Provision of fertility services for women at increased risk of complications during fertility treatment or pregnancy: an Ethics Committee opinion

This opinion addresses the ethics of providing fertility treatment to women at elevated risk from fertility treatment or pregnancy. It is ethically appropriate for providers to treat women who are at elevated risk provided that the women are carefully assessed, that specialists in their medical condition are consulted as appropriate, and that they are fully informed about the risks, benefits, and alternatives, which may include oocyte or embryo donation, use of a gestational surrogate, declining fertility treatment, and adoption. Providers also may conclude that the medical risks of fertility treatment for a given patient are too high, in which case it is ethical for them for them to decline to provide treatment. Such determinations must be made in a medically objective and unbiased manner, and patients must be fully informed of the decision and its rationale. Counseling for these women should incorporate the most current knowledge available, with cognizance of the woman’s personal determinants in relation to her reproductive desires. In this way, both the physician and the patient will optimize decision making in an ethically sound, patient-supportive context. This document replaces the document of the same name, last published in 2016 (Fertil Steril 2016;106:1319-23). (Fertil Steril® 2022;117:713-9. ©2022 by American Society for Reproductive Medicine.)

El resumen está disponible en Español al final del artículo.

Key Words: Assisted reproductive technology, complications, ethics, fertility treatment, high-risk pregnancy

KEY POINTS

- All patients presenting for fertility services should be assessed for their risk of medical complications during treatment and pregnancy.
- Clinicians should thoroughly counsel women who are at increased risk of complications during fertility treatment or pregnancy regarding these risks. This counseling should involve specialists in maternal-fetal medicine or those with expertise in the woman’s particular medical condition. Counseling should include fertility- and pregnancy-related risks to the woman and risks to the resulting child. Such counseling should occur in advance of a decision to initiate or decline to provide treatment.
- Reproductive liberty is a core value in the provision of fertility care and includes the right of individuals to make informed choices about whether and how to reproduce. Reproductive liberty also means the right to receive fertility care in a nondiscriminatory manner. Clinicians may ethically treat a woman at elevated risk if she is fully informed of her risks, benefits, and alternatives.
- Clinicians may also decline to provide care when such decisions arise from evidence-based, reasoned judgments that the risks of morbidity or mortality from fertility treatment or pregnancy are too high for treatment to be provided ethically and with professional integrity. In situations where a physician either provides or declines to provide reproductive assistance to a high-risk woman, it is appropriate to recommend that the patient obtain a second opinion from experts both within and outside the field of reproductive medicine.
- Whenever possible, physicians should encourage patients to reduce their modifiable risk factors. In cases where the patient is unable or unwilling to modify her risk, physicians may differ regarding whether or not to treat her. In such cases, it is acceptable for physicians to decline to provide fertility treatment when such decisions are based on medical considerations and applied without bias.
- Clinicians may differ about what constitutes a reasonable level of risk during fertility treatment or pregnancy. It is ethically appropriate to decline to provide fertility treatment when the physician determines that the risks of complications to the...
woman or her resulting child are unacceptably high, as long as such judgments are made in a nondiscriminatory fashion and without bias. Counseling in these cases should include a discussion of alternatives to carrying a pregnancy, such as gestational surrogacy, adoption, or foregoing fertility treatment. The impact of cost and how it may limit available options should be included as part of this discussion.

- Clinicians should encourage high-risk women to involve their parenting partners, if present, in deciding whether to undergo fertility treatment. However, the woman carrying the pregnancy has the ultimate autonomy about whether to proceed with treatment, since she bears the medical risk to her health from the pregnancy. To protect patient autonomy, reasonable efforts should be made to ensure that women at increased risk of complications choose to initiate fertility treatment independently and without undue influence from others.

- When clinicians determine that a fertility treatment or the resulting pregnancy may pose increased risk, consideration should be given to providing care in a setting that can best meet the patient’s needs. Often, the involvement of a center with expertise in treating a particular medical condition during part or all of the patient’s care will be helpful in achieving this goal.

