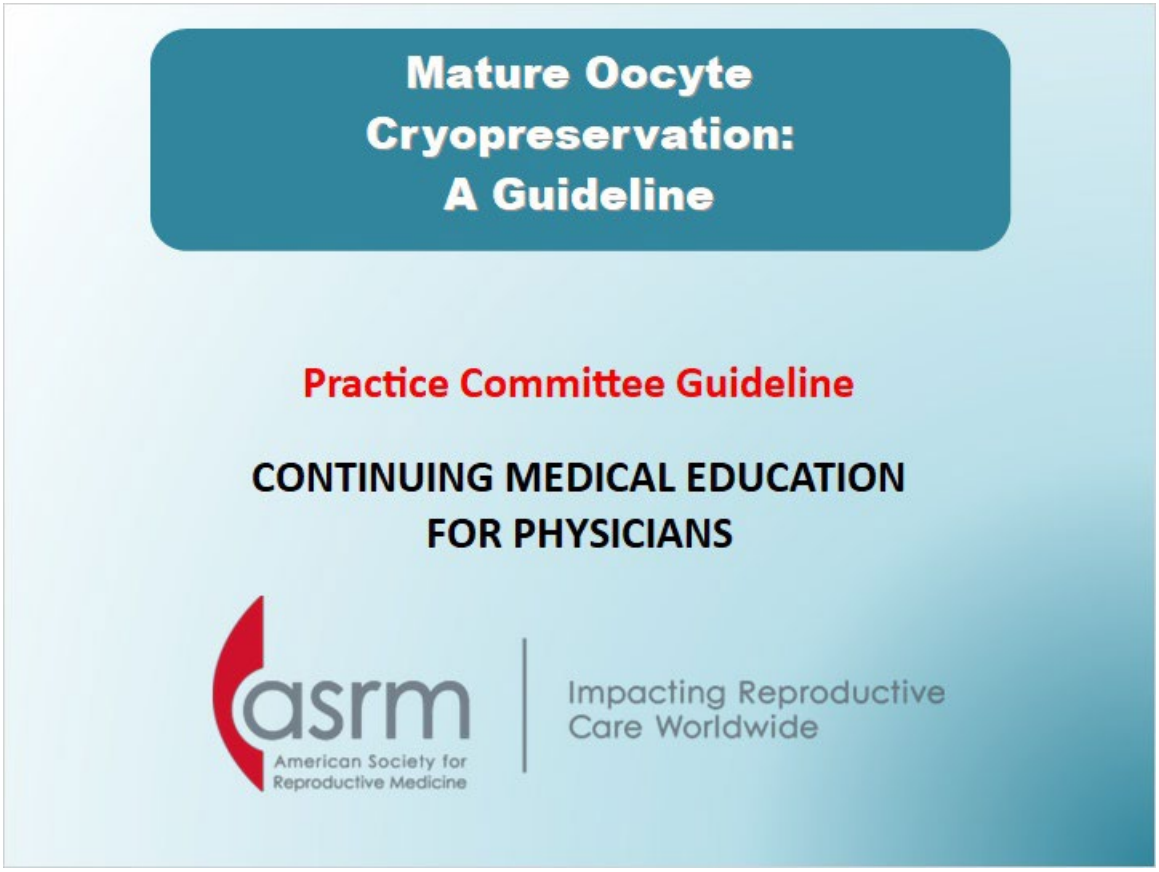
MD120 Lesson 5

1. MD120_L5

1.1 Mature Oocyte Cryopreservation:



Notes:

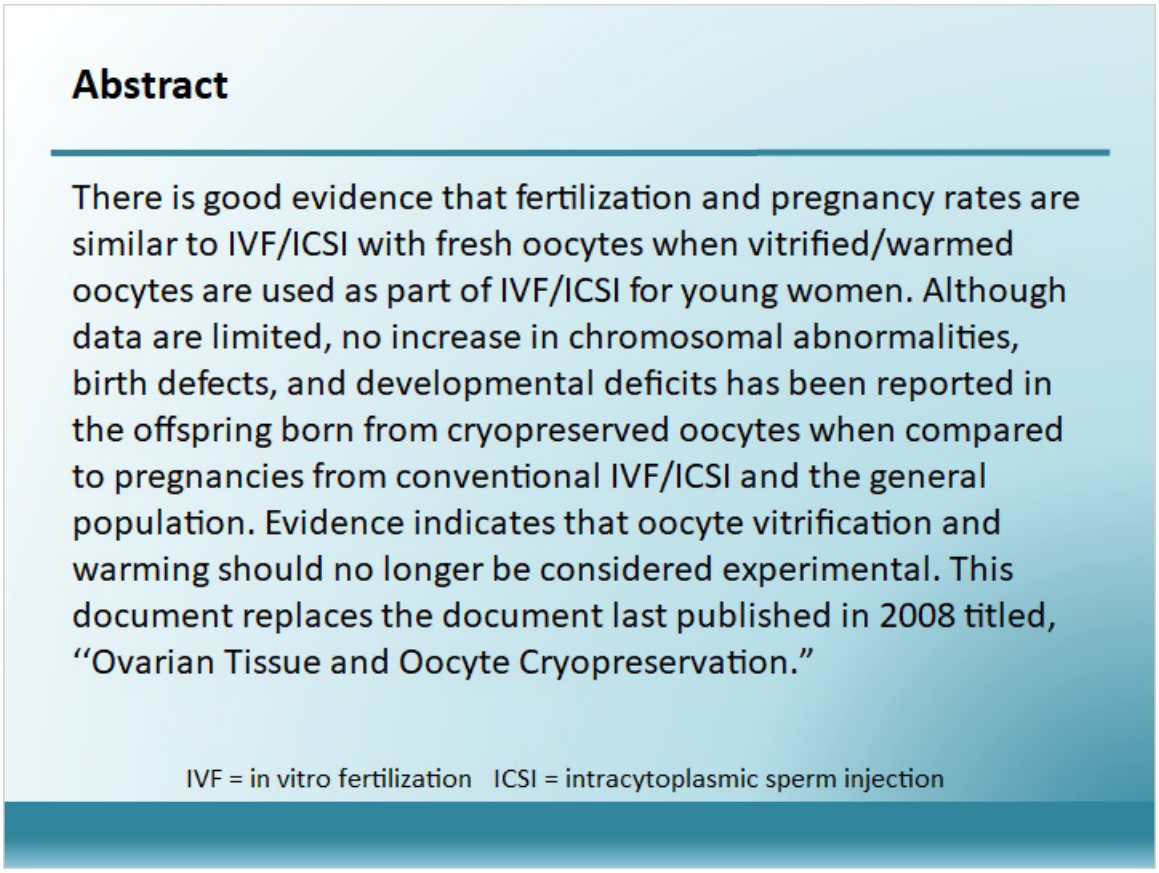
Welcome to the American Society for Reproductive Medicine's eLearning modules. The subject of this presentation is the Practice Committee Guideline on Mature Oocyte Cryopreservation.

1.2 Acknowledgments

Notes:

This report was developed under the direction of the Practice Committee of the American Society for Reproductive Medicine (ASRM) in collaboration with the Society for Assisted Reproductive Technology (SART) as a service to its members and other practicing clinicians. Although this document reflects appropriate management of a problem encountered in the practice of reproductive medicine, it is not intended to be the only approved standard of practice or to dictate an exclusive course of treatment. Other plans of management may be appropriate, taking into account the needs of the individual patient, available resources, and institutional or clinical practice limitations. The Practice Committees and the Board of Directors of ASRM and SART have approved this report. It has been reviewed by the SART presidential chain and edited based on their comments.

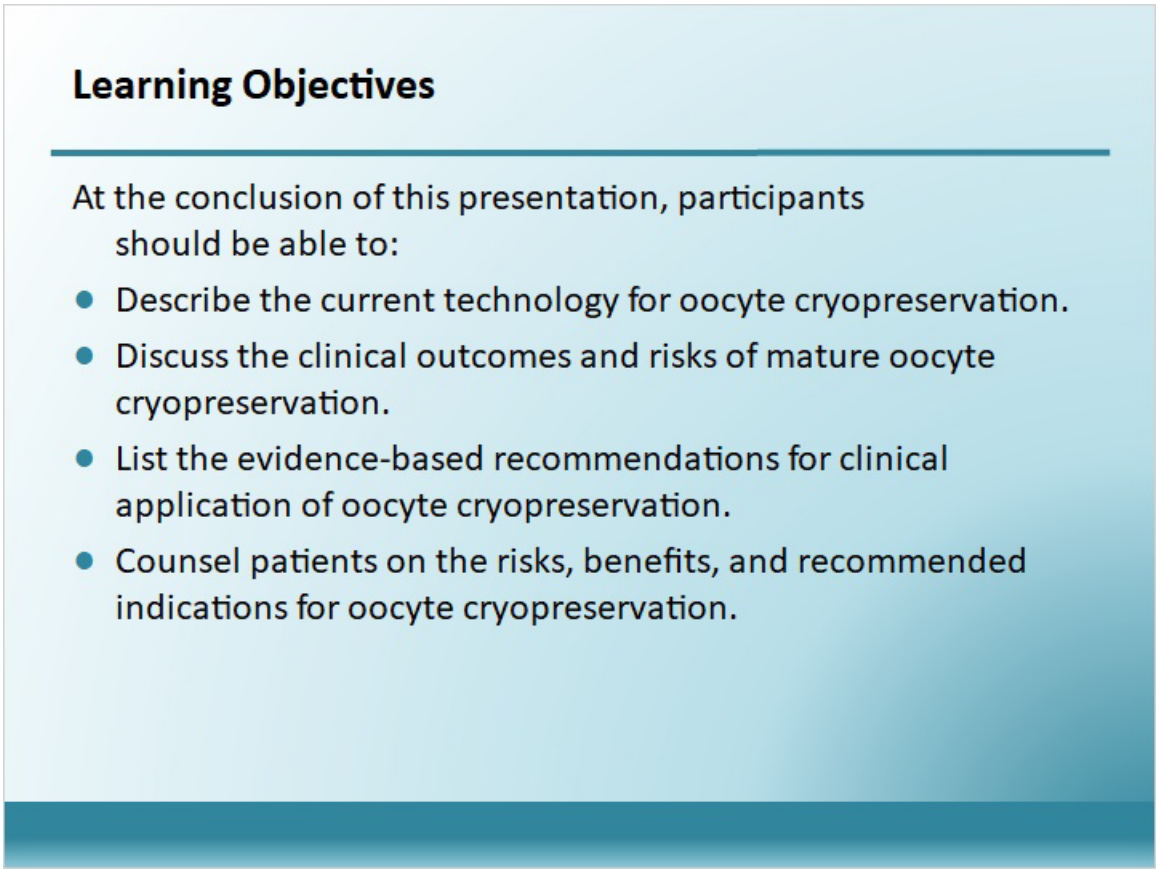
1.3 Abstract



Notes:

There is good evidence that fertilization and pregnancy rates are similar to IVF/ICSI with fresh oocytes when vitrified/warmed oocytes are used as part of IVF/ICSI for young women. Although data are limited, no increase in chromosomal abnormalities, birth defects, and developmental deficits has been reported in the offspring born from cryopreserved oocytes when compared to pregnancies from conventional IVF/ICSI and the general population. Evidence indicates that oocyte vitrification and warming should no longer be considered experimental. This document replaces the document last published in 2008 titled, ‘‘Ovarian Tissue and Oocyte Cryopreservation.”

1.4 Learning Objectives



Notes:

At the conclusion of this presentation, participants should be able to:

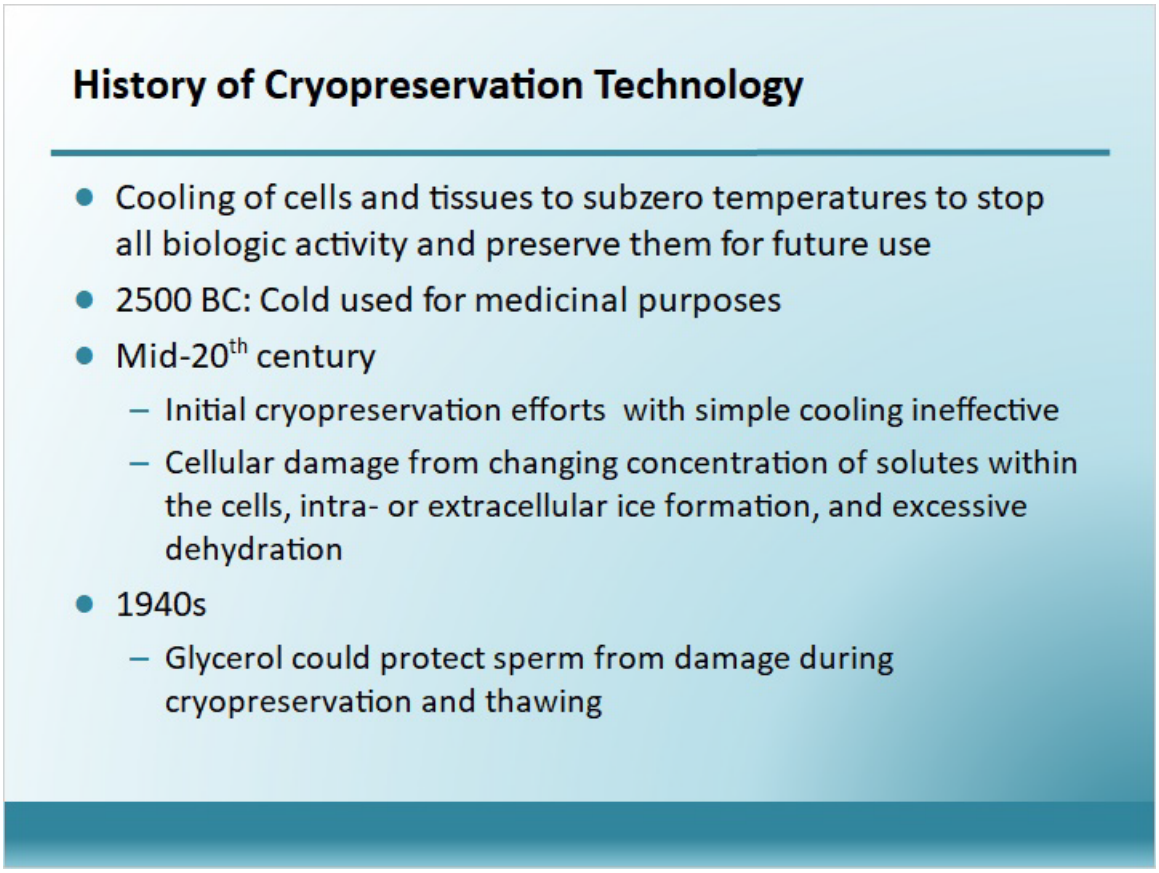
Describe the current technology for oocyte cryopreservation.

Discuss the clinical outcomes and risks of mature oocyte cryopreservation.

List the evidence-based recommendations for clinical application of oocyte cryopreservation.

Counsel patients on the risks, benefits, and recommended indications for oocyte cryopreservation.

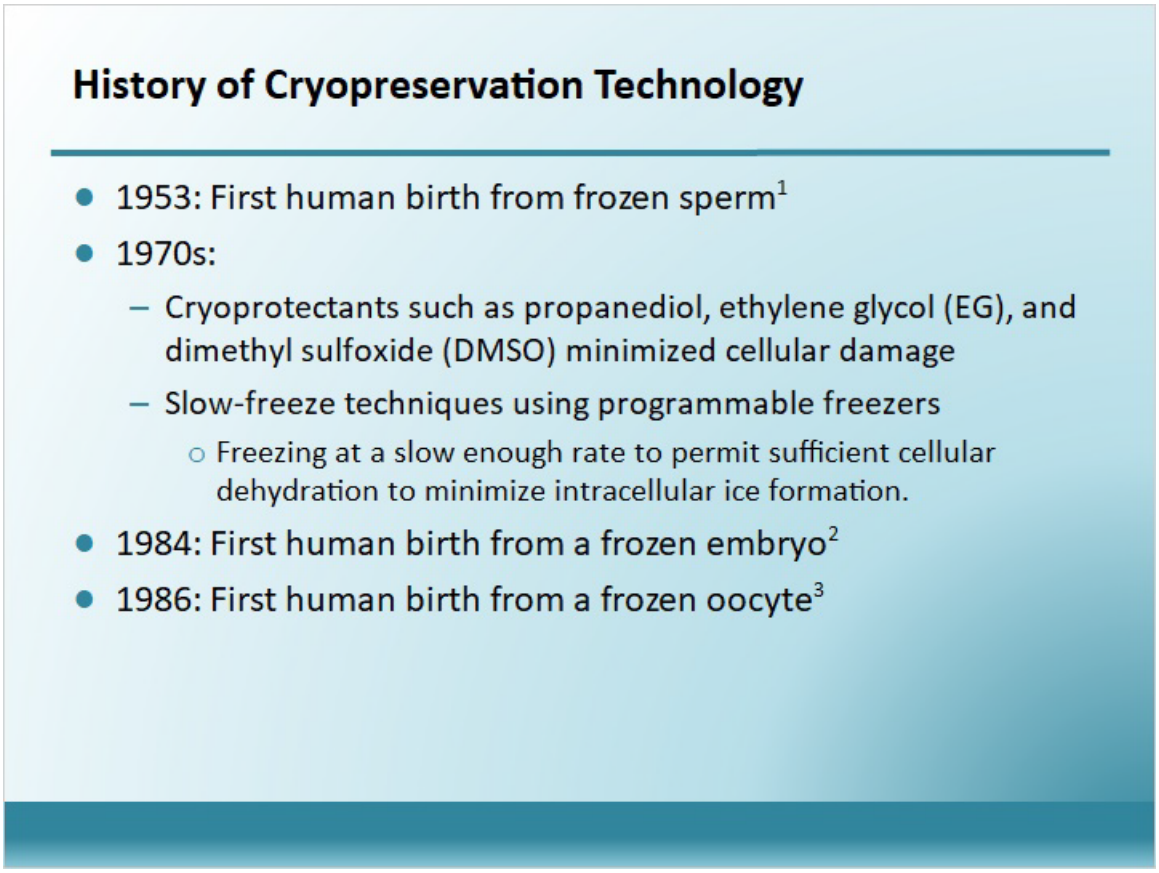
1.5 History of Cryopreservation Technology



Notes:

Cryopreservation refers to the cooling of cells and tissues to subzero temperatures in order to stop all biologic activity and preserve them for future use. The science of cryobiology can be traced as far back as 2500 BC, when early civilizations used cold for medicinal purposes. However, cryopreservation of cells and tissues did not become a reality until the mid-20th century. Initial efforts at cryopreservation were ineffective because simple cooling techniques led to cellular damage from changing concentration of solutes within the cells, intra- or extracellular ice formation, and excessive dehydration. In the 1940s, it was discovered that glycerol could protect sperm from damage during cryopreservation and thawing.

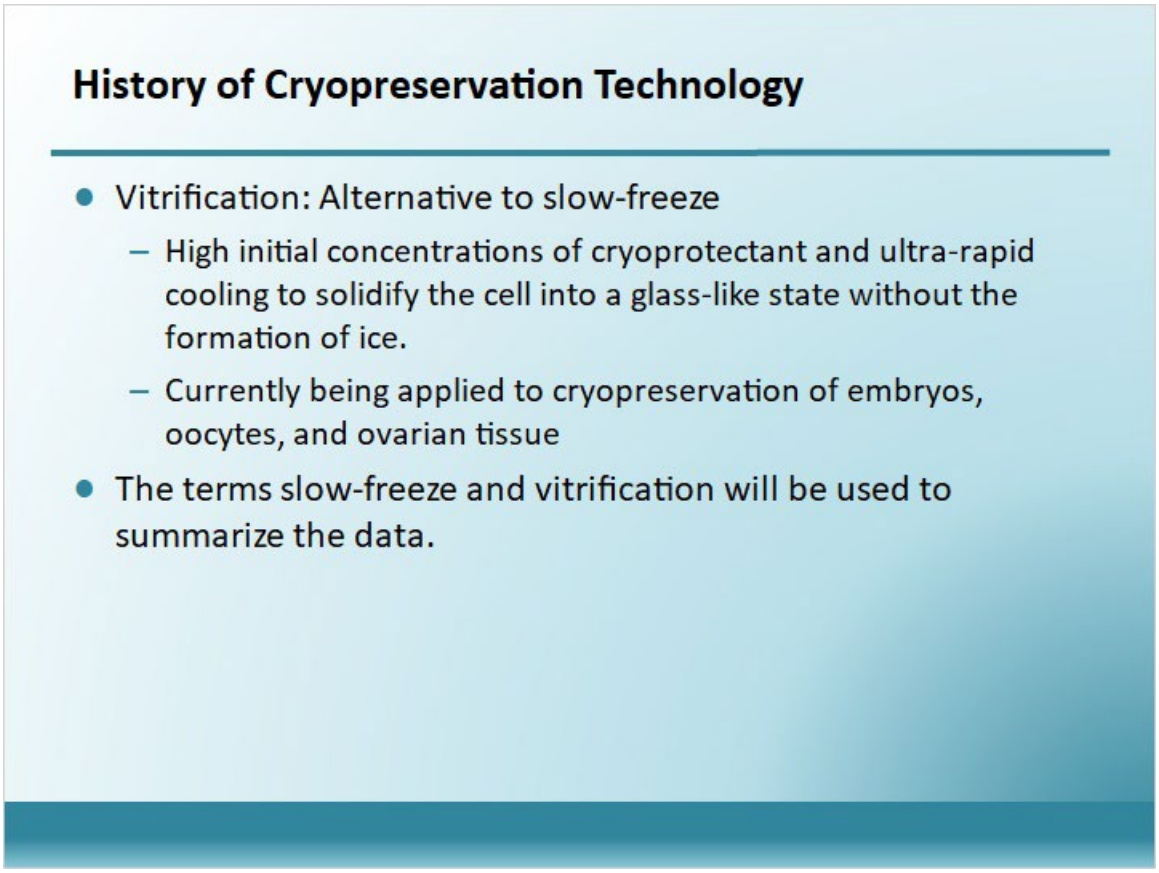
1.6 History of Cryopreservation Technology



Notes:

The first human birth from frozen sperm was reported in 1953 (1). In the 1970s other cryoprotectants such as propanediol, ethylene glycol (EG), and dimethyl sulfoxide (DMSO) were identified and found to minimize cellular damage. In addition, slow-freeze techniques using programmable freezers were developed to allow for freezing to occur at a slow enough rate to permit sufficient cellular dehydration to minimize intracellular ice formation. These improvements led to the first human birth from a frozen embryo, reported in 1984 (2). In 1986, the first human birth from a frozen oocyte was reported (3).

