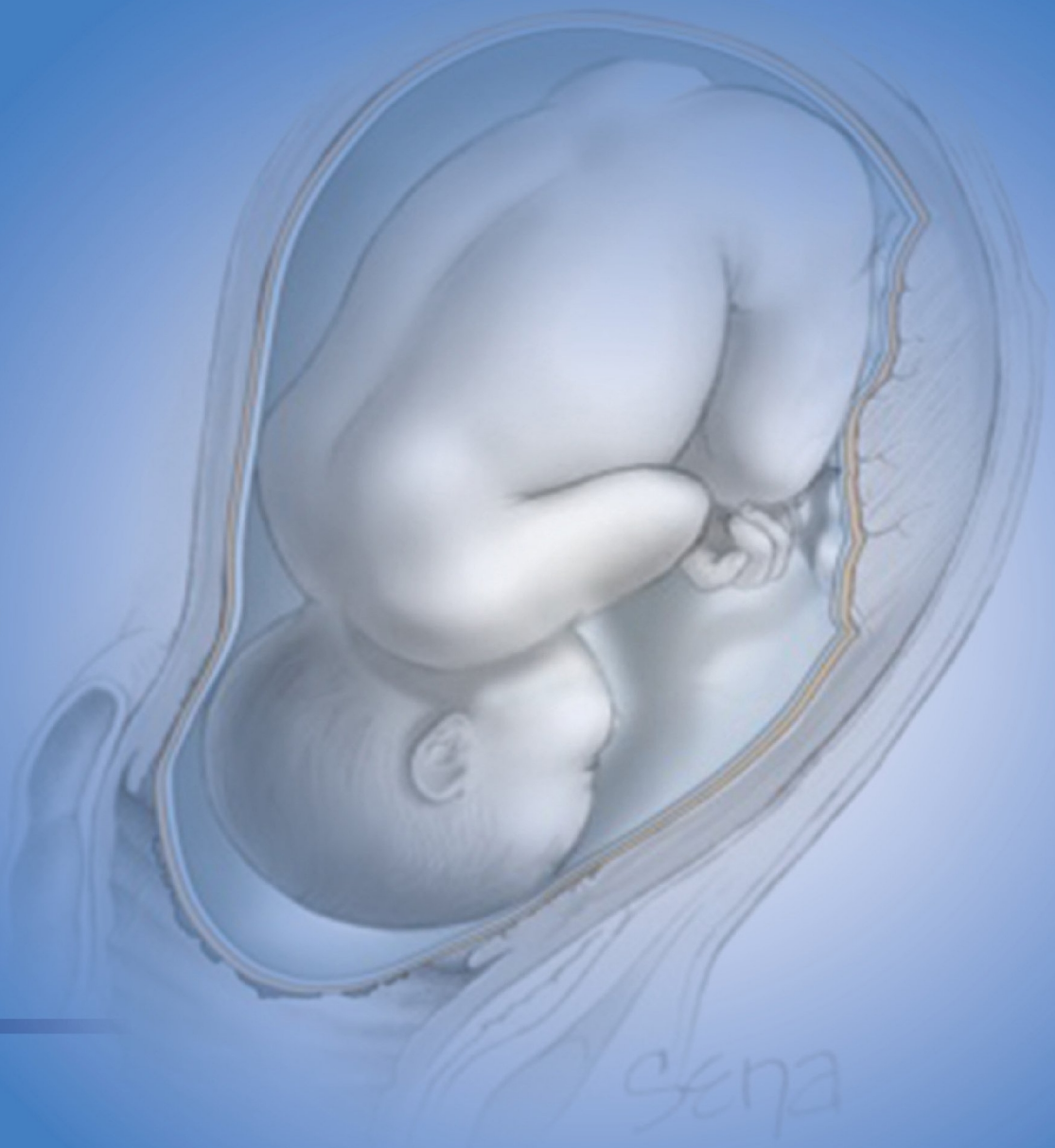
26TH EDITION

Williams OBSTETRICS



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Williams OBSTETRICS

26TH EDITION

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Editor of *Williams Obstetrics*
18th through 26th Editions

In the early 1970s, as I was finishing my residency at Charity Hospital of New Orleans, the 14th edition of *Williams Obstetrics* was published. The residents in our program were totally enamored with the textbook because it was a clinical manual derived from the editors' personal experiences and from contemporary, evidence-based literature.

During my last year, my chairman, Dr. Abe Mickal, invited me to attend a national meeting where I first met four obstetricians who would have an immeasurable impact on my life—Drs. Jack Pritchard, Paul MacDonald, Norman Gant, and Peggy Whalley. Following that, I was invited to Dallas to spend time at the University of Texas Southwestern and Parkland Hospital. As I followed Dr. Pritchard through Labor & Delivery and his clinical research laboratory, I became hooked on "Parkland Obstetrics" and later that year began a fellowship that was the nascent subspecialty of Maternal–Fetal Medicine. It also began a lifelong friendship with Jack Pritchard that I will always treasure.

Beginning with the 15th edition of *Williams Obstetrics*, the author-editors were Drs. Pritchard, MacDonald, and Gant. After publication of the 17th edition, these mentors asked me to assume the senior editor role. I was immediately struck by the awesome responsibility of shepherding the book that many people called "the bible of obstetrics."

Over the years, and now as we publish this 26th edition, I reflect on the evolution of obstetrics, and hence the complexity of sustaining a textbook designed to cover the breadth of obstetrics. As essential fields such as sonography, genetics, and fetal medicine were developed, we enlisted the help of extremely talented leaders in their respective fields to ensure that the book adequately presented these innovations. As for my role in this and other editions, I can only promise the readers that the quality of the book has been foremost in my mind and led me to spend literally tens of thousands of hours to help prepare the past nine editions. To this end, the editors have always strived to put the best product forward because of the tremendous responsibility that we shoulder regarding the care of women and their unborn children. The textbook has been one of the great passions in my life, and I will miss the challenge.

