

Survival Rates of Frozen-Thawed Oocytes Remain Constant as Female Age Increases

Anupama Rambhatla

arambhatla88@gmail.com

Stanford University

Kyle Le

Shady Grove Fertility Center

Kerry Flannagan

US Fertility

Jing Wu

US Fertility

Jerry Wang

US Fertility

Amalia Namath

National Institutes of Health

Allison Eubanks

National Institutes of Health

Atoosa Ghofranian

Icahn School of Medicine at Mount Sinai

Jensen Reckhow

Icahn School of Medicine at Mount Sinai

Joshua Lim

Shady Grove Fertility Center

Taer Han

Shady Grove Fertility Center

Rebecca Brohammer

Fertility Centers of Illinois

Luis Hoyos

IVF Florida Reproductive Associates

Kate Devine

Shady Grove Fertility Center

Ruth Bunker Lathi

Stanford University

Phillip Romanski

Reproductive Medicine Associates of New York

Ravi Agarwal

Reproductive Science Center

Research Article

Keywords: Oocyte cryopreservation, oocyte survival, oocyte thaw, fertility preservation

Posted Date: October 23rd, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-11236398/v1>

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Additional Declarations: No competing interests reported.

Abstract

Purpose

To evaluate survival rates of vitrified oocytes by age.

Methods

This retrospective, multi-center cohort study included women ≤ 45 years who underwent autologous oocyte thaw following planned oocyte cryopreservation between January 2013 and September 2024. Baseline characteristics included age at freeze and thaw, BMI, AMH, and race. The primary outcome was oocyte survival after warming by age. Secondary outcomes included fertilization and blastulation rates, as well as outcomes by year of cryopreservation and warming. A modified Poisson regression model with generalized estimating equations was used, with statistical significance set at $p < 0.05$.

Results

A total of 1,339 patients underwent 1,427 oocyte vitrification cycles. Mean age at vitrification was 36.1 years, and mean duration of cryostorage prior to warming was 2.3 years. The mean number of metaphase II oocytes warmed per patient was 13, with a mean of 11.5 surviving. Overall, oocyte survival was 88.2%. Survival rates for patients < 35 , 35–37, 38–40, 41–42, and ≥ 43 years were 87.4%, 88.7%, 88.1%, 88.4%, and 88.4%, respectively. Survival differed significantly by clinical site. Mean fertilization rate was 72.2%. Mean blastulation rate was 39.8% and declined significantly with increasing age, from 43.7% in patients < 35 to 34.6%, 30.6%, and 31.7% in the 38–40, 41–42, and ≥ 43 age groups.

Conclusion

Oocyte survival does not decline with advancing female age, suggesting no association with early meiotic errors on survival. While fertilization rates remain stable, blastulation rates decrease with age. Improved survival by year of cryopreservation and warming suggests ongoing advances in laboratory techniques.

Introduction

The use of cryobiology has been applied to medicine dating back to 2500 BC. Since then, its use in reproductive medicine has allowed significant advancements in the field, including the first human birth from frozen sperm in 1953 [1] a frozen embryo in 1984 [2, 3], and a frozen oocyte in 1986 [4]. Improvements in freezing techniques using vitrification, a process of cryopreservation that freezes the cell into a glass-like state without the formation of ice crystals, has led to an increase in survivability of vitrified-warmed oocytes, making oocyte cryopreservation a more effective and reliable option for single

women [5]. With this improvement in efficiency, the American Society for Reproductive Medicine (ASRM) decreed that oocyte cryopreservation was no longer experimental, increasing access to those patients desiring fertility preservation and reproductive autonomy [3]. The decision was made after several studies suggested vitrification resulted in better oocyte survival and embryologic outcomes compared to slow freeze techniques, and vitrified oocytes performed equally as well as fresh oocytes [3, 5, 6–8].

One potential concern related to the use of vitrified oocytes was whether meiotic errors and ultimately embryo aneuploidy rates would be affected by the freeze-thaw process. During vitrification, the meiotic spindle disappears along with other morphologic changes to the oocyte, leading to initial concerns regarding the overall integrity and ploidy status of vitrified metaphase II (MII) oocytes [3, 9]. However, a small randomized control trial (RCT) by Forman et al. demonstrated no difference in aneuploidy among vitrified oocytes versus fresh oocytes, further establishing oocyte vitrification as a feasible option for fertility preservation [10].

