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Psychological morbidity following spinal cord injury and among those without spinal cord injury: the impact of chronic centralized and neuropathic pain

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Abstract

Study Design: Longitudinal cohort study of privately-insured beneficiaries with and without traumatic spinal cord injury (SCI).

Objectives: Compare the incidence of and adjusted hazards for psychological morbidities among adults with and without traumatic SCI, and examine the effect of chronic centralized and neuropathic pain on outcomes.

Setting: Privately-insured beneficiaries were included if they had an ICD-9-CM diagnostic code for traumatic SCI (n=9,081). Adults without SCI were also included (n=1,474,232).

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Author Contributions:

MP and EM were responsible for designing the conceptual framework of the study. PL and NK conducted the statistical analyses. MM, GR, and JK contributed substantially to the data interpretation and the article preparation. All authors provided writing support and contributed to the editing of the final manuscript.

Statement of Ethics:

This study was deemed exempt by the Institutional Review Board at the researchers' institution.

Data Availability

All data accessed for this study were purchased through the Clinformatics™ Data Mart Database, a de-identified nationwide claims database of all beneficiaries from a single private payer. Thus, data are not eligible or available for public data access.

Conflict of Interest:

The authors declare that they have no conflicts of interest.

Methods: Incidence of common psychological morbidities were compared at 5-years of enrollment. Survival models were used to quantify unadjusted and adjusted hazard ratios for incident psychological morbidities.

Results: Adults with SCI had a higher incidence of *any* psychological morbidity (59.1% vs. 30.9%) as compared to adults without SCI, and differences were to a clinically meaningful extent. Survival models demonstrated that adults with SCI had a greater hazard for *any* psychological morbidity (HR: 1.67; 95%CI: 1.61, 1.74), and all but one psychological disorder (impulse control disorders), and ranged from HR: 1.31 (1.24, 1.39) for insomnia to HR: 2.10 (1.77, 2.49) for post-traumatic stress disorder. Centralized and neuropathic pain was associated with all psychological disorders, and ranged from HR: 1.31 (1.23, 1.39) for dementia to HR: 3.83 (3.10, 3.68) for anxiety.

Conclusions: Adults with SCI have a higher incidence of and risk for common psychological morbidities, as compared to adults without SCI. Efforts are needed to facilitate the development of early interventions to reduce risk of chronic centralized and neuropathic pain and psychological morbidity onset/progression in this higher risk population.

Keywords

spinal cord injury; centralized pain; neuropathic pain; depression; anxiety; post-traumatic stress disorder

Introduction

Traumatic spinal cord injury (SCI) is a sudden and life changing event that impacts health, functioning, societal participation, and quality of life. In the United States, about 17,810 individuals acquire a new traumatic SCI each year, while there are an estimated 294,000 people living with the condition¹. The extent of functional impairment among individuals living with SCIs depends on the location and extensiveness of damage to the spinal cord; individuals with higher level injuries (e.g., cervical vs. lumbar region) and more severe damage experience greater impairments. In most cases, traumatic SCI is considered a permanent condition, with any restoration of function limited to the first two years after injury and then usually only resulting in only minor changes to functional ability, but potentially longer-term effects involving changes in quality of life and psychological health.

While it is a misperception that depression and poor quality of life are necessary consequences of SCI²⁻⁴, research on the psychological impact of traumatic SCI has consistently found higher levels of psychological morbidity among this group than the general population⁵⁻⁷, with rates that reflect occurrence in a significant minority (not majority) of people living with the condition (e.g., depression is roughly 22% prevalent following traumatic SCI⁵). Most recently, Peterson and colleagues used claims data from privately insured beneficiaries to compare the longitudinal incidence of psychological morbidity of adults with SCI and a matched cohort of adults without SCI and noted higher rates of adjustment reaction, anxiety disorders, depressive disorders, alcohol dependence, drug dependence, dementia, insomnia, and psychological multi-morbidity as compared with adults without SCIs⁶.

Unfortunately, less is known about the timing of the development of these psychological conditions and the occurrence of comorbid factors following SCI. For example, even if the occurrence of psychological morbidities is not premorbid, it is often hard to determine if increased rates are associated with SCI itself or with the comorbid medical conditions that adults with SCI experience at higher rate^{1, 8–12}. Perhaps the least understood risk factor for psychological morbidity after SCI is chronic pain. There is evidence suggesting that the magnitude and presence of chronic pain following SCI results in both adaptive and maladaptive structural plasticity of sensorimotor regions, alongside altered metabolism of brain areas involved with descending pain modulation, pain perception and sensory integration¹³.

