



anxiety-related responses to pain or trauma<sup>34</sup>) are thought to mechanically enhance pain sensitivity<sup>40,47</sup> and disrupt memory consolidation.<sup>13</sup> Consistent with these frameworks, high levels of acute pain, anxiety, and stress symptoms increase the likelihood of persistent pain and PTSS after injury.<sup>45,52,53</sup> Moreover, PTSS and chronic pain share several psychological characteristics,<sup>25,57</sup> including symptoms of anxiety,<sup>5</sup> catastrophizing,<sup>18</sup> depression,<sup>55</sup> pain and PTSS-related avoidance,<sup>37</sup> and low self-efficacy.<sup>11,22</sup>

Many studies have shown an association between symptoms of PTSD/PTSS and pain, but few have characterized the nature of this association. One notable exception was the study by Liedl et al,<sup>38</sup> which found that pain intensity was associated with arousal, intrusion, and avoidance PTSS at baseline, 3-, and 12-months following injury. Moreover, arousal symptoms at 3 months contributed to the maintenance of pain at 12-month postinjury, and pain intensity 3 months after injury was predictive of intrusion, avoidance, and arousal PTSS. However, pain intensity is only 1 part of pain experience that has been shown to play a relatively small role in long-term disability. Rather, several other factors including the cognitive and psychological aspects of pain experience have a greater impact on long-term outcomes.<sup>3,48,49</sup> A better understanding of the factors associated with PTSS and the multidimensional features of pain is therefore necessary to enable the development of targeted therapeutic approaches in the clinic.

This observational cohort study examined the association between the psychological aspects of both pain and PTSS. We hypothesized that more severe PTSS (intrusions, avoidance, negative alterations in cognitions and mood, and hyperarousal) would be associated with more severe pain outcomes (ie, pain severity, interference, pain-related disability, catastrophizing, self-efficacy, and kinesiophobia). We hypothesized that the association between PTSS and pain-related disability would be mediated by the severity of psychological distress (anxiety and depression symptoms), and detrimental cognitive-behavioral pain appraisals (catastrophizing, kinesiophobia, and self-efficacy).

## 2. Method

### 2.1 Study design and setting

Participants were recruited if they received their definitive care at The Alfred Hospital after traumatic injury and were registered in the Victorian Orthopaedic Trauma Outcomes Registry (VOTOR)<sup>72</sup> or the Victorian State Trauma Registry (VSTR).<sup>17</sup> In addition to the 12-month structured interview for the registry, all participants completed outcome measures of pain and psychological well-being at 12- to 14-months following injury. Potential participants were not referred to the study if they were distressed or required a proxy to participate during the registry interview. Distress was evaluated qualitatively by the registry interviewers, all of whom had worked in this role for several years, and may have included expressions of self-harm or suicidal ideation, or inability to complete the registry interview due to expressions of distress.

The VSTR monitors major trauma cases and systems in Victoria, Australia, and collects admission and outcomes data on all patients admitted to 138 hospitals in the state. The principle inclusion criteria for inclusion in VSTR include (1) admission to intensive care unit for  $\geq 24$  hours and mechanically ventilated; (2) significant injury to 2 or more body regions (ie, an Abbreviated Injury Scale (AIS) score of  $\geq 2$  in 2 or more body regions, signifying moderate-severe injuries) or a total Injury Severity Score (ISS) greater than 12; (3) urgent surgery for intracranial, intrathoracic or intra-abdominal injury, or fixation of pelvic or spinal fractures; or

(4) electrical injuries, drowning, and asphyxia. Patients admitted to hospital for  $>3$  days for traumatic injury may also be included if they do not meet any exclusion criteria that indicate that the injury was less severe or due to an isolated limb injury. Patients are included in VOTOR if they have sustained an orthopedic (bone or soft tissue) injury and were admitted to 1 of 4 Victorian hospitals for  $>24$  hours. Patients who have soft tissue injuries that were managed conservatively do not enter VOTOR, and therefore were not eligible for participation in the present study.

All eligible trauma cases are automatically registered to VSTR and VOTOR, respectively. Prior to the first interview at 6 months, patients are provided information about the registry and given the opportunity to opt off. Both registries have less than 1 percent of cases who opt off. The registries comprise prehospital and hospital admission data (eg, clinical observations and transport mode), injury event, diagnoses, procedures, and injury severity (VSTR only). Interviews at 6-, 12- and 24-months collect information on physical function (12-item Health Survey, SF12; Glasgow Outcome Scale Extended, GOS-E), health-related quality of life (EQ-5D), pain (numerical rating scale of pain intensity “right now”), and work outcomes (work status; return to same organisation; return to same role).

These recruitment sources ensured that the cohort was drawn from a major trauma service in the state of Victoria, Australia, and details about the initial trauma and hospitalization were not reliant on participant recollection.

### 2.2. Materials and procedures

The study protocol was approved by the Alfred Hospital (study: 290/13) and Monash University (study: CF13/3276 - 2013001633) Human Research Ethics Committees, and all participants gave informed consent. Registry data were collected at hospital discharge and through interview 12 months following the injury. Participant demographics, injury-related details, and hospitalization details (eg, length of stay, discharge location) were obtained from VOTOR and VSTR, together with the 12-month follow-up interview data. Following the 12-month registry interview, psychological and pain-related measures were administered by study researchers, through telephone interview, online, or in hard copy, according to participant preference. Participants also indicated their level of health care use for pain in the previous 3 months.

### 2.3. Injury severity

Injury severity was measured by the Injury Severity Score (ISS), which is calculated from the maximum Abbreviated Injury Scale (AIS) 2005 Update 2008 score in 3 different body regions (each maximum AIS score is squared and then summed).<sup>8</sup> The AIS codes injury severity from 1 = “minor,” 2 = “moderate,” 3 = “serious,” 4 = “severe,” 5 = “critical” and 6 = “maximal (currently untreatable).” There are 9 AIS body regions: head, face, neck, thorax, abdomen, spine, upper extremity, lower extremity, and external or other body regions. In all cases, AIS was coded retrospectively by a trained and experienced AIS coder. The method of AIS coding is consistent across all health services, with coding occurring after the definitive care discharge to ensure that all information about the injury was available for accurate coding. The AIS coders were all trained in the rules and guidelines for AIS coding, including the ranking of sources and reliability of injury information. As AIS is not included in the VOTOR registry, AIS scores for 90 cases who were only registered to VOTOR and had sustained isolated limb injuries with an ISS  $<12$ , were assigned AIS codes based on the *International Classification of Diseases*