Given the relatively short time frame that oocyte cryopreservation has been in use, there is a paucity of data on thaw outcomes, as the majority of oocytes remain cryopreserved for future use or are discarded when they are no longer needed. According to the 2021 Society of Advanced Reproductive Technology (SART) data, though the absolute number of planned oocyte cryopreservation cycles increased annually from 2012 to 2018, only 11% of those cycles have resulted in oocyte thaw, thereby limiting what is known about oocyte survival [11].

With the increase observed in fertility preservation cycles, several investigators have developed tools to help predict the chance of a successful pregnancy using vitrified-warmed oocytes [8, 12, 13]. One of the most widely used live birth probability calculators was developed by Goldman and colleagues to aid physicians in counseling patients [13]. This calculator estimates the probabilities of having at least one, two, or three live births based on a woman's age and the number of oocytes cryopreserved. However, several assumptions were made, including an assumed 95% survival of cryopreserved oocytes for women less than age 36, and an 85% survival for women aged 36 and older [13]. These age-based survival rates were decided based on internal data as well as survival rates based on available data from smaller studies prior to 2013 [3, 5, 13]. Since the development of this tool, a few larger studies have reported their clinic's survival rates of vitrified oocytes, which ranged from 68% – 82% [14–17]. A recent systematic review and meta-analysis evaluated 17,418 oocyte retrieval cycles on a global scale and found an aggregate survival of 81.4% [18]. Other predictive models also demonstrated significant heterogeneity in estimating future success. These more recent studies call into question the accuracy of widely available predictive models using oocyte survival rates that may be higher than the results reported by most centers.

Since the publication of the most commonly used oocyte success rate tools, embryology labs have gained a significant amount of experience with oocyte vitrification and warming and thus it is reasonable that oocyte survivability may have changed over the last decade. Since oocyte survivability is one of the main components that contributes to the calculated chance of live birth with vitrified oocytes, age

specific outcome data on oocyte survivability and usability are in need of an update. Therefore, the primary objective of this study was to evaluate survival rates of vitrified-warmed oocytes by age, as well as embryologic outcomes to determine whether age at freeze has a negative impact on oocyte survival and overall usability.

Methods

Design:

We conducted a retrospective, multi-center cohort study of all patients who underwent autologous oocyte thaw cycles following planned oocyte cryopreservation between January 1st, 2013 and September 11th, 2024. By 2013, all clinics included in this study were using only vitrification for planned oocyte cryopreservation.

Subjects:

All patients who underwent a planned oocyte cryopreservation cycle prior to age 46 were reviewed. Exclusion criteria included cycles where oocyte vitrification occurred at an external center, if oocyte cryopreservation was performed prior to gonadotoxic treatments, or any donor cycle (oocyte donor or recipient). Additionally, we excluded cycles that cryopreserved metaphase I (MI) oocytes in addition to metaphase II (MII) oocytes, which is an individualized decision made in some poor prognosis cases. For patients who underwent multiple cryopreservation cycles, data were aggregated into a twelve-month period from the index cycle. Thaw cycles that included oocytes from more than one cycle were only included if the cryopreservation cycles occurred within a twelve-month period of time.

Variables and Data Collection:

Demographic and outcome variables were collected from the electronic medical record system. Outcome variables included primary diagnosis, body mass index (BMI), age at oocyte cryopreservation, age at thaw, number of years oocytes remained frozen prior to warming, anti-Mullerian hormone level (AMH) and antral follicle count (AFC) at cryopreservation, peak estradiol level, total number of MII oocytes cryopreserved, number of MII oocytes warmed, number of MII oocytes that survived warming and were subsequently injected with sperm, number of oocytes fertilized (2pn), and the number of usable blastocysts. The primary outcome was oocyte survival after warming stratified by the SART age group categorization. Secondary outcomes evaluated fertilization (defined as number of thawed MII oocytes fertilized/number of MII oocytes successfully inseminated) and blastulation (defined as number of usable blastocysts/total number of oocytes fertilized) rates stratified by the SART age group categorization.

