baseline predictors along with their associated psychometric measures and procedures is included in Appendix Table 1. Sociodemographic data were collected via self-report and included age, race, ethnicity, height, weight, marital status, household income, and years of education. The Structured Clinical Interview for DSM-IV (SCID-I) (First et al., 2005) was used to assess current and past mood and anxiety disorders, age at first MDD onset, and number of prior MDD episodes. Self-report measures were used to assess depressive (Beck Depression Inventory second edition (Beck et al., 1996)) and anxiety (Generalized Anxiety Disorder 7-item scale (Spitzer et al., 2006)) symptoms, pain intensity (McGill Pain Questionnaire short form (Melzack, 1987)), pain catastrophizing (Pain Catastrophizing Scale (Sullivan et al., 1995)), and functional impairment (Sheehan Disability Scale (Sheehan, 1983)).

To evaluate the influence of timing of baseline assessment relative to trauma exposure, days since index trauma was examined as a predictor. Number of prior traumatic life events was assessed using the LEC (Gray et al., 2004). Childhood abuse and neglect were determined by the Childhood Trauma Questionnaire (CTQ) (Bernstein et al., 1994). Trauma-related cognitive appraisals (i.e., negative cognitions about the self, negative cognitions about the world, self-blame) were assessed with the Posttraumatic Cognitions Inventory (PTCI) (Foa et al., 1999). Primary control coping (i.e., problem-solving, emotion regulation, emotional expression), secondary control coping (i.e., cognitive reappraisal, acceptance, distraction, positive thinking), and disengagement coping (i.e., avoidance, wishful thinking, denial) were assessed with the Responses to Stress Questionnaire (RSQ) (Connor-Smith et al., 2000). Cognitive flexibility was assessed with the trail-making, design fluency, and color-word inhibition subtests of the Delis-Kaplan Executive Function System (D-KEFS) (Delis et al., 2001). Ability to develop and maintain appropriate problem-solving strategies across changing stimulus conditions was assessed with the Wisconsin Card Sorting Test (WCST) (Heaton & Staff, 1993).

Table 1. Descriptive and Clinical Characteristics at Baseline Assessment for Recent Interpersonal Violence Survivors Who Developed New PTSD Onsets During the Study (PTSD +) and Those Who Did Not (PTSD –).

	Mean (*SD*) or *n* (%)		PTSD + vs. PTSD –
Baseline Feature	PTSD + (*n* = 7)	PTSD - (*n* = 51)	*t* or $\chi 2$
Sociodemographic			
Age (years)	25.0 (2.0)	23.7 (3.4)	1.49
Race			1.06
White/Caucasian	4 (57%)	29 (57%)	
Black/African American	3 (43%)	16 (31%)	
Asian	0 (0%)	6 (12%)	
Hispanic	0 (0%)	4 (8%)	0.00
Education (years)	14.0 (1.5)	14.8 (1.9)	1.07
Marital status			0.94
Single	6 (86%)	45 (88%)	
Married	0 (0%)	1 (2%)	
Engaged	0 (0%)	2 (4%)	
Living with partner	1 (14%)	3 (6%)	
Cognitive appraisal			
PTCI – self	3.9 (1.1)	2.6 (1.0)	3.01**
PTCI – world	5.3 (1.0)	4.2 (1.1)	2.60*
PTCI – self-blame	4.3 (1.0)	3.2 (1.0)	2.66*
Coping			
Primary control (RSQ)	0.15 (0.03)	0.20 (0.04)	2.99**
Secondary control (RSQ)	0.22 (0.06)	0.26 (0.05)	2.44*
Disengagement (RSQ)	0.15 (0.02)	0.14 (0.03)	0.71
Executive function			
Perseverative response % (WCST)	13.7 (6.6)	10.5 (6.3)	1.24
Learning-to-learn index (WCST)	–6.4 (13.2)	–1.9 (6.9)	1.31
TM switching vs. number (D-KEFS)	9.1 (2.2)	9.0 (1.9)	0.16
Design Fluency switching (D-KEFS)	12.6 (3.2)	11.9 (3.4)	0.53

(*continued*)

Table 1. continued

	Mean (*SD*) or *n* (%)		PTSD + vs. PTSD –
Baseline Feature	PTSD + (*n* = 7)	PTSD - (*n* = 51)	*t* or $\chi 2$
CW inhibition/switching (D-KEFS)	10.7 (2.5)	10.3 (3.8)	0.29
Diurnal secretion			
Cortisol AUCg	4,729 (1,232)	4,551 (3,176)	0.15
Cortisol awakening response	1.4 (2.9)	1.6 (6.7)	0.07
Cortisol diurnal slope	–0.6 (0.3)	–0.6 (0.3)	0.23
Alpha-amylase AUCg	44,484 (39,740)	59,551 (37,338)	0.98
Alpha-amylase awakening response	–15.0 (21.9)	2.3 (25.0)	1.74
Alpha-amylase diurnal slope	0.2 (0.3)	0.4 (0.4)	1.22
TSST reactivity			
Pre-stress cortisol	1.3 (0.4)	4.0 (10.3)	0.64
Cortisol reactivity	1.6 (1.7)	3.1 (6.2)	0.54
Pre-stress alpha-amylase	95.9 (86.8)	80.7 (62.9)	0.53
Alpha-amylase reactivity	172.6 (154.8)	45.5 (49.1)	1.83
Reactivity HR (peak – pre-TSST)	13.2 (9.0)	10.7 (21.4)	0.25
Recovery HR (peak – post-TSST)	15.0 (11.3)	14.7 (9.4)	0.07
Prolonged cortisol secretion			
Hair cortisol concentration	30.6 (16.0)	19.1 (21.2)	1.13
Pain			
Pain catastrophizing	20.7 (11.6)	10.4 (8.4)	2.66*
Sensory pain (MPQ)	7.5 (6.5)	4.5 (5.2)	1.27
Affective pain (MPQ)	3.3 (2.4)	1.9 (2.0)	1.58
Pain interference (PROMIS)	19.5 (8.2)	13.5 (6.5)	2.05*
Psychiatric diagnoses			
Major depression (current)	3 (43%)	4 (8%)	3.94*
Prior major depressive episodes	9.7 (9.0)	2.7 (3.0)	1.34