DEDICATION

KENNETH LEVENO, MD
1941–2020

Dr. Kenneth Leveno was a vocal and stalwart defender of evidence-based obstetrics. Sadly, he passed away in May 2020. Ken joined the Department of Obstetrics & Gynecology at the University of Texas Southwestern after completing a Maternal–Fetal Medicine fellowship in 1978. In 1984, he was appointed Chief of Obstetrics at Parkland Memorial Hospital—a role in which he served for the next 20 years. During that time and afterwards, he worked tirelessly to achieve a level of excellence in obstetrical care for indigent women of Dallas County. His inspiring leadership and innovations raised the quality of care at the community obstetrics clinics, the high-risk prenatal clinics at Parkland, and the inpatient units, which include the Obstetrical Triage Unit, Labor & Delivery, postpartum wards, and the High-Risk Pregnancy Unit. Early on, he also designed a computerized database to measure quality indicators and provide an underpinning for clinical research. Indeed, his contributions to these programs were reverently referred to by us as *Parkland Obstetrics.*

Ken Leveno's leadership extended well beyond the hospital that he loved. He was a leader in American obstetrics by his defining of clinical research. Through his hundreds of peer-reviewed publications, his clinical opinions, and his willingness to engage in national debates, he helped shape obstetrical practices worldwide. In 1993, Ken began serving as an editor for *Williams Obstetrics*—a task that he regarded as a privilege and a responsibility. He co-authored the 19th through the current 26th editions. Last and importantly, he mentored the careers of many Maternal–Fetal Medicine fellows and young faculty who have gone on to achieve national reputations in the care of women. Ken will be greatly missed.

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PREFACE

Over its 26 editions, *Williams Obstetrics* has aimed to serve practicing obstetricians and midwives in the bedside care of their patients. With its detailed explanations of disease pathophysiology and treatment fundamentals, it provides a bedrock text for residents who are training in Obstetrics or in Family Medicine specialties. Fellows in Maternal–Fetal Medicine will benefit from its additional discussions of complicated pathology and management. Last, *Williams Obstetrics* can aid specialists who act as consultants for gravidas with non-pregnancy-related disorders. Specifically, each chapter in Section 12 focuses on a specific organ system, the normal physiological changes and frequent disorders of that system in pregnancy, and suitable treatment options.

For this 26th edition, we continue to present the detailed staples of basic obstetrics such as maternal anatomy and physiology, preconceptional and prenatal care, labor, delivery, and the puerperium. These accompany detailed discussions of obstetrical complications exemplified by preterm labor, hemorrhage, hypertension, and many more. To emphasize the "M" in Maternal–Fetal Medicine, we continue to instruct on the many medical and surgical disorders that can complicate pregnancy. And, our second patient—the fetus—has accrued especial attention with an entire section devoted to diagnosis and treatment of fetal disorders. For all of these, we once again emphasize the science-based practice of clinical obstetrics. Expert clinical pearls add depth to these discussions and are written for busy practitioners—those "in the trenches." To integrate all our content, the reader of one chapter may be referred to a different chapter that contains complementary content. This offers a more global understanding of a given topic.

To accomplish our teaching goals, the text has been updated with more than 3000 new literature citations through 2021. Many of the nearly 900 figures are new, and these graphs, sonograms, magnetic resonance images, photographs, photomicrographs, and data graphs are all in vivid color. Much of the original artwork was rendered by our own medical illustrators.

As before, we continue to incorporate contemporaneous guidelines from professional and academic organizations such as the American College of Obstetricians and Gynecologists, the Society for Maternal–Fetal Medicine, the Centers for Disease Control and Prevention, the National Institutes of Health, and other authoritative sources. Many of these data are distilled into nearly 100 tables, in which information has been arranged in an easy read-and-use format. In addition, several diagnostic and management algorithms are available to quickly guide practitioners. Although we strive to cite numerous sources and provide multiple evidence-based options for such management schemes, we also include our own clinical experiences drawn from the large obstetrical service at Parkland Hospital. We are convinced that these are disciplined examples of evidence-based obstetrics but quickly acknowledge that they do not constitute the sole method of management.

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ACKNOWLEDGMENTS

In the creation and production of this textbook, we were fortunate to have the assistance and support of countless talented professionals both within and outside the Department of Obstetrics and Gynecology. To begin, we acknowledge that an undertaking of this magnitude would not be possible without the unwavering support provided by our recent Chairman Dr. Steven Bloom and Vice-Chairman Dr. Barry Schwarz, whose financial and academic endorsement has been essential. Dr. Bloom has served as an editor for the 22nd through 25th editions but now has assumed the important role of Associate Dean of Clinical Sciences at the University of Texas Southwestern Medical Center.

In constructing such an expansive academic compilation, the expertise of many colleagues was needed to add vital, evidence-based content. It was indeed fortuitous for us to have access to a trove of collaborators from our medical center. From our own Department of Obstetrics and Gynecology, Dr. Shivani Patel was essential to the production of our book and is an invaluable addition to our team. We benefitted from her obstetrical expertise, writing talent, and ability to translate difficult concepts into teaching pearls. Faculty with specific expertise included Dr. Claudia Werner, who lent valuable insight into the management of cervical dysplasia. Our nationally known pelvic anatomist, Dr. Marlene Corton, prepared graphic masterpieces for the anatomy chapter with artist Lew Calver. We also are grateful to the numerous faculty and residents who added seminal clinical photographs to our text.

In addition to these contributors, we relied heavily on our colleagues in the Division of Maternal–Fetal Medicine. These professionals, in addition to providing expert consultation, graciously assisted us by covering clinical duties when writing and editing were especially time consuming. These include Drs. Scott Roberts, Oscar Andujo, Vanessa Rogers, Charles Brown, Julie Lo, Robyn Horsager, Patricia Santiago-Muñoz, Mark Peters, Elaine Duryea, Jamie Morgan, Morris Bryant, Shena Dillon, Anne Ambia, Robert Martin, Robert Stewart, Stephan Shivvers, Ashley Zink, Sarah Happe, and Christina Herrera.

We also emphasize that production of *Williams Obstetrics* would not be feasible without the help of our Maternal–Fetal Medicine fellows and our residents in Obstetrics and Gynecology. Their insatiable curiosity serves to energize us to find new and effective ways to convey age-old truths, new data, and cutting-edge concepts. Their logical and critical questions lead us to weaknesses in the text, and thereby always help us to improve our work. In addition, we sincerely thank them for their vigilance in capturing photographs of spectacular examples of both obstetrical pathology and normal findings.

