Consensus Statement

Care Levels for Fetal Therapy Centers

Ahmet A. Baschat, MD, Sean B. Blackwell, MD, Debnath Chatterjee, MD, James J. Cummings, MD, Stephen P. Emery, MD, Shinjiro Hirose, MD, Lisa M. Hollier, MD, MPH, Anthony Johnson, DO, Sarah J. Kilpatrick, MD, PhD, Francois I. Lukes, MD, PhD, M. Kathryn Menard, MD, MPH, Lawrence B. McCullough, PhD, Julie S. Moldenhauer, MD, Anita J. Moon-Grady, MD, George B. Mychaliska, MD, Michael Narvey, MD, Mary E. Norton, MD, Mark D. Rollins, MD, PhD, Eric D. Skarsgard, MD, Kuojen Tsao, MD, Barbara B. Warner, MD, MSi, Abigail Wilpers, WHNP-BC, PhD, and Greg Ryan, MB

Fetal therapies undertaken to improve fetal outcome or to optimize transition to neonate life often entail some level of maternal, fetal, or neonatal risk. A fetal therapy center needs access to resources to carry out such therapies and to manage maternal, fetal, and neonatal complications that might arise, either related to the therapy per se or as part of the underlying fetal or maternal condition. Accordingly, a fetal therapy center requires a dedicated operational infrastructure and necessary resources to allow for appropriate oversight and monitoring of clinical performance and to facilitate multidisciplinary collaboration between the relevant specialties. Three care levels for fetal therapy centers are proposed to match the anticipated care complexity.

From the Department of Gynecology & Obstetrics, Johns Hopkins Center for Fetal Therapy, Johns Hopkins University, Baltimore, Maryland; the Department of Obstetrics, Gynecology & Reproductive Sciences and the Division of Pediatric General and Thoracic Surgery, Department of Surgery, McGovern Medical School, University of Texas Health Science Center at Houston, Houston, Texas; the Department of Anesthesiology, Children’s Hospital Colorado/Colorado Fetal Care Center, University of Colorado School of Medicine, Aurora, Colorado; the Department of Pediatrics & Bioethics, Albany Medical College, Albany, New York; the Division of Maternal-Fetal Medicine, Department of Obstetrics, Gynecology & Reproductive Sciences, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania; Division of Pediatric, General, Thoracic and Fetal Surgery, Department of Surgery, UC Davis Medical Center, Sacramento, California; the Division of Maternal-Fetal Medicine, Department of Obstetrics & Gynecology, and the Center for Medical Ethics and Health Policy, Baylor College of Medicine, Houston, Texas; the Department of Obstetrics & Gynecology, Cedars-Sinai Medical Center, Los Angeles, California; the Department of Surgery, Warren Alpert Medical School of Brown University, and Hasbro Children’s Hospital, Providence; Rhode Island; the Division of Maternal-Fetal Medicine, Department of Obstetrics & Gynecology, UNC School of Medicine, Chapel Hill, North Carolina; the Center for Fetal Diagnosis and Treatment, Children’s Hospital of Philadelphia, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, Pennsylvania; the Division of Pediatric Cardiology, Department of Clinical Pediatrics, and the Department of Obstetrics, Gynecology & Reproductive Sciences, University of California, San Francisco, San Francisco, California; the Department of Pediatric Surgery, C.S. Mott Children’s Hospital, University of Michigan, Ann Arbor, Michigan; the Division of Neonatology, Department of Paediatrics, University of Manitoba, Winnipeg, Manitoba, Canada; the Department of Anesthesiology, Mayo Clinic, Rochester, Minnesota; the Department of Surgery, Centre for Surgical Research, BC Children’s Hospital, University of British Columbia, Vancouver, British Columbia, Canada; the Division of Newborn Medicine, Department of Pediatrics, Washington University School of Medicine in St. Louis, St. Louis, Missouri, Yale University School of Nursing, Orange, Connecticut; and the Ontario Fetal Centre, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, Canada.

The North American Fetal Therapy Network is supported through funding by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (SR11HD059293-05).

The Board of the American Pediatric Surgical Association supports the development of a framework for the safe and ethical provision of care to fetuses and mothers. Organizations and their level of support of this document are listed in Appendix 1, available online at http://links.lww.com/AOG/C709.

Each author has confirmed compliance with the journal’s requirements for authorship.

Corresponding author: Ahmet A. Baschat, MD, Department of Gynecology & Obstetrics, Johns Hopkins Center for Fetal Therapy, Johns Hopkins University, Baltimore, MD; email: abascha1@jhmi.edu.

Financial Disclosure

Ahmet A. Baschat disclosed receiving royalties from UpToDate. James J. Cummings disclosed that he receives funding from ONY Biotech, Amherst, NY—first as a consultant, then later as a part-time employee. During the time this report was being prepared, he served as chair of a national committee (American Academy of Pediatrics, Fetus and Newborn). This was a voluntary, uncompensated position. Sarah J. Kilpatrick disclosed receiving funding from Contemporary OB/GYN, and Kaneka Corporation, and the textbook, Obstetrics—Normal and Problem Pregnancies. She also disclosed receiving royalties from UpToDate. Anita J. Moon-Grady is an unpaid board member for the Fetal Heart Society and a board member of the AIUM. She reported that this article discusses off-label use of approved intravascular devices, such as balloon catheters. The other authors did not report any potential conflicts of interest.