(*continued*)

Table 1. continued

Baseline Feature	Mean (*SD*) or *n* (%) PTSD + (*n* = 7)	PTSD - (*n* = 51)	PTSD + vs. PTSD – *t* or $\chi 2$
GAD (current)	1 (14%)	8 (16%)	0.00
Panic disorder (current)	2 (29%)	1 (2%)	4.29*
Agoraphobia (current)	1 (14%)	0 (0%)	1.38
Stress and psychiatric symptoms			
Stress levels major events (PES)	14.0 (6.6)	7.7 (5.8)	2.46*
Stress levels daily hassles (PES)	45.9 (26.9)	29.7 (19.1)	1.98
Depressive (BDI-II)	30.3 (9.3)	13.4 (9.5)	4.39***
GAD severity (GAD-7)	13.6 (6.1)	5.8 (4.6)	4.03***
Trait anxiety (STAI)	57.3 (9.3)	43.7 (9.6)	3.51**
Peri-traumatic dissociation (PDEQ)	20.9 (8.7)	22.0 (7.3)	0.37
Trauma characteristics			
Childhood trauma (CTQ)	70.4 (23.3)	45.1 (15.3)	3.79***
Number of traumatic events (LEC)	8.0 (5.3)	7.2 (2.9)	0.65
Days since index trauma	22.9 (5.3)	48.2 (24.6)	6.36***
Disability			
Impairment family life (SDS)	4.3 (3.0)	1.7 (2.4)	2.43*
Impairment social life (SDS)	4.5 (1.9)	1.9 (2.2)	2.76**
Impairment school/work (SDS)	4.8 (2.1)	2.0 (2.3)	2.85**

***$p < .001$; **$p < .01$; *$p < .05$.

Note. PTSD = posttraumatic stress disorder; PTCI = Posttraumatic Cognitions Inventory; RSQ = Responses to Stress Questionnaire; WCST = Wisconsin Card Sorting Test; D-KEFS = Delis–Kaplan Executive Function System; AUC_g = area under the curve; HR = heart rate; MPQ = McGill Pain Questionnaire short form; PROMIS = Patient-Reported Outcomes Measurement Information System; GAD = generalized anxiety disorder; PES = Perceived Events Scale; BDI-II = Beck Depression Inventory second edition; STAI = State-Trait Anxiety Inventory; PDEQ = Peri-traumatic Dissociative Experiences Questionnaire; CTQ = Childhood Trauma Questionnaire; LEC = Life Events Checklist; SDS = Sheehan Disability Scale.

Diurnal cortisol and alpha-amylase secretion patterns were determined using ten saliva samples obtained over two consecutive days. Cortisol and alpha-amylase reactivity to the social-evaluative stress task (Trier Social Stress Test; TSST) (Kirschbaum et al., 1993) was determined using four pre-TSST samples collected at 30-minute intervals and seven post-TSST samples collected at 10-minute intervals. For diurnal secretion and reactivity measures, free cortisol levels were determined by chemiluminescence immunoassay (Kirschbaum & Hellhammer, 1989) and alpha-amylase levels by a quantitative enzyme kinetic method (Nater et al., 2007). Intra- and inter-assay coefficients of variation for these assays were below 6%. Prolonged HPA activity was determined by hair cortisol concentrations from 3 cm hair segments as described previously (Morris et al., 2017). Intra- and inter-assay coefficients of variation for this assay were below 12%. Throughout the TSST, heart rate reactivity and recovery were determined from continuously recorded heart rate using a Polar H7 chest-strap (Polar, Finland) and Actigraph wristwatch.

Outcome Measures

Severity of posttraumatic stress symptoms at all assessments was determined using the Clinician-Administered PTSD Scale interview for DSM-IV (CAPS-IV) (Blake et al., 1995). The CAPS-IV has excellent psychometric properties (Weathers et al., 2001) and was administered by a clinical psychologist (MCM) or by a trained research assistant under his supervision. Multilevel models examined predictors of CAPS-IV severity scores across assessments. ML models examined two outcomes: posttraumatic stress symptom severity at 6-month assessment and PTSD diagnostic status. PTSD status was defined as developing PTSD over the follow-up period and computed using the "F1/I2" rule (Weathers et al., 1999).

