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Society for Maternal-Fetal Medicine Consult Series #71: Management of previable and periviable preterm prelabor rupture of membranes

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Previable and periviable preterm prelabor rupture of membranes are challenging obstetrical complications to manage given the substantial risk of maternal morbidity and mortality, with no guarantee of fetal benefit. The following are the Society for Maternal-Fetal Medicine recommendations for the management of previable and periviable preterm prelabor rupture of membranes before the period when a trial of neonatal resuscitation and intensive care would be considered appropriate by the healthcare team and desired by the patient: (1) we recommend that pregnant patients with previable and periviable preterm prelabor rupture of membranes receive individualized counseling about the maternal and fetal risks and benefits of both abortion care and expectant management to guide an informed decision; all patients with previable and periviable preterm prelabor rupture of membranes should be offered abortion care, and expectant management can also be offered in the absence of contraindications (GRADE 1C); (2) we recommend antibiotics for pregnant individuals who choose expectant management after preterm prelabor rupture of membranes at ≥24 0/7 weeks of gestation (GRADE 1B); (3) antibiotics can be considered after preterm prelabor rupture of membranes at 20 0/7 to 23 6/7 weeks of gestation (GRADE 2C); (4) administration of antenatal corticosteroids and magnesium sulfate is not recommended until the time when a trial of neonatal resuscitation and intensive care would be considered appropriate by the healthcare team and desired by the patient (GRADE 1B); (5) serial amnioinfusions and amniopatch are considered investigational and should be used only in a clinical trial setting; they are not recommended for routine care of previable and periviable preterm prelabor rupture of membranes (GRADE 1B); (6) cerclage management after previable or periviable preterm prelabor rupture of membranes is similar to cerclage management after preterm prelabor rupture of membranes at later gestational ages; it is reasonable to either remove the cerclage or leave it in situ after discussing the risks and benefits and incorporating shared decision-making (GRADE 2C); and (7) in subsequent pregnancies after a history of previable or periviable preterm prelabor rupture of membranes, we recommend following guidelines for management of pregnant persons with a previous spontaneous preterm birth (GRADE 1C).

Key words: abortion, antibiotics, cerclage, expectant management, infection, maternal morbidity, maternal mortality, neonatal morbidity, neonatal mortality, periviable, preterm prelabor rupture of membranes, previable, prophylaxis

Introduction

Preterm prelabor rupture of membranes (PPROM) is defined as membrane rupture before labor that occurs before 37 0/7 weeks of gestation.[1] PPROM occurs in <1% of all pregnancies,[2–6] but is associated with substantial maternal and neonatal infectious morbidity and mortality.[7–14] Continuing pregnancy after previable and periviable PPROM incurs maternal risk with no direct maternal benefit and no guarantee of fetal benefit.[15] Furthermore, management has become more complicated by abortion restrictions that took effect in many states after the Supreme Court decision in

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Dobbs v Jackson Women's Health Organization.[16] The death of Savita Halappanavar in Ireland from sepsis after previable PPROM highlights the grave consequences of denying abortion care for patients with previable and periviable PPROM and the need for clinicians to have clear guidance on management options.[17,18] The objective of this Consult is to review the maternal and neonatal risks of expectant management with and without intervention and abortion care for patients with previable and periviable PPROM, and to outline management options that should be available to all patients in these circumstances.

What are previable and periviable preterm prelabor rupture of membranes?

Defining viability is complicated because it represents a physiological continuum impacted by gestational age and other clinical factors described below.[19] The timing of viability shifts according to the availability of medical advances that facilitate providing a trial of neonatal intensive care. For the purposes of this document, "viable" denotes the period when a fetus is able to survive outside the uterus, and this definition is not based on gestational age alone. "Previable" denotes the period when a fetus would not survive outside the uterus and thus is not a candidate for life-sustaining interventions.[20] "Periviable" denotes the period when the fetus may survive outside the uterus with life-sustaining interventions but still with a high risk of death or severe morbidities. Consensus from a 2013 multidisciplinary joint workshop with participants from 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 defined the periviable period as 20 0/7 to 25 6/7 weeks of gestation.[20] As detailed in a summary of the workshop, rates of neonatal survival to discharge in this period range from 23% to 27% for births at 23 weeks of gestation, 42% to 59% for births at 24 weeks of gestation, and 67% to 76% for births at 25 weeks of gestation.[20] Deliveries before 23 weeks of gestation have a 5% to 6% neonatal survival rate, and the rate of serious morbidity is 98% to 100% among the survivors.[21] In addition to gestational age, other important factors affecting viability include estimated fetal weight, multiple gestations, fetal genetic diseases, and fetal anomalies.[20,21] This document focuses on the management of PPROM during the previable and periviable periods when a trial of neonatal resuscitation and intensive care are not considered appropriate by the healthcare team or not desired by the pregnant patient. Management of periviable PPROM when neonatal resuscitation and intensive care are considered appropriate by the healthcare team and desired by the patient generally should follow previous guidelines for PPROM and periviable birth (Table).[1,21,22]

What are the management options after a diagnosis of previable and periviable preterm prelabor rupture of membranes?

