

The Utilization of Assisted Reproductive Technologies – It is not just for Fertility Treatment

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Disclosures


- Ferring
- Natera



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Objectives

- Utilization of ART in the US
- Changes in trends for ART
- Outcomes for fertility preservation
- Patient attitudes toward banking
- A unique population – the physician



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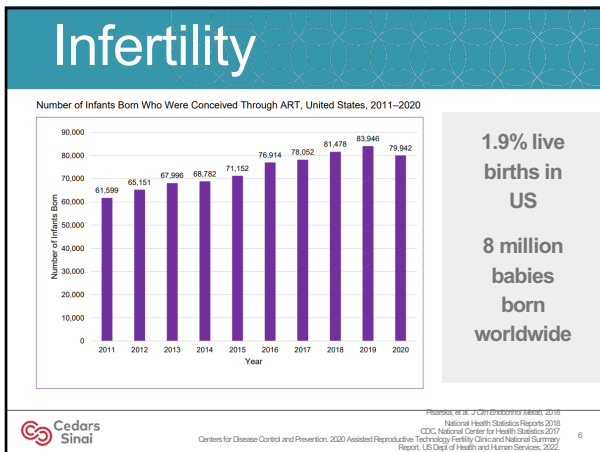
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Assisted Reproductive Technologies in vitro fertilization

The diagram illustrates the IVF process. It starts with a 'Vaginal Probe Ultrasound' showing an internal view of the reproductive system. This leads to an 'Ultrasound' image of an ovary. The next step is 'Egg Retrieval', shown as a needle aspirating an egg from the ovary. This is followed by 'Embryo Transfer', shown as an embryo being placed into the uterus. The Cedars Sinai logo is in the bottom left, and the number 7 is in the bottom right.

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Intracytoplasmic Sperm Injection

The image shows three sequential microscopic views of an egg cell. In the first, a needle is approaching the egg. In the second, the needle is inserted into the cytoplasm. In the third, a sperm cell is being injected into the egg. The Cedars Sinai logo is in the bottom left, and the number 8 is in the bottom right.

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Success rates

Percentage of Embryo Transfers That Resulted in Live-Birth Delivery, by Patient Age and Egg or Embryo Source, United States, 2020

| Patient Age (Years) | Donor Eggs or Embryos (%) | Patient Eggs or Embryos (%) |
|---------------------|---------------------------|-----------------------------|
| <30 | 42.8% | 42.0% |
| 30 | 48.4% | 42.7% |
| 31 | 48.8% | 42.2% |
| 32 | 44.1% | 41.7% |
| 33 | 48.5% | 41.4% |
| 34 | 47.3% | 40.9% |
| 35 | 42.0% | 39.6% |
| 36 | 44.6% | 38.1% |
| 37 | 43.3% | 37.3% |
| 38 | 41.2% | 35.4% |
| 39 | 43.5% | 32.8% |
| 40 | 40.8% | 30.2% |
| 41 | 44.4% | 26.4% |
| 42 | 42.4% | 23.0% |
| 43 | 41.0% | 16.1% |
| 44 | 38.4% | 14.0% |
| 45 | 41.1% | 12.9% |
| >45 | 37.6% | 10.6% |

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New Beginnings

ASRM PAGES

Mature oocyte cryopreservation: a guideline

The Practice Committees of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology
Society for Reproductive Medicine and Society for Assisted Reproductive Technology, Birmingham, Alabama


As of October 2012, the ASRM states "evidence indicates that oocyte vitrification and warming should no longer be considered experimental."