Copyright © 2022 The Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

ISSN: 0029-7844/22
Fetal therapy, performed for the benefit of the fetus and neonate, has evolved markedly over the past three decades.\textsuperscript{1,2} This is reflected in the increasing membership of fetal therapy centers in the North American Fetal Therapy Network and by the number and complexity of interventions cumulatively performed at these centers.\textsuperscript{3,4} All fetal interventions, whether medical or surgical, are by definition performed on a pregnant individual before separation of the fetus from the placenta at birth. As such, they may entail maternal risks in either the current or future pregnancies, as well as fetal or neonatal risks. Although this document refers to fetal interventions, recommendations are intended to prioritize safety for both the pregnant individual and their fetus or neonate based on the available evidence.

To perform any fetal intervention, provide all the associated care needs, address any potential risks, and assess outcomes, a fetal therapy center requires a dedicated operational infrastructure, which encourages and facilitates the close collaboration of health care professionals from maternal, fetal, nursing, anesthetic, and pediatric specialties.\textsuperscript{5–7} Several of these specialties, specifically obstetrics and maternal–fetal medicine, pediatric surgery, and neonatology, already have established levels of care.\textsuperscript{8–10} These are based on the guiding principle of matching resources with the anticipated complexity of care to achieve optimal outcomes at an institutional and regional level.\textsuperscript{8–11} These care levels are independently assigned for each of these specialties and may not coexist at the same level at a single institution. Guidelines issued by the American College of Obstetricians and Gynecologists (ACOG), the Society for Maternal-Fetal Medicine (SMFM), and American Academy of Pediatrics have outlined the general operational infrastructure necessary for centers to perform fetal diagnostic and therapeutic procedures but have not stratified these guidelines by the risk profile of individual interventions.

**GOAL**

The purpose of this document is to propose levels of care for fetal therapy centers based on the anticipated complexity of an intervention for both pregnant individuals and their neonates. Our recommendations will also consider the obstetric, neonatal, pediatric (medical and surgical), and ethical care resources that should be in place to support such fetal interventions. Our guiding principle is to provide maternal safety and autonomy while also addressing the anticipated care needs of the fetus and neonate.

**FETAL INTERVENTIONS AND THE PRACTICE OF FETAL THERAPY**

The goal of fetal therapy may be to achieve a prenatal cure, attenuate or improve sequelae for the infant, or optimize the transition to postnatal life. When presented with a prenatal diagnosis, a pregnant individual may choose to pursue expectant management, fetal therapy, pregnancy termination, active neonatal care, or palliation.\textsuperscript{12–17} It is the duty of the fetal therapy center to support those decisions with the appropriate level of care, regardless of the management choice.

A fetal therapy center must provide a pregnant individual with an understanding of the fetal condition and the relative maternal and fetal risks and benefits of any proposed intervention when considering management options. The ability to appropriately counsel patients relies on diagnostic capabilities that enable an estimate of fetal risk based on an accurate prenatal diagnosis and an understanding of the natural history of the disease and its overall prognosis.

The risks of any fetal intervention depend on the 1) technical details of the procedure, including its complexity, fetal status, degree of compromise, and gestational age; 2) presence of maternal comorbidities (eg, high body mass index [BMI, calculated as weight in kilograms divided by height in meters squared], obstetric risk factors for preterm birth, or membrane rupture; and 3) operator and center experience.\textsuperscript{18–27}

A comprehensive maternal assessment of psychosocial, familial, social, moral, religious, ethical, and financial influences are elements to be considered in the planning of the patient’s care.\textsuperscript{28,29} Risk–benefit assessment will differ according to the specific intervention and by practitioner and fetal therapy center. If
Respiratory technologist or anesthetic assistant: fetal management during interventions
Pediatric cardiology: Prenatal diagnosis and consultation, postnatal management, fetal hemodynamic monitoring during complex procedures or transplacental medical therapy, neonatal cardiac care

Additional care services
Social work and spiritual support: coordination of social services, patient advocacy
Patient services coordinator, financial counselor: scheduling of appointments, financial planning assistance, and insurance authorization across all involved care specialties
Data coordinator: tracking and facilitating the reporting of outcomes-related data of the fetal therapy center
Interpreting and cultural diversity specialist: consultation, consent, follow-up services, with availability especially when multiple therapeutic options are being entertained
Family planning: safe pregnancy termination and contraception counseling
Palliative care: palliative neonatal care, perinatal hospice services

Research regulatory and ethics
Institutional research review boards: oversight of experimental and research-related interventions
Medical ethicist: consultation and oversight as needed for research and ethical questions that arise during clinical care
Database and information technology support: data collection for sharing, reporting, quality improvement, and research

members, spouses, partners, or even health care professionals themselves, to undergo or decline any fetal therapy. A thorough discussion with patients needs to clearly present the full range of therapeutic options, their risks and benefits for the fetus, as well as any potential risks to the pregnant individual in the current or future pregnancies. An important conversation that should precede any fetal intervention, particularly in a sick or very premature fetus, is the management of procedure-related fetal complications, specifically addressing whether delivery or nonintervention is to be undertaken, with clear discussion of all consequences. These conversations are best held in collaboration with maternal–fetal medicine specialists, neonatologists, and additional specialists as required by the condition and may benefit from the involvement of an unbiased and specially trained independent advocate, such as the patient's primary health care professional, perinatal nurse, or religious advisor.

UNIVERSAL CORE COMPONENTS AND OPERATIONAL RESPONSIBILITIES OF A FETAL THERAPY CENTER

Certain resources are fundamental to optimize the provision of care and to minimize any fetal therapy procedure–related risks. Universal core components of a fetal therapy center as designated by several professional societies are summarized in Box 1.2,5,7 The need for additional resources that may be required for specific interventions should be considered in the context of the proposed fetal therapy center care levels.