Data Analysis

Variables were examined for distributional properties and cases screened for univariate outliers. Three out-of-range values for diurnal cortisol and alpha-amylase levels were winsorized at three standard deviations. Missing data were handled using maximum-likelihood estimation in multilevel models. Missing values in predictor data were imputed using the random forest proximity algorithm library "randomForest" in ML analyses (Liaw & Wiener, 2002).

Multilevel modeling.

Trajectories of posttraumatic stress symptom severity (CAPS-IV total scores at baseline, 1-, 3-, and 6-month assessments) were examined with multilevel

models specified using hierarchical linear models (HLM v.8) (Raudenbush et al., 2019). Multilevel models consisted of a within-person (level 1) submodel describing how symptom severity changed over time and a between-person (level 2) submodel describing how these changes varied across participants. A within-person variable denoting number of days since the index traumatic event was included in all models to account for between-person variability in the timing of assessments. Separate multilevel models were run to test the following groups of predictors: sociodemographic (i.e., age, race, ethnicity, years of education, marital status); cognitive appraisal; coping; executive function (i.e., perseverative responses and learning-to-learn index [WCST]; trail making switching vs. number [D-KEFS]; design fluency switching [D-KEFS]; color-word inhibition/switching [D-KEFS]); diurnal cortisol/alpha-amylase secretion (i.e., daily output, cortisol awakening response, diurnal cortisol slope); TSST measures (i.e., pre-stress cortisol/alpha-amylase, cortisol/alpha-amylase reactivity, heart rate reactivity and recovery); psychiatric diagnoses (i.e., current MDD, prior depressive episodes, current generalized anxiety disorder (GAD), current Panic Disorder, current Agoraphobia); stress and psychiatric symptoms (i.e., stress levels from major events and daily hassles, depressive symptoms, GAD severity, trait anxiety, peri-traumatic dissociation); trauma characteristics (i.e., childhood trauma exposure, number of prior traumatic events); disability (i.e., impairment in family life, social life, school/work). Multilevel models were focused on cross-level interactions between baseline predictors and days since trauma.

Machine learning (ML).

Gradient Boosting Machine (GBM) methods were used to predict posttraumatic stress symptom severity and PTSD onset using the all available predictors; this ML method assembles small decision trees in order to build prediction models for regression and classification problems. Two GBM algorithms were performed: a model predicting PTSD onset and a model predicting PTSD symptom severity at 6-month follow-up. Both models specified baseline posttraumatic stress symptom severity (CAPS-IV total score) as a predictor and were compared to the benchmark of a model predicting PTSD status during the study from baseline posttraumatic stress symptom severity only. Including a large number of features (n = 137) in ML models (Appendix Table 1) can produce AUC values near "1"; in such cases of overfitting, a model performs well at capturing noise in the current dataset but performs poorly at predicting future data (Yarkoni & Westfall, 2017). For smaller studies in which the creation of separate training and testing subsamples for validation purposes may not be feasible, the optimism correction provides a useful alternative (Peña-Bautista et al., 2019). This method uses

boot-strapping models to calculate an optimism value, which is then subtracted from the original AUC. Due to the small sample size, these GBM algorithms were considered exploratory. The performance of ML models were compared to a logistic regression model including baseline posttraumatic stress symptom severity only.

Results

Sample Characteristics

Descriptive statistics for demographic and select predictors are presented separately for individuals who developed PTSD at follow-up and those who did not, along with statistical tests for between-group comparisons at baseline (Table 1). Baseline assessments were conducted at a mean duration of 45.1 days (SD = 24.6 days) since their index trauma. Of the 58 women who experienced recent interpersonal violence, 15 (26%) already met PTSD diagnostic criteria and 7 (12%) developed new PTSD onsets over follow-up assessments. Women who developed PTSD reported more negative cognitive appraisals, less use of adaptive coping strategies, greater pain catastrophizing, higher stress levels, greater childhood trauma exposure, more severe depressive and anxiety symptoms, greater functional impairment, and more severe PTSD symptoms at baseline compared to women who did not develop PTSD. However, the PTSD group had a shorter duration since index trauma at baseline compared to the non-PTSD group.

Multilevel Models Predicting Posttraumatic Stress Symptom Severity

Within-person relations between theory-driven predictors at baseline assessment and changes in posttraumatic symptom severity over time were examined with multilevel models. A preliminary model including only time as a predictor revealed that CAPS-IV total severity scores declined by 1.2 points each week (Figure 1). Multilevel models revealed three general patterns of associations between baseline predictors and PTSD trajectories: (1) risk factors that were associated with high and stable posttraumatic stress symptom severity over time; (2) risk factors that were associated with high initial posttraumatic stress symptom severity but rapid declines in severity over time; and (3) protective factors that were associated with lower posttraumatic stress symptom severity over time.

