

Planned oocyte cryopreservation to preserve future reproductive potential: an Ethics Committee opinion

Ethics Committee of the American Society for Reproductive Medicine

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Planned oocyte cryopreservation is an ethically permissible procedure that may help individuals avoid future infertility. Because planned oocyte cryopreservation is new and evolving, it is essential that those considering using it be informed about the uncertainties regarding its efficacy and long-term effects. This replaces the document of the same name, last published in 2017. (Fertil Steril® 2024;121:604–12. ©2023 by American Society for Reproductive Medicine.)

El resumen está disponible en Español al final del artículo.

Key Words: Oocyte, reproduction, ethics, cryopreservation, fertility

KEY POINTS

- For individuals attempting to extend their reproductive window in the face of expected reproductive aging, and for transgender men who will experience the loss of female gametes in the process of transitioning from female to male, advanced oocyte cryopreservation (“OC”) is ethically permissible. The Ethics Committee will refer to this procedure as “planned oocyte cryopreservation” or “planned OC.” Planned OC serves legitimate interests in reproductive autonomy.
- Planned OC is relatively new, and uncertainties exist regarding its efficacy, appropriate use, and long-term effects.
- Providers should ensure that individuals who request planned OC are informed about its efficacy, safety, costs, benefits, and risks, including the unknown long-term health effects for offspring. Because of the uncertainties that accompany this developing procedure, there are distinct obligations regarding disclosure and informed decision-making. Providers should disclose their own clinic-specific statistics, or lack thereof, for successful freeze-thaw and live birth. Patients should be informed that medical benefits are uncertain and harms that are not fully understood may emerge from planned OC.
- To improve scientific understanding of planned OC, including efficacy, advisability, and long-term effects, medical professionals offering this procedure are encouraged to collect outcome data, conduct research, and report planned OC cycles to the Society for Assisted Reproductive Technology.

The ability to cryopreserve gametes and embryos has created important reproductive options. It has given individuals facing the potential loss of reproductive capacity, such as those receiving gonadotoxic medical treatment, the chance to have biologically related children in the future. The history of cryopreservation of sperm, embryos, and oocytes is set forth in the American Society for

Reproductive Medicine (ASRM) Practice Committee document, “Evidence-based outcomes after oocyte cryopreservation for donor oocyte in vitro fertilization and planned oocyte cryopreservation: a guideline” (1). Although the first human birth from a previously frozen oocyte occurred in 1986, laboratory techniques such as vitrification and intracytoplasmic sperm injection have led to a marked improvement in the

efficacy of oocyte cryopreservation (OC) (2).

Oocyte cryopreservation was classified initially by ASRM as experimental. In 2012, the ASRM Practice Committee removed the experimental label after a thorough review of the scientific literature. The report concluded that in vitro fertilization (IVF) and pregnancy rates with cryopreserved oocytes compared favorably to those with fresh oocytes. In addition, short-term studies of the health of offspring from OC revealed no increases in congenital anomalies compared with other IVF offspring (2). Although the ASRM Practice Committee and Ethics Committee approved the use

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of OC for patients facing therapies likely to be gonadotoxic (2–4), the Practice Committee declined at that time to recommend OC “for the sole purpose of circumventing reproductive aging in healthy women” on the grounds that there were insufficient data on the “safety, efficacy, ethics, emotional risks, and cost-effectiveness” for that indication (2).

Since that time, further research on efficacy has been reassuring (5, 6). Increasing numbers of women are seeking planned OC, and increasing numbers of physicians are providing it (7–13). Additionally, planned OC expands reproductive options for transgender men, who will experience the loss of female gametes in the process of transitioning from female to male. In 2014, ASRM published a fact sheet on its patient education website, describing how individuals may use OC even when they are not facing a fertility-threatening disease (14). All these factors point to planned OC as a medical innovation that is moving into practice, raising “ethical issues involving evaluation of evidence, balancing benefits and harms, supporting patient autonomy, avoiding conflict of interest, and promoting advances in health care” (15). This Committee Opinion addresses the ethical issues that arise when OC is used by individuals whose goal is to protect their ability to have children in the future, apart from an immediate threat from gonadotoxic therapy.

