Anesthesiologists as Peripartum Physicians:

New Paradigms to Improve Maternal Outcomes

Jennifer M. Banayan, MD

Assistant Professor
Department of Anesthesia and Critical Care
University of Chicago
Chicago, Illinois

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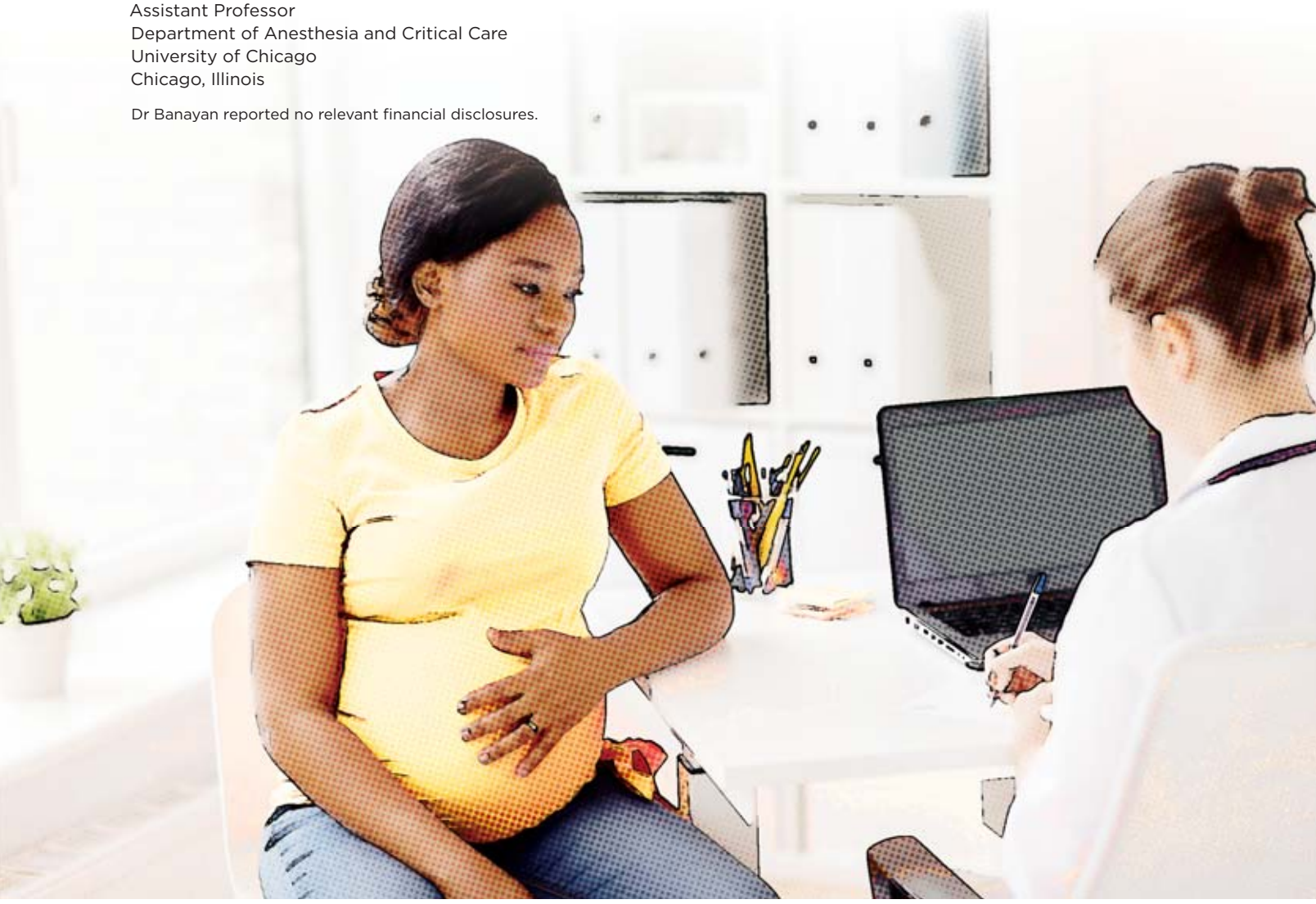

Maternal mortality in the United States has lately been increasing.[1] Anesthesiologists need to act as peripartum physicians and work with others to improve maternal safety.