Generally, when a woman becomes pregnant, she anticipates that at the end of her pregnancy both she and her newborn will be healthy. In most cases, this is the outcome. Indeed, maternal mortality in the United States is approximately 17.8 per 100,000 women (1). There is some controversy as to whether overall maternal mortality is increased or decreased in women using in vitro fertilization (IVF) (2–4). Regardless of the baseline risk to women conceiving with IVF, some women are at higher risk of having complications during either fertility treatment or the ensuing pregnancy due to underlying disease, preexisting conditions, or both. Women who do not need help conceiving usually decide whether to try to become pregnant or continue their pregnancy in the privacy of their own homes and within their individual social structures. For those women who will require medical assistance to conceive, a discussion of the risks and benefits of pregnancy can occur between the woman, her partner (if she has one), and reproductive and other medical professionals before conception. When prospective patients are at increased treatment- or pregnancy-related risks, the provider’s approach to counseling should take these risks into account. Women at high risk of complications resulting from fertility treatment or pregnancy include, for example, those with Turner syndrome, end-stage renal disease, or a history of cardiomyopathy. In addition to routine counseling in advance of initiating fertility treatment, which would include a discussion regarding risks such as ovarian hyperstimulation syndrome (OHSS) and multiple gestation, reproductive endocrinologists should take particular care to counsel women about treatment- or pregnancy-related risks that are specific to their medical condition so that they are able to make informed decisions regarding their reproductive care. Physicians may benefit from using a preconception risk-stratification tool that has been developed to help assess and counsel women who are at increased risk of complications during treatment or pregnancy (5).

**Risks Inherent to Fertility Treatment**

Women who undergo fertility treatment may face increased risks resulting from their treatment, the pregnancy itself, or both. Stimulation-related risks include OHSS and an increased incidence of thromboembolic events, such as deep venous thrombosis and pulmonary embolism. In addition, transvaginal oocyte retrieval may be difficult or impossible for women with obesity or for those in whom surgery has displaced the ovaries out of the pelvis (6, 7). When fertility treatments result in multiple gestations, the risks include a higher incidence of prematurity, gestational diabetes, and pre-eclampsia. These risks can be minimized by avoiding controlled ovarian hyperstimulation cycles with intrauterine insemination in favor of IVF and by adhering to protocols that strictly limit the number of embryos transferred during IVF (8). Although these risks apply to some extent to all women undergoing fertility treatment, certain populations of women are at higher risk of complications during induction of ovulation. These include women with medical conditions, such as underlying thrombophilias, who are at increased risk of clotting disorders, women with obesity, and women with polycystic ovary syndrome. These also include women with psychiatric disorders that may be exacerbated by the hormonal changes of ovarian stimulation, the increased stress that fertility treatments can induce, and the decision to discontinue their psychotropic medication (9).

**Relative vs. Absolute Contraindications to Pregnancy**

For most women, even those with significant comorbidities, pregnancy remains a reasonable option. Women with underlying medical conditions may require increased monitoring by subspecialists in maternal-fetal medicine during pregnancy, as well as consultation with specialists outside the field of obstetrics. They may also benefit from receiving some or all of their care at a medical center with expertise in treating their particular medical condition. Reproductive endocrinologists play a vital role in identifying women who are at increased risk of treatment- and pregnancy-related complications and in delineating the magnitude of this increase as part of the fertility evaluation. This may include obtaining background studies and seeking consultation from experts to assist in counseling the patient so that she is fully informed of her risks when entering treatment and pregnancy and ensuring that she starts fertility treatment and becomes pregnant in as healthy a state as possible. It also includes having a plan of care that includes the provision of a safe and seamless transfer of care to a provider or center that can best meet her needs once she becomes pregnant.

For most preexisting conditions and comorbidities, pregnancy will be possible with appropriate planning. Although it is true that women may choose to become pregnant without...
assistance, regardless of the risk that this poses to them, it is less clear whether it is ethical for physicians to offer or decline to offer fertility treatment in cases where fertility treatment or pregnancy poses elevated risks to the woman or her pregnancy. When reproductive endocrinologists determine that the risk of treatment- or pregnancy-related complications is extremely elevated, declining to provide fertility services may be ethically appropriate. Before making this determination, reproductive endocrinologists should seek consultation from specialists expert in the patient’s particular condition to further delineate her risk. When care is denied, it should be done after careful consideration of the medical facts and without discrimination. It is ethically acceptable for clinicians, based on their evidence-based and unbiased assessments of risk, to decline to provide fertility treatment to women at high risk of complications in themselves or their children.

