



## **Obstetric Care Consensus**

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# Obstetric Care Consensus #11, Pregnancy at age 35 years or older



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 found in younger pregnant populations, even in healthy individuals with no other comorbidities. There are several studies that suggest that 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 obstetrical care with anticipated delivery at the age of 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 of women aged 35 years or older. The mean age of women having their first birth in 2020 was 27.1 years vs 21.4 years in 1970.<sup>1,2</sup> 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 those found in younger pregnant populations, even in healthy individuals with no other comorbidities.

This document seeks to provide evidence-based clinical recommendations for minimizing adverse outcomes 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 (Definition), this document will focus

on pregnancy with anticipated delivery at the age of 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 obstetrical care with anticipated delivery at the age of 35 years or older within the framework of routine pregnancy care.

### **Definition**

Historically, advanced maternal age has been defined as 35 years or older at estimated date of delivery. This age cutoff was selected on the basis of evidence of declining fertility and concern surrounding increasing risks for genetic abnormalities identified in the offspring of pregnant women aged 35 years or older.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 seems to be on a continuum, such that risks increase with increasing age at the time of the pregnancy.<sup>6,7</sup> Likewise, studies evaluating the effect of chronic medical conditions such as diabetes mellitus, hypertension, and obesity, which may exacerbate pregnancy-related morbidity, seem 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 to 39, 40 to 44, 45 to 49, 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 suggesting that advancing age at the time of pregnancy is associated with greater disparities in severe maternal morbidity and mortality. <sup>15–18</sup> 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 obstetrical and gynecologic care. In original portions of this document, the authors seek to use gender-inclusive 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 <a href="https://www.acog.org/clinical-information/policy-and-position-statements/state-ments-of-policy/2022/inclusive-language">https://www.acog.org/clinical-information/policy-and-position-statements/state-ments-of-policy/2022/inclusive-language</a>.

#### **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. <sup>19</sup> The description below is specific to this Obstetric Care Consensus document.

#### Literature search

A literature search for the period from 2000 to November 2021 was performed for clinical questions 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. Medical Subject Headings (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 the age of 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).

# 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 the age of 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 or older are at higher risk for complications such as gestational diabetes mellitus, 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 birthweight. 10,23,24 More extensive evaluation of the data demonstrates that risks for adverse maternal and neonatal outcomes are on a

### **SUMMARY OF CONSENSUS RECOMMENDATIONS**

### Antepartum care

We suggest that pregnancy with anticipated delivery at the 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 years or older in the setting of at least 1 other moderate risk factor. (GRADE 1B. Strong recommendation, moderate-quality evidence.)

Given increased rates of multiple gestations for pregnant individuals with anticipated delivery at the age of 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 the age of 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.)

continuum, with risks increasing progressively with advancing age, particularly older than 40 years. <sup>8,9,11,12</sup> 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 US population database of nearly 34 million deliveries characterized pregnancy-related morbidity risk by age. Overall, women aged 35 years or older were at increased risk of pregnancy-related morbidity compared with those aged 25 to 29 years. When evaluated in age-based increments (35–39, 40–44, and 45–54 years), the risk increased with increasing age (relative risk [RR], 1.36; 95% confidence interval [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). In addition, the investigators evaluated obstetrical complications such as preeclampsia, cesarean delivery, postpartum hemorrhage, and gestational diabetes mellitus and found that advancing maternal age at the time of pregnancy was an independent risk factor for all of these obstetrical outcomes. These risks increased incrementally, so that pregnant women in the 45 to 54-year age group were at the highest risk. <sup>25</sup>

Chronic medical disorders such as obesity, hypertension, and diabetes mellitus are more prevalent in pregnant individuals aged 35 years or 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. <sup>26–28</sup> Studies have shown that pregnant women aged 35 years or older are 2 to 4 times more likely to have chronic hypertension and nearly twice as likely to have type 2 diabetes mellitus as pregnant women aged 25 to 29 years. <sup>26,29</sup> Similarly, women aged older than 40 years had 2 to 3 times the risk of gestational diabetes mellitus compared with younger individuals. <sup>12,29</sup> Even after controlling for baseline characteristics of prepregnancy hypertension and diabetes mellitus, older women remained at significant risk of developing preeclampsia and gestational diabetes mellitus.