Fortunately, increasing access and ability to analyze large datasets, including medical claims data, provides the opportunity examine large enough cohorts while also providing control groups to account for personal and demographic variables. Such information may lead to improved precision medicine approaches to provide efficient care coordination and diminished secondary disease risk. The objective of this study was to examine the risk (likelihood) of psychological morbidity among adults with traumatic SCI as compared to adults without SCI, controlling for the impact associated with chronic centralized and neuropathic pain and other medical conditions.

Methods

Data Source

This is a retrospective cohort study of adults with traumatic SCI whose diagnosis could have existed across any patient care setting. This study used a national, private insurance claims database, Clinformatics DataMart Database (OptumInsight, Eden Prairie, MN). This is a de-identified administrative claims database of over 80 million adults and children with commercial insurance representing those on a single, large U.S. private payer who had both medical and pharmacy coverage throughout the enrollment. Enrolled beneficiaries' emergency department, outpatient, and inpatient encounters are captured.

Sample Selection

All individuals 18 years of age and older at the time of enrollment were eligible for this analysis. Enrollment years included 2007–2017. We excluded individuals with less than 12 months of continuous enrollment to require sufficient claim history. All medical claims excluding laboratory and outpatient pharmacy was considered to identify prevalence or treatment for these conditions during the enrollment period.

Identification of Patients with a SCI—All members with a diagnosis of traumatic SCI were identified using International Classification of Diseases, Ninth revision, Clinical Modification (ICD-9-CM) (Supplementary Table S1). Members with SCI prior to 2007 were excluded due to poorer coverage of diagnosis codes during 2001 to 2006 in the database. Members without a diagnosis code in any position when they were 18 years or older during enrollment were excluded. To allow adequate longitudinal follow up for all patients with

SCI, only those that had four or more continuous years of enrollment following their starting date of enrollment within the study period were included.

A comparison cohort of controls without SCI or other neurological disabilities were also identified using the same aforementioned inclusion criteria. Additional exclusion criteria for identifying the control cohort included removal of any individual with other physically disabling neurological disorders (e.g., non-SCI paraplegia, non-SCI quadriplegia, non-SCI hemiplegia, cerebral palsy, spina bifida, and multiple sclerosis). Among remaining members without SCI, a 20% simple random sample of members was selected to represent the control group. Post-hoc analyses of demographic characteristics were compared between the 20% sample of controls and all controls and confirmed that there was no bias in control cohort attributable to random selection (Figure 1).

Psychological Morbidities—Provider-diagnosed psychological health disorders were identified based on a single encounter that included at least one of pertinent ICD-9 or ICD-10 codes (in any position) (see Supplementary Table S1). The primary outcome was time in days to incident psychological morbidity as a composite outcome following enrollment on the plan. Secondary outcomes were component incident psychological morbidity, including: (1) insomnia, (2) adjustment disorders, (3) anxiety disorders and post-traumatic stress disorder (PTSD), (4) delirium/dementia/amnesic or other cognitive disorder, (5) dementias, (6) impulse control disorders, (7) mood disorders, (8) personality disorders, (9) alcohol-related disorders, and (10) substance-related disorders.

Chronic Centralized and Neuropathic Pain—Physician-diagnosed pain disorders were identified based on a single encounter that included at least one of pertinent ICD-9 or ICD-10 codes (see Supplemental File 1 for list). The pain disorders were categorized as chronic centralized and neuropathic pain, and included chronic pain, central pain syndrome, chronic pain syndrome, psychogenic pain, fibromyalgia, and neuralgia and neuritis.

Covariates—Explanatory covariates included age group split into three categories (18–44, 45–64, 65 or older), sex, race, educational attainment, household net worth, and a modified Elixhauser comorbidity index. The Elixhauser comorbidity index was modified to removed four conditions that would be correlated with incident psychological morbidity: alcohol abuse, drug abuse, psychoses, and depression. Therefore, the revised index only considers 27 comorbidities (Supplemental Table S2).

Statistical Analysis

Bivariate analyses of baseline demographic characteristics between patients with SCI and controls were examined. For categorical variables, column percentages were compared between both groups using effect size calculations with Cohen's *h*. The Cohen's *h* effect size calculation was used to calculate a standardized mean difference (SMD) since, due to large sample sizes, being statistically overpowered would not provide clinically meaningful differences in proportions between groups. For continuous variables, means and standard deviations as well as medians with upper and lower bounds on interquartile ranges were

calculated. Cohen's *d* SMD were calculated for continuous variables to ascertain clinically meaningful differences between groups.