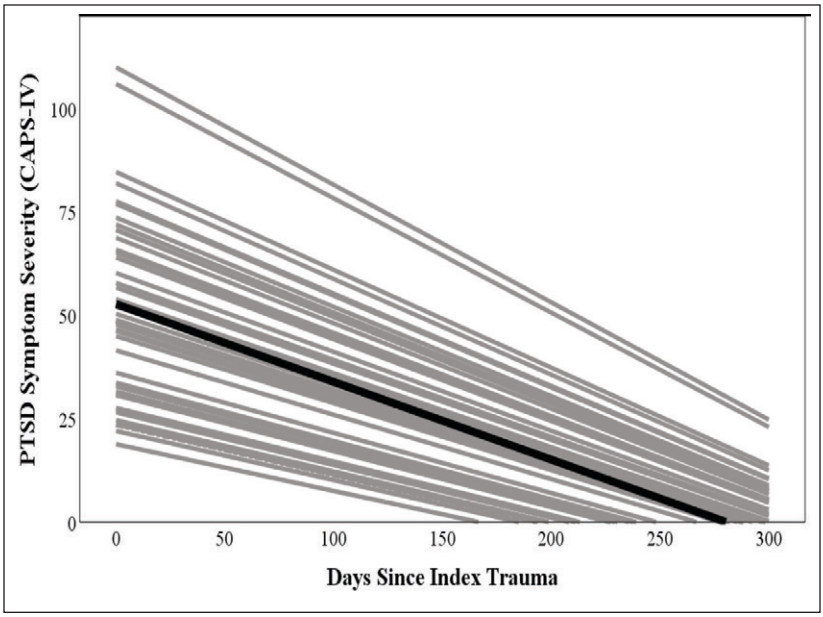

Figure 1. Multilevel modeling estimates of change in PTSD symptom severity following interpersonal violence (gray lines = individual survivor trajectories; black line = average trajectory).

Risk factors. The following factors were associated with high and stable posttraumatic stress symptom severity over time: self-blame, GAD severity, childhood trauma exposure, and impairment across multiple domains (family, social, work). Women reporting more self-blame exhibited higher baseline posttraumatic stress symptom severity ($b = 9.953$, $SE = 3.084$, $p = .002$) but severity did not change significantly over time ($b = –0.018$, $SE = 0.016$, $p = .261$). Greater GAD severity was associated with higher baseline posttraumatic stress symptom severity ($b = 2.387$, $SE = 0.706$, $p = .002$) but severity did not change significantly over time ($b = –0.002$, $SE = 0.004$, $p = .587$). Survivors with greater childhood trauma exposure exhibited higher baseline posttraumatic stress symptoms severity ($b = 0.661$, $SE = 0.147$, $p < .001$) but no changes in severity over time ($b = –0.001$, $SE = 0.001$, $p = .201$). Greater impairment in family ($b = 4.613$, $SE = 1.009$, $p < .001$), social ($b = 2.777$, $SE = 1.298$, $p = .038$), and work ($b = 5.208$, $SE = 1.042$, $p < .001$) domains, were each associated with higher baseline posttraumatic stress symptom severity but did not predict changes in severity over time.

The following factors were associated with high initial posttraumatic stress symptom severity and declining severity over time: negative cognitions about the self and world, perseverative responses on the WCST, and depressive symptoms. Survivors with more negative cognitions about the self and world exhibited a pattern of higher baseline posttraumatic stress symptom severity (self subscale: b=14.545, SE=2.368, p<.001; world subscale: b=10.736, SE=3.320, p=.002) and more rapid decline in severity over time (self subscale: b = –0.045, SE = 0.010, p < .001; world subscale: b = –0.028, SE = 0.014, p = .047). Survivors with higher percentages of perseverative responses on the WCST exhibited a pattern of higher baseline posttraumatic stress symptom severity (b = 2.264, SE = 0.712, p = .003) and more rapid decline in symptoms over time (b = –0.010, SE = 0.004, p = .012). Women reporting higher depressive symptoms showed higher baseline posttraumatic stress symptoms severity (b = 1.084, SE = 0.416, p = .013) and more rapid decline in severity over time (b = –0.006, SE = 0.003, p = .024).

Protective factors.
Greater use of primary control coping was associated with a blunted pattern of lower baseline posttraumatic stress symptom severity (b = –8.515, SE = 2.815, p = .004) and slower decline in severity over time (b = 0.023, SE = 0.011, p = .047).

The following factors were not significantly associated with baseline posttraumatic stress symptom severity or changes in severity over time: sociodemographic characteristics, secondary control coping, disengagement coping, diurnal cortisol/alpha-amylase secretion, stress reactivity, or psychiatric diagnostic measures.

ML Approach to PTSD Prediction

Exploratory GBM predicting PTSD onsets identified 27 relevant variables (Table 2) and yielded an optimism-corrected AUC of 0.96. The baseline CAPS-IV-only logistic regression model predicting PTSD over follow-up yielded an AUC of 0.91. A full GBM model explained 34% of variability in CAPS-IV severity scores at 6-month follow-up and identified 18 relevant variables. Baseline CAPS-IV severity scores alone explained 27% of variability in CAPS-IV severity scores at 6-month follow-up. Predictors identified by both full GBM models included age of onset of first MDD episode, baseline PTSD symptom severity, pain interference, overall pain severity, functional impairment (social, family, work/school), number of prior depressive episodes, childhood trauma exposure, GAD severity, and days since index trauma.