Oocyte Vitrification, Warming, and Fertilization:

Oocyte vitrification and warming were performed in a manner similar as previously described in literature [19]. Two hours after oocyte retrieval, oocytes were briefly exposed to hyaluronidase solution aliquot

(Hyase). Following this, they were mechanically denuded to remove any cumulus or corona cells using progressively smaller pipettes until the smallest size of 140 μ L. Next, oocytes were assessed for maturity, looking for the presence of a polar body and assessing the zona pellucida. The mature oocytes were then exposed to a series of cryoprotectants. This included 200 μ L of equilibrium solution [ES; 15 ml of 40 ml Human Tubal Fluid w/ HEPES (mHTF) + 10 ml SSS [mHTF + 20% Quinn's Advantage Serum Protein Substitute (SPS)]] and 15 ml of 6.0ml ethylene glycol (EG) + 6.0ml dimethyl sulfoxide (DMSO) + 28 ml 15% EG/DMSO] and placed onto a non-heated surface in the hood for twelve minutes. Then, mature oocytes were placed in 2 x 200 μ L of vitrification solution (VS; M-199 N'-2-hydroxyethylpiperazine-N0-2-ethanesulfonic acid buffered medium + 20% dextran serum substitute; Irvine Scientific) at room temperature (approximately 25° C). They were then loaded onto the Cryolock (BioDeseno), which was promptly plunged into liquid nitrogen with care to avoid bubbling.

For warming of vitrified oocytes, the Cryolock was plunged into one drop of thawing solution [TS; 5ml WS [16 ml mHTF + 4 ml SSS (mHTF + 20% SPS)] + 3.423g sucrose [1.0M sucrose + wash solution (WS)]] for one minute at 37° C. Next, the oocytes were moved to diluent solution (DS; 5 ml WS + 5 ml TS) for three minutes at room temperature. After DS solution, the oocytes were then exposed to WS for five minutes at room temperature, and then a second WS well for three minutes at 37° C. The oocytes were evaluated post-warming to ensure the integrity of the oolemma membranes, which indicates that the oocytes have survived the process. The polar bodies may degenerate during this process so they were also evaluated. Post-warm survival was defined as the total number of MII oocytes that survived the warming process divided by the total number of vitrified MIIs.

Intracytoplasmic sperm injection (ICSI) was performed on all mature oocytes after 2–4 hours of re-equilibration in 20% SPS. After ICSI, the inseminated oocytes were moved to a 10% SPS + gentamicin insemination dish for up to 7 days (Irvine Scientific) and evaluated for fertilization on day 1, and for blastulation between days 5–7 following ICSI.

Statistical Analysis:

We compared demographic and clinical characteristics across age groups with the use of means and standard deviations (SD), medians and interquartile ranges (IQR), or N (%) as appropriate. We compared both the mean (SD) and median (IQR) of our primary (percent MII oocytes surviving the warming process) and secondary (percent MII oocytes fertilized and percent fertilized oocytes completing blastulation) outcomes by age category. We further estimated risk ratios (RR) and 95% confidence intervals (CI) for each outcome comparing age categories with the use of Poisson regression models fitted with generalized estimating equations (GEE) to account for correlation between multiple freeze cycles per patient. Analyses were completed in R version 4.3.1 (Vienna, Austria), and significance set to a $p < 0.05$.

Results

A total of 1,399 patients met inclusion criteria for this study. Patient demographics by age group are listed in Table 1. The mean age at freeze was 36.1 years (standard deviation (SD) 3.5), and mean age of thaw was 38.5 (SD 4). Oocytes remained cryopreserved, on average, for 2.3 years prior to usage. However, there was a noticeably shorter time until these oocytes were used in the older age groups. For example, the average time oocytes remained cryopreserved prior to use was 3 years in the 35–37 group (SD 2.2), compared to only 0.3 years in the 43 + group (SD 0.2). Mean BMI for all patients was 25.2 kg/m² (SD 5.1), and was similar across each age group. Median AMH was 2.4 [IQR, 1.2–4.4] for the entire study cohort, with an expected age-related decline seen in the older age groups.

