Severe maternal morbidity: Fundamental concepts

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ABSTRACT

PURPOSE OF REVIEW Despite the importance of severe maternal morbidity (SMM) as a medical concern, there is a lack of consensus on several issues related to this topic. This article reviews fundamental concepts associated with SMM, and provides a historical and scientific perspective on these critical issues.

RECENT FINDINGS SMM is defined as the population rate of serious illnesses in pregnancy, childbirth, or the puerperium. The SMM rate depends on the component severe maternal illnesses included in composite SMM, the rigor with which these components are defined, and the data sources used for surveillance (among others). These issues pose a serious challenge for spatiotemporal comparisons of SMM, especially for between-country comparisons of composite SMM rates. The different severe maternal illnesses included within composite SMM display substantial heterogeneity in terms of frequency, clinical burden of illness, and population impact. Other concerns include the need to address SMM in early pregnancy hospitalizations and postpartum readmissions; the need for nuanced interpretation of adjusted rates; and whether assigning a singular underlying severe illness is preferable to assigning one or more severe illnesses for each woman. Finally, the heterogeneity of the composite measure warrants careful consideration of the need for an all-inclusive composite outcome versus a more restricted/ specific outcome depending on the study question or surveillance priority. Prevention programs addressing SMM need to focus on component illnesses and identify opportunities for intervention based on case reviews or epidemiologic analyses of risk factors for the specific illness.

SUMMARY There is a lack of consensus on several concepts related to SMM, and this calls for a careful consideration of the clinical and epidemiologic issues related to quantifying and interpreting SMM rates.

Key words: Severe maternal morbidity; definition; types; case fatality; maternal health.

INTRODUCTION

Severe maternal morbidity (SMM) is a significant medical and social concern as severe illnesses in pregnancy, childbirth and the puerperium have acute and debilitating effects on pregnant women and people (hereafter abbreviated as pregnant women). These severe illnesses occur at a critical period in the lives of reproductive age women and often result in long-term physical and mental sequelae. In addition to the above-mentioned burden of illness that makes severe maternal conditions a legitimate target for clinical and public health prevention initiatives, the secular decline in maternal mortality worldwide [1] also provides an opportunity for increasing the focus on these potentially devastating maternal outcomes associated with pregnancy. Not surprisingly, the volume of scientific literature on SMM has increased over 10-fold in recent years: Medline listed fewer than 20 articles per year with SMM as a medical subject heading in the early 1990s, and this has risen to over 200 such articles each year since 2015.

Despite the importance of SMM as a substantive epidemiologic topic, there are several issues in the contemporary scientific literature on which there remains a significant lack of consensus. These includes propositions on diverse issues including the definition of SMM, component conditions to be included within composite SMM (i.e., its types and subtypes), epidemiologic issues pertinent to the interpretation of surveillance findings, and the purpose of SMM surveillance. For instance, the World Health Organization (WHO), equates SMM with "near miss", and recommends that the "same classification of underlying causes [be] used for both maternal deaths and near misses" [2]. However, this injunction is rarely followed, and most contemporary studies on SMM are not based on each case of severe maternal illness being assigned a singular underlying illness or cause.

In this article, we provide a selective review of some of the fundamental concepts related

to SMM, and provide a historical and scientific perspective on this topic of significant relevance to maternal health.

DEFINITION

Many studies on SMM do not formally define the term and instead provide an operationalized listing of the component conditions used for identifying cases of severe maternal illness (e.g., eclampsia, maternal Intensive Care Unit (ICU) admission and acute renal failure) [3-34]. Such lists are typically based on a previously identified set of severe maternal conditions (e.g., SMM list identified by the Centers for Disease Control and Prevention [9,14]) or a previously described list with modifications. Two general definitions of SMM that attempt to address its conceptual essence (i.e., without focusing on the specific components) are presented below and briefly discussed along with an alternative definition based on traditional medical concepts and terminology. Definitions of SMM in the current literature include

1. *Severe acute maternal morbidity, preferably termed 'near miss,' is defined as 'A woman who nearly died but survived a complication that occurred during pregnancy, childbirth or within 42 days of termination of pregnancy' [35].*
2. *Severe maternal morbidity includes unexpected outcomes of labor and delivery that can result in significant short- or long-term health consequences [36].*

The first of these definitions, proposed by the WHO [35], draws on previously articulated definitions of near-miss [37], severe obstetric morbidity [38], and severe acute maternal morbidity [39], and restricts the definition of SMM to cases of near-fatal maternal illness. The second definition, proposed by Centers for Disease Control and Prevention [36] refers to 'unexpected outcomes of labor and delivery' with significant immediate or delayed health consequences. The latter definition limits SMM to 'unexpected' outcomes of labor and delivery

without specification of the time at risk, whereas the former definition extends the period during which complications can arise to also include the antepartum and postpartum periods.

In considering a reasonable alternative to these definitions of SMM, it is instructive to consider medical concepts and terminology related to clinical and community (population) medicine, and to morbidity and mortality in particular [40,41]. Medical disciplines are classified into those dealing with individuals (i.e., clinical medicine) and those dealing with populations (i.e., community medicine [40,41]; also termed public or population health). Morbidity, per its original epidemiologic definition, refers to the population counterpart of illness (in the individual), whereas mortality (also a community medicine/public health concept) refers to the population counterpart of death (of the individual) [40,41]. Thus, SMM is defined as the population rate of serious illnesses in pregnancy, childbirth or the puerperium, while maternal mortality is defined as the population rate of maternal death in pregnancy, childbirth or the puerperium.