Table 2. Relevant Baseline Features (>1%) in Gradient Boosting Machine Model Predicting PTSD Onsets.

PTSD Onsets			
Baseline Features	Influence (%)	Baseline Features (Continued)	Influence (%)
Age of first MDD onset	6.849	Age	2.494
Household income	4.816	Childhood trauma total score (CTQ)	2.264
Pre-stress cortisol (TSST)	4.619	Childhood physical neglect (CTQ)	2.109
Baseline PTSD severity (CAPS-IV)	4.160	Depressive symptoms (BDI-II)	2.076
Alpha-amylase reactivity	4.112	Alpha-amylase AUCg	1.917
Cortisol AUCg	4.016	Alpha-amylase daily slope	1.805
Primary control coping (RSQ)	3.735	DF attempted designs (D-KEFS)	1.283
Alpha-amylase awakening response	2.882	Impairment family life (SDS)	1.223
Days since index trauma	2.837	Resting heart rate (pre-TSST)	1.164
Number of prior MDEs	2.698	Impairment school/work (SDS)	1.080
VAS pain severity (MPQ-SF)	2.691	Weight	1.071
Failure to maintain set (WCST)	2.636	Pain interference (PROMIS)	1.069
Childhood sexual abuse (CTQ)	2.590	Hair cortisol concentration	1.025
Impairment social life (SDS)	2.577		

Note. MDD = major depressive disorder; TSST = Trier Social Stress Test; AUC_g = area under the curve (daily output); RSQ = Responses to Stress Questionnaire; MDE = major depressive episode; VAS = visual analogue scale; MPQ-SF = McGill Pain Questionnaire Short Form; WCST = Wisconsin Card Sorting Test; CTQ = Childhood Trauma Questionnaire; SDS = Sheehan Disability Scale; BDI-II = Beck Depression Inventory second edition; DF = Design Fluency; D-KEFS = Delis–Kaplin Executive Function System; PROMIS = Patient-Reported Outcomes Measurement Information System.

Discussion

Identifying recent trauma survivors who will develop PTSD and could benefit from preventive interventions remains a significant challenge. A wide range of biopsychosocial factors are implicated in theoretical models of

PTSD (Ehlers & Clark, 2000; Yehuda et al., 1998; Zoladz & Diamond, 2013), yet evidence suggests these factors each exhibit only small-to-medium effects. This 6-month longitudinal study following young women who experienced recent interpersonal violence sought to address two key challenges: (1) how are individual risk and protective factors associated with trajectories of posttraumatic stress symptom trajectories?; and (2) how accurately can a broad set of biopsychosocial factors identify interpersonal trauma survivors who will develop PTSD?

Multilevel models identified predictors associated with three distinct patterns of change in posttraumatic stress symptom severity. Survivors who exhibited a high and stable pattern of posttraumatic stress symptoms were characterized by greater self-blame, GAD severity, childhood trauma exposure, and impairment in multiple domains (family, social, work). A pattern of high initial posttraumatic stress symptoms that declined significantly over time was associated with negative cognitions about the self and world, perseverative responses on the WCST, and depressive symptoms. Although seemingly counter-intuitive, these findings are not unexpected; whereas stability is expected in chronic posttraumatic stress, some level of recovery for survivors is expected in the acute aftermath of trauma. Survivors with more severe baseline symptoms have more opportunity to demonstrate recovery than those less severe baseline symptoms. However, despite the faster rate of improvement, at the end of the acute recovery phase, they remain more likely than survivors with lower baseline symptoms to have clinically significant symptoms. Finally, greater use of primary control coping was associated with a pattern of lower posttraumatic stress symptom severity over time. None of the biological measures of diurnal secretion (cortisol, alpha-amylase), prolonged cortisol secretion (hair cortisol concentrations), or stress reactivity (cortisol, alpha-amylase, heart rate) were associated with PTSD trajectories. Taken together, these findings point to a subset of individual factors associated with elevated posttraumatic stress symptom severity over follow-up, including two (i.e., self-blame, GAD severity) that may be targeted by early cognitive behavioral interventions for PTSD (Kearns et al., 2015).

Exploratory ML methods were used to enhance predictive accuracy for posttraumatic stress symptom severity and PTSD diagnosis. GBM models including an extensive array of theory-driven features as well as baseline posttraumatic stress symptom severity performed somewhat better than a logistic regression model including only baseline posttraumatic stress symptom severity. The performance of the GBM model predicting new PTSD onsets over follow-up (AUC = 0.96) compared favorably to ML studies predicting PTSD screening status three months after emergency room hospitalization (AUC = 0.85) (Papini et al., 2018), posttraumatic stress symptom

trajectories among individuals admitted to emergency rooms (AUC = 0.82) (Galatzer-Levy et al., 2017), and posttraumatic stress symptom trajectories among soldiers deployed to Afghanistan (AUC = 0.88) (Karstoft, Statnikov, et al., 2015). However, bootstrap-based optimism-corrected AUCs for GBM models in the present study should be interpreted with caution in light of the ongoing debate regarding their ability to address overfitting in smaller samples (Iba et al., 2020). These findings support the feasibility of predicting PTSD onset among recent survivors of interpersonal violence.

