



Reviews of Natural Infant Deaths Due to Prematurity

National Center Guidance Report

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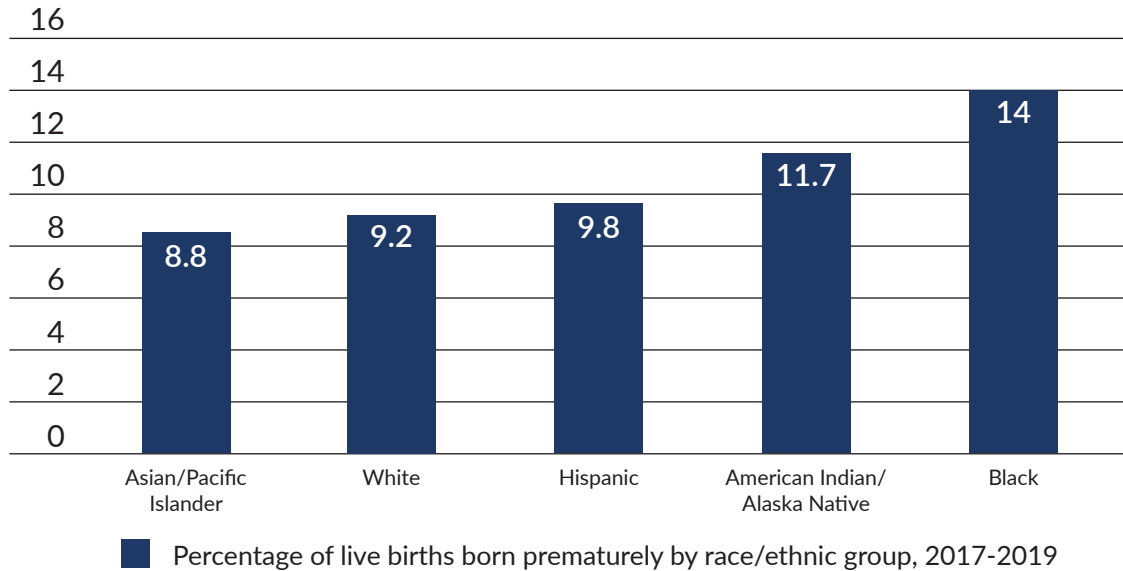
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Introduction and Scope of the Problem

Preterm birth, defined by the Centers for Disease Control and Prevention (CDC) as an infant born before 37 completed weeks gestation, is one of the most significant contributors to infant mortality. In 2020, preterm birth affected one of every ten infants born in the United States. Little progress has been made in the last several years. In fact, the preterm birth rate has increased from 9.6% in 2015 to 10.1% in 2020. Racial and ethnic differences in preterm birth rates persist. In 2020, the rate of preterm birth among Black, non-Hispanic persons (14.4%) was about 50 percent higher than the rate of preterm birth among white or Hispanic persons (9.1% and 9.8%, respectively).¹

In the United States, the preterm birth rate for Black birthing persons is 51% higher than the rate for all other birthing persons.



Preterm babies have a higher risk of complications that could lead to death within the first year of life. Their lungs and digestive systems are often not fully developed, and they face a higher risk of brain damage. More than one-third of US infant deaths are attributed to premature birth.² Infant gestational age is classified into these four categories:

Late preterm: Infants born between 34 – 37 weeks gestation

Moderately Preterm: Infants born between 32 – 34 weeks gestation

Very Preterm: Infants born between 28 – 32 weeks gestation

Extremely Preterm: Infants born less than 28 weeks gestation

Preterm newborns had a **3.8-fold higher risk of infant death** (17.9%) than term newborns (4.7%).³ Infants born very preterm and extremely preterm are at the greatest risk for medical complications and death.⁴



These numbers do not explain how to prevent these disparities and infant mortality attributable to preterm births. Effective review of preterm infant deaths by fatality review teams can lead to an increased understanding of the causes, contributors, and factors placing parents and families at risk for the tragedy of a loss due to prematurity. **This guidance is intended to support fatality reviews of natural infant deaths due to prematurity.**

Causes and Contributors

Preterm birth is a complex cluster of problems, often with overlapping factors of influence. The Institute of Medicine (United States) Committee on Understanding Premature Births has categorized causes of preterm birth into five categories which will be discussed further.⁵ They are:

1. Sociodemographic and community factors
2. Medical and pregnancy complications
3. Behavioral and psychosocial contributors
4. Gene-environment interaction
5. Environmental toxicants

Sociodemographic and Community Factors

Age

Birthing persons at both ends of the age spectrum are at an increased risk for preterm birth. Young age (giving birth at less than 16 years old) is associated with a twofold greater risk for preterm delivery than the risk for giving birth between 18 and 29.⁶ Giving birth over the age of 35 also increases the risk for preterm delivery, and the risk seems to be even higher among birthing persons over 35 years of age delivering their first-born child.⁷

