

# The status of oocyte cryopreservation in the United States

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**Objective:** To determine the current status of oocyte cryopreservation across the United States, and the perceived indications for its use.

**Design:** Cross-sectional survey of all IVF Centers in the United States.

**Setting:** Telephone and fax based survey of all IVF practice or laboratory directors, conducted March to June of 2009.

**Patient(s):** None.

**Intervention(s):** None.

**Main Outcome Measure(s):** Prevalence of oocyte cryopreservation, acceptable indications and age groups, number of oocyte cryopreservation cycles performed and thawed, fertilization and pregnancy rates, number of live births.

**Result(s):** Of 442 centers contacted, 282 (64%) responded in 49 states. In these centers 143 (51%) programs currently offer oocyte cryopreservation, with a geographic trend toward the western-located clinics. Of all programs, 36% offer oocyte cryopreservation only for cancer patients or as an alternative to embryo cryopreservation after IVF, whereas 64% of programs offer it electively in women of advancing maternal age. For elective indications, 87% of programs accept patients aged 35–37 years, 49% consider age 38–40 years as acceptable, whereas only 26% of programs cryopreserve oocytes beyond age 40 years. Three hundred thirty-seven live births resulting from 857 thawed cycles (39.3% pregnancy rate [PR]) were reported across all centers.

**Conclusion(s):** Oocyte cryopreservation is offered in more than 50% of ART clinics in the United States. Most programs that perform oocyte cryopreservation for cancer indications offer it for elective delay of childbearing as well. These data suggest a growing acceptance for this technology within our field. (Fertil Steril® 2010;94:2642–6. ©2010 by American Society for Reproductive Medicine.)

**Key Words:** Oocyte cryopreservation, elective indications, regional trends, ART, survey, statistics

There is much debate in the United States regarding the clinical applicability of oocyte cryopreservation. In 2007, the American Society for Reproductive Medicine Practice Committee reported, “due to its experimental status and lack of outcome data, it should not be offered electively to fertile women as a means of postponing childbearing (1).” However, assisted reproductive technology (ART) programs are faced with an increasing demand for this technology both for use in women facing potentially gonadotoxic cancer therapies, and electively, in women of advancing maternal age. Because the current societal trend is to delay childbearing until career goals are met, an increasing number of women are interested in oocyte cryopreservation as a means of preserving their fertility.

The first pregnancies from oocyte cryopreservation were reported two decades ago (2), but the overall oocyte survival, fertilization, and pregnancy rates (PR) remained low compared with cryopreserved embryos, discouraging the use of this technology (3–6). Recently, however, with changes in cryopreservation technique

and particularly with the introduction of intracytoplasmic sperm injection (ICSI), recent studies are reporting PRs that are comparable to embryo cryopreservation (7–9). It is estimated that there are approximately 1,000 live births worldwide resulting from oocyte cryopreservation (10).

Oocyte cryopreservation has a wide range of clinical applications. Particularly for patients facing a new diagnosis of cancer, it may be used for fertility preservation when sterilizing therapies, such as chemotherapy and radiation, are necessary. It can increase the utility and flexibility of ART by avoiding embryo cryopreservation after IVF in patients who are opposed to freezing embryos, and by rescuing cycles complicated by failure to obtain sperm. Finally, it can improve synchronization in oocyte donation cycles, and provide a means of donor egg banking.

Perhaps most controversial is the extension of this technology to otherwise fertile young women who wish to preserve their reproductive potential. Opponents of elective use cite the lack of outcome data, the small number of live births, and the lack of proven long-term safety. However, as the number of live births increase and as this technology is refined, an increasing number of ART facilities are offering oocyte cryopreservation to young, fertile women as means of “insurance” against their biological clock. This question of whether it is ethical to offer elective cryopreservation brings many gender equality issues to the reproductive forefront (11–13). Now that the technological success of oocyte cryopreservation is catching up with its demand, will our field embrace it and if so,

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**TABLE 1****Responding ART clinics.**

Characteristics of responding clinics	Response rate (total = 282, 64%)
Type of clinic	
Academic	71/282 (25%)
Community	211/282 (75%)
Geographic location <sup>a</sup>	
Northeast	64/282 (23%)
South	76/282 (27%)
Midwest	62/282 (22%)
West	78/282 (28%)
Annual no. of IVF cycles	
Median	200
Range	5–3,600
Total	85,139
No. of physicians	
Median	2.0
Range	1–22
Main payment type	
Private insurance	64/282 (23%)
Public insurance	7/282 (2.6%)
Out of pocket	87/282 (31%)
Mix	124/282 (44%)
Main patient ethnicity	
White	211/282 (75%)
Hispanic	8/282 (3%)
Asian	5/282 (2%)
Mix	56/282 (20%)
Oocyte cryopreservation status	
Yes	144/282 (51%)
No	138/282 (49%)
Indications for oocyte cryopreservation <sup>b</sup>	
Elective/any indication	159/241 (66%)
Cancer related	43/241 (18%)
Any except elective	79/241 (33%)
Acceptable age groups for elective indication <sup>c</sup>	
<35 y	218/218 (100%)
35–37 y	181/218 (83%)
38–40 y	109/218 (50%)
>40 y	56/218 (26%)

<sup>a</sup> US Census Bureau territories were used to designate which geographic region a state belonged to.

