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# Assessment and Prediction of Cardiovascular Contributions to Severe Maternal Morbidity

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## Abstract

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Severe maternal morbidity (SMM) refers to any unexpected outcome directly related to pregnancy and childbirth that results in both short-term delivery complications and long-term consequences to a women's health. This affects about 60,000 women annually in the United States. Cardiovascular contributions to SMM including cardiac arrest, arrhythmia, and acute myocardial infarction are on the rise, probably driven by changing demographics of the pregnant population including more women of extreme maternal age and an increased prevalence of cardiometabolic and structural heart disease. The utilization of SMM prediction tools and risk scores specific to cardiovascular disease in pregnancy has helped with risk stratification. Furthermore, health system data monitoring and reporting to identify and assess etiologies of cardiovascular complications has led to improvement in outcomes and greater standardization of care for mothers with cardiovascular disease. Improving cardiovascular disease-related SMM relies on a multipronged approach comprised of patient-level identification of risk factors, individualized review of SMM cases, and validation of risk stratification tools and system-wide improvements in quality of care. In this article, we review the epidemiology and cardiac causes of SMM, we provide a framework of risk prediction clinical tools, and we highlight need for organization of care to improve outcomes.

**Keywords**

cardio-obstetrics; cardiovascular disease; severe maternal morbidity

Severe maternal morbidity (SMM) refers to any unexpected adverse outcome directly related to pregnancy and childbirth that results in both short-term delivery complications and long-term consequences to a women's health.[1] SMM rates have been steadily increasing in the United States over the last several decades; an estimated 60,000 women were affected by SMM in 2014; and this number is likely underreported.[2–4] Cardiovascular disease is the leading cause of maternal mortality in high-income countries and cardiovascular-related SMM are among the most commonly reported causes.[5] The rise in overall SMM and cardiovascular contributions are associated with increasing maternal age, increased use of assisted reproductive techniques often leading to higher-order pregnancies, and changes in the overall cardiovascular health of women of reproductive age.[6] The rising prevalence of congenital heart disease, diabetes mellitus, prepregnancy obesity, and hypertension are primary contributors driving obstetric intensive care unit admissions.[7] Given such a rise in SMM rates from cardiac causes, for the purpose of this review, we will focus on high-risk cardiac patients that can be recognized earlier in their pregnancy. Early recognition of high-risk patients allows for individualized counseling regarding contraception, optimization of cardiovascular care prior to pregnancy, appropriate risk stratification, management of high-risk cases by Cardio-Obstetric teams, and individualized care plans during pregnancy to improve care and reduce overall rates of SMM from cardiovascular disease.

Common approaches for the identification of maternal morbidity include the use of clinical disease-specific criteria, organ-system dysfunction criteria, or intervention and management criteria.[8] Several organizations have attempted to stratify maternal morbidity based on severity. The World Health Organization (WHO) uses the organ-system criteria to subcategorize maternal morbidity, and the WHO definition of maternal near miss is the

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survival of a near-death event during pregnancy, delivery, or within 42 days after the end of pregnancy.[8–10] Professional and governmental organizations differ in their approach to identifying and evaluate the events or conditions which lead to SMM.[8–10] In contrast to the WHO's organ-system criteria, the Centers for Disease Control and Prevention (CDC) uses the International Classification of Disease diagnosis and procedure codes to identify cases of SMM.[11] This approach toward case identification in the United States is the result of using epidemiologic data sets for population-based surveillance. For simplicity, clinical entities described throughout this review are aligned with the definitions of SMM established by the CDC.

We first describe the epidemiology of SMM, including recent trends and disparities in cardiovascular contributions to SMM. We focus on cardiovascular risk assessment and cardiovascular disease associated with SMM and then provide an overview of current early maternal warning triggers and predictors of SMM, with the goal of encouraging better risk assessment and optimization of the quality of maternity care.

## EPIDEMIOLOGY AND TRENDS IN SMM

From 1993 to 2014, SMM has steadily risen from 49.5 to 144 cases per 10,000 delivery hospitalizations, an increase of approximately 200%.[11] This has primarily been driven by blood transfusions, which have increased nearly 400% from 24.5 cases per 10,000 delivery hospitalizations to 122.3 in 2014.[11] However, without including transfusions, the rate of SMM increased by about 20% over the same time frame, from 28.6 to 35.0 cases per 10,000 delivery hospitalizations.[11] After transfusion, the leading causes of rising SMM per 10,000 delivery hospitalizations between 1993 and 2014 are acute renal injury (1.3–5.2, 300%), acute respiratory distress syndrome (2.0–6.1, 205%), cardiac arrest, ventricular fibrillation (VF), or arrhythmia requiring cardioversion (0.4–1.1, 175%), and acute myocardial infarction (AMI) or aneurysm (0.1–0.2, 100%).[11] Rates of multi-systemic disease have increased as well, with rates of maternal shock increasing 173%, from 1.1 to 3.0, and sepsis increasing 75%, from 2.4 to 4.2 cases per 10,000 delivery hospitalizations.[11]

Rates of acute congestive heart failure or pulmonary edema have decreased by 7.7%, from 2.6 to 2.4 cases per 10,000 delivery hospitalizations.[11] Decreases in ischemic and hemorrhagic stroke have also been noted (1.3–0.9, 31%), and improvements have been realized in procedural safety, as decreases have been observed in rates of heart failure or cardiac arrest during surgeries or procedures (0.5–0.3, 40%) and in severe complications of anesthesia (2.3–0.3, 87% per 10,000 delivery hospitalizations). Further, rates of eclampsia have decreased (4.1–2.0, 51.2% per 10,000 delivery hospitalizations).[11]

## RISK FACTORS FOR SMM.

With the rising number of women affected by SMM, several risk factors have been identified (Figure 1).[12] These include demographic factors such as older or younger maternal age, and Black race/ethnicity.[3,13–15] Maternal smoking and other substance use as well as nulliparity and history of prior cesarean deliveries also increase a woman's risk for SMM.[16–20] Further, concomitant metabolic conditions, such as obesity,[21] diabetes mellitus,[22] as well as specific

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cardiovascular diseases such as hypertension,[23] heart failure, arrhythmia, valvular disease, and congenital defects lead to increased risk of SMM.[11,17,24] Early identification of these risk factors is critical to mitigate the risk of SMM.

