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ARTICLE

Prescription medications dispensed following a nontraumatic spinal cord dysfunction: a retrospective population-based study in Ontario, Canada

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Abstract

Study design Retrospective cohort study.

Objectives To examine the prevalence of polypharmacy for individuals with nontraumatic spinal cord dysfunction (NTSCD) following inpatient rehabilitation and to determine associated risk factors.

Setting Ontario, Canada.

Methods Administrative data housed at ICES, Toronto, Ontario were used. Between 2004 and 2015, we investigated prescription medications dispensed over a 1-year period for persons following an NTSCD-related inpatient rehabilitation admission. Descriptive and analytical statistics were conducted. Using a robust Poisson multivariable regression model, relative risks related to polypharmacy (ten or more drug classes) were calculated. Main independent variables were sex, age, income quintile, and continuity of care with outpatient physician visits.

Results We identified 3468 persons with NTSCD during the observation window. The mean number of drug classes taken post-inpatient rehabilitation was 11.7 (SD = 6.0), with 4.0 different prescribers (SD = 2.5) and 1.8 unique pharmacies (SD = 1.0). Significant predictors for post-discharge polypharmacy were: being female, lower income, higher comorbidities prior to admission, lower Functional Independence Measure at discharge, previous number of medication classes dispensed in year prior to admission, and lower continuity of care with outpatient physician visits. The most common drugs dispensed post-inpatient rehabilitation were antihypertensives (70.0%), laxatives (61.6%), opioids (59.5%), and antibiotics (57.8%).

Conclusion Similar to previous research with traumatic spinal cord injury, our results indicate that polypharmacy is prevalent among persons with NTSCD. Additional research examining medication therapy management for NTSCD is suggested.

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Introduction

Spinal cord injury/dysfunction is often a devastating lifelong condition that results in significant impairments, morbidity, and lower life expectancies [1]. Most individuals with spinal cord damage experience episodic secondary health complications (e.g., urinary tract infections, spasticity, constipation, respiratory infections) and multiple chronic conditions (e.g., chronic pain, diabetes, heart disease, fatigue, osteoporosis, depression) [2, 3]. Pharmacotherapy is often provided for these complications and multimorbidity rendering persons with spinal cord injury/dysfunction at risk for polypharmacy [4].

In the general population, polypharmacy (e.g., often defined as five or more drugs) can sometimes be problematic because it may increase the risk of drug therapy problems, potentially inappropriate prescribing, challenges with adherence, and negative health outcomes [5]. Although limited and mostly focused on traumatic spinal cord injury (TSCI), previous studies have identified a high prevalence of polypharmacy among persons with spinal cord injury/dysfunction [4]. For example, a large cohort by Kitzman and colleagues used administrative health data in the United States to examine the prevalence of polypharmacy and drug therapy problems in 4800 hospitals over three years among patients with and without injury/dysfunction [6]. Slightly more than half of the cohort (56%; $n = 7399$ of a total 13,160) was on ≥5 concomitant prescription medications. Moreover, 23% of the cohort was on ≥10 prescription medications as compared with 7% for the age- and sex-matched control group. Polypharmacy was identified as an important factor contributing to drug-related problems, as persons with injury/dysfunction who were taking five or more medications were 3.7 times more likely to have a drug-related problem compared with comparison control group. While Kitzman and colleagues used population-based data with large, generalizable sample size, the analysis was not stratified by type of injury/dysfunction (i.e., nontraumatic, traumatic), and did not examine the factors associated with polypharmacy.

A recent scoping review conducted by Cadel and colleagues identified possible negative clinical outcomes associated with polypharmacy, such as drug therapy problems (e.g., intoxication by negative drug interactions), and bowel complications (e.g., diarrhea, constipation) [4]. Factors related to polypharmacy included older age, higher level of injury, and greater severity of injury. Cadel and colleagues concluded more research is needed in this area; particularly with nontraumatic spinal cord dysfunction (NTSCD), with minimal studies specifying the mechanism of injury or examining polypharmacy by injury [4]. Given the age-related etiologies associated with NTSCD such as cancer and degeneration of the spinal column [7], it is important to further investigate the prevalence of polypharmacy within this group. To address this gap, the current study aimed to describe the prevalence of polypharmacy among persons with NTSCD using administrative health data and examine factors that impact the likelihood of polypharmacy in this population.

