JAMA Psychiatry | Original Investigation

Utility of Wrist-Wearable Data for Assessing Pain, Sleep, and Anxiety Outcomes After Traumatic Stress Exposure

Laura D. Straus, PhD; Xinming An, PhD; Yinyao Ji, MS; Samuel A. McLean, MD, MPH; Thomas C. Neylan, MD; and the AURORA Study Group

IMPORTANCE Adverse posttraumatic neuropsychiatric sequelae after traumatic stress exposure are common and have higher incidence among socioeconomically disadvantaged populations. Pain, depression, avoidance of trauma reminders, reexperiencing trauma, anxiety, hyperarousal, sleep disruption, and nightmares have been reported. Wrist-wearable devices with accelerometers capable of assessing 24-hour rest-activity characteristics are prevalent and may have utility in measuring these outcomes.

OBJECTIVE To evaluate whether wrist-wearable devices can provide useful biomarkers for recovery after traumatic stress exposure.

DESIGN, SETTING, AND PARTICIPANTS Data were analyzed from a diverse cohort of individuals seen in the emergency department after experiencing a traumatic stress exposure, as part of the Advancing Understanding of Recovery After Trauma (AURORA) study. Participants recruited from 27 emergency departments wore wrist-wearable devices for 8 weeks, beginning in the emergency department, and completed serial assessments of neuropsychiatric symptoms. A total of 19 019 patients were screened. Of these, 3040 patients met study criteria, provided informed consent, and completed baseline assessments. A total of 2021 provided data from wrist-wearable devices, completed the 8-week assessment, and were included in this analysis. The data were randomly divided into 2 equal parts (n = 1010) for biomarker identification and validation. Data were collected from September 2017 to January 2020, and data were analyzed from May 2020 to November 2022.

EXPOSURES Participants were recruited for the study after experiencing a traumatic stress exposure (most commonly motor vehicle collision).

MAIN OUTCOMES AND MEASURES Rest-activity characteristics were derived and validated from wrist-wearable devices associated with specific self-reported symptom domains at a point in time and changes in symptom severity over time.

RESULTS Of 2021 included patients, 1257 (62.2%) were female, and the mean (SD) age was 35.8 (13.0) years. Eight wrist-wearable device biomarkers for symptoms of adverse posttraumatic neuropsychiatric sequelae exceeded significance thresholds in the derivation cohort. One of these, reduced 24-hour activity variance, was associated with greater pain severity (r = −0.14; 95% CI, −0.20 to −0.07). Changes in 6 rest-activity measures were associated with changes in pain over time, and changes in the number of transitions between sleep and wake over time were associated with changes in pain, sleep, and anxiety. Simple cutoffs for these biomarkers identified individuals with good recovery for pain (positive predictive value [PPV], 0.85; 95% CI, 0.82-0.88), sleep (PPV, 0.63; 95% CI, 0.59-0.67, and anxiety (PPV, 0.76; 95% CI, 0.72-0.80) with high predictive value.

CONCLUSIONS AND RELEVANCE These findings suggest that wrist-wearable device biomarkers may have utility as screening tools for pain, sleep, and anxiety symptom outcomes after trauma exposure in high-risk populations.

Author Affiliations: Author affiliations are listed at the end of this article.

Group Information: The AURORA Study Group authors appear at the end of the article.

Corresponding Author: Samuel A. McLean, MD, MPH, Institute for Trauma Recovery, Department of Psychiatry, University of North Carolina at Chapel Hill, 304 MacNider Hall, CB# 7160, Chapel Hill, NC 27599-7160 (samuel_mclean@med.unc.edu); Thomas C. Neylan, MD, Department of Neurology, University of California, San Francisco, 4150 Clement St, San Francisco, CA 94121 (thomas.neylan@ucsf.edu).

Up to 90% of individuals experience at least 1 traumatic event.[1] While most individuals recover, adverse posttraumatic neuropsychiatric sequelae (APNS) are common and produce morbidity.[2] Common APNS symptoms include pain and other somatic symptoms, depression, avoidance of trauma reminders, trauma reexperiencing, anxiety, hyperarousal, sleep disruption, and nightmares. These symptoms are associated with negative consequences, including emotional distress, functional impairments,[3,4] and reduced quality of life.[5,6]

More than 1 in 5 individuals in the US use a wrist-wearable device capable of accelerometry.[7] Wrist-wearable devices can assess 24-hour rest, wake, and activity pattern characteristics that have been associated with alterations in pain, fatigue, and mood[8-10] and might influence clinical and psychological outcomes. For example, sleep quality and daytime activity have been found to influence pain, posttraumatic stress, and other symptoms.[11-19] To our knowledge, no large study has used wrist-wearable devices to examine neuropsychiatric sequelae following traumatic stress exposure.

In this study, we used longitudinal wrist-wearable data obtained from a socioeconomically disadvantaged adult population presenting to emergency departments (EDs) after traumatic stress exposure. We obtained serial assessments of 10 common neuropsychiatric symptom domains to identify 24-hour rest, wake, and activity characteristics associated with APNS symptom outcomes. We sought to derive and validate rest-activity characteristics associated with specific APNS symptoms, and changes in rest-activity characteristics associated with changes in APNS symptoms over time. We hypothesized that such characteristics could be identified.

Methods

Study Overview and Sample Characteristics

Data were obtained from the Advancing Understanding of Recovery After Trauma (AURORA) study. The AURORA study collected a combination of prospective data from a diverse sample of trauma survivors recruited from EDs in the early aftermath of trauma. The full AURORA study methodology has been published elsewhere,[2] and we have followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.[20] The AURORA study protocol was approved by the Institutional Review Board at the University of North Carolina at Chapel Hill. Qualifying traumatic events included motor vehicle collision, physical assault, sexual assault, fall more than 10 ft, and mass casualty incidents. AURORA study enrollment began in September 2017; participants who had completed the 8-week period of follow-up assessment by January 2020 were included in this analysis. Individuals were eligible if they presented to one of 27 EDs within the AURORA study network within 72 hours of the trauma, were aged 18 to 65 years, and were able to speak and read English. Individuals were excluded if they had a solid organ injury Grade of 1 or greater per the American Association for the Surgery of Trauma, had significant hemorrhage, required operative intervention, or were likely to be admitted

Key Points

Question Can 24-hour rest-activity characteristics from wrist-wearable devices predict adverse posttraumatic neuropsychiatric symptoms following traumatic stress exposure?

Findings In this cohort study including 2021 participants observed over time after traumatic stress exposure, reduced 24-hour activity variance based on wrist accelerometry identified individuals with greater pain severity. Changes in several rest-activity measures were associated with changes in pain, sleep, and anxiety over time, and simple thresholds for these biomarkers identified individuals with good recovery for pain, sleep, and anxiety with high predictive value.

Meaning These findings suggest that wrist-activity biomarkers may have utility as screening tools for adverse pain, sleep, and anxiety symptom outcomes after trauma exposure.

for more than 72 hours. A total of 3040 patients met all these criteria, provided informed consent, and completed baseline ED assessments. Of these, 2021 provided watch data, completed the 8-week assessment after ED enrollment, and were included in this analysis.