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Medical Indications for Oocyte Cryopreservation

- Postmenarchal women facing gonadotoxic therapies
- Cancer patients (chemotherapy, pelvic radiation)
- Patients undergoing oophorectomies
- Genetic conditions predisposing to primary ovarian insufficiency
- Fragile X premutation
- Mosaic monosomy X

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Elective/Social Egg Freezing – Social Media (2014)

"Perk Up: Facebook and Apple Now Pay for Women to Freeze Eggs"

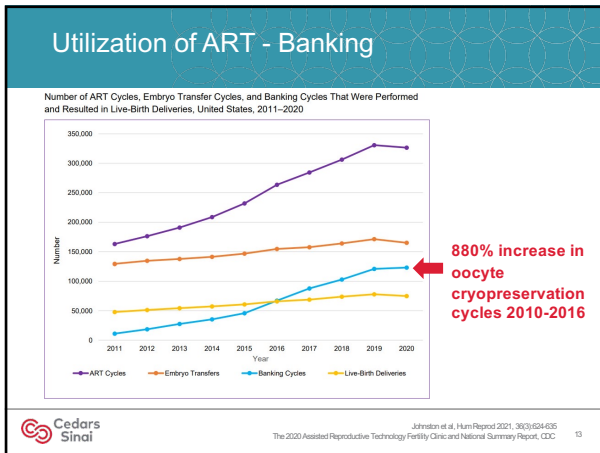
"Cold Comfort: Tech Jobs and Egg Freezing"

"Career women are having 'egg-freezing' parties"

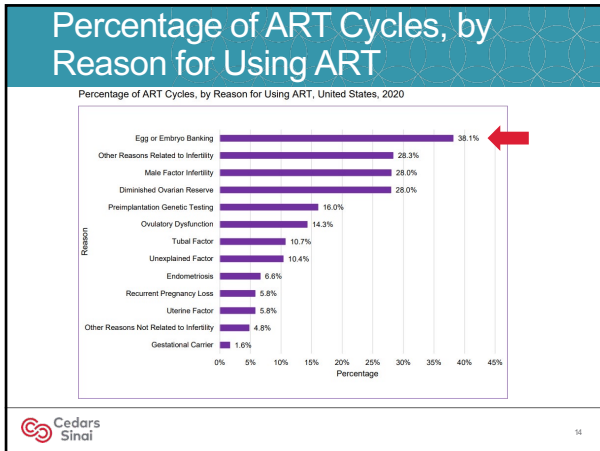
"5 Celebrities Who Froze Their Eggs"

 Cedars Sinai [Perk Up: Facebook and Apple Now Pay for Women to Freeze Eggs. \(nbnews.com\)](http://nbnews.com) 12

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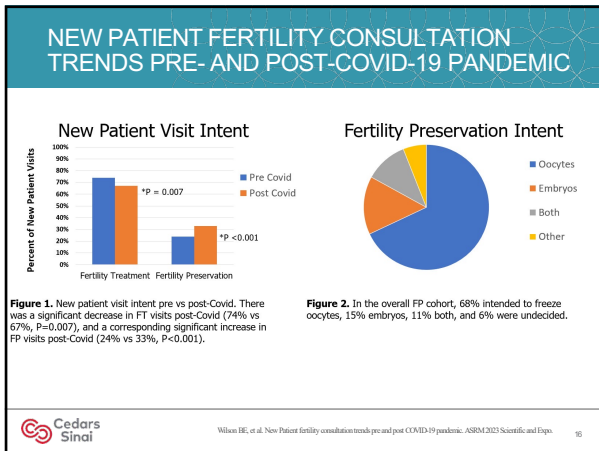
ART - Now

"All the years and years and years of speculation... It was really hard. I was going through IVF, drinking Chinese teas, you name it. I was throwing everything at it. I would've given anything if someone had said to me, 'Freeze your eggs. Do yourself a favor.' You just don't think it. So here I am today. The ship has sailed."

December 2022

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NEW PATIENT FERTILITY CONSULTATION TRENDS PRE- AND POST-COVID-19 PANDEMIC

| Demographics of Fertility Preservation Cohort | Pre-Covid | Post-Covid | P value |
|--|-----------|------------|---------|
| AMH (ng/mL ± SD) | 2.2±2.3 | 2.7±2.5 | 0.03* |
| Insurance coverage (% of all new patients) | 0.62% | 30.40% | <0.001* |
| Proceeded to treatment (% of all new patients) | 37% | 45% | 0.086 |

Table 1. Demographics of fertility preservation cohort. *P<0.05 is statistically significant.