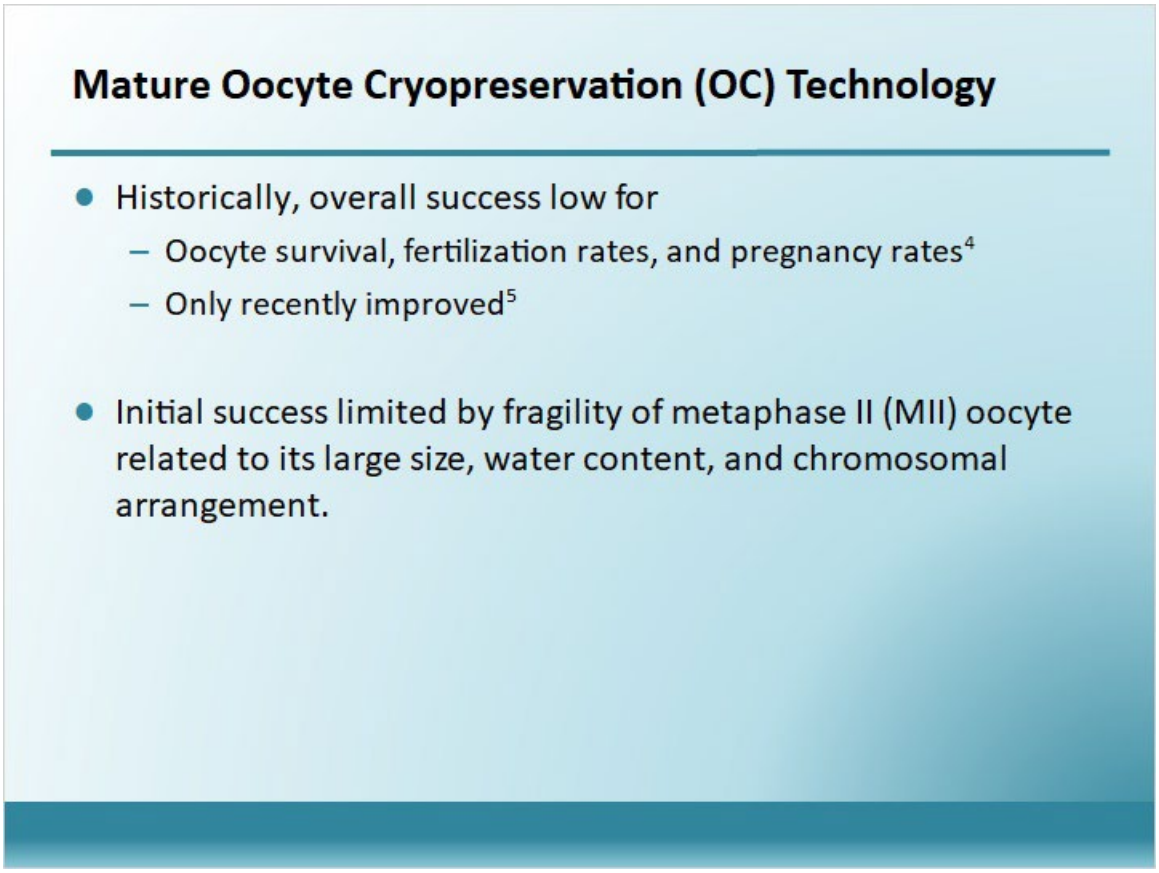
1.7 History of Cryopreservation Technology



Notes:

Over the past decade, an alternative to slow-freeze, vitrification, has been developed. Vitrification is the process of cryopreservation using high initial concentrations of cryoprotectant and ultra-rapid cooling to solidify the cell into a glass-like state without the formation of ice. Vitrification is currently being applied to the cryopreservation of embryos, oocytes, and ovarian tissue. While various methods of slow-freeze and vitrification have been used, for the purpose of this document the terms slow-freeze and vitrification will be used to summarize the data.

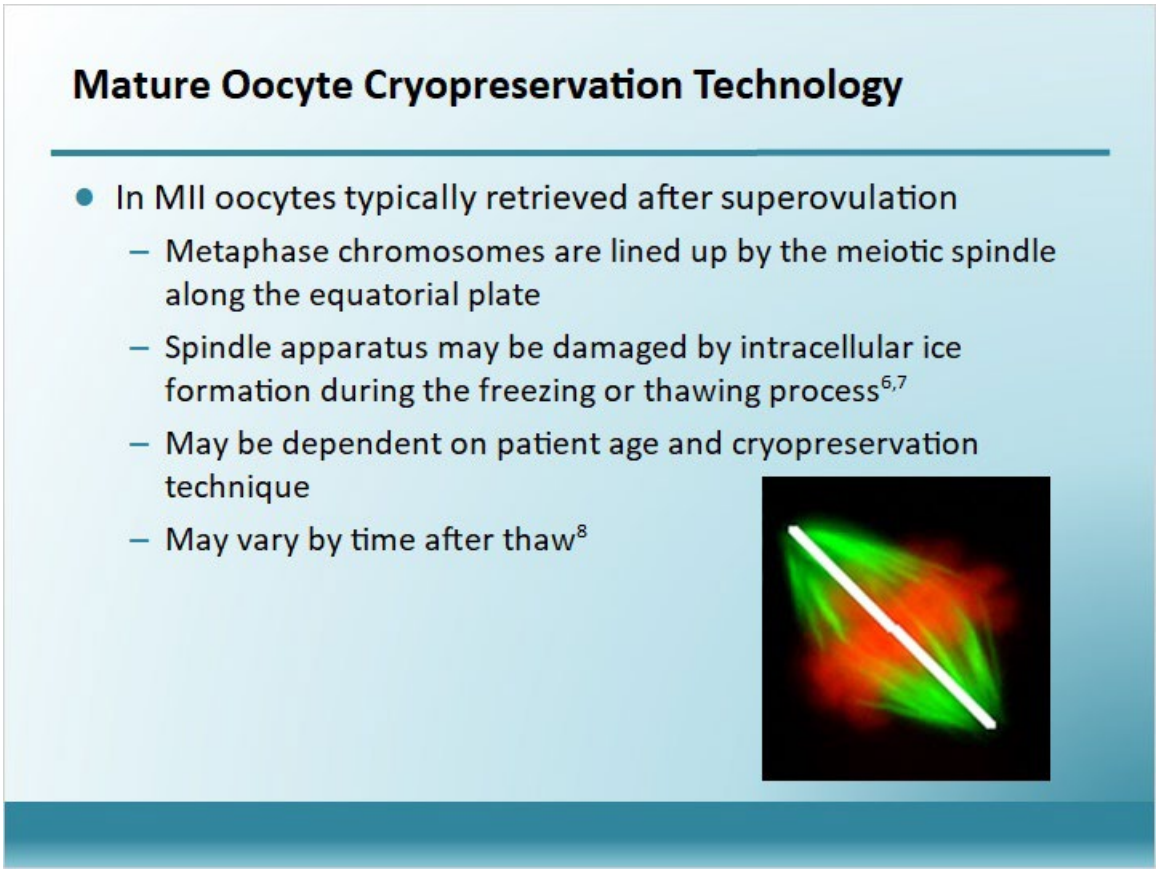
1.8 Mature Oocyte Cryopreservation (OC) Technology



Notes:

Historically, overall success with respect to oocyte survival, fertilization rates, and pregnancy rates was low(4) and has only recently improved(5). Initial success was limited by the fragility of the metaphase II (MII) oocyte related to its large size, water content, and chromosomal arrangement.

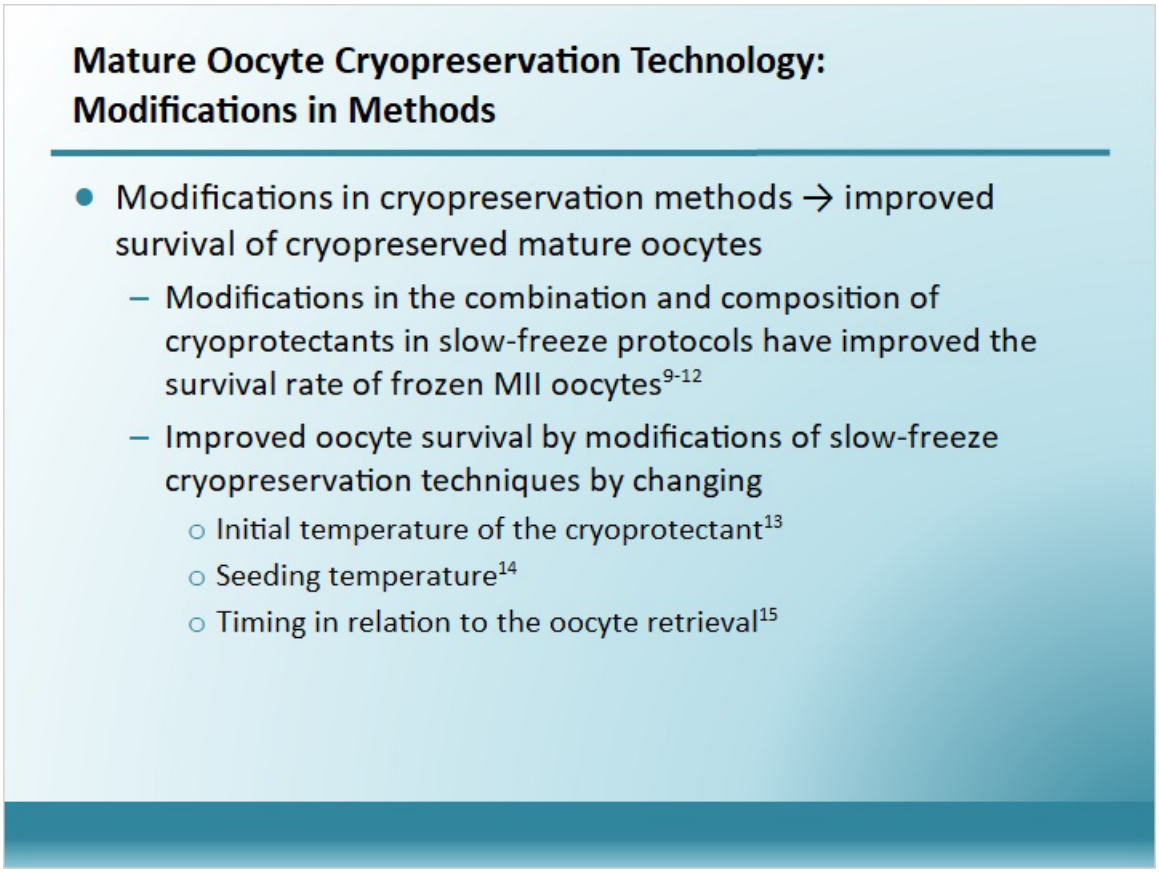
1.9 Mature Oocyte Cryopreservation Technology



Notes:

In mature oocytes (MII), typically retrieved after superovulation, the metaphase chromosomes are lined up by the meiotic spindle along the equatorial plate. Studies have documented that the spindle apparatus may be damaged by intracellular ice formation during the freezing or thawing process (6,7), and these abnormalities may be dependent on patient age and cryopreservation technique and may vary by time after thaw(8).

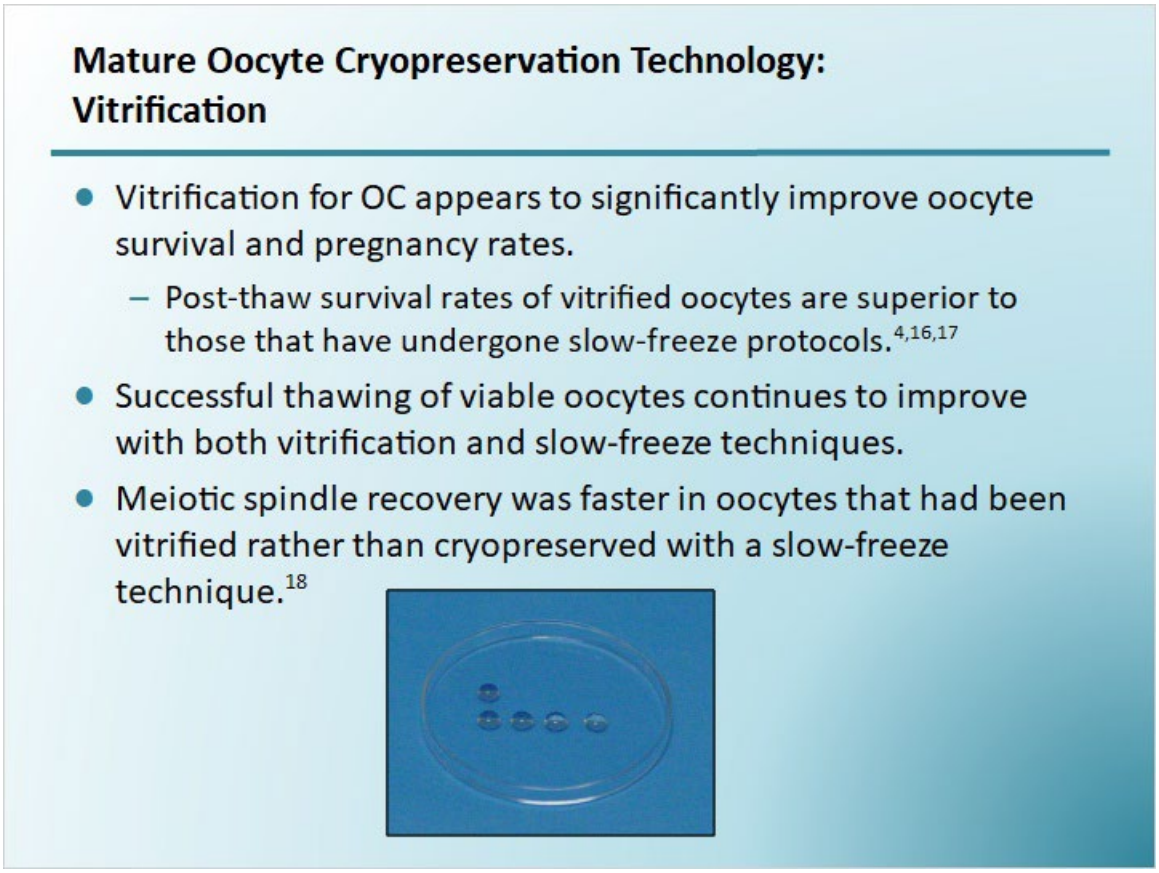
1.10 Mature Oocyte Cryopreservation Technology:



Notes:

Modifications in cryopreservation methods over the past few years may be responsible for improved survival of cryopreserved mature oocytes. For example, modifications in the combination and composition of cryoprotectants in slow-freeze protocols have improved the survival rate of frozen MII oocytes (9-12). Numerous studies also have reported improved oocyte survival by modifications of slow-freeze cryopreservation techniques such as changing the initial temperature of the cryoprotectant (13), the seeding temperature (14), and timing in relation to the oocyte retrieval (15).

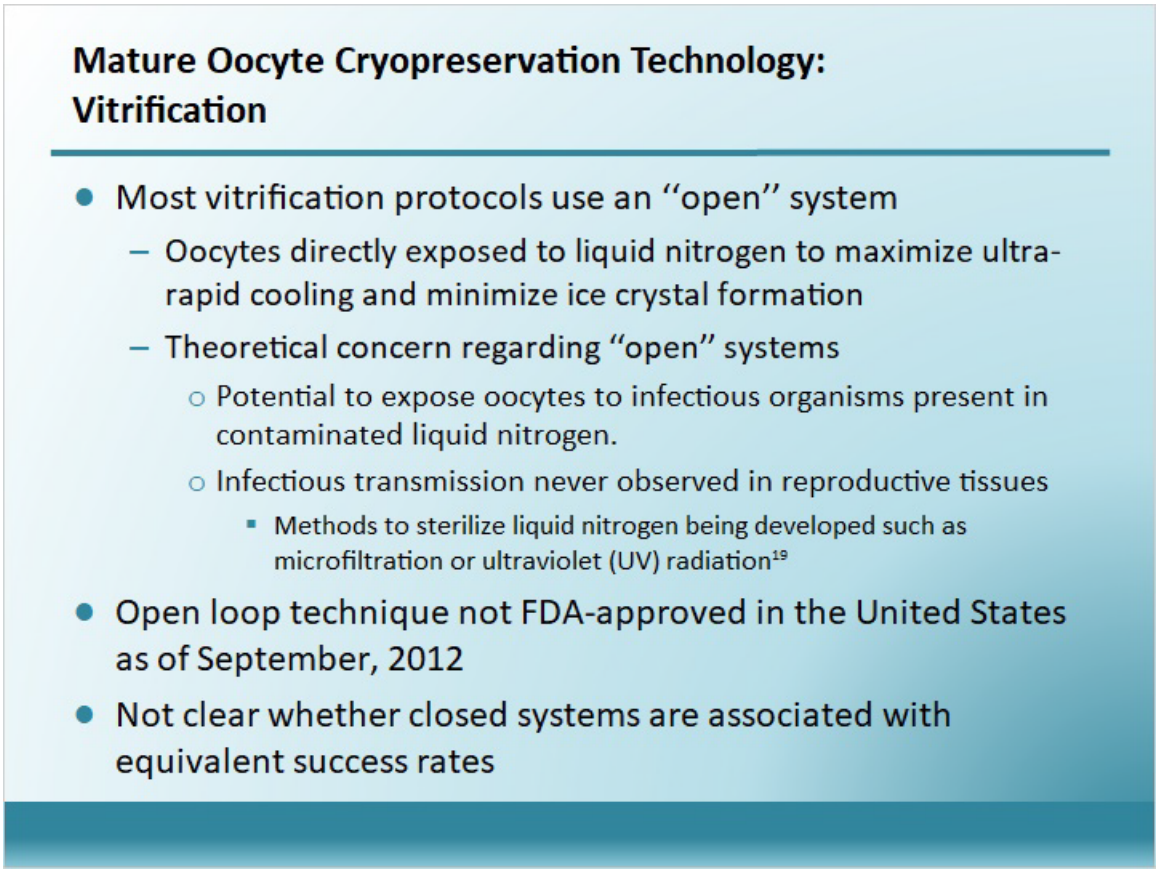
1.11 Mature Oocyte Cryopreservation Technology:



Notes:

Recent studies suggest that vitrification for oocyte cryopreservation significantly improves oocyte survival and pregnancy rates. In humans, most studies suggest that post-thaw survival rates of vitrified oocytes are superior to those that have undergone slow-freeze protocols (4, 16, 17). It should be noted that successful thawing of viable oocytes continues to improve with both vitrification and slow-freeze techniques. In addition, a study reported that meiotic spindle recovery was faster in oocytes that had been vitrified rather than cryopreserved with a slow-freeze technique(18).

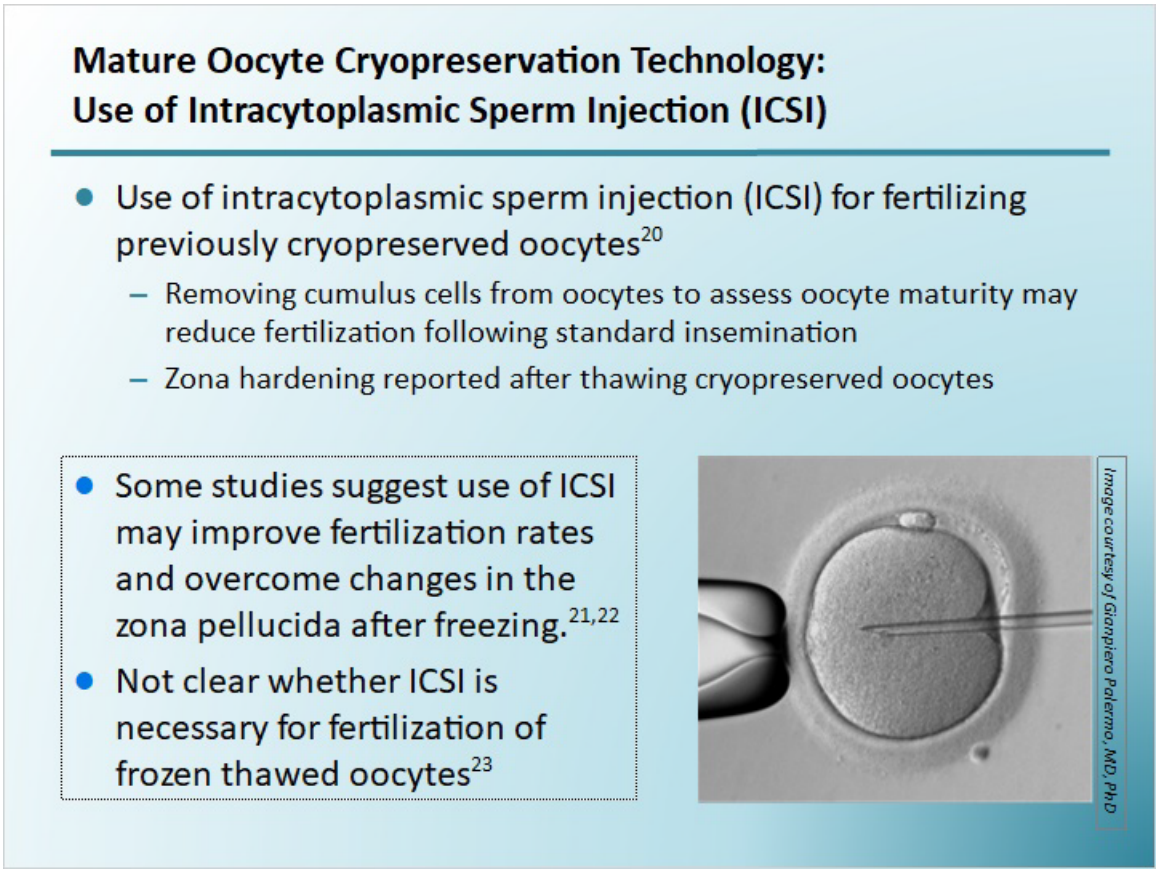
1.12 Mature Oocyte Cryopreservation Technology:



Notes:

Most vitrification protocols use an ''open'' system, in which oocytes are directly exposed to liquid nitrogen to maximize ultra-rapid cooling and minimize ice crystal formation. A theoretical concern regarding such ''open'' systems is their potential to expose oocytes to infectious organisms present in contaminated liquid nitrogen. While infectious transmission has never been observed in reproductive tissues, methods to sterilize liquid nitrogen are being developed such as microfiltration or ultraviolet (UV) radiation (19). As of September, 2012, the open loop technique was not FDA-approved in the United States (US). Closed systems also exist, but it is not clear whether they are associated with equivalent success rates.