All patients with sufficient continuous enrollment within the study period of four years were retained to enable sufficient follow-up. For the SCI cohort, we used a one year look back period of enrollment prior to the enrollment to capture comorbidity history and to examine if any prevalent psychological outcomes existed. Any patient with SCI with evidence of prevalent psychological morbidity in the one year lookback was removed from the cohort.

To examine disease-free survival of individuals with SCI compared to controls, those patients that had no evidence of composite psychological morbidity in each group were plotted using Kaplan-Meier product limit survival curves for a three-year period. To establish incidence in claims, we used a one-year lookback period from the index date in each group to obtain evidence of any service utilization with a diagnosis of any psychological morbidity. These patients were excluded from the product-limit survival curves and other subsequent analyses.

To estimate the unadjusted and adjusted hazard of the composite and each psychological morbidity, a series of survival models were developed. For each psychological morbidity, all patients that had evidence of the specific psychological morbidity were excluded from the model. For example, if depression was being considered as the incident outcome, all patients with prevalent depression in the one year prior to the index date would be excluded from the model. Therefore, sample sizes of patients included for each outcome varied based on evidence of prevalent disease in the one year prior to the index date. Survival models were then used to quantify unadjusted and adjusted hazard ratios for each incident psychological morbidity. Appropriate survival models were based on distributional assumptions that included testing Weibull, lognormal, exponential, gamma, logistic, loglog, and Normal distribution with respect to the follow-up in days by minimizing critical model fit statistics. Critical assessment of Akaike Information Criterion (AIC) was used as a basis for minimization amongst all candidate distributions. Use of the parametric Weibull regression for incident psychological outcome was applied stepwise. To examine the effects of incremental adjustment on the exposure variable (SCI), a series of models for each psychological outcome was evaluated. The final model (Model 5) examining the effect of chronic centralized and neuropathic pain was implemented due to the known associations between chronic pain in SCI, as well as between chronic pain and psychological morbidity. All patients were right censored if they did not experience the outcome in the follow-up period or disenrolled from the plan. Both unadjusted and all adjusted hazard ratios and 95% confidence intervals for the exposure to SCI were calculated.

All analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC). Statistical testing was two-tailed with a significance level of 0.01 and effect sizes used a 0.2 meaningful difference (i.e., SMD) cutoff.

Results

The mean time in the plan for eligible enrollees was 10.8 (25th Percentile: 8.0; 75th Percentile: 13.0) and 8.5 (25th Percentile: 6.0; 75th Percentile: 10.3) years for patients with SCI vs controls respectively (Table 1). Adults living with SCI had a higher 4-year incidence of any psychological morbidity (59.1% vs. 30.9%) as compared to adults without SCI, and differences were to a clinically meaningful extent. Moreover, adults with SCI had significantly higher incidence of all of the psychological outcomes, including insomnia, adjustment disorders, anxiety disorders and PTSD, delirium/dementia/amnestic or other cognitive disorder, dementia, mood disorders, alcohol-related disorders, substance-related disorders, and central pain syndrome, as compared to adults without SCI (all $P < .01$ and SMD 0.2) (Table 2).

A Kaplan-Meier curve for the unadjusted disease-free survival for any psychological morbidity in adults with SCI and controls are demonstrated in Figure 2. Unadjusted survival models demonstrated a robust increased hazard ratio (HR) for each of the incident psychological morbidities among adults with SCI, and ranged from HR: 1.73 (1.60, 1.87) for adjustment disorders to HR: 5.07 (4.79, 5.37) for delirium/dementia/amnestic/other cognitive disorder (all $p < 0.001$). Fully adjusted survival models demonstrated that adults with SCI had a greater hazard for *any* psychological morbidity (HR: 1.67; 95% CI: 1.61, 1.74) (Supplemental Table S3), and all but one psychological disorder (impulse control disorders), and ranged from HR: 1.31 (1.24, 1.39) for insomnia to HR: 2.10 (1.77, 2.49) for PTSD (Table 3).

Centralized and neuropathic pain was also associated with all psychological disorder (Model 5), including insomnia (HR: 1.88; 95% CI: 1.83, 1.94), adjustment disorders (HR: 1.59; 95% CI: 1.52, 1.66), anxiety disorders (HR: 1.73; 95% CI: 1.68, 1.77), PTSD (HR: 3.38; 95% CI: 3.11, 3.67), delirium/dementia/amnestic/other cognitive disorders (HR: 1.39; 95% CI: 1.33, 1.45), dementias (HR: 1.31; 95% CI: 1.24, 1.39), impulse control disorders (HR: 2.39; 95% CI: 1.93, 2.95), mood disorders (HR: 1.74; 95% CI: 1.69, 1.79), personality disorders (HR: 2.71; 95% CI: 2.42, 3.03), alcohol-related disorders (HR: 1.76; 95% CI: 1.66, 1.86), and substance-related disorders (HR: 3.74; 95% CI: 3.63, 3.8).

