

Research article

# The association of age, pain, and fatigue with physical functioning and depressive symptoms in persons with spinal cord injury

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**Context/objective:** To describe the relationship of pain and fatigue with physical and psychological functioning in adults with spinal cord injury (SCI).

**Design:** Cross-sectional survey.

**Setting:** Community-based survey.

**Participants:** Convenience sample of individuals with SCI.

**Intervention:** Not applicable.

**Outcome measures:** Physical functioning (Patient-Reported Outcomes Measurement Information System (PROMIS) Physical Functioning item bank items), depression (Patient Health Questionnaire-9 (PHQ-9)), pain severity (0–10 Numerical Rating Scale (NRS)), and fatigue (0–10 NRS).

**Results:** Pain and fatigue were independently associated with depression, but only pain was associated with physical functioning. Additionally, depression was more severe among middle-aged participants relative to younger or older participants. Physical functioning declined with increasing age, as well as with higher level of injury.

**Conclusions:** The findings support the need for continued development of effective treatments for both pain and fatigue in order to prevent and mitigate the negative effects these symptoms can have on functioning.

**Keywords:** Pain, Fatigue, Spinal cord injuries, Depression, Mood, Function, Physical, Outcomes, Rehabilitation, Model system

Spinal cord injuries (SCI) are associated with a variety of symptoms and health conditions thought to be secondary to the original injury, such as pain, fatigue, pressure ulcers, urinary tract infections, pneumonia, and deep vein thrombosis.<sup>1–3</sup> Approximately, one-third of individuals with SCI describe experiencing pain of severe intensity.<sup>4</sup> Similarly, fatigue is also common among individuals with disabilities (including SCI), and more severe in disabled populations than in the general population.<sup>5</sup> Several studies have reported a positive association between pain and fatigue among persons with SCI,<sup>6,7</sup> and both pain and fatigue are negatively associated with physical functioning and mood.<sup>6,8–13</sup> However, although these symptoms often

co-occur, understanding their *independent* contributions to physical and psychological functioning is necessary for delineating their relative importance, as well as for designing interventions to improve functioning in this population.

With regard to physical functioning, pain has been reported to interfere with everyday activity on an average of 16 out of 90 days among persons with SCI.<sup>4</sup> Among persons with SCI living in the community, pain has a number of negative consequences including effects on ability to fall asleep (58%), exercise (35%), do household chores (39%), and work outside the home (34%).<sup>8</sup> Fatigue is reported to interfere with physical functioning at a similarly high level, with 57% of participants with SCI reporting fatigue severe enough to interfere with everyday functioning.<sup>6</sup> Similarly, McColl *et al.*<sup>9</sup> observed associations between fatigue,

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health problems, and increased disability among individuals with SCI.

Previous research has also shown negative associations of pain and fatigue with psychological functioning.<sup>9–13</sup> For example, pain was associated with higher levels of depressive symptoms in a sample of community-dwelling men with SCI,<sup>14</sup> and both pain and fatigue are associated with poorer social integration and overall mental health.<sup>12</sup> Given that 29% of persons with SCI require depression treatment within 6 years of injury,<sup>15</sup> it is particularly important to identify factors, such as pain and fatigue, that may be associated with the onset and persistence of depression.

Only a small body of literature has explored the effect of aging on the experience of pain and fatigue in SCI. Expanding this literature is important given that a person aging with SCI may experience cumulative effects of secondary conditions in addition to unrelated age-related chronic diseases. Furthermore, aging may be associated with greater difficulty accessing sustained social and instrumental support that can mitigate the impact of disability. Few studies have explored whether pain and fatigue change over the course of the lifespan in persons with SCI. Most of these studies conclude that pain problems in persons with SCI do not often improve over time, and often increase in severity.<sup>12,16,17</sup> However, one longitudinal study reported that changes in pain were regionally distinct in SCI, with upper-extremity pain increasing with age and lower-extremity pain decreasing over time (presumably due to an increase in shoulder pain associated with long-term manual wheelchair use).<sup>18</sup> Further, there is evidence that older persons with SCI report higher levels of fatigue than do members of the general population<sup>5</sup> and that younger persons with SCI are less likely to report fatigue than older persons.<sup>9</sup> Finally, there is evidence that certain organ systems (especially the cardiovascular system) may age at an accelerated rate in persons with SCI,<sup>19</sup> potentially putting older individuals with SCI at higher risk for accelerated functional decline.