1.13 Mature Oocyte Cryopreservation Technology:

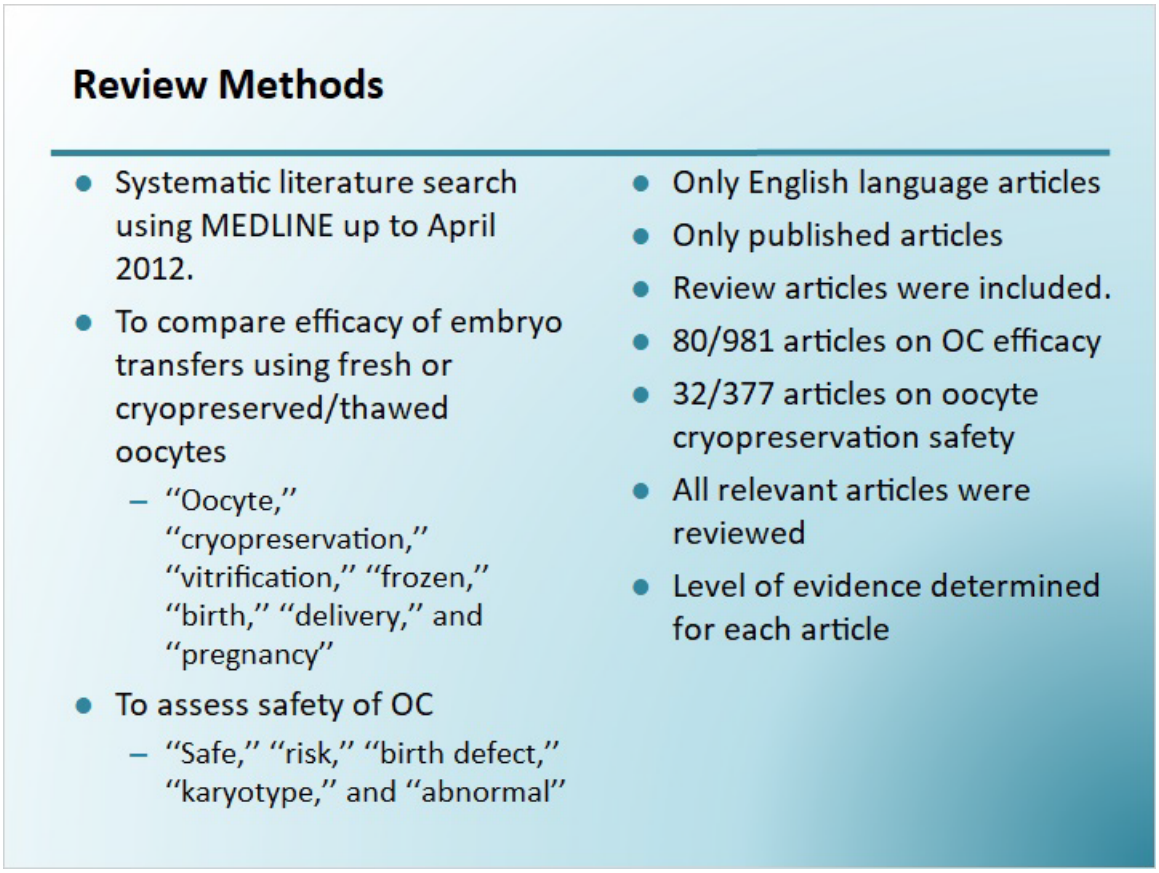


Notes:

Cryopreservation protocols usually involve removing cumulus cells from oocytes in order to assess oocyte maturity. Because removing cumulus cells may reduce fertilization following standard insemination and because zona hardening has been reported after thawing cryopreserved oocytes,

intracytoplasmic sperm injection (ICSI) is generally used for fertilizing previously cryopreserved oocytes (20). While some studies suggest that the use of ICSI may improve fertilization rates and overcome changes in the zona pellucida after freezing(21, 22), it is not clear whether ICSI is necessary for fertilization of frozen thawed oocytes(23).

1.14 Review Methods

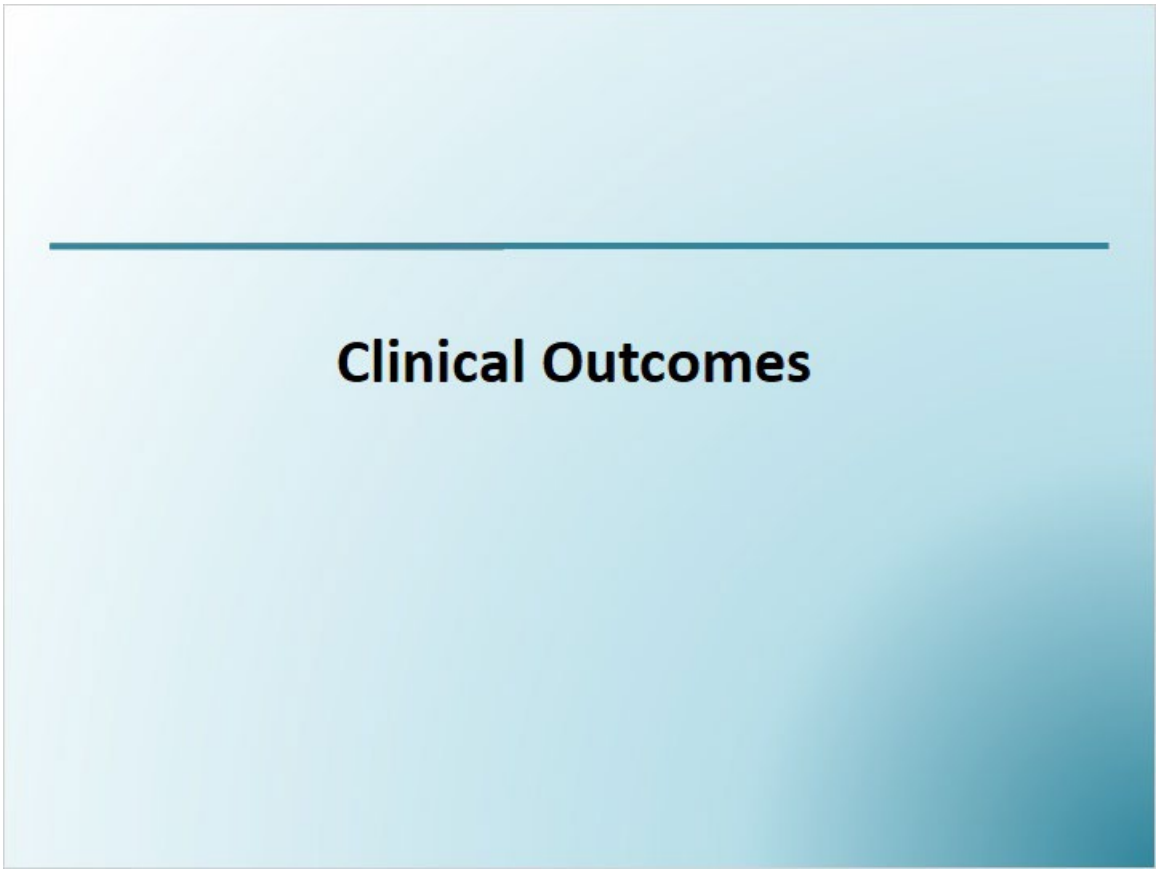


Notes:

To evaluate the efficacy and safety of mature oocyte cryopreservation the Committee performed a systematic literature search using the MEDLINE site up to April 2012. In order to compare the efficacy (clinical pregnancy and live-birth rates) of embryo transfers using fresh or cryopreserved/thawed oocytes, the search utilized combinations of medical subject headings ''oocyte,'' ''cryopreservation,'' ''vitrification,'' ''frozen,'' ''birth,'' ''delivery,'' and ''pregnancy.'' In order to assess the safety of oocyte cryopreservation, the search included the terms ''safe,'' ''risk,'' ''birth defect,'' ''karyotype,'' and ''abnormal'' to the search. Only English language articles were selected, and the search was restricted to published articles.

Review articles were included. The relevance of included articles was assessed by an epidemiologist with subsequent consultation by the Committee. A total of 981 articles on oocyte cryopreservation efficacy was identified initially and 80 were determined to be relevant. Three hundred seventy-seven articles were initially identified in the oocyte cryopreservation safety search and 32 were found to be relevant. All relevant articles were reviewed and the level of evidence was determined for each article.

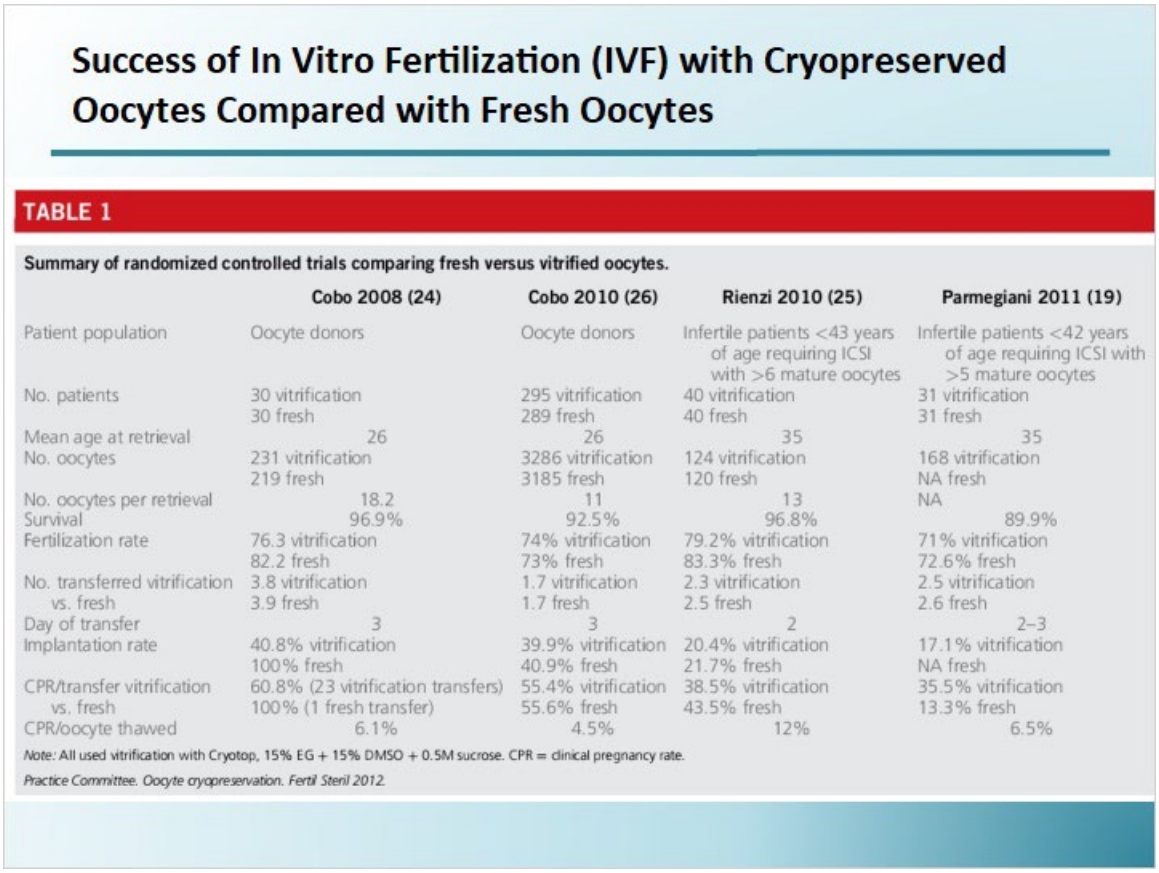
1.15 Clinical Outcomes



Notes:

This section will discuss clinical outcomes for oocyte cryopreservation.

1.16 Success of In Vitro Fertilization (IVF) with Cryopreserved Oocytes Compared with Fresh Oocytes



Success of In Vitro Fertilization (IVF) with Cryopreserved Oocytes Compared with Fresh Oocytes

TABLE 1

Summary of randomized controlled trials comparing fresh versus vitrified oocytes.

	Cobo 2008 (24)	Cobo 2010 (26)	Rienzi 2010 (25)	Parmegiani 2011 (19)
Patient population	Oocyte donors	Oocyte donors	Infertile patients <43 years of age requiring ICSI with >6 mature oocytes	Infertile patients <42 years of age requiring ICSI with >5 mature oocytes
No. patients	30 vitrification 30 fresh	295 vitrification 289 fresh	40 vitrification 40 fresh	31 vitrification 31 fresh
Mean age at retrieval	26	26	35	35
No. oocytes	231 vitrification 219 fresh	3286 vitrification 3185 fresh	124 vitrification 120 fresh	168 vitrification NA fresh
No. oocytes per retrieval	18.2	11	13	NA
Survival	96.9%	92.5%	96.8%	89.9%
Fertilization rate	76.3 vitrification 82.2 fresh	74% vitrification 73% fresh	79.2% vitrification 83.3% fresh	71% vitrification 72.6% fresh
No. transferred vitrification vs. fresh	3.8 vitrification 3.9 fresh	1.7 vitrification 1.7 fresh	2.3 vitrification 2.5 fresh	2.5 vitrification 2.6 fresh
Day of transfer	3	3	2	2–3
Implantation rate	40.8% vitrification 100% fresh	39.9% vitrification 40.9% fresh	20.4% vitrification 21.7% fresh	17.1% vitrification NA fresh
CPR/transfer vitrification vs. fresh	60.8% (23 vitrification transfers) 100% (1 fresh transfer)	55.4% vitrification 55.6% fresh	38.5% vitrification 43.5% fresh	35.5% vitrification 13.3% fresh
CPR/oocyte thawed	6.1%	4.5%	12%	6.5%

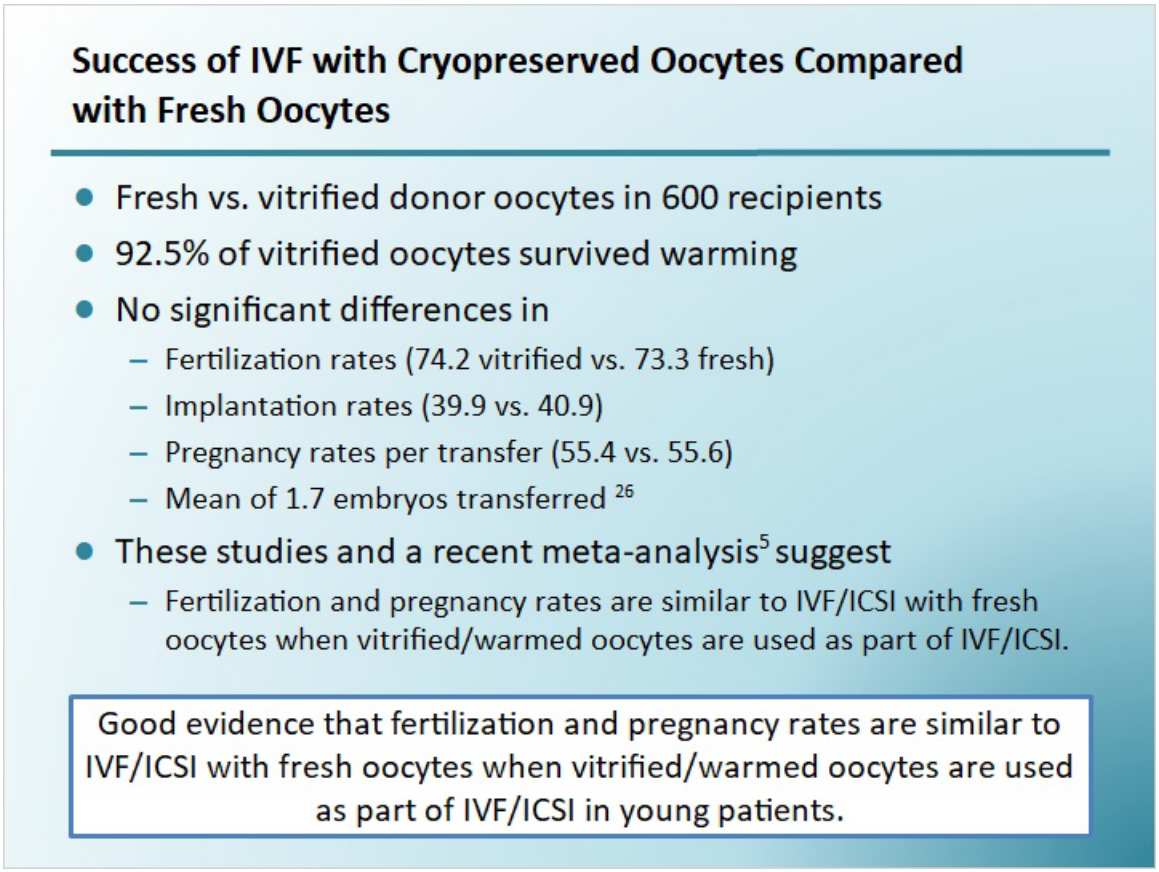
Note: All used vitrification with Cryotop, 15% EG + 15% DMSO + 0.5M sucrose. CPR = clinical pregnancy rate.

Practice Committee. Oocyte cryopreservation. Fertil Steril 2012.

Notes:

The literature search identified only four randomized controlled trials comparing outcomes with cryopreserved and fresh oocytes in IVF/ICSI cycles (19, 24-26)(Table 1). All studies used a similar open vitrification protocol (Cryotop® device, 15% EG + 15% DMSO + 0.5 M sucrose) and were conducted in Europe. Two of these studies were conducted in egg donor/recipient cycles, and 2 were conducted in infertile couples with supernumerary oocytes available to vitrify and warm only if pregnancy was not achieved in the fresh cycle. Overall, oocyte survival after vitrification and warming ranged between 90% and 97%, fertilization rates were between 71% and 79%, implantation rates were 17%-41%, and clinical pregnancy rates per transfer ranged from 36%-61%. The clinical pregnancy rate (CPR) per thawed oocyte ranged from 4.5%-12%.

