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Individuals with spinal cord injury have greater odds of substance use disorders than non-sci comparisons

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ABSTRACT

Background: Individuals with spinal cord injury (SCI) are disproportionately affected by numerous physical and behavioral health disparities, but the literature lacks a clear understanding of the association between SCI and substance use disorders. Identifying such behavioral health disparities in persons with disabilities is an increasingly central focus for public health researchers and represents a critical first step for prevention.

Method: The present study utilized a large database of deidentified electronic health records to examine the association between SCI and substance use disorders related to alcohol, cannabis, opioid, and nicotine. Examining data from patients 16 years or older who had patient encounters at the Penn State Hershey Medical Center from January 1, 1997 to April 30, 2018, the current study included data from 1,466,985 unique patients – 6192 of which held SCI diagnoses. Age-adjusted odds ratios were calculated using logistic regression.

Results: Compared to non-SCI patients, individuals with SCI were at increased odds of having alcohol use disorder (OR: 4.19, 95% CI [3.67, 4.80]), cannabis use disorder (OR: 7.83, 95% CI [6.32, 9.69]), opioid use disorder (OR: 7.97, 95% CI [6.59, 9.66]), and nicotine use disorder (OR: 4.66, 95% CI [4.40, 4.94]). Patient sex did not moderate any of the four associations.

Conclusion: This study provides early indication that individuals with SCI may be disproportionately at-risk for substance use disorders and provides a foundation for future mechanistic and translational research. This evidence is a valuable step towards improving the health and quality of life for individuals with SCI.

1. Introduction

Acquiring a spinal cord injury (SCI) represents a major life event that is often associated with serious physical and psychosocial health concerns (Craig et al., 2015; Devivo, 2012; Geyh et al., 2012; Post and van Leeuwen, 2012). Individuals with SCI face unique stressors and live with numerous health disparities that negatively impact quality of life (Craig et al., 2009; Noonan et al., 2014; Rivers et al., 2018; Tomasone et al., 2013). As examples of these disparities, researchers have found evidence that, compared to non-SCI individuals, those with SCI are at greater risk for developing depression and anxiety disorders (Graupensperger et al., 2018; Le and Dorstyn, 2016; Williams and Murray, 2015), often experience severe pain (Ataoglu et al., 2013; Craig et al., 2013; Ullrich et al., 2013), and report comparatively low indices of well-being (Hetz et al., 2011; Rivers et al., 2018; Tomasone et al., 2013). Alongside these health concerns, there is also preliminary evidence that substance use may be more prevalent among individuals who have acquired an SCI (Tétrault and Courtois, 2014).

There is an emerging understanding that SCI is linked to patterns of substance use, yet existing research is limited by inconsistent evidence. With regard to these findings on specific substances, alcohol use disorders have been the most widely studied within this population. Several studies have reported greater prevalence of alcohol use disorders in individuals with SCI compared to non-SCI individuals (Heinemann et al., 1989; Kolakowsky-Hayner et al., 2002; Meyers et al., 1988), though other studies have reported contradictory findings (Tate et al., 2004; Young et al., 1995). Although fewer studies have investigated the association between SCI and illicit substance use, cannabis use rates are commonly reported to be higher in individuals with SCI (Heinemann et al., 1991; Hwang et al., 2012; Tate et al., 2004; Young et al., 1995). Several studies have similarly reported that individuals with SCI have greater odds of nicotine and tobacco use (Hwang et al., 2012; Meyers et al., 1988). Lastly, there is emerging evidence that individuals with SCI are more likely to be prescribed higher doses of opioids for longer periods of time and are at greater risk for experiencing adverse drug events from prescription use (Hand et al.,

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2018a, 2018b). Whereas these findings signal that those with SCI may face risks related to substance use, there is not yet evidence of whether those with SCI are at greater risk for developing opioid use disorders. This is a topic that is particularly timely to investigate, considering evidence of spikes in opioid use and related overdose deaths (e.g., Seth et al., 2018). In summarizing the existing literature in this domain, there is early indication that those with SCI may be at-risk for using a range of substances. However, more precise estimates are needed to better understand the scope of these disparities and to guide subsequent translational research efforts.