A large meta-analysis that combined 10 cohort studies of more than 1000 patients per study comparing pregnant women aged 35 years or older with pregnant women aged 20 to 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 mellitus, and hypertension, and analyzed data in 5year age increments. Although not as pronounced as in previous cohort studies, age alone was a risk factor for obesity, gestational diabetes mellitus, and hypertension, and women aged 35 years or 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 or older, including low birthweight, 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.<sup>30</sup>

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 1 other moderate risk factor. (GRADE 1B)

Pregnant women aged 35 years or older have been found to be at increased risk for preeclampsia in several observational cohort studies. 3,8-10,12,13,21,31 The risk seems linear, with increasing age at the time of pregnancy leading to increased risk for hypertensive disorders of pregnancy. One large meta-analysis evaluating maternal and neonatal outcomes in women aged 35 years or 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. The increased risk remained even when controlling for preexisting conditions independently associated with preeclampsia such as hypertension and diabetes mellitus.

A retrospective cohort study evaluating maternal outcomes of older-aged pregnant women used the age of 35 to 39 years for the referent group for comparison with pregnant women aged 40 years and older. 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 to 44 years (RR, 1.32; 95% CI, 1.25–1.4)

and more than doubled for pregnant women aged 45 to 59 years (RR, 2.21; 95% CI, 1.89–2.58). Consistent with other studies, within each age group adverse outcomes increased relative to 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; I250%), preterm birth (pooled RR, 0.80; 95% CI, 0.67–0.95; 13 studies; I2549%), small for gestational age neaontes or fetal growth restriction (RR, 0.82; 95% CI, 0.68–0.99; 16 studies; I2541.0%), and perinatal mortality (pooled RR, 0.79; 95% CI, 0.66–0.96; 11 studies; I250%) 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/d), ideally between 12 and 16 weeks of gestation, continued daily until delivery in individuals at high risk for preeclampsia. The USPSTF determined that age of 35 years or older is a moderate risk factor for developing preeclampsia. Therefore, individuals with pregnancies at the age of 35 years or older who have at least 1 high-risk factor or at least 1 additional moderate-risk factor qualify for low-dose aspirin therapy. 32-34 Other moderaterisk factors include nulliparity, obesity (ie, BMI >30), family history of preeclampsia (ie, mother or sister), Black race (as a proxy for underlying racism), lower income, personal history factors (eg, low birthweight or small for gestational age neonates, previous adverse pregnancy outcome, >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 mellitus; 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 moderaterisk factors, regardless of 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, and not biological propensities. 32,34

Given the increased rates of multiple gestations for pregnant individuals with anticipated delivery at the age of 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.<sup>35</sup> Analysis of National Vital Statistics System (NVSS) data from 2018 demonstrates an increased rate of twin births with increasing

TABLE 1
Chromosomal abnormalities in second-trimester pregnancies according to maternal age at term<sup>a,b</sup>

	Trisomy 21	Trisomy 18	Trisomy 13	Sex chromosome aneuploidy (Obstetric Care Consensus, XY, XYY, 45, X)	Microarray or rare chromosomal abnormality	All chromosomal abnormalities
Age 20	8/10,000 1 in 1250	2/10,000 1 in 5000	1/10,000 1 in 10,000	34/10,000 1 in 294	37/10,000 1 in 270	82/10,000 1 in 122
Age 25	10/10,000 1 in 1,000	2/10,000 1 in 5000	1/10,000 1 in 10,000	34/10,000 1 in 294	37/10,000 1 in 270	84/10,000 1 in 119
Age	14/10,000	4/10,000	2/10,000	34/10,000	37/10,000	91/10,000
30	1 in 714	1 in 2500	1 in 5,000	1 in 294	1 in 270	1 in 110
Age	34/10,000	9/10,000	4/10,000	35/10,000	37/10,000	119/10,000
35	1 in 294	1 in 1111	1 in 2,500	1 in 285	1 in 270	1 in 84
Age	116/10,000	30/10,000	14/10,000	51/10,000	37/10,000	248/10,000
40	1 in 86	1 in 333	1 in 714	1 in 196	1 in 270	1 in 40

Data from

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Modified from American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics et al. 41

<sup>a</sup> Not all chromosomal abnormalities increase with maternal age;; <sup>b</sup> Copy number variants are independent of maternal age at pregnancy.