Self-reported Data Collection and Preparation

Sociodemographic characteristics, including race and ethnicity, were assessed via survey items.[2] Following the baseline ED visit, participants completed a rotating battery of smartphone-based questionnaires consisting of 10 common APNS symptom domains: pain,[21,22] depressive symptoms,[23-26] sleep discontinuity,[27] nightmares,[28-30] somatic symptoms,[21,31] difficulty with concentration, thinking, or fatigue,[32-35] avoidance of trauma reminders, trauma reexperiencing, anxiety,[36,37] and hyperarousal.[38-41] As detailed elsewhere,[2] these questions were chosen to capture symptoms of the most common APNS syndromes of pain, postconcussive syndrome, posttraumatic stress disorder, and depression. Each survey item was administered at 6 time points within the first 8 weeks posttrauma using the Mindstrong Discovery application (eTable 1 in Supplement 1). These survey items were used as indicator variables to develop measurement models for each APNS symptom domain, and factor scores for each symptom were computed for each participant at each time point. Joint measurement models including all 6 time points within the first 8 weeks after trauma exposure were developed to define each symptom domain. As noted elsewhere,[2] 8 weeks was chosen as the time frame for assessment because of critical changes in the first few days and weeks after trauma exposure that signal transition from either persistent APNS symptoms or recovery.[22,42,43] Temporal correlations of these indicator variables were introduced to improve model fit if the temporal autocorrelations were not fully explained by the joint measurement model. Model fit indices (eg, comparative fit index, Tucker-Lewis index, standardized root mean square residual) were used to evaluate the fit of each measurement model.[44]

Wrist-Wearable Data Collection and Preparation

Participants were instructed to wear the research watch (Verily Life Sciences[45]) at least 21 hours a day throughout the

8-week study period. In addition to this project, the Verily study watch is currently being used to examine rest-activity biomarkers in other large-scale cohort health studies.[46,47] Participants were sent home with the watch, a charging dock, and a connectivity hub with 4G LTE for data upload. The device collected continuous 3-axis accelerometry data at 30 Hz. Prior to feature extraction, days with missing data percentage larger than 20% were excluded, as well as days in which the participant was categorized as having no activity (wrist-wearable device not worn). Accelerometer data were then converted to activity counts.[48] Briefly, z-axis accelerometry data were filtered using a 0.25-11 Hz bandpass to eliminate the gravitational artifacts and very slow movements.[49] Afterwards, the maximum absolute values inside 1-second windows were taken and summed for each 30-second epoch.[48] Sleep/wake activity patterns were then calculated from each nonoverlapping 30-second accelerometry epoch using the Cole-Kripke algorithm.[50] Cosinor rhythmometry features were used to capture each participant's circadian rhythm.[51] Specifically, a cosine model was fit to the data: $Y(t) = M + K \cos(2\pi t/\tau + \varphi)$, where M is the mesor, K is the amplitude, and φ is the acrophase. The mesor describes the baseline activity of the participant for the day, and the amplitude indicates the difference in daytime and nighttime activities. This algorithm was applied to 24-hour segments of data, and the number of transitions between sleep and wake and percentage of the 24-hour period scored as sleep were calculated. Means and SDs of activity counts for each 24-hour period were also calculated. The most active 10 hours and least active 5 hours, indicating the average daily activity in the wake period and the nighttime activity, respectively, were also derived using the movement data.[52] See eTable 2 in Supplement 1 for rest-activity descriptive statistics.

Rest-Activity Biomarker Derivation, Validation, and Evaluation

For each self-report survey, mean 24-hour wrist-wearable device rest-activity characteristics from the day prior to and the day of self-reported symptom data collection were used as candidate rest-activity biomarkers for corresponding self-reported symptoms. Given this, participants without self-report survey data for a symptom and/or no watch data within the 2 days prior to the survey were excluded from analysis for that symptom. We endeavored to identify rest-activity characteristics associated with the severity of specific APNS symptoms either at a point in time between participants or over time within participants. These 2 types of biomarkers were indicated by cross-sectional and longitudinal associations, respectively, based on repeated measures. Biomarkers with cross-sectional (between-participant) associations helped differentiate participants with respect to APNS symptoms at a point in time. Biomarkers with longitudinal (within-participant) associations helped differentiate the change of the APNS symptoms within participants over time. We used a bivariate linear mixed model to evaluate the correlation for each pair of rest-activity features and symptoms and partition it into between-participant and within-participant correlations based on repeated measures. More specifically, between-

participant and within-participant correlations were derived from the between-participant and within-participant covariance matrix, respectively.[53]

Statistical Analysis

Following initial quality check of rest-activity variables, the data were randomly divided into 2 equal parts (n = 1010) for biomarker identification and validation. The same identification and validation data set was used for all analyses. P values were calculated using the z test. False-discovery rate P value of .05 was used to define biomarkers that passed identification; these biomarkers were then evaluated in the validation data set. A Bonferroni-corrected 2-tailed P value of .05 was used to identify biomarkers that passed the validation step. To explore the potential utility of validated biomarkers to identify change in self-reported symptoms over time, simple cutoffs were used, where symptom worsening or improvement was defined as the symptom outcome measure and biomarker increase or decrease was used as the predictor. Each of these values was generated by subtracting the last symptom or biomarker value (obtained in the final 8-week assessment) from the first value (obtained in week 1). We then assessed the sensitivity, specificity, and positive predictive value (ie, probability of correctly identifying a case) of increasing or decreasing biomarker value for increasing or decreasing symptom score. Because several biomarkers were identified for pain, we constructed a composite biomarker for this outcome comprised of individual biomarkers that were not strongly correlated with each other (eFigure 1 in Supplement 1). To create the composite biomarker, we built a linear mixed model, with pain as the dependent variable and individual biomarkers as predictors, and used the predicted pain score from this linear mixed model as the composite biomarker. Missing data are common in large-scale, longitudinal naturalistic samples; to help explore the potential influence of missing data, we evaluated the association between watch data and self-reported data missingness. All correlations were weak (less than 0.1), suggesting that completion rate did not bias main outcome associations, and thus missing data were considered missing at random (eTable 3 in Supplement 1).

Analyses were conducted using R version 4.0.1 (The R Foundation) and SAS version 9.4 (SAS Institute). For additional information on study methods, see the eMethods in Supplement 1. For data flow pathways for self-report and watch data, see eFigure 2 in Supplement 1. For sample R code for data processing, see the eAppendix in Supplement 1.

Results

Sociodemographic and Clinical Characteristics

Of 2021 included patients, 1257 (62.2%) were female, and the mean (SD) age was 35.8 (13.0) years (**Table 1**). A total of 1014 (50.2%) were Black, 227 (11.2%) were Hispanic, 694 (34.3%) were White, and 77 (3.8%) were another race (including American Indian or Alaska Native, Asian, and Native Hawaiian or Other Pacific Islander). A total of 1595 (79.3%) did not have a college degree, and 1160 (64.2%) earned $35 000 per year or

less. A total of 1519 patients (75.2%) had experienced motor vehicle collision as the traumatic event leading to study inclusion. Median symptom scores indicated a substantial burden of APNS symptoms during the weeks after trauma (**Figure**). For most symptoms, median severity exhibited gradual modest improvement over the study period. Pain scores demonstrated an initial steep decline in the first week after trauma, followed by gradual modest improvement.