Racism

Significant racial-ethnic disparities in preterm birth rates exist in the United States. Racial differences in socioeconomic condition, behaviors (including the use of prenatal care), stress, infection, and genetics do not fully account for the disparities. In 2017–2019, the March of Dimes convened a workgroup with biomedical, clinical, and epidemiologic expertise to review knowledge of the causes of the persistent Black-White disparity in preterm birth. Multiple databases were searched to identify hypothesized causes examined in peer-reviewed literature; 33 hypothesized causes were reviewed for whether they plausibly affect preterm birth and either occur more/less frequently and/or have a larger/smaller effect size among Blacks vs. Whites. **The study found that racism, as a chronic stressor, affected preterm birth through the body's physiologic response to stress (e.g., neuroendocrine, immune, inflammatory, and vascular mechanisms). It also identified risk was increased by cumulative physiologic wear and tear due to chronic stress associated with overcoming barriers to educational and occupational success.**⁸ In other words, racism and its effects significantly contribute to these disparities.

Community-level risk

Community factors, such as adverse neighborhood conditions, have a negative effect on the health of residents. Availability of goods and services such as grocery stores and recreational facilities, public safety, quality of housing, as well as poverty, presence of crime, and residential stability all play a role in contributing to socioeconomic disadvantage. Factors that affect the quality of the physical environment include toxicants, noise, water quality, and air pollution to which a pregnant person may be exposed.

Medical and Pregnancy Complications

Medical conditions

A number of medical conditions are associated with an increased risk of preterm birth. Examples of some of the most common medical problems that may lead to preterm birth are listed below:

Chronic hypertension	Hypertensive disorders of pregnancy
Systemic lupus erythematosus	Infection
Restrictive lung disease	Cardiac disease
Hyperthyroidism	Asthma
Pregestational diabetes and Gestational diabetes	Renal disorders

Any condition altering or limiting the placental delivery of oxygen and nutrients to the developing fetus could result in an early birth or fetal growth restriction. Preterm birth is strongly associated with periodontal disease (also called gum disease), infections that affect the urinary tract (kidney, bladder, ureters, and urethra), and genital or vaginal infections.

Weight

Being underweight pre-pregnancy has consistently been associated with preterm birth. Conversely, overweight and obese birthing persons also have increased risks of preterm delivery, especially extremely preterm delivery.⁹

Status and timing of previous pregnancies

One of the leading risk factors for preterm birth is a previous preterm birth. Timing of pregnancies, or interpregnancy interval, has been found by numerous investigators to play a role in preterm birth. Interpregnancy intervals are the time between the end of one pregnancy and the conception of another. Short (<12 months), very short (<6 months), and long (≥ 120 months) inter-pregnancy intervals have been found to be associated with increased odds of preterm birth. An interpregnancy interval of 18 to 23 months has the lowest preterm birth risk.¹⁰

Uterine overdistension plays a key role in the onset of preterm labor, associated with conditions such as multiple gestations, polyhydramnios (an excessive volume of amniotic fluid), and macrosomia (a newborn that is much larger than average, generally more than 4,000 grams or 8 pounds, 13 ounces).

Multiple gestations

Birthing persons carrying multiples (twins, triplets, or more) are at an increased risk for early delivery and other complications. Multiple gestations are more common with assisted reproductive technology than pregnancies that result from natural conception. This guidance document will not discuss assisted reproductive technology in detail. To learn more, read [Perinatal Risks Associated with Assisted Reproductive Technology](https://bit.ly/3EZohQ5) (URL: <https://bit.ly/3EZohQ5>).

Reproductive organ abnormalities

Two important additional medical conditions leading to preterm birth are implantation errors and vascular lesions of the placenta. The most commonly occurring placental implantation abnormalities are low-lying placenta and placenta previa. Low lying placenta is a placenta that ends very close to the cervical opening but does not cover it. Placenta previa is when a placenta completely or partially obstructs the cervix. Vascular lesions of the placenta are commonly associated with preterm birth and preterm premature rupture of membranes (PPROM)—when the membranes rupture before the onset of labor at a gestational age before term. The proposed mechanism linking vascular lesions to preterm birth is related to uteroplacental ischemia.¹¹

Lastly, birthing persons with specific abnormalities of the reproductive organs are at greater risk for preterm labor and birth than persons who do not have these abnormalities. It has been shown that a shortened cervix is a powerful indicator of preterm births in singleton and twin gestations. The shorter the cervical length, the higher the risk of spontaneous preterm birth.¹²