Leadership

A fetal therapy center should have a medical director—a physician with experience in maternal and fetal care and, specifically, in maternal–fetal interventions. The medical director is responsible for operational oversight of delivery of clinical care and ensuring patient safety. The medical director should work in partnership with a nursing director, who supervises the nursing staff and shares in the oversight of patient care and center operations. Others may be appointed in allied leadership roles, depending on the operational setup at a particular fetal therapy center. Although fetal therapy is not a recognized subspecialty, its practice demands advanced understanding and training in fetal physiology; expertise in prenatal diagnosis, fetal imaging, and surveillance; and operative skills to safely perform fetal interventions.

Staffing

A fetal therapy center requires a multidisciplinary and closely collaborative group of health care personnel. In addition to providing safe and effective fetal therapy, a center’s team should facilitate a positive care environment and experience by providing pregnant individuals and their families with access to resources that facilitate managing their expectations and coping with their stress and grief. Nurses with expertise in fetal diagnosis and prenatal care play a central role in fetal therapy centers and may be involved in the patients’ and referring health care professionals’ initial contact with the center, throughout prenatal evaluation, counseling, fetal intervention, and follow-up.33,34 A financial counselor or insurance specialist may assist in reviewing a patient’s health care coverage and initiate insurance authorization if required. A nurse coordinator or licensed social worker may help manage the psychosocial needs of the patient and family and act as an advocate. Geneticists and genetic counselors can refine the genetic testing strategy, discuss results with families, and help to arrange relevant autopsy examinations when indicated. Key members of any team are practitioners who are skilled in performing the fetal interventions. Other medical specialists should be involved as required in each case. A perinatal or pediatric palliative care service is important for cases in which a fetal death or complicated neonatal course are anticipated.

A data coordinator is invaluable in ensuring that key indicators of care quality and outcome are monitored and can be audited and reported to internal and external registries, funding agencies, and patients, as needed.2 Given the ethical challenges entailed in certain, particularly innovative, fetal interventions, the involvement of the institutional ethics committee in such circumstances is vital.2,28–30

Diagnostic Services

A fetal therapy center needs to have access to appropriate diagnostic services for all conditions that they intend to manage. This includes imaging specialists skilled in the performance of detailed fetal ultrasonography, fetal echocardiography and cardiovascular imaging, and magnetic resonance imaging. Imaging expertise has to include prognostic staging for conditions such as congenital pulmonary airway malformations,34 congenital diaphragmatic hernia,35 congenital heart disease,36,37 fetal hydrops,38 and twin–twin transfusion syndrome,39–41 as well as ultrasonography for procedural guidance. Magnetic resonance images should be interpreted by a board-certified imaging radiologist with specific expertise in fetal magnetic resonance imaging. For complex cardiac conditions, a pediatric cardiologist with expertise in fetal echocardiography and postnatal cardiac management must be involved.
Facilities Needed to Offer Fetal Therapy and Maternal, Fetal, and Neonatal Care

Appropriate clinical facilities should be identified where fetal interventions can be performed and where postprocedure monitoring and recovery of the pregnant patient and fetus(es) can occur. Depending on the nature of the procedure and gestational age, this may be in the imaging facility, fetal medicine unit, operating room, or labor and delivery suite. After fetal viability, all fetal therapy procedures should be performed in areas with access to a labor and delivery suite and neonatal intensive care unit (NICU). Operative and monitoring equipment needs to be available and should be regularly serviced. The capacity for rapid provision of red blood cells or platelets for intrauterine transfusion as well as medications for fetal administration are necessary at any fetal therapy center.

Policies, Organization, Conduct, and Governance

Fetal therapy centers should offer evidence-based therapies that are subject to institutional oversight and provide transparent and complete reporting of maternal and fetal outcomes. Innovative interventions, including any that entail substantial modification to accepted protocols or procedures, should be undertaken only with prior in-depth discussion, review, and consensus-based approval by the relevant subspecialists and potential consultation with an institutional ethics committee or panel. Research must be conducted with institutional review board approval and oversight, including registration as a clinical trial when appropriate. The fetal therapies that are offered, their eligibility criteria, as well as the mechanisms to introduce new therapies should be clearly established at each institution and reviewed periodically as part of a formal institutional or departmental quality-assurance process.

Fetal Therapy Oversight

A multidisciplinary fetal therapy advisory committee ideally includes representation from a variety of health care workers, including maternal–fetal medicine specialists, pediatric surgeons, anesthesiologists, neonatologists, geneticists, social workers, nurses, perinatal medical ethicists, and other ad hoc members, as appropriate, who may or may not be involved in the direct care of the patient. The composition, role, and responsibilities of such a committee may be modified depending on the specific needs of a fetal therapy center and could range from quality assurance or audit through clinical oversight. Committee members might review proposed interventions that are considered (locally) innovative or experimental, evaluate research proposals before their submission, participate in trial-related data safety monitoring boards, or conduct case reviews.

Maintenance of Competency and Center Performance

Achieving optimal maternal and fetal outcomes is dependent on a number of factors, including practitioner and team experience, local resources and setting, case volume, ongoing audit, and maintenance of competency of the whole health care team. The association between surgical volume and improved outcomes has been attributed to multiple factors, including team proficiency and their ability to recognize, triage, and manage specific complications within a particular health care system.

For those who choose pregnancy termination, a process should be in place to ensure access, including referral to another accommodating practitioner or facility if abortion services are not available at the fetal center.

