

Original Article

Cite this article: Brown HK *et al.* (2025) A population-based cohort study of perinatal mental illness following traumatic brain injury. *Epidemiology and Psychiatric Sciences* **34**, e19, 1–9. <https://doi.org/10.1017/S2045796025000150>

Received: 21 November 2024

Revised: 27 February 2025


Accepted: 28 February 2025

Keywords:

brain injuries; cohort study; mental disorders; perinatal care; traumatic brain injury

Corresponding author: Hilary K. Brown;
Email: hk.brown@utoronto.ca

A population-based cohort study of perinatal mental illness following traumatic brain injury

Hilary K. Brown^{1,2,3,4} , Kinwah Fung⁴, Andrea Mataruga⁴, Rachel Strauss⁴, Vincy Chan^{5,6}, Natalie Urbach⁷, Tatyana Mollayeva^{5,6}, Angela Colantonio^{5,6,8,9}, Eyal Cohen^{4,8,10,11,12}, Cindy-Lee Dennis^{13,14}, Joel G. Ray^{4,8,15}, Natasha R. Saunders^{4,8,10,11,12} and Simone N. Vigod^{2,3,4,16}

¹Department of Health & Society, University of Toronto Scarborough, Toronto, ON, Canada; ²Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada; ³Women's College Research Institute, Women's College Hospital, Toronto, ON, Canada; ⁴ICES, Toronto, ON, Canada; ⁵KITE Research Institute-Toronto Rehabilitation Institute, University Health Network, Toronto, ON, Canada; ⁶Rehabilitation Sciences Institute, Temerty Faculty of Medicine, University of Toronto, Toronto, ON, Canada; ⁷School of Medicine, Queen's University, Kingston, ON, Canada; ⁸Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, ON, Canada; ⁹Department of Occupational Science and Occupational Therapy, Temerty Faculty of Medicine, University of Toronto, Toronto, ON, Canada; ¹⁰Hospital for Sick Children, Toronto, ON, Canada; ¹¹Edwin SH Leong Centre for Healthy Children, University of Toronto, Toronto, ON, Canada; ¹²Department of Pediatrics, Temerty Faculty of Medicine, University of Toronto, Toronto, ON, Canada; ¹³Lawrence Bloomberg Faculty of Nursing, University of Toronto, Toronto, ON, Canada; ¹⁴Lunenfeld-Tannenbaum Research Institute, Mount Sinai Hospital, Toronto, ON, Canada; ¹⁵Li Ka Shing Knowledge Institute, Unity Health Toronto, Toronto, ON, Canada and ¹⁶Department of Psychiatry, Temerty Faculty of Medicine, University of Toronto, Toronto, ON, Canada

Abstract

Aims. To examine the risk of perinatal mental illness, including new diagnoses and recurrent use of mental healthcare, comparing women with and without traumatic brain injury (TBI), and to identify injury-related factors associated with these outcomes among women with TBI.

Methods. We conducted a population-based cohort study in Ontario, Canada, of all obstetrical deliveries to women in 2012–2021, excluding those with mental healthcare use in the year before conception. The cohort was stratified into women with no remote mental illness history (to identify new mental illness diagnoses between conception and 365 days postpartum) and those with a remote mental illness history (to identify recurrent illnesses). Modified Poisson regression generated adjusted relative risks (aRRs) (1) comparing women with and without TBI and (2) according to injury-related variables (i.e., number, severity, timing, mechanism and intent) among women with TBI.

Results. There were $n = 12,724$ women with a history of TBI (mean age: 27.6 years [SD, 5.5]) and $n = 786,317$ without a history of TBI (mean age: 30.6 years [SD, 5.0]). Women with TBI were at elevated risk of a new mental illness diagnosis in the perinatal period compared to women without TBI (18.5% vs. 12.7%; aRR: 1.31, 95% confidence interval [CI]: 1.24–1.39), including mood and anxiety disorders. Women with a TBI were also at elevated risk for recurrent use of mental healthcare perinatally (35.5% vs. 27.8%; aRR: 1.18, 95% CI: 1.14–1.22), including mood and anxiety, psychotic, substance use and other mental health disorders. Among women with a history of TBI, the number of TBI-related healthcare encounters was positively associated with an elevated risk of new-onset mental illness.

Conclusions. These findings demonstrate the need for providers to be attentive to the risk for perinatal mental illness in women with a TBI. This population may benefit from screening and tailored mental health supports and treatment options.

Introduction

Perinatal mental illness is a common and costly complication of childbearing, affecting one in five women and other birthing people in pregnancy and postpartum (O'Hara and Wisner, 2014). Perinatal mental illnesses, including widespread disorders such as depression and anxiety and rare but serious illnesses such as bipolar and psychotic disorders, can have major negative impacts on long-term maternal and child wellbeing (Kingston and Tough, 2014; Meltzer-Brody and Stuebe, 2014). Traumatic brain injury (TBI) is an injury to the brain caused by an external force and can range from mild to severe (World Health Organization, 2006). One-third of people with TBI are female (Thurman *et al.*, 1999). There are nearly 400 emergency department visits and 50 hospitalizations per 100,000 females per year in Canada (Public Health Agency of Canada, 2020), with intimate partner violence being an important contributor

(Haag *et al.*, 2022). Outside of pregnancy, women with TBI are at higher risk for mental illness than women without TBI as well as men with TBI (Chan *et al.*, 2022a; Farace and Alves, 2000; Perry *et al.*, 2016; Yeh *et al.*, 2020). Yet, little is known about the risk for perinatal mental illness in this population.

