

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

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Disclosures

- Ferring
- Natera

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



And here she is...

THE LOVELY LOUISE



LOUISE BROWN, bright-eyed at 18 hours old: The test tube baby in hospital yesterday

Daily Mail World Exclusive Picture by Bill Cross © World Copyright Associated Newspapers Group Ltd., 1978. Full story and more pictures inside



LIFE

'CATS' LEAPS ONTO BROADWAY
The hottest theater ticket in the country

SAVING AFRICA'S BIG ANIMALS
A radical plan to butcher some of them and sell their meat

November 1982/\$2.00

TEST-TUBE BABY BOOM

Elizabeth Carr, America's first in vitro baby, at the lab where she was conceived



© Life Magazine



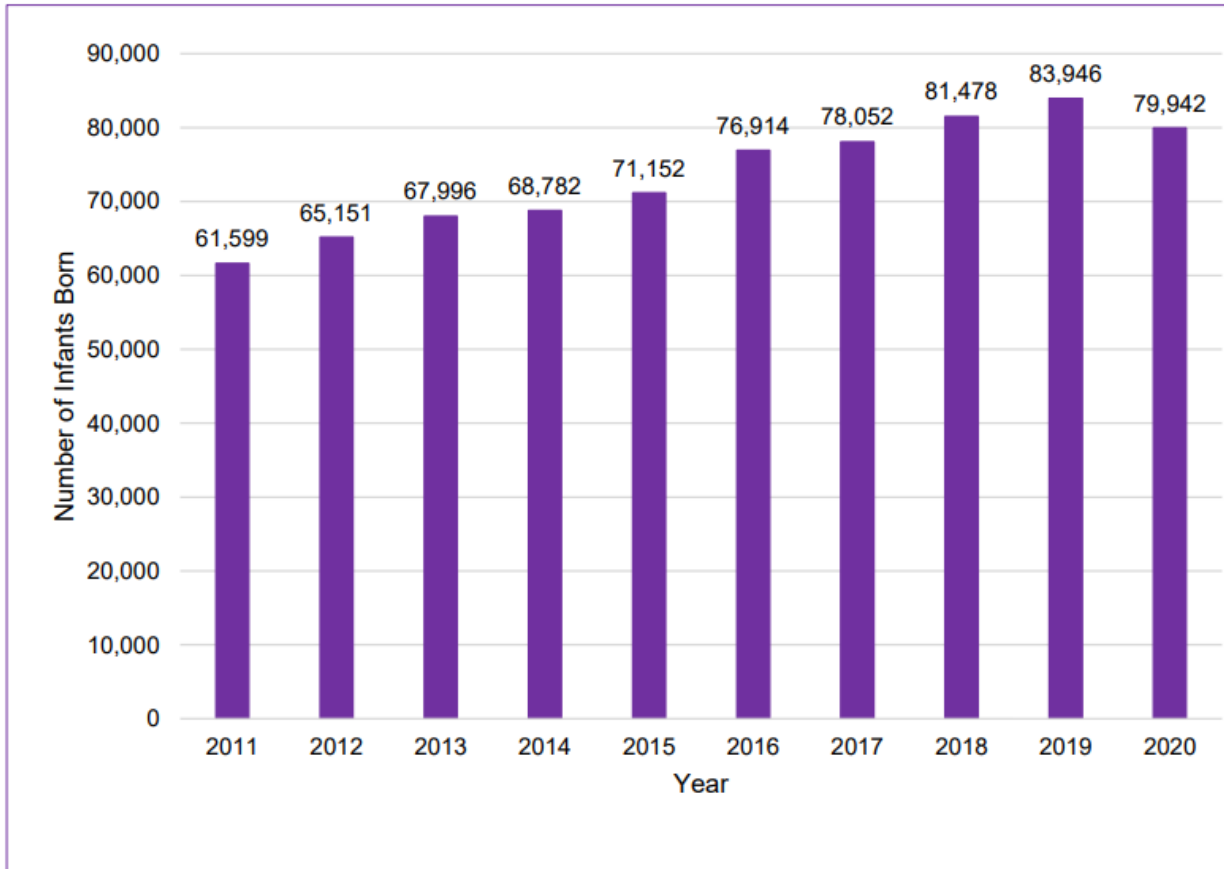
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© Boston Globe via Getty Images