A salient limitation of the existing evidence base is that it is predominately derived from studies with small samples, which may partially explain the inconsistent findings. Whereas these studies reflect challenges in recruiting large samples when collecting data from clinical populations, larger scale studies are necessary to clarify estimates of prevalence and risk. Identifying the broader patterns of substance use in a large clinical sample is a critical first step towards prevention as it provides foundational knowledge to improve the screening practices of substances that are particularly at-risk. It also entails the potential to advance prevention strategies oriented toward supporting health and well-being during the years following spinal cord injury. Specifically, identifying such risk holds translational value for informing ambulatory care and rehabilitation practices. For example, the knowledge that individuals with SCI are disproportionately affected by health concerns related to physical inactivity led researchers to develop telephone-based counseling services that can effectively help this population increase and sustain leisure time physical activity (Tomasone et al., 2018a).

The purpose of the current study was to query a large database of deidentified patient medical records to identify the prevalence rates of individuals with SCI who have been diagnosed as having substance use disorders related to alcohol, cannabis, opioids, and nicotine. The current study sought to estimate the odds of these substance use disorders to identify whether individuals with SCI are disproportionately at-risk when compared to non-SCI individuals. This exploratory epidemiological research is a necessary step towards substance use prevention for this vulnerable population of individuals with SCI.

2. Method

2.1. Data source

Data were obtained from deidentified electronic health records (EHR) stored within the National Institutes of Health-supported Informatics for Integrating Biology and the Bedside (i2b2) database and query tool (Murphy et al., 2010). Medical records for all individuals who had patient encounters at the Penn State Milton S. Hershey Medical Center[1] beginning in 1997 are included within this database, which is updated monthly and contains data for nearly 1.5 million unique patients. Data are recorded to patients' EHR for every patient encounter at any facility associated with the Hershey Medical Center (i.e. inpatient and outpatient) and are submitted by certified coders based on health care providers' observations, diagnoses, and treatments during the course of care. These diagnoses are coded using the International Classification of Disease (ICD) procedural and diagnostic codes (versions 9 and 10) that are provided as unique patient 'counts'. ICD codes are particularly useful because they are standardized and are coded immediately following patient encounters. Patient counts are searchable through the i2b2 database using a 'query' designated by the researcher, and a patient is counted once if he/she meets the criteria specified by the query.

[1] The Hershey Medical Center (located in Hershey, Pennsylvania), is a 548-bed hospital that averages over one-million outpatient visits and nearly 75,000 emergency visits per year.

For the sake of the current study, we extracted EHR data pertaining to patient diagnoses (identified using ICD codes) for all individuals over the age of 16 that had patient encounters from January 1, 1997, to April 30, 2018. A full description of each ICD code used to identify individuals as being diagnosed with SCI and/or a substance use disorders is available in the online supplement. Codes 344 ('other paralytic syndromes') and G82 ('paraplegia or quadriplegia') were excluded from search queries, as these conditions may not be directly associated with SCI (e.g., cerebral palsy), and may lead to overestimation (Hagen et al., 2009). Regarding diagnoses of substance use disorders, the ICD nomenclature classifies disorders as either 'dependence' or 'abuse' for a wide range of specific substances, and have been extensively validated (Hasin et al., 2006). Criteria for dependence entails at least three of the following criteria co-occurring within a 12-month period: Tolerance, withdrawal, continued use despite problems, impaired control, neglect of activities, and spending a great deal of time in substance-related activity (Hasin et al., 2006). The ICD nomenclature treats dependence and abuse hierarchically in that only individuals without dependence are diagnosed with abuse. The criteria for substance abuse to be considered a diagnosable disorder is that (a) patient demonstrates clear evidence that the substance use contributed physical or psychological harm, (b) the harm caused by substance use was clearly identifiable and specifiable, (c) that pattern of harmful use has persisted for at least one month or has occurred repeatedly in a 12-month period, and (d) symptoms do not meet criteria for any other mental or behavioral disorder related to substance in the same time period (with the exception of 'acute intoxication'; Hasin et al., 2006). It is important to note that the diagnosis of Z72.0 ('Tobacco use not otherwise specified') was treated as a disorder for the sake of the current study. This decision was made because there is no code for tobacco 'abuse' but Z72.0 includes harmful use of tobacco and is otherwise a valid indicator of tobacco.