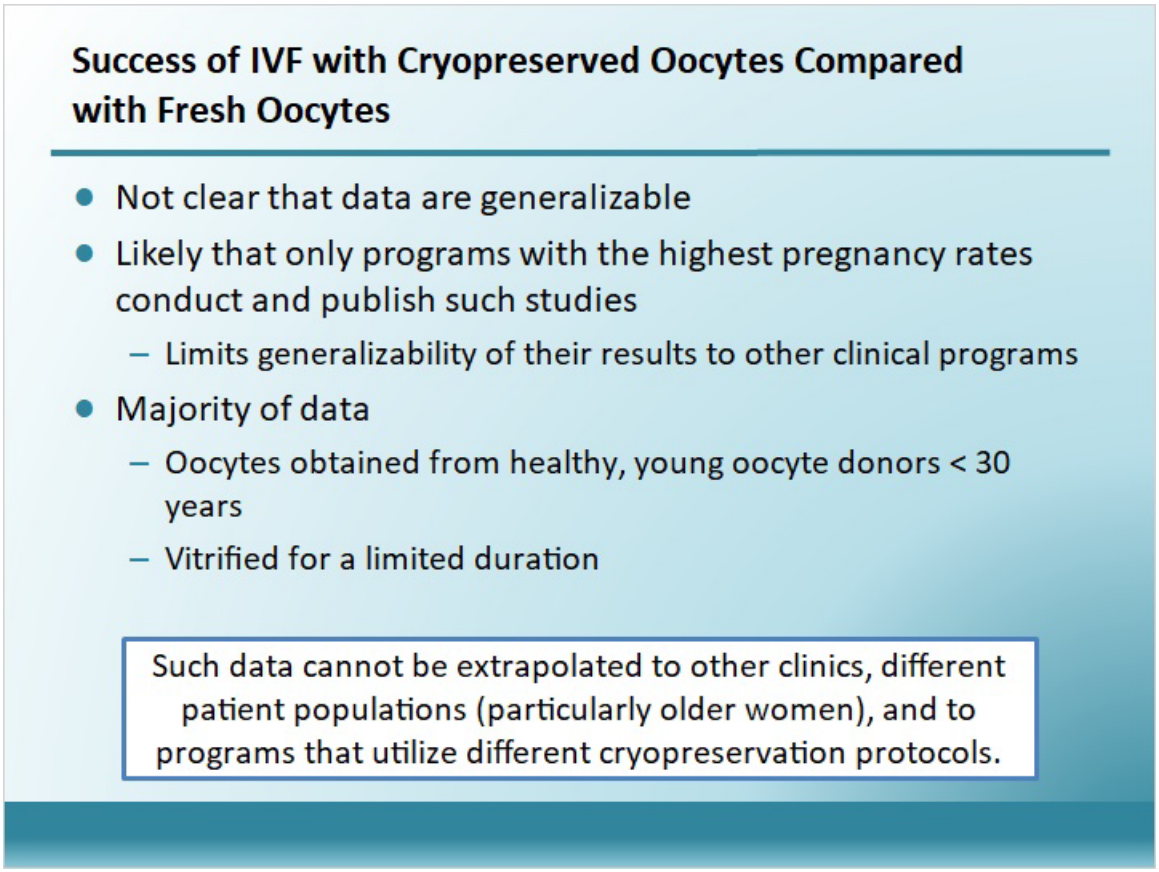
1.17 Success of IVF with Cryopreserved Oocytes Compared with Fresh Oocytes



Notes:

The largest and most compelling randomized controlled trial (RCT) compared the use of fresh versus vitrified donor oocytes in 600 recipients. The investigators found that 92.5% of vitrified oocytes survived warming and that there were no significant differences in fertilization rates (74.2 vitrified vs. 73.3 fresh), implantation rates (39.9 vs. 40.9) and pregnancy rates per transfer (55.4 vs. 55.6) between groups, with a mean of 1.7 embryos transferred(26). These studies and a recent meta-analysis (5) suggest that fertilization and pregnancy rates are similar to IVF/ICSI with fresh oocytes when vitrified/warmed oocytes are used as part of IVF/ICSI. In summary, there is good evidence that fertilization and pregnancy rates are similar to IVF/ICSI with fresh oocytes when vitrified/warmed oocytes are used as part of IVF/ICSI in young patients.

1.18 Success of IVF with Cryopreserved Oocytes Compared with Fresh Oocytes



Notes:

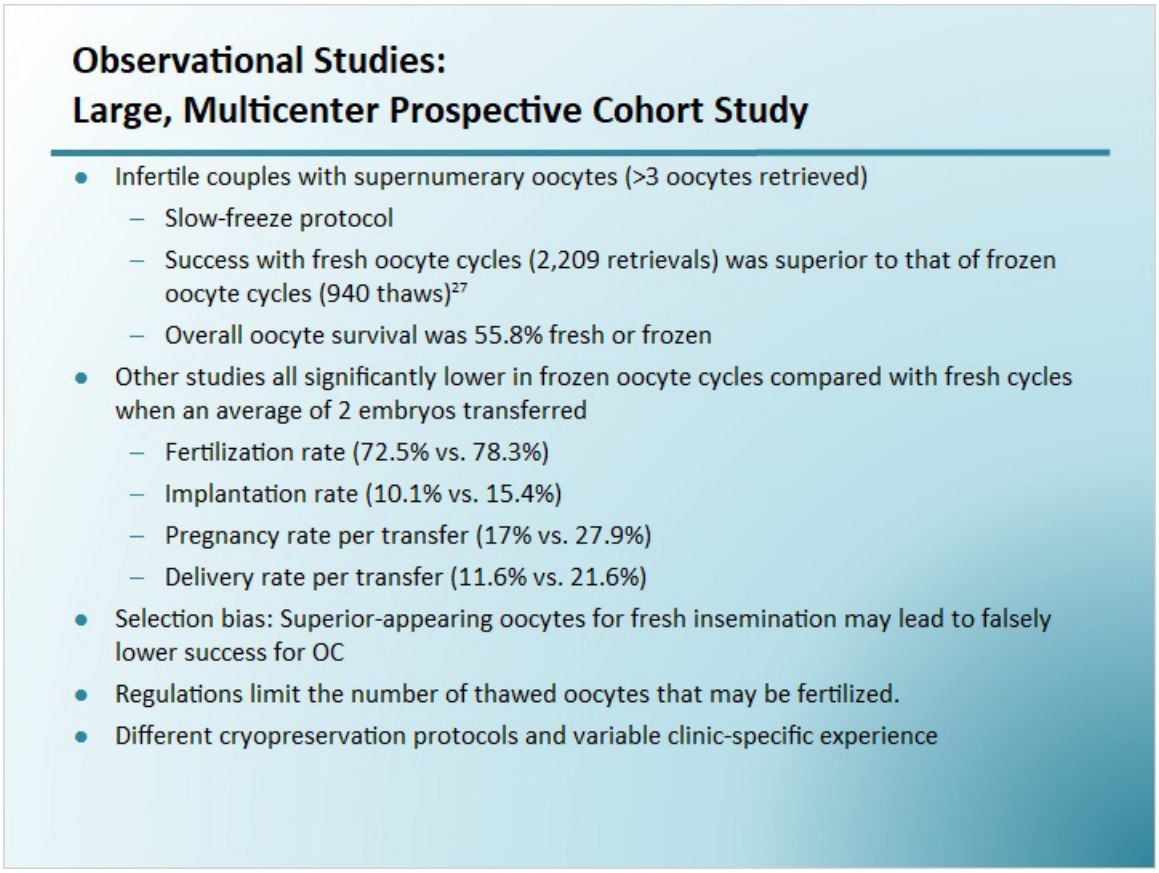
However, given the limited number of randomized controlled trials, it is not clear that these data are generalizable. Indeed, it is likely that only programs with the highest pregnancy rates conduct and publish such studies, limiting the generalizability of their results to other clinical programs. In addition, the majority of these data derives from experience using oocytes obtained from healthy, young oocyte donors under the age of 30 years, which have been vitrified for a limited duration. Therefore, such data cannot be extrapolated to other clinics, different patient populations (particularly older women), and to programs that utilize different cryopreservation protocols.

1.19 Observational Studies

Notes:

Given these limitations, it is useful also to consider the results of observational studies comparing success rates using fresh and cryopreserved oocytes. The largest of these observational studies have been conducted in Italy, where Italian law limited the number of oocytes that may be fertilized as part of IVF. For this reason, programs in Italy have been offering OC to couples with additional oocytes available at retrieval for many years. These data are important because they reflect success rates at various clinical programs rather than only at programs with particular expertise.

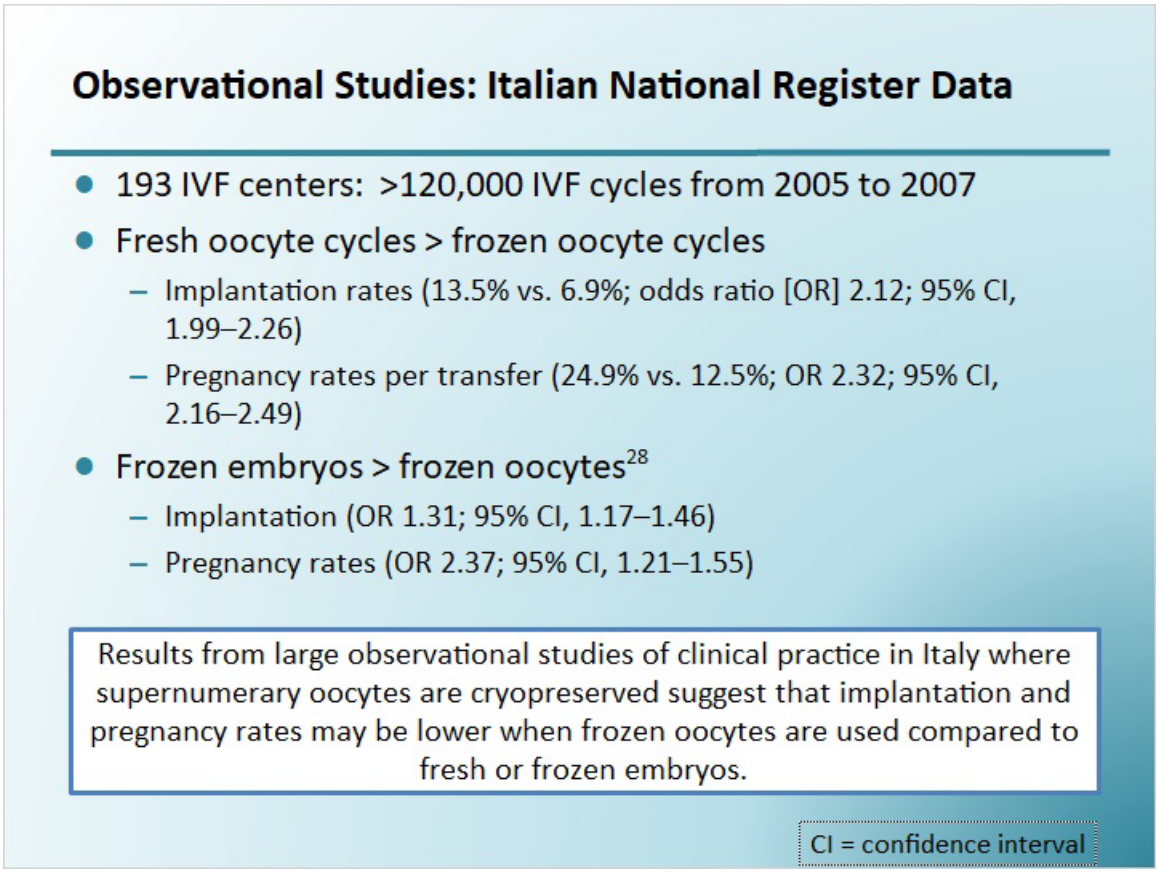
1.20 Observational Studies:



Notes:

A large Italian multicenter prospective cohort study of infertile couples with supernumerary oocytes (>3 oocytes retrieved) cryopreserved using a slow-freeze protocol demonstrated that success with fresh oocyte cycles (2,209 retrievals) was superior to that of frozen oocyte cycles (940 thaws) (27). The overall oocyte survival was 55.8% fresh or frozen; other studies comparing the fertilization rate (72.5% vs. 78.3%), implantation rate (10.1% vs. 15.4%), pregnancy rate per transfer (17% vs. 27.9%), and delivery rate per transfer (11.6% vs. 21.6%) were all significantly lower in frozen oocyte cycles compared with fresh cycles when an average of 2 embryos were transferred. It should be recognized that the lower success rates observed in this study may be due in part to selection bias as selection of superior-appearing oocytes for fresh insemination may lead to falsely lower success for oocyte cryopreservation and because regulations limit the number of thawed oocytes that may be fertilized. In addition, different cryopreservation protocols (slow-freeze) and variable clinic-specific experience may contribute to these findings as well.

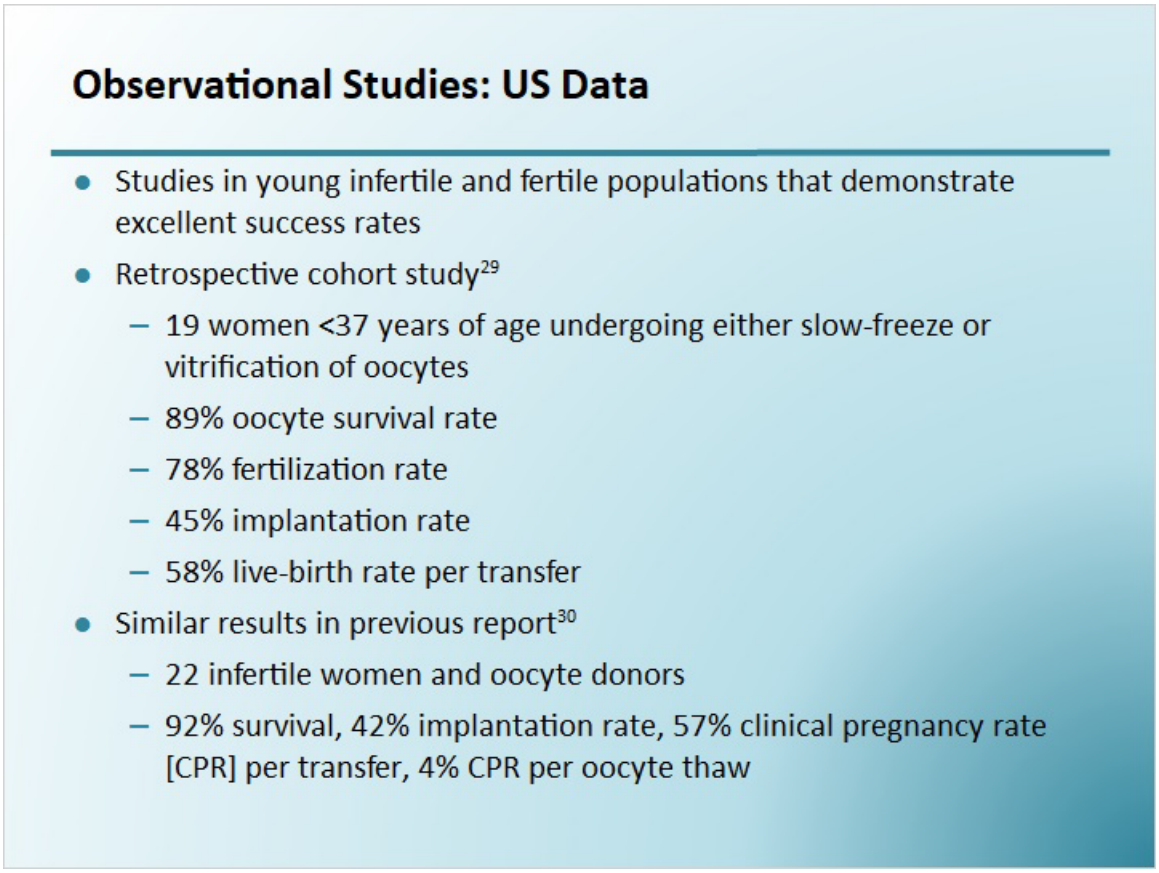
1.21 Observational Studies: Italian National Register Data



Notes:

Similarly, an analysis of Italian national register data from 193 IVF centers and over 120,000 IVF cycles from 2005 to 2007 also demonstrated that implantation rates (13.5% vs. 6.9%; odds ratio [OR] 2.12; 95% confidence interval [CI], 1.99-2.26) and pregnancy rates per transfer (24.9% vs. 12.5%; OR 2.32; 95% CI, 2.16-2.49) were higher with fresh oocyte cycles compared to frozen oocyte cycles. In addition, while frozen embryo cycles were limited, they found that implantation (OR 1.31; 95% CI, 1.17-1.46) and pregnancy rates (OR 2.37; 95% CI, 1.21-1.55) were higher when frozen embryos were used compared to frozen oocytes (28). In summary, results from large observational studies of clinical practice in Italy where supernumerary oocytes are cryopreserved suggest that implantation and pregnancy rates may be lower when frozen oocytes are used compared to fresh or frozen embryos.

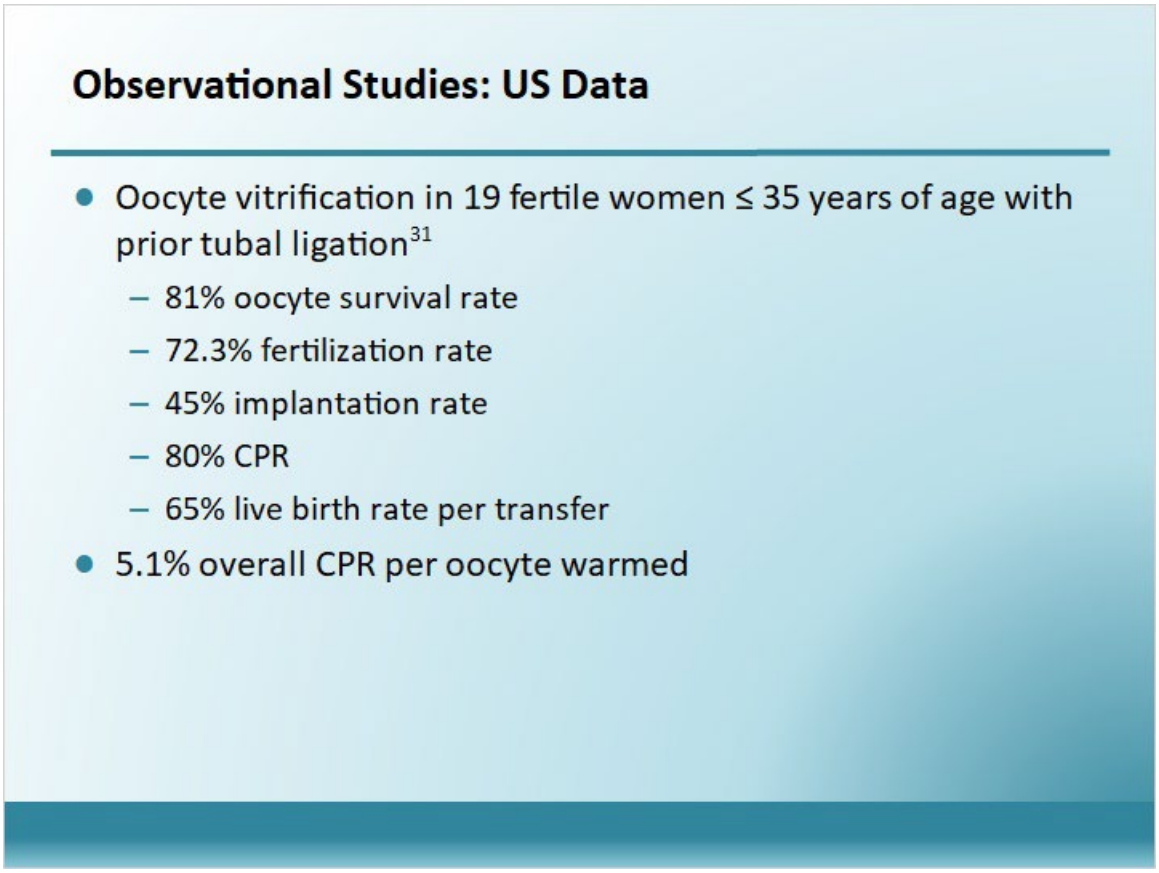
1.22 Observational Studies: US Data



Notes:

Because IVF practices in Europe differ considerably from those in the United States, it is also relevant to summarize recent observational data on the success of oocyte cryopreservation in the US even though samples sizes are limited in these reports. Several studies have been conducted in young infertile and fertile populations that demonstrate excellent success rates. A retrospective cohort study of 19 women less than 37 years of age undergoing either slow-freeze or vitrification of oocytes reported an oocyte survival rate of 89%, a fertilization rate of 78%, an implantation rate of 45%, and a live-birth rate per transfer of 58%(29). The same group previously reported the results of oocyte cryopreservation/thaw cycles in 22 infertile women and oocyte donors and reported similar results (92% survival, 42% implantation rate, 57% clinical pregnancy rate [CPR] per transfer, and 4% CPR per oocyte thaw)(30).

1.23 Observational Studies: US Data

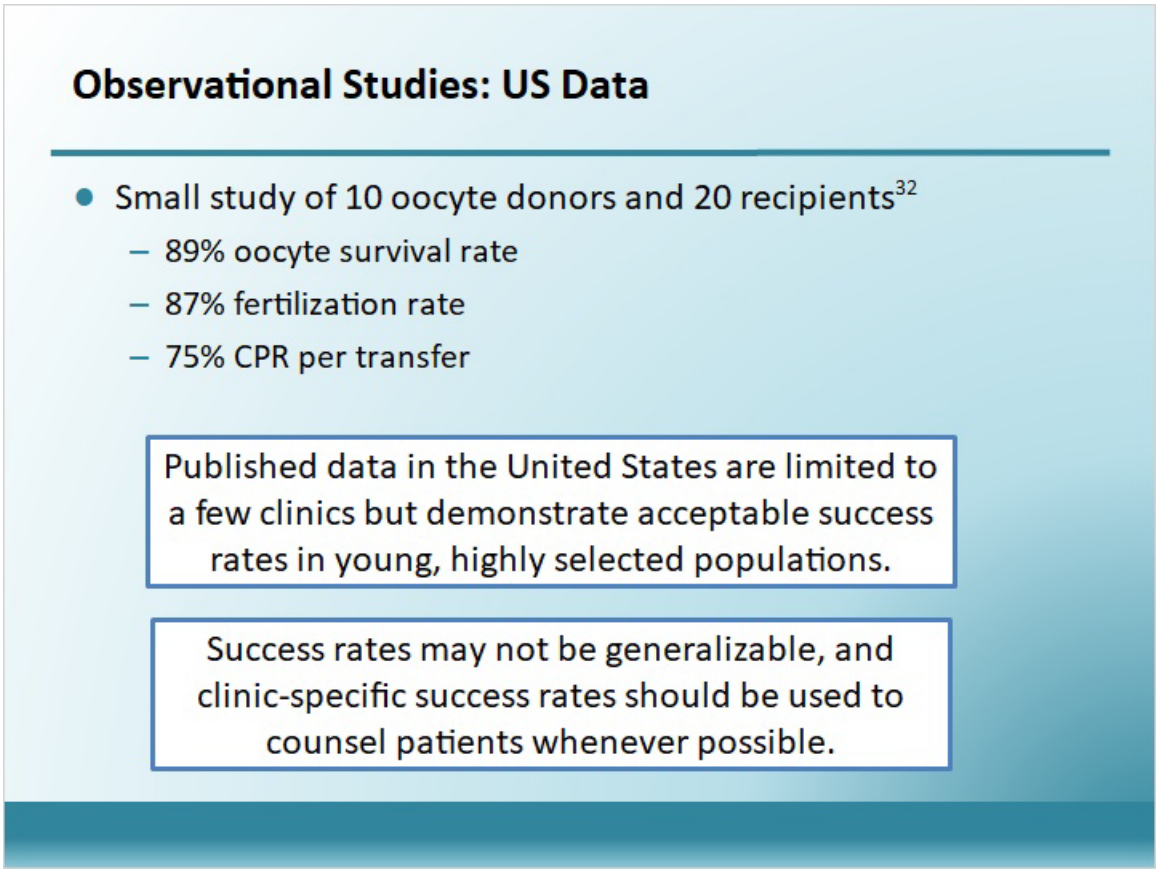


Notes:

A study of oocyte vitrification in 19 fertile women 35 years of age or younger with a prior tubal ligation

demonstrated a survival rate of 81%, fertilization rate of 72.3%, implantation rate of 45%, and CPR of 80%, and live-birth rate per transfer of 65% (31). Overall, the CPR per oocyte warmed was 5.1% in this study.