Women with TBI may be differentially susceptible to mental illness perinatally. The social (e.g., violence; Langlois *et al.*, 2006) and health disparities (e.g., neurological comorbidities; Chan *et al.*, 2017; Haag *et al.*, 2016) experienced by women with TBI are risk factors for perinatal mental illness (Brown *et al.*, 2019; Yang *et al.*, 2022). The specific sequelae of TBI may also contribute to an elevated risk. People with TBI often report ongoing physical, cognitive, social and emotional symptoms, such as headaches, irritability, sleep issues, executive function limitations and problem-solving difficulties (Kieffer-Kristensen and Teasdale, 2011; Mollayeva *et al.*, 2016; Pryor, 2004). Such issues may be exacerbated in the perinatal period, especially postnatally when women experience sleep deprivation and childcare stressors (e.g., infant crying; Pryor, 2004). Perinatal hormonal fluctuations could also impact the vulnerable brain (Brunton and Russell, 2010). In a study of 208 women, Colantonio *et al.* (2010) found 50% of women with a history of TBI reported 'postpartum problems' vs. 24% of those without TBI. The third most common problem was depression, reported by 19% of women with TBI. To date, however, there is no population-level evidence on this topic; such evidence is essential for strategizing health service provisions. Therefore, in a population-based cohort study, we compared the risks of new mental illness diagnoses and recurrent use of mental healthcare from conception to 365 days post-delivery in women with vs. without TBI. We also examined injury-related factors associated with these outcomes among women with a TBI.

Method

Study design and setting

We undertook a population-based cohort study in Ontario, Canada, using data from ICES (Toronto), an independent, non-profit organization that holds complete, reliable administrative health data derived from the healthcare encounters of Ontario's 14.7 million residents (Williams and Young, 1996). We accessed and analysed the following datasets at ICES, linked at the individual level using a unique encoded identifier: the Canadian Institute for Health Information Discharge Abstract Database, including the derived MOMBABY dataset; the Ontario Mental Health Reporting System; the National Ambulatory Care Reporting System; the Ontario Health Insurance Plan dataset; the Registered Persons Database; the Immigration, Refugees and Citizenship Canada Permanent Resident Database; and the Census (Table S1). Use of data for this project was authorized under section 45 of Ontario's *Personal Health Information Protection Act* (PHIPA), which does not require ethics board review. We followed the Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) guidelines in our reporting (von Elm *et al.*, 2008).

Study population

We identified 15- to 49-year-old females (based on sex recorded on provincial health insurance cards) with an obstetrical delivery (i.e., livebirth or stillbirth after 20 weeks gestation) conceived between 1 April 2012 and 31 March 2021. Conception dates were estimated by subtracting gestational age at birth, most often ascertained

using first trimester ultrasound, from the delivery date (You *et al.*, 2008). We excluded those who used mental health services in the year before conception because they were considered to be in active treatment for mental illness (Figure S1). One of the strongest risk factors for perinatal mental illness is history of mental illness (O'Hara and Wisner, 2014), and there is a bi-directional relationship between TBI and mental illness in the general population (Chan *et al.*, 2022a; Liao *et al.*, 2012; McHugo *et al.*, 2017; Yeh *et al.*, 2020). Thus, we stratified our cohort by remote history of mental illness, defined based on ≥ 2 physician visits within 2 years of each other, or ≥ 1 emergency department visits or hospital admissions with a mental illness diagnosis between database inception and 1-year pre-conception. This allowed us to ascertain new mental illness diagnoses and recurrent use of mental healthcare perinatally (Figure 1).

Measures

We used a validated Centers for Disease Control and Prevention algorithm (Hedegaard *et al.*, 2016; Table S2) to identify women with a TBI recorded in the 'most responsible diagnosis' field in ≥ 1 emergency department visits or hospitalizations in the 10 years before conception. This algorithm has a positive predictive value of 96.9% relative to clinician-documented TBI (Warwick *et al.*, 2020). We also (1) examined TBI recorded in any diagnostic field (which better captures individuals with polytrauma but also captures those with a prior TBI unrelated to the encounter; Public Health Agency of Canada, 2020) and (2) used a sensitive definition of TBI (which includes open wounds of the head, fracture of the orbital floor and crushing injuries of the face and head – which often accompany, but do not necessarily indicate, TBI) (Brown *et al.*, 2024). Those without TBI in the 10 years before conception were the referent.

In those with a TBI recorded in the 'most responsible diagnosis' field in the 10 years before conception, we additionally measured injury-related variables: (1) the number of acute healthcare encounters for TBI (separated by ≥ 24 hours); (2) severity of the most severe TBI, based on a combination of hospital admission and discharge destination (i.e., emergency department visit only, or hospital admission and discharged home or to another facility; Brown *et al.*, 2024); and (3) time since the most recent acute healthcare encounter for TBI. For the TBI most proximal to conception, we also ascertained the (4) mechanism of injury (i.e., motor vehicle collision, struck by/against, falls, other; Hedegaard *et al.*, 2016) and (5) intent (i.e., intentional, unintentional/undetermined/other; Centers for Disease Control and Prevention, 2015).

Perinatal mental illness was defined as a healthcare encounter for mental illness between conception and 365 days postpartum, captured in ≥ 1 visits to a primary care provider, paediatrician, obstetrician or psychiatrist; emergency department visits; or hospital admissions with a mental illness diagnosis (Table S3). Perinatal mental illness was then further categorized by (a) timing (i.e., prenatal, with the first encounter occurring during pregnancy; or postpartum, with the first encounter occurring within 365 days of delivery) and (b) diagnosis (i.e., a mood or anxiety, psychotic, substance use, or other mental health disorder, or self-harm; these categories were derived from all healthcare encounters in the perinatal period and were not mutually exclusive). In additional analyses, we required ≥ 2 outpatient visits (as 1 visit may be a rule-out).

Covariates were maternal age and parity, neighbourhood income quintile, rural residence, immigration status (derived from the Immigration, Refugees and Citizenship Canada Permanent Resident Database), history of recent severe violence (captured

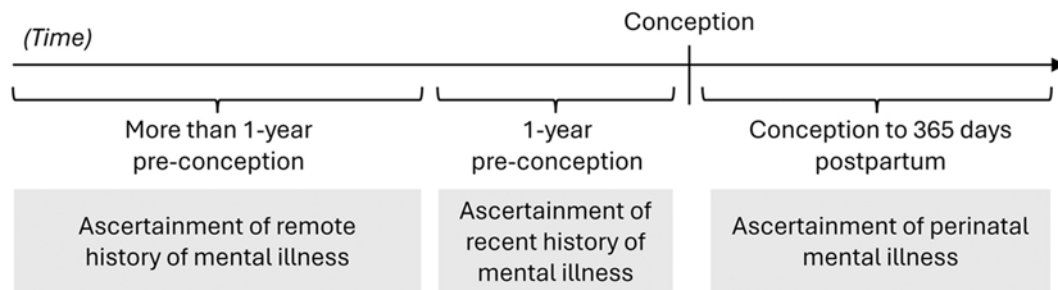


Figure 1. Illustration of the cohort design. We excluded women who used mental health services in the 1-year pre-conception because they were considered to be in active treatment for mental illness. We then stratified our cohort by remote history of mental illness status, defined based on ≥ 2 physician visits within 2 years of each other, or ≥ 1 emergency department visits or hospital admissions with a mental illness diagnosis between database inception and 1-year pre-conception. This allowed us to ascertain new mental illness diagnoses (in those without a remote history of mental illness) and recurrent use of mental healthcare (in those with a remote history of mental illness) perinatally.