## DISPARITIES IN SMM.

In the United States, significant disparities exist in the incidence of SMM across racial and ethnic groups, by age, region, income, and by type of hospital where the patient received care.[25] Non-Hispanic White mothers had the lowest incidence of SMM, at 105 cases per 10,000 births from 2016 to 2017, in comparison to 163 in Hispanic mothers, 153 in non-Hispanic Asian mothers, and 138 cases in all other race/ethnic groups.[25] Non-Hispanic Black mothers experienced 226 cases of SMM per 10,000 births, more than twice as many as non-Hispanic White mothers.[25] This corresponds with the disparity in maternal mortality experienced between these groups, with a rate of 37.3 deaths per 100,000 live births in non-Hispanic Black mothers in 2018 compared to 14.9 and 11.9 deaths in the non-Hispanic White and Hispanic population, respectively.[26] Corroborating these results, a recent analysis of the National Inpatient Sample found that from 2012 to 2015, the incidence of SMM was significantly higher in women of all other racial and ethnic categories than in non-Hispanic White women.[27] Another study of the National Inpatient Sample found that the incidence of SMM and mortality was almost 2-fold higher among Indigenous women than among non-Hispanic White women, with the highest incidence among rural residents both on and off reservations.[28]

Differences in the incidence of SMM exist based on geographical location in the US. Mothers in the Northeast experienced the highest rates, at 173 events, followed by those in the South and the West, at 147 and 132 events per 10,000 births, respectively.[25] Mothers in the Midwest experienced the lowest incidence of SMM, at 110 events per 10,000 births in the 2016 to 2017 period.[25] Importantly, women living in rural areas are more susceptible to SMM than those living in urban areas.[28]

Sociodemographic data suggest that income level and type of hospital where care was received may also influence the rate of SMM.[25] Mothers from the lowest income quartile experienced a markedly higher rate of SMM than those from other income quartiles, at 175 events per 10,000 births in comparison to 137, 124, and 115 in the second, third, and fourth quartiles, respectively based on recent data.[25] Further, women who gave birth at public hospitals experienced dramatically higher rates of SMM than those who gave birth in private non-profit or for-profit hospitals, at 190 events per 10,000 births in comparison to 136 and 118 events, respectively.[25]

In short, social determinants of health such as neighborhood toxicity, food insecurity, poverty, and rural areas might have significant underpinnings on severe maternal morbidity; these factors need further exploration.

## CLINICAL SCOPE OF SMM: FOCUS ON CARDIOVASCULAR INDICATORS

SMM can be categorized into cardiac and non-cardiac causes, which themselves can be further divided into respiratory, obstetric, renal, hematologic, infectious, and procedural

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causes. These indicators are summarized in Table 1.[11,29] This review will focus on cardiac indicators of SMM.

## ACUTE MYOCARDIAL INFARCTION.

The incidence of AMI in reproductive-age women is low; however, pregnancy increases a woman's risk of AMI 3- to 4-fold.[30] The estimated incidence of pregnancy-associated myocardial infarction (PAMI) is 0.6 to 1.0 per 10,000 pregnancies.[31] PAMI risk increases with increasing maternal age and multigravida pregnancies.[30–32] A study of 165 cases of PAMI in pregnant women included 68 (54%) that had undergone coronary angiography.[32] In these women, 29% had normal arteries, 43% had atherosclerosis, 21% had intracoronary thrombus without atherosclerosis, and 16% had dissection.[32] An examination of 150 contemporary cases noted coronary artery dissection (43%) as the leading cause of PAMI, often presenting in the final trimester or early in the postpartum period.[33] Pregnancy-related dissection of the left anterior descending or the left main coronary artery was more likely to result in heart failure, ventricular arrhythmias, and cardiogenic shock.[33] While the diagnosis of AMI in women is often underrecognized; PAMI should be considered in patients presenting with cardiac arrest, chest pain, or dyspnea, as well as those with electrocardiographic changes and elevated cardiac enzymes.[34] Elevations in creatine kinase and creatine kinase myocardial band can occur during labor and delivery; however, troponin elevation is more specific to cardiac injury and should warrant expeditious workup.[35]

## CARDIAC ARREST.

Data from 1998 to 2011 suggest that cardiac arrest occurs in 1 in 12,000 admissions for delivery.[36] Common causes include hemorrhage, heart failure, hypertension, sepsis, and amniotic fluid embolus.[36,37] While the overall mortality after cardiac arrest is high, recent data suggest that survival after maternal cardiac arrest is as high as 58.9% (99% CI: 54.8% −63.0%).[36] Obstetrical conditions associated with cardiac arrest include abnormal placental insertion, polyhydramnios, malignancy, respiratory disease, hypertension, and gestational diabetes mellitus.[38]

## ARRHYTHMIA.

Supraventricular tachycardia (SVT) is the most common type of sustained arrhythmia in pregnancy; however, the prevalence of atrial fibrillation (AF) and ventricular arrhythmias are increasing in frequency and have been shown to contribute to maternal morbidity and mortality.[39,40] Specifically, the prevalence of SVT is approximately 24 per 100,000 hospital admissions in pregnant women compared to a prevalence of 2 for AF and flutter and 2 for ventricular tachycardia and VF.[40] The mechanism leading to increased arrhythmia burden in pregnancy is unknown; however, it is likely due to a combination of autonomic changes, hormonal fluctuations, and hemodynamic shifts throughout gestation leading to increased cardiac output and physical stress on cardiac myocytes.[41] Women of older maternal age, particularly between ages 41 and 50 years, experience an increased burden of arrhythmia, which is associated with greater frequency of in-hospital death (5.9%) and maternal or fetal complications (36.5%).[39] Notably, ventricular tachycardia and VF are rare compared

