

Pregnancy at Age 35 Years or Older

Committee on Clinical Consensus—Obstetrics | Society for Maternal-Fetal Medicine

This Obstetric Care Consensus was developed jointly by the American College of Obstetricians and Gynecologists' Committee on Clinical Consensus—Obstetrics in collaboration with Angela Gantt, MD, MPH, and the Society for Maternal-Fetal Medicine in collaboration with Torri D. Metz, MD, MS, and with the assistance of Jeffrey A. Kuller, MD, and Judette M. Louis, MD, MPH, on behalf of the Society for Maternal-Fetal Medicine, and Alison G. Cahill, MD, MSCI, and Mark A. Turrentine, MD, on behalf of the American College of Obstetricians and Gynecologists.

SUMMARY

Centers for Disease Control and Prevention data from 2020 demonstrate the continued upward trend in the mean age of pregnant individuals in the United States. Observational studies demonstrate that pregnancy in older individuals is associated with increased risks of adverse pregnancy outcomes—for both the pregnant patient and the fetus—that might differ from those in a younger pregnant population, even in healthy individuals with no other comorbidities. There are several studies that suggest advancing age at the time of pregnancy is associated with greater disparities in severe maternal morbidity and mortality. This document seeks to provide evidence-based clinical recommendations for minimizing adverse outcomes associated with pregnancy with anticipated delivery at an advanced maternal age. The importance and benefits of accessible health care from prepregnancy through postpartum care for all pregnant individuals cannot be overstated. However, this document focuses on and addresses the unique differences in pregnancy-related care for women and all those seeking obstetric care with anticipated delivery at age 35 years or older within the framework of routine pregnancy care. This Obstetric Care Consensus document was developed using an a priori protocol in conjunction with the authors listed above.

BACKGROUND

Purpose

Centers for Disease Control and Prevention (CDC) data from 2020 demonstrate the continued upward trend in the mean age of pregnant individuals in the United States. Nearly 19% of all pregnancies and 11% of all first pregnancies in the United States were in women aged 35 years and older (1). The mean age of women having their first birth in 2020 was 27.1 years compared with 21.4 years in 1970 (1, 2). This trend is not unique to the United States. Globally there has been a

trend toward initiating pregnancy later, with most countries noting an increasing age at first pregnancy (3, 4), thereby supporting the importance of addressing the risks associated with pregnancy later in life. Observational studies demonstrate that pregnancy in older individuals is associated with increased risks of adverse pregnancy outcomes—for both the pregnant patient and the fetus—that might differ from a younger pregnant population, even in healthy individuals with no other comorbidities.

This document seeks to provide evidence-based clinical recommendations for minimizing adverse outcomes

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associated with pregnancy with anticipated delivery at an advanced maternal age. To align with literature that has historically used 35 years as the threshold to determine advanced maternal age (see Definition), this document will focus on pregnancy with anticipated delivery at age 35 years or older. However, it should be noted that this is an arbitrary threshold and, as discussed later, some risks associated with older age may not influence outcomes until later ages (ie, 40 years and older). The importance and benefits of accessible health care from prepregnancy through postpartum care for all pregnant individuals cannot be overstated. However, this document focuses on and addresses the unique differences in pregnancy-related care for women and all those seeking obstetric care with anticipated delivery at age 35 years or older within the framework of routine pregnancy care.

Definition

Historically, *advanced maternal age* has been defined as women who are 35 years or older at estimated date of delivery. This age cutoff was selected based on evidence of declining fertility and concern surrounding increasing risks for genetic abnormalities identified in the offspring of pregnant women older than age 35 years (5). More recent studies, such as the FASTER (First- and Second-Trimester Evaluation of Risk) trial and the NBDPS (National Birth Defects Prevention Study), have demonstrated a significant association between chromosomal abnormalities and possible congenital malformations in children born to women aged 35 years or older. However, the association appears to be on a continuum such that risks increase with increasing age at the time of the pregnancy (6, 7). Likewise, studies evaluating the effect of chronic medical conditions such as diabetes, hypertension, and obesity, which may exacerbate pregnancy-related morbidity, appear to demonstrate an increasing risk with increasing age at the time of pregnancy (8–14). Therefore, recognizing the possibility of progressive age-related risk, recent studies have commonly divided the age of individuals pregnant at age 35 years and older into 5-year increments: 35–39 years, 40–44 years, 45–49 years, and 50 years and older, which better stratifies the possible pregnancy risks associated with advancing age. To promote use of objective and more precise terminology, this document will use phrasing such as “pregnancy with anticipated delivery at [a specific age or age range] or older.”

Health Disparities

There are several studies that suggest advancing age at the time of pregnancy is associated with greater disparities in severe maternal morbidity and mortality (15–18). This underscores the need for clinical guidance to directly address these disparities and to promote equitable care. This is further addressed in the Methods, Consensus Recommendations, and Discussion sections.

Use Of Language

The American College of Obstetricians and Gynecologists (ACOG) and the Society for Maternal-Fetal Medicine (SMFM) recognize and support the gender diversity of all patients who seek obstetric and gynecologic care. In original portions of this document, the authors seek to use gender-inclusive language or gender-neutral language. When describing research findings, this document uses gender terminology reported by investigators. To review ACOG’s policy on inclusive language, see Inclusive Language at <https://www.acog.org/clinical-information/policy-and-position-statements/statements-of-policy/2022/inclusive-language>.

METHODS

This Obstetric Care Consensus document was developed using an a priori protocol in conjunction with the authors listed above. The a priori protocol was modeled after the Clinical Consensus methodology, a full description of which is published separately (19). The description below is specific to this Obstetric Care Consensus document.

Literature Search

A literature search was performed from 2000 to November 2021 for clinical questions as noted in the outline, which included considerations for the prepregnancy, antepartum, intrapartum, and postpartum periods. ACOG medical librarians searched Cochrane Library, Cochrane Collaboration Registry of Controlled Trials, EMBASE, PubMed, and MEDLINE for human-only studies written in English. MeSH terms and keywords can be found in Appendix 1 (available online at <http://links.lww.com/AOG/C770>). Search terms for racial and ethnic disparities in maternal and fetal outcomes for pregnancies that occurred at age 35 years or older were incorporated into the literature review, and recommendations were drafted with the intent to promote health equity and reduce these disparities. A bridge literature search was completed in November 2021. Any updated literature was incorporated into the text and recommendations, as appropriate.

Study Selection

Qualifying studies passed both title and abstract screen and full-text screen and met the following inclusion criteria: conducted in countries ranked very high on the United Nations Human Development Index (20), included female participants, and included all study designs. Studies were included in the evidence map if they passed full-text screen by the authors and were cited in the article to support a recommendation (Appendix 2, available online at <http://links.lww.com/AOG/C771>).



Summary of Consensus Recommendations

Antepartum Care

We suggest that pregnancy with anticipated delivery at age 35 years or older be recognized as a risk factor for adverse maternal, fetal, and neonatal outcomes when counseling patients and determining management plans. Nuanced counseling will be dependent on specific age and comorbidities. (GRADE 2C. Weak recommendation, low-quality evidence.)

We recommend daily low-dose aspirin for the reduction of preeclampsia for pregnant individuals aged 35 or older in the setting of at least one other moderate risk factor. (GRADE 1B. Strong recommendation, moderate-quality evidence.)

Given increased rates of multiple gestations for pregnant individuals with anticipated delivery at age 35 years or older, we suggest a first-trimester ultrasonogram. (GRADE 2C. Weak recommendation, low-quality evidence.)

We recommend that prenatal genetic screening (serum screening with or without nuchal translucency ultrasonography or cell-free DNA screening) and diagnostic testing (chorionic villus sampling or amniocentesis) options be discussed and offered to all pregnant individuals regardless of age or risk of chromosomal abnormality. After review and discussion, every patient has the right to pursue or decline prenatal genetic screening and diagnostic testing. (GRADE 1A. Strong recommendation, high-quality evidence.)

We suggest a detailed fetal anatomic ultrasonogram for pregnant individuals with anticipated delivery at age 35 years or older given the increased risk of aneuploidy and potential increased risk of congenital anomalies in this population. (GRADE 2C. Weak recommendation, low-quality evidence.)

Due to increased risk of both large-for-gestational-age and small-for-gestational-age neonates, we suggest an ultrasonogram for growth assessment in the third trimester for pregnant individuals with anticipated delivery at age 40 years or older. (GRADE 2C. Weak recommendation, low-quality evidence.)

We suggest offering antenatal fetal surveillance for pregnant individuals with anticipated delivery at age 40 years or older given the increased risk of stillbirth. (GRADE 2B. Weak recommendation, moderate-quality evidence.)

We recommend proceeding with delivery in well-dated pregnancies at 39 0/7–39 6/7 weeks of gestation for individuals with anticipated delivery at age 40 years or older due to increasing rates of neonatal morbidity and stillbirth beyond this gestational age. (GRADE 1B. Weak recommendation, moderate-quality evidence.)

We suggest counseling that vaginal delivery is safe and appropriate if there are no other maternal or fetal indications for cesarean delivery. Counseling should include a discussion of the risks of cesarean delivery, the patient's comorbidities, and the patient's preferences and goals. Advancing patient age alone is not an indication for cesarean delivery. (GRADE 2B. Strong recommendation, moderate-quality evidence.)

Health Equity

We recommend that obstetrician–gynecologists and other obstetric care professionals be aware of the disproportionate rates of most adverse maternal and perinatal outcomes in Black and American Indian and Alaska Native pregnant individuals aged 35 years and older. We recommend that they understand ways racism contributes to perpetuating these outcomes. (Grade 1B. Strong recommendation, moderate-quality evidence.)

Consensus Voting and Recommendation Development

At a meeting of the Committee on Clinical Consensus–Obstetrics, a quorum of two thirds of eligible voting members was met, and the Committee held a formal vote for each proposed recommendation. Eligible voting members included representatives from both ACOG and SMFM. All recommendation statements met or exceeded the 75% approval threshold required for consensus.