Methods

Using administrative health data housed at ICES, Toronto, Ontario (www.ices.on.ca), we conducted a retrospective cohort study. ICES is a nonprofit research institute funded by the Ontario Ministry of Health and Long-Term Care. As a prescribed entity under privacy legislation in Ontario, ICES is authorized to collect and use healthcare data for the purposes of health system evaluation and improvement. The datasets contain records of all publicly funded healthcare encounters within the province of Ontario, Canada. As Canada's most populous province, Ontario represents ~40% of the Canadian population with over 14 million residents. Ontario has a universal health system under the Canada Health Act that funds all medically necessary care by physicians, hospitals, inpatient rehabilitation, and some other beneficiary care. A comprehensive list of drugs is publicly funded through the Ontario Drug Benefit (ODB) program for individuals of 65 years and older and individuals <65 years who receive financial social assistance or have catastrophic drug costs.

These datasets were linked using encoded identifiers and analyzed at ICES. The National Rehabilitation Reporting System (NRS) provided information individuals who received inpatient rehabilitation care (e.g., admission and discharge dates, transfer information, and diagnostic codes). The Discharge Abstract Database (DAD) provided hospital admission and discharge information (e.g., dates, transfer information, the most responsible diagnosis and up to 24 secondary diagnostic codes [based on International Classification of Disease, Tenth Revision Canada, ICD-10-CA codes]). The National Ambulatory Care Reporting System (NACRS) provided information related to emergency department visits, and same day surgeries (e.g., diagnostic codes). The Ontario Health Insurance Plan (OHIP) database provided information on outpatient physician visits (e.g., physician specialty, service date and location, and diagnostic codes). The ODB database provided records of drugs dispensed in community pharmacies. In Canada, every drug product has a different identifier (drug identification number). The Ontario Registered Persons database provided basic demographic information (e.g., sex, age, date of birth, residential postal code), and vital statistics information (e.g., death date).

Study population

Individuals who were admitted to inpatient rehabilitation with a NTSCD between April 1, 2004 and March 31, 2015 were included. Individuals were excluded if they died before the end of their index episode of care, if they were not living in the community for at least 275 days in the year after their index episode of care [8], or if they were not ODB eligible in the year after their index episode of care (Fig. 1). These last two exclusions were done to ensure that adequate data were available in the ODB database.

Study variables

Main outcome: polypharmacy

Our primary outcome was the prevalence of polypharmacy within the NTSCD population during a 1-year period after their index episode of care. An episode of care began with the initial inpatient rehabilitation stay and continued through transfer (if any) to another inpatient rehabilitation, complex continuing care, long-term care, or home. Individuals could be at home for up to 14 days between periods of inpatient stays and still be considered to be in the same episode of care, to account for temporary discharges home (e.g., waiting for a bed in rehabilitation or complex care). Episodes of care ended when more than 14 days elapsed without institutional care.

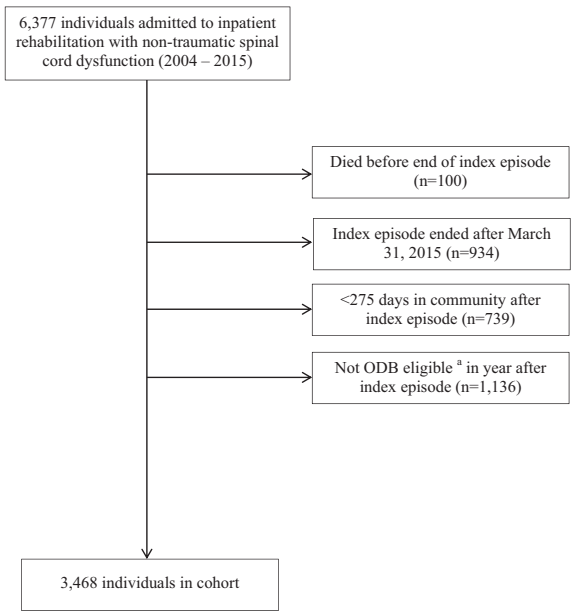

Fig. 1 Flow chart of individuals admitted to an inpatient rehabilitation hospital with nontraumatic spinal cord dysfunction between 2004 and 2015 in Ontario, Canada. [a]Not ODB eligible refers to not receiving publicly-funded drugs through the Ontario Drugs Benefit program in the year following index episode.