in emergency department visits in the 2 years before conception; Saunders *et al.*, 2021) and comorbidities (ascertained using Adjusted Clinical Groups in the 2 years before conception; Johns Hopkins Bloomberg School of Public Health, 2009) (Table S4).

Statistical analyses

Baseline characteristics of women with and without TBI in the history of mental illness strata were measured using descriptive statistics and compared using standardized differences (Austin, 2009).

To address the first objective, we used modified Poisson regression (Zou, 2004) to estimate the relative risk (RR) and 95% confidence interval (CI) of perinatal mental illness, overall and by timing and type as defined above, comparing women with and without TBI. Therein, new mental illness was determined in those without a history of mental illness and recurring mental illness was estimated in those with a history of mental illness. Generalized estimating equations (Zou and Donner, 2013) were used to account for clustering due to the inclusion of more than one birth per woman in the study period. Multivariable models included age, parity, income quintile, rurality, immigration status, history of violence and comorbidities.

For the second objective, we used modified Poisson regression to examine injury-related factors associated with any new and recurring perinatal mental illness in women with TBI, using the same model covariates.

In sensitivity analyses, we tested the impacts of variations of the exposure and outcome definitions on the results; we examined TBI recorded in any diagnostic field (Hedegaard *et al.*, 2016) (sensitivity analysis 1); used the more sensitive definition of TBI (Public Health Agency of Canada, 2020) (sensitivity analysis 2) and required ≥ 2 outpatient visits in our definition of perinatal mental illness (sensitivity analysis 3). Finally, we stratified the analyses by maternal age, to explore whether age-related stressors could impact results (sensitivity analysis 4).

SAS version 9.4 (SAS Institute Inc., Cary, NC) was used.

Results

Among women without a history of mental illness, there were 5,647 women with a TBI recorded in the 10 years before conception, and 507,309 without a TBI. Among those with a history of mental illness, there were 7,077 with a TBI and 279,008 without a TBI. In both cohorts, compared to women without TBI, those with TBI

were more likely to be younger, primiparous, living in a rural area, non-immigrant and a victim of violence (Table 1).

Women with TBI were at elevated risk of both new-onset (18.5% vs. 12.7%; adjusted RR [aRR]: 1.31, 95% CI: 1.24–1.39) and recurrent mental illness perinatally (35.5% vs. 27.8%; aRR: 1.18, 95% CI: 1.14–1.22) compared to women without a TBI (Table 2). Risks were similar for both prenatal and postpartum mental illness presentations. Among women without a history of mental illness, those with TBI were at elevated risk for new-onset mood and anxiety disorders in the perinatal period; among women with a history of mental illness, those with TBI were at risk for recurrent mood and anxiety, psychotic, substance use and other mental health disorders perinatally (Table 2).

Among women with TBI without a history of mental illness, multiple TBI-related healthcare encounters were associated with an elevated risk of new-onset mental illness perinatally in unadjusted analyses. Among those with a history of mental illness, time since the most recent TBI-related healthcare encounter and intentional injuries were associated with recurrent mental illness risk (Table 3). However, with the exception of multiple TBI-related healthcare encounters, none of these variables were statistically significant after adjustment.

Findings were similar to the main analysis when we examined TBI in any diagnostic field (sensitivity analysis 1; Table S5); used the more sensitive definition of TBI (sensitivity analysis 2; Table S6) and required ≥ 2 outpatient visits in our perinatal mental illness definition (sensitivity analysis 3; Table S7 and Table S8). Effect sizes were slightly larger in younger women (15–34 years) compared to older women (35–49 years) (sensitivity analysis 4; Table S9).

Discussion

In the first study of its kind, we used whole-population data to show women with a TBI recorded in an acute healthcare encounter in the 10 years before conception were at elevated risk of both new-onset and recurrent mental illness perinatally vs. those without TBI. Findings were similar for prenatal and postpartum mental illness, with mood and anxiety disorders being the most common type of mental illness observed in both groups. In women with a TBI, having multiple acute healthcare encounters for TBI was associated with a higher risk of new mental illness perinatally. Results were robust under variations of both the TBI and outcome definitions. Our data show the need for screening for perinatal mental illness in women with TBI and for tailored prevention and treatment efforts to reduce the risk of perinatal mental illness.

Table 1. Baseline characteristics of women with a TBI in the 10 years before conception and those without a TBI. Reported as *n* (%) unless otherwise indicated. Cells with sample sizes <6 suppressed to minimize re-identification risk