Management options for previable and periviable PPROM include expectant management and abortion care. After diagnosis of previable and periviable PPROM, pregnant individuals should be assessed for signs and symptoms of infection, hemorrhage, and ongoing labor, which could

TABLE
Summary of American College of Obstetricians and Gynecologists and Society for Maternal-Fetal Medicine guidelines for intervention with threatened periviable birth

Intervention	20 0/7 to 21 6/7 wk	22 0/7 to 22 6/7 wk	23 0/7 to 23 6/7 wk	24 0/7 to 24 6/7 wk	25 0/7 to 25 6/7 wk
Neonatal assessment for resuscitation	Not recommended 1A	Consider 2B	Consider 2B	Recommended 1B	Recommended 1B
Antenatal corticosteroids	Not recommended 1A	Consider 2C	Consider 2B	Recommended 1B	Recommended 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 PPROM	Consider 2C	Consider 2C	Consider 2B	Recommended 1B	Recommended 1B
Intrapartum antibiotics for group B streptococci prophylaxis	Not recommended 1A	Not recommended 1A	Consider 2B	Recommended 1B	Recommended 1B
Cesarean delivery for fetal indication	Not recommended 1A	Not recommended 1A	Consider 2B	Consider 1B	Recommended 1B

PPROM, preterm prelabor rupture of membranes.

Adapted from Cahill et al,[22] 2021 and Obstetric Care Consensus No. 6: Periviable birth.[21]

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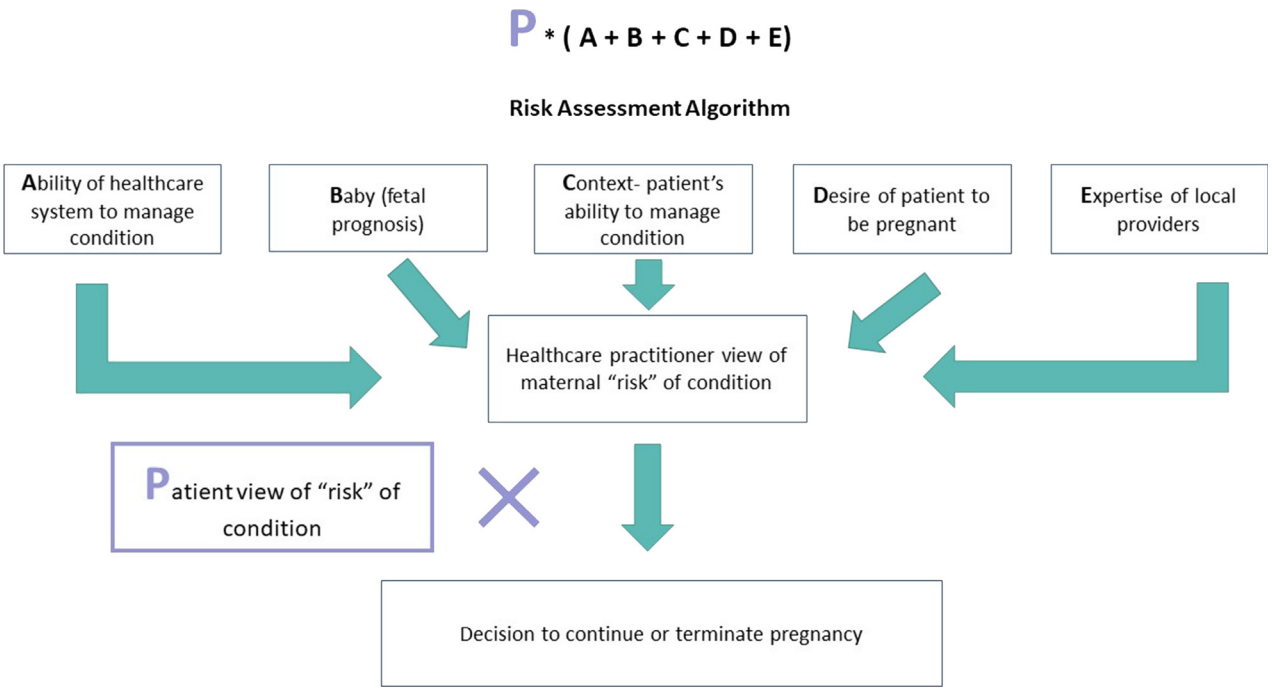
preclude expectant management as an option.[1] Notably, clinical symptoms of infection may be less overt at earlier gestational ages.[1] Although intraamniotic infection is often diagnosed clinically on the basis of maternal temperature ≥38°C and ≥1 other signs or symptoms of infection (eg, maternal tachycardia, purulent cervical discharge, fetal tachycardia, uterine tenderness),[23] some cases of intraamniotic infection may not initially present with a maternal fever.[24] Thus, the diagnosis of intraamniotic infection and appropriate intervention with antibiotics and abortion care should not be delayed because of the absence of maternal fever.[25] Similarly, although amniocentesis may be helpful in diagnosing intraamniotic infection, it should not delay clinical management as described above. Other contraindications to expectant management, including hemorrhage and fetal demise, should prompt abortion care or delivery and evacuation of uterine contents.[1,12,26] Decisions regarding the type of abortion care (procedural or medication abortion) should prioritize the safety of the pregnant person with consideration of maternal stability, gestational age, and availability of clinicians able to provide procedural abortion care.[27,28] A recent single-center study at a tertiary academic medical care center compared maternal outcomes after procedural abortion (dilation and evacuation [D&E]) and medication abortion (induction of labor) among patients with PPROM from 14 0/7 to 23 6/7 weeks of gestation.[29] In this cohort, 77 of 123 patients (62.6%) underwent D&E, and time to uterine evacuation was not different between the groups (D&E, 14.3 hours vs induction of labor, 11.5 hours). Complications were more frequent after induction of labor than after D&E (hemorrhage >500 cc, 28.3% vs 9.1% [$P<.01$]; infection, 23.9% vs 1.3% [$P<.01$]; and retained tissue requiring an additional procedure, 17.4% vs 1.3% [$P<.01$]; respectively).

What are the key ethical considerations when treating pregnant patients with previable and periviable preterm prelabor rupture of membranes?