Introduction

Pregnancy and childbirth are the leading causes of death among young women in many countries around the world.[1] Globally, 800 women die in childbirth every day.[1] In the US, despite spending $98 billion a year on hospitalizations related to pregnancy—more than any other country—the maternal mortality rate is higher than many other countries. In fact, the World Health Organization (WHO) ranks the US 46th out of 184 countries on maternal mortality.[2] Even more concerning is that the US is the only developed country in which maternal mortality has increased since 1990.[3] Since 1987, the US maternal mortality rate has more than doubled.[1]

Maternal Mortality and Morbidity

These findings are surprising, especially considering that maternal mortality in the US had decreased dramatically between 1925 and 1987.[4] Improved survival was attributed to advances in medical care, more deliveries in hospitals, more infants being delivered by providers trained in obstetric care, development and use of medications to control hemorrhage and blood pressure, and improvement in aseptic technique.[5] But instead of continuing improvement in maternal survival, we are witnessing the opposite in this country over the past 3 decades.[6]

In addition, severe maternal morbidity has more than doubled in the 21st century, affecting 50,000 women every year.[7] Unfortunately, because there is no general consensus on the definition of maternal morbidity, comparison between nations is difficult. The Euro-Peristat project, which attempts to establish a European perinatal information system, identifies indicators such as eclampsia, hysterectomy, embolization, blood transfusion, or a stay of more than 24 hours in an intensive care unit while pregnant as maternal morbidity.[8] The WHO proposed a definition for maternal "near-miss" as a woman who nearly died but survived a complication during pregnancy, childbirth, or within 42 days of termination of pregnancy.[9]

In other publications, clinical diagnoses such as wound infection, hemorrhage, embolism, acute renal failure, stroke, and acute myocardial infarction are examples of complications resulting in longer hospital stay and higher medical costs.[7] Most importantly, anesthesiologists should realize that even with different definitions of morbidity, the overall trend in the US indicates that maternal morbidity is rising.

Maternal Risk Factors

The reasons for the increase in morbidity are unclear but several possible explanations exist. First, there is an increased incidence of parturients of advanced maternal age: 15% of all US births are to women over the age of 35 years.[10] This age demographic carries a disproportionate share of maternal mortality.[11] Advanced maternal age increases a patient's risk for a coexisting disease, such as hypertension, preeclampsia, amniotic fluid embolism, venous thromboembolism (VTE) , hemorrhage, and diabetes.[12]

Second, compared with other developed countries, the US has a disproportionately high rate of cesarean deliveries.[13] Currently, the cesarean delivery rate is 32%[14]; in Sweden, the rate is half that.[15] Not only does a cesarean delivery increase the chance of a complication, such as surgical hemorrhage, VTE, or perioperative infection, but it also can cause complications in subsequent pregnancies. Repeat cesarean deliveries lead to an increased incidence of placental implantation abnormalities such as placenta accreta—a potentially devastating disease process.[16]

The most compelling explanation for increased maternal mortality may be related to the surge in chronic health conditions in the parturient, such as hypertension, diabetes, and chronic heart disease.[7,17-19] Cardiac disease has become the main cause of maternal mortality, and congenital heart disease (CHD) accounts for more than half of all cardiac disease in pregnancy.[20] Our success in managing and treating patients who were born with CHD has resulted in a 43% increase over a 10-year period (1998-2007) in parturients presenting with a history of CHD.[21] Pregnant women with CHD have a 13% incidence of peripartum pulmonary edema, arrhythmias, stroke, or cardiac death.[22]

Despite the fact that more than half of US women who become pregnant are over a healthy weight,[23] obesity itself is not an independent risk factor for maternal mortality.[24] Nevertheless, obese patients have a higher risk for developing preeclampsia, gestational diabetes, or sleep apnea. They also may have anatomy that leads to difficulties in epidural placement and increases their rate for a cesarean delivery or difficult airway.

Causes of Maternal Mortality and Morbidity

Historically, the most common causes of maternal death have been hemorrhage, hypertensive disorders, thromboembolic events, and infections.[11,25] Recently, the fraction of deaths due to these conventional causes has declined, and a significant proportion of maternal deaths is now attributable to cardiovascular conditions and other coexisting medical diseases (Figure 1).[11,25] In addition to being concerned with obstetric complications, such as hemorrhage or hypertension in pregnancy, the anesthesiologist is confronted with preexisting disease, such as peripartum cardiomyopathy or with Fontan physiology.

Cardiovascular Disease

Cardiovascular disease is now the leading cause of maternal mortality in the US, surpassing hemorrhage, hypertensive disorders of pregnancy, infection, and thrombotic pulmonary embolism.[11] The mechanisms underlying the increase in maternal cardiovascular deaths are incompletely understood. A rising incidence of risk factors for cardiovascular disease, such as advanced maternal age, obesity, hypertension,

and diabetes, may be responsible. Another possibility is the growing number of women with congenital heart defects who have reached childbearing age.[26] The hemodynamic changes of pregnancy, such as increased cardiac output, may challenge a patient with cardiac disease. For example, pulmonary hypertension in pregnancy is associated with high mortality despite numerous advances in therapies.[27] Patients with cyanotic heart disease are poor candidates for pregnancy and have unacceptably high mortality rates.[28,29]

