#### INTERIM UPDATE





# **BSTETRIC CARE**

INTERIM UPDATE: This Obstetric Care Consensus is updated as highlighted to reflect updated supporting evidence regarding the spectrum of outcomes for infants born in the periviable period.

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#### Periviable Birth

ABSTRACT: Approximately 0.5% of all births occur before the third trimester of pregnancy, and these very early deliveries result in the majority of neonatal deaths and more than 40% of infant deaths. A recent executive summary of proceedings from a joint workshop defined periviable birth as delivery occurring from 20 0/7 weeks to 25 6/7 weeks of gestation. When delivery is anticipated near the limit of viability, families and health care teams are faced with complex and ethically challenging decisions. Multiple factors have been found to be associated with short-term and long-term outcomes of periviable births in addition to gestational age at birth. These include, but are not limited to, nonmodifiable factors (eg, fetal sex, weight, plurality), potentially modifiable antepartum and intrapartum factors (eg, location of delivery, intent to intervene by cesarean delivery or induction for delivery, administration of antenatal corticosteroids and magnesium sulfate), and postnatal management (eg, starting or withholding and continuing or withdrawing intensive care after birth). Antepartum and intrapartum management options vary depending upon the specific circumstances but may include short-term tocolytic therapy for preterm labor to allow time for administration of antenatal steroids, antibiotics to prolong latency after preterm premature rupture of membranes or for intrapartum group B streptococci prophylaxis, and delivery, including cesarean delivery, for concern regarding fetal well-being or fetal malpresentation. Whenever possible, periviable births for which maternal or neonatal intervention is planned should occur in centers that offer expertise in maternal and neonatal care and the needed infrastructure, including intensive care units, to support such services. This document describes newborn outcomes after periviable birth, provides current evidence and recommendations regarding interventions in this setting, and provides an outline for family counseling with the goal of incorporating informed patient preferences. Its intent is to provide support and guidance regarding decisions, including declining and accepting interventions and therapies, based on individual circumstances and patient values.

Approximately 0.5% of all births occur before the third trimester of pregnancy, and these very early deliveries result in the majority of neonatal deaths and more than 40% of infant deaths (1). When delivery is anticipated near the limit of viability, families and health care teams are faced with complex and ethically challenging decisions. Decision making often needs to adapt to changing clinical circumstances before and after delivery. This document describes newborn outcomes after periviable birth, provides current evidence and recommendations regarding interventions in this setting, and provides an outline for family counseling with the goal of incorporating informed patient preferences. Its intent is to provide support and guidance regarding decisions, including both declining and accepting interventions and therapies, based on individual circumstances and patient values.

#### Background

#### What is considered the periviable period?

Numerous terms have been used to refer to newborns delivered near the limit of viability whose outcomes range from certain or near-certain death to likely survival with a high likelihood of serious morbidities. A recent executive summary

of proceedings from a joint workshop sponsored by the Society for Maternal–Fetal Medicine, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), the Section on Perinatal Pediatrics of the American Academy of Pediatrics, and the American College of Obstetricians and Gynecologists, in which a diverse group of experts were invited to participate, defined *periviable birth* as delivery occurring from 20 0/7 weeks to 25 6/7 weeks of gestation (2). (For consistency and clarity in this document, gestational age summarized in weeks of gestation refers to the completed week of gestation and the next 6 days; for example, "24 weeks of gestation" refers to 24 0/7 weeks through 24 6/7 weeks of gestation and "before 24 weeks of gestation" refers to before 24 0/7 weeks of gestation.)

### • What is the spectrum of outcomes for infants born in the periviable period?

From the 1950s through 1980, newborn death was virtually ensured with delivery of an infant, even one that was appropriately grown, at or before 24 weeks of gestation (3, 4). It remains true in the present day that delivery before 23 weeks of gestation typically results in neonatal death (5–6% survival [5, 6]), and among rare survivors, significant morbidity is universal (98–100% [5, 6]). However, a recent study demonstrated that wide variation in practices exists regarding the initiation of resuscitation and active treatment at these very early gestational ages and that this variation explains some of the betweenhospital differences in survival and survival without impairment, particularly at 22 weeks and 23 weeks (6). At more advanced gestational ages, however, practices

and outcomes are more consistent across tertiary care institutions. A review of studies published over the past three decades reveals a progressive increase in the rate of survival for infants born at 22, 23, 24, and 25 weeks of gestation (Fig. 1) (5–11). Data published for newborns delivered in the United States, England, and Australia within the past decade have indicated rates of survival to discharge of 23-27% for births at 23 weeks, 42-59% for births at 24 weeks, and 67-76% for births at 25 weeks of gestation (5–7, 12). Long-term outcomes are summarized in Figure 2. A follow-up study of a cohort of infants born at 22-26 weeks of gestation in England in 2006 found a progressive decrease in the proportion of children at age 30 months with severe or moderate impairment (defined as cerebral palsy, blindness, profound hearing loss, or developmental quotient 2 SDs or more below the mean) with increasing gestational age at birth: 45% at 22-23 weeks, 30% at 24 weeks, and 17% at 25 weeks of gestation (13). Similarly, a recent systematic review found that the incidence of moderate-to-severe neurodevelopmental impairment among survivors at 4-8 years decreased progressively with each week gained in gestational age at birth: 43% at 22 weeks, 40% at 23 weeks, 28% at 24 weeks, and 24% at 25 weeks of gestation (10); notably, although the combined rate decreased, the rate of severe neurodevelopmental impairment alone did not decrease significantly with increasing gestational age in this study. In 2017, a study described survival and neurologic outcomes among more than 4,000 births from 2001 to 2011 that were between 22 weeks and 24 weeks of gestation at 11 centers in the United States. The authors reported that the rate