Behavioral and Psychosocial Contributors

Substance use

Cigarette smoking is among the most prevalent, preventable causes of prematurity and adverse pregnancy outcomes. Smoking is strongly related to placental abruption, reduced birth weight, and infant mortality.¹³ High levels of alcohol during pregnancy, defined as four or more drinks during a single occasion (binge drinking) or more than eight drinks a week, can have adverse effects on fetal development. There is consistent support for a negative impact for heavier users of alcohol. For example, birthing persons who have more than one drink per day, on average, have an increased risk of preterm birth. Substance use before and during pregnancy has been linked repeatedly to adverse birth outcomes, including preterm birth. Birthing persons with reported drug abuse/dependence during pregnancy were at increased risk of having a preterm birth. All but those using cannabis were at risk of having an early-term delivery. Cocaine use and polysubstance use were at the highest risk of birth at < 32 weeks.¹⁴

Nutrition

Nutritional deficiencies (e.g., iron, folic acid, zinc, vitamin D, calcium, magnesium, and imbalances of ω -3 and ω -6 polyunsaturated fatty acids) and inadequate intake of nutrient-dense foods are associated with preterm birth.¹⁵



Employment and activity

The impact of employment on preterm birth is difficult to determine. Factors such as the socioeconomic conditions in the geographic location, the nature of the work, and the implications that employed birthing persons are more likely to have economic resources and access to medical care make it difficult to draw inferences that employment is a risk factor for preterm birth. One study has found that among pregnant persons who worked, a moderate excess risk was observed for those working more than 42 hours a week, standing for more than six hours a day, and for those with low job satisfaction.¹⁶ Jobs involving increased squatting and lifting, or overnight shifts have also been associated with early delivery. Recreational or leisure physical activity (not intense physical activity) has the potential to be a protective factor in reducing the risk of preterm birth. One study has found that the longer in pregnancy the activity continues, the lower the risk for preterm birth.¹⁷

Stress

Stress can be defined as any type of change that causes physical, emotional, or psychological strain. Stress is the body's response to anything that requires attention or action. Psychosocial stress involves life demands that may strain or exceed a person's adaptive resources and can result in biological or psychosocial responses (fight or flight) that may compromise health. Considerable research links stress to preterm birth through stress-induced physiological mechanisms, including inflammation, immune dysregulation, and effects on behaviors.¹⁸ Stress during pregnancy can cause the release of increased levels of catecholamines and cortisol, which could prematurely activate placental corticotropin-releasing hormone, thereby precipitating the biological cascade leading to the onset of preterm labor. Extensive research indicates that social support can buffer the negative effects of stress, thereby protecting against poor health outcomes, including preterm birth.¹⁹

Significant life events

“Life events” are significant events that occur throughout an individual’s life, such as divorce, death, or illness of a close family member, getting a new job, or losing a job. More recently, scientists have been looking into childhood adversity or ACEs (Adverse Childhood Experiences) and linking them to risk for preterm birth.²⁰

Mental health disorders

Recent studies suggest that anxiety may be a potentially important risk factor for preterm birth. Depression has been repeatedly associated with preterm birth. Elevated depression levels, particularly in early- to mid-pregnancy, appear to increase the risk of preterm birth and a small for gestation (low birth weight) infant.²¹

Intimate partner violence

Intimate partner violence (IPV) can directly affect the growing fetus through physical or sexual trauma or indirectly due to increased stress, inadequate nutrition, and poor prenatal care. IPV is a pattern of assaultive and coercive behavior that may include physical injury, psychological abuse, sexual assault, progressive isolation, stalking, deprivation, intimidation, and reproductive coercion.²² Abuse starts in pregnancy for one in six birthing persons, with more than 320,000 reports of abuse by an intimate partner during pregnancy each year.²³ Researchers have recently concluded that intimate partner violence doubles the risk of preterm birth and low birth weight birth.²⁴

Pregnancy intention

The term *unintended* refers to those pregnancies that are unwanted or mistimed (i.e., they occur earlier than desired). Generally, pregnancy intendedness is measured by self-report by using standard survey questions that can distinguish between whether a child was wanted now, not now but at some point (mistimed), or not at all (unwanted). Since these questions are often answered after conception, there may be retrospective bias. Nearly half (45%) of the 6.1 million pregnancies in the US each year are unintended.²⁵ The public health impact of unintended pregnancy is considerable: birthing persons who carry an unintended pregnancy to term are more likely to delay prenatal care, use alcohol and tobacco, and experience low infant birth weight, preterm birth, and maternal morbidity and mortality.²⁶

Gene environment

Several observations indicate that genetic differences contribute to the risk of preterm birth. **Birthing persons born preterm or who have a family history of preterm birth are more likely to deliver early.**²⁷ Familial and intergenerational influences on preterm birth may be attributable to shared environmental factors, genetic factors, or both. In one large genome-wide association study of 43,568 birthing persons of European ancestry, six gene variants were found to be associated with risk for preterm birth. The genes were involved in a range of functions, including uteroplacental circulation, development of the female reproductive system, cell energy and metabolism, endocrine, vascular and metabolic functions, and inflammatory response.²⁸ More research is needed to tease out the epigenetic effect from environmental exposures and chronic stress associated with socioeconomic hardship as plausible contributors to preterm birth.