(10) *Australian Modification (ICD-10-AM)* diagnosis codes by a Certified Abbreviated Injury Scale Specialist. These cases were included to give a spectrum of relatively minor and major injuries. The methods followed in this study were in line with best practice for injury and registry projects and is valid for coding isolated limb injuries where the nature, location, and type of injury are clear in the *ICD-10* diagnosis codes and injury descriptions.<sup>31</sup>

## 2.4. Brief Pain Inventory

The Brief Pain Inventory (BPI) is a self-report questionnaire assessing pain intensity and pain interference.<sup>20</sup> Participants rated their pain intensity from 0 = "no pain" to 10 = "pain as bad as you can imagine" when completing the questionnaire, as well as the usual, least, and worst pain intensity in the past week. Pain interference with general activity, walking ability, work, sleep, enjoyment of life, mood, and relationships were rated from 0 "did not interfere" to 10 "interfered completely." Total scores for pain severity and interference subscale were obtained by calculating the average of all item responses for the respective subscale (Cronbach  $\alpha$  = 0.92 for pain severity and 0.95 for pain interference in the present cohort). Scores  $\geq 4$  are classified as moderate, and  $\geq 7$  as severe, given that persons at or above this threshold tend to have greater analgesic requirements and appraise their pain to be moderate severe.<sup>6,27</sup>

## 2.5. Posttraumatic Stress Disorder Checklist

The Posttraumatic Stress Disorder Checklist (PCL-C) is a brief self-report inventory for *Diagnostic and Statistical Manual of Mental Disorders-IV-TR* PTSS<sup>74</sup> experienced within the past month. The PCL-C produces a total score ranging from 17 to 85, measuring overall symptomatology. The 17 items were sorted into 4 subscales, corresponding to the four-cluster symptom structure of PTSS in the *DSM-V*: Criterion B: re-experiencing symptoms (PCL-C items 1-5, Cronbach  $\alpha$  = 0.90); Criterion C: avoidance symptoms (PCL-C items 6-7,  $\alpha$  = 0.79); Criterion D: negative alterations to cognition and mood (PCL-C items 8-12,  $\alpha$  = 0.87); and Criterion E: hyperarousal symptoms (PCL-C items 13-17,  $\alpha$  = 0.84), in line with recent recommendations.<sup>51</sup> Cluster symptom scores were generated by summing the items belonging to each criterion. The *DSM-IV* symptoms that are missing with this conversion method specifically relate to the presence of distorted cognitions and negative emotional states (Criterion D); and reckless or self-destructive behavior (Criterion E). All other *DSM-V* symptoms are measured in the PCL-C. Determination of probable PTSD was based on exceeding a threshold of  $\geq 36$ , which has been recommended as clinically suggestive in pain cohorts<sup>71</sup> in addition to meeting PTSD criteria A to E<sup>1</sup>; that is, trauma exposure (Criterion A), and indicating that in the past month they have been bothered by at least 1 Cluster B and C symptom, and at least 2 Cluster D and E symptoms "moderately," "quite a bit," or "extremely." As the study did not involve a detailed clinical interview, it is not known whether participants also met Criterion F (symptoms lasting > 1 month), Criterion G (symptoms causing distress or impairment) or Criterion H (symptoms are not due to other causes). Cronbach  $\alpha$  for the total scale in the present sample was 0.95.

## 2.6. Hospital Anxiety and Depression Scale

The Hospital Anxiety and Depression Scale (HADS) is a self-report screening measure of clinical depression and anxiety validated for use in a nonclinical setting.<sup>76</sup> It comprises 2 subscales, measuring anxiety (HADS-A) and depression (HADS-D), with 7

items each. Items are rated on a 4-point Likert scale and summed to produce subscale scores that range from 0 to 21. Higher scores indicate more severe symptoms and scores of  $\geq 11$  represent a probable clinical disorder.<sup>76</sup> Cronbach  $\alpha$  in the present sample were 0.74 (anxiety) and 0.85 (depression).

## 2.7. Pain Catastrophizing Scale

The Pain Catastrophizing Scale (PCS) is a self-report measure of catastrophic thoughts and feelings as a response to anticipated or actual pain comprising 13 items that are rated on a 5-point Likert scale.<sup>66</sup> The PCS comprises 3 subscales of magnification, rumination, and helplessness, with a total score range from 0 to 52, with higher scores indicating that catastrophic thoughts or feelings occur more often. A score of  $\geq 30$  is considered clinically elevated.<sup>65</sup> Cronbach  $\alpha$  for the total scale in the present sample was 0.94.

## 2.8. Pain Self-Efficacy Questionnaire

The Pain Self-Efficacy Questionnaire (PSEQ) is a self-report measure of confidence in performing everyday tasks, despite being in pain.<sup>44</sup> It comprises 10 items such as "I can enjoy things, despite the pain" rated on a scale from 0 to 6, with higher scores indicating greater confidence. Ratings are summed to produce a total score ranging from 0 to 60, with scores <30 indicating moderately low self-efficacy and <20 severely low self-efficacy in clinical samples.<sup>44</sup> Cronbach  $\alpha$  for the present sample was 0.93.

## 2.9. Tampa Scale of Kinesiophobia

The Tampa Scale of Kinesiophobia (TSK) is a self-report measure of kinesiophobia, with 17 items relating to fear of pain or reinjury because of movement (eg, "I'm afraid that I might injure myself if I exercise," or "Simply being careful that I do not make any unnecessary movements is the safest thing I can do to prevent my pain from worsening").<sup>41</sup> Respondents indicate their agreement with each item on a 4-point scale. The TSK is summed so that higher scores indicate greater fear of movement, with a range from 0 to 51, where scores >40 indicate clinically elevated kinesiophobia.<sup>35</sup> Cronbach  $\alpha$  for this sample was 0.78.

## 2.10. Roland-Morris Disability Questionnaire

The Roland-Morris Disability Questionnaire (RMDQ) is a measure of functional status and physical disability in the context of pain.<sup>50</sup> It was originally developed for back pain; however, a modified generic version has been validated as a generic tool of pain-related disability.<sup>58</sup> This study used the 18-item generic version, which comprised a list of 18 statements relating to different activities and impairments, such as "I get dressed more slowly because of my pain," and respondents are asked to indicate which items "describe you lately." These responses are then summed to produce a total score from 0 to 18, with higher scores representing more impairment. A score of  $\geq 7$  represents moderate impairment, whereas  $\geq 12$  represents severe impairment.<sup>64</sup> Cronbach  $\alpha$  in this sample was 0.87.