Infertility

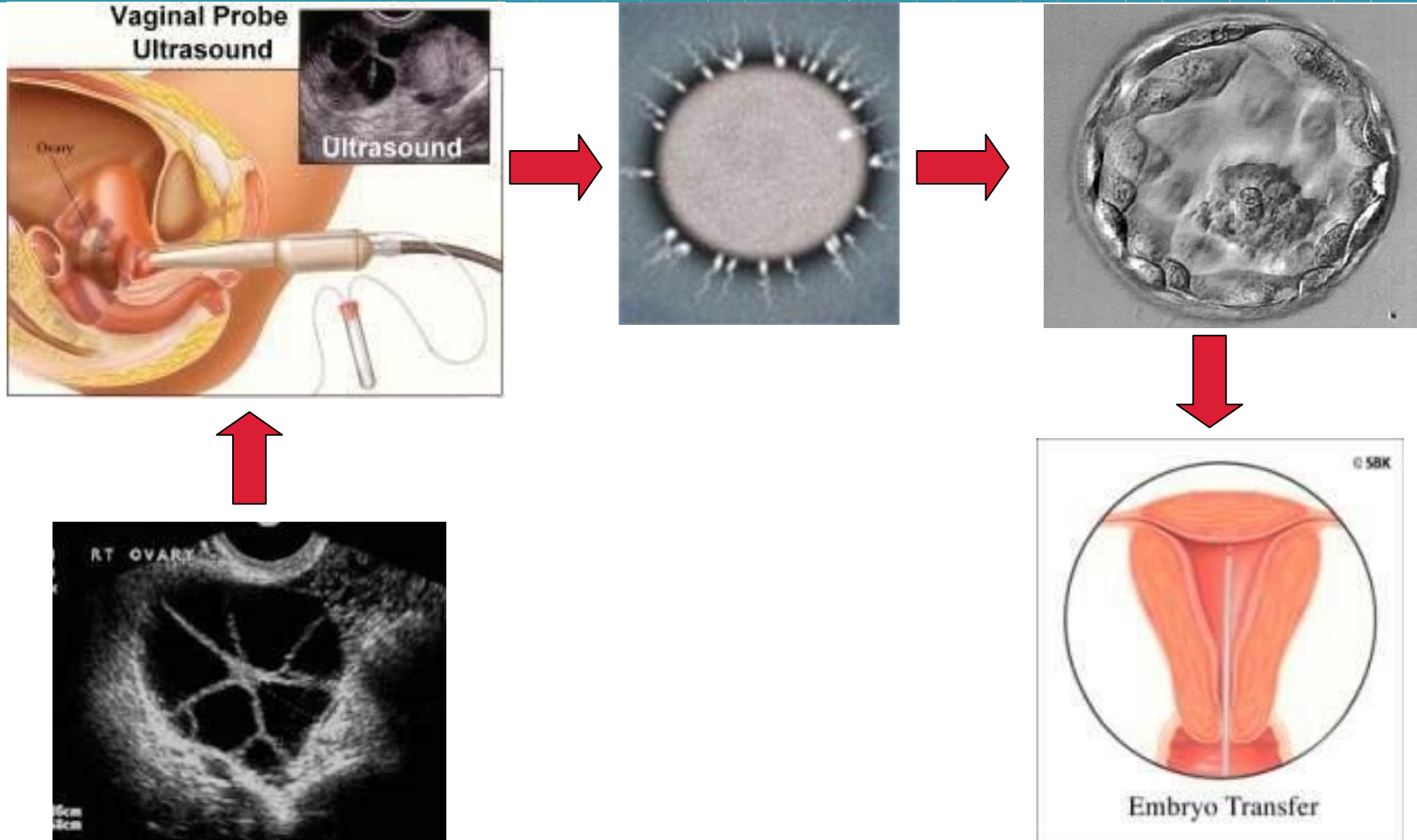
Number of Infants Born Who Were Conceived Through ART, United States, 2011–2020