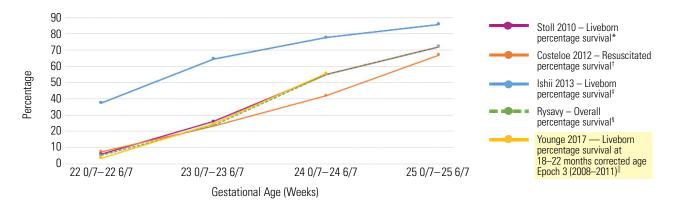


Figure 1. Percentage of survival by gestational age. ←

\*Stoll BJ, Hansen NI, Bell EF, Shankaran S, Laptook AR, Walsh MC, et al. Neonatal outcomes of extremely preterm infants from the NICHD Neonatal Research Network. Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. Pediatrics 2010;126:443–56.

<sup>†</sup>Costeloe KL, Hennessy EM, Haider S, Stacey F, Marlow N, Draper ES. Short term outcomes after extreme preterm birth in England: comparison of two birth cohorts in 1995 and 2006 (the EPICure studies). BMJ 2012;345:e7976.

‡Ishii N, Kono Y, Yonemoto N, Kusuda S, Fujimura M. Outcomes of infants born at 22 and 23 weeks' gestation. Neonatal Research Network, Japan. Pediatrics 2013;132:62–71.

§Rysavy MA, Li L, Bell EF, Das A, Hintz SR, Stoll BJ, et al. Between-hospital variation in treatment and outcomes in extremely preterm infants. Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. N Engl J Med 2015;372:1801–11.

Younge N, Goldstein RF, Bann CM, Hintz SR, Patel RM, Smith PB, et al. Survival and neurodevelopmental outcomes among periviable infants. Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. N Engl J Med 2017;376:617–28.

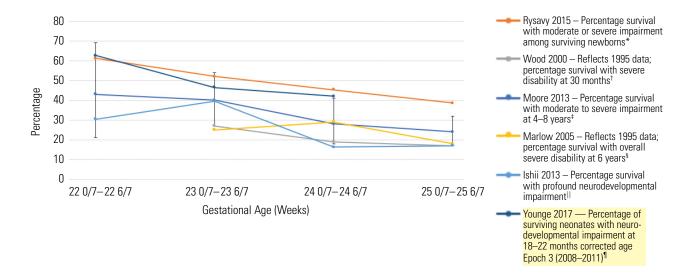


Figure 2. Percentage of surviving neonates with severe or moderate disability by gestational age.  $\Leftarrow$ 

of survival and survival without neurodevelopmental impairment increased over this period whereas the rate of survival with such impairment did not change, arguing that the observed overall increase in survival was not simply a tradeoff for life with significant impairment. The absolute change in survival without impairment was just 4%, however, and most neonates in the most recent 2008–2011 epoch died (64%) or were severely impaired (16%). Among those born at 22 0/7-22 6/7 weeks, death rates were 97-98% with just 1% surviving without neurodevelopmental impairment. In contrast from 2008 to 2011 at 24 0/7 weeks to 24 6/7 weeks of gestation, 55% of neonates survived and 32% survived without evidence of neurodevelopmental impairment at 18-22 months of corrected age. Overall, these data led the authors to conclude that "despite improvements over time, the incidence of death, neurodevelopmental impairment, and other adverse outcomes remains high" (14). In considering all these outcome studies, it also should be emphasized that although summary data often are grouped into segments of weeks, outcomes for deliveries at the extreme may be closer to those of the adjacent week than to those at the other extreme of the same week (eg, outcomes at 23 6/7 weeks may be more similar to those at 24 0/7 weeks than to those at 23 0/7 weeks of gestation).

#### **Clinical Considerations and Management**

What tools are available to obstetrician-gynecologists, other obstetric providers, and families to predict outcomes of periviable birth?

Because of the wide range of outcomes associated with periviable birth, counseling should attempt to include accurate information that is as individualized as possible regarding anticipated short-term and long-term outcomes. Nevertheless, it is important to realize that outcomes that have been reported in the medical literature may have some biases because of a variety of factors, including study inclusion criteria (eg, whether studies include all births or are limited to liveborn infants, nonanomalous newborns, liveborn resuscitated newborns, or neonatal intensive care unit [NICU] admissions only), variation in management between centers, and changes in NICU practices over time (eg, administration of antepartum steroids, resuscitative efforts, NICU admission criteria; see Table 1) (5, 9-11, 15-20). In addition, a precise understanding of outcomes in survivors is further confounded by differing definitions of "major" and "minor" disabilities used in studies.