The comparison samples were drawn from the same database and were age- and sex-matched patients who had *not* been diagnosed with SCI using the relevant ICD codes. Given that the data were deidentified, the Institutional Review Board at the Pennsylvania State University considered this research to be exempt.

2.2. Analytical procedures

To test whether individuals with SCI are disproportionately affected by substance use disorders, separate logistic regressions were computed to determine odds ratios (OR) for the associations between having SCI and having diagnoses pertaining to (a) alcohol use disorders, (b) cannabis use disorders, (c) opioid use disorders, and (d) nicotine use disorders – compared to a non-SCI comparison sample. To account for known confounders, we stratified samples by sex, given that men are more likely than women to acquire SCI (Singh et al., 2014), and are more likely to develop alcohol (Hughes et al., 2016), cannabis (Kerridge et al., 2018), opioid (Kerridge, 2016), and nicotine disorders (Evans-Polce et al., 2015). Analyses were also adjusted by age, to account for that fact that people acquire SCI as they age and because people of different ages have varying profiles of substance use. The strength of associations were determined using ORs with corresponding 95% confidence intervals (CI). Sex-stratified ORs were also contrasted to determine whether sex moderated any associations. As suggested by Chen et al. (2010), we presently interpret ORs as indices of effect size that are considered small ($d = .2$; $OR = 1.5$), moderate ($d = .5$; $OR = 2.7$) and large ($d = .8$; $OR = 4.6$).

3. Results

3.1. Demographics

In total, the current study included data from 1,466,985 unique patients ages 16 years or older. Of these, 6192 had diagnoses related to

Table 1
Sample prevalence of disorders related to alcohol, cannabis, opioid, and nicotine use - stratified by age and sex.

