

## ORIGINAL ARTICLE

# Understanding age effects associated with changes in secondary health conditions in a Canadian spinal cord injury cohort

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**Study design:** Longitudinal cohort.

**Objectives:** To determine whether changes in secondary health conditions (SHC) associated with spinal cord injury (SCI) were effectively modeled from a longitudinal or cross-sectional perspective, and whether the changes in SHCs were attributable to age or years post-injury (YPI).

**Setting:** Toronto Rehabilitation Institute, Lyndhurst Centre.

**Methods:** Telephone survey methods were used to collect data on (1) demographics, (2) impairment, (3) health status, and (4) self-reported SHCs at two time intervals (1995–1997; 2003–2004) from 344 adults with SCI. Generalized estimating equations were applied to model the longitudinal and cross-sectional effects.

**Results:** Health status decreased over time ( $P < 0.0005$ ), whereas the number of SHCs increased ( $P < 0.0001$ ). Regardless of age or YPI, the longitudinal component of aging better predicted SHC occurrence and was associated with spasticity [odds ratio, OR = 1.055 (95% confidence interval, CI, 1.018 to 1.093,  $P < 0.01$ )], kidney problems [OR = 1.154 (95% CI, 1.084 to 1.229,  $P < 0.0001$ )], cardiac problems [OR = 1.168 (95% CI, 1.060 to 1.286,  $P < 0.01$ )], high blood pressure [OR = 1.121 (95% CI, 1.058 to 1.188,  $P < 0.0001$ )], chronic pain [OR = 1.058 (95% CI, 1.021 to 1.096,  $P < 0.01$ )], and arthritis/joint pain [OR = 1.113 (95% CI, 1.075 to 1.152,  $P < 0.0001$ )].

**Conclusion:** Within a relatively short period of time, persons with SCI experienced substantive declines in health. The findings suggest that a longitudinal perspective is more sensitive for predicting the risk of self-reported SHCs than a cross-sectional one.

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**Keywords:** spinal cord injury; aging; secondary health conditions; health status; generalized estimating equations

## Introduction

Despite the increase in the number of studies examining the relationship between aging and secondary health conditions (SHC) after spinal cord injury (SCI), there are several challenges to understanding the nature of this relationship.<sup>1</sup> Some problems highlighted by Coll<sup>2</sup> include whether changes in SHCs over time are suitably represented by cross-sectional analysis, whether they are related more to age or years-post injury (YPI), and whether the patterns of SHC occurrences are linear or nonlinear. One way of addressing these limitations is the use of relatively novel

statistical methods designed to separate the cross-sectional and longitudinal effects within a longitudinal study.<sup>3</sup>

The separation of aging effects is illustrated in a recent paper by Coll,<sup>2</sup> in which generalized estimating equations (GEE) analysis to a longitudinal data set from the National Model Systems SCI database was applied. GEE analysis uses the generalized linear model to estimate more efficient and unbiased regression parameter estimates, as it accounts for data consisting of repeated measures that may be correlated within a subject.<sup>4</sup> Coll<sup>2</sup> examined whether changes in SHC occurrences across three data collection phases were attributable to longitudinal age (years of aging between data collection intervals), cross-sectional age, or cross-sectional YPI. The models identified that the longitudinal effect of aging was associated with the majority of changes in SHCs

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over time. That is, regardless of current age or YPI, the outcome changed over time. For instance, the occurrence of pain and stiffness over various body regions (that is shoulder, elbow, hand, and hip) increased in the cohort across the data collection intervals.

When examining whether the changes in outcomes were more associated with age or YPI, the majority of SHCs were not associated with either of these effects. Only shoulder pain/stiffness was associated with age, neck and back pain/stiffness was associated with YPI, and smoking was associated with both age and YPI. As well, the occurrences of certain SHCs were nonlinear (that is, neck and back pain/stiffness, constipation, smoking, and nausea), suggesting that the risk of these SHCs was not constant. The findings of this study highlighted that longitudinal designs are warranted, as the cross-sectional variables failed to detect the effects of aging in predicting the risk of SHCs associated with SCI.