This edition is heavily populated with seminal examples of sonographic findings. We are grateful for the efforts of Mary Gibbs, RDMS; Rafael Levy, RDMS; Michael Davidson, RDMS; and the many talented sonographers at Parkland Hospital.

Thanks to generous funding from the McGraw-Hill Companies, this 26th edition now contains more than 200 color illustrations. Most of these were crafted by several skilled medical illustrators who include Ms. Marie Sena, Ms. Erin Frederickson, and Ms. SangEun Cha. All of these talented artists trained here at UT Southwestern under the instruction of Mr. Lewis Calver. Additional artistic support came from Mr. Joseph Varghese, Ms. Shreya Tiwari, Dr. Sudhi Singh, and Mr. Manoj Kumar Choudhry. Their work at Thomson Digital provided the full-color graphs and line art used to enhance this edition. Their team tirelessly coordinated efforts between author and artist and graciously accommodated our numerous changes and tweaks.

Production of the 5000-page manuscript would not have been possible without a dedicated team. Once again, we are deeply indebted to Ms. Dawn Wilson and Ms. Melinda Epstein for their untiring efforts with manuscript production. Ms. Regina Williams also provided excellent, cheerful, conscientious manuscript assistance. Mr. Charles Richards offered knowledgeable and responsive information technology support. For these and many more that go unnamed, we could not have done our job without their expertise.

It again has been a privilege to work with the dedicated professionals from McGraw-Hill Education. We have had the pleasure to work with Executive Editor Mr. Jason Malley in production of our textbook and are grateful for his support of *Williams Obstetrics*. Senior Project Development Editor Ms. Christie Naglieri has again brought her considerable knowledge to this edition of our book. Her dedication to creating the best textbook supported our efforts, and we appreciate her productive, gracious style. We thank Ms. Leah Carton, who provided professional, timely, and ever-sunny aid. Mr. Richard Ruzycka served as production supervisor for this edition of the textbook, and our book benefits from his years of experience.

Our text took its final shape under the watchful care of our compositors at Aptara, Inc. We thank Ms. Indu Jawwad for her talents in graciously and masterfully coordinating and overseeing composition. Her dedicated attention to detail and organization were vital to completion of our project. She has created many editions with us, and we consider her an essential team member. At Aptara, Mr. Mahender Singh carried out the crucial task of quality control. He also assisted, along with Mr. Rajesh Chander, Mr. Kamlesh Bhatt, and Mr. Anil Varghese, in creating beautiful chapter layouts to highlight our content aesthetically and informatively. This edition's chapters were also posted and available online for use prior to print publication. We thank Mr. Braj Bhushan and Mr. Ashish Kumar Sharma for preparing this content so brilliantly. Special thanks go to Mr. Greg Feldman. As copyeditor, Greg added

precision and clarity to our efforts. His endurance and pleasant professionalism through many challenging chapters has made our text better.

Last, we acknowledge our significant debt to the women who have entrusted themselves and their unborn children to us for obstetrical care. The clinical expertise and many images provided in this text would not have been possible without their collaborative spirit to help us advance obstetrical knowledge. We also offer enthusiastic and heartfelt appreciation to our families and friends. Without their patience, generosity, love, and encouragement, this task would have been impossible.

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Williams OBSTETRICS

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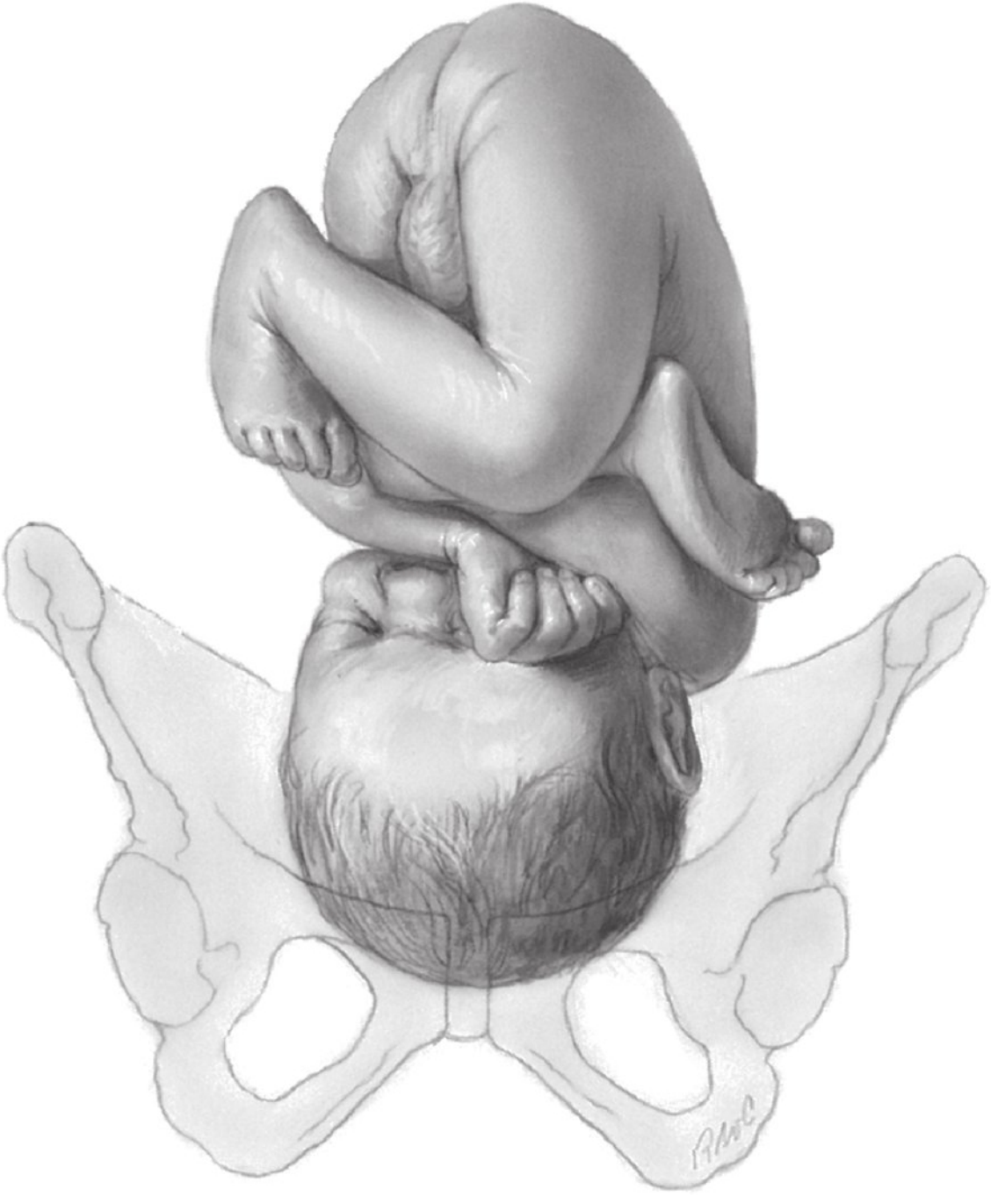
SECTION 1