Although the ovarian stimulation and oocyte retrieval required for OC are medical procedures that are well-tested, used worldwide, and regarded as safe, caution is warranted. There is a risk of misplaced confidence in the effectiveness of this procedure, as well as scientific unknowns concerning long-term and transgenerational offspring health. Mindful of these cautions, however, this Committee finds the use of OC for those attempting to extend their reproductive potential for the future to be ethically permissible after informed consent.

The Ethics Committee previously supported OC for individuals facing immediate, medically induced loss of fertility (4). But there are many less-immediate developments that could also threaten a person’s ability to have children in the future. These developments include diseases, ovarian insufficiency, traumatic injury, the planned female-to-male gender transition, and the fertility loss that occurs with reproductive aging. Planned OC may also benefit those seeking children in response to unanticipated future events such as remarriage or the death of an existing child (16).

After the 2022 Supreme Court’s reversal of *Roe v. Wade*, there is no longer a federally protected constitutional right to abortion at any stage of pregnancy, and states may regulate abortion under a “rational basis” standard rather than the previous “strict scrutiny” standard (17). The impacts on reproductive choice and autonomy for patients, providers, and third-party participants in assisted reproductive technology therapy are still unfolding and may vary depending on state laws that extend or restrict access to abortion and reproductive care. To the extent a restrictive, applicable state law may explicitly or implicitly apply to IVF preimplantation embryos, additional considerations as to where to create or store IVF embryos and cryopreserving gametes rather than embryos should be considered. This may increase demand for OC.

TERMINOLOGY

The appropriate language to describe the process of preserving oocytes for future fertility is unsettled. “Oocyte cryopreservation” or “OC” is the most generic terminology and does not distinguish the rationale for oocyte preservation. When OC is used in contexts other than to avoid immediate gonadotoxic effects, observers have criticized terms like “social egg freezing,” “freezing for nonmedical reasons,” and “elective” OC. Such terms may trivialize the fact that the treatment is being undertaken to avert infertility that, when it arises, will in fact be a medical condition (18, 19). The Ethics Committee concurs. Researchers in the United Kingdom have suggested the term “oocyte cryopreservation for Anticipated Gamete Exhaustion” or “AGE” (18). The Committee believes a more general term is merited, however, because the circumstances that lead to the use of the oocytes may be other than advancing age. The critical difference between the OC examined in this opinion and that which is done when gonadotoxic therapy is imminent is its nonemergent nature. It is being undertaken as a matter of planning before a medical indication has materialized and will be referred to as “planned oocyte cryopreservation” or “planned OC.” The Ethics Committee recognizes that when many individuals who plan to cryopreserve oocytes identify as female or women, not all do. The committee aims to use gender-neutral language wherever possible.

RATIONALES FOR PLANNED OC

For decades, women in the United States have been having children at older ages. Nationwide, the rate of first births to women ages 35–39 years has been rising since the 1970s, although it has recently plateaued; the rate of first births to women ages 40–44 years has been rising since the early 1980s (20, 21). Many factors contribute to this trend, but it is well-recognized that increased access to education and participation in the workplace is central. The critical periods of advancement in these pursuits usually take place when individuals are in their 20s and 30s, corresponding with the time at which ovarian reserve begins to decline (22).

This trend is sometimes described as “delaying” or “postponing” childbearing, statements that suggest affirmative choice or even blame that individuals have brought the difficulty on themselves (23). Rather, the data show that many people who want to have children face conflicts about their preferred life path in a culture where the optimal time for educational and career advancement coincides directly with the period that the body is best suited for reproduction. One study cited the lack of a partner as the most common reason individuals elect to undergo planned OC (24). Many individuals report that their life circumstances (partnership, marriage, and finances) are not as they desire them, or as society supports or regards as acceptable, and these circumstances are what prevented them from starting a family at an earlier time (25–29). Finally, what may appear to be affirmative delay may actually be the unwitting product of a “knowledge gap”: the widespread and persistent overestimation of both reproductive potential at a given age

and the ability of reproductive medicine to restore that potential (30).

Given these societal and personal reasons for procreation later in life, a biological truth comes into play: older females increase the risk of infertility because of reduced oocyte quantity and quality, increased chromosomal abnormalities, and increased rates of pregnancy loss. Fertility and offspring health are affected by men's age, too, although not until men are older, generally past age 40 or 50 years. For both sexes, the more time that passes before they reproduce, the greater the chance that some illness, life circumstance, or accident may impair their fertility or reproductive outcomes.

