Severe maternal morbidity and mental health-related hospitalizations or emergency department visits after delivery: A nation-wide study in Canada

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Abstract

Background: Severe maternal morbidity (SMM) is a composite of near-fatal events occurring during pregnancy or the puerperium. SMM is known to cause significant physical and emotional trauma, resulting in both short-term and long-term health complications. Short term psychological complications of SMM range from depressive symptoms to psychiatric admission or prescription medication for mental illness. SMM subtypes like severe pre-eclampsia have been associated with long term outcomes of severe mental illness, including psychiatric admission for depression. It is plausible that composite SMM is also associated with long-term severe mental health outcomes, including mental-health related hospitalization or emergency department visits.

Objectives and hypotheses: The primary objective is to assess for an association between any SMM in the first recorded birth, with hospitalization or ED visit for mental illness up to 13 years after the index birth hospitalization, as compared to no SMM in the first recorded birth.

Methods: Using data from the Canadian Institute of Health Information Discharge Abstract Database (DAD) and the National Ambulatory Care Reporting System (NACRS) we performed a longitudinal cohort study of 2,112,518 Canadian postpartum individuals aged 18-55 years with a first recorded hospital birth between April 1, 2008 and March 31, 2021. The primary study outcome was a composite of mental health-related hospitalization and/or ED visits occurring 43 days or more after the index birth hospitalization. The composite was defined by an ICD-10-CA code for a mood or anxiety disorder, substance-related or addictive disorder, schizophrenia spectrum or other psychotic disorder, or suicidality or self-harm event We used univariable and multivariable Cox regression models to generate crude and adjusted hazard ratios (HRs).

Results: A total of 2,112,518 individuals gave birth over the study period; after exclusions, our analytic cohort included 35,825 SMM-affected individuals and 1,543,567 were non SMM-affected individuals (mean age 29.7±5.4 and 30.7 ±6.0, respectively). SMM-affected individuals were more likely to be older, to deliver pre-term, to have a stillbirth, to have a cesearean section, and to have experienced a non-severe hypertensive disorder of pregnancy or gestational diabetes compared with individuals who did not have an SMM. Overall, 43,066 individuals had a mental health-related hospitalization or ED visit (73.2 per 10 000); among these, 1287 had a recorded SMM (96.1 per 1000), and 41 779 did not (72.7 per 1000) (crude HR 1.31 [95% CI 1.24-1.39]). After adjustment for delivery year, comorbidity, maternal age, urban or rural residential status and income quintile, the adjusted HR was 1.26 (95% 1.19-1.34.

Conclusion: Results from this study suggest a relationship between composite SMM and long-term mental health-related hospitalization or ED visit. As pregnancy complications become increasingly prevalent in Canada, it is increasingly crucial to understand the association between these events and adverse mental health outcomes. Given the disruptive nature of severe obstetric complications, and the potential for long-term mental health complications, it is important to extend clinical monitoring for these conditions among postpartum individuals beyond the first year postpartum.

Resume

Contexte : La morbidité maternelle grave (MMS) est un ensemble d'événements quasi mortels survenant pendant la grossesse ou la puerpéralité. On sait que la MMS provoque un traumatisme physique et émotionnel important, entraînant des complications sanitaires à court et à long terme. Les complications psychologiques à court terme du SMM vont des symptômes dépressifs à l'admission en psychiatrie ou à la prescription de médicaments pour une maladie mentale. Des sous-types de MMS, comme la pré-éclampsie sévère, ont été associés à des résultats à long terme de maladie mentale sévère, y compris l'admission en psychiatrie pour dépression. Il est plausible que le SMM composite soit également associé à des conséquences à long terme sur la santé mentale, y compris des hospitalisations liées à la santé mentale ou des visites aux urgences.

Objectifs et hypothèses : L'objectif principal est d'évaluer l'existence d'une association entre tout SMM lors de la première naissance enregistrée et une hospitalisation ou une visite aux urgences pour maladie mentale jusqu'à 13 ans après l'hospitalisation de la naissance index, par rapport à l'absence de SMM lors de la première naissance enregistrée.

Méthodes : À l'aide des données de la Base de données sur les congés des patients (BDCP) de l'Institut canadien d'information sur la santé et du Système national d'information sur les soins ambulatoires (SNISA), nous avons réalisé une étude de cohorte longitudinale portant sur 2 112 518 Canadiennes âgées de 18 à 55 ans ayant accouché pour la première fois à l'hôpital entre le 1er avril 2008 et le 31 mars 2021. Le principal résultat de l'étude était un composite d'hospitalisations liées à la santé mentale et/ou de visites aux urgences survenant 43 jours ou plus après l'hospitalisation de l'accouchement index. Le composite était défini par un code CIM-10-CA pour un trouble de l'humeur ou de l'anxiété, un trouble lié à une substance ou une dépendance, le spectre de la schizophrénie ou un autre trouble psychotique, ou un événement de suicidalité ou d'automutilation. Nous avons utilisé des modèles de régression de Cox univariables et multivariables pour générer des rapports de risque bruts et ajustés (HR).

Résultats : Au total, 2 112 518 personnes ont donné naissance au cours de la période d'étude ; après exclusion, notre cohorte analytique comprenait 35 825 personnes affectées par le SMM et 1 543 567 personnes non affectées par le SMM (âge moyen 29,7±5,4 et 30,7 ±6,0, respectivement). Les personnes affectées par le SMM étaient plus susceptibles d'être plus âgées, d'accoucher avant terme, d'avoir une mortinaissance, d'avoir une césarienne et d'avoir souffert d'une hypertension non sévère pendant la grossesse ou d'un diabète gestationnel que les personnes qui n'étaient pas affectées par le SMM. Globalement, 43 066 personnes ont été hospitalisées ou se sont rendues aux urgences pour des raisons de santé mentale (73,2 pour 10 000) ; parmi elles, 1 287 avaient un SMM enregistré (96,1 pour 1 000) et 41 779 n'en avaient pas (72,7 pour 1 000) (HR brut 1,31 [IC à 95 % 1,24-1,39]). Après ajustement pour l'année d'accouchement, la comorbidité, l'âge maternel, le statut résidentiel urbain ou rural et le quintile de revenu, le HR ajusté était de 1,26 (95 % 1,19-1,34).

Conclusion : Les résultats de cette étude suggèrent une relation entre le SMM composite et l'hospitalisation à long terme liée à la santé mentale ou la visite à l'urgence. Les complications de la grossesse devenant de plus en plus fréquentes au Canada, il est de plus en plus crucial de comprendre l'association entre ces événements et les effets néfastes sur la santé mentale. Compte tenu de la nature perturbatrice des complications obstétricales graves et du risque de complications à long terme sur le plan de la santé mentale, il est important d'étendre la surveillance clinique de ces conditions chez les personnes en post-partum au-delà de la première année post-partum.

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Preface and Contributions of the Authors

This thesis was written following the manuscript-based thesis guidelines. I performed the literature review, established the methods and design, analyzed, and interpreted the data, and wrote the manuscript.

Drs. Natalie Dayan, Robert Platt and Ugochinyere Vivian Ukah assisted and supervised with the development of study design, statistical analyses, interpretation of data, and critical revision and editing of the manuscript. Dr. Gabriel Shapiro provided statistical and content expertise throughout the study development and data analysis. Dr. Xiangfei Meng assisted with the editing of the manuscript and critical revision. Drs. Sarka Lisonkova, Natalie Auger, Joel G. Ray, Isabelle Malhamme and Darine El-Chaâr are co-authors on the manuscript and provided expert advice on the theoretical aspects of the study, interpreted data and will revise the manuscript for important intellectual content. They did not contribute to my thesis as committee members. Dr. Dayan acquired the funding for this study.

Introduction

Severe maternal morbidity (SMM)- a composite of potentially life-threatening conditions and clinical interventions indicative of a near-fatal event during pregnancy or up to 42 days postpartum- is currently estimated to occur in 1.5% of Canadian births.[1–3] Typically, SMM includes serious maternal complications like severe pre-eclampsia, obstetric hemorrhage, sepsis, which are identified by International Classification of Disease (ICD) codes in administrative data.[3] It is likely that SMM will become increasingly prevalent in the years to come, in response to trends among reproductive age individuals, including delayed childbearing, the rising prevalence of obesity and associated cardiometabolic comorbidities, and the use of assisted reproductive technologies.[4–7]

Severe pregnancy complications are known to be traumatic events, which can affect both physical and psychological long-term health. Composite SMM and SMM subtypes have been associated with a variety of physical complications, ranging from short to long-term including an increased risk of premature mortality and all-cause and cardiovascular rehospitalization.[8,9] Notably, severe pre-eclampsia- one of the more prevalent SMM subtypes- has been associated with negative short- and long-term mental health conditions ranging from depressive symptoms to more severe outcomes.[10] On the other hand, two studies found null associations between postpartum hemorrhage and adverse mental health, demonstrating the variation in the nature of the relationships between severe pregnancy complications and mental health conditions.[11,12] Nonetheless, composite SMM has been associated with hospitalization and prescription for mental health conditions, including depression, anxiety and psychosis, up to the first postpartum year.[13,14] Information about the long-term mental health implications of individual morbidity-types and overall SMM is lacking. This data is particularly lacking in the Canadian context, despite how potentially informative it is for clinical postpartum care pathways and surveillance approaches.

Therefore, the overall aim of this thesis is to measure the associations between overall SMM and prevalent SMM types and mental health conditions, in a population-based cohort of Canadian deliveries.

Background

1. Severe Maternal Morbidity

1.1 What is SMM?

Severe maternal morbidity (SMM) is a term referring to life-threatening pregnancy complications that would have resulted in death, if not for chance or timely clinical care. SMM was first conceptualized as a population health metric for pregnant and postpartum people in response to declining mortality rates in industrialized countries and has evolved through a delphi process for the purposes of maternal health surveillance. [15,16]

Today, SMM is measured by most maternal surveillance programmes. There are slight international variations in the operational definitions used for SMM, despite an early World Health Organization (WHO) proposal of 25 standardized clinical, laboratory and management criteria to identify near miss cases.[15] In some developing countries, the utility of the WHO criteria is limited by inadequate laboratory resources. Therefore, several studies examining SMM in the Global South have excluded the laboratory criteria and adjusted the threshold for blood transfusion from the WHO definition [3,17,18]

In contrast, in the Global North, SMM definitions are typically operationalized by diagnostic and procedural codes in hospital discharge abstracts using administrative health data. However, variability still exists among these definitions due to efforts to optimize surveillance across different healthcare systems, and a lack of consensus among perinatal experts about which indicators truly reflect a dire maternal health situation in all circumstances. In addition, public health agencies intermittently refine their SMM definitions in their efforts to accurately capture SMM. In the United States, published guidelines from the Centres for Disease Control (CDC) have defined SMM by a composite of 18 indicators.[3,19] In Australia, experts have developed and validated a composite SMM definition of 14 diagnoses and 11 procedures.[20] The Canadian definition has evolved to the currently used 44-indicator composite through rigorous formal assessment by the Canadian Perinatal Surveillance System branch of the Public Health Agency of Canada. In Canada, SMM includes events occurring during pregnancy, at birth or within 42 days of delivery that are associated with a high case fatality rate and/or prolonged hospital stay (>7 days). [2]

1.2 Incidence

Despite the aforementioned variation across definitions, temporal trends consistently indicate that SMM is increasing in the Global North. [2,4,19] In Canada, the incidence of SMM increased about 7% between fiscal years 2003/2004 and 2016/2017, when it was calculated at 15.2 per 1,000 births (95% CI 15.9−16.3). [21–24] In the United States, the SMM rate was 14 per 1,000 deliveries in 2014- nearly 200% greater than the rate in 1993. [25] Similarly, studies in Australia demonstrate that the incidence of SMM events has increased by about 15% between 2001 and 2017. [26] Surveillance conducted across these and other countries in the Global North indicates that hypertensive and hemorrhagic morbidities are often the most prevalent conditions, and blood transfusion tends to be the most prevalent intervention. It remains unclear whether the variability in reported SMM rates is solely a reflection of the differences in monitoring and reporting these events, or if this variation is also related to different practices or patient populations leading to different outcomes. [21,2526]

1.3 The Canadian context for SMM

As mentioned, formal surveillance of SMM in Canada is led by the Canadian Perinatal Surveillance System (CPSS) since 2004. [27] SMM was first defined by a list of maternal conditions associated with maternal critical

illness, associated with prolonged maternal hospitalization or with high case fatality rates as agreed by expert clinicians. [27] This definition was refined through formal assessments and expanded to include severe pre-eclampsia and Hemolysis and Elevated Liver enzymes and Low Platelets (HELLP). Today, SMM comprises 44 indicators which are grouped by etiology, use of specific procedures, or by organ system into 13 general subtypes (severe preeclampsia, HELLP syndrome, and eclampsia; severe hemorrhage; maternal ICU admission; surgical complications; hysterectomy; sepsis; embolism, shock, and disseminated intravascular coagulation (DIC); assisted ventilation; cardiac conditions; acute renal failure; severe uterine rupture; cerebrovascular accidents; and other SMM).[2] The SMM indicators are identified using 76 diagnosis codes (International Classification of Diseases and Related Health Problems, 10th Revision (ICD-10CA)), 24 intervention codes (the Canadian Classification of Health Interventions (CCI)), and three variables specifically collected by the Canadian Institute for Health Information. The composite definition has been validated against maternal data in the Canadian Institute of Health Information (CIHI) Discharge Abstract Database (DAD) by KS Joseph and colleagues, revealing high sensitivities and high specificities, especially for diagnoses like postpartum hemorrhage and interventions including transfusions. [2,28]

1.4 Adverse sequelae of SMM

SMM has been linked to several health complications occurring up to decades after delivery. Survivors of SMM have twice (95% CI: 1.87–2.23) the risk of rehospitalization in the first postpartum year and are also more likely to experience heart failure and venous and arterial thromboembolic events up to 26 months postpartum, than those without SMM. [29–31] Long-term cardiovascular dysfunction is also associated with SMM; in particular, survivors of hemorrhagic, cardiovascular and hypertensive SMM types are at increased risk of heart disease and cardiomyopathy more than a decade postpartum [32,33] At extremes, these individuals have 77% (95% CI: 72%–82%) higher risk of cardiovascular hospitalization up to 31 years postpartum. [9] Most importantly, those who experience SMM have 189% (95% CI 93%-333%) greater risk of cardiovascular-specific mortality and 18% greater risk of all-cause mortality up to 29 years postpartum. [8,34]

In addition, as survivors of critical illness, SMM-affected individuals often experience some form of disability in the aftermath of SMM as these events compromise functional ability. In fact, individuals have reported compromised mobility, sexual function and health status after SMM, as well as limited ability to perform basic activities of daily living up to six months postpartum.[35,36]

2. Perinatal mental health

2.1 Epidemiology of postpartum mental illness

Childbirth, and ensuing social changes associated with the early stages of parenthood can present emotional and psychological challenges. [37] The perinatal period is characterized by fluctuations of estradiol and progesterone, which may affect neurotransmitters such as serotonin, GABA, dopamine and norepinepherine. [38–43] Exposure to trauma, acute and chronic stress and reproductive hormones all result in the upregulation of cortisol and pro-inflammatory cytokines, potentially leading to overall dysregulation of both the hypothalamic-pituitary axis (HPA) and the hypothalamic-pituitary-gonadal (HPG) axis. These rapid psychophysiological changes are strongly implicated in the pathogenesis of postpartum mental health disorders, particularly postpartum depression (PPD), anxiety and postpartum psychosis. [44,45] Additionally, genetics and history of mental illness are pivotal risk factors due to the heritability associated with postpartum mental illness, and the propensity for one disorder to trigger

others. [46–48] Functional ability is a crucial mediator of postpartum mental illness, as impaired functioning is often associated with increased severity of postpartum mental health conditions, especially in relation to an individual's ability to care for the infant. [49]

It is common for individuals to experience some form of emotional disturbance after childbirth. In fact, up to 50% of postpartum individuals will experience transient postpartum blues, while around 17% of postpartum individuals report experiencing depressive symptoms, and approximately 10% report symptoms of anxiety. [50–54]However, for a subset of postpartum individuals, this emotional disturbance can progress to more serious mental health complications. Postpartum psychosis, a rare but serious mental health complication often requiring hospitalization occurs in 0.089 to 2.6 per 1000 births. [55,56] Suicidal ideation is a symptom of many mental health disorders, impacting up to 12% (95% CI 11–14) of pregnant and postpartum individuals globally. [46,57] This is critical, because estimates show that 13-36% of maternal deaths in the first postpartum year can be attributed to suicide. [58–61] The prevalence of postpartum substance abuse remains unclear, however a systematic review of alcohol and illicit drug use among postpartum women indicated that the prevalence of postpartum alcohol use ranges from 30.1%–49%, while the prevalence of postpartum drug use is approximately 4.5%–8.5%. [47]

2.2 Diagnostic approaches to postpartum mental illness

Researchers and clinicians use three main approaches to identify postpartum mental illness along a spectrum of severity. The gold standard definition is derived from a detailed clinical interview and using diagnostic criteria from the Diagnostic and Statistical Management (DSM). In research, self-reported symptoms are often sought using validated screening tools and mental health conditions are positively identified based on validated cut-off scores. Cases of mental illness can also be identified for research by case defining algorithms - a combination of hospital discharge abstracts, emergency department visits, outpatient mental health visits and/or pharmacy data found in administrative datasets.

2.2.1 Definitions of mental health disorders using administrative health data

Mental health conditions can be identified by ICD codes in physician billing codes and hospital discharge abstracts. A recent systematic review exclusively based on the DAD tested the validity of five existing definitions for depression from Alaghehbandan et al, Noyes et al and Singh et al, as well as six increasingly inclusive definitions developed by these authors. [62 63–65] All newly developed definitions were at least 99% specific with positive predictive values (PPV) of at least 89% and negative predictive values (NPV) of at least 91%. [62]. All definitions reported higher sensitivities in ICD-10(34.2-35.6%) than ICD-9 (28.9-32.9%). Another study by Doktorchik examined six case defining algorithms for depression against chart review by medical abstractors. According to Doktorchik and colleagues,[66] the most valid DAD-based algorithm was 2 depression claims within a one-year period, or one hospitalization with a depression diagnosis.[66]

There have been very few attempts to validate definitions for mental health conditions beyond depression. Kurdyak and colleagues tested four algorithms for schizophenia spectrum disorders. In this study, the most valid defining algorithm for schizophrenia, schizoaffective disorder and psychosis not otherwise specified (NOS) was hospitalization or 3 medical doctor (MD) visits within 36 months. This definition reported a 98.8% sensitivity (95% CI 96.5-100), 49% specificity (95% CI 42-56), a PPV of 45.7% (95% CI 38.5-58) and a NPV of 99.0% (95% CI 97.0-100). One of the only attempts at validating a definition for suicide attempts and deliberate self-harm was a study by Randall that compared the validity of ICD-10 codes for intentional self-harm, self-harm of

undetermined intent and accidental poisonings from hospital discharge data against clinical assessment using the Columbia Classification Algorithm of Suicide Assessment.[67]

3. Associations between SMM and mental illness

3.1. Pregnancy complications and short-term postpartum metal health conditions

Inquiry into the relationship between overall SMM and mental illness is still nascent. However, existing research supports a possible association between various pregnancy complications and mental health conditions after delivery. One such study including 180 participants examined de novo PPD, defined as a score of 10 or more on the Edinburgh Postnatal Depression Scale (EDPS). According to this study, the odds of new-onset PPD are approximately three times greater in individuals with pre-eclampsia and almost four times higher in individuals with severe pre-eclampsia, compared to individuals with normal pregnancies.[68] Eckerdal and colleagues examined the odds of self-reported PPD at 6 weeks postpartum after postpartum hemorrhage, in a cohort of 446 Swedish individuals. These researchers found that individuals with severe postpartum hemorrhage (defined as blood loss of >= 1000 mL) had 81% (95% CI 0.91–3.57) greater odds of PPD, identified by >=12 on the EDPS but reported wide confidence intervals that crossed the null. [12]. Notably, these two studies have been constrained by small sample sizes.