Given the limitations associated with longitudinal designs (for example subject attrition and cohort effects), along with conflicting results between longitudinal and cross-sectional analyses on aging (for example Charlifue *et al.*,<sup>5</sup> Kerr and Thompson<sup>6</sup>), there is a need to apply analysis techniques that maximize the potential of longitudinal data to clarify how health status in persons with SCI changes over time. The purpose of this study was to (1) describe changes in health status in an aging Canadian cohort of SCI individuals, (2) determine whether changes in SHC occurrences are adequately represented by longitudinal and/or cross-sectional effects, and (3) assess whether these change are associated with cross-sectional age or YPI.

## Materials and methods

### Participants

All participants were former patients of Toronto Rehab's Spinal Cord Rehabilitation Program, and were recruited from an existing long-term follow-up database and hospital health records. Data were collected through telephone survey at two time points: 1995–1997 (Time 1) and 2003–2004 (Time 2). At Time 1, data on 851 participants with SCI were collected. However, 176 participants had missing data that could not be verified from hard copies of the questionnaires and were excluded from the analysis. At Time 2, 344 participants were successfully re-contacted (see Table 1). Seventy participants had died, and 261 were lost to follow-up, representing a 38.9% attrition rate.

This study was approved by the Research Ethics Board of Toronto Rehab, and we certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed.

### Measures

The AT Jousse Long-Term Follow-Up Questionnaire is a nonstandardized survey designed to collect data on (1) socio-demographics, (2) mortality, (3) impairment, (3) health status, (4) SHCs, and (5) mobility. At Time 2, the questionnaire was updated to collect data on quality of life (see Tonack *et al.*<sup>7</sup>).

**Table 1** Demographic and impairment characteristics at Time 1 and Time 2 (*n* = 344)

	Time 1 and Time 2		Time 1		Time 2	
	Number	%	Number	%	Number	%
<i>Gender</i>						
Men	293	85.2				
Women	51	14.8				
<i>Impairment</i>						
Incomplete tetraplegia	62	32.7				
Complete tetraplegia	81	13.2				
Incomplete paraplegia	92	32.8				
Complete paraplegia	109	21.4				
<i>Etiology</i>						
Traumatic	319	92.7				
Non-traumatic	25	7.3				
<i>Age</i>						
Mean			42.9		49.8	
Range			16–80		24–86	
<i>Years post-injury</i>						
Mean			12.2		19.07	
Range			<1–52		7–58	
<i>Marital status</i>						
Married/common-law			164	47.7	175	50.9
Single/divorced/separated/widowed			180	52.3	169	49.1
<i>Education</i>						
≥ Post-secondary			NA		147	42.7
< Post-secondary					197	57.3
<i>Employment</i>						
Working (full or part-time/student/etc.)			204	59.3	225	65.4
Not working (unemployed/retired)			140	40.7	119	34.6

### Socio-demographics and impairment

The variables of interest were age, gender, marital status, employment, and level of education (data on education were only collected at Time 2). Impairment data included self-report etiology of injury/disease, date of injury/disease onset, level of injury/lesion, and severity (motor and sensory complete or incomplete).

### Health status and secondary health complications

A 10-point numeric scale was used to assess health status, with 1 being 'poor' and 10 being 'excellent'. SHC occurrence(s) were collected by asking participants, 'Have you had any of the following conditions in the past year?': spasticity, pressure ulcers, bladder infections, kidney problems, bowel problems, cardiac problems, high blood pressure, respiratory complications, arthritis/joint pain, chronic pain, and psychological distress. Data on additional SHCs were collected at Time 2, and can be found in Hitzig *et al.*<sup>8</sup>

### Procedure

At the Time 1 interval, data were collected through telephone interview and were stored in a database. Before the Time 2 data collection interval, the data from Time 1 were transferred into a new database system, and data integrity was verified by examining existing hard copies of the Time 1 data case-report forms. The new long-term follow-up database had several programmed control checks to minimize data entry error. The data were screened and verified with hard copies of the questionnaire and/or health records.