When individuals seek children at a time when their own oocyte quality is compromised, whether because of age, disease, or another cause, they traditionally have had the option to undergo IVF treatment with donor oocytes. Planned OC provides an additional option in this circumstance: when they have previously banked their own oocytes, they may be able to use them for family building. Compared with using donor oocytes, planned OC offers benefits that include maintaining a genetic connection to the offspring, the potentially reduced cost of planned OC compared with multiple cycles of IVF or the use of donor oocytes (23), and avoiding the complexities of working with a reproductive third party. Although planned OC ultimately will be ineffective in some percentage of cases (the value of which is dependent on patient age at the time of cryopreservation and the number of oocytes frozen), it will allow some individuals and couples who otherwise would have had to forego biological parenthood the chance to have genetically related children.

Data on the long-term safety and efficacy of planned OC are incomplete because most oocytes cryopreserved for autologous use have yet to be thawed and utilized. Fortunately, several recent studies have reported outcome data and led to an increased understanding of determinants that predict success, including age at cryopreservation and ovarian reserve (21, 25, 26, 28, 31). Embryos from previously vitrified oocytes show rates of fertilization, implantation, and clinical pregnancy that are comparable to those for embryos from fresh oocytes, although there can be considerable variation among clinics (31–35). Although only short-term, birth reports indicate no increase in congenital abnormalities in infants from cryopreserved oocytes compared with other IVF infants (33, 36, 37). Observational studies of offspring conceived after OC, although limited, show no increased risks compared with the use of fresh oocytes (38). Medical professionals offering planned OC and IVF treatment are strongly encouraged to undertake long-term outcome studies of maternal and fetal health. The Society for Assisted Reproductive Technology will contribute to a greater understanding of success rates as planned OC cycle data from fertility clinics is currently being collected.

ETHICAL ARGUMENTS IN FAVOR OF PLANNED OC TO PRESERVE FUTURE FERTILITY

A range of viewpoints on planned OC has been presented by researchers and commentators (11, 21, 24–29). Although several commentators raise questions and concerns about

planned OC, most conclude it should be available to those who are fully informed and wish to use it (26, 28). The European Society of Human Reproduction and Embryology approved the use of planned OC for fertility preservation in 2012 (30). This section examines the arguments in favor of the planned OC.

The leading argument for planned OC is that it may increase reproductive options, thus enhancing reproductive autonomy. This argument proceeds on several levels. First, planned OC may improve one's ability to organize their education, work, and family building with less pressure from their "biological clock." A planned OC may allow one time to establish suitable relationships or life circumstances to prepare for having and raising children. It reduces the pressure to have a child when not yet psychologically, socially, or situationally ready (19, 39, 40).

Planned OC further enhances autonomy by potentially eliminating the need for third parties, such as oocyte donors, with the associated complexities and costs. Planned OC also avoids problems from "second parties;" that is, it can allow individuals to control their preserved gametes without the risk that a partner may retract consent to future use, as can happen with frozen embryos. The disputes over embryos that may erupt when gamete providers separate or divorce can pose clinical, emotional, and legal difficulties, all of which are avoidable when individual gametes, rather than embryos, are preserved for later use. Planned OC also provides an option for those who prefer not to form and then cryopreserve embryos (29).

This Committee finds that planned OC is compatible with beneficence, the ethical precept obligating physicians to act for the patient's welfare. As described above, planned OC represents a preventive strategy that may enhance reproductive potential and the health of offspring. Although cryopreserving oocytes in this context is not undertaken in response to an immediate disease, it is undertaken with the goal of preventing infertility in the future. It is worth observing that there is little when any, criticism of those choosing to cryopreserve sperm to protect their future fertility (11). Although the costs, physical demands, and risks of sperm vs. oocyte preservation are certainly different, the benefit considerations are comparable.

Planned OC may also promote social justice by reducing the obstacles women currently face because their reproductive window is narrower than men's. By extending the time when women may start a family, planned OC can lessen the effects of educational and workplace constraints that disparately burden one sex; thus, oocyte cryopreservation can contribute to equality for men and women (11, 21, 30).

ETHICAL ARGUMENTS AGAINST PLANNED OC TO PRESERVE FUTURE FERTILITY

This section examines the arguments that raise caution against planned OC. Certain objections revolve around the procedure: a nonmaleficence argument that the intervention is too physically invasive and risky to perform when there is no immediate threat of infertility (41) and that studies

have not yet established whether there is a “shelf life” for cryopreserved oocytes or the long-term safety for offspring.