Table 1
Patient Demographics

N, freeze cycles	All-comers	< 35	35–37	38–40	41–42	43+
	1427	415	509	388	80	35
Age at freeze, mean (SD)	36.1 (3.5)	31.8 (2.3)	36 (0.8)	38.9 (0.8)	41.4 (0.5)	43.7 (0.8)
Age at thaw, mean (SD)	38.5 (4)	34 (3.8)	39.1 (2.3)	41 (1.8)	42.5 (1.1)	43.9 (0.8)
Number of years vitrified, mean (SD)	2.3 (2.1)	2.2 (2.4)	3 (2.2)	2.1 (1.8)	1.1 (1.1)	0.3 (0.2)
BMI at cryopreservation, mean (SD)	25.2 (5.1)	25 (5.3)	24.6 (4.6)	25.6 (5.1)	26.8 (5.7)	27.7 (6.1)
AMH at cryopreservation, median (IQR)	2.4 (1.2, 4.4)	3.4 (1.9, 5.7)	2.3 (1.2, 4)	2.1 (1.1, 3.9)	1.5 (0.8, 2.4)	0.9 (0.6, 2.2)
Race						
Caucasian	802 (56.2)	252 (60.7)	301 (59.1)	193 (49.7)	39 (48.8)	17 (48.6)
African American	132 (9.3)	32 (7.7)	29 (5.7)	44 (11.3)	18 (22.5)	9 (25.7)
Asian	206 (14.4)	58 (14)	76 (14.9)	59 (15.2)	11 (13.8)	2 (5.7)
Hispanic	71 (5)	15 (3.6)	25 (4.9)	26 (6.7)	2 (2.5)	3 (8.6)
Other	71 (5)	17 (4.1)	27 (5.3)	21 (5.4)	6 (7.5)	0 (0)
Unknown/refused	145 (10.2)	41 (9.9)	51 (10)	45 (11.6)	4 (5)	4 (11.4)

Survival outcomes of vitrified-warmed oocytes are demonstrated in Table 2. Amongst the entire cohort, a total of 21,841 oocytes were cryopreserved for the indication of planned oocyte cryopreservation. A total of 18,606 MII oocytes were ultimately warmed from 1,427 freeze cycles. The mean number of MII

oocytes thawed per cycle was 13 (SD 8.1), while the mean number that survived the warming process per cycle was 11.5 (7.3). There was an expected age-based decline in the number of oocytes retrieved per cycle. The overall survival following warming of MII oocytes for all age groups was 88.2% (SD 15.8). As seen in Fig. 1, survival did not differ by age group. The mean survival for women aged < 35 was 87.4% (SD 15.5). This was compared to 88.7% in women aged 35–37 [RR 1.02 (1.0–1.04)], 88.1% in women aged 38–40 [RR 1.02 (0.99–1.04)], 88.4% in women aged 41–42 [RR 0.99 (0.92–1.06)], and 88.4% in women aged 43+ [RR 1.02 (0.97–1.06)]. The median survival per age group is demonstrated in Fig. 2.

Table 2
Oocyte Survival Outcomes

N, patients	All-comers	< 35	35–37	38–40	41–42	43+	p-value
	1339	403	482	358	79	34	
N, freeze cycles	1427	415	509	388	80	35	
# of MII warmed	18606	5758	6832	4800	869	347	
# of MII warmed per cycle, mean (SD)	13 (8.1)	13.9 (8.4)	13.4 (7.6)	12.4 (7.9)	10.9 (8.3)	9.9 (9.1)	
# of MII that survived warming per cycle, mean (SD)	11.5 (7.3)	12.1 (7.7)	11.9 (7)	11 (7.2)	9.3 (6.5)	8.8 (8.4)	
% survival after thaw (N survived/N thawed)							
Median (IQR)	93.8 (81.8, 100)	92.9 (80, 100)	93.3 (83.3, 100)	95.2 (81.8, 100)	100 (84.6, 100)	96.4 (79.6, 100)	
Mean (SD)	88.2 (15.8)	87.4 (15.5)	88.7 (14.2)	88.1 (17.3)	88.4 (19)	88.4 (15.6)	
RR (95% CI)		Ref	1.02 (1, 1.04)	1.02 (0.99, 1.04)	0.99 (0.92, 1.06)	1.02 (0.97, 1.06)	0.50

We did find a difference in survival across the various clinical sites, with median survival ranging from 84.9% (IQR 17.7) to 89.4% (IQR 14.1) [Site 1 RR 1.0 (0.96, 1.03), Site 2 RR (Ref), Site 3 RR 0.95 (0.92, 0.99), Site 4 RR 1.0 (0.95, 1.04)] (Table 3). There was no difference in survival outcomes based on the year oocytes were frozen. Additionally, there was no difference in survival rates when evaluating length of time oocytes remained cryopreserved for ($p = 0.35$).