OVERVIEW



CHAPTER 1

Overview of Obstetrics

The science and clinical practice of obstetrics focuses on human reproduction. The specialty promotes the health and well-being of the pregnant woman and her fetus through quality perinatal care. Such care entails recognition and treatment of complications, supervision of labor and delivery, initial care of the newborn, and management of the puerperium. Postpartum care promotes health and provides family planning options.

Evidence-based medicine dominates the modern practice of obstetrics. As described by Williams in this textbook's first edition, we too strive to present the scientific evidence for current obstetrical care. Still, high-quality data do not support most recommendations (Brock, 2021). Thus, much of our practice stems from expert-based opinions and historical experiences (Society for Maternal-Fetal Medicine, 2021). To help bridge knowledge gaps, we also rely on authoritative sources such as the American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine, as well as agencies such as the Centers for Disease Control and Prevention (CDC) and National Institutes of Health (NIH).

VITAL STATISTICS

The importance of obstetrics is demonstrated by the use of maternal and neonatal outcomes as an index of health and life quality among nations. Intuitively, indices showing poor obstetrical and perinatal outcomes could be assumed to reflect medical care deficiencies for the entire population.

The National Vital Statistics System of the United States collects statistics on births and deaths, including fetal deaths. Legal authority for collection resides individually with the 50 states; two regions—the District of Columbia and New York City; and five territories—American Samoa, Guam, the Northern Mariana Islands, Puerto Rico, and the Virgin Islands. The standard birth certificate includes information on medical and lifestyle risks, labor and delivery factors, and newborn characteristics. Importantly, the current death certificate contains a pregnancy checkbox (Hoyert, 2020).

Definitions

Standard definitions are encouraged by the World Health Organization as well as the American Academy of Pediatrics and the American College of Obstetricians and Gynecologists (2019a). Uniformity allows data comparison between states or regions and between countries. Still, not all definitions are uniformly applied. For example, uniformity is incomplete among states regarding birthweight and gestational age criteria for reporting fetal deaths (American College of Obstetricians and Gynecologists, 2020a). Not all states follow this recommendation. Specifically, 28 states stipulate that losses beginning at 20 weeks' gestation should be recorded as fetal deaths; eight states report all products of conception as fetal deaths; and still others use a minimum birthweight of 350 g, 400 g, or 500 g to define fetal death. To further the confusion, the National Vital Statistics Reports tabulates fetal deaths from pregnancies that are 20 weeks' gestation or older (Centers for Disease Control and Prevention, 2020a). This is problematic because the 50th percentile for fetal weight at 20 weeks approximates 325 to 350 g—considerably less than the 500-g definition. In fact, a birthweight of 500 g corresponds closely with the 50th percentile for 22 weeks' gestation.

Definitions recommended by the National Center for Health Statistics and the CDC are as follows:

Perinatal period. The interval between the birth of a neonate born after 20 weeks' gestation and the 28 completed days after that birth. When perinatal rates are based on birthweight, rather than gestational age, recommendations define the perinatal period as commencing at the birth of a 500-g neonate.

Birth. The complete expulsion or extraction from the mother of a fetus after 20 weeks' gestation. As described above, in the absence of accurate dating criteria, fetuses weighing <500 g are usually not considered births but rather are termed *abortuses* for purposes of vital statistics.

Birthweight. Neonatal weight determined immediately after delivery or as soon thereafter as feasible. It should be expressed to the nearest gram.

Birth rate. The number of live births per 1000 population.

Fertility rate. The number of live births per 1000 females aged 15 through 44 years.

Live birth. The term used to record a birth whenever the newborn at or sometime after birth breathes spontaneously or shows any other sign of life such as a heartbeat or definite spontaneous movement of voluntary muscles. Heartbeats are distinguished from transient cardiac contractions, and respirations are differentiated from fleeting respiratory efforts or gasps.

Stillbirth or fetal death. The absence of signs of life at birth.

Early neonatal death. Death of a liveborn neonate during the first 7 days after birth.

Late neonatal death. Death after 7 days but before 29 days.

Stillbirth rate or fetal death rate. The number of stillborn neonates per 1000 neonates born, including live births and stillbirths.

Neonatal mortality rate. The number of neonatal deaths per 1000 live births.

Perinatal mortality rate. The number of stillbirths plus neonatal deaths per 1000 total births.

Infant death. All deaths of liveborn infants from birth through 12 months of age.

Infant mortality rate. The number of infant deaths per 1000 live births.

Low birthweight. A newborn whose weight is <2500 g.

Very low birthweight. A newborn whose weight is <1500 g.

Extremely low birthweight. A newborn whose weight is <1000 g.

Term neonate. A neonate born any time after 37 completed weeks' gestation and up until 42 completed weeks' gestation (260 to 294 days). The American College of Obstetricians and Gynecologists and Society for Maternal-Fetal Medicine encourage specific gestational age designations (2019a). *Early term* refers to neonates born at 37 completed weeks up to $38^{6/7}$ weeks. *Full term* denotes those born at 39 completed weeks up to $40^{6/7}$ weeks. Last, *late term* describes neonates born at 41 completed weeks up to $41^{6/7}$ weeks.

Preterm neonate. A neonate born before 37 completed weeks (the 259^{th} day). A neonate born before 34 completed weeks is early preterm, whereas a neonate born between 34 and 36 completed weeks is late preterm.

Postterm neonate. A neonate born any time after completion of the 42nd week, beginning with day 295.

Abortus. A fetus or embryo removed or expelled from the uterus in the first half of gestation—20 weeks or less, or in the absence of accurate dating criteria, born weighing <500 g.