Environmental toxicants

Where families live and work may also increase the risk of preterm birth. Air pollution, water quality, exposure to agricultural chemicals, environmental tobacco smoke, dioxin, and lead have been extensively studied. Multiple studies have found that birthing persons who live in an area with high levels of air pollution are more likely to deliver early than those who live in less polluted areas.²⁹ Residential proximity to highways was also found to be related to the risk for preterm birth.³⁰

It cannot be understated that there is a disproportionate burden of environmental pollution on poor people and persons of color. Racial residential segregation, a consequence of racism at structural and interpersonal levels, is associated with social and economic disadvantage and environmental toxicity. Black and brown people are significantly more likely to experience toxic exposures (e.g., air, traffic, water, industrial) linked to preterm birth.³¹



Preparing to Review Cases

Fatality review leaders should consider the needs of the fatality review team that are unique to deaths related to preterm birth. The records available in these cases are likely to be more medically dense. With training, team members will be prepared to review deaths that contain more medical information.

Consider Unconscious Bias and Health Equity

Fatality review teams obtain information to provide context on the death of an unborn baby, infant, or child. Social factors such as geography, access to education, experience with discrimination, trauma (including historical trauma), and access to physical and behavioral healthcare can contribute to premature mortality. Residential, educational, and occupational segregation impacts access to high-quality education, employment opportunities, healthy foods, and physical and behavioral health care. Combined, these structural inequities have long-lasting health impacts, including adverse birth outcomes and infant mortality.

The fatality review process is not a time to assign blame for poor outcomes, even if there were behavioral contributors that increased risk. Rather, it is an opportunity to determine how systems-level factors influence families' options, access, and behaviors.

Case review teams should provide an opportunity for members to consider how unconscious bias may contribute to assumptions in case review with every case, regardless of the cause of death. A tool for recognizing bias and discriminating in medical and social service records is available at: https://ncfrp.org/wp-content/uploads/FIMRTools-Recognizing-bias-in-records-abstraction_TipSheet.pdf (URL: <https://bit.ly/3P8y6iZ>)

Educate Team Members

Before holding a review of infant deaths due to prematurity, it may be helpful to educate review team members on some of the common causes and contributors to preterm births. Having accurate information about the condition of the infant and the factors contributing to a death will ensure team members all understand the case in the same way. Non-medical team members will benefit from an overall understanding of the common terms, prevalence, and expected outcomes. Consider providing team members with fact sheets, using information from reliable sources, such as the CDC or a state or local health department. The March of Dimes has extensive information for the US and state-specific “report cards” that explore key indicators on preterm birth, measures on infant mortality, and social drivers of health. To access the report cards, go to: <https://www.marchofdimes.org/mission/reportcard.aspx>. (URL: <https://bit.ly/38G4jgY>)

Convene the Right Partners

Typically, membership on a Fetal and Infant Mortality Review (FIMR) case review team will include obstetricians, midwives, doulas, pediatricians, nurses, social workers, public health professionals, child welfare, home visitors, and many disciplines who care for and touch the lives of childbearing parents and families. Core members of Child Death Review (CDR) teams usually include representatives from law enforcement, child protective services, prosecutor/district attorney, medical examiner, public health, pediatrician, and emergency medical services. To examine cases involving preterm birth, teams may want to consider adding a variety of review members with added expertise, such as:

- Racial & ethnic consumer advocacy groups
- Perinatologists, or Maternal Fetal Medicine specialists
- Infectious disease specialists
- Neonatologists
- Perinatal bereavement professionals
- March of Dimes
- Health plans

Review to Improve and Prevent

The goal of fatality review teams is to recommend and implement prevention strategies based on in-depth, multidisciplinary case reviews of deaths. In cases where an infant or child dies due to an injury, prevention strategies may seem straightforward. Still, preterm birth is the result of a complex cluster of problems, often with overlapping factors of influence. It can be challenging for teams to determine why a preterm birth and subsequent infant death occurred. This can complicate the process of making recommendations. **In these instances, teams should consider what factors may have increased risk, even if there is no direct causal relationship between risk factors and outcomes.**

Regardless of whether a team determines that an infant death that was due to prematurity could have been prevented, it is important to focus on what services were, or should have been, available to families and if there were ways service delivery and care could be improved in these instances.

Whether a team determines a specific death could have been prevented or not, the review process is an opportunity to learn about service systems in these cases. Team findings can meaningfully contribute to continuous quality improvement in the systems that serve all families.