SEVERE MATERNAL MORBIDITY: COMPONENTS

Operationalizing the above-mentioned definition of SMM (as the population rate of serious illnesses in pregnancy, childbirth, or the puerperium) requires specification of a list of severe maternal illnesses. Three different approaches have been used in the literature for identifying the severe illnesses that constitute composite SMM, and these include targeting specific disease conditions (e.g., severe pre-eclampsia), identifying severe maternal illness based on interventions (e.g., assisted ventilation, and maternal ICU admission) and/or using criteria that indicate organ system dysfunction (e.g., oxygen saturation <90% for ≥60 minutes) [35]. Each approach has its strengths and limitations: using diseases and interventions to identify cases of severe maternal illness is relatively simple, although the former can lead to false positive cases (due to the

inclusion of mild or moderate disease), and variability in the illness-severity threshold for interventions (e.g., ICU admission) can complicate spatiotemporal and other comparisons. Using organ system dysfunction to identify severe maternal illnesses represents an accurate method of identifying cases of severe maternal illness, although this may not be feasible for population surveillance if it requires close clinical monitoring and documentation [35,42].

A WHO systematic review examined approaches to SMM surveillance and recommended the prospective identification of cases of organ system dysfunction as the most reliable and accurate method for identifying near-miss cases [35,42]. This method of SMM surveillance involves the prospective follow-up of women with potentially life-threatening conditions in order to identify those with organ system dysfunction. The proposed list of potentially life-threatening conditions to be monitored included hemorrhagic disorders (e.g., postpartum hemorrhage), hypertensive disorders (e.g., severe pre-eclampsia and eclampsia), other systemic disorders (e.g., sepsis) and severe management indicators (e.g., ICU admission) [35]. Under this proposal, organ system dysfunction is to be ascertained using specific clinical criteria (e.g., acute cyanosis and respiratory rate >40 or <6 per minute), laboratory-based criteria (e.g., oxygen saturation <90% for ≥60 minutes and serum creatinine >300 μmoles per L) and management-based criteria (e.g., red cell transfusion ≥5 units, and hysterectomy following infection/hemorrhage) [35]. However, such a system of SMM surveillance has not been widely implemented on a population basis, given the onerous nature of such prospective data collection.

The methods that have been most commonly used to develop the list of SMM components include expert clinical opinion and literature review, assessments of illness severity based on prolonged length of hospital stay and case fatality, and medical chart review to identify and confirm cases of severe illness [34]. Most lists of severe maternal illnesses include cardiac,

respiratory, hepatic and renal failure; hemorrhage, thrombotic and infectious morbidity; and critical interventions [34].

More recently, assessments of SMM have included severe morbidity components that identify severe maternal mental illness [31]. The rationale for this inclusion is based on increasing recognition of mental health conditions as a leading cause of maternal death [23], the classification of suicide as cause of direct maternal death by the WHO [43] and the recognition of the postpartum period as an at-risk period for maternal mental health problems. Cases of severe maternal mental illness are identified using suicide attempts, acute psychosis, and any hospitalisation with a primary diagnosis of a psychiatric disorder in pregnancy or within 42 days of delivery [31].

DATA SOURCES FOR SMM SURVEILLANCE

Contemporary surveillance for SMM relies on one of two types of data sources for information on cases of severe maternal illnesses, namely, a) hospitalization databases (or other registries) with data routinely abstracted from medical charts and b) medical charts. Hospitalization databases in many high-income countries are often used for estimating the (population) rate of SMM as such routinely collected information is readily available, with virtually all cases of severe maternal illness in the population included in the data source. The data collated in such databases are coded using diagnostic and intervention classification systems, such as the International Statistical Classification of Diseases and Related Health Problems (ICD), although abstraction and coding may lead to a lack of detail, omissions and errors which may limit accurate ascertainment of illness severity. The opposite challenge confronts SMM surveillance based on medical charts: surveillance based on data extracted on an ad hoc basis from the primary medical chart requires the cooperation of all hospitals in a given geographic area in

order to obtain population rates. However, available details in the medical chart permit a more accurate identification of cases of severe maternal illness.

Lists of SMM components developed for use with medical charts tend to be more clinically nuanced compared with those developed for use with hospitalization databases. For instance, information on the number of units of blood or packed cells transfused can be combined with the volume of blood loss (and prior hemoglobin status) to determine severity of the hemorrhage when surveillance is based on medical chart review. A recent exhaustive review [34] of the components of SMM identified 40 studies in the literature: 32 lists of SMM components were identified for use with hospitalization databases, and 13 lists were identified for use with medical charts. The frequency of composite SMM ranged from 1.3 per 1,000 deliveries to 35.4 per 1,000 deliveries (median 11.4 per 1,000 deliveries) in studies based on hospitalization databases, while the studies based on lists designed for use with medical charts yielded a frequency ranging from 3.8 to 28.4 per 1,000 women delivered (median 6.7 per 1,000) [34]. However, variability in the data sources, component conditions included in composite SMM, diagnoses and procedures used to identify component conditions and the risk period over which complications were assessed makes between-study comparisons of the frequency of SMM challenging.