Table 3
Survival Rates Across Various Clinical Sites

Clinic	Median Survival (%)	RR	95% CI
Site 1	89.4	1.0	0.96, 1.03
Site 2	89.3	—	Ref
Site 3	84.9	0.95	0.92, 0.99
Site 4	87.7	1.0	0.95, 1.04

After adjusting for age and clinical site, we found a significant difference in survival rates between the different clinics ($p < 0.01$). Similar to our unadjusted model, there was no difference in survival rates when evaluating length of vitrification between the different age groups after adjusting for age and clinical site ($p = 0.18$). There was, however, a significant difference in survival rates based on when an oocyte was cryopreserved (Table 4). Namely, oocytes were less likely to survive if cryopreserved between 2013–2015, compared to 2016–2018 [RR 1.05 (1.02–1.08), $p < 0.01$], 2019–2021 [RR 1.09 (1.06–1.12), $p < 0.01$], and 2022–2024 [RR 1.06 (1.02–1.1), $p < 0.01$]. Oocytes were more likely to survive the warming process if thawed after 2018, with significance noted in 2019–2021 [RR 1.08 (1.0–1.17), $p = 0.036$] (Table 5). After adjusting for the year of cryopreservation and year of warming, we found a significant difference in survival rates if an oocyte was warmed after 2018, regardless of the year of cryopreservation (Table 6).

Table 4
Survival Outcomes by Year of Cryopreservation

Year of Cryopreservation	RR	CI	P-value
2013–2015	Ref	Ref	—
2016–2018	1.051	1.021, 1.082	< 0.01
2019–2021	1.09	1.060, 1.120	< 0.01
2022–2024	1.057	1.020, 1.096	< 0.01

Table 5
Survival Outcomes by Year of Thaw

Year of Thaw	RR	CI	P-value
2013–2015	—	—	Ref
2016–2018	1.05	0.97, 1.13	0.2
2019–2021	1.08	1.00, 1.17	0.036
2022–2024	1.07	0.99, 1.16	0.079

Table 6
Association between Year of Cryopreservation-Year of Thaw

Year of Cryopreservation : Year of Thaw	RR	95% CI	p-value
2013–2015 : 2013–2015	—	—	
2013–2015 : 2016–2018	1.051	0.965, 1.143	0.254
2013–2015 : 2019–2021	1.091	1.011, 1.177	0.026
2013–2015 : 2022–2024	1.095	1.000, 1.200	0.05
2016–2018 : 2016–2018	1.097	1.016, 1.184	0.018
2016–2018 : 2019–2021	1.132	1.051, 1.219	0.001
2016–2018 : 2022–2024	1.113	1.031, 1.201	0.006
2019–2021: 2019–2021	1.152	1.072, 1.238	0
2019–2021: 2022–2024	1.144	1.064, 1.231	0
2022–2024 : 2022–2024	1.113	1.033, 1.199	0.005

The mean fertilization rate of previously vitrified oocytes was 72.2% for all ages (SD 21.1). There was no difference observed in fertilization rates across the different age groups (Table 7). Those patients less than 35 years old had an average fertilization rate of 72.9% (SD 20.9). The mean fertilization in those aged 35–37 was 73.0% [RR 1.0 (0.96–1.03)], 71.0% in those aged 38–40 [RR 0.97 (0.94–1.01)], 69.9% in those aged 41–42 [RR 0.95 (0.89–1.01)], and finally 71.8% in the 43 + group.

Table 7
Embryology Outcomes

	All-comers	< 35	35–37	38–40	41–42	43+	p-value
% 2PN (N fertilized/N inseminated)							
Median (IQR)	75 (62.5, 87.2)	75 (61.7, 88.2)	75 (62.5, 87.5)	75 (62.5, 85.7)	71.4 (62, 83.3)	69.2 (51.5, 92.9)	
Mean (SD)	72.2 (21.1)	72.9 (20.9)	73 (20)	71 (22.7)	69.9 (21.9)	71.8 (21.2)	
RR (95% CI)		Ref	1 (0.96, 1.03)	0.97 (0.94, 1.01)	0.95 (0.89, 1.01)	0.93 (0.84, 1.03)	0.19
Blastulation rate (N blasts/N fertilized)							
Median (IQR)	38.5 (21.4, 57.1)	41.7 (25, 63.6)	41.3 (25, 60)	33.3 (17.4, 50)	28.6 (11.1, 50)	22.2 (0, 50)	
Mean (SD)	39.8 (26.1)	43.7 (27.9)	42.4 (24.9)	34.6 (23.8)	30.6 (25.4)	31.7 (33.2)	
RR (95% CI)		Ref	0.98 (0.91, 1.05)	0.82 (0.75, 0.89)	0.65 (0.54, 0.78)	0.54 (0.41, 0.69)	< 0.01