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age of the pregnant woman, from 17.1 per 1000 births in individuals younger than aged 20 years to as high as 51.1 per 1000 births in individuals aged 40 to 54 years. 35 Women aged 30 to 39 years have a rate of twinning double that of individuals younger than aged 20 years, and those aged older than 40 years have a rate of twinning that is triple that of women aged younger than 20 years.<sup>35</sup> 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 NVSS data. A retrospective cohort study from Belgium (N=41,618) similarly demonstrated 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 or older).36

There is an increased risk of 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 (Multifetal Gestations: Twin, Triplet, and Higher-Order Multifetal Pregnancies) provides an in-depth review of multifetal pregnancy, including the associated risks, complications, and management.<sup>37</sup>

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 because of 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 use, 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 with maternal age. In comparison, the use of young donor eggs yielded similar live-birth rates regardless of maternal age at the time of pregnancy.<sup>38</sup>

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

Thus, although aneuploidy is not exclusive to individuals aged 35 years or older, pregnant individuals should be aware that aneuploidy risk increases with age. Clinicians should be prepared to discuss options and availability of prenatal tests, both screening and diagnostic. If available, a genetic counselor may offer additional information regarding aneuploidy risk and options for carrier screening. All Regardless, the decision to test and the decision to pursue a specific test should be shared between the clinician and patient according to patient values and test availability, regardless of cost.

We suggest a detailed fetal anatomic ultrasound examination for pregnant individuals with anticipated delivery at the age of 35 years or older or older given the increased risk of aneuploidy. (GRADE 2C)

Early studies suggest that the 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 the age of 35 years or older. 42-45 More recent studies have conflicting results and challenge the assumption that the 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 or older than in 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 of 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

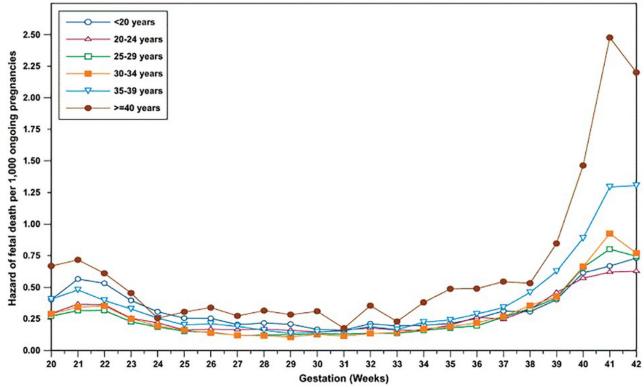
Using smaller data sets, other recent studies have not demonstrated lower rates of nonchromosomal-related fetal structural anomalies in pregnant individuals aged 35 years or older. These studies have demonstrated similar rates of such anomalies across all age groups of pregnant women. <sup>28,46,48</sup> Pregnant individuals aged 35 years or 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 in Medicine in the setting of maternal age of 35 years or older. However, it is worth noting that the increased risk in congenital malformations at the time of anatomic survey may be less than historically observed on the basis of 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 neonates are more common with increasing maternal age. In a prospective cohort study of 11,328 deliveries in Spain, rates of macrosomia increased progressively, reaching 12% in women younger than age 35 years, 12.6% in women aged 35 to 39 years, and 15.4% in women aged 40 years or older. Similarly, the rate of small-for-gestational-age neonates increased across the same age categories (14.0%, 15%, and 17.4%, respectively). The association between abnormal birthweight and age 40 years or older remained significant after adjustment for tobacco use, gestational diabetes mellitus, and hypertension, with odds ratios (ORs) of 1.29 (95% CI, 1.04–1.59) for small-forgestational-age and 1.27 (95% CI, 1.01–1.59) for large-forgestational-age. So





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In a retrospective cohort study (N=41,618), rates of birthweight <2500 g increased with maternal age, with groups aged 25 to 34 years (6.7%), 35 to 39 years (6.9%), 40 to 44 years (10.0%), and 45 years or 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 birthweight >4500 g with increasing age, observed in groups aged 25 to 34 years (0.72%), 35 to 39 years (1.14%), and 40 to 44 years (1.17%), with a slight decrease in prevalence at 45 years or older (0.95%). Similarly, a retrospective cohort study using NVSS data demonstrated an increase in small-forgestational-age neonates (birthweight <5%ile) in women aged older than 40 years.

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

Although growth ultrasonograms may already be performed in clinical practices given the associated birthweight 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 on the basis of other comorbidities or pregnancy complications.