Cardiomyopathy is the largest subcategory of cardiac-related mortality, and peripartum cardiomyopathy (PPCM) is a major cause of morbidity and mortality.[30] PPCM is diagnosed when all other causes of heart failure are excluded and typically presents during the third trimester of pregnancy or immediately postpartum.[31] It is estimated that 33% to 67% of women diagnosed with PPCM experience a long-term reduction in cardiac function, and the related mortality rate is 9% to 50%.[31]

Hemorrhage

Obstetric hemorrhage is the most common cause of maternal mortality worldwide.[32] Although mortality from hemorrhage is decreasing in the US and globally, there is an increase in the incidence of postpartum hemorrhage as well as in hemorrhage-related morbidity in this country.[33] It has been suggested that clinicians tend to underestimate blood loss at birth, delay intervention, miss early warning signs, and do not resuscitate adequately.[34] Many studies have referred to hemorrhage-related mortality as preventable.[35,36]

In an effort to increase awareness and recognition of hemorrhage, the American Congress of Obstetricians and Gynecologists (ACOG) revised the definition of *early postpartum hemorrhage* to "cumulative blood loss of ≥1,000 mL operating room (OR) blood loss accompanied by signs and symptoms of hypovolemia within 24 hours following the birth process. Cumulative blood loss of 500-999 mL alone should trigger increased supervision and potential intervention as clinically indicated."[34]

Earlier this year, the World Maternal Antifibrinolytic (WOMAN) trial was published.[37] This international, randomized, double-blind, placebo-controlled trial evaluated the effects of the early administration of tranexamic acid (TXA) during postpartum hemorrhage. Over 20,000 women with a diagnosis of postpartum hemorrhage (from cesarean or vaginal delivery) at 193 hospitals in 21 mostly low- to moderate-resource

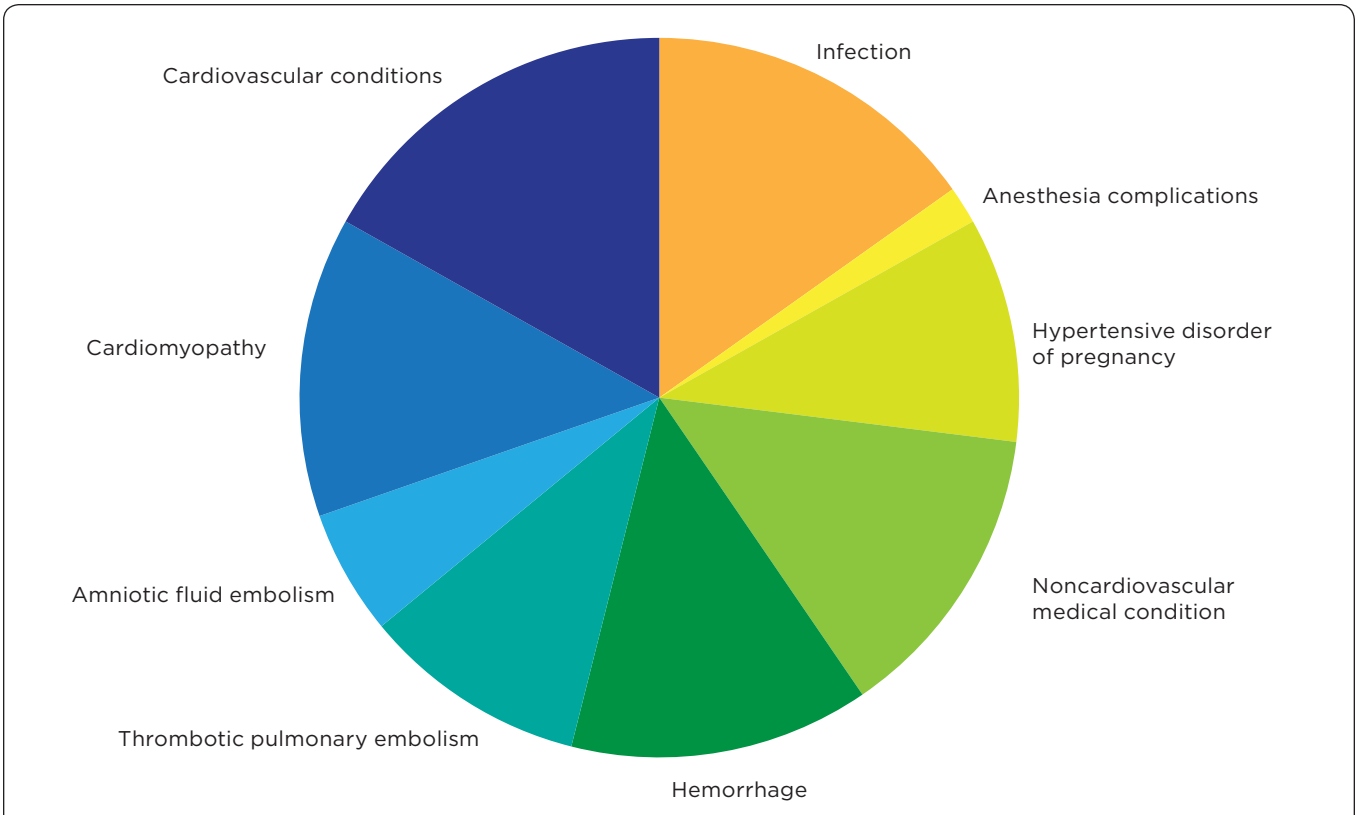

Figure 1. Causes of pregnancy-related mortality in the United States: 2006-2010.