The Society for Maternal-Fetal Medicine maternal risk assessment algorithm[30] summarizes the complex medical and contextual factors that affect maternal risk in pregnancy: (1) the ability of the healthcare system to manage the condition, (2) the prognosis for the fetus and neonate, (3) the pregnant patient's ability to manage the condition, (4) the desire of the individual to be pregnant, and (5) the expertise of local or available healthcare practitioners (Figure 1). Integration of these factors with the patient's tolerance or view of the risk can inform decision-making regarding pregnancy management after previable and periviable PPROM.

For stable pregnant individuals with previable or periviable PPROM who desire ongoing pregnancy and do not have contraindications to expectant management, an ethical framework can help the pregnant patient weigh the risks and benefits of each management option to both themself and

FIGURE 1
Society for Maternal-Fetal Medicine risk assessment algorithm[30]



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their fetus.[31] The principles of beneficence ("doing good") and nonmaleficence ("refraining from infliction of harm") can guide decisions regarding treatment to improve the life of another while not increasing harm or prolonging life associated with significant suffering.[31] Clinicians should respect pregnant individuals' autonomy to make decisions that best align with their core values after counseling that provides all medically appropriate options for informed decision-making. Finally, justice requires providing equitable care to all pregnant individuals and not treating pregnant patients differently from other patients simply because they are pregnant.

Applying ethical principles to any issue during and after pregnancy is unique because the benefits and risks for both the pregnant person and the fetus or neonate must be considered. Ethical care of pregnant patients requires that maternal medical benefit take priority when maternal and fetal benefit intractably conflict. However, the pregnant patient may exercise their autonomy by choosing to prioritize perceived fetal benefit over maternal medical benefit. Of note, recognition of the pregnant patient's authority to prioritize perceived fetal benefit over their own medical benefit does not imply that clinicians are ethically obligated to offer any requested course of action. In such circumstances, clinicians' counseling should exclude interventions where there is an absence of reasonable evidence for fetal benefit.[32] Nonetheless, counseling given to pregnant patients on the medically appropriate options in a clinical scenario must reflect ethical commitments to prioritize maternal medical benefit and respect the authority of pregnant patients to accept certain risks to their own health in pursuit of perceived fetal benefit.

How should pregnant individuals with previable and periviable preterm prelabor rupture of membranes be counseled about management options?

The scenario of previable and periviable PPROM is unique because continuing the pregnancy has substantial maternal risk and no direct maternal benefit apart from the potential emotional benefit of attempting to improve outcomes for the fetus, and abortion has no fetal or neonatal benefit apart from potentially preventing suffering after the birth of an extremely premature neonate.[33,34] **We recommend that pregnant patients with previable and periviable PPROM receive individualized counseling about the maternal and fetal risks and benefits of both abortion care and expectant management to guide an informed decision. All patients with previable and periviable PPROM should be offered abortion care. Expectant management can also be offered in the absence of contraindications (GRADE 1C).**[35–38]

Initial counseling may be performed by clinicians with the necessary training and knowledge, with additional consultation by a maternal–fetal medicine subspecialist or neonatologist as needed to ensure that the pregnant person understands the maternal and fetal risks and neonatal prognoses of each management option. Referral to a tertiary care center may be needed depending on the availability of these services to ensure that the pregnant individual can make an informed decision. Patients should receive counseling on all management options, even if those options are not immediately available, with appropriate referrals as indicated. In addition, pregnant persons have the right to change their minds regarding the management of previable and periviable PPROM and should have access to timely procedural and medication abortion care, if desired, after an initial trial of expectant management. Documentation of the counseling and shared decision-making process is important and should be readdressed if the patient desires or the clinical scenario changes.

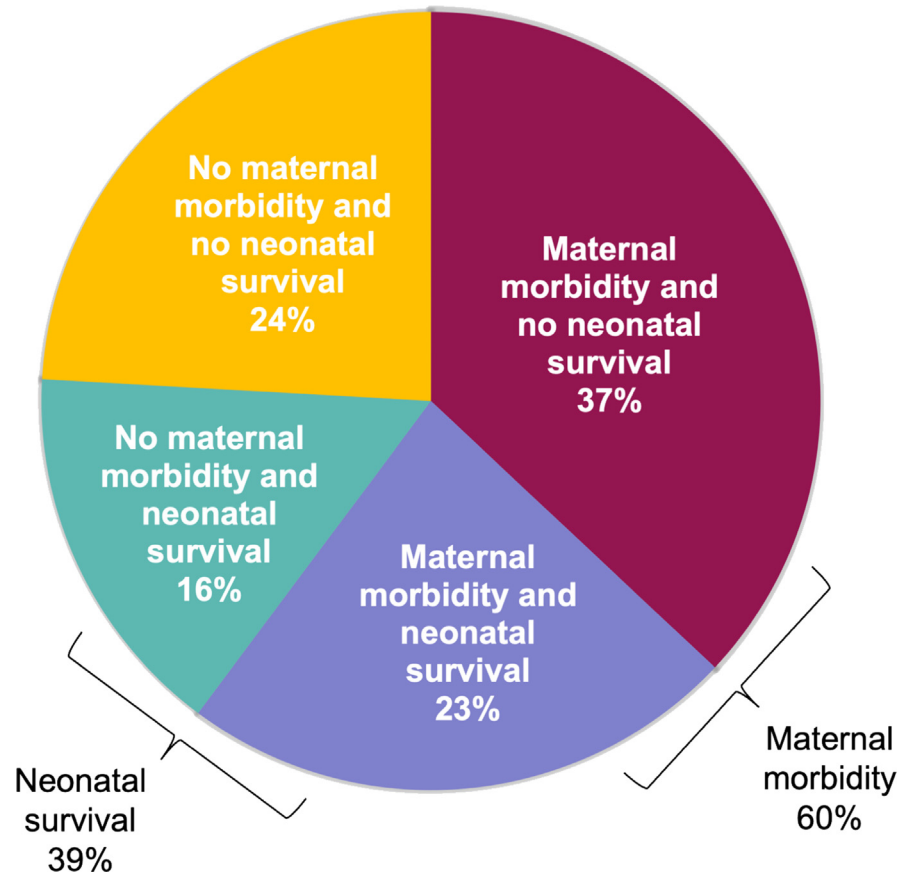
What are the maternal risks associated with expectant management of previable and periviable preterm prelabor rupture of membranes compared with abortion care?