The physical demands of planned OC fall safely within the acceptable bounds of reproductive medicine. It is no more invasive than oocyte donation, which is supported by the ASRM as a matter of reproductive choice and which provides no personal health or reproductive benefits to the donor (ASRM Financial Compensation of Oocyte Donors). Planned OC is apt to carry less physical risk than OC before gonadotoxic therapy because the patient is not already afflicted with a serious disease or possibly postponing its treatment (21). The most common risk, that of ovarian hyperstimulation syndrome, is reduced (although not absent) in planned OC because there is no embryo transfer at the end of the stimulation cycle. In addition, gonadotropin-releasing hormone agonist triggers, used in the context of gonadotropin-releasing hormone antagonist cycles, can further decrease the chance of the development of ovarian hyperstimulation (42).

Another set of objections is rooted in the fact that many oocytes ultimately remain unused, such that both the procedure and its expense may prove to have been unnecessary; individuals may not seek to preserve their oocytes until they are at an age when the oocytes are already compromised (29), and planned OC may provide a false sense of security about an individual’s ability to have children in the future (43). These concerns are synergistic: the younger the age at which individuals bank their oocytes, the less likely they will be utilized given that there is more time for their life plan to unfold (28). Such differences are inherent when prophylactic medical treatments are undertaken, however, and are not unique to planned OC. Similar considerations arise in the decision to cryopreserve oocytes before gonadotoxic therapy; that is, the patient’s need for the oocytes is not certain, the timing of retrieval may be late relative to their age and health, and there may be a risk of false security. Researchers are investigating the question of the optimal window, both biologically and financially, in which to undergo planned OC, and recommendations to guide patients on the advisability of planned OC will continue to emerge (23, 44). In the end, however, the choice to use planned OC and to incur uncertain risks for the prospect of uncertain benefits can be made only by individuals for themselves.

The issue of false security is highlighted when planned OC is referred to as an “insurance policy” for future childbearing, raising a concern that it will lead to an overly confident reliance on the preserved oocytes. This concern presupposes without basis that the women have other available options, such as immediate marriage or reproduction, that they will dismiss because of the cryopreserved oocytes (17). To the extent that the risk is based on a misunderstanding of the likely success rates of planned OC, it is best addressed through education and informed consent. Physicians and those acting in concert with them should avoid overstatements that may invite or allow misplaced confidence. More broadly, however, in medical contexts, it is not uncommon for patients to grapple with choices about medical options where overreliance is a risk. Patients should be trusted to comprehend information when full and appropriate medical counseling is

presented and should not have options removed because of a potentially biased underestimation of their capabilities (45).

Research on this topic may also make a difference. There are ongoing studies on the quality and number of oocytes, by age and hormone levels, needed to have a particular chance of pregnancy when those oocytes are used (23, 32, 44, 46). This information should be communicated to patients. Learning that at age 38 years, approximately 25–30 cryopreserved oocytes are required to have a reasonable chance of having one child helps mitigate the risk of overreliance (5, 46, 47). This research does raise a further issue: planned OC is expensive (23), is usually self-pay (even for OC for many cancer patients at this time), and will often require multiple cycles to attain a reasonable chance of having a child in the future. These factors mean there will be economic and probably racial and ethnic disparities in access to planned OC (25, 47, 48). Few employers offer planned OC as a health benefit, although the trend, at least among some very large employers, appears to be on the rise (49). As it stands, however, only a small subset of those who are interested in using planned OC will find it affordable; the inequitable result is that the educational, career, and life-planning benefits will accrue only to a few. That being said, there are some who contend that corporate coverage of planned OC may confine reproductive autonomy in that it encourages delay of childbearing (49).

Concerns about planned OCs on societal grounds are sometimes voiced. Here one finds the objections that planned OC may promote delayed childbearing, that older parenthood is not fair to children, and that planned OC lets workplaces and the broader society “off the hook” from having to alter policies and demands that constrain individuals’ choices and hinder their success (33, 50), and that planned OC invites a risk of commercial exploitation. Later childbearing is already happening for reasons described previously. When people exercise this aspect of reproductive autonomy, planned OC offers a chance to mitigate the potentially devastating costs of infertility, childlessness, the inability to have the desired number of children, and the increased risks of adverse pregnancy outcomes. Expressions of concern about older parenthood may be tinged with sexism when one considers that parenthood by older men rarely draws the same criticism (11). Moreover, the Committee addressed an analogous issue in its opinion on OC before gonadotoxic therapy and concluded that the risk that offspring will be born to a person with a potentially shortened lifespan is not a reason to deny him or her reproductive treatment (3).