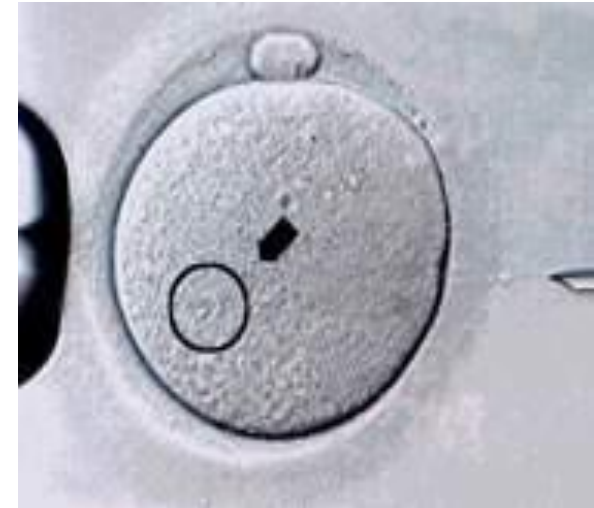
**1.9% live
births in
US**

**8 million
babies
born
worldwide**

Assisted Reproductive Technologies in vitro fertilization

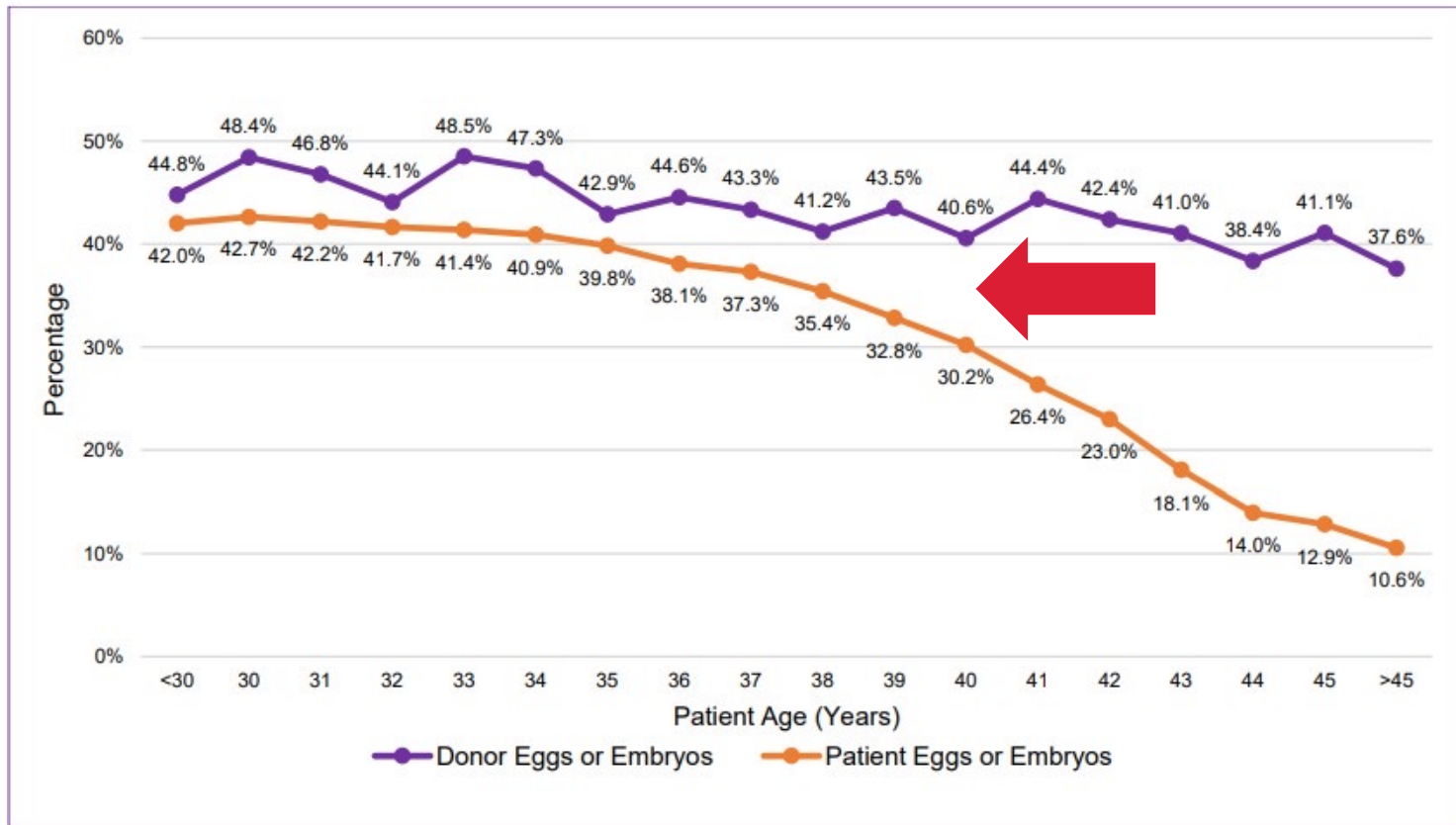


Intracytoplasmic Sperm Injection



Success rates

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



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.”

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

Elective/Social Egg Freezing – Social Media (2014)

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

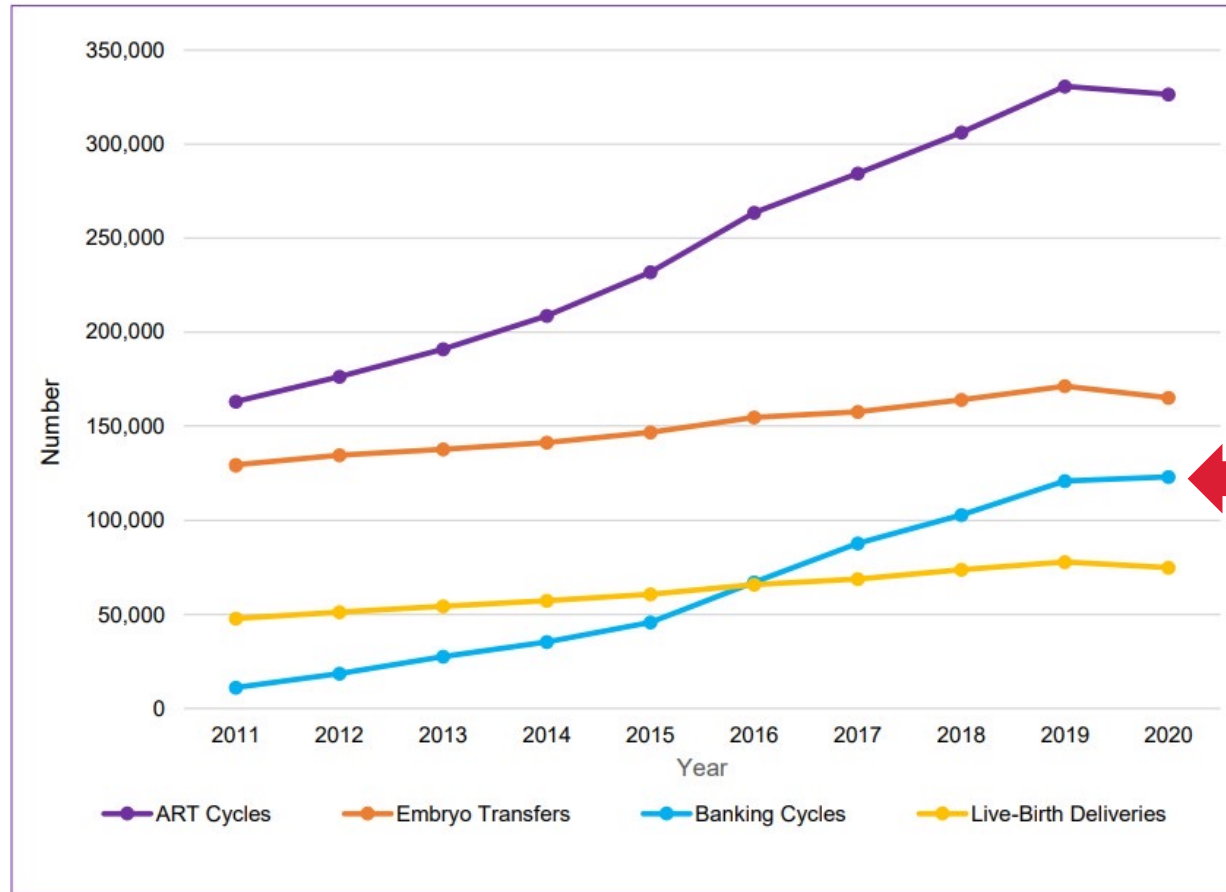
“Cold Comfort: Tech Jobs and Egg Freezing”

“Career women are having ‘egg-freezing’ parties”

“5 Celebrities Who Froze Their Eggs”