Compared with abortion care, expectant management of previable and periviable PPROM increases the risk of multiple maternal complications, including infection, hemorrhage, and death.[7,38] Although it would be unethical to conduct a randomized clinical trial to compare outcomes following expectant management with outcomes following abortion care after previable and periviable PPROM, several retrospective cohort studies address this question. A study using electronic health record data collected from 2011 to 2018 at 3 hospitals in different US geographic regions evaluated outcomes with expectant management compared with abortion care following PPROM at 14 0/7 to 23 6/7 weeks of gestation. Individuals with contraindications to expectant management (defined as chorioamnionitis or active heavy bleeding) and those with spontaneous delivery within 24 hours of PPROM were excluded from the analysis. Of the 208 included pregnant individuals, 108 (51.9%) chose expectant management, and 100 (48.1%) chose abortion care. Pregnant individuals who chose expectant management had PPROM at a later mean gestational age (21 6/7 weeks; interquartile range [IQR], 15 0/7–23 6/7) than those who chose abortion care (18 6/7 weeks; IQR, 14 0/7–23 6/7; $P<.001$). After adjustment for gestational age at PPROM and other key confounders, the authors found a higher incidence of composite maternal morbidity with expectant management compared with abortion care (60.2% vs 33.0%; adjusted odds ratio [aOR], 3.47; 95% confidence interval [CI], 1.52–7.93).[12] It is important to note that regardless of the management decision after previable and periviable PPROM, there was a high incidence of maternal morbidity, which included $\geq$1 of the following: intraamniotic infection (defined as clinical chorioamnionitis documented by a physician and prompting treatment with antibiotics), endometritis, sepsis, unplanned operative procedure after delivery, injury requiring repair, unplanned hysterectomy, unplanned hysterotomy (excluding cesarean), uterine rupture, hemorrhage of >1000

mL, transfusion, admission to the maternal intensive care unit, acute renal insufficiency, venous thromboembolism, pulmonary embolism, and readmission to the hospital within 6 weeks. The most common complication was intraamniotic infection, which occurred in 38.0% of those who chose expectant management, as opposed to 13.0% of those who chose abortion care (odds ratio [OR], 4.10; 95% CI, 2.03–8.26).[12] Postpartum hemorrhage was also more than doubled with expectant management compared with abortion care (23.1% vs 11.0%; OR, 2.44; 95% CI, 1.13–5.26). No adverse maternal outcomes were significantly more common among pregnant individuals who underwent abortion care compared with those who had expectant management. Overall, of the patients who initially selected expectant management, 37% experienced maternal morbidity without neonatal survival, 23% had maternal morbidity and an infant who survived to hospital discharge, 24% had no maternal morbidity and no neonatal survival, and only 16% avoided maternal morbidity and had an infant who survived to discharge (Figure 2). This study was limited to short-term outcomes and did not evaluate long-term maternal or offspring morbidities.[2,39]

Increased risks of maternal morbidity with expectant management of previable and periviable PPROM were also observed in a retrospective cohort study of 99 pregnancies with PPROM before 24 0/7 weeks of gestation at 2 tertiary-

FIGURE 2
Outcomes after expectant management of PPROM at <24 weeks of gestation



Adapted from Sklar et al,[12] a retrospective cohort study of pregnant individuals with PPROM at <24 weeks of gestation at multiple US centers comparing outcomes based on initial trial of expectant management vs abortion care. The most common outcome after trial of expectant management after PPROM <24 weeks was maternal morbidity and no neonatal survival. Maternal morbidity included ≥1 of the following: intraamniotic infection (defined as clinical chorioamnionitis documented by a physician and prompting treatment with antibiotics), endometritis, sepsis, unplanned operative procedure after delivery, injury requiring repair, unplanned hysterectomy, unplanned hysterotomy (excluding cesarean), uterine rupture, hemorrhage of >1000 mL, transfusion, admission to the maternal intensive care unit, acute renal insufficiency, venous thromboembolism, pulmonary embolism, and readmission to the hospital within 6 weeks. Rates of neonatal survival were based on all pregnancies with PPROM <24 weeks that had trial of expectant management. Other studies have shown that earlier gestational ages at PPROM are associated with lower rates of neonatal survival compared with PPROM at later gestational ages.[2]

PPROM, preterm prelabor rupture of membranes.

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level maternity hospitals in Canada from 2009 to 2015.[10] Intraamniotic infection (defined as clinical diagnosis of chorioamnionitis with histologic confirmation) was also more common among pregnant individuals who had expectant management compared with those who had abortion care (58.1% vs 8%; $P<.0001$). Although postpartum hemorrhage did not differ between groups (14.9% vs 20%; $P=.56$), antepartum hemorrhage or abruption were more common with expectant management compared with abortion care (41.9% vs 19%; $P=.02$).[10]

High rates of maternal morbidity were also observed in a Texas cohort of pregnant individuals from September 2021 to May 2022 after legislation in Texas banned virtually all abortions after embryonic cardiac activity can be detected.[40,41] Among 28 pregnant individuals with a medical indication for delivery at <22 weeks of gestation (n=26 with PPROM), expectant management was associated with higher rates of maternal morbidity compared with immediate intervention with labor induction.[42] Maternal morbidity, including complications such as clinical chorioamnionitis and hemorrhage, occurred in 43% of the cohort overall, with nearly doubled rates among those who had expectant management compared with immediate intervention, and only 1 neonate was still alive at the time of publication.