CONSENSUS RECOMMENDATIONS AND DISCUSSION

Antepartum Care

We suggest that pregnancy with anticipated delivery at age 35 years or older be recognized as a risk factor for adverse maternal, fetal, and neonatal outcomes when counseling patients and determining management plans. Nuanced

counseling will be dependent on the pregnant individual's specific age and comorbidities. (GRADE 2C)

There are numerous observational and cohort studies evaluating the influence of age at the time of delivery on outcomes for pregnant individuals and their neonates. Overall, when compared with those of younger ages, women aged 35 years and older are at higher risk for complications such as gestational diabetes, preeclampsia, labor dystocia, and cesarean delivery (8, 9, 21, 22). Older women are also at risk of delivering a neonate who is born preterm (spontaneous or iatrogenic), requires neonatal intensive care unit admission, and has low birth weight (10, 23, 24). More extensive evaluation of the data demonstrates that risks for adverse maternal and neonatal outcomes are on a continuum, with risks increasing progressively with advancing age, particularly older than 40 years (8, 9, 11, 12). Thus, pregnancy counseling and



pregnancy care recommendations can be tailored better toward the individual if specific patient age is considered.

A retrospective cohort analysis using a large U.S. population database of nearly 34 million deliveries characterized pregnancy-related morbidity risk by age (25). Overall, women older than age 35 years were at increased risk of pregnancy-related morbidity compared with those aged 25–29 years. When evaluated in age-based increments (35–39 years, 40–44 years, 45–54 years), the risk increased with increasing age (relative risk [RR] 1.36, 95% CI 1.33–1.39; RR 1.83, 95% CI 1.77–1.89; and RR 3.33, 95% CI 3.03–3.66, respectively) (25). In addition, the investigators evaluated obstetric complications such as preeclampsia, cesarean delivery, postpartum hemorrhage, and gestational diabetes and found that advancing maternal age at the time of pregnancy was an independent risk factor for all of these obstetric outcomes. These risks increased incrementally such that pregnant women in the 45–54-year age group were at the highest risk (25).

Chronic medical disorders such as obesity, hypertension, and diabetes are more prevalent in pregnant individuals aged 35 years and older. Several large population-based studies have demonstrated small but statistically significant increases in body mass index (BMI, calculated as weight in kilograms divided by height in meters squared) with advancing maternal age (26–28). Studies have shown that pregnant women aged 35 years and older are two to four times more likely to have chronic hypertension and nearly twice as likely to have type 2 diabetes mellitus as pregnant women aged 25–29 years (26, 29). Similarly, women older than age 40 years had two to three times the risk of gestational diabetes compared with younger individuals (12, 29). Even after controlling for baseline characteristics of prepregnancy hypertension and diabetes, older women remained at significant risk of developing preeclampsia and gestational diabetes.

A large meta-analysis that combined 10 cohort studies of more than 1,000 patients per study comparing pregnant women aged 35 years and older with pregnant women aged 20–34 years confirmed the pregnancy risks associated with advancing age of the pregnant woman (30). The study controlled for prepregnancy conditions such as obesity, diabetes, and hypertension and analyzed data in 5-year age increments. Although not as pronounced as prior cohort studies, age alone was a risk factor for obesity, gestational diabetes, and hypertension, and women aged 35 years and older were more likely to undergo labor induction or cesarean delivery. Similarly, there was a small increased risk to neonates born to women aged 35 years and older, including low birth weight, preterm birth, low 5-minute Apgar score, and neonatal intensive care unit admission. The risk for each

of these outcomes increased with increasing age increments of the pregnant woman (30).

We recommend daily low-dose aspirin for the reduction of preeclampsia for pregnant individuals aged 35 years or older in the setting of at least one other moderate risk factor. (GRADE 1B)

Pregnant women aged 35 years and older have been found to be at increased risk for preeclampsia in several observational and cohort studies (3, 8–10, 12, 13, 21, 31). The risk appears linear, with increasing age at the time of pregnancy leading to increased risk for hypertensive disorders of pregnancy. One large meta-analysis evaluating the maternal and neonatal outcomes in women aged 35 years and older found that the risk for preeclampsia progressively increased with increasing age; however, the difference was statistically significant only in women aged 40 years and older (30). The increased risk remained even when controlling for pre-existing conditions independently associated with preeclampsia such as hypertension and diabetes.

A retrospective cohort study evaluating maternal outcomes of older-aged pregnant women used age 35–39 years as the referent group for comparison with pregnant women aged 40 years and older (11). Even when using the older referent group, there was an increase in preeclampsia with advancing age older than 40 years in the pregnant women. The RR for preeclampsia increased by 30% for women aged 40–44 years (RR 1.32, 95% CI 1.25–1.4) and more than doubled for pregnant women aged 45–59 years (RR 2.21, 95% CI 1.89–2.58) (11). Consistent with other studies, adverse outcomes increased within each age group compared with the referent group.

In their systematic review, the U.S. Preventive Services Task Force (USPSTF) found evidence of a reduction in risk for preeclampsia (pooled RR 0.85, 95% CI 0.75–0.95; 16 studies; I²=0%), preterm birth (pooled RR 0.80, 95% CI 0.67–0.95; 13 studies; I²=49%), small for gestational age or fetal growth restriction (RR 0.82, 95% CI 0.68–0.99; 16 studies; I²=41.0%), and perinatal mortality (pooled RR 0.79, 95% CI 0.66–0.96; 11 studies; I²=0%) in individuals at increased risk for preeclampsia who took low-dose aspirin prophylaxis (32).

ACOG, SMFM, and the USPSTF recommend initiating low-dose aspirin therapy (81 mg/day), ideally between 12 and 16 weeks of gestation and continued daily until delivery in individuals at high risk for preeclampsia. The USPSTF determined that age 35 years and older is a moderate risk factor for developing preeclampsia. Therefore, individuals with pregnancies at age 35 years or older who have at least one high risk factor or at least one additional moderate risk factor qualify for low-dose



aspirin therapy (32–34). Other moderate risk factors include nulliparity, obesity (ie, BMI higher than 30), family history of preeclampsia (ie, mother or sister), Black race (as a proxy for underlying racism), lower income, personal history factors (eg, low birth weight or small for gestational age, previous adverse pregnancy outcome, longer than 19-year pregnancy interval), and in vitro fertilization (32, 34). High risk factors include history of preeclampsia, especially when accompanied by an adverse outcome; multifetal gestation; chronic hypertension; pregestational type 1 or 2 diabetes; kidney disease; autoimmune disease (ie, systemic lupus erythematosus, antiphospholipid syndrome); and combinations of multiple moderate-risk factors (32, 34).

Additionally, low-dose aspirin can also be considered if the patient has only one or more of the following moderate risk factors, regardless of their age: Black race (as a proxy for underlying racism) or lower income. The underlying risk to health is racism and not race. However, there are not yet adequate tools for measuring the known effect of racism on health. Therefore, in this document, Black race serves as a proxy for underlying racism. These factors are associated with increased risk due to environmental, social, structural, and historical inequities shaping health exposures, access to health care, and the unequal distribution of resources, not biological propensities (32, 34).

Given increased rates of multiple gestations for pregnant individuals with anticipated delivery at age 35 years or older, we suggest a first-trimester ultrasonogram. (GRADE 2C)

The incidence of multifetal gestation increases with advancing age at the time of pregnancy (35). Analysis of National Vital Statistics data from 2018 demonstrates an increased rate of twin births with increasing age of the pregnant woman, from 17.1 per 1,000 births in individuals younger than age 20 years to a high of 51.1 per 1,000 births in individuals aged 40–54 years (35). Women aged 30–39 years have a rate of twinning double that of individuals younger than age 20 years, and those who are older than 40 years have a rate of twinning that is triple that of women younger than age 20 years (35). Some of the increased risk for multiple gestation is likely due to increased use of ovulation induction and assisted reproductive technology; however, the proportion of twin pregnancies that result from assisted reproductive technology is not delineated in vital statistics data. A retrospective cohort study from Belgium (N=41,618) similarly demonstrates increasing rates of twin gestation with increasing age of the pregnant woman (2.8% at 25–34 years, 4.5% at 35–39 years, 5.5% at 40–44 years, and 10.9% at 45 years and older) (36).

There is an increased risk for nearly all pregnancy-related morbidities for pregnant individuals and neonates in multifetal gestations. Identification of a multifetal gestation, therefore, influences pregnancy management. The optimal time for determination of the number of fetuses is the first trimester and chronicity in the late first or early second trimester. ACOG's Practice Bulletin on *Multifetal Gestations: Twin, Triplet, and Higher-Order Multifetal Pregnancies* provides an in-depth review of multifetal pregnancy, including the associated risks, complications, and management (37).

We recommend that prenatal genetic screening (serum screening with or without nuchal translucency ultrasonography or cell-free DNA screening) and diagnostic testing (chorionic villus sampling or amniocentesis) options be discussed and offered to all pregnant individuals regardless of age or risk of chromosomal abnormality. After review and discussion, every patient has the right to pursue or decline prenatal genetic screening and diagnostic testing. (GRADE 1A)

From birth to menopause, there is a natural and progressive decrease in oocytes and oocyte quality. This gradual decline accelerates during the fourth decade of life, likely due to changes in a myriad of hormone levels regulating the ovaries. Thus, an individual's fertility rate will decline with increasing age, regardless of environment, exogenous hormone usage, or sexual activity. There is increasing risk for aneuploidy (Table 1) and spontaneous abortion with declining fertility. The mechanism is likely related to increased chromosomal nondisjunction in the final stages of meiosis before ovulation. Several studies evaluating in vitro fertilization success rates have demonstrated that, despite normal-appearing embryos, the frequency of spontaneous abortion or aneuploidy increases based on the maternal age. In comparison, utilization of young donor eggs yielded similar live-birth rates regardless of maternal age at the time of pregnancy (38).

Not all chromosome abnormalities increase as maternal age increases. Sex chromosome trisomies, specifically 47, XXX and 47, XXY increase with increasing maternal age. In contrast, sex chromosome monosomy (ie, 45, X) does not appear to be affected by maternal age (39, 40). Likewise, copy number variants are independent of maternal age at pregnancy (41). Paternal age may affect chromosomal abnormalities but is beyond the scope of this document.