Adapted from reference 11.

countries were randomly assigned to receive 1 g of intravenous TXA or placebo with standard hemorrhage care. A second dose of TXA could be administered if bleeding continued. Primary end points were hysterectomy and death. Death from postpartum hemorrhage was significantly reduced in women who received TXA (1.5% vs 1.9% in placebo group; *P*=0.045), specifically in those who received TXA within 3 hours of giving birth. However, the reduction in all-cause mortality in women receiving TXA was not statistically significant. Thromboembolic events were not significantly higher in the TXA group.

This study indicates that TXA may reduce death from postpartum hemorrhage, especially if it is administered soon after hemorrhage begins.[37] However, it should be noted that the study had a major limitation in that the power calculation and hypothesis were changed after data collection was initiated. Furthermore, how these data should be extrapolated to high-resource countries, such as the US, that have much lower fatality rates from hemorrhage, remains unclear. In addition, the anesthesiologist should exercise care with TXA, because accidental administration into the intrathecal space may result in death within 24 hours.[38-40]

Hypertension in Pregnancy

Failure to manage hypertension adequately or recognize clinical manifestations of preeclampsia, such as hemolysis, thrombocytopenia, elevated liver enzymes, and pulmonary edema, is common and can lead to grave complications.[41] In the preeclamptic patient, the systolic blood pressure is an important precursor to hemorrhagic stroke.[42] Consequently, a systolic blood pressure of 160 mm Hg or greater in a pregnant patient is a hypertensive emergency and requires immediate intervention by a clinician.[43] Administration of antihypertensive agents in a timely fashion is essential and potentially lifesaving. More than half of maternal deaths from hypertension are potentially avoidable.[41]

The ACOG has created standardized evidence-based guidelines, including dosing regimens for intravenous labetalol and hydralazine and oral nifedipine (when intravenous access is problematic), for the initial management of acute severe hypertension in pregnancy.[42]

Venous Thromboembolism

Venous thromboembolism is a leading cause of maternal mortality and severe morbidity. Maternal thromboembolism in the US increased more than 70% from 1998 to 2009,[7] but it is largely considered preventable.[11] Thromboembolism prophylaxis is effective in decreasing maternal mortality.[44] Widespread VTE prophylaxis in the United Kingdom (UK) has resulted in a reduction of maternal deaths.[45]

In response to these findings, several organizations have made recommendations regarding thromboprophylaxis. The Hospital Corporation of America recommended pneumatic compression devices for all women undergoing a cesarean delivery.[46] The Joint Commission issued a sentinel event alert requiring that sequential compression devices before a cesarean delivery remain in place until the patient is fully ambulatory.[47] The Joint Commission also recommended that high-risk antepartum and postpartum patients should be chemically anticoagulated.

The ACOG published a statement on the prevention of VTE that included early ambulation, pneumatic compression devices, and risk stratification regarding pharmacologic thromboprophylaxis.[48] The National Partnership for Maternal Safety (NPMS) recommends that clinicians assess patients for VTE risk throughout pregnancy, during prenatal visits, hospitalizations during pregnancy, delivery hospitalization, and during discharge from delivery hospitalizations.[48,49] Two different risk assessment tools, the Caprini and Padua scoring systems, can be used to identify patients at highest risk for developing VTE.[49] For patients at highest risk, more aggressive VTE prophylactic strategies may be considered.

The expected increase in the proportion of parturients receiving anticoagulation therapy around delivery may complicate the safe administration of neuraxial anesthesia. A table in the VTE bundle summarizes the recommendations for timing of neuraxial anesthesia in relation to pharmacologic prophylaxis.[49]

Sepsis

Infection is one of the leading causes of US maternal mortality, and severe sepsis and sepsis-related deaths continue to rise.[50] In the UK, a study reported that the source of sepsis in 40% of women with severe sepsis was pneumonia/respiratory infections.[51] These findings corroborate another UK study that suggested a large percentage of maternal sepsis deaths were due to influenza.[51] Risk factors for maternal morbidity from sepsis include lower socioeconomic status, younger age, multiple gestations, and cesarean delivery.[51]

