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Pre-injury health status and excess mortality in persons with traumatic brain injury: A decade-long historical cohort study

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Abstract

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Author Contributions

TM, VC, ME and AC conceived the original concept and initiated the work. ME designed and optimized statistical analyses for this work. MH carried out the analyses with the support of ME, AC, TM, VC, and MS. All authors discussed the results weekly. TM wrote the manuscript. All authors read the paper and commented on the text.

Credit Author Statement

Tatyana Mollayeva, Vincy Chan, Michael Escobar and Angela Colantonio conceived the original concept, obtained funding, and initiated the work.

Michael Escobar designed and optimized statistical analyses for this work.

Mackenzie Hurst carried out the analyses with the support of Michael Escobar, Angela Colantonio, Tatyana Mollayeva, Vincy Chan, and Mitchell Sutton. All authors discussed the results weekly.

Tatyana Mollayeva wrote the manuscript and visualized hypotheses for the study.

All authors read the paper and commented on the text.

Competing Interests

The authors declare no financial and non-financial competing interests.

Ethical approval and informed consent

Approval: The study protocol was approved by the ethics committees at the clinical (Toronto Rehabilitation Institute-University Health Network) and academic (Institute for Clinical Evaluative Sciences) institutions. All methods were carried out in accordance with the relevant guidelines and regulations. Informed consent: This research utilised encrypted administrative health data with no access to personal information.

Availability of materials and data

The datasets generated during and/or analysed during the current study are available in the ICES repository, [www.ices.on.ca/DAS<http://www.ices.on.ca/DAS], under accession DAS 2016–257(2018 0970 084 000). Data sharing agreements prohibit ICES from making the datasets publicly available; however, access may be granted to those who meet pre-specified criteria for confidential access. The full dataset creation plan and underlying analytic code are available from the authors upon request, understanding that the computer programs may rely upon coding templates or macros that are unique to ICES and are therefore either inaccessible or may require modification.

An increasing number of patients are able to survive traumatic brain injuries (TBIs) with advanced resuscitation. However, the role of their pre-injury health status in mortality in the following years is not known. Here, we followed 77,088 consecutive patients (59% male) who survived the TBI event in Ontario, Canada for more than a decade, and examined the relationships between their pre-injury health status and mortality rates in excess to the expected mortality calculated using sex- and age-specific life tables. There were 5,792 deaths over the studied period, 3,163 (6.95%) deaths in male and 2,629 (8.33%) in female patients. The average excess mortality rate over the follow-up period of 14 years was 1.81 (95% confidence interval =1.76–1.86). Analyses of follow-up time windows showed different patterns for the average excess rate of mortality following TBI, with the greatest rates observed in year one after injury. Among identified pre-injury comorbidity factors, 33 were associated with excess mortality rates. These rates were comparable between sexes. Additional analyses in the validation dataset confirmed that these findings were unlikely a result of TBI misclassification or unmeasured confounding. Thus, detection and subsequent management of pre-injury health status should be an integral component of any strategy to reduce excess mortality in TBI patients. The complexity of pre-injury comorbidity calls for integration of multidisciplinary health services to meet TBI patients' needs and prevent adverse outcomes.

Keywords

Age; Comorbidity; Environmental exposures; Injury severity; Health services; Mortality; Life tables; Risk; Sex differences; Traumatic brain injury

Introduction

Traumatic brain injury (TBI), defined 'as an alteration in brain function or other evidence of brain pathology caused by an external force'[1], has long intrigued researchers and clinicians because of its multifaceted presentation and, more recently, because of the multiple additional clinically-relevant entities (i.e., comorbid conditions), previously existing, adding complexity and complication to the study and management of TBI[2,3]. These entities are widespread in TBI and have been shown to encompass not only aspects of a person's health, both mental and physical, but also factors external to the human body, the environment, which people often have little to no control[3].

Although evidence exists for relationships between certain pre-existing comorbid disorders and both in-hospital and all-cause mortality[4,5], uncertainty surrounds the magnitude of these associations, and the contributions of different comorbidities to the development of long-term adverse outcomes[6]. Chronic medical disorders, mental health disorders and alcohol and drug use, and a range of comorbid conditions through comorbidity indices are the most commonly reported predictors of all-cause mortality (supplementary table 1)[6–15]; however, a variety of non-diagnostically specific ways were used to study and categorize these comorbidities and/or comorbidity indices[6]. By focusing almost exclusively on selective comorbid disorders within an individual, both mental and physical, that are collected via self-report measures or chart abstractions from clinical files[6], clinicians and researchers may miss opportunities to risk-stratify patients with less common comorbidities, and those emerging from environmental adversities. Likewise, the burden of different comorbid disorders differs between male and female patients with TBI[7], and it is possible that certain comorbidities may be more relevant and offer better predictive ability when studying mortality risk in the sexes, bringing forth another objective for the study of mortality in TBI – sex-specific analysis. Finally, temporal separation of the comorbidity and TBI event, to protect against reverse causality bias, has received little attention in the scientific literature[6–15], but is highly relevant in the context of TBI-mortality prevention research. The present study addresses the gaps outlined above by following a large cohort of persons across the spectrum of TBI severity over more than a decade, evaluating the relationship between a comprehensive set of comorbidity factors preceding TBI and all-cause mortality. We hypothesized that TBI-preceding systemic comorbid disorders that require continuous treatment and disorders that arise from adverse environmental conditions that are difficult to modulate would increase the mortality risk in male and female persons across TBI severities beyond the expected mortality based on the person's age and sex. We also hypothesized that TBI severity and biological sex will have an impact on the strength of the association between pre-existing comorbid disorders and all-cause mortality (Figure 1).