Thus, although aneuploidy is not exclusive to individuals older than age 35 years, pregnant individuals should be aware that aneuploidy risk increases with age. Clinicians should be prepared to discuss options and availability of



Table 1. Chromosomal Abnormalities in Second-Trimester Pregnancies Based on Maternal Age at Term*†

	Trisomy 21	Trisomy 18	Trisomy 13	Sex Chromosome Aneuploidy (XXX, XY, XYY, 45, X)	Microarray or Rare Chromosomal Abnormality	All Chromosomal Abnormalities
Age 20	8 per 10,000 1 in 1,250	2 per 10,000 1 in 5,000	1 per 10,000 1 in 10,000	34 per 10,000 1 in 294	37 per 10,000 1 in 270	82 per 10,000 1 in 122
Age 25	10 per 10,000 1 in 1,000	2 per 10,000 1 in 5,000	1 per 10,000 1 in 10,000	34 per 10,000 1 in 294	37 per 10,000 1 in 270	84 per 10,000 1 in 119
Age 30	14 per 10,000 1 in 714	4 per 10,000 1 in 2,500	2 per 10,000 1 in 5,000	34 per 10,000 1 in 294	37 per 10,000 1 in 270	91 per 10,000 1 in 110
Age 35	34 per 10,000 1 in 294	9 per 10,000 1 in 1,111	4 per 10,000 1 in 2,500	35 per 10,000 1 in 285	37 per 10,000 1 in 270	119 per 10,000 1 in 84
Age 40	116 per 10,000 1 in 86	30 per 10,000 1 in 333	14 per 10,000 1 in 714	51 per 10,000 1 in 196	37 per 10,000 1 in 270	248 per 10,000 1 in 40

*Not all chromosomal abnormalities increase as maternal age increases.

†Copy number variants are independent of maternal age at pregnancy.

Data from:

1. Srebniak MI, Joosten M, Knäpen MF, Arends LR, Polak M, van Veen S, et al. Frequency of submicroscopic chromosomal aberrations in pregnancies without increased risk for structural chromosomal aberrations: systematic review and meta-analysis. *Ultrasound Obstet Gynecol* 2018;51:445–52. doi: 10.1002/uog.17533
2. Hook EB. Rates of chromosome abnormalities at different maternal ages. *Obstet Gynecol* 1981;58:282–5.
3. Gravholt CH, Juul S, Naeraa RW, Hansen J. Prenatal and postnatal prevalence of Turner's syndrome: a registry study. *BMJ* 1996;312:16–21. doi: 10.1136/bmj.312.7022.16
4. Snijders RJ, Sebire NJ, Nicolaides KH. Maternal age and gestational age-specific risk for chromosomal defects. *Fetal Diagn Ther* 1995;10:356–67. doi: 10.1159/000264259
5. Snijders RJ, Sundberg K, Holzgreve W, Henry G, Nicolaides KH. Maternal age- and gestation-specific risk for trisomy 21. *Ultrasound Obstet Gynecol* 1999;13:167–70. doi: 10.1046/j.1469-0705.1999.13030167.x
6. Forabosco A, Percesepe A, Santucci S. Incidence of non-age-dependent chromosomal abnormalities: a population-based study on 88965 amniocenteses. *Eur J Hum Genet* 2009;17:897–903. doi: 10.1038/ejhg.2008.265
7. Crider KS, Olney RS, Cragan JD. Trisomies 13 and 18: population prevalences, characteristics, and prenatal diagnosis, metropolitan Atlanta, 1994–2003. *Am J Med Genet A* 2008;146A:820–6. doi: 10.1002/ajmg.a.32200
8. Irving C, Richmond S, Wren C, Longster C, Embleton ND. Changes in fetal prevalence and outcome for trisomies 13 and 18: a population-based study over 23 years. *J Matern Fetal Neonatal Med* 2011;24:137–41. doi: 10.3109/14767051003758879

Modified from Screening for fetal chromosomal abnormalities. ACOG Practice Bulletin No. 226. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2020;136:e48–69. doi: 10.1097/AOG.0000000000004084

prenatal tests, both screening and diagnostic. If available, a genetic counselor may offer additional information regarding aneuploidy risk and options for carrier screening (41). Regardless, the decision to test and the decision to pursue a specific test should be shared between the clinician and patient based on patient values and test availability, regardless of cost.

We suggest a detailed fetal anatomic ultrasound examination for pregnant individuals with anticipated delivery at age 35 years or older given the increased risk of

aneuploidy and potential increased risk of congenital anomalies in this population. (GRADE 2C)

Early studies suggest that risk of a major congenital anomaly affecting a fetus, such as congenital cardiac disease and cardiac malformations, neural tube defects, renal anomalies, extremity anomalies, and diaphragmatic hernias, increases with pregnancy at age older than 35 years (42–45). More recent studies have conflicting results and challenge the assumption that age of the pregnant woman alone is a risk factor for a major



congenital anomaly (28, 46–48). The largest of these was a retrospective cohort study evaluating congenital anomalies in singleton pregnancies without aneuploidy (47). All patients underwent a second-trimester detailed fetal anatomic ultrasound examination. Detailed ultrasound examinations involve visualization of additional structures that would not typically be assessed in a basic ultrasound examination (49). These investigators found lower rates of congenital fetal anomalies in pregnant women aged 35 years and older compared with younger individuals (adjusted odds ratio [aOR] 0.59, 95% CI 0.52–0.66). The anomalies that contributed most to the observed reduction were neural tube defects, renal anomalies, and abdominal wall defects. The frequency of congenital cardiac anomalies was similar across both age groups. An analysis comparing individuals aged 40 years and older with all other individuals demonstrated a similar decreased risk for congenital anomalies with older age. Perhaps improved prenatal diagnostic tests such as first-trimester screening and increased access to invasive testing more accurately identified a euploid pool for analysis. In addition, the authors hypothesize an “all or nothing” phenomenon in which fewer congenital malformations are noted during pregnancy because the increased rate of spontaneous abortion associated with advancing age at the time of pregnancy reduces the number of ongoing anomalous pregnancies (47).

Using smaller data sets, other recent studies have not demonstrated lower rates of non-chromosomal-related fetal structural anomalies in pregnant individuals older than age 35 years. These studies have demonstrated similar rates of such anomalies across all age groups of pregnant women (28, 46, 48). Pregnant individuals aged 35 years and older were at no greater risk than those in the younger referent groups.

In general, a detailed fetal anatomic ultrasound examination (Current Procedural Terminology code 76811) is recommended by ACOG, SMFM, and the American Institute of Ultrasound Medicine in the setting of maternal age older than 35 years (49). However, it is worth noting that the increased risk in congenital malformations at the time of anatomic survey may be less than historically observed based on increased availability of aneuploidy screening, higher rates of miscarriage, and early ultrasonogram capability. Given the known increased risk of aneuploidy, a detailed fetal anatomic ultrasound examination is suggested, particularly for individuals without aneuploidy screening or testing.

Due to increased risk of both large-for-gestational-age and small-for-gestational-age neonates, we suggest an ultrasonogram for growth assessment in the third trimester for

pregnant individuals with anticipated delivery at age 40 years or older. (GRADE 2C)

Both large-for-gestational-age and small-for-gestational-age occurs in neonates at higher frequencies as maternal age increases. In a prospective cohort study of 11,328 deliveries in Spain, rates of macrosomia increased progressively, with 12% in women younger than age 35 years, 12.6% in women aged 35–39 years, and 15.4% in women aged 40 years or older (50). Similarly, small for gestational age increased across the same age categories (14.0%, 15%, and 17.4%, respectively). The association between abnormal birth weight and age 40 years or older remained significant after adjustment for tobacco use, gestational diabetes, and hypertension, with odds ratios (ORs) of 1.29 (95% CI 1.04–1.59) for small for gestational age and 1.27 (95% CI 1.01–1.59) for large for gestational age (50).

In a retrospective cohort study (N=41,618), rates of birth weight less than 2,500 g increased with increasing maternal age, classified as 25–34 years (6.7%), 35–39 years (6.9%), 40–44 years (10.0%), and 45 years and older (16.4%). Some of the observed risk is likely secondary to an increased rate of preterm birth. The authors also found an increased frequency of birth weight higher than 4,500 g with increasing age, classified as 25–34 years (0.72%), 35–39 years (1.14%), and 40–44 years (1.17%), with a slight decrease in prevalence at 45 years and older (0.95%) (36). Similarly, a retrospective cohort study using National Vital Statistics Data demonstrated an increase in small for gestational age (birth weight less than 5%ile) in women older than age 40 years (51).

Although the above data demonstrate increased risk of growth abnormalities in fetuses of women older than age 40 years, there is insufficient evidence to recommend ultrasonography for growth assessment in the third trimester for individuals aged 35–39 years in the absence of other risk factors for large-for-gestational-age or small-for-gestational-age neonates.

Although growth ultrasonograms may already be performed in clinical practices given the associated birth weight abnormalities, there are no data to guide recommendations regarding timing or frequency of ultrasound assessments in individuals aged 40 years and older. In many cases, ultrasonogram timing and frequency will be dictated based on other comorbidities or pregnancy complications.