Patients should be provided with meaningful counseling regarding the differences between absolute and relative risk. An increase in the relative risk when the absolute risk is low may be of different ethical significance than an increase in the relative risk when the absolute risk is high. For example, for an absolute risk of 1 per 1,000, a 100% increase in the relative risk brings the risk to 2 per 1,000. However, for an absolute risk of 1 per 10, a 100% increase in the relative risk brings the risk to 2 per 10. Some discussions in the literature point out the importance of explaining this distinction to patients in determining what risks are reasonable (10).

**Risks Associated with Underlying Medical Conditions or Disease Predisposition**

Examples of comorbidities that may confer exceedingly high absolute risks in pregnancy include Turner syndrome, which carries a 3.3% risk of potentially life-threatening complications (11, 12) and a 2% risk of death (13). Some patients with Turner syndrome, particularly those with an aortic size index >2.0 cm/m², are at particular risk for pregnancy-associated morbidity and mortality. According to the American Society for Reproductive Medicine Practice Committee, this finding is an absolute contraindication for attempting pregnancy (13). Another example is a subsequent pregnancy in women with peripartum cardiomyopathy. One study reported a 9% mortality rate in pregnancies in which persistent left ventricular dysfunction was present (14). A final example is primary pulmonary hypertension, in which maternal mortality rates as high as 33% have been reported (15, 16).

In cases of significantly heightened absolute risk, counseling is crucial. The level of risk that a woman judges to be acceptable will likely depend on a constellation of factors. These include the risk to her and her pregnancy, her level of risk aversion, and the development of a plan of action in case complications occur. Unfortunately, the inability to afford alternatives, such as a gestational carrier, may also inform her willingness to undertake risk. Additionally, the availability and extent of her support system and social structure may play a role in the level of risk that she is willing to accept. This includes the presence and willingness of someone to provide care for her during the pregnancy as well as someone to care for the resulting offspring if she becomes too sick to do so or in the event of her death. This also includes whether she already has people who depend on her for care, such as other children or older dependent adults. Women may differ in the decisions they make, based on their unique situation, coupled with the potential risks that fertility treatment and pregnancy may pose for them. Fertility preservation and pregnancy in patients with cancer may also raise ethical issues regarding risks during treatment and pregnancy; these issues are discussed in detail elsewhere (17).

**Modifiable Risk Factors**

Modifiable risk factors can include ones relating to underlying health conditions, such as obesity, smoking, and poorly controlled diabetes. Modifiable risk factors can affect both fertility treatment and pregnancy. Reflecting a commitment to patient safety, clinicians and patients should work toward decreasing risk whenever possible. Sometimes the modifications involve clinical treatment decisions, and at other times they involve improving patient health. An example of a modifiable risk factor is the number of embryos to transfer (8). With single-embryo transfer, the risk of twins and high-order multiple births can be significantly reduced. Similarly, limiting the amount of gonadotropins used to stimulate the ovaries, using an alternative protocol and ovulation trigger, and cryopreserving all embryos for later use can decrease the risks associated with OHSS (18).

There are times when it is not the fertility treatment but the resulting pregnancy that confers increased risk. Women with uncontrolled medical conditions such as diabetes or hypertension may benefit from a delay of fertility treatment until the disease is adequately controlled. Delaying fertility treatment must be balanced with the risk of declining fertility with increasing age. One option to consider is performing IVF in a timely fashion and cryopreserving the embryos or oocytes, thus delaying pregnancy until the modifiable risk factors are decreased. For example, a woman with a diagnosis of breast cancer may benefit from timely IVF, but a delay in transferring her embryos until she has completed the prescribed course of adjuvant therapy is advisable.