## 2.11. EuroQol: EQ-5D-3L

The EQ-5D 3 level questionnaire measures general health outcomes relating to current problems within 5 domains of mobility, self-care, usual activities, pain or discomfort, and anxiety

or depression.<sup>68</sup> The response to the pain or discomfort domain was used in this study, which was rated from 1 (no pain or discomfort), 2 (moderate pain or discomfort), or 3 (extreme pain or discomfort).

## 2.12. Statistical analyses

The analyses were performed using IBM SPSS Statistics 22, and Stata Version 14.0. Treatment of missing data involved imputation with unweighted mean substitution at the individual participant and scale, or subscale, level. That is, the average of the completed items for the respective subscale was imputed before calculation of the total scale or subscale scores. Only the total sub/scale scores were used in analyses. Participants missing more than 1 item on a subscale were coded as missing for that measure consistent with the scale scoring recommendations, and methods used in previous studies.<sup>61</sup> This resulted in imputation of only 53 values (0.15% of data points) for the BPI severity ( $n = 1$ ) and interference ( $n = 7$ ) subscales, PSEQ ( $n = 5$ ), TSK ( $n = 8$ ), PCS ( $n = 13$ ), HADS Anxiety ( $n = 4$ ) and Depression ( $n = 10$ ) subscales, and the PCL-C ( $n = 6$ ).

As many variables were not normally distributed, Mann-Whitney  $U$  tests examined group differences (probable PTSD/no PTSD) in the distribution of pain intensity, anxiety, catastrophizing, depression, kinesiophobia, disability, and self-efficacy, and bootstrapping with case resamples was performed. Effect sizes were based on those recommended by Cohen,<sup>21</sup> with 0.2 (small), 0.5 (moderate), 0.8 (large).

Canonical correlation was used to examine the association between PTSS (Cluster B, C, D, and E symptoms) and pain outcomes (pain severity [BPI], interference [BPI], disability [RMDQ], catastrophizing [PCS], kinesiophobia [TSK], and self-efficacy [PSEQ]). Canonical correlation estimates variates, which are the linear combination of variables comprised in the set of independent (ie, PTSS) and dependent (ie, pain-related characteristics) variables. Each latent canonical variate reflects the relative linear relationship between the independent and dependent variables. The Redundancy Index (RI) reflects the variance shared between each independent, or dependent variable, and the variate, multiplied by the total variance explained by the variate (ie, the Canonical Root). Higher RI is desirable as this shows that a high proportion of variance in the dependent variables is explained by the independent variables, and vice versa. Canonical cross-loadings indicate the relative contribution of each variable to the variate. Sensitivity analyses examined the impact of injury severity (ie, having an isolated injury) and of each PTSS cluster on the canonical correlation. The data met the assumptions for canonical correlation with high linearity and low multicollinearity (preliminary regression analyses had tolerance inflation factors  $>0.2$ , and variance inflation factors  $<10$ ). The data were not normally distributed; however, canonical correlation can proceed without the strict assumption of normality, especially in the presence of strong linearity and  $>10$  cases per variable.<sup>29</sup>

Mediation analyses were used to determine the strength of the direct and indirect relationship between PTSS (total PCL-C score) and pain-related disability (RMDQ) through pain (ie, pain self-efficacy, kinesiophobia, and catastrophizing) and psychological characteristics (depression and anxiety). Participants' missing data were excluded in a listwise manner. We controlled for key demographics (age, sex, and education), injury factors (ISS and hospital length of stay) and pain severity (BPI severity), as univariate analyses showed that each of these factors was associated with either PTSS or pain-related disability. Socioeconomic position (measured by the Index of Relative

Socio-Economic Disadvantage [IRSAD], based on participant postcode and national census surveys<sup>7</sup>) was not associated with either PTSS or pain-related disability ( $P > 0.90$ ), so was not included in the covariates. Mediation was tested using the Sobel-Goodman mediation test in Stata 14.0 with bootstrapping with 1000 case resamples, which is a nonparametric mediation method. The assumptions of mediation require a significant association between predictor (ie, independent variable) and mediator (path a), mediator and outcome (ie, dependent variable, path b), and a direct association between predictor and outcome (path c) that is reduced, or becomes nonsignificant, when adjusting for the mediator (path c'). Using these criteria, mediation through anxiety was not pursued as there was no direct association between anxiety and pain-related disability (b path, 95% confidence interval [CI]:  $-0.15$  to  $0.15$ ). A significant indirect effect was based on the examination of the CIs, whereby the effect was significant when the bias-corrected bootstrapped CI did not include zero.

The sample size met the requirements to detect small-moderate effects for canonical correlation, as small to moderate levels of shared variance (ie,  $R$  of 0.3 to 0.5) require samples that have at least 40 cases per variable (ie,  $>400$  for the present study).<sup>10</sup> Likewise, the sample was sufficient for detection of a moderate bias-corrected bootstrapped-mediated (indirect) effect, which requires a minimum sample of 377 to 400 cases.<sup>26</sup>

## 3. Results

### 3.1. Cohort overview

A total of 732 persons were referred to the study during their 12-month follow-up registry interview with the VOTOR or VSTR between October 2013–2015 and 433 participated; see **Figure 1** for STROBE diagram of participant recruitment and eligibility screening. The cohort participated on average 13.47 months ( $SD = 1.58$ ) after their injury.

The cohort was predominantly male ( $n = 324$ , 74.8%) and aged 17–75 years at the time of their injury ( $M = 44.83$ ,  $SD = 14.16$ ). The sample reflected a range of cultural identities including Australian ( $n = 269$ , 62.1%), European ( $n = 111$ , 25.6%), Asian ( $n = 15$ , 3.5%), Pacific Islander ( $n = 9$ , 2.1%), American ( $n = 2$ ), and African ( $n = 1$ ); data on cultural identity were missing from 26 participants. The most common injuries were from falls ( $n = 140$ , 32.3%), or transport-related incidents including injury sustained as a cyclist or pedestrian (69, 15.9%), or an occupant of a motor vehicle ( $n = 66$ , 15.2%) or motorcycle ( $n = 65$ , 15.01%). The majority of participants ( $n = 392$ , 90.5%) had at least 1 fracture. Injury characteristics are shown in **Table 1**, and the pain and psychological characteristics are presented in **Table 2**.