We suggest offering antenatal fetal surveillance for pregnant individuals with anticipated



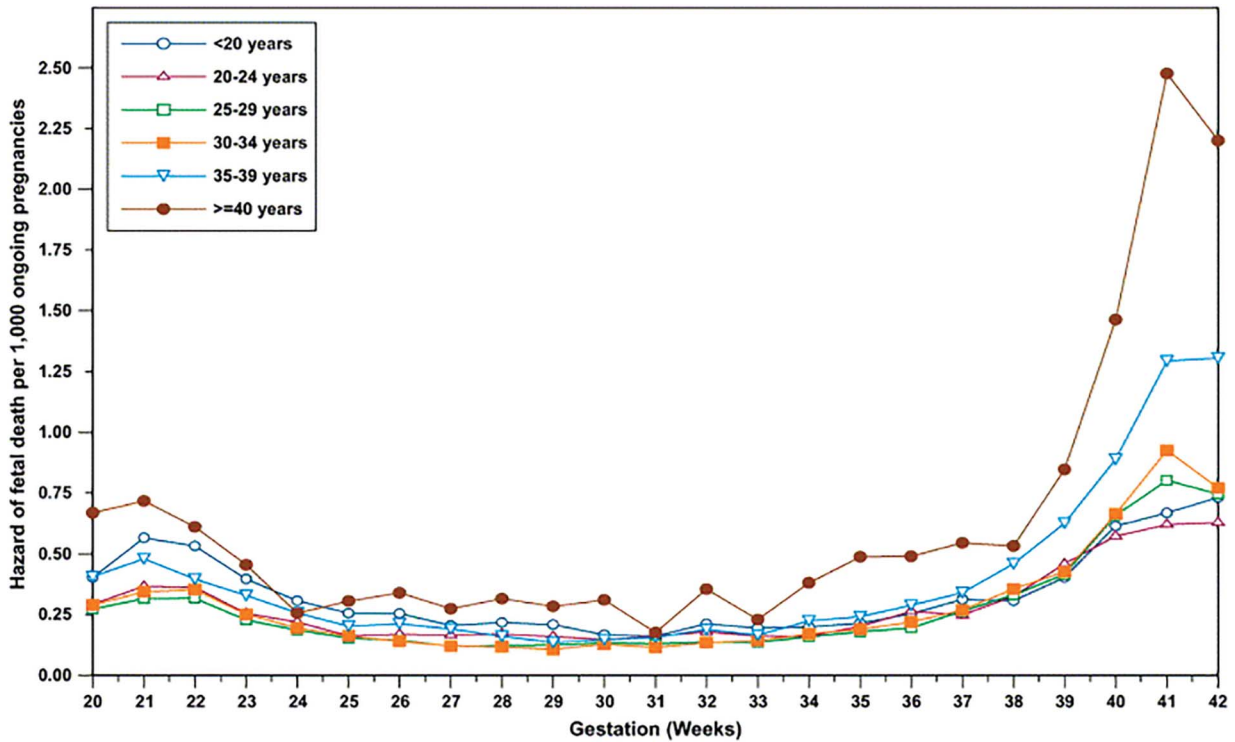


Figure 1. Risk of Fetal Death per 1,000 Ongoing Pregnancies by Week of Gestation. Reprinted from Reddy UM, Ko CW, Willinger M. Maternal age and the risk of stillbirth throughout pregnancy in the United States. *Am J Obstet Gynecol* 2006;195:764–70. doi: 10.1016/j.ajog.2006.06.019. Copyright 2006, with permission from Elsevier.

delivery at age 40 years or older given the increased risk of stillbirth. (GRADE 2B)

There is increased stillbirth risk associated with advancing age at the time of pregnancy. In 2013, the stillbirth rate in the United States among all pregnant individuals was nearly 6.0 per 1,000 pregnancies that extended beyond 20 weeks of gestation. Rates were highest in older women: 10.1 stillbirths per 1,000 births for women aged 40–44 years and 13.8 per 1,000 births in women older than age 45 years (52). Notably, the association between stillbirth and age of the pregnant woman persisted with age 35 years and older, even when controlling for confounding risk factors such as hypertension and diabetes.

Using the National Center for Health Statistics data set of nearly 5.5 million singleton pregnancies without congenital anomalies, one study sought to determine risk of fetal death for ongoing pregnancies by gestational week and patient age (53). In this data set, the risk of stillbirth increased with increasing gestational age for all ongoing pregnancies beyond 37 weeks of gestation; however, there is a distinct increased risk associated with age at the time of pregnancy (53) (Fig. 1). The risk of stillbirth at 37 to 41 weeks of gestation was 1 in 382 ongoing pregnancies for women aged 35–39 years

and 1 in 267 ongoing pregnancies for women 40 years and older (53). The cumulative risk for stillbirth per 1,000 pregnancies through 41 weeks of gestation increased for older women, with a risk of 6.2 in those younger than aged 35 years, 7.9 in those aged 35–39 years, and 12.8 in those aged 40 years and older. By 41 weeks of gestation, the RR for stillbirth was threefold higher for those aged 40 years and older compared with those younger than age 35 years.

Another study sought to determine the stillbirth rate by gestational age and age ranges of pregnant women using the CDC database of more than 6.3 million singleton pregnancies (54). After excluding pregnancies complicated by congenital anomalies and maternal medical comorbidities, the stillbirth rate was calculated by age at delivery in 5-year increments. Age was an independent risk factor for stillbirth, with a rapid increase in stillbirth rate occurring between 37 and 41 weeks of gestation. The authors created a cumulative risk model and found that the risk of stillbirth in women aged 40–44 years at 39 weeks of gestation was comparable with the risk at 42 weeks in women aged 25–29 years (54).

A study analyzing birth data from Scotland evaluated the association between age at the time of pregnancy and unexplained stillbirth from 1997–2003,



using a referent group of women aged 20–24 years (55). Those who were aged 35–39 years had increased odds of stillbirth for any pregnancy (aOR 1.54, 95% CI 1.21–2.19) and for nulliparous pregnancies (aOR 1.81, 95% CI 1.10–2.98). Those who were aged 40 years or older had increased odds of stillbirth for any pregnancy (aOR 2.24, 95% CI 1.45–3.83). The result was no longer statistically significant when the population was narrowed only to nulliparous pregnant patients older than age 40 years (aOR 2.03, 95% CI 0.63–6.52), likely secondary to a smaller sample size in this subset (55).

A retrospective cohort study of all women with singleton pregnancies at a single institution from 1989–2004 (N=126,402) found that age 40 years and older was associated with stillbirth at 28–31 weeks of gestation (aOR 2.93, 95% CI 1.76–4.92), 32–36 weeks of gestation (aOR 1.73, 95% CI 1.05–2.83), and 40–41 weeks of gestation (aOR 2.28, 95% CI 1.18–4.4) (56). Other retrospective cohort studies similarly demonstrate increased risk of stillbirth for women aged 40 years and older, with more modest or no association between age 35–39 years and stillbirth (36, 57–60).

The benefit of antenatal fetal surveillance to reduce the risk of stillbirth in this population remains unknown secondary to a lack of interventional trials or adequately powered observational studies to examine the rare outcome of stillbirth (61, 62). Nonetheless, ACOG and SMFM have already established guidance that “suggests surveillance for conditions for which stillbirth is reported to occur more frequently than 0.8 per 1,000 (the false-negative rate of a biophysical profile [or modified biophysical profile]) and which are associated with a relative risk or odds ratio for stillbirth of more than 2.0 compared with pregnancies without the condition.” (63) Based on this rationale, available data support offering antenatal fetal surveillance for pregnant individuals with anticipated delivery at age 40 years and older given the increased risk of stillbirth. However, for individuals aged 35–39 years, there is insufficient evidence to recommend routine antenatal fetal surveillance in the absence of other risk factors for stillbirth, and whether to offer surveillance to these individuals should be individualized.

There are no data on which to base recommendations regarding the timing and frequency of antenatal surveillance. Stillbirth risk for women older than age 40 years begins to increase at 34 weeks of gestation, with the greatest rise in risk occurring at 39 weeks of gestation and beyond (53). Based on data that demonstrate a steady increase in the risk of stillbirth beginning at 33 weeks of gestation (53) (Table 1) and existing studies that initiate fetal surveillance between 32 and 36 weeks of gestation (61, 62), it is reasonable to initiate

antenatal fetal surveillance between 32 and 36 weeks of gestation.

We recommend proceeding with delivery in well-dated pregnancies at 39 0/7–39 6/7 weeks of gestation for individuals 40 years and older due to increasing rates of neonatal morbidity and stillbirth beyond this gestational age. (GRADE 1B)

Because of the increased stillbirth rates in older individuals, several cohort studies have evaluated the potential benefits of induction of labor before 40 weeks of gestation as a preventative strategy for stillbirth. A national cohort study in Denmark evaluated stillbirth rates in 830,000 births over 12 years, during which a national effort to increase induction of labor as a modality to decrease stillbirth was implemented. The results demonstrated a significant decrease in stillbirth rates during this period after the 37th week of gestation. Women at high risk for stillbirth, including those older than age 40 years, were included in this targeted intervention of earlier induction of labor (64). Other studies have been underpowered to detect a difference in stillbirth (4).

Both observational and randomized controlled trial data demonstrate no increased risk of adverse neonatal outcomes and potential benefit of induction of labor between 39 0/7 and 39 6/7 weeks of gestation. A retrospective cohort study demonstrated a nadir in the risk of adverse neonatal outcomes at 39 weeks of gestation for women of all ages. The largest magnitude of RR for neonatal morbidity with advancing gestational age was identified among women older than age 40 years (adjusted RR 1.24, 95% CI 1.01–1.52 at 40 weeks of gestation) (65).

One randomized controlled trial specifically evaluated the effect of induction of labor compared with expectant management on the rate of cesarean delivery in women aged 35 years and older (66). More than 600 women were randomized to labor induction between 39 0/7 and 39 6/7 weeks of gestation compared with expectant management up to 42 weeks of gestation. Participants in this study did not have antenatal surveillance unless indicated for reasons other than advanced patient age at the time of pregnancy. Overall, there was no difference between groups in the cesarean delivery rate (32% induction of labor vs 33% expectant management, RR 0.99, 95% CI 0.87–1.14). There were also no differences in secondary maternal outcomes such as intra-partum and postpartum complications or neonatal outcomes such as stillbirth or neonatal intensive care unit admission (66).