**Situations in Which Risk to the Patient Also Confers Risk to the Resulting Child**

In some situations, a woman entering a risky pregnancy is also endangering the health and well-being of her intended child. One example is the case of vascular Ehlers-Danlos syndrome. This is an autosomal dominant genetic disorder that can have severe vascular complications (aortic dissection and arterial rupture) and that has one of the highest maternal mortality rates of any condition. There are various reports in the literature of maternal mortality among patients with vascular Ehlers-Danlos syndrome, with one study reporting an overall risk of 6.5% (19–21). Women with Ehlers-Danlos syndrome who undertake pregnancy not only endanger their lives but also have a 50% chance of transmitting the very disease that places them at high risk of death to their offspring.
These situations raise especially difficult ethical questions. Preimplantation genetic testing for the purpose of selecting an unaffected child is an option, but the pregnancy would still put the woman at increased risk of complications. Choosing to transfer an unaffected embryo into a gestational carrier would remove both the pregnancy-related risks to the patient and the disease-related risks to the resulting child. In such cases, attention should be paid not only to the wishes of the woman, but also to the cost of genetic analysis and third-party reproduction. Cost may be a barrier to care for many women, and this may lead them to choose riskier options. Such options may be acceptable when the woman is fully informed of the risks that she is taking and those that she is potentially conferring on any resulting children. In other situations, such as women at high risk for severe preeclampsia (e.g., because of a history of preeclampsia, a history of renal transplantation, or presence of systemic lupus erythematosus), the risks to the mother also confer risks to the child, primarily relating to prematurity. Decisions to provide or decline to provide fertility treatment are best made carefully and after insightful deliberation and expert consultation among the patient, her physician, and outside experts when warranted.

**ETHICAL CONSIDERATIONS**

Reproductive liberty is a core value in the provision of fertility care and includes the right of individuals to make informed choices about whether and how to reproduce. For those women at elevated risk who may need assistance in becoming pregnant, the importance of reproductive choice supports their access to treatment. Nonetheless, different interests in reproduction may be at issue, and women and their physicians may weigh these interests differently. For some women, fertility treatment may enable them to bear a child with their own gametes and the gametes of their chosen partner. Others may be able to provide their own oocytes and transfer the resulting embryos into a gestational carrier, achieving a genetically related child without the experience or risk of pregnancy. For still others, such as patients with premature ovarian insufficiency or those whose ovarian reserve has been adversely affected by chemotherapy, pregnancy may be achieved, but only with donated gametes; these women may want the experience of pregnancy and birth but will not be able to have a genetically related child.

The value of reproductive choice is a primary consideration in favor of treating women at elevated risk. In such contexts, it is especially important to ensure that choices are made without pressure and are well informed. Patients may lack needed information, may receive misleading information from other sources, or may be pressured by family members or cultural contexts to try to achieve pregnancy or the birth of a genetically related child. In light of these concerns, providers must work with patients to explore their reasons for choosing treatment and their understanding of the risks and alternatives. Providers should make a reasonable effort to ensure that patients fully appreciate the risks to themselves and their potential offspring. Providers must counsel patients about alternatives that might be available to them, such as oocyte donation or use of a gestational carrier.

Conversely, providers may be concerned that women at elevated risk may be under especially strong personal or social pressures to achieve reproduction. These pressures may make informed consent difficult, in which case the reproductive choice argument is undermined. Some ethicists have argued that professional duties require providers to act in the best health-related interests of their patients. If so, providers who believe that ovarian stimulation or pregnancy is not in the best health-related interests of a patient will choose not to offer fertility treatment to the patient (22). In such cases, it is reasonable to obtain a second opinion to ensure that the physician’s clinical assessment is reasonable and made without bias.

Providers may also be concerned that pregnancy in some high-risk women poses risks to the fetus. In women with human immunodeficiency virus infection, for example, American Society for Reproductive Medicine has taken the position that it is ethical to provide fertility care if all reasonable precautions are undertaken to guard against maternal transmission of human immunodeficiency virus infection to the fetus (23). Other high-risk situations include women with uncontrolled diabetes, which increases the risk of congenital anomalies and prematurity in the resulting children.

Another concern is that some women at higher risk may not survive pregnancy or may be unable to care for their children until they reach adulthood (24). This argument may also apply to women conceiving at advanced ages (25). These issues should be explored with the women before initiating care. They should be encouraged to involve their partners, when appropriate, in these discussions.