On the other hand, another study by Liu and colleagues found a null association between postpartum haemorrhage and PPD up to the first year postpartum [69]. This study included 486,722 full-term pregnancies and defined PPD as an ICD code for depression or postpartum depression in outpatient or inpatient hospitalization records or an outpatient prescription for an antidepressant. Though this study has a large sample size, the authors did not account for comorbidity or socioeconomic status- two major confounders of this relationship.

We know of only two existing administrative data studies that examined mental illness after composite SMM, although they examined short-term outcomes and neither of them use Canadian data. [13,14]Lewkowitz and colleagues performed a retrospective cohort study of 1 229 835 pregnancies in the US to determine the risk of ED presentation or readmission to an inpatient hospital for psychiatric illness after SMM. This study demonstrated that individuals who experience SMM have 74% (95% CI 58% – 91%) greater odds of composite psychiatric morbidity (inpatient admission or ED visit for suicide attempt, depression, anxiety, post-traumatic stress disorder, psychosis, acute stress reaction, or adjustment disorder) up to a year after discharge. However, the SMM definition is limited to events during the delivery hospitalization. [13]

Similarly, a study of 699,236 deliveries in Sweden demonstrated that individuals who experience SMM have significantly greater odds of being treated for a psychiatric disorder (aOR 1.22 [95% CI 1.03–1.45]) and being prescribed psychotropic medications (aOR 1.40[95% CI 1.24–1.58]) in the first postpartum year. Specifically, they found greater odds of treatment for neuroses (aOR 1.35[95% CI 1.09–1.69]) and having a prescription for anxiolytics/hypnotics (aOR 1.36[95% CI 1.18–1.58]) or antidepressants (aOR 1.35 [95% CI 1.17–1.55]).[14] However, it is possible that uncontrolled confounding is present in these estimates because this study did not exclude individuals with previous mental illness or adjust for comorbidity or other relevant perinatal factors.

3.2. SMM and long-term postpartum mental health conditions

The demonstrated focus on short term outcomes fuels persisting uncertainty about the long-term impact that SMM may have on mental health. However, existing research suggests that common SMM subtypes like severe pre-eclampsia and obstetric hemorrhage are associated with long-term psychological sequelae. Parry-Smith and colleagues examined the association between SMM and mental health conditions, identified by ICD codes in

administrative data, in a cohort of 42,327 deliveries from England. These researchers found that postpartum hemorrhage is associated with a 10% increase in the risk of postnatal depression (95%CI: 1%-21%) up to 7 years postpartum but did not find any significant relationship with anxiety or severe mental illness. These researchers adjust for hypertensive disorders but did not account for other comorbidities and include teens in their analysis, potentially introducing bias.[70]

Likewise, a prospective cohort study of 1,210,963 Quebec deliveries in administrative data by Auger and colleagues found that pre-eclampsia was associated with 16% (95% CI 9%-23%) greater risk of depression hospitalization up to 28 years after delivery, compared to no pre-eclampsia. [10] Notably, they also demonstrated that the risk varies according to time after delivery- in this study, risks were more pronounced after the first year postpartum. However, these researchers include multiple gestation as a confounder in analyses, which many regard to be an effect modifier of the relationship.

The long-term psychological consequences of SMM are less well studied. A more refined understanding of trajectories of mental health over time and across provinces can enable the planning of appropriate mental health services and programmes for high-risk groups. Big data provides large sample sizes to evaluate rare mental health conditions and enables the analysis of regional and temporal trends. To address these gaps, we undertook this population-based cohort study within Canada to examine the association between SMM and mental-health related hospitalizations or ED visits over a 13-year period.

Summary and rationale for current study

Rates of SMM have been increasing, partially due to the increasing number of individuals with comorbid conditions in their reproductive ages. SMM can be seen as a traumatic experience which may result in hyperactivation of stress response pathways, ultimately causing lasting negative health outcomes. [5,71–75] SMM – both as a composite and as individual subtype - have been associated with physical complications in the immediate postpartum and up to decades beyond the first postpartum year. [32,33] More importantly, composite SMM has been associated with severe mental illness occurring up to the first year postpartum. [13,14] Some individual SMM subtypes - namely pre-eclampsia and obstetric hemorrhage- have been associated with hospitalization for mental illness years after birth. [10,70] However, despite the initial evidence demonstrating the relationship between SMM and severe mental illness in the short term, and the established long-term health implications of SMM, research examining long-term mental health complications after SMM is scarce. Therefore, in this thesis we assessed the relationship between SMM and mental health conditions requiring hospitalization or ED visit in a nationwide cohort to address these knowledge gaps. Such an effort is direly needed to anticipate and address the needs of postpartum individuals and, more importantly, is indispensable to any clinical effort to identify high risk postpartum individuals for extended clinical monitoring.

Objectives and Hypotheses

Overall objective:

The overall objective of this work is to assess the association between any SMM in the first recorded birth, and hospitalization or ED visit for mental health condition up to 13 years after the index birth hospitalization, as compared to no SMM in the first recorded birth.

Specific objectives:

1. To examine associations between SMM and a composite of hospitalization or ED visit for mental health condition, in Canada overall and by province up to 13 years after the index birth hospitalization

Hypothesis: Given that severe pregnancy complications can lead to dysregulation of neuromodulator pathways, we hypothesize that the risk of hospitalization or ED visit for a mental health condition will be higher in individuals who experienced SMM, as compared to those who did not have SMM.

2. To examine associations between SMM and mental health related- (i) hospitalizations and (ii) ED visit, analysed separately, overall and by province up to 13 years after the index birth hospitalization

Hypothesis: Given the high prevalence of mood and anxiety disorders postpartum and the relative rarity of psychosis and other schizophrenia spectrum disorders, we hypothesize that the association between SMM and hospitalization or ED visit for mood and anxiety disorders will be highest, while the association between SMM and schizophrenia spectrum and other psychotic disorders will be the lowest

3. To examine associations between SMM subtypes (that is, severe hemorrhage, severe pre-eclampsia/eclampsia, maternal ICU admission, sepsis, assisted ventilation, hysterectomy, surgical complications, cardiovascular SMM, cerebrovascular SMM, severe uterine rupture, embolism, shock and disseminated intravascular coagulation) where possible and a composite of hospitalization or ED visit for mental health condition up to 13 years after the index birth hospitalization

Hypothesis: Given the heterogeneity of composite SMM and the various etiological pathways associated with each SMM subtype, we hypothesize that there will be some variations in the association between each SMM subtype and hospitalization or ED visit

Additional Methods

To enhance the readability of this work, I have included below the definition of the exposure (SMM) and the outcome (severe mental health related visits) in abbreviated Tables. Tables including complete diagnostic codes are also included in the manuscript supplement.

Table 1: Diagnostic Categories Comprising Severe Maternal Morbidity and Associated Specific Diagnostic Code Descriptors

SMM Categories	**SMM Diagnostic Codes**
Severe preeclampsia, HELLP, eclampsia	Severe pre-eclampsia, HELLP syndrome
	eclampsia
Severe hemorrhage	Placenta previa with haemorrhage and red cell transfusion
	Antepartum hemorrhage with coagulation defect
	Placental abruption with coagulation defect
	Intrapartum hemorrhage with coagulation defect
	Intrapartum hemorrhage with red cell transfusion
	Postpartum hemorrhage with red cell transfusion, procedures to the uterus or hysterectomy
	Curettage with red cell transfusion
Maternal ICU admission	Maternal ICU admission
Surgical complications	Complications of obstetric surgeries and procedures
	Evacuation of incisional hematoma with RBC transfusion
	Repair of bladder, urethra, or intestine
	Reclosure of caesarean wound with RBC transfusion
Hysterectomy	Caesarean hysterectomy
	Hysterectomy using an open approach (without bladder neck suspension, suspension of vaginal vault or pelvic floor repair
Sepsis	Puerperal sepsis
	Septicemia during labor
Embolism, shock, DIC	Obstetric shock
	Obstetric embolism
	Disseminated intravascular coagulation

Assisted ventilation	Assisted ventilation through endotracheal tube
	Assisted ventilation through tracheostomy
Cardiac conditions	Cardiac complications of anesthesia
	Cardiomyopathy
	Cardiac arrest and resuscitation
	Myocardial infarction
	Pulmonary edema and heart failure
Acute renal failure	Acute renal failure
	Dialysis
Severe uterine rupture	Rupture of the uterus with red cell transfusion, procedures to the uterus or hysterectomy
Cerebrovascular Accident	Cerebral venous thrombosis in pregnancy
	Cerebral venous thrombosis in the puerperium
	Subarachnoid and intracranial hemorrhage, cerebral infarction
Other types	Acute fatty liver with red cell transfusion or plasma transfusion
	Hepatic failure
	Cerebral edema or coma
	Pulmonary, cardiac and CNS complications of anaesthesia during pregnancy, labour, delivery or the puerperium
	Status asthmaticus
	Adult respiratory distress syndrome
	Acute abdomen
	Surgical or manual correction of inverted uterus for vaginal births only
	Sickle cell anemia with crisis
	Acute psychosis
	Status epilepticus
	HIV disease

Outcome

The outcome included composites of psychiatric conditions grouped according to diagnostic category.

Table 2: Categories of Mental Health Conditions and Individual Diagnoses

Mental health category	Individual diagnoses
Mood and Anxiety Disorders	Mood disorder due to known physiological condition
	Manic episode
	Bipolar disorder
	Depressive episode
	Major depressive disorder, recurrent
	Persistent mood (affective) disorders
	Unspecified mood (affective) disorders
	Anxiety disorder due to known physiological condition
	Phobic anxiety disorders
	Other anxiety disorders
	Obsessive compulsive disorder
	Reaction to severe stress, and adjustment disorders
	Other specified nonpsychotic mental disorders
	Nonpsychotic mental disorder, unspecified
	Mental and behavioral disorders associated with the puerperium, not elsewhere classified
Suicidality or Deliberate Self Harm	Intentional self-harm
	Poisoning
	Contact with sharp object
Schizophrenia spectrum and other psychotic disorders	Psychotic disorder with hallucinations due to known physiological condition
	Psychotic disorder with delusions due to known physiological condition
	Schizophrenia
	Delusional disorders
	Brief psychotic disorder
	Shared psychotic disorders

	Schizoaffective disorders
	Other psychotic disorder not due to substance or known physiological condition
	Unspecified psychosis not due to a substance or known physiological condition
	Puerperal psychosis
Substance-related and addictive disorders	Alcohol related disorders
	Opioid related disorders
	Cannabis related disorders
	Sedative, hypnotic or anxiolytic related disorders
	Cocaine related disorders
	Other stimulant related disorders
	Hallucinogen related disorders
	Nicotine dependence
	Inhalant related disorders
	Other psychoactive substance related disorders
	Abuse of nonpsychoactive substances

Covariates

A-priori selected covariates with subcategories are shown below.

For comorbidity, we elected to include clinical conditions which are known to pre-dispose individuals to pregnancy complications or have been linked to negative maternal outcomes. These conditions chosen were those which are often included in comorbidity indexes, such as the Batemen and Charlson indexes, and have been validated for use in an obstetric comorbidity index by Amy Metcalfe and others. [76]

Covariate	Subcategories
Maternal age at delivery	18-24
	25-29
	30-34
	35-39
	40-44
	>= 45
Income quintile	Lowest quintile
	Second quintile
	Third quintile

	Fourth quintile
	Highest quintile
Fiscal year of birth	2008/09
	2009/10
	2010/11
	2011/12
	2012/13
	2013/14
	2014/15
	2015/16
	2016/17
	2017/18
	2018/19
	2019/20
	2020/21
Province	Alberta
	British Columbia
	Manitoba
	New Brunswick
	Newfoundland and Labrador
	Nova Scotia
	Ontario
	Prince Edward Island
	Saskatchewan
Comorbidity	Pre-existing hypertension
	Diabetes mellitus
	Chronic kidney disease
	Chronic liver disease
	Cardiovascular condition
	Sickle cell disease
	HIV
	Autoimmune syndrome
	Asthma
	Obesity
	Smoking
Non-severe hypertensive disorders of pregnancy	
Gestational diabetes	
Pre-term birth	Gestational age < 37
	Gestational age >= 37
Still birth	
Delivery mode	Cesearean
	Vaginal
	Obstetric Not Otherwise Specified

Hospital type	Teaching tertiary care hospital
	Community hospital

Statistical Analysis

We used a direct acyclic graph (DAG; see below) to select variables for inclusion in our models. We chose to adjust for maternal age at delivery (continuous), comorbidity, income quintile, fiscal year and urban or rural/remote residence because we had identified these a priori as important covariates and they were related to SMM and mental health-related hospitalization or ED visit in our cohort. We did not adjust for preterm birth and stillbirth, as we believe these would introduce collider stratification bias. We did not adjust for delivery mode as we preserve the temporal order and felt that delivery mode would be caused by SMM. We did not adjust for non-severe hypertensive disorders of pregnancy or gestational diabetes because they were not related to SMM and mental health-related hospitalization or ED visit in our cohort.

In secondary analyses we excluded births in Ontario from the cohort, because mental health hospitalizations in this province are reported both through CIHI and also through the Ontario Mental Health Reporting Services – a data source that was unavailable to us. Thus, it is possible that mental health hospitalizations were incompletely captured with our approach.

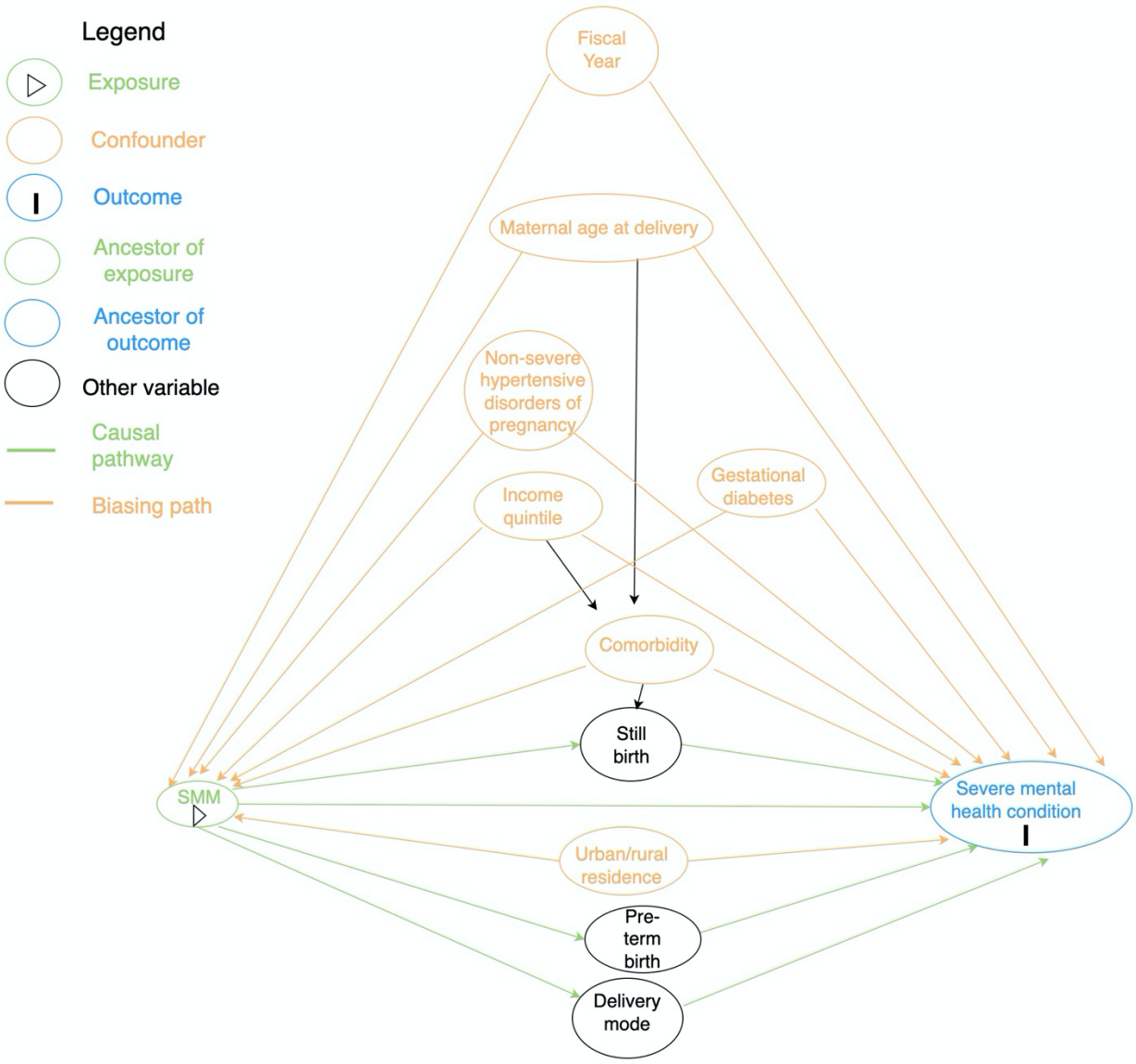

Figure 1. Directed Acyclic Graph of Relationships between Variables in Our Study

Multivariable regression model of choice: the Cox Proportional Hazards model

We chose to use cox proportional hazards model to estimate the association between SMM and our outcomes in our study because of cox proportional hazards model account for time, can be used to model time-varying covariates and accounts for loss to followup, which were important factors to be considered given the long followup.

There are three main assumptions which must be met for appropriate use of the Cox proportional hazards model

1. independence of survival times between distinct individuals in the sample,
2. a multiplicative relationship between the predictors and the hazard
3. a constant hazard ratio over time.

Verification of assumptions

We plotted log(-log(survival) vs log(time) plots and plotted the Schoenfield residuals over time to verify the proportional hazards assumption. In the event of a violation, we elected to include interaction terms between covariates and time in the model.