Baseline characteristics	No history of mental illness			History of mental illness		
	TBI ^a (<i>n</i> = 5,647)	No TBI (<i>n</i> = 507,309)	Standardized difference ^b	TBI ^a (<i>n</i> = 7,077)	No TBI (<i>n</i> = 279,008)	Standardized difference ^b
Age (years), mean (SD)	27.53 ± 5.39	30.48 ± 4.92	0.57	27.57 ± 5.60	30.76 ± 5.24	0.59
15–19 years	373 (6.6)	9,669 (1.9)	0.23	485 (6.9)	5,910 (2.1)	0.23
20–24 years	1,340 (23.7)	47,254 (9.3)	0.40	1,786 (25.2)	28,452 (10.2)	0.40
25–29 years	1,937 (34.3)	149,506 (29.5)	0.10	2,207 (31.2)	73,825 (26.5)	0.10
30–34 years	1,391 (24.6)	198,183 (39.1)	0.31	1,778 (25.1)	103,947 (37.3)	0.26
35–39 years	525 (9.3)	87,545 (17.3)	0.24	677 (9.6)	55,294 (19.8)	0.29
40–44 years	75–79	14,330 (2.8)	0.10	136 (1.9)	10,843 (3.9)	0.12
45–49 years	<6	822 (0.2)	0.04	8 (0.1)	737 (0.3)	0.03
Multiparous	2,404 (42.6)	286,972 (56.6)	0.28	3,578 (50.6)	168,042 (60.2)	0.20
Neighbourhood income quintile (Q)						
Q1 (lowest)	1,087 (19.2)	99,363 (19.6)	0.01	1,714 (24.2)	55,992 (20.1)	0.10
Q2	1,122 (19.9)	100,684 (19.8)	0.00	1,537 (21.7)	55,288 (19.8)	0.05
Q3	1,244 (22.0)	108,677 (21.4)	0.01	1,394 (19.7)	58,100 (20.8)	0.03
Q4	1,222 (21.6)	110,038 (21.7)	0.00	1,365 (19.3)	59,694 (21.4)	0.05
Q5 (highest)	954 (16.9)	87,339 (17.2)	0.01	1,041 (14.7)	49,172 (17.6)	0.08
Missing	18 (0.3)	1,208 (0.2)	0.02	26 (0.4)	762 (0.3)	0.02
Rural residence						
Urban	4,463 (79.0)	456,131 (89.9)	0.30	5,814 (82.2)	249,007 (89.2)	0.20
Rural	1,176 (20.8)	50,663 (10.0)	0.30	1,247 (17.6)	29,637 (10.6)	0.20
Missing	8 (0.1)	515 (0.1)	0.01	16 (0.2)	364 (0.1)	0.02
Immigration status						
Long-term resident	4,889 (86.6)	334,523 (65.9)	0.50	6,562 (92.7)	231,299 (82.9)	0.30
Refugee	136 (2.4)	25,171 (5.0)	0.14	151 (2.1)	9,616 (3.4)	0.08
Family or economic class immigrant	622 (11.0)	147,615 (29.1)	0.46	364 (5.1)	38,093 (13.7)	0.29
History of violence	141 (2.5)	774 (0.2)	0.21	313 (4.4)	1,164 (0.4)	0.26
Stable chronic conditions	983 (17.4)	101,693 (20.0)	0.07	1,570 (22.2)	65,652 (23.5)	0.03
Unstable chronic conditions	630 (11.2)	54,534 (10.7)	0.01	1,083 (15.3)	37,580 (13.5)	0.05
Injury-specific variables						
≥2 TBI acute healthcare encounters	390 (0.1)	–	–	728 (0.3)	–	–
Most severe injury						
A hospitalization, discharged to facility	36 (0.0)	–	–	44 (0.0)	–	–
A hospitalization, discharged home	237 (0.0)	–	–	267 (0.1)	–	–
Emergency department visit only	5,374 (1.0)	–	–	6,766 (2.4)	–	–
≤2 years since most recent TBI acute healthcare encounter	1,372 (0.3)	–	–	1,623 (0.6)	–	–

(Continued)

Table 1. (Continued.)

Baseline characteristics	No history of mental illness			History of mental illness		
	TBI ^a (n = 5,647)	No TBI (n = 507,309)	Standardized difference ^b	TBI ^a (n = 7,077)	No TBI (n = 279,008)	Standardized difference ^b
Most recent TBI mechanism						
Motor vehicle collision	1,390 (0.3)	–	–	1,632 (0.6)	–	–
Struck by/against	2,296 (0.4)	–	–	2,985 (1.0)	–	–
Fall	1,724 (0.3)	–	–	2,087 (0.7)	–	–
Other	230–234	–	–	370–374	–	–
Missing	<6	–	–	<6	–	–
Most recent TBI intentional	260 (0.1)	–	–	571 (0.2)	–	–

^aIncludes individuals with a TBI recorded in 'the most responsible diagnosis' field in the 10 years before conception. Individuals TBI recorded outside of the 'most responsible diagnosis' field and those with injuries that often accompany TBI (n = 41,494) are excluded.

^bStandardized differences >0.10 indicate clinically meaningful differences between groups.

There is a considerable body of literature showing the lasting impacts of TBI on mental health, mostly from professional athlete and veteran samples primarily comprised of men (Perry *et al.*, 2016). Growing evidence shows mental health is affected even more often in women with TBI than men with TBI (Farace and Alves, 2000), underscoring the importance of sex and gender-based analyses of this association. Yet, despite the importance of the perinatal period in the life course of women, including the known elevated baseline risk of mental health concerns in this period (Howard and Khalifeh, 2020), very few studies have examined the risk of perinatal mental illness associated with TBI. In their study of 208 women, Colantonio *et al.* (2010) found that depression in the postpartum period was more commonly reported in women with TBI compared to those without TBI. However, the analysis did not account for a pre-pregnancy history of mental illness, nor did it examine prenatal mental illness or diagnoses other than depression. Our study adds to the literature by showing that, in a women without active mental illness going into pregnancy, those with TBI were at elevated risk of new-onset and recurrent mental illness both pre- and postnatally, and for a range of types of mental health disorders. Our analysis of injury-related risk factors for perinatal mental illness among women with TBI is also novel, showing patients with multiple TBIs might be at greatest risk. Other injury-related variables, such as time since injury, appeared to be less important after accounting for other factors, including violence.

The impact of TBI on perinatal mental health may be indirect or direct. TBI is associated with social and health disparities that carry risks for perinatal mental illness (Chan *et al.*, 2017; Haag *et al.*, 2016). One particularly important factor is violence (Howard *et al.*, 2013). Intimate partner violence is a leading cause of TBI in women, and injuries to the head, face and neck are the most common physical injuries in women affected by intimate partner violence (Haag *et al.*, 2022; Sheridan and Nash, 2007). Indeed, in our cohort, a history of violence was much more common in women with than without TBI. The strength of the relation between TBI and perinatal mental illness was reduced after controlling for violence, and, among women with TBI, intentional injuries were associated with a particularly high risk of perinatal mental illness. Together, these data show the importance of violence in the observed associations. However, after adjustment for this and other covariates, elevated risk of perinatal mental illness remained. Some of this remaining risk may be due to a

direct relation between TBI and perinatal mental illness. For example, TBI is associated with headaches, dizziness, reduced noise tolerance, irritability, sleep problems, and executive functioning and problem-solving difficulties (Kieffer-Kristensen and Teasdale, 2011; Mollayeva *et al.*, 2016; Pryor, 2004) that might be exacerbated perinatally when women have reduced opportunities for self-care and encounter additional stressors such as sleep deprivation. Perinatal hormonal fluctuations could also play a role (Brunton and Russell, 2010). Future studies should examine these potential mechanisms.