Developing relevant, agreed-on outcome measures for specific interventions that are frequently evaluated and monitored will help to prospectively evaluate fetal intervention risks, as well as the overall performance of fetal therapy treatments. Outcomes relevant for any fetal intervention include 1) preterm prelabor rupture of membranes (PROM), preterm birth, mode of delivery, stillbirth, or neonatal death; 2) maternal complications such as hemorrhage, infection, pulmonary edema, or intensive care unit (ICU) admission; 3) the frequency with which the intended treatment outcome was achieved; and 4) the effect on future fertility and pregnancy outcomes. Core outcome sets are being developed in fetal medicine and currently exist for twins, twin–twin transfusion syndrome, congenital diaphragmatic hernia, fetal
myelomeningocele closure, and fetal growth restriction. Centers should also develop or participate in needs-specific continuing medical education and quality-improvement programs, which may include the use of simulation training models, to help develop and maintain their competence in specific fetal interventions.

**FETAL THERAPY CENTER CARE LEVELS—PRINCIPAL CONSIDERATIONS**

A fetal therapy center needs to have all of the resources to carry out fetal interventions and to manage any maternal, fetal, or neonatal complications that might arise. We are proposing a three-tiered model to optimize the delivery of care at each level of case complexity, which may entail regionalized concentration of some subspecialized health care services. The underlying fetal condition, type of intervention, and expected treatment outcomes are the primary factors determining these proposed tiers and resource settings. Intervention-related risks can occur independent of experience or case volume, and, particularly, maternal complication rates tend to be underreported. Patient safety requires a care setting that, at the very least, can manage common (greater than 1%) as well as infrequent but severe complications. The care level documents for maternal, neonatal, and pediatric surgery provide the underlying framework that was adapted for fetal therapy centers.

**Maternal Levels of Care**

Aside from accredited birth centers, maternal care settings have been stratified into four levels in the United States. Of these, levels III (subspecialty care) and IV (regional perinatal center) have board-certified obstetricians, maternal–fetal medicine subspecialists, obstetric anesthesiologists, and adult subspecialists, with ICU facilities onsite that accept individuals who are pregnant or in the postpartum period; both levels III and IV allow access to the full range of expertise that may be necessary for any maternal or fetal intervention. Onsite ICU care at a level IV center allows for primary or co-management by a maternal–fetal medicine team with expertise in complex medical conditions and critically ill or unstable pregnant or postpartum patients.

**Neonatal Levels of Care**

Within the four neonatal care levels, level III and IV NICUs have attendant neonatologists, nurse practitioners, respiratory technologists, and pediatric anesthesiology services either onsite or readily available at an adjacent institution. Although level III NICUs can provide prolonged support for all degrees of prematurity, the ability to provide onsite subspecialty care, including the surgical management of complex congenital abnormalities, is limited to level IV NICUs or pediatric intensive care units (PICUs). Neonatal outcomes are improved the closer the delivery occurs to a pediatric center that can provide a full range of medical and surgical care. All fetal interventions that may potentially result in (iatrogenic) preterm delivery after viability require, at least, level III NICU support. Complex neonatal management challenges, including those encountered with congenital anomalies, may benefit from access to a level IV NICU with subspecialty resources. Surgical care of newborns with congenital anomalies is optimized in the highest-level pediatric surgery facility, which is required for level IV NICU or PICU designation.

**Considerations for Selecting the Necessary Level of Care**

Before performing any fetal intervention, factors such as gestational age; fetal condition; and procedure-related maternal, fetal, or preterm delivery risks, as well as the potential need to deliver outside the patients’ community, must be evaluated to determine whether the case can be managed locally or if transfer to a higher-level facility should be considered. It is important that each fetal therapy center has strong institutional backing and that specific policies are in place to support a collaborative, multispecialty model.

**Risk Profile and Complexity of Fetal Interventions**

The overall risk profile and complexity of any fetal intervention is related to its degree of invasiveness and the required interventional setup. These factors also determine the type of anesthesia or analgesia required, as well as the need for maternal and fetal monitoring during and after the procedure. Neonatal risks are determined by the potential risk of delivery soon after the intervention, gestational age at the time of intervention, and the neonatal management needs specific to the fetal condition. Therefore, neonatal care needs can range from management of prematurity to multidisciplinary management of coexisting conditions. We propose that fetal interventions be categorized at three levels: 1) needle-based, 2) percutaneous, and 3) open or laparotomy. These levels dictate the resource setting in which these procedures can be performed safely.
Ultrasonography-Guided Needle-Based Fetal Therapy Interventions

For these procedures, a fine needle is advanced into a target under continuous ultrasonographic guidance. This approach is used for chorionic villous sampling, amniocentesis, amnioinfusion, amnioreduction, fetal fluid drainage, fetal blood sampling, intrauterine transfusion of blood products, fetal or placental interstitial vascular occlusion, and fetal cardiac interventions (Table 1). Needle-based procedures typically require only local anesthesia but may occasionally require intravenous conscious sedation and, very rarely, neuraxial anesthesia. The principal maternal risks include postprocedural pain, preterm PROM, preterm labor, and the need for emergent delivery for fetal distress (Table 1). After viability, intraoperative fetal surveillance may be used to identify any signs of compromise that might require either intrauterine resuscitation or delivery. After the procedure, maternal monitoring for obstetric complications and fetal heart rate monitoring after viability are performed.