Serious maternal complications such as sepsis and death are difficult to study because few studies use population-based data, and most rely on single- or multisite institutional resources. However, maternal sepsis has been reported to occur in up to 6.8% of cases of previable and periviable PPROM,[2,10,12,33,43] and rates are higher with expectant management compared with abortion care.[38] In an analysis from the French national confidential enquiry into maternal deaths, 7 maternal deaths were found to be associated with expectant management of PPROM at 14 0/7 to 24 6/7 weeks of gestation during a 14-year period, an incidence rate of 45 per 100,000 patients with previable PPROM,[7] with a baseline French maternal mortality rate of 8 to 12 per 100,000 births.[44] Investigation revealed that none of the patients showed signs of infection at the time of admission, and all received prophylactic antibiotics, but infection led to death in 6 of the 7 women. Although the median interval between PPROM and the first signs of infection was 5 days (IQR, 1–10 days), once infection was identified, the median time to death was only 18 hours (IQR, 12–120 hours), illustrating how rapidly the clinical condition can deteriorate.[7]

What are the average latency and perinatal outcomes associated with expectant management of previable and periviable preterm prelabor rupture of membranes?

Because expectant management of previable and periviable PPROM provides no direct medical benefit to the pregnant individual, the likelihood of neonatal survival and morbidity is often paramount to decision-making. The primary goal of expectant management after previable PPROM in patients who desire ongoing pregnancy is to reach a gestational age when the neonate can survive with life-sustaining interventions after birth. For many parents, the goal is neonatal survival without major disability. The average latency, or time between PPROM and delivery, varies substantially across studies of previable and periviable PPROM, with reported duration ranging from 7 days (IQR, 3–29) to 51 days (IQR, 19–107).[2,4,9,10,45] Latency has been inversely associated with gestational age at PPROM (ie, the earlier PPROM occurs, the longer the latency period can be expected).[1,4,46] However, in at least 1 study of pregnant individuals with previable and periviable PPROM at 14 to 24 weeks of gestation who underwent expectant management, latency did not vary by gestational age at PPROM (after PPROM at <20 weeks: median, 8 days; IQR, 1–161; after PPROM at 20 to 21 weeks: median, 4.5 days; IQR, 2–106; after PPROM at 22 to 23 weeks: median, 12 days; IQR, 1–112).[47]

A better measure of latency after previable and periviable PPROM may be the proportion of individuals whose pregnancies reach viability after expectant management. A prospective cohort study of 98 pregnant individuals who had PPROM at 13 0/7 to 23 6/7 weeks of gestation at a tertiary academic care center and 8 affiliated secondary hospitals in Amsterdam (PPROMEXIL-III cohort) found that 40% of individuals who underwent expectant management achieved viability, defined in this study as 24 weeks of gestation, with a median latency of 9 days (IQR, 2.6–52.3).[2] In the Canadian cohort, only 27% of individuals who underwent expectant management achieved viability with a median latency of 7 days (IQR, 3–29).[10] Notably, there was wide variation in latency in both of these studies, and neither evaluated differences in latency based on gestational age at the time of PPROM.

Even after achieving a live birth at a viable gestational age, there remains a high risk of neonatal morbidity and mortality. Estimates of overall neonatal survival vary in published literature from as low as 17% to as high as 80%, likely due to differences in inclusion criteria, populations studied, and improvements in care over time.[8,12,33,43,47–52] For example, survival estimates may be falsely elevated in studies that only include individuals who achieve a certain amount of latency or are delivered at a viable gestational age. Similarly, if studies only analyze neonates admitted to the neonatal intensive care unit, then the survival estimate will not include all those with intrauterine fetal demise, delivery before viability with demise, or demise in the delivery room. In a retrospective cohort study of pregnant individuals with PPROM at <24 weeks of gestation in multiple US centers, only 42 of 108 (38.8%) pregnant individuals who initially opted for expectant management had a neonate who survived to hospital discharge.[12] A total of 26.9% underwent abortion care because of complications during expectant management, 11.1% had an intrauterine fetal demise, 9.3% had neonates who died during labor or in the delivery room, and 13.8% had neonates who died in the neonatal intensive care unit. Other recent studies that reported overall survival

among all those who attempted expectant management found slightly lower rates of neonatal survival to discharge of 25% to 28%.[2,9,10]

One of the major concerns with previable PPROM is lack of sufficient amniotic fluid volume during the period of critical fetal lung development, which can result in pulmonary hypoplasia and death or severe pulmonary disease[14,53]; however, pulmonary hypoplasia is difficult to predict antenatally.[2] In the PPROMEXIL-III cohort, 4 out of 10 live-born neonates who did not survive to discharge were diagnosed with pulmonary hypoplasia, suggesting it may be a large contributor to neonatal mortality.[1] Respiratory distress and bronchopulmonary dysplasia are common among surviving neonates, with incidences up to 50% to 80%.[2,4,8–10,33,43,48,49,54] Other less common neonatal complications such as skeletal deformities, intraventricular hemorrhage, necrotizing enterocolitis, sepsis, and retinopathy of prematurity have been observed in up to 5% to 25% of cases.[4,10,33,45]

Not only are neonates born after previable and periviable PPROM at risk for short-term morbidities, but many of these complications lead to chronic disease and long-term health problems.[14] In the PPROMEXIL-III cohort, which included follow-up of 13 children to the age of 2 to 5 years, 9 (69.2%) had normal neurodevelopment according to the Bayley-III or Wechsler Preschool and Primary Scale of Intelligence tests.[2] However, 50% of children at age 2 and 57% of children at age 5 had respiratory problems requiring treatment with respiratory medications. Similarly, a matched cohort study of 10-year-old children who were delivered after PPROM at 18 to 27 weeks of gestation demonstrated that previable or periviable PPROM was associated with worse lung function, mild pulmonary hypertension, and lower peak oxygen consumption compared with children who were delivered at similar gestational ages but after PPROM at 28 weeks of gestation.[39] In addition, children with a history of previable or periviable PPROM had more motor difficulties and a trend toward more learning and attention problems.[39]

Are there clinical factors that can predict outcomes with expectant management of previable and periviable preterm prelabor rupture of membranes?

