

## Ten-year outcomes following traumatic brain injury: A population-based cohort

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### Abstract

*Primary objective:* To quantify the 10 year health service use (HSU) and mortality outcomes for people with a traumatic brain injury (TBI).

*Research design:* A population-based matched cohort study using linked administrative data from Manitoba, Canada (Manitoba Injury Outcome Study).

*Methods and procedures:* An inception cohort (1988–1991) of hospitalized cases with TBI aged 18–64 years ( $n = 1290$ ) was identified and matched to a non-injured comparison group ( $n = 1290$ ). Survival analysis, Negative binomial and Poisson regression were used to quantify associations between injury and HSU/mortality outcomes for 10 years following the TBI event.

*Main outcome and results:* The majority of deaths (47.2%) occurred in the first 60 days following injury. Excluding the first 60 days, the adjusted 10 year mortality remained elevated (mortality rate ratio = 1.48, 95% CI = 1.02–2.15). After adjusting for demographic characteristics and pre-existing health status, the TBI cohort had more post-injury hospitalizations (rate ratio (RR) = 1.54, 95% CI = 1.39–1.71), greater cumulative lengths of stay (RR = 5.14, 95% CI = 3.29–8.02) and a greater post-injury physician claims rate (RR = 1.44, 95% CI = 1.35–1.53) than the non-injured cohort.

*Conclusions:* People who sustain a TBI and survive the initial acute phase of care experience substantially increased long-term morbidity compared to the general population, regardless of the level of injury severity.

**Keywords:** *Epidemiology, traumatic brain injury, data linkage, outcomes, mortality, morbidity, health service utilization*

### Introduction

Knowing the true nature and extent of the needs of people who have experienced traumatic brain injury (TBI) is critically important for the appropriate planning and management of acute trauma care and long-term community services. In a study which demonstrated a sustained and substantial post-injury readmission rate, ranging from 23% after 12 months to 17% at 5 years post-injury [1], Marwitz et al. noted the need to consider costs of short- and long-term care when quantifying the

importance of TBI as a public health issue. These authors also noted the scarcity of available information on which to base sound cost estimates. Current epidemiological data clearly establishes TBI as an important public health problem, with the burden falling disproportionately on younger people, males, low socio-economic groups, those with poor education levels and Indigenous people [2–5]. This descriptive epidemiology is not sufficiently complete or detailed to support the required public health response [6, 7].

While current clinical literature suggests the physical, psychological and cognitive effects of TBI may continue for many years after the event [8–10], there are few large, population-based studies of long-term morbidity and mortality [11–13]. Conclusions from previous studies have been limited by the study methods used. These include small sample sizes [10, 14, 15], non-population-based sampling [14, 16, 17], the lack of population comparison groups [8, 18] or controlling for potential confounders such as pre-injury health status [19–21] and excessive loss to follow-up [22, 23]. Most are injury severity specific with the length of follow-up rarely beyond 5 years [8, 16, 18, 24].

Many studies have obtained their research populations from specialized rehabilitation programmes or tertiary level trauma centres and neurosurgical units [14] rather than population-based sampling methods [11, 25]. However, the literature indicates as few as 10–25% of all people with brain injuries ever receive formal rehabilitation [16, 17, 26] and not all people with a TBI are admitted to specialist tertiary care. In addition, people with language barriers, those with known psychiatric conditions, history of substance misuse or severe neurological deficits are often excluded from studies due to difficulties of participation and informed consent [11, 27, 28]. As a result, large proportions of people with a TBI are omitted from research selection and little is known about their recovery or long-term morbidity.

It is important to estimate what observed outcomes in people with a TBI are results of the injury and what would be present due to natural attrition, ageing, presence of comorbid conditions or other confounders. The use of a non-injured comparison group can provide data on the presence of the outcomes of interest in a comparative non-injured population and assist in quantifying outcomes that are likely to be due to the injury. While life expectancy and disease incidence tables or population 'norms' from national health surveys have been used in injury studies for comparison [18], these methods assume the health status of the injured cases was equal to that of the general population prior to the injury [29, 30]. Outcome studies of clinical case series cannot test this assumption and few population-based studies that compare injured and non-injured people have been reported in the literature [31].

While some attempts have been made to look at differences in health status in study participants pre- and post-injury using self-reported retrospective recall, studies using this method acknowledge inevitable biases [20, 24, 32, 33]. Some studies relying on patient self-recall to rate their health

status prior to the injury have reported health states as similar or better than the general population [34–36]. This is possibly due to a 'response shift', where the individual re-evaluates their prior health state in light of their traumatic injury experience, leading to more positive self-assessment of pre-injury health [29, 37]. In contrast, studies assessing pre-injury health status using medical morbidity data have found people with injuries have higher comorbidities and ill health than non-injured people [31].