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to SVT, and are most often seen in women with preexisting structural disease such as hypertrophic cardiomyopathy and arrhythmogenic right ventricular cardiomyopathy.[42,43]

## HEART FAILURE OR CARDIAC ARREST DURING SURGERY OR PROCEDURE.

Acute heart failure or cardiac arrest during a procedure occurs in 1.1 per 10,000 delivery hospitalizations in the United States in 2014.[11] The etiology of arrest is unknown in most cases; the most common causes include postpartum/antepartum hemorrhage, amniotic fluid/thrombotic embolism, myocardial infarction, complications of anesthesia, and sepsis.[11,37] Rare causes of arrest include provocation of the Bezold-Jarisch reflex (bradycardia, hypotension, and peripheral vasodilation) during spinal anesthesia,[44] administration of misoprostol, a prostaglandin E1 analog which can cause coronary artery vasospasm,[45] or arrest prompted by cesarean section done for severe preeclampsia.[46] Though cardiac arrest is highly morbid with only 13 to 71% of mothers surviving to discharge, a recent study demonstrates that survival rates are higher amongst maternal in-hospital arrests compared to nonmaternal in-hospital cardiac arrests (45.1% vs 26.5%).[38,47–49]

## PULMONARY EDEMA/ACUTE HEART FAILURE AND CARDIOGENIC SHOCK.

Acute pulmonary edema/heart failure occurred in 2.4 cases per 10,000 delivery hospitalizations in the United States in 2014.[11] In severe cases mechanical ventilation may be necessary, which itself is an indicator of severe maternal morbidity. Certain conditions are well known to increase the risk of symptomatic heart failure during pregnancy, including known preexisting dilated or hypertrophic cardiomyopathy, or valvular diseases such as mitral stenosis, aortic stenosis, or mitral or aortic insufficiency, or ventricular dysfunction of any cause.[50,51] One case report shows the development of stress cardiomyopathy prompted by emergency cesarean section.[52,53] Other factors associated with heart failure include use of tocolytic agents, severe preeclampsia, and iatrogenic hypervolemia.[54–57] Some forms of congenital heart disease also increase the risk of developing heart failure or arrhythmia during pregnancy.[58]

Peripartum cardiomyopathy is defined as clinical heart failure in the absence of any other identifiable causes with evidence of left ventricular systolic dysfunction with an ejection fraction <45% with or without left ventricular dilatation. Peripartum cardiomyopathy occurs in the last month or within 5 months postdelivery.[59–61] As many as 60% of patients present postpartum.[62] It can progress to overt shock, which complicated 3 per every 10,000 delivery hospitalizations in the United States in 2014.[11]

## VALVULAR HEART DISEASE.

In women with significant mitral stenosis, the increased intravascular volume and heart rate during pregnancy can precipitate arrhythmia and pulmonary edema.[63–65] The etiology of mitral stenosis is commonly rheumatic, and in many women, the initial diagnosis is not made until cardiovascular decompensation occurs as a result of pregnancy.[65] Patients with

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severe aortic stenosis have a reduced ability to accommodate increased intravascular volume due to a fixed outflow tract obstruction, and thus may develop pulmonary edema, peripheral edema, or AF or other SVT.[63,65–67] Aortic stenosis in women is often due to a bicuspid aortic valve and may be known prior to pregnancy.[68] Isolated mild-to-moderate left-sided valvular insufficiency with normal ventricular function generally does not markedly increase heart failure risk during pregnancy, as the decreased systemic vascular resistance during pregnancy favors forward flow.[69,70]

## AORTIC DISSECTION.

Aortic dissection is a major cause of cardiovascular maternal mortality and morbidity, accounting for 11% of cardiac maternal deaths in the United Kingdom.[71] Most cases occur in women with heritable aortopathy such as Marfan or Loeys-Dietz syndromes; although cases have been reported with bicuspid aortic valve as well.[72] Delayed diagnosis is a significant contributor to poor outcomes and therefore a high index of suspicion is required to diagnose and treat this condition in a timely manner.

## IDENTIFICATION OF SMM

Professional societies vary in their recommendations for screening and detection of conditions leading to SMM; however, there is consensus that quality improvement methods and validation studies of current techniques are necessary, as identification of SMM is crucial for the prevention of maternal morbidity and mortality at the hospital level. Current methods used for screening and detection of SMM for hospital or center-based reviews involve different approaches for categorization of illness, each with unique strengths and weaknesses.

In 2016, the Society for Maternal-Fetal Medicine (SMFM) and American College of Obstetricians and Gynecologists (ACOG) released joint recommendations for the detection of SMM which highlighted a 2-step screening and review process.[1] SMFM and ACOG recommend screening for SMM based on the following criteria: 1) transfusion of 4 or more units of blood; and 2) intensive care unit admission of a pregnant or postpartum woman[1] (grade 1B). These 2 criteria have independently and in conjunction demonstrated a high positive predictive value, sensitivity, and specificity for the identification of SMM.[1,73–75] The recommendations further specify that any case that meets one or both stated criteria should not be automatically considered SMM but rather should be further reviewed, as some cases may be due to a progression of a known underlying disease and thus unavoidable. The review process should include a full evaluation including characterization of the diagnoses and events, a thorough examination for any avoidable outcomes, and a search for opportunities for change in systems of care provisions. The SMFM and ACOG also recommend including institution-specific screening criteria as appropriate (grade 1C); however, additional details for choosing screening criteria are not outlined.[1]

As previously described, the CDC uses diagnosis-specific criteria from hospital discharge data to identify SMM cases at the population level. The initial list included 25 SMM indicators based on the International Classification of Diseases-9th Revision procedure

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codes from 2012.[29] In 2015, the CDC reevaluated the SMM indicators based on the available validation data and revised International Classification of Diseases-Tenth Revision code diagnoses and procedures. The updated list includes 21 indicators to track SMM discharge data with both International Classification of Diseases-9th Revision and International Classification of Diseases-10th Revision codes (Table 1). The use of hospital discharge data is the most common method of screening in the United States; however, this method has been critiqued as SMM may not be well-documented or coded in records, leading to underestimates of the true number of cases, and a low positive predictive value as a result.[1,73] Studies have also shown that approximately 15% of cases may occur after the initial delivery hospitalization, which further emphasizes a need for a review of current practices to ensure these cases are appropriately captured and evaluated.[2]

## STRATEGIES FOR REDUCING SMM

In this section, we outline risk reduction of SMM with a focus on early identification of patients based on tools that have been well-validated and incorporated by health systems to reduce complications and improve multidisciplinary collaboration and management of those at risk.