Prioritize the Family Experience

Even the most committed care provider cannot speak on behalf of a family. Analyzing and abstracting available records provides only part of the story. Teams may want to consider engaging with partners who serve birthing persons and infants born preterm, asking them to help the team consider what the family may have experienced through the pregnancy, birth, and death of the child.

An important feature of the FIMR model is the inclusion of parental interviews. They should be attempted in all case reviews of infants dying from prematurity. The parental interview will inform the team about navigating care and referral systems, what aspects are working well, and what family needs remain unmet.

Data Collection

The National Fatality Review Case Reporting System (NFR-CRS) is a web-based data system that allows for data entry and provides standardized data reports and basic data visualizations. The National Center offers consistent technical support to equip fatality review teams to collect standardized case review information to drive prevention. The NFR-CRS collects variables on birthing parents, risk factors, socioeconomic and demographic factors, environmental factors, and life stressors that may have played a role in an infant death due to prematurity. This information is gathered through a rigorous abstraction process of relevant case records and, for FIMR, through a parental interview. NFR-CRS data should be used in conjunction with other data sources.

Other Data Sources

These additional data sources can provide regional, population-level data on preterm birth. Fatality review teams and their partners often choose to examine fatality review findings and data alongside population-level statistics to have a clear understanding of the overall burden of poor outcomes as well as the rich information collected through multidisciplinary case reviews. Examples of population-level data available at the state level include:

- Vital records (includes all live births and fetal deaths)
- Census data (consists of all people or households)
- The Census Bureau's American Community Survey (represents all people or households)
- Pregnancy Risk Assessment Monitoring (*PRAMS*—represents all live births)
- Behavioral Risk Factor Surveillance System (*BRFSS*—represents adults)

CDC's Division of Reproductive Health is engaged in various research and science-to-practice activities aimed at understanding and reducing preterm birth. CDC scientists collaborate with many partners, including state health departments, university researchers, and other health care professionals to understand why preterm births occur and what can be done to help prevent them. <https://www.cdc.gov/reproductivehealth/maternalinfanthealth/pretermbirth.htm>

March of Dimes Peristats provides access to maternal and infant health data for the US and by state or region, including more than 60,000 graphs, maps, and tables. National and state summaries on preterm birth focus on prevalence, causes and contributors, helping families connect to services and support, and educating communities. <https://www.marchofdimes.org/peristats/ViewTopic.aspx?reg=99&top=3&lev=0&slev=1>

Diagnostic Tests

The goals of diagnostic evaluation are to detect the conditions that predispose a pregnant patient to premature labor and determine the most effective course of treatment and prevention. Diagnostic tests should include an evaluation of the fetus's condition so that it can be determined whether there is a need to deliver the baby.

Pelvic Examination

A pelvic exam will allow the provider to determine how much a pregnant patient's cervix has opened and thinned. An assessment can be performed to find out how far the baby has moved down the birth canal. The exam can also check for leaking fluid in the vagina, which may indicate that the amniotic sac has ruptured.



Ultrasound or Transvaginal Ultrasound

An ultrasound creates pictures of the fetus. A transvaginal ultrasound is an internal scan of the female reproductive organs. It involves inserting a small ultrasound probe, called a transducer, into the vagina to produce incredibly detailed images of the organs in the pelvic region. Transvaginal ultrasonography may help predict patients at risk for spontaneous preterm birth at < 35 weeks' gestation.³²

Monitoring Contractions

If a pregnant patient thinks they are having contractions, a provider may use a tocodynamometer, an instrument that measures the force of uterine contractions, to determine the regularity, frequency, and force of contractions which may indicate preterm labor.

Fetal Fibronectin Screening

Fetal fibronectin is a protein that helps the amniotic sac stay attached to the uterine lining. The protein begins to break down as the body prepares for birth, so detecting the presence of fetal fibronectin in vaginal discharge in the second and third trimesters of pregnancy may indicate an increased risk of preterm labor. To test for fetal fibronectin, a provider will swab the cervix and test the secretions for the protein.





Records Needed

The following is a list of records typically needed to effectively review deaths related to preterm birth. Whether records will be available at the review meeting through the various participating CDR members or records are abstracted in advance by the FIMR staff and put into a de-identified case summary, these are the critical sources of information needed:

- Birth certificate
- Health records of the birthing person, including:
 - Preexisting health conditions
 - Prenatal care records (OB/GYN history, past pregnancies)
 - Labor and delivery records (antepartum, delivery, postpartum)
 - Emergency department records (birthing person's visits to ED during pregnancy)
 - Relevant lab results
 - Placental pathology
- Infant health records for:
 - Newborn/NICU care
 - Well and sick visits
 - Immunizations
- Social work consults, inpatient and outpatient
- Any support services utilized, including WIC and Family Planning
- Mental health records and services
- Substance use disorder records and services
- Home visitation service summaries
- Parental/family interview, if available
- Insurance coverage
- Death certificates

Key Questions to Ask During the Review Meeting

Because risk factors for infant deaths related to prematurity are multifaceted, with overlapping factors of influence, fatality review teams may need to ask different questions during these case reviews. Teams should carefully examine the family medical history, including stressors and exposures the birthing person may have encountered before or during pregnancy. Teams may choose to use the following questions to understand the case better and capture all the pertinent data with an eye toward prevention.