Lastly, an intriguing body of literature has emerged regarding the association of age with psychological functioning, including depression and emotional responses to difficult medical conditions. Among persons with<sup>20,21</sup> and without disabilities,<sup>22,23</sup> depressive symptoms tend to follow an inverse “U-shaped curve” across the lifespan. That is, depression is more prevalent among middle-aged persons relative to younger and older persons. Moreover, emotional reactivity to pain appears to vary with age: one study of adults with chronic pain found that older persons reported less

emotional response to pain than did younger adults;<sup>24</sup> another study in cancer patients suggested that older adults might be less bothered by physical activity restrictions relative to younger adults.<sup>25</sup> Finally, a large population-based cohort study observed that older adults reported better quality of life and better mood relative to younger adults, despite having pain that was both more intense and of longer duration than younger adults.<sup>26</sup> In essence, it appears that age may act as a buffer against the negative effects of pain and disease on physical and psychological functioning.<sup>27</sup> Confirmation of the inverse U-shaped association between age and depression in samples of persons with SCI would assist researchers and clinicians in identifying potential vulnerabilities in persons with SCI at different points in the lifespan.

The present study was conducted to build upon the existing literature on pain and fatigue in persons with SCI by (1) investigating the independent associations of pain and fatigue with depressive symptoms and physical functioning among persons with SCI and (2) testing the hypothesis that age moderates these relationships. Guided by prior research, we predicted that pain and fatigue would be associated with lower levels of physical functioning and higher levels of depressive symptoms. We hypothesized that increased age would be associated with attenuated associations between pain and depression and stronger associations among pain, fatigue, and impaired physical functioning.

## Methods

### Measures

#### Criterion variables: physical functioning and depressive symptoms

Physical activity was measured with items from the 124-item Patient-Reported Outcomes Measurement Information System (PROMIS) Physical Functioning item bank.<sup>28–30</sup> A unique aspect of the PROMIS item bank is that it has been developed to allow for any subset of items to be used to estimate the latent trait, in this case physical activity.<sup>31</sup> Thus, consistent with this purpose of the development of the PROMIS item bank, study investigators chose 12 items from this bank for their applicability for use in persons with disabilities. The PROMIS physical functioning item bank is measured on a 5-point scale from “without any difficulty” to “unable to do” and examines a person’s ability to perform a variety of physical activities. Items ask individuals to rate the difficulty they have completing a wide range of activities, including difficulty: (1) putting on and taking off a coat or jacket; (2) walking more than a mile; (3) carrying a bag of groceries for a

short distance; (4) preparing simple meals for themselves or for others; (5) doing housework like vacuuming or sweeping floors; (6) moving around on a slippery surface outdoors; (7) doing vigorous activities, such as playing sports; (8) standing up from sitting on a low, soft couch; (9) washing and drying their body; (10) making a bed, including spreading and tucking in bed sheets; (11) getting up off the floor from lying on their back without help; and (12) going for a walk of at least 15 minutes. Scores are transformed into *t*-scores with higher scores in the PROMIS physical function domain indicating better physical functioning.