SMM components developed for use with hospitalization databases contrast starkly with lists developed for use with surveillance involving more rigorous data collection. Thus, estimates of the rates of specific severe morbidity types ascertained from routine hospitalization databases may be less accurate than those ascertained using a more rigorous methodology based on medical charts. For this reason, the International Network of Obstetric Surveillance Systems advocates the use of uniform definitions for SMM types, the use of a common data collection

methodology, and specific data collections tools [44]. A core set of SMM conditions under the SMM umbrella has been identified for international studies, and definitions for each condition have been formalized using a Delphi process [45]. The definitions were formulated with a view to ensuring consistent and accurate identification of cases (e.g., uterine rupture defined as "a visually confirmed, complete rupture of the myometrium and serosa") [45].

Widespread use of electronic medical records will likely facilitate the availability of detailed information on severe maternal illnesses on a population basis. Future studies may permit more accurate and routine assessment of SMM when diagnoses, interventions, organ system dysfunction and other details (such as laboratory values) become part of a standardized electronic medical record that is implemented across the population.

FREQUENCY OF SMM

One of the earlier lists for quantifying SMM was developed for use with hospitalization data in Canada, and based on diagnoses/procedures during the delivery admission that were deemed to represent a near-fatal condition [7]. This list included 11 diagnoses identified using ICD version 9 (ICD-9) codes and 3 procedures identified using the Canadian Classification of Diagnostic, Therapeutic, and Surgical Procedures. The SMM rate based on this formulation was 4.4 per 1,000 deliveries in Canada (excluding Quebec) in 1991-2001, and notably, blood transfusion was not considered a SMM type, except when it occurred in conjunction with postpartum hemorrhage [7].

Another list developed in the United States also used ICD-9 diagnoses and procedure codes for severe maternal complications, and was subsequently revised with the addition of other severe complications identified based on a review of associated in-hospital mortality rates [14]. The final list included 25 diagnoses/procedures and yielded a population frequency of 12.9

per 1,000 deliveries in 2008-2009, with blood transfusion contributing to 75% of cases [14].

The Canadian list of SMM elements was revised in 2010 with diagnoses based on ICD-10 codes and procedures based on the Canadian Classification of Health Interventions [12], and subsequently revised again in 2019-2020 [24,25]. Types and subtypes of severe maternal illnesses were identified based on clinical knowledge and rates of prolonged hospitalization and case fatality. The final list of SMM components included 13 SMM types and 46 subtypes [24,25]. The formulation did not include blood transfusion as a SMM type per se, although blood transfusion was used to qualify the severity of other conditions (such as hemorrhage). The frequency of SMM was 16.1 per 1,000 deliveries in 2012-2016, and the most frequent SMM type was severe pre-eclampsia, HELLP syndrome and eclampsia [24].

Although estimates of the magnitude of SMM are highly dependent on the data source and the list of component severe maternal illnesses included in the SMM composite, there are other extraneous issues that can significantly affect the estimated SMM rate. First, as mentioned, the definition of SMM components can vary between jurisdictions and this can affect spatial comparisons of SMM. For instance, postpartum hemorrhage is defined based on a blood loss of ≥500 ml for vaginal deliveries and ≥750 ml for cesarean deliveries in Australia [10,46], a blood loss of ≥500 ml for vaginal deliveries and ≥1,000 ml for cesarean deliveries in Canada [47] and a blood loss of ≥1,000 ml (irrespective of the mode of delivery) in Sweden [48]. Similarly, severe primary postpartum hemorrhage as defined by the International Network of Obstetric Surveillance Systems involves blood loss exceeding 2000 ml and/or the need for transfusion of at least four units of red blood cells within 24 hours after the end of pregnancy [45], whereas information on the volume of blood loss and the number of pints of red blood cells transfused is not recorded in hospitalization databases in Canada [24]. Perhaps more concerning is variability

within populations: bias in the assessment of maternal health disparities between subpopulations (e.g., by rural/urban residence, socioeconomic status or race/ethnicity) could occur if hospitals predominantly serving specific subpopulations varied in terms of underreporting severe maternal illnesses.

SMM IN NON-DELIVERY ADMISSIONS

Most studies of SMM tend to focus on delivery admissions and relatively few studies provide details regarding the frequency and subtypes of severe maternal illness occurring in early pregnancy, and among non-delivery antepartum hospitalizations, and postpartum readmissions. One study from France which examined SMM occurring in the antepartum period (i.e., prior to labour onset) showed that such cases constituted 23% of cases among all delivery admissions [49].

Severe maternal illnesses among hospitalizations involving early pregnancy outcomes have a different profile from those occurring at delivery, with ectopic pregnancy and abortion-related complications predominating. A Canadian study of hospitalizations for abortive outcomes (ICD-10 O00-O08) in 2008-2017 documented a maternal ICU admission rate of 3.4 per 1,000 such hospitalizations (Joseph KS; unpublished communication). Most of these admissions were related to complications following ectopic pregnancy, molar pregnancy or spontaneous abortion and included severe morbidity associated with hysterectomy, assisted ventilation, curettage with blood transfusion, acute renal failure, cardiac complications and repair of the bladder, urethra or intestine. The severity of the illness associated with ectopic pregnancy was highlighted by the recent United Kingdom and Ireland Confidential Enquiries, which documented a mortality rate of 0.82 per 100,000 maternities (n=12) in 2021-2022 for deaths due to an early pregnancy-related cause. All 12 deaths occurred due to complications associated with ectopic pregnancy [50].