Discussion

Research on adults living with SCI has consistently found higher rates of psychological conditions among this population but have been limited in design and/or size to small clinical cohorts or large cross sectional studies^{6, 7, 14, 15}. This study provides clear longitudinal evidence that adults with traumatic SCI are at increased risk for developing both general psychological morbidity as well as most specific psychological conditions.

Moreover, we have shown for the first time in a large, longitudinal cohort of adults living with traumatic SCIs, that chronic centralized and neuropathic pain is robustly associated with all psychological morbidity. In fact, in most cases, chronic centralized and neuropathic pain was more highly associated with psychological morbidity than was the exposure of SCI. These findings lend strong support for the awareness around and improved referral

networks for early pain phenotyping and management after SCI. Moreover, understanding the mechanisms of pain in this population is vital, as response to pain treatment varies depending on pain etiology. Given that pain perception may arise from nociceptive, neuropathic, or nociplastic mechanisms, future studies are needed to understand the phenotypes of chronic pain among adults with SCI which will be crucial for prescribing the most appropriate and effective pain management interventions. For example, some treatments for pure nociceptive pain, such as narcotics, have been demonstrated to be harmful in centralized pain conditions, such as fibromyalgia¹⁶. As an important example, long-term opioid use in fibromyalgia has been associated with poorer outcomes than in individuals who are not receiving opioids¹⁷.

The overall incidence of psychological morbidity found in this study was 59.1% among adults with SCI versus 30.9% in the control group. This cohort of private insurance beneficiaries with SCI were diagnosed with a psychological condition at an unadjusted rate that is 2.41 times higher than that of adults without SCI. Moreover, the fully adjusted HR (in Model 5) indicates that adults with SCI experience a 79% increased risk of developing any psychological morbidity than adults without SCI with the same demographic factors and comorbid conditions. Of note, our use of HRs, rather than odds ratios (ORs) helps to reduce the impact of selection bias associated with the identified endpoint, as they represent instantaneous risk over the follow-up period used for the study (in this case 4 years).

Given the results from this study, closer attention should be paid to the relative impact of chronic pain conditions on the risk for each of the identified types of psychological conditions. The case of delirium, dementia, amnesic and other cognitive disorders and dementias is particularly notable as individuals with SCI had an unadjusted risk of 5.07 times the rate of diagnosis and an adjusted rate of 2.34 when controlling for demographic variables; a risk of 1.96 when controlling for both demographic and comorbid conditions; and a risk of 1.94 when controlling for demographic, comorbid conditions and income. In contrast, controlling for demographic characteristics actually appears to increase risk of diagnosis of certain conditions, including adjustment and alcohol-related disorders. These findings highlight the contribution of comorbid conditions in the development of psychological morbidities among persons with SCI, while also suggesting a role of personal characteristics (e.g., age, race, gender) in their diagnosis^{18, 19–21}. Unfortunately, only a minority of adults with SCI see mental health professionals after that period unless they are receiving treatment through a veterans' affairs (VA) facility where it is an integrated component of annual evaluations^{15, 22}. Rather, in most outpatient medical settings, psychological issues are not regularly assessed nor addressed unless the patient verbalizes a relevant problem, or the provider notes physical signs.

While the frequency of psychological problems identified by this and other studies should prompt physicians to integrate monitoring of and screening for psychological sequelae among patients with SCI as a standard part of clinical practice²³, this is unlikely to occur so long as providers do not feel that they have either the qualifications or the resources to address these issues. Given the findings of this study and that of others, physicians need to be able to identify a qualified mental health provider – whether a psychologist, psychiatrist or social worker - to whom they can refer the distressed patient with SCI to for treatment

before they may feel comfortable readily asking about psychological issues. Unfortunately, a myriad of issues limits the availability of psychological support for this high-risk group of patients, including the lack of integration of or insurance coverage for mental health services and limited availability of rehabilitation psychologists and psychiatrists. As long as there is limited availability of these services, chronic centralized pain and psychological morbidity among patients with traumatic SCI is likely to remain unaddressed.