Utilization of ART - Banking

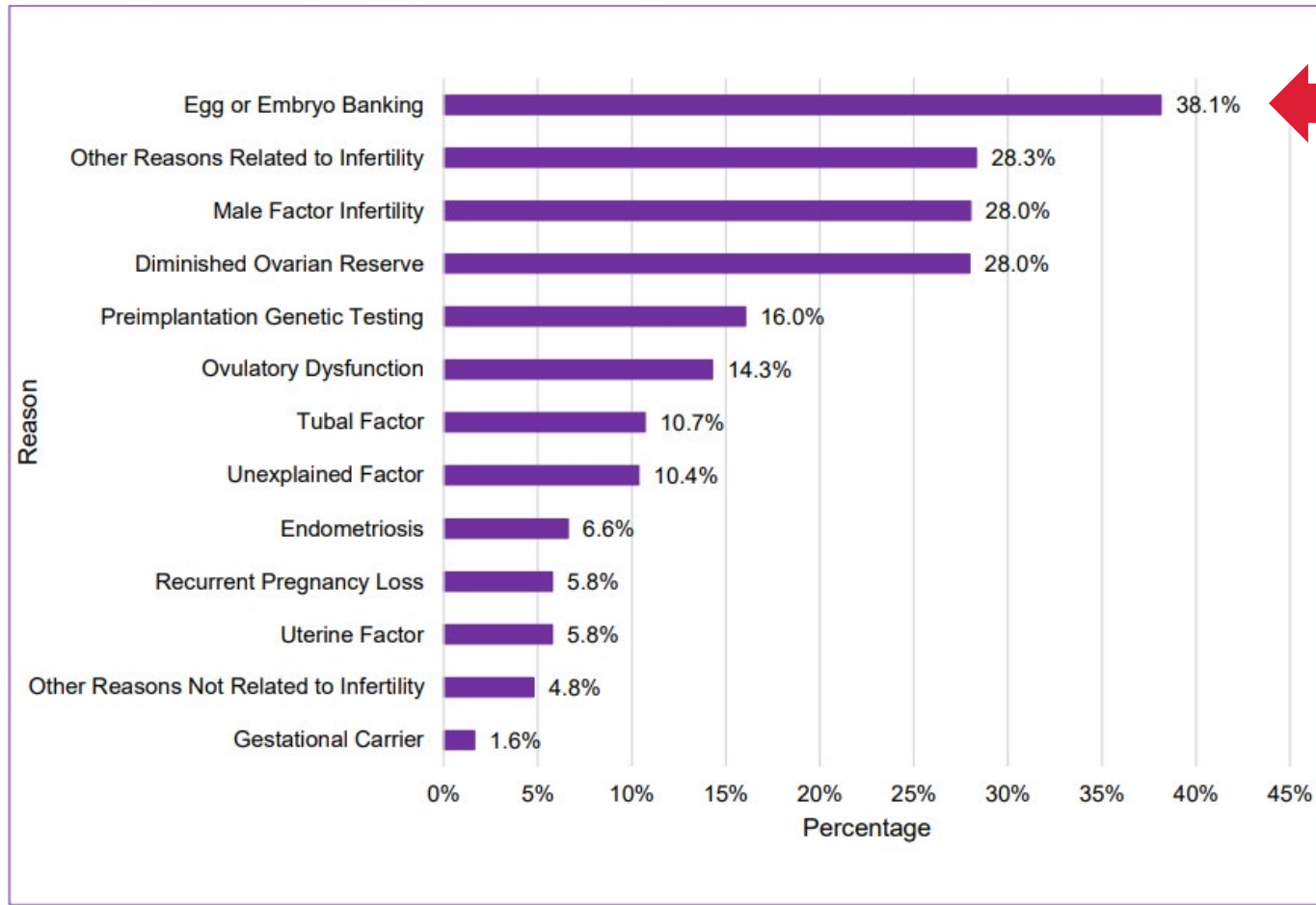
Number of ART Cycles, Embryo Transfer Cycles, and Banking Cycles That Were Performed and Resulted in Live-Birth Deliveries, United States, 2011–2020



880% increase in oocyte cryopreservation cycles 2010-2016

Percentage of ART Cycles, by Reason for Using ART

Percentage of ART Cycles, by Reason for Using ART, United States, 2020



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

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

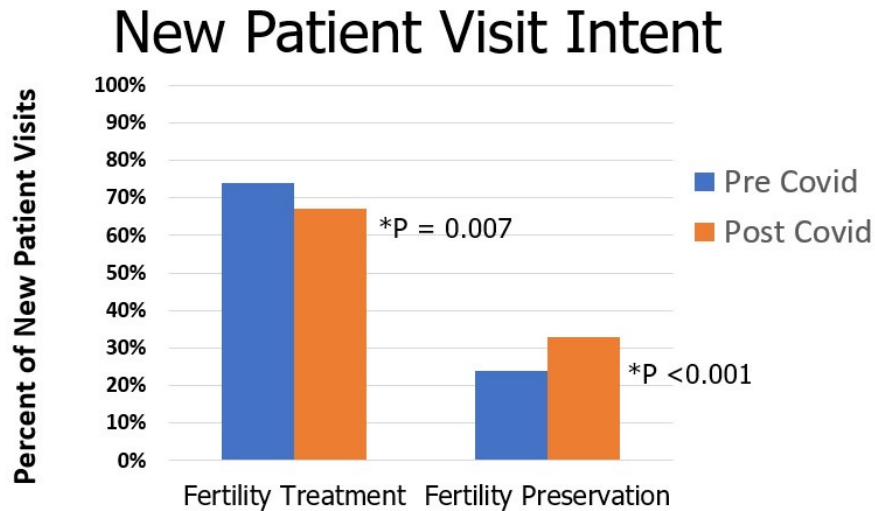


Figure 1. New patient visit intent pre vs post-Covid. There was a significant decrease in FT visits post-Covid (74% vs 67%, $P=0.007$), and a corresponding significant increase in FP visits post-Covid (24% vs 33%, $P<0.001$).