Despite the increase in international literature on long-term outcomes following injury, few studies have follow-up greater than 12 months [24] and outcome studies greater than 5 years post-injury are rare [8, 14, 16]. Estimating the true burden from TBI requires an understanding of the increased risk of premature mortality and the extent and duration of morbidity for people who have been injured.

One of the most crucial sources of bias in cohort studies and also a major problem in most injury outcome studies is loss to follow-up [22, 23, 38]. Corrigan et al. [38, p. 153] report 'one third to one half of subjects in studies of long-term outcomes of traumatic brain injury are not included in outcome samples because of the inability to track subjects after they leave inpatient treatment'. Kristman et al. [23] found as little as 20% loss of data or subjects was associated with considerable bias of findings. Minimizing losses to follow-up are essential for improving the quality of TBI outcome research.

Of the few existing population-based injury outcome studies, an association has been found between TBI and an increase in all-cause mortality as well as post-injury health service use, which in some studies remained up to 50 years after injury [12, 13]. Despite this, there is limited information on hospital readmissions, ongoing outpatient visits, physician visits or long-term care provision for individuals who have sustained a TBI. Few studies have described the distribution of these outcomes by severity of the injury sustained. There is a particular need for population-based epidemiological studies of outcomes for people with a TBI to provide better empirical data relating to post-hospital deaths and long-term disabling sequelae [7, 11, 39].

The Manitoba Injury Outcome Study (MIOS) was developed using data linkage to provide a study that would overcome the above-mentioned design limitations and provide population-based epidemiological data. While some findings from MIOS have been previously published [21, 40–42], the aim of this paper is to further examine the specific TBI results to produce the first detailed population-based account of nature and extent of long-term TBI outcomes. Specifically the objectives of this descriptive study are to measure injury

outcomes over 10 years following TBI in terms of (i) death rates, (ii) hospitalizations, (iii) cumulative length of stay in hospital and (iv) physician claims, adjusting for age, gender, injury severity and pre-injury health status.

## Methods and procedures

### *Study design*

MIOS is a population-based retrospective matched cohort study with a follow-up period of 10 years, which uses linked administrative health data from Manitoba, Canada. Full details of the methods of this study have been previously published [21, 40–43]. The study was conducted in accordance with a protocol approved by the University of Manitoba Research Ethics Board, Manitoba Health's Health Information Privacy Committee and the University of Queensland Ethics Committee, Australia.

### *Setting and data sources*

The provision of health care in Canada is based on a system of universal medical care insurance. This entitles all eligible residents in the population access to publicly provided or insured health services [44]. Manitoba Health maintains databases of health provider claims for a population of 1.14 million residents for reimbursement of services provided (hospital, physician and nursing care services) as well as a population registry of those persons in the province eligible for health coverage [45, 46]. The databases have been used extensively in health research and are described in detail elsewhere [47, 48]. All data were de-identified prior to study investigator access.

### *Participants*

All persons with an injury, aged 18–64 years, resident in the province of Manitoba, who were hospitalized with a injury between 1 January 1988 and 31 December 1991 were identified ( $n = 21\,032$ ). For the purposes of this paper, a sub-set of people with TBI were selected ( $n = 1290$ ). The cohort included all individuals who had a TBI based on CDC guidelines [49] using the International Classification of Diseases, Ninth edition, Clinical Modification (ICD-9-CM), in the first or second diagnostic fields of their hospital record. During the inception period, the first injury-related hospital admission was designated as the index case record.

A comparison cohort of people not hospitalized for an injury during the same time period was randomly selected from the total remaining

population, identified from the Manitoba population registry. Non-injured persons were individually matched to injured cases on Aboriginal status, age, gender and geographical location of residence (partial postcode) at the date of admission of the injured case. Residents of nursing care homes, patients in extended hospital care and persons not resident in the province for 12 months before the admission date on the index record were excluded from both cohorts (for the purposes of extracting baseline data).

### *Pre-injury health service use and comorbidity measures*

Pre-existing health conditions were determined from health service use (HSU) records during the 12-month period prior to the index injury for both the injured and comparison cohort individuals [21]. Group differences were identified by classifying primary diagnoses under the 18 disease chapters of ICD-9-CM and combining the frequency of use of hospital and ambulatory physician services for each of these conditions. Two levels of severity of comorbidity were then defined. A 'mild condition' was one which involved one-to-three physician claims and no hospitalizations; a 'moderate-severe condition' was defined as four or more physician claims or at least one hospitalization for that condition. Individuals were coded as not having a condition if they had no contact with the health services. The Dartmouth-Manitoba version of the Charlson Comorbidity Index (CCI) [50] was also used to quantify pre-existing comorbidity for the two cohorts.