In age-adjusted analyses, the odds of proceeding with fertility preservation treatment was not associated with fertility preservation insurance coverage (OR 1.09, 95% CI 0.82-1.46).

Cedars Sinai | Wilson JE, et al. New Patient fertility consultation trends pre and post COVID-19 pandemic. ASRM 2023 Scientific and Educ. 17

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Doyle et al, Fertility & Sterility 2016

- 2009-2015
- 1171 oocyte cryopreservation cycles for 875 women
- 117 (10%) returned to use their oocytes


| | Vitrified Oocytes | Control Group | P-value |
|-------------------------|-------------------|---------------|---------|
| Age at OC | 34.9 | 35.5 | NS |
| # oocytes used | 8.0 | 10.1 | 0.0002 |
| Fertilization rate | 70% | 72% | NS |
| Implantation rate | 43% | 35% | 0.046 |
| Clinical pregnancy rate | 57% | 44% | 0.011 |
| Live birth rate | 39% | 35% | NS |

 Cedars Sinai Doyle et al Fert Steril 2016; 105:459-66 19

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Efficiency Per Oocyte

- **Vitrified-warmed oocytes to live born child efficiency = 6.4%**
- Ranges between 5.2% to 7.4% depending on age at the time of planned OC
- 55 live born-children
 - 5 children for women 41-42yo at the time of planned OC


 Cedars Sinai Doyle et al Fert Steril 2016; 105:459-66 20

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Predicted Probabilities

FIGURE 1

Predicted probabilities of having at least one, two, and three live-born children according to the number of mature oocytes cryopreserved for elective fertility preservation, according to age at oocyte retrieval and the associated oocyte-to-live-born child efficiency estimates: (A) 30–34 years, 8.2% efficiency; (B) 35–37 years, 7.3% efficiency; (C) 38–40 years, 4.5% efficiency; (D) 41–42 years, 2.5% efficiency.


 Cedars Sinai Doyle et al Fert Steril 2016; 105:459-66 21

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Leung et al Repro Biomed Online 2021


- 2006-2020
- 921 women underwent planned oocyte cryopreservation cycles
- 68 (7.4%) returned to use their oocytes

| | <38yo | ≥38yo | P-value |
|--|-------|-------|---------|
| Age at OC | 36.6 | 39.6 | 0.02 |
| Time interval between OC and thaw, years | 4.1 | 3.2 | NS |
| # oocytes used | 14.5 | 14.2 | NS |
| Clinical pregnancy rate | 54.5% | 39.3% | NS |
| Live birth rate | 48.5% | 28.6% | NS |
| Cumulative live birth rate per pt | 38.9% | 25.0% | NS |

 Cedars Sinai Leung et al RBMO 2021; 43(4): 671-679 22

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- Only 7.4% of patients (68/921) return to use their oocytes
- **32% (22/68) achieved a live birth**
- 22% (15/68) did not have an embryo for transfer
- No patient ≥40yo at the time of planned oocyte cryopreservation was successful

 Cedars Sinai Leung et al RBMO 2021; 43(4): 671-679 23

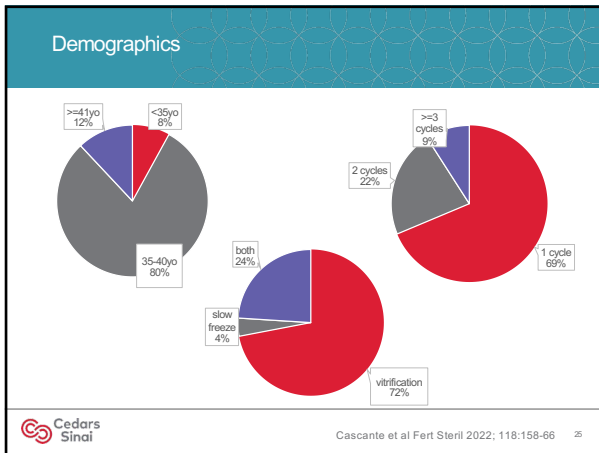
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Cascante et al Fertility & Sterility 2022