Induced termination of pregnancy. The purposeful interruption of an intrauterine pregnancy that has the intention other than to produce a liveborn neonate and that does not result in a live birth. This definition excludes retention of products of conception following fetal death.

Direct maternal death. The death of the mother that results from obstetrical complications of pregnancy, labor, or the puerperium and from interventions, omissions, incorrect treatment, or a chain of events resulting from any of these factors. An example is maternal death from exsanguination after uterine rupture.

Indirect maternal death. A maternal death that is not directly due to an obstetrical cause. Death results from previously existing disease or a disease developing during pregnancy, labor, or the puerperium that was aggravated by maternal physiological adaptation to pregnancy. An example is maternal death from complications of mitral valve stenosis.

Late maternal death. Death of a woman from direct or indirect obstetrical causes more than 42 days but less than 1 year after the pregnancy's end.

Nonmaternal death. Death of the mother that results from accidental or incidental causes not related to pregnancy. An example is death from an automobile accident or concurrent malignancy.

Pregnancy-associated death. The death of a woman, from any cause, while pregnant or within 1 calendar year of termination of pregnancy, regardless of the duration and the site of pregnancy.

Pregnancy-related death. A pregnancy-associated death that results from: (1) complications of pregnancy itself, (2) the chain of events initiated by pregnancy that led to death, or (3) aggravation of an unrelated condition by the physiological or pharmacological effects of pregnancy and that subsequently caused death.

Maternal mortality ratio. The number of maternal deaths that result from the reproductive process per 100,000 live births. Used more commonly, but less accurately, are the terms *maternal mortality rate* or *maternal death rate*. The term *ratio* is more accurate because it includes in the numerator the number of deaths regardless of pregnancy outcome—for example, live births, stillbirths, and ectopic pregnancies—whereas the denominator includes the number of live births.

PREGNANCY RATES IN THE UNITED STATES

According to the CDC, the fertility rate of women aged 15 to 44 years in the United States in 2019 was 58 live births per 1000 women. This rate began slowly trending downward in 1990 and has now dropped below that for replacement births to sustain the population level. This indicates a population decline. The birth rate decreased for all major ethnic and racial groups, for adolescents and unmarried women, and for

TABLE 1-1. Total Pregnancies and Outcomes in the United States in 2019

Outcome	Number or Percent
Total births	3,747,540
Cesarean deliveries	31.7%
Primary cesarean delivery	21.6%
Vaginal birth after cesarean	13.8%
Preterm births (<37 weeks)	10.0%
Low birthweight (<2500 g)	8.0%
Very low birthweight (<1500 g)	1.4%
Induced abortions	862,320

Data from Guttmacher 2019b; Martin, 2021.

those aged 20 to 24 years. For women older than 30 years, the birth rate rose slightly. Almost half of newborns in 2019 in the United States were minorities: Hispanic—25 percent; African-American—15 percent; and Asian—4 percent (Martin, 2021).

The total number of pregnancies and their outcomes in 2019 are shown in Table 1-1. According to the Guttmacher Institute (2019b), 45 percent of births in the United States are unintended at the time of conception. But, the overall proportion of unintended births has declined since 2008. Unmarried women, black women, and women with less education or income are more likely to have an unplanned pregnancy.

OBSTETRICAL CARE MEASURES

Several indices are used to assess obstetrical and perinatal outcomes as measures of medical care quality. As noted, the *perinatal mortality rate* includes the number of stillbirths and neonatal deaths per 1000 total births. In 2016, this rate was 6 deaths per 1000 births (Fig. 1-1). This rate has been unchanged for several years (Gregory, 2018). Rates of fetal death at 28 weeks' gestational age or more have declined since 1990, whereas rates for those between 20 and 27 weeks are static.

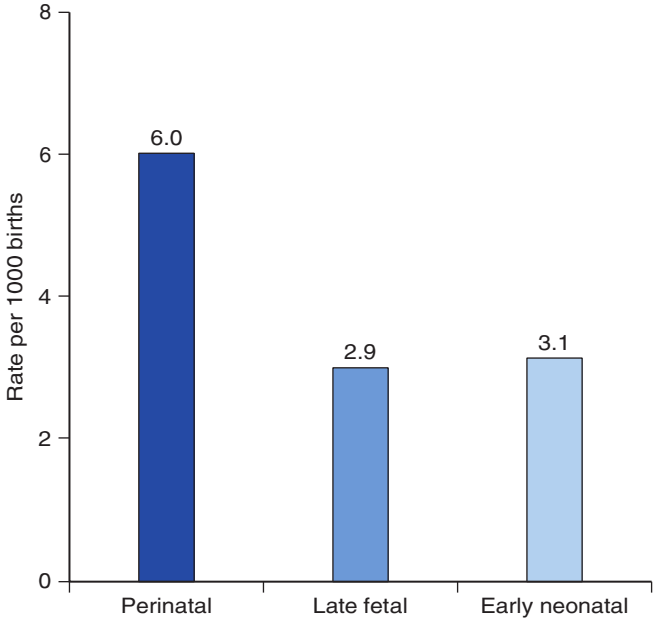


FIGURE 1-1 Perinatal, late-fetal, and early-neonatal mortality rates per 1000 births in the United States in 2016. (Data from Gregory, 2018).

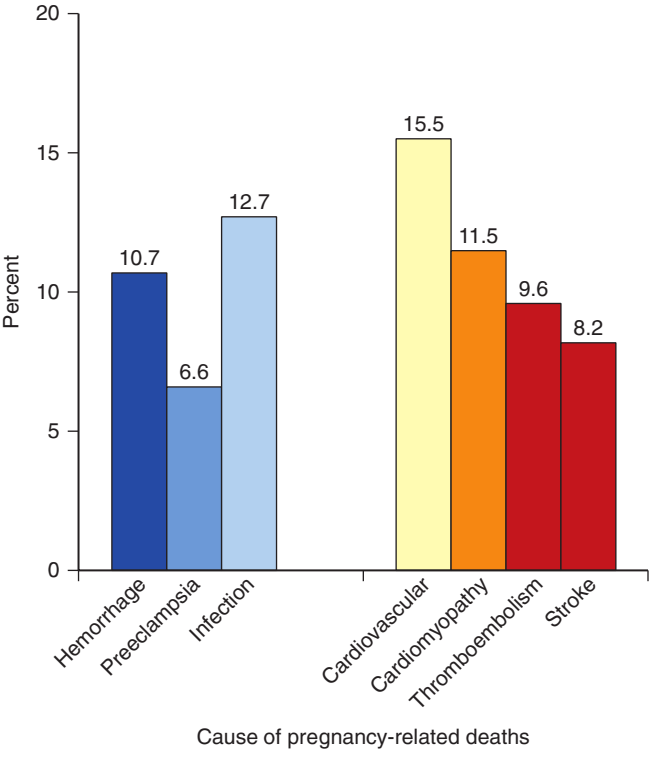


FIGURE 1-2 Some causes of and their contributions to pregnancy-related maternal deaths in the United States from 2014–2017. (Data from Centers for Disease Control and Prevention, 2020c).