Strengths and Weaknesses

A major strength of this study is the large and longitudinal sample of adults living with traumatic SCI. It can be challenging to gather data on these clinical sub-populations, and little is known about mental health outcomes among individuals with SCI at the population level. Moreover, most large administrative claims databases do not contain some socioeconomic indicators such as net worth, race, and location (division). Herein, we provide incidence estimates and adjusted hazards for psychological morbidity while considering numerous sociodemographic variables from samples representing all states in the US. Lastly, while clinical trials may be considered the “gold standard” in clinical research, cohort studies are less expensive, include broader patient populations, and are more efficient. In fact, there is little evidence to support the superiority of clinical trials over observational studies²⁴.

Our study also has several limitations that should be acknowledged. First, we were unable to determine several basic clinical characteristics of the SCI cohort (e.g., the severity of disability, exact time after injury, type of paralysis) through claims-based data. However, we suspect that our sample may be more reflective of a healthier, higher functioning segment of the traumatic SCI, because they had to be enrolled in private insurance, either by purchasing their own insurance, or by being covered through employment or marriage to someone who had private insurance. Therefore, results and comparisons to adults without SCI are likely conservative estimates, and the true extent of psychological morbidity may be underestimated in this study. Moreover, the accuracy of the psychological diagnoses which are used in these analyses are unclear, especially as clinician bias has been found to result in the over-diagnosis of depression and other psychological conditions among patients with SCI^{3, 18}. In addition, people with SCI may come in contact with the healthcare system more frequently and therefore there may be more opportunities to make diagnoses.

Importantly, administrative claims data may be prone to inaccurate coding of medical diagnoses, such as SCI, as well as chronic diseases, which may affect our incidence estimates. While validation studies have shown that using >1 claim for a medical condition improves the ability to identify beneficiaries with that medical condition^{25, 26}, single claim-based algorithms have been reported to have moderate-to-high positive predictive value (~80%) or specificity (up to 96%)^{25, 27, 28}. However, the accuracy of identifying medical conditions using claims data depends on the number of years for the study period²⁷ and the medical condition examined^{25, 27–29}. Along those lines, our use of a one year lookback period may not be sufficient to capture a true clean period. Finally, we cannot rule out time-varying confounding since baseline measurements of all covariates were included in our final models. Thus, whether having a traumatic SCI “causes” an elevated

risk for earlier-onset psychological morbidity, or if changes in other health parameters (e.g., diabetes, a known predictor of psychological morbidity) themselves, are a cause of poor mental health, is an interesting topic. Thus, we were unable to determine if other competing risks or unmeasured confounding (i.e., other risk factors [e.g., family history of mental health disorders, lack of physical activity, loss of functional independence, etc.]) may have influenced the observed findings. This would lend credence to additional follow-up work to understand the care pathway to success for these patients.

Conclusion

In conclusion, adults with SCI have an elevated risk of developing a variety of psychological morbidities compared to the general adult population of privately insured beneficiaries without SCI, and it appears that centralized and neuropathic pain is a major driver of these outcomes. Individuals with SCI frequently utilize healthcare services as part of their routine clinical care. Therefore, improving clinical screening strategies and developing efficient referral resources for coordinated care may help reduce the burden of mental health disorders in this high need population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Spinal Cord Injury (SCI) Cohort