For participants reporting moderate to severe pain or discomfort on the EQ-5D ( $n = 204$ ), most ( $n = 150$ ; 73.5%) reported receiving at least one medical and other health care treatment for their pain in the previous 3 months. Moreover, participants who had probable PTSD (median = 6 clinical service episodes, interquartile range = 15, range: 0–60) reported twice the clinical service use for their pain in the previous 3 months compared with those without probable PTSD (median = 1, interquartile range = 5, range: 0–56);  $z$  ( $N = 421$ ) =  $-5.98$ ,  $P < 0.0001$ ,  $r = 0.29$ .

### 3.2. Association between probable posttraumatic stress disorder, posttraumatic stress disorder symptoms severity, and pain outcomes

Ninety two (21.2%) participants had probable PTSD (data missing from 2 participants). The majority of these participants ( $n = 67$ ,

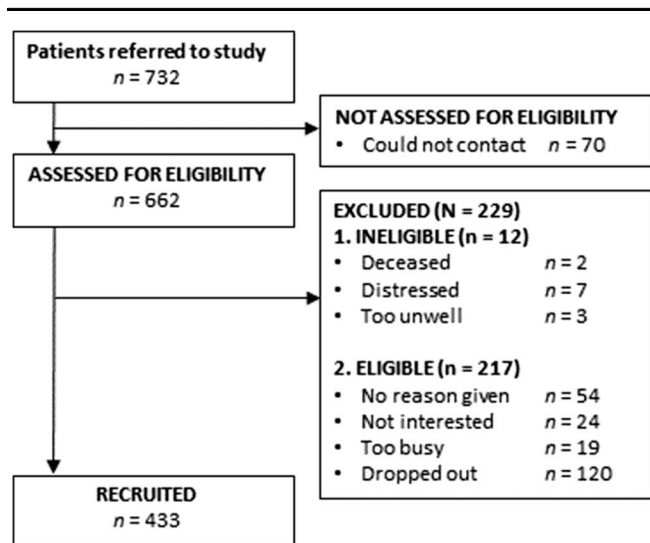


Figure 1. STROBE diagram of participant recruitment.

72.8%) reported current moderate or extreme problems with pain or discomfort on the EQ-5D, compared with 137 (40.4%) participants who did not have probable PTSD (risk ratio = 1.81, 95% CI: 1.51–2.17,  $P < 0.0001$ ). Conversely, 204 (47.3%) participants reported moderate or extreme problems with pain or discomfort, of whom 67 (32.8%) had probable PTSD compared with 25 (11.0%) of the 227 participants who did not report any problems with pain (risk ratio = 2.98, 95% CI: 1.96–4.53,  $P < 0.0001$ ). Participants who had probable PTSD reported significantly worse pain, pain-related disability, anxiety, and depression, with large effect sizes; see **Figure 2**.

Using canonical correlation, we examined the association between PTSS and the psychological and pain outcomes. Only 2 latent variates predicted the pain outcomes from PTSS ( $P < 0.01$ ). **Table 3** displays the canonical functions, canonical correlations, percentage variance explained, and redundancy indices. The shared variance and redundancy indices suggest that only the first canonical variate was meaningful, with

**Table 1**  
Injury Characteristics of the cohort (N = 433).

	n	%
Moderate-critical injury (AIS body regions)		
Head	99	22.9
Face	35	8.1
Neck	6	1.4
Thorax	133	30.7
Abdomen	39	9.0
Spine	146	33.7
Upper extremity	139	32.1
Lower extremity	183	42.3
Unspecified	5	1.2
Attribution of fault		
Self	215	49.7
Another person	111	25.6
Other or unknown	107	24.7
Discharge location		
Home	304	70.2
Rehabilitation	129	29.8
Compensation status		
Compensable injury	169	39.0
Noncompensable injury	264	61.0

only minimal overlap in the second variate. Examination of the canonical cross-loadings for the first variate showed that PTSS predominantly explained variance in pain catastrophizing and self-efficacy. On the other hand, the pain outcomes predominantly explained variance in Cluster D symptoms (negative alterations in cognition and mood), followed by Cluster E (hyperarousal), C (avoidance), and B (re-experiencing) symptoms.

Multiple sensitivity analyses were undertaken to further interpret the canonical correlation results, see **Table 4**. First, the total variance explained, canonical cross-loadings, and redundancy indices did not change substantially when we excluded the ninety cases who had isolated orthopaedic injuries, highlighting that the results were not strongly influenced by injury complexity or severity. Second, in the whole sample, the canonical cross-loadings, shared variance, and redundancy indices were remarkably stable when Cluster B was omitted, suggesting that re-experiencing symptoms did not contribute markedly to the association between pain and PTSS. However, omission of Cluster C symptoms (avoidance) reduced the amount of variance in PTSS explained by the pain outcome variate by approximately one-third. Considering the canonical cross-loadings for Cluster C were otherwise quite low in all other canonical functions, avoidance symptoms appear to be especially important in relation to pain outcomes because of their relationship with the other PTSS clusters. Omission of Cluster D (negative changes to cognition and affect) increased the variance in pain severity that was explained by the remaining PTSS (ie, Clusters B, C, and E) by 3-fold (ie, from  $-0.12$  to  $-0.35$ ). Removal of Cluster D also increased the amount of variance in Clusters E (hyperarousal; ie, from 0.17 to 0.51) and C (avoidance; ie, from 0.028 to 0.22) by 3–7-fold, respectively, that was explained by the pain variate. Finally, omission of Cluster E had minimal impact on the cross-loadings of Clusters B and C symptoms, but markedly increased the contribution of Cluster D, highlighting that negative changes to cognition and affect covary greatly with hyperarousal symptoms in the context of pain after traumatic injury.

Pairwise correlations were conducted to further examine the association between pain severity and specific Cluster D symptoms. The strongest association was between pain severity and Item 9 (loss of interest;  $r^2 = 0.54$ ,  $P < 0.001$ ), followed by the dissociative symptoms—Item 12 (feeling foreshortened future;  $r^2 = 0.48$ ,  $P < 0.001$ ), Item 10 (feeling cut off;  $r^2 = 0.47$ ,  $P < 0.001$ ) and Item 11 (feeling emotionally numb;  $r^2 = 0.37$ ,  $P < 0.001$ )—with the weakest association with Item 8 (impacts on memory;  $r^2 = 0.32$ ,  $P < 0.001$ ); see supplementary figures for heatmap and density plots for these associations (available at <http://links.lww.com/PR9/A11>).

Altogether the canonical correlations and sensitivity analyses highlight that the association between pain and PTSS of hyperarousal and avoidance shares a great deal of variance with negative changes to cognition and mood, especially the specific symptoms of lost interest and dissociation.