We suggest offering antenatal fetal surveillance to pregnant individuals with anticipated 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 1000 pregnancies that extended beyond 20 weeks of gestation. Rates were highest in older women: 10.1 stillbirths per 1000 births for women aged 40 to 44 years and 13.8 per 1000 births in women older than age 45 years. Notably, the association between stillbirth and age of the pregnant woman persisted with age of 35 years or 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 the risk of fetal death for ongoing pregnancies by gestational week and patient age.<sup>53</sup> In this data set, the risk of stillbirth increased with 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<sup>53</sup> (Figure). The risk of stillbirth at 37 to 41 weeks of gestation was 1 in 382 ongoing pregnancies for women aged 35 to 39 years, and 1 in 267 ongoing pregnancies for women 40 years and older.<sup>53</sup> The cumulative risk of stillbirth per 1000 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 to 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 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 >6.3 million singleton pregnancies. <sup>54</sup> 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 to 44 years at 39 weeks of gestation was comparable with the risk at 42 weeks in women aged 25 to 29 years. <sup>54</sup>

A study analyzing birth data from Scotland evaluated the association between age at the time of pregnancy and unexplained stillbirth from 1997 to 2003, using a referent group of women aged 20 to 24 years. Those aged 35 to 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 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 aged older than 40 years (aOR, 2.03; 95% CI, 0.63–6.52), which was 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 to 2004 (N=126,402) found that age of older than 40 years was associated with stillbirth at 28 to 31 weeks of gestation (aOR, 2.93; 95% CI, 1.76–4.92), 32 to 36 weeks of gestation (aOR, 1.73; 95% CI, 1.05–2.83), and 40 to 41 weeks of gestation (aOR, 2.28; 95% CI, 1.18–4.4). 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 of 35 to 39 years and stillbirth.

The benefit of antenatal fetal surveillance in reducing 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 still-birth. 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 RR or OR for stillbirth of more than 2.0 compared with pregnancies without the condition." According to this rationale, available data support offering antenatal fetal surveillance for pregnant individuals with anticipated delivery at the age of older than 40 years given the increased risk of stillbirth. However, for individuals aged 35 to 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 aged older than 40 years begins to increase at 34 weeks of gestation, with the greatest rise in risk occurring at ≥39 weeks of gestation. On the basis of data demonstrating a steady increase in the risk of stillbirth beginning at 33 weeks of gestation (Table 1) and existing studies that initiate fetal surveillance between 32 and 36 weeks of gestation, 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 because of 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 aged older than 40 years, were included in this targeted intervention of earlier induction of labor. <sup>64</sup> Other studies have been underpowered to detect a difference in stillbirth. <sup>4</sup>

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 aged older than 40 years (adjusted RR, 1.24; 95% CI, 1.01–1.52 at 40 weeks of gestation).

One randomized controlled trial specifically evaluated the effect of induction of labor compared with that of expectant

TABLE 2 Comparison of outcomes between planned elective cesarean delivery and planned vaginal delivery among women aged 35 years 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)
CL confidence interval			

Cl. confidence interval

Modified from Lavecchia et al. 95 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,

Committee on Clinical Consensus—Obstetrics, Society for Maternal-Fetal Medicine. Pregnancy at age 35 years or older. Am J Obstet Gynecol 2023.

management on the rate of cesarean delivery in women aged 35 years or 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 intrapartum 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 6106 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.<sup>67</sup> In a prespecified 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 that of women aged 25 to 29 years at >41 weeks of gestation. 53,54 Therefore, delivery in well-dated pregnancies at ≥39 weeks of gestation 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 to 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 NVSS 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 to 39 years and nearly 48% for women aged older than 40 years.<sup>69</sup> 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 to 39 years and 45 to 49 years, respectively. 70 A large retrospective study of 1.3 million births in California demonstrated a similar stepwise increase, with a cesarean delivery rate of 40.5% in women aged 35 to 39 years, 47.3% in women aged 40 to 44 years, 55.6% in women aged 45 to 49 years, and 62.4% in women aged 50 years and older.<sup>29</sup> 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 to 34 years (8.9%), 35 to 39 years (15.2%), 40 to 44 years (17.8%), and 45 years or older (27.3%).36 A 2010 systematic review identified 21 studies with ORs between 1.39 and 2.76 for the association between age of 35 years or older 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 morbidity. A retrospective cohort study using data from the Healthcare Cost and Utilization Project Nationwide Inpatient Sample compared outcomes of women aged 35 years or older who had a planned primary elective cesarean delivery with those of women 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). 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 obstetrical care professionals be aware of the disproportionate rates of most adverse maternal and perinatal outcomes in Black, American Indian, and Alaska Native pregnant individuals aged 35 years or older. We recommend that they understand the ways in which 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 of those who identify as non-Hispanic White. 15 The top 5 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 to 39 years and 3.6 for women aged 40 vears and older. 16

Similarly, fetal outcomes including preterm birth (both spontaneous and iatrogenic), small for gestational age neonates, 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 (10.7/1000 live births and 7.9/1000 live births, respectively) is double the rate of 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 the effect of 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 or 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 suggested 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 remain lower in Hispanic 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, and 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 obstetrical 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 antiracist policies and practices within their healthcare systems and follow an antiracist framework when conducting research.