<sup>b</sup> Two hundred forty-one clinics answered the survey questions regarding acceptable indications. “Elective” refers to oocyte cryopreservation for the purposes of delaying childbearing in otherwise fertile women. “Cancer related” refers to fertility preservation when sterilizing therapies such as chemotherapy or radiation are necessary. “Any except elective” refers to both cancer-related indications and “IVF-related indications” including alternative to freezing embryos, and rescue situations in which the partner is unable to produce a semen sample on the day of retrieval.

<sup>c</sup> Two hundred eighteen clinics answered the survey questions regarding acceptable age groups for elective indication.

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**MATERIALS AND METHODS**

This study was approved by the University of Southern California Institutional Review Board. The Centers for Disease Control (CDC) 2006 National ART report was queried to produce a list of all ART clinics in the United States. According to the Fertility Clinic Success Rate and Certification Act, all ART clinics are required to submit ART cycle data to the CDC. There were 426 fertility clinics in operation in 2006 that provided and verified data on the outcomes of all ART cycles started in their clinics. Of those, 31 clinics had either closed since 2006, were not performing IVF, or became affiliated with another larger IVF laboratory, leaving 395 ART clinics. We also surveyed 47 nonreporting clinics, for a total number of 442 possible survey responses (14).

From March–June of 2009, each ART clinic’s laboratory director or practice director was contacted at least twice either by telephone, fax, or email, to request completion of a two-page survey. The first part of the survey contained demographic questions: practice type (community vs. academic), number of IVF cycles per year, number of physicians in the practice, location of the practice, insurance type of the patients, patient ethnicity. The second part of the survey contained questions regarding oocyte cryopreservation status: whether the center currently offers oocyte cryopreservation and for how long, whether they plan to in the future, acceptable indications for oocyte cryopreservation, acceptable age groups for elective oocyte cryopreservation, method of cryopreservation, and preliminary outcome data such as number of oocyte cryopreservation cycles, number of cycles thawed, estimated fertilization and PRs, and number of live births. The Society of Assisted Reproductive Technology (SART) data for 2006 or the CDC clinic summary was used to obtain the distribution of diagnoses in each clinic.

Correlations between survey data and oocyte cryopreservation status were analyzed using  $\chi^2$  and Fisher’s exact tests for categorical variables, independent *t*-tests and Pearson’s correlations for normally distributed continuous variables, and Mann-Whitney *U* tests and Spearman correlations for non-normally distributed continuous variables. Statistical significance is defined as  $P < .05$  and a statistical trend is defined as  $P = .05–.099$ . Statistical analysis was performed using SAS, version 9.2 (SAS Institute, Inc., Cary, NC).

**RESULTS**

Of 442 clinics contacted, 282 clinics responded to the survey across 49 states, yielding a response rate of 64% (Table 1). The distribution of types of clinics (community vs. academic) and geographic location of the responding clinics is similar to the distribution of all IVF clinics. In addition, the responding clinics encompassed a wide range of clinic sizes. The total number of IVF cycles among responding clinics was 85,139, which represents 60% of the total number of IVF cycles performed in the United States in 2007 according to the CDC. (142,435 cycles) (14).

Of the responding clinics, 51% currently offer oocyte cryopreservation. Of those clinics that do not, 55% plan to in the near future, another 19% might in the future, whereas 26% do not plan on offering it at all, the most common reason being “not enough demand.” Oocyte cryopreservation status is associated with location; western-located clinics are most likely to offer oocyte cryopreservation ( $P = .04$ ). Centers that offer cryopreservation have a higher median number of IVF cycles and a higher median number of physicians than centers that do not ( $P < .0001$ ).

Of all programs 66% would offer oocyte cryopreservation electively (“elective-willing”). Elective-willing programs were more likely to actually offer oocyte cryopreservation at the time of this survey ( $P = .04$ ). Among the clinics already cryopreserving oocytes, “elective use” is cited as the most common indication (Table 2), followed by IVF-related reasons (18%), and cancer-related reasons (18%).