### *Injury severity*

Injury Severity Scores (ISS) were generated by ICDMAP-90© software from Johns Hopkins University. An ISS of 16 or greater was considered to be a major injury, an ISS of 9–15 a moderate injury and a mild injury was defined as an ISS of 1–8 [51, 52].

### *Outcome measures*

For all study participants, death status (and date of death) was obtained from the population registry for the 10 years following the date of injury. Hospitalization data provided a further two outcome measures, the total number of hospitalizations and cumulative length of stay (LOS) for the 10 years post-injury. While hospitalization for the index injury was not included in the number of hospitalizations, the resulting number of days stay in hospital was included in the LOS following the injury event. The number of ambulatory physician

claims for the 10 years post-injury provided the fourth outcome measure. The fifth outcome measure was the time from the index injury until the first admission to a nursing care home during the 10-year follow-up period.

#### *Calculation of person-years (PYs) at risk*

Using the information from the population registry, the total time a person was in the province, alive and eligible for health coverage, was calculated for the 10 years following the date of the index injury.

#### *Analysis*

Analysis was conducted using SAS version 9.2, STATA version 8 and SPSS version 12. The statistical significance of differences between groups for rates of HSU and presence of comorbid conditions was assessed by chi-squared statistics for categorical data and the Mann–Whitney U-test for continuous data with non-normal distributions. All tests were two-sided with a 5% level of significance. Mortality rates were calculated as the number of deaths in a cohort divided by the sum of the person-years for that cohort, divided by 10 000.

Survival analysis was conducted using the Kaplan–Meier method and Cox proportional hazards model to analyse the time from the injury event until death. Hazard ratios estimated from the Cox regression were used as measures of rate ratios. A group-by-time interaction term was added to test the proportional hazards assumption [53]. Evidence of non-proportionality was demonstrated ( $p < 0.001$ ), thus rate ratios (RRs) were calculated for each year following the injury, in addition to a pooled estimate for the total 10 years. Survival analysis was also conducted using the Kaplan–Meier method and Cox proportional hazards model to analyse the time from the injury event until the first admission to a nursing care home.

Negative binomial regression was used to estimate crude and adjusted RRs between exposure (injury) and outcome (HSU) for hospitalizations and the number of physicians claims [54, 55]. Examining the frequency distribution and the goodness of fit revealed that the negative binomial regression model was a better fit than the Poisson model for the hospital and physician claims data. The post-injury LOS data showed a better fit with the model estimated using over-dispersed Poisson regression.

Those factors shown to be associated with both the exposure and the outcomes in univariate analysis were included in the model as potential confounders. Colinearity existed between the numbers of pre-injury hospitalizations, pre-injury cumulative LOS

and number of hospital-defined comorbidities; and also the number of pre-injury physician claims and the number of physician-defined comorbidities. On the basis of clinical relevance, only pre-injury cumulative LOS and the number of pre-injury physician claims were included in the multivariate analyses. Matching variables were included in the model, because it has been shown that where cohort members have different lengths of follow-up, confounding by matching variables may occur over time [56]. The final model included age, gender, place of residence, pre-injury CCI, pre-injury cumulative hospital LOS, pre-injury physician claims, generated scores for pre-injury mental health, musculoskeletal conditions and previous injuries.

Attributable risk percentages (AR%) were calculated as the adjusted RR minus one, divided by the adjusted RR, multiplied by 100 [56]. The AR% was used to estimate the proportion of mortality and long-term HSU where injury was a component cause.

## **Results**

### *Characteristics of the cohort*

There was an over-representation of males (69.1%) and younger people aged 18–34 years (61.2%) among the 1290 people with a TBI. Fewer people with a TBI were aged between 45–64 years (23.0%). The mean age at the time of inception was 33.6 years. Almost half of all the injured people resided in rural regions of the province at the time of the injury (46.9%) (Table I). Three categories of external causes accounted for 82.6% of all the causes of brain injuries—transport-related incidents 42.3%, accidental falls 24.2% and attempted homicide or injury inflicted by others 16.1%. A quarter of the cases were severely injured, with ISS scores of 16 or greater (26.6%) (Table I).

Persons with a TBI had higher CCI scores, more hospitalizations, increased LOS in hospital and a greater number of physician claims than the comparison group in the 12 months before the injury (all variables significant;  $p < 0.001$ ) (Table I). People with a TBI were more likely to have been admitted to hospital or seen a physician multiple times for a mental health condition, musculoskeletal condition or for a previous injury in the 12-month period prior to sustaining the TBI (all variables significant;  $p < 0.001$ ) (Table I). Further details of these results have been published elsewhere [21].

### *Ten-year follow-up*

Over the 10-year follow-up period, there was no significant difference in the number of members of

Table I. Place of residence, injury severity scores and pre-injury health status of the injured and non-injured cohorts.