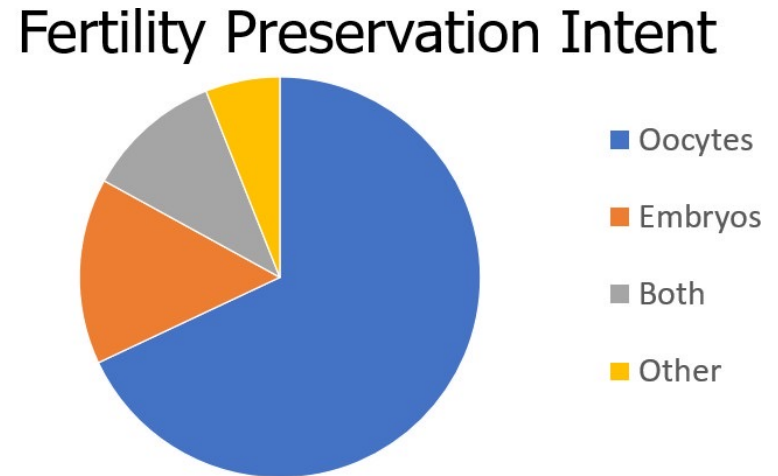


Figure 2. In the overall FP cohort, 68% intended to freeze oocytes, 15% embryos, 11% both, and 6% were undecided.

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).

Success Rates

Doyle et al, Fertility & Sterility 2016

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

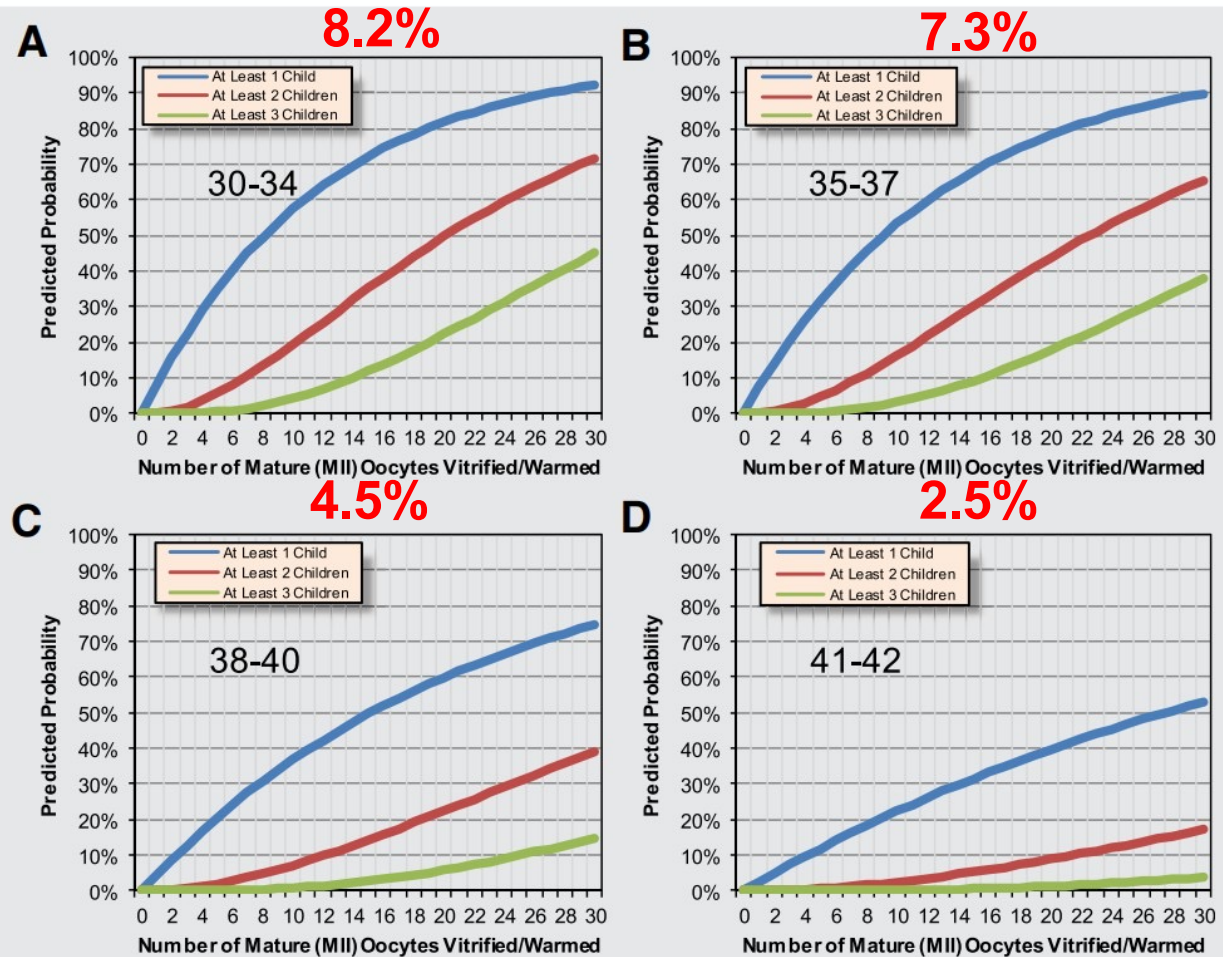
	Vitrified Oocytes	Control Group	P-value
Age at OC	34.9	35.5	NS
# oocytes used	8.0	10.1	0.0002
Fertilization rate	70%	72%	NS
Implantation rate	43%	35%	0.046
Clinical pregnancy rate	57%	44%	0.011
Live birth rate	39%	35%	NS

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

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.

Doyle. Autologous vitrified oocyte IVF outcomes. *Fertil Steril* 2016.