Derivation and Validation of Cross-Sectional Biomarkers
We first sought to identify cross-sectional, point-in-time rest-activity biomarkers that identified individuals experiencing high APNS symptoms at a point in time. Eight wrist-wearable device biomarkers for 5 APNS symptoms exceeded significance thresholds in the derivation cohort (**Table 2**). One of these biomarkers, reduced daily activity variance, passed the validation step for cross-sectional association with increased pain ($r = -0.14$; 95% CI, -0.20 to -0.07; adjusted $P < .008$) (Table 2).

Derivation and Validation of Individual State Biomarkers
We next sought to identify changes in rest-activity biomarkers associated with changes in specific APNS symptoms during the initial 8 weeks after trauma (state biomarkers). A total of 13 APNS symptom biomarkers passed the initial derivation step, and 9 APNS symptom biomarkers passed validation (**Table 3**). Among these 9 validated state biomarkers, 7 were associated with changes in pain symptom severity, 1 was associated with changes in sleep quality, and 1 was associated with changes in anxiety. Increased maximum daily activity over time, increased average activity of the individual's most active 10 hours, increased average daily activity, increased baseline activity, and increased variation in daily activity were all associated with reduced pain over time. Reduction in the number of sleep/wake transitions was associated with reductions in self-reported pain, sleep disturbance, and anxiety over time (Table 3).

Utility of Example State Biomarkers
The potential utility of state biomarkers as screening tools for posttrauma outcomes was then assessed, using cutoff scores (**Table 4**). Worsening and improvement in self-reported symptoms was defined as symptom severity in the eighth week minus symptom severity in the first week greater than 0 and less than 0, respectively. Similarly, cutoff scores for change in rest-activity characteristics were defined based on positive vs negative change in rest-activity score at these 2 time points. We obtained high positive predictive values for symptom improvement and high negative predictive values for symptom worsening, suggesting rest-activity measures derived from wrist-wearable devices may have utility as initial screening measures for APNS. In addition, a composite biomarker for pain was developed using a linear mixed model based on the multiple derived and validated rest-activity pain biomarkers. When multiple predictive biomarkers for pain were combined, positive and negative predictive values were similar (Table 4). For additional results, including state biomarkers for subgroups of participants, see eTables 4 and 5 in Supplement 1.

Table 1. Demographic Information

Characteristic	No. (%)
Total, No.	2021
Sex	
Female	1257 (62.2)
Male	764 (37.8)
Race and ethnicity[a]	
Black	1014 (50.2)
Hispanic	227 (11.2)
White	694 (34.3)
Other race	77 (3.8)
Age, mean (SD), y	35.8 (13.0)
Highest grade completed in formal education	
<High school	242 (12.0)
High school graduate	518 (25.6)
Some college	835 (41.3)
College graduate	419 (20.7)
Income, $	
>35 000	647 (32.0)
19 000-35 000	557 (27.6)
<19 000	603 (29.8)
Marital status	
Married or cohabitating	811 (40.1)
Separated, divorced, widowed, or not cohabitating	284 (14.1)
Annulled or never married	915 (45.3)
Trauma type	
Motor vehicle collision	1519 (75.2)
Physical assault	195 (9.6)
Sexual assault	13 (0.6)
Other	294 (14.6)

[a] Race and ethnicity data were collected via survey items. The other race category includes American Indian or Alaska Native, Asian, and Native Hawaiian or Other Pacific Islander races.

Discussion

Most individuals experience traumatic events, and many individuals who come to the ED for care after traumatic stress struggle with 1 or more persistent APNS. This is particularly true for individuals from socioeconomically disadvantaged populations.[54] Wrist-wearable devices with accelerometry are common, and 24-hour rest-activity characteristics obtained from wearable devices might identify those who will recover from trauma in high-risk populations. We derived and validated cross-sectional and longitudinal associations between 24-hour activity patterns and APNS symptoms during the 8 weeks following a traumatic event, a high-risk period during which individuals transition to symptom recovery or persistence. To our knowledge, this study is the first to examine such associations. We identified 1 cross-sectional rest-activity biomarker of an APNS symptom: reduced daily activity variance was a biomarker for increased pain. In addition, we identified 9 rest-activity biomarkers that changed with APNS symptoms over time. Six activity-related biomarkers changed with pain: increased maximum daily activity over time, increased

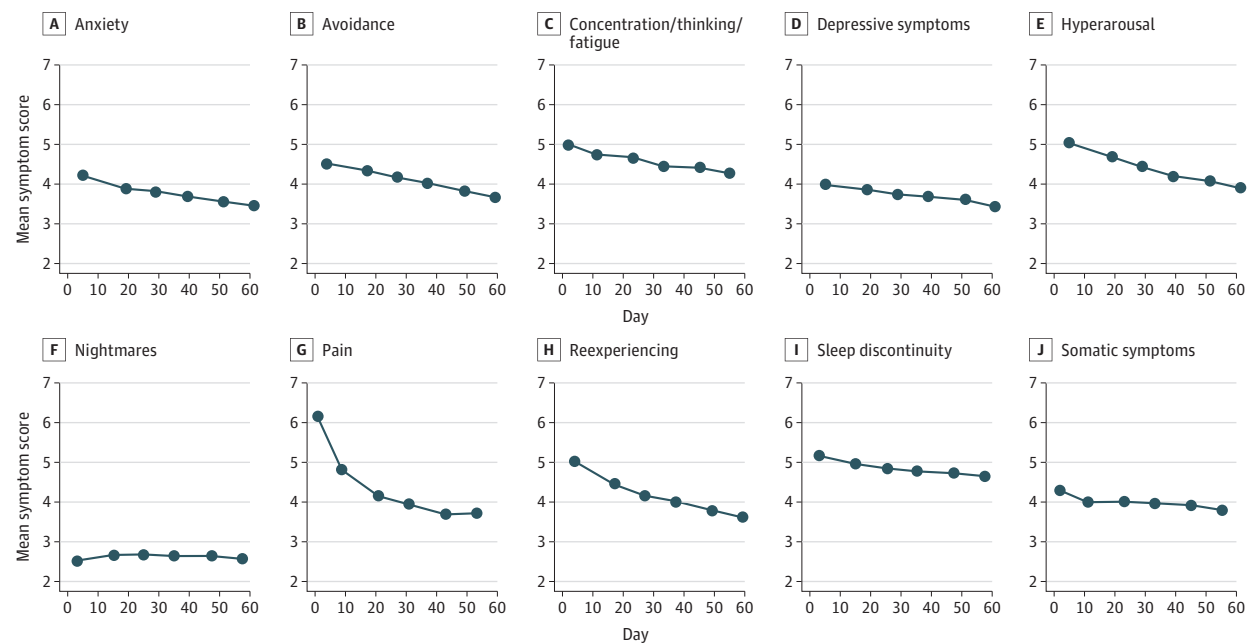Figure. Trajectory of Median Symptom Scores Over the First 8 Weeks After Trauma

Table 2. Wrist-Wearable Rest-Activity Biomarkers Associated With the Severity of Specific Adverse Posttraumatic Neuropsychiatric Symptoms at a Point in Time[a]