The ARRIVE (A Randomized Trial of Induction Versus Expectant Management) study randomized 6,106 nulliparous, low-risk women to induction of labor between 39 0/7 and 39 6/7 weeks of gestation compared with expectant management. The study had adequate power to evaluate a composite primary outcome of perinatal death or severe neonatal complications and a principal



secondary outcome of cesarean delivery. There was no difference in the primary perinatal outcome between the induction group and the expectant management group (RR 0.80, 95% CI 0.64–1.00; $P=.049$). There were decreased rates of cesarean delivery (18.6% vs 22.2%, RR 0.84, 95% CI 0.76–0.93, $P<.001$) and hypertensive disorders of pregnancy (9.1% vs 14.1%, RR 0.64, 95% CI 0.56–0.74, $P<.001$) with induction of labor (67). In a pre-specified subgroup analysis of women aged 35 years or older compared with those younger than age 35 years, there were no differences in the results for the primary neonatal composite outcome or cesarean delivery.

Timing of delivery is a shared decision-making process, with consideration of maternal and fetal factors. The rate of stillbirth at 39 weeks of gestation in women aged 40 years and older is nearly the same as the rate of stillbirth for women aged 25–29 years who are beyond 41 weeks of gestation (53, 54). Therefore, delivery in well-dated pregnancies at 39 weeks of gestation or later for individuals aged 40 years and older should be considered. In the absence of additional maternal or fetal comorbidities, the evidence for elevated stillbirth risk in individuals aged 35–39 years is not sufficient to support a clear recommendation regarding timing of delivery beyond routine practice. Nonetheless, induction of labor after 39 0/7 weeks of gestation decreased cesarean delivery rates and incidence of hypertensive disorders

of pregnancy, even in a low-risk population, with no increase in adverse neonatal outcomes (67, 68).

We suggest counseling that vaginal delivery is safe and appropriate if there are no other maternal or fetal indications for cesarean delivery. Counseling should include a discussion of the risks of cesarean delivery, the patient's comorbidities, and the patient's preferences and goals. Advancing patient age alone is not an indication for cesarean delivery. (GRADE 2B)

The 2016 National Vital Statistics data highlight a significant difference in overall cesarean delivery rate related to age at the time of pregnancy. The cesarean delivery rate was 40% for women aged 35–39 years and nearly 48% for women older than age 40 years (69). A population-based cohort study analyzed 10 years of Washington State birth certificate data and found a progressive increase in cesarean delivery with increasing age of the pregnant woman. Pregnant women younger than age 35 years had a 20% cesarean delivery rate, compared with nearly 26% and 37% for pregnant women aged 35–39 years and 45–49 years, respectively (70). A large retrospective study of 1.3 million births in California demonstrated a similar stepwise increase, with a

Table 2. Outcomes for Planned Elective Cesarean Delivery Compared With Planned Vaginal Delivery Among Women 35 Years of Age or Older

Outcome	Elective Cesarean Delivery, n=35,170	Planned Vaginal Delivery, n=406,897	Adjusted Odds Ratio (95% CI)
In-hospital death	25.6/100,000	4.4/100,000	5.63 (2.52–12.55)
Hemorrhage requiring hysterectomy	0.09	0.05	1.81 (1.25–2.61)
Any hysterectomy	0.16	0.08	1.81 (1.36–2.40)
Postpartum hemorrhage	1.11	2.52	0.44 (0.39–0.48)
Disseminated intravascular coagulation	0.24	0.11	2.13 (1.69–2.69)
Blood transfusion	0.92	0.44	2.07 (1.84–2.34)
Uterine rupture	0.01	0.03	0.30 (0.10–0.94)
Anesthetic complications	0.55	0.31	1.78 (1.53–2.07)
Cardiac arrest	0.56	0.10	5.39 (4.54–6.38)
Acute renal failure	10.0	0.01	3.39 (1.78–6.46)
Assisted ventilation or intubation	0.11	0.02	4.81 (3.27–7.08)
Major puerperal infection	0.41	0.19	2.21 (1.85–2.65)
Sepsis	0.04	0.02	2.27 (1.25–4.14)
In-hospital wound dehiscence	0.16	0.02	8.69 (6.13–12.32)

Modified from Lavecchia M, Sabbah M, Abenhaim HA. Effect of planned mode of delivery in women with advanced maternal age. *Matern Child Health J* 2016;20:2318–27. doi: 10.1007/s10995-016-2055-4. All significant results are presented. With the exception of in-hospital death, all numbers are reported as percentages. Models are adjusted for age, race, income, hospital type, hospital location and type of insurance.



cesarean delivery rate of 40.5% in women aged 35–39 years, 47.3% in women aged 40–44 years, 55.6% in women aged 45–49 years, and 62.4% in women aged 50 years and older (29). Although the rates in each age category were lower in a retrospective cohort study in Belgium (N=41,618), there remained a stepwise increase in the rate of primary cesarean delivery with increasing age of the pregnant woman, classified as 25–34 years (8.9%), 35–39 years (15.2%), 40–44 years (17.8%), and 45 years and older (27.3%) (36). A 2010 systematic review identified 21 studies with ORs between 1.39 and 2.76 for the association between age older than 35 years and cesarean delivery. However, a meta-analysis could not be performed to obtain a pooled estimate given the heterogeneity of the results (71). Despite numerous observational, population-based studies demonstrating an association between older age at the time of pregnancy and cesarean delivery (18, 29, 31, 70, 72–94), most of these studies do not detail the indication for cesarean delivery, and the etiology of the higher rate remains unknown.

Because cesarean delivery is associated with increased maternal morbidity compared with vaginal birth, the observed increased rates of cesarean delivery with advancing age of the pregnant individual likely translate to increased maternal morbidities. A retrospective cohort study using data from the Healthcare Cost and Utilization Project Nationwide Inpatient Sample compared outcomes for women older than age 35 years who had a planned primary elective cesarean delivery with those who had a planned vaginal birth. Planned primary elective cesarean delivery was associated with a higher in-hospital mortality ratio and numerous other serious complications (Table 2) (95). These risk data can be used when counseling older patients regarding planned mode of delivery.

Advancing patient age alone is not an indication for cesarean delivery. Decisions regarding mode of delivery need to incorporate counseling regarding the risks of cesarean delivery, individual comorbidities, and patient preferences.

HEALTH EQUITY

We recommend that obstetrician–gynecologists and other obstetric care professionals be aware of the disproportionate rates of most adverse maternal and perinatal outcomes in Black and American Indian and Alaska Native pregnant individuals aged 35 years and older. We recommend that they understand the ways racism contributes to perpetuating these outcomes. (GRADE 1B)

The maternal mortality rates for individuals who identify as American Indian and Alaska Native and non-

Hispanic Black are more than double and triple, respectively, the rate for those who identify as non-Hispanic White (15). The top five causes of maternal death—cardiovascular conditions, infection or sepsis, hemorrhage, thrombotic embolism, and cerebrovascular accidents—are more common in populations disproportionately affected by racism and historical inequities. An observational study that evaluated the CDC Pregnancy Mortality Surveillance System data for maternal mortality trends determined a pregnancy-related mortality risk ratio of 3.2 for non-Hispanic Black women compared with non-Hispanic White women. This ratio increased to 4.9 for non-Hispanic Black women aged 35–39 years and 3.6 for women aged 40 years and older (16).

Similarly, fetal outcomes including preterm birth (both spontaneous and iatrogenic), small for gestational age, and stillbirth occur more frequently in some racial and ethnic groups that are disproportionately affected by social and structural barriers to care and inequitable access to care. The infant mortality rate for non-Hispanic Black and American Indian and Alaska Native infants (10.7/1,000 live births and 7.9/1,000 live births, respectively) is double the rate for non-Hispanic White infants (96). Evaluation of adverse fetal or neonatal outcomes collected from the National Center for Health Statistics database demonstrates that fetal risk progressively increased with increasing patient age of 30 years and older at the time of pregnancy. The risk was most pronounced in individuals who identified as non-Hispanic Black and American Indian and Alaska Native (17). Another study evaluated chronic stress (weathering) and race on the risk of preterm birth. Overall, they determined that the risk of preterm birth increased for all populations aged 35 years and older but significantly more in the non-Hispanic Black population (18).

There are fewer and sometimes conflicting data regarding other vulnerable populations. Studies using earlier databases suggest comparable, if not slightly better, outcomes for Hispanic populations compared with non-Hispanic White populations (16, 18, 97). Although severe maternal morbidity and mortality rates in Hispanic women remain lower than in non-Hispanic Black and American Indian and Alaska Native populations, prevalence of these adverse outcomes exhibited the highest increase in Hispanic women (98). More research regarding these shifts is warranted, as well as a better understanding of how these risks may change with advancing age at the time of pregnancy.

Given these disparities in maternal and infant health outcomes, obstetrician–gynecologists and other obstetric care professionals should consider systems-based and individual strategies to reduce racial and ethnic disparities in care and outcomes. At a systems



level, strategies may include conducting internal assessments of barriers and facilitators to providing equitable care, implementing unconscious bias and communication training, and advocating for patient input in decision making. In addition to reflecting on their own biases, individual clinicians can advocate for anti-racist policies and practices within their health care systems and follow an anti-racist framework when conducting research.

FURTHER RESEARCH

The definition of advanced maternal age (35 years and older) has led to research that, in many instances, dichotomizes patient age to younger than 35 years and 35 years and older. As demonstrated in numerous observational studies, age-related risks increase with increasing age. Therefore, some of the findings of increased risks associated with pregnancies in women aged 35 years or older may be largely driven by pregnancies in individuals who have pregnancies at older ages, such as older than 40 years or older than 45 years. Future research should clearly delineate risk by age category to allow for recommendations for individuals within a specific age range based on evidence and use objective, clear phrasing.

There are no robust data evaluating whether antenatal fetal surveillance reduces the risk of stillbirth in this population, and there are limited data regarding the timing and frequency of testing. There are also limited data regarding disparities and whether the risks associated with older age of a pregnant individual are increased in different populations, including different racial and ethnic populations (Hispanic ethnicity and Asian and American Indian and Alaska Native populations). Prior research has also grouped all patients of Hispanic ethnicity in a single group, whereas various countries of origin and community-level factors may also influence outcomes. More granular data regarding race and ethnicity will need to be collected as part of future analyses.