Age/Sex	Total *N*		Alcohol		Cannabis		Opioid		Nicotine	
	SCI	non-SCI	SCI	non-SCI	SCI	non-SCI	SCI	non-SCI	SCI	Non-SCI
All (16+)	6192	**1,460,793**	**227 (3.7%)**	**12,571 (0.8%)**	**89 (1.4%)**	2926 **(0.2%)**	**111 (1.7%)**	3435 **(0.2%)**	1690 **(27.3%)**	**103,559 (7.1%)**
M	3,368	678,994	176 (5.2%)	8859 (1.3%)	67 (2.0%)	1900 (0.2%)	66 (2.0%)	1821 (0.3%)	1059 (31.4%)	57,844 (8.5%)
F	2,824	781,799	51 (1.8%)	3712 (0.5%)	22 (0.8%)	1026 (0.1%)	45 (1.6%)	1614 (0.2%)	631 (22.3%)	45,715 (5.8%)
16-30	**1,014**	**333,312**	**17 (1.7%)**	1599 **(0.5%)**	**16 (1.6%)**	**894 (0.3%)**	**15 (1.4%)**	**812 (0.2%)**	**90 (8.9%)**	8004 **(2.4%)**
M	519	163,912	14 (2.7%)	976 (0.6%)	13 (2.5%)	556 (0.3%)	9 (1.7%)	420 (0.3%)	52 (10.0%)	4022 (2.5%)
F	495	169,400	3 (0.6%)	623 (0.4%)	3 (0.6%)	338 (0.2%)	6 (1.2%)	392 (0.2%)	38 (7.7 %)	3982 (2.4%)
31-45	**980**	**272,851**	**57 (5.8%)**	3359 **(1.2%)**	**27 (2.8%)**	1047 **(0.4%)**	**24 (2.4%)**	1179 **(0.4%)**	**271 (27.7%)**	**18,423 (6.8%)**
M	533	117,778	46 (8.6%)	2290(1.9%)	21 (3.9%)	669 (0.6%)	17 (3.2%)	619 (0.5%)	169 (31.750	8,817 (7.5%)
F	447	155,073	11 (2.5%)	1069 (0.6%)	6 (1.3%)	378 (0.2%)	7 (1.6%)	560 (0.4%)	102 (22.8%)	9606 (6.2%)
46-60	**1,572**	**314,617**	**84 (5.3%)**	4022 **(1.3%)**	**30 (1.9%)**	**715 (0.2%)**	**34 (2.2%)**	**919 (0.3%)**	**538 (34.2%)**	**27,506 (8.7%)**
M	857	142,069	63 (7.4%)	2831 (2.0%)	20 (2.3%)	472 (0.3%)	18 (2.1%)	496 (0.3%)	310 (36.1%)	14,209 (10.0%)
F	715	172,548	21 (0.3%)	1191 (0.7%)	10 (1.3%)	243 (0.1%)	16 (2.2%)	423 (0.2%)	228 (31.9%)	13,297 (7.7%)
61-75	**1,618**	**282,353**	**53 (3.2%)**	2704 **(1.0%)**	**16 (1.0%)**	**254 (0.1%)**	**35 (2.1%)**	**452 (0.2%)**	**492 (30.4%)**	**28,415 (10.1%)**
M	919	136,014	39 (4.2%)	2069 (1.5%)	13 (1.4%)	189 (0.1%)	20 (2.1%)	253 (0.2%)	331 (24.3%)	17,267 (12.7%)
F	699	146,339	14 (2.0%)	635 (0.4%)	3 (0.4%)	65 (0.04%)	15 (2.1%)	199 (0.1%)	161 (23.0%)	11,148 (7.6%)
75+	**1,008**	**257,660**	**16 (1.5%)**	**887 (0.3%)**	**0 (0%)**	**16 (< 0.1%)**	**3 (0.3%)**	**73 (< 0.1%)**	**299 (29.7%)**	**21,211 (8.2%)**
M	540	119,221	14 (2.6%)	693 (0.6%)	0 (0%)	14 (< 0.1%)	2 (0.4%)	33 (< 0.1%)	197 (36.5%)	13,529 (11.3%)
F	468	138,439	2 (0.4%)	194 (0.1%)	0 (0%)	2 (< 0.1%)	1 (0.2%)	40 (< 0.1%)	102 (21.8%)	7682 (5.5%)

Note: SCI = Spinal Cord Injury. M = Male, F = Female.

SCI (prevalence of 0.4%). Prevalence rates for substance use disorders, stratified by age and sex, are listed in Table 1. Age was stratified into 15 year increments to align with the standardized age classifications maintained by the International Spinal Cord Injury Core Data Set (Biering-Sørensen et al., 2017). From a descriptive perspective, the prevalence of all four currently investigated categories of substance use disorders were higher in individuals with SCI than non-SCI and were higher in men than in women. It should be noted that, although the demographic details presented in Table 1 are stratified by age, we adjusted for age within the logistic regression models to account for the potential confounding effect of age (as opposed to conducting separate regressions by age).

3.2. Odds of substance use disorders among individuals with SCI

The results of the logistic regression models, which describe the strength of association between SCI and substance use disorders, are presented in Table 2. Compared to non-SCI patients, individuals with SCI were at increased odds of having alcohol use disorder (OR: 4.19, 95% CI [3.67, 4.80]), cannabis use disorder (OR: 7.83, 95% CI [6.32, 9.69]), opioid use disorder (OR: 7.97, 95% CI [6.59, 9.66]), and nicotine use disorder (OR: 4.66, 95% CI [4.40, 4.94]). All associations were statistically significant (i.e., confidence intervals do not include the null value of 1), with effect sizes ranging from moderate to large. Tests for moderation revealed that no significant differences were found between men and women, as shown by overlapping 95% confidence intervals in all cases.