Construct	Variable	Correlation (95% CI)	P value	Adjusted P value
Pain	Daily activity variance	−0.14 (−0.20 to −0.07)	<.001	<.001
Somatic symptoms	Percentage of the 24-h period scored as wake	−0.09 (−0.13 to −0.01)	.02	.21
	No. of transitions between sleep and wake	−0.07 (−0.10 to 0.03)	.25	>.99
Nightmares	Percentage of the 24-h period scored as wake	−0.06 (−0.11 to 0.02)	.16	>.99
Depressive symptoms	Percentage of the 24-h period scored as wake	−0.05 (−0.12 to 0.01)	.12	>.99
Pain	Percentage of the 24-h period scored as wake	−0.04 (−0.11 to 0.02)	.18	>.99
Hyperarousal	Percentage of the 24-h period scored as wake	−0.03 (−0.09 to 0.05)	.57	>.99
Nightmares	No. of transitions between sleep and wake	−0.03 (−0.08 to 0.05)	.64	>.99

[a] Results are based on the validation set (50% of the overall sample; n = 1010); 95% CIs and P values were calculated with R package psych.

average activity of the individual's most active 10 hours, increased average daily activity, increased baseline activity, increased variation in daily activity, and increased peak activity. We created a composite biomarker comprised of these measures, which did not outperform the individual measures. One sleep-related biomarker was associated with changes in pain, sleep, and anxiety symptoms over time. Simple biomarker or symptom change cutoffs suggest that these biomarkers might have utility as initial screening tools to identify individuals with potential good recovery in these domains who might not need further evaluation. In clinical practice, they could serve as ancillary data to help patients and physicians identify whether symptoms are improving or worsening after trauma. Notably, the magnitude of associations between individual rest-activity biomarkers and APNS outcomes were small, and no single biomarker achieved both high positive and negative predictive value for APNS symptom change. Given this, these biomarkers would likely have the most utility if used to augment other measures, such as self-report. Additionally, it should be noted that these biomarkers

performed similarly to other objective measures commonly used in clinical practice.[55,56]

Across the 10 APNS symptom domains evaluated, rest-activity biomarkers demonstrated the strongest associations with pain. For example, pain was the only cross-sectional (ie, between-participant(biomarker that passed both the derivation and validation assessments. Specifically, individuals with more severe pain at a point in time demonstrated diminished daily activity variance, indicating less movement during the day and greater sleep disruption during the night. This finding is consistent with prior research suggesting pain conditions are associated with blunted rest-activity rhythms.[8-10] Pain also showed negative within-participant correlations of daily activity over time, indicating that as pain increased over time for an individual, daily activity and variance of daily activity decreased. Participants with worsening pain over the study period also showed increasing number of transitions between sleep and wake. These findings are consistent with other studies that have found temporal relationships between pain severity, activity,

Table 3. Changes in Wrist-Wearable Rest-Activity Biomarkers
Associated With Changes in Symptom Domain Outcomes Over Time[a]

Construct	Variable	Correlation (95% CI)	P value	Adjusted P value
Pain	Maximum daily activity	−0.15 (−0.18 to −0.12)	<.001	<.001
	Average activity of most active 10 h	−0.14 (−0.17 to −0.11)	<.001	<.001
	Average daily activity	−0.13 (−0.16 to −0.10)	<.001	<.001
	Baseline activity[b]	−0.13 (−0.16 to −0.09)	<.001	<.001
	SD of daily activity	−0.12 (−0.15 to −0.09)	<.001	<.001
	Peak activity timing	−0.07 (−0.11 to −0.04)	<.001	<.001
	Percentage of the 24-h period scored as wake	−0.05 (−0.09 to −0.02)	.001	.02
Depressive symptoms	Maximum daily activity	−0.04 (−0.07 to 0)	.04	.64
	Percentage of the 24-h period scored as wake	−0.02 (−0.05 to 0.01)	.25	>.99
Pain	No. of transitions between sleep and wake	0.13 (0.10 to 0.16)	<.001	<.001
Sleep discontinuity	No. of transitions between sleep and wake	0.10 (0.06 to 0.13)	<.001	<.001
Anxiety	No. of transitions between sleep and wake	0.06 (0.03 to 0.09)	<.001	.007
Depressive symptoms	No. of transitions between sleep and wake	0.05 (0.02 to 0.09)	.002	.03
Somatic symptoms	No. of transitions between sleep and wake	0.04 (0.01 to 0.08)	.003	.06

[a] Results are based on the validation set (50% of the overall sample; n = 1010).

[b] Mesor from the circadian rhythm cosine model; 95% CIs and P values were calculated with R package psych.

Table 4. Prediction of Symptom Trajectory Using Biomarker Trajectory[a]

Outcome	Sample with outcome, No. (%)	Feature variable	Sensitivity	Specificity	PPV[b]	NPV[b]	Accuracy
Worsening[c]							
Pain	139 (17)	Maximum daily activity	0.44	0.63	0.20	0.84	0.60
Pain	139 (17)	Average activity of most active 10 h	0.42	0.67	0.21	0.85	0.63
Pain	139 (17)	No. of transitions between sleep and wake	0.38	0.60	0.17	0.82	0.56
Pain	139 (17)	Average daily activity	0.44	0.67	0.22	0.85	0.63
Pain	139 (17)	Baseline activity[c,d]	0.42	0.67	0.21	0.85	0.63
Pain	139 (17)	SD of daily activity	0.40	0.67	0.20	0.84	0.62
Pain	139 (17)	Peak activity timing	0.42	0.58	0.18	0.83	0.56
Sleep	315 (39)	No. of transitions between sleep and wake	0.37	0.69	0.43	0.63	0.56
Anxiety	197 (24)	No. of transitions between sleep and wake	0.36	0.66	0.25	0.76	0.58
Pain	139 (17)	Composite biomarker	0.42	0.68	0.21	0.85	0.64
Improvement[c]							
Pain	660 (83)	Maximum daily activity	0.63	0.44	0.84	0.20	0.60
Pain	660 (83)	Average activity of most active 10 h	0.67	0.42	0.85	0.21	0.63
Pain	660 (83)	No. of transitions between sleep and wake	0.60	0.38	0.82	0.17	0.56
Pain	660 (83)	Average daily activity	0.67	0.44	0.85	0.22	0.63
Pain	660 (83)	Baseline activity	0.67	0.42	0.85	0.21	0.63
Pain	660 (83)	Standard deviation of daily activity	0.67	0.40	0.84	0.20	0.62
Pain	660 (83)	Peak activity timing	0.58	0.42	0.83	0.18	0.56
Sleep	500 (61)	No. of transitions between sleep and wake	0.69	0.37	0.63	0.43	0.56
Anxiety	612 (76)	No. of transitions between sleep and wake	0.66	0.36	0.76	0.25	0.58
Pain	660 (83)	Composite biomarker	0.68	0.42	0.85	0.21	0.64

[a] Results are based on the validation set (50% of the overall sample; n = 1010).

[b] Positive predictive value indicates the probability of correctly identifying that an individual fits the category, while negative predictive value indicates the probability of correctly identifying that an individual does not fit the category.