Control Cohort

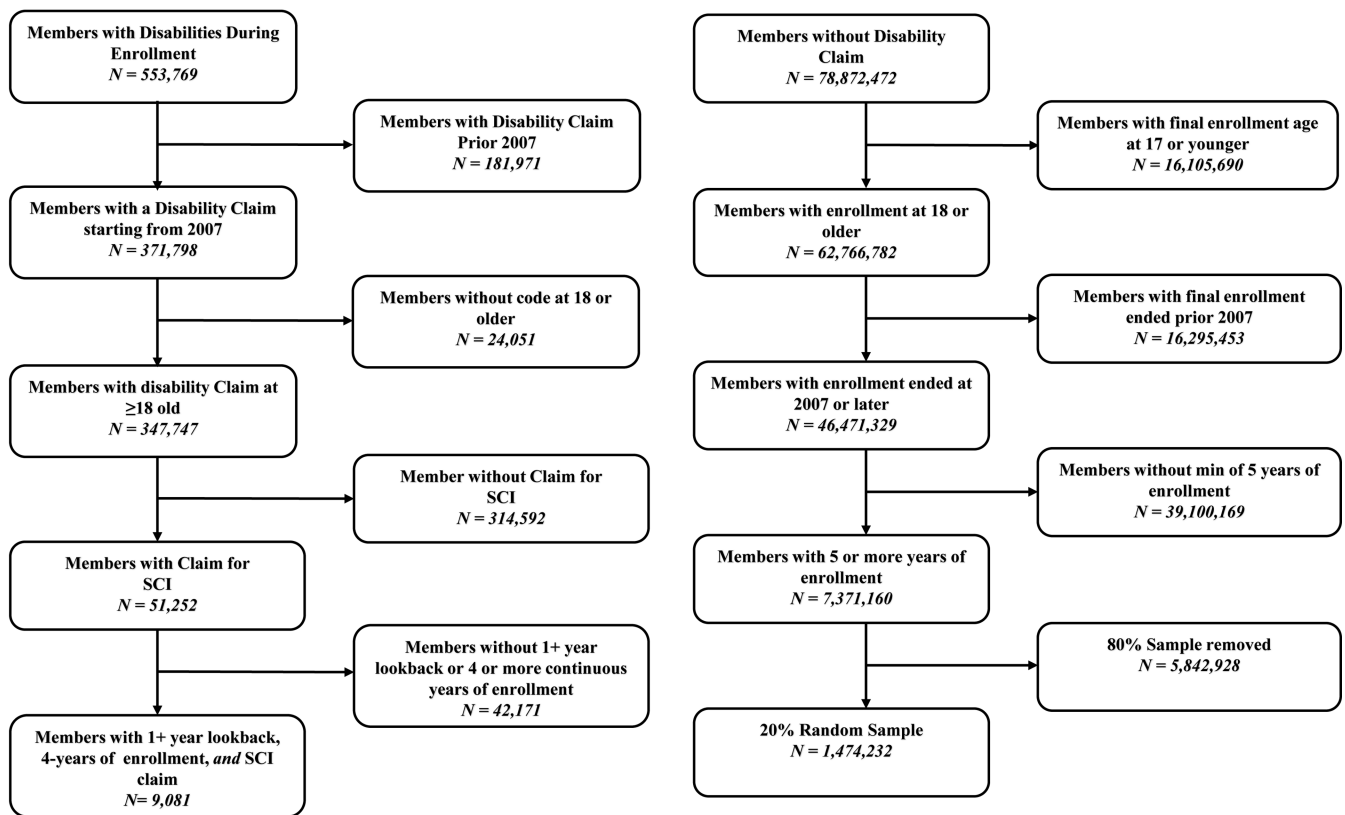


Figure 1. Flow chart of subject inclusion and exclusion for final case and control cohorts.