Percutaneous Fetal Interventions

Percutaneous interventions include ultrasonography-guided bipolar cord coagulation, radio frequency ablation, shunt procedures, and fetoscopy for laser umbilical cord occlusion, laser ablation of placental vascular anastomoses, fetoscopic endotracheal occlusion, amniotic band resection, and percutaneous fetal myelomeningocele closure (Table 2). Fetoscopic interventions or bipolar forceps procedures are performed using a combination of ultrasonographic guidance and direct visualization, entering the uterus directly or through a sheath. Percutaneous fetoscopic fetal myelomeningocele closure notably may employ multiple ports. Anesthetic requirements increase correspondingly with increasing invasiveness, procedure duration, and complexity, from local anesthesia to conscious intravenous sedation (monitored by the anesthesiology team) to general anesthesia.

Table 1. Ultrasonography-Guided Needle-Based Fetal Interventions

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Reported Procedural Risks</th>
<th>Required Resources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fetal blood sampling and transfusion</td>
<td>Maternal: urgent delivery</td>
<td>Maternal: L&amp;D unit if viable; OB anesthesiology for intravenous conscious sedation or, rarely, neuraxial anesthesia</td>
</tr>
<tr>
<td>Needle size: 22-20 gauge (outer diameter 0.71–0.91 mm)</td>
<td>Fetal: puncture site bleeding 20–30%; transient bradycardia 5–10%; fetal death 0.4%; up to 25% for complicated fetal disease and hydrops</td>
<td>Neonatal: premature delivery (average gestational age at birth: 31–35 wk; condition-specific)</td>
</tr>
<tr>
<td>Fetal cardiac interventions</td>
<td>Maternal: postoperative pain up to 32%; postoperative nausea or vomiting up to 26%</td>
<td>Maternal: L&amp;D unit if viable; OB anesthesiology for sedation; neuraxial, general anesthesia as required</td>
</tr>
<tr>
<td>Needle size 18-16 gauge (outer diameter 1.27–1.65 mm)</td>
<td>Fetal: transient hemopericardium 18–28%; bradycardia up to 32%; IUFD by 48 h 10–30%</td>
<td>Neonatal: premature delivery (less than 37 wk up to 20%); fetal death before discharge up to 61%</td>
</tr>
<tr>
<td>Radiofrequency, microwave, or interstitial laser ablation</td>
<td>Maternal: myometrial bleeding less than 1%</td>
<td>Maternal: dedicated intervention setting, OB anesthesiology for intravenous conscious sedation and, rarely, neuraxial anesthesia; L&amp;D unit for postprocedure monitoring</td>
</tr>
<tr>
<td>Instrument size: 18-16 gauge (outer diameter 1.27–1.65 mm)</td>
<td>Fetal: miscarriage within 2 wk 3%; thermal injury of co-twin 2%; co-twin death 10–16%; PPROM within 2 wk 2–9%</td>
<td>Neonatal: premature delivery (less than 32 wk 9–18%; less than 37 wk 9–18%)</td>
</tr>
</tbody>
</table>

L&D, labor and delivery; OB, obstetric; NICU, neonatal intensive care unit; IUFD, intrauterine fetal death; PPROM, preterm prelabor rupture of membranes.* Not typically used but may be required on a case-by-case basis in the absence of fetal compromise.
neuraxial or general anesthesia. After these types of procedures, surgical complications such as trocar site bleeding, intraperitoneal amniotic fluid or CO₂ leakage, and, occasionally, even pulmonary edema or need for ICU admission may be encountered. These risks, as well as the potential obstetric complications of preterm PROM and preterm labor, require maternal and fetal postprocedure monitoring on a labor and