Multiple factors have been found to be associated with short-term and long-term outcomes of periviable

<sup>\*</sup>Rysavy MA, Li L, Bell EF, Das A, Hintz SR, Stoll BJ, et al. Between-hospital variation in treatment and outcomes in extremely preterm infants. Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. N Engl J Med 2015;372:1801–11.

<sup>&</sup>lt;sup>1</sup>Wood NS, Marlow N, Costeloe K, Gibson AT, Wilkinson AR. Neurologic and developmental disability after extremely preterm birth. EPICure Study Group. N Engl J Med 2000;343:378–84.

<sup>&</sup>lt;sup>‡</sup>Moore GP, Lemyre B, Barrowman N, Daboval T. Neurodevelopmental outcomes at 4 to 8 years of children born at 22 to 25 weeks' gestational age: a meta-analysis. JAMA Pediatr 2013;167:967–74.

<sup>§</sup>Marlow N, Wolke D, Bracewell MA, Samara M. Neurologic and developmental disability at six years of age after extremely preterm birth. EPICure Study Group. N Engl J Med 2005;352:9–19.

Ishii N, Kono Y, Yonemoto N, Kusuda S, Fujimura M. Outcomes of infants born at 22 and 23 weeks' gestation. Neonatal Research Network, Japan. Pediatrics 2013;132:62–71.

Younge N, Goldstein RF, Bann CM, Hintz SR, Patel RM, Smith PB, et al. Survival and neurodevelopmental outcomes among periviable infants. Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. N Engl J Med 2017;376:617–28.

births in addition to gestational age at birth (Table 1). These include, but are not limited to, nonmodifiable factors (eg, fetal sex, weight, plurality), potentially modifiable antepartum and intrapartum factors (eg, location of delivery [21], intent to intervene by cesarean delivery [22] or induction of labor, administration of antenatal corticosteroids and magnesium sulfate), and life-sustaining interventions and postnatal management (eg, starting or withholding and continuing or withdrawing intensive care after birth).

Birth weight and gestational age, alone or in combination, often have been used as predictors of outcome and as criteria for offering resuscitation. However, in recognition of the effect of other clinical factors and in an attempt to create a better prediction tool, the NICHD Neonatal Research Network developed a tool to estimate outcomes among liveborn infants that was based on prospectively collected information for live births at 22–25 weeks of gestation in 19 academic NICU centers (available at <a href="https://neonatal.rti.org">https://neonatal.rti.org</a>). The estimated outcomes are probabilities derived from data obtained from 4,446 infants born at 400–1,000 g without major congenital anomalies who were admitted to a level III or IV Neonatal Research Network hospital between 1998 and

2003 and monitored until 18-22 months' corrected age. Using these data, the combination of five variables-1) gestational age, 2) birth weight, 3) exposure to antenatal corticosteroids, 4) sex, and 5) plurality—was found to be more predictive of outcomes than gestational age and birth weight alone. The NICHD estimator estimates frequencies of outcomes for all live births and for resuscitated newborns receiving mechanical ventilation. In addition to NICHD data and estimates, other organizations may have access to data from their own networks that can be useful for counseling, and they should be encouraged to use available contemporary data to develop and evaluate alternative prediction tools. After delivery, a number of initial illness severity scoring systems have been used in newborn care to predict death or adverse neurologic outcomes (23).

#### • What are the limitations of these tools and how should this information be incorporated into family counseling?

Prediction models for estimating neonatal outcomes after periviable birth were developed based on populations of neonates born during a given period, but as medical care advances, these models (if not updated based on more

Table 1. Factors That Affect the Reliability of Estimates of Survival or the Actual Outcomes Among Periviable Births

Variable	Effect				
Factors Affecting Reliability of Est	imates of Probability of Clinical Outcomes				
Data source	International, national, regional, and single-institution data reflect variations in regional and local practices.				
Cohort selection	Exclusion of newborns not surviving to NICU admission results in inclusion of those with higher potential for survival and higher reported rates of survival. Inclusion of nonresuscitated infants or stillbirths reduces overall reported rates of survival. Inclusion of anomalous infants may decrease reported survival estimates.				
Gestational age assignment	In vitro fertilization and ovulation induction provide accurate gestational age assignment. Dating by last menstrual period assumes accurate recollection of this date as well as conception on day 14. Ultrasonography initially performed at less than 24 weeks of gestation estimates gestational age within 5–14 days.*				
Factors Potentially Affecting Clinic	ral Outcomes				
Nonmodifiable risk factors	Race and ethnicity, plurality (singleton versus multiple gestation), infant sex, birth weight, gestational age				
Modifiable obstetric practices	Antenatal interventions (eg, corticosteroids, tocolysis, antibiotics for preterm PROM, or magnesium for neuroprotection), site and mode of delivery				
Modifiable neonatal practices	Initial resuscitation and subsequent care (eg, approaches to ventilation and oxygenation, nutritions support, and treatment of newborn infections)				
Approaches to comfort care	Influenced by institutional and physician philosophies, parental wishes, and religious convictions				
Regional/hospital legal and practice guidelines	Policies concerning neonatal resuscitation				

Abbreviations: NICU, neonatal intensive care unit; PROM, premature rupture of membranes.