Among all responding clinics, attitudes toward acceptable indications are associated with location. Northeastern programs are most likely to offer it for nonelective reasons (45.2%), whereas western

for what indications? The aim of this study was to determine the current status of oocyte cryopreservation across the United States, including regional differences, and the perceived acceptability of indications for its use.

**TABLE 2****Characteristics of ART clinics offering oocyte cryopreservation.**

Characteristics of ART clinics offering oocyte cryopreservation	Clinics offering oocyte cryopreservation (n = 143)
Type of clinic	
Academic	38/143 (27%)
Community	105/143 (73%)
Geographic location	
Northeast	35/143 (24%)
South	29/143 (20%)
Midwest	31/143 (22%)
West	48/143 (34%)
Annual no. of IVF cycles	
Median	300
Range	5–3,600
Indications for oocyte cryopreservation	
Elective/any indication	91/142 (64%)
Cancer related	26/142 (18%)
Any except elective	25/142 (18%)
Acceptable age groups for elective indication <sup>a</sup>	
<35 y	126/126 (100%)
35–37 y	109/126 (87%)
38–40 y	75/126 (60%)
>40 y	42/126 (26%)

<sup>a</sup> Centers designating 35–37, 38–40, and >40 years old as acceptable age groups were more likely to offer oocyte cryopreservation ( $P < .001$ ,  $P < .001$ ,  $P < .005$ , respectively).

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programs are most likely to offer it for elective reasons (81.4%,  $P = .007$ ). This relationship persists when considering only those centers that are currently performing oocyte cryopreservation at the time of this survey ( $P = .02$ ). Centers that classified themselves as academic were less likely to believe that elective oocyte cryopreservation is acceptable (53.33%) than community centers (70.37%), with a trend toward significance ( $P = .06$ ).

Acceptable age categories for elective cryopreservation were similar between responding clinics and those clinics already performing oocyte cryopreservation. Half of all clinics considered age 38–40 years to be an acceptable age for elective oocyte cryopreservation. Centers designating >40 years old as an acceptable age group were more likely to currently offer oocyte cryopreservation ( $P < .005$ ) at the time of the survey. They were also larger practices, with higher median number of IVF cycles ( $P = .001$ ), number of doctors ( $P = .001$ ), number of oocyte cryopreservation cycles already performed ( $P = .07$ ), and number of thawed cycles ( $P = .04$ ).

Considering the distribution of infertility diagnoses, centers with higher amounts of tubal infertility were less likely to offer oocyte cryopreservation at all ( $P < .0001$ ). Elective-willing centers had a lower median percentage of tubal disease ( $P = .042$ ) and a higher median percentage of patients with decreased ovarian reserve ( $P = 0.04$ ).

Insurance type was not associated with whether or not a center offers oocyte cryopreservation when all insurance possibilities are included ( $P = .75$ ). However, centers accepting mainly out of pocket

**TABLE 3****Oocyte cryopreservation outcomes.**

Oocyte cryopreservation outcomes	Total responses (n = 140)
No. of years offered	
Median	2.0 y
Range	0.17–10 y
Method	
Slow freeze	23/140 (16%)
Vitrification	78/140 (56%)
Both	39/140 (28%)
No. of oocyte cryopreservation cycles	
Median	5
Range	0–200
Total	1,847
No. of thawed cycles	
Median	1
Range	0–120
Total	857
Fertilization rates	
Median	67%
Range	0–100%
Pregnancy rates	
Median	33%
Range	0–100%
No. of live births	
Median	1
Range	0–50
Total	337

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payments tended to be more willing to offer elective oocyte cryopreservation (73.1%) than those accepting only private insurance (58.3%,  $P = .09$ ). Clinics taking solely public insurance were the least likely to electively freeze oocytes ( $P = .014$ ). Similarly, patient ethnicity was not associated with whether a clinic offers oocyte cryopreservation or whether a clinic is “elective-willing.”

Oocyte cryopreservation outcome data is shown in Table 3. A total of 337 live births from 1,845 cryopreservation cycles were reported, with an overall PR of 39%. Elective-willing centers have been offering oocyte cryopreservation for a longer period of time ( $P = .041$ ), have a larger median number of cycles performed ( $P = .0015$ ), cycles thawed ( $P = .0029$ ), and number of live births ( $P = .0017$ ), than those centers who offer it for only nonelective reasons. With regard to method of cryopreservation, centers using only the slow freeze method had a longer duration of offering oocyte cryopreservation ( $P = .07$ ) and a marginally higher PR ( $P = .063$ ).