As demonstrated in Fig. 1, there was a significant decline in blastulation rates with increasing age groups (Fig. 1). The mean blastulation for women < 35 was 43.7% (SD 27.9). This was similar to the 42.4% [RR 0.98 (0.91–1.05)] blastulation rate for women aged 35–37. In contrast, a significant difference was observed in the 38–40, 41–42, and 43 + age groups, with mean blastulation rates decreasing to 34.6% [RR 0.82 (0.75–0.89)], 30.6% [RR 0.65 (0.54–0.780)], and 31.7% [RR 0.54 (0.41–0.69)], respectively.

Discussion

The primary aim of this study was to evaluate whether oocyte survival following warming was impacted by age of cryopreservation. As planned oocyte cryopreservation continues to gain popularity, our knowledge of oocyte disposition will continue to increase as more oocytes are warmed for use. At this time, however, SART estimates only 11% of vitrified oocytes have been utilized in the US, similar to global numbers [11, 17, 18, 20]. Therefore, it is imperative we have a proper understanding of both the survival rates of vitrified-warmed oocytes, as well as their reproductive potential, to appropriately counsel patients who already have, or will pursue fertility preservation in the future.

For those patients who returned with the intent to utilize their cryopreserved oocytes, 85% were warmed for use. Overall survival for all age groups was 88.2%. This is higher than previously reported survival rates in prior studies [14–17]. We did not find a difference in survival rates between different age groups,

as other studies have demonstrated [15, 16]. Similar to prior studies, we did not find a difference in survival based on the number of years an oocyte remained cryopreserved for [16, 18, 21]. This can provide additional reassurance to patients that oocyte stability is maintained irrespective of how long an oocyte is cryopreserved for. Overall, many patients in our study cohort had 100% survival of their oocytes, irrespective of age, with median survival for all ages of 93.8% (Fig. 2). In our study, we found survival rates to not be normally distributed. This is an interesting finding that will help to inform follow-up studies that will evaluate for more specific causes of oocytes that do not survive the warming process.

In 2010, Smith et al established equivalent, if not improved survival outcomes of oocytes using vitrification compared to slow-freeze cycles [6]. Since then, several studies have compared survival of vitrified oocytes to donor oocytes, as well as evaluating overall survival outcomes from their clinics. Seshadri et al compared outcomes of 1490 vitrified oocytes from egg donors to age-matched controls using ICSI and autologous oocytes in a fresh cycle. The authors demonstrated an overall survival of 73.6% of vitrified-warmed oocytes from egg donors [14]. Another study assessed survival outcomes of both slow-freeze and vitrified oocytes and found no difference between SART age groups [16]. In this study, survival rates ranged from 66.6% to 78%, and approximately 60% of cycles originated from slow-freeze cycles. Most recently, Kirubarajan et al performed a systematic review and meta-analysis of 27 studies. They included over 24,000 oocytes with an aggregate survival of 81.4% [18]. However, age of freeze was not provided in this review. Our study differs in that we examined oocyte disposition and reproductive potential from vitrification cycles only to better assess current practices. To our knowledge, this is the largest study evaluating thaw outcomes of vitrified oocytes specifically by age.

Similar to initial models which found consistent fertilization rates across all ages, we found no difference in fertilization rates between age groups, with mean fertilization of 72.2% [8, 13]. Likewise, another study evaluating blastulation outcomes in embryo cryopreservation cycles found no difference in fertilization rates based on maternal age, except in those older than 44 [22]. Fertilization rates between fresh and frozen oocytes have previously been demonstrated to be equivalent, and in the range of 71–79% [3, 5]. Our overall fertilization rate is comparable to these studies.