Modified from Raju TN, Mercer BM, Burchfield DJ, Joseph GF Jr. Periviable birth: executive summary of a joint workshop by the Eunice Kennedy Shriver National Institute of Child Health and Human Development, Society for Maternal–Fetal Medicine, American Academy of Pediatrics, and American College of Obstetricians and Gynecologists. Obstet Gynecol 2014;123:1083–96.

<sup>\*</sup>Method for estimating due date. Committee Opinion No. 611. American College of Obstetricians and Gynecologists. Obstet Gynecol 2014;124:863-6.

recent information) may not provide estimates with an accuracy equivalent to that initially reported. Prediction of outcome frequencies based on gestational age, birth weight, or both in combination with other predictors provides only a point estimate reflecting a population average and cannot predict with certainty the outcome for an individual newborn. Further, gestational age is a key component of any predictive model and may not be known accurately in all cases. Also, defining outcomes based on completed weeks arbitrarily eliminates the differences between a fetus at 23 0/7 weeks and one at 23 6/7 weeks of gestation as well as the similarities between a fetus at 23 6/7 weeks and one at 24 0/7 weeks of gestation. Furthermore, before delivery, newborn birth weight can only be estimated. The inherent inaccuracy of ultrasound-estimated fetal weight introduces a degree of uncertainty to the prediction of newborn outcomes. In addition, how parents weigh and value these potential outcomes (ie, death, degree of neurodevelopmental impairment) can vary widely, and individual values need to be incorporated into decision making. Finally, the response of an individual neonate to resuscitation can never be known with certainty before delivery. Thus, when a specific estimated probability for an outcome is offered, it should be stated clearly that this is an estimate for a population and not a prediction of a certain outcome for a particular patient in a given institution. It is not known if and how the use of these tools improves care, patient-centered outcomes, or families' satisfaction with decision making. These limitations highlight the need for further research and development of improved prediction models and counseling tools. However, at present, the NICHD estimator (available at www.nichd.nih.gov/about/org/der/branches/ppb/ programs/epbo/Pages/epbo\_case.aspx?start=13:15:46) remains the most widely available resource to estimate the likelihood of perinatal morbidity and mortality.

#### What are the considerations of periviable delivery for maternal health?

The effect of periviable delivery on maternal health is an important consideration that should be incorporated into counseling. In the setting of possible periviable birth, interventions intended to delay delivery or to improve newborn outcomes often are undertaken but may affect maternal outcomes. Although some interventions (eg, antenatal corticosteroid administration or magnesium sulfate for neuroprotection) pose relatively low risk to the pregnant woman and offer the prospect of a fetal benefit, others (eg, emergent cerclage placement or classical cesarean delivery) may result in significant short-term and long-term maternal morbidity. Risks to a pregnant woman's short-term and long-term health need to be evaluated in the context of a newborn's predicted outcome and the degree to which the intervention in question is predicted to improve this outcome. Although maternal risks associated with individual interventions may not vary widely with a neonate's gestational age, expectations for anticipated benefit to neonatal outcome may more strongly support undertaking such risks at later gestational ages.

Because preterm birth frequently is associated with fetal malpresentation, whether to undertake a cesarean delivery for malpresentation is a relatively common question related to periviable gestation. Earlier cesarean delivery is associated with a higher likelihood that the needed hysterotomy will be a vertical uterine incision (classical hysterotomy) extending into the upper muscular portion of the uterus. Hysterotomy that involves the muscular portion of the uterus has been associated with more frequent perioperative morbidities than low transverse cesarean delivery and also leads to the recommendation for repeat cesarean delivery in future pregnancies because of the increased risk of uterine rupture with labor. In addition, recent data indicate that regardless of incision type, periviable cesarean delivery results in an increased risk of uterine rupture in a subsequent pregnancy (24). Finally, cesarean delivery is associated with future reproductive risks, which increase further with each additional repeat cesarean delivery.

Maternal morbidity and mortality may arise not just with interventions surrounding periviable pregnancy management but also with decisions not to intervene. For example, decisions to delay delivery (so-called "expectant management") in the setting of preterm premature rupture of membranes (PROM) may result in maternal infection (25, 26) or, in the setting of severe preeclampsia, may result in hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome or other complications of worsening preeclampsia (27). These examples emphasize that patients, obstetrician-gynecologists, and other obstetric providers should together consider such risks in the context of the parents' goals of care (resuscitative compared with palliative); the potential for newborn survival with immediate delivery; the likelihood of extended latency to improve newborn outcomes; and the likelihood of severe adverse maternal outcomes with attempted pregnancy prolongation, individual interventions proposed for fetal or neonatal benefit, or both.

## • What obstetric and pediatric resources should be available in institutions that provide care for periviable birth? When should transport occur, if needed?

Periviable infants do not survive without life-sustaining interventions immediately after delivery. The circumstances prompting periviable birth are, in many cases (eg, preeclampsia with severe features), also likely to require advanced care and resources to improve a woman's outcome. Delivery of a pregnancy in the periviable period at a center with a level III–IV NICU, level III–IV maternal care designation, or both, allows for immediate resuscitation with additional needed ancillary supports (eg, respiratory technology, newborn imaging 24 hours daily) and advanced maternal care to optimize outcomes for the neonate and woman (28).