Methods

The study protocol was approved by the ethics committees at the clinical and academic institutions affiliated with the authors. The findings were reported in compliance with the STROBE guidelines for cohort studies[16].

Study design and data sources

Data for this retrospective cohort study were obtained from the Institute for Clinical Evaluation Sciences (ICES)[17], which houses high-quality health administrative data on various publicly funded services to residents, including individual-level information on emergency department (ED) and acute care hospitalisations within Ontario, Canada. Diagnoses are indicated by the ICD-10 Canadian Enhancement (ICD-10-CA) [18]. All residents diagnosed with TBIs (ICD-10-CA codes S02.0, S02.1, S02.3, S02.7, S02.8, S02.9, S04.0, S07.1, and S06; supplementary table 2) of any severity and by any mechanism in an ED or acute care hospital between April 1, 2002 and March 31, 2016 were considered in this study (supplementary figure 1). To protect against overfitting and for internal validation, the data was split into three datasets, i.e. training, validation, and testing, with an allocation of 50%, 25%, and 25%, respectively[19]. Frequencies were calculated for the complete and testing datasets, and the training and validation datasets were used for model building and internal validation.

Predictors

Health status preceding TBI was evaluated as a predictor in our statistical models. From all possible ICD-10 codes classifying patients' health conditions, a previous data mining and validation study identified 43 factors (supplementary table 3) that differentiated patients with TBI from those with other diagnoses, individually matched based on age, sex, income level, and place of residence[3]. These comorbidity factors were significantly overrepresented in TBI patients compared to the reference patients in the five years preceding their TBI event. Each factor was considered a predictor and was studied individually.

Outcome

The primary outcome was excess mortality rates attributable to each of the 43 comorbidity factors preceding TBI, by sex and injury severity. Age- and sex-specific mortality rates were derived from a cause-elimination life table of the general population generated by Statistics Canada[18] and calculated excess mortality rates by differentiating the age- and sex-specific mortality rates (background mortality) from the reported mortality for each TBI patient, by each year interval, depending on whether the patient survived their TBI.

Covariates

Age, sex, socioeconomic standing, TBI severity and mechanism, and selective survivorship are important in the study of mortality. Injury severity was defined according to a previously published severity classifications [20,21]. Injury mechanism was determined using major external cause of injury group codes (E codes)[22], divided into falls, struck by/against object, motor vehicle accidents, other transport injury, intent (intentional or unintentional), and sports-related injury.

Statistical approach

Analysis of patients' first TBI

Due to ICES confidentiality policies, we were unable to obtain the exact dates for TBI-related hospital visits. Instead, two variables were attributed to each hospital visit: number of days from index date (i.e., first TBI event) to admission date and fiscal year of the admission date. To calculate the number of days to the censor date, the TBI event date was set as the first day of the fiscal year. Previous research considered mortality within a 30-day window to be TBI-related mortality[23]. A histogram representing the death distribution by day after the TBI event was constructed for all TBI patients. This histogram peaked around the index date, with little change after 100 days, and dropping drastically 30 days after the index date. The 30-day window, therefore, was determined as a TBI-related mortality window, and all patients alive 31 days after their first TBI were studied.

Discrete-time survival analysis—To calculate the excess mortality rate, the discrete-time method was used [24]. This required conversion from a person-record to a person-year dataset, which was achieved by creating a new entry for every year the patient remained in the cohort; the number of records in the new person-year dataset equalled the total sum of patient-years spent in the cohort. The patient's age was modified for each year he/she remained in the cohort, and the binary variable 'death' was set to zero for all person-year records except the last year. At that point, the patient was either censored or would have died in that year (assigned the value of zero or one, respectively). Subsequently, the sex-, age-, and calendar year-specific death rates in the general population, extracted from life tables[18], were age- and sex-matched to each surviving TBI patient of that year and used as an offset term to calculate excess mortality rate[25].

Poisson distribution—To determine the mortality rate per year for each TBI patient, a Poisson distribution was used to convert the binary variable 'death' to the mortality rate in that particular year[26]. A general linear model with a log-link function was used [27], where the outcome variable was the excess mortality rate in that year for a TBI patient versus that for someone from the general population with the same sex and age in that fiscal year of death, and the predictor variable was the TBI-preceding health status. The results were adjusted for age, income quintile, place of residence (urban vs. rural), injury mechanism, and fiscal year since the first TBI, for each comorbidity factor preceding TBI, and reported for male and female patients separately, by injury severity.

Age effects—Next, we accounted for possible effects of age. Since the offset term is based on the age-specific hazard for that particular year, it is already controlled for any increase in risk caused by patient age. However, age might have an additional effect in TBI patients compared to the general population. Thus, linear, quadratic, cubic, and quartic age effects were modelled. The results highlighted wide confidence intervals (CIs) for the cubic and quartic models. Follow-up likelihood-ratio tests revealed the quadratic age effect was optimal, which was used in the modelling process.

Effects of follow-up year on mortality rate—The assumption that the mortality rate after the first TBI (supplementary figures 2 and 3) remained unchanged throughout subsequent years and that any observed changes between years would only derive from age increases was tested. Our results highlighted that this was not the case; the percentages of patient deaths decreased with time post-TBI.

To better understand this phenomenon, least-square means were used to compare excess mortality rates in all follow-up years (supplementary figure 4). Excess mortality rates for each subsequent year were further tested in a categorical and binary effect of ≥ 2 years post-TBI. The Akaike[28] and Bayesian[29] information criteria were considered (supplementary table 4); the categorical effect was shown to be optimal. All statistical analyses were conducted using SAS software (version 9.410, SAS Inc., Cary, NC).