- Is there a detailed family history?
- Consider the pregnancy history of recurrent miscarriages or other early pregnancy losses, including previous preterm births. Do the biological parents or other family members have medical problems, such as hypertension, diabetes, or cardiovascular disease?
- Consider the personal medical history of the birthing person.
 - Was there a history of previous preterm birth?
 - Were there exposures to environmental toxins? Medications?
 - Were there any co-morbid conditions identified?
 - Was there identification of recent illnesses, including COVID-19?
 - Did the birthing person experience anxiety, depression, or other mental health concerns?
- If the birthing person had any medical conditions that may require special care during pregnancy, such as anemia, epilepsy, diabetes, or high blood pressure, was preconception and interconception care and counseling available?
- Was prenatal care comprehensive, acceptable, accessible, appropriate, and culturally responsive?
- Did prenatal care include assessing and providing services for risks due to sexually transmitted infections, substance use disorders, domestic violence, social support, housing, employment, and transportation?
- Were the family's mental health and stress issues identified and addressed?
- Were there any times when the family felt treated differently or unfairly in seeking and receiving care and services?
- Was there any bias identified in the provision of care and services?
- Were there adequate and appropriate resources in place to support the parents/family?
- Were there any services the family needed or could have benefited from that they could not access or receive?

Opportunities for Prevention

There is increasing evidence that a variety of interventions have the potential to prevent a large proportion of preterm births significantly and safely.³³ The goal of all interventions is not just to prolong pregnancy but rather to give the newborn infant the best chance of surviving with as few complications as possible. Depending on the particular clinical situation, the treatment of choice might be to prolong the pregnancy or deliver the baby. Early detection and diagnosis of preterm labor is critical to determine the best interventions and strategies. Preterm birth prevention strategies can be broken down into these broad categories: medical and non-medical interventions.

Medical Interventions

Preventing nonmedically indicated late preterm birth

There are medical indications in pregnancy for which evidence supports delivery versus expectant management in the early-term period. However, the risk of adverse outcomes is greater for babies delivered in the early-term period than neonates delivered at 39 weeks of gestation, including infant death. Multiple studies have shown increased rates of adverse long-term infant outcomes associated with late-preterm and early-term delivery compared with full-term delivery. ACOG and the SMFM have made the following recommendation: Nonmedically indicated delivery, including cesarean delivery, inductions of labor, and cervical ripening, should not occur before 39 0/7 weeks of gestation.³⁴

Progesterone supplementation

In birthing persons with a past history of preterm birth, progesterone has been shown to significantly reduce the risk of preterm birth.³⁵ Progesterone is the hormone responsible for uterine growth and prevention of contractions. Administered two ways, vaginal progesterone **may** help prevent preterm birth in birthing persons shown to have a short cervix on ultrasound imaging in mid-pregnancy. Progesterone injections are a kind of progesterone called 17 alpha-hydroxyprogesterone caproate (17P) and may be administered to persons with a singleton pregnancy and previous spontaneous preterm birth.

Tocolysis

Tocolysis is an obstetrical treatment to prolong gestation in patients who are experiencing preterm labor. This is achieved through the administration of medications that may inhibit contractions of uterine smooth muscle. The primary medicines used are beta-adrenergic receptor agonists, calcium channel blockers, magnesium sulfate, nonsteroidal anti-inflammatories, and oxytocin inhibitors.³⁶ The primary goal of tocolysis is to postpone premature delivery by 48 hours to allow pregnant patients to be transferred to a center specialized in the management of preterm deliveries and thus administer corticosteroids for the possibility of reducing neonatal organ immaturity.³⁷

Cerclage

When a weakened cervix starts to shorten and open too early in a pregnancy, it can cause late miscarriage or preterm birth. Cervical cerclage, also known as a cervical stitch, is a treatment for cervical weakness that uses sutures or synthetic tape to reinforce the cervix. Recent research shows us that after cerclage was placed in patients with a previous preterm delivery, 69% of the successive pregnancies delivered at term (>37 weeks), and 17% delivered between 28-37 weeks. In general, with a singleton pregnancy, the overall success rate for cervical cerclage is 80%.³⁸ However, cerclage was associated with higher rates of fever, vaginal discharge, and vaginal bleeding, together with a significant increase in delivery by Cesarean section.