	Injured ( <i>n</i> = 1290)		Non-injured ( <i>n</i> = 1290)		Significance <sup>c</sup>
	<i>n</i>	%	<i>n</i>	%	
Place of residence at the time of the injury event <sup>a</sup>					
Urban	381	29.5	393	30.5	<i>p</i> = 0.63
Rural	605	46.9	613	47.5	
Remote	304	23.6	284	22.0	
Injury Severity Score <sup>b</sup>					
Minor (ISS 1–8)	786	66.6	na	na	na
Moderate (ISS 1–15)	81	6.9	na	na	na
Severe (ISS ≥16)	314	26.6	na	na	na
Health Status and service use in the 12 months prior to date of injury event					
Charlson Comorbidity Index (Score of 1 or more)	71	5.50	15	1.16	<i>p</i> < 0.001
Number of persons with a Mental Health condition <sup>c</sup>	56	4.34	29	2.25	<i>p</i> < 0.001
Number of persons with a Musculoskeletal condition <sup>c</sup>	63	4.88	30	2.33	<i>p</i> < 0.001
Number of persons with a prior injury/poisoning <sup>c</sup>	118	9.15	35	2.71	<i>p</i> < 0.001
Mean number of physicians claims (range) <sup>d</sup>	3.46	(0–161)	2.28	(0–118)	<i>p</i> < 0.001
Mean number of hospitalizations (range) <sup>d</sup>	0.13	(0–6)	0.09	(0–6)	<i>p</i> < 0.001
Mean length of stay in days (range) <sup>d</sup>	0.28	(0–103)	0.18	(0–55)	<i>p</i> < 0.001

<sup>a</sup>Place of residence matched on partial postcode, thus there are small differences in actual numbers.

<sup>b</sup>It was not possible to assign AIS scores to all cases, no Injury Severity Score (ISS) calculated for 109 cases.

<sup>c</sup>Presence of moderate–severe condition defined by four or more physician claims or at least one hospitalization for that condition in the 12 months prior to the injury date.

<sup>d</sup>Geometric mean calculated due to non-normal distributions.

<sup>e</sup>Determined by Mann-Whitney U-test or  $\chi^2$  statistics.

Table II. Mortality rates per 10 000 person-years (PYs) for injured and non-injured cohorts, by time periods.

Time period	Number of deaths				Unadjusted rate ratio	95% Confidence interval
	Injured ( <i>n</i> = 1290)		Non-injured ( <i>n</i> = 1290)			
	Deaths	/10 000 PYs	Deaths	/10 000 PYs		
0–60 days	77	3843.3	1	47.2	78.99	10.99–567.86
61–366 days	7	58.5	5	39.8	0.52	0.47–4.61
Year 2	14	120.4	0	0.0	na	na
Year 3	7	62.2	5	42.4	1.47	0.47–4.62
Year 4	7	63.7	2	17.2	3.70	0.77–17.82
Year 5	12	111.9	12	104.8	1.07	0.48–2.37
Year 6	10	95.2	4	35.5	2.68	0.84–8.54
Year 7	6	58.4	4	36.1	1.62	0.46–5.73
Year 8	6	59.3	4	36.6	1.62	0.46–5.73
Year 9	12	120.7	6	55.9	2.16	0.81–5.76
Year 10	5	54.9	8	81.0	0.68	0.22–2.07
Total	163	153.0	51	45.0	3.35	2.45–4.59

the injured cohort who left the province or were unable to be located (11.6%), than members of the comparison cohort (13.6%) (*p* = 0.1).

### Mortality

Of the injured cohort, 12.6% died (*n* = 163) compared with 4.0% of the comparison cohort (*n* = 51). The injured cohort had a 10-year all-cause mortality rate (MR) of 153.0/10 000 PYs

compared with 45.0/10 000 PYs in the non-injured, giving an unadjusted MRR of 3.35 (95% CI = 2.45–4.59) (Table II).

The greatest rate of mortality in the cohort of people with TBI occurred in the first 60 days following the injury, with 47.2% (*n* = 77) of all the injured case deaths occurring, with an associated unadjusted MRR 78.99-times that of the non-injured (95% CI = 10.99–567.86). When the first 60 days were excluded from the analysis,

the overall unadjusted 10-year MRR for people with a TBI remained significant but decreased from 3.35 (95% CI=2.45–4.59) to 1.83 (95% CI=1.29–2.60). However, year-by-year analysis indicated that after the first 60 days there was no significant difference in mortality for any individual time period between the injured and non-injured cohorts, although the mortality rates were consistently higher in the cohort of people with TBI (Table II).

Some of the elevated risk in the 10 year crude MRR diminished after adjusting for demographic characteristics at the time of injury and pre-injury health status, from 3.35 to an adjusted ratio of 3.10 (95% CI=2.24–4.30) (Table III). Excluding the first 60 days post-injury, the adjusted MRR decreased to 1.48 (96% CI=1.02–2.15).