The Patient Health Questionnaire-9 (PHQ-9) was used to evaluate depressive symptoms. The PHQ-9 is a nine-item measure that asks participants to rate how frequently they were bothered by the nine diagnostic symptoms of major depression in the past 2 weeks. The 4-point scale ranges from “not at all” (0) to “nearly every day” (3). The total score on the PHQ-9 can range from 0 to 27, with higher scores representing higher levels of depressive symptoms and scores above 10 consistent with a clinically significant depressive disorder. It is widely accepted as a valid measure for use in populations with physical disease and disabilities, including SCI.<sup>32,33</sup>

#### **Predictor variables: pain severity and fatigue**

Pain severity and fatigue were measured using Numerical Rating Scales (NRSs), with participants rating the severity of symptoms over the past week on 0–10 scales, with 0 = “none” and 10 = “very severe”. Symptom severity is commonly assessed using NRSs, which have been demonstrated to be valid measures of pain and fatigue.<sup>34–36</sup>

#### *Procedures*

Participants were eligible if they were 18 years of age or older, could read, write, and understand English, and had a self-reported diagnosis of SCI. Participants were recruited through (1) invitation letters sent to individuals who had previously participated in studies conducted at the University of Washington (UW Disability Registry, composed of participants who previously participated in the Quality of Life in Persons with Disabilities Survey and were originally recruited from the Northwest Regional Spinal Cord Injury Model System and the University of Washington Center on Outcomes Research in Rehabilitation), as well as (2) other print advertisements and word of mouth. A total of 558 individuals responded to these invitation letters and advertisements. Surveys were sent to 540 individuals who met inclusion criteria. A total

of 492 surveys were completed and returned (91% response rate). Participants received a check for \$25 for their participation. This study was approved by the Institutional Review Board at the University of Washington and informed consent was obtained from all participants. One paper comparing the severity of fatigue with USA norms across age cohorts in a sample that included almost all of the participants in the current paper has already been published.<sup>5</sup>

#### *Data analysis*

Data were first examined to ensure the assumptions of multiple regression were met. After confirming the absence of significant skew, kurtosis, outliers, or heteroscedasticity for any predictor or criterion variable (parameters: skew <2.0, kurtosis <2.0, visual inspection of scatterplot of residuals), we then computed descriptive statistics (mean, standard deviation, and range) on study variables. We next computed Pearson correlation coefficients between predictor and criterion variables to determine their zero-order associations in order to verify our hypothesis that pain and fatigue would be associated with each other and, also, that they would be associated with physical functioning and depression.

Two parallel regression analyses were conducted to test the two hypotheses regarding whether pain and fatigue made independent contributions to the prediction of physical functioning and depression (represented by the PROMIS Physical Functioning scale and PHQ-9 score, respectively) after controlling for chronological age and level of injury. The control variables were selected due to the literature supporting associations of age with both physical and psychological functioning, as well as the likely significant impact of level of injury on physical functioning. (We carefully considered how to include level of injury, including using a continuous variable and a number of categorizations representing cutoffs for aspects of functioning and complete or incomplete injury. This exploration revealed that controlling for level of injury was important, but that the method by which we categorized level of injury did not alter the results. Thus, we chose to report the continuous variable for level of injury as it is most intuitive to interpret alongside the other continuous variables.) All predictor variables were centered before being entered into the model in order to minimize potential problems associated with multi-collinearity. Variables were entered as follows: centered chronological age variable and continuous level of injury were entered in step one, (centered) age<sup>2</sup> was entered in step two to test for a possible quadratic (i.e. inverse U-shaped) association between age and the criterion variables, average pain

severity and fatigue (0–10 NRS ratings) were entered in step three, age × pain severity and age × fatigue severity interaction terms were entered in the fourth step (to test for the moderation of linear age), and age<sup>2</sup> × pin severity and age<sup>2</sup> × fatigue severity interaction terms were entered in the fifth step to test for quadratic age effects. The beta weights and significance levels of each predictor were examined to evaluate their associations.