Induction of lung maturation with corticosteroids

Corticosteroids are a class of drugs used to reduce inflammation in the body by reducing the production of certain chemicals. Administration of corticosteroids to a pregnant person prior to an anticipated preterm birth is one of the most effective therapies available to improve newborn outcomes.³⁹ Corticosteroids help accelerate fetal lung maturation by increasing surfactant production in the fetal lungs, which increases the pulmonary artery blood flow. It is important to note that this is a therapy and not a preventive measure. The use of antenatal steroids is a well-known treatment to reduce the risk of neonatal respiratory distress syndrome, a common cause of mortality and morbidity in premature infants.



Antibiotic Treatment

While there is plenty of evidence that infections are associated with preterm birth, studies are mixed on whether antibiotics are effective in preventing preterm birth.⁴⁰ Urinary tract infections, genital tract infections such as bacterial vaginosis, pyelonephritis, and appendicitis have been found to be related to preterm birth. However, the use of antibiotics to prevent and treat infections during pregnancy is different from the use of antibiotics prophylactically to treat preterm labor. The evidence concerning the use of antibiotics in preterm labor is inconsistent.⁴¹ Prevention with antibiotics after PPRM, preterm premature of the membranes, may increase the time from rupture to delivery, lower the risk of infection in the vagina and uterus, and reduce the risk of fetal infection.

Non-medical Interventions

Alleviate stress

A large case-control study recently investigated the effect of stress during pregnancy on the risk of preterm birth. The authors concluded that it was critical to identify and possibly alleviate the causes of and exposure to stress during pregnancy and try to decrease the preterm birth rate.⁴² The recommendations for reducing stress during pregnancy included eating healthy foods, getting plenty of sleep and exercise, and possibly cutting back on unnecessary activities. Relaxation activities like prenatal yoga or meditation are recommended. A strong support network is protective and can help reduce the effects of stress. The support network can include a partner, family, and/or friends. Home visitors connect families to needed health, mental health, child care, and other services and work with families to identify strategies for managing stress and social isolation.⁴³

Bed rest

There is no evidence supporting or disputing bed rest at home or in the hospital to prevent preterm birth. Although bed rest in the hospital or at home is used widely as the first step of treatment, there is no evidence that this practice is beneficial.⁴⁴

Two additional strategies have been widely adopted for preventing preterm birth:

- Managing health conditions and adopting healthy behaviors before becoming pregnant - or preconception care.
- Avoiding harmful substances and maintaining healthy behaviors during pregnancy. Tobacco use and tobacco exposure in birthing persons are key modifiable risk factors for infant death. There is compelling evidence to support a dose-response relationship between smoking in pregnancy and preterm birth. The more and the longer a birthing person smokes in pregnancy, the higher the associated morbidity and mortality.⁴⁵ Therefore, **any** reduction in tobacco use during pregnancy can help prevent preterm birth, including total abstinence.



Recommendations

The CDC recommends five specific strategies⁴⁶ to reduce the risk of preterm birth and complications:

- 1. Persons of childbearing age need access to preconception care services, including screening, health promotion, and interventions that will enable them to achieve high levels of wellness, minimize risks, and enter pregnancy in optimal health.**
- 2. Pregnant persons at risk for preterm delivery need to be identified and offered access to effective treatments to prevent preterm birth, such as those outlined in Opportunities for Prevention above.**
- 3. Discourage nonmedically indicated elective deliveries, especially before 39 0/7 weeks.**
- 4. Achieve optimal birth spacing and prevent unintended pregnancies.**
- 5. Visit a healthcare professional regularly. Anyone planning a pregnancy should be encouraged to see a health care provider and start prenatal care as soon as a pregnancy is confirmed.**

Fatality review teams can document findings and make recommendations based on case reviews. The following are some of the kinds of recommendations fatality review teams may make in cases of deaths of infants due to prematurity. Some of these recommendations may focus on prevention of poor outcomes, and others may focus on needed systems improvements identified in case reviews.



Improving Health Care Services

- **Prioritize** regular annual physicals or well check visits for persons of childbearing age
- **Ensure** all birthing persons have available preconception care (before pregnancy), interconception care (between pregnancies), and counseling
- **Improve** the quality of prenatal care to ensure that care is acceptable, accessible, appropriate, and culturally-sensitive
- **Ensure** all birthing persons have postpartum care options available that include contraception, pregnancy planning, and preconception care