Bias analyses

The objective of quantitative bias analysis is to adjust an observed estimate of effect and its variance for a specified bias by making assumptions about the parameters that control the degree of bias. When adjusting for misclassification, assumptions are made about the sensitivity (Se) and specificity (Sp) of the misclassified variable (possibly within levels of another variable) and 'corrected' data is back calculated using the specified parameters. [76]

We used methods described by Lash, Fox and Fink (shown below) to assess the impact of misclassification by previous mental illness on our estimates.[7776]

Table 3. A Table Displaying Two by Two Tables of SMM and Mental Health Related Hospitalization or ED Visit in the Observed Data, Both Overall and Stratified by Previous Mental Illness

Observed data								
	Total			PrevSMI			No PrevSMI	
	SMM	No SMM		SMM	No SMM		SMM	No SMM
SMI	a	b		a_1	b_1		a_0	b_0
No SMI	c	d		c_1	d_1		c_0	d_0
Total	m	n		m_1	n_1		m_0	n_0

1. The odds ratio (OR) for the relationship between SMM and SMI were calculated for the observed data

   (a x d)/(b x c)

2. The OR was adjusted for the confounder, previous mental illness.

   $(a_1 \times d_1/m_1 + n_1 + a_0 \times d_0/m_0 + n_0)/(b_1 \times c_1/ m_1 + n_1 + b_0 \times c_0/ m_0 + n_0)$

Table 4. Two by Two Tables of SMM and Mental Health Related Hospitalization or ED Visit in the Corrected Data, Both Overall and Stratified by Previous Mental Illness

Corrected data								
	Total			PrevSMI			No PrevSMI	
	SMM	No SMM		SMM	No SMM		SMM	No SMM
SMI	A	B		A_1	B_1		A_0	B_0
No SMI	C	D		C_1	D_1		C_0	D_0
Total	M	N		M_1	N_1		M_0	N_0

3. Corrected data cells were calculated as follows:

   $^{A}_{1} = [^{a}_{1} - a(1-Sp_1)]/[(Se_1-(1-Sp_1)]$

   $B_1 = [^{b}_{1} - b(1-Sp_1)]/[(Se_1-(1-Sp_1)]$

   $C_1 = [^{c}_{1} - c(1-Sp_1)]/[(Se_1-(1-Sp_1)]$

   $D_1 = [^{d}_{1} - d(1-Sp_1)]/[(Se_1-(1-Sp_1)]$

   $A_0 = a - {}^{A}_{1}$

   $B_0 = b - {}^{B}_{1}$

   $C_0 = c - {}^{C}_{1}$

   $D_0 = d - {}^{D}_{1}$

4. Sp_1 and Se_1 were estimated by averaging the calculated sensitivity and specificity from existing validation studies of mental illness in the DAD. See table below

   Table 5. Validity of Definitions for the Diagnostic Categories of Mental Health Conditions in The Primary Outcome using Hospitalization in DAD

	Mood and anxiety disorders	Schizophrenia spectrum and other psychotic disorders	Substance abuse and other addictive disorders	Suicidality and self harm	All conditions
Sensitivity (%)	5.3	87.1	82.6	42.4	54.4

Specificity (%)	99.6	69.9	96.8	97.4	90.9
Source	Doktorchik 2019[66]	Kurdyak 2015[78]	Quan 2008[79]	Randall 2017[67]	

Note: There are no studies validating mood and anxiety disorders, so we used a study validating a definition for depression in DAD

Definitions for the diagnostic categories of mental health conditions used in our study are more inclusive than the validated definitions in the study above, and therefore, are likely to be less specific and more sensitive

5. The OR for the relationship between SMM and SMI was calculated for the corrected data

   $(A \times D)/(B \times C)$

6. The OR for the corrected data was then adjusted for previous mental illness

   $(A_1 \times D_1/M_1 + N_1 + A_0 \times D_0/M_0 + N_0)/(B_1 \times C_{1/} M_1 + N_1 + B_0 \times C_0/ M_0 + N_0)$

Preface to manuscript

Epidemiologic studies have demonstrated a potential link between severe pregnancy complications and mental health outcomes, although these studies are limited to short term outcomes or single diagnoses. Indeed, there is much to learn about the long-term mental-health implications of severe pregnancy complications, yet only a few studies have examined this relationship with composite exposures like SMM. The literature is even more scarce in the Canadian context where perinatal care is covered under universal health insurance while mental health care is out-of-pocket and variable in accessibility.

Therefore, the purpose of this study was to measure the association between SMM and mental health-related hospitalization or ED visit for a composite of mental health conditions, up to 13 years after the index delivery. We also elected to assess how this relationship changes according to SMM subtype and between composite SMM and different diagnostic groups of mental health conditions.

This study will be submitted to the Journal of the American Medical Association for publication in June 2023.

Manuscript

Severe maternal morbidity and mental health-related hospitalizations or emergency department visits after delivery: A nation-wide study in Canada

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Key Points

Question: Is severe maternal morbidity associated with long-term mental health related hospitalizations or emergency department visits after delivery?

Findings: In this cohort study of 1 543 567 Canadian individuals, mental health outcomes were compared between 35 825 individuals who had severe morbidity during pregnancy or up to 42 days postpartum, and 1 981 326 individuals who had no severe morbidity. Severe maternal morbidity was associated with a 1.3-fold increased rate of hospitalization or emergency department visit for a mental health condition up to 13 years postpartum.

Meaning: Severe maternal morbidity appears to be linked with adverse mental health conditions beyond the immediate postpartum period.

Abstract

Importance: Severe maternal morbidity, a composite of near-fatal events occurring during pregnancy or within 42 days after delivery, may lead to both short- and long-term chronic health issues for the mother. The association between severe maternal morbidity and serious mental health-related outcomes after birth has not been well studied.

Objective: To assess the relationship between severe maternal morbidity in the first recorded birth and hospitalization or emergency department visits for a mental health condition up to 13 years after the index birth hospitalization.

Design: Population-based retrospective cohort study of individuals with first births between April 2008 and March 2021

Setting: All provinces and territories in Canada, excluding Quebec.

Participants: Postpartum individuals aged 18-55 years with a first hospital delivery between 2008 and 2021

Intervention(s) (for clinical trials) or Exposure(s) (for observational studies): The exposure was severe maternal morbidity occurring any time after 20 weeks' gestation and up to 42 days after first delivery. Severe maternal morbidity was defined based on the validated Canadian Perinatal Surveillance System definition criteria and included conditions such as sepsis, severe pre-eclampsia or eclampsia, and severe hemorrhage requiring transfusion or intervention.

Main Outcome(s) and Measure(s): The outcome was hospitalization and/or emergency department visits for mental health-related issues including mood or anxiety disorder, substance-related or addictive disorder, schizophrenia spectrum or other psychotic disorder, or suicidality or self-harm event, occurring 43 days or more after the first birth hospitalization. Cox regression models were used to obtain adjusted hazard ratios with 95% confidence intervals, adjusted for baseline comorbidity, maternal age at delivery, income quintile, urban or rural residence and delivery year.

Results: A total of 2 026 594 individuals were included in our final cohort which comprised of 45 268 individuals with severe maternal morbidity (2.2%). Our analytic cohort included 1 543 567 individuals, comprising 35 825 SMM-affected individuals. Of these, 43 066 individuals had a mental health-related hospitalization or emergency department visit (73.2 per 10 000); among these, 1 287 had severe maternal morbidity (96.1 per 1000), and 41 779 did not (72.7 per 1000) (crude hazard ratio 1.31 [95% CI 1.24-1.39]). Severe maternal morbidity was associated with an increased risk of mental health related hospitalization or emergency department visit, compared with no severe maternal morbidity (adjusted HR 1.26 [95% 1.19-1.34]).

Conclusion: Our study reveals a moderate increased risk of mental health-related hospitalization or emergency department visit up to 13 years after a delivery complicated by severe maternal morbidity. Enhanced surveillance and provision of postpartum mental health resources may be especially important in those who have experienced severe maternal morbidity.

Introduction

Severe maternal morbidity (SMM) is increasingly prevalent, affecting approximately 2% of pregnancies in North America.[1,2] While existing definitions vary, SMM typically includes life-threatening conditions occurring in pregnancy or soon after delivery such as severe hemorrhage, severe pre-eclampsia/eclampsia and sepsis.[1,3–5] Over the past two decades, SMM has become a principal indicator of maternal health and quality care in the Global North where maternal mortality is rare.[4,6] Individuals who survive SMM are more likely to develop chronic health conditions including cardiovascular diseases,[7,8] long-term impaired functional ability, and chronic pain.[9,10] Furthermore, SMM-affected individuals appear to have a reduced life expectancy relative to individuals with unaffected pregnancy.[7,11] It is possible that SMM could also impact psychological health due to long-term vascular dysfunction and a trauma-induced exaggerated stress response. [12–15] Despite this, less is known about mental health after SMM, although up to 36% of mortality in the first year postpartum is due to suicide.[16]

Available studies examining mental health outcomes after pregnancy complications suggest a link between adverse pregnancy outcomes and postpartum mental health. However, these studies have only examined individual conditions like preeclampsia [17–19]and often have relatively short follow-up.[20,21] Two large cohort studies in the US and Sweden noted that SMM survivors have 74% and 22% higher odds respectively of psychiatric illness in the first year postpartum, compared to those who do not have SMM. [20,21] A UK cohort demonstrated a 10% increased risk of hospitalization for postnatal depression in survivors of postpartum hemorrhage up to several decades after delivery, compared with those who have not had a postpartum hemorrhage,[22] while a study in Québec demonstrated that preeclampsia is associated with a 16% increase in the risk of hospitalization for depression up to 28 years after delivery.[17]

Knowledge of the short-term and long-term risk of severe mental health conditions after SMM and its subtypes is lacking in the Canadian context and could help inform the need for enhanced postpartum supportive resources. We therefore performed a pan-Canadian cohort study examining mental health-related hospitalizations and emergency department (ED) visits after SMM up to 13 years postpartum, compared with no SMM. We hypothesized that individuals who experienced SMM will have increased risk of postpartum severe mental health conditions identified using hospitalization and ED presentation, and that these risks will likely vary over time and by SMM subtype.

Methods

Study design and data sources

We performed a longitudinal cohort study of individuals aged 18 to 55 years with a first recorded hospital delivery between April 1, 2008 and March 31, 2021 in Canada (excluding Québec). Clinical and demographic information was extracted from the Canadian Institute of Health Information (CIHI) Discharge Abstract Database (DAD), which includes administrative, clinical, and demographic information on all hospital deliveries, and accounts for approximately 98% of all deliveries in Canada, excluding Québec. [23,24] Up to 25 diagnostic codes and 20 intervention codes are captured for each record in the DAD. The accuracy of the DAD records has been validated against medical records, demonstrating high specificity and sensitivity for most maternal conditions and high specificity and low-to-moderate sensitivity for most mental health conditions. [25,26]

The CIHI-DAD and National Ambulatory Care Reporting System (NACRS) datasets were linked through unique patient identifiers. NACRS includes patient data from EDs for all provinces except Québec.[23,27] Most provinces submit data to NACRS, but coverage of ED data is variable across provinces and each fiscal year.[27,28] In both CIHI-DAD and NACRS, diagnostic and procedural codes using International Classification of Diseases Canadian implementation, version 10 (ICD-10-CA) and the Canadian Classification of Health Intervention (CCI) respectively were used to characterize the sample and define study exposure and outcome. [23,29]

Study population

We included individuals with a first recorded liveborn or stillborn delivery between 20 weeks' and 43 weeks' gestation.[30] We excluded teens (maternal age at delivery <18 years) and older individuals (maternal age at delivery >55 years) because these outlier age groups may require specialized obstetric as well as postpartum mental health care. [31,32] We further excluded individuals with a previous mental health hospitalization or ED visit up to 2 years before the index birth hospitalization, as well as duplicate delivery records, delivery records with missing identifiers, out-of-hospital deliveries, and individuals with ectopic pregnancies.

Study exposure

Exposure was SMM occurring at any time between 20 weeks' gestation and 42 days after the first recorded birth hospitalization; individuals without SMM at hospitalization for first birth were considered unexposed. SMM was defined as the presence of one or more of the 44 indicators in the validated Canadian Perinatal Surveillance System composite definition, captured by ICD-10-CA and CCI codes in the DAD. The SMM composite included severe preeclampsia or eclampsia, severe hemorrhage (peripartum hemorrhage or placental abruption with a coagulation defect, and transfusion for intrapartum hemorrhage, postpartum hemorrhage, placenta previa, or complications of curettage), cardiac complications (cardiomyopathy, cardiac arrest and resuscitation, myocardial infarction, pulmonary edema and heart failure, complications of anesthesia), cerebrovascular accidents, acute renal failure or dialysis, embolism, shock, disseminated intravascular coagulation, sepsis, uterine rupture, hysterectomy, surgical complications, assisted ventilation, intensive care unit admission, and other serious disorders (acute fatty liver, hepatic failure, cerebral edema or coma, and similar conditions) (eTable 1 in Supplement). [1] We excluded psychosis from the SMM definition because it is part of the composite outcome. HIV and prevalent hypertensive heart disease were also excluded from the exposure as our interest was in acute conditions with onset during the peripartum period. [1,33]

We further examined individual SMM subtypes where possible (obstetric hemorrhage; sepsis, severe preeclampsia/eclampsia, maternal ICU admission, assisted ventilation etc) [1,34] as secondary exposures, and as hemorrhagic and non-hemorrhagic given that severe hemorrhage was the most prevalent SMM subtype in our study.

Study outcomes

The primary study outcome was a composite of mental health-related hospitalization and/or ED visit occurring 43 days or more after the index birth hospitalization. The composite outcome was identified using ICD-10-CA codes for a (1) mood or anxiety disorder, (2) substance-related or addictive disorder, (3) schizophrenia spectrum or other psychotic disorder, or (4) suicidality or self-harm event, captured in the DAD or NACRS.[35] (eTable 2 in Supplement). We also assessed each component of these mental health outcomes individually. We further

assessed hospitalization and ED visits separately, as those requiring hospitalization may differ in important ways from those leading to an ED visit with subsequent discharge to the community. [36]

Covariates

Covariates were selected *a priori* as potential confounders and effect modifiers in multivariate models, guided by the use of a directed acyclic graph (eFigure 1 in Supplement) and were captured within 2 years prior to index birth hospitalization. These included: maternal age at delivery (continuous, and by category 18-24, 25-29, 30-34, 35-39, 40-44 and ≥45),[37] income quintile, year and province of birth, and maternal comorbid conditions (0, 1 or 2 or more of pre-existing hypertension, diabetes mellitus, chronic kidney disease, chronic liver disease, cardiovascular condition, sickle cell disease, HIV, autoimmune syndrome such as systemic lupus erythematosus, asthma, obesity or smoking), urban or rural residential status, and hospital type (teaching tertiary care hospital versus community hospital). We also collected the following variables but elected not to consider them as confounders due to the potential for collider stratification bias [38] as they may be a consequence of the exposure: pregnancy characteristics of the index birth (i.e., non-severe hypertensive disorders of pregnancy (yes/no), gestational diabetes (yes/no), pre-term birth (gestational age < 37 weeks or gestational age >= 37 weeks), stillbirth (yes/no), and mode of delivery (cesarean, vaginal or obstetric delivery not otherwise specified).

Statistical Analysis

We described baseline maternal demographic and pregnancy characteristics for the cohort, stratified according to the presence or absence of SMM in first recorded birth. We described continuous variables using means and standard deviations (SD) or medians and interquartile ranges (IQR). Dichotomous variables and categorical variables were described with frequencies and percentages. We generated graphs of SMM in any recorded birth over time and mental health-related hospitalization or ED visit within two years of the index delivery date over time.

For our main analyses, we defined the index delivery date as the admission date of first recorded hospital birth, starting on April 1, 2008. To limit the potential for bias introduced by sporadic unavailability of NACRS data across provinces, we restricted the cohort to individuals whose index delivery occurred in a province and year with available NACRS follow-up data. We calculated incidence rates per 10 000 person-years with 95% confidence intervals (CI) for composite and individual outcomes. Univariable and multivariable Cox proportional hazards models were used to calculate crude and adjusted hazard ratios (HRs) and 95% CIs, respectively, estimating the relationship between SMM and mental health-related hospitalization or ED visit, with years as the time unit of analysis for follow-up. Multivariable models were adjusted for *a priori* selected covariates. In secondary analyses, we re-ran our models to assess associations between SMM and (i) hospitalization, and (ii) ED visits separately. We assessed for variation in the associations between individual SMM subtypes and mental health hospitalization or ED visit and for each of the four outcome diagnostic categories (mood or anxiety disorders, schizophrenia spectrum and other psychotic disorders, substance abuse and other related disorders and suicidality or self-harm). Finally, we split the follow-up time axis into: <= 1 year postpartum, between 1 and 5 years postpartum, and > 5 years postpartum, to assess how proximity to delivery affects the relationship between SMM and mental health-related hospitalization or ED visit. In all models, follow-up was initiated 43 days after first recorded hospital birth admission and records were censored on death, subsequent pregnancy or end of study follow-up (March 2021). We conducted a complete case analysis after assessing the frequency of missingness in the dataset to be less than 5% and therefore, unlikely to meaningfully impact estimates.[39]

In a sensitivity analysis we re-defined the primary hospitalization outcome to include ICD-10-CA codes found in all 25 DAD diagnostic code fields to assess hospitalization *with* as opposed to *for* a mental health condition.[40] We re-ran models among individuals with mental health conditions prior to the index pregnancy to assess for worsening/exacerbated disease post-delivery. In a bias analysis, we used methods described by Lash, Fox and Fink[41] to estimate the impact of misclassification of previous mental illness in our cohort on our estimates. As these methods are not appropriate for time to event data, we computed odds ratios of the relationship between SMM and mental health-related hospitalization or ED visit and adjusted these for misclassification of previous mental illness.

Ethics approval

The study was approved by the research ethics board of the McGill University Health Centre (MUHC), Nagano identifier 2022-8041. Since the study used secondary aggregate data, the need for individual informed consent was waived. We followed Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for reporting this study[42] and analyzed data using SAS version 9.4

Results

Study flow

Of 2 112 518 eligible deliveries over the period, we identified 2 026 594 individuals with their first hospital delivery in all provinces and territories in Canada, excluding Québec, of which 45 268 (2.2%) had a recorded SMM. The analytic cohort included 1 579 392 individuals, of which 35 825 were (2.2%) had a recorded SMM. (Figure 1)

The overall prevalence of SMM increased from about 1.5% of deliveries in fiscal years 2006/2007 to about 2.2% in 2020/2021. Similarly, the percentage of individuals experiencing mental health-related hospitalizations and ED visits within two years of delivery increased. (Figure 2)

Baseline characteristics of study sample

The mean age at delivery of individuals in the study population was 30+/-5.4 years (Table 1). Compared with non SMM-affected individuals, those with SMM were more likely to be older at the index delivery, to reside in the lowest income quintile neighbourhoods or rural or remote areas, and to have comorbidities. Individuals with SMM were also more likely to experience a non-severe hypertensive disorder of pregnancy or gestational diabetes, deliver pre-term, have a stillbirth, deliver by cesarean section and to have their index delivery in a teaching tertiary care hospital.