It is also important to note that the relationship between TBI and mental illness is likely bi-directional, with research showing TBI can lead to new-onset mental illness (Chan *et al.*, 2022a; Perry *et al.*, 2016; Yeh *et al.*, 2020), but may also be a consequence of pre-existing mental illness due to factors such as risk-taking behaviours and adverse life experiences (Liao *et al.*, 2012; McHugo *et al.*, 2017). While it is possible a history of mental illness could have preceded some cases of TBI in our cohort, it is notable that the relationship between TBI and perinatal mental illness persisted in women without any history of mental illness, and also increased with a rising number of prior TBI-related healthcare encounters, adding strength to the assertion that the perinatal period is a time of particular vulnerability for mental illness among women with a TBI.

Limitations

Our findings should be interpreted in the context of a few limitations. We examined TBI in the 'most responsible diagnosis' field, to capture incident, rather than existing, TBI. While this approach has a positive predictive value of 97% (Hedegaard *et al.*, 2016), we may have misclassified women with polytrauma, wherein a more severe injury was listed as the most responsible diagnosis. However, findings were similar in an additional analysis in which we examined TBI in any diagnostic field. Our reliance on acute care data to capture TBI likely resulted in the inclusion of more moderate to severe injuries; we may have misclassified TBI status and underestimated the occurrence of multiple TBIs in women who did not seek healthcare for their injury or who only received outpatient care. We also may have misclassified TBI status in women whose injuries occurred more than 10 years before conception, as Ontario's emergency department visit dataset only dates back

Table 2. Unadjusted and adjusted associations between TBI in the 10 years before conception and perinatal mental illness

	No history of mental illness (<i>n</i> = 512,956)			History of mental illness (<i>n</i> = 286,085)		
	<i>N</i> (%) with outcome	Unadjusted RR (95% CI)	Adjusted RR (95% CI) ^b	<i>N</i> (%) with outcome	Unadjusted RR (95% CI)	Adjusted RR (95% CI) ^b
Any perinatal mental illness						
No history of TBI	64,523 (12.7)	1.00 (Referent)	1.00 (Referent)	77,613 (27.8)	1.00 (Referent)	1.00 (Referent)
History of TBI ^a	1,047 (18.5)	1.46 (1.38–1.54)	1.31 (1.24–1.39)	2,512 (35.5)	1.27 (1.23–1.31)	1.18 (1.14–1.22)
Prenatal mental illness						
No history of TBI	22,825 (4.5)	1.00 (Referent)	1.00 (Referent)	30,724 (11.0)	1.00 (Referent)	1.00 (Referent)
History of TBI	350 (6.2)	1.38 (1.24–1.52)	1.31 (1.18–1.45)	983 (13.9)	1.26 (1.18–1.33)	1.20 (1.13–1.28)
Postpartum mental illness						
No history of TBI	41,698 (8.2)	1.00 (Referent)	1.00 (Referent)	46,889 (16.8)	1.00 (Referent)	1.00 (Referent)
History of TBI	697 (12.3)	1.50 (1.40–1.61)	1.31 (1.22–1.41)	1,529 (21.6)	1.28 (1.23–1.34)	1.17 (1.12–1.23)
Mood or anxiety disorder						
No history of TBI	59,012 (11.6)	1.00 (Referent)	1.00 (Referent)	72,484 (26.0)	1.00 (Referent)	1.00 (Referent)
History of TBI	976 (17.3)	1.48 (1.40–1.57)	1.34 (1.26–1.42)	2,320 (32.8)	1.25 (1.21–1.30)	1.18 (1.14–1.22)
Psychotic disorder						
No history of TBI	233 (0.0)	1.00 (Referent)	1.00 (Referent)	469 (0.2)	1.00 (Referent)	1.00 (Referent)
History of TBI	<6	**	**	24 (0.3)	2.01 (1.33–3.02)	1.65 (1.07–2.54)
Substance use disorder						
No history of TBI	1,072 (0.2)	1.00 (Referent)	1.00 (Referent)	2,349 (0.8)	1.00 (Referent)	1.00 (Referent)
History of TBI	28 (0.5)	2.33 (1.60–3.40)	1.04 (0.71–1.54)	149 (2.1)	2.49 (2.11–2.94)	1.41 (1.18–1.67)
Another mental illness						
No history of TBI	6,358 (1.3)	1.00 (Referent)	1.00 (Referent)	6,626 (2.4)	1.00 (Referent)	1.00 (Referent)
History of TBI	87 (1.5)	1.23 (0.99–1.52)	1.27 (1.02–1.58)	253 (3.6)	1.50 (1.32–1.70)	1.42 (1.25–1.61)
Self-harm						
No history of TBI	214 (0.0)	1.00 (Referent)	1.00 (Referent)	313 (0.1)	1.00 (Referent)	1.00 (Referent)
History of TBI	7 (0.1)	2.80 (1.25–6.25)	1.54 (0.72–3.29)	26 (0.4)	3.25 (2.18–4.86)	1.52 (0.99–2.33)

^aIncludes individuals with a TBI recorded in 'the most responsible diagnosis' field in the 10 years before conception. Individuals TBI recorded outside of the 'most responsible diagnosis' field and those with injuries that often accompany TBI (*n* = 41,494) are excluded.

^bAdjusted model controls for maternal age, parity, neighbourhood income quintile, rurality, immigrant status, history of violence, and stable and unstable chronic conditions.

**Suppressed due to small sample sizes <6.

to 2002. Further, we were unable to measure injury severity (e.g., using the Glasgow Coma Scale), an important limitation given such scores are predictive of later functional outcomes (Dos Reis Zuniga *et al.*, 2024).