Because sepsis is difficult to diagnose,[52] there is a variety of different approaches to improve early detection of an infection. The Saving Mothers' Lives report has a list of early warning criteria to prompt a clinician to consider an evolving sepsis diagnosis.[53] Tachycardia greater than 100 beats per minute, tachypnea greater than 20 breaths per minute, or a temperature above 38°C combined with a clinical symptom such as chest or abdominal pain, diarrhea, vomiting, vaginal discharge, or postpartum uterine tenderness should trigger aggressive intervention, including early broad-spectrum antibiotics, fluid resuscitation, and consideration of vasopressors (norepinephrine is the first-line recommendation) as needed to maintain adequate blood pressure (mean arterial pressure, 65 mm Hg).[54] Although not specifically studied in the parturient, the "Sepsis Six"—a bundle of therapies aimed at reducing mortality from sepsis in the UK (Figure 2)[55]—may be adapted for the obstetric population.

Anesthesia-Related Causes

Mortality related to anesthesia is rare and becoming less common.[11] It is estimated to occur at about 1.2 per million live births—a 60% decline since 1979.[44] The Society of Obstetric Anesthesia and Perinatology (SOAP) Serious Complications Repository (SCORE) project aimed to identify the incidence of serious complications related to obstetric anesthesia. Standardized forms were collected from 30 institutions in the US, with more than 307,000 deliveries.

Anesthetic complications were extremely rare, with incidences of epidural hematoma of approximately 1 in 250,000; epidural abscess, approximately 1 in 60,000; and serious neurologic injury, approximately 1 in 35,000.[56] High neuraxial block (1/4,336) and failed intubation (1/533) occurred most commonly.[56] Despite the concern about a "cannot ventilate/cannot intubate" situation, the SCORE study did not report any cases of serious aspiration or hypoxemic arrest secondary to a lost airway. In fact, among the 5,332 general anesthetics administered with an approximate 10% failed intubation rate, there was not even one report of hypoxemic arrest.[56] Other studies have also shown that airway difficulty in the obstetric population is becoming similar to the general population.[57] Failed intubation and its associated complications may have decreased in parturients as a result of better preparedness, earlier neuraxial intervention, and better airway equipment.

In comparison with the aforementioned severe complications, unintentional dural punctures occur much more frequently, with an approximate incidence of 1 in 144.[56] These errors may very rarely lead to serious complications, such as herniation, central vein thrombosis, or intracranial hemorrhage, and therefore unintentional dural punctures were not mentioned as a leading cause of maternal anesthetic complications.

Interventions

Fortunately, maternal mortality and morbidity, particularly hemorrhage and hypertension in pregnancy, may be avoidable. Up to 93% of hemorrhage-related deaths and 60% of hypertension-related deaths may be preventable.[35] This indicates that by implementing protocols, increasing awareness and education, and appropriately triaging patients to optimal care centers, we can reduce maternal mortality. Anesthesiologists' input is vital to successful implementation of these interventions. In particular, there are 3 measures that have been implemented to improve maternal care:

1. National Partnership for Maternal Safety (NPMS) and Maternal Safety Bundles
2. Maternal Early Warning Systems
3. Maternal Levels of Care

National Partnership for Maternal Safety and Maternal Safety Bundles

The NPMS, housed within ACOG's Council on Patient Safety in Women's Healthcare, was formed in response to the rise in US maternal mortality and morbidity. Its mission is to "continually improve patient safety in women's healthcare through multi-disciplinary collaboration that drives cultural change." The core of the NPMS is its commitment to multidisciplinary cooperation. The publication of the bundles in a variety of sources, including anesthesia, obstetrics, nursing, and midwifery journals, is a testament to this commitment. Although ACOG has published practice bulletins and committee opinions for years, they have not been multidisciplinary in nature.

The goal of the NPMS is to reduce maternal morbidity and mortality in the US by 50%. One means of accomplishing this reduction is to create bundles. Bundles are a set of evidence-based practices that improve outcomes. A variety of existing evidence-based recommendations, such as the ACOG practice bulletins, are