The observation window for drug claims began after the episode of care and lasted for a 1-year period. We chose to begin follow-up for polypharmacy after the index episode of care due to the high readmission rates with this population [9, 10] and the inability for the administrative databases to capture drugs dispensed while in hospital. Based on our previous work with TSCI, polypharmacy was defined using a threshold of ten or more drug classes [11]. We used cumulative polypharmacy, which is an established approach for pharmacoepidemiology research [12]. All unique drug classes received were summed over the observation period. Drug classes were defined as drugs with similar therapeutic or pharmacologic use, using the third level of the World Health Organization's Anatomical Therapeutic Chemical drug classification (ATC) system [13].

Independent variables of interest

Our main independent variables were sex, age, continuity of care, and income quintile. Based on Cadel and colleagues review [4], we also included the following variables in the model: morbidity, functional status, length of stay in rehabilitation, and the number of drug classes dispensed in the year prior to inpatient rehabilitation admission.

Continuity of care was defined as the proportion of physician visits (office, home, phone) to the provider frequented most often in the post-discharge observation year divided by all physician visits [14]. High continuity was defined as at least 75% of visits with the same physician and low continuity was defined as <50% of visits made to the same physician. Continuity of care was not calculated if an individual had fewer than three visits in the observation period.

We used postal code and census information to determine neighborhood income quintile for each individual. We also used established methods to calculate prevalence of the following chronic diseases prior to inpatient rehabilitation admission: asthma, congestive heart failure, chronic obstructive pulmonary disease, hypertension, diabetes, rheumatoid arthritis, and dementia [15–22]. ICES databases were used for determination of chronic diseases, mostly using the DAD, NACRS, OHIP, and ODB [15–22]. Morbidity burden was determined using the Johns Hopkins ACG® System Ver. 10. For the 2 years prior to the inpatient rehabilitation admission, the number of Aggregated Diagnosis Groups (ADGs) from hospitalization, emergency department, and physician office visits were calculated. A higher number of ADGs indicated greater morbidity [23]. Functional status was determined at discharge by the Functional Independence Measure (FIM), with higher scores indicating more independence [24].

Statistical analysis

We used means (standard deviations), medians (interquartile ranges), and proportions to describe demographic and clinical characteristics. Differences between groups were tested using chi squared tests for categorical characteristics, *t*-tests for means, Wilcoxon–Mann–Whitney tests for medians, and the Cochran–Armitage test for ordinal characteristics. We used the exact McNemar's test for differences in drugs dispensed before and after inpatient rehabilitation. A test was considered statistically significant at an alpha level of 0.05. Factors were examined independently in univariate Poisson regression models with polypharmacy (10+ different drug classes dispensed) as a binary outcome. Statistically significant factors were included in the final Poisson multivariable regression model with robust standard errors [25]. Relative risks (RRs) and 95% confidence limits were calculated. SAS version 9.4 (SAS Institute Inc., Cary, NC, USA; www.sas.com) was used to analyze the data.

Results

Overall, there were 3468 individuals who had an admission to inpatient rehabilitation for NTSCD between April 1, 2004 and March 31, 2015 (Fig. 1) and who met our inclusion/exclusion criteria. The median age (interquartile range) at admission was 70 (62–77), with almost even sex distribution (49.7% female; Table 1). The median length of stay for inpatient rehabilitation was 30 days (IQR = 16–52), and the mean FIM score at discharge was 106.2 (standard deviation [SD] = 16.1). The majority of persons resided in an urban setting (92.6%). Healthcare utilization in the year prior to inpatient rehabilitation was relatively high, with an average of 7.7 (SD = 7.1) specialist visits, 9.6 (SD = 8.5) family physician visits, and 12.4 (SD = 39.0) home care visits. The mean number of preadmission ADGs was 10.1 (SD = 4.0), with 20.3% of persons having high comorbidity. The majority of persons had a previous diagnosis of arthritis (79.8%), while 68.9% had hypertension, 30.6% had diabetes, 27.2% had coronary syndrome, 24.5% had cancer, and 23.1% had mood/anxiety disorders (see Table 1).

Post-injury healthcare utilization and prescription drugs dispensed

The mean number of drug classes taken following inpatient rehabilitation was 11.7 (SD = 6; median 11 (IQR = 7–16); see Table 2), with 62.7% on ten or more unique drug classes and 89% on five or more. There was an average of 4.0 different prescribers (SD = 2.5) and 1.8 unique pharmacies (SD = 1.0) used over the observation window. Continuity

Table 1 Characteristics of individuals with an inpatient rehabilitation admission for nontraumatic spinal cord dysfunction between 2004 and 2015, in Ontario, Canada.