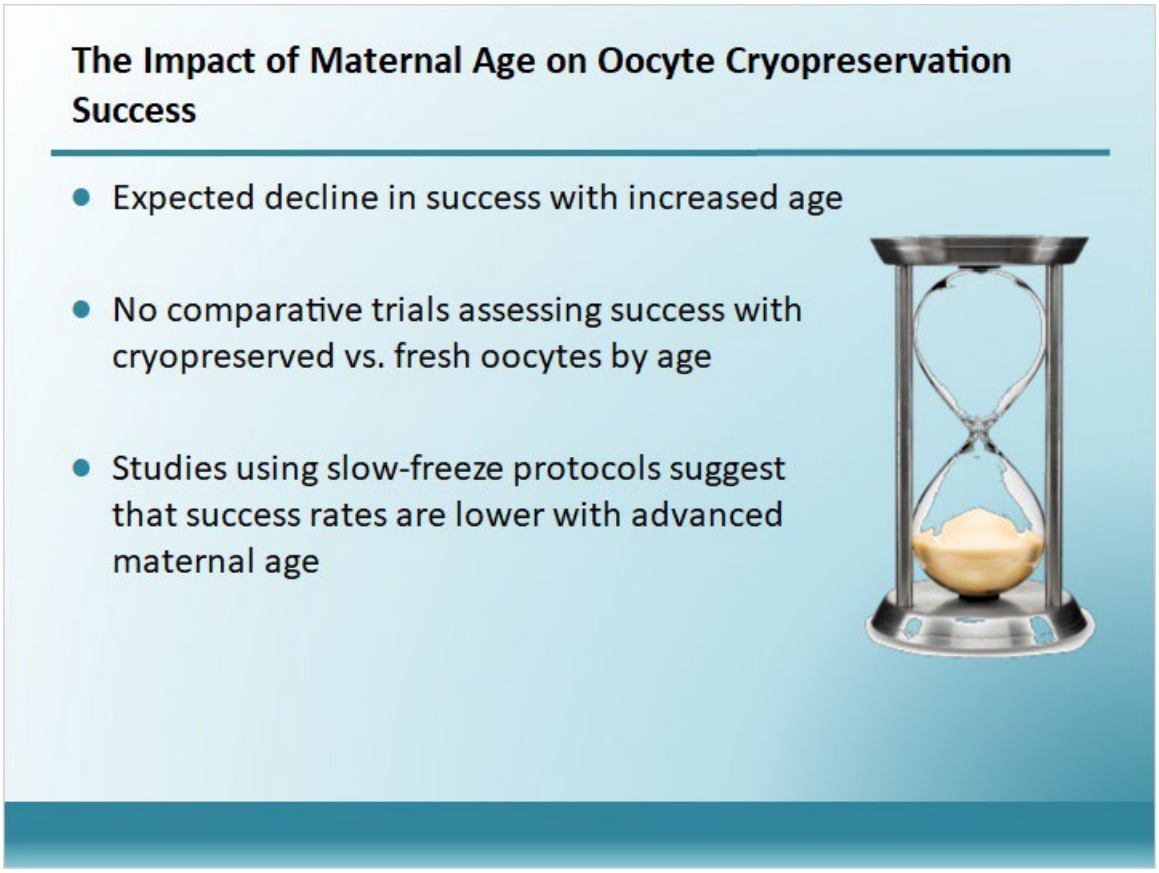
1.24 Observational Studies: US Data



Notes:

Finally, another group reported similar success rates in a small study of 10 oocyte donors and 20 recipients (89% oocyte survival rate, 87% fertilization rate, 75% CPR per transfer) (32). In summary, published data in the United States are limited to a few clinics but demonstrate acceptable success rates in young, highly selected populations. It is important to recognize that success rates may not be generalizable, and clinic-specific success rates should be used to counsel patients whenever possible.

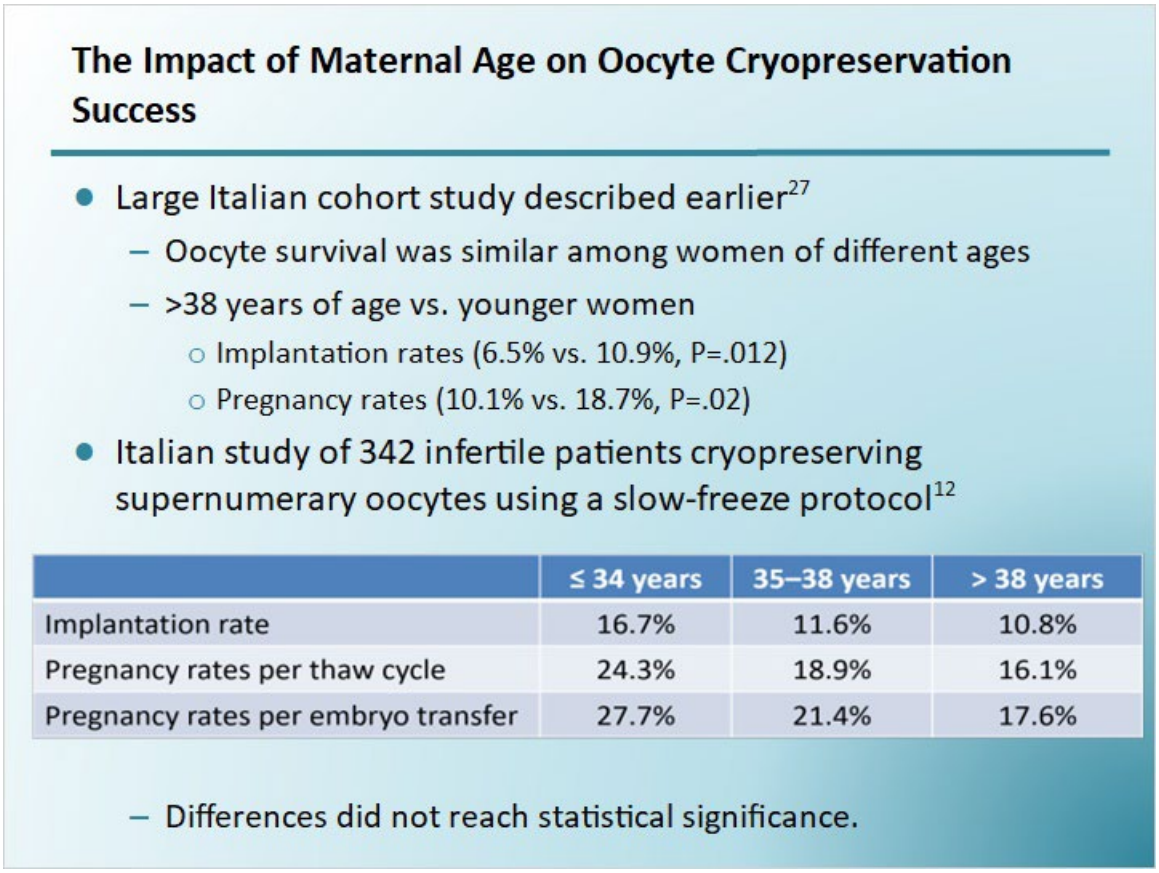
1.25 The Impact of Maternal Age on Oocyte Cryopreservation Success



Notes:

Several observational studies have assessed the impact of age on the success of oocyte cryopreservation. As with fresh oocytes, there is an expected decline in success with increased age. There are no comparative trials assessing success with cryopreserved vs. fresh oocytes by age. However, several studies using slow-freeze protocols suggest that success rates are lower with advanced maternal age.

1.26 The Impact of Maternal Age on Oocyte Cryopreservation Success

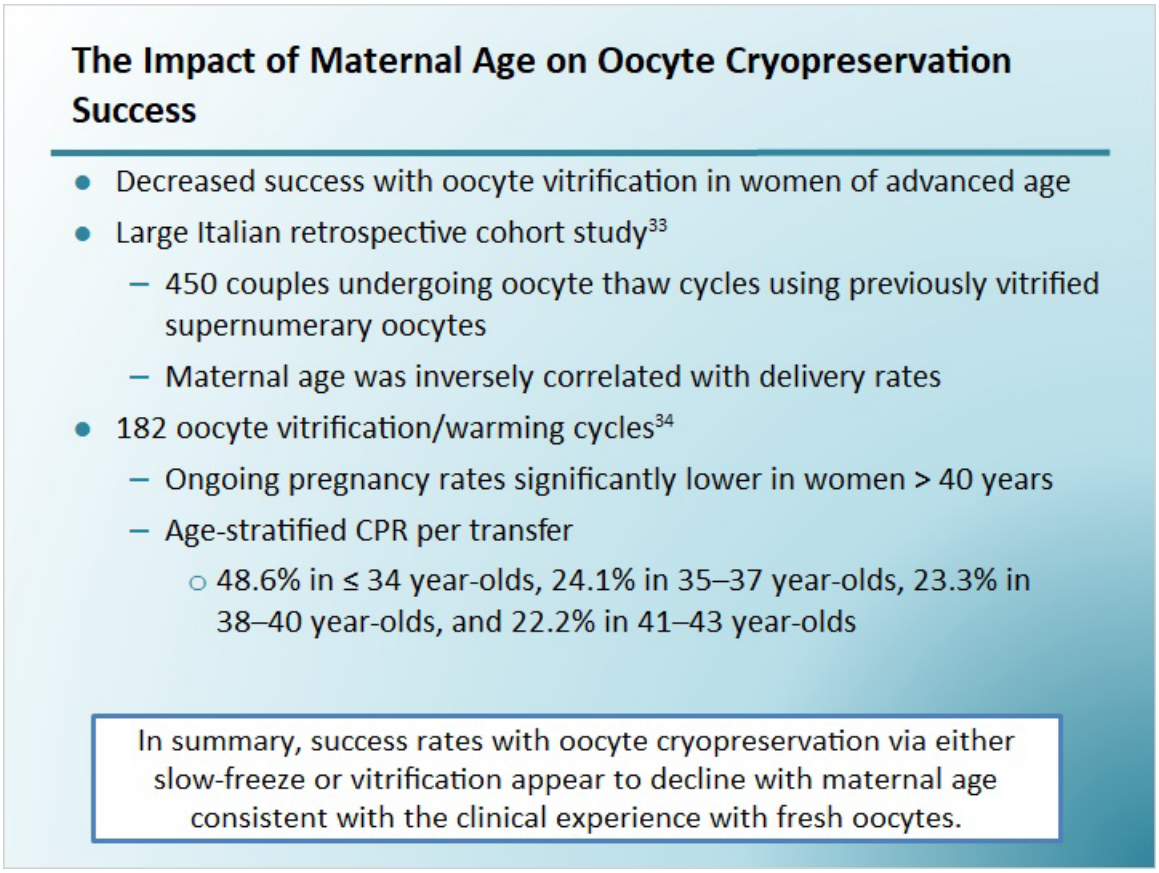


	≤ 34 years	35–38 years	> 38 years
Implantation rate	16.7%	11.6%	10.8%
Pregnancy rates per thaw cycle	24.3%	18.9%	16.1%
Pregnancy rates per embryo transfer	27.7%	21.4%	17.6%

Notes:

In the large Italian cohort study described earlier, oocyte survival was similar among women of different ages and women over 38 years of age had lower implantation rates (6.5% vs. 10.9%, P=.012) and pregnancy rates (10.1% vs. 18.7%, P=.02) compared to younger women (27). Another Italian study of 342 infertile patients cryopreserving supernumerary oocytes using a slow-freeze protocol reported pregnancy rates in three groups of women by age (12). Implantation rates were 16.7%, 11.6%, and 10.8%; pregnancy rates per thaw cycle were 24.3%, 18.9%, and 16.1%; and pregnancy rates per embryo transfer were 27.7%, 21.4%, and 17.6% in women≤34 years, 35-38 years, and over 38 years, respectively. While success appeared to be lower in older women, differences did not reach statistical significance.

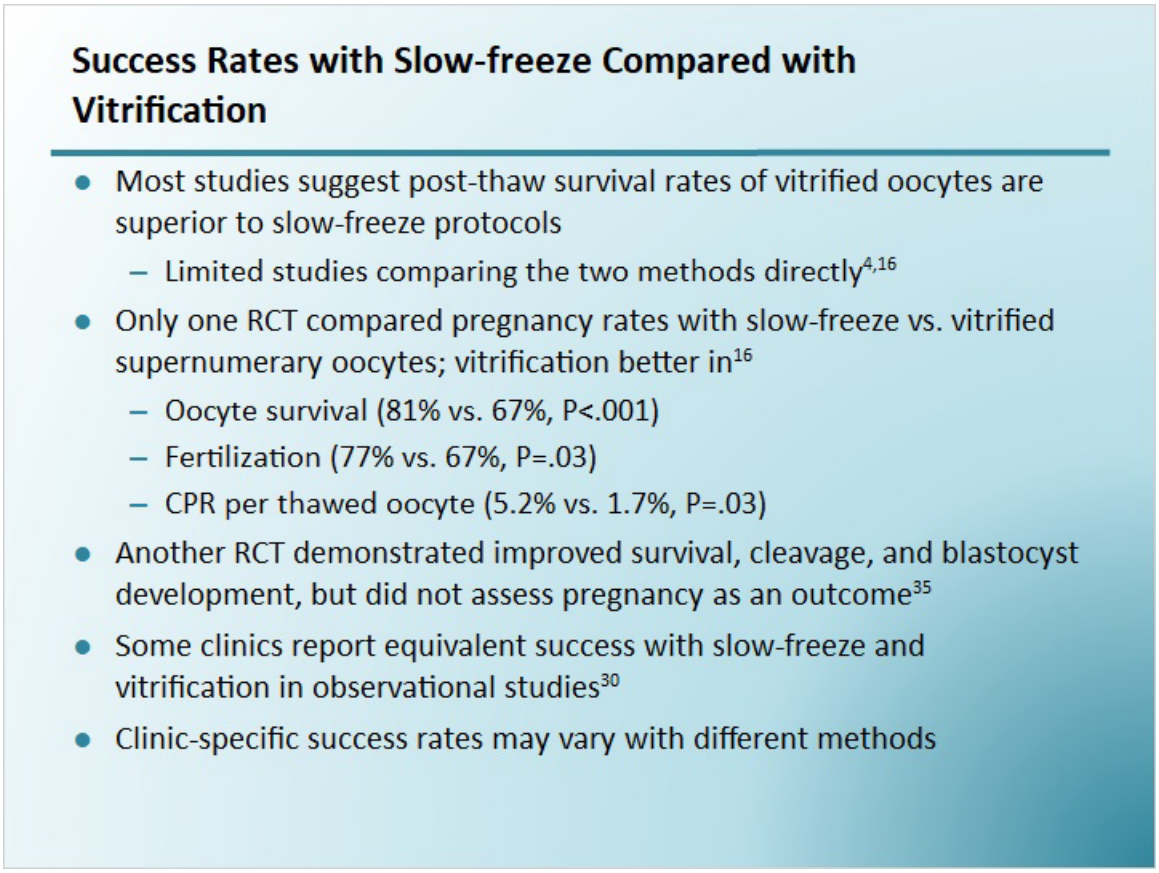
1.27 The Impact of Maternal Age on Oocyte Cryopreservation Success



Notes:

Several studies also have observed decreased success with oocyte vitrification in women of advanced age. A large Italian retrospective cohort study of 450 couples undergoing oocyte thaw cycles using previously vitrified supernumerary oocytes found that maternal age was inversely correlated with delivery rates (33). Another report also noted that ongoing pregnancy rates in 182 oocyte vitrification/warming cycles were significantly lower in women over 40 years of age (34). In this study, age-stratified CPR per transfer were: 48.6% in≤ 34 year-olds, 24.1% in 35-37 year-olds, 23.3% in 38-40 year-olds, and 22.2% in 41-43 year-olds. In summary, success rates with oocyte cryopreservation via either slow-freeze or vitrification appear to decline with maternal age consistent with the clinical experience with fresh oocytes.

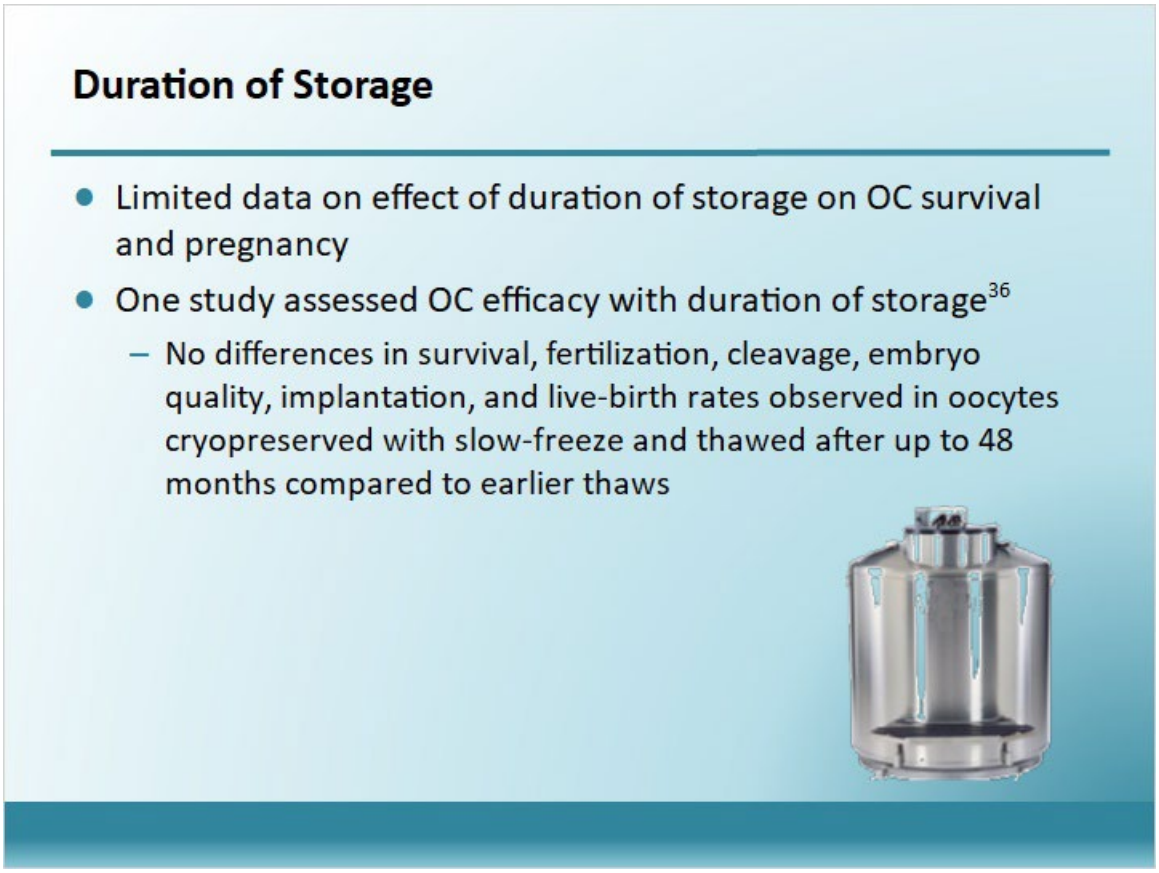
1.28 Success Rates with Slow-freeze Compared with



Notes:

Most studies suggest that post-thaw survival rates of vitrified oocytes are superior to those that have undergone slow-freeze protocols, but there are limited studies comparing the two methods directly (4, 16). Only one RCT was identified in the literature search that compared pregnancy rates with slow-freeze vs. vitrified supernumerary oocytes and demonstrated that vitrification resulted in better oocyte survival (81% vs. 67%, P<.001), fertilization (77% vs. 67%, P=.03), and CPR per thawed oocyte (5.2% vs. 1.7%, P=.03) compared to slow-freeze (16). Similarly another RCT demonstrated improved survival, cleavage, and blastocyst development, but did not assess pregnancy as an outcome(35). Nonetheless, some clinics report equivalent success with slow-freeze and vitrification in observational studies (30), and it is likely that clinic-specific success rates may vary with different methods of cryopreservation.