Of *infant deaths*, the rate approximated 6 deaths per 1000 live births in 2018 compared with nearly 7 in 2001 (Centers for Disease Control and Prevention, 2020b). The four leading causes—congenital malformations, preterm birth, low birthweight, and maternal pregnancy complications—accounted for almost half of all infant deaths. Neonates born at the lowest gestational ages and birthweights add substantively to these mortality rates. For example, 17 percent of all infant deaths in 2018 were in those born preterm and with a low birthweight (Centers for Disease Control and Prevention, 2020d). Of particular interest are neonates with birthweights <500 g, for whom neonatal intensive care can now be offered (Chap. 45, p. 785).

Of *maternal deaths*, rates dropped precipitously in the United States during the 20th century. Pregnancy-related deaths are so uncommon as to be measured per 100,000 births. The CDC maintains data on pregnancy-related maternal deaths in its Pregnancy Mortality Surveillance System (PMSS). Its latest report described 3410 pregnancy-related deaths between 2011 and 2015 (Petersen, 2019b). Approximately 5 percent were early-pregnancy maternal deaths due to ectopic gestation or abortive outcomes. The deadly obstetrical triad of hemorrhage, preeclampsia, and infection accounted for a third of all deaths (Fig. 1-2). Thromboembolism, cardiomyopathy, and other cardiovascular disease together accounted for another third. Other significant contributors were amniotic fluid embolism (5.5 percent) and cerebrovascular accidents (8.2 percent). Anesthesia-related deaths were at an all time low—only 0.4 percent. Similar

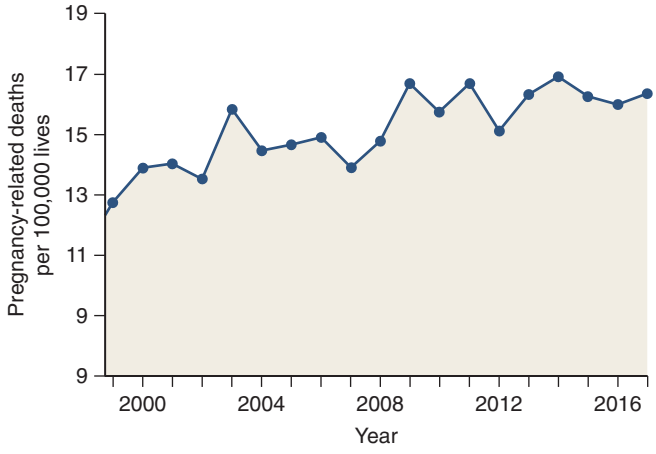


FIGURE 1-3 Trends in pregnancy-related maternal mortality in the United States from 1999–2017. (Data from Centers for Disease Control and Prevention, 2020c).

causes were reported for selected cohorts by MacDorman and associates (2017).

The pregnancy-related maternal mortality ratio was 17 deaths per 100,000 live births in 2017 (Fig. 1-3). The cause of this rise during the last 30 years may simply be that more women are dying, however, other factors explain this increase (Joseph, 2017). First, the number of pregnant women with severe chronic health conditions, which place women at higher risk, is greater (Centers for Disease Control and Prevention, 2020c). Second, the increased proportion of births to women older than 40 years contributes to higher mortality rates (Petersen, 2019b). Another is an artificial elevation caused by the International Statistical Classification of Diseases, 10th Revision (ICD-10), implemented in 1999. Additionally, improved reporting of maternal mortality contributes to the rise (MacDorman, 2016, 2017). Last, implementation of the pregnancy checkbox on the death certificate was associated with an increased identification of maternal deaths (Rossen, 2020). Thus, after accounting for the checkbox, predicted maternal mortality rates did not change significantly from 1999 through 2017.

Another consideration is the obvious disparity of higher mortality rates among black, Hispanic, and white women as shown in Figure 1-4. Racial disparities stem from health-care

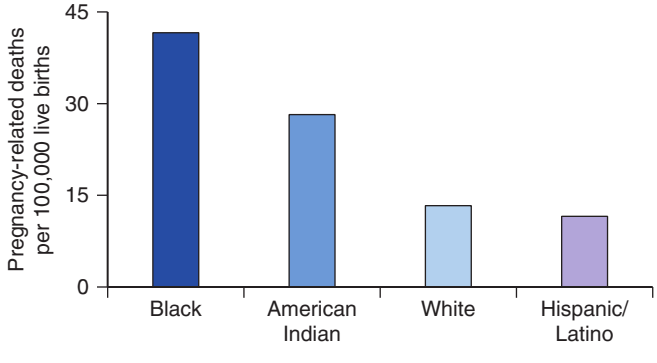


FIGURE 1-4 Pregnancy-related mortality ratio by race/ethnicity in the United States from 2014–2017. (Data from Centers for Disease Control and Prevention, 2020c).

availability, access, or use (Petersen, 2019a). The maternal mortality rate is also disparately high in rural compared with metropolitan areas (Maron, 2017).

Importantly, many maternal deaths are considered preventable. In one report, up to a third of pregnancy-related deaths in white women and up to half of those in black women were deemed preventable (Berg, 2005). One evaluation of an insured cohort reported that 28 percent of 98 maternal deaths were preventable (Clark, 2008). Thus, further efforts are imperative for obstetrics and described on page 6.

Severe Maternal Morbidity

This is defined as unintended events of labor and delivery resulting in serious short- or long-term consequences to a woman. Indicators serve as one measure to guide prevention (Table 1-2). The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine (2016) have provided lists of suggested screening topics for this purpose.

