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Stillbirth

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Stillbirth, defined as fetal death at 20 or more weeks of gestation or 350 g or greater in birth weight, is a tragic outcome for families and clinicians.[1] Stillbirth affects approximately 5.7 per 1000 births in the US—equivalent to 21 000 annually—and can occur antenatally (83%) or intrapartum (17%).[2] This rate has remained relatively stable over the past 2 decades, despite substantial reductions in infant and childhood mortality.[3,4] Stillbirth prevention is complex because many cases of stillbirth are unexplained, and there are substantial disparities in incidence by geographic region, socioeconomic status, and maternal race.[5]

Supplemental content

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Causes and Risk Factors for Stillbirth

Although no etiology is found in up to 40% of stillbirths, there are numerous established risk factors and causal pathways.[2] The most common risk factors (with approximate stillbirth incidence per 1000 births extrapolated from odds ratios) include maternal chronic diseases like diabetes (stillbirths in approximately 14.3 of 1000 births) and obesity (9.7 of 1000), exposures like tobacco (9.1 of 1000), multiple gestation (14.3 of 1000), demographic characteristics including Black race (12.0 of 1000) and advanced maternal age (especially ≥40 years; 13.7 of 1000), and history of prior stillbirth (33.6 of 1000).[1,6]

Placental causes of stillbirth, attributed to 24% of cases, include placental insufficiency, a clinical diagnosis of inadequate placental supply to the fetus, which is associated with fetal growth restriction (estimated fetal weight less than the 10th percentile for gestational age), and placental abruption.[2,5] Umbilical cord occlusion related to cord knots, prolapse, or thrombosis cause approximately 10% of stillbirths.[2,5] Nearly 14% of stillbirths occur secondary to fetal genetic or structural anomalies.[2,5] Infection (ie, group B streptococcus, *Escherichia coli*, syphilis) causes 13% of stillbirths through several mechanisms: fetal infection leading to malformations or sepsis, placental infection causing placental insufficiency, or severe maternal infection.[2,5] Maternal medical conditions, particularly those that are severe or poorly controlled—including hypertensive disorders, pregestational diabetes, kidney disease, systemic lupus erythematosus, antiphospholipid antibody syndrome, thyroid disease, and intrahepatic cholestasis of pregnancy—are considered causative in approximately 17% of stillbirths.[2,5] Approximately 25% of stillbirths in the US are considered preventable.

The recommended evaluation after stillbirth includes fetal autopsy, placental pathology, fetal genetic testing (chromosomal microarray with or without karyotype), assessment for fetal-maternal hemorrhage (fetal bleeding into the maternal circulation), and maternal testing for antiphospholipid antibodies, hemoglobin A_{1c}, and syphilis if not performed during pregnancy.[1,5] Even with complete evaluation, the cause of stillbirth is determined in only 76% of cases.[2,5] It is also important to provide patients with appropriate bereavement and mental health support following stillbirth, given its strong association with depression, anxiety, and posttraumatic stress disorder (with 4% risk of an acute psychiatric event).

Prenatal Care to Prevent Stillbirth

Routine prenatal care integrates anticipatory guidance for normal pregnancy with mitigation of maternal risk factors and screening for potential adverse pregnancy outcomes such as stillbirth. Stillbirth prevention includes ultrasonography when abnormal fetal growth is suspected in the second and third trimesters, universal screening for gestational diabetes, and blood pressure monitoring to detect hypertensive disorders of pregnancy. These standard elements of prenatal care are recommended to all patients, regardless of risk profile.

A Dual Framework for Stillbirth Prevention

Risk stratification for stillbirth is difficult due to the numerous mechanisms for stillbirth, the high prevalence of risk factors, and the frequency of unexplained stillbirths. Nonetheless, obstetric clinicians use a 2-tiered prevention strategy in patients deemed to be at increased risk (**Table**). The first—or primary—level of prevention involves mitigating modifiable risks for stillbirth starting in the preconception period and continuing through pregnancy. These strategies include cessation of smoking and substance use, glycemic control (hemoglobin A_{1c} <7%) for patients with diabetes, blood pressure control (<140/90 mm Hg) for patients with hypertension, and weight management (goal pregravid body mass index <25 [calculated as weight in kilograms divided by height in meters squared]) (eTable in the Supplement). Additionally, low-dose aspirin to prevent preeclampsia and other adverse outcomes may be prescribed after 12 weeks of gestation for patients at high risk.[5] Primary prevention also involves optimizing delivery timing, which includes cautioning against continuing pregnancy past 42 weeks, consideration of elective, risk-reducing induction of labor for nulliparous patients at 39 weeks of gestation, and making recommendations for delivery before 39 weeks of gestation based on maternal comorbidities or fetal/placental complications, which are largely based on expert opinion.[1,8]

A secondary level of prevention involves identifying and interrupting ongoing pathways leading to stillbirth. This predominantly takes the form of antenatal physiologic testing, which most commonly includes nonstress tests (NSTs) and biophysical profiles (BPPs). NSTs and BPPs are assessments of fetal well-being using fetal heart rate monitoring and ultrasonography, respectively (Table).[1,5,7,9] Both can ascertain risk for fetal acidemia caused by inadequate blood flow and gas exchange across the placenta, which can lead to stillbirth if uninterrupted. Normal results of these tests are associated with a risk of approximately 0.1% of impending stillbirth related to placental insufficiency in the following week.[7] An abnormal result may indicate increased risk of impending stillbirth and should prompt either additional fetal monitoring or expedited