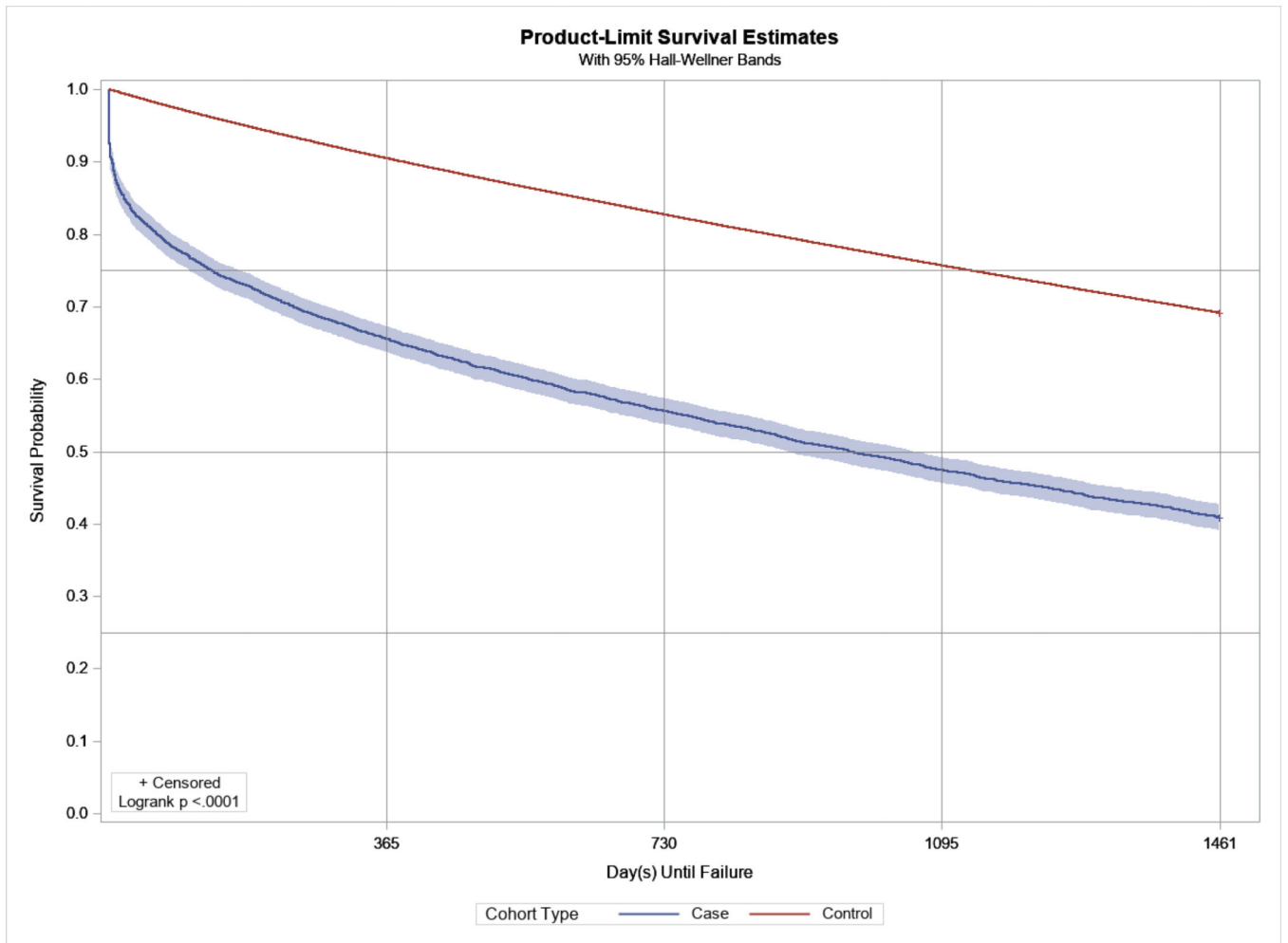


Figure 2. Disease-free survival and Kaplan-Meier product-limit survival curves (3-year) for adults with SCI (blue) and without SCI (red), for *any* psychological morbidity.

Table 1.

Descriptive characteristics among adults with SCI (case) or without SCI (control).

Spinal Cord Injury	Case	Control
Overall	9081 (100%)	1474232 (100%)
Full Enrollment Length		
<i>Mean (SD)</i>	10.8 (3.4)	8.5 (3.2)
<i>Median (Q1-Q3)</i>	10.3 (8.0–13.0)	7.6 (6.0–10.3)
Years Post Eligibility Start Date[†]		
<i>Mean (SD)</i>	6.0 (1.7)	5.3 (1.5)
<i>Median (Q1-Q3)</i>	5.6 (4.7–7.0)	4.7 (4.2–5.8)
Age Group		
<i>18–44</i>	1384 (15.2%)	542106 (36.8%)
<i>45–64</i>	2547 (28.0%)	512676 (34.8%)
<i>65 or Older</i>	5150 (56.7%)	419450 (28.5%)
Gender		
<i>Female</i>	5252 (57.8%)	774282 (52.5%)
<i>Male</i>	3829 (42.2%)	699950 (47.5%)
Race		
<i>Asian</i>	263 (2.9%)	56134 (3.8%)
<i>Black</i>	637 (7.0%)	117545 (8.0%)
<i>Hispanic</i>	718 (7.9%)	129689 (8.8%)
<i>Unknown</i>	1758 (19.4%)	285255 (19.3%)
<i>White</i>	5705 (62.8%)	885609 (60.1%)
Education		
<i><High School Diploma</i>	58 (0.6%)	8418 (0.6%)
<i>High School Diploma</i>	2386 (26.3%)	354512 (24.0%)
<i><Bachelor Degree</i>	4999 (55.0%)	784246 (53.2%)
<i>Bachelor Degree</i>	1451 (16.0%)	284927 (19.3%)
<i>Unknown/Missing</i>	187 (2.1%)	42129 (2.9%)
Net Worth		
<i>Unknown</i>	1554 (17.1%)	250582 (17.0%)
<i><\$25K</i>	1479 (16.3%)	222644 (15.1%)
<i>\$25K–\$149K</i>	1622 (17.9%)	258445 (17.5%)
<i>\$150K–\$249K</i>	886 (9.8%)	151485 (10.3%)
<i>\$250K–\$499K</i>	1376 (15.2%)	245106 (16.6%)
<i>\$500K</i>	2164 (23.8%)	345970 (23.5%)

[†]All adults with SCI have their Index Date set the same as start of eligibility date (start of 2007, year when turned 18, or enrollment start date, whichever was the latest)

Table 2.