Results

Among the Ontario population of 12 and 14 million people in 2002 and 2016, respectively[30], 319,700 patients had their first TBI-related visit in either an emergency department (ED) or acute care hospital between the fiscal years 2002/03 and 2015/16. Of these, 11,347 (3.55%) patients died within 30 days following their TBIs and were excluded from analysis. The final sample was randomly split into training (50%; n = 154,177), validation (25%; n = 77,088), and testing (25%; n = 77,088) datasets (supplementary figure 1).

The 77,088 patients in the testing dataset comprised of 59% male and 41% female patients. The most common causes of TBI were falls (n = 33,800 [43.85%]; male: n = 17,518 [38.48%]; female: n = 16,282 [51.59%]) and being struck by/against an object (n = 27,407 [35.55%]; male: n = 18,383 [40.38%]; female: n = 9024 [28.59%]). Injury severity was not established in 12,629 (16.38%) male and 11,011 (14.28%) female patients; among these, most cases were recorded as concussion without a specified length of unconsciousness (ICD-10-CA code S06.0). Accidents and intentional injury accounted for 92% and 8% of

TBIs, respectively. Of all injuries, 26% were sports-related, and 13% were related to motor vehicle accidents (Table 1 and supplementary table 5).

Among the 43 pre-injury comorbidity factors, orthopaedic injuries (Factor 4 [41%]), disorders of elderly (Factor 3 [26%]), airway/lung disorders (Factor 19 [26%]), metabolic disorders (Factor 11 [24%]), and cardiovascular disorders (Factor 1 [17%]) had the highest occurrence. Factors related to medical procedure complications (Factor 31 [5%]), pharmacology emergencies (Factors 24 [0.9%], 25 [0.6%], and 41 [0.1%]), toxicology (Factor 20 [0.4%]), and environmental exposure (Factors 43 [0.12%], 32 [0.2%], and 42 [0.34%]) occurred less frequently (Figure 2).

There were 5792 (7.51%) deaths over the study period, including 3163 (6.95%) deaths in male and 2629 (8.33%) in female patients. Most deaths (n = 1648; 28.45%) occurred within 1-year post-TBI diagnosis, after which these percentages decreased for the next 6 years, within the range of 15.78–5.70%, reaching a minimum of 0.27% at year 14. This was true for both sexes, although the frequencies were higher in female than in male patients across most years and injury severities (Table 1).

The average excess mortality rate over the entire follow-up period was 1.81 (95% CI=1.76−1.86). Analyses of follow-up time windows showed different patterns for the average excess mortality rate post-TBI, with the greatest difference observed in year one post-injury (Figure 3 and supplementary figure 2).

Older age, urban residence, and lowest income quintile were associated with excess mortality rates (supplementary table 5). Among the 43 factors preceding TBI, 33 were associated with excess mortality rate after adjusting for relevant covariates. Among the high-frequency factors, Factors 1 (cardiovascular disorders and other), 3 (disorders of elderly and medical issues), 4 (orthopaedic injuries and other), 11 (metabolic disorders and abdominal symptoms), and 19 (acute and chronic disorders of airways and lungs) were associated with excess risk of dying at 1.56 (95% CI=1.42–1.70), 1.88 (95% CI=1.72–2.03), 1.36 (95% CI=1.24–1.49), 1.57 (95% CI=1.43–1.71), and 1.45 (95% CI=1.33–1.59), respectively. Among low-frequency factors, Factors 9 (liver disorders, others), 20 (alcohol-related emergencies), 22 (narcotic poisoning), and 33 (cold exposure, hypothermia) were associated with greater risks of excess mortality at 4.17 (95% CI=3.36–5.17), 4.45 (95% CI=2.78–7.12), 4.48 (95% CI=2.46–4.92), and 4.51 (95% CI=2.09–9.73), respectively (supplementary tables 6 and 7). The estimates varied by severity, but the results were comparable between sexes, although marginal factor-related differences were observed (Figure 4).

All detected associations, except for Factors 38 (adult, child abuse, sexual assault), 40 (reproductive organ infections, other), and 42 (toxic effects of gases, fumes, vapours), were internally validated via retesting with the validation dataset (supplementary figure 5).

Discussion

In this large representative cohort of persons with universal healthcare insurance (N=77, 088 patients, 57% males) who survived a TBI event, almost eight percent died over a period of 14 years following injury. When sex- and age-specific general population mortality rates were considered, the mortality risk for the TBI cohort remained elevated for most of the examined years. Among comorbidity factors preceding injury, 33 were strongly associated with excess mortality rates; the ten with the largest effects, irrespective of injury severity and sex, were (in no specific order): (1) alcohol related emergencies and emergencies and adversities due to substance use (Factors 20, 14), (2) liver disorders and others (Factor 9), (3) schizophrenia, delusional disorder (Factor 21), (4) epilepsy, seizures, brain lesions (Factor 26), (5) adult and child abuse, sexual assault (Factor 28), (6) poisoning due to narcotics, hormones and cardiovascular drugs, pain killers and anti-inflammatory drugs (Factors 22, 24, 25), and (7) exposure to the cold/hypothermia (Factor 33). These results suggest that pre-injury comorbidities with underlying pathophysiological processes due to systemic disorders, neuropharmacology, lifestyle, environment, and healthcare practices[31] could be mechanistic links in the relationship between TBI and excess mortality.