- **Improve** local provider knowledge of preconception health care issues
- **Improve** emergency response and transport systems (risk-appropriate care)
- **Increase** vaccination rates for all children, persons planning a pregnancy, pregnant, and newly delivered persons
- **Foster** family support services, including evidence-based home visiting, to improve the social/psychological environment for birthing persons and families at risk
- **Encourage** all local providers' comprehensive assessment of and provision of services for risks due to STIs and substance abuse, including alcohol, smoking, intimate partner violence, depression, social support, housing, employment, transportation, etc.
- **Eliminate** barriers to adequate nutrition for birthing persons, education, and access to folic acid
- **Equip** birthing persons to manage chronic conditions like diabetes and obesity
- **Support** workplace safety regulations in the public and private sector
- **Support** environmental work to reduce pollution and exposure to chemicals in the environment and drinking water
- **Normalize** exploration of family health history
- **Prioritize** reproductive life planning
- **Invest** in trauma-informed smoking and alcohol cessation
- **Enhance** communication between providers and patients, focusing on health literacy and cultural differences
- **Streamline** referral processes
- **Develop** resource lists for families
- **Advocate** for parental, medical, and bereavement leave in the workplace
- **Standardize** bereavement support referrals

Strengthening Families and Communities

- **Implement** strategies to reduce implicit bias in health care settings
- **Strengthen** father involvement with families
- **Enhance** service coordination and systems integration
- **Create** reproductive social capital in communities
- **Invest** in community building and urban renewal
- **Develop** and distribute community resource directories to make consumers and providers aware of where to go for help and services
- **Provide** mentoring, support, outreach, and advocacy at the community level utilizing paraprofessionals, indigenous health workers, and faith-based initiatives
- **Develop** systems to provide transportation and childcare to those seeking prenatal care
- **Hold** forums to raise awareness of infant mortality issues among consumers, providers, and policymakers
- **Develop** local community/business/health care partnerships to broaden the number of community collaborators
- **Enhance** community education to include unplanned/unwanted pregnancy prevention, including teen pregnancy prevention services and early detection of signs and symptoms of preterm labor
- **Support** the building of health care facilities in underserved communities
- **Provide** accessible primary care focused on meeting the needs of marginalized individuals in the community

Conclusion

Preterm birth continues to be a leading cause of infant morbidity and mortality in the US. Around the world, an estimated 15 million babies are born too early every year. That is more than 1 in 10 babies. **Approximately 1 million children die** each year due to complications of preterm birth.⁴⁷ Many survivors face a lifetime of disability, including learning disabilities and visual and hearing problems. Effective review of fetal and infant deaths by fatality review teams can lead to an increased understanding of the causes, contributors, and factors placing parents and families at risk for the tragedy of a loss due to preterm birth.

Effective review of these cases requires preparation and education. Case review teams will need to consider the available data and the experiences of the families of children who die due to prematurity. Case review findings can inform valuable prevention efforts. Team recommendations can also catalyze improvements to the community and healthcare services that serve all birthing families.

Societal and community factors play an essential role in the risk for preterm birth. Adverse neighborhood conditions (e.g., residential segregation; concentrated poverty; high crime rates; lack of goods, services, and recreational activities; and lack of access to quality health care) and diminished opportunities (e.g., inferior education and employment; housing market discrimination; and low wages) contribute to the stress of communities and the pregnant people who live in them. Exploring broader social policies to improve the health of birthing persons, particularly in African Americans and other communities at high risk, could reduce preterm birth and associated disparities.⁴⁸



The National Center welcomes inquiries related to case reviews of infant deaths due to prematurity at info@ncfrp.org.

Resources

Centers for Disease Control and Prevention: <https://www.cdc.gov/reproductivehealth/maternalinfanthealth/pretermbirth.htm>

World Health Organization: <https://www.who.int/news-room/fact-sheets/detail/preterm-birth>

Society for Maternal-Fetal Medicine, Preterm Birth Tool Kit: <https://www.smfm.org/publications/231-smfm-preterm-birth-toolkit>

American College of Obstetricians and Gynecologists, Preterm (Premature) Labor and Birth: <https://www.acog.org/womens-health/faqs/preterm-labor-and-birth>

Support for Patients and Families, March of Dimes: <https://www.marchofdimes.org/complications/preterm-labor-and-premature-baby.aspx>

Premature Birth, Mayo Clinic: <https://www.mayoclinic.org/diseases-conditions/premature-birth/symptoms-causes/syc-20376730>

Strategies to Prevent Preterm Birth - NCBI - National Institutes of Health: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4237124/>

National Center Resources:

- Webinar: *Effective Review of Natural Infant Deaths*: <https://ncfrp.org/center-resources/archived-webinars/>
- Quick Look: *Infants Born Prematurely*: <https://ncfrp.org/center-resources/quick-looks/prematurity/>
- Health Equity Tool Kit: https://ncfrp.org/wp-content/uploads/NCRPCD-Docs/Health_Equity_Toolkit.pdf
- Enhancing Fatality Review with Lessons from Brain Science: https://ncfrp.org/wp-content/uploads/Brain_Science_Guidance_Jan2021.pdf
- National Fatality Review-Case Reporting System: <https://ncfrp.org/data/nfr-crs/>

Endnotes

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