Contrary to expectation, ML statistical models including a broad range of cognitive and neurobiological predictors exhibited similar predictive performance to a logistic regression model including only baseline PTSD (CAPS-IV) symptom severity scores.

[i] An analysis of 2,473 trauma survivors from 10 longitudinal studies assessed within 60 days of trauma exposure yielded a similar result: logistic regression predicting endpoint PTSD (AUC = 0.85) from baseline CAPS-IV scores performed comparably to a full model with sociodemographic and traumatic event characteristics (AUC = 0.86) (Shalev et al., 2019). Notably, a recent study found a larger improvement in performance between a full ML model with diverse (i.e., hospital, psychosocial, census) predictors (AUC = 0.85) and a logistic regression including a brief, 4-item PTSD severity screening tool (AUC = 0.78) (Papini et al., 2018). Taken together, ML findings from the present study and prior research have two important implications. First, the predictive accuracy of the CAPS-IV interview for identifying interpersonal violence survivors who will develop PTSD is high and is not substantially improved by including additional cognitive and neurobiological risk factors. Second, semi-structured clinical interviews offer improved predictive accuracy compared to brief self-report screening measures. Given that the CAPS-IV interview is time-intensive and requires trained raters, future studies are needed to assess the feasibility of including the CAPS interview in routine risk screening with trauma survivors.

Primary control engagement coping in response to social stressors emerged as an important feature predicting posttraumatic stress symptom trajectories in multilevel models as well as PTSD onsets in ML. Specifically, women who reported greater use of problem-solving, emotional expression, and emotion regulation strategies relative to other coping strategies were less likely to develop PTSD. Greater use of these types of coping was associated with a pattern of low posttraumatic stress symptom severity over time. Prospective studies have yielded inconsistent support for problem-focused coping, finding both positive (Spurrell & McFarlane, 1993) and negative (Johnsen et al., 2002) associations with posttraumatic stress symptoms. One reason for these discrepancies could be the tendency for trauma-exposed

individuals to report greater use of all types of coping strategies, which underscores the importance of assessing the relative use of different strategies within individuals (Connor-Smith et al., 2000). Our findings suggest that a higher proportion of primary control coping (relative to other coping strategies) is an important determinant of resilience among survivors of interpersonal violence.

Multilevel modeling and ML approaches converged on a similar set of stress- and trauma-related predictors. GBM models confirmed the importance of PTSD predictors identified in previous ML studies, including depression (Papini et al., 2018), childhood trauma exposure (Galatzer-Levy et al., 2017; Karstoft, Statnikov, et al., 2015), pain (Karstoft, Galatzer-Levy, et al., 2015), and impaired functioning at work (Karstoft, Galatzer-Levy, et al., 2015). Age of first MDD onset emerged as the most important predictor in both GBM models; marginal effects analyses showed elevated risk for women with first onset occurring before age 17. Earlier MDD onset is associated with greater recurrences, more negative cognitive appraisals, greater functional impairment, and more frequent suicide attempts (Zisook et al., 2007). Early emergence of depression may serve as a marker for other PTSD risk factors such as childhood sexual abuse (Teicher et al., 2009). Alternately, younger age of MDD onset may increase PTSD risk indirectly through the development of negative cognitive style (Zisook et al., 2007).

Multilevel models and ML findings also highlighted a novel set of PTSD predictors among a unique cohort of survivors of recent interpersonal violence. Cognitive processes such as updating, cognitive flexibility, and inhibition (collectively referred to as executive function), emerged as important predictors of both PTSD onsets and posttraumatic stress symptom severity at 6-month follow-up. Executive functions allow individuals to maintain and manipulate information for goal-directed activity while controlling impulses (Miyake et al., 2000). Individuals with PTSD generally exhibit poorer performance on executive function measures compared to controls (Polak et al., 2012). Executive function deficits could increase posttraumatic stress symptoms by making it difficult for trauma survivors to disengage their attention from trauma reminders and to inhibit hyperarousal symptoms (Aupperle et al., 2012). Recent evidence further suggests that better cognitive flexibility in the immediate aftermath of trauma predicted lower subsequent posttraumatic stress symptom severity (Ben-Zion et al., 2018). The present findings advance this literature by showing that measures of cognitive flexibility and inhibition are important predictors of PTSD over and above the influence of other cognitive variables such as coping and appraisals (Morris et al., 2015).

Neuroendocrine measures of diurnal stress response system activity and stress reactivity improved predictive accuracy for PTSD onsets in ML models. Prior meta-analyses identified circulating cortisol levels, heart rate, and blood pressure in emergency room settings, as predictors of subsequent PTSD (Morris et al., 2016). ML models have confirmed urinary cortisol (Galatzer-Levy et al., 2017) and heart rate (Papini et al., 2018) as important features associated with posttraumatic stress symptoms. Pre-trauma cortisol reactivity has also been associated with elevated risk for posttraumatic stress symptoms among soldiers exposed to traumatic events during deployment (Steudte-Schmiedgen et al., 2015). Neurobiological models of PTSD emphasize diurnal cortisol secretion (Steudte-Schmiedgen et al., 2016) and sympathetic nervous system (SNS) dysregulation (Schumacher et al., 2013) as important PTSD risk factors. To our knowledge, this study is the first to include indices of cortisol/alpha-amylase stress reactivity and diurnal secretion in ML classification models for PTSD. Results highlight the importance of both HPA (cortisol: higher anticipatory pre-stress levels, higher daily output, higher hair cortisol concentrations) and SNS (alpha-amylase: higher stress reactivity, lower daily output, lower awakening response, steeper negative slope across the day) factors for prediction of PTSD onset. These findings add to a nascent literature showing altered alpha-amylase awakening responses in individuals with PTSD (Thoma et al., 2012) and altered alpha-amylase reactivity in maltreated women compared to healthy controls (Mielock et al., 2017).