There is growing evidence from human studies on the effect of alcohol in persons with TBI on mortality, given the metabolic and neurological effects of alcohol[33]. Several population-based cohort studies reported that alcohol intoxication at the time of injury was not associated with in-hospital or long-term mortality or improved survivorship, taking into account TBI severity, age and sex[34,35,36]; one study[37] reported the opposite – that alcohol intoxication increases risk of mortality. Such discrepancies may be due to the numerous dose-related effects of alcohol, the time of exposure in relation to the injury, temporary versus continuous effects[38], or genetic susceptibility[39]. It has also been noted that alcohol intoxication at the time of injury affects the accuracy of injury severity assessment[40]. Our findings highlighted the effect of alcohol-related emergencies and adverse effects of alcohol in the time preceding TBI on mortality in persons who survived the injury event; we also observed wide confidence intervals pertaining to the effect and differences in the magnitude of the effect based on TBI severity and biological sex. These results can reasonably be explained by relative and not absolute elimination of compensatory responses and disruption of physiological regulation that protects the living organism against severe threats and sustained life in response to TBI long after the injury. Future studies looking at genetic vulnerability to the metabolic and neurological effects of alcohol would provide further insight into this relationship in TBI.

Our findings on neurological (epilepsy, seizures, brain lesions [41,42,43]) and gastrointestinal disorders (systemic hepato-renal disorders[42,44,45]) increasing mortality risk are consistent with the findings of previous studies, pointing to potentially disrupted immune-to-brain communication pathways[46], a complex array of defensive mechanisms aimed at tissue repair after injury, which is crucial for survival. Future studies should look at immune response to a TBI event in persons with systemic disorders.

A past study described links between abuse and sexual assault and TBI events, with women significantly more likely to die from a head injury due to assault as compared to men[47]. In this study such events were rare, however in both the complete and testing datasets, men who visited ED or acute care as a result of abuse or assault in the five years preceding their TBI had increased risk of mortality years after moderate and severe TBI. This is significant and may point to a less thorough approach to surveillance of abuse and assault in men.

Knowledge about factors infrequently co-occurring with TBI, described here and previously[3], is essential for preventive medicine. Exposure to cold/hypothermia, which was present in 0.15% of the sample, increased the overall excess mortality rate by 4.51 (95% 0=2.09–9.73). This has clinical implications, as several other episodes of excess mortality associated with cold exposure have been described recently, tightly linked to older age, male sex, mental illness, and homelessness[48,49].

Perhaps the most unique finding of this study is the magnitude of excess mortality due to adverse effects of psychoactive drugs and other medications preceding TBI. Drug therapy are frequently cited as the largest cause of adverse events post–hospital discharge, and it has been estimated that 13% of adverse drug events after discharge from the hospital result in an ED visit or rehospitalization[50,51]. Other research reported that narcotic analgesics frequently cause opioid induced respiratory depression, a combination of lowered level of consciousness, decreased respiratory drive, and upper airway obstruction, and are implicated in cerebral hypoxia and falls with or without loss of consciousness.[52] The link between adverse effects of medications and excess mortality in our study is noteworthy, and endorses attention to principles of quaternary prevention[53].

Aside from the ten comorbidities described above, diabetes mellitus and stroke, along with cardiovascular and respiratory disorders (previously reported in the literature in relation to mortality in TBI[3,6–14]) were shown to be associated with excess mortality across injury severities and in both biological sexes. These disorders have been reported to impact surgical care and rehabilitation outcomes in TBI[54,55], adding to the challenge of balancing the risk-benefit ratio of feasible therapies [56], limiting TBI-related treatment options[57]. Drug management of the comorbid disorders described above often requires multi-drug prescriptions[58]. Polypharmacy may indirectly increase risks related to TBI[3], which are often preventable by accounting for pharmacological interactions. There has been a recent call to utilise a minimally disruptive approach[59] when deciding on pharmacological management of conditions to reduce the likelihood of drug interactions and medical errors post-injury[53].

Our finding on the association between history of Alzheimer's disease and dementia and excess mortality across injury severities and sexes, are novel and could be used to inform care of patients with these conditions. Dementia and other TBI-preceding comorbidities are linked to reduced tolerance to rehabilitation interventions; for instance, elderly patients and patients with gait or balance deficits, often associated with orthopaedic injuries of elderly, may be excluded from rehabilitation interventions post-TBI [60,61], which may negatively influence long-term survivorship, independent of TBI-related processes. The present research calls for greater focus on comorbidity in the coordination of care and rehabilitation, to prevent long-term adverse effects in persons who survived their injury.

Our research addresses many limitations of previously published observational studies. The study includes over 77,000 patients from a population-based cohort and consequently has a large number of death events, allowing us to control for all available confounders. The use of population-based sex- and age-specific life tables is particularly important because these variables could confound associations between TBI-preceding comorbidity and mortality. Further, we stratified our results by sex accounting for differential help-seeking behaviours and contact with healthcare providers[62]. Finally, we used rigorous methods for dealing with age and selective survivorship effects.

Our study has limitations. Despite being internally validated in a large cohort, the 43 factors preceding TBI were not medical diagnoses with well-defined criteria[5]. Therefore, excess mortality rates may incorporate some imprecision, similar to that of other parameters, e.g., differences between physiological and chronological age [63,64] or frailty being a relative vs. absolute state. However, herein, health status, depicted by our pre-TBI comorbidity factors, incorporated environmental adversities, and therefore more accurately represents clinical situations by reflecting the complex personal and social factors presenting in TBI patients[65]. By limiting our sample to patients presenting to emergency and acute care facilities, mortality rates may have been overestimated because these individuals may represent more severe TBI cases, injury-preceding comorbidities, or both [66]. However, this approach has the advantage of investigating patients who access services in healthcare settings that are non-differential and free at the point of care. Although validated algorithms were used to define TBI severity, patient misclassification is possible, resulting in miscalculated TBI-related predictors. Finally, while health-related information routinely collected for administrative purposes provides a unique resource to study pre-TBI comorbidity and long-term outcomes in TBI patients, this approach is limited in its ability to identify continued unhealthy exposures after TBI.