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

- 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 ≥ 40 yo at the time of planned oocyte cryopreservation was successful

- **2004-2020**

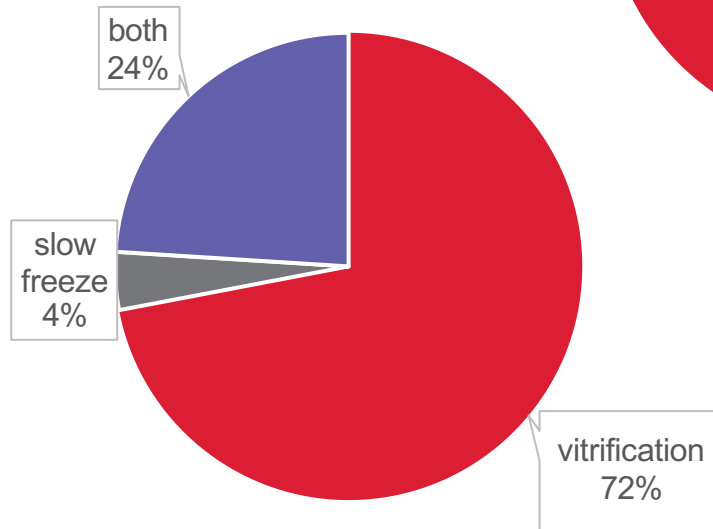
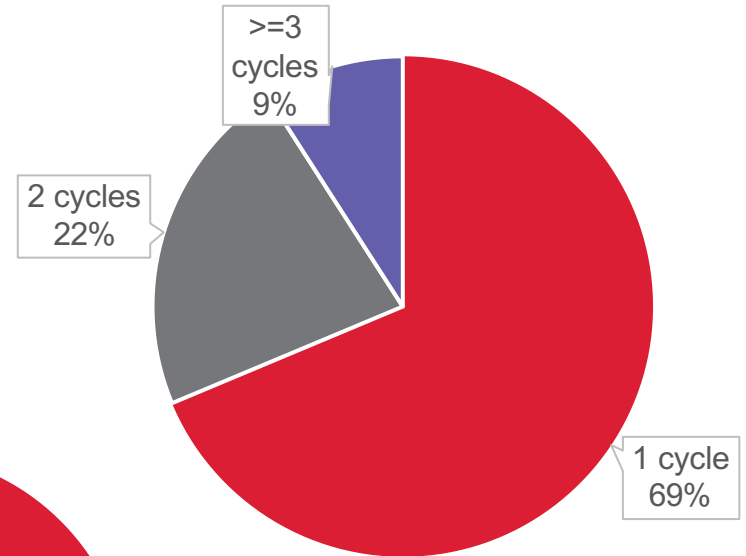
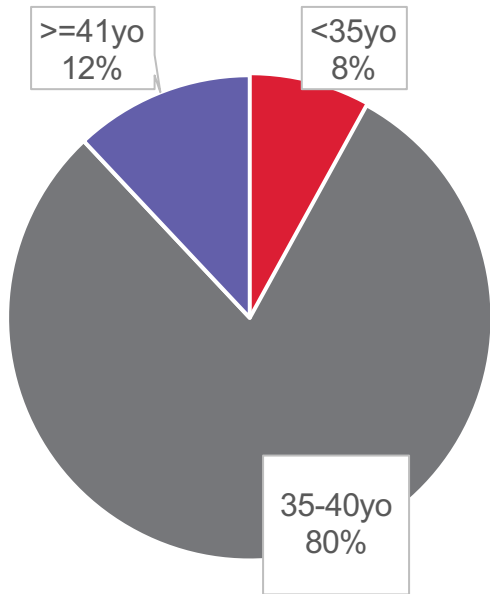
- **543 patients underwent 800 oocyte cryopreservation cycles, 605 thaws, 436 transfers**

- **332 pts (61%) had ≥ 1 embryo transfer**

- **166 pts (31%) had no transfer**

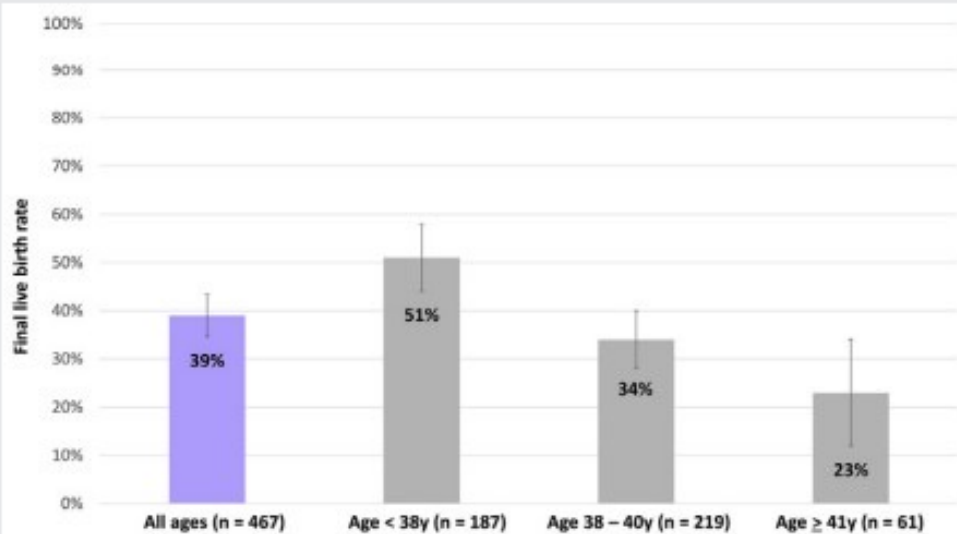
- No oocytes survived
- No fertilization
- Embryo arrest
- No euploid embryos

Demographics



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%

FIGURE 2



Final live birth rate per patient by age at the first cryopreservation; 95% confidence intervals are shown. Live births include 1 pregnancy with an unknown outcome (ongoing at last contact). The median number of oocyte cryopreservation cycles for each group was 1. n = number of patients.