Incidence rates of Mental Health-Related Outcomes

A total of 43 066 individuals (73 per 10 000 person-years [95% CI 72.6-73.9]) were hospitalized or visited the ED for a mental health condition, and 1 536 326 had no record of a mental health-related hospitalization or ED visit. Rates of mental-health related hospitalization or ED visit decreased with increasing age and income quintile, and were highest in rural or remote areas, and for those who had two or more comorbidities, preterm births, stillbirths and vaginal deliveries. (Table 2)

Association between SMM and Hospitalization or ED visit for Mental Health Conditions

SMM was associated with an increased risk of mental health-related hospitalization or ED visit (crude HR 1.31 [95% CI 1.24-1.39], which did not change significantly after adjusting for covariates (adjusted HR (aHR) 1.26 [95% CI 1.19-1.34]) (Table 3) and did not vary substantially by province (Figure 4). Specifically, SMM-affected individuals were found to be at significantly increased risk of hospitalization or ED visit for substance abuse (aHR 1.22 [95% CI 1.09-1.38]), mood and anxiety disorders (aHR 1.23 [95% CI 1.16-1.31]), and suicidality or self-harm (aHR 1.54 [95% CI 1.26-1.88]).

Results showed moderately elevated risk of mental health-related hospitalization or ED visit after severe hemorrhage (aHR 1.16 [95% CI 1.04-1.28]), severe pre-eclampsia (aHR 1.19[95% CI 1.03-1.38]), assisted ventilation (aHR 1.37 [95% CI 1.10-1.72]) and sepsis (aHR 1.33[95% CI 1.17-1.51]), compared with no SMM. The risk was highest among those with embolism, shock and disseminated intravascular coagulation (aHR 1.71[95% CI 1.38-2.12]) and those who were admitted to the maternal ICU (aHR 1.43 [95% CI 1.31-1.65]), when compared with no SMM. Individuals with hemorrhagic and nonhemorrhagic SMM types had a similar risk of mental health-related hospitalization or ED visit (non-hemorrhagic aHR 1.30 [95% CI 1.22-1.39] hemorrhagic aHR 1.16 [95% CI 1.04-1.28]). (Figure 3)

Those with SMM had strongly increased risk of hospitalization and a moderately increased risk of ED visit for the composite of mental health conditions, compared to those who did not have an SMM (hospitalization aHR 1.42 [95% CI 1.22-1.64], ED visit (aHR 1.25[95% CI 1.18-1.33]). Results showed increased risk of hospitalization and ED visit respectively, for mood and anxiety disorders and substance abuse and other addictive disorders. On the other hand, while results also showed that those with SMM had a strongly increased risk of hospitalization for schizophrenia spectrum and other psychotic disorders (aHR 1.53 [95% CI 1.21-2.06]), their relative risk for ED visit (aHR 1.02 [95% CI 0.77-1.34]) for the same conditions was unaffected. (Table 3)

Sensitivity Analyses

SMM-affected individuals had the highest relative risk of hospitalization or ED visit for a mental health condition in the first year postpartum (aHR 1.38 [95% CI 1.24-1.53]). This observed association weakened after the first postpartum year but remained relatively constant thereafter - for individuals with ≥ 1 year and less than 5 years of follow-up aHR was 1.23 (95% CI 1.14-1.34) and for individuals with more than 5 years of follow-up, aHR was 1.21 (95% CI 1.07-1.37). When we assessed mental health-related hospitalization or ED visit in individuals with previous mental illness, absolute rates of mental health visits were substantially higher, but calculated aHR 1.21 (95% CI 1.10-1.34) was not appreciably different from the result from the primary analysis. (eTable 3 in Supplement)

Bias Analysis

In the observed data where previous mental illness is misclassified, the calculated odds ratio (OR) which was adjusted for previous mental illness was 1.25, demonstrating 25% higher odds of mental health-related hospitalization among SMM-affected individuals compared to those without SMM. However, after completing the bias analysis, the calculated odds ratio in the corrected data which was adjusted for previous mental illness was 0.99. This suggests no difference between the odds of mental health-related hospitalization among those with SMM and those without SMM. According to these results, the OR from the observed data was biased away from the null by approximately 26%.

Summary of findings

In this pan-Canadian longitudinal cohort study, individuals who experienced SMM had a moderately increased risk of hospitalization or ED visits for mental health conditions up to 13 years after a first hospital delivery, compared with those who did not experience SMM. The risk of a mental health-related hospitalization or ED visit was highest during the first postpartum year and diminished in intensity but remained elevated from baseline throughout the follow-up period. Individuals who were treated in a maternal ICU during pregnancy and those with an embolism, shock or disseminated intravascular coagulation had the highest risk of mental health-related hospitalization or ED visit. SMM-affected individuals had moderately increased risk of hospitalization and/or ED visit for mood and anxiety disorders and substance abuse disorders, but their risk of hospitalization and/or ED visit for suicidality and self-harm was particularly high, as was their risk hospitalization for schizophrenia spectrum and other psychotic disorders.

Comparison to other studies

Our results expand on previous work in the United States (US) and Swedish contexts.[20,21] The former analysed 1 229 835 pregnancies and found that severe maternal morbidity was associated with a 74% higher odds of hospital admission for depression, anxiety, and psychosis in the first year postpartum. Differences in risk estimates between this study and ours could be due to a variety of factors including differing patient populations and health care systems, the SMM definition and the short follow-up period. These authors did not find an association between SMM and suicidality in their study, whereas in our study, SMM was associated with a strong increase in risk of hospitalization or ED visit for suicidal behaviour or self-harm.[20] The latter assessed 25 674 deliveries and found that SMM is associated with higher odds of inpatient psychiatric treatment for mood disorders, neuroses and behavioural disorders in the first postpartum year. Estimates from this analysis (aOR 1.22 [95% CI 1.03–1.45]) are similar to ours, even though these researchers did not exclude individuals with previous mental illness or adjust for maternal comorbidity. [21]

Interpretation of findings

In Canada, approximately 1 in every 65 births will be complicated by SMM, resulting in around 5500 SMM-affected births per year.[24,43] Our analysis suggests that approximately 1 in every 10 SMM-affected individuals will subsequently experience a mental health condition severe enough to warrant either an ED visit or inpatient admission. The reason for the elevated risk of mental health-related hospitalization and/or ED visits among SMM-affected individuals is unknown. Putative explanations typically involve the dysregulation of neuromodulator pathways secondary to vascular dysfunction, immune dysregulation and stress. [12,44–46] Disseminated intravascular coagulation, sepsis and shock are conditions that occur secondary to several other morbidities, including postpartum hemorrhage and severe pre-eclampsia. These severe complications are characterized by extremely high systemic volumes of pro-inflammatory cytokines and endothelial dysfunction, which are thought to provoke depression, anxiety and psychosis by disrupting the hypothalamic-pituitary axis (HPA) and the hypothalamic-pituitary-gonadal (HPG) axis.[12,13,45,47] Also, SMM during delivery is often accompanied by an ICU admission, which typically results in separation of parent and neonate.[48–50] It is possible that the stress and associated spike in cortisol levels related to this separation could lead to psychological trauma during postpartum.[15,50–52]

Resources and health service mandates are often province-specific, rendering the provision of postpartum mental health supports inconsistent across Canada. Although ample research supports the efficacy of psychological and psychosocial interventions such as cognitive behavioural therapy (CBT), interpersonal therapy (IPT) and pharmacotherapy for treating postpartum mental health conditions, many individuals cannot access treatment due to high cost, inefficient referral pathways and long wait times.[53–55] Further, Canadian perinatal health care providers report significant gaps in training, screening tool use, and timely and culturally safe treatment of perinatal mental health concerns.[56,57] This is crucial, as high risk individuals such as those with material deprivation, those residing in rural and remote areas, immigrants and those in lower income quintiles face the greatest barriers to accessing care; these individuals are also most likely to experience pregnancy complications such as SMM.[33,58–61]

In contrast to other international public health agencies such as Australia's Centre of Perinatal Excellence, the UK National Institute for Health and Care Excellence and the US Preventive Services Task Force, the Canadian Task Force for Preventative Health Care does not recommend routine screening for perinatal mental illness in primary care settings. British Columbia, New Brunswick, Saskatchewan, Alberta and Nova Scotia are the only provinces where maternal mental health screening is recommended and facilitated through programs. This is important, because evidence shows that early detection leads to favourable outcomes and that screening alone results in clinical benefits, and some research indicates that screening is cost effective.[62–65]

However, screening alone does not effectively address barriers to perinatal mental healthcare access. [66]Despite the existence of routine screening programs, Alberta and Saskatchewan both had high rates of mental health related hospitalizations or ED visits, and SMM-affected individuals in Alberta had an increased risk of these events. Recently, provinces have focused their efforts on improving the accessibility of mental health services, by increasing the supply of mental health workers, including providers for specialized needs, and using virtual technologies to address geographic barriers. [58] In Ontario, the country's most populous province, these programs include the Champlain Building Access to Specialists through eConsultation (BASE) program, the Local Health Hubs project, the Ontario Psychiatric Outreach Program (OPOP) and Extension for Community Healthcare Outcomes (ECHO) Ontario Mental Health.[58]

Strengths and limitations

The study has several strengths including the large sample size, which facilitated the analysis of a rare exposure and outcome. Other strengths include the population-based nature of the study, relatively long follow-up period and use of robust, validated definitions.

Limitations relate to the retrospective observational nature of this study using administrative health data prone to missing variables and various biases. We were unable to determine loss-to-follow-up due to migration or death out of hospital. We were unable to account for potential confounders like race and ethnicity and it is likely these variables are contributing to observed associations. We defined SMM using the validated definition from Canadian Perinatal Surveillance System, which limits generalizability to studies in other populations. In addition, in our analyses SMM was treated as a fixed exposure in the first recorded birth as opposed to a time-varying exposure, potential limiting the generalizability of the results to any SMM-affected pregnancy. Due to the unavailability of outpatient data, the cohort likely included individuals who are being treated for a mental health condition in an outpatient setting, and there is also likely to be some misclassification of individuals with less severe mental health conditions in our outcome. We estimated the misclassification of individuals with previous mental illness may have biased results about away from the null. We attempted to limit the potential for bias in estimates from sporadic reporting of ED data to NACRS across provinces by restricting our analytic cohort to records in provinces with available follow-up ED data, but we are likely underestimating the true result.

Conclusion

In this study SMM was associated with hospitalization or ED visit for mental health conditions several years after the postpartum period. Morbidities like severe pre-eclampsia, severe hemorrhage, sepsis, assisted ventilation, embolism, shock and disseminated intravascular coagulation and maternal ICU admission were also associated with long-term hospitalization or ED visit for mental health conditions. Individuals with SMM would benefit from targeted psychological postpartum care and additional supportive resources.

References

1. Dzakpasu S, Deb-Rinker P, Arbour L, et al. Severe Maternal Morbidity in Canada: Temporal Trends and Regional Variations, 2003-2016. *J Obstet Gynaecol Can*. 2019;41(11):1589-1598.e16. doi:10.1016/j.jogc.2019.02.014

2. Metcalfe A, Sheikh M, Hetherington E. Impact of the ICD-9-CM to ICD-10-CM transition on the incidence of severe maternal morbidity among delivery hospitalizations in the United States. *Am J Obstet Gynecol*. 2021;225(4):422.e1-422.e11. doi:10.1016/j.ajog.2021.03.036

3. Chen J, Cox S, Kuklina EV, Ferre C, Barfield W, Li R. Assessment of Incidence and Factors Associated With Severe Maternal Morbidity After Delivery Discharge Among Women in the US. *JAMA Netw Open*. 2021;4(2):e2036148. doi:10.1001/jamanetworkopen.2020.36148

4. Geller SE, Koch AR, Garland CE, MacDonald EJ, Storey F, Lawton B. A global view of severe maternal morbidity: moving beyond maternal mortality. *Reprod Health*. 2018;15(1):98. doi:10.1186/s12978-018-0527-2

5. Say L, Souza JP, Pattinson RC. Maternal near miss – towards a standard tool for monitoring quality of maternal health care. *Best Pract Res Clin Obstet Gynaecol*. 2009;23(3):287-296. doi:10.1016/j.bpobgyn.2009.01.007

6. England N, Madill J, Metcalfe A, et al. Monitoring maternal near miss/severe maternal morbidity: A systematic review of global practices. Salinas-Miranda A, ed. *PLOS ONE*. 2020;15(5):e0233697. doi:10.1371/journal.pone.0233697

7. Ukah UV, Dayan N, Potter BJ, Paradis G, Ayoub A, Auger N. Severe Maternal Morbidity and Long-Term Risk of Cardiovascular Hospitalization. *Circ Cardiovasc Qual Outcomes*. 2022;15(2):e008393. doi:10.1161/CIRCOUTCOMES.121.008393

8. Ukah UV, Auger N. Severe maternal morbidity and risk of cardiovascular disease: Recent advances. *Kardiol Pol*. 2022;80(6):638-643. doi:10.33963/KP.a2022.0119

9. Angelini CR, Pacagnella RC, Parpinelli MA, et al. Quality of Life after an Episode of Severe Maternal Morbidity: Evidence from a Cohort Study in Brazil. *BioMed Res Int*. 2018;2018:1-10. doi:10.1155/2018/9348647

10. Silveira C, Parpinelli MA, Pacagnella RC, et al. A cohort study of functioning and disability among women after severe maternal morbidity. *Int J Gynecol Obstet*. 2016;134(1):87-92. doi:10.1016/j.ijgo.2015.10.027

11. Ray JG, Park AL, Dzakpasu S, et al. Prevalence of Severe Maternal Morbidity and Factors Associated With Maternal Mortality in Ontario, Canada. *JAMA Netw Open*. 2018;1(7):e184571. doi:10.1001/jamanetworkopen.2018.4571

12. Bauer ME, Teixeira AL. Inflammation in psychiatric disorders: what comes first?: Inflammation in psychiatric disorders. *Ann N Y Acad Sci*. 2019;1437(1):57-67. doi:10.1111/nyas.13712

13. Berk M, Williams LJ, Jacka FN, et al. So depression is an inflammatory disease, but where does the inflammation come from? *BMC Med*. 2013;11(1):200. doi:10.1186/1741-7015-11-200

14. Jermy BS, Hagenaars S, Coleman JRI, Vassos E, Lewis CM. Risk factor profiles for depression following childbirth or a chronic disease diagnosis: case–control study. *BJPsych Open*. 2022;8(6):e182. doi:10.1192/bjo.2022.586

15. McGowan S. Does the maternal experience of childbirth affect mother-infant attachment and bonding? *J Health Visit*. 2014;2(11):606-616. doi:10.12968/johv.2014.2.11.606

16. Lommerse K, Knight M, Nair M, Deneux-Tharaux C, van den Akker T. The impact of reclassifying suicides in pregnancy and in the postnatal period on maternal mortality ratios. *BJOG Int J Obstet Gynaecol*. 2019;126(9):1088-1092. doi:10.1111/1471-0528.15215

17. Auger N, Low N, Paradis G, Ayoub A, Fraser WD. Preeclampsia and the longitudinal risk of hospitalization for depression at 28 years. *Soc Psychiatry Psychiatr Epidemiol*. 2021;56(3):429-436. doi:10.1007/s00127-020-01920-x

18. Chen L, Wang X, Ding Q, Shan N, Qi H. Development of Postpartum Depression in Pregnant Women with Preeclampsia: A Retrospective Study. *BioMed Res Int*. 2019;2019:1-7. doi:10.1155/2019/9601476

19. Eckerdal P, Kollia N, Löfblad J, et al. Delineating the Association between Heavy Postpartum Haemorrhage and Postpartum Depression. *PLOS ONE*. 2016;11(1):e0144274. doi:10.1371/journal.pone.0144274

20. LEWKOWITZ AK, ROSENBLOOM JI, KELLER M, et al. Association Between Severe Maternal Morbidity and Psychiatric Illness Within One Year of Hospital Discharge After Delivery. *Obstet Gynecol*. 2019;134(4):695-707. doi:10.1097/AOG.0000000000003434

21. Wall-Wieler E, Carmichael SL, Urquia ML, Liu C, Hjern A. Severe maternal morbidity and postpartum mental health-related outcomes in Sweden: a population-based matched-cohort study. *Arch Womens Ment Health*. 2019;22(4):519-526. doi:10.1007/s00737-018-0917-z

22. Parry-Smith W, Okoth K, Subramanian A, et al. Postpartum haemorrhage and risk of mental ill health: A population-based longitudinal study using linked primary and secondary care databases. *J Psychiatr Res*. 2021;137:419-425. doi:10.1016/j.jpsychires.2021.03.022

23. Canadian Institute for Health Information. Data Quality Documentation, National Ambulatory Care Reporting System—Multi-Year Information. Published online 2012.

24. Statistics Canada. Live births, by month. doi:10.25318/1310041501-ENG

25. Joseph KS, Mahey J. Validation of perinatal data in the Discharge Abstract Database of the Canadian Institute for Health Information. *Chronic Dis Can*. 2009;29(3):96-101. doi:10.24095/hpcdp.29.3.01

26. Kurdyak P, Lin E, Green D, Vigod S. Validation of a Population-Based Algorithm to Detect Chronic Psychotic Illness. *Can J Psychiatry Rev Can Psychiatr*. 2015;60(8):362-368.

27. Data Quality Documentation, National Ambulatory Care Reporting System— Current-Year Information, 2020–2021. Published online 2021.

28. Data Quality Documentation, National Ambulatory Care Reporting System— Current-Year Information, 2013–2014. Published online 2014.

29. Canadian Institute for Health Information. Data Quality Documentation, Discharge Abstract Database—Multi-Year Information. Published online 2012.

30. Platt RW, Abrahamowicz M, Kramer MS, et al. Detecting and eliminating erroneous gestational ages: a normal mixture model. *Stat Med*. 2001;20(23):3491-3503. doi:10.1002/sim.1095

31. Huybrechts KF, Bateman BT, Pawar A, et al. Maternal and fetal outcomes following exposure to duloxetine in pregnancy: cohort study. *BMJ*. Published online February 19, 2020:m237. doi:10.1136/bmj.m237

32. Maconochie N, Doyle P, Prior S, Simmons R. Risk factors for first trimester miscarriage-results from a UK-population-based case-control study. *BJOG Int J Obstet Gynaecol*. 2007;114(2):170-186. doi:10.1111/j.1471-0528.2006.01193.x

33. Urquia ML, Wanigaratne S, Ray JG, Joseph KS. Severe Maternal Morbidity Associated With Maternal Birthplace: A Population-Based Register Study. *J Obstet Gynaecol Can*. 2017;39(11):978-987. doi:10.1016/j.jogc.2017.05.012

34. Dzakpasu S, Deb-Rinker P, Arbour L, et al. Severe maternal morbidity surveillance: Monitoring pregnant women at high risk for prolonged hospitalisation and death. *Paediatr Perinat Epidemiol*. 2020;34(4):427-439. doi:10.1111/ppe.12574

35. Dayan N, Velez MP, Vigod S, et al. Infertility treatment and postpartum mental illness: a population-based cohort study. *CMAJ Open*. 2022;10(2):E430-E438. doi:10.9778/cmajo.20210269

36. Smith MW, Stocks C, Santora PB. Hospital Readmission Rates and Emergency Department Visits for Mental Health and Substance Abuse Conditions. *Community Ment Health J*. 2015;51(2):190-197. doi:10.1007/s10597-014-9784-x

37. Rademaker D, Hukkelhoven CWPM, van Pampus MG. Adverse maternal and perinatal pregnancy outcomes related to very advanced maternal age in primigravida and multigravida in the Netherlands: A population-based cohort. *Acta Obstet Gynecol Scand*. 2021;100(5):941-948. doi:10.1111/aogs.14064

38. Hernán MA, Robins JM. Estimating causal effects from epidemiological data. *J Epidemiol Community Health*. 2006;60(7):578-586. doi:10.1136/jech.2004.029496

39. Harrell , FE. *Regression Modeling Strategies: With Applications to Linear Models, Logistic and Ordinal Regression, and Survival Analysis*. Springer International Publishing; 2015. doi:10.1007/978-3-319-19425-7

40. Canadian Institute for Health Information. Ontario Mental Health Reporting System Data Quality Documentation. Published online 2020.