- 2004-2020
- 543 patients underwent 800 oocyte cryopreservation cycles, 605 thaws, 436 transfers
- 332 pts (61%) had ≥1 embryo transfer
- 166 pts (31%) had no transfer
 - No oocytes survived
 - No fertilization
 - Embryo arrest
 - No euploid embryos

 Cedars Sinai Cascante et al Fert Steril 2022; 118:158-66 24

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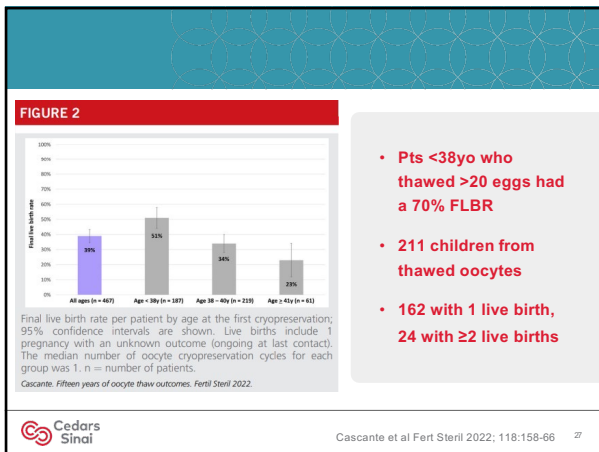


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| | |
|--|--------------------------------|
| Median age | 38.3 (36.8-39.7) Oldest 44y |
| Median time from freeze to thaw, years | 4.2 (2.9-5.6) |
| Median # oocytes | 12 (8-18) |
| Oocyte survival | 79% |
| Final live birth rate | 39% |

Cedars Sinai | Cascante et al Fert Steril 2022; 118:158-66 26

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The New York Times

'Sobering' Study Shows Challenges of Egg Freezing

Data from a fertility center showed many women did not get pregnant because of the age at which they froze their eggs and because they did not preserve enough of them.



Egg center a message at a fertility clinic in Maryland. "I always tell patients, 'There's not a baby in the frozen. There's a chance to get pregnant,'" said one fertility expert, according to The Washington Post via Getty Images.

1/3 of patients who return to use frozen eggs are successful

Cedars Sinai ["Sobering" Study Shows Challenges of Egg Freezing - The New York Times \(nytimes.com\)](#)

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How do we counsel women on elective fertility preservation?

- "Live birth rates are improved when oocyte cryopreservation is performed in younger compared to older women" (ASRM 2021 Guideline)
- Optimal age is ≤ 35 yo
- Newest data suggest 32 – 35 yo (Bakkensen et al, Fertility Sterility, 2022)
- Fertility preservation is not a guarantee

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32 is the New 35

TABLE 2

Probability of live birth and cost-effectiveness by delayed reproduction treatment strategy

| Treatment strategy | Probability of ≥ 1 LB | Probability of 2 LB | Average individual cost | Maximum individual cost | Cost per percentage point increase in success, 1 LB | Cost per percentage point increase in success, 2 LB |
|--|----------------------------|---------------------|-------------------------|-------------------------|---|---|
| Desires 1 child | | | | | | |
| No OC + IVF/PGT | 50% | 0% | \$62,308 | \$84,536 | Ref | |
| OC | 73% | 0% | \$30,523 | \$37,992 | -\$1,376 | |
| Desires 2 children | | | | | | |
| No OC + IVF/PGT without embryo banking | 76% | 19% | \$79,057 | \$145,018 | Ref | Ref |
| No OC + IVF/PGT with embryo banking | 78% | 48% | \$79,728 | \$97,802 | \$278 | \$23 |
| OC 1 cycle + IVF/PGT | 93% | 61% | \$76,100 | \$122,528 | -\$176 | -\$71 |
| OC 2 cycles | 94% | 77% | \$52,479 | \$63,092 | -\$1,441 | -\$458 |

See Figure 1 and methods for a detailed description of each treatment strategy. Negative cost per percentage point increase in live birth reflects a net cost savings. OC, oocyte cryopreservation; IVF/PGT, in vitro fertilization with preimplantation genetic testing for aneuploidy; LB, live birth; Ref, referent strategy.