We found a significantly lower blastulation rate in patients 38 years and older. These findings are similar to Romanski et al who demonstrated blastocyst conversion rates begin to decline after the age of 40 [22]. These results can be explained by an age-based decline in oocyte quality, with several studies noting decreased blastulation in older age groups [15, 22]. With fewer eggs retrieved per cycle and diminishing blastulation rates in the older age groups, patients should be counseled on the likely need for additional cycles for a reasonable chance of success for a future pregnancy.

One of the most important aspects in caring for patients pursuing planned oocyte cryopreservation relies on managing patient expectations regarding the number of eggs cryopreserved in the context of their future family goals. Currently established oocyte cryopreservation success tools may over or underestimate patient success by incorporating oocyte survival rates that may now be less accurate

compared to current laboratory outcomes; our data provides age-specific survival rates that can lead to better patient counseling, specifically, that there is no decline observed in oocyte survival rates with increasing age. Interestingly, we did see a significant difference in oocyte survival based on the year an oocyte was cryopreserved as well as the year of warming, suggesting improvements in both vitrification and warming techniques contributed to improved survival in more recent years. We did find that survival was not consistent across various clinical sites, and more specifically, one clinic had lower survival rates compared to others in our cohort. It is imperative that each individual clinic disclose their own clinic-specific statistics on survival outcomes for appropriate patient counseling [23] and it would be useful if publicly available counseling tools allowed users to modify the oocyte survival to more accurately reflect the outcomes of their clinics.

Strengths of our study include a multi-center database encompassing 18,606 oocytes that were warmed for use. As our study period spanned over 10 years, we had the opportunity to capture over 1300 women who returned to utilize previously vitrified oocytes. To our knowledge, this is the largest study to evaluate outcomes from autologous vitrified oocytes only, which represents the current standard of care for patients undergoing planned oocyte cryopreservation cycles. This data will help provide more appropriate counseling on oocyte survival outcomes and chance of success in the future.

We acknowledge there are limitations to our study. As with any retrospective study, our results are limited by the reliance on existing records within each clinics' medical record system. Although incomplete charts were manually reviewed, this can still introduce potential bias which may affect the accuracy and generalizability of our findings. We excluded patients who underwent oocyte cryopreservation for medical indications as some studies have suggested lower AMH levels in cancer patients prior to gonadotoxic treatment compared to age-matched controls [24]. Therefore, our results may not be generalizable to those undergoing medically indicated fertility preservation prior to gonadotoxic treatment. As demonstrated in our results, individual clinics in our study demonstrated a significant difference in survival rates, therefore the results of this study may not be generalizable to every clinic. Clinicians should be aware of potential variations in vitrification and warming techniques, and most importantly, the experience level of embryologists and lab staff, as these variables may all affect individual clinic results.

Conclusion

Survival rates of vitrified oocytes is not associated with increasing female age. Similarly, fertilization rates remain constant for all age groups, however a significant decline is noted in blastulation rates in older age groups, which can be attributed to increasing aneuploidy. Future studies should aim to identify explanations for oocytes that do not survive the warming process to better understand why this occurs and to possibly continue to improve upon current oocyte survival rates.

Declarations

Author Contribution

Anupama Rambhatla MD: conceptualization, data curation, formal analysis, investigation, methodology, writing (original), writing (review and editing) Kyle Le MD: conceptualization, data curation, methodology, writing (original) Kerry Flannagan PhD: conceptualization, formal analysis, methodology, validation, writing (review and editing) Jing Wu MD: formal analysis, methodology, validation, writing (review and editing) Jerry Wang MS: data curation, methodology Amalia Namath MD: investigation, writing (review and editing) Allison Eubanks MD: investigation, writing (review and editing) Atoosa Ghofranian MD: investigation, writing (review and editing) Jensen Reckhow MD: investigation, writing (review and editing) Joshua Lim BS: methodology, writing (original draft) Taer Han BS: methodology, writing (original draft) Rebecca Brohammer BS: data curation, investigation Luis R Hoyos MD: Conceptualization, supervision, writing (review and editing) Kate Devine MD: Conceptualization, supervision, writing (review and editing) Ruth B Lathi MD: Conceptualization, supervision, writing (review and editing) Phillip Romanski MD: Conceptualization, data curation, formal analysis, investigation, methodology, supervision, validation, writing (original draft), writing (review and editing) Ravi Agarwal MD: Conceptualization, data curation, formal analysis, investigation, methodology, supervision, validation, writing (original draft), writing (review and editing) All authors reviewed the manuscript.