Cascante. *Fifteen years of oocyte thaw outcomes. Fertil Steril* 2022.

- **Pts <38yo who thawed >20 eggs had a 70% FLBR**
- **211 children from thawed oocytes**
- **162 with 1 live birth, 24 with ≥2 live births**

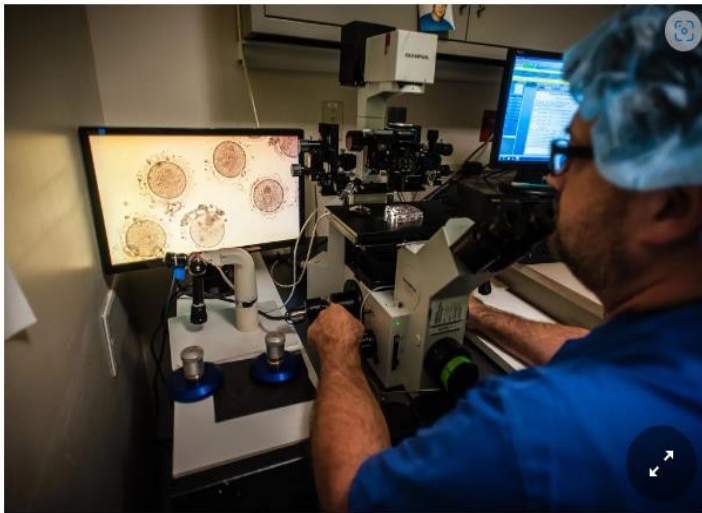
'Sobering' Study Shows Challenges of Egg Freezing

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.

Give this article



161



Eggs under a microscope at a fertility clinic in Maryland. "I always tell patients, 'There's not a baby in the freezer. There's a chance to get pregnant,'" said one fertility expert. Andre Chung for The Washington Post, via Getty Images

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

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**

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	<i>Ref</i>	
OC	73%	0%	\$30,333	\$37,992	-\$1,376	
Desires 2 children						
No OC + IVF/PGT without embryo banking	76%	19%	\$79,057	\$145,018	<i>Ref</i>	<i>Ref</i>
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.

Patient experiences following elective oocyte cryopreservation

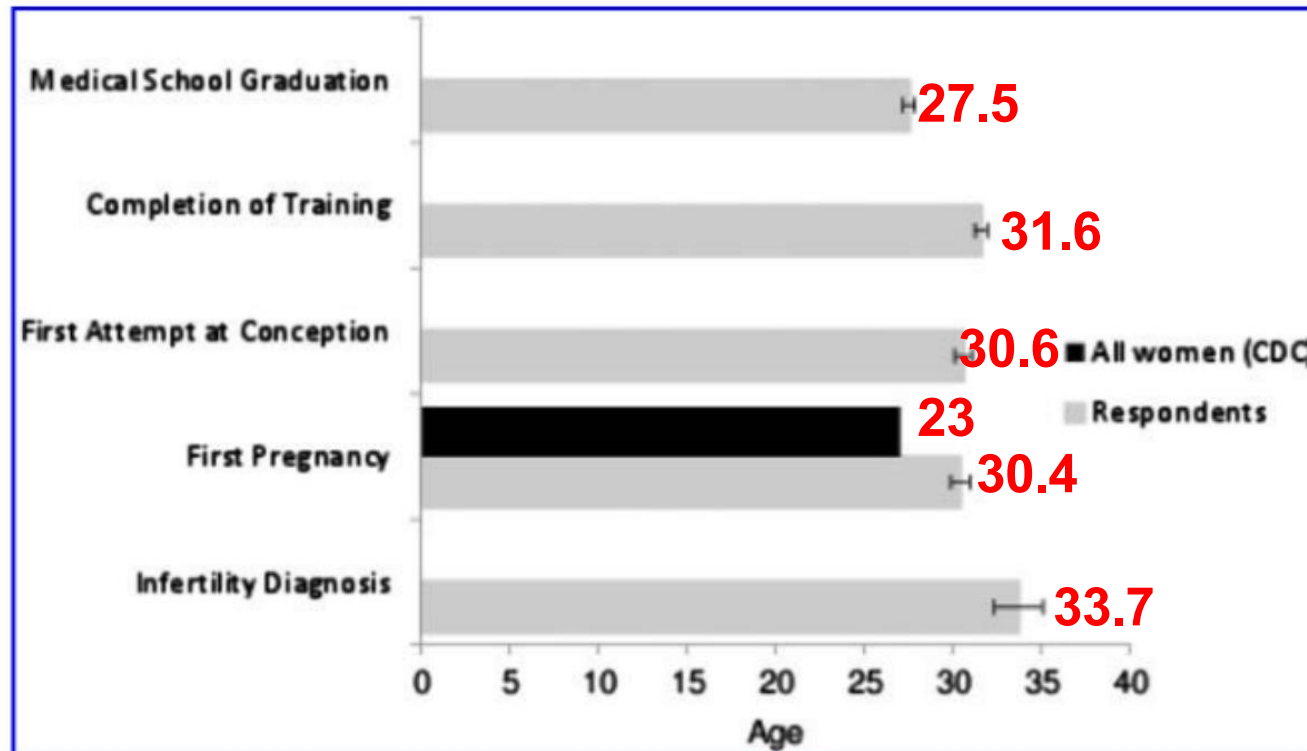
- **Stoop et al, Hum Reproduction, 2015**
 - 95% would choose to do planned OC again
 - 96% would recommend planned OC to others
 - 76% wish that froze eggs at a younger age
- **Greenwood et al, Fertility Sterility, 2018**
 - 88% increased control over reproductive planning
 - 89% happy they froze eggs 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

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**

Fertility considerations in female physicians



Fertility considerations in female physicians

Perspective FREE PREVIEW



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.