At the Time 2 interval, information letters were mailed to potential participants, who were then contacted by trained telephone interviewers to obtain informed consent for participation. After the first month of interviews, randomly selected questionnaires were reviewed to assess the reliability and consistency of the data by cross-referencing injury characteristics with the participants' health records. Hospital charts were reviewed to obtain missing data regarding date of birth, date of injury, and/or impairment.

### Analysis

Descriptive statistics were used to report the demographic and impairment characteristics of the cohort and the frequency of SHCs at Time 1 and Time 2 ( $n=344$ ). Chi-square ( $\chi^2$ ) analyses and dependent samples  $t$ -tests were conducted to assess changes in SHC occurrence and health status. As well, Pearson correlation coefficients were calculated to see whether the total number of SHCs was associated with health status for each time interval: 1995–1997 and 2003–2004, respectively.

We adopted a modeling strategy similar to that of Coll,<sup>2</sup> who adapted the models of Neuhaus and Kalbfleisch.<sup>3</sup> In our model, age and years post-injury (YPI) were partitioned into cross-sectional and longitudinal components to evaluate whether changes in SHCs were longitudinal in nature or if they could be effectively modeled by cross-sectional analysis. To estimate cross-sectional differences among participants, along with the longitudinal changes within participants, we modeled age by using the chronological age of the participant at Time 1 (*Cross-sectional Age*) and the time difference between the two interviews (*Longitudinal Age*). A significant *Cross-Sectional Age* effect indicates a cross-sectional difference in which participants who differ in age would be expected to also differ in a selected outcome. A significant *Longitudinal Age* effect reveals that the outcome is better modeled longitudinally, and shows, on average, that a person who gains a year of age can expect to have a changed outcome. If the effects of *Cross-Sectional* and *Longitudinal Age* are equal, then the outcome can only be effectively accounted for by using a cross-sectional model. For YPI, we used the YPI of the sample at Time 1. Given the broad age and YPI span of the cohort, the use of first age and YPI, along with the time term (*Longitudinal Age*), is a suitable means for describing the data.<sup>9</sup>

On the basis of the earlier stated modeling rationale, GEE were used to investigate whether longitudinal changes in

SHCs are represented sufficiently by cross-sectional analysis. For each dichotomous outcome (SHC = 1 or absence = 0), the effects of *Cross-Sectional Age*, YPI, and *Longitudinal Age* were evaluated, while controlling for impairment and employment status. Impairment was dichotomized into severity (complete = 0 vs incomplete = 1) and level (paraplegia = 0 vs tetraplegia = 1). Employment status (working = 1 and not working = 0) was controlled because  $\chi^2$  analyses detected associations between employment status (at both Time 1 and Time 2) with a number of the SHC outcomes. Further,  $t$ -tests revealed that persons who were not working (unemployed or retired) had significantly more SHCs and lower self-perceptions of health than persons who were working (employed and/or student and/or volunteer).

To determine whether the risk of an SHC was related more to age or YPI, an analysis of the models without the *Longitudinal Age* term was conducted. For these models, a significant age effect indicates that age is the primary factor, whereas the opposite is held true if YPI is significant.

The use of GEE methods is a more appropriate means for analyzing longitudinal data. Longitudinal studies are those in which the outcome variable is repeatedly measured on the same individual on several occasions. As a result, the observations collected over time are not independent of each other, and techniques based on this assumption, such linear or logistic regression analyses cannot be directly used in longitudinal studies.<sup>10</sup>