Providers may reasonably differ on the level of elevated risk they are willing to accept in treating patients. In making such judgments, providers may benefit from seeking the assistance of specialists in the patient’s condition, both to minimize the risks of fertility care and pregnancy and to ensure that judgments are fully informed. Providers must also be careful to guard against discrimination arising from nonmedical factors or unrelated to patient well-being when providing or declining to provide fertility care.

**PHYSICIAN AUTONOMY: CHOOSING TO PROVIDE OR DENY TREATMENT**

In providing fertility treatment, physicians have the professional responsibility to assess the baseline health of the woman and her treatment- and pregnancy-associated risks. When patients face increased risks that are modifiable in ways that reduce the risks, efforts should be made to decrease these risks (26). Some examples include weight loss, smoking cessation, and blood sugar regulation in patients with diabetes. In cases where patients are unable or unwilling to modify their risks, physicians may differ regarding whether or not to treat them. So, long as treatment decisions are based on reasonable medical considerations and applied without discrimination or bias, physician autonomy should be respected.

In some cases, the physician may be concerned that the evidence suggests that the risks of morbidity and mortality
for the woman and potentially her offspring may be too high to justify treatment. In such cases, the reproductive endocrinologist should seek expert advice, including relevant practice guidelines (13), regarding the actual risks to the woman and her offspring. Asking the woman to obtain a second opinion should be considered as part of a reasonable effort to ensure that there is consensus regarding the level of risk to her, her pregnancy, and the resulting child. When declining to provide treatment, physicians must ensure that these decisions are made after careful consideration of the medical facts and without bias toward the woman or her partner. Such bias could include the physician’s feelings about the patient’s age, ethnicity, socioeconomic status, parenting unit, and medical condition or disability. The physician may also be biased in cases where the underlying disease is caused by behavioral factors such as smoking or alcohol intake. It is important for physicians to fully assess their reasons for denying care and to ensure that they are not discriminatory.

CONCLUSIONS

When women are at elevated risk from fertility treatment or pregnancy, decisions about whether to proceed with treatment are often difficult. In such cases, clinicians must carefully assess the patient and may benefit from consultation with specialists who are knowledgeable about the patient’s medical diagnosis and her pregnancy-related risks. Clinicians must thoroughly counsel patients about the risks of treatment, methods of modifying risks, and available alternatives, which may include oocyte and embryo donation, gestational surrogacy, adoption, and forgoing treatment. Clinicians must make reasonable efforts to ensure that patients’ decisions are voluntary and that they are not being pressured by external circumstances. On the basis of unbiased, evidence-based judgments, clinicians may also conclude that the medical risks to the patient are too high for them to ethically provide care, thereby resulting in a decision to decline to provide treatment. Such decisions must be made in a sound, patient-supportive, and nondiscriminatory context.

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REFERENCES

Prestación de servicios de fertilidad para mujeres con mayor riesgo de complicaciones durante tratamientos de fertilidad o embarazo: dictamen del comité de ética.

Esta opinión aborda la ética de proporcionar tratamiento de fertilidad a mujeres con alto riesgo durante tratamientos de fertilidad o embarazo. Es éticamente apropiado para los proveedores tratar mujeres que tienen un riesgo elevado siempre que en su condición médica sean consultados según corresponda, y que estén completamente informadas sobre los riesgos, beneficios y alternativas, que puede incluir la donación de ovocitos o embriones, el uso de un sustituto gestacional, rechazar el uso de tratamientos de fertilidad y la adopción. Los proveedores también pueden concluir que los riesgos médicos del tratamiento de fertilidad para un paciente dado son demasiado altos, en cuyo caso es ético que se nieguen a ofrecer tratamiento. Dichas determinaciones deben hacerse de manera médicamente objetiva e imparcial, y los pacientes deben estar plenamente informados de la decisión y sus fundamentos. El asesoramiento para estas mujeres debe incorporar la información más actualizada disponible, con conocimiento de los determinantes personales de la mujer en relación con sus deseos reproductivos. De esta manera, ambos el médico y el paciente optimizarán la toma de decisiones en un contexto éticamente sano y de apoyo al paciente. Este documento reemplaza el documento del mismo nombre, publicado por última vez en 2016.