Mortality rates also increased as severity of the injury increased (Table III). While there was no significant difference in mortality comparing the injured and non-injured cohorts for the people who had a minor or moderate TBI, people with severe brain injuries were 9.9-times more likely to die than their non-injured counterparts (95% CI=5.45–18.05). These results were not affected when adjusted for known confounders. People with a severe TBI who survived the first 60 days following the injury continued to have significant risk of mortality during the remaining years of follow-up (adjusted MRR=4.16, 95% CI=1.96–8.84).

#### *Health service use*

People with a TBI had higher rates of HSU in almost every year of the post-injury study period than members of the non-injured cohort, for each of the outcome measures (Figure 1). During the same period of time, the non-injured cohort demonstrated a consistent pattern of increasing rates of HSU. The distribution of rates of placement in nursing care homes was less consistent, probably because the overall numbers of placements in care homes during the 10 year period were small in both cohorts (28 people in the injured cohort and five in the comparison cohort).

For each measure, the greatest difference in HSU between the injured and comparison cohorts occurred in the first year following the injury (Figure 1). After adjusting for demographic characteristics and pre-injury health status, the injured cohort continued to have significantly greater HSU than the comparison cohort for all outcome measures.

After adjusting for demographic characteristics and pre-existing health status, the injured cohort had 1.54-times the number of all-cause post-injury hospitalizations (95% CI=1.39–1.71), 5.14-times

the number of days post-injury in hospital for all-causes (95% CI=3.29–8.02) and 1.44-times the number of post-injury physician claims (95% CI=1.35–1.53) (Table IV). The adjusted AR% suggested that 35.1% of all post-injury hospitalizations ( $n=1227$ ), 80.5% of all the time spent in hospital ( $n=105.13$ ) and 30.6% of physician claims ( $n=21\ 239$ ) in the injured cohort could be attributed to being injured (results not shown).

Hospital discharge rates were similar for each of the three levels of severity of injury, measured by the ISS (Table IV). In contrast, the rates of LOS in hospital and rate ratios increased with the severity of the injury (Table IV). Those with a minor injury had a rate of days LOS of 1.54/PY (adjusted RR=1.89, 95% CI=1.40–2.54) compared to 2.90/PY in those with moderate injuries (adjusted RR=3.79, 95% CI=0.44–32.36) and 15.46/PY in those with an ISS score of 16 or more (adjusted RR=14.02, 95% CI=5.97–32.19). Rates of all-cause post-injury physician claims increased as the severity of the injury increased, as did the adjusted RRs (Table IV).

When the primary diagnosis of all post-injury hospitalizations and physician claims was examined and ranked by RRs, the greatest differences were seen for subsequent injuries and mental health disorders (results not shown). In the 10 years following the TBI, the injured cohort had a 3.9-times higher rate of admissions to hospital with an injury diagnosis (injured 41.1/1000 PYs and non-injured 10.6/1000 PYs) and a 2.4-times higher rate of injury related physician claims (injured 94.2/100 PYs) than the non-injured people (39.6/100 PYs). However, less than 25% of all subsequent injury admissions had a primary diagnosis relating to skull fractures, intracranial injury or open wounds to the head. Approximately 15% of the injury admissions had a primary diagnosis as a medical or surgical complication or late effect of injury. It is not possible to determine from these data whether these were directly related to the original TBI. The remaining 60% of injury admissions had primary diagnoses unrelated to a head or brain injury.

In the 10 years following the TBI, the injured cohort were found to have 2.82-times the number of mental health related hospitalizations (95% CI=1.84–4.33), after controlling for pre-injury mental health and all other confounders. This increased risk was also demonstrated with physician claims with the injured cohort having an adjusted rate of mental health claims 1.92-times that of the non-injured cohort (95% CI=1.63–2.27) [41].

Table III. Adjusted mortality rates per 10 000 person-years (PYs) for injured and non-injured cohorts, by injury severity.

Injury Severity Score (ISS) <sup>a</sup>	Deaths				/10 000 PYs	Unadjusted rate ratio	95% Confidence interval	Adjusted rate ratio <sup>b</sup>	95% Confidence interval	Adjusted rate ratio <sup>b</sup> excluding first 60 days	95% Confidence interval
	Injured (n = 1290)		Non-injured (n = 1290)								
	Deaths	/10 000 PYs	Deaths	/10 000 PYs							
Minor ISS 1-8 (n = 786)	42	60.5	29	42.0	1.44	0.90-2.32	1.12	0.68-1.89	0.91	0.53-1.55	
Moderate ISS 9-15 (n = 81)	10	142.2	5	71.4	2.00	0.68-5.84	na <sup>c</sup>	na	na <sup>c</sup>	na	
Severe ISS ≥ 16 (n = 314)	101	486.7	12	43.1	9.92	5.45-18.05	10.30	5.58-18.99	4.16	1.96-8.84	
Total	163	153.0	51	45.0	3.35	2.45-4.59	3.10	2.24-4.30	1.48	1.02-2.15	

<sup>a</sup>It was not possible to assign AIS scores to all cases, no Injury Severity Score (ISS) calculated for 109 cases.