## PREDICTORS OF SMM.

The use of scoring tools has reduced the overall rates of SMM through the early identification of patients at risk for SMM. Several validated risk tools (Table 2) have been developed that include patient comorbidities to predict these life-threatening complications of pregnancy and childbirth, and they allow for earlier identification and treatment.[76–80] Additionally, these tools allow for direct comparisons of SMM rates across patient groups, comorbidities, and health care institutions. Several examples of these tools are further described below.

1. California Maternal Quality Care Collaborative (CMQCC): The CMQCC developed an obstetric comorbidity scoring system using data from birth hospitalizations in California (2016–2017) to predict rates of SMM and non-transfusion related SMM.[81,82] This scoring system helps in comparing SMM rates across different patient populations with a wide range of comorbidities. Using International Classification of Diseases codes and clinical modifications of diagnosis codes, 27 patient-level risk factors for SMM were identified. Researchers used machine learning methods to rank the risk factors based on adjusted risk ratios.[82] These results were then used to assign scores to each comorbidity which subsequently was summed to a single score. This was compared to a prior obstetric comorbidity index (OB-CMI) and validated in California and national data sets.[82] Several cardiac comorbidities and risk factors were included in the obstetric comorbidity scoring system, such as preexisting cardiac disease, chronic hypertension, acute myocardial infarction, cardiac arrest/VF, conversion of cardiac rhythm, heart failure, and cardiogenic shock.[82] This system enabled the comparison of total SMM rates and non-

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transfusion SMM rates between various hospitals and emphasizes the importance of standardized metrics for analyzing SMM.[81]

2. OB-CMI: The OB-CMI is a comorbidity-based screening tool to identify patients at risk of SMM during labor and delivery.[83] In one study, the OB-CMI score of 2,800 pregnant patients at >23 weeks' gestation was initially calculated on presentation to the labor and delivery floor.[83] This score was subsequently re-calculated at 12-hour intervals. The median OB-CMI score for women with SMM was 5 (OB-CMI score ranged from 0 to 15 for patients in the study) and for those without SMM was 1. The frequency of SMM ranged from 0.41% in patients with a score of 0 to 18.75% for those with a score >9. The OB-CMI score allows for prospective identification of women at risk of SMM. Thus, routine use of this scoring system can help in early identification of women at heightened SMM risk and allow for early intervention.

3. Maternal Early Warning Criteria: The maternal early warning system includes maternal early warning criteria to identify patients at increased risk of SMM.[84–86] The maternal early warning criteria includes a list of abnormal parameters that should prompt an urgent bedside evaluation. A retrospective cohort comprising 19,000 laboring patients with live births from 2004 to 2014 was used to create a 3-part SMM risk scoring system based on antepartum, intrapartum, or combined risk scores to predict SMM.[77] In this cohort, the primary outcome was maternal morbidity including amniotic fluid embolism, organ failure, transfusion, sepsis, shock, thrombotic events, anesthesia complications, and hysterectomy. Antepartum, intrapartum, and combined risk scores were generated which subsequently helped in the prediction of SMM.[77]

In patients with preexisting cardiac conditions (particularly heart failure, coronary disease, arrhythmias, valvular disease, aortopathy, and congenital heart disease), pregnancy increases the risk of developing serious cardiovascular complications given the profound cardiac changes that occur during this period.[87] While the currently available risk assessment tools consider several comorbidities that contribute to SMM, cardiac-specific tools can aid in risk-stratifying pregnant women with cardiac conditions that could lead to life-threatening complications.

Three major risk assessment tools (Table 3) have been described in the literature and validated for clinical practice based on population-based studies of patients with various cardiovascular diseases.[76,88] In addition, one risk prediction tool has been specifically designed to predict cardiovascular indicators of SMM among pregnant and postpartum women with or without preexisting cardiovascular disease.[89] While the final risk assessment tool performed well on internal validation, it has not been externally validated and is currently not being used in clinical practice.[89]

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## PUBLIC REPORTING AND DEVELOPMENT OF HOSPITAL SAFETY AND QUALITY METRICS

Standardized case-based review of SMM can help in the identification of systemic weaknesses and help reduce the overall rates of SMM from both cardiac and non-cardiac causes. As an illustrative example, a state-wide SMM review was conducted across all obstetric hospitals in Illinois to better understand maternal health and identify factors contributing to the rising rates of SMM.[75] In this retrospective analysis, about 400 SMM cases were reviewed. Women who were multiparous, non-Hispanic Black, had public insurance, were aged 35 or older, or had poor prenatal care were more likely to have SMM. While the most common cause of SMM was haemorrhage (48%) followed by preeclampsia and eclampsia (20%), this review revealed that in 42% of SMM cases, there were identifiable opportunities to improve care.[75] The main contributors to SMM included health care professional factors during intrapartum and postpartum periods such as communication issues between physicians and lack of policies and procedures related to massive transfusion. Patient factors contributing to SMM were not explored in this analysis. This study showed that comprehensive state-wide reviews at hospitals providing obstetric care can identify contributing factors and quality improvement opportunities to help reduce rates of SMM.