Accordingly, whenever possible, periviable births for which maternal or neonatal intervention is planned should occur in centers that offer expertise in maternal and neonatal care and the needed infrastructure, including intensive care units, to support such services (28–30). Efforts should be made to transfer women before delivery, if feasible, because antenatal transfer has been associated with improved neonatal outcome when compared with transport of a neonate after delivery (31, 32). It similarly stands to reason that transfer of a parturient for advanced care before her condition worsens may improve her outcome as well.

To facilitate needed transfers, hospitals without the optimal resources for maternal, fetal, and neonatal care needed for periviable birth should have policies and procedures in place to facilitate timely transport to a receiving hospital. Protocols with guidelines for the initial management and safe transport of the periviable gestation should include recommendations for such treatments as antenatal corticosteroids, magnesium sulfate for neuroprotection, tocolytic therapy, antibiotics for latency after preterm PROM, and group B streptococci prophylaxis.

In some cases, circumstances may preclude antenatal maternal transport because of a rapidly evolving clinical situation or because of maternal instability due to severe illness. In such cases, neonatal transport after delivery may be needed, and protocols also should be in place to facilitate postpartum consultation and transfer. Final decisions regarding interventions to be initiated before transfer, as well as the optimal timing and method of transport, should be individualized and made in consultation with the accepting physician.

#### • What are the benefits and risks of obstetric interventions for anticipated or inevitable periviable birth?

As in any pregnancy, obstetric interventions should be undertaken only after a discussion with the family regarding individual risks and benefits of management options in addition to alternate approaches. In order to facilitate informed decision making, this discussion should include an unbiased presentation of data related to the chance of both survival and long-term neurodevelopmental impairment. This discussion also should present the option of nonintervention. In light of the high likelihood of death and the significant degree of neurodevelopmental impairment that may result from periviable birth, the American Academy of Pediatrics has stated that parents should be given the choice for palliative care alongside the option to attempt resuscitation. Clinicians should recognize that parental goals of care may be oriented toward optimizing survival or minimizing pain and suffering and should formulate an antenatal plan of care in accordance with these parental goals. Rather than treat patients based upon algorithms organized solely by gestational age, a plan of care should be informed primarily by whether the goal is to optimize the chance of survival or minimize the likelihood of suffering.

Given the potential for maternal and perinatal morbidity and mortality, the option of pregnancy termination should be reviewed with the patient. Individual obstetrician-gynecologists and other obstetric providers or institutions may have objections to discussing or providing this option, but in the case of such objections, there should be a system in place to allow families to receive counseling about their options and access to such care (33). The management plan for ongoing pregnancies should be reassessed and follow-up counseling should be provided as the clinical situation develops and gestational age increases. Initiation of interventions to help improve outcome (eg, administration of antenatal antibiotics or corticosteroids) does not mandate that all other interventions (eg, cesarean delivery or newborn resuscitation) subsequently be undertaken. Further interventions should be considered in the context of clinical circumstances at that time. Accurate pregnancy dating is of particular importance in the periviable period, and the best estimate of gestational age should be used for counseling and decision making (34).

Obstetric interventions often considered in pregnancies at risk of periviable delivery include treatments to delay delivery as well as efforts to improve newborn outcomes should delivery occur despite such efforts. Treatment options vary depending upon the specific circumstances but may include short-term tocolytic therapy for preterm labor to allow additional time for administration of antenatal steroids, emergent cerclage, antibiotics to prolong latency after preterm PROM or for intrapartum group B streptococci prophylaxis, and delivery (including cesarean delivery) for concern regarding fetal well-being or fetal malpresentation.

Data regarding the use of obstetric interventions during the periviable period, especially for gestational ages less than 24 weeks, however, are limited, as these gestational ages were not included in many studies, especially those performed in the 1970s and 1980s. Even the studies that included subjects in the periviable gestational age range typically had small numbers in these groups, with corresponding limited power to evaluate the effect of interventions. As a result, most recommendations for management in the periviable gestational age range are extrapolated from data available for women who gave birth between 26 weeks and 34 weeks of gestation.

Guidance offered in this document for the management of the pregnancy at risk of periviable birth is based, therefore, on a mix of direct evidence, data extrapolated from more advanced gestational ages, and expert opinion. This guidance, summarized in Table 2 and Table 3, is considered in more detail below. There are a few perspectives that serve to frame these recommendations:

Recommendations presented in this document vary in some aspects from those published and summarized previously (2) in part because of further stratification of advice offered for anticipated deliveries between 23 0/7 weeks and 25 6/7 weeks of gestation. Outcomes vary widely across this gestational age range, as do the quantity and quality of available data supporting various proposed interventions. The recommendations are intended to provide guidance that will facilitate implementation of the 2014 NICHD workshop recommendations.