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Reported Procedural Risks</th>
<th>Required Resources</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Shunting procedures</strong>&lt;sup&gt;103–110&lt;/sup&gt;</td>
<td>Maternal: myometrial bleeding less than 1%</td>
<td>Maternal: L&amp;D unit if viable; OB anesthesiology for intravenous conscious sedation or, rarely, neuraxial anesthesia</td>
</tr>
<tr>
<td>Instrument diameter: 6–9 French (1.83–3 mm)</td>
<td>Fetal: shunt failure or dislodgement 8–35%; Chorioamnion separation up to 7.7%; PPROM up to 10%; fetal death up to 12%</td>
<td>Fetal: trained intervention team; medications for fetal administration as required</td>
</tr>
<tr>
<td></td>
<td>Neonatal: premature delivery (less than 34 wk up to 56%); NICU admission up to 83%; neonatal death up to 22%</td>
<td>Neonatal: ICU if viable, with subspecialty access as dictated by the fetal disease</td>
</tr>
<tr>
<td><strong>Bipolar or fetoscopic cord coagulation</strong>&lt;sup&gt;6,95–97&lt;/sup&gt;</td>
<td>Maternal: trocar site bleeding 1–3%</td>
<td>Maternal: dedicated intervention setting; L&amp;D unit; OB anesthesiology for intravenous conscious sedation or neuraxial anesthesia as required</td>
</tr>
<tr>
<td>Instrument diameter: 1.5–5 mm</td>
<td>Fetal: co-twin death 8–14%; PPROM at less than 32 wk 23–34%; chorioamnion separation 5–10%</td>
<td>Fetal: trained intervention team with specific procedural expertise at the expected level of complexity</td>
</tr>
<tr>
<td></td>
<td>Neonatal: premature delivery (less than 32 wk 23–34%); neonatal death 6–12%</td>
<td>Neonatal: NICU if viable, with subspecialty access if more severe fetal disease is present</td>
</tr>
<tr>
<td><strong>Fetoscopic laser surgery</strong>&lt;sup&gt;18,22,74,76,132,133&lt;/sup&gt;</td>
<td>Maternal: pulmonary edema 1–8%; ICU admission 1–2%; trocar site bleeding 5–7%; maternal blood transfusion up to 2.9%; intra-abdominal fluid leakage 1–7%</td>
<td>Maternal: dedicated intervention setting; L&amp;D unit; OB anesthesiology for intravenous conscious sedation or neuraxial anesthesia as required; blood bank; ICU availability</td>
</tr>
<tr>
<td>Instrument diameter: 5–12 French (1.5–4 mm)</td>
<td>Fetal: PPROM in less than 24 h 3–4%; chorioamnion separation 5–10%; placental abruption 1–3%; PPROM at less than 32 wk 19–34%</td>
<td>Fetal: trained intervention team with specific procedural expertise at the expected level of complexity</td>
</tr>
<tr>
<td></td>
<td>Neonatal: preterm birth at less than 33 wk up to 36%</td>
<td>Neonatal: NICU if viable; access to pediatric cardiology for severe fetal disease</td>
</tr>
<tr>
<td><strong>FETO</strong>&lt;sup&gt;76,114,120,121,134&lt;/sup&gt;</td>
<td>Maternal: abdominal hemorrhage 0.5%</td>
<td>Maternal: dedicated intervention setting; L&amp;D unit; OB anesthesiology for intravenous conscious sedation or neuraxial anesthesia as required; blood bank; ICU availability</td>
</tr>
<tr>
<td>Instrument diameter: 10 French (3.3 mm)</td>
<td>Fetal: fetal death 2%; unscheduled balloon removal up to 56%; unscheduled EXIT procedure up to 7%</td>
<td>Fetal: expertise with FETO procedure; on-call multidisciplinary team for emergent balloon removal or EXIT procedure</td>
</tr>
<tr>
<td></td>
<td>Neonatal: PTB at less than 34 wk up to 31%; postnatal balloon removal up to 17%</td>
<td>Neonatal: NICU; PICU; pediatric surgery; pediatric anesthesiology; pediatric cardiology; ECMO; pediatric ENT</td>
</tr>
<tr>
<td><strong>Percutaneous fetoscopic MMC closure</strong>&lt;sup&gt;116–119,130&lt;/sup&gt;</td>
<td>Maternal: pulmonary edema 2%; abdominal CO₂ leak 20–33%</td>
<td>Maternal: dedicated intervention setting; L&amp;D unit; OB anesthesiology for intravenous conscious sedation; neuraxial or general anesthesia as required; blood bank; adult ICU</td>
</tr>
<tr>
<td>Instrument diameter 10–15 French (3.3–5 mm), up to 4 ports</td>
<td>Fetal: PPROM at less than 34 wk 67%</td>
<td>Fetal: fetal MFM surgeon; pediatric neurosurgery</td>
</tr>
<tr>
<td></td>
<td>Neonatal: PTB at less than 35 wk up to 23%; CSF leakage at birth up to 32%</td>
<td>Neonatal: NICU with subspecialty care; pediatric neurosurgery; pediatric anesthesiology</td>
</tr>
</tbody>
</table>

PPROM, preterm prelabor rupture of membranes; NICU, neonatal intensive care unit; L&D, labor and delivery; OB, obstetric; ICU, intensive care unit; EXIT, ex utero intrapartum treatment; PTB, preterm birth; FETO, fetoscopic endotracheal occlusion; PICU, pediatric intensive care unit; ECMO, extracorporeal membrane oxygenation; ENT, ear, nose, and throat; MMC, myelomeningocele; CSF, cerebrospinal fluid; MFM, maternal–fetal medicine.
delivery unit, and, occasionally, access to adult ICU services. Patients undergoing fetoscopic endotracheal occlusion may require the emergent removal of a tracheal balloon, necessitating 24/7 availability of an ex utero intrapartum treatment (EXIT) team in the event that a balloon is still in situ if preterm labor occurs and cannot be removed either by ultrasonography-guided needle puncture or fetoscopically. After delivery, neonates with spina bifida or congenital diaphragmatic hernia are likely to need management in a level III–IV NICU or PICU.