Other countries have adopted similar approaches such as the UK Obstetric Surveillance System, (UKOSS), a national system developed to study rare disorders of pregnancy.[90,91] These studies included identification of specific conditions as opposed to prospective surveillance of all SMM.[90–93] UKOSS has examined outcomes for pregnant women with mechanical heart valves, and myocardial infarction, and conducted the UKOSS CAPS (Cardiac Arrest in Pregnancy study).[93] CAPS looked at nationwide surveillance data collected in the United Kingdom between 2011 and 2014. The data included detailed clinical information related to 66 maternal cardiac arrests.[92] In this population, anesthetic complications (16 of 59 events) were the primary etiology of arrest, followed by hypovolemia (13 of 59 events).[92,93] Study results also suggested that prompt perimortem cesarian sections could reduce rates of SMM and improve maternal survival as the median duration from collapse to C-section delivery was lower in survivors compared to those who did not survive. This is an example of the use of population-based data to better understand the factors surrounding cardiac arrest in pregnancy and aid in improving current practice involving maternal cardiopulmonary resuscitation.[92] Several countries have modeled surveillance systems based on UKOSS and together currently form the International Network of Obstetric Survey and Systems.[94] The large-scale collaborations of UKOSS and International Network of Obstetric Survey and Systems can provide meaningful information on cardiovascular risk factors and processes to improve care for rare conditions in pregnancy.[95]

Another way to improve quality of care includes the development of bundles for specific cardiac and non-cardiac conditions which can cause SMM. A safety ‘bundle’ is essentially a series of checklists and protocols derived from evidence-based research focused on reducing adverse outcomes. One example is the *Safe Motherhood Initiative*

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from the *American College of Obstetrics and Gynecology District II* which has developed standardized obstetric care bundles for various conditions in New York.[96,97] These are hospital-level safety bundles created to improve consistency in the diagnosis and management of various conditions that contribute to SMM. In this initiative, 127 New York based hospitals participated to provide standardized care to patients and reduce rates of SMM.[96] Bundles were created for hemorrhage, hypertension, and venous thromboembolism. For pregnant patients with hypertension, the bundles focused on early identification of patients with chronic hypertension and prompt diagnosis of gestational hypertension, preeclampsia, and eclampsia.[97] Treatment algorithms were published on the timely use of antihypertensives including labetalol, hydralazine, and nifedipine. Checklists were devised indicating the appropriate next steps in patients with hypertensive emergency, preeclampsia, and eclampsia. These included prompt cardiology consultation, medication use, frequent blood pressure checks, and appropriate laboratory testing.[96,97] An early analysis of the hypertensive bundle showed improvements in timely recognition and treatment of severe hypertension for at-risk patients; however, it also highlighted the need for greater funding and resources required to properly implement them.[98] A similar health initiative was carried out by the CMQCC in California. Beyond creating an obstetric comorbidity scoring system, the CMQCC led maternal mortality reviews and created Maternal Quality Improvement Toolkits specifically aimed to improve prevention and care related to obstetric hemorrhage, hypertensive disorders of pregnancy, sepsis, and reducing primary cesarean deliveries in California hospitals.[99] These toolkits improved maternal mortality and morbidity throughout the state of California.[100–102] Specifically, implementation of the toolkit for hypertensive disorders of pregnancy across 23 hospitals led to improvement in treatment compliance, a decrease in the incidence of eclampsia, and an overall reduction in severe maternal morbidity.[102] Another example is the Cardiac Conditions in Obstetrical Care bundle created by the Alliance for Innovation on Maternal Health which incorporates multidisciplinary care training, cardiac screening, patient education, and systems learning after individual cases.[103] Recognizing that SMM can emerge in the immediate postpartum period, the Alliance for Innovation on Maternal Health has been focused on the creation and implementation of care bundles to standardize postpartum care.[2]

To improve rates of SMM related to cardiac risk factors, it is important to focus on devising and providing logistical support for implementation of bundles like those created by the CMQCC and the *Safe Motherhood Initiative* for hypertension. This in conjunction with the utility of cardiac risk assessment tools as discussed above can provide early identification of patients at significant risk of cardiac-related SMM.[76–80,82,83,104,105] As such systems develop, increased use of electronic health records offers the opportunity to develop artificial intelligence screening tools which may also help physicians identify high-risk patients.[106] Further, patients with known preexisting high-risk cardiac disease who are planning pregnancy should have a multidisciplinary approach involving care provided by a cardiologist and a maternal-fetal medicine specialist.[107–109]

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## THE ROLE OF A CARDIO-OBSTETRICS TEAM IN THE MANAGEMENT OF SMM.

Pregnancy poses a unique and complex cardiac risk in patients with preexisting cardiac disease given the physiological changes that occur during pregnancy.[24,110,111] Cardio-obstetrics is an evolving subspecialty crucial to address the specific cardiac needs of these patients.[112–114] It is important that all cardiologists understand the cardiovascular causes of SMM when caring for these patients to identify at-risk patients earlier and follow them closely during the antepartum, intrapartum, and postpartum periods.[5] There is emerging data that a cardio-obstetrics–based approach to the care of these patients is associated with improved outcomes for women with both simple and complex cardiovascular conditions during pregnancy.[115] This close interdisciplinary collaboration has been shown to reduce overall cardiac-related rates of SMM.[116]

Most studies observing cardio-obstetrics teams have included patients with known, preexisting cardiac disease. However, cardiovascular decompensation may occur for the first time during pregnancy among patients without known pre-existing cardiac disease. Since the prompt diagnosis of an underlying cardiovascular condition and early intervention is imperative in pregnant patients at risk for cardiovascular SMM, it is paramount that these patients are identified early during pregnancy with detailed evaluation and screening for underlying cardiovascular disease. Figure 2 summarizes a checklist that allows for early identification of patients with undiagnosed heart disease and enables optimization of cardiac risk factors in the antepartum, intrapartum, and postpartum periods.[117]

## CONCLUSIONS

Although SMM from cardiac causes is rising,[117] many of these events are preventable through the identification of patient-, physician-, and system-level factors contributing to this rise (Central Illustration).[118] At the patient level, recognition of individual risks including advanced maternal age, prior history of cesarean section, and preexisting conditions are necessary to help physicians provide individualized care plans and better optimize cardiovascular comorbidities prior to pregnancy. The use of multidisciplinary cardio-obstetric teams for patients at especially high risk has been shown to improve maternal care and outcomes. Recognizing the growing risk of SMM, individual systems have spearheaded efforts to create cardiovascular disease specific risk scores and prediction tools. Still others have been able to utilize existing tools and data to create educational and clinical care bundles for hospital systems. Such efforts, though isolated to individual states and systems, have been crucial for early recognition, risk stratification, and timely referrals of individuals with high cardiac risk and have demonstrated reduction in SMM on multiple occasions. Furthermore, health system data monitoring and reporting at the national level has also led to better outcomes and increased standardization of care for mothers with cardiovascular disease.