- In formulating a plan of care for periviable neonates, clinicians should discuss with parents whether their goal is optimizing survival or minimizing suffering. The approach to antenatal and postdelivery care may differ dramatically depending on parental preferences regarding resuscitation.
- A recommendation regarding assessment for resuscitation is not meant to indicate that resuscitation should always either be undertaken or deferred, or that every possible intervention need be offered. A stepwise approach concordant with neonatal circumstances and condition and with parental wishes is appropriate. Care should be reevaluated regularly and potentially redirected based on the evolution of the clinical situation. Assessment at birth, for example, may include confirmation that comfort measures are most appropriate.
- A decision to proceed with resuscitation always should be informed by individual circumstances, including specific clinical issues (especially, for example, estimated fetal weight and the most precise estimate of gestational age), family values and

- wishes, and ongoing evaluation of fetal or neonatal condition. In some cases, decisions will be informed by local institutional policy and relevant laws, of which obstetrician-gynecologists and other obstetric providers should be aware. Accordingly, the guidelines offer recommendations with regard to the gestational ages at which assessment for resuscitation rather than resuscitation itself should be undertaken. Such assessment is meant in most cases to refer to that provided by neonatologists or other pediatric providers, separate from that offered by obstetrician-gynecologists and other obstetric providers.
- A decision not to undertake resuscitation of a liveborn infant should not be seen as a decision to provide no care, but rather a decision to redirect care to comfort measures.
- Continuous electronic fetal heart rate monitoring is not separately considered as an intervention because in most cases its use will be linked to plans regarding cesarean delivery for fetal indications. Even if cesarean delivery for fetal indication is not planned, if arrangements have been made for resuscitation of a potentially viable liveborn neonate, electronic fetal heart rate monitoring may be considered if it is believed that intrauterine resuscitation will affect the newborn's outcome.
- The less directive recommendation of "consider" is assigned to some guidance because of the very limited evidence regarding use of a given intervention in a particular gestational age range (because available

Table 2. Recommendations for Periviable Birth 🗢	
Recommendations	Grade of Recommendations
Based on anticipated neonatal or maternal complications, antepartum transport to a center with advanced levels of neonatal or maternal care is recommended when feasible and appropriate.	Best practice
Prenatal and postnatal counseling regarding anticipated short-term and long-term neonatal outcome should take into consideration anticipated gestational age at delivery, as well as other variables that may alter the likelihood of survival and adverse newborn outcomes (eg, fetal sex, multiple gestation, the presence of suspected major fetal malformations, antenatal corticosteroid administration, birth weight, and response to initial newborn resuscitation).	Best practice
Family counseling should be provided by a multidisciplinary team that includes obstetrician—gynecologists and other obstetric providers, maternal—fetal medicine specialists, if available, and neonatologists who can address their individual and shared considerations and perspectives. Maternal and neonatal outcomes should be considered. Follow-up counseling should be provided when there is relevant new information about the maternal and fetal status or the newborn's evolving condition.	Best practice
A predelivery plan, made with the parents, family, or both, should be recognized as a general plan of approach, which may be modified as the neonate's condition and response is evaluated by the neonatal providers. A recommendation regarding assessment for resuscitation is not meant to indicate that resuscitation should always either be undertaken or deferred, or that every possible intervention need be offered. A stepwise approach concordant with neonatal circumstances and condition and with parental wishes is appropriate. Care should be reevaluated regularly and potentially redirected based on the evolution of the clinical situation.	Best practice

Recommendations regarding specific interventions, tailored to gestational age and other clinical data, and taking into account individual family preferences and values, are summarized in Table 3.

**Table 3.** General Guidance Regarding Obstetric Interventions for Threatened and Imminent Periviable Birth by Best Estimate of Gestational Age\* ←

	20 0/7 weeks to	22 0/7 weeks to	23 0/7 weeks to	24 0/7 weeks to	25 0/7 weeks to
	21 6/7 weeks	22 6/7 weeks	23 6/7 weeks	24 6/7 weeks	25 6/7 weeks
Neonatal assessment for resuscitation*	Not recommended 1A	Consider 2B	Consider 2B	Recommended 1B	Recommended 1B
Antenatal corticosteroids	Not recommended 1A	Not recommended 1A	Consider 2B	Recommended 1B	Recommended 1B
Tocolysis for preterm labor to allow for antenatal corticosteroid administration	Not recommended	Not recommended	Consider	Recommended	Recommended
	1A	1A	2B	1B	1B
Magnesium sulfate for neuroprotection	Not recommended 1A	Not recommended 1A	Consider 2B	Recommended 1B	Recommended 1B
Antibiotics to prolong latency during expectant management of preterm PROM if delivery is not considered imminent	Consider 2C	Consider 2C	Consider 2B	Recommended 1B	Recommended 1B
Intrapartum antibiotics for group B streptococci prophylaxis†	Not recommended	Not recommended	Consider	Recommended	Recommended
	1A	1A	2B	1B	1B
Cesarean delivery for fetal indication <sup>‡</sup>	Not recommended	Not recommended	Consider	Consider	Recommended
	1A	1A	2B	1B	1B

Abbreviation: PROM, premature rupture of membranes.

evidence suggests limited benefit with significant potential risk) or if antenatal interventions will be altered by the intention to perform newborn resuscitation or to provide comfort care.