When weighing the risks and benefits of expectant management vs abortion care after previable or periviable PPROM, identifying clinical factors that predict outcomes could help individualize counseling. Among all baseline maternal and obstetrical characteristics, later gestational age at PPROM and higher residual amniotic fluid volume are most consistently associated with improved perinatal survival. In most[2,9,10,55] but not all studies[4,45] of previable or periviable PPROM, neonatal survival is more likely when PPROM occurs at later gestational ages. For example, in the PPROMEXIL-III cohort, there were no surviving neonates after PPROM at <16 weeks of gestation; in contrast, approximately 20% survived after PPROM at 16 0/7 to 19 6/7 weeks of gestation, 30% survived after PPROM at 20 0/7 to 21 6/7 weeks of gestation, and 41% survived after PPROM at 22 0/7 to 23 6/7 weeks of gestation.[2]

Residual amniotic fluid volume after PPROM is also associated with differential neonatal outcomes. Compared with nonsurviving neonates, surviving neonates were less likely to be born to pregnant individuals who had oligohydramnios or anhydramnios after PPROM.[4,10,55] However, anhydramnios does not definitively preclude survival, as previous studies have reported rates of anhydramnios ranging from 7% to 38% among surviving neonates.[4,10,55] Gestational age at PPROM and oligohydramnios were found to be independent factors associated with severe respiratory morbidity in a retrospective cohort study of individuals with PPROM at 20 0/7 to 28 6/7 weeks of gestation.[56] However, this and other previous studies are limited by their inclusion of characteristics not known until the time of delivery in the multivariable models, which may bias the results. Although these factors may aid in counseling about the relative risks of neonatal mortality, they remain limited in their ability to accurately predict pregnancy outcomes and should not be used to withhold management options.

In addition to predicting neonatal survival, the ability of clinical factors to predict maternal morbidity after previable and periviable PPROM has also been investigated. In a case–control study of 174 pregnant individuals with PPROM at 14 0/7 to 22 6/7 weeks of gestation, maternal age >35 years and twin gestation were associated with higher odds of composite maternal morbidity including sepsis, intensive care unit admission, acute renal insufficiency, need for uterine curettage or hysterectomy, deep vein thrombosis, pulmonary embolus, need for blood transfusion, need for readmission, or maternal death (aOR, 4.00; 95% CI, 1.48–10.8; and aOR, 5.62; 95% CI, 2.21–14.2; respectively).[57] Consideration of maternal risk after previable and periviable PPROM based on underlying medical and obstetrical characteristics should also be incorporated into the shared decision-making process.

For pregnant individuals undergoing expectant management of previable and periviable preterm prelabor rupture of membranes, what are the antepartum interventions that improve perinatal outcomes?

Antibiotics

Broad-spectrum antibiotics are recommended for the management of PPROM at <34 weeks of gestation and can be considered at 20 0/7 to 23 6/7 weeks to prolong latency and reduce neonatal morbidity.[1,21] The recommended antibiotic regimen includes a 7-day course of antibiotic therapy with a combination of intravenous ampicillin and erythromycin for 48 hours followed by oral amoxicillin and erythromycin for an additional 5 days based on data from a randomized clinical trial.[58]

Azithromycin can be used as an alternative to erythromycin in settings where it is not available given that observational studies have found no evidence of decreased efficacy and potential benefit with decreased rates of chorioamnionitis.[59] Amoxicillin–clavulanic acid should be avoided because it has been associated with increased risk of necrotizing enterocolitis.[60]

There are limited data surrounding antibiotic use specifically after previable and periviable PPROM. Retrospective observational studies evaluating factors associated with neonatal survival after previable and periviable PPROM have shown that surviving neonates were more likely to be born to pregnant persons who received antibiotics, and antibiotic use was associated with longer latency.[9,55] However, the optimal antibiotic type, dose, and timing of administration after previable and periviable PPROM are unknown, and considerable variation exists in current clinical practice.[45,61–63] Regarding antibiotic timing, a retrospective cohort study of 94 pregnant individuals with PPROM at 16 0/7 to 23 6/7 weeks of gestation demonstrated that administration of antibiotics <24 hours after PPROM vs >24 hours after PPROM did not impact maternal or neonatal outcomes.[64] Key limitations of this study include the small sample size and small difference in antibiotic timing between the groups, with median time to antibiotic administration of 0 days in the immediate group vs 1 day (IQR, 1–2 days) in the delayed group. In summary, **we recommend antibiotics for pregnant individuals who choose expectant management after PPROM at ≥24 0/7 weeks (GRADE 1B).[65] Antibiotics can be considered after PPROM at 20 0/7 to 23 6/7 weeks of gestation (GRADE 2C)**.[65] Given the lack of evidence of clear benefit of antibiotics following previable PPROM at <20 weeks, we recommend shared decision-making reviewing potential benefits and risks of the use of antibiotics at the time of PPROM diagnosis vs at a later gestational age.