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## ABBREVIATIONS AND ACRONYMS

| | |
|---|---|
| **ACOG** | American College of Obstetricians and Gynecologists |
| **AF** | atrial fibrillation |
| **AMI** | acute myocardial infarction |
| **CDC** | Centers for Disease Control and Prevention |
| **CMQCC** | California Maternal Quality Care Collaborative |
| **OB-CMI** | obstetric comorbidity index |
| **PAMI** | pregnancy-associated myocardial infarction |
| **SMFM** | Society for Maternal-Fetal Medicine |
| **SMM** | severe maternal morbidity |
| **SVT** | supraventricular tachycardia |
| **UKOSS** | UK Obstetric Surveillance System |
| **VF** | ventricular fibrillation |
| **WHO** | World Health Organization |

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## HIGHLIGHTS

- SMM affects about 60,000 women annually in the U.S.
- Cardiovascular contributions to SMM are on the rise.
- SMM prediction tools and cardiovascular disease risk can improve risk stratification.
- Improving cardiovascular disease-related SMM relies on a multipronged approach.

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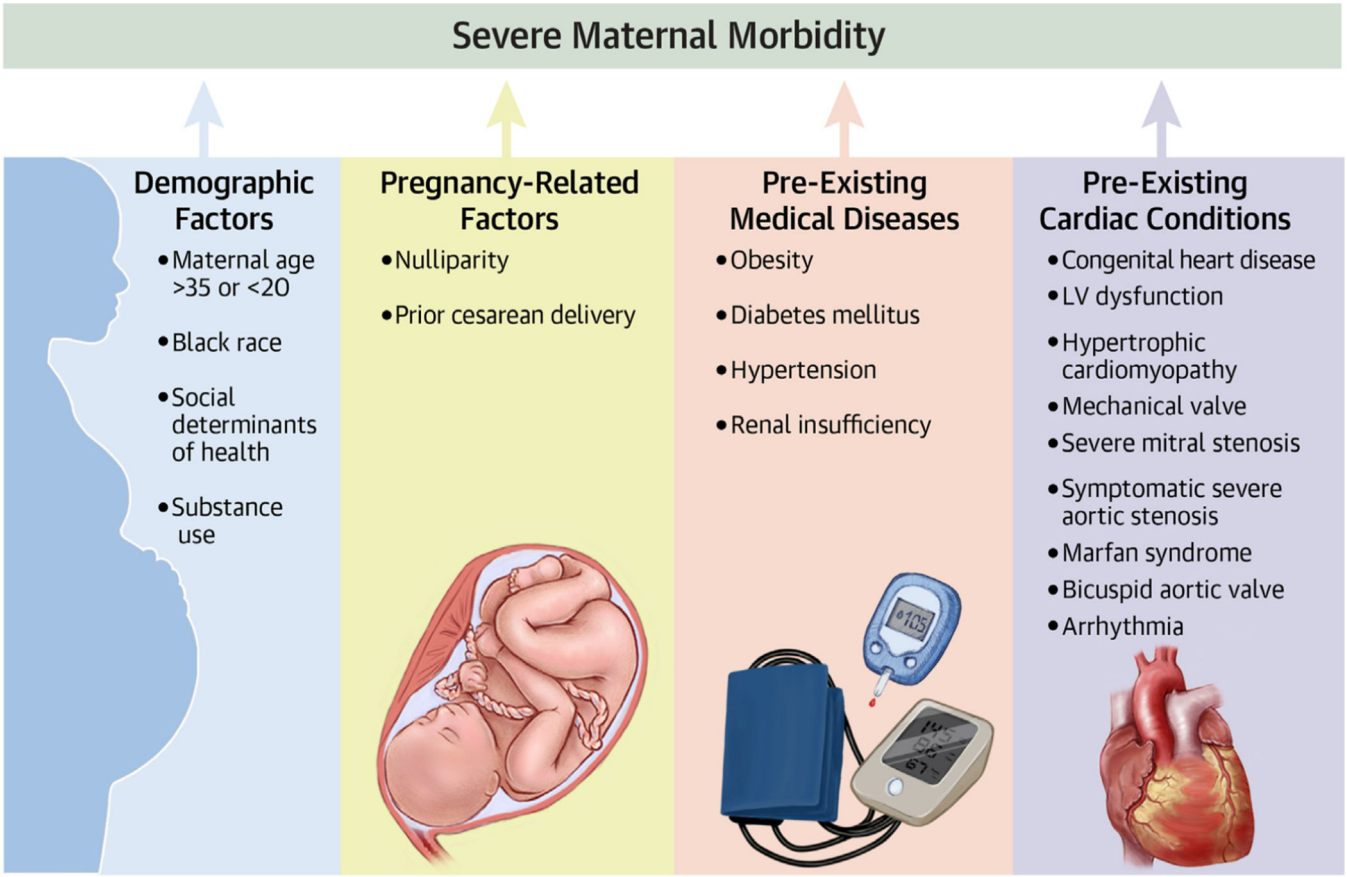


**FIGURE 1. Factors Implicated in the Development of SMM**

LV = left ventricular; SMM = severe maternal morbidity.