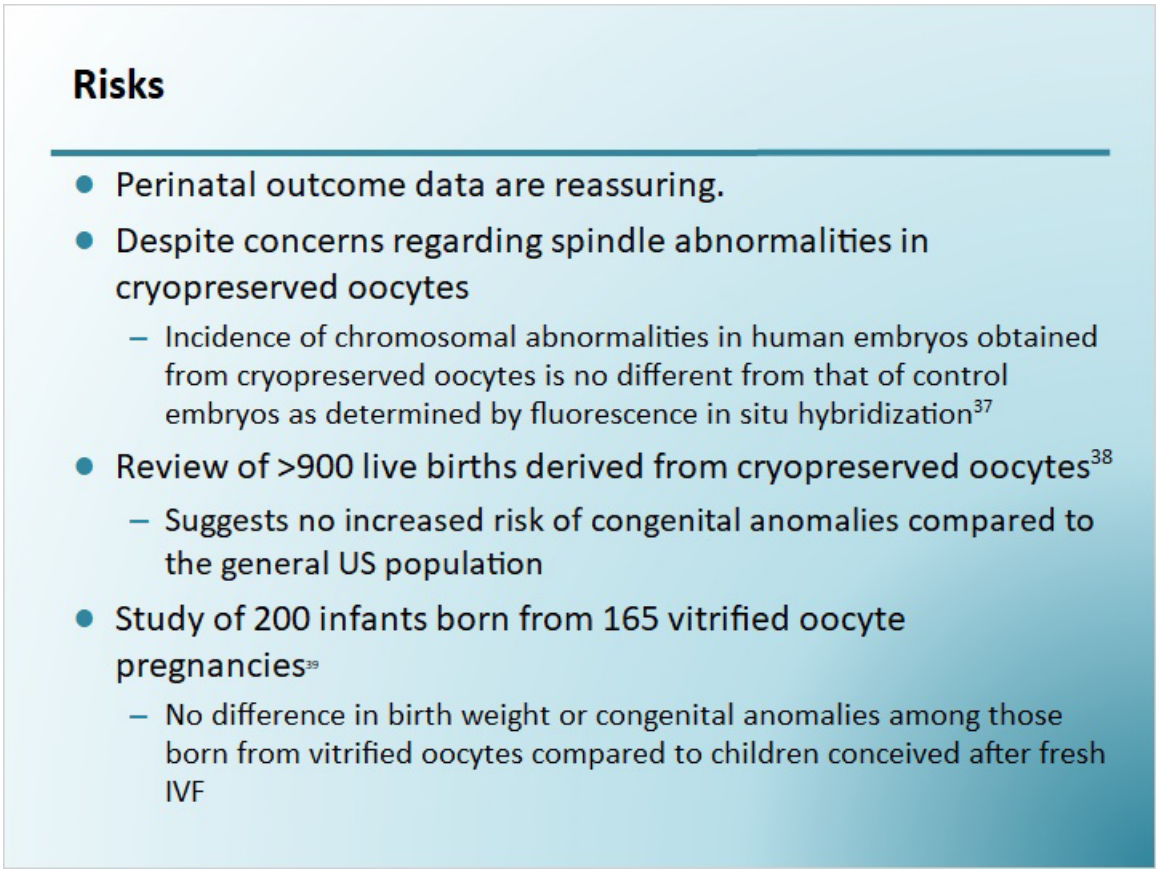
1.29 Duration of Storage



Notes:

Limited data exist regarding the effect of duration of storage on oocyte cryopreservation survival and pregnancy. One study was identified in the literature search that assessed oocyte cryopreservation efficacy with duration of storage. In this study, no differences in survival, fertilization, cleavage, embryo quality, implantation, and live-birth rates were observed in oocytes cryopreserved with slow-freeze and thawed after up to 48 months compared to earlier thaws (36).

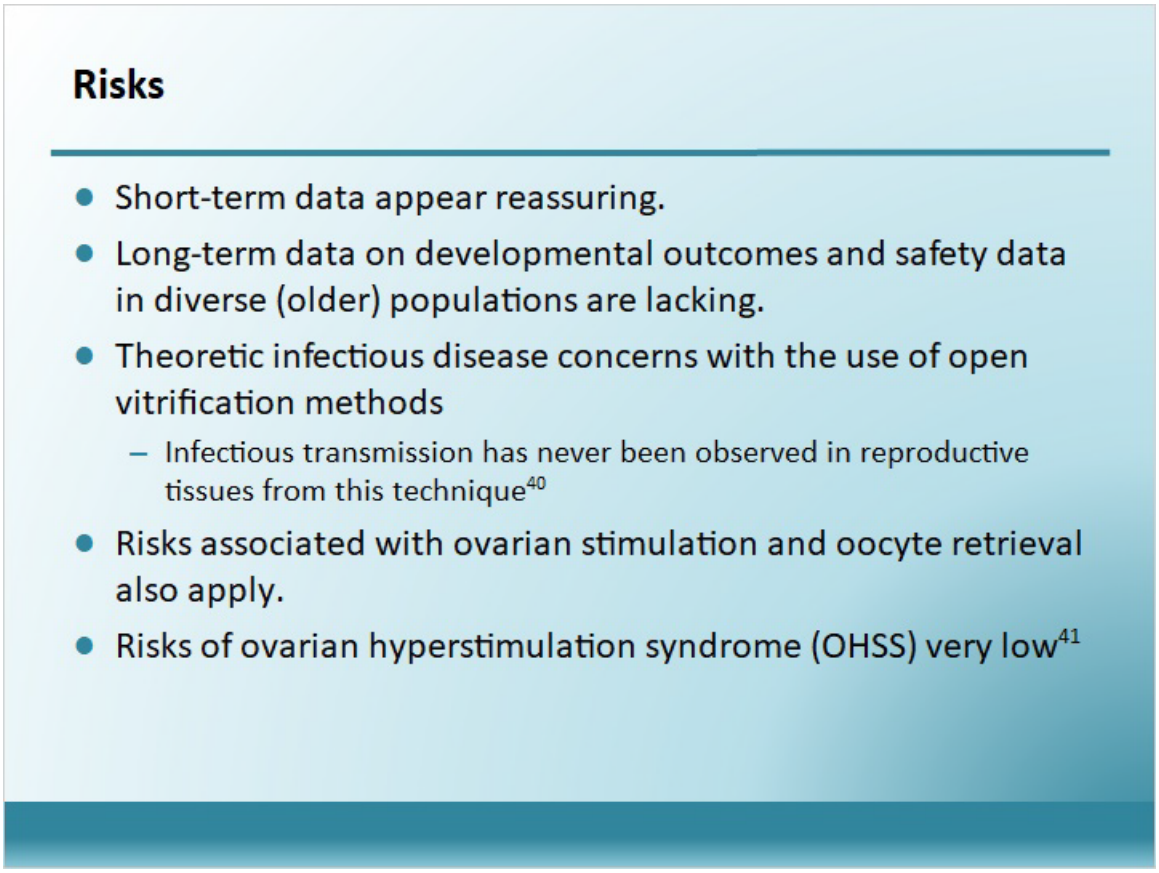
1.30 Risks



Notes:

While there are a limited number of established pregnancies and deliveries derived from cryopreserved oocytes, perinatal outcome data are reassuring. Despite concerns regarding spindle abnormalities in cryopreserved oocytes, the incidence of chromosomal abnormalities in human embryos obtained from cryopreserved oocytes is no different from that of control embryos as determined by fluorescence in situ hybridization (37). A recent review of over 900 live births derived from cryopreserved oocytes, principally using slow-freeze, suggests that there is no increased risk of congenital anomalies compared to the general US population (38). In addition, a study of 200 infants born from 165 vitrified oocyte pregnancies revealed no difference in birth weight or congenital anomalies among those born from vitrified oocytes compared to children conceived after fresh IVF (39).

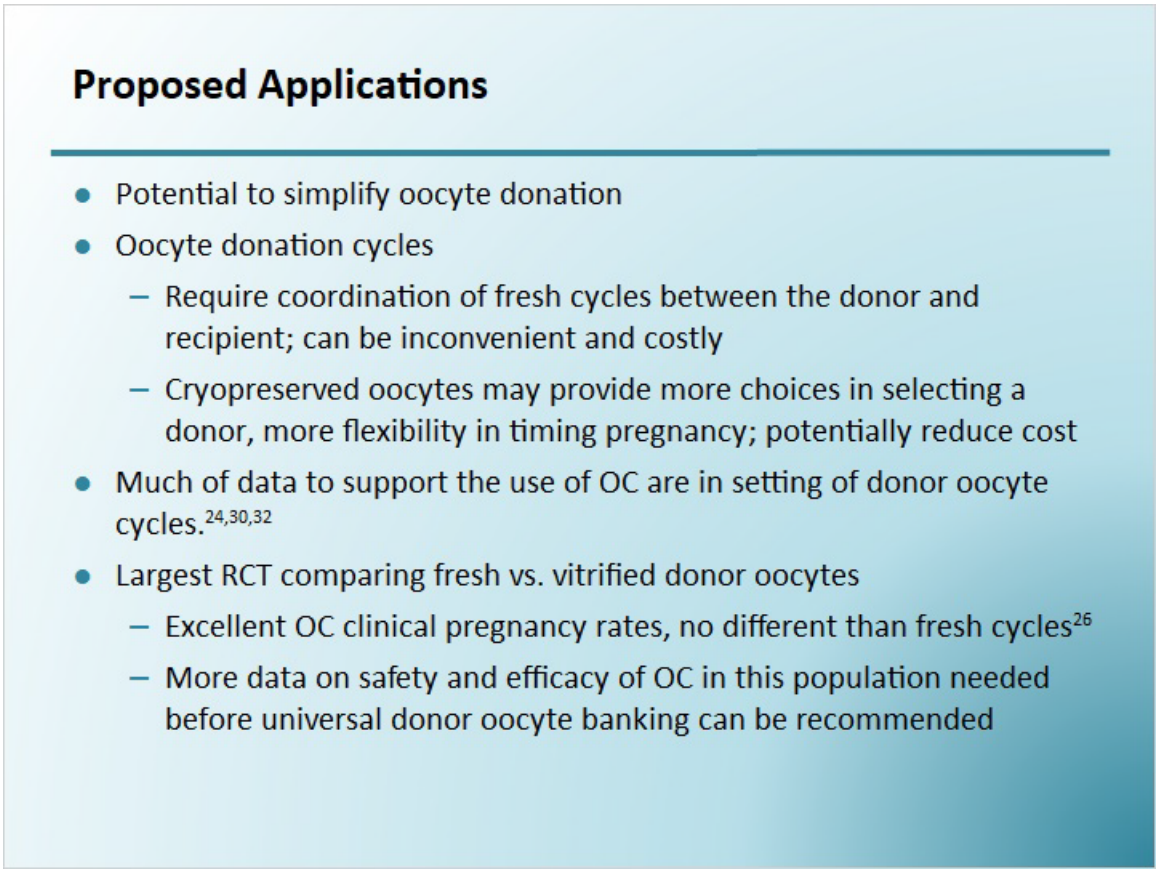
1.31 Risks



Notes:

While short-term data appear reassuring, long-term data on developmental outcomes and safety data in diverse (older) populations are lacking. As previously discussed, there also are theoretic infectious disease concerns with the use of open vitrification methods. However, infectious transmission has never been observed in reproductive tissues from this technique(40). The well-described risks associated with ovarian stimulation and oocyte retrieval also apply. Since embryo transfer is not being performed in most individuals cryopreserving oocytes, the risks of ovarian hyperstimulation syndrome (OHSS) are very low (41).

1.32 Proposed Applications



Notes:

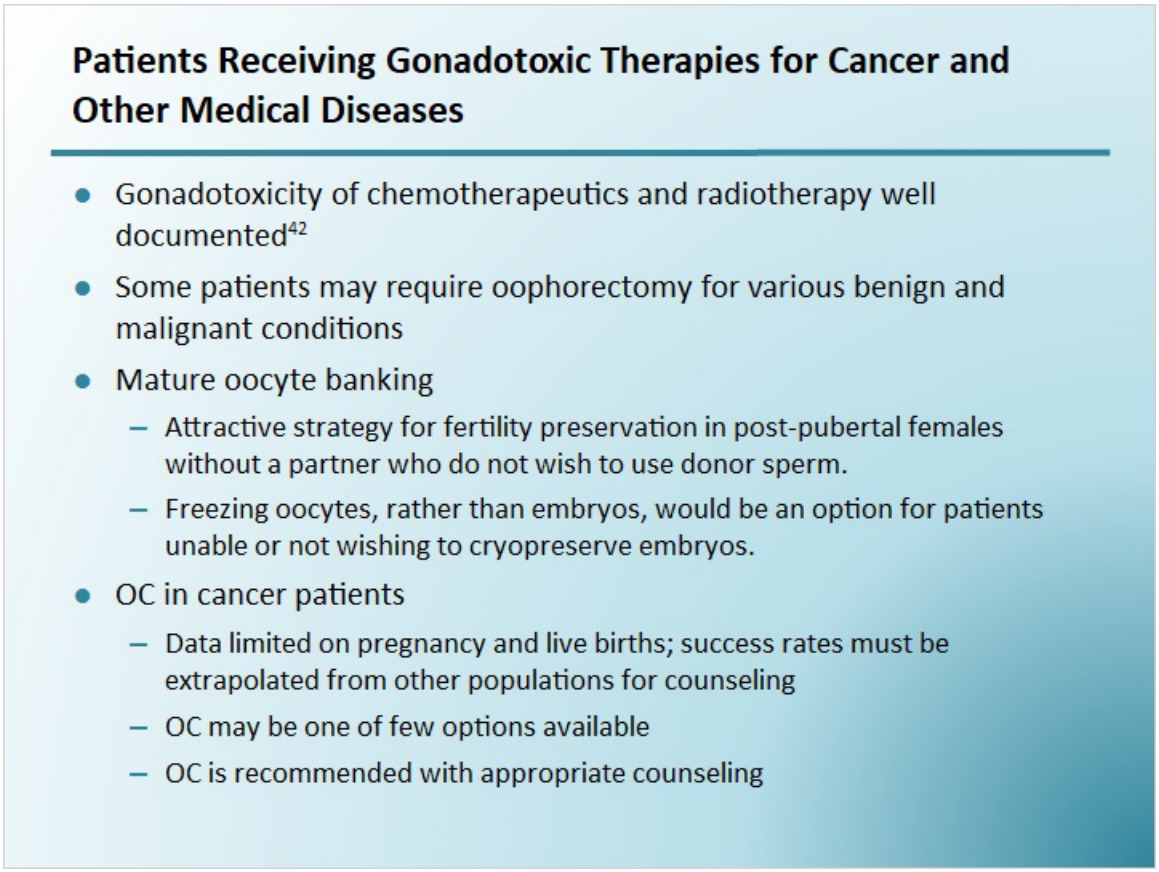
Successful oocyte cryopreservation has the potential to simplify oocyte donation. Currently, oocyte donation cycles require coordination of fresh cycles between the donor and recipient, which can be inconvenient and costly. Use of cryopreserved oocytes may provide women with more choices in selecting a donor and more flexibility in timing pregnancy and potentially reduce the cost. Indeed, much of the best data to support the use of OC are in the setting of donor oocyte cycles (24, 30, 32). The largest RCT comparing fresh vs. vitrified donor oocytes in 600 recipients revealed excellent clinical pregnancy rates, no different than in fresh cycles (26) (Table 1). However, while these data are reassuring, more widespread clinic-specific data on the safety and efficacy of oocyte cryopreservation in this population are needed before universal donor oocyte banking can be recommended.

1.33 Medical Indications

Notes:

This section covers medical indications for oocyte cryopreservation.

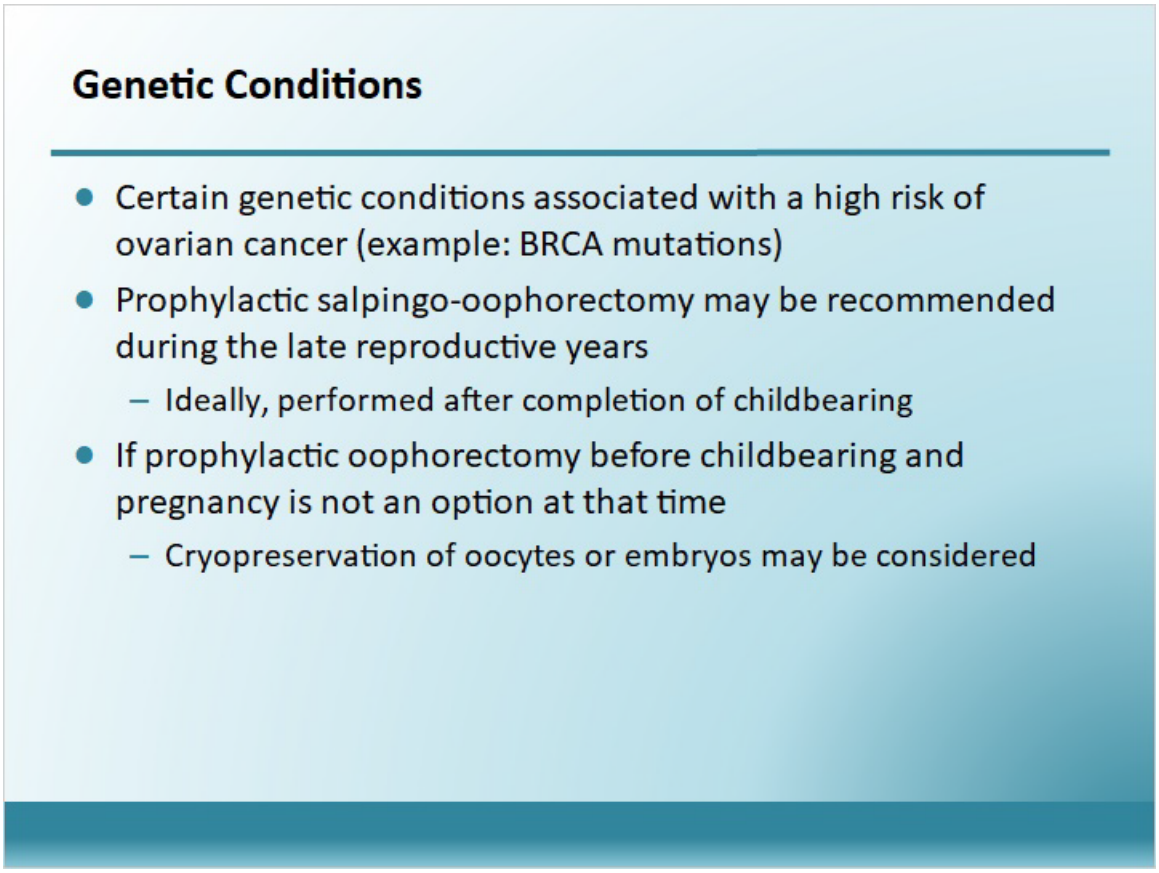
1.34 Patients Receiving Gonadotoxic Therapies for Cancer and Other Medical Diseases



Notes:

The gonadotoxicity of chemotherapeutics and radiotherapy has been well documented (42). In addition, some patients may require oophorectomy for various benign and malignant conditions. Mature oocyte banking is an attractive strategy for fertility preservation in post-pubertal females without a partner and who do not wish to use donor sperm. Freezing oocytes, rather than embryos, would be an option for patients unable or not wishing to cryopreserve embryos. Data on pregnancy and live births from oocyte cryopreservation in cancer patients are very limited, and success rates must be extrapolated from other populations for patient counseling. However, in this population at high risk for infertility, oocyte cryopreservation may be one of the few options available and therefore is recommended with appropriate counseling.

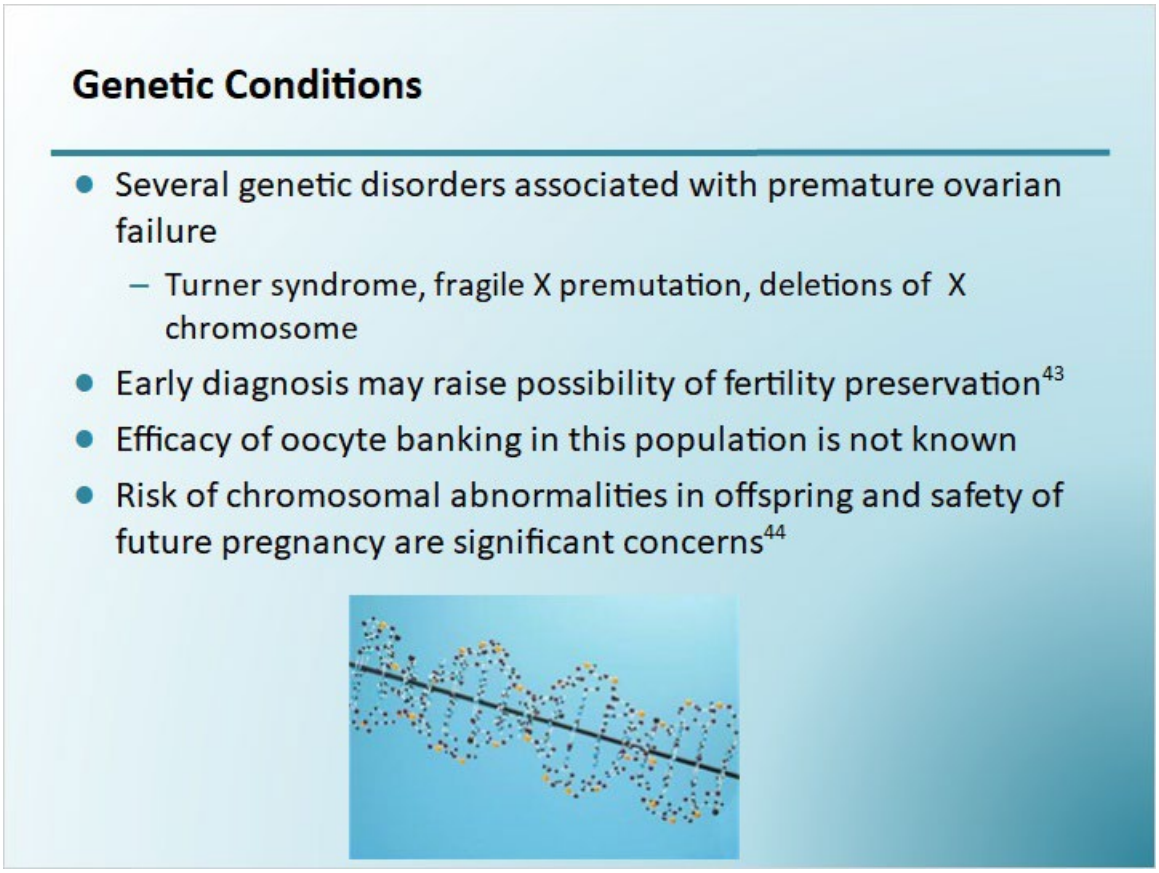
1.35 Genetic Conditions



Notes:

Certain genetic conditions, such as BRCA mutations, are associated with a high risk of ovarian cancer, and prophylactic salpingo-oophorectomy may be recommended during the late reproductive years. Ideally, this procedure is performed after completion of childbearing. However, in the event that prophylactic oophorectomy is recommended before childbearing and pregnancy is not an option at that time, cryopreservation of oocytes or embryos may be considered.