4. Discussion

Despite emerging research indicating patterns of substance use among those with SCI, there are nevertheless few studies on these associations and existing evidence is largely clouded by inconsistent findings. We targeted this knowledge gap by utilizing a large database of deidentified EHRs to investigate the association between SCI and substance use disorders related to alcohol, cannabis, opioid, and nicotine use. Stating the core findings of this research, we found evidence that SCI is moderately associated with alcohol and nicotine use disorders, and strongly associated with cannabis and opioid use disorders. Individuals with SCI had increased odds of being diagnosed with a substance use disorder.

Identifying and mitigating behavioral health disparities in persons with disabilities is an increasingly central focus for public health researchers (Krahn et al., 2015). The current study answers the call for research that is able to inform programs, policies, and practices that promote the health of people with disabilities made within the *Healthy People 2020* initiative (Bundara Sinclair et al., 2018). The knowledge that individuals with SCI are at increased odds for having substance use disorders holds implications for rehabilitation and ambulatory care. Given this increased risk, it is critical that health care providers screen and closely monitor patients with SCI to identify substance use behaviors. This increased rate of substance use disorders demonstrates the need to implement policies and programs aimed at preventing substance use in patients with SCI. Such preemptive strategies could be implemented during the course of standard early-stage rehabilitation settings (e.g., inpatient physical rehabilitation). Researchers have previously demonstrated that psychosocial health outcomes can be effectively targeted as secondary effects of behavioral interventions designed for physical rehabilitation (Nooijen et al., 2017). Beyond immediate rehabilitation, patients' family and caregivers are sources of support that may play a key role in the prevention of substance use disorders. For example, researchers have designed a family and caregiver-based intervention to target coping skills and emotion regulation in individuals with SCI (Dyck et al., 2016). There is also an emerging

Table 2
Logistic regressions to assess the association between spinal cord injury and disorders related to alcohol, cannabis, opioids, and nicotine.

	Alcohol	Cannabis	Opioids	Nicotine
All SCI	**4.19 [3.67, 4.80]**	**7.83 [6.32, 9.69]**	**7.97 [6.59, 9.66]**	**4.66 [4.40, 4.94]**
Male	3.86 [3.32, 4.51]	7.65 [5.97, 9.79]	7.50 [5.85, 9.62]	4.59 [4.26, 4.95]
Female	3.83 [2.90, 5.07]	6.52 [4.27, 9.98]	8.16 [6.05, 11.01]	4.49 [4.11, 4.92]

Note: Regressions are age-adjusted and odds ratios are contrasted with non-SCI comparison sample. SCI = spinal cord injury. Brackets contain 95% confidence intervals.

body of evidence showing that patients with SCI can be targeted through telephone interventions including empowerment (Houlihan et al., 2016) and physical activity (Tomasone et al., 2018b), which represent a promising avenue for continued long-term substance abuse prevention. Although the current findings are a necessary first step towards prevention, additional work further along the translational spectrum is needed to better understand these associations and how we can reduce these behavioral health disparities (Fishbein et al., 2016).

Alongside the direct public health implications, the large effect sizes found for these associations provide a foundation for future research that is essential to identify *mechanisms* of these associations and to identify which individuals with SCI are more (or less) at risk of developing substance use disorders. Identifying potential mediators and moderators on this association would provide valuable information for prevention efforts within treatment and rehabilitation. When explaining substance use patterns, investigators anticipate that increased substance use may result from processes such as: (a) increases in depression and/or anxiety (Shamji et al., 2016), (b) initial access and use of substances during care, prompting addiction (e.g., pain medication misuse; Krause et al., 2015) (c) dysfunctional coping (Smedema and Ebener, 2010), and (d) sensation seeking or attempt to 'escape' reality (Saunders and Krause, 2011). Findings also vary in relation to the nature of the injury: Whereas those who acquire an SCI are at increased risk for using of harmful substances (Radnitz and Tirch, 1995), contradicting results indicate that those with pediatric-onset SCI are less likely to use substances compared to age-matched non-SCI comparisons (Hwang et al., 2012). Ultimately, identifying third variables will enhance our understanding of the association between SCI and substance use, and is valuable future direction for researchers in this domain.