Conclusion

We observed that comorbidities preceding TBI substantially increased excess mortality across injury severities and in both sexes, even after adjusting for other proxies of mortality. Early attention to comorbidity preceding TBI diagnosis, as an opportunity to intervene to prevent adverse TBI outcome, cannot be underestimated.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Pre-injury health status and mortality after traumatic brain injury were studied
- Age and sex-specific life tables were used to calculate excess mortality rates
- The excess mortality rates over the follow-up period were comparable between sexes
- 33 pre-injury comorbidity factors were associated with excess mortality rates
- Attention to pre-injury health status is needed to reduce excess mortality.

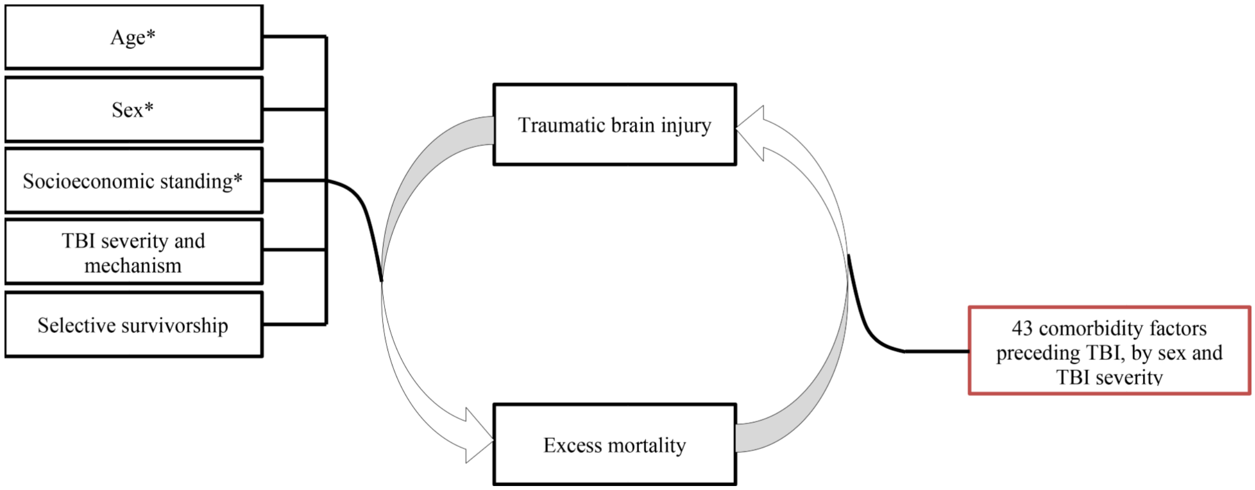


Figure 1.
Hypothesized relationships related to excess mortality outcome after TBI. Red colour indicates primary hypothesis. Black colour indicates covariates, some (*) previously described. TBI=traumatic brain injury.

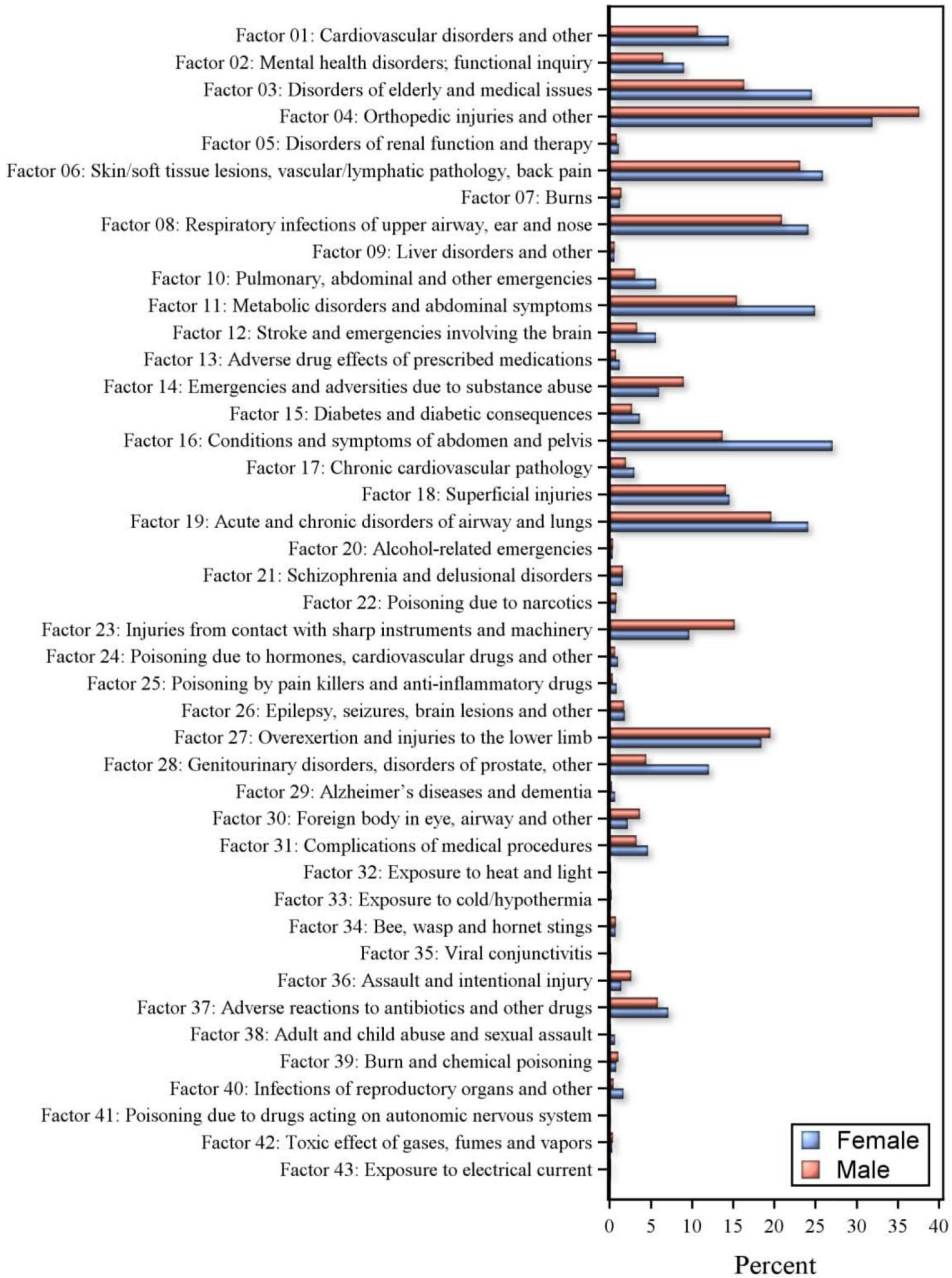


Figure 2.