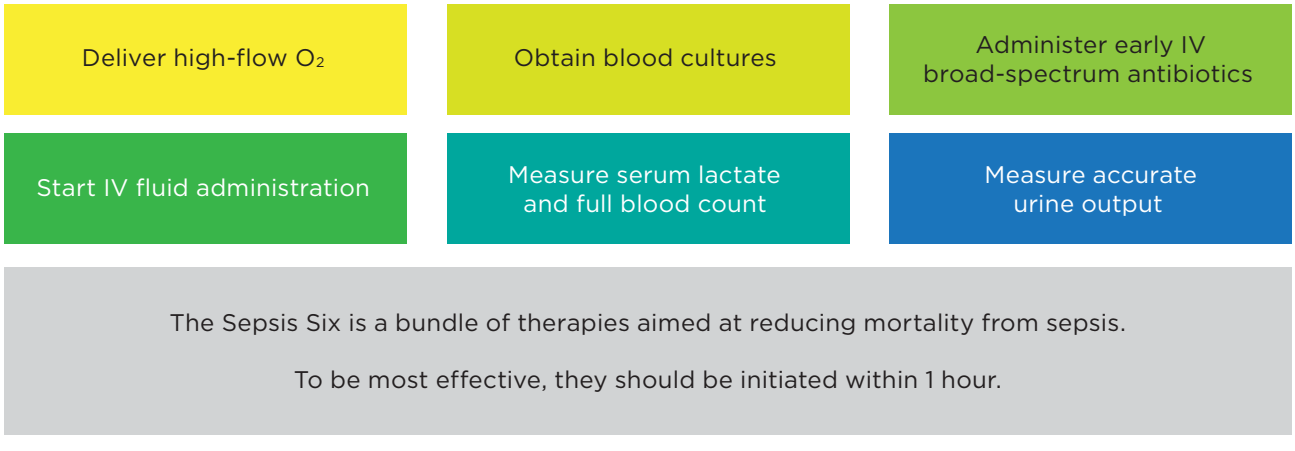

Figure 2. The Sepsis Six.

Adapted from reference 55.

available in a readily accessible format. Additionally, individual facilities are encouraged to modify the bundle to meet local needs and adapt to local resources. Maternal Safety Bundles address a variety of topics (Figure 3). Each bundle is formatted into 4 sections: Readiness, Recognition and Prevention, Response, and Reporting/System Learning.

The experience in California offers an excellent example of the way implementing bundles or toolkits can reduce maternal mortality. Between 2002 and 2004, 207 deaths occurred in California, and nearly 40% of them were considered preventable.[58] In response, the California Maternal Quality Care Collaborative (CMQCC) created a free online hemorrhage toolkit available to anyone. The toolkit included a collection of articles, guidelines, implementation guides, and educational documents with the goal of preventing mortality and morbidity in the parturient. Hospitals that used the CMQCC toolkit experienced a 20.8% reduction in severe maternal morbidity from hemorrhage over one year. The hospitals that did not adopt the CMQCC toolkit had a 1.2% reduction that was not significant.[32]

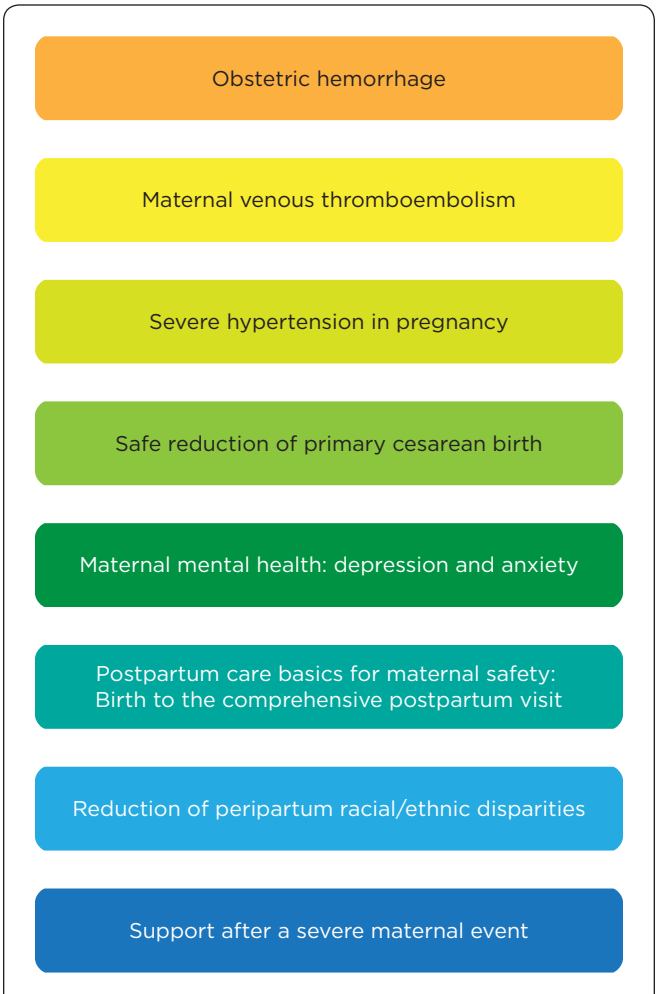

Figure 3. National Partnership for Maternal Safety: maternal safety bundle topics.