This is not to say that individuals should have pregnancies at any age. Studies indicate that the risks of maternal and neonatal harm increase with the increasing age of the woman carrying the pregnancy (51). This, again, is important information that needs to be conveyed when considering OC (52).

It would be beneficial when workplace and societal norms evolved to achieve equality for women and obviated the draw of so-called “medicalization,” that is, the “tendency to seek medical answers to social problems” (30). However, it does not follow that planned OC, as an available preventive procedure, should be withheld until these ideals are realized. Rather, it is fair to proceed on both fronts concomitantly.

This Committee supports insurance coverage for fertility treatments that expand reproductive choice, including planned OC. The US Department of Defense moved in a positive direction in 2016 when it proposed a temporary pilot program to pay for the preservation of sperm and oocytes for active-duty service members (53). Disappointingly, the program never materialized because it was contained in a budget that ultimately did not become law (54). The Ethics Committee encourages employers and lawmakers to enact policies that reduce the burden of childbearing and child-raising and that promote equality for all in the workplace and around the world. It is important, however, that women are not subjected to pressure to cryopreserve their oocytes and delay childbearing as a demonstration that they are committed to their careers (29).

Commentators have identified the risk of commercial exploitation when planned OC is offered by employers or marketed by those who profit from it (29, 49, 55). The Ethics Committee is concerned about coercion and the line between education and inappropriately aggressive marketing. Messaging in the media or through in-person gatherings may have the benefit of educating women about the decline in future reproductive potential, although they are still good candidates for unassisted reproduction or planned OC, but it may also generate disproportionate fear or encourage action that is not in their best interest (18, 26). In that regard, this Committee disapproves of arrangements in which medical practices hire firms to hold marketing sessions and then pay those firms for each person who becomes a patient. Such arrangements may also raise legal and ethical concerns; practices considering them should obtain legal advice on the laws and issues that are implicated.

MEDICAL RISKS AND INFORMED CONSENT

Providers should ensure that all who request planned OC are informed about efficacy, safety, benefits, and risks, including the unknown long-term health effects for offspring. Because planned OC is a developing procedure, disclosure and informed decision-making should be consistent with the Ethics Committee Opinion, “Moving innovation to practice: a committee opinion,” which emphasizes the importance of shared decision-making to help patients assess the value the treatment may or may not have for them (10).

First, physicians and those advising potential patients about planned OC should convey that the most assured and lowest-cost way to have a family is to try to conceive through sexual intercourse or donor insemination at a relatively early age (before the mid-30s, keeping in mind the time required to have subsequent children, when desired). Conversations about planned OC should identify all of the options for forming a family: early unassisted reproduction, assisted reproduction with their own oocytes, oocyte donation, embryo donation, adoption, or living childfree. These options should be reviewed again, as appropriate, when patients return to use their cryopreserved oocytes. At the same time, clinicians must be mindful not to interpose their own judgments about an individual’s priorities and life plans (17). Some patients presenting for planned OC may do so as a means to deliber-

ately “buy time” to reach a career goal, for example. That prerogative is a matter of personal autonomy; it is not for a physician to substitute his or her differing values.

Those advising patients about planned OC need to be clear about what is and is not yet known. Factors such as the suitable range of ages for planned OC and the number of oocytes needed are still being determined and may vary widely according to clinic experience. Patients may wish to consult with an independent mental health professional before choosing a planned OC to further explore their expectations, motivations, and any concerns surrounding the procedure. In an initial study of 201 women, almost half (49%) subsequently experienced some regret about their decision to cryopreserve oocytes. Factors that increased regret included having fewer oocytes to freeze than anticipated and receiving inadequate information or emotional support (56).