### 3.3. Indirect relationships between posttraumatic stress disorder symptoms and pain-related disability

A linear regression showed that PTSS (PCL-C total score) alone explained 38.2% (adj.  $R^2$ ) of the variance in pain disability (RMDQ), which increased to 59.9% when also accounting for age ( $b = 0.039$ ,  $SE = 0.012$ ,  $P = 0.001$ ), sex ( $b = -0.16$ ,  $SE = 0.39$ ,  $P = 0.69$ ), education level ( $b = 0.046$ ,  $SE = 0.13$ ,  $P = 0.72$ ), pain severity ( $b = 1.22$ ,  $SE = 0.10$ ,  $P < 0.0001$ ), hospital stay

**Table 2****Clinical characteristics of the sample (n = 433).**

Measure	M (SD)	95% confidence interval*		Proportion with clinically meaningful scores		
		Lower limit	Upper limit	Criterion	N (%)	
Pain severity (BPI)	2.61 (2.05)	2.41	2.82	Moderate	≥4	100 (23.1)
				Severe	≥7	12 (2.8)
Pain interference	2.70 (2.54)	2.46	2.96	Moderate	≥4	87 (20.1)
				Severe	≥7	34 (7.9)
Pain and discomfort (EQ-5D)	1.52 (0.58)	1.47	1.58	Moderate	2	187 (43.2)
				Extreme	3	17 (3.9)
Pain-related disability	5.88 (5.41)	5.36	6.40	Moderate	≥7	103 (23.8)
				Severe	≥12	79 (18.2)
Catastrophizing	9.71 (10.99)	8.69	10.89	Clinically elevated	≥30	34 (7.9)
Kinesiophobia	37.57 (7.79)	36.86	38.33	Clinically elevated	>40	153 (35.3)
Pain self-efficacy	45.49 (14.24)	44.13	46.95	Moderate	≤30	49 (11.3)
				Severe	≤20	29 (6.7)
Anxiety	7.02 (3.76)	6.65	7.39	Clinically Probable score	≥11	75 (17.3)
Depression	4.49 (4.12)	4.07	4.88	Clinically Probable score	≥11	44 (10.2)
PTSD: total score	32.21 (14.86)	30.81	33.70	Clinically Probable score	>36	137 (31.6)
PTSD: Cluster B (intrusion)	8.92 (4.62)	8.47	9.35	PTSD Cluster criteria†		97 (22.4)
PTSD: Cluster C (avoidance)	3.66 (2.12)	3.46	3.86	PTSS >36 and Cluster criteria†		92 (21.2)
PTSD: Cluster D (cognition and mood)	9.22 (4.91)	8.75	9.69			
PTSD: Cluster E (hyperarousal)	10.18 (4.96)	9.69	10.63			

No participants had missing subscale scores; pain intensity: average pain intensity in the past week from BPI (cutoff:  $\geq 5$ )<sup>36</sup>; Anxiety: Hospital Anxiety and Depression Scale, Anxiety subscale (cutoff:  $\geq 11$ )<sup>76</sup>; Catastrophizing: Pain Catastrophizing Scale<sup>65</sup>; Depression: Hospital Anxiety and Depression Scale, Depression subscale (cutoff:  $\geq 11$ )<sup>76</sup>; Kinesiophobia: Tampa Scale of Kinesiophobia (cutoff:  $>40$ )<sup>35</sup>; Pain Self-Efficacy: Pain Self-Efficacy Questionnaire (cutoff:  $<30$  moderate,  $<20$  severe)<sup>44</sup>; PTSS: posttraumatic checklist, PTSD mean (SD) pertain to the total PCL-C score (cutoff: total score  $>36$ ).

\* 1000 bias-corrected bootstrap samples.

† Cluster criteria = moderate or higher for at least 1 Clusters B and C symptom, and at least 2 Clusters D and E symptoms<sup>71</sup>; Pain-related disability: Roland-Morris Disability Questionnaire (cutoff:  $\geq 7$  moderate disability,  $\geq 7$  severe disability).<sup>64</sup> PTSD, posttraumatic stress disorder; PTSS, PTSD symptoms.

( $b = 0.14$ ,  $SE = 0.024$ ,  $P < 0.0001$ ), and ISS ( $b = -0.006$ ,  $SE = 0.019$ ,  $P = 0.74$ );  $F(7,410) = 89.98$ ,  $P < 0.0001$ . Preliminary linear regressions showed that the predictor (PCL-C total score) was significantly associated with each of the mediators, and that each mediator, except for anxiety, was significantly associated with pain-related disability (RMDQ) while controlling for demographics (age, sex, and education), ISS, length of hospital stay and pain severity.