**Results**

*Participants*

The final sample of 481 participants included 67% (*n* = 320) men and 34% (*n* = 161) women. Average age was 50.01 years (SD = 14.00; range = 21–89 years). For supplemental analyses, participants were divided into five age-based cohorts: less than 45 years old (*n* = 166, 35%), 45–54 years old (*n* = 120, 25%), 55–64 years old (*n* = 126, 26%), 65–74 years old (*n* = 54, 11%), and 75 years old and older (*n* = 15, 3%). The overwhelming majority of our participants reported their race/ethnicity as Caucasian (*n* = 420, 87.3%) and highly educated (the majority reported completion of at least some

college). Table 1 provides descriptive data stratified by injury subgroup (i.e. tetraplegia versus paraplegia, complete versus incomplete injury).

*Means, standard deviations, and associations among study variables*

Descriptive analyses for the predictor and outcome variables are presented in Table 2. As demonstrated in the zero-order correlations reported in Table 3, pain and fatigue were significantly associated with physical and psychological functioning; age was significantly associated with physical functioning.

*Regression analyses*

The results for the regression analysis for physical functioning are reported in Table 4. The overall model was significant ( $F(9, 472) = 15.44, P < 0.05$ ) and accounted for 22.7% of the variance in PROMIS Physical Functioning scores. In step 1, age ( $\beta = -0.13, P = 0.02$ ) and level of injury ( $\beta = -0.44, P < 0.001$ ) were significantly associated with physical functioning and accounted for 20.3% of the variance in physical functioning. These negative associations indicate that

**Table 1 Demographics of the study sample**

|                                    | Tetraplegia, complete (N = 66) | Tetraplegia, incomplete (N = 158) | Tetraplegia, unsure (N = 20) | Paraplegia, complete (N = 130) | Paraplegia, incomplete (N = 97) | Paraplegia, unsure (N = 16) |
|------------------------------------|--------------------------------|-----------------------------------|------------------------------|--------------------------------|---------------------------------|-----------------------------|
| Age (M years (SD))                 | 50.1 (13.9)                    | 49.9 (13.9)                       | 48.3 (15.7)                  | 49.1 (13.6)                    | 51.4 (14.3)                     | 49.9 (16.0)                 |
| Gender (%)                         |                                |                                   |                              |                                |                                 |                             |
| Male                               | 83.3                           | 67.1                              | 70.0                         | 67.7                           | 52.6                            | 62.5                        |
| Female                             | 16.7                           | 32.9                              | 30.0                         | 32.3                           | 47.4                            | 37.5                        |
| Ethnicity (%)                      |                                |                                   |                              |                                |                                 |                             |
| African American                   | 10.6                           | 7.6                               | 15.0                         | 7.7                            | 6.2                             | 12.5                        |
| Asian                              | 3.0                            | 1.9                               | 0.0                          | 1.5                            | 3.1                             | 0.0                         |
| Caucasian                          | 81.8                           | 86.7                              | 85.0                         | 89.2                           | 90.7                            | 87.5                        |
| Hispanic                           | 3.0                            | 0.6                               | 0.0                          | 2.3                            | 1.0                             | 0.0                         |
| Native American                    | 4.5                            | 3.8                               | 0.0                          | 2.3                            | 2.1                             | 0.0                         |
| American Indian/<br>Alaskan Native |                                |                                   |                              |                                |                                 |                             |
| Pacific Islander                   | 0.0                            | 1.3                               | 0.0                          | 0.0                            | 0.0                             | 0.0                         |
| Other                              | 0.0                            | 1.9                               | 0.0                          | 0.8                            | 0.0                             | 0.0                         |
| Education (%)                      |                                |                                   |                              |                                |                                 |                             |
| 9th grade or less                  | 1.5                            | 0.6                               | 0.0                          | 2.3                            | 1.0                             | 0.0                         |
| 10–11 grades                       | 1.5                            | 1.9                               | 5.0                          | 1.5                            | 1.0                             | 0.0                         |
| High school graduate or GED        | 15.2                           | 15.2                              | 30.0                         | 20.0                           | 11.3                            | 31.3                        |
| Vocational or technical school     | 7.6                            | 8.2                               | 10.0                         | 10.8                           | 9.3                             | 18.8                        |
| Some college                       | 27.3                           | 26.6                              | 5.0                          | 24.6                           | 24.7                            | 31.3                        |
| College graduate                   | 27.3                           | 29.7                              | 30.0                         | 30.0                           | 34.0                            | 18.8                        |
| Graduate or professional school    | 19.7                           | 17.7                              | 20.0                         | 10.8                           | 18.6                            | 0.0                         |
| Duration of SCI (M years (SD))     | 19.3 (11.2)                    | 16.2 (10.7)                       | 19.5 (14.8)                  | 16.7 (10.4)                    | 19.4 (12.5)                     | 15.6 (11.1)                 |