Mental illness variables were captured in healthcare encounters in the publicly funded healthcare system. We may have under-ascertained perinatal mental illness for women who did not seek care for their symptoms, or who received private services (e.g., private psychologists). On the other hand, we may have over-ascertained perinatal mental illness by only requiring one outpatient visit (or one emergency department visit or hospital admission). Nevertheless, findings were similar using a more strict definition requiring two or more outpatient visits.

Finally, we had no information on race/ethnicity, gender identity, social supports and healthcare seeking behaviours. We

also likely underestimated experiences of violence. These factors may have influenced our results.

Implications

Perinatal mental illness is associated with significant adverse maternal, child and family outcomes, as well as healthcare costs (Moore *et al.*, 2021), highlighting the importance of prevention, timely identification and effective treatment. Our findings suggest women with TBI may be a high-risk group that could benefit from additional support to reduce their risk of perinatal mental illness. Such supports should start before conception and might include occupational therapy to optimize the management of TBI-related symptoms and other social risk factors, and mental health information for women planning a pregnancy. Perinatally,

Table 3. Injury-related factors associated with perinatal mental illness among women with a TBI in the 10 years before conception^a

	No history of mental illness (n = 512,956)			History of mental illness (n = 286,085)		
	N (%) with outcome	Unadjusted RR (95% CI)	Adjusted RR (95% CI) ^a	N (%) with outcome	Unadjusted RR (95% CI)	Adjusted RR (95% CI) ^a
Number of TBI acute healthcare encounters						
1	947 (18.0)	1.00 (Referent)	1.00 (Referent)	2,240 (35.3)	1.00 (Referent)	1.00 (Referent)
≥2	100 (25.6)	1.41 (1.17–1.71)	1.34 (1.12–1.61)	272 (37.4)	1.06 (0.96–1.18)	1.03 (0.93–1.14)
Most severe injury						
Emergency department visit only	1,010 (18.8)	1.00 (Referent)	1.00 (Referent)	2,395 (35.4)	1.00 (Referent)	1.00 (Referent)
A hospitalization	37 (13.6)	0.72 (0.53–0.97)	0.71 (0.52–0.97)	117 (37.6)	1.06 (0.91–1.24)	1.05 (0.90–1.22)
Time since most recent TBI acute healthcare encounter						
≥3 years	781 (18.3)	1.00 (Referent)	1.00 (Referent)	1,888 (34.6)	1.00 (Referent)	1.00 (Referent)
≤2 years	266 (19.4)	1.03 (0.91–1.17)	1.01 (0.89–1.15)	624 (38.4)	1.08 (1.01–1.16)	1.05 (0.98–1.13)
Most recent TBI mechanism						
Other	48 (20.5)	1.00 (Referent)	1.00 (Referent)	138 (37.2)	1.00 (Referent)	1.00 (Referent)
Struck by/against	450 (19.6)	0.94 (0.71–1.24)	0.93 (0.71–1.22)	1,038 (34.8)	0.93 (0.81–1.07)	0.93 (0.81–1.07)
Motor vehicle collision	265 (19.1)	0.92 (0.69–1.23)	0.96 (0.73–1.28)	564 (34.6)	0.93 (0.80–1.08)	0.95 (0.82–1.10)
Fall	284 (16.5)	0.80 (0.60–1.06)	0.81 (0.62–1.08)	772 (37.0)	0.99 (0.86–1.14)	1.00 (0.87–1.16)
Most recent TBI intent						
Unintentional/undetermined/other	988 (18.4)	1.00 (Referent)	1.00 (Referent)	2,280 (35.1)	1.00 (Referent)	1.00 (Referent)
Intentional	59 (22.7)	1.24 (0.98–1.58)	1.12 (0.86–1.47)	232 (40.6)	1.16 (1.04–1.29)	1.07 (0.95–1.21)

^aAdjusted model controls for maternal age, parity, neighbourhood income quintile, rurality, immigrant status, history of violence and stable and unstable chronic conditions.

additional preventive measures might include in-home support from public health nurses to help women compensate for executive functioning impairment and cope with sensory overload, as well as respite services to reduce sleep deprivation in women without adequate support. To facilitate early entry into treatment, women with TBI should be screened for mental illness antenatally and early in the postpartum period. Mental health interventions should be tailored to their needs. For example, given the relationship between violence and TBI (Haag *et al.*, 2022), trauma-informed care approaches may be beneficial (Sperlich *et al.*, 2017). Given many individuals with TBI experience treatment-resistant mental illness (Naraparaeddy *et al.*, 2020), knowledge of a history of TBI should be used to inform the types of therapies and medications used.

These efforts require that providers be aware of a woman's history of TBI. Providers should be educated about TBI with a sex and gender lens, as this has been identified as a gap in care (Hanafy *et al.*, 2022). Such training should include how to accommodate someone with a TBI and referral networks. This is necessary given reports from women of being dismissed by providers when reporting symptoms (Haag *et al.*, 2016). Toolkits such as the 'Battered and Brain Injured' toolkit provide education and resources on TBI and intimate partner violence (www.abitoolkit.ca).

These efforts require collaboration between rehabilitation and mental healthcare providers, suggesting the benefits of integrated

care approaches that promote coordinated, patient-centred care (Chan *et al.*, 2022b). This is particularly important as both TBI and mental health diagnoses can serve as exclusion criteria for many services.

Conclusion

In a large, population-based study, history of TBI was associated with increased risk of new-onset and recurrent mental illness in the perinatal period. These findings demonstrate the need for providers to be attentive to the risk for perinatal mental illness in women with a TBI. This population may benefit from mental illness preventive efforts, screening and tailored treatment options.

Supplementary material. The supplementary material for this article can be found at <https://doi.org/10.1017/S2045796025000150>.

Availability of data and materials. Data used for this study were housed at ICES, an independent not-for-profit corporation. The dataset used in this study is held securely in coded form at ICES. While the data sharing agreements that govern the dataset prohibit making it publicly available, access may be granted to those who meet specified criteria for confidential access. External individuals must apply for access through ICES' Data and Analytic Services (DAS), a division of ICES established to provide data and analytic services to 'third party researchers'. The dataset that approved third party researchers would be permitted to access would be adjusted to ensure the risk of re-identification of

any underlying individuals is low. Information about the application process, including the DAS Data Request Form and the criteria for access, including, for example, confirmation of approval by a Research Ethics Board, are available at <https://www.ices.on.ca/DAS/Submitting-your-request>. For general information visit www.ices.on.ca/DAS or email das@ices.on.ca.