Bakkensen. Cost-effectiveness of planned OC. *Fertil Steril* 2022.

Cedars Sinai Bakkensen Fertil Steril 2022;118:875-84 30


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Patient experiences following elective oocyte cryopreservation

- Stoop et al, Hum Reproduction, 2015
- 95% would choose to do planned OC again
- 96% would recommend planned OC to others
- 76% wish that froze eggs at a younger age

- Greenwood et al, Fertility Sterility, 2018
- 88% increased control over reproductive planning
- 89% happy they froze eggs even if they never use them

- Seyhan et al, Reproductive Sciences, 2021
- 72% felt more secure in reproductive potential
- 98.8% would recommend to a friend




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Fertility considerations in female physicians

Stentz et al, Journal of Women's Health 2016

- 2012-2013 random survey of 600 female physicians from AMA
- 55% response rate (n=327)
- 54% of respondents from OBGYN/Pediatrics/Family Medicine
- 32% of respondents from Medicine/Subspecialties
- 9% of respondents from hospital based specialists
- 4% of respondents from Surgery/Subspecialties


• 1 in 4 were diagnosed with infertility – the mean age at diagnosis was 33.7 years



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Fertility considerations in female physicians

| Milestone | Respondents | All women (CDQ) |
|-----------------------------|-------------|-----------------|
| Medical School Graduation | 27.5 | - |
| Completion of Training | 31.6 | - |
| First Attempt at Conception | 23 | 30.6 |
| First Pregnancy | 23 | 30.4 |
| Infertility Diagnosis | - | 33.7 |



Stentz et al, Journal of Women's Health 2016

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Fertility considerations in female physicians

Perspective FREE PERSPECTIVE

THE NEW ENGLAND JOURNAL OF MEDICINE

One in Four — The Importance of Comprehensive Fertility Benefits for the Medical Workforce

Erica C. Kaye, M.D., M.P.H.

The New York Times

A Medical Career, at a Cost: Infertility

Physicians are raising awareness of the reproductive toll that work stress, long hours, sleep deprivation and years of training can exact.

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Fertility considerations in female physicians

JAMA Network Open

View Article

JAMA Network Open. 2022 Oct 31;5(10):e2337558.
Published online 2022 Oct 31. doi: 10.1001/jamanetworkopen.2022.37558.
10.1001/jamanetworkopen.2022.37558

PMCID: PMC9629435
PMD: 36315148

31% reported infertility, n=1004

Family Planning, Fertility, and Career Decisions Among Female Oncologists

Original Research—General Obstetrics/Gynecology

AMERICAN ACADEMY OF OBSTETRICIANS AND GYNECOLOGISTS
F O G I N O B A T I O N

30.4% reported infertility, n=398

Outcomes of Your and Your Partner's Fertility: A Cross-Sectional Study of American Academies of Obstetrics and Gynecology Members 2021

The American Journal of Surgery 2023;126(10):13-19

Access this article at [SciendoDirect](#)

The American Journal of Surgery
JOURNAL HOMEPAGE: www.ajsonline.com/ajsonline/home

54% reported infertility, n=351

Forward Article
Fertility & childbearing outcomes of female plastic surgeons: How far have we come in 25 years?
Kuhjra Hemal¹, Juliana Remark¹, Wendy Chen¹, Debra A. Bourne^{1*}

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Fertility considerations in female physicians