REFERENCES

- Osterman M, Hamilton B, Martin JA, Driscoll AK, Valenzuela CP. Births: final data for 2020. *Natl Vital Stat Rep* 2021;70:1–50. doi: 10.15620/cdc:112078
- Mathews TJ, Hamilton BE. Mean age of mother, 1970–2000. *Natl Vital Stat Rep* 2002;51:1–13. doi: 10.1111/1471-0528.12659
- Laopaiboon M, Lumbiganon P, Intarat N, Mori R, Ganchimeg T, Vogel JP, et al. Advanced maternal age and pregnancy outcomes: a multicountry assessment. *BJOG* 2014;121(suppl 1):49–56. doi: 10.1111/1471-0528.12659
- Walker KF, Bradshaw L, Bugg GJ, Thornton JG. Causes of antepartum stillbirth in women of advanced maternal age. *Eur J Obstet Gynecol Reprod Biol* 2016;197:86–90. doi: 10.1016/j.ejogrb.2015.11.032
- Hook EB. Rates of chromosome abnormalities at different maternal ages. *Obstet Gynecol* 1981;58:282–5.
- Cleary-Goldman J, Malone FD, Vidaver J, Ball RH, Nyberg DA, Comstock CH, et al. Impact of maternal age on obstetric outcome. *FASTER Consortium. Obstet Gynecol* 2005;105:983–90. doi: 10.1097/01.AOG.0000158118.75532.51
- Gill SK, Broussard C, Devine O, Green RF, Rasmussen SA, Reefhuis J, et al. Association between maternal age and birth defects of unknown etiology: United States, 1997–2007. *National Birth Defects Prevention Study. Birth Defects Res A Clin Mol Teratol* 2012;94:1010–8. doi: 10.1002/bdra.23049
- Rademaker D, Hukkelhoven CW, van Pampus MG. Adverse maternal and perinatal pregnancy outcomes related to very advanced maternal age in primigravida and multigravida in the Netherlands: a population-based cohort. *Acta Obstet Gynecol Scand* 2021;100:941–8. doi: 10.1111/aogs.14064
- Claramonte Nieto M, Meler Barrabes E, Garcia Martínez S, Gutierrez Prat M, Serra Zantop B. Impact of aging on obstetric outcomes: defining advanced maternal age in Barcelona. *BMC Pregnancy Childbirth* 2019;19:342–3. doi: 10.1186/s12884-019-2415-3
- Schimmel MS, Bromiker R, Hammerman C, Chertman L, Iosco-vich A, Granovsky-Grisaru S, et al. The effects of maternal age and parity on maternal and neonatal outcome. *Arch Gynecol Obstet* 2015;291:793–8. doi: 10.1007/s00404-014-3469-0
- Arya S, Mulla ZD, Plavsic SK. Outcomes of women delivering at very advanced maternal age. *J Womens Health (Larchmt)* 2018;27:1378–84. doi: 10.1089/jwh.2018.7027
- Marozio L, Picardo E, Filippini C, Mainolfi E, Berchiolla P, Cavallo F, et al. Maternal age over 40 years and pregnancy outcome: a hospital-based survey. *J Matern Fetal Neonatal Med* 2019;32:1602–8. doi: 10.1080/14767058.2017.1410793
- Smithson SD, Greene NH, Esakoff TF. Pregnancy outcomes in very advanced maternal age women. *Am J Obstet Gynecol MFM* 2022;4:100491. doi: 10.1016/j.ajogmf.2021.100491
- Dongarwar D, Tahseen D, Aliyu MH, Saliu HM. Pregnancy outcomes among Asian Americans of advanced maternal age, 1992–2018. *J Obstet Gynaecol Res* 2021;47:2117–25. doi: 10.1111/jog.14790
- Centers for Disease Control and Prevention. Maternal and infant health. Accessed May 19, 2022. <https://www.cdc.gov/reproductivehealth/maternalinfanthealth/index.html>
- Creanga AA, Syverson C, Seed K, Callaghan WM. Pregnancy-related mortality in the United States, 2011–2013. *Obstet Gynecol* 2017;130:366–73. doi: 10.1097/AOG.0000000000002114
- Schummers L, Hacker MR, Williams PL, Hutcheon JA, Vanderwee TJ, McElrath TF, et al. Variation in relationships between maternal age at first birth and pregnancy outcomes by maternal race: a population-based cohort study in the United States. *BMJ Open* 2019;9:e033697–033697. doi: 10.1136/bmjopen-2019-033697
- Kim SY, Park JY, Bak SE, Jang YR, Wie JH, Ko HS, et al. Effect of maternal age on emergency cesarean section. *J Matern Fetal Neonatal Med* 2019 Mar 25 [Epub ahead of print]. doi: 10.1080/14767058.2019.1593958
- ACOG methodology: clinical consensus methodology. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2021;138:523–6. doi: 10.1097/AOG.0000000000004520



20. United Nations Development Programme. Table 1. Human Development index and its components. In: Human development report 2019. Accessed May 19, 2022. <http://hdr.undp.org/sites/default/files/hdr2019.pdf>
21. Scime NV, Chaput KH, Faris PD, Quan H, Tough SC, Metcalfe A. Pregnancy complications and risk of preterm birth according to maternal age: a population-based study of delivery hospitalizations in Alberta. *Acta Obstet Gynecol Scand* 2020;99:459–68. doi: 10.1111/aogs.13769
22. Bergholt T, Skjeldestad FE, Pyykönen A, Rasmussen SC, Tapper AM, Bjarnad ttir RI, et al. Maternal age and risk of cesarean section in women with induced labor at term - a Nordic register-based study. *Acta Obstet Gynecol Scand* 2020;99:283–9. doi: 10.1111/aogs.13743
23. Cakmak Celik F, Aygun C, Kucukoduk S, Bek Y. Maternal and neonatal outcomes in advanced maternal age: a retrospective cohort study. *J Matern Fetal Neonatal Med* 2017;30:2452–6. doi: 10.1080/14767058.2016.1253058
24. Posthumus AG, Birnie E, van Veen MJ, Steegers EA, Bonsel GJ. An antenatal prediction model for adverse birth outcomes in an urban population: the contribution of medical and non-medical risks. *Midwifery* 2016;38:78–86. doi: 10.1016/j.midw.2015.11.006
25. Sheen JJ, Wright JD, Goffman D, Kern-Goldberger AR, Booker W, Siddiq Z, et al. Maternal age and risk for adverse outcomes. *Am J Obstet Gynecol* 2018;219:390.e1–15. doi: 10.1016/j.ajog.2018.08.034
26. Timofeev J, Reddy UM, Huang CC, Driggers RW, Landy HJ, Laughon SK. Obstetric complications, neonatal morbidity, and indications for cesarean delivery by maternal age. *Obstet Gynecol* 2013;122:1184–95. doi: 10.1097/AOG.0000000000000017
27. Barton JR, Sibai AJ, Istwan NB, Rhea DJ, Desch CN, Sibai BM. Spontaneously conceived pregnancy after 40: influence of age and obesity on outcome. *Am J Perinatol* 2014;31:795–8. doi: 10.1055/s-0033-1359716
28. Frederiksen LE, Ernst A, Brix N, Braskhøj Lauridsen LL, Roos L, Ramlau-Hansen CH, et al. Risk of adverse pregnancy outcomes at advanced maternal age. *Obstet Gynecol* 2018;131:457–63. doi: 10.1097/AOG.0000000000002504
29. Osmundson SS, Gould JB, Butwick AJ, Yeaton-Massey A, El-Sayed YY. Labor outcome at extremely advanced maternal age. *Am J Obstet Gynecol* 2016;214:362.e1–7. doi: 10.1016/j.ajog.2015.09.103
30. Pinheiro RL, Areia AL, Mota Pinto A, Donato H. Advanced maternal age: adverse outcomes of pregnancy, a meta-analysis. *Acta Med Port* 2019;32:219–26. doi: 10.20344/amp.11057
31. Islam MM, Bakheit CS. Advanced maternal age and risks for adverse pregnancy outcomes: a population-based study in Oman. *Health Care Women Int* 2015;36:1081–103. doi: 10.1080/07399332.2014.990560
32. Davidson KW, Barry MJ, Mangione CM, Cabana M, Caughey AB, et al. Aspirin use to prevent preeclampsia and related morbidity and mortality: US Preventive Services Task Force recommendation statement. *JAMA* 2021;326:1186–91. doi: 10.1001/jama.2021.14781
33. Low-dose aspirin use during pregnancy. ACOG Committee Opinion No. 743. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2018;132:e44–52. doi: 10.1097/AOG.0000000000002708
34. American College of Obstetricians and Gynecologists. Low-dose aspirin use for the prevention of preeclampsia and related morbidity and mortality. ACOG Practice Advisory. Accessed May 19, 2022. <https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2021/12/low-dose-aspirin-use-for-the-prevention-of-preeclampsia-and-related-morbidity-and-mortality>
35. Martin JA, Osterman MJK. Is twin childbearing on the decline? Twin births in the United States, 2014–2018. *NCHS Data Brief* 2019;(351):1–8. doi: 10.1111/1471-0528.12659
36. Jacquemyn Y, Martens E, Martens G. Pregnancy at late premenopausal age: outcome of pregnancies at 45 years and older in Flanders, Belgium. *J Obstet Gynaecol* 2014;34:479–81. doi: 10.3109/01443615.2014.911831
37. Multifetal gestations: twin, triplet, and higher-order multifetal pregnancies. ACOG Practice Bulletin No. 231. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2021;137:e145–62. doi: 10.1097/AOG.0000000000004397
38. Female age-related fertility decline. Committee Opinion No. 589. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2014;123:719–21. doi: 10.1097/01.AOG.0000444440.96486.61
39. Lei Y, Dong M. Association of maternal age with fetal sex chromosome aneuploidies [in Chinese]. *Zhejiang Da Xue Bao Yi Xue Ban* 2019;48:409–13. doi: 10.3785/j.issn.1008-9292.2019.08.10
40. Li H, Mao Y, Jin J. The correlation between maternal age and fetal sex chromosome aneuploidies: a 8-year single institution experience in China. *Mol Cytogenet* 2021;14:25. doi: 10.1186/s13039-021-00545-2
41. Screening for fetal chromosomal abnormalities. ACOG Practice Bulletin No. 226. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2020;136:e48–69. doi: 10.1097/AOG.0000000000004084
42. Reefhuis J, Honein MA. Maternal age and non-chromosomal birth defects, Atlanta–1968–2000: teenager or thirty-something, who is at risk? *Birth Defects Res A Clin Mol Teratol* 2004;70:572–9. doi: 10.1002/bdra.20065
43. Shnorhavorian M, Bittner R, Wright JL, Schwartz SM. Maternal risk factors for congenital urinary anomalies: results of a population-based case-control study. *Urology* 2011;78:1156–61. doi: 10.1016/j.urology.2011.04.022
44. Ciancimino L, Laganà AS, Chiofalo B, Granese R, Grasso R, Triolo O. Would it be too late? A retrospective case-control analysis to evaluate maternal-fetal outcomes in advanced maternal age. *Arch Gynecol Obstet* 2014;290:1109–14. doi: 10.1007/s00404-014-3367-5
45. Hollier LM, Leveno KJ, Kelly MA, McIntire DD, Cunningham FG. Maternal age and malformations in singleton births. *Obstet Gynecol* 2000;96:701–6. doi: 10.1016/s0029-7844(00)01019-x
46. Okmen Ozkan B, Köroğlu N, Turkgeldi LS, Cetin BA, Aslan H. Advanced maternal age and risk of non-chromosomal anomalies: data from a tertiary referral hospital in Turkey. *J Matern Fetal Neonatal Med* 2019;32:749–52. doi: 10.1080/14767058.2017.1390741
47. Goetzinger KR, Shanks AL, Odibo AO, Macones GA, Cahill AG. Advanced maternal age and the risk of major congenital anomalies. *Am J Perinatol* 2017;34:217–22. doi: 10.1055/s-0036-1585410
48. Best KE, Rankin J. Is advanced maternal age a risk factor for congenital heart disease? *Birth Defects Res A Clin Mol Teratol* 2016;106:461–7. doi: 10.1002/bdra.23507
49. Wax J, Minkoff H, Johnson A, Coleman B, Levine D, Helfgott A, et al. Consensus report on the detailed fetal anatomic ultrasound examination: indications, components, and qualifications. *J Ultrasound Med* 2014;33:189–95. doi: 10.7863/ultra.33.2.189