Studies of SMM carried out among postpartum readmissions reveal a relatively lower population frequency (compared with SMM at the delivery admission) and a different profile of severe maternal illness [14,51,52]. A study from California [51] showed that the inclusion of postpartum readmissions led to a 23% higher rate of SMM (45% higher if blood transfusion was excluded from the list of SMM components). Another study from Massachusetts [52] showed that the inclusion of SMM among prenatal and postpartum admissions increased the rate of SMM by 22%. Rates of sepsis and acute myocardial infarction were particularly over-represented among postpartum readmission in California [51], while sepsis and blood transfusions were the most common cases among both the prenatal and postpartum admissions in Massachusetts [52].

ATTRIBUTING SEVERE MATERNAL ILLNESS TO A SINGULAR CAUSE

As mentioned, the WHO recommends that the "same classification of underlying causes [be] used for both maternal deaths and near misses" [2]. The WHO classification of the cause of maternal death has a simple structure that facilitates tabulation by individual underlying causes, which are distinct from conditions contributing to fatal outcomes. However, between-country and regional differences in definitions and assignment of causes of death can hinder meaningful comparisons [53-56]. Such differences in underlying cause-of-death assignment have been previously highlighted by the case of a woman with pre-eclampsia who suffered severe hemorrhage and died as a consequence [56]. Members of the Maternal Mortality Committee from the United Kingdom (UK) assigned postpartum hemorrhage as the underlying cause of death to this case, whereas members of the Dutch Maternal Mortality Committee favoured pre-eclampsia as the appropriate choice for the underlying cause of death [56].

The imperative to identify a singular underlying cause of maternal death or attributing

cases of severe maternal illness to a single underlying illness is based on public health concepts rooted in traditional ideas regarding cause and effect [57], rather than contemporary, multi-factorial models of causation [41,58-61]. Simplicity is the strongest argument for a single underlying cause/illness, while the lack of a comprehensive, albeit more complex, etiologic perspective is the most significant weakness of this method [61]. Attributing a case of severe maternal illness to multiple different causes/illnesses results in the number of severe maternal illnesses exceeding the number of women with severe illness. Nevertheless, such assignment provides an etiologic perspective that is consistent with modern models of causation [41,58-61], with each severe illness receiving appropriate attention and spurring efforts aimed at prevention and optimal management. Thus, assigning a case of severe maternal illness or death complicated by pre-eclampsia and severe hemorrhage to both these conditions ensures that efforts will be directed at the prevention and management of both conditions [61].

Although the WHO recommends assigning a single underlying illness to each case of severe maternal illness [2], most studies of SMM in the literature identify and count all severe maternal illnesses attributed to each case. Most commonly, SMM rates are estimated in terms of the number of women with at least one severe maternal illness. Some studies have quantified the exponential increase in case fatality rates among women who have 1 severe maternal illness, 2 severe maternal illnesses, 3 severe maternal illnesses, etc. [62].

Both the WHO recommendation regarding the need to assign a singular illness as the underlying cause of a case of severe maternal illness [2], and the alternative of potentially assigning multiple causes for each case, require structured case reviews that provide a considered assessment of each case in terms of cause(s) and avenues for prevention. Detailed reviews of all cases of severe maternal illness (similar to those carried out by Confidential Enquiries into

maternal death in the United Kingdom, and by the Maternal Mortality Review Committees in the United States) may or may not be not be feasible given the frequency of SMM, although specific SMM types judged to require attention could be selected for review on a periodic basis (as carried out by the Confidential Enquiry into specific severe maternal morbidity in the United Kingdom [50]).

ROLE OF ADJUSTMENT IN COMPARISONS OF SEVERE MATERNAL MORBIDITY

Although adjustment for confounding is de rigueur in epidemiologic studies of causal relationships, adjustment in surveillance studies may require a more nuanced interpretation. The difference arises because surveillance results are spatio-temporally specific, unlike causal relationships which are generally free of place-time anchors. For instance, the SMM rate in Canada in 2012-2016 (16.1 per 1,000 deliveries, as mentioned above [24]), is meaningless without the place-time referent, whereas the smoking-lung cancer relation is free of this restraint (even if the population in which the relationship was quantified is anchored to some time and place).

This nuance associated with interpreting adjusted SMM rates may be illustrated by asking whether temporal trends in SMM (e.g., when comparing SMM in a country in 2010 vs 2025) should be adjusted for maternal age? If the unadjusted temporal contrast in SMM rates shows a doubling over a 15-year period, and the age-adjusted comparison shows no difference, what does this imply with regard to the temporal change in SMM? Similarly, one could ask what SMM adjusted for pre-pregnancy chronic disease implies. Adjustment for maternal age may serve an explanatory role insofar as (a temporal increase in) advanced maternal age may account for the temporal increase in SMM, and similarly adjustment for pre-pregnancy chronic disease may significantly attenuate or abolish a temporal increase in SMM. Nevertheless, the temporal deterioration in maternal health quantified by the increase in unadjusted SMM rates represents a

population phenomenon. The higher SMM rate for the more recent period quantifies a higher clinical and population burden of maternal illness relative to the previous period (irrespective of the explanation provided by the adjustment for risk factors)

Similar nuanced considerations would also be required for interpreting unadjusted and adjusted estimates of SMM in comparisons between regions and subpopulations (e.g., by socioeconomic status, and race/ethnicity). If adjustment for pre-pregnancy chronic disease attenuates racial/ethnic disparities in SMM, this provides a potential explanation for the observed severe morbidity difference but does not imply any lesser need in terms of health care inputs for addressing the clinical and population burden of illness in the specific at-risk race/ethnicity group.