## **Further research**

The definition of advanced maternal age (35 years or older) has led to research that, in many instances, dichotomizes patient age to younger than 35 years and 35 years or older. As demonstrated in numerous observational studies, agerelated 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 40 years or older or 45 years or older. Future research should clearly delineate risk by age category to allow evidence-based recommendations for individuals within a specific age range 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, American Indian, and Alaska Native populations). Previous 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.

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All American College of Obstetricians and Gynecologists (ACOG) Committee members and authors have submitted a conflict of interest disclosure statement related to this published product. Any potential conflicts have been considered and managed in accordance with ACOG's Conflict of Interest Disclosure Policy. The ACOG policies can be found on acog.org. For products jointly developed with other organizations, conflict of interest disclosures by representatives of the other organizations are addressed by those organizations. The ACOG has neither solicited nor accepted any commercial involvement in the development of the content of this published product.

All authors and committee members have filed a disclosure of interests delineating personal, professional, business, or other relevant financial or nonfinancial interests in relation to this publication. Any substantial conflicts of interest have been addressed through a process approved by the Society for Maternal-Fetal Medicine (SMFM) Board of Directors. SMFM has neither solicited nor accepted any commercial involvement in the specific content development of this publication.

This document has undergone an internal peer review through a multilevel committee process within SMFM. This review involves critique and feedback from the SMFM Publications and Document Review Committees and final approval by the SMFM Executive Committee. SMFM accepts sole responsibility for the document content. SMFM publications do not undergo editorial and peer review by the American Journal of Obstetrics & Gynecology. The SMFM Publications Committee reviews publications every 18 to 24 months and issues updates as needed. Further details regarding SMFM publications can be found at <a href="https://www.smfm.org/publications">www.smfm.org/publications</a>.

The Society for Maternal-Fetal Medicine (SMFM) recognizes that obstetric patients have diverse gender identities and is striving to use gender-inclusive language in all of its publications. SMFM will be using terms such as "pregnant person/persons" or "pregnant individual/individuals" instead of "pregnant woman/women" and will use the singular pronoun "they." When describing study populations used in research, SMFM will use the gender terminology reported by the study investigators.

# **Appendices**

# Supplemental digital content

- A. Literature search strategy: http://links.lww.com/AOG/ C770
- B. Evidence Map: http://links.lww.com/AOG/C771

GRADE of recommendation	Clarity of risk and benefit	Quality of supporting evidence	Implications	Suggested language
1A. Strong recommendation, nigh-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> <li>We strongly recommend.</li> <li>We recommend that.should be performed or administered.</li> <li>We recommend that.is indicated, beneficial, or effective.</li> </ul>
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> <li>We recommend.</li> <li>We recommend that should be performed or administered.</li> <li>We recommend that is (usually) indicated, beneficial, or effective.</li> </ul>
1C. Strong recommendation, ow-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> <li>We recommend.</li> <li>We recommend that should be performed or administered.</li> <li>We recommend that is (perhaps) indicated, beneficial, or effective.</li> </ul>
GRADE of Recommendation	Clarity of Risk and Benefit	Quality of Supporting Evidence	Implications	Suggested Language
2A. Weak recommendation, nigh-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> <li>We suggest.</li> <li>We suggest that it may or might be reasonable.</li> </ul>
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> <li>We suggest.</li> <li>We suggest that it may or might be reasonable.</li> </ul>

Consensus

GRADE of Recommendation	Clarity of Risk and Benefit	Quality of Supporting Evidence	Implications	Suggested Language
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> <li>We suggest it is an option.</li> <li>We suggest that it may or might be reasonable.</li> </ul>
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> <li>We recommend.</li> <li>We recommend that it should be performed or administered.</li> <li>We recommend that it is (usually) indicated, beneficial, or effective.</li> </ul>

Recommendations are classified as either strong<sup>1</sup> or weak,<sup>2</sup> and quality of evidence is classified as high (A), moderate (B), and low (C).<sup>99</sup> Thus, the recommendations can be one of the following six possibilities: 1A, 1B, 1C, 2A, 2B, 2C.

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