## Results

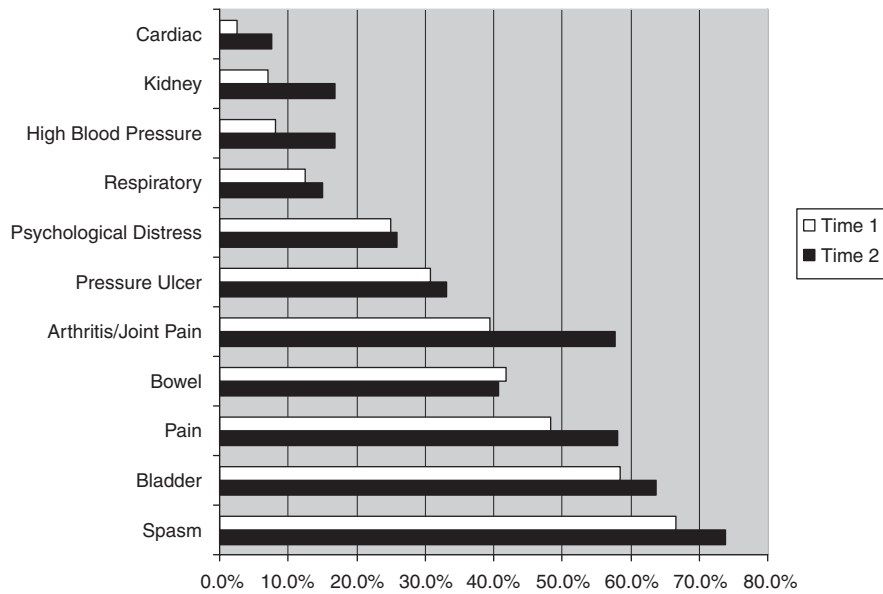
### Changes in health status

The frequency of each self-reported SHC increased ( $P < 0.0001$ ) over time except for bowel problems, which decreased ( $P < 0.0001$ ; see Figure 1). The mean total number of SHCs was higher at Time 2 ( $t(344) = -6.855$ ,  $P < 0.0005$ ;  $M = 4.1$ ; s.d. = 1.96) than at Time 1 ( $M = 3.4$ ; s.d. = 1.91). Similarly, the mean health status at Time 1 ( $M = 7.3$ ; s.d. = 1.82) decreased ( $t(338) = 2.320$ ,  $P < 0.0005$ ) by Time 2 ( $M = 7.1$ ; s.d. = 1.76). There was an association between total number of SHCs and perceived health status at Time 1 ( $r = -0.40$ ;  $P \leq 0.001$ ) and at Time 2 ( $r = -0.37$ ;  $P \leq 0.001$ ). Hence, poorer perceptions of health were associated with a higher number of self-reported SHCs.

### Cross-sectional and longitudinal aging and YPI effects

The resulting odds ratios (ORs; per 1 year of change) from the GEE analysis of the cross-sectional and longitudinal aging and YPI effects are presented in Table 2. When the OR is  $> 1.0$ , the more likely the event (SHC) is expected to occur with increasing age or YPI. Conversely, when the OR is  $< 1.0$ , the likelihood of the SHC occurring with increasing age or YPI is low.

More than half of the SHCs examined were positively associated with *Longitudinal Age*. The outcomes with only significant longitudinal effects included spasticity [OR = 1.055 (95% confidence interval, CI, 1.018 to 1.093,  $P \leq 0.01$ )], kidney problems [OR = 1.154 (95% CI, 1.084 to 1.229,  $P \leq 0.0001$ )], high blood pressure [OR = 1.121 (95% CI,