Acknowledgements. Parts of this material are based on data and/or information compiled and provided by the Canadian Institute for Health Information (CIHI) and the Ontario Ministry of Health (MOH). However, the analyses, conclusions, opinions and statements expressed in the material are solely those of the authors, and do not reflect those of CIHI or MOH; no endorsement is intended or should be inferred. Parts or whole of this material are based on data and/or information compiled and provided by Immigration, Refugees and Citizenship Canada (IRCC) current to 11 August 2023. However, the analyses, conclusions, opinions and statements expressed in the material are those of the author(s), and not necessarily those of IRCC. This document used data adapted from the Statistics Canada Postal CodeOM Conversion File, which is based on data licensed from Canada Post Corporation, and/or data adapted from the Ontario Ministry of Health Postal Code Conversion File, which contains data copied under license from ©Canada Post Corporation and Statistics Canada. This does not constitute an endorsement by Statistics Canada of this product.

Financial support. This study was supported by ICES, which is funded by an annual grant from the Ontario Ministry of Health (MOH) and the Ministry of Long-Term Care (MLTC). The research reported in this publication was supported by the Canadian Institutes of Health Research under award # FRN173436. This research was undertaken, in part, thanks to funding from the Canada Research Chairs Program to Dr. Hilary K. Brown (CRC-2019-00158), Dr. Tatyana Mollayeva (CRC-2021-00074) and Dr. Angela Colantonio (CRC-2019-00019). The analyses, conclusions, opinions and statements expressed herein are solely those of the authors and do not reflect those of the funding; no endorsement is intended or should be inferred.

Competing interests. Eyal Cohen reports paid membership on the Committee to Evaluate Drugs, which advises Ontario's Ministry of Health on public drug policy. Natasha Saunders receives an honorarium from the BMJ Group (Archives of Disease in Childhood). Simone N. Vigod receives royalties from UpToDate for authorship of materials on depression and pregnancy.

Ethical standards. ICES is a prescribed entity under Ontario's Personal Health Information Protection Act (PHIPA). Section 45 of PHIPA authorizes ICES to collect personal health information, without consent, for the purpose of analysis or compiling statistical information with respect to the management of, evaluation or monitoring of, the allocation of resources to or planning for all or part of the health system. Projects that use data collected by ICES under section 45 of PHIPA, and use no other data, are exempt from research ethics board review. The use of the data in this project is authorized under section 45 and approved by ICES' Privacy and Legal Office.

References

- Austin PC (2009) Using the standardized difference to compare the prevalence of a binary variable between two groups in observational research. *Communications in Statistics – Simulation and Computation* **38**, 1228–1234.
- Brown HK, Strauss R, Fung K, Mataruga A, Chan V, Mollayeva T, Urbach N, Colantonio A, Cohen E, Dennis CL, Ray JG, Saunders N and Vigod SN (2024) Mental illness in the 2 years prior to pregnancy in a population with traumatic brain injury: A cross-sectional study. *Canadian Journal of Psychiatry* **69**, 607–617.
- Brown HK, Wilton D, Ray J, Dennis CL, Guttman A and Vigod S (2019) Chronic physical conditions and risk for perinatal mental illness: A population-based retrospective cohort study. *PLoS Medicine* **16**, e1002864.
- Brunton PJ and Russell JA (2010) Endocrine induced changes in brain function during pregnancy. *Brain Research* **1364**, 198–215.
- Centers for Disease Control and Prevention (2015) *ICD-9 Framework for Presenting Injury Mortality Data*. Atlanta: Centers for Disease Control and Prevention.
- Chan V, Marcus L, Burlic D, Mann RE, Toccalino D, Cusimano MD, Ilie G and Colantonio A (2022a) Social determinants of health associated with psychological distress stratified by lifetime traumatic brain injury status and sex: Cross-sectional evidence from a population sample of adults in Ontario, Canada. *PLoS One* **17**, e0273072.
- Chan V, Mollayeva T, Ottenbacher KJ and Colantonio A (2017) Clinical profile and comorbidity of traumatic brain injury among younger and older men and women: A brief research notes. *BMC Research Notes* **10**, 371.
- Chan V, Toccalino D, Omar S, Shah R and Colantonio A (2022b) A systematic review on integrated care for traumatic brain injury, mental health, and substance use. *PLoS One* **17**, e0264116.
- Colantonio A, Mar W, Escobar M, Yoshida K, Velikonja D, Rizoli S, Cusimano M and Cullen N (2010) Women's health outcomes after traumatic brain injury. *Journal of Women's Health* **19**, 1109–1116.
- Dos Reis Zuniga RD, de Cassia Almeida Vieira R, Fontoura Solla DJ, Godoy DA, Kolias A, de Amorim RLO, de Andrade AF, Teixeira MJ and Paiva WS (2024) Long-term outcome of traumatic brain injury persists with initial GCS of 3–5. *World Neurosurgery: X* **23**, 100361.
- Farace E and Alves WM (2000) Do women fare worse: A meta-analysis of gender differences in traumatic brain injury outcome. *Journal of Neurosurgery* **93**, 539–545.
- Haag HL, Caringal M, Sokoloff S, Kontos P, Yoshida K and Colantonio A (2016) Being a woman with acquired brain injury: Challenges and implications for practice. *Archives of Physical Medicine and Rehabilitation* **97**, S64–S70.
- Haag HL, Jones D, Joseph T and Colantonio A (2022) Battered and brain injured: Traumatic brain injury among women survivors of intimate partner violence: A scoping review. *Trauma, Violence, & Abuse* **23**, 1270–1287.
- Hanafy S, Amodio V, Haag HL, Colquhoun H, Lewko J, Quilicio E, Riopelle R, Archambault P, Colantonio A, Lindsay S and Mollayeva T (2022) Is it prime time for sex and gender considerations in traumatic brain injury? Perspectives of rehabilitation care professionals. *Disability & Rehabilitation* **44**, 684–692.
- Hedegaard H, Johnson RL, Warner M and Chen L-H (2016) Proposed framework for presenting injury data using the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnosis codes. *National Health Statistics Report* **22**, 1–20.
- Howard LM and Khalifeh H (2020) Perinatal mental health: A review of progress and challenges. *World Psychiatry: Official Journal of the World Psychiatric Association (WPA)* **19**, 313–327.
- Howard LM, Oram S, Galley H, Trevillion K and Feder G (2013) Domestic violence and perinatal mood disorders: Systematic review and meta-analysis. *PLoS Medicine* **10**, e1001452.
- Johns Hopkins Bloomberg School of Public Health (2009) *The Johns Hopkins CGH System: Technical Reference Guide Version 9.0*. Baltimore: Johns Hopkins Bloomberg School of Public Health.
- Kieffer-Kristensen R and Teasdale TW (2011) Parental stress and marital relationships among patients with brain injury and their spouses. *Neuro Rehabilitation* **28**, 321–330.
- Kingston D and Tough S (2014) Prenatal and postpartum maternal mental health and school-age child development: A systematic review. *Maternal & Child Health Journal* **18**, 1728–1741.
- Langlois JA, Rutland-Brown W and Wald MM (2006) The epidemiology and impact of traumatic brain injury: A brief overview. *Journal of Head Trauma Rehabilitation* **21**, 375–378.
- Liao CC, Chiu WT, Yeh CC, Chang HC and Chen L (2012) Risk and outcomes for traumatic brain injury in patients with mental disorders. *Journal of Neurology, Neurosurgery & Psychiatry* **83**, 1186–1192.
- McHugo GJ, Krassenbaum S, Donley S, Corrigan JD, Bogner J and Drake RE (2017) The prevalence of traumatic brain injury among people with co-occurring mental health and substance use disorders. *Journal of Head Trauma Rehabilitation* **32**, E65–E74.
- Meltzer-Brody S and Stuebe A (2014) The long-term psychiatric and medical prognosis of perinatal mental illness. *Best Practice and Research: Clinical Obstetrics and Gynaecology* **28**, 49–60.