From safehealthcareforeverywoman.org/patient-safety-bundles/

Studies such as those published by Shields et al are more examples of proof that instituting comprehensive protocols for the treatment of maternal hemorrhage can improve patient safety.[59,60] Shields et al looked at outcomes before and after instituting a hemorrhage protocol at one institution and demonstrated a decrease in transfusions and a nonsignificant decrease in development of disseminated intravascular coagulation (DIC) after protocol implementation.[60] The investigators found a significant reduction in blood product use. There was also a reduction in the number of patients who required a hysterectomy when a comprehensive maternal hemorrhage protocol was instituted at a health care system that had 29 different delivery units and more than 60,000 deliveries.[59] These findings are evidence that increasing education and resources and providing toolkits may have a positive effect on patient outcomes.

Example of a Maternal Bundle: Hemorrhage

The Obstetric Hemorrhage Patient Safety Bundle was published in 2015.[34] The bundle outlines areas for improvement, including better recognition and appreciation of blood loss amount, increased attention to clinical signs of hemorrhage, faster restoration of blood volume, and greater emphasis on intervening decisively.[41] The goals of the hemorrhage bundle are to limit the proportion of hemorrhagic episodes that become severe, decrease the need for blood product transfusion, and decrease the frequency of coagulopathy.

The bundle is divided into 4 sections:

1. readiness,
2. recognition and prevention,
3. response, and
4. reporting/system learning

In the readiness section, supplies and systems needed to prepare for hemorrhage are listed. Each center should have hemorrhage kits and carts with medications and equipment at hand. A partnership with the facility's local blood bank should be made to prepare for rapid availability of blood products. Creating a massive transfusion protocol is also recommended to receive blood products immediately from the blood bank in case of a hemorrhage emergency. The recognition and prevention section recommends clinician assessment of every patient that measures cumulative blood loss during delivery and postpartum (eg, weighing of bedding and pads rather than visual estimates). The response section contains standard, stage-based emergency management plans for hemorrhage and detailed support programs for all patients and families. Finally, the reporting/system learning section recommends multidisciplinary reviews after severe hemorrhage episodes and tips for debriefing and perinatal quality improvement committees.

Maternal Early Warning Systems

Another proposed approach to reduce maternal morbidity and mortality is the adoption of Maternal Early Warning Systems. This method derives from the knowledge that abnormalities in vital signs or laboratory values precede a critical illness.[61] Promptly recognizing a patient's deteriorating condition may improve outcomes after timely interventions. Hemorrhage, sepsis, hypertensive crisis, and VTE are conditions that can be missed or not corrected in a timely fashion.[52] In 2007, The Confidential Enquiry into Maternal Deaths (now renamed the Centre for Maternal and Child Enquiries), in the UK, recommended an obstetric early warning system for identification of clinical deterioration, called the Modified Early Obstetric Warning System (MEOWS).[53] The MEOWS tracks temperature, blood pressure, heart rate, respiratory rate, oxygen saturation, level of consciousness, and pain scores. Thresholds are set for serious triggers known as "red triggers" or moderate triggers known as "yellow triggers." The triggers activate an escalation pathway to be followed.

The MEOWS has been found to be highly sensitive (89%) and moderately specific (79%).[61,62] A UK survey of the benefits of MEOWS observed that 91% of survey respondents agreed that any early warning system helps prevent obstetric morbidity, and 45% of them recommended the use of MEOWS.[63] The NPMS also has published Maternal Early Warning Criteria, which is similar to the UK's MEOWS.[52] A list of the criteria established by the NPMS is shown in Figure 4. Women who meet any of the criteria should receive a bedside evaluation by a clinician who considers a differential diagnosis, responds in a therapeutic manner, and activates resources in an emergency situation.[52]

Levels of Maternal Care

Maternal morbidity is higher in low-volume versus high-volume facilities (1,000-1,200 births per year).[64] Hemorrhage and infection occur more frequently in low-volume facilities. A recent study found more anesthesia-related adverse events in low-volume facilities.[65] The causes of these findings are unknown; they may be related to difficulty in recruiting and retaining high-quality professionals or to other institutional resources, such as blood bank availability. Whatever the cause, the findings underscore the need to standardize the assessment of maternal and neonatal care capabilities at each facility in the US. The ACOG and the Society for Maternal–Fetal Medicine published their consensus statement, "Levels of Maternal Care," which was endorsed by SOAP.[66]

One of the objectives of this statement is to introduce "uniform designations for centers of maternal care" that are distinct (yet still complementary) from the levels of neonatal care already in place. Currently, various states have implemented levels of maternal care, but the variability in nomenclature can contribute to confusion. The statement describes a uniform classification system for facilities (Table).[66] The goal is to ensure that appropriate personnel, space, equipment and technology are available based on these designations to provide consistent levels of care and to develop a geographically distributed network that promotes an integrated approach for peripartum care.

By specifically outlining each facility's capabilities, the type of health care providers present in each, and examples of patients who would be candidates for each type of facility, the statement establishes well-defined thresholds for transferring women to facilities to optimize their care. The transfer may occur prenatally or during the intrapartum or postpartum period.