Considering third variables also raises a critical point pertaining to the timing of diagnoses. Although the majority of studies have focused on substance use disorders that develop following SCI, there is also evidence that substance use patterns may increase risk of acquiring a SCI (Tate et al., 2004). Notably, researchers have found that many SCIs are acquired from accidents during which the individual was intoxicated by alcohol, illicit substances, or even a mixture the two (e.g., McKinley et al., 1999). This may indicate that some SCI patients have substance use issues even prior to injury. Researchers would be wise to track these lifestyle behaviors over time, beginning with injury onset, to identify critical periods for substance use. This point, however, is likely to differ across substances. For example, it is expected that opioid use may be particularly linked to the post-injury phase resulting from prescription pain medications, while alcohol use disorder may play a more salient role in injury acquisition (e.g., impaired driving). Regardless of temporality, the current findings indicate that there is a troubling link between SCI and substance use. The current results support a call to better understand screening and care for substance use *throughout* the SCI care process and to identify best practices for those who already have substance use disorders prior to injury, in contrast to the needs of those who may be at risk for developing substance use disorders following SCI.

4.1. Limitations

Although the i2b2 database is readily accessed to investigate associations between health conditions that would be difficult to collect prospectively, this data source also holds several limitations. Despite being a large database (i.e., nearly 1.5 million patients), the generalizability is limited given that all patients were treated within the same hospital system. Furthermore, although the database entails standardized diagnoses of substance use disorders by licensed clinicians (as opposed to self-report) the ICD codes do not capture some details of diagnoses. Regarding SCI, ICD codes do not provide indices of injury severity, etiology (i.e., traumatic or non-traumatic), or time since injury. This limitation precluded us from controlling for these factors or from examining how long after injury individuals with SCI are most at-risk of developing a substance use disorder. As a related point, the current analyses could not distinguish whether individuals' substance use disorder was diagnosed before or after the spinal cord injury diagnosis.

The use of ICD codes is also critical to how substance use findings are interpreted. The results herein captured *disordered* use and *abuse* of substances that met a threshold for diagnosis but does not entail broader patterns of substance use that may nevertheless impact health. Some of the substance use disorders had very low prevalence in our sample (e.g., marijuana: 0.2% of non-SCI participants), which demonstrates that the findings primarily represent patients that have reached a problematic level of use. Lastly, we speculate that those with SCI may have more patient encounters in a given year than most non-SCI individuals, which may provide greater opportunity for health care providers to recognize and identify substance use disorders.

A final point of consideration pertains to the use of big data sources such as electronic medical records. Big data sources possess great potential for discovery, especially considering ongoing advances in coding tools, technology, and data sharing (Jensen et al., 2012). Nevertheless, a note of caution is required when evaluating electronic medical records. The data contained within these sources should not be relied upon as a sole source for characterizing population prevalence, because broader epidemiological studies may necessitate unique operational definitions of health conditions, including criteria for substance use disorders (Khoury and Ioannidis, 2014). The exploratory and descriptive nature of this research means that these records represent an opportunity for early-stage hypothesis-generating explorative research using descriptive clinical diagnoses. Findings from these data sources should then be used to warrant and inform deeper and more intensive investigations.

4.2. Conclusion

The current research provides evidence for a relatively strong association between SCI and substance use disorders related to alcohol, cannabis, opioid, and nicotine. This early indication that individuals with SCI are disproportionately at-risk for substance use disorders provides a foundation for prevention scientists to further investigate why this disparity may exist and highlights the need for long-term rehabilitation efforts to develop strategies that protect this vulnerable population. Replication is needed to examine the extent that this association generalizes. Nevertheless, the findings are a valuable step towards prevention and towards ultimately improving the health and quality of life for individuals with SCI.

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Contributors

All authors have made significant contributions to all stages of the current research. They have each approved of the submitted manuscript in its present form.

Declaration of Competing Interest

The authors have no conflict of interest, including specific financial interests and relationships and affiliations relevant to the subject of this manuscript.

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Appendix A. Supplementary data

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