Comorbidity factors preceding injury in males and females with TBI in Ontario, Canada 2002–2016.

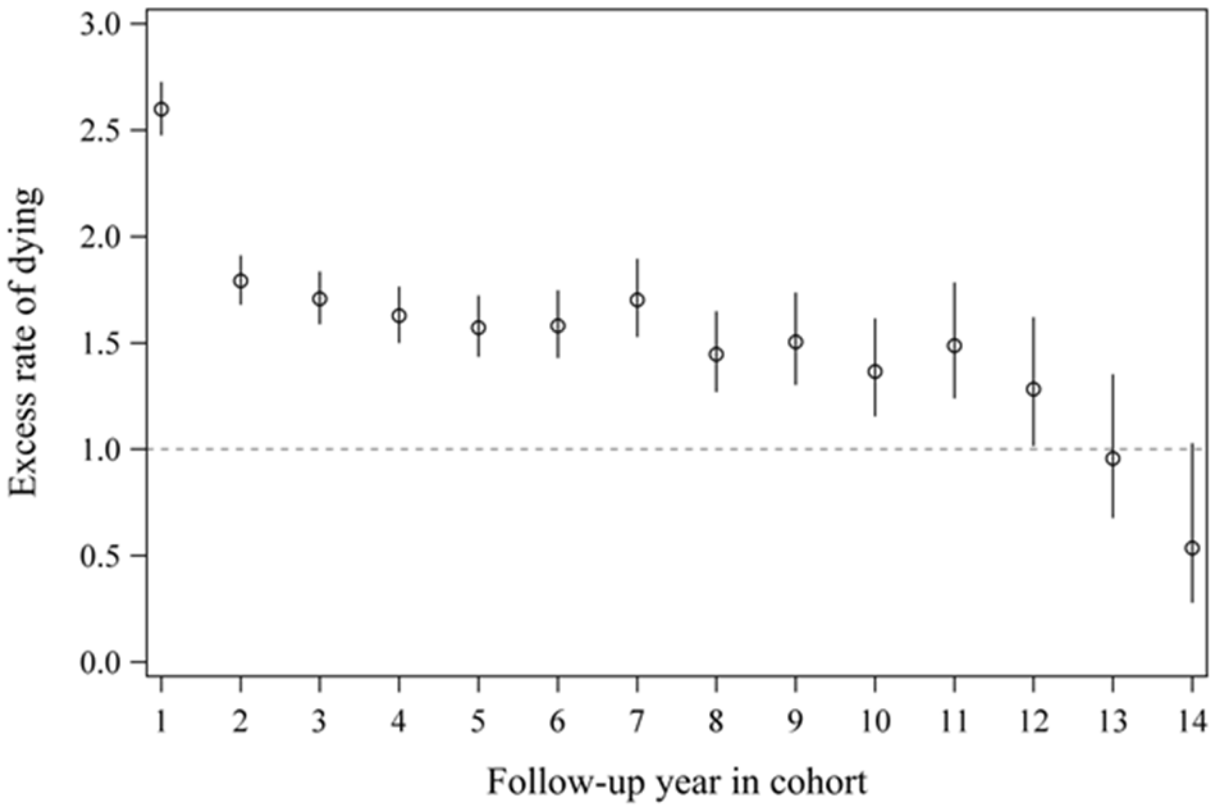
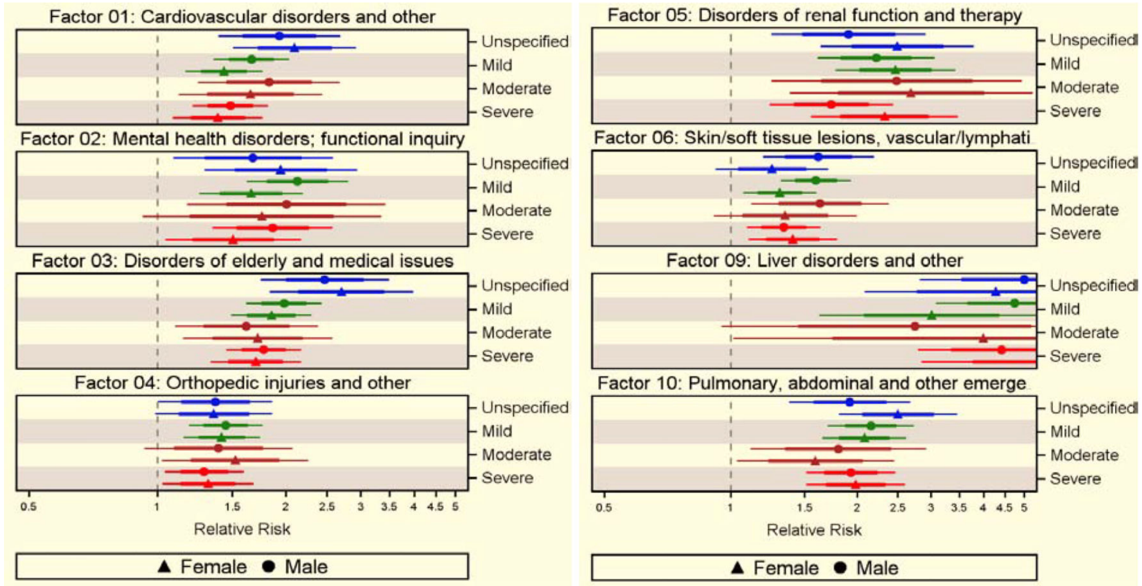
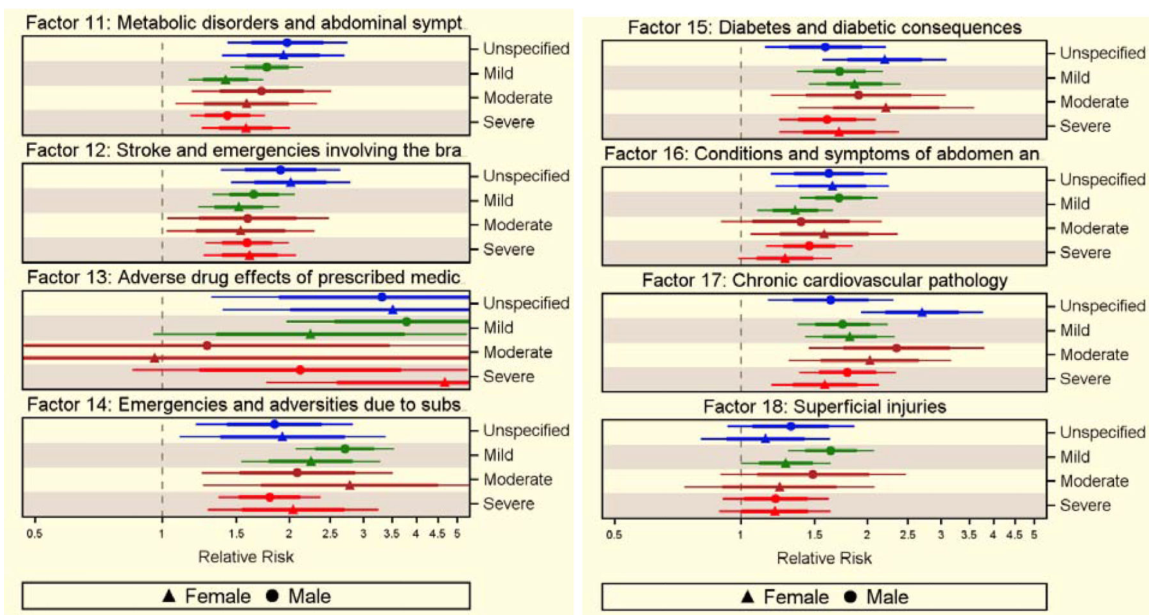