Table. Antenatal Testing and Risk of Stillbirth

Test	Description	Patient population	Abnormal result	Risk of stillbirth within 1 wk of normal result[7]
Nonstress test (NST)	Fetal heart rate monitoring for accelerations	Testing based on risk factors; ad hoc testing for acute concerns (ie, decreased fetal movement)	Nonreactive: <2 accelerations in 40 min	1.9/1000
Biophysical profile	Ultrasonography assessment of fetal breathing, movement, tone, and amniotic fluid, with or without NST	Testing based on risk factors; ad hoc testing for acute concerns (ie, decreased fetal movement)	≤6/10 (≥1 Component abnormal and nonreactive NST); 4/10 or less is highly abnormal	0.8/1000
Umbilical artery Doppler velocimetry	Doppler velocimetry of the umbilical artery performed in fetuses with growth restriction (estimated fetal weight or abdominal circumference <10th percentile for gestational age)	Testing in setting of fetal growth restriction	Elevated systolic:diastolic ratio >95th percentile for gestational age or absent or reversed end-diastolic flow	Not well quantified (risk of stillbirth if absent or reversed end-diastolic flow is approximately 20%)
Fetal movement awareness	Awareness of quantity and pattern of typical fetal movements	All pregnant patients >28 wk	Perceived decrease or <10 movements in 2 h	Not well quantified

(and possibly urgent) delivery, depending on the degree of abnormality and gestational age.

Expert consensus recommends NSTs and BPPs in the third trimester of pregnancy based on the presence of stillbirth risk factors.[10] Kick count, a maternal self-assessment of the volume or pattern of fetal movement in a designated period such as 2 hours, is a low-technology method to assess fetal well-being. Although pregnant individuals are typically asked about awareness of fetal movement as part of routine prenatal care, there is no universally accepted best practice to quantify fetal movement.[5] In addition, the limited trial data available do not support a reduction in stillbirth with routine fetal movement counting. However, pregnant individuals reporting decreased fetal movement after viability, around 22 weeks, should undergo prompt assessment to evaluate fetal well-being.

Given the low absolute risk of stillbirth (0.6%) and the limited data supporting the effectiveness of the prevention tools outlined here, it is important to incorporate patient preferences in clinical decision-making. Although surveillance with NSTs and BPPs may reduce risk of stillbirth, antenatal monitoring can cause anxiety, disrupt employment, and increase risk of unnecessary interventions including iatrogenic preterm birth. Equitable access to antenatal testing is important to prevent widening inequities in stillbirth incidence by socioeconomic status, geography, and health literacy.

Health systems can consider these patient-level factors as well as hospital resources in determining recommendations for antenatal testing, balancing the population-level goal of stillbirth reduction with risk-appropriate individual clinical recommendations and avoidance of overuse in low-risk patients. Developing evidence-based criteria for antenatal testing and delivery timing may help to minimize harm from stillbirth prevention efforts while maximizing benefit.

Conclusions

Modifying known maternal risk factors and utilizing risk-appropriate antenatal testing can help reduce the incidence of stillbirths. However, current approaches to preventing stillbirth are limited by the unexplained nature of many stillbirths and the difficulty identifying pregnancies at highest risk.

ARTICLE INFORMATION

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Submissions: The Women's Health editors welcome proposals for features in the section. Submit yours to linda.brubaker@jamanetwork.org.

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Supplemental Online Content

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eTable. Primary Prevention of Stillbirth

This supplemental material has been provided by the authors to give readers additional information about their work.

eTable. Primary Prevention of Stillbirth

Intervention Type	Examples
Medical optimization of chronic disease before and during pregnancy	Blood pressure control, glycemic control, weight management, control of other chronic disease (ie: autoimmune conditions, thyroid disorders, renal disease, obstructive sleep apnea)
Treatment of antiphospholipid antibody syndrome	Prophylactic or therapeutic anticoagulation based on history and low dose aspirin
Avoiding toxic exposures	Smoking and substance use cessation (particularly cocaine, amphetamines)
Prenatal supplementation and prophylaxis	All pregnancies: Prenatal vitamin with folic acid Preeclampsia risk factors: Low dose aspirin
Screening for fetal anatomic abnormalities or abnormal growth	Anatomic survey ultrasound in the second trimester with additional ultrasounds based on maternal/fetal risk factors
Screening for fetal genetic conditions	Routine screening for fetal aneuploidy (typically through cell free DNA technology) or diagnostic testing for fetal aneuploidy (chorionic villus sampling or amniocentesis)
Screening and management of pregnancy complications	Including maternal red cell alloimmunization, gestational diabetes, hypertensive disorders of pregnancy, intrahepatic cholestasis of pregnancy
Delivery timing	Late preterm or early term delivery based on risk factors, consideration of delivery at 39 weeks for low-risk patients, timely induction of post-term pregnancies (beyond 41 weeks)