CLINICAL BURDEN ASSOCIATED WITH SEVERE MATERNAL ILLNESS

Although all the severe maternal illnesses included within the SMM rubric have serious acute and potentially long-term consequences for affected women, the illnesses vary in terms of their clinical burden. A few studies have quantified the clinical burden associated with each severe maternal illness in terms of frequency, the proportion of cases of each severe maternal illness that result in a prolonged hospitalization (≥7 days), and case fatality rates [24]. Such a characterization of SMM provides an overview of the clinical burden associated with different components of SMM, and highlights the clinical heterogeneity within composite SMM.

Figure 1 shows the frequency of each major type of severe maternal illness, and the rates of prolonged hospital stay and case fatality associated with each such illness in Canada (excluding Quebec), 2012-2016 [24]. Although this information is spatiotemporally specific, the data source is a hospitalization database, and the definitions of the maternal conditions may be idiosyncratic to Canada, the relative contribution of each maternal condition to the overall frequency of

composite SMM and the propensity of these conditions to result in a prolonged hospitalization or death is informative. The details of the clinical burden associated with each SMM type is best evaluated against the overall frequency of SMM in Canada (excluding Quebec) in 2012-2016, which was 16.1 per 1,000 deliveries. Among women with any severe maternal illness, 18.8% had a prolonged hospital stay (compared with 1.3% among those without any SMM) and the case fatality rate was 2.0 per 1,000 women delivered (compared with 0.004 per 1,000 deliveries among those without any SMM) [24].

The most common components of SMM were severe pre-eclampsia, HELLP syndrome and eclampsia (559 per 100,000 deliveries), severe hemorrhage (500 per 100,000 deliveries), surgical complications (194 per 100,000 deliveries), ICU admission (192 per 100,000 deliveries) and sepsis (91 per 100,000 deliveries) [24]. On the other hand, the clinical burden associated with each SMM type, expressed in terms of prolonged hospitalization rates, showed that the highest rates of hospital stay ≥7 days were associated with acute renal failure/dialysis (53% of such cases has a prolonged stay), assisted ventilation (48%), ICU admission (37%), cardiac conditions (35%) and obstetric embolism/shock/disseminated intravascular coagulation (28%) [24]. The SMM types with the highest case fatality were cardiac conditions (41 deaths per 1,000 deliveries with a cardiac condition), cerebrovascular accidents (37 per 1,000 deliveries), assisted ventilation (31 per 1,000 deliveries), obstetric embolism, shock and disseminated intravascular coagulation (20 per 1,000 deliveries) and acute renal failure/dialysis (14 per 1,000 deliveries; Figure 1) [24].

POPULATION BURDEN ASSOCIATED WITH SMM

The population attributable fraction (PAF) expresses the proportion of cases of any outcome (e.g., disease and death) in a population that is caused by a particular risk factor and represents the proportion of the outcome that could be prevented if the risk factor was eliminated from the

population [63,64]. The PAF calculation addresses both the frequency of the risk factor and its propensity to cause the outcome in question. Composite SMM in Canada (excluding Quebec), 2012-2016, was associated with a PAF of 18% for prolonged hospitalization and a PAF of 88% for death. It should be noted that the use of interventions to identify severe maternal illness complicates the interpretation of SMM components somewhat, as these interventions represent markers for severe illnesses and life-saving therapies/procedures (see below).

Figure 2 shows the PAFs associated with each SMM component for prolonged hospitalization and death. The severe maternal illnesses contributing the most toward prolonged hospitalization were severe pre-eclampsia, HELLP syndrome and eclampsia (PAF 8.8%), and severe hemorrhage (4.0%). Contributions of severe maternal illness to death during the delivery admission were much larger, with the largest contributors being cardiac conditions (70.6%), severe hemorrhage (37.2%) and obstetric embolism, shock and disseminated intravascular coagulation (37.2%). These calculations assume a causal relationship between each severe maternal illness and prolonged hospitalization/death, and that the PAFs associated with the different SMM components are not mutually exclusive (i.e., the PAFs can add to over 100%) [63,64].

Figure 2 also shows the PAFs associated with life-saving interventions such as assisted ventilation and maternal ICU admission (which, as mentioned, serve as proxies for severe maternal illness). The PAF associated with each intervention represents the proportion of prolonged hospitalization/death that would be prevented if the maternal illnesses requiring such intervention were prevented. Thus, for instance, cases of SMM requiring maternal ICU admission contributed to 4.3% of all prolonged hospitalizations, and 47% of maternal deaths. Since ICU admission serves as a proxy for severe maternal illness, these estimates are best

viewed in terms of their contribution to specific outcomes. Thus, it is illustrative to acknowledge that ICU admissions (and all SMM) contribute minimally to prolonged hospital stay, whereas 47% of maternal deaths are ICU associated. Also, noteworthy is the large fraction of maternal deaths that do not reach the ICU, which may imply the need to enable high intensity interventions in non-ICU settings such as the delivery room. Note also that the PAF estimates for each severe maternal illness (e.g., cardiac conditions) are not affected by the calculation of intervention-associated PAFs since multiple conditions were attributed to each case of severe maternal illness (e.g., cardiac conditions and maternal ICU admission).