[c] Worsening and improvement in self-report symptoms was defined as symptom severity in week 8 minus symptom severity in week 1 greater than 0 and less than 0, respectively. Similarly, cutoff scores for change in rest-activity characteristics were defined based on positive vs negative change in rest-activity score at these 2 time points. Prediction was made based on the change in rest-activity characteristic and its correlation with the symptom. For example, if the rest-activity characteristic was positively correlated with the symptom and it increased between week 1 and 8, we would predict the symptom was worsening.

[d] Mesor from the circadian rhythm cosine model.

and sleep quality in the immediate aftermath of traumatic events.[57,58]

In addition to pain, we also observed temporal associations in trauma survivors between changes in rest-activity measures and self-reported anxiety and sleep quality. Worsening sleep continuity (as measured by sleep/wake transitions) over the 8-week study period was associated with worsening self-reported difficulties with anxiety and sleep quality, while

improving sleep continuity was associated with improvements in self-reported anxiety and sleep quality. This finding makes sense in the context of research suggesting sleep problems and anxiety symptoms are related to each other bidirectionally[15] and that sleep problems prior to[29,59] or in the immediate aftermath of traumatic events is a vulnerability factor for other difficulties, such as posttraumatic stress disorder and depression.[60,61] In this study, improving sleep consolidation was associated with improving self-reported anxiety symptoms over the study period, suggesting that interventions to improve sleep consolidation may be helpful to implement soon after trauma to improve other long-term mental health outcomes. Brief behavioral interventions for sleep[62,63] can be delivered by telehealth, which may be particularly practical to implement for patients presenting to EDs.

Limitations

Limitations should be considered when interpreting our study results. All trauma survivors enrolled presented to the ED for evaluation; the generalizability of study findings to patients who do not present to the ED is not known. In addition, most were survivors of motor vehicle collisions, and the generalizability of study findings to other types of trauma is also unknown. Additionally, analyses required concurrent accelerometry and self-reported data. While missing data were not correlated with any of our specific outcome measures, there could be other potential missing data patterns we could not account for. We applied the sleep-wake detection algorithm to 24-hour data instead of a participant-identified sleep period, raising the possibility that sedentary segments could be confused as sleep. However, passive monitoring with accelerometers without concurrent sleep diaries is naturalistic and performed in other large-scale studies.[64] Study evaluation was limited to the 8 weeks immediately following a traumatic event. Future studies should examine wrist-wearable biomarker associations with APNS symptoms and symptom changes over longer time durations. Finally, existing users of wearable technology are generally more health conscious, wealthier, insured, and have higher education and access to wireless technologies,[7,46] which differed from the population of this study. While our study more closely resembles the population likely to present to the ED after experiencing trauma, there may be challenges implementing wearable-based assessment and intervention tools in this group in clinical practice. However, given this, we found no specific patterns regarding missing data for wearable devices vs self-report, suggesting that our results are at least internally valid.

Conclusions

Wrist-wearable devices are common and frequently use built-in accelerometers to detect 24-hour activity patterns.[65] Thus, a proportion of the population may be using devices capable of yielding useful information to help screen for trauma survivors with high pain levels at a point in time and/or poor pain, sleep, and/or anxiety recovery over time. In the future, such biomarkers might be useful to identify trauma survivors who merit further evaluation for adverse trauma outcomes, particularly in vulnerable populations. Such biomarkers might also be useful to help clinicians and patients evaluate their responses to treatment interventions for pain, sleep, or anxiety and to help patients understand how their activity, rest, and sleep affect their health.

Author Affiliations: San Francisco VA Medical Center, San Francisco, California (Straus); Department of Psychiatry, University of California, San Francisco (Straus, Neylan); Institute for Trauma Recovery, Department of Anesthesiology, University of North Carolina at Chapel Hill (An); Institute for Trauma Recovery, Department of Psychiatry, University of North Carolina at Chapel Hill (Ji, McLean); Department of Emergency Medicine, University of North Carolina at Chapel Hill (McLean); Department of Neurology, University of California, San Francisco (Neylan).

The AURORA Study Group Authors: Ayse S. Cakmak, PhD; Anne Richards, MD, MPH; Gari D. Clifford, DPhil; Mochuan Liu, MS; Donglin Zeng, PhD; Stacey L. House, MD, PhD; Francesca L. Beaudoin, MD, PhD; Jennifer S. Stevens, PhD; Sarah D. Linnstaedt, PhD; Laura T. Germine, PhD; Kenneth A. Bollen, PhD; Scott L. Rauch, MD; John P. Haran, MD, PhD; Alan B. Storrow, MD; Christopher Lewandowski, MD; Paul I. Musey, MD; Phyllis L. Hendry, MD; Sophia Sheikh, MD; Christopher W. Jones, MD; Brittany E. Punches, PhD, RN; Michael C. Kurz, MD; Robert A. Swor, DO; Lauren A. Hudak, MD, MPH; Mark J. Seamon, MD; Elizabeth M.

Datner, MD; Anna M. Chang, MD; Claire Pearson, MD; David A. Peak, MD; Roland C. Merchant, MD, MPH, ScD; Robert M. Domeier, MD; Niels K. Rathlev, MD; Brian J. O'Neil, MD; Paulina Sergot, MD; Leon D. Sanchez, MD, MPH; Steven E. Bruce, PhD; Mark W. Miller, PhD; Robert H. Pietrzak, PhD, MPH; Jutta Joormann, PhD; Deanna M. Barch, MD, PhD; Diego A. Pizzagalli, PhD; John F. Sheridan, PhD; Steven E. Harte, PhD; James M. Elliott, PhD; Ronald C. Kessler, PhD; Kerry J. Ressler, MD, PhD; Karestan C. Koenen, PhD.

Affiliations of The AURORA Study Group Authors: Department of Psychiatry, University of California, San Francisco (Richards); Institute for Trauma Recovery, Department of Anesthesiology, University of North Carolina at Chapel Hill (Linnstaedt); Institute for Trauma Recovery, Department of Psychiatry, University of North Carolina at Chapel Hill (Liu); School of Electrical and Computer Engineering, Georgia Institute of Technology, Atlanta (Cakmak); VA San Francisco Health Care System, San Francisco, California (Richards); Department of Biomedical Informatics, Emory University School of Medicine, Atlanta, Georgia (Clifford); Department of Biomedical Engineering, Georgia Institute of Technology, Emory University, Atlanta (Clifford); Department of Biostatistics, University of North Carolina at Chapel Hill (Liu); Department of Biostatistics, Gillings School of Global Public Health, University of North

Carolina at Chapel Hill (Zeng); Department of Emergency Medicine, Washington University School of Medicine, St Louis, Missouri (House); Department of Epidemiology, Brown University, Providence, Rhode Island (Beaudoin); Department of Emergency Medicine, Brown University, Providence, Rhode Island (Beaudoin); Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta (Stevens); Institute for Technology in Psychiatry, McLean Hospital, Belmont, Massachusetts (Germine, Rauch); The Many Brains Project, Belmont, Massachusetts (Germine); Department of Psychiatry, Harvard Medical School, Boston, Massachusetts (Germine, Rauch, Pizzagalli, Ressler); Department of Psychology and Neuroscience, University of North Carolina at Chapel Hill (Bollen); Department of Psychiatry, McLean Hospital, Belmont, Massachusetts (Rauch); Department of Emergency Medicine, University of Massachusetts Chan Medical School, Worcester (Haran); Department of Emergency Medicine, Vanderbilt University Medical Center, Nashville, Tennessee (Storrow); Department of Emergency Medicine, Henry Ford Health System, Detroit, Michigan (Lewandowski); Department of Emergency Medicine, Indiana University School of Medicine, Indianapolis (Musey); Department of Emergency Medicine, University of Florida College of Medicine, Jacksonville (Hendry, Sheikh); Department of Emergency Medicine, Cooper