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**FIGURE 2.**
The Antenatal Visit Checklist in Screening for Cardiovascular Disease 117

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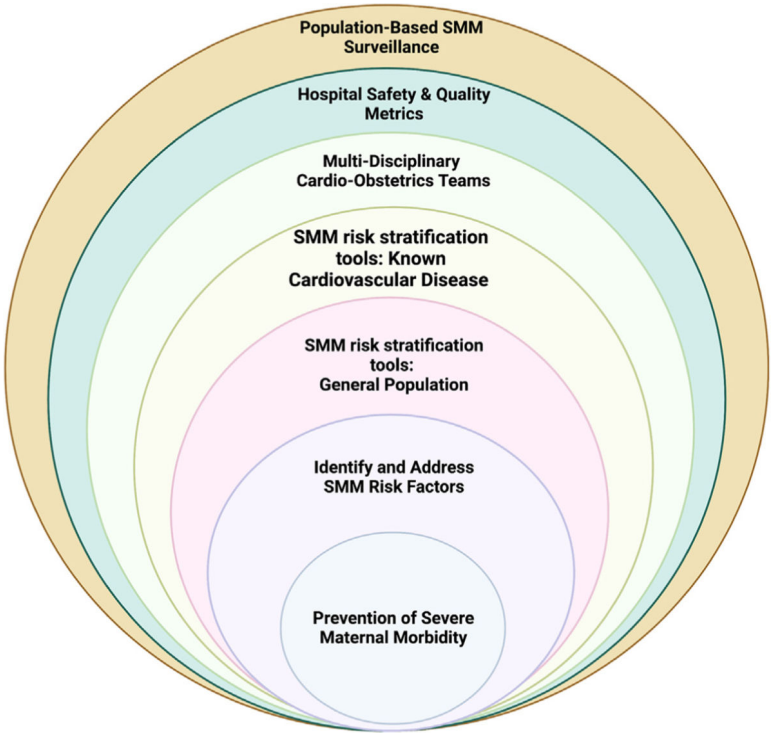


**CENTRAL ILLUSTRATION. Stages of Opportunities to Address SMM**
Thakkar A, et al. JACC Adv. 2023;2(2):100275.

Prevention of severe maternal morbidity requires a multi-layered approach beginning with identifying and managing SMM risk factors such as demographics, pregnancy-related risk factors, and preexisting cardiovascular conditions. Examples of SMM risk stratification tools in the general population include *MEWC* (maternal early warning criteria), *CMQCC* (California Maternal Quality Care Collaborative), and OB-CMI (Obstetric Comorbidity Index) Examples of SMM risk stratification tools in women with known CVD include ZAHARA I (Zwangerschap bij vrouwen met een Aange- boren HARtAfwijking-II), mWHO (modified World Health Organization) and CARPREG I/II (Cardiac Disease in Pregnancy). CVD = cardiovascular disease; SMM = severe maternal morbidity.

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*JACC Adv*. Author manuscript; available in PMC 2023 August 09.

**TABLE 1**

Indicators of SMM: Cardiac, and Non-Cardiac Causes

| Organ System | Severe Maternal Morbidity Indicators | Description |
|---|---|---|
| Cardiovascular | Acute myocardial infarction | Positive cardiac biomarkers above 99th percentile, and at least one of the following: symptoms of ischemia, new ischemic ECG changes, development of pathological Q waves, imaging evidence of loss of viable myocardium or regional wall motion abnormalities, identification of coronary thrombus[119] |
| | Aortic aneurysm | Segmental full-thickness dilation (involving all 3 tissue layers) with least a 50% increase in diameter compared with the expected diameter[120] |
| | Cardiac arrest or ventricular fibrillation | Cessation of cardiac mechanical function[37] |
| | Cardioversion | Termination of arrhythmia by electrical shock that depolarizes the tissue involved in a reentrant circuit[121] |
| | Heart failure or cardiac arrest during surgery or procedure | Characteristic symptoms and evidence of cardiac dysfunction as a cause, or inability to pump blood to meet metabolic demands of peripheral organs or only able to do so with high filling pressures |
| | Acute heart failure or pulmonary edema | Acute dyspnea, peripheral or pulmonary edema associated with elevated intracardiac filling pressures[122] |
| | Puerperal cerebrovascular disorders | A widespread group of disorders resulting from either vasospasm and endothelial dysfunction (causing brain ischemia, cerebral hemorrhage, posterior reversible encephalopathy syndrome), or arterial or venous obstruction (causing cerebral edema, hemorrhage, and intracranial hypertension)[123] |
| | Shock | A state of cellular/tissue hypoxia due to reduced oxygen delivery or utilization, increased oxygen consumption, or a combination of these etiologies[124] |
| Pulmonary | Acute respiratory distress syndrome | Respiratory symptoms beginning within 1 wk of a clinical insult, bilateral opacities on chest imaging not fully explained by pleural effusions, lobar/lung collapse, or pulmonary nodules, respiratory failure not fully explained by pulmonary edema due to cardiac dysfunction, and $PaO_2/FiO_2$ ratio <300 mmHg with positive end-expiratory pressure or continues positive airway pressure of at least 5 cm $H_2O$[125] |
| | Ventilation | Delivery of positive pressure to the lungs via face mask, endotracheal tube, or tracheostomy tube[126] |
| | Tracheostomy | Cannulation of the anterior wall of the trachea for ventilation[126] |
| Obstetric | Amniotic fluid embolism | Sudden onset of cardiorespiratory arrest or hypotension with evidence of respiratory compromise, with disseminated intravascular coagulation, with onset during labor or within 30 min of placental delivery, and with absence of fever during labor[127] |
| | Eclampsia | New onset tonic-clonic seizures in the absence of other causative conditions[128] |
| | Hysterectomy | Surgical removal of the uterus[129] |
| Renal | Acute renal failure | Increase in serum creatinine by >0.3 mg/dL within 48 h, or increase in serum creatinine to >1.5 times baseline, which is known or presumed to have occurred within the prior 7 d, or urine volume <0.5 mL/kg/h for 6 h |
| Hematologic | Disseminated intravascular coagulation | A clinical and laboratory diagnosis, based on findings of thrombocytopenia, coagulation factor consumption, and fibrinolysis in the appropriate setting without another unifying explanation for these laboratory findings[130] |
| | Sickle cell disease crisis | Acute increase in sickled erythrocytes causing vascular injury/stasis, coagulopathy, inflammation, reperfusion injury, and extreme pain.[131] |
| | Blood product transfusion | The infusion of donated blood products, including erythrocytes, platelets, plasma, cryoprecipitate, and immunoglobulin. |