Prolonged length of hospital stay may be affected by extraneous factors that complicate interpretation. For instance, maternal death can lead to a short duration hospital stay and is better assess among survivors. Also, hospital stay may be extended for social or medical reasons (e.g., achieving diabetes control in a vulnerable person who does not have an adequate social support network).

PURPOSE OF QUANTIFYING SMM

SMM quantifies the magnitude of one aspect of maternal (ill) health in a population and is similar to maternal mortality, which quantifies a different but closely related dimension of population maternal health. SMM is also similar to maternal mortality insofar as these two entities are etiologically heterogeneous: SMM is a composite entity that encompasses many different severe maternal illnesses, while maternal mortality includes maternal deaths from diverse causes (such as the many severe maternal illnesses that comprise SMM).

SMM surveillance quantifies the magnitude of severe maternal illnesses in a specific population at a particular time. The quantification of this composite entity and its types and subtypes represents a ‘community diagnosis’ that carries implications similar to diagnosis at the

individual level [41]. Beyond the diagnostic information conveyed (e.g., "the magnitude of SMM in Population A is high, and this is in part because of high rates of severe pre-eclampsia/ eclampsia"), the quantification of SMM may also provide clues to community etiognosis (e.g., a lack of antenatal care), and community prognosis (e.g., high maternal mortality). These elements of community 'gnosis' [41] can serve as inputs for clinical and public health initiatives directed at improving critical aspects of maternal health.

The quantification of SMM in a population permits spatiotemporal comparisons and benchmarking that can help to identify and address disparities between populations (e.g., through rural vs urban comparisons) and within the same population over time. However, as discussed, SMM is an extremely heterogeneous entity and this can complicate the interpretation of temporal, regional and other subpopulation differences in composite SMM. The heterogeneity can arise artefactually due to data sources, definitions of underlying illnesses and procedures, and coding/charting practices and also for substantive reasons that involve the component conditions included in composite SMM. Two populations with similar rates of composite SMM, and different proportions of specific SMM types, may vary significantly with regard to the clinical and population burden (e.g., in terms of the need for prolonged hospital stay and maternal death).

Although the definition of SMM refers to the magnitude of all severe maternal illnesses in a population, the heterogeneity of the composite measure warrants a careful consideration of the need for an all-inclusive outcome versus a more restricted/specific measure depending on the study question or surveillance priority. For instance, a surveillance program monitoring temporal trends in maternal ICU admission in a population (as a measure of SMM) could provide epidemiologically meaningful tracking of this dimension of maternal health, if the criteria for

admission to ICU remain unchanged over the surveillance period. On the other hand, surveillance of composite SMM among women with pre-eclampsia may fail to reveal changes in the (combined) frequency of SMM types that may have an inverse relationship e.g., pulmonary edema (that can occur due to excessive fluid administration) and acute kidney injury (that can be caused by fluid restriction) [65].

Regional comparisons of SMM may also be more accurately carried out with comparisons involving specific SMM components (which can be more accurately defined and quantified) as compared with contrasts of composite SMM. Similarly, scientific studies (regarding antecedents of severe maternal illness [66,67], recurrence risk [68,69], long-term consequences [70,71] and association with neonatal and other outcomes [72-74]) may need to carefully consider whether specification of one or more specific severe maternal illness is preferable to a heterogeneous composite outcome.

Prevention programs addressing SMM also need to focus on the component illnesses that are deemed to be a priority (based on frequency, clinical burden or population burden) and investigate these occurrences in detail in order to identify opportunities for intervention. Such investigations could be of qualitative (i.e., clinical case reviews of specific severe illnesses) or quantitative (i.e., epidemiologic analyses of risk factors for specific severe illnesses) depending on the frequency of the component severe illness.

CONCLUSION

SMM has emerged as a focus of clinical and public health concern in recent years, although several fundamental concepts would benefit from being more carefully considered and articulated. The definition of SMM as a population phenomenon requires attention in order to distinguish it from severe maternal illness occurring at the individual level. Numerous lists of

component conditions have been compiled in order to quantify SMM in a more comprehensive manner, and this is partly responsible for the varying magnitude of SMM in different populations and in the same population at different time periods. Differences between surveillance studies based on hospitalization databases versus (primary) medical charts are recognized as a source of heterogeneity, as are differences in the definitions of maternal illnesses that constitute the components of SMM. Substantial heterogeneity is also evident with regard to the clinical and population burden associated with SMM components. Other fundamental concepts to be considered and addressed in studies of SMM include the need to include severe maternal illness occurring in early pregnancy, non-delivery hospitalizations and postpartum readmission; interpretation of unadjusted and adjusted rates of SMM; and whether assigning a singular underlying illness for each case of severe maternal illness is preferable to assigning one or more severe illnesses to each case. Finally, the heterogeneity of the composite measure warrants a careful consideration of the need for an all-inclusive outcome versus a more restricted and specific measure depending on the study question, surveillance priority and the feasibility of accurate measurement. Prevention programs addressing SMM need to focus on component illnesses and identify opportunities for intervention based on clinical reviews or epidemiologic analyses of risk factors for the specific illness. Surveillance of SMM and studies on SMM need to consider these issues, and appropriately design the SMM outcome depending on the question being addressed.

Conflict of Interest
The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent
This article does not contain any studies with human or animal subjects performed by any of the authors.