	Overall cohort $n = 3468$	<66 Years of age $n = 1159$	≥66 Years of age $n = 2309$
Demographics			
Female, *n* (%)	1722 (49.7)	531 (45.8)	1191 (51.6)[a]
Age, median (IQR)	70 (62–77)	55 (44–62)	75 (70–80)[a]
Urban residence, *n* (%)	3210 (92.6)	1059 (91.4)	2151 (93.2)[a]
Income quintile, *n* (%)[a,b]			
1 (low)	807 (23.3)	348 (30.0)	459 (19.9)
2	664 (19.1)	226 (19.5)	438 (19.0)
3	667 (19.2)	233 (20.1)	434 (18.8)
4	678 (19.6)	193 (16.7)	485 (21.0)
5 (high)	635 (18.3)	150 (12.9)	485 (21.0)
Healthcare services utilization prior to admission			
Visits, mean ± SD			
Acute hospitalizations	0.4 ± 0.8	0.4 ± 0.9	0.4 ± 0.7
Emergency department	1.6 ± 2.2	2.1 ± 2.9	1.4 ± 1.8[a]
Family physician	9.6 ± 8.5	9.6 ± 11.0	9.6 ± 6.9
Home care	12.4 ± 39.0	12.7 ± 42.8	12.2 ± 36.9
Specialist	7.7 ± 7.1	6.7 ± 7.5	8.1 ± 6.9[a]
Continuity of care, *n* (%)[a,c]			
Low	1609 (46.4)	514 (44.3)	1095 (47.4)
Medium	1262 (36.4)	396 (34.2)	866 (37.5)
High	508 (14.6)	186 (16.0)	322 (13.9)
Length of stay (in days) for index admission, median (IQR)	30 (16–52)	36 (20–61)	29 (15–47)[a]
Preexisting comorbidities, *n* (%)			
Acute myocardial infarction (AMI)	6 (0.2)	≤5[d]	≤5[d]
Asthma	602 (17.4)	226 (19.5)	376 (16.3)[a]
Cancer	835 (24.1)	220 (19.0)	615 (26.6)[a]
Cardiac arrythmia	389 (11.2)	42 (3.6)	347 (15.0)[a]
Chronic heart failure	298 (8.6)	39 (3.4)	259 (11.2)[a]
Chronic obstructive pulmonary disease (COPD)	360 (10.4)	80 (6.9)	280 (12.1)[a]
Coronary syndrome (excluding AMI)	944 (27.2)	129 (11.1)	815 (35.3)[a]
Dementia	95 (2.7)	13 (1.1)	82 (3.6)[a]
Diabetes	1060 (30.6)	267 (23.0)	793 (34.3)[a]
Hypertension	2390 (68.9)	519 (44.8)	1871 (81.0)[a]
Mood disorders	802 (23.1)	341 (29.4)	461 (20.0)[a]
Other mental illnesses	279 (8.0)	177 (15.3)	102 (4.4)[a]

Table 1 (continued)

	Overall cohort $n = 3468$	<66 Years of age $n = 1159$	≥66 Years of age $n = 2309$
Osteoarthritis	2766 (79.8)	775 (66.9)	1991 (86.2)[a]
Osteoporosis	365 (10.5)	63 (5.4)	302 (13.1)[a]
Rheumatoid arthritis	170 (4.9)	39 (3.4)	131 (5.7)[a]
Renal failure	256 (7.4)	64 (5.5)	192 (8.3)[a]
Stroke	223 (6.4)	44 (3.8)	179 (7.8)[a]
Healthcare characteristics			
ADG quintile, *n* (%)[a,e]			
1 (low)	639 (18.4)	282 (24.3)	357 (15.5)
2	867 (25.0)	298 (25.7)	569 (24.6)
3	684 (19.7)	212 (18.3)	472 (20.4)
4	573 (16.5)	168 (14.5)	405 (17.5)
5 (high)	705 (20.3)	199 (17.2)	506 (21.9)
ADG score, median (IQR)[e]	10 (8–13)	9 (7–12)	11 (8–13)[a]
Functional Independence Measure (FIM), mean ± SD			
At admission	80.0 ± 16.8	80.6 ± 17.9	79.8 ± 16.1
At discharge	106.2 ± 16.1	106.4 ± 17.8	106.1 ± 15.1

AMI acute myocardial infarction, *COPD* chronic obstructive pulmonary disease, *ADG* Aggregated Diagnosis Groups, *IQR* interquartile range, *FIM* Functional Independence Measure, *SD* standard deviation.

[a]Significant difference based on an alpha level of 0.05. Differences between groups were tested using chi squared tests for categorical characteristics, *t*-tests for means, Wilcoxon–Mann–Whitney tests for medians, and the Cochran–Armitage test for ordinal characteristics.