Figure 3.
Excess mortality rate for patients with TBI versus general population (individually matched by age and sex), by fiscal year remained in cohort.


Factor 01: Cardiovascular disorders and other
Factor 02: Mental health disorders; functional inquiry
Factor 03: Disorders of elderly and medical issues
Factor 04: Orthopedic injuries and other
Factor 05: Disorders of renal function and therapy
Factor 06: Skin/soft tissue lesions, vascular/lymphati
Factor 09: Liver disorders and other
Factor 10: Pulmonary, abdominal and other emerge
Unspecified
Mild
Moderate
Severe
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5
Relative Risk
Female
Male


Factor 11: Metabolic disorders and abdominal sympt
Factor 12: Stroke and emergencies involving the bra
Factor 13: Adverse drug effects of prescribed medic
Factor 14: Emergencies and adversities due to subs
Factor 15: Diabetes and diabetic consequences
Factor 16: Conditions and symptoms of abdomen an
Factor 17: Chronic cardiovascular pathology
Factor 18: Superficial injuries
Unspecified
Mild
Moderate
Severe
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5
Relative Risk
Female
Male

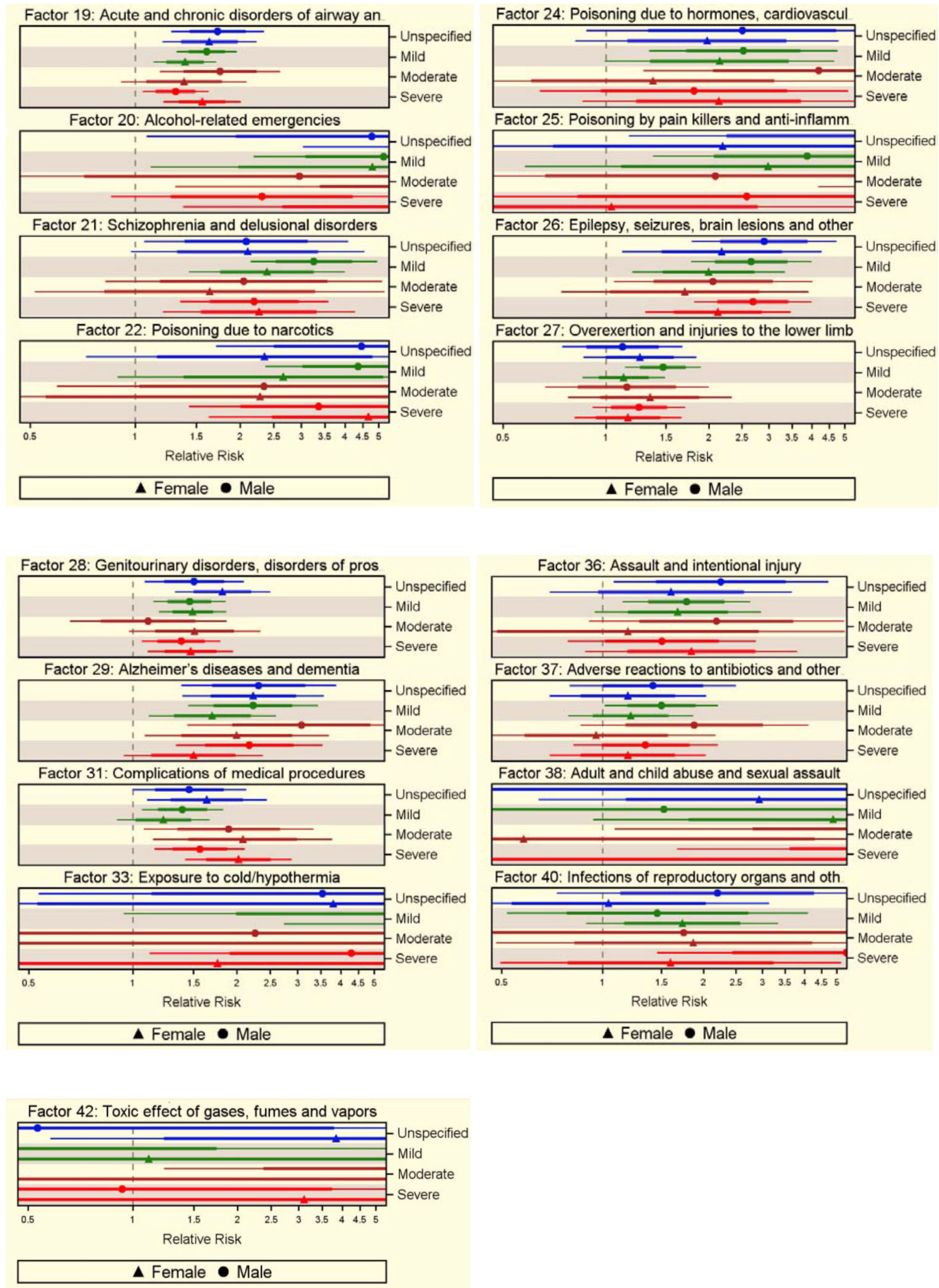


Figure 4.

Excess rate of death due to 33 health status factors preceding TBI, with 95% CI, without (denser line) and with (thinner line) Bonferroni adjustment, by sex and injury severity, controlling for potential confounders of excess rate of death.

Table 1.

Characteristics of patients with traumatic brain injury overall, and by sex and outcome by year after injury event

VARIABLES	Overall N (%) 77,088 (100)	Female patients (N, %) 31,560 (40.94)	Male patients (N, %) 45,528 (59.06)
Socio-demographic characteristics			
Age at first TBI, years old			
Mean (SD)	33.96 (24.26)	37.70 (25.71)	31.37 (22.85)
Median (IQR)	25.00 (15.00 – 51.00)	31.00 (16.00 – 57.00)	23.00 (14.00 – 46.00)
Income Q1 (poorest)	15,124 (19.62)	6,073 (19.24)	9,051 (19.88)