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Figure legends

Figure 1. Types of severe maternal morbidity: relative frequency per 100,000 deliveries (Panel A), proportion of cases requiring a prolonged (≥7 days) hospital stay (Panel B), and case fatality rates per 1,000 deliveries (Panel C), Canada (excluding Quebec), 2012-2016. SPE denotes severe pre-eclampsia; HELLP denotes HELLP syndrome; ICU: Intensive Care Unit admission; DIC: disseminated intravascular coagulation and CVA: cerebrovascular accident.

* Case fatality rates for severe pre-eclampsia, HELLP syndrome and eclampsia, sepsis, and severe uterine rupture were based on small numbers (i.e., estimates are unstable).

Figure 2. Population attributable fractions (PAF) expressing the contribution of each severe morbidity type to prolonged (≥7 days) hospital stay (Panel A) and case fatality (Panel B), Canada (excluding Quebec), 2012-2016. SPE denotes severe pre-eclampsia; HELLP denotes HELLP syndrome; ICU: Intensive Care Unit admission; DIC: disseminated intravascular coagulation and CVA: cerebrovascular accident.

* Case fatality PAFs for severe pre-eclampsia, HELLP syndrome and eclampsia, sepsis and severe uterine rupture were based on small numbers (i.e., estimates are unstable).

Figure 1.

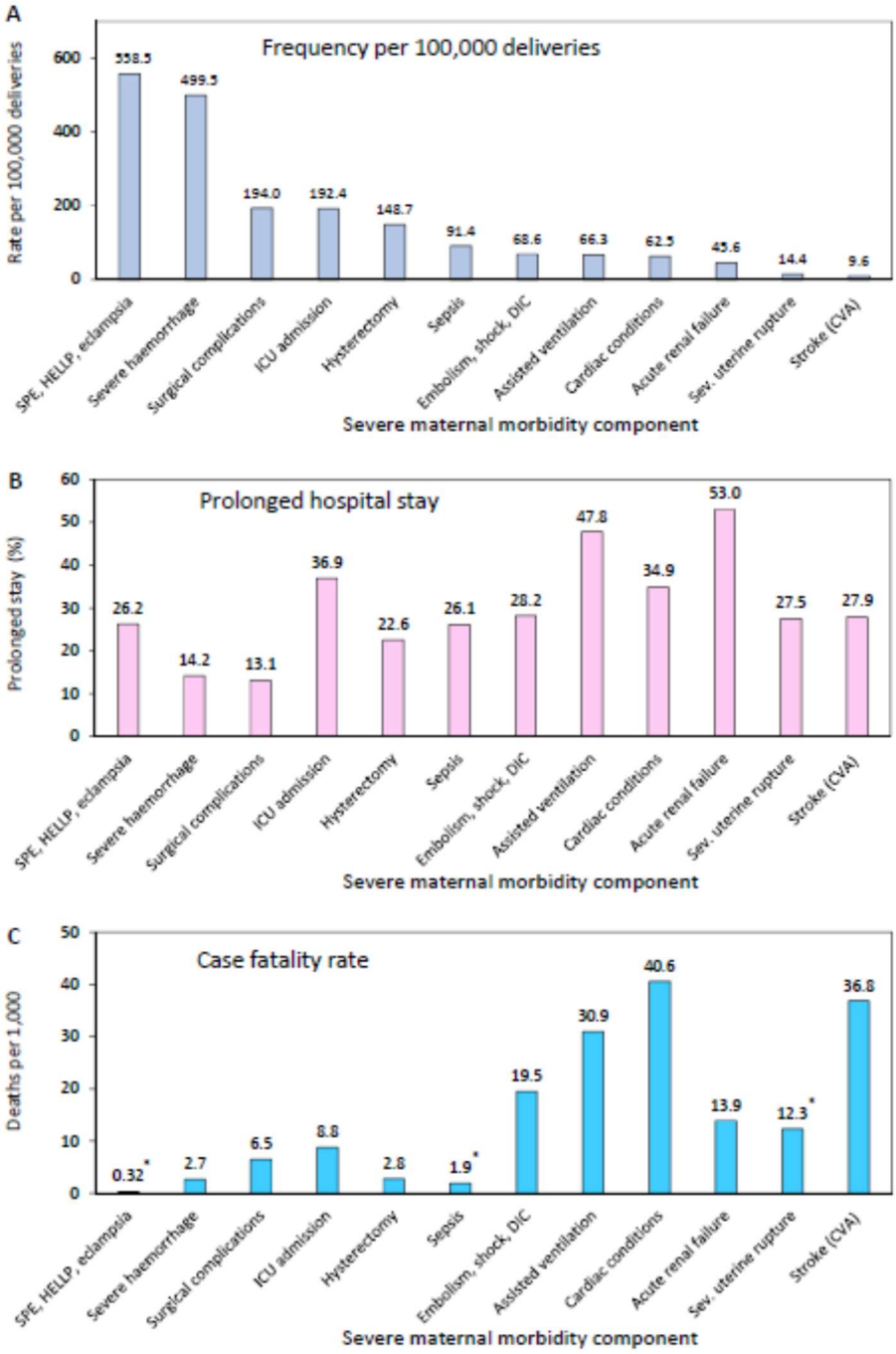
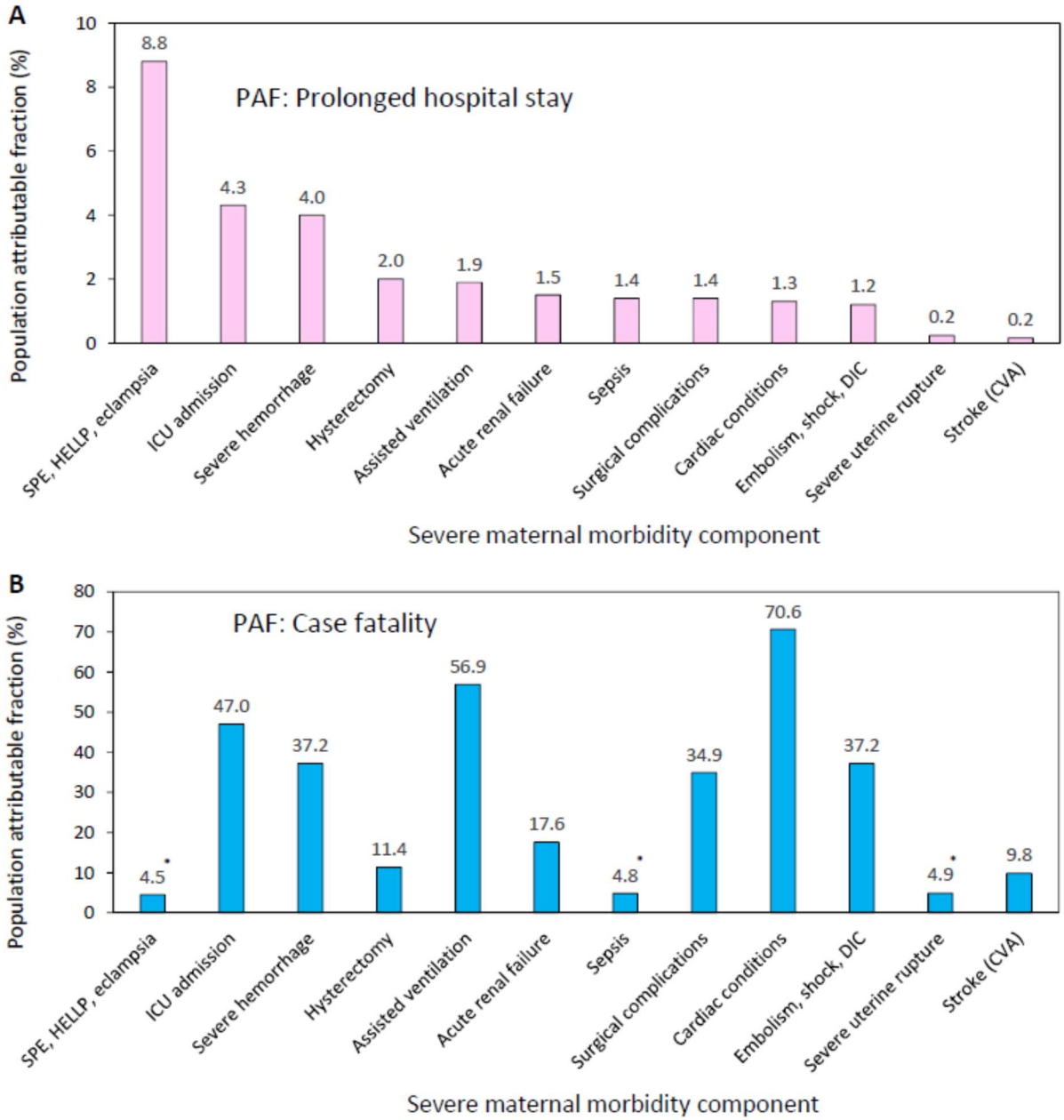