[b]Values do not add up due to missing values.

[c]Continuity of care $= \frac{\text{All physician office visits to usual source of care } (n)}{\text{All physician office visits } (n)}$.

[d]Cell sizes <6 are suppressed for privacy.

[e]ADG refers to Aggregated Diagnosis Groups from the Johns Hopkins ACG® System. This system classifies health conditions in administrative health data over 2 years. Larger numbers of ADGs reflect higher comorbidity levels.

of care was relatively low as 47.8% of the cohort had <50% of their outpatient visits with the same physician after inpatient rehabilitation. Overall, there were significant increases in the majority of drug classes dispensed following inpatient rehabilitation (Table 3). The most commonly dispensed drug classes during this period were antihypertensives (70.0%), laxatives (61.6%), opioids (59.5%), antibiotics (57.8%), cholesterol lowering medications (46.6%), and proton pump inhibitors (44.5%).

Predictors of the likelihood of polypharmacy

A number of variables were significantly associated with the risk of polypharmacy (10+ different drug classes dispensed) following inpatient rehabilitation (Fig. 2). Notable significant risk factors included being female (RR = 1.06; 95% confidence interval [CI] 1.02–1.11), low

Table 2 Healthcare characteristics of individuals 1 year after inpatient rehabilitation for nontraumatic spinal cord dysfunction between 2004 and 2015, in Ontario, Canada.

	Overall cohort $n = 3468$	<66 Years of age $n = 1159$	≥66 Years of age $n = 2309$
Healthcare services utilization			
Visits, mean ± SD			
Acute hospitalization	0.4 ± 0.9	0.5 ± 1.0	0.4 ± 0.8[a]
Emergency department	1.2 ± 2.3	1.6 ± 2.9	1.0 ± 1.8[a]
Family physician	9.7 ± 8.4	9.9 ± 9.8	9.5 ± 76
Home care	58.3 ± 96.5	59.0 ± 98.0	57.9 ± 95.8
Specialist	8.5 ± 7.1	8.9 ± 7.9	8.4 ± 6.7
Continuity of care, *n* (%)			
Low	1658 (47.8)	562 (48.5)	1096 (47.5)
Medium	1274 (36.7)	419 (36.2)	855 (37.0)
High	466 (13.4)	152 (13.1)	314 (13.6)
Medication characteristics			
Number of drug classes, mean ± SD	11.7 ± 6.0	10.5 ± 6.4	12.4 ± 5.6[a]
Number of unique prescribers, mean ± SD	4.01 ± 2.5	4.0 ± 2.8	4.0 ± 2.3
Number of unique pharmacies, mean ± SD	1.8 ± 1.0	1.8 ± 1.1	1.8 ± 1.0
Healthcare characteristics			
ADG score, median (IQR)[b]	8 (5–10)	8 (5–10)	8 (5–10)
ADG Quintile, *n* (%)[a,b]			
1 (low)	574 (16.6)	196 (16.9)	378 (16.4)
2	748 (21.6)	262 (22.6)	486 (21.0)
3	731 (21.1)	228 (19.7)	503 (21.8)
4	632 (18.2)	204 (17.6)	428 (18.5)
5 (high)	783 (22.6)	269 (23.2)	514 (22.3)

IQR interquartile range, *SD* standard deviation.

[a]Significant difference based on an alpha level of 0.05. Differences between groups were tested using chi squared tests for categorical characteristics, *t*-tests for means, Wilcoxon–Mann–Whitney tests for medians, and the Cochran–Armitage test for ordinal characteristics.

[b]ADG refers to Aggregated Diagnosis Groups from the Johns Hopkins ACG® System. This system classifies health conditions in administrative health data over 2 years. Larger numbers of ADGs reflect higher comorbidity levels.

continuity of care (RR = 1.07; 95% CI 1.02–1.12), low income (RR = 1.09; 95% CI 1.03–1.16), ≤102 FIM score (RR = 1.30; 95% CI 1.21–1.41), 103–111 FIM score (RR = 1.19; 95% CI 1.04–1.29), and 112–117 FIM score (RR = 1.14; 95% CI 1.06–1.24). Higher number of drug classes used prior to injury (RR = 1.86; 95% CI 1.75–1.98) was also significantly associated with an increase in risk of

Table 3 Prescription medications dispensed to individuals with nontraumatic spinal cord dysfunction 1 year before and 1 year after an inpatient rehabilitation episode between 2004 and 2015, in Ontario, Canada.