**Figure 1** Frequencies of self-reported secondary health conditions at Time 1 and Time 2.

**Table 2** Odds ratios (OR, per 1-year change) of secondary health conditions

	Cross-sectional age		Cross-sectional YPI		Longitudinal Age	
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Spasticity	0.981 (0.962 to 1.001)	0.056	1.007 (0.984 to 1.029)	0.568	1.055 (1.018 to 1.093)	0.003**
Pressure ulcers	0.988 (0.971 to 1.005)	0.160	1.022 (1.001 to 1.044)	0.045*	1.013 (0.970 to 1.057)	0.562
Bladder infections	0.974 (0.958 to 0.990)	0.002**	0.997 (0.976 to 1.019)	0.812	1.030 (0.990 to 1.071)	0.142
Kidney problems	1.012 (0.990 to 1.034)	0.296	0.979 (0.950 to 1.008)	0.159	1.154 (1.084 to 1.229)	0.000***
Bowel complications	1.015 (0.997 to 1.033)	0.096	0.972 (0.944 to 1.013)	0.540	0.992 (0.962 to 1.038)	0.970
Cardiac	1.054 (1.020 to 1.089)	0.002**	1.016 (0.978 to 1.056)	0.403	1.168 (1.060 to 1.286)	0.002**
High blood pressure	1.009 (0.986 to 1.032)	0.462	0.979 (0.944 to 1.013)	0.216	1.121 (1.058 to 1.188)	0.000**
Respiratory complications	1.027(1.004 to 1.051)	0.024*	0.989 (0.965 to 1.014)	0.400	1.031 (0.977 to 1.088)	0.262
Chronic pain	1.005 (0.988 to 1.022)	0.567	0.993 (0.973 to 1.014)	0.509	1.058 (1.021 to 1.096)	0.002**
Arthritis/joint pain	1.013 (0.996 to 1.034)	0.131	1.004 (0.982 to 1.027)	0.701	1.113 (1.075 to 1.152)	0.000***
Psychological distress	0.993 (0.975 to 1.011)	0.451	0.977 (0.954 to 1.001)	0.060	0.999 (0.957 to 1.043)	0.964

Abbreviations: YPI, years post-injury; CI, confidence intervals.

\*Significant at the 0.05 level; \*\*significant at the 0.01 level; \*\*\*significant at the 0.001 level.

1.058 to 1.188,  $P \leq 0.0001$ ), chronic pain [OR = 1.058 (95% CI, 1.021 to 1.096,  $P \leq 0.01$ )], and arthritis/joint pain [OR = 1.113 (95% CI, 1.075 to 1.152,  $P \leq 0.0001$ )]. Regardless of YPI or age, the risk for these SHCs increased over time.

Both the longitudinal [OR = 1.168 (95% CI, 1.060 to 1.286,  $P \leq 0.01$ )] and cross-sectional [OR = 1.054 (95% CI, 1.020 to 1.089,  $P \leq 0.01$ )] effects were positive and significant for

cardiac complications. Hence, the risk of cardiac problems increases with age and with time.

Only a few cross-sectional effects were detected for the SHCs modeled. For *Cross-Sectional Age*, a negative association was detected with bladder infections [OR = 0.974 (95% CI, 0.974 to 0.990,  $P < 0.01$ )], whereas a positive association was found with respiratory complications [OR = 1.027 (95% CI, 1.004 to 1.051,  $P < 0.05$ )]. This indicates that the risk of

bladder infections decreased with age, whereas the risk of respiratory complications increased. As well, the occurrence of pressure ulcers was positively associated with YPI [OR=1.022 (95% CI, 1.001 to 1.044,  $P \leq 0.05$ )]. Hence, the risk of having a pressure ulcer increases with duration of SCI.

In regard to whether the change in a particular SHC was related more to age or to YPI, the majority of cross-sectional effects were not significant. Similar to the models including the longitudinal component, positive *Cross-Sectional Age* effects were detected with cardiac [OR=1.052 (95% CI, 1.019 to 1.085,  $P < 0.01$ )] and respiratory [OR=1.027 (95% CI, 1.004 to 1.051,  $P < 0.05$ )] complications. As well, a negative association was found with bladder infections [OR=0.974 (95% CI, 0.958 to 0.990,  $P < 0.01$ )]. No significant YPI effects were detected.