Though important for PTSD classification, neuroendocrine measures were not individually associated with posttraumatic stress symptom trajectories in multilevel models. That is, while their inclusion in ML models enhanced predictive accuracy for PTSD, neuroendocrine measures did not predict patterns of change in posttraumatic stress symptom severity. This divergence between ML and multilevel model findings illustrates the inherent trade-offs between accuracy and interpretability in these approaches. One possible interpretation of this divergence is that neuroendocrine measures are not directly associated with posttraumatic stress symptom trajectories, but rather influence PTSD risk through complex interactions with other biopsychosocial factors (Galatzer-Levy et al., 2017).

Limitations

This study identified a subset of features using two powerful and complementary statistical approaches that showed promise for PTSD prediction; many of these features can be evaluated using relatively brief and

well-validated measures. Overall, study findings should be interpreted with caution until replicated in larger samples due to the small number of interpersonal trauma survivors (n=58) and new PTSD onsets (n=7). Although the performance of exploratory GBM models was adjusted to account for small sample size and high ratio of features to participants, results should be considered preliminary until replicated in larger samples of interpersonal violence survivors and their applicability tested for survivors of other types of traumatic life events (e.g., combat) as well as male survivors. Variability in duration from traumatic event to baseline assessment could have influenced predictive models, despite the inclusion of "days since index trauma" as a predictor in both all models. Women using oral contraceptives—which could influence HPA function - were not excluded; such a criterion would have rendered recruitment prohibitively difficult. The lack of a prospective design precludes determination of whether alterations in predictors of PTSD were present before – or were consequences of - exposure to the index traumatic event. It is important to note that trauma survivors reported a mean of more than 7 prior traumatic events at baseline, which makes it difficult to parse the relative influence of past from present trauma on current PTSD symptom severity. Rather, it is likely that prior traumatic events sensitize survivors to developing PTSD following subsequent exposures (Cougle et al., 2009). It is important to note that the predictive features identified by ML models may not represent mechanisms of risk or resilience for PTSD. Conversely, theory-driven and empirically-supported risk and resilience factors for PTSD may not emerge as relevant predictors in ML models. Certain features identified by GBM models, such as household income, are less amenable to individual-level interventions. Other features that emerged as PTSD predictors are potentially malleable, including cognitive factors (i.e., cognitive flexibility, coping, appraisals), and could inform the refinement of existing early interventions for PTSD (Kearns et al., 2015). Although predictors were examined in relation to distinct patterns of change in PTSD symptom severity, the relatively modest sample size precluded a data analytic approach that could assign individuals to these trajectories. Larger studies of interpersonal trauma survivors using latent growth modeling techniques are needed to evaluate whether the predictors identified in this study are associated with trajectory membership (Galatzer-Levy et al., 2018). Finally, the present study did not evaluate risk factors for other types of posttraumatic psychopathology, including anxiety and depressive disorders, which commonly emerge following interpersonal violence exposure (Perkonigg et al., 2000).

Conclusion

This study sought to identify factors that contributed to posttraumatic stress symptom severity among women who recently experienced interpersonal violence and to enhance predictive accuracy for developing PTSD. Higher levels of self-blame, GAD severity, childhood trauma exposure, and impairment across multiple domains was associated with a pattern of elevated posttraumatic stress symptom severity over time. A semi-structured clinical interview-based measure of baseline PTSD symptom severity demonstrated excellent predictive accuracy, suggesting that improved screening in emergency room or forensic medical exam settings for PTSD risk could be accomplished. Hence, the benefits of improved prediction must be weighed against the time, cost, and feasibility of screening for additional risk and protective factors. Improving our capacity to predict PTSD is especially critical for survivors of interpersonal violence who have received less attention in this literature (Morris & Rao, 2013) despite being at elevated risk compared to survivors of other traumatic life events.

Author Note

The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported, in part, by grants from the National Institutes of Health (K01 MH101403, U54 MD007593, U54MD007586, R01MH108155, R01MD010757 and R01DA040966).

Note

1. There are no statistical tests appropriate for contrasting AUC values between optimism-corrected and logistic regression models, nor for contrasting R^2 values between non-nested models.

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Appendix A1. Baseline Features Included in Multilevel Models and Machine Learning Analyses.