41. Fox MP, MacLehose RF, Lash TL. SAS and R code for probabilistic quantitative bias analysis for misclassified binary variables and binary unmeasured confounders. *Int J Epidemiol*. Published online May 4, 2023:dyad053. doi:10.1093/ije/dyad053

42. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: Guidelines for reporting observational studies. *Int J Surg*. 2014;12(12):1495-1499. doi:10.1016/j.ijsu.2014.07.013

43. Centre for Surveillance and Applied Research PHA of C. *Perinatal Health Indicators Data Tool, 2020 Edition*. Public Health Agency of Canada; 2020.

44. Bouzinova EV, Norregaard R, Boedtkjer DMB, et al. Association Between Endothelial Dysfunction and Depression-Like Symptoms in Chronic Mild Stress Model of Depression. *Psychosom Med*. 2014;76(4):268-276. doi:10.1097/PSY.0000000000000062

45. Maes M, Kubera M, Obuchowiczwa E, Goehler L, Brzeszcz J. Depression's multiple comorbidities explained by (neuro)inflammatory and oxidative & nitrosative stress pathways. *Neuro Endocrinol Lett*. 2011;32(1):7-24.

46. Szpunar MJ, Malaktaris A, Baca SA, Hauger RL, Lang AJ. Are alterations in estradiol, cortisol, and inflammatory cytokines associated with depression during pregnancy and postpartum? An exploratory study. *Brain Behav Immun - Health*. 2021;16:100309. doi:10.1016/j.bbih.2021.100309

47. Achtyes E, Keaton SA, Smart L, et al. Inflammation and kynurenine pathway dysregulation in post-partum women with severe and suicidal depression. *Brain Behav Immun*. 2020;83:239-247. doi:10.1016/j.bbi.2019.10.017

48. Baskett TF. Epidemiology of obstetric critical care. *Best Pract Res Clin Obstet Gynaecol*. 2008;22(5):763-774. doi:10.1016/j.bpobgyn.2008.06.002

49. Einav S, Leone M. Epidemiology of obstetric critical illness. *Int J Obstet Anesth*. 2019;40:128-139. doi:10.1016/j.ijoa.2019.05.010

50. Ray JG, Urquia ML, Berger H, Vermeulen MJ. Maternal and neonatal separation and mortality associated with concurrent admissions to intensive care units. *CMAJ Can Med Assoc J*. 2012;184(18):E956-E962. doi:10.1503/cmaj.121283

51. Slomian J, Honvo G, Emonts P, Reginster JY, Bruyère O. Consequences of maternal postpartum depression: A systematic review of maternal and infant outcomes. *Womens Health*. 2019;15:1745506519844044. doi:10.1177/1745506519844044

52. van Veenendaal NR, van Kempen AAMW, Broekman BFP, et al. Association of a Zero-Separation Neonatal Care Model With Stress in Mothers of Preterm Infants. *JAMA Netw Open*. 2022;5(3):e224514. doi:10.1001/jamanetworkopen.2022.4514

53. Hooykas A. Time for Action: Why Canada Needs A National Perinatal Mental Health Strategy Now More Than Ever. Published online 2021. https://cpmhc.ca/report.

54. Howard LM, Khalifeh H. Perinatal mental health: a review of progress and challenges. *World Psychiatry*. 2020;19(3):313-327. doi:10.1002/wps.20769

55. Martín-Gómez C, Moreno-Peral P, Bellón JA, et al. Effectiveness of psychological, psychoeducational and psychosocial interventions to prevent postpartum depression in adolescent and adult mothers: study protocol for a systematic review and meta-analysis of randomised controlled trials. *BMJ Open*. 2020;10(5):e034424. doi:10.1136/bmjopen-2019-034424

56. DeRoche C, Hooykaas A, Ou C, Charlebois J, King K. Examining the gaps in perinatal mental health care: A qualitative study of the perceptions of perinatal service providers in Canada. *Front Glob Womens Health*. 2023;4:1027409. doi:10.3389/fgwh.2023.1027409

57. Hicks LM, Ou C, Charlebois J, et al. Assessment of Canadian perinatal mental health services from the provider perspective: Where can we improve? *Front Psychiatry*. 2022;13:929496. doi:10.3389/fpsyt.2022.929496

58. Friesen E. The landscape of mental health services in rural Canada. *Univ Tor Med J*. 2019;96(2).

59. Hansotte E, Payne SI, Babich SM. Positive postpartum depression screening practices and subsequent mental health treatment for low-income women in Western countries: a systematic literature review. *Public Health Rev*. 2017;38:3. doi:10.1186/s40985-017-0050-y

60. Vigod SN, Bagadia AJ, Hussain-Shamsy N, Fung K, Sultana A, Dennis CLE. Postpartum mental health of immigrant mothers by region of origin, time since immigration, and refugee status: a population-based study. *Arch Womens Ment Health*. 2017;20(3):439-447. doi:10.1007/s00737-017-0721-1

61. Oot A, Huennekens K, Yee L, Feinglass J. Trends and Risk Markers for Severe Maternal Morbidity and Other Obstetric Complications. *J Womens Health*. 2021;30(7):964-971. doi:10.1089/jwh.2020.8821

62. ACOG Committee Opinion No. 757: Screening for Perinatal Depression. *Obstet Gynecol*. 2018;132(5):e208-e212. doi:10.1097/AOG.0000000000002927

63. Premji S, McDonald SW, Metcalfe A, et al. Examining postpartum depression screening effectiveness in well child clinics in Alberta, Canada: A study using the All Our Families cohort and administrative data. *Prev Med Rep*. 2019;14:100888. doi:10.1016/j.pmedr.2019.100888

64. Premji S, McDonald SW, McNeil DA, Spackman E. Maximizing maternal health and value for money in postpartum depression screening: a cost-effectiveness analysis using the All Our Families cohort and administrative data in Alberta, Canada. *J Affect Disord*. 2021;281:839-846. doi:10.1016/j.jad.2020.11.051

65. Verbeke E, Bogaerts A, Nuyts T, Crombag N, Luyten J. Cost-effectiveness of mental health interventions during and after pregnancy: A systematic review. *Birth*. 2022;49(3):364-402. doi:10.1111/birt.12623

66. McPhail J, Loitz CC, Zaychkowsky C, et al. Opportunistic postpartum depression symptom screening at well-child clinics in Alberta, 2012–2016. *Can J Public Health*. 2021;112(5):938-946. doi:10.17269/s41997-021-00521-8

Tables and Figures

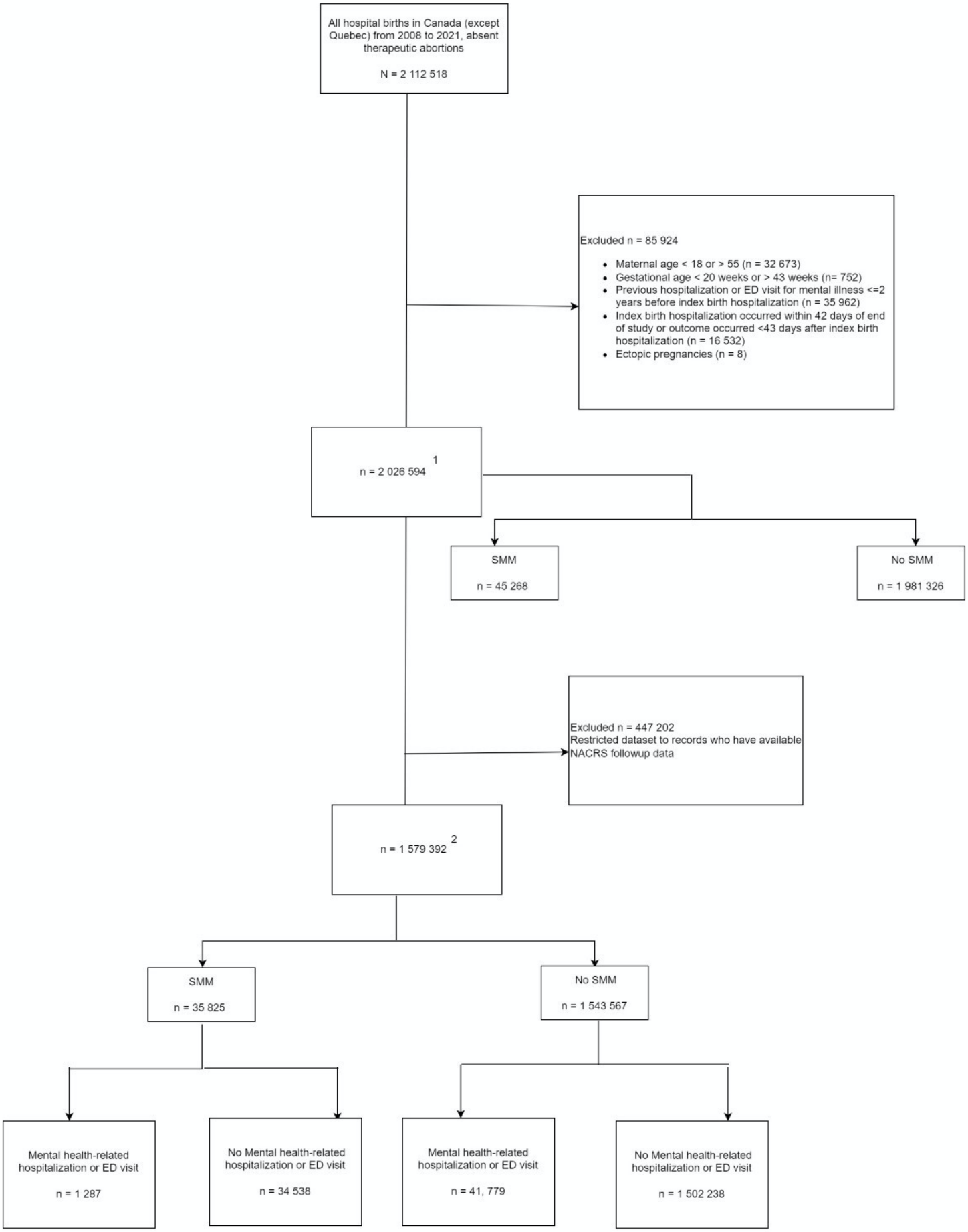
Figure legends

Figure 1: The Study Flow Chart

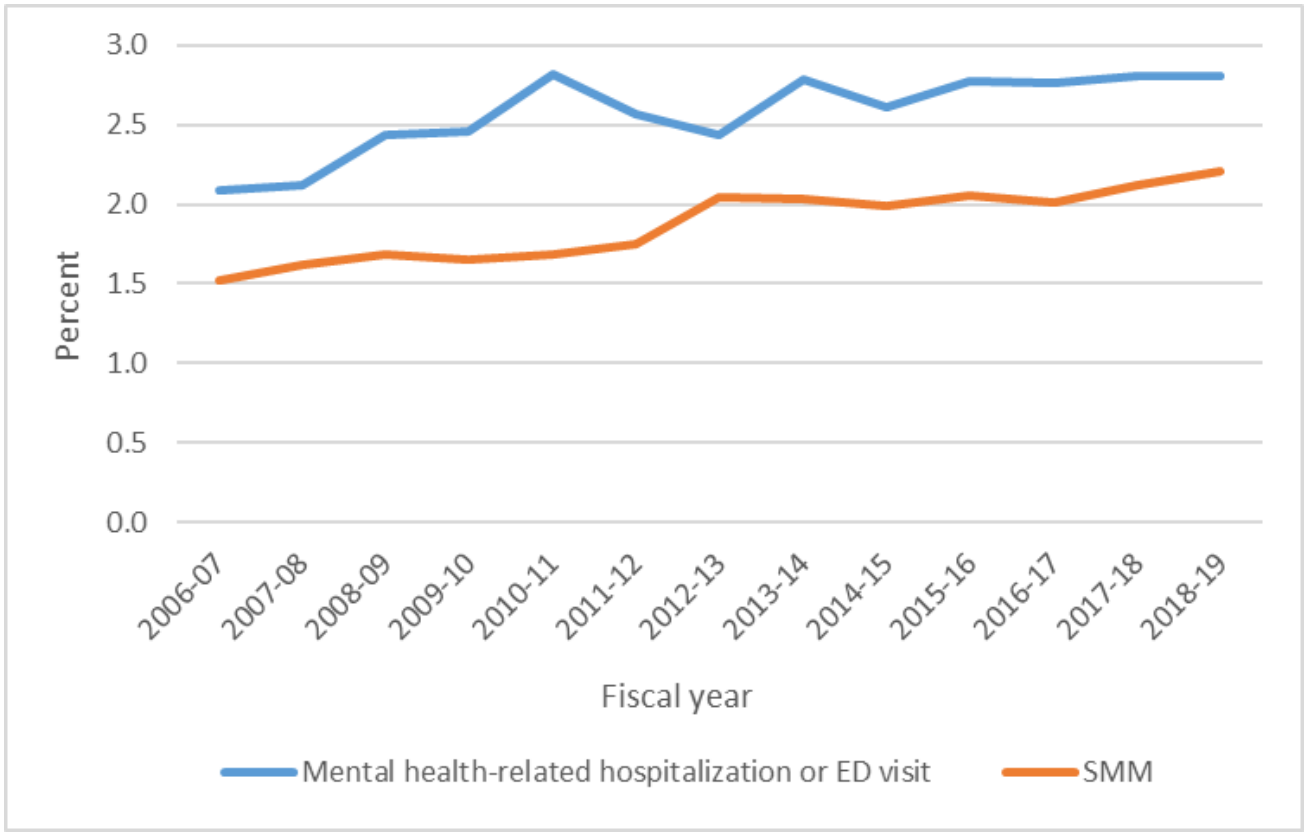
Figure 2: A Graph Displaying the Percentage of Deliveries with SMM and the Percentage of Deliveries with A Mental Health-Related Hospitalization or ED Visit Within Two Years of Index Delivery Over Between Fiscal Years 2006/2007 and 2018/2019 in Canada (excluding Québec)

Figure 3: Forest Plot of Adjusted Hazard Ratios for the Relationship Between SMM Subtypes and Mental Health-Related Hospitalization or ED Visit

Figure 4: Forest Plot of Hazard Ratios for the Relationship Between SMM and Mental Health-Related Hospitalization or ED Visit, by Province/Territory



1 This cohort was used to calculate outcomes of mental health-related hospitalization alone
2 This cohort was used to calculate outcomes that included ED visits. That is, mental health-related hospitalization or ED visit and mental health-related ED visit