There were no statistically significant group differences with the exception of a difference in gender distribution for tetraplegia complete versus paraplegia incomplete.

**Table 2** Descriptive statistics for physical functioning, depression, fatigue, pain, and age

|                                       | Mean  | SD    | Range       | Skew  | Kurtosis |
|---------------------------------------|-------|-------|-------------|-------|----------|
| PROMIS Physical Functioning (T-score) | 32.59 | 9.72  | 13.96–59.91 | –0.09 | –0.08    |
| PHQ-9 Depression                      | 5.83  | 5.06  | 0–27        | 1.23  | 1.17     |
| Average pain over past week           | 4.51  | 2.66  | 0–10        | –0.06 | –0.97    |
| Average fatigue over past week        | 4.10  | 2.53  | 0–10        | 0.19  | –0.71    |
| Age                                   | 50.02 | 14.02 | 21–88       | –0.03 | –0.52    |

**Table 3** Zero-order correlation matrix of physical functioning, depression, fatigue, pain, and age

|   | 1       | 2       | 3       | 4    |
|---|---------|---------|---------|------|
| 1. PROMIS Physical Functioning          |         |         |         |      |
| 2. PHQ-9 Depression                     | –0.05   |         |         |      |
| 3. Average pain severity over past week | –0.09*  | 0.36*** |         |      |
| 4. Average fatigue over past week       | –0.10*  | 0.53*** | 0.45*** |      |
| 5. Age                                  | –0.12** | 0.04    | 0.04    | 0.01 |

\* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ .

**Table 4** Regression model predicting PROMIS Physical Functioning score

| Variable   | B     | t     | P value | R <sup>2</sup> Δ | F(R <sup>2</sup> Δ) | P value |
|--|-------|-------|---------|------------------|---------------------|---------|
| Block 1  |       |       |         | 0.203            | 61.142              | <0.0001 |
| Age (centered)                                   | –0.13 | –3.12 | 0.002   |                  |                     |         |
| Level of injury                                  | 4.35  | 10.67 | <0.0001 |                  |                     |         |
| Block 2  |       |       |         | 0.000            | 0.02                | 0.89    |
| Age <sup>2</sup> (centered)                      | 0.01  | 0.14  | 0.89    |                  |                     |         |
| Block 3  |       |       |         | 0.016            | 4.82                | 0.008   |
| Pain (centered)                                  | –0.11 | –2.44 | 0.015   |                  |                     |         |
| Fatigue (centered)                               | –0.03 | –0.62 | 0.54    |                  |                     |         |
| Block 4  |       |       |         | 0.001            | 3.24                | 0.72    |
| Age (centered) × pain (centered)                 | –0.04 | –0.80 | 0.43    |                  |                     |         |
| Age (centered) × fatigue (centered)              | 0.01  | 1.94  | 0.85    |                  |                     |         |
| Block 5  |       |       |         | 0.007            | 2.19                | 0.11    |
| Age <sup>2</sup> (centered) × pain (centered)    | 0.03  | 0.46  | 0.65    |                  |                     |         |
| Age <sup>2</sup> (centered) × fatigue (centered) | 0.11  | 1.85  | 0.07    |                  |                     |         |