Smith et al, JAMA Network, 2022

Table 1. Themes and Subthemes Regarding Fertility Knowledge Among Women in Medicine That Arose From Qualitative Interviews With 16 Physicians

| Theme | Subthemes | Exemplary quotations* |
|--|-----------------------------|--|
| Fertility knowledge | Inadequate formal education | "The majority of what I learned about from a fertility standpoint was basic sort of how the reproductive system works... I do think that aging and fertility is something that we were told about, but referring in words (over 35) something we didn't hear about." (1006) "I think it [age and infertility] was briefly touched upon in medical school during my OB/GYN rotation, but not much more than at age 35 your risk for Down syndrome goes up markedly... I wouldn't say that it was really emphasized at all. I don't think that I had any sort of opportunity to go to an REI [reproductive endocrinology and infertility] clinic... I think that was something that I learned in residency." (1008) |
| | | "I would add it to your residency orientation, because I think you're capturing people in their 20s for the most part. I think that's an ideal age, and I think that if people have it in the back of their mind, they are going to be more cognizant..." (1006) |
| | | "Medical school is when people are still considering different fields and telling us different fields may affect their fertility choices and options... so, before you're in the time where you're really thinking about starting a family, to have the information ahead of time would be good." (1008) |
| Improving medical education for medical trainees | | "I would add it to your residency orientation, because I think you're capturing people in their 20s for the most part. I think that's an ideal age, and I think that if people have it in the back of their mind, they are going to be more cognizant..." (1006) "Medical school (when people are still considering different fields and telling us different fields may affect their fertility choices and options... so, before you're in the time where you're really thinking about starting a family, to have the information ahead of time would be good." (1008) |

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Fertility considerations in female physicians

Smith et al. BMC Medical Education (2023) 23:147
<https://doi.org/10.1186/s12909-023-04075-w> BMC Medical Education

RESEARCH Open Access

Anxiety, attitudes, and education about fertility among medical students in the United States **65% reported plans to delay childbearing (planned age of 31 +/- 2 years). n=351**

D. Grace Smith^{1*}, Abigail Ross², Elena HogentEsch³, Rachel Okine⁴, Marissa L. Bonus⁵, Eve C. Feinberg³ and Lia A. Bernardi³

Research Report

Childbearing Decisions in Residency: A Multicenter Survey of Female Residents **61% reported they were delaying childbearing. n=1537**

Shobha W. Stack, PhD, MD, Reshma Jaggi, MD, DPhil, J. Sybil Biermann, MD, Gina P. Lundberg, MD, Karen L. Law, MD, Caroline K. Milne, MD, Sigrid G. Williams, MD, MPH, Tracy C. Burton, MD, Cindy L. Larson, MA, and Jennifer A. Best, MD




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Fertility considerations in female physicians

Research Report

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| Reason | Percentage |
|---|------------|
| Discouraged to have children during residency by senior faculty | 5% |
| Other | 10% |
| Desire to not delay taking my board exam | 13% |
| Fellowship or job start date restrictions | 15% |
| My partner is not ready | 20% |
| Residency training might increase pregnancy complications | 27% |
| Parental leave would burden my colleagues | 35% |
| Finances | 42% |
| Lack of access to childcare (i.e., daycare) | 46% |
| Desire to not extend my residency training | 53% |
| Busy work schedule | 93% |

Figure 1 Self-reported reasons for delaying childbearing among 274 female residents participating in a multicenter survey of female residents, 2017. Responses are not mutually exclusive; respondents indicated up to 3 selections. The survey is available as Supplemental Digital Appendix 1 at <http://links.lww.com/ACADMED/A984>.

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Conclusions


- ART is not only for infertility
- The number of oocyte/embryo cryopreservation cycles is increasing exponentially on a national level
- We are young in every way, with the exception of our ovaries (i.e. we are limited by our ovarian reserve)
 - Live birth rates are improved when oocyte cryopreservation is performed in younger compared to older women
 - Ideal time for oocyte cryopreservation is ≤ 32 yo
 - Number of oocytes 20 (may need more than 1 cycle)
 - Not a guarantee (1/3 are successful)



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Conclusions

- >90% of women are happy they underwent planned oocyte cryopreservation
 - Most women wish they did so at a younger age
- Female physicians are a unique population –
 - Delaying childbearing during medical training
 - 1 in 4 female physicians is diagnosed with infertility
- Counseling regarding future family building should be addressed at all well women visits and in the medical school curriculum


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Our patients for participating in our studies to improve outcomes!


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