3.0
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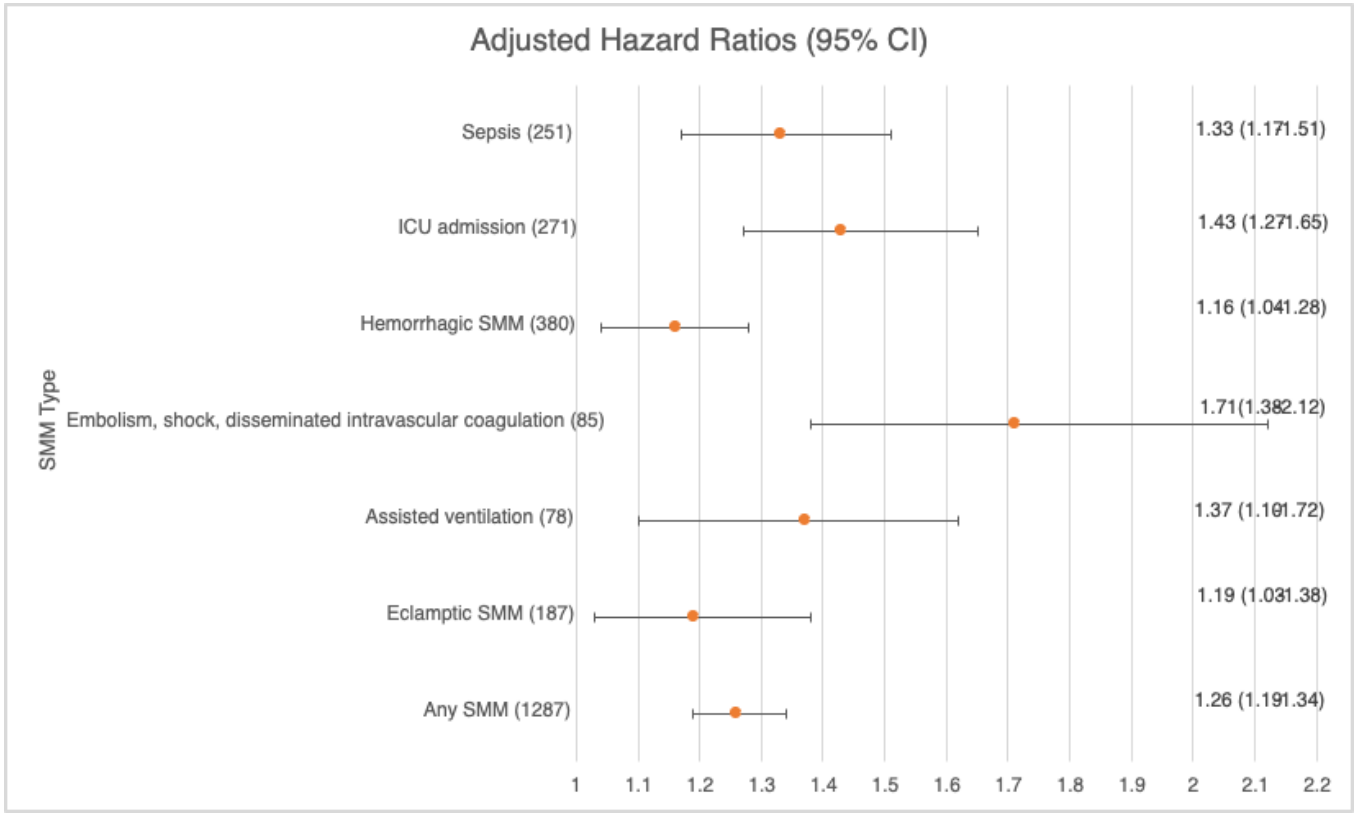
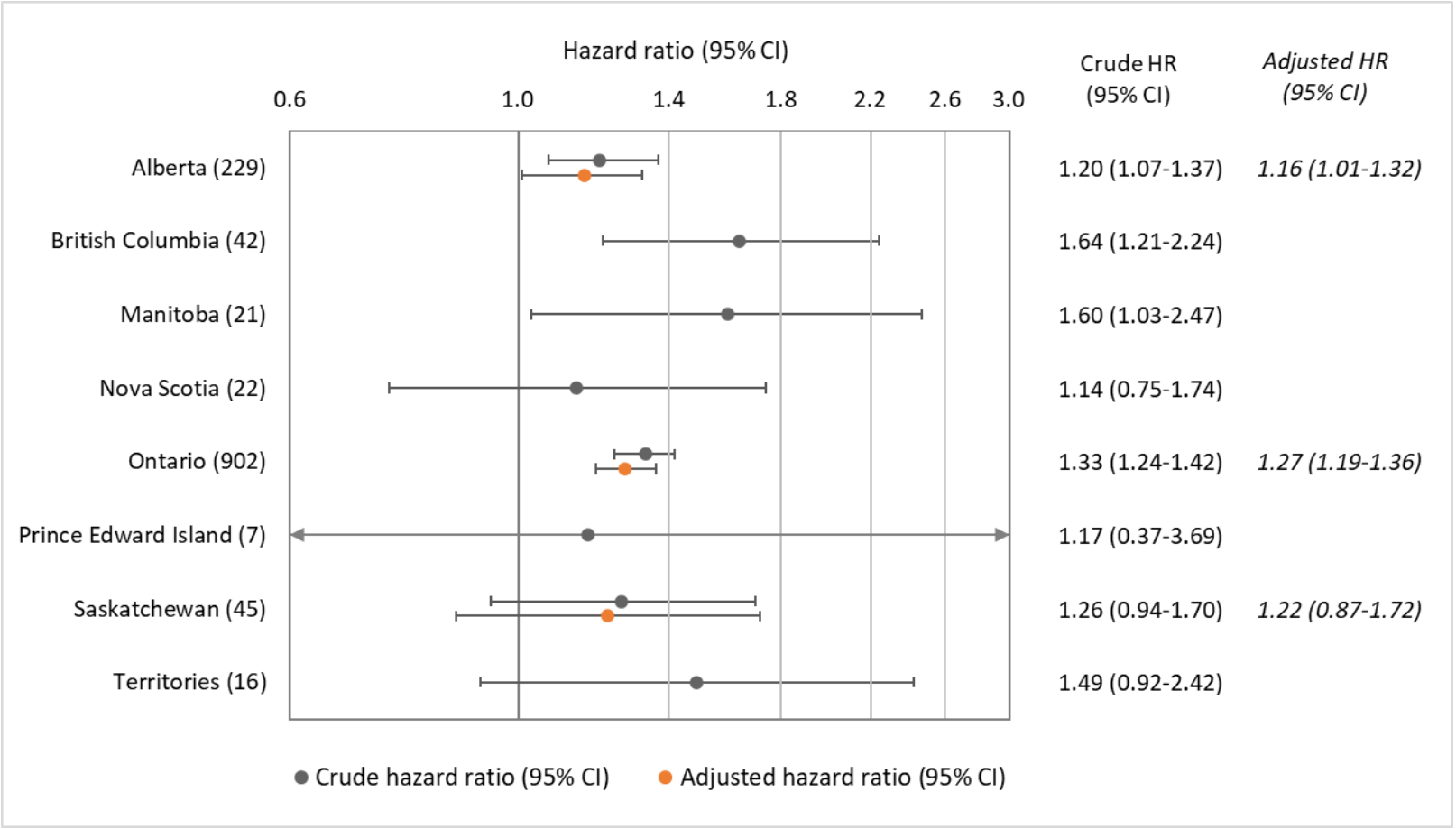
Fiscal year
Mental health-related hospitalization or ED visit
SMM



Note: Hazard ratios compare SMM to reference group No SMM



Note: Numbers in parentheses next to provinces represent the number of women with both SMI and SMM. Adjusted hazard ratios are shown for provinces where the number of women with both a mental health-related hospitalization or ED visit and SMM is ≥45. Estimates were not reportable for New Brunswick and Newfoundland and Labrador due to small cell counts.

Table 1. Baseline characteristics of study cohort at first recorded hospital delivery, stratified according to the presence or absence of severe maternal morbidity (N=2 026 594).

	No SMM		SMM		Standardized difference
	N	%	N	%	
All	1981326	97.77	45268	2.23	
Maternal age at delivery (y)					
Mean +/-SD	29.7 +/- 5.4		30.7+/-6.0		
18-24	348196	17.6	7752	17.1	-0.01
25-29	603142	30.4	11810	26.1	-0.10
30-34	647450	32.7	14228	31.4	-0.03
35-39	308039	15.5	8480	18.7	0.09
40-44	69319	3.5	2618	5.8	0.11
>=45	5089	0.3	380	0.8	0.07
Income quintile					
Lowest quintile	38560	1.9	869	1.9	0.00
Second quintile	458050	23.1	11438	25.3	0.05
Third quintile	409264	20.7	9274	20.5	0.00
Fourth quintile	399593	20.2	8820	19.5	-0.02
Highest quintile	376461	19	8355	18.4	-0.02
Missing	299398	15.1	6512	14.4	-0.02
Delivery Year					
2008-09	214662	10.8	3986	8.8	-0.07

	2009-10	184980	9.3	3481	7.7	-0.06
	2010-11	164617	8.3	3198	7.1	-0.05
	2011-12	156169	7.9	3281	7.2	-0.03
	2012-13	150845	7.6	3682	8.1	0.02
	2013-14	146380	7.4	3552	7.8	0.02
	2014-15	146069	7.4	3408	7.5	0.00
	2015-16	143140	7.2	3595	7.9	0.03
	2016-17	141685	7.2	3432	7.6	0.02
	2017-18	139173	7	3550	7.8	0.03
	2018-19	136925	6.9	3544	7.8	0.03
	2019-20	139204	7	3459	7.6	0.02
	2020-21	117492	5.9	3107	6.9	0.04
Province						
	Alberta	343552	17.3	8788	19.4	0.05
	British Colombia	316336	16	7047	15.5	-0.01
	Manitoba	99824	5	2382	5.3	0.01
	New Brunswick	48059	2.4	1205	2.7	0.02
	Newfoundland and Labrador	32529	1.6	913	2	0.03
	Nova Scotia	60551	3.1	1339	3	-0.01
	Ontario	971530	49	21028	46.5	-0.05
	Prince Edward Island	9102	0.5	194	0.4	-0.01
	Saskatchewan	90960	4.6	2140	4.7	0.00
	Northern Territories	8884	0.4	232	0.5	0.01

Comorbidity[1]					
0	1714004	86.5	33553	74.1	-0.32
1	244864	12.4	9395	20.8	0.23
>=2	22458	1.1	2320	5.1	0.23
Urban/rural residence					
Urban	1686506	85.1	37670	83.2	-0.05
Rural/Remote	257049	13	6750	14.9	0.05
Missing	37771	1.9	848	1.9	0.00
Non-severe hypertensive disorders of pregnancy					
Yes	1862445	94	40386	89.2	-0.17
No	118881	6	4882	10.8	0.17
Gestational diabetes					
Yes	159854	8.1	5132	11.3	0.11
No	1821472	91.9	40136	88.7	-0.11
Gestational age (weeks)					
Median(IQR)	39(38,40)		38(36,40)		
<=22	4201	0.2	317	0.6	0.06
22-27	12103	0.6	1497	3.3	0.20
28-32	18028	0.9	2418	5.4	0.26
33-36	117785	5.9	6764	15	0.30
>=37	1828550	92.3	34290	75.7	-0.46
Missing	670	0	16	0	0.00
Pre-term birth					

Yes	152117	7.7	10962	24.2	0.46
No	1828546	92.3	34290	75.7	-0.46
Missing	663	0	16	0	0.00
Still birth					
Yes	9668	0.5	714	1.6	0.11
No	1971658	99.5	44554	98.4	-0.11
Delivery mode					
Cesearean	608337	30.7	24171	53.4	0.47
Vaginal	1094914	55.3	14731	32.6	-0.47
Obstetric delivery not otherwise specified	278075	14	6366	14.1	0.00
Hospital type					
Teaching tertiary hospital	870796	43.9	23502	51.9	0.16
Community	1099919	55.5	21506	47.5	-0.16
Missing	10611	0.5	260	0.6	0.01

[1]Comorbidity includes pre-existing hypertension, diabetes mellitus, chronic kidney disease, chronic liver disease, cardiovascular condition, sickle cell disease, HIV, autoimmune syndrome such as systemic lupus erythematosus, asthma, obesity and smoking

Table 2. Frequency and incidence rates of mental health-related hospitalizations or emergency department visits according to characteristics of first recorded hospital delivery (N=1 579 372)

	Number of mental-health related hospitalizations or ED visits	Number of person-years	Incidence rate per 10,000 person-years (95% CI)

Total cohort (1 579 372)	43066	5879735	73.24(72.55-73.94)
Maternal age at delivery (y)			
18-24	14922	871259	171.27(168.52-174.01)
25-29	11113	1543777	71.99(70.64-73.32)
30-34	9903	1929888	51.31(50.30-52.32)
35-39	5564	1188251	46.83(45.59-48.06)
40-44	1462	322437	45.34(43.02-47.67)
>= 45	102	24122	42.29(34.08-50.49)
Income quintile			
Lowest quintile	13299	1435654	92.63(91.06-94.21)
Second quintile	9382	1223606	76.68(75.12-78.23)
Third quintile	8078	1172466	68.90(67.40-70.40)
Fourth quintile	6761	1070181	63.18(61.67-64.68)
Highest quintile	4699	852590	55.11(53.54-56.69)
Missing	847	125238	
Comorbidity[1]			
0	35264	5065994	69.61(68.88-70.34)
1	6722	738654	91.00(88.83-
>=2	1080	75088	143.83(135.25-152.41)
Urban/rural residence			
Urban	34834	5180595	67.24(66.53-67.95)
Rural/Remote	7421	576117	128.81(125.88-131.74)
Missing	811	123023	
Non-severe hypertensive disorders of pregnancy			
Yes	2731	345853	78.96(76.00-81.93)

No	40335	5533882	72.89(72.18-73.60)
Gestational diabetes			
Yes	3064	476944	64.24(61.97-66.52)
No	40002	5402791	74.04(73.32-74.77)
Gestational age (weeks)			
<=23	133	9893	134.44(111.59-157.29)
23-28	384	42355	90.66(81.59-99.73)
28-33	591	64899	91.06(83.72-98.41)
33-36	3451	383662	89.95(86.95-92.95)
>=36	38471	5376772	71.55(70.84-72.27)
Missing	36	2155	
Pre-term birth (Gestational age at delivery < 37 weeks)			
Yes	4559	500809	91.03(88.39-93.68)
No	38471	5376772	71.55(70.84-72.27)
Missing	36	2154	
Still birth			
Yes	245	20979	116.78(102.16-131.40)
No	42821	5858756	73.09(72.40-73.78)
Delivery mode			
Caesarean	13438	1916645	70.11(68.93-71.30)
Vaginal	24750	3228415	76.66(75.71-77.62)
Obstetric delivery NOS	4878	734675	66.40(64.53-68.26)
Hospital type			

	Teaching tertiary care hospital	14658	2290466	64.00(62.96-65.03)
	Community hospital	27792	3539042	78.53(77.61-79.45)
	Missing	616	50228	

Table 3. Severe maternal morbidity and associated rate and risk of mental health-related hospitalization and/or emergency department visits, 2008 - 2021. Also shown are rates and risks of specific mental health diagnoses (N = 1 579 372).

	Mental health-related hospitalization or ED visit [2]					Mental health-related hospitalization					Mental health-related ED visit [2]				
SMM	n/N	Total person-years	Incidence rates (IRs) per 10,000 person-years	Crude HR (95% CI)	Adjusted HR[3] (95% CI)	n/N	Total person-years	IRs per 10,000 person-years	Crude HR (95% CI)	Adjusted HR[3] (95% CI)	n/N	Total person-years	IRs per 10,000 person-years	Crude HR (95% CI)	Adjusted HR[3] (95% CI)
Any mental health condition															
Overall	43066/ 1579392	5879735	73.2	-	-	11176/ 2026594	8597956	13.0	-	-	40432/ 1579392	5887822	68.7	-	-
SMM	1287/ 35825	133969	96.1	1.31(1.24-1.39)	1.26(1.19-1.34)	388/ 45268	194634	19.9	1.57(1.35-1.81)	1.42(1.22-1.64)	1193/ 35825	134267	88.9	1.29(1.22-1.37)	1.25(1.18-1.33)
No SMM	41779/ 1543567	5745766	72.7	ref	ref	10788/ 1981326	8402962	12.8	ref	ref	39239/ 1981326	5753556	68.2	ref	ref
Mood or anxiety disorder															
Overall	34997/ 1579392	5907143	59.2	-	-	6575/ 2026594	8614661	7.63	-	-	33260/ 1579392	5912667	56.25	-	-
SMM	1016/ 35825	134861	75.3	1.28(1.20-1.36)	1.23(1.16-1.31)	230/ 45268	195179	11.78	1.56(1.37-1.78)	1.49(1.31-1.70)	959/ 35825	135034	71.02	1.27(1.19-1.35)	1.23(1.15-1.31)
No SMM	33981/ 1543567	5772282	58.9	ref	ref	6345/ 1981326	8419482	7.54	ref	ref	32301/ 1543567	5777633	55.91	ref	ref
Schizophrenia spectrum and other psychotic disorders															
Overall	2501/ 1579392	6028454	4.15	-	-	1295/ 2026594	8637258	1.50	-	-	2142/ 1579392	6029524	3.55	-	-
SMM	70/ 35825	138352	5.06	1.24(0.98-1.57)	1.18(0.93-1.50)	47/ 45268	195921	2.40	1.63(1.21-2.17)	1.53(1.21-2.06)	51/ 35825	138425	3.68	1.04(0.80-1.37)	1.02(0.77-1.34)

No SMM	2431 /1543567	5890102	4.13	ref	ref	1248/ 1981326	8441338	1.48	ref	ref	2091/ 1543567	5891098	3.55	ref	ref
Substance abuse and other related disorders															
Overall	10240/ 1579392	6004512	17.05	-	-	3774/ 2026594	8628700	4.374	-	-	9306/ 1579392	6007100	15.49	-	-
SMM	313/ 35825	137636	22.74	1.30(1.16-1.46)	1.22(1.09-1.38)	132/ 45268	195631	6.75	1.56(1.31-1.86)	1.47(1.22-1.74)	283/ 35825	137734	20.55	1.33(1.19-1.50)	1.23(1.09-1.39)
No SMM	9927/ 15435657	5866877	16.92	ref	ref	3642/ 1981326	8433069	4.32	ref	ref	9023/ 1543567	5869366	15.37	ref	ref
Suicidality or self-harm															
Overall	2888/ 1579392	6027271	4.79	-	-	1272 /2026594	8637163	1.473	-	-	2559/ 1579392	6028407	4.24	-	-
SMM	106/ 35825	138258	7.67	1.60(1.31-1.95)	1.54(1.26-1.88)	48/ 45268	195937	2.45	1.68(1.26-2.25)	1.49(1.31-1.70)	91/ 35825	138301	6.58	1.57(1.27-1.93)	1.23(1.15-1.31)
No SMM	2782/ 1543567	5889013	4.72	ref	ref	1224/ 1981326	8441226	1.45	ref	ref	2468/ 1542567	5890106	4.19	ref	ref

[2]Alberta contributes ED data for followup from 2010-2021, British Columbia contributed ED data for followup from 2008-2010 and 2011-2021, Manitoba contributes ED data for followup from 2009-2021, New Brunswick contributes no ED data for followup, Newfoundland and Labrador contribute no ED data for followup Nova Scotia contributes ED data for followup from 2008-2021, Ontario contributes ED data for followup from 2008-2021, Saskatchewan contributes ED data for followup from 2010-2021, the Northern Territories contribute ED data for followup from 2008-2021

[3]Hazard ratios have been adjusted for maternal age at delivery, income quintile, comorbidity, delivery year and urban or rural residential status

Thesis Discussion

In this thesis, we examined the association between SMM - both overall and by subtype - and a composite of inpatient hospitalizations or ED visit for mental health conditions capturing mood, anxiety, substance use, psychotic disorders and suicidality. Using the DAD and NACRS administrative datasets from CIHI, we conducted a large nationwide longitudinal cohort study of individuals who delivered liveborn or stillborn neonates between 20 and 43 weeks' gestation in Canada (excluding Québec). We used complete case analysis because less than 5% of values in our dataset were missing.

The results of our longitudinal study of more than 2 million Canadian deliveries suggested that composite SMM is associated with a moderately increased risk of hospitalization or ED visit for a mental health condition up to 13 years after delivery, as compared to no SMM. Results showed that the risk of mental health-related hospitalization or ED visit was highest in the first year postpartum, but remained elevated for several years postpartum. Our findings suggest that when compared with those who do not have SMM, individuals who experience SMM have the greatest risk of future hospitalization or ED visit for suicidality and self-harm, then schizophrenia-spectrum and psychotic disorders, followed by mood and anxiety disorders, and finally substance use and other related disorders.

The risk of mental-health related hospitalization or ED visit was highest in individuals who were admitted to the maternal ICU and those who had an embolism, shock and disseminated intravascular coagulation during pregnancy. The risk of mental health-related hospitalization or ED visit after SMM was found to higher in those with hemorrhagic as compared with nonhaemorrhagic SMM.

Among SMM-affected individuals, the relative risk was higher for mental health hospitalizations even though the frequency was higher for mental health-related ED visit, suggesting that SMM confers risk for the most serious type of mental health issues. Analyses of the regional variation in the associations between SMM and mental health-related hospitalization or ED visit were limited by small sample sizes. Despite this, we found a higher relative risk of mental health-related hospitalization or ED visit after any SMM compared to no SMM in Alberta and Ontario. In our stratified analysis among individuals with previous mental illness, the relative risk of mental health-related hospitalization or ED visit after SMM was not appreciably different from the result in the primary analysis where these individuals were excluded.

Contributions to the literature

The work done here expands on available knowledge about the relationship between SMM and severe mental health outcomes, including hospitalization or ED visits. We demonstrate evidence of a relationship between severe pregnancy complications and long-term risk of mental health-outcomes. The elevated risk estimate among individuals with a maternal ICU admission could indicate that any critical illness during or around a delivery, and associated separation from their infant may trigger for stressful and potentially lasting traumatic responses in the mother .[37,81,82]

In accordance with evidence from studies by Lewkowitz et al[13] and Wall-Wieler et al,[14] our findings suggest that the first postpartum year is a critical time for clinical monitoring and psychological assessment, especially after surviving a life-threatening event in pregnancy. That our results showed persistent elevated risk of mental health-related hospitalization or ED visit, including for suicidal behaviours beyond the fifth postpartum year suggest that monitoring may need to be extended for certain high-risk subgroups. Unlike our study, neither of these studies use the Canadian definition of SMM, which includes antepartum events, postpartum events and events that occur during the delivery hospitalization. Other important differences are those related to healthcare system structure and patient population. [13,14]

Provincial variation in results is likely due to differences in health service mandates and resource availability and might suggest the need for more standardized efforts at perinatal mental health care. This work adds to the obstetric literature around the long-term health implications of severe pregnancy complications and is useful for developing appropriate clinical postpartum care pathways for high-risk individuals. This study also highlights the need for additional supportive mental health resources during, and more importantly, beyond the first postpartum year after delivery.