<sup>b</sup>Adjusted for age, gender, place of residence and comorbidities in 12 months prior to injury date (including CCI, cumulative LOS, number of physician claims, pre-existing psychiatric condition, pre-existing musculoskeletal condition and previous injuries).

<sup>c</sup>Model did not converge.

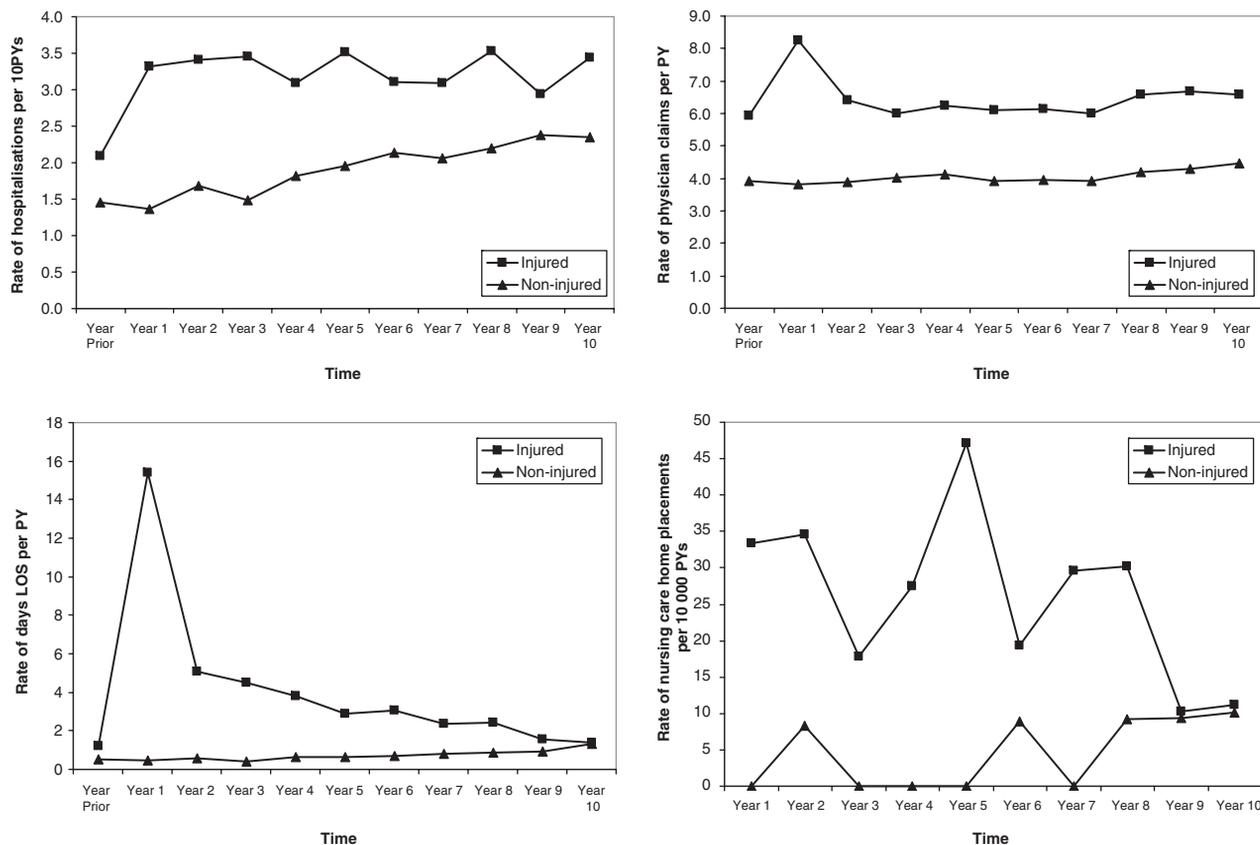


Figure 1. Rates of health service use for TBI and comparison cohorts, for 12 months pre-injury and 10 years post-injury ( $n = 1290$  pairs).

Table IV. Rates of health service use for injured and non-injured cohorts, by injury severity, with unadjusted and adjusted rate ratios.