A
Frequency per 100,000 deliveries
Rate per 100,000 deliveries
558.5
499.5
194.0
192.4
148.7
91.4
68.6
66.3
62.5
45.6
14.4
9.6
SPE, HELLP, eclampsia
Severe haemorrhage
Surgical complications
ICU admission
Hysterectomy
Sepsis
Embolism, shock, DIC
Assisted ventilation
Cardiac conditions
Acute renal failure
Sev. uterine rupture
Stroke (CVA)
Severe maternal morbidity component
B
Prolonged hospital stay
Prolonged stay (%)
26.2
14.2
13.1
36.9
22.6
26.1
28.2
47.8
34.9
53.0
27.5
27.9
Severe maternal morbidity component
C
Case fatality rate
Deaths per 1,000
0.32*
2.7
6.5
8.8
2.8
1.9*
19.5
30.9
40.6
13.9
12.3*
36.8
Severe maternal morbidity component

Figure 2.


A
PAF: Prolonged hospital stay
Population attributable fraction (%)
10
8
6
4
2
0
8.8
4.3
4.0
2.0
1.9
1.5
1.4
1.4
1.3
1.2
0.2
0.2
SPE, HELLP, eclampsia
ICU admission
Severe hemorrhage
Hysterectomy
Assisted ventilation
Acute renal failure
Sepsis
Surgical complications
Cardiac conditions
Embolism, shock, DIC
Severe uterine rupture
Stroke (CVA)
Severe maternal morbidity component
B
PAF: Case fatality
Population attributable fraction (%)
80
70
60
50
40
30
20
10
0
4.5 *
47.0
37.2
11.4
56.9
17.6
4.8 *
34.9
70.6
37.2
4.9 *
9.8
SPE, HELLP, eclampsia
ICU admission
Severe hemorrhage
Hysterectomy
Assisted ventilation
Acute renal failure
Sepsis
Surgical complications
Cardiac conditions
Embolism, shock, DIC
Severe uterine rupture
Stroke (CVA)
Severe maternal morbidity component