Limitations

Administrative datasets are excellent resources often leveraged for research because they are population-based and allow assessment of rare exposures and outcomes over time. However, there are limitations associated with these data sources, and researchers who use them to perform observational studies must address their potential for misclassification of exposures and outcomes and confounding.

1. Misclassification

Administrative datasets are susceptible to misclassification, often due to errors in coding and data entry. Misclassification can either be differential - when the sensitivity and specificity of the outcome varies by exposure status - or non-differential. The outcome in this study was a composite of mental health conditions, which are diagnosed by the attending physician. Previous validation studies in administrative data have demonstrated that ICD codes for depression, schizophrenia spectrum and other psychotic disorders, suicidality and self-harm and substance abuse and other addictive disorders have low to moderate sensitivity and high specificity, when compared with physician assessments.[66,67,79,80] Also we did not have access to outpatient clinical assessments, which limited our ability to identify individuals with mental health conditions that did not require hospitalization. A bias analysis assessing the impact that misclassification of previous mental illness on estimates showed that misclassification of individuals with previous mental illness biased results away from the null. However, given the length of time between the exposure and outcome and how little is known about the relationship between severe pregnancy complications and severe mental health outcomes, it is unlikely any of this misclassification will differ by

exposure status, so misclassification of the outcome is most likely to be non-differential and would be expected to bias our findings toward the null. That is, our estimate is likely an under-estimate of the link between SMM and mental health outcomes. Significant exposure misclassification is unlikely, as our exposure was defined by the validated SMM composite from the Canadian Perinatal Surveillance System and includes severe conditions which are less likely to be misdiagnosed by clinicians or incorrectly coded by trained abstractors. On the other hand, it is likely that some of the confounding variables are misclassified, adding bias to our estimates. For instance, it is well documented that definitions of comorbid conditions have low to moderate sensitivity and specificity in administrative data.[80] Finally, due to the data sources used, this study doesn't capture data on completed suicide, only suicide attempts that resulted in a hospitalization or ED visit, potentially underestimating the relationship between SMM and suicidality or self-injurious behaviours.

2. Confounding

Confounding impacts all non-randomized study designs. Observational studies are particularly susceptible to bias from residual confounding from both measured and unmeasured confounders. In our case we were unable to account for important confounders related to race and ethnicity as these are not captured by DAD or NACRS. It is possible that these variables could be contributing to observed associations.

3. Selection bias

The cohort for this study was identified from hospital discharge abstracts from administrative datasets, which record approximately 98% of all Canadian deliveries, therefore selection bias is unlikely. We used a directed acyclic graph and tested crude associations between variables for collinearity to determine which covariates we should include in adjusted models in order to limit the possibility of selection bias by adjustment for colliders.

4. Missing Data

It is common for observational data to have missing data. Based on prior validation studies and DAD and NACRS data quality reports, we assumed that data were missing at random. Further, all variables were assessed and found to have less than 5% missingness, the threshold under which it is safe to assume that deletion in complete case analysis will not meaningfully impact estimates in large datasets, according to Stavseth et al. [83]

5. External validity

This study uses Canadian data and examines outcomes indicative of severe mental health conditions, identified by hospitalization or ED visits. Given the absence of outpatient mental health

data, it is likely that this limits generalizability to other populations and individuals with less severe mental health conditions. In addition, in our analyses SMM was treated as a fixed exposure in the first recorded birth as opposed to a time-varying exposure, potential limiting the generalizability of the results to any SMM-affected pregnancy.

We elected not to perform regression analyses in instances where there were less than 45 SMM-affected individuals with the outcome, and therefore were unable to perform provincial analyses of mental health-related hospitalization and mental health-related ED visits. Also, we were unable to determine loss-to-follow-up due to migration or death out of hospital.

Conclusion

Individuals who have SMM are at moderately increased risk of mental health-related hospitalization or ED visit for years after the immediate postpartum period. SMM survivors are at strongly increased risk of hospitalization or ED visit for suicidality or self-harm. Future studies should examine the relationship between severe pregnancy complications and mental health conditions in individual provinces and should also examine outcomes including outpatient visits and pharmacy data.

References

1. Chen J, Cox S, Kuklina EV, Ferre C, Barfield W, Li R. Assessment of Incidence and Factors Associated With Severe Maternal Morbidity After Delivery Discharge Among Women in the US. *JAMA Netw Open*. 2021;4(2):e2036148. doi:10.1001/jamanetworkopen.2020.36148

2. Dzakpasu S, Deb-Rinker P, Arbour L, et al. Severe maternal morbidity surveillance: Monitoring pregnant women at high risk for prolonged hospitalisation and death. *Paediatr Perinat Epidemiol*. 2020;34(4):427-439. doi:10.1111/ppe.12574

3. Geller SE, Koch AR, Garland CE, MacDonald EJ, Storey F, Lawton B. A global view of severe maternal morbidity: moving beyond maternal mortality. *Reprod Health*. 2018;15(1):98. doi:10.1186/s12978-018-0527-2

4. Arya S, Mulla ZD, Plavsic SK. Outcomes of Women Delivering at Very Advanced Maternal Age. *J Womens Health*. 2018;27(11):1378-1384. doi:10.1089/jwh.2018.7027

5. Lebenbaum M, Zaric GS, Thind A, Sarma S. Trends in obesity and multimorbidity in Canada. *Prev Med*. 2018;116:173-179. doi:10.1016/j.ypmed.2018.08.025

6. Schummers L, Hutcheon JA, Hacker MR, et al. Absolute risks of obstetric outcomes risks by maternal age at first birth: a population-based cohort. *Epidemiol Camb Mass*. 2018;29(3):379-387. doi:10.1097/EDE.0000000000000818

7. Tulandi T, King L, Zelkowitz P. Public Funding of and Access to In Vitro Fertilization. *N Engl J Med*. 2013;368(20):1948-1949. doi:10.1056/NEJMc1213687

8. Ukah UV, Dayan N, Potter BJ, Ayoub A, Auger N. Severe Maternal Morbidity and Risk of Mortality Beyond the Postpartum Period. *Obstet Gynecol*. 2021;137(2):277. doi:10.1097/AOG.0000000000004223

9. Ukah UV, Dayan N, Potter BJ, Paradis G, Ayoub A, Auger N. Severe Maternal Morbidity and Long-Term Risk of Cardiovascular Hospitalization. *Circ Cardiovasc Qual Outcomes*. 2022;15(2):e008393. doi:10.1161/CIRCOUTCOMES.121.008393

10. Auger N, Low N, Paradis G, Ayoub A, Fraser WD. Preeclampsia and the longitudinal risk of hospitalization for depression at 28 years. *Soc Psychiatry Psychiatr Epidemiol*. 2021;56(3):429-436. doi:10.1007/s00127-020-01920-x

11. Chen L, Wang X, Ding Q, Shan N, Qi H. Development of Postpartum Depression in Pregnant Women with Preeclampsia: A Retrospective Study. *BioMed Res Int*. 2019;2019:1-7. doi:10.1155/2019/9601476

12. Eckerdal P, Kollia N, Löfblad J, et al. Delineating the Association between Heavy Postpartum Haemorrhage and Postpartum Depression. *PLOS ONE*. 2016;11(1):e0144274. doi:10.1371/journal.pone.0144274

13. LEWKOWITZ AK, ROSENBLOOM JI, KELLER M, et al. Association Between Severe Maternal Morbidity and Psychiatric Illness Within One Year of Hospital Discharge After Delivery. *Obstet Gynecol*. 2019;134(4):695-707. doi:10.1097/AOG.0000000000003434

14. Wall-Wieler E, Carmichael SL, Urquia ML, Liu C, Hjern A. Severe maternal morbidity and postpartum mental health-related outcomes in Sweden: a population-based matched-cohort study. *Arch Womens Ment Health*. 2019;22(4):519-526. doi:10.1007/s00737-018-0917-z

15. Pattinson R, Say L, Souza JP, Broek N van den, Rooney C. WHO maternal death and near-miss classifications. *Bull World Health Organ*. 2009;87:734-734A. doi:10.1590/S0042-96862009001000002

16. Say L, Souza JP, Pattinson RC. Maternal near miss – towards a standard tool for monitoring quality of maternal health care. *Best Pract Res Clin Obstet Gynaecol*. 2009;23(3):287-296. doi:10.1016/j.bpobgyn.2009.01.007

17. Goldenberg RL, Saleem S, Ali S, et al. Maternal near miss in low-resource areas. *Int J Gynaecol Obstet Off Organ Int Fed Gynaecol Obstet*. 2017;138(3):347-355. doi:10.1002/ijgo.12219

18. Nelissen E, Mduma E, Broerse J, et al. Applicability of the WHO Maternal Near Miss Criteria in a Low-Resource Setting. *PLOS ONE*. 2013;8(4):e61248. doi:10.1371/journal.pone.0061248

19. Callaghan WM, Creanga AA, Kuklina EV. Severe maternal morbidity among delivery and postpartum hospitalizations in the United States. *Obstet Gynecol*. 2012;120(5):1029-1036. doi:10.1097/aog.0b013e31826d60c5

20. Jayaratnam S, De COSTA C, Howat P. Developing an assessment tool for maternal morbidity 'near-miss'– A prospective study in a large Australian regional hospital. *Aust N Z J Obstet Gynaecol*. 2011;51(5):421-425. doi:10.1111/j.1479-828X.2011.01330.x

21. Dzakpasu S, Deb-Rinker P, Arbour L, et al. Severe Maternal Morbidity in Canada: Temporal Trends and Regional Variations, 2003-2016. *J Obstet Gynaecol Can*. 2019;41(11):1589-1598.e16. doi:10.1016/j.jogc.2019.02.014

22. Public Health Agency of Canada. Perinatal Health Indicators for Canada 2011. Published online 2012.

23. Public Health Agency of Canada. Perinatal Health Indicators for Canada 2013: a Report of the Canadian Perinatal Surveillance System. Published online 2013.

24. Public Health Agency of Canada, Deb-Rinker P, Decou ML. Perinatal Health Indicators For Canada 2017. Published online June 2017.

25. American College of Obstetricians and Gynecologists and the Society for Maternal–Fetal Medicine, Kilpatrick SK, Ecker JL. Severe maternal morbidity: screening and review. *Am J Obstet Gynecol*. 2016;215(3):B17-22. doi:10.1016/j.ajog.2016.07.050

26. Duke GJ, Maiden MJ, Huning EYS, Crozier TM, Bilgrami I, Ghanpur RB. Severe acute maternal morbidity trends in Victoria, 2001–2017. *Aust N Z J Obstet Gynaecol*. 2020;60(4):548-554. doi:10.1111/ajo.13103

27. Joseph KS, Liu S, Rouleau J, et al. Severe Maternal Morbidity in Canada, 2003 to 2007: Surveillance Using Routine Hospitalization Data and ICD-10CA Codes. *J Obstet Gynaecol Can*. 2010;32(9):837-846. doi:10.1016/S1701-2163(16)34655-2

28. Joseph KS, Mahey J. Validation of perinatal data in the Discharge Abstract Database of the Canadian Institute for Health Information. *Chronic Dis Can*. 2009;29(3):96-101. doi:10.24095/hpcdp.29.3.01

29. Cartus AR, Jarlenski MP, Himes KP, James AE, Naimi AI, Bodnar LM. Adverse Cardiovascular Events Following Severe Maternal Morbidity. *Am J Epidemiol*. 2022;191(1):126-136. doi:10.1093/aje/kwab208

30. Harvey EM, Ahmed S, Manning SE, Diop H, Argani C, Strobino DM. Severe Maternal Morbidity at Delivery and Risk of Hospital Encounters Within 6 Weeks and 1 Year Postpartum. *J Womens Health*. 2018;27(2):140-147. doi:10.1089/jwh.2017.6437

31. Matas JL, Mitchell LE, Sharma SV, Louis JM, Salemi JL. Severe maternal morbidity at delivery and postpartum readmission in the United States. *Paediatr Perinat Epidemiol*. 2021;35(6):627-634. doi:10.1111/ppe.12762

32. Burlina S, Dalfrà MG, Chilelli NC, Lapolla A. Gestational Diabetes Mellitus and Future Cardiovascular Risk: An Update. *Int J Endocrinol*. 2016;2016:1-6. doi:10.1155/2016/2070926

33. Grand'Maison S, Pilote L, Okano M, Landry T, Dayan N. Markers of Vascular Dysfunction After Hypertensive Disorders of Pregnancy: A Systematic Review and Meta-Analysis. *Hypertension*. 2016;68(6):1447-1458. doi:10.1161/HYPERTENSIONAHA.116.07907

34. Lykke JA, Langhoff-Roos J, Lockwood CJ, Triche EW, Paidas MJ. Mortality of mothers from cardiovascular and non-cardiovascular causes following pregnancy complications in first delivery: Pregnancy complications and subsequent maternal mortality. *Paediatr Perinat Epidemiol*. 2010;24(4):323-330. doi:10.1111/j.1365-3016.2010.01120.x

35. Norhayati MN, Nik Hazlina NH, Aniza AA. Immediate and long-term relationship between severe maternal morbidity and health-related quality of life: a prospective double cohort comparison study. *BMC Public Health*. 2016;16(1):818. doi:10.1186/s12889-016-3524-9

36. Silveira C, Parpinelli MA, Pacagnella RC, et al. A cohort study of functioning and disability among women after severe maternal morbidity. *Int J Gynecol Obstet*. 2016;134(1):87-92. doi:10.1016/j.ijgo.2015.10.027

37. Kendall-Tackett K. A new paradigm for depression in new mothers: the central role of inflammation and how breastfeeding and anti-inflammatory treatments protect maternal mental health. *Int Breastfeed J*. 2007;2(1):6. doi:10.1186/1746-4358-2-6

38. Batt MM, Duffy KA, Novick AM, Metcalf CA, Epperson CN. Is Postpartum Depression Different From Depression Occurring Outside of the Perinatal Period? A Review of the Evidence. *FOCUS*. 2020;18(2):106-119. doi:10.1176/appi.focus.20190045

39. Langan Martin J, McLean G, Cantwell R, Smith DJ. Admission to psychiatric hospital in the early and late postpartum periods: Scottish national linkage study. *BMJ Open*. 2016;6(1):e008758. doi:10.1136/bmjopen-2015-008758

40. Lysell H, Dahlin M, Viktorin A, et al. Maternal suicide – Register based study of all suicides occurring after delivery in Sweden 1974–2009. *PLOS ONE*. 2018;13(1):e0190133. doi:10.1371/journal.pone.0190133

41. Meltzer-Brody S, Rubinow D. An Overview of Perinatal Mood and Anxiety Disorders: Epidemiology and Etiology. In: Cox E, ed. *Women's Mood Disorders*. Springer International Publishing; 2021:5-16. doi:10.1007/978-3-030-71497-0_2

42. Schiller C, Dichter G, Bizzell J, et al. Reproductive Hormones Regulate Affect and Reward Circuit Function in Women. *Biol Psychiatry*. 2020;87(9):S217. doi:10.1016/j.biopsych.2020.02.564

43. Szpunar MJ, Malaktaris A, Baca SA, Hauger RL, Lang AJ. Are alterations in estradiol, cortisol, and inflammatory cytokines associated with depression during pregnancy and postpartum? An exploratory study. *Brain Behav Immun - Health*. 2021;16:100309. doi:10.1016/j.bbih.2021.100309

44. Berk M, Williams LJ, Jacka FN, et al. So depression is an inflammatory disease, but where does the inflammation come from? *BMC Med*. 2013;11(1):200. doi:10.1186/1741-7015-11-200

45. Maes M, Kubera M, Obuchowiczwa E, Goehler L, Brzeszcz J. Depression's multiple comorbidities explained by (neuro)inflammatory and oxidative & nitrosative stress pathways. *Neuro Endocrinol Lett*. 2011;32(1):7-24.

46. Amiri S, Behnezhad S. The global prevalence of postpartum suicidal ideation, suicide attempts, and suicide mortality: A systematic review and meta-analysis. *Int J Ment Health*. 2021;50(4):311-336. doi:10.1080/00207411.2021.1959814

47. Chapman SLC, Wu LT. Postpartum Substance Use and Depressive Symptoms: A Review. *Women Health*. 2013;53(5):479-503. doi:10.1080/03630242.2013.804025

48. Smid MC, Terplan M. What Obstetrician–Gynecologists Should Know About Substance Use Disorders in the Perinatal Period. *Obstet Gynecol*. 2022;139(2):317. doi:10.1097/AOG.0000000000004657

49. Slomian J, Honvo G, Emonts P, Reginster JY, Bruyère O. Consequences of maternal postpartum depression: A systematic review of maternal and infant outcomes. *Womens Health*. 2019;15:1745506519844044. doi:10.1177/1745506519844044

50. Goodman JH, Watson GR, Stubbs B. Anxiety disorders in postpartum women: A systematic review and meta-analysis. *J Affect Disord*. 2016;203:292-331. doi:10.1016/j.jad.2016.05.033

51. Liu X, Wang S, Wang G. Prevalence and Risk Factors of Postpartum Depression in Women: A Systematic Review and Meta-analysis. *J Clin Nurs*. 2022;31(19-20):2665-2677. doi:10.1111/jocn.16121

52. Meltzer-Brody S, Howard LM, Bergink V, et al. Postpartum psychiatric disorders. *Nat Rev Dis Primer*. 2018;4:18022. doi:10.1038/nrdp.2018.22

53. Shorey S, Chee CYI, Ng ED, Chan YH, Tam WWS, Chong YS. Prevalence and incidence of postpartum depression among healthy mothers: A systematic review and meta-analysis. *J Psychiatr Res*. 2018;104:235-248. doi:10.1016/j.jpsychires.2018.08.001

54. Falah-Hassani K, Shiri R, Dennis CL. The prevalence of antenatal and postnatal co-morbid anxiety and depression: a meta-analysis. *Psychol Med*. 2017;47(12):2041-2053. doi:10.1017/S0033291717000617

55. Maguire J. Hormonal and immunological factors in postpartum psychosis. In: *Biomarkers of Postpartum Psychiatric Disorders*. Elsevier; 2020:159-179. doi:10.1016/B978-0-12-815508-0.00012-6

56. Jones I. Postpartum psychosis: an important clue to the etiology of mental illness. *World Psychiatry*. 2020;19(3):334-336. doi:10.1002/wps.20780

57. Haglund A, Lysell H, Larsson H, Lichtenstein P, Runeson B. Suicide Immediately After Discharge From Psychiatric Inpatient Care: A Cohort Study of Nearly 2.9 Million Discharges. *J Clin Psychiatry*. 2019;80(2). doi:10.4088/JCP.18m12172

58. Chin K, Wendt A, Bennett IM, Bhat A. Suicide and Maternal Mortality. *Curr Psychiatry Rep*. 2022;24(4):239-275. doi:10.1007/s11920-022-01334-3

59. Lommerse K, Knight M, Nair M, Deneux-Tharaux C, van den Akker T. The impact of reclassifying suicides in pregnancy and in the postnatal period on maternal mortality ratios. *BJOG Int J Obstet Gynaecol*. 2019;126(9):1088-1092. doi:10.1111/1471-0528.15215

60. Lisette RC, Crystal C. Psychiatric emergencies in pregnancy and postpartum. *Clin Obstet Gynecol*. 2018;61(3):615-627. doi:10.1097/GRF.0000000000000377

61. Grigoriadis S, Wilton AS, Kurdyak PA, et al. Perinatal suicide in Ontario, Canada: a 15-year population-based study. *CMAJ Can Med Assoc J*. 2017;189(34):E1085-E1092. doi:10.1503/cmaj.170088

62. Fiest KM, Jette N, Quan H, et al. Systematic review and assessment of validated case definitions for depression in administrative data. *BMC Psychiatry*. 2014;14(1):289. doi:10.1186/s12888-014-0289-5

63. Alaghehbandan R, MacDonald D, Barrett B, Collins K, Chen Y. Using Administrative Databases in the Surveillance of Depressive Disorders—Case Definitions. *Popul Health Manag*. 2012;15(6):372-380. doi:10.1089/pop.2011.0084

64. Singh JA. Accuracy of Veterans Affairs Databases for Diagnoses of Chronic Diseases. *Prev Chronic Dis*. 2009;6(4):A126.