To study severe maternal morbidity (SMM), the CDC analyzed more than 50 million maternity records from 1998 to 2009 (Callaghan, 2012). They reported that 129 per 10,000 women had at least one indicator for SMM (Table 1-2). Thus, for every maternal death, approximately 200 women experience severe morbidity. As shown in Figure 1-5, SMM rates have increased during the past 15 years, and this trend is attributed to better documentation and a rise the blood transfusion rate. These numbers are greatest in smaller hospitals with <1000 deliveries annually (Hehir, 2017). Last, as with mortality rates,

TABLE 1-2. Severe Maternal Morbidity Indicators

Acute myocardial infarction
Acute renal failure
Adult respiratory distress syndrome
Amnionic fluid embolism
Cardiac arrest/ventricular fibrillation
Cardiac monitoring
Cardiac surgery
Conversion of cardiac rhythm
Disseminated intravascular coagulation
Eclampsia
Heart failure during procedure
Hysterectomy
Injuries of thorax, abdomen, and pelvis
Intracranial injuries
Puerperal cerebrovascular disorders
Pulmonary edema
Severe anesthesia complications
Sepsis
Shock
Sickle-cell crisis
Thrombotic embolism
Tracheostomy
Ventilation

Summarized from the Centers for Disease Control and Prevention, 2021.

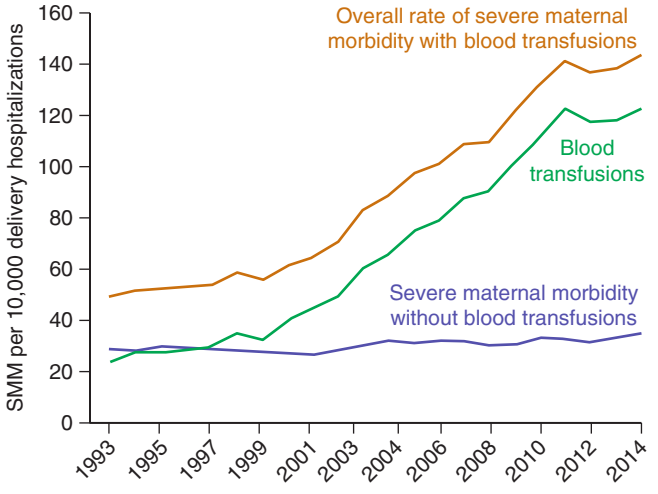


FIGURE 1-5 Rates of severe maternal morbidity (SMM) per 10,000 delivery hospitalizations. Women who received blood transfusions account for the greatest fraction of SMM. (Data from Centers for Disease Control and Prevention, 2021).

there are serious racial and ethnic disparities for SMM, and black women are disproportionately affected (Creanga, 2014).

Near Misses

Lowering medical error rates serves to diminish risks for maternal death and SMM. The terms *near misses* or *close calls* were introduced and defined as unplanned events caused by error that do not result in patient injury but have this potential (Institute for Safe Medication Practices, 2009). These are more common than injury events, but for obvious reasons, they are more difficult to identify and quantify. Systems designed to encourage reporting have been installed in various institutions and allow focused safety efforts (Clark, 2012; King, 2012; Shields, 2017). The World Health Organization (WHO) also implemented such a system. It has been validated in Brazil and accurately correlates with maternal death rates (Souza, 2012). A similar system in Britain is the *UK Obstetric Surveillance System—UKOSS* (Knight, 2005, 2008). In the United States, one is the *National Partnership for Maternal Safety* (D'Alton, 2016; Main, 2015).

TIMELY TOPICS IN OBSTETRICS

Various topics have been in the forefront since the 25th edition of this textbook. Here, we discuss several of these.

COVID-19 Pandemic

In early 2020, the severe acute respiratory syndrome (SARS)-CoV-2 virus spread rapidly around the globe, creating the greatest public health crisis since the influenza pandemic of 1918 (Chap. 67, p. 1187). As of early 2021, the disease caused by this virus and commonly known as COVID-19 is estimated to have infected more than 181 million people and caused nearly 4 million deaths (World Health Organization, 2021). Expectedly, the healthcare and political landscapes in the United States changed dramatically because of the pandemic.

Following the January 2020 declaration of a Global Health Emergency by the WHO, citywide lockdowns, state-mandated shelter-in-place orders, and public mask mandates were all implemented to help control early viral spread. Healthcare systems scrambled to acquire COVID-19 tests and personal protective equipment for staff. Wards dedicated solely to COVID-19 care opened in hospitals throughout the nation to handle substantial patient volume. Despite these measures, more than 500,000 individuals—including more than 3000 healthcare workers—died in the United States in 2020 from the infection.

Maternity wards were not spared, and traditional models of prenatal care were transformed. Namely, virtual care and drive-through prenatal care models aimed to reduce exposure risk to patients and staff (Holcomb, 2020; Turrentine, 2020). Asymptomatic or mild infections were common in pregnancy (Adhikari, 2020). Still, the effects of COVID-19 on pregnancy are not completely understood, and the effect of pregnancy on disease course is controversial. Management of severe COVID-19 infection in pregnancy requires interdisciplinary care and an understanding of pregnancy physiology and viral pathophysiology.

Preventive measures—including mRNA vaccines—have been shown to be safe and highly effective in disease prevention. However, this critical information was delayed following exclusion of pregnant individuals from initial clinical trials (Adhikari, 2021; Polack, 2020). In a report describing over 800,000 pregnancies, Chinn and colleagues (2021) found that 2.2 percent (18,715) of these women had COVID-19. When compared with women without such infections, these women had significantly increased adverse outcomes to include preterm birth, ICU admissions, intubations and mechanical ventilation, and maternal deaths. In 2021 the FDA approved COVID-19 vaccines for pregnant women.

Knowledge gained during the SARS-CoV-2 pandemic will undoubtedly shape healthcare moving forward (Cook, 2021). Indeed, a combined in-person plus audio-only virtual prenatal care model may most effectively provide services to vulnerable patients who lack internet access (Duryea, 2021).