Medical School of Rowan University, Camden, New Jersey (Jones); Department of Emergency Medicine, Ohio State University College of Medicine, Columbus (Punches); Ohio State University College of Nursing, Columbus (Punches); Department of Emergency Medicine, University of Alabama School of Medicine, Birmingham (Kurz); Department of Surgery, Division of Acute Care Surgery, University of Alabama School of Medicine, Birmingham (Kurz); Center for Injury Science, University of Alabama at Birmingham (Kurz); Department of Emergency Medicine, Oakland University William Beaumont School of Medicine, Rochester, Michigan (Swor); Department of Emergency Medicine, Emory University School of Medicine, Atlanta, Georgia (Hudak); Perelman School of Medicine, University of Pennsylvania, Philadelphia (Hudak, Seamon); Department of Surgery, Division of Traumatology, Surgical Critical Care and Emergency Surgery, University of Pennsylvania, Philadelphia (Seamon); Department of Emergency Medicine, Einstein Healthcare Network, Philadelphia, Pennsylvania (Datner); Department of Emergency Medicine, Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania (Datner); Department of Emergency Medicine, Jefferson University Hospitals, Philadelphia, Pennsylvania (Chang); Department of Emergency Medicine, Wayne State University, Ascension St. John Hospital, Detroit, Michigan (Pearson); Department of Emergency Medicine, Massachusetts General Hospital, Boston (Peak); Department of Emergency Medicine, Brigham and Women's Hospital, Boston, Massachusetts (Merchant, Sanchez); Department of Emergency Medicine, Saint Joseph Mercy Hospital, Ypsilanti, Michigan (Domeier); Department of Emergency Medicine, University of Massachusetts Medical School-Baystate, Springfield (Rathlev); Department of Emergency Medicine, Wayne State University, Detroit Receiving Hospital, Detroit, Michigan (O'Neil); Department of Emergency Medicine, McGovern Medical School at UTHealth, Houston, Texas (Sergot); Department of Emergency Medicine, Harvard Medical School, Boston, Massachusetts (Sanchez); Department of Psychological Sciences, University of Missouri, St Louis (Bruce); National Center for PTSD, Behavioral Science Division, VA Boston Healthcare System, Boston, Massachusetts (Miller); Department of Psychiatry, Boston University School of Medicine, Boston, Massachusetts (Miller); National Center for PTSD, Clinical Neurosciences Division, VA Connecticut Healthcare System, West Haven, Connecticut (Pietrzak); Department of Psychiatry, Yale School of Medicine, New Haven, Connecticut (Pietrzak); Department of Psychology, Yale University, New Haven, Connecticut (Joormann); Department of Psychological and Brain Sciences, Washington University in St Louis (Barch); Division of Depression and Anxiety, McLean Hospital, Belmont, Massachusetts (Pizzagalli, Ressler); Division of Biosciences, Ohio State University College of Dentistry, Columbus (Sheridan); Institute for Behavioral Medicine Research, OSU Wexner Medical Center, Columbus, Ohio (Sheridan); Department of Anesthesiology, University of Michigan Medical School, Ann Arbor (Harte); Department of Internal Medicine–Rheumatology, University of Michigan Medical School, Ann Arbor (Harte); Kolling Institute, University of Sydney, St Leonards, Australia (Elliott); Faculty of Medicine and Health, University of Sydney, Northern Sydney Local Health District, Sydney, Australia (Elliott); Physical Therapy and Human Movement Sciences, Feinberg School of Medicine, Northwestern University, Chicago, Illinois (Elliott); Department of Health Care Policy, Harvard Medical School, Boston, Massachusetts (Kessler); Department of Epidemiology, Harvard T. H. Chan School of Public Health, Harvard University, Boston, Massachusetts (Koenen); Department of Sociology, University of North Carolina at Chapel Hill (Bollen).

REFERENCES

1. Kilpatrick DG, Resnick HS, Milanak ME, Miller MW, Keyes KM, Friedman MJ. National estimates of exposure to traumatic events and PTSD prevalence using *DSM-IV* and *DSM-5* criteria. *J Trauma Stress*. 2013;26(5):537-547. doi:10.1002/jts.21848

2. McLean SA, Ressler K, Koenen KC, et al. The AURORA study: a longitudinal, multimodal library of brain biology and function after traumatic stress exposure. *Mol Psychiatry*. 2020;25(2):283-296. doi:10.1038/s41380-019-0581-3

3. Momartin S, Silove D, Manicavasagar V, Steel Z. Comorbidity of PTSD and depression: associations with trauma exposure, symptom severity and functional impairment in Bosnian refugees resettled in Australia. *J Affect Disord*. 2004;80 (2-3):231-238. doi:10.1016/S0165-0327(03)00131-9

4. Dobie DJ, Kivlahan DR, Maynard C, Bush KR, Davis TM, Bradley KA. Posttraumatic stress disorder in female veterans: association with self-reported health problems and functional impairment. *Arch Intern Med*. 2004;164(4):394-400. doi:10.1001/archinte.164.4.394

5. Clapp JD, Beck GJ, Palyo SA, Grant DM. An examination of the synergy of pain and PTSD on quality of life: additive or multiplicative effects? *Pain*. 2008;138(2):301-309. doi:10.1016/j.pain.2008.01.001

6. Gormsen L, Rosenberg R, Bach FW, Jensen TS. Depression, anxiety, health-related quality of life and pain in patients with chronic fibromyalgia and neuropathic pain. *Eur J Pain*. 2010;14(2):127.e1-127.e8. doi:10.1016/j.ejpain.2009.03.010

7. Chandrasekaran R, Katthula V, Moustakas E. Patterns of use and key predictors for the use of wearable health care devices by US adults: insights from a national survey. *J Med internet Res*. 2020;22 (10):e22443. doi:10.2196/22443

8. Wilson AC, Palermo TM. Physical activity and function in adolescents with chronic pain: a controlled study using actigraphy. *J Pain*. 2012;13 (2):121-130. doi:10.1016/j.jpain.2011.08.008

9. Korszun A, Young EA, Engleberg NC, Brucksch CB, Greden JF, Crofford LA. Use of actigraphy for monitoring sleep and activity levels in patients with fibromyalgia and depression. *J Psychosom Res*. 2002;52(6):439-443. doi:10.1016/S0022-3999(01)00237-9

10. Neikrug AB, Donaldson G, Iacob E, Williams SL, Hamilton CA, Okifuji A. Activity rhythms and clinical correlates in fibromyalgia. *Pain*. 2017;158(8): 1417-1429. doi:10.1097/j.pain.0000000000000906