65. Noyes K, Liu H, Lyness JM, Friedman B. Medicare Beneficiaries With Depression: Comparing Diagnoses in Claims Data With the Results of Screening. *Psychiatr Serv*. 2011;62(10):1159-1166. doi:10.1176/ps.62.10.pss6210_1159

66. Doktorchik C, Patten S, Eastwood C, et al. Validation of a case definition for depression in administrative data against primary chart data as a reference standard. *BMC Psychiatry*. 2019;19(1):9. doi:10.1186/s12888-018-1990-6

67. Randall JR, Roos LL, Lix LM, Katz LY, Bolton JM. Emergency department and inpatient coding for self-harm and suicide attempts: Validation using clinician assessment data. *Int J Methods Psychiatr Res*. 2017;26(3):e1559. doi:10.1002/mpr.1559

68. Chen L, Wang X, Ding Q, Shan N, Qi H. Development of Postpartum Depression in Pregnant Women with Preeclampsia: A Retrospective Study. *BioMed Res Int*. 2019;2019:9601476. doi:10.1155/2019/9601476

69. Liu C, Butwick A, Sand A, Wikström AK, Snowden JM, Stephansson O. The association between postpartum hemorrhage and postpartum depression: A Swedish national register-based study. *PLOS ONE*. 2021;16(8):e0255938. doi:10.1371/journal.pone.0255938

70. Parry-Smith W, Okoth K, Subramanian A, et al. Postpartum haemorrhage and risk of mental ill health: A population-based longitudinal study using linked primary and secondary care databases. *J Psychiatr Res*. 2021;137:419-425. doi:10.1016/j.jpsychires.2021.03.022

71. Baghlaf H, Spence AR, Czuzoj-Shulman N, Abenhaim HA. Pregnancy outcomes among women with asthma. *J Matern Fetal Neonatal Med*. 2019;32(8):1325-1331. doi:10.1080/14767058.2017.1404982

72. Petca A, Miron BC, Pacu I, et al. HELLP Syndrome—Holistic Insight into Pathophysiology. *Medicina (Mex)*. 2022;58(2):326. doi:10.3390/medicina58020326

73. Phipps EA, Thadhani R, Benzing T, Karumanchi SA. Pre-eclampsia: pathogenesis, novel diagnostics and therapies. *Nat Rev Nephrol*. 2019;15(5):275-289. doi:10.1038/s41581-019-0119-6

74. Sibai BM, Lindheimer M, Hauth J, et al. Risk factors for preeclampsia, abruptio placentae, and adverse neonatal outcomes among women with chronic hypertension. National Institute of Child Health and Human Development Network of Maternal-Fetal Medicine Units. *N Engl J Med*. 1998;339(10):667-671. doi:10.1056/NEJM199809033391004

75. Vest AR, Cho LS. Hypertension in Pregnancy. *Curr Atheroscler Rep*. 2014;16(3):395. doi:10.1007/s11883-013-0395-8

76. Metcalfe A, Lix L, Johnson J, et al. Validation of an obstetric comorbidity index in an external population. *Bjog*. 2015;122(13):1748-1755. doi:10.1111/1471-0528.13254

77. Fox MP, MacLehose RF, Lash TL. SAS and R code for probabilistic quantitative bias analysis for misclassified binary variables and binary unmeasured confounders. *Int J Epidemiol*. Published online May 4, 2023:dyad053. doi:10.1093/ije/dyad053

78. Fox M, Lash T, MacLehose R. *Applying Quantitative Bias Analysis to Epidemiologic Data*. Springer International Publishing AG

79. Kurdyak P, Lin E, Green D, Vigod S. Validation of a Population-Based Algorithm to Detect Chronic Psychotic Illness. *Can J Psychiatry Rev Can Psychiatr*. 2015;60(8):362-368.

80. Quan H, Li B, Duncan Saunders L, et al. Assessing Validity of ICD-9-CM and ICD-10 Administrative Data in Recording Clinical Conditions in a Unique Dually Coded Database. *Health Serv Res*. 2008;43(4):1424-1441. doi:10.1111/j.1475-6773.2007.00822.x

81. van Veenendaal NR, van Kempen AAMW, Broekman BFP, et al. Association of a Zero-Separation Neonatal Care Model With Stress in Mothers of Preterm Infants. *JAMA Netw Open*. 2022;5(3):e224514. doi:10.1001/jamanetworkopen.2022.4514

82. McGowan S. Does the maternal experience of childbirth affect mother-infant attachment and bonding? *J Health Visit*. 2014;2(11):606-616. doi:10.12968/johv.2014.2.11.606

83. How handling missing data may impact conclusions: A comparison of six different imputation methods for categorical questionnaire data - Marianne Riksheim Stavseth, Thomas Clausen, Jo Røislien, 2019. Accessed June 1, 2023. https://journals.sagepub.com/doi/full/10.1177/2050312118822912

Supplementary Thesis Tables

eTable 1: Canadian Perinatal Surveillance System Definition for Severe Maternal Morbidity with Accompanying ICD-10 and CCI codes

SMM type	SMM subtype	ICD-10 CA and CCI codes
SPE, HELLP, eclampsia	Severe pre-eclampsia, HELLP syndrome	O14.1, O14.2
	eclampsia	O15
Severe hemorrhage	Placenta previa with haemorrhage and red cell transfusion	O44.1 + RBCTRNSF='Y
	Antepartum hemorrhage with coagulation defect	O46.0
	Placental abruption with coagulation defect	O45.0
	Intrapartum hemorrhage with coagulation defect	O67.0
	Intrapartum hemorrhage with red cell transfusion	O67 + RBCTRNSF='Y'
	Postpartum hemorrhage with red cell transfusion, procedures to the uterus or hysterectomy	O72 + any of the following: RBCTRNSF='Y', or (1.RM.13, 1.KT.51, 5.PC.91.LA or 5.PC.91. HV) + RBCTRNSF = 1, or (5.MD.60.RC, 5.MD.60.RD, 5.MD.60.KE, 5.MD.60. CB or 1.RM.89.LAb), or 1.RM.87.LA-GX Note: 1.RM.89.LA is included only if codes 1. PL.74, 1.RS.74 or 1.RS.80 are NOT also present
	Curettage with red cell transfusion	(5.PC.91.GA, 5.PC.91.GC or 5.PC.91. GD) + RBCTRNSF='Y

Maternal ICU admission	Maternal ICU admission	FTSPCU in ('10','20','25','30','35','40','45','60', '80')
Surgical complications	Complications of obstetric surgeries and procedures	O75.4
	Evacuation of incisional hematoma with RBC transfusion	5.PC.73.JS + RBCTRNSF='Y'
	Repair of bladder, urethra, or intestine	5.PC.80.JR, 1.NK.80 or 1.NM.80
	Reclosure of caesarean wound with RBC transfusion	(5.PC.80.JM or 5.PC.80.JH) + RBCTRNSF='Y'
Hysterectomy	Caesarean hysterectomy	5.MD.60.RC, 5.MD.60.RD, 5.MD.60.KE, 5.MD.60.CB
	Hysterectomy using an open approach (without bladder neck suspension, suspension of vaginal vault or pelvic floor repair	1.RM.89.LAc (exclude if 1.PL.74, 1.RS.74 or 1.RS.80 code also present) or 1.RM.87.LA-GX Note: 1.RM.89.LA is included only if codes 1.PL.74, 1. RS.74 or 1.RS.80 are NOT also present
Sepsis	Puerperal sepsis	O85
	Septicemia during labor	O75.3
Embolism, shock, DIC	Obstetric shock	O75.1, R57, T80.5 or T88.6
	Obstetric embolism	O88
	Disseminated intravascular coagulation	D65
Assisted ventilation	Assisted ventilation through endotracheal tube	1.GZ.31.CA-ND
	Assisted ventilation through tracheostomy	1.GZ.31.CR-ND
Cardiac conditions	Cardiac complications of anesthesia	O74.2, O89.1
	Cardiomyopathy	O90.3, I42, I43
	Cardiac arrest and resuscitation	I46, I49.0, 1.HZ.09, 1.HZ.30

	Myocardial infarction	I21, I22
	Pulmonary edema and heart failure	I50, J81
Acute renal failure	Acute renal failure	O90.4, N17, N19 or N99.0
	Dialysis	1.PZ.21
Severe uterine rupture	Rupture of the uterus with red cell transfusion, procedures to the uterus or hysterectomy	(O71.0 or O71.1) + any of the following: RBCTRNSF='Y', or (1.RM.13, 1.KT.51, 5.PC.91.LA or 5.PC.91. HV) + RBCTRNSF='Y', or (5.MD.60.RC, 5.MD.60.RD, 5.MD.60.KE, 5.MD.60. CB or 1.RM.89.LA), or 1.RM.87.LA-GX a Note: 1.RM.89.LA is included only if codes 1. PL.74, 1.RS.74 or 1.RS.80 are NOT also present
Cerebrovascular Accident	Cerebral venous thrombosis in pregnancy	O22.5
	Cerebral venous thrombosis in the puerperium	O87.3
	Subarachnoid and intracranial hemorrhage, cerebral infarction	I60, I61, I62, I63 or I64
Other types	Acute fatty liver with red cell transfusion or plasma transfusion	O26.6 + (RBCTRNSF='Y' or PLSTRNSF='Y')
	Hepatic failure	K71 or K72
	Cerebral edema or coma	G93.6 or R40.2
	Pulmonary, cardiac and CNS complications of anaesthesia during pregnancy, labour, delivery or the puerperium	O29.0, O29.1, O29.2, O89.0, O89.1, O89.2, O74.0, O74.1, O74.2 or O74.3
	Status asthmaticus	J45.01, J45.11, J45.81 or J45.91

	Adult respiratory distress syndrome	J80
	Acute abdomen	K35, K37, K65, N73.3 or N73.5
	Surgical or manual correction of inverted uterus for vaginal births only	5.PC.91.HQ or 5.PC.91.HP, restricted to vaginal births (i.e., absence of caesarean code 5.MD.60)
	Sickle cell anemia with crisis	D57.0
	Acute psychosis	F53.1 or F23
	Status epilepticus	G41
	HIV disease	B20-24, O98.7

eTable 2: Indicators of Mental Illness Included in Primary Outcome Composite with Accompanying ICD-10-CA codes

Outcome	Individual diagnoses	ICD-10-CA codes
Substance-Related and Addictive Disorders	Abuse of non-psychoactive substances	F55
	Abuse of psychoactive substances	F10 to F19
Mood and Anxiety Disorders	Mood disorder due to known physiological condition	F06.3
	Manic episode	F30
	Bipolar disorder	F31
	Depressive episode	F32
	Major depressive disorder, recurrent	F33
	Persistent mood (affective) disorders	F34
	Unspecified mood (affective) disorders	F39

	Anxiety disorder due to known physiological condition	F06.4
	Phobic anxiety disorders	F40
	Other anxiety disorders	F41
	Obsessive compulsive disorder	F42
	Reaction to severe stress, and adjustment disorders	F43
	Other specified nonpsychotic mental disorders	F48.8
	Nonpsychotic mental disorder, unspecified	F48.9
	Mental and behavioral disorders associated with the puerperium, not elsewhere classified	F53
Suicidality or Deliberate Self Harm	Intentional self-harm	X60-X84,
	Poisoning	Y10-Y19,
	Contact with sharp object	Y28, Note when DX10CODE1 not equal F06-F99 (DXTYPE = alldx or DXTYPE = 9)
Schizophrenia spectrum and other psychotic disorders	Psychotic disorder with hallucinations due to known physiological condition	F06.0
	Psychotic disorder with delusions due to known physiological condition	F06.2
	Schizophrenia	F20 (excl. F20.4)
	Delusional disorders	F22
	Brief psychotic disorder	F23
	Shared psychotic disorders	F24
	Schizoaffective disorders	F25

	Other psychotic disorder not due to substance or known physiological condition	F28
	Unspecified psychosis not due to a substance or known physiological condition	F29
	Puerperal psychosis	F53.1
Substance-related and addictive disorders	Alcohol related disorders	F10
	Opioid related disorders	F11
	Cannabis related disorders	F12
	Sedative, hypnotic or anxiolytic related disorders	F13
	Cocaine related disorders	F14
	Other stimulant related disorders	F15
	Hallucinogen related disorders	F16
	Nicotine dependence	F17
	Inhalant related disorders	F18
	Other psychoactive substance related disorders	F19
	Abuse of nonpsychoactive substances	F55

eTable 3: Covariates in Our Study with Accompanying ICD-10-CA codes

Covariate	Subcategories	ICD-10-CA codes
Maternal age at delivery	<=19	
	20-24	

	25-29	
	30-34	
	35-39	
	>=40	
Income quintile	Lowest quintile	
	Second quintile	
	Third quintile	
	Fourth quintile	
	Highest quintile	
Year of birth	2008	
	2009	
	2010	
	2011	
	2012	
	2013	
	2014	
	2015	
	2016	
	2017	
	2018	
	2019	
	2020	
Province	Alberta	
	British Columbia	
	Manitoba	
	New Brunswick	
	Newfoundland and Labrador	
	Nova Scotia	

	Ontario	
	Prince Edward Island	
	Saskatchewan	
Comorbidity	Pre-existing hypertension	O10, O11, I10-I16, I27, I27.2, K76., B65. I45
	Diabetes mellitus	E10, E11, E13, O24, E74.8
	Chronic kidney disease	N18.^^,N03-N05, N07, N08, N11.1, N11.9, N19.^^, N25.0, N25.1, N25.8, N25.9, N26, Z49.0-Z49.2 or Z99.2
	Chronic liver disease	B18.0, B18.1, B18.2, B18.8, B18.9, K70.^, K71.1, K71.3-K71.5, K 71.7, K72.^, K74.^, K75.4, K76.0,K76.2-K76.9, Z94.4
	Cardiovascular condition	P29.8, P29.9, I05-I09, I20.^, I25.^, I27.8, I30.^, I31.^, I33.^-I28.^ 1.40.^, I44.^, I45.^,I47.^-I49.^,Q20.^, Q21.^, Q23.^, Q24
	Sickle cell disease	D57
	HIV	B20, O98.72
	Autoimmune syndrome	L93, M30, M32, M33, M34,M35 or M36
	Asthma	J45.^ or O99.5
	Obesity	Z68.31, Z68.32, Z68.33, Z68.34, Z68.35, Z68.36, Z68.37, Z68.38, Z68.39 or O99.21
	Smoking	O99.33x, Z71.6, F17.210, F17.213, F17.218, F17.219
Non-severe hypertensive disorders of pregnancy	Moderate pre-eclampsia	O13, O14

Gestational diabetes		O24
Pre-term birth	Gestational age < 37 Gestational age >= 37	O60
Still birth		O36.4, O31, Z37.1, Z37.4
Delivery mode	Cesearean	
	Vaginal	
	Obstetric Not Otherwise Specified	
Hospital type	Teaching tertiary care Community hospital	

eTable 4: Associations of Severe Maternal Morbidity with the Risk of Hospitalization and/or ED Visit Capturing a Mental Health Condition Recorded in Any of the Twenty-Five Diagnostic DAD Fields

	Mental health-related hospitalization or ED visit				
SMM	Total mental health-related hospitalization or ED visits (n)	Total person-years	Incidence rates (IRs) per 10,000 person-years	Crude HR (95% CI)	Adjusted HR[3] (95% CI)
Any	1479	133200	111.04	1.39(1.32-1.46)	1.33(1.26-1.39)
None	45532	5732934	79.42	ref	ref

[3]Hazard ratios have been adjusted for maternal age at delivery, income quintile, comorbidity, delivery year and urban or rural residential status

eTable 5: Associations of Severe Maternal Morbidity with the Risk of Mental Health-Related Hospitalization or ED Visit Among Individuals with Previous Mental Illness

	Mental health-related hospitalization or ED visit				
	Total mental health-related hospitalization or ED visits (n)	Total person-years	Incidence rates (IRs) per 10,000 person-years	Crude HR (95% CI)	Adjusted HR[3] (95% CI)
Overall	10149	126949	799.45		

Any SMM	429	4041	1061.62	1.30(1.18-1.44)	1.21(1.10-1.34)
No SMM	9720	122908	790.8354	ref	ref

[3]Hazard ratios have been adjusted for maternal age at delivery, income quintile, comorbidity, delivery year and urban or rural residential status

eTable 6: Associations of Severe Maternal Morbidity with the Risk of Mental Health-Related Hospitalization or ED Visit Among Individuals with Varying Followup Times

Followup Time	**Total mental health-related hospitalization or ED visits (n)**	**Total person-years**	**Incidence rates (IRs) per 10,000 person-years**	**Crude HR (95% CI)**	**Adjusted HR[3](95% CI)**
			followup <=1 year		
Overall	10885	173254	628.2683		
Any SMM	356	3707	960.3453	1.57(1.41-1.74)	1.52(1.37-1.69)
No SMM	10529	169547	621.0077	ref	ref
			>1 year and <=5 years		
Overall	22491	2057417	109.3167		
Any SMM	670	47458	141.1775	1.25(1.15-1.35)	1.27(1.18-1.38)
No SMM	21821	2009960	108.5643	ref	ref
			>5 years		
Overall	9690	3649064	26.55475		
Any SMM	261	82804	31.52022	1.25(1.10-1.41)	1.21(1.07-1.37)
No SMM	9429	3566250	26.43954	ref	ref

[3]Hazard ratios have been adjusted for maternal age at delivery, income quintile, comorbidity, delivery year and urban or rural residential status