	Before			After		
	Overall cohort $n = 3468$	<66 Years of age $n = 1159$	≥66 Years of age $n = 2309$	Overall cohort $n = 3468$	<66 Years of age $n = 1159$	≥66 Years of age $n = 2309$
Pain medications, *n* (%)						
Acetaminophen	634 (18.3)	110 (9.5)	524 (22.7)	1181 (34.1)[a]	312 (26.9)	869 (37.6)
Opioids	1700 (49.0)	422 (36.4)	1278 (55.4)	2062 (59.5)[a]	749 (64.6)	1313 (56.9)
Systemic NSAIDs[b]	1588 (45.8)	361 (31.2)	1,227 (53.1)	1234 (35.6)[a]	399 (26.9)	835 (36.2)
Co-analgesic medications, *n* (%)						
Antidepressants						
Tricyclics and other NRIs	465 (13.4)	136 (11.7)	329 (14.3)	662 (19.1)[a]	286 (24.7)	376 (16.3)
SNRIs	276 (8.0)	92 (7.9)	184 (8.0)	380 (11.0)[a]	167 (14.4)	213 (9.2)
Benzodiazepines	834 (24.1)	225 (19.4)	609 (26.4)	1007 (29.0)[a]	365 (31.5)	642 (27.8)
Muscle relaxants	95 (2.7)	13 (1.1)	82 (3.6)	553 (16.0)[a]	318 (27.4)	235 (10.2)
Pregabalin and gabapentin	471 (13.6)	123 (10.6)	348 (15.1)	1049 (30.3)[a]	423 (36.5)	626 (27.1)
Other anticonvulsants	113 (3.3)	59 (5.1)	54 (2.3)	142 (4.1)[a]	74 (6.4)	68 (2.9)
Supportive care medications						
Antidiarrheal drugs	32 (0.9)	11 (1.0)	21 (0.9)	61 (1.8)[a]	16 (1.4)	45 (2.0)
Laxatives	1085 (31.3)	221 (19.1)	864 (37.4)	2137 (61.6)[a]	667 (57.6)	1470 (63.7)
Urinary antispasmodics	204 (5.9)	44 (3.8)	160 (6.9)	385 (11.1)[a]	120 (10.4)	265 (11.5)
Dermatological medications, *n* (%)						
Antifungals, antibiotics, and antiseptics	544 (15.7)	112 (9.7)	432 (18.7)	768 (22.2)[a]	236 (20.4)	532 (23.0)
Topical steroids	665 (19.2)	119 (10.3)	546 (23.7)	735 (21.2)[a]	209 (18.0)	526 (22.8)
Cardiovascular medications, *n* (%)						
Anticoagulants						
Antiplatelet drugs	148 (4.3)	12 (1.0)	136 (5.9)	207 (6.0)[a]	20 (1.7)	187 (8.1)
Heparins	51 (1.5)	13 (1.1)	28 (1.7)	101 (2.9)[a]	45 (3.9)	56 (2.4)
Novel oral anticoagulants	36	≤5[b]	31	98 (2.8)[a]	9 (0.8)	89 (3.9)
Warfarin	184 (5.3)	14 (1.02)	170 (7.4)	338 (9.8)[a]	80 (6.9)	258 (11.2)
Antihypertensives	2126 (61.3)	306 (26.4)	1820 (78.8)	2429 (70.0)[a]	533 (46.0)	1896 (82.1)
Cholesterol lowering medications	1397 (40.3)	173 (14.9)	1224 (53.0)	1617 (46.6)[a]	326 (28.1)	1291 (55.9)
Diabetes medications, *n* (%)						
Glyburide and chlorpropamide	157 (4.5)	21 (1.8)	136 (5.9)	109 (3.1)[a]	20 (1.7)	89 (3.9)
Insulin	186 (5.4)	42 (3.6)	144 (6.2)	233 (6.7)[a]	69 (6.0)	164 (7.1)
Other oral antidiabetic agents	557 (16.1)	96 (8.3)	461 (20.0)	658 (19.0)[a]	173 (14.9)	485 (21.0)
Other medications, *n* (%)						
Antipsychotics	207 (6.0)	115 (9.9)	92 (4.0)	319 (9.2)[a]	175 (15.1)	144 (6.2)
Osteoporosis prevention drugs	513 (14.8)	50 (4.3)	463 (20.1)	604 (17.4)[a]	102 (8.8)	502 (21.7)
Proton pump inhibitors	1128 (32.5)	237 (20.5)	891 (38.6)	1542 (44.5)[a]	442 (38.1)	1100 (47.6)
Stimulants	32 (0.9)	19 (1.6)	13 (0.6)	29 (0.8)[a]	15 (1.3)	14 (0.6)
Systemic antibiotics	1589 (45.8)	360 (31.1)	1229 (53.2)	2005 (57.8)[a]	634 (54.7)	1371 (59.4)
Vitamins and minerals	528 (15.2)	89 (7.7)	439 (19.0)	889 (25.6)[a]	200 (17.3)	689 (9.8)