11. Lautenbacher S, Kundermann B, Krieg J-C. Sleep deprivation and pain perception. *Sleep Med Rev*. 2006;10(5):357-369. doi:10.1016/j.smrv.2005.08.001

12. McLean SA, Clauw DJ, Abelson JL, Liberzon I. The development of persistent pain and psychological morbidity after motor vehicle collision: integrating the potential role of stress response systems into a biopsychosocial model. *Psychosom Med*. 2005;67(5):783-790. doi:10.1097/01.psy.0000181276.49204.bb

13. Smagula SF, Krafty RT, Thayer JF, Buysse DJ, Hall MH. Rest-activity rhythm profiles associated with manic-hypomanic and depressive symptoms. *J Psychiatr Res*. 2018;102:238-244. doi:10.1016/j.jpsychires.2018.04.015

14. Luik AI, Zuurbier LA, Direk N, Hofman A, Van Someren EJ, Tiemeier H. 24-Hour activity rhythm and sleep disturbances in depression and anxiety: a population-based study of middle-aged and older persons. *Depress Anxiety*. 2015;32(9): 684-692. doi:10.1002/da.22355

15. Richards A, Kanady JC, Neylan TC. Sleep disturbance in PTSD and other anxiety-related disorders: an updated review of clinical features, physiological characteristics, and psychological and neurobiological mechanisms. *Neuropsychopharmacology*. 2020;45(1):55-73. doi:10.1038/s41386-019-0486-5

16. Geneen LJ, Moore RA, Clarke C, Martin D, Colvin LA, Smith BH. Physical activity and exercise for chronic pain in adults: an overview of Cochrane Reviews. *Cochrane Database Syst Rev*. 2017;4(4): CD011279. doi:10.1002/14651858.CD011279.pub2

17. Pigeon WR, Moynihan J, Matteson-Rusby S, et al. Comparative effectiveness of CBT interventions for co-morbid chronic pain & insomnia: a pilot study. *Behav Res Ther*. 2012;50 (11):685-689. doi:10.1016/j.brat.2012.07.005

18. Belleville G, Cousineau H, Levrier K, St-Pierre-Delorme M-È. Meta-analytic review of the impact of cognitive-behavior therapy for insomnia on concomitant anxiety. *Clin Psychol Rev*. 2011;31 (4):638-652. doi:10.1016/j.cpr.2011.02.004

19. Anderson E, Shivakumar G. Effects of exercise and physical activity on anxiety. *Front Psychiatry*. 2013;4:27. doi:10.3389/fpsyt.2013.00027

20. Vandenbroucke JP, von Elm E, Altman DG, et al; STROBE initiative. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. *Ann Intern Med*. 2007;147(8):W163-W194. doi:10.7326/0003-4819-147-8-200710160-00010-w1

21. Moldofsky H, Rothman L, Kleinman R, Rhind SG, Richardson JD. Disturbed EEG sleep, paranoid cognition and somatic symptoms identify veterans with post-traumatic stress disorder. *BJPsych Open*. 2016;2(6):359-365. doi:10.1192/bjpo.bp.116.003483

22. Ulirsch JC, Weaver MA, Bortsov AV, et al. No man is an island: living in a disadvantaged neighborhood influences chronic pain development after motor vehicle collision. *Pain*. 2014;155(10): 2116-2123. doi:10.1016/j.pain.2014.07.025

23. Gold PW, Chrousos GP. Organization of the stress system and its dysregulation in melancholic and atypical depression: high vs low CRH/NE states. *Mol Psychiatry*. 2002;7(3):254-275. doi:10.1038/sj.mp.4001032

24. Doerig N, Krieger T, Altenstein D, et al. Amygdala response to self-critical stimuli and symptom improvement in psychotherapy for depression. *Br J Psychiatry*. 2016;208(2):175-181. doi:10.1192/bjp.bp.114.149971

25. Gollan JK, Buchanan A, Connolly M, et al. Differences in the neural correlates of affective responses in depressed and healthy women. *Psychiatry Res*. 2015;234(3):336-345. doi:10.1016/j.pscychresns.2015.10.006

26. Liu CH, Ma X, Song LP, et al. Abnormal spontaneous neural activity in the anterior insular and anterior cingulate cortices in anxious depression. *Behav Brain Res*. 2015;281:339-347. doi:10.1016/j.bbr.2014.11.047

27. Koren D, Arnon I, Lavie P, Klein E. Sleep complaints as early predictors of posttraumatic stress disorder: a 1-year prospective study of injured survivors of motor vehicle accidents. *Am J Psychiatry*. 2002;159(5):855-857. doi:10.1176/appi.ajp.159.5.855

28. Kobayashi I, Sledjeski EM, Spoonster E, Fallon WF Jr, Delahanty DL. Effects of early nightmares on the development of sleep disturbances in motor vehicle accident victims. *J Trauma Stress*. 2008;21(6):548-555. doi:10.1002/jts.20368

29. Bryant RA, Creamer M, O'Donnell M, Silove D, McFarlane AC. Sleep disturbance immediately prior to trauma predicts subsequent psychiatric disorder. *Sleep*. 2010;33(1):69-74. doi:10.1093/sleep/33.1.69

30. van Liempt S, van Zuiden M, Westenberg H, Super A, Vermetten E. Impact of impaired sleep on the development of PTSD symptoms in combat veterans: a prospective longitudinal cohort study. *Depress Anxiety*. 2013;30(5):469-474. doi:10.1002/da.22054

31. McAndrew LM, Lu SE, Phillips LA, Maestro K, Quigley KS. Mutual maintenance of PTSD and physical symptoms for Veterans returning from deployment. *Eur J Psychotraumatol*. 2019;10(1):1608717. doi:10.1080/20008198.2019.1608717

32. Scott JC, Matt GE, Wrocklage KM, et al. A quantitative meta-analysis of neurocognitive functioning in posttraumatic stress disorder. *Psychol Bull*. 2015;141(1):105-140. doi:10.1037/a0038039

33. Christensen H, Griffiths K, Mackinnon A, Jacomb P. A quantitative review of cognitive deficits in depression and Alzheimer-type dementia. *J Int Neuropsychol Soc*. 1997;3(6):631-651. doi:10.1017/S1355617797006310

34. Zakzanis KK, Leach L, Kaplan E. On the nature and pattern of neurocognitive function in major depressive disorder. *Neuropsychiatry Neuropsychol Behav Neurol*. 1998;11(3):111-119.