In an era when informed decision making by the patient is emphasized, publishing each birthing center's available resources is necessary. This information helps patients and their families consider options. Many patients choose to deliver at their local hospital for the

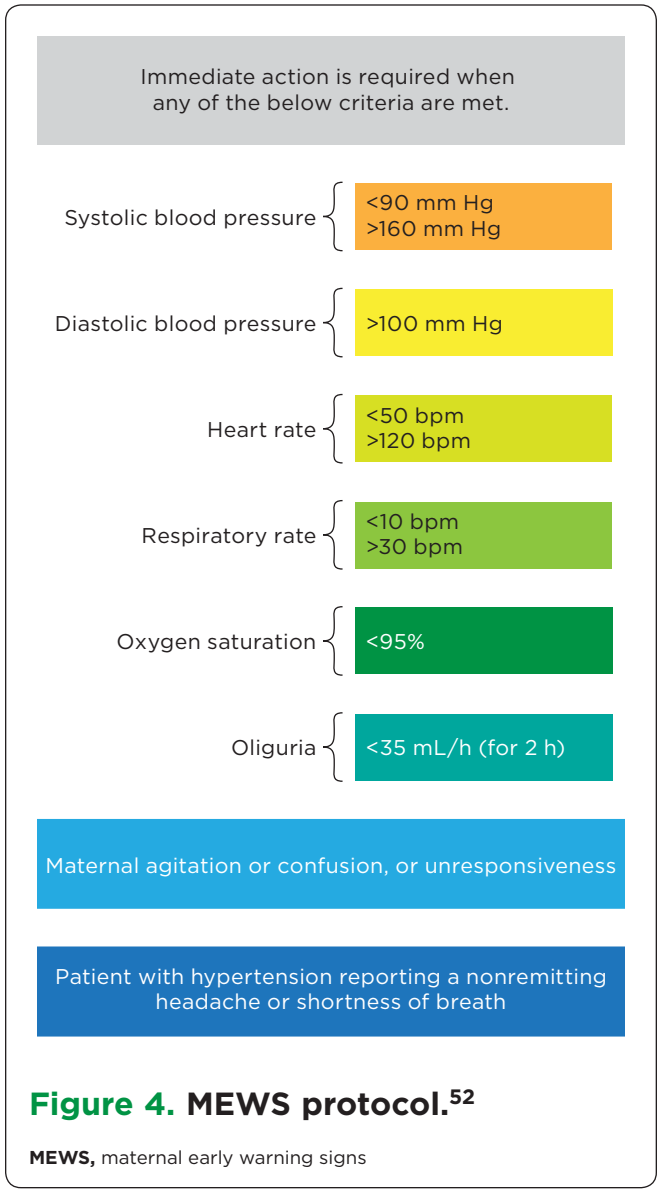

Figure 4. MEWS protocol.[52]

MEWS, maternal early warning signs

convenience of proximity, especially for a low-risk pregnancy. The publication on Levels of Maternal Care is not meant to discourage a decision that prioritizes patient convenience but rather to ensure that high-risk patients are aware of resources available at all institutions they may consider for their care.[67]

Conclusion

After many years of improvement, there has been a recent increase in maternal morbidity and mortality in the US. Recognizing that a large proportion of maternal mortality and morbidity is preventable is the key to improving outcomes. Several programs, in this country and abroad, have had promising early returns in improving maternal outcomes.

As anesthesiologists, we must take an active role in implementing maternal bundles or maternal levels of care, and utilize a maternal early warning system. Now, more than ever, anesthesiologists must act as peripartum physicians and collaborate with other caregivers to optimize maternal safety.

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Table. Levels of Maternal Care

	Birth Center	Level I	Level II	Level III	Level IV
Capabilities: (Each level of care assumes the capabilities of all levels below it)	Can manage a low-risk woman with uncomplicated singleton term pregnancy, vertex presentation, uncomplicated birth	Can manage an uncomplicated pregnancy but also can manage an unanticipated maternal, fetal, or neonatal complication until patient can be transferred	Can manage a high-risk antepartum, intrapartum, or postpartum condition	Can care for complex maternal medical conditions, obstetric complications, and fetal conditions	Can manage the most complex, critically ill pregnant women and fetuses
Anesthesia resources	Not available	Anesthesia services available	Anesthesia services available at all times. Board-certified anesthesiologist with special training or experience in obstetrics available for consultation	Anesthesia services available at all times. Board-certified anesthesiologist with special training or experience in obstetrics is in charge of obstetric anesthesia services.	Anesthesia services available at all times. Board-certified anesthesiologist with special training or experience in obstetrics is in charge of obstetric anesthesia services.
Obstetrics surgeon	Not available	Available for emergency cesarean delivery	OB/GYN available at all times	OB/GYN on site at all times	OB/GYN on site at all times

Based on reference 66.

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