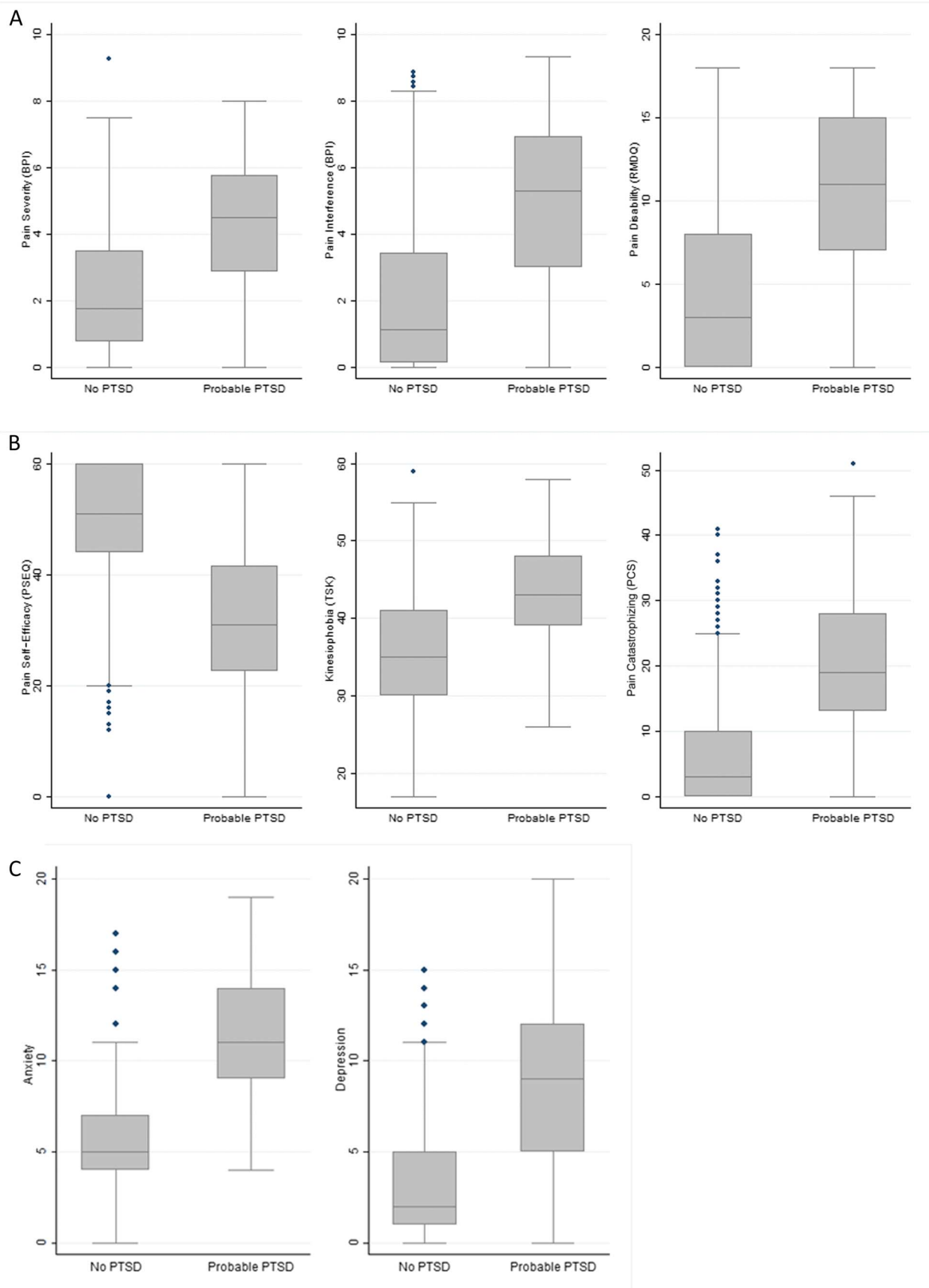
We therefore proceeded to examine the strength of the direct and indirect (through self-efficacy, depression, kinesiophobia, and catastrophizing) relationships between PTSS and pain-related disability using the Sobel-Goodman test. Each analysis tested a single mediator in turn and showed significant indirect effects through self-efficacy ( $n = 409$ ), depression ( $n = 418$ ), kinesiophobia ( $n = 415$ ), and catastrophizing ( $n = 417$ ); see **Figure 3**. The amount of variance explained in each model was remarkably consistent (ranging from 59.4% to 59.9%), and the proportion of the total effect that was mediated ranged from 23.9% for kinesiophobia (adj  $R^2 = 59.9\%$ ), to 25.5% for catastrophizing (adj  $R^2 = 59.9\%$ ), 37.8% for pain self-efficacy (adj  $R^2 = 59.4\%$ ), and 60.4% for depression (adj  $R^2 = 59.9\%$ ). Each model controlled for pain severity, which was significantly associated with each mediator (PSEQ:  $\beta = -2.9$ ;  $-0.44$ ,  $-0.29$ ; TSK:  $\beta = 0.039$ ;  $0.016$ ,  $0.063$ ; PCS:  $\beta = 2.44$ ;  $2.03$ ,  $2.84$ ; Depression:  $\beta = 0.35$ ;  $0.17$ ,  $0.21$ ), education (associated with PSEQ only,  $\beta = -0.89$ ;  $-1.59$ ,  $-0.19$ ), age (associated with catastrophizing [ $\beta = -0.079$ ;  $-0.13$ ,  $-0.032$ ] and kinesiophobia [ $\beta = 0.039$ ;  $0.016$ ,  $0.063$ ]), sex (only associated with depression,  $\beta = -0.64$ ;  $-1.21$ ,  $-0.074$ ), length of hospital stay (associated

with kinesiophobia,  $\beta = 0.14$ ;  $0.092$ ,  $0.18$ ), and ISS. While ISS was not associated with any mediators when adjusting for all other factors it remained in each analysis, given that there was such high variability in injury severity within the sample.

The preliminary regression results, and mediation tests, showed that the majority of variance in pain-related disability was associated with the demographic characteristics (especially sex, education, and length of hospital stay), pain severity and PTSS. While, there were meaningful and significant indirect associations (in order of greatest to lowest magnitude) through depression, pain self-efficacy, catastrophizing, and kinesiophobia, the unique indirect effects were small ( $\beta < 0.1$ ), highlighting that the magnitude of the indirect effects was most likely attributable to the large effect of PTSS on pain-related disability, together with the demographic characteristics, and pain severity.

#### 4. Discussion

The present study found that 1 in 3 people who had been admitted to hospital for traumatic injury had elevated PTSS 12 months later. This is consistent with findings from other recent prospective studies.<sup>16</sup> Those who had probable PTSD also reported markedly higher anxiety, catastrophizing, depression, kinesiophobia, pain severity and pain-related disability, and lower self-efficacy. Having current problems with pain and discomfort 12 months after injury was more strongly associated with probable PTSD than the reverse. A small but meaningful association between PTSS and pain-related disability was



**Figure 2.** Box plots comparing patients with probable PTSD and those without symptomatic PTSD for (A) pain severity ( $z$  [N = 430] = 8.48,  $P < 0.0001$ ,  $r = 0.41$ ), pain interference ( $z$  [N = 431] = 9.07,  $P < 0.0001$ ,  $r = 0.44$ ), and pain disability ( $z$  [N = 431] = 8.72,  $P < 0.0001$ ,  $r = 0.42$ ); (B) pain catastrophizing ( $z$  [N = 430] = 9.74,  $P < 0.0001$ ,  $r = 0.47$ ), kinesiophobia ( $z$  [N = 428] = 8.25,  $P < 0.0001$ ,  $r = 0.40$ ), and self-efficacy ( $z$  [N = 422] = 9.20,  $P < 0.0001$ ,  $r = 0.45$ ); and (C) anxiety ( $z$  [N = 430] = 11.58,  $P < 0.0001$ ,  $r = 0.56$ ), and depression ( $z$  [N = 431] = 10.80,  $P < 0.0001$ ,  $r = 0.52$ ). PTSD, posttraumatic stress disorder.

**Table 3**

Summary of the canonical functions, correlations, explained and shared variance, and redundancy indices for the independent (posttraumatic stress disorder clusters) and dependent (pain outcomes) variables (n = 418).