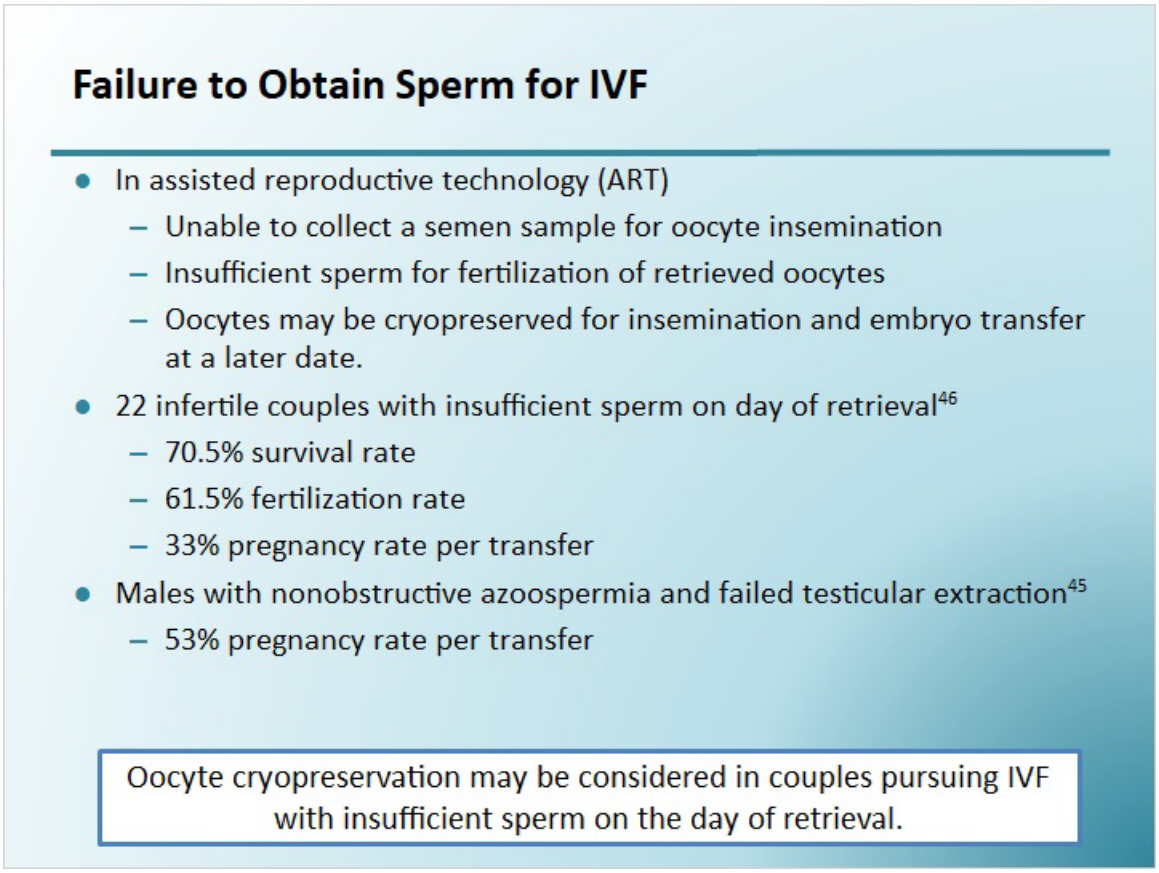
1.36 Genetic Conditions



Notes:

In addition, several genetic disorders have been associated with premature ovarian failure, such as Turner syndrome, fragile X premutation, and deletions of the X chromosome. Early diagnosis of these conditions may raise the possibility of fertility preservation in these populations (43). However, the efficacy of oocyte banking in this population is not known, and the risk of chromosomal abnormalities in offspring and the safety of future pregnancy are significant concerns(44).

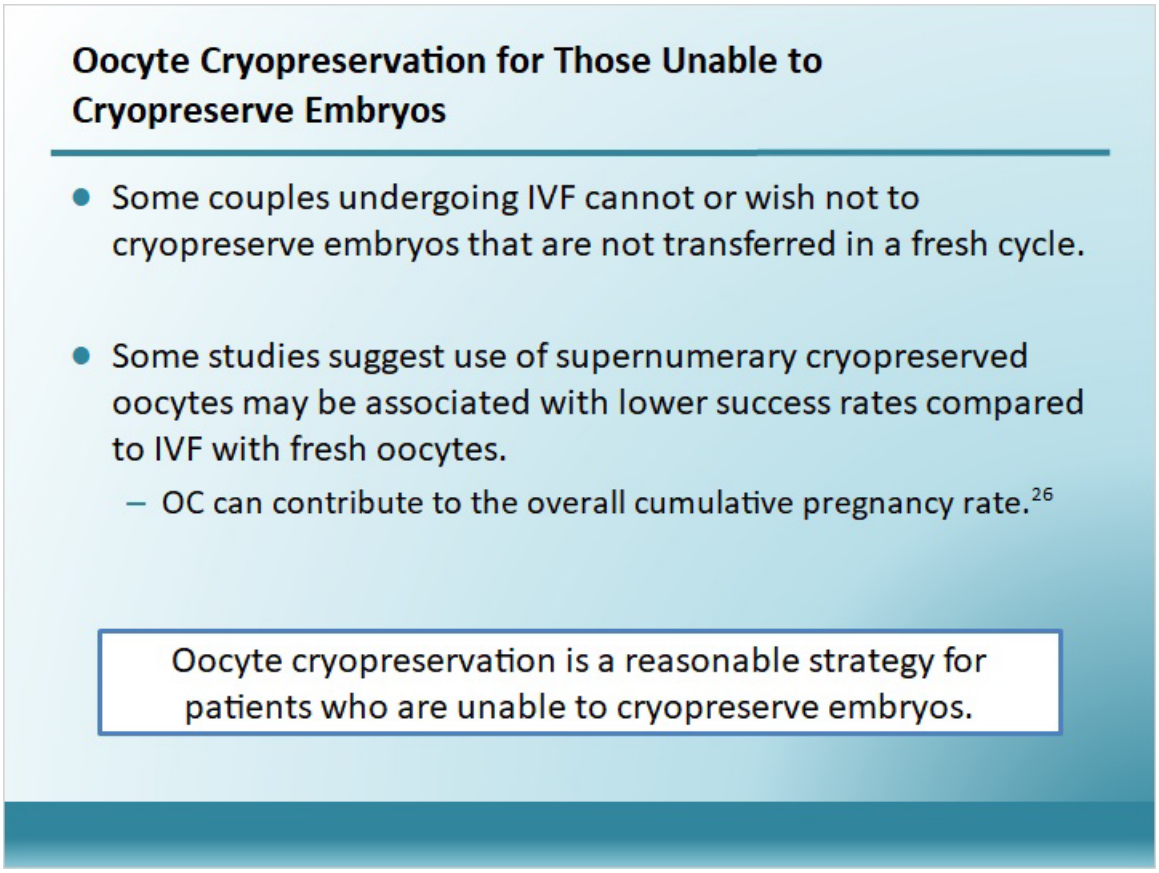
1.37 Failure to Obtain Sperm for IVF



Notes:

Occasionally, the male partner of a couple undergoing IVF is unable to collect a semen sample for oocyte insemination on the day of the oocyte retrieval. In addition, males with severe male infertility may have insufficient sperm for fertilization of retrieved oocytes. In such instances, oocytes may be cryopreserved for insemination and embryo transfer at a later date. Two studies have reported success rates of oocyte cryopreservation in such situations(45, 46). One study assessing the success of oocyte cryopreservation in 22 infertile couples with insufficient sperm on the day of the retrieval reported a survival of 70.5%, a fertilization rate of 61.5%, and a pregnancy rate per transfer of 33% (46). Another study reported a pregnancy rate of 53% per transfer after oocyte cryopreservation in female partners of males with nonobstructive azoospermia and failed testicular extraction (45). Therefore, oocyte cryopreservation may be considered in couples pursuing IVF with insufficient sperm on the day of retrieval.

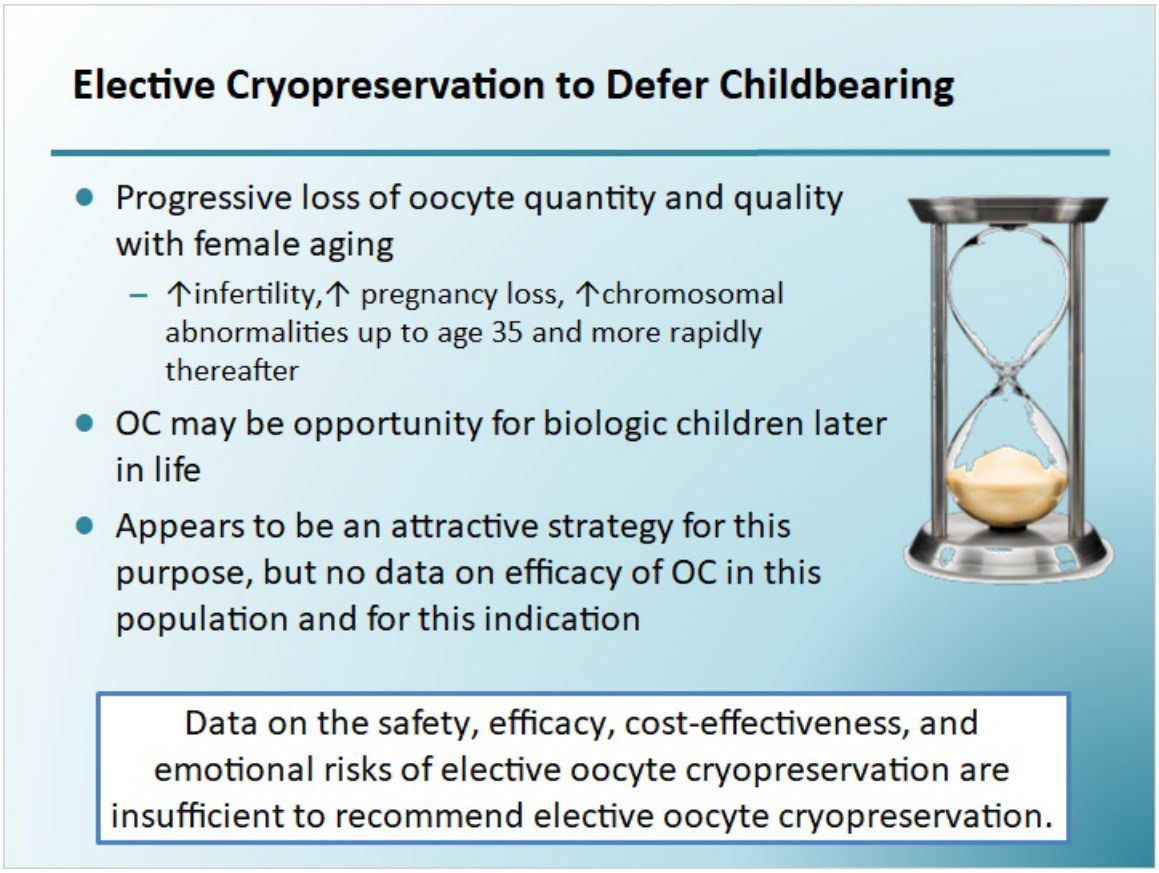
1.38 Oocyte Cryopreservation for Those Unable to



Notes:

Some couples undergoing IVF cannot or wish not to cryopreserve embryos that are not transferred in a fresh cycle. While some studies suggest the use of supernumerary cryopreserved oocytes may be associated with lower success rates compared to IVF with fresh oocytes, oocyte cryopreservation can contribute to the overall cumulative pregnancy rate (26). Therefore, oocyte cryopreservation is a reasonable strategy for patients who are unable to cryopreserve embryos.

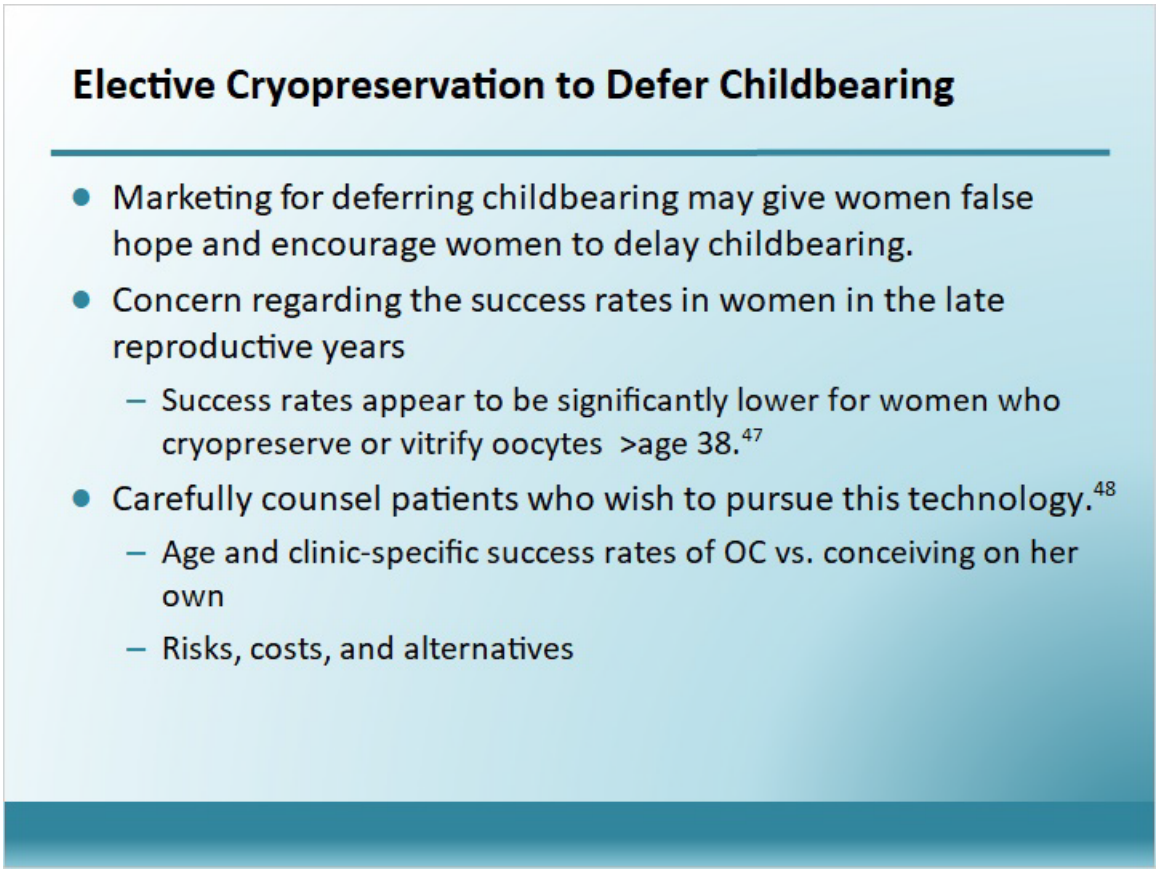
1.39 Elective Cryopreservation to Defer Childbearing



Notes:

Since there is a progressive loss of oocyte quantity and quality that occurs with female aging, the prevalence of infertility and the incidence of pregnancy loss and chromosomal abnormalities increase steadily up to age 35 and more rapidly thereafter. Technologies such as OC may allow women to have an opportunity to have biologic children later in life. While this technology may appear to be an attractive strategy for this purpose, there are no data on the efficacy of oocyte cryopreservation in this population and for this indication. Data on the safety, efficacy, cost-effectiveness, and emotional risks of elective oocyte cryopreservation are insufficient to recommend elective oocyte cryopreservation.

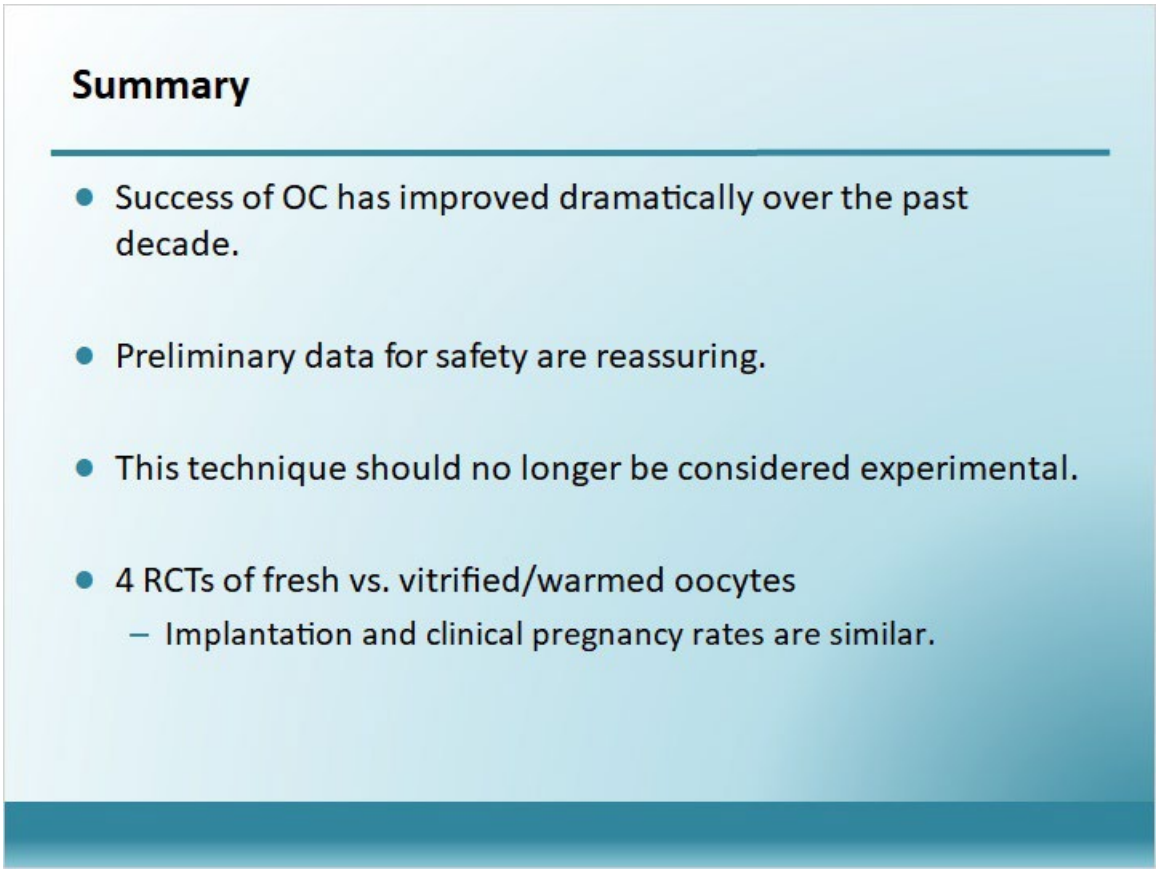
1.40 Elective Cryopreservation to Defer Childbearing



Notes:

Marketing this technology for the purpose of deferring childbearing may give women false hope and encourage women to delay childbearing. In particular, there is concern regarding the success rates in women in the late reproductive years who may be the most interested in this application. As described above, success rates appear to be significantly lower for women who cryopreserve or vitrify oocytes over the age of 38(47). Patients who wish to pursue this technology should be carefully counseled about age and clinic-specific success rates of oocyte cryopreservation vs. conceiving on her own and risks, costs, and alternatives to using this approach(48).