Overall model:  $F(9, 472) = 15.44$ ,  $P < 0.05$ .

younger participants reported higher levels of physical functioning than those who were relatively older, and participants with lower levels of injury reported higher levels of physical functioning relative to participants with relatively higher levels of injury. In step 2, age<sup>2</sup> was not associated with physical functioning. In step 3, pain ( $\beta = -0.11$ ,  $P = 0.015$ ) was significantly associated with physical functioning and accounted for an additional 1.6% of the variance in physical functioning; fatigue was not associated with physical functioning. The direction of the relationship of pain and physical functioning indicates that higher levels of pain were associated with less physical activity. The interaction terms (steps 4 and 5) did not significantly contribute to the variance in physical functioning.

The overall regression model for depressive symptoms was significant ( $F(9, 472) = 22.18$ ,  $P < 0.0001$ ) and

accounted for 29.9% of the variance (see Table 5). In the first step, age and level of injury were not significantly associated with depression and did not significantly contribute to the prediction of variance in depression. In step 2, age<sup>2</sup> was significantly associated with depression ( $\beta = -0.09$ ,  $P < 0.05$ ) and accounted for 0.9% of the variance in PHQ-9 depression scores. To better understand this quadratic association, we examined the depression scores for each of five age cohort groups: (1) younger than 45 years old (PHQ-9  $M = 5.50$ ); (2) 45–54 years old (PHQ-9  $M = 5.98$ ); (3) 55–64 years old (PHQ-9  $M = 6.29$ ); (4) 65–74 years old (PHQ-9  $M = 5.55$ ); and (5) 75 years old and older (PHQ-9  $M = 5.53$ ). These results indicate an inverse U-shaped pattern such that participants between 45 and 64 years old reported the highest levels of depression, with the younger and older participants

**Table 5 Regression model predicting PHQ-9 Depression score**

| Variable   | B     | t     | P value | R <sup>2</sup> Δ | F(R <sup>2</sup> Δ) | P value |
|--|-------|-------|---------|------------------|---------------------|---------|
| Block 1  |       |       |         | 0.002            | 0.54                | 0.58    |
| Age (centered)                                   | 0.05  | 1.00  | 0.32    |                  |                     |         |
| Level of injury                                  | 0.01  | 0.27  | 0.79    |                  |                     |         |
| Block 2  |       |       |         | 0.009            | 4.16                | 0.04    |
| Age <sup>2</sup> (centered)                      | -0.09 | -2.04 | 0.04    |                  |                     |         |
| Block 3  |       |       |         | 0.286            | 96.20               | <0.0001 |
| Pain (centered)                                  | 0.14  | 3.28  | 0.001   |                  |                     |         |
| Fatigue (centered)                               | 0.46  | 10.56 | <0.0001 |                  |                     |         |
| Block 4  |       |       |         | 0.000            | 0.05                | 0.95    |
| Age (centered) × pain (centered)                 | 0.00  | -0.06 | 0.95    |                  |                     |         |
| Age (centered) × fatigue (centered)              | 0.01  | 0.31  | 0.76    |                  |                     |         |
| Block 5  |       |       |         | 0.001            | 0.49                | 0.62    |
| Age <sup>2</sup> (centered) × pain (centered)    | -0.04 | -0.72 | 0.47    |                  |                     |         |
| Age <sup>2</sup> (centered) × fatigue (centered) | 0.05  | 0.85  | 0.40    |                  |                     |         |

Overall model:  $F(9, 472) = 22.18, P < 0.0001$ .

reporting lower levels of depression than the middle-aged participants; however, the differences between the age cohorts in depressive symptoms were not statistically significant ( $F = 0.53, n.s.$ ). In step 3, pain and fatigue accounted for an additional 28.5% of the variance in PHQ-9 Depression scores ( $F\Delta = 96.20, P < 0.0001$ ). Both pain ( $\beta = 0.14, P = 0.001$ ) and fatigue ( $\beta = 0.46, P < 0.0001$ ) made independent significant contributions to the criterion. The direction of the relationship indicates that more pain and more fatigue were associated with greater depressive symptomatology. The interaction terms entered in steps 4 and 5 did not contribute significantly to the model.