35. Henry J, Crawford JR. A meta-analytic review of verbal fluency deficits in depression. *J Clin Exp Neuropsychol*. 2005;27(1):78-101. doi:10.1080/138033990513654

36. Boffa JW, Norr AM, Raines AM, Albanese BJ, Short NA, Schmidt NB. Anxiety sensitivity prospectively predicts posttraumatic stress symptoms following a campus shooting. *Behav Ther*. 2016;47(3):367-376. doi:10.1016/j.beth.2016.02.006

37. Olatunji BO, Fan Q. Anxiety sensitivity and post-traumatic stress reactions: evidence for intrusions and physiological arousal as mediating and moderating mechanisms. *J Anxiety Disord*. 2015;34:76-85. doi:10.1016/j.janxdis.2015.06.002

38. Pole N. The psychophysiology of posttraumatic stress disorder: a meta-analysis. *Psychol Bull*. 2007;133(5):725-746. doi:10.1037/0033-2909.133.5.725

39. Jovanovic T, Sakoman AJ, Kozarić-Kovačić D, et al. Acute stress disorder versus chronic posttraumatic stress disorder: inhibition of fear as a function of time since trauma. *Depress Anxiety*. 2013;30(3):217-224. doi:10.1002/da.21991

40. Orr SP, Metzger LJ, Lasko NB, et al; Harvard/Veterans Affairs Post-traumatic Stress Disorder Twin Study Investigators. Physiologic responses to sudden, loud tones in monozygotic twins discordant for combat exposure: association with posttraumatic stress disorder. *Arch Gen Psychiatry*. 2003;60(3):283-288. doi:10.1001/archpsyc.60.3.283

41. Shalev AY, Peri T, Brandes D, Freedman S, Orr SP, Pitman RK. Auditory startle response in trauma survivors with posttraumatic stress disorder: a prospective study. *Am J Psychiatry*. 2000;157(2):255-261. doi:10.1176/appi.ajp.157.2.255

42. Sterling M, Hendrikz J, Kenardy J. Similar factors predict disability and posttraumatic stress disorder trajectories after whiplash injury. *Pain*. 2011;152(6):1272-1278. doi:10.1016/j.pain.2011.01.056

43. Hu J, Bortsov AV, Ballina L, et al. Chronic widespread pain after motor vehicle collision typically occurs through immediate development and nonrecovery: results of an emergency department-based cohort study. *Pain*. 2016;157(2):438-444. doi:10.1097/j.pain.0000000000000388

44. Hu L, Bentler PM. Cutoff criterion for fit indexes in covariance structure analysis: conventional criteria versus new alternatives. *Struct Equ Modeling*. 1999;6:1-55. doi:10.1080/10705519909540118

45. Alphabet I. Developing a sensor-based wearable for continuous monitoring. Accessed August 26, 2022. https://verily.com/solutions/study-watch/

46. Smuck M, Odonkor CA, Wilt JK, Schmidt N, Swiernik MA. The emerging clinical role of wearables: factors for successful implementation in healthcare. *NPJ Digit Med*. 2021;4(1):45. doi:10.1038/s41746-021-00418-3

47. Arges K, Assimes T, Bajaj V, et al. The Project Baseline Health Study: a step towards a broader mission to map human health. *NPJ Digit Med*. 2020;3(1):84. doi:10.1038/s41746-020-0290-y

48. Borazio M, Berlin E, Kücükyildiz N, Scholl P, Van Laerhoven K. Towards benchmarked sleep detection with wrist-worn sensing units. Paper presented at: 2014 IEEE International Conference on Healthcare Informatics; September 15-17, 2014; Verona, Italy.

49. Ancoli-Israel S, Cole R, Alessi C, Chambers M, Moorcroft W, Pollak CP. The role of actigraphy in the study of sleep and circadian rhythms. *Sleep*. 2003;26(3):342-392. doi:10.1093/sleep/26.3.342

50. Kosmadopoulos A, Sargent C, Darwent D, Zhou X, Roach GD. Alternatives to polysomnography (PSG): a validation of wrist actigraphy and a partial-PSG system. *Behav Res Methods*. 2014;46(4):1032-1041. doi:10.3758/s13428-013-0438-7

51. Cornelissen G. Cosinor-based rhythmometry. *Theor Biol Med Model*. 2014;11(1):16. doi:10.1186/1742-4682-11-16

52. Van Someren EJ, Swaab DF, Colenda CC, Cohen W, McCall WV, Rosenquist PB. Bright light therapy: improved sensitivity to its effects on rest-activity rhythms in Alzheimer patients by application of nonparametric methods. *Chronobiol Int*. 1999;16(4):505-518. doi:10.3109/07420529908998724

53. Huang Q, Railkar R. PROC MIXED: calculate correlation coefficients in the presence of repeated measurements. Accessed February 19, 2020. https://www.pharmasug.org/proceedings/2019/ST/PharmaSUG-2019-ST-321.pdf

54. Chiu KB, deRoon-Cassini TA, Brasel KJ. Factors identifying risk for psychological distress in the civilian trauma population. *Acad Emerg Med*. 2011;18(11):1156-1160. doi:10.1111/j.1553-2712.2011.01206.x

55. Wootton D, Feldman C. The diagnosis of pneumonia requires a chest radiograph (x-ray)—yes, no or sometimes? *Pneumonia (Nathan)*. 2014;5(1)(suppl 1):1-7. doi:10.15172/pneu.2014.5/464

56. Leman P. Validity of urinalysis and microscopy for detecting urinary tract infection in the emergency department. *Eur J Emerg Med*. 2002;9(2):141-147. doi:10.1097/00063110-200206000-00008

57. Borchgrevink GE, Kaasa A, McDonagh D, Stiles TC, Haraldseth O, Lereim I. Acute treatment of whiplash neck sprain injuries. a randomized trial of treatment during the first 14 days after a car accident. *Spine (Phila Pa 1976)*. 1998;23(1):25-31. doi:10.1097/00007632-199801010-00006

58. Finan PH, Goodin BR, Smith MT. The association of sleep and pain: an update and a path forward. *J Pain*. 2013;14(12):1539-1552. doi:10.1016/j.jpain.2013.08.007

59. Neylan TC, Kessler RC, Ressler KJ, et al. Prior sleep problems and adverse post-traumatic neuropsychiatric sequelae of motor vehicle collision in the AURORA study. *Sleep*. 2021;44(3):zsaa200. doi:10.1093/sleep/zsaa200

60. Babson KA, Feldner MT. Temporal relations between sleep problems and both traumatic event exposure and PTSD: a critical review of the empirical literature. *J Anxiety Disord*. 2010;24(1):1-15. doi:10.1016/j.janxdis.2009.08.002

61. Spoormaker VI, Montgomery P. Disturbed sleep in post-traumatic stress disorder: secondary symptom or core feature? *Sleep Med Rev*. 2008;12(3):169-184. doi:10.1016/j.smrv.2007.08.008

62. Troxel WM, Germain A, Buysse DJ. Clinical management of insomnia with brief behavioral treatment (BBTI). *Behav Sleep Med*. 2012;10(4):266-279. doi:10.1080/15402002.2011.607200

63. Maguen S, Gloria R, Huggins J, et al. Brief behavioral treatment for insomnia improves psychosocial functioning in veterans: results from a randomized controlled trial. *Sleep*. 2021;44(3):zsaa205. doi:10.1093/sleep/zsaa205

64. Doherty A, Jackson D, Hammerla N, et al. Large scale population assessment of physical activity using wrist worn accelerometers: the UK Biobank study. *PLoS One*. 2017;12(2):e0169649. doi:10.1371/journal.pone.0169649

65. Baron KG, Duffecy J, Berendsen MA, Cheung Mason I, Lattie EG, Manalo NC. Feeling validated yet? a scoping review of the use of consumer-targeted wearable and mobile technology to measure and improve sleep. *Sleep Med Rev*. 2018;40:151-159. doi:10.1016/j.smrv.2017.12.002