Fertility considerations in female physicians



JAMA Netw Open. 2022 Oct; 5(10): e2237558.

PMCID: PMC9623435

Published online 2022 Oct 31. doi: 10.1001/jamanetworkopen.2022.37558:

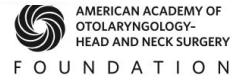
PMID: [36315148](#)

10.1001/jamanetworkopen.2022.37558

31% reported infertility.
n=1004

Family Planning, Fertility, and Career Decisions Among Female Oncologists

Original Research—General Otolaryngology



30.4% reported infertility.
n=398

Pregnancy and Fertility Trends Among Female Otolaryngologists

The American Journal of Surgery 225 (2023) 13–19

Otolaryngology—
Head and Neck Surgery
2022, Vol. 167(4) 650–656
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Otolaryngology—Head and Neck
Surgery Foundation 2021
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The American Journal of Surgery

journal homepage: www.elsevier.com/locate/amjsurg



54% reported infertility.
n=351

Featured Article

Fertility & childbearing outcomes of female plastic surgeons: How far have we come in 25 years?



Kshipra Hemal^a, Juliana Remark^a, Wendy Chen^b, Debra A. Bourne^{c,*}

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 ^a
Fertility knowledge	Inadequate formal education	<p>"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 infertility in women under 35 is something we didn't hear about." (1010)</p> <p>"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] clinic or had any exposure to that in medical school." (1001)</p>

"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

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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 HogenEsch³, Rachel Okine⁴, Marissa L. Bonus³, Eve C. Feinberg⁵ and Lia A. Bernardi⁵

Research Report

Childbearing Decisions in Residency: A Multicenter Survey of Female Residents

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. Larison, MA, and Jennifer A. Best, MD

61% reported they were delaying childbearing. n=1537

Fertility considerations in female physicians

Research Report

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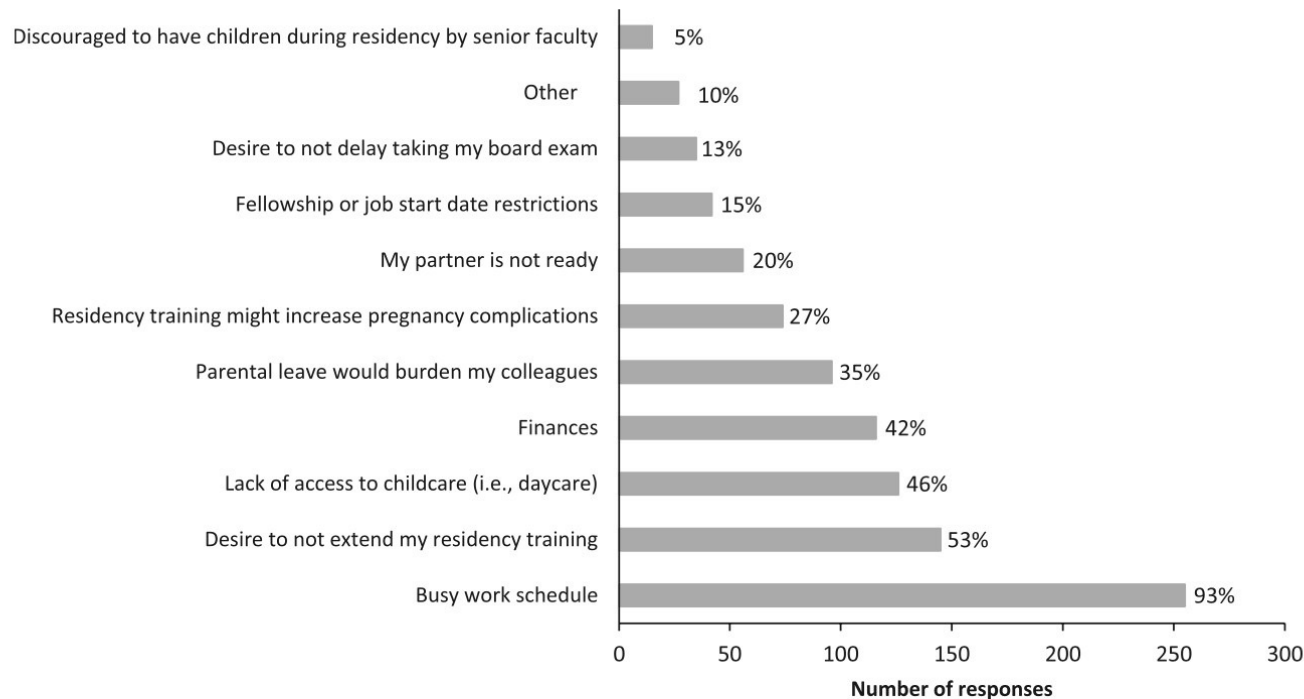


Figure 1 Self-reported reasons for delaying childbearing among 274 female residents participating in a multicenter survey of female residents, 2017. Responses are not mutually exclusive; respondents indicated up to 3 selections. The survey is available as Supplemental Digital Appendix 1 at <http://links.lww.com/ACADMED/A984>.

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)

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**

Acknowledgements

- *Pisarska Lab*
 - *Tania Gonzalez, PhD*
 - *Amy Flowers, PhD*
 - *Bryn Willson, MD*
 - *Katherine VanHise, MD*
- *Prenatal Biorepository*
 - *Allynson Novoa*
 - *Akhila Swarna*
- *Faculty*
 - *Erica Wang, MD MAS*
 - *Jessica Chan, MD MSCE*
- *Fellows*
 - *Bryn Willson, MD*
 - *Katherine VanHise, MD*
 - *Ally Kosturakis, MD*
- *CFRM Staff*



PI:
**Margareta
Pisarska, MD**

***Our patients for
participating in our
studies to improve
outcomes!***