In communicating with potential patients about planned OC success rates, centers need to be specific about the extent of their experience with planned OC and their own results. At a minimum, they should disclose the survival of oocytes after thawing as well as their own pregnancy and live birth rates as they become available. National statistics can supplement this information, but studies indicate it takes experience to become skilled at oocyte vitrification and thawing, and patients deserve to understand their provider’s degree of experience (35). In that regard, the prior statement of this committee applies:

- A patient should be informed when the intervention has been adopted recently by the practice. The provider should share evidence relevant to the expectation that the new intervention is likely to be successful for the patient and how the risks may differ from those of standard treatment. It is important to point out to the patient that published success rates may not be achieved in a setting where a treatment or procedure has been adopted recently. The personal experience of providers with the new techniques or procedures should be discussed, whether the patient asks or not, and potential conflicts of interest should be disclosed (10).
- Potential patients should be informed, for example, when no patients have yet returned for thawing, fertilization, and transfer, such that the facility’s live birth results after OC are not yet established. Some facilities, such as those that provide only egg banking, are not required to report to the Society for Assisted Reproductive Technology or the Centers for Disease Control and Prevention the outcomes of cycles using oocytes they cryopreserved. This lack of reported data also should be disclosed and explained to prospective patients.
- Consent forms for planned OC should contain information on the process for oocyte cryopreservation, including potential and uncertain risks along with limited safety and outcome data. Patients should be cautioned that this is an emerging technology and that they may not receive any medical benefit from going through the procedure and may incur harm.
- Consent forms should also address the future disposition of cryopreserved oocytes. Patients should indicate their

disposition preferences in the event of death and any wishes regarding posthumous reproduction and inheritance rights (43). The facilities that store oocytes should communicate to patients their policies regarding the consequences of any loss, destruction, or theft of a patient's gametes or nonpayment of storage fees. It is acceptable for consent forms to offer the option of donating unused oocytes for research and for facilities to provide it as a possible disposition when oocytes are unclaimed. In such cases, explicit consent is required, and consent forms should follow the recommendations in the Ethics Committee opinion, "Informed consent and the use of gametes and embryos for research" (57).

- Consent forms should also include any clinic policies regarding the upper age limit for the future use of cryopreserved oocytes for the purpose of reproduction.

AREAS REQUIRING ADDITIONAL STUDY

Because the use of planned OC increases, researchers are encouraged to continue to investigate factors that will shed light on how best to offer and use planned OC. Topics include the pregnancy potential of oocytes retrieved at different ages with different markers for reproductive aging (antimüllerian hormone, follicle-stimulating hormone, and antral follicle count); the health effects on those who are stimulated to produce oocytes when young; and the health effects for offspring, including long-term studies. Physicians who are providing planned OC should collect and share these data with patients and, to the extent possible, with the profession.

It also will be beneficial to continue to generate data on the social aspects of planned OC: the experiences and motivations of those who elect to cryopreserve oocytes, their experiences when attempting to use those oocytes, and the reflections of those who never use them. Recent research suggests that some individuals will experience decisional regret over having cryopreserved oocytes, a development that needs to be better understood and addressed (56, 58). Because lack of a partner is often offered as a reason for seeking planned OC, researchers should examine issues of male as well as female "procreative consciousness and decision-making" (59). In that regard, the availability of planned OC also creates opportunities for health professionals to fill the "knowledge gap" by educating the public about the limits of female fertility. In so doing, we may achieve an estimable goal: that fewer women will discover they are already in the phase of greatest fertility decline without ever having been taught of its existence.

CONCLUSION

The Committee concludes that planned OC may allow individuals who, in earlier times, would have faced infertility and childlessness to potentially have a child to whom they are genetically linked. Planned OC is an ethically permissible medical treatment that may enhance reproductive autonomy and promote social equality. As with any relatively new treatment, however, uncertainties exist regarding its efficacy and long-term effects. Patients considering this treatment must be apprised of these unknowns, whereas practitioners are

strongly encouraged to gather and share data to add to scientific understanding about planned OC.

Acknowledgments

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Criopreservación planificada de ovocitos para preservar el potencial reproductivo futuro: un dictamen del Comité de Ética

La criopreservación planificada de ovocitos es un procedimiento éticamente permitido que puede ayudar a las personas a evitar la infertilidad en el futuro. Dado que la criopreservación planificada de ovocitos es un procedimiento nuevo y en evolución, es esencial que quienes se planteen utilizarlo estén informados sobre las incertidumbres relativas a su eficacia y efectos a largo plazo. (Sustituye al documento del mismo nombre, publicado por última vez en 2017).