Canonical function	Canonical correlation	Canonical root	P	PTSD clusters			Pain outcomes		
				% Variance explained	Shared variance	Redundancy index	% Variance explained	Shared variance	Redundancy index
1	0.765	0.585	<0.001	39.4	0.740	0.433	67.4	0.505	0.296
2	0.212	0.045	0.008	0.4	0.092	0.004	7.9	0.059	0.003
3	0.131	0.017	0.131	—	—	—	—	—	—

indirectly attributable to elevated symptoms of kinesiophobia (ie, fear of reinjury or exacerbation of pain), catastrophizing and depression, and lower self-efficacy. These indirect associations suggest that PTSS and persistent pain may have additive associations with disturbed mood, especially if the co-occurrence of symptoms impacts on participation in meaningful occupational and recreational activities.

#### 4.1. Theoretical implications

Several theoretical models of the co-occurrence of PTSD/PTSS and persistent pain have been proposed: mutual maintenance, shared/triple vulnerability, and diathesis-stress. These models emphasize the mechanistic and high association between pain severity, vulnerability to anxiety-related cognitive, emotional and behavioural reactions to pain, and attentional biases towards threat in the development of both persistent pain and PTSS.<sup>25</sup> Previous studies have found that shared vulnerability symptoms play a large role—more so than symptoms like low mood<sup>32</sup>—in the persistence of pain after surgery<sup>34</sup> or injury.<sup>52</sup> The

associations that we identified between specific PTSS and pain outcomes support the presence of shared mechanisms, especially the perception of more severe pain, and greater physiological and cognitive reactivity to both the trauma and to pain. Specifically, pain severity and catastrophizing were strongly associated with hyperarousal symptoms, but this association was masked by the severity of trauma-related changes to cognition and mood, suggesting that changes to cognition and mood and hyperarousal covary strongly in the context of pain after injury. Of all the changes to cognition and mood symptoms, pain severity showed the strongest association with the degree to which participants felt that they had lost interest in things that they used to enjoy, followed by dissociative PTSS (especially feeling a foreshortened future or feeling cut off), suggesting that having more severe pain at 12 months postinjury synergistically covaries with losing interest and feelings of hopelessness. Posttraumatic stress avoidance symptoms also showed a strong association with pain outcomes, but this was largely because avoidance symptoms shared a high degree of variance with the other PTSS clusters. Whether the strong relationships between the cognitive

**Table 4**

Sensitivity analysis of the respective role of injury severity\* and the independent variables (posttraumatic stress disorder clusters) for first canonical function.

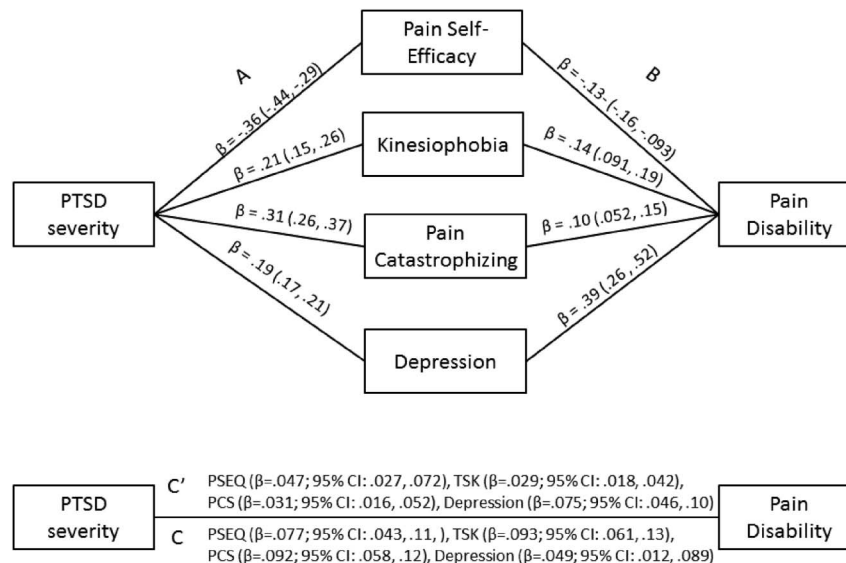
	All clusters	All clusters*	Results after omission of			
			PTSD Cluster B	PTSD Cluster C	PTSD Cluster D	PTSD Cluster E
Canonical correlation (R)	0.765	0.776	0.761	0.765	0.710	0.760
Canonical root (R <sup>2</sup> )	0.585	0.602	0.579	0.585	0.504	0.578
Independent variate						
Canonical cross-loadings						
PTSD: Cluster B	0.140	0.186	—	0.153	0.172	0.212
PTSD: Cluster C	0.028	0.008	0.084	—	0.220	0.025
PTSD: Cluster D	0.532	0.517	0.540	0.170	—	0.613
PTSD: Cluster E	0.170	0.150	0.238	0.162	0.508	—
Shared variance	0.740	0.738	0.775	0.479	0.783	0.739
Redundancy	0.566	0.573	0.590	0.366	0.556	0.561
Dependent variate						
Canonical cross-loadings						
Pain severity	−0.120	−0.095	−0.123	−0.120	−0.351	−0.133
Pain interference	0.206	0.133	0.218	0.210	0.135	0.191
Pain catastrophising	0.345	0.383	0.320	0.345	0.302	0.379
Kinesiophobia	0.095	0.111	0.101	0.093	0.093	0.096
Pain self-efficacy	−0.258	−0.269	−0.270	−0.256	−0.230	−0.254
Pain disability	0.085	0.081	0.082	0.086	0.095	0.079
Shared variance	0.505	0.507	0.506	0.505	0.516	0.500
Redundancy	0.296	0.305	0.293	0.296	0.260	0.289

PTSD: Cluster B (intrusion), Cluster C (avoidance), Cluster D (negative changes to cognition and affect), Cluster E (hyperarousal).

\* The data reported in this column excluded patients with isolated orthopaedic injuries to determine whether the variance explained in pain or PTSD symptoms, and respective their association with each other, were impacted by injury severity.

PTSD, posttraumatic stress disorder.





**Figure 3.** Direct and indirect effects between PTSD symptom severity and pain-related disability (RMDQ), through pain self-efficacy (PSEQ), kinesiophobia (TSK), pain catastrophizing (PCS) and depression (HADS), while controlling for age at injury, sex, education, injury severity (ISS, hospital length of stay), and pain severity. CI, confidence interval; PTSD, posttraumatic stress disorder.

and affective dimensions of pain and PTSS (ie, catastrophizing, self-efficacy, avoidance, mood/affect), and between the physiological symptoms of PTSD (ie, hyperarousal) and pain severity arise due to shared vulnerability or mutual maintenance, however, cannot be confirmed from the present results given the cross-sectional nature of this study.