Health Service Use <sup>a</sup>	Injured ( $n = 1290$ )		Non-injured ( $n = 1290$ )		Unadjusted rate ratio	95% Confidence interval	Adjusted rate ratio <sup>b</sup>	95% Confidence interval
	Adms	/10 PYs	Adms	/10 PYs				
<b>Hospitalizations</b>								
Minor ISS 1–8 ( $n = 786$ )	2268	3.27	1377	1.99	1.68	1.46–1.94	1.40	1.23–1.59
Moderate ISS 9–15 ( $n = 81$ )	219	3.11	121	1.73	1.85	1.19–2.85	1.41	0.95–2.11
Severe ISS $\geq 16$ ( $n = 314$ )	600	2.89	485	1.74	1.84	1.42–2.39	1.78	1.40–2.28
Total	3505	3.29	2181	1.92	1.8	1.58–1.98	1.54	1.39–1.71
<b>Cumulative LOS in hospital</b>								
Minor ISS 1–8	29.27	1.54	12.81	0.68	2.28	1.61–3.22	1.89	1.40–2.54
Moderate ISS 9–15	5.59	2.90	1.19	0.62	4.67	1.23–17.79	3.79	0.44–32.36
Severe ISS $\geq 16$	87.84	15.46	8.55	1.12	13.80	5.20–36.64	14.02	5.97–32.19
Total	130.6	4.48	24.3	0.79	5.7	3.29–9.93	5.14	3.29–8.02
<b>Physician claims</b>								
Minor ISS 1–8	43 717	6.30	27 839	4.03	1.59	1.46–1.75	1.32	1.23–1.43
Moderate ISS 9–15	4395	6.25	3018	4.31	1.61	1.21–2.15	1.41	1.13–1.75
Severe ISS $\geq 16$	14 466	6.97	11 592	4.16	1.85	1.58–2.16	1.68	1.45–1.93
Total	69 410	6.51	45 964	4.06	1.7	1.56–1.80	1.44	1.35–1.53

<sup>a</sup>It was not possible to assign AIS scores to all cases, no Injury Severity Score (ISS) calculated for 109 cases.

<sup>b</sup>Adjusted for age, gender, place of residence and comorbidities in 12 months prior to injury date (including CCI, cumulative LOS, number of physician claims, pre-existing psychiatric condition, pre-existing musculoskeletal condition and previous injuries).

**Discussion**

The aim of this study was to quantify the short- and long-term population-based burden of morbidity and mortality attributable to TBI in working-age

adults and to describe the role of pre-existing health status as a confounder in the relationship between injury and outcome. Through the use of linked administrative datasets and a retrospective matched

cohort design, this study sought to overcome some of the methodological limitations of previous TBI outcome studies. The findings of this study have implications for advancing current estimates of the burden of injury and informing public health policy for the appropriate planning and management of acute trauma care and long-term community services.

People with a TBI were found to have an increased prevalence of morbidity prior to sustaining the injury when compared with matched non-injured counterparts. While there are few TBI outcome studies similar in scope and methods to the current study, these findings were consistent with the pre-morbid results of another injury study with similar methods [57]. Comorbid health has also been shown to relate to injury outcome. Several clinical studies have measured comorbidities using a number of different methods, mostly reliant on the diagnostic fields of the index hospital admission record [32, 52, 58]. These studies found a consistent association between the presence of comorbid conditions and increased risk of inpatient mortality following injury. Smaller and less consistent associations were found in the few studies considering comorbidity and non-fatal outcomes [59–61].

As comorbidities are associated with both the occurrence of injury and the risk of adverse outcomes from injury, there is a potential for these conditions to confound the relationship between injury and outcome. The results of the present study demonstrated a small but consistent reduction in the findings by adjusting for the presence of comorbidities.

While this study demonstrated that cumulative excess mortality existed for the injured cohort over the 10 years following the injury (adjusted MRR=3.10), the greatest risk of mortality existed in the acute phase and early weeks following the injury. Almost half (47.2%) of all deaths for people with a TBI occurred during the first 60 days after the injury event. While more people with a TBI died in the remaining 10 years compared with the non-injured (adjusted MRR=1.48), there was no individual year of significant increased risk. However, the small number of events in each time period may account for this. These findings indicate current estimates of mortality, based on the acute hospitalised period alone, substantially underestimate the true attributable burden of deaths from TBI.

These findings are consistent with the results of the few population-based injury mortality studies with a non-injured comparison group reported in the literature [25, 57, 62–64]. Despite variation in study methods and different types of injury considered, the reviewed studies found a positive association

between injury and increased total long-term mortality exceeding that of the general population. Four of the studies found total mortality up to 18 years post-injury, including the inpatient period, ranged between 10.1–15.5% [25, 57, 64, 65]. In the current study, the proportion of mortality in working-age adults, over the 10 years of follow-up, who had a TBI, was comparable at 12.6%.

The one population-based TBI outcome study of all-cause mortality up to 18 years post-injury reported unadjusted MRRs ranging from 1.10–5.29-times that of the general population [25]. Brown et al. [25] reported that the mortality rate in the first 6 months for moderate-to-severe TBI cases was 5.29-times that of the general population and mild TBI cases had 1.33-times the general population mortality. Their study reported that after 6 months post-injury, no cases had increased rates of mortality compared to the general population.