**DISCUSSION**

These data reflect the status of oocyte cryopreservation in the United States as of mid-2009. More than 50% of the responding ART clinics currently offer oocyte cryopreservation. The responses to our survey indicate that there are geographic trends not only in terms of oocyte cryopreservation status, but also in terms of acceptable indications. Independent of whether currently offering oocyte cryopreservation, the majority of programs (66%) believe that it is acceptable to use this technology to preserve fertility while delaying childbearing. Even among the programs that do not currently cryopreserve

oocytes but who plan to in the future, 64% believe that elective indications are acceptable.

Are these results truly representative of all ART centers in the United States? Although our response rate is less than 100%, we believe that the distribution of survey responses is truly representative of the whole; 64% of the total number of CDC reporting and nonreporting clinics responded to the survey. This population of responding clinics also performs 60% of the total number of IVF cycles in the United States. Thus we do not believe that the responding clinics over or under-represent US clinics as a whole (14). Our response group encompasses a wide range of ART clinic sizes, and the distribution of community versus academic centers (75% vs. 25%) is similar to the actual distribution. Finally, the geographic distribution of responding clinics is similar to the geographic distribution of all US ART clinics, with the highest percentage of ART clinics located in the western and northeastern states.

Although our reported outcome data are likely an approximation, we believe that the number of live births that we obtained is likely an underestimate, as not all ART centers responded to the survey. In our study, there were 337 live births reported across 64% of all ART clinics. From these data, one could extrapolate to estimate approximately 500 live births from oocyte cryopreservation in the United States alone. This is consistent with previous studies looking at international data. In the study by Noyes et al. (10), performed in 2008, more than 900 live births were tabulated from 58 separate reports worldwide.

This study has several weaknesses. We were unable to obtain a 100% response rate to the survey, thus we are missing outcome data and attitudes on oocyte cryopreservation from several large centers. However, we believe the cohort of clinics that did respond is representative in terms of size, type of practice, and location. It is also possible that clinics already performing oocyte cryopreservation were more likely to respond to the survey. Although we cannot account for this, the attitudes of those clinics that did respond are clearly still important and relevant. Finally, although all telephone interviews were conducted by the same interviewer, we attempted to minimize bias by using the same set of straightforward questions for each interview.

The American Society for Reproductive Medicine Practice Committee designates oocyte cryopreservation as “experimental since efficacy and safety are unproven,” and thus should only be performed under Institutional Review Board (IRB) protocol. Although IRB status was not directly ascertained in this survey, the majority of programs that currently offer oocyte cryopreservation voluntarily offered that it was under IRB protocol. Multiple programs commented on the difficulty of obtaining IRB approval as the reason

they did not offer oocyte cryopreservation. Several clinics responded, “IRB approval isn’t needed for freezing embryos so why should it be necessary for freezing oocytes?” The Human Oocyte Preservation Experience (HOPE) registry is a multicenter observational registry tracking the outcome of oocyte cryopreservation cycles. Their preliminary data demonstrates that more than 60% of clinics are offering oocyte cryopreservation, of which only 66% have IRB approval (15).

Among the most hotly debated is the elective use of oocyte cryopreservation as a means of preserving natural fertility for women who wish to delay childbearing. Our study suggests that the elective arena is actually where the majority of the demand for this technology lies. The programs performing elective oocyte cryopreservation are the same programs with the highest number of oocyte cryopreservation cycles ( $P=.002$ ), the highest number of thawed cycles ( $P=.003$ ), the highest PRs, and the highest number of live births ( $P=.002$ ). Because demonstrating further efficacy and safety will require larger numbers of subjects, especially in older age groups, this subpopulation of infertile women should be included in IRB protocols, rather than excluded.

Our data also suggest an association between centers performing elective oocyte cryopreservation and the percentage of patients with decreased ovarian reserve ( $P=.02$ ). In our survey, 52% of programs would cryopreserve oocytes electively in women aged 38–40 years, whereas only 26% of programs would cryopreserve oocytes beyond the age of 40 years. Elective oocyte cryopreservation as a truly preventative approach would ideally be before the age of 35 years; however, we are not yet at the point of educating all 30–35-year-old women to warn them about the risks of delaying childbearing. Such a preventative approach would depend more on the general obstetrician gynecologist, as these are the practitioners who routinely see and treat these younger women. Thus, if we are to restrict the preventative use of this technology to any age group, then more of an effort needs to be made to routinely educate younger women about the risks of delaying childbearing. Conversely, if a patient is considering freezing oocytes at an age more than 35 years, then to truly perform “informed consent,” we still need reference data in these older age groups to appropriately counsel her about risks and benefits.

In conclusion, oocyte cryopreservation is now offered in more than 50% of ART clinics in the United States, with a geographic trend toward western states. Although its application for elective purposes remains controversial, two-thirds of programs currently performing oocyte cryopreservation do so for elective indications. These data suggest a growing acceptance for this technology within our field.

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