Incidence of any and all psychological morbidities among adults with and without SCI with one-year clean enrollment period.

Spinal Cord Injury	[†] <i>No Outcome at Baseline</i>	
	<i>Case/Denominator</i>	<i>Control/Denominator</i>
Insomnia	1292/8532 (15.1%)*	105424/1433868 (7.4%)
Adjustment disorders	654/8836 (7.4%)*	62556/1450761 (4.3%)
Anxiety disorders	2006/7851 (25.6%)*	200415/1382550 (14.5%)
PTSD	147/9031 (1.6%)*	8306/1470937 (0.6%)
Delirium/Dementia/Amnesic/Other Cognitive Disorder	1403/8385 (16.7%)*	49250/1457864 (3.4%)
Dementias	756/8895 (8.5%)*	25981/1468871 (1.8%)
Impulse control disorders	19/9073 (0.2%)	1612/1473687 (0.1%)
Mood disorders	2075/7368 (28.2%)*	171236/1363578 (12.6%)
Personality disorders	83/9048 (0.9%)	4717/1472497 (0.3%)
Alcohol-related disorders	465/8777 (5.3%)*	33513/1463413 (2.3%)
Substance-related disorders	896/8773 (10.2%)*	58915/1464738 (4.0%)

* $P < .01$ and standard mean difference (SMD) 0.2

[†] Denominators for both cases and controls reflect a one-year clean period during their enrollment for the specific condition. For instance, among cases (SCI), there exist 8,532 patients whose first year of enrollment had no evidence of insomnia; therefore, inferred incident insomnia could be estimated for this subset of the full SCI cohort. As a result, all patient cohorts' denominators dynamically change conditional on the incident outcome being measured to ensure a clean period in the first year of enrollment

Table 3.

Survival models with parametric Weibull regression was completed stepwise for each incident psychological outcome to examine the effects of incremental adjustment on the exposure variable (SCD).

Psychological Morbidities	Model 1	Model 2	Model 3	Model 4
Insomnia	2.14 (2.02, 2.26) ***	1.74 (1.64, 1.83) ***	1.42 (1.34, 1.50) ***	1.41 (1.33, 1.49) ***
Adjustment disorders	1.73 (1.60, 1.87) ***	2.04 (1.88, 2.20) ***	1.77 (1.64, 1.92) ***	1.75 (1.62, 1.89) ***
Anxiety disorders	1.84 (1.76, 1.92) ***	1.79 (1.71, 1.88) ***	1.48 (1.41, 1.55) ***	1.47 (1.41, 1.54) ***
PTSD	2.84 (2.41, 3.36) ***	3.42 (2.89, 4.05) ***	2.52 (2.13, 2.98) ***	2.50 (2.11, 2.96) ***
Delirium/Amnesic/Other Cognitive Disorder	5.07 (4.79, 5.37) ***	2.34 (2.21, 2.48) ***	1.96 (1.85, 2.07) ***	1.94 (1.84, 2.05) ***
Dementia	4.86 (4.50, 5.24) ***	1.80 (1.67, 1.94) ***	1.53 (1.42, 1.64) ***	1.52 (1.41, 1.64) ***
Impulse control disorders	1.92 (1.22, 3.02) **	2.29 (1.45, 3.61) ***	1.55 (0.98, 2.46)	1.55 (0.98, 2.44)
Mood Affective Disorders	2.41 (2.31, 2.52) ***	2.12 (2.03, 2.22) ***	1.69 (1.62, 1.77) ***	1.69 (1.61, 1.77) ***
Personality Disorders	2.81 (2.25, 3.50) ***	3.19 (2.55, 3.98) ***	2.05 (1.64, 2.57) ***	2.04 (1.63, 2.55) ***
Alcohol-related disorders	1.74 (1.56, 1.93) ***	1.83 (1.64, 2.03) ***	1.52 (1.36, 1.69) ***	1.51 (1.36, 1.68) ***
Substance-related disorders	2.51 (2.35, 2.69) ***	2.32 (2.17, 2.49) ***	1.68 (1.57, 1.80) ***	1.69 (1.58, 1.81) ***

Model 1: Unadjusted

Model 2: Model 1 + Demographic variables (age, sex, race, geographic region).

Model 3: Model 1 + Model 2 + Modified Elixhauser Comorbidity Index

Model 4: Model 1 + Model 2 + Model 3 + Education + Net Worth

* As with incidence estimates (Table 2), all survival models used cases (SCI) and control cohorts consistent with Table 2, which required a one-year clean period with no evidence of the condition being measured

*** P-value < 0.001