Intrusion PTSS were traditionally thought to enhance pain because flashbacks and re-experiencing episodes may explicitly elicit painful sensations.<sup>67,75</sup> Alternatively, Cho et al<sup>19</sup> proposed that persistent pain is a reminder of the trauma that triggers hyperarousal symptoms and avoidance, thereby exacerbating pain-related disability. Contrary to both of these proposals, however, we only found a weak association between intrusion symptoms and pain. This is consistent with other recent studies that have also shown no meaningful association between posttraumatic re-experiencing and coping with pain.<sup>42</sup>

#### 4.2. Clinical implications

Considering the high co-occurrence of PTSS and pain, which affects up to half of those who have sustained a traumatic injury<sup>33</sup> as early as 3 months postinjury<sup>63</sup> and impacts enormously on function and quality of life, it is important to circumvent the onset of both conditions with a view to the likely contributing mechanisms. Early prevention efforts should include optimal management of acute pain and distress. In the subacute phase and beyond, several interventions have been found to be effective at preventing or attenuating the severity of PTSD after traumatic injury, including cognitive behavioural therapy<sup>15,24,46</sup> and prolonged exposure.<sup>59</sup> For early interventions targeting pain, however, only a handful of studies have shown reductions in the severity of pain through early mobilization<sup>54,73</sup> or multidisciplinary assessment and treatment.<sup>14</sup> Altogether, few interventions acknowledge the importance of assessing and treating symptoms of both pain and PTSD concurrently, highlighting that this is a field of clinical practice requiring substantial development.

The present findings highlight that a fifth of injured persons have probable PTSD, and almost half report current moderate to extreme problems with pain at 12 months after traumatic injury.

These rates are markedly higher than population lifetime incidence of PTSD (7.8 percent)<sup>39</sup> and musculoskeletal pain conditions (30.7 percent)<sup>30</sup>, in the Australian community. Given that high PTSS was associated with significantly worse psychopathology and pain, it is likely that injured persons with both conditions will differ both psychologically and behaviorally from those without PTSD. In particular, patients with both PTSS and pain may have specific symptom profiles (eg, as per the pain traumatization framework<sup>34</sup>), with greater psychological distress, hyperarousal, hypersensitivity, avoidance, and negative alterations in cognition and mood. Moreover, several studies have found that PTSS, fear avoidance,<sup>19</sup> and sensory hypersensitivity<sup>47</sup> are associated with worse pain and functional impairments after injury.<sup>23</sup> After traumatic injury, high kinesiophobia and low pain self-efficacy lead to greater pain-related disability because these appraisals reduce the likelihood of engaging in activities.<sup>9,70</sup> Evidently, it is important to screen and assess key aspects of both pain and PTSS when an injured person presents for treatment of either condition after traumatic injury.

While further research is required, it is clear that people with persistent pain and PTSS have a complex clinical profile that may necessitate more intensive therapy.<sup>62</sup> For instance, more frequent sessions, longer duration of treatment, or graded approaches that first manage mechanisms and clinical features common to both conditions may be required. It may be necessary to first address common avoidance of thoughts, feelings, or activities related to the trauma or pain, and hypersensitivity and stress regulation mechanisms. Moreover, as elevated symptoms of depression, kinesiophobia and catastrophizing, and lower self-efficacy mediated the relationship between PTSD symptoms and pain-related disability, therapy may need to target reducing fear of pain and improving confidence in performing everyday tasks despite pain, which together may lead to longer term improvements in mood. For instance, clinicians could provide education about pain<sup>43</sup> and trauma-related thoughts and attitudes,<sup>12</sup> and use prolonged exposure techniques<sup>56</sup> during rehabilitation alongside medication management, cognitive behavioural therapy, functional rehabilitation, and patient-centered goal-setting.

### 4.3. Limitations and future research

This study had some limitations that should be considered. First, those who were notably distressed during the registry interview were not invited to participate. The current study may therefore have underrepresented the incidence, severity, and patterns of PTSS in persons hospitalized after traumatic injury. All participants had sustained moderate to severe injuries that required hospitalization, and the findings may not generalize to those with less severe injuries. We only used self-report measures of pain and psychological outcomes, including PTSS, and cross-validation with clinical interview would be beneficial. Moreover, the study commenced before the PCL-5 was released, so we used a modified scoring method to generate the current *DSM-V* symptom scores. While this conversion method has been empirically supported and shows 95% accuracy,<sup>51</sup> it probably missed identifying some probable PTSD cases, given that 3 *DSM-V* symptoms are not measured in the PCL-C. Finally, our study was cross-sectional, and the direction of the association between pain and PTSS cannot be assumed.

Future research should adopt prospective longitudinal designs with more assessment points to able to control for extraneous factors such as health care service use before and after injury, or previous trauma, pain, and psychopathology. Longitudinal designs would also enable the evaluation of whether relationships between PTSD symptoms, psychological characteristics, and disability change over time. Finally, investigation into whether the present findings can be replicated in other clinical samples (eg, after minor injury or surgical procedures) would add to the generalizability of the findings, and further inform the theoretical frameworks for the co-occurrence of PTSS and chronic pain. The development and evaluation of mechanism-based treatments for the prevention and management of pain and PTSS is now a priority. Considering acute pain<sup>45</sup> and anxiety<sup>52</sup> increase the likelihood of developing both persistent pain and PTSS, preventive interventions should span the acute and subacute periods.

### 5. Conclusions

Chronic pain and PTSS after traumatic injury are both significant health problems in the community, and their co-occurrence is common in rehabilitation and pain management settings.<sup>25,33</sup> The present findings highlight the associations between PTSS and pain, which support the presence of shared mechanisms and vulnerabilities, particularly between pain severity, hyperarousal, and cognitive responses to the trauma and pain. Psychological aspects of pain had strong associations with PTSS. Moreover, depression, self-efficacy, catastrophizing, and kinesiophobia mediated the relationship between PTSS and disability. Taken together, these findings have implications for treating persons with both pain and PTSS, and emphasise the significance of addressing common features during rehabilitation.

### Disclosures

The authors have no conflict of interest to declare.

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Data availability statement: Requests for access to data from this study would require approval from the data custodians (<http://www.med.monash.edu.au/epidemiology/traumaepi/traumareg/>) and appropriate governance and ethics approvals from the Monash Research Office (<https://www.monash.edu/researchoffice>).

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### Appendix A. Supplemental digital content

Supplemental digital content associated with this article can be found online at <http://links.lww.com/PR9/A11>.

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