#### Antenatal Corticosteroids

Corticosteroid administration before anticipated preterm birth is one of the most important antenatal therapies available to improve newborn outcomes (35–38). Specific data on the use of steroids in the periviable period are supported by a combination of laboratory data on the response of lung tissue and clinical observational studies (35, 39, 40). Data from a Eunice Kennedy Shriver NICHD Neonatal Research Network observational cohort revealed a significant reduction in death and neurodevelopmental impairment at 18-22 months for infants who had been exposed to antenatal corticosteroids and born at 23 weeks of gestation (83.4% versus 90.5%), 24 weeks of gestation (68.4% versus 80.3%), and 25 weeks of gestation (52.7% versus 67.9%) (35). At 22 weeks of gestation, no significant difference in these outcomes was noted (90.2% versus 93.1%)

(35). In this study, antenatal corticosteroid exposure also decreased incidence of death, intraventricular hemorrhage, periventricular leukomalacia, and necrotizing enterocolitis in infants born between 23 weeks and 25 weeks of gestation.

#### Magnesium Sulfate for Neuroprotection

Maternal treatment with magnesium sulfate has been shown to improve neurologic outcomes when administered before anticipated early preterm birth. The use of magnesium sulfate for this indication has been studied in five randomized controlled trials, with enrollment started as early as 24 weeks of gestation (19, 41). Although data specific to the periviable period are not available, antenatal magnesium sulfate treatment has been shown to reduce the incidence of any cerebral palsy (relative risk, 0.68; 95% confidence interval, 0.54–0.87) without increasing mortality (relative risk, 1.04; 95% confidence interval, 0.92–1.17) when administered before 30 weeks of gestation (19). Given these findings, magnesium sulfate prophylaxis is recommended if periviable delivery of a potentially viable infant is anticipated.

<sup>\*</sup>Survival of infants born in the periviable period is dependent on resuscitation and support. Between 22 weeks and 25 weeks of gestation, there may be factors in addition to gestational age that will affect the potential for survival and the determination of viability. Importantly, some families, concordant with their values and preferences, may choose to forgo such resuscitation and support. Many of the other decisions on this table will be linked to decisions regarding resuscitation and support and should be considered in that context.

<sup>&</sup>lt;sup>†</sup>Group B streptococci carrier, or carrier status unknown

<sup>&</sup>lt;sup>‡</sup>For example, persistently abnormal fetal heart rate patterns or biophysical testing, malpresentation

#### Antibiotics for Pregnancy Prolongation After Pre-term Labor or Premature Rupture of Membranes

Administration of broad-spectrum antibiotics during expectant management of preterm PROM has been shown to prolong pregnancy and reduce newborn infections (42). Alternatively, antibiotic treatment of women with preterm labor and intact membranes has been shown to have no effect on pregnancy prolongation or on the improvement of newborn outcomes; indeed, the combination of amoxicillin-clavulanic acid in the setting of preterm labor may worsen long-term outcomes for the offspring (43). Thus, although data specific to the periviable period are not available, broad-spectrum antibiotic treatment to prolong pregnancy during expectant management of periviable preterm PROM generally is recommended at 24 weeks of gestation and beyond. Conversely, there are inadequate data to help obstetriciangynecologists and other obstetric providers balance any potential efficacy at earlier gestational ages against potential risks. In the setting of preterm labor with intact membranes, because of the lack of evidence of benefit and the potential risks, such treatment is not recommended.

#### Tocolytic Therapy for Preterm Labor

Studies suggest that nifedipine and indomethacin tocolysis of women in preterm labor with intact membranes may delay delivery between 48 hours and 72 hours after 26 weeks of gestation, but specific data for pregnancies treated before 26 weeks of gestation are lacking (44, 45). Theoretically, a brief delay of delivery with tocolytic therapy for preterm labor could reduce neonatal morbidity and mortality in the periviable period, particularly if antenatal steroids can be administered. However, although some studies have found that tocolytics delay delivery for a short time, improvements in actual neonatal outcomes have not been consistently demonstrated (46). Because there is some evidence of brief pregnancy prolongation but no consistent data suggesting improved newborn outcomes at any gestational age, a specific and strong recommendation in favor of or against tocolytic therapy for preterm labor cannot be made.

#### Cervical Cerclage

Placement of an emergency ("rescue") cerclage when the fetal membranes are visible at or past the external cervical os can be considered in the absence of uterine contractions or preterm PROM or other contraindications to placement (eg, labor, intraamniotic infection) at less than 24 weeks of gestation (47). Observational and randomized controlled studies of emergency cerclage placement based on physical examination findings of dilation have revealed an association between cerclage placement and pregnancy prolongation, as well as increased live births and neonatal survival, when compared with those treated without cerclage (48–51).

#### Cesarean Delivery

Routine cesarean delivery is not recommended for the indication of periviable delivery alone because it has not been shown to decrease mortality or intraventricular hemorrhage after early preterm birth (52). Randomized controlled trials comparing cesarean delivery with vaginal delivery have not been done in the periviable period. Although limited retrospective data provide some support for cesarean delivery in the presence of malpresentation, delivery for women in the periviable period should be individualized, recognizing increased maternal morbidity associated with cesarean delivery, particularly if the need for classical cesarean delivery is anticipated (7, 53–55). Cesarean delivery before 22 weeks of gestation is appropriate only for maternal indications (eg, placenta previa or uterine rupture).

#### How should information regarding potential maternal and newborn interventions and outcomes be presented to facilitate family decision making?