**Discussion**

Findings from the present study confirm our hypothesis that pain and fatigue are associated with depression, and partially support our parallel hypothesis for associations of these variables with physical functioning by indicating that pain, but not fatigue, is associated with physical functioning in persons with SCI. Specifically, regression analyses revealed an association of more depressive symptoms with middle age and with higher levels of pain and fatigue. In contrast, lower levels of physical functioning were associated with older age, higher level of injury, and more severe pain. We were also interested in testing the moderating effects of age; our results indicated that while age is associated with depression and physical functioning, it does not moderate the relationships of pain and fatigue with depression or with physical functioning. Taken together, these findings build upon previous studies that considered only associations of either pain *or* fatigue with functioning in persons with SCI<sup>6,8,9</sup> by identifying independent associations of pain and fatigue (when considered

together) with depression. However, inconsistent with our findings in studies investigating other disability groups,<sup>20,37</sup> only pain, and not fatigue, was associated with physical functioning when both variables were included in the same model.

The findings of independent associations of pain and fatigue with depression closely mirror previous findings for SCI<sup>9-13</sup> and for other disabilities we have studied, such as post-polio syndrome<sup>20</sup> and muscular dystrophy.<sup>37</sup> By identifying independent associations of pain and fatigue with depression, the results demonstrate that pain and fatigue are not merely proxy measures of each other. Instead, they make independent contributions to depression, which suggests that both clinical issues should be carefully evaluated and treated so as to minimize their respective potential negative influences on depression.

Although the association of pain with physical functioning was consistent with the extant literature, the absence of an association between fatigue and physical functioning diverged from previous findings.<sup>6,8,9</sup> This effect may be explained via the strong association between the level of injury and physical functioning, which is not surprising in the context of SCI. It is likely that some participants were simply unable to perform certain activities (e.g. walking more than a mile, doing vigorous activities). Relatedly, and also not surprising, participants' total scores on the PROMIS physical functioning measure were lower than we have observed for persons with other disabilities<sup>20,37</sup> (although not sufficiently low to create a floor effect). In fact, although not reported in this manuscript, we conducted the same analyses on versions of the PROMIS measure with additional items removed and also on other physical functioning measures from this

survey and the results remained the same. Taken together, despite the restrictions of the condition itself on physical functioning, pain still had a statistically significant association with physical functioning among this population of persons with SCI.

As with all studies of physical functioning, the results must be interpreted carefully, with specific attention to what was measured and what conclusions can be made as a result. In the present study, participants were asked to indicate their difficulty with daily tasks that are primarily home-based self-care activities. At the same time, it is important to note that we did not consider whether a patient can or cannot do the activity (i.e. ability), whether the measured activities are important to the participant, whether these deficits subsequently interfere with community participation, or whether these findings have implications for subjective well-being or quality of life.<sup>38</sup> Additionally, we do not know how a participant's self-reported functioning relates to their actual ability or functioning, and whether pain would be associated in all types of measurement.<sup>39</sup> Taken together, the results of the present study have specific implications for the relationship of pain with poorer physical functioning in the domains measured, but future research is needed to understand how these results relate to other aspects of physical functioning.