When the decision is made to administer antibiotics after previable and periviable PPROM, it is reasonable to follow similar recommendations for antibiotic regimen and duration of treatment as for PPROM at later gestational ages, given the lack of data. Modifications to the antibiotic regimen may be necessary if inpatient hospitalization for intravenous therapy is deferred. Nevertheless, caution is advised against prolonged or repeated antibiotic courses beyond what would be used for PPROM at later gestational ages to optimize antibiotic stewardship.[1]

UNNUMBERED TABLE
Summary of recommendations

#	Recommendation	Grade
1	We recommend that pregnant patients with previable and periviable PPROM receive individualized counseling about the maternal and fetal risks and benefits of both abortion care and expectant management to guide an informed decision. All patients with previable and periviable PPROM should be offered abortion care. Expectant management can also be offered in the absence of contraindications.	1C
2	We recommend antibiotics for pregnant individuals who choose expectant management after PPROM at ≥24 weeks of gestation.	1B
3	Antibiotics can be considered after PPROM at 20 0/7 to 23 6/7 weeks of gestation.	2C
4	Administration of antenatal corticosteroids and magnesium sulfate is not recommended until the time when a trial of neonatal resuscitation and intensive care would be considered appropriate by the healthcare team and desired by the patient.	1B
5	Serial amnioinfusions and amniopatch are considered investigational and should be used only in a clinical trial setting; they are not recommended for routine care of previable and periviable PPROM.	1B
6	Cerclage management after previable and periviable PPROM is similar to cerclage management after PPROM at later gestational ages; it is reasonable to either remove the cerclage or leave it in situ after discussing the risks and benefits and incorporating shared decision-making.	2C
7	In subsequent pregnancies after a history of previable or periviable PPROM, we recommend following guidelines for management of pregnant persons with a previous spontaneous preterm birth.	1C

PPROM, preterm prelabor rupture of membranes.

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Antenatal corticosteroids, magnesium sulfate

Regarding other antenatal interventions that may be used during expectant management of PPROM at later gestational ages, **administration of antenatal corticosteroids and magnesium sulfate is not recommended until the time when a trial of neonatal resuscitation and intensive care would be considered appropriate by the healthcare team and desired by the patient (GRADE 1B).**[21,22] Given that the primary focus of this Consult is the management of previable and periviable PPROM before the period when neonatal resuscitation and intensive care are pursued, an in-depth discussion on the appropriate timing of these interventions is beyond the scope but can be found elsewhere.[21]

Inpatient vs outpatient management

High-quality evidence to inform decisions regarding inpatient vs outpatient management during expectant management of previable and periviable PPROM is lacking. It is reasonable for individuals to be observed for a period of time in the hospital to ensure stability without evidence of preterm labor, abruption, or infection before discharge home. Outpatient management with close monitoring for signs or symptoms of maternal complications such as hemorrhage or infection is often preferred when the pregnant person desires expectant management during the period when

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Society for Maternal-Fetal Medicine grading system: GRADE (Grading of Recommendations Assessment, Development and Evaluation) recommendations[83,a]

Grade of recommendation	Clarity of risk and benefit	Quality of supporting evidence	Implications
1A. Strong recommendation, high-quality evidence	Benefits clearly outweigh risks 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 recommendation that 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 risks 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 that 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 risks and burdens, or vice versa	Evidence from observational studies, unsystematic clinical experience, or randomized controlled trials with serious flaws Any estimate of effect is uncertain	Strong recommendation that 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; alternative 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 randomized controlled trials with serious flaws Any estimate of effect is uncertain	Very weak recommendation; alternatives may be equally reasonable
Best practice	Recommendation in which either (1) there is an 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 (2) recommendation to the contrary would be unethical		

[a] Adapted from Guyatt et al,[84] 2008.

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UNNUMBERED TABLE
Organization recommendations

The content of this document reflects the national guidelines related to preterm prelabor rupture of membranes.

Organization	Title	Year of publication
American College of Obstetricians and Gynecologists	Practice Bulletin No.142: Cerclage for the management of cervical insufficiency[81]	2014
American College of Obstetricians and Gynecologists	Committee Opinion No. 712: Intrapartum Management of Intraamniotic Infection[23]	2017
American College of Obstetricians and Gynecologists	Prelabor Rupture of Membranes: ACOG Practice Bulletin, Number 217[1]	2020

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neonatal resuscitation and intensive care would not be pursued for fetal benefit. Before hospital discharge for a trial of outpatient expectant management, it is important to provide detailed instructions about the signs and symptoms of PPROM complications that the pregnant individual should monitor.[1] These include but are not limited to daily temperature monitoring to screen for maternal fever and infection, contractions, vaginal bleeding, discolored or malodorous vaginal discharge, and abdominal pain.[1] In addition, it is common for patients to be seen frequently (often weekly) in an outpatient setting for close monitoring, including assessment of maternal vital signs, fetal heart rate, physical examination, and possible laboratory evaluation for signs of infection such as leukocytosis.[66] Hospital readmission should occur if there are contraindications to continued expectant management, such as hemorrhage, infection, or fetal demise, or after reaching a point when a trial of neonatal resuscitation and intensive care would be considered appropriate by the healthcare team and desired by the patient so that antenatal corticosteroids, magnesium sulfate, and antepartum fetal surveillance may be initiated as appropriate.[1,21]