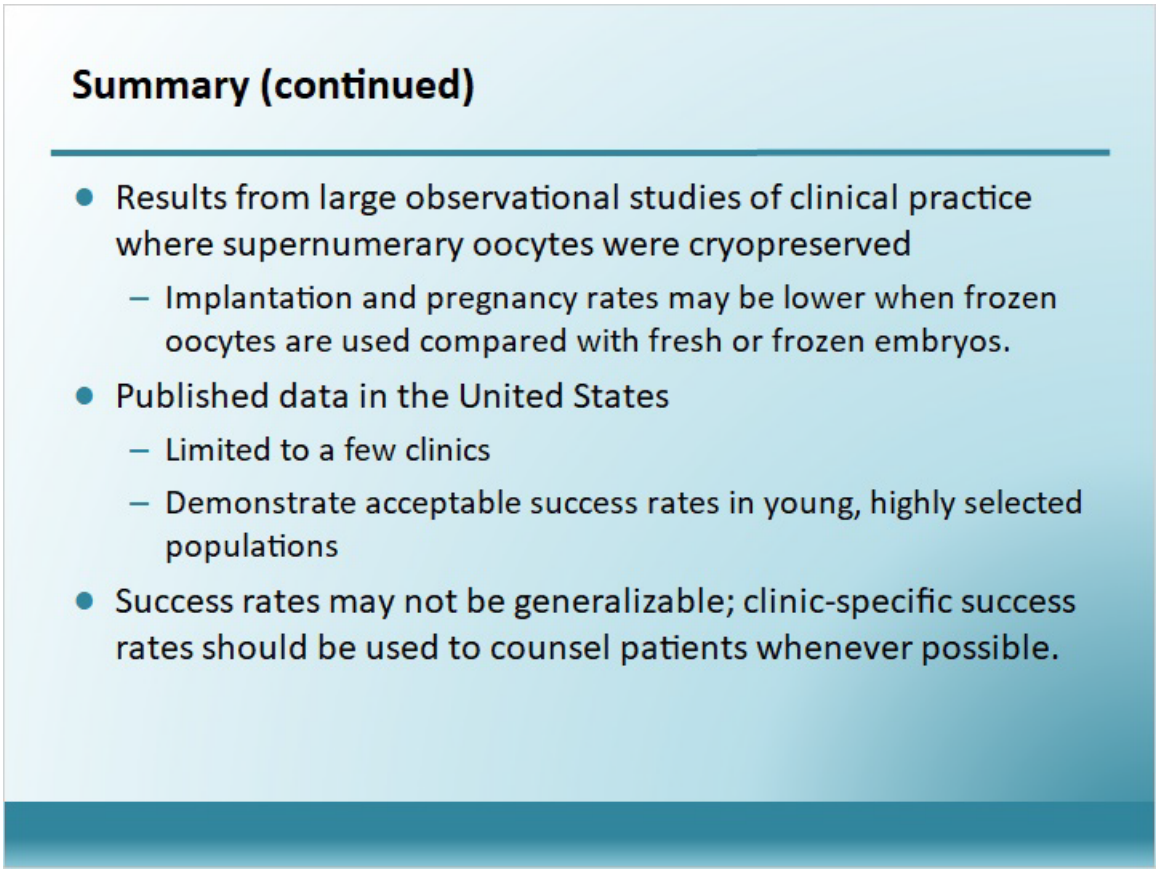
1.41 Summary



Notes:

The success of oocyte cryopreservation has improved dramatically over the past decade, and preliminary data for safety are reassuring. Therefore, this technique should no longer be considered experimental. Four randomized controlled trials of fresh vs. vitrified/warmed oocytes indicate that implantation and clinical pregnancy rates are similar.

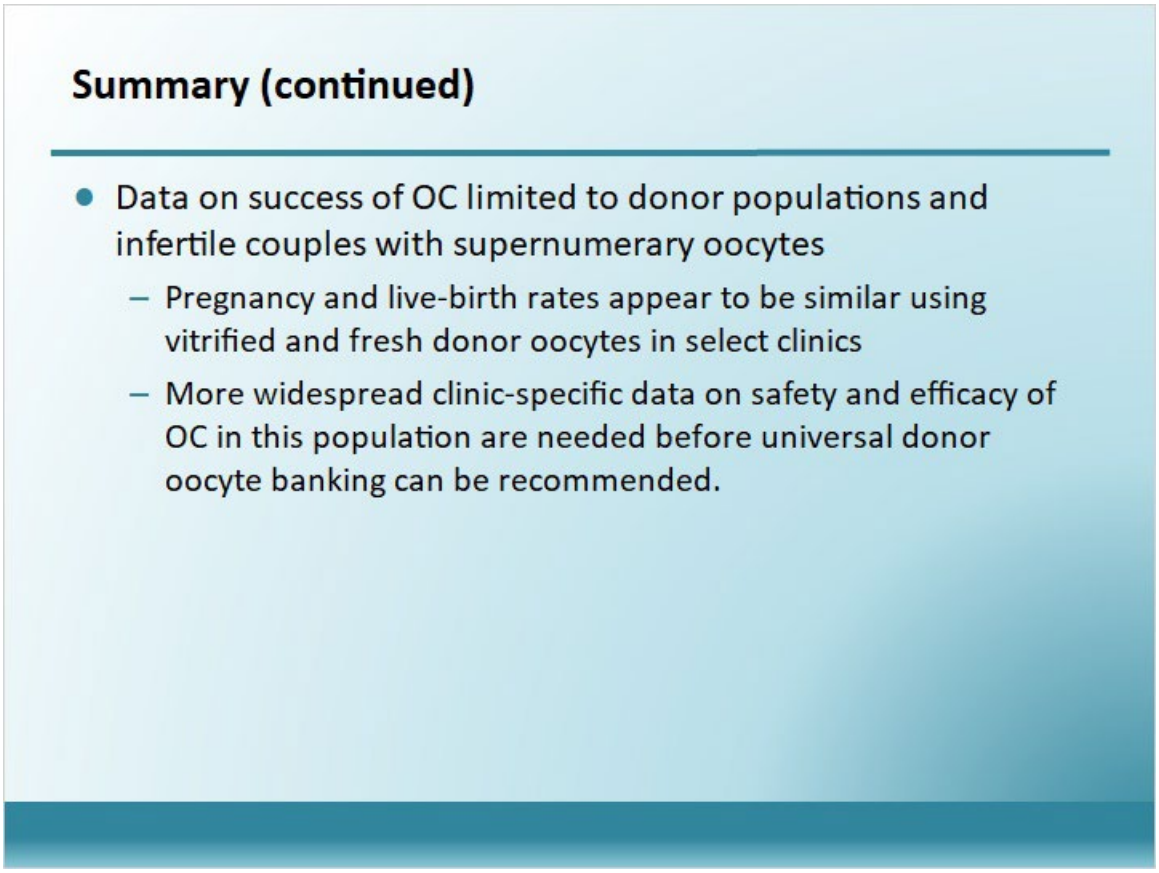
1.42 Summary (continued)



Notes:

However, results from large observational studies of clinical practice where supernumerary oocytes were cryopreserved suggest that implantation and pregnancy rates may be lower when frozen oocytes are used compared with fresh or frozen embryos. Published data in the United States are limited to a few clinics but demonstrate acceptable success rates in young, highly selected populations. It is important to recognize that success rates may not be generalizable, and clinic-specific success rates should be used to counsel patients whenever possible.

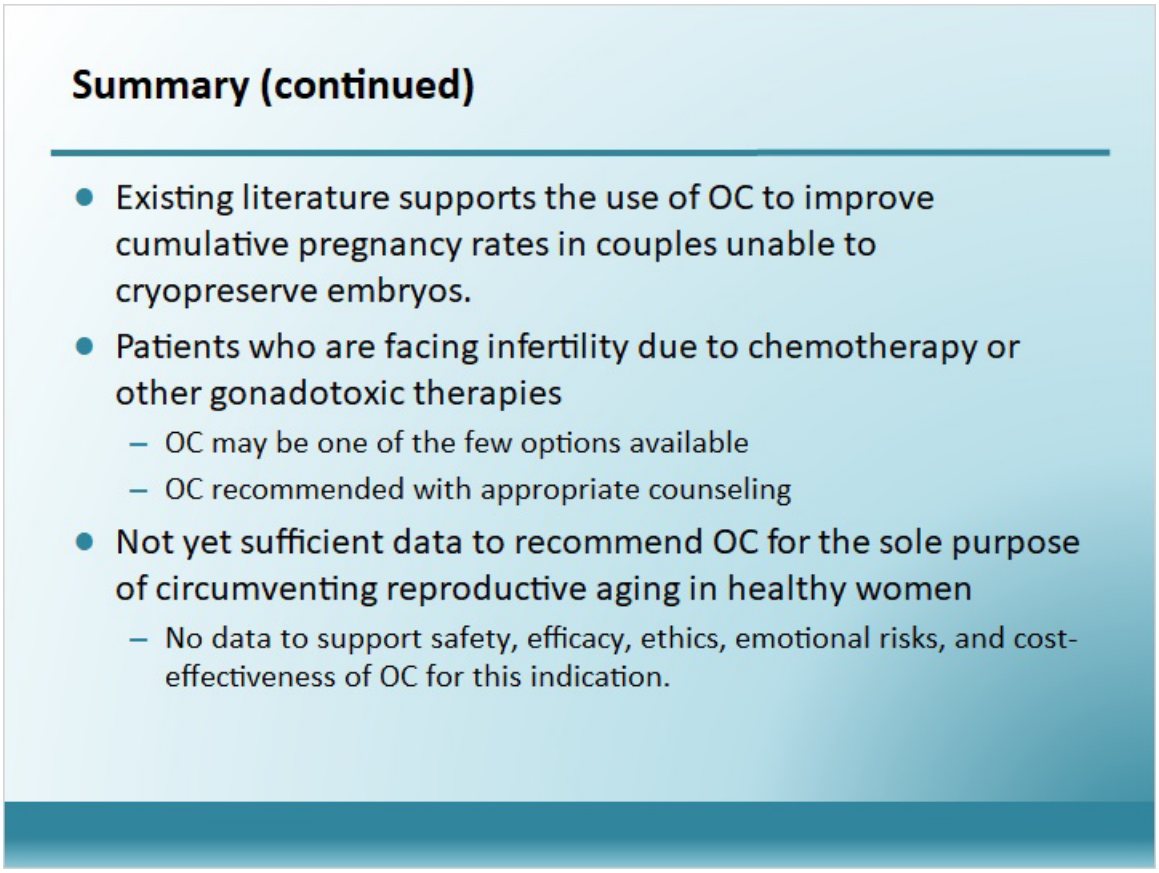
1.43 Summary (continued)



Notes:

Although a variety of clinical applications have been proposed for the use of oocyte cryopreservation, data on the success of oocyte cryopreservation are limited to donor populations and infertile couples with supernumerary oocytes. While pregnancy and live-birth rates appear to be similar using vitrified and fresh donor oocytes in select clinics, more widespread clinic-specific data on the safety and efficacy of oocyte cryopreservation in this population are needed before universal donor oocyte banking can be recommended.

1.44 Summary (continued)

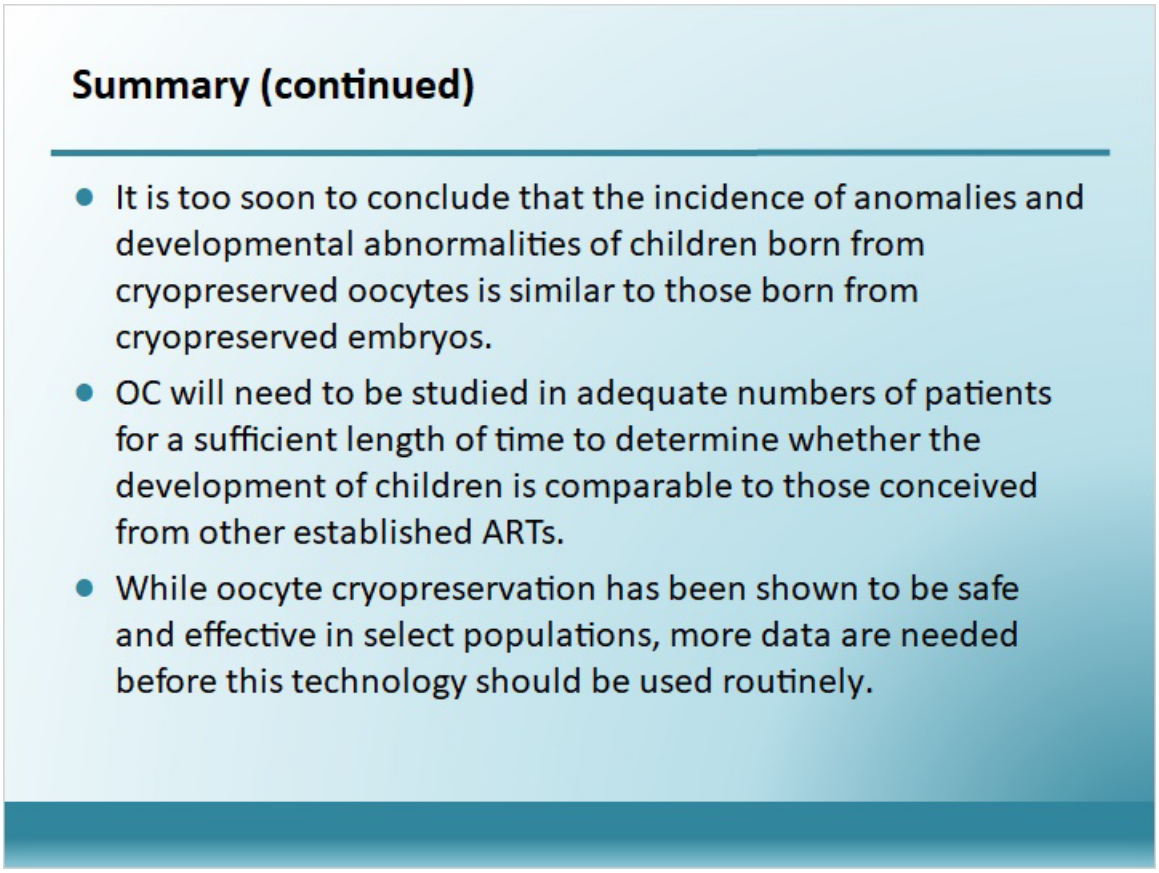


Notes:

The existing literature supports the use of oocyte cryopreservation to improve cumulative pregnancy rates in couples who are unable to cryopreserve embryos. In the case of patients who are facing infertility due to chemotherapy or other gonadotoxic therapies, oocyte cryopreservation may be one of the few options available and therefore is recommended under these circumstances with appropriate counseling. On the other hand, there are not yet sufficient data to recommend oocyte cryopreservation for the sole purpose of circumventing

reproductive aging in healthy women because there are no data to support the safety, efficacy, ethics, emotional risks, and cost-effectiveness of oocyte cryopreservation for this indication.

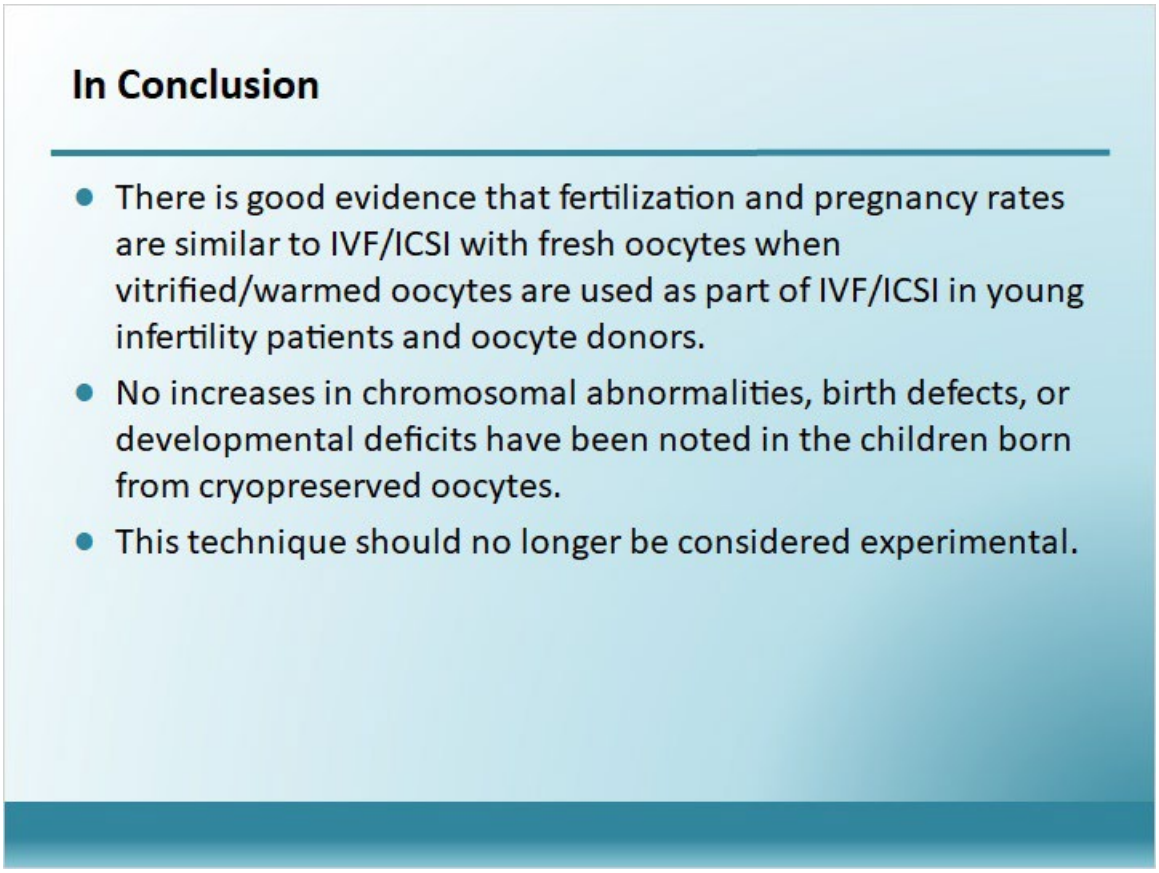
1.45 Summary (continued)



Notes:

In addition, while data are reassuring at this point, it is too soon to conclude that the incidence of anomalies and developmental abnormalities of children born from cryopreserved oocytes is similar to those born from cryopreserved embryos. Oocyte cryopreservation will need to be studied in adequate numbers of patients for a sufficient length of time to determine whether the development of children is comparable to those conceived from other established assisted reproduction techniques. While oocyte cryopreservation has been shown to be safe and effective in select populations, more data are needed before this technology should be used routinely.

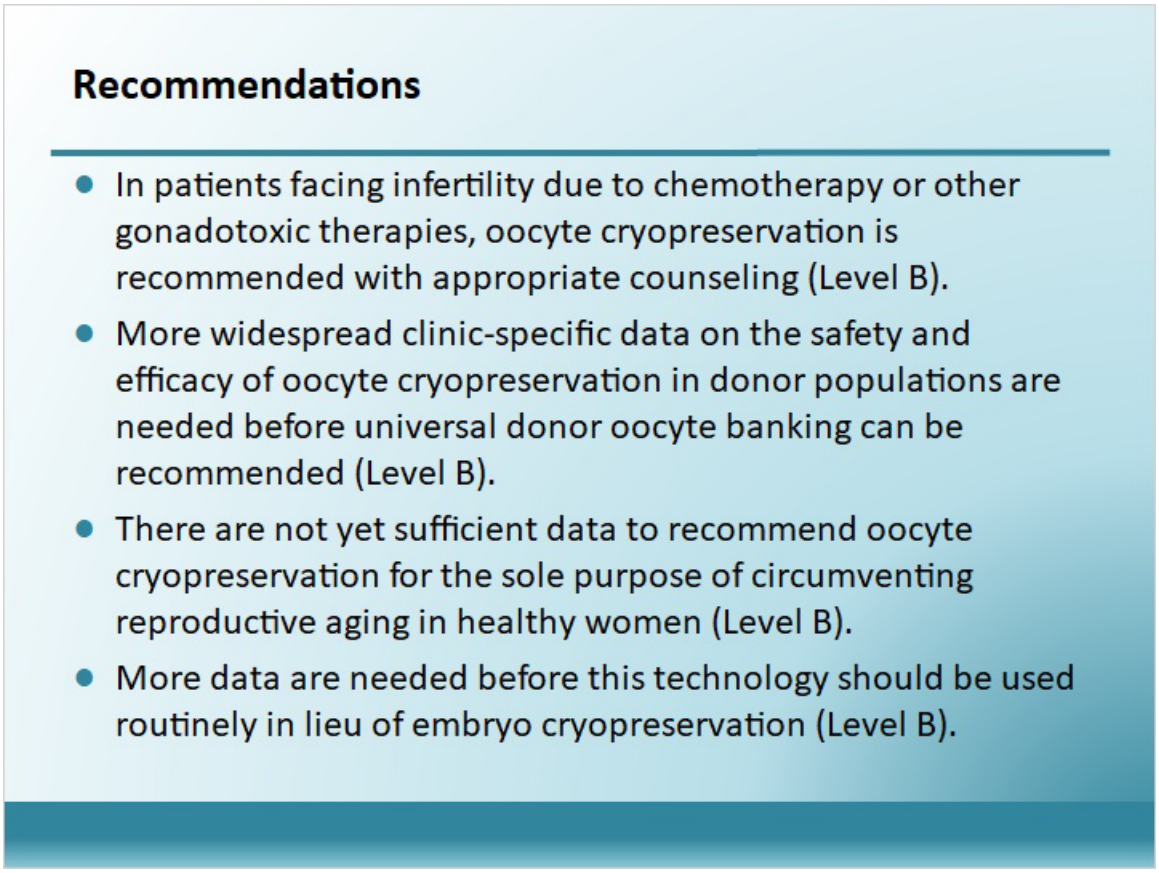
1.46 In Conclusion



Notes:

In conclusion, there is good evidence that fertilization and pregnancy rates are similar to IVF/ICSI with fresh oocytes when vitrified/warmed oocytes are used as part of IVF/ICSI in young infertility patients and oocyte donors. No increases in chromosomal abnormalities, birth defects, or developmental deficits have been noted in the children born from cryopreserved oocytes. This technique should no longer be considered experimental.

1.47 Recommendations



Notes:

In patients facing infertility due to chemotherapy or other gonadotoxic therapies, oocyte cryopreservation is recommended with appropriate counseling (Level B).

More widespread clinic-specific data on the safety and efficacy of oocyte cryopreservation in donor populations are needed before universal donor oocyte banking can be recommended (Level B).

There are not yet sufficient data to recommend oocyte cryopreservation for the sole purpose of circumventing reproductive aging in healthy women (Level B).

More data are needed before this technology should be used routinely in lieu of embryo cryopreservation (Level B).

1.48 Thank you!

Notes:

Thank you for participating in this educational activity.