Maternal Mortality—a Call to Arms

Almost 700 women in the United States die each year from pregnancy or its complications, and many deaths are deemed preventable. As a result, obstetricians and other stakeholders have united to address these tragedies (Chescheir, 2015). Because maternal deaths are inextricably linked to SMM indicators (see Table 1-2), several programs have been designed by national organization to avoid these events. Noted earlier, the Pregnancy Mortality Surveillance System (PMSS) collects national pregnancy-related death data to guide prevention efforts. Another, the Alliance for Innovation on Maternal Health (AIM) program, creates patient *safety bundles*, which describe evidence-based best practices for various obstetrical settings. The Joint Commission recommends that birthing centers establish protocols and implement simulation efforts (Barbieri, 2015). Moreover, national working groups target specific risks, such as thromboembolism (D'Alton, 2016).

In addition to pregnancy, the puerperium is a vulnerable period as well. One specific national effort is to establish

dedicated 1-year postpartum follow-up to ensure ongoing care. Important targets are medical disorders such as hypertension, diabetes, other cardiovascular diseases, and their consequences. To emphasize puerperal care, the concept of a "fourth trimester" has been introduced (Chap. 36, p. 634). Moreover, legislation—the MOMMA's Act—aims to expand Medicaid postpartum coverage from 60 days to 12 months (Bailey, 2021). As stated by Surgeon General Jerome Adams, "We must act now; our nation and our mothers deserve better." (Frieden, 2020).

Opioid Use Disorder

During 1999 to 2014, the national prevalence of opioid use disorder in pregnant women rose 333 percent from 1.5 to 6.5 cases per 1000 deliveries (Centers for Disease Control and Prevention, 2018). In addition to the complexities of maternal addiction, opioid use has led to an unprecedented increase in the incidence of the *neonatal opioid withdrawal syndrome* (Chap. 33, p. 605). To combat the associated adverse effects on women and their pregnancies, the American College of Obstetricians and Gynecologists (2019b) has stressed an active role by obstetricians. The College recommends universal screening by questionnaire, as well as care given to affected women by a multidisciplinary team. Therapeutic use of opioids is curtailed as best possible. Treatment of opioid use disorder with methadone or buprenorphine is challenging and discussed in Chapter 64 (p. 1150). Despite efforts, a significant decline in the prevalence of these disorders in gravidas is not in sight.

Advances in Prenatal Genetics

Several technologies help detect fetal genetic abnormalities. Since the last edition, noninvasive prenatal screening that uses cell-free DNA (cfDNA) has become commonplace in prenatal care (Zhang, 2019). Another promising technique is chromosomal microarray analysis (CMA) performed on samples of chorionic villi or amnionic fluid. These tests provide sophisticated information about gains and losses of DNA segments as small as 50 to 100 kilobases. However, although the yield with CMA is superior to that with fetal karyotyping, *most* birth defects occur in the setting of normal CMA and karyotype results.

As knowledge of the human genome has expanded, the role of specific DNA sequence abnormalities has gained attention. As an example, evaluation of fetal skeletal dysplasia may include panels of tests in which next-generation sequencing is used to identify mutations in specific genes. Whole exome sequencing (WES) analyzes all coding regions of DNA, which together account for 1.5 percent of the genome. In pregnancies with structural fetal abnormalities, and in which CMA and karyotype results are normal, WES has identified clinically significant abnormalities in approximately 10 percent of fetuses (Lord, 2019; Petrovski, 2019). In one series of fetuses with unexplained nonimmune hydrops, WES detected diagnostic genetic variants in nearly 30 percent (Sparks, 2020).

Although promising, WES technology at this time is not recommended for routine use in prenatal diagnosis (American College of Obstetricians and Gynecologists, 2020b). Limitations include high rates of genetic variants of uncertain significance, long turnaround times, and high costs. Comprehensive counseling is needed because WES may detect or suspect a finding that is unrelated but medically actionable. Genomic tests are reviewed in Chapter 16 (p. 324), and elements of counseling are discussed in Chapter 17 (p. 334).

Placenta Accreta Spectrum

Since our last edition, the cesarean delivery rate has been static and approximates 32 percent. However, rates of pregnancies complicated by placenta accreta spectrum (PAS) have grown substantially. An incidence as high as 1 case in 300 deliveries has been cited (American College of Obstetricians and Gynecologists, 2018). Sequelae of these dangerous syndromes are discussed in Chapter 43 (p. 765). To address these risks, specialized accreta surgical teams at tertiary care centers and greater antepartum transfer to these centers are both on the rise. As one prevention, national efforts have worked to avoid the *primary* cesarean delivery. However, despite these efforts, PAS will likely continue as a significant risk for SMM.

Progestogens to Prevent Preterm Birth

Progesterone derivatives to forestall preterm birth have been studied for decades. One—intramuscular 17-alpha-hydroxyprogesterone caproate (17-OHPC)—was approved by the U.S. Food and Drug Administration (FDA) under the accelerated approval process and contingent on demonstration of efficacy in a second trial. The drug is marketed as *Makena*, and subsequent, observational studies, described in Chapter 45 (p. 795), have led to questions of its efficacy (Nelson, 2021).

In 2019, results of the confirmatory trial of *Makena* efficacy—the PROLONG trial—failed to show its benefits compared with placebo for prevention of birth before 35 weeks (Blackwell, 2020). Later in 2019, an FDA Advisory Committee voted 9 to 7 to withdraw interim accelerated approval. Analyses by the committee included cross-study comparisons and subgroup analyses that did not show 17-OHPC benefits (Fig. 45-6, p. 796). In late 2020, the FDA Center for Drug Evaluation and Research (CDER) recommended drug withdrawal from the market.

Subsequently, obstetricians became polarized regarding "off label" use of the drug because it *appears safe* (Chang, 2020; Greene, 2020; Sibai, 2020). Despite findings from the PROLONG trial and the FDA's CDER, both the American College of Obstetricians and Gynecologists (2021) and the Society for Maternal-Fetal Medicine (2020) continued to endorse 17-OHPC use. This, however, is with the proviso that "uncertainty regarding benefit" be shared with the patient during decision-making. Last, the EPPPIC Group (2021) performed a metaanalysis of randomized trials evaluating progestogens for preterm birth prevention. Although not statistically significant, they concluded progestogens, which include 17-OHPC, reduced births at less than 34 weeks. The FDA's CDER (2021) continues to recommend withdrawal of 17-OHPC from the market. At this time, however, thousands of women continue to receive 17-OHPC despite its questionable efficacy.

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