Clinically, these findings support the aggressive treatment of pain and fatigue among persons with SCI for the improvement of physical functioning and mood. A number of effective pharmacological, non-pharmacological, and multidisciplinary management approaches exist for persons with pain and SCI.<sup>40-45</sup> In contrast, less support exists for treatments that address fatigue. Modafinil has emerged as an effective treatment for fatigue in persons with disabilities,<sup>46</sup> but only one small study has been conducted on persons with SCI.<sup>47</sup> Given the simultaneous and independent association of pain and fatigue with psychological functioning, it may prove beneficial to identify methods that treat both conditions simultaneously.

Beyond pain and fatigue, the data also revealed associations of age with both physical and psychological functioning. Increasing age was associated with decreasing physical functioning; suggesting that declines in physical functioning may be related to the aging process. Given the possibility that age could be a proxy for time since injury, we conducted *post hoc* regressions with both age and time since injury as predictor variables. While the two variables are moderately correlated with each other, we found that chronological age, but not time since injury, was a significant predictor

of physical functioning. Thus, this finding supports the conclusion that the aging process is negatively associated with physical functioning. Moreover, the interactions of age with pain and age with fatigue were not significantly associated with either depression or physical functioning. Although the interpretation of null findings must be made with caution, these findings do not support the study hypothesis that pain and fatigue play an increasingly strong (or a diminishingly important) role in physical functioning or depression as individuals with SCI age.

Yet, with regard to depression, age did demonstrate a quadratic relationship with psychological functioning, wherein individuals in middle age reported the highest levels of depression. This finding is consistent with the growing body of literature suggesting an inverse U-shaped association between age and depression among persons with<sup>20,21</sup> and without disabilities<sup>22,23,48</sup> and is clinically important. Extant literature suggests that this U-shaped association may be the result of declining functional capacity in the context of high-performance expectations during middle age<sup>48</sup> followed by an increased sense of control and concomitant lower stress during retirement years.<sup>49</sup> In the setting of SCI, it may be the case that the disparity between actual levels of functioning and societal expectations of the same is particularly pronounced during middle age, thus suggesting the possibility that higher levels of depression in this group may reflect perceptions of lower quality-of-life. Growing replication of these findings suggests two aims for clinicians: (1) actively assess for emergence of depression in persons with SCI, particularly as these individuals enter midlife and (2) proactively prepare individuals with SCI for challenges they may face in middle age with regard to home life, work, and physical abilities, with the aim of minimizing or preventing the appearance of depressive symptoms.

The current study is strengthened by the use of a community-based survey that allowed for the inclusion of a large sample (481) of individuals with SCI. Survey methodology is particularly effective in this population for accessing participants who may have limited ability to present for in-person participation. However, as with any survey research, there are a number of limitations. First, this is a convenience sample of individuals who were motivated to participate in this study. Second, this was a cross-sectional study and thus allows only for the identification of associations between variables without causal conclusions. Third, data were self-reported, meaning that the results reflect participants' perception of their symptoms and functioning; data collected through a different method (e.g. family member/

health care provider observation) could potentially reveal different absolute levels of variables of interest and different relationships among them. Lastly, we acknowledge that the assessment of physical functioning in persons with SCI is challenging, particularly when including a heterogeneous sample with widely varying physical abilities. At minimum, we recommend future researchers control for level of injury in their analyses, as we have done here. However, we also recognize that it may ultimately be best to utilize a measure that more specifically targets this population.

### Conclusions

Pain and fatigue affect depression and physical functioning in persons with disabilities.<sup>9–13,20,37</sup> In the present study of persons with SCI, we observed similarities and differences in these associations relative to those observed in other populations. Specifically, pain – in addition to level of injury – was associated with physical functioning, and both pain and fatigue were associated with depression, highlighting the importance of monitoring both pain and fatigue as persons age with SCI. Close monitoring and appropriate early intervention will assist patients and healthcare providers in proactively managing the risks for decline in physical and psychological functioning in this population.

### Acknowledgement

This paper is based on original research conducted in the Department of Rehabilitation Medicine at the University of Washington. Funding for this study was provided through a grant from the Department of Education, NIDRR grant number H133B080024.

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