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| Organ System | Severe Maternal Morbidity Indicators | Description |
|---|---|---|
| | Air and thrombotic embolism | Air embolism encompasses the entry of air from the atmosphere to either the venous or the arterial circulation. Thrombotic embolism refers to the mobilization of formed thrombus from one vascular territory to another.[132] |
| Infectious | Sepsis | Organ dysfunction caused by a dysregulated host response to an infection.[1] |
| Procedural | Severe anesthesia complications | Complications related to the act of anesthesia itself, including cardiac arrest or arrhythmia, central nervous system complications, aspiration pneumonitis, and other respiratory complications. |

ECG = electrocardiography; SMM = severe maternal morbidity.

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**TABLE 2**

Predictors and Reporting of SMM

| Predictive Tools | | Tool | Use |
|---|---|---|---|
| | | California Maternal Quality Care Collaborative (CMQCC) | • Obstetric comorbidity scoring system to predict rates of SMM and non-transfusion SMM |
| | | Obstetric Comorbidity Index (OB-CMI) | • Comorbidity-based screening tool to identify patients at risk of SMM at labor and delivery in real time |
| | | Maternal Early Warning Criteria (MEWC) | • Early warning system to identify at-risk patients who should be assessed promptly at bedside |
| Reporting & Quality Metrics | Standardized Case-Based Reviews | Initiative | Illustrative examples of outcomes |
| | | Illinois State Review | • SMM could be reduced by improving care coordination and communication at the system level as well as improving recognition of high-risk cases |
| | | CMQCC Toolkit for Hypertensive Disorders of Pregnancy | • Improvement in hospital-wide treatment compliance led to overall reduction in incidence of eclampsia and SMM |
| | | UK Obstetric Surveillance System (UKOSS) | • Demonstrated that cesarian sections performed in a timely manner could reduce rates of SMM and improve maternal survival |
| | | International Network of Obstetric Survey & Systems (INOSS) | • International surveillance demonstrated great variability in management of obstetric hemorrhage prior to peripartum hysterectomy across Europe |
| | ACOG District II's Safe Motherhood Initiative | Hypertensive bundle | • preliminary analysis in recognition and treatment of severe hypertension are promising; however, continued funding and support are needed to continue progress |

ACOG = American College of Obstetricians and Gynecologist; SMM = severe maternal morbidity.

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**TABLE 3**

Cardiovascular Risk Assessment Scores and Classifications[133]

| Modified WHO Classification | ZAHARA Risk Score (Weighted Risk Score Based on Factors of Poor Predictive Outcomes) | CARPREG II Risk Predictors (Weighted Risk Score Based on Lesion, Imaging Parameters and Patient Factors) |
|---|---|---|
| Class I: No detectable increase in maternal mortality and no/mild increase in morbidity (uncomplicated and repaired ASD, VSD, PDA, and MVP, atrial and ventricular ectopic beats) | Mechanical valve prosthesis (4.25)<br>Evidence of left-side obstruction (aortic valve peak gradient >50 mm Hg or AVA <1.0 $cm^2$ (2.50) History of arrhythmia (1.50) | Prior cardiac events or arrhythmias (3)<br>NYHA functional class III-IV or cyanosis (3)<br>Mechanical valve (3) Systemic LV dysfunction (EF <55%) (2) |
| Class II: Small increase in maternal mortality and moderate increase in morbidity (Unoperated ASD, VSD, TOF, and ventricular arrhythmias. Depending on the individual mild LV dysfunction, HCM, Marfan without aortic dilatation, repaired coarctation of aorta) | Use of cardiac medication pre-pregnancy (1.50)<br>Repaired and unrepaired cyanotic heart disease (1.0) | High-risk valve disease (2) Pulmonary hypertension (RVSP >49 mm Hg (2) |
| | Moderate to severe atrioventricular valve dysfunction (possibly related to underlying LV dysfunction) (0.75) | High-risk aortopathy (2) Coronary artery disease (2) No prior cardiac intervention (1)<br>Late pregnancy assessment (1) |
| Class III: Significantly increased maternal mortality and morbidity. (Mechanical valve, systemic right ventricle, Fontan circulation, unrepaired cyanotic heart disease, aortic root dilatation in Marfan and bicuspid valve) | Baseline NYHA functional classification >II (0.75) | |
| Class IV: Extremely high-risk maternal mortality and morbidity (Cardiomyopathy with LVEF <30%, pulmonary hypertension, native severe coarctation, severe mitral and aortic stenosis) | | |
| Maternal cardiovascular complication risks: class I, 2.5%−5%; class II, 5.7%−10.5%; class II-III, 10%−19%; class III, 19%−27%; class IV, 40%−100% | Weighted risk score: Maternal cardiovascular complications risk:<br><0.5 points 5 2.9%,<br>0.5–1.5 points 5 7.5% 1.51–2.50 points 5 17.5% 2.51–3.5 points 5 43.1% >3.5 points 5 70% | Weighted risk score: Maternal cardiac complications risk:<br>0–1 = 5%<br>2 = 10%<br>3 = 15%<br>4 = 22%<br>>4 = 41% |

Adapted with permission from Sharma et al.[133]

ASD = atrial septal defect; AVA = aortic valve area; CARPREG = cardiac disease in pregnancy; EF = ejection fraction; HCM = hypertrophic cardiomyopathy; LV = left ventricular ; LVEF = left ventricular ejection fraction; MVP = mitral valve prolapse; NYHA = New York Heart Association; PDA = patent ductus arteriosus; RVSP = right ventricular systolic pressure; TOF = teratology of Fallot; VSD = ventricular septal defect; ZAHARA = Zwangerschap bij vrouwen met een Aange-boren HARtAfwijking-II.

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