**Fetal Interventions Requiring Laparotomy**

Fetal interventions requiring a maternal laparotomy and hysterotomy (ie, “open fetal surgery”) include open fetal myelomeningocele closure, resection of fetal tumors such as a sacrococcygeal teratoma, and the EXIT procedure for airway obstruction. Although open fetoscopic fetal myelomeningocele closure avoids a hysterotomy, the maternal laparotomy itself carries comparable operative risks (Table 3). Open procedures are performed under general anesthesia, aided by neuraxial anesthesia, for intrapartum and postpartum pain management and require more sophisticated intraoperative maternal and fetal monitoring. The procedural setup, as well as the requisite operator and multidisciplinary team expertise, is most demanding for these procedures, and access to the highest level of maternal (level III or IV) and neonatal care resources is required. After a procedure, the pregnant patient and fetus need to be monitored in a labor and delivery setting, with ready access to ICU resources if needed.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Reported Procedural Risks</th>
<th>Required Resources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Open fetoscopic MMC closure</td>
<td>Maternal: pulmonary edema up to 9%</td>
<td>Maternal: dedicated intervention setting; L&amp;D unit; OB anesthesiology for neuraxial or general anesthesia and postoperative pain management as required; blood bank; adult ICU</td>
</tr>
<tr>
<td></td>
<td>Fetal: PPROM at less than 37 wk up to 25–38%</td>
<td>Fetal: fetal MFM surgeon; pediatric neurosurgery; pediatric surgery; pediatric anesthesiology</td>
</tr>
<tr>
<td></td>
<td>Neonatal: premature delivery (less than 35 wk 45–52%); perinatal death 3–6%; dehiscence at repair site 4.3–13%</td>
<td>Neonatal: NICU with subspecialty care; pediatric neurosurgery</td>
</tr>
<tr>
<td>Open fetal MMC closure</td>
<td>Maternal: pulmonary edema 2–6% (up to 27.8% for open fetal surgeries)</td>
<td>Maternal: dedicated intervention setting; L&amp;D unit; OB anesthesiology for neuraxial or general anesthesia and postoperative pain management as required; blood bank; adult ICU</td>
</tr>
<tr>
<td>(ie, with laparotomy and hysterotomy)</td>
<td>Intraoperative blood transfusion 1–6% (fetal myelomeningocele repair), 9–13% for other open fetal surgery; ICU admission up to 24.6%; intubation for more than 48 h up to 2.3%</td>
<td></td>
</tr>
<tr>
<td>Open fetal surgery</td>
<td>Maternal: intraoperative atony and hemorrhage</td>
<td>Maternal: dedicated intervention setting; L&amp;D unit; OB anesthesiology for neuraxial or general anesthesia and postoperative pain management as required; blood bank; adult ICU</td>
</tr>
<tr>
<td></td>
<td>Fetal: bradycardia requiring resuscitation 5–10%; PPROM at less than 37 wk 32–46%; fetal death up to 4.3%</td>
<td>Fetal: fetal MFM surgeon; pediatric neurosurgery; pediatric surgery; pediatric anesthesiology</td>
</tr>
<tr>
<td></td>
<td>Neonatal: premature delivery (less than 35 wk 45–52%); perinatal death 3–6%; dehiscence at repair site in current or future pregnancies 4.3–13%</td>
<td>Neonatal: NICU with subspecialty care, eg, pediatric neurosurgery or other condition-specific specialties</td>
</tr>
<tr>
<td>EXIT procedures</td>
<td>Maternal: intraoperative atony and hemorrhage</td>
<td>Maternal: dedicated intervention setting; L&amp;D unit; OB anesthesiology for neuraxial or general anesthesia as required; blood bank; adult ICU</td>
</tr>
<tr>
<td></td>
<td>Fetal: perinatal death 3–14%, usually attributable to primary pathology</td>
<td>Fetal: multidisciplinary intervention team</td>
</tr>
<tr>
<td></td>
<td>Neonatal: premature delivery (average gestational age 31–36 wk)</td>
<td>Neonatal: NICU with subspecialty care</td>
</tr>
</tbody>
</table>

MMC, myelomeningocele; PPROM, preterm prelabor rupture of membranes; L&D, labor and delivery; OB, obstetric; ICU, intensive care unit; MFM, maternal–fetal medicine; NICU, neonatal intensive care unit.
PROPOSED LEVELS OF CARE FOR FETAL THERAPY CENTERS

The care level of a fetal center is defined by the presence of resources tailored to the level of complexity of the intervention and ability to manage anticipated maternal, fetal, and neonatal complications. Based on the complexity and risk profile of fetal interventions, three levels of fetal care are proposed.

Level I

A level I fetal therapy center should be capable of offering fetal interventions that may be associated with the obstetric risks of preterm PROM and preterm birth but that would be very unlikely to require maternal medical subspecialty or ICU care (Box 2). Neonatal risks should not exceed those of moderate prematurity (ie, 32–37 weeks of gestation), and a neonate should be unlikely to require any subspecialty medical or surgical care. Maternal care resources should meet ACOG–SMFM level III obstetric care center standards, and the NICU should be level III. After a procedure, maternal and fetal monitoring should be supervised by the maternal–fetal medicine team members of the fetal therapy center. In experienced hands, needle-based procedures and transplacental medical therapy can be performed at a level I fetal therapy center (Box 2). After viability, interventions carrying a risk for fetal distress should be performed with ready access to a labor and delivery unit and NICU. If any procedure is felt to be beyond the expertise of the local practitioners, or if the local supportive care resources are insufficient, referral to an institution where these needs can be met should be initiated if feasible.

Box 2. Proposed Fetal Therapy Levels and Specific Resource Setting

<table>
<thead>
<tr>
<th>Level</th>
<th>Definition: fetal therapies with low maternal and fetal risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level I</td>
<td>Personnel: fetal therapy center team, supported by institutional infrastructure</td>
</tr>
<tr>
<td>Maternal care level: at least level III</td>
<td></td>
</tr>
<tr>
<td>NICU care level: at least level III</td>
<td></td>
</tr>
<tr>
<td>Examples of procedures: fetal blood sampling, uncomplicated IUT, fetal shunt placement, radiofrequency or interstitial laser ablation, fetal antiarrhythmic treatment*</td>
<td></td>
</tr>
<tr>
<td>Additional consideration: mechanism in place to evaluate case complexity before interventions and transfer care to a higher level fetal therapy center if required</td>
<td></td>
</tr>
<tr>
<td>Level II</td>
<td>Definition: fetal therapies with low or high maternal risk but low neonatal risks</td>
</tr>
<tr>
<td>Personnel: fetal therapy center team, supported by institutional infrastructure</td>
<td></td>
</tr>
<tr>
<td>Maternal care level: at least level III</td>
<td></td>
</tr>
<tr>
<td>NICU care level: at least level III</td>
<td></td>
</tr>
<tr>
<td>Pediatric surgery care level: level I for all conditions for which a fetal intervention is offered</td>
<td></td>
</tr>
<tr>
<td>Examples of procedures: all procedures performed at level I centers, plus complicated IUT,t fetoscopic laser ablation for TTTS, ultrasonography-guided cord or vascular occlusions, fetoscopic amniotic band resection, fetal cardiac interventions,† uncomplicated EXIT procedures§</td>
<td></td>
</tr>
<tr>
<td>Level III</td>
<td>Definition: all fetal therapies, irrespective of their risk level</td>
</tr>
<tr>
<td>Personnel: fetal therapy center team, supported by institutional infrastructure</td>
<td></td>
</tr>
<tr>
<td>Maternal care level: at least level III</td>
<td></td>
</tr>
<tr>
<td>NICU care level: level IV</td>
<td></td>
</tr>
<tr>
<td>Pediatric surgery: level I for all conditions</td>
<td></td>
</tr>
<tr>
<td>Examples of procedures: all procedures performed at level I and II centers irrespective of the level of fetal compromise or procedural challenge, plus FETO balloon placement and retrieval, complex multidisciplinary fetoscopic procedures, open fetal surgery, 24/7 availability of EXIT procedures</td>
<td></td>
</tr>
</tbody>
</table>