50. Zapata-Masias Y, Marqueta B, Gomez Roig MD, Gonzalez-Bosquet E. Obstetric and perinatal outcomes in women ≥ 40 years of age: associations with fetal growth disorders. *Early Hum Dev* 2016;100:17–20. doi: 10.1016/j.earlhumdev.2016.04.010

51. Palatnik A, De Cicco S, Zhang L, Simpson P, Hibbard J, Egede LE. The association between advanced maternal age and diagnosis of small for gestational age. *Am J Perinatol* 2020;37:37–43. doi: 10.1055/s-0039-1694775

52. MacDorman MF, Gregory EC. Fetal and perinatal mortality: United States, 2013. *Natl Vital Stat Rep* 2015;64:1–24. doi: 10.1111/1471-0528.12659

53. Reddy UM, Ko CW, Willinger M. Maternal age and the risk of stillbirth throughout pregnancy in the United States. *Am J Obstet Gynecol* 2006;195:764–70. doi: 10.1016/j.ajog.2006.06.019

54. Bahtiyar MO, Funai EF, Rosenberg V, Norwitz E, Lipkind H, Buhimschi C, et al. Stillbirth at term in women of advanced maternal age in the United States: when could the antenatal testing be initiated? *Am J Perinatol* 2008;25:301–4. doi: 10.1055/s-2008-1076605

55. Sutan R, Campbell D, Prescott GJ, Smith WC. The risk factors for unexplained antepartum stillbirths in Scotland, 1994 to 2003. *J Perinatol* 2010;30:311–8. doi: 10.1038/jp.2009.158

56. Hoffman MC, Jeffers S, Carter J, Duthely L, Cotter A, Gonzalez-Quintero VH. Pregnancy at or beyond age 40 years is associated with an increased risk of fetal death and other adverse outcomes. *Am J Obstet Gynecol* 2007;196:e11–3. doi: 10.1016/j.ajog.2006.10.862

57. Canterino JC, Ananth CV, Smulian J, Harrigan JT, Vintzileos AM. Maternal age and risk of fetal death in singleton gestations: USA, 1995–2000. *J Matern Fetal Neonatal Med* 2004;15:193–7. doi: 10.1080/14767050410001668301

58. Mutz-Dehbalala I, Scheier M, Jerabek-Klestil S, Brantner C, Windbichler GH, Leitner H, et al. Perinatal mortality and advanced maternal age. *Gynecol Obstet Invest* 2014;77:50–7. doi: 10.1159/000357168

59. Reddy UM, Laughon SK, Sun L, Troendle J, Willinger M, Zhang J. Prepregnancy risk factors for antepartum stillbirth in the United States. *Obstet Gynecol* 2010;116:1119–26. doi: 10.1097/AOG.0b013e3181f903f8

60. Miller DA. Is advanced maternal age an independent risk factor for uteroplacental insufficiency? *Am J Obstet Gynecol* 2005;192:1974–2. doi: 10.1016/j.ajog.2005.02.050

61. Fox NS, Rebarber A, Silverstein M, Roman AS, Klausner CK, Saltzman DH. The effectiveness of antepartum surveillance in reducing the risk of stillbirth in patients with advanced maternal age. *Eur J Obstet Gynecol Reprod Biol* 2013;170:387–90. doi: 10.1016/j.ejogrb.2013.07.035

62. Levine LD, Srinivas SK, Par E, Mehta-Lee SS. The impact of antenatal testing for advanced maternal age on cesarean delivery rate at an urban institution. *Am J Perinatol* 2015;32:101–6. doi: 10.1055/s-0034-1376312

63. Indications for outpatient antenatal fetal surveillance. ACOG Committee Opinion No. 828. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2021;137:e177–97. doi: 10.1097/AOG.0000000000004407

64. Hedegaard M, Lidgaard Ø, Skovlund CW, Mørch LS, Hedegaard M. Reduction in stillbirths at term after new birth induction paradigm: results of a national intervention. *BMJ Open* 2014;4:e005785. doi: 10.1136/bmjopen-2014-005785

65. Valent AM, Newman T, Chen A, Thompson A, DeFranco E. Gestational age-specific neonatal morbidity among pregnancies complicated by advanced maternal age: a population-based retrospective cohort study. *J Matern Fetal Neonatal Med* 2016;29:1485–90. doi: 10.3109/14767058.2015.1051955

66. Walker KF, Bugg GJ, Macpherson M, McCormick C, Grace N, Wildsmith C, et al. Randomized trial of labor induction in women 35 years of age or older. *N Engl J Med* 2016;374:813–22. doi: 10.1056/NEJMoa1509117

67. Grobman WA, Rice MM, Reddy UM, Tita AT, Silver RM, Mallett G, et al. Labor induction versus expectant management in low-risk nulliparous women. *N Engl J Med* 2018;379:513–23. doi: 10.1056/NEJMoa1800566

68. American College of Obstetricians and Gynecologists. Clinical guidance for integration of the findings of the ARRIVE trial: labor induction versus expectant management in low-risk nulliparous women. ACOG Practice Advisory. Accessed May 19, 2022. <https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2018/08/clinical-guidance-for-integration-of-the-findings-of-the-arrive-trial>

69. Martin JA, Hamilton BE, Osterman MJ, Driscoll AK, Drake P. Births: final data for 2016. *Natl Vital Stat Rep* 2018;67:1–55. doi: 10.1111/1471-0528.12659

70. Richards MK, Flanagan MR, Littman AJ, Burke AK, Callegari LS. Primary cesarean section and adverse delivery outcomes among women of very advanced maternal age. *J Perinatol* 2016;36:272–7. doi: 10.1038/jp.2015.204

71. Bayrampour H, Heaman M. Advanced maternal age and the risk of cesarean birth: a systematic review. *Birth* 2010;37:219–26. doi: 10.1111/j.1523-536X.2010.00409.x

72. Kanmaz AG, İnan AH, Beyan E, Ögür S, Budak A. Effect of advanced maternal age on pregnancy outcomes: a single-centre data from a tertiary healthcare hospital. *J Obstet Gynaecol* 2019;39:1104–11. doi: 10.1080/01443615.2019.1606172

73. Callaway LK, Lust K, McIntyre HD. Pregnancy outcomes in women of very advanced maternal age. *Aust N Z J Obstet Gynaecol* 2005;45:12–6. doi: 10.1111/j.1479-828X.2005.00333.x

74. Casteleiro A, Paz-Zulueta M, Par s-Bravo P, Ruiz-Azcona L, Santiba ez M. Association between advanced maternal age and maternal and neonatal morbidity: a cross-sectional study on a Spanish population. *PLoS One* 2019;14:e0225074. doi: 10.1371/journal.pone.0225074

75. Molina-García L, Hidalgo-Ruiz M, Arredondo-Lopez B, Colomino-Cepri n S, Delgado-Rodríguez M, Martínez-Galiano JM. Maternal age and pregnancy, childbirth and the puerperium: obstetric results. *J Clin Med* 2019;8:672. doi: 10.3390/jcm8050672

76. Salman L, Shmueli A, Chen R, Ashwal E, Hirsch L, Yogev Y, et al. Choice of scheduled cesarean delivery versus trial of labor for advanced maternal age primiparous women. *J Matern Fetal Neonatal Med* 2019;32:979–84. doi: 10.1080/14767058.2017.1397121

77. Muto H, Ishii K, Nakano T, Hayashi S, Okamoto Y, Mitsuda N. Rate of intrapartum cesarean section and related factors in older nulliparous women at term. *J Obstet Gynaecol Res* 2018;44:217–22. doi: 10.1111/jog.13522