Declaration of Generative AI and AI-assisted technologies

There were no generative AI or AI-assisted technologies used in the preparation of this manuscript.

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Figures

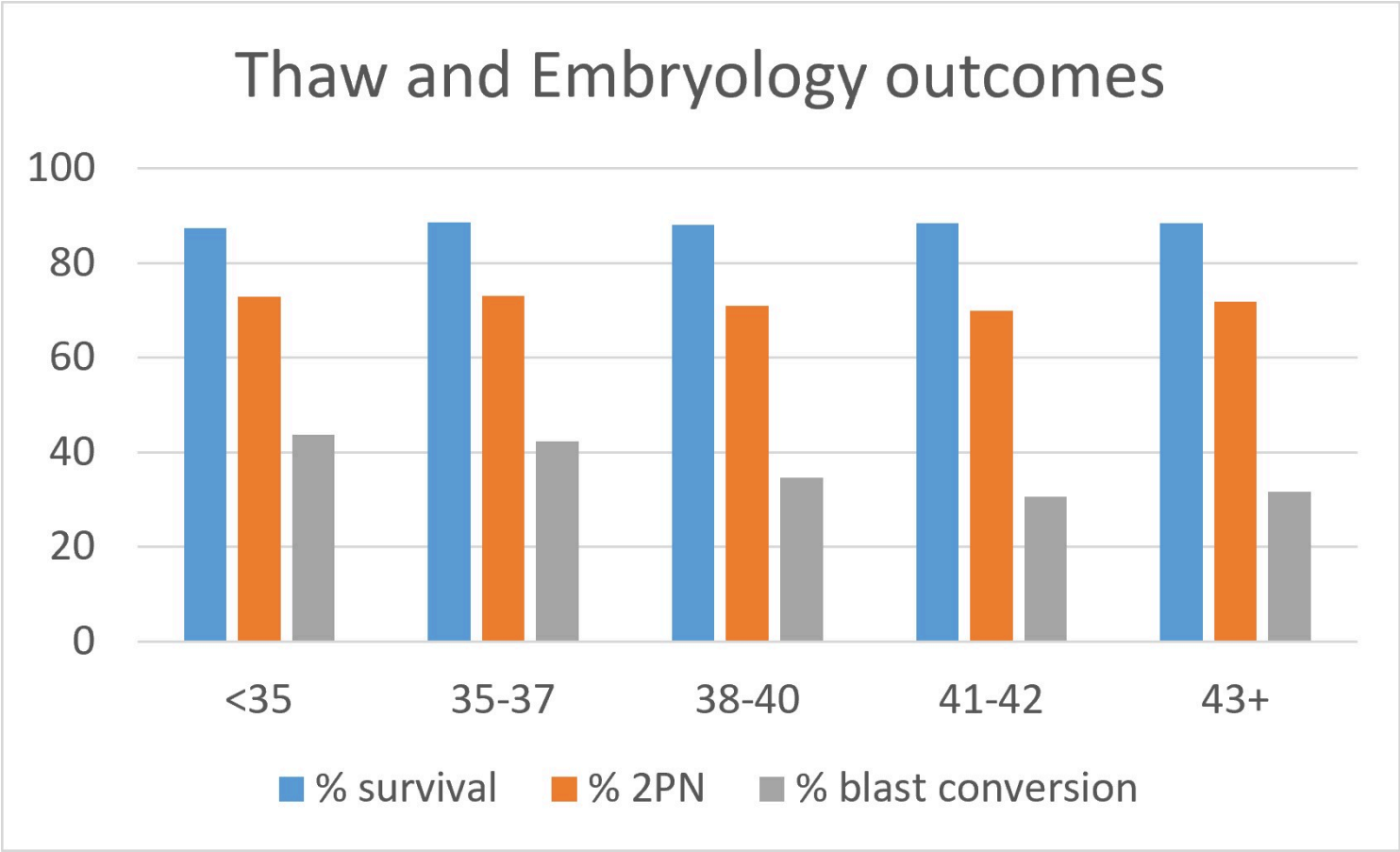


Figure 1

Thaw and Embryology Outcomes