NICU, neonatal intensive care unit; IUT, intrauterine transfusion; TTTS, twin–twin transfusion syndrome; EXIT, ex utero intrapartum treatment; FETO, fetoscopic tracheal occlusion.

*Maternal digoxin, sotalol, flecainide, or amiodarone treatment should be undertaken with input from and neonatal follow-up with a fetal–pediatric cardiology specialist.

†Complicated IUT refers to procedures performed at less than 20 weeks of gestation or in the presence of a compromised or hydropic fetus or with high maternal body mass index.

‡To be undertaken only if disease-specific pediatric care services are present, ideally at that institution or else by remote virtual consultation.

§Uncomplicated EXIT procedures refers to procedures that can be scheduled electively, well in advance, and for which all required resources are available.
Level II

A level II fetal therapy center should be capable of offering fetal interventions that also carry risks that might necessitate maternal ICU admission or could result in very preterm birth after viability (Box 2). Although most level II fetal centers will be capable of managing the majority of maternal risks associated with any particular fetal intervention, the pediatric specialty resources to manage some of the more challenging neonatal issues may not be immediately available. Maternal care resources should comply with ACOG–SMFM level III or IV obstetric care center standards, but a level III NICU is sufficient (Box 2). Level II fetal care centers should be capable of offering the full range of procedures performed at a level I center but could also manage more complex ultrasonography-guided procedures and fetoscopies as well pregnant patients with comorbid conditions or high BMIs (Box 2). After viability, fetal therapy should be offered only for conditions for which the appropriate level of neonatal care is available. A level II center might, on a case-by-case basis, be capable of performing a prescheduled EXIT procedure, presuming onsite availability of the relevant pediatric airway expertise.

Level III

A level III fetal therapy center can offer the full range of minimally invasive and open fetal interventions and can manage all levels of maternal and neonatal risk or complications that might be encountered with such procedures (Box 2). These centers will have level III or IV maternal care services, with ready access to a level IV NICU or PICU with the full range of pediatric subspecialties. A level IV maternal care center allows co-management or close collaboration between ICU and maternal–fetal medicine subspecialists. A level III fetal center can offer the complete range of fetal therapy, including all therapies offered at level I and II centers, fetoscopic endotracheal occlusion for congenital diaphragmatic hernia, and all open fetal surgical procedures. It can also manage fetal conditions such as compromised congenital pulmonary airway malformations, fetal hydrops, congenital diaphragmatic hernia, and spina bifida. The center should also have the capability to rapidly assemble complex medical teams on a 24/7 basis (eg, for EXIT).\(^\text{132}\)

SUMMARY

Development of a fetal therapy center is a multidisciplinary endeavor guided by the principles of fetal therapy, including the need to provide maternal safety and autonomy while also optimizing fetal, neonatal, and maternal outcomes. The fetal interventions offered should reflect the available expertise, resources, and degree of institutional support. This document proposes three levels of care for fetal therapy centers. Our intention is to provide guidance for the optimal care setting in which fetal interventions can be offered. Multidisciplinary care is fundamental to the establishment and operation of a fetal therapy center. The proposed fetal levels of care are aligned with existing levels of care for maternal, neonatal, and surgical care. In the absence of any central, national, or international regulatory body at present, it is the responsibility of the leadership at each fetal therapy center to ensure appropriate staff credentialing, resource planning, quality benchmarking, and outcome reporting for any intervention offered at that institution. This document is intended as a guide for the optimal resources that ought to be in place to facilitate fetal therapy. It is not intended to impede the development of new fetal centers, but rather to assist them in considering the necessary components to ensure patient safety and procedural success. As the technology, instrumentation, and procedures in fetal therapy evolve, different resources may be suggested. The overarching goal is continued advancement of fetal therapy through provision of safe and effective treatment of fetal disease.

REFERENCES


75. Practical approaches to risk minimisation for medicinal products: report of CIOMS Working Group IX. Council for International Organizations of Medical Sciences (CIOMS); 2014.

PEER REVIEW HISTORY
Received December 3, 2021. Received in revised form January 30, 2022. Accepted February 3, 2022. Peer reviews and author correspondence are available at http://links.lww.com/AOG/C710.

Save 20% on Books Published by Wolters Kluwer
As a special benefit, all members of the American College of Obstetricians and Gynecologists are eligible to receive a 20% discount on books published by Wolters Kluwer when ordering online at www.lww.com.

To take advantage of this special offer, enter the code WGA330WW in the promotion code box during the online ordering process.

For information on Wolters Kluwer books and to place an order, visit www.lww.com.