NSAIDs nonsteroidal anti-inflammatory drugs, *NRIs* norepinephrine reuptake inhibitors, *SNRIs* serotonin–norepinephrine reuptake inhibitors.

[a]Comparison between overall cohort before and after rehabilitation hospitalization; significant difference based on an alpha level of 0.05 using the exact McNemar's test for differences.

[b]Cell sizes <6 suppressed for privacy.

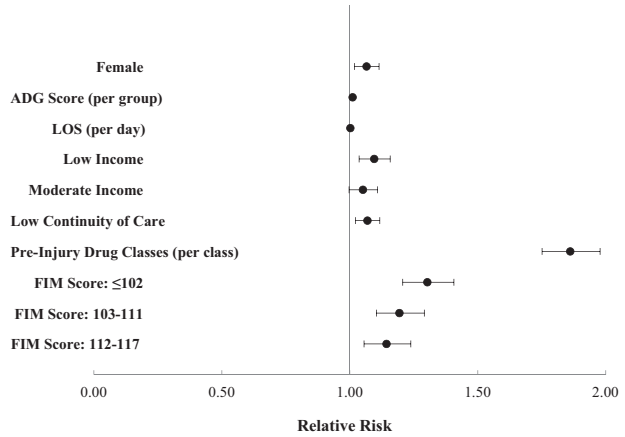

Fig. 2 Forest plot of statistically significant risk factors for polypharmacy (10+ drug classes) among individuals with an inpatient rehabilitation admission for nontraumatic spinal cord dysfunction between 2004 and 2015, in Ontario, Canada. Reference categories are indicated in brackets: female (male), low income (high income), moderate income (high income), low continuity of care (high continuity of care), ≤102 FIM score (117+ FIM score), 103–111 FIM score (117+ FIM score), and 112–117 FIM score (117+ FIM score). ADG Aggregated Diagnosis Groups (measure of morbidity), FIM Functional Independence Measure, LOS length of stay.

polypharmacy after inpatient rehabilitation. Morbidity (RR = 1.01; 95% CI 1.01–1.02 per ADG) and length of stay in inpatient rehabilitation (RR = 1.00; 95% CI 1.00–1.00 per day) were statistically significant but the RRs were small. Age was not statistically significant.

Discussion

The present study found the prevalence of polypharmacy to be high among persons with NTSCD, with more than half of the cohort on ten or more different drug classes. However, prior to inpatient rehabilitation, persons with NTSCD had significant preexisting morbidity and prescription drug claims. The most common pre-inpatient rehabilitation comorbidities included those related to cardiovascular, cancer, and mental health. The most common prescribed drugs following inpatient rehabilitation were related to cardiovascular disease, bowel care, pain, and infections. Notable risk factors associated with polypharmacy following inpatient rehabilitation among persons with NTSCD were related to sex, income, continuity of care, previous drug claims, morbidity, and function.

Importantly, our findings reinforce the impact of medical complexity among persons with NTSCD. In comparison with the general older adult Canadian population and older adults with TSCI, persons with NTSCD in our cohort had significantly higher rates of polypharmacy. Our findings indicated that 68% of persons with NTSCD >66 years of age were on ten or more different drug classes, and 94% were on five or more different drug classes. Comparatively, the Canadian Institute for Health Information has reported 26.5% of older adults (65 years and older) are on ten or more prescribed drugs, while 66% are on five or more drugs [26]. Similarly, persons with NTSCD have higher prevalence of polypharmacy compared with TSCI, as we previously identified 56% of older adults with TSCI being prescribed ten or more drugs [11].