The current study also found no significantly increased risk in long-term mortality for people who sustained minor or moderately severe brain injuries. However, in contrast to Brown et al., in this study people with a severe TBI who survived the first 60 days following the injury continued to have significant risk of mortality during the remaining years of follow-up (adjusted MRR=4.16, 95% CI=1.96–8.84).

While no population-based TBI morbidity studies were found in the literature that were similar in methods to the current study [13], these findings confirm previous clinical case series studies that suggested the needs of people with a TBI continue for many years following acute care, even after accounting for attrition, ageing and pre-existing comorbid conditions. After controlling for known potential confounding factors, people with a TBI had 1.54-times the rate of hospital separations, 1.44-times the number of physician claims and 5.14-times the cumulative LOS in hospital in the 10 years after the injury, than the non-injured cohort.

While this study found little difference in rates of hospitalizations and physician claims across the different levels of injury severity, the greatest excess was seen for length of inpatient care, which included the inpatient stay from the index injury event. As the severity of the TBI increased, cumulative lengths of time in hospital increased from 1.54 days/PY for those with a minor injury to 15.46 days/PY for those people with the most severe brain injuries. After adjusting for other known confounders, those people with the most severe injuries had 14-times the length of stay in hospital compared to the rest of the non-injured population, over the 10 year follow-up period.

These findings were consistent with the results of the few population-based studies of post-injury HSU with a non-injured comparison group [57, 63, 66–68]. Despite variation in methods, these studies also found a positive association between injury and increased HSU, which exceeded that of the general population. Across the studies, RRs of hospitalizations post-injury comparing the injured and non-injured ranged from 2.0–2.6.

The pattern of rates of HSU for different time periods post-injury was consistent with the findings of other studies [57, 63, 66]. The first 12 months after injury appeared to be a time of high need for health care, reflected by repeat or lengthy hospital admissions and high rates of physician claims. Rates of hospitalizations for the injured cases peaked in year 1 post-injury, decreased considerably in the following 2–5 years, but at no time during follow-up did rates decrease to that of the non-injured. The non-injured comparison group demonstrated a consistent pattern of increasing HSU for each of the different outcome measures over the decade of follow-up.

### Study limitations and strengths

There are a number of limitations in the use of administrative databases for epidemiological research. These largely relate to the quality of the HSU data and the extent to which they can be considered a measure of health status. However, extensive research and validity studies have been conducted on the Manitoban data by a number of different groups, the results of which support the assumptions underpinning this study [45, 69, 70]. While, to some extent, confounding by factors other than pre-existing morbidity was addressed by the matched study design, some unmeasured potential confounders remain. These include aspects of socioeconomic status, risk-taking and health behaviours associated with both the injury and outcome, over and above the matched variables, which were not included in the administrative datasets.

The nature of the administrative data prevented any effort to explore reasons for the higher rates of measured outcomes for people with TBI compared to the uninjured sample. In contradistinction to clinical studies [1] where reasons for post injury re-hospitalization can be explored, the use of administrative data to quantify population burden on injury provide only the population summaries rather than detailed causal explanations.

A second important limitation is that in order to obtain a sufficient follow-up period, the sample included in the study were injured more than

16 years ago. While the findings would reflect the outcomes of injured patients in the population at that time, advances in trauma care, rehabilitation and service provision has changed what is currently available and therefore the study findings may not represent the outcomes of people injured today. Thus the generalizability of the data presented in the study needs to be done with caution.

The strengths that set this study apart from previous injury outcome studies are that it was a large-scale population-based study with a long follow-up time, accurate pre- and post-injury measures and a sample size sufficient for quantitative analysis. The injured cohort was a population-based series of incidence cases, which avoids the biases inherent in most clinical study samples. This is one of the few studies that used a population-based non-injured comparison group. The ability to link the provincial population registry to individual HSU data provided outcome measures and comprehensive follow-up of the large sample, which enabled more accurate mortality and HSU estimates.

The results of this study can be generalized to other populations from high-income countries where the demographic characteristics, distribution of injury and health care systems are similar. While generalizing the results of this study needs to be done with some caution, the study sample and the consistency of findings suggest they are sufficiently robust to be relevant across different communities.

### Conclusion

This study is one of the first population-based injury outcome studies to quantify the burden of HSU for individuals and long-term mortality using linked longitudinal data. For people who have sustained a TBI and survived the initial acute phase of care, a considerable increased risk of excess hospitalizations, increased lengths of stay in hospital care and increased rates of physician claims remained across almost every year of follow-up regardless of the level of injury severity. These needs increased as the severity of the injury increased, after accounting for normative use of services in a matched population over the same time period.

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