The medical team plays a key role in helping the family navigate the complex decisions needed regarding periviable delivery and in giving the patient and her family the opportunity to express their values and preferences (56, 57). However, except in the rare case when the patient is not competent to do so, only the pregnant woman can provide consent for maternal interventions. The counseling process should concurrently address clinical considerations regarding the pregnant woman, her fetus, and the newborn (if delivered). This information is optimally addressed by a multidisciplinary team that includes obstetricians, neonatologists and, when available, maternal-fetal medicine subspecialists, who can speak to their individual and combined considerations and perspectives (58). Because of the complexity and ramifications of management decisions in the periviable period, other health care team members (eg, bioethicists, social workers, palliative care experts, spiritual care providers, and nurses) may provide important contributions to the counseling process as well as psychological and emotional support. Ideally, counseling by the obstetric and neonatology teams will occur simultaneously or will occur in such a way that each team keeps the other informed of the content of their discussions. These efforts will help to optimize coordination so as to avoid the provision of conflicting information to the patient and her family. These efforts should include the acknowledgement of when data are uncertain and consensus cannot be obtained.

It is important that the health care team provide accurate, balanced, and unbiased information and guidance. Because obstetrician-gynecologists and other obstetric providers may have divergent opinions and practices based on personal beliefs or professional experiences, it is preferable that institutions develop consensus guidelines regarding counseling about outcomes and a general approach to resuscitation of the periviable

newborn. Effective communication within the health care team will identify conflicts of conscience that may arise. Advanced knowledge of these issues can allow the team to develop strategies that recognize differences in obstetrician–gynecologists' or other obstetric providers' personal beliefs without impairing patient counseling or care.

The family should be counseled regarding short-term and long-term consequences that are anticipated in the context of evolving clinical findings for their newborn. Family counseling should recognize the fact that additional information may become available subsequent to initial conversations that may change recommendations and decision making. It is recognized that those attending a delivery or providing neonatal care may not be the same as those who have counseled patients and made plans for their care. Efforts should be made and systems should be put in place to ensure that established plans are communicated and respected as teams hand off and assume responsibility for a patient's care.

Optimally, the family should be counseled before delivery regarding possible pregnancy and newborn outcomes, with adequate time available for the woman and her family to process the information needed to make an informed decision. However, delivery may occur quickly in some cases, precluding adequate time for full discussion of all options and expectations before birth. In this circumstance, the family should be counseled with relevant information about the newborn's condition at and after birth as soon as is practical after delivery. Regardless of when counseling is initiated, follow-up counseling should be provided when there is relevant new information about the maternal and fetal status or the newborn's evolving condition. In line with recommendations already emphasized, maternal transport should be recommended when appropriate and feasible.

When a decision has been made to withhold or withdraw life-sustaining treatment after birth, the newborn should receive individualized compassionate care that is directed toward providing warmth, minimizing discomfort, and allowing the family to spend as much time with their newborn as desired. It should be emphasized that decisions to redirect care do not mean forgoing all care but instead mean focusing on the palliative care that is appropriate based on the clinical circumstances. Bereavement care for the family is of great importance in this situation. Creating memories (eg, by making footprints or taking photographs) often is appreciated by the family.

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Obstetric Care Consensus documents will use Society for Maternal-Fetal Medicine's grading approach: http://www.ajog.org/article/S0002-9378%2813%2900744-8/fulltext. Recommendations are classified as either strong (Grade 1) or weak (Grade 2), and quality of evidence is classified as high (Grade A), moderate (Grade B), and low (Grade C)\*. Thus, the recommendations can be 1 of the following 6 possibilities: 1A, 1B, 1C, 2A, 2B, 2C.

Grade of Recommendation	Clarity of Risk and Benefit	Quality of Supporting Evidence	Implications			
1A. Strong recommendation, high-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa.	Consistent evidence from well-performed randomized controlled trials or overwhelming evidence of some other form. Further research is unlikely to change 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.			
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 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.			
1C. Strong recommendation, low-quality evidence	Benefits appear 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, and applies to most patients. Some of the evidence base supporting the recommendation is, however, of low quality.			
2A. Weak recommendation, high-quality evidence	Benefits closely balanced with risks and burdens.	Consistent evidence from well- performed randomized controlled trials or overwhelming evidence of some other form. Further research is unlikely to change confidence in the estimate of benefit and risk.	Weak recommendation, best action may differ depending on circumstances or patients or societal values.			
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 effect on confidence in the estimate of benefit and risk and may change the estimate.	Weak recommendation, alternativ approaches likely to be better for some patients under some circumstances.			
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 from randomized controlled trials with serious flaws. Any estimate of effect is uncertain.	Very weak recommendation, other alternatives may be equally reasonable.			
Best practice	Recommendation in which either (i) there is enormous amount of indirect evidence that clearly justifies strong recommendation (direct evidence would be challenging, and inefficient use of time and resources, to bring together and carefully summarize), or (ii) recommendation to contrary would be unethical.					
*Guyatt GH, Oxman AD, Vist GE, K ommendations. GRADE Working G		al. GRADE: an emerging consensus on ratir	ng quality of evidence and strength of rec-			
	l adopts GRADE (Grading of Recommend II). Am J Obstet Gynecol 2013;209:163—	ations Assessment, Development, and Evalu 5.	uation) for clinical guidelines. Society for			

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