Baseline Feature	Measures
Demographics	Age, height, weight, race, ethnicity, education (years completed), family income, marital status
PTSD	Clinician-Administered PTSD Scale for DSM-IV [total severity score]; PTSD Checklist for DSM-IV (PCL-IV)
Cognitive appraisals	Posttraumatic Cognitions Inventory (PTCI) [negative cognitions about the self, negative cognitions about the world, self-blame subscales]
Coping	Responses to Stress Questionnaire (RSQ): Adult Interpersonal Stress version [primary control coping, secondary control coping, disengagement coping subscales]
Depression	Beck Depression Inventory 2nd Ed. (BDI-II) [total score]; SCID-IV [current/past diagnosis; number of prior depressive episodes, age of first depressive episode onset]
Anxiety	Generalized Anxiety Disorder 7-item scale (GAD-7) [total score]; Spielberger State-Trait Anxiety Inventory (STAI) [trait anxiety score]; SCID-IV (current/past diagnosis of GAD, Panic Disorder, Agoraphobia, OCD)]
Trauma	Life Events Checklist (LEC) [number of prior traumatic events, number of categories of traumatic events]; Childhood Trauma Questionnaire (CTQ) [total score, physical abuse, sexual abuse, emotional abuse, physical neglect, emotional neglect] Peritraumatic Dissociation Scale (PDQ) [total score]; type of index trauma (sexual assault, physical assault)
Stressors	Perceived Events Scale: Young Adult Version [total stress levels for major/daily life events, number of major/daily life events, total stress levels for dependent/independent major/daily life events]
Executive function	D-KEFS trail making [visual scanning, number sequencing, letter sequencing, letter switching, motor speed, composite score, switch vs. visual contrast, switch vs. number contrast, switch vs. letter sequencing contrast, switch vs. number + letter contrast, switch vs. motor contrast, all errors]; D-KEFS design fluency (filled dots, empty dots, switching, composite, filled + empty, switch vs. filled + empty, total set loss, total repeated designs, percent design accuracy]

(*continued*)

Appendix A1. continued

Baseline Feature	Measures
	D-KEFS color word [color naming, word reading, inhibition, inhibition/switching, composite naming + reading, inhibition vs. color naming, inhibition/switching vs. naming + reading, inhibition/switching vs. inhibition, inhibition/switching vs. word reading, color naming errors percentile, word reading errors percentile, inhibition errors, inhibition/switching errors] Wisconsin Card Sorting Test (WCST) [number trials administered, total correct, total correct errors raw, percent errors raw, perseverative responses raw, percent perseverative responses raw, nonperseverative errors raw, percent nonperseverative errors, conceptual responses, percent conceptual responses, categories completed, trials to complete first category, failure to maintain set, learning to learn index]
Pain	PROMIS Pain Interference short form: 8-item [total score]; McGill Pain Questionnaire short form (MPQ-SF) [sensory pain, affective pain, visual analogue pain strength, overall pain description]; Pain Catastrophizing Scale [total score]
Functional impairment	Sheehan Disability Scale (SDS) [family life impairment, social life impairment, work/school impairment]
Healthcare utilization	Medical hospital visits (past 3 months), emergency room visits (past 3 months), other hospital or treatment center visits (past 3 months); visits with a medical doctor or nurse practitioner or physician's assistant (past 3 months); visits with a counselor or mental health provider (past 3 months)
Stress response system	For diurnal secretion and reactivity measures, free cortisol levels were determined by commercial chemiluminescence immunoassay and alpha-amylase levels were determined by a quantitative enzyme kinetic method. Intra- and inter-assay coefficients of variation for these assays were below 6% Reactivity to the Trier Social Stress Test (TSST): Salivary cortisol and alpha-amylase reactivity was determined using four pre-TSST samples collected at 30-minute intervals and seven post-TSST samples collected at 10-minute intervals. Reactivity index was computed as the difference between cortisol/alpha-amylase levels for the final pre-TSST sample and the maximum post-TSST level.

(*continued*)

Appendix A1. continued

Baseline Feature	Measures
	Throughout the TSST, we also obtained continuously recorded heart rate using a Polar H7 chest-strap (Polar, Finland) and Actigraph wrist watch; we computed mean resting heart rate (over a 20-minute period prior to the TSST instructions), anticipatory heart rate (over 5 minutes immediately preceding the TSST), mean heart rate during the 10-minute TSST, and recovery heart rate (over a 20-minute period immediately following the TSST). Diurnal secretion: Diurnal cortisol and alpha-amylase secretion was determined by saliva samples collected at home using cotton swabs (Sarstedt Inc., Netwon, NC) obtained at five established times (waking, 30 minutes after awakening, before lunch, 3pm, 9pm or bedtime) over two consecutive days. Participants were instructed to refrain from brushing teeth, eating, drinking caffeine, or engaging in rigorous exercise within 30 minutes of each sample. Sample times were recorded by participants and confirmed using MEMS 6 TrackCaps (Aardex Ltd., Switzerland). Daily output was computed using the area under the curve with respect to ground (AUCg) formula; average AUCg was determined across both collection days. Cortisol and alpha-amylase awakening responses were determined by the mean change from awakening to 30 minutes after awakening across both collection days. Diurnal cortisol and alpha-amylase slopes were determined based on regression coefficients estimated individually for each participant's daily samples and an average was taken across both collection days. Prolonged HPA secretion was determined by hair cortisol concentrations from 3cm hair segments as described previously. Intra- and inter-assay coefficients of variation for this assay are below 12%.

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