Income Q2	14,839 (19.25)	6,025 (19.09)	8,814 (19.36)
Income Q3	15,203 (19.72)	6,302 (19.97)	8,901 (19.55)
Income Q4	16,166 (20.97)	6,678 (21.16)	9,488 (20.84)
Income Q5 (wealthiest)	15,756 (20.44)	6,482 (20.54)	9,274 (20.37)
Rural residence	12,779 (16.58)	5,069 (16.06)	7,710 (16.93)
TBI-related characteristics			
Cause: Falls	33,800 (43.85)	16,282 (51.59)	17,518 (38.48)
Cause: Struck by/against object	27,407 (35.55)	9,024 (28.59)	18,383 (40.38)
Cause: Motor vehicle accident	9,667 (12.54)	3,916 (12.41)	5,751 (12.63)
Cause: Other transport injury	3,304 (4.29)	1,304 (4.13)	2,000 (4.39)
Cause: Other cause	4,383 (5.69)	1,526 (4.84)	2,857 (6.28)
Unintentional injury	71,040 (92.15)	30,433 (96.43)	40,607 (89.19)
Intentional injury	6,111 (7.93)	1,120 (3.55)	4,991 (10.96)
Sport-related injury	19,882 (25.79)	5,978 (18.94)	13,904 (30.54)
Number of deaths during the study period			
1st year after TBI event	1,648 (2.14)	704 (2.23)	944 (2.07)
2nd year after TBI event	914 (1.38)	401 (1.51)	513 (1.29)
3rd year after TBI event	726 (1.26)	356 (1.58)	370 (1.05)
4th year after TBI event	572 (1.15)	266 (1.41)	306 (0.99)
5th year after TBI event	455 (1.07)	221 (1.39)	234 (0.87)

VARIABLES	Overall N (%) 77,088 (100)	Female patients (N, %) 31,560 (40.94)	Male patients (N, %) 45,528 (59.06)
6th year after TBI event	375 (1.04)	183 (1.38)	192 (0.84)
7th year after TBI event	330 (1.07)	159 (1.43)	171 (0.87)
8th year after TBI event	224 (0.87)	103 (1.13)	121 (0.72)
9th year after TBI event	186 (0.86)	86 (1.15)	100 (0.71)
10th year after TBI event	136 (0.77)	59 (0.97	77 (0.67)
11th year after TBI event	115 (0.83)	48 (1.02)	67 (0.74)
12th year after TBI event	70 (0.69)	29 (0.84)	41 (0.61)
13th year after TBI event	32 (0.49)	NR	NR
14th year after TBI event	9 (0.27)	< 6	< 6

Abbreviations: IQR, interquartile range; TBI, traumatic brain injury. NR, not reportable due to residual disclosure.