The higher rates of polypharmacy among persons with NTSCD are important for clinical and research considerations. Clinically, these findings suggest the importance for overall awareness of polypharmacy among this population. Understanding subpopulations who may be more at risk for polypharmacy and associated potential harm are important. Adverse drug events increase with polypharmacy and the potential for drug to drug interactions, side effects, compromised medication adherence, morbidity, and mortality [5]. We identified persons most at risk are women, those with multimorbidity, decreased functional independence, lower income, and lower continuity of care. Hand and colleagues also identified women, those experiencing polypharmacy and morbidity at increased risk for drug therapy problems for all types of injury/dysfunction [27]. Medication reviews and deprescribing opportunities (e.g., tapering opioids) may be warranted for further clinical and research considerations.

Similar to previous research on TSCI [11], continuity of care was an important predictor of polypharmacy, that is, the higher continuity, the less risk for polypharmacy. Persons with NTSCD in our cohort had a mean of four different prescribers and visited 1.8 different pharmacies in the observation window. Given the medical complexity and prevalence of polypharmacy, it is important for informational continuity which may be enhanced by sharing electronic medical records and by establishing a continued relationship with providers, such as a usual pharmacy [28].

These findings reinforce the importance for conversations around medication self-management and medication-taking behavior among persons with NTSCD during their inpatient rehabilitation. For example, educational components may include improving health literacy, such as understanding what medications are prescribed for, how to take them, side effects to watch out for and who to follow up with should there be any additional concerns [28]. Moreover, previous research has shown medication-taking behavior can be compromised if there are mental health concerns [29]. Approximately 31% of our cohort had either a mood disorder or another mental illness diagnosis prior to their inpatient rehabilitation stay. Clinicians should be sensitive to challenges with taking medications as recommended among persons with NTSCD who also have concomitant mental health concerns.

Strengths and limitations

There are a few limitations of this study. In using administrative health data, we were unable to identify persons who are on private plans or those who pay out-of-pocket. In addition, we were not able to capture prescriptions that were prescribed but never dispensed or were dispensed in an inpatient setting. Thus, our findings represent a conservative estimate of polypharmacy in this population. We mitigated this by starting the observation window after the initial inpatient episode of care to minimize the unaccounted inpatient prescriptions. While we identified the first inpatient rehabilitation stay for individuals during our observation window, we do not know the time of diagnosis for a NTSCD. While those <65 who are receiving drug coverage due to social assistance or catastrophic drug coverage may be uniquely different than those over 65 who are receiving coverage due to age, we did not find any differences in findings with sensitivity analyses. We chose to use cumulative polypharmacy to be consistent with how others report polypharmacy to which we were comparing our data (e.g., the Canadian Institute for Health Information), rather than simultaneous or continuous polypharmacy. There is no gold standard on the best method for capturing polypharmacy. Finally, we were not able to capture over-the-counter medications or natural health products or identify the indications for the medications. There are several strengths to this study, including the use of population-level data to examine prevalence of polypharmacy. We used the ATC system for classifying medications, which is an internationally adopted system such that our results will be more easily compared with future research in this area. We were also able to capture almost all prescription medications dispensed to persons over the age of 65, using the ODB database.

Future directions

Future research examining medication therapy management for NTSCD would be warranted. The present study identified high rates of polypharmacy and associated risk factors; however, more research is needed to understand prescription drug use and the types of drugs used over time. We identified for example more than half of the cohort is prescribed opioids, and future research would be useful to monitor trends in opioid use over time following inpatient rehabilitation. Future research examining the impact of morbidity and function on polypharmacy would be useful. Further, qualitative research is warranted to explore perceptions of medications, factors related to adherence and self-management, and more specifically, how persons with NTSCD are integrating medications into their everyday life.

Summary

There is limited research to date examining polypharmacy among persons with NTSCD. This study identified a high prevalence of polypharmacy. Risk factors associated with polypharmacy were female sex, low income, high morbidity, lower functional status, and low continuity of care.

Data availability

The dataset from this study is held securely in coded form at ICES. While data sharing agreements prohibit ICES from making the dataset publicly available, access may be granted to those who meet prespecified criteria for confidential access, available at www.ices.on.ca/DAS.

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Author contributions SJTG conceptualized the study. SJTG, SLH, TP, TaP, and AKL obtained acquisition of study funding and designing the study. SJTG, M-EH, DMC, and AJC, prepared, coordinated, and guided the data analyses and interpretations. DMC and AJC analyzed the data. All authors assisted with overall interpretation and contextualization. SJTG, M-EH and QG assisted with the first draft of the manuscript. All authors critically reviewed and approved manuscript.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethics approval The use of data in this project was authorized under section 45 of Ontario's Personal Health Information Protection Act, which does not require review by a Research Ethics Board. However, we received Research Ethics Board approval from the University of Toronto (#34063).

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