- Mollaveya T, Mollaveya S and Colantonio A** (2016) The risk of sleep disorder among persons with mild traumatic brain injury. *Current Neurology and Neuroscience Reports* **16**, 55.
- Moore JE, McLemore MR, Glenn N and Zivin K** (2021) Policy opportunities to improve prevention, diagnosis, and treatment of perinatal mental health conditions. *Health Affairs* **40**, 1534–1542.
- Naraparaeddy BR, Narapareddy L, Lin A, Wigh S, Nanavati J, Dougherty J, Nowrangi M and Roy D** (2020) Treatment of depression after traumatic brain injury: A systematic review focused on pharmacological and neuromodulatory interventions. *Psychosomatics*, **61**(5), 481–497.
- O'Hara MW and Wisner KL** (2014) Perinatal mental illness: Definition, description and aetiology. *Best Practice and Research: Clinical Obstetrics and Gynaecology* **28**, 3–12.
- Perry DC, Sturm VE, Peterson M, Piper CF, Bullock T, Boeve BF, Miller BL, Guskiewicz KM, Berger MS, Kramer JH and Welsh-Bohmer KA** (2016) Association of traumatic brain injury with subsequent neurological and psychiatric disease: A meta-analysis. *Journal of Neurosurgery* **124**, 511–526.
- Pryor J** (2004) What environmental factors irritate people with acquired brain injury? *Disability & Rehabilitation* **26**, 974–980.
- Public Health Agency of Canada** (2020) *Injury in Review, 2020 Edition: Spotlight on Traumatic Brain Injuries across the Life Course*. Ottawa: Public Health Agency of Canada.
- Saunders NR, Plumtre L, Diong C, Gandhi S, Schull M, Guttman A and Paterson JM** (2021) Acute care visits for violence and maltreatment before vs. during the COVID-19 pandemic in Ontario, Canada. *JAMA Health Forum* **2**, e211983.
- Sheridan DK and Nash KR** (2007) Acute injury patterns of intimate partner violence victims. *Trauma, Violence, & Abuse* **8**, 281–289.
- Sperlich M, Seng JS, Li Y, Taylor J and Bradbury-Jones C** (2017) Integrating trauma-informed care into maternity care practice: Conceptual and practical issues. *Journal of Midwifery & Women's Health* **62**, 661–672.
- Thurman DJ, Alverson C, Dunn KA, Guerrero J and Sniezek JE** (1999) Traumatic brain injury in the United States: A public health perspective. *Journal of Head Trauma Rehabilitation* **14**, 602–615.
- von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC and Vandenbroucke JP STROBE Initiative** (2008) The Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies. *Journal of Clinical Epidemiology* **61**, 344–349.
- Warwick J, Slavova S, Bush J and Costich J** (2020) Validation of ICD-10-CM surveillance codes for traumatic brain injury inpatient hospitalizations. *Brain Injury* **34**, 1763–1770.
- Williams JI and Young WA** (1996) *Summary of Studies on the Quality of Health Care Administrative Databases in Canada*. Ottawa: Canadian Medical Association.
- World Health Organization** (2006) *Neurological Disorders: Public Health Challenges*. Geneva: World Health Organization.
- Yang K, Wu J and Chen X** (2022) Risk factors for perinatal depression in women: A systematic review and meta-analysis. *BMC Psychiatry* **22**, 63.
- Yeh T-C, Chien W-C, Chung C-H, Lian C-S, Chang H-A, Kao Y-C, Yeh HW, Yang YJ and Tzeng NS** (2020) Psychiatric disorders after traumatic brain injury: A nationwide population-based cohort study and the effects of rehabilitation therapies. *Archives of Physical Medicine and Rehabilitation* **101**, 822–831.
- You JJ, Alter DA, Stukel TA, McDonald SD, Laupacis A, Liu Y and Ray JG** (2008) Proliferation of prenatal ultrasonography. *Canadian Medical Association Journal* **182**, 143–151.
- Zou G** (2004) A modified Poisson regression approach to prospective studies with binary data. *American Journal of Epidemiology* **159**, 702–706.
- Zou G and Donner A** (2013) Extension of the modified Poisson regression model to prospective studies with correlated binary data. *Statistical Methods in Medical Research* **22**, 661–670.