Serial amnioinfusions and amniopatch

Investigators have attempted to use serial amnioinfusions and techniques that reseal the amniotic membrane to improve outcomes after previable PPROM. The 2 largest trials that randomly assigned patients with PPROM at 16 0/7 to 23 6/7 weeks of gestation to serial amnioinfusions until 28 to 34 weeks of gestation or expectant management found no reduction in perinatal morbidity within each trial population, and the results did not change when they were pooled together (pooled 66.1% vs 71.4%; relative risk, 0.92; 95% CI, 0.72–1.19).[67–69] Although limited by sample size, there were also no reductions in potential risks such as infection, abruption, hemorrhage, or spontaneous onset of labor with amnioinfusion compared with expectant management.[67–69] Similarly, an amniopatch, or injection of autologous platelet concentrate and cryoprecipitate,[70] has not significantly improved perinatal morbidity after previable PPROM. A retrospective cohort study of pregnant individuals with PPROM at 17 to 23 weeks of gestation found that only 1 of 7 individuals had complete resealing of the membrane after an amniopatch and delivered at 39 weeks of gestation without complications.[71] Although there seemed to be evidence of longer latency (median, 30 days; IQR, 3–123; vs median, 14 days; IQR, 0–67; P=.14), later gestational age at delivery (median, 25.3 weeks; IQR, 21.4–39.0; vs median, 24.4 days; IQR, 0–67; P=.49), and less histologic chorioamnionitis (57.1% vs 76.2%; P=.37) with amniopatch, these differences were not statistically significant and were limited by a small sample size.[71] On the basis of these findings, **serial amnioinfusions and amniopatch are considered investigational and should be used only in a clinical trial setting; they are not recommended for routine care of previable and periviable preterm prelabor rupture of membranes (GRADE 1B).**

Should transvaginal cervical cerclage be removed after previable and periviable preterm prelabor rupture of membranes?

There is a lack of consensus surrounding cerclage management after PPROM at any gestational age.[72] Currently, there is only a single randomized clinical trial evaluating the efficacy of cervical cerclage removal after PPROM at 22 0/7 to 32 6/7 weeks of gestation vs expectant management with cerclage retention in situ.[72] After enrolling 56 participants, the trial was stopped early because of futility, with no evidence of pregnancy prolongation with cerclage retention compared with removal (1-week prolongation in 45.8% with cerclage retention vs 56.2% with cerclage removal; P=.58). Although there was limited power to assess secondary outcomes, cerclage retention did not significantly increase the rates of chorioamnionitis (41.6% vs 25.0%; P=.25), postpartum endometritis (12.5% vs 3.1%; P=.30), composite neonatal morbidity (56% vs 50%; P=.91), or perinatal

mortality (16% vs 12%; $P=.52$) compared with cerclage removal. Although some retrospective cohort studies have shown longer latency with cerclage retention, there may also be an associated increase in infectious morbidity.[73–78] These data are not specific to the previable and periviable periods. **Cerclage management after previable or periviable PPROM is similar to cerclage management after PPROM at later gestational ages; it is reasonable to either remove the cerclage or leave it in situ after discussing the risks and benefits and incorporating shared decision-making (GRADE 2C).**

What are the risks in subsequent pregnancies after a history of previable or periviable preterm prelabor rupture of membranes?

There is limited evidence regarding best practices for management of subsequent pregnancies after a history of previable or periviable PPROM. In a retrospective cohort study of 108 pregnant women with a history of ≥1 pregnancies complicated by PPROM at <24 weeks of gestation, there was a high risk of recurrent preterm birth.[79] Nearly 50% of immediate subsequent pregnancies resulted in recurrent preterm birth, with 30% at <34 weeks of gestation, 23% at <28 weeks of gestation, and 17% at <24 weeks of gestation. Notably, only 45% of participants received either progesterone or cerclage for prevention of recurrent preterm birth, but outcomes were similar regardless of these interventions. The only factor that was independently associated with recurrent preterm birth after previable PPROM was a history of another previous preterm birth.[79] Cerclage placement for management of subsequent pregnancies after a previous previable PPROM was associated with increased odds of preterm birth in a retrospective cohort study in Israel (63.2% vs 10.9%; OR, 14.0; 95% CI, 3.97–49.35).[80] Although this study was limited by small sample size (n=74) and a heterogeneous population with multiple differences in baseline characteristics between those who received a cerclage and those who did not, it encourages caution in the management of subsequent pregnancies to avoid causing harm. On the basis of limited existing data, **in subsequent pregnancies after a history of previable or periviable PPROM, we recommend following guidelines for management of pregnant persons with a previous spontaneous preterm birth (GRADE 1C)**.[1,81,82] History-indicated cerclage should be reserved for individuals with classic historical features of cervical insufficiency or an unexplained second-trimester loss in the absence of placental abruption.[81]

Future directions and conclusion

Previable and periviable PPROM represent serious obstetrical complications with high rates of maternal and neonatal morbidity and mortality. Pregnant individuals require counseling about all management options, including abortion care, and individuals who elect expectant management should be provided with the most realistic estimate of perinatal survival and morbidities based on the best available evidence. Data from the multicenter US retrospective cohort study help contextualize the overall outcome of expectant management after previable PPROM; only approximately 15% had neonatal survival to discharge without maternal morbidity, whereas more than one-third had both perinatal demise and maternal morbidity, and the remaining 50% of individuals experienced either maternal morbidity or perinatal demise (Figure 2).[12] Among surviving neonates, there is still a high risk of chronic pulmonary disease and other long-term morbidities.[2,39] Additional research will help inform individual management decisions, such as the timing of antibiotics. Monitoring adverse outcomes among pregnant individuals who are unable to access abortion care because of lack of clarity about exceptions to state abortion restrictions will be important to add to the existing literature and may help drive legislative and institutional changes. Until that time, it is imperative that all pregnant individuals with previable and periviable PPROM be counseled about all management options, including abortion care, and be able to seek second opinions and appropriate management based on personal circumstances and priorities. Individuals should understand the risk of serious maternal complications with expectant management of previable and periviable PPROM, with only small chances of neonatal survival without major morbidity. Informed consent, respect for patient autonomy, and shared decision-making aligned with the pregnant individual's values and incorporating the best available data should ultimately guide management decisions after previable and periviable PPROM.

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