78. Nakano T, Muto H, Ishii K, Hayashi S, Okamoto Y, Mitsuda N. Factors associated with emergency cesarean delivery during induction of labor in nulliparous women aged 35 years or older at term. *J Obstet Gynaecol Res* 2018;44:1747–51. doi: 10.1111/jog.13708

79. Dunn L, Kumar S, Beckmann M. Maternal age is a risk factor for caesarean section following induction of labour. *Aust N Z J Obstet Gynaecol* 2017;57:426–31. doi: 10.1111/ajo.12611



80. Fayed AA, Wahabi H, Mamdouh H, Kotb R, Esmail S. Demographic profile and pregnancy outcomes of adolescents and older mothers in Saudi Arabia: analysis from Riyadh Mother (RAHMA) and Baby cohort study. *BMJ Open* 2017;7:e016501. doi: 10.1136/bmjopen-2017-016501
81. Ogawa K, Urayama KY, Tanigaki S, Sago H, Sato S, Saito S, et al. Association between very advanced maternal age and adverse pregnancy outcomes: a cross sectional Japanese study. *BMC Pregnancy Childbirth* 2017;17:349. doi: 10.1186/s12884-017-1540-0
82. Leonard SA, Main EK, Carmichael SL. The contribution of maternal characteristics and cesarean delivery to an increasing trend of severe maternal morbidity. *BMC Pregnancy Childbirth* 2019;19:16. doi: 10.1186/s12884-018-2169-3
83. Berezcky LK, Kiss SL, Szab B. Increased frequency of gestational and delivery-related complications in women of 35 years of age and above. *J Obstet Gynaecol* 2015;35:115–20. doi: 10.3109/01443615.2014.940294
84. Favilli A, Acanfora MM, Bini V, Radicchi R, Di Renzo GC, Gerli S. Single indication of labor induction with prostaglandins: is advanced maternal age a risk factor for cesarean section? A matched retrospective cohort study. *J Matern Fetal Neonatal Med* 2013;26:665–8. doi: 10.3109/14767058.2012.746658
85. Canto MJ, Reus A, Cortés S, Ojeda F. Pregnancy outcome in a Spanish population of women beyond age 40 delivered above 32 weeks' gestation. *J Matern Fetal Neonatal Med* 2012;25:461–6. doi: 10.3109/14767058.2011.629246
86. Kozinszky Z, Orvos H, Zoboki T, Katona M, Wayda K, P I A, et al. Risk factors for cesarean section of primiparous women aged over 35 years. *Acta Obstet Gynecol Scand* 2002;81:313–6. doi: 10.1034/j.1600-0412.2002.810406.x
87. Diejomaoh MF, Al-Shamali IA, Al-Kandari F, Al-Qenae M, Mohd AT. The reproductive performance of women at 40 years and over. *Eur J Obstet Gynecol Reprod Biol* 2006;126:33–8. doi: 10.1016/j.ejogrb.2005.07.014
88. Chibber R. Child-bearing beyond age 50: pregnancy outcome in 59 cases "a concern?" *Arch Gynecol Obstet* 2005;271:189–94. doi: 10.1007/s00404-003-0577-7
89. Takahashi H, Watanabe N, Sugibayashi R, Aoki H, Egawa M, Sasaki A, et al. Increased rate of cesarean section in primiparous women aged 40 years or more: a single-center study in Japan. *Arch Gynecol Obstet* 2012;285:937–41. doi: 10.1007/s00404-011-2099-z
90. Carolan M, Davey MA, Biro MA, Kealy M. Older maternal age and intervention in labor: a population-based study comparing older and younger first-time mothers in Victoria, Australia. *Birth* 2011;38:24–9. doi: 10.1111/j.1523-536X.2010.00439.x
91. Wang Y, Tanbo T, Abyholm T, Henriksen T. The impact of advanced maternal age and parity on obstetric and perinatal outcomes in singleton gestations. *Arch Gynecol Obstet* 2011;284:31–7. doi: 10.1007/s00404-010-1587-x
92. Prasad M, Ghosh S, Al-Taher H. Obstetric outcome in women over the age of 40 years. *J Obstet Gynaecol* 2000;20:24–6. doi: 10.1080/01443610063408
93. Roos N, Sahlin L, Ekman-Ordeberg G, Kieler H, Stephansson O. Maternal risk factors for postterm pregnancy and cesarean delivery following labor induction. *Acta Obstet Gynecol Scand* 2010;89:1003–10. doi: 10.3109/00016349.2010.500009
94. Chan BC, Lao TT. Effect of parity and advanced maternal age on obstetric outcome. *Int J Gynaecol Obstet* 2008;102:237–41. doi: 10.1016/j.ijgo.2008.05.004
95. Lavecchia M, Sabbah M, Abenhaim HA. Effect of planned mode of delivery in women with advanced maternal age. *Matern Child Health J* 2016;20:2318–27. doi: 10.1007/s10995-016-2055-4
96. Ely DM, Driscoll AK. Infant mortality in the United States, 2019: data from the period linked birth/infant death file. *Natl Vital Stat Rep* 2021;70:1–18. doi: 10.15620/cdc:111053
97. Moaddab A, Dildy GA, Brown HL, Bateni ZH, Belfort MA, Sangi-Haghpeykar H, Clark SL. Health care disparity and pregnancy-related mortality in the United States, 2005–2014. *Obstet Gynecol* 2018;131:707–12. doi: 10.1097/AOG.0000000000002534
98. Bornstein E, Eliner Y, Chervenak FA, Grünebaum A. Racial disparity in pregnancy risks and complications in the US: temporal changes during 2007–2018. *J Clin Med* 2020;9:1414. doi: 10.3390/jcm9051414



Society for Maternal-Fetal Medicine Grading System: GRADE Recommendations

GRADE of Recommendation	Clarity of Risk and Benefit	Quality of Supporting Evidence	Implications	Suggested Language
1A. Strong recommendation, high-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa.	Consistent evidence from well-performed randomized, controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk.	Strong recommendations; can apply to most patients in most circumstances without reservation. Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.	<ul style="list-style-type: none"> ●We strongly recommend... ●We recommend that...should be performed or administered... ●We recommend that...is indicated, beneficial, or effective...
1B. Strong recommendation, moderate-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa.	Evidence from randomized, controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise) or very strong evidence of some other research design. Further research (if performed) is likely to have an impact on our confidence in the estimate of benefit and risk and may change the estimate.	Strong recommendation and applies to most patients. Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.	<ul style="list-style-type: none"> ●We recommend... ●We recommend that...should be performed or administered... ●We recommend that...is (usually) indicated, beneficial, or effective...
1C. Strong recommendation, low-quality evidence	Benefits seem to outweigh risk and burdens, or vice versa.	Evidence from observational studies, unsystematic clinical experience, or from randomized, controlled trials with serious flaws. Any estimate of effect is uncertain.	Strong recommendation that applies to most patients. Some of the evidence-base practices supporting the recommendation are, however, of low quality.	<ul style="list-style-type: none"> ●We recommend... ●We recommend that...should be performed or administered... ●We recommend that...is (perhaps) indicated, beneficial, or effective...

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Society for Maternal-Fetal Medicine Grading System: GRADE Recommendations (continued)

GRADE of Recommendation	Clarity of Risk and Benefit	Quality of Supporting Evidence	Implications	Suggested Language
2A. Weak recommendation, high-quality evidence	Benefits closely balanced with risks and burdens.	Consistent evidence from well-performed randomized, controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk.	Weak recommendation; best action may differ depending on circumstances or patients or societal values.	<ul style="list-style-type: none"> ●We suggest... ●We suggest that...may or might be reasonable...
2B. Weak recommendation, moderate-quality evidence	Benefits closely balanced with risks and burdens, some uncertainty in the estimates of benefits, risks, and burdens.	Evidence from randomized, controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise) or very strong evidence of some other research design. Further research (if performed) is likely to have an impact on our confidence in the estimate of benefit and risk and may change the estimate.	Weak recommendation; alternative approaches likely to be better for some patients under some circumstances.	<ul style="list-style-type: none"> ●We suggest... ●We suggest that...may or might be reasonable...
2C. Weak recommendation, low-quality evidence	Uncertainty in the estimates of benefits, risks, and burdens; benefits may be closely balanced with risks and burdens.	Evidence from observational studies, unsystematic clinical experience, or randomized, controlled trials with serious flaws. Any estimate of effect is uncertain.	Very weak recommendation; other alternatives may be equally reasonable.	<ul style="list-style-type: none"> ●We suggest...is an option ●We suggest that...may or might be reasonable...

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Society for Maternal-Fetal Medicine Grading System: GRADE Recommendations (continued)

GRADE of Recommendation	Clarity of Risk and Benefit	Quality of Supporting Evidence	Implications	Suggested Language
Best Practice	Recommendation in which either (1) there is enormous amount of indirect evidence that clearly justifies a strong recommendation, direct evidence would be challenging and inefficient use of time and resources, to bring together and carefully summarize or (2) a recommendation to the contrary would be unethical.			<ul style="list-style-type: none"> ●We recommend... ●We recommend that...should be performed or administered... ●We recommend that...is (usually) indicated, beneficial, or effective...
<p>Obstetric Care Consensus documents use the Society for Maternal-Fetal Medicine's grading approach: https://www.ajog.org/article/S0002-9378%2820%2932576-X/fulltext.</p> <p>Recommendations are classified as either strong (1) or weak (2), and quality of evidence is classified as high (A), moderate (B), and low (C).[*] Thus, the recommendations can be one of the following six possibilities: 1A, 1B, 1C, 2A, 2B, 2C.</p> <p>[*]Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. <i>BMJ</i> 2008;336:924–6. doi: 10.1136/bmj.39489.470347.AD</p> <p>Society for Maternal-Fetal Medicine. SMFM Special Statement: SMFM Grading of Recommendations Assessment, Development, and Evaluation update. <i>Am J Obstet Gynecol</i> 2021.</p>				

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APPENDICES

Supplemental Digital Content

A. Literature search strategy: <http://links.lww.com/AOG/C770>

B. Evidence Map: <http://links.lww.com/AOG/C771>

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409 12th Street SW, Washington, DC 20024-2188

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