## Discussion

The findings of this study suggest that aging with an SCI, even across a relatively short period of time, is associated with significant decreases in self-reported health status. Within a 5- to 8-year period, the perceived health status of the cohort decreased, whereas the total number and individual number of self-reported SHCs increased. Interestingly, the more frequent but relatively 'benign' conditions, such as bladder problems and spasticity, showed smaller increases over time than the less frequent SHCs that have implications for co-morbidities and life expectancy. Although still relatively low, the reports of cardiac complications and high blood pressure doubled between Time 1 and Time 2. This is particularly concerning given the prevalence of metabolic syndrome,<sup>11</sup> and the mortality and morbidity associated with cardiac events among persons with SCI.<sup>12</sup> Similarly, there were noticeable increases in the frequency of joint/arthritis pain and kidney problems. With regard to the GEE analyses, the regression-adjusted ORs revealed significant and positive associations between *Longitudinal Age* and the majority of the SHCs examined. Hence, irrespective of age or YPI, the odds of reporting high blood pressure, chronic pain, arthritis/joint pain, spasticity, and kidney problems increased over time for the cohort.

It is difficult to determine whether the increases in these particular SHCs are accelerated because of SCI<sup>13</sup> or are normative, as the able-bodied population is also at risk of increased cardiovascular health-related problems, renal impairment, respiratory ailments, and joint/arthritis pain with advancing age.<sup>14</sup> There is some compelling evidence for the former,<sup>15,16</sup> but further work is required to clarify these relationships<sup>17</sup> and to determine whether they are unique to one body system or consistent across several biological systems.<sup>18</sup> Unfortunately, the findings of our study cannot account for the rate of change in SHCs of the cohort, as we only collected data at two time intervals. As a result, we do not know whether the occurrence of these SHCs get progressively worse over time, or whether they follow a nonlinear progression. Regardless, the increase in prevalence of conditions such as musculoskeletal pain can cause greater

functional impairments, and can lead to the development of depressive symptoms over time.<sup>19</sup>

When trying to determine whether the occurrence of a particular SHC was associated more with age or YPI, it was not surprising that the only associations detected were with cardiac and respiratory complications. These SHCs are modeled effectively from a cross-sectional perspective, as they are typical conditions found in the aging able-bodied population as well.<sup>14</sup> The finding that pressure ulcers were associated with increased duration of SCI is consistent with other studies, but there are likely other influential factors (for example difficulty with practicing good skin care) contributing to the increased risk of developing a pressure ulcer over time.<sup>20</sup> Similarly, there were several associations detected between certain SHCs and impairment (for example a complete injury was associated with pressure ulcers and bladder infections, and spasticity was associated with tetraplegia), indicating that the development of certain conditions (for example bowel problems) is a consequence of the nature and severity of the SCI itself.<sup>21</sup>

Our findings are comparable to those of Coll,<sup>2</sup> whose data were also better represented by longitudinal effects than by the cross-sectional ones. Overall, only three of the self-reported SHCs were associated with *Cross-Sectional Age*, and none were associated with YPI. However, the magnitude of the longitudinal regression-adjusted ORs predicting the occurrence of an SHC was much higher in Coll's study than in ours. This discrepancy may be attributed to the fact that Coll<sup>2</sup> examined a different set of SHCs across three rather than two time intervals, which were of longer duration than those in this study.

There were also methodological limitations that may have affected our conclusions. Our data consist of self-reported impairment and SHC occurrence. Self-report data exclude the clinician perspective, and do not capture the severity or impact of the SHC. Although definitions of study terms were provided to respondents if requested, these were not standardized at either Time 1 or Time 2. We are currently using the Secondary Conditions Scale<sup>22</sup> in our current phase of data collection (Time 3) to address these issues.

This study also had problems typically associated with longitudinal designs, including interim participant mortality and attrition, and changes in data collection procedures, which we have outlined in the methods. This study may also be subject to several forms of bias, such as observer expectation bias and reporting bias.<sup>23</sup>

At this time, we are beginning to understand the implications of aging with an SCI on an individual's health, and the findings of this study highlight that a cross-sectional approach is a limited means for advancing our knowledge on the topic. The use of appropriate statistical methods, such as GEE analysis, in longitudinal studies is critical for identifying whether changes attributed to aging are inherent in living with an SCI or whether there are modifiable risk factors that can be targeted to minimize future problems. The prevalent SHCs associated with aging reported in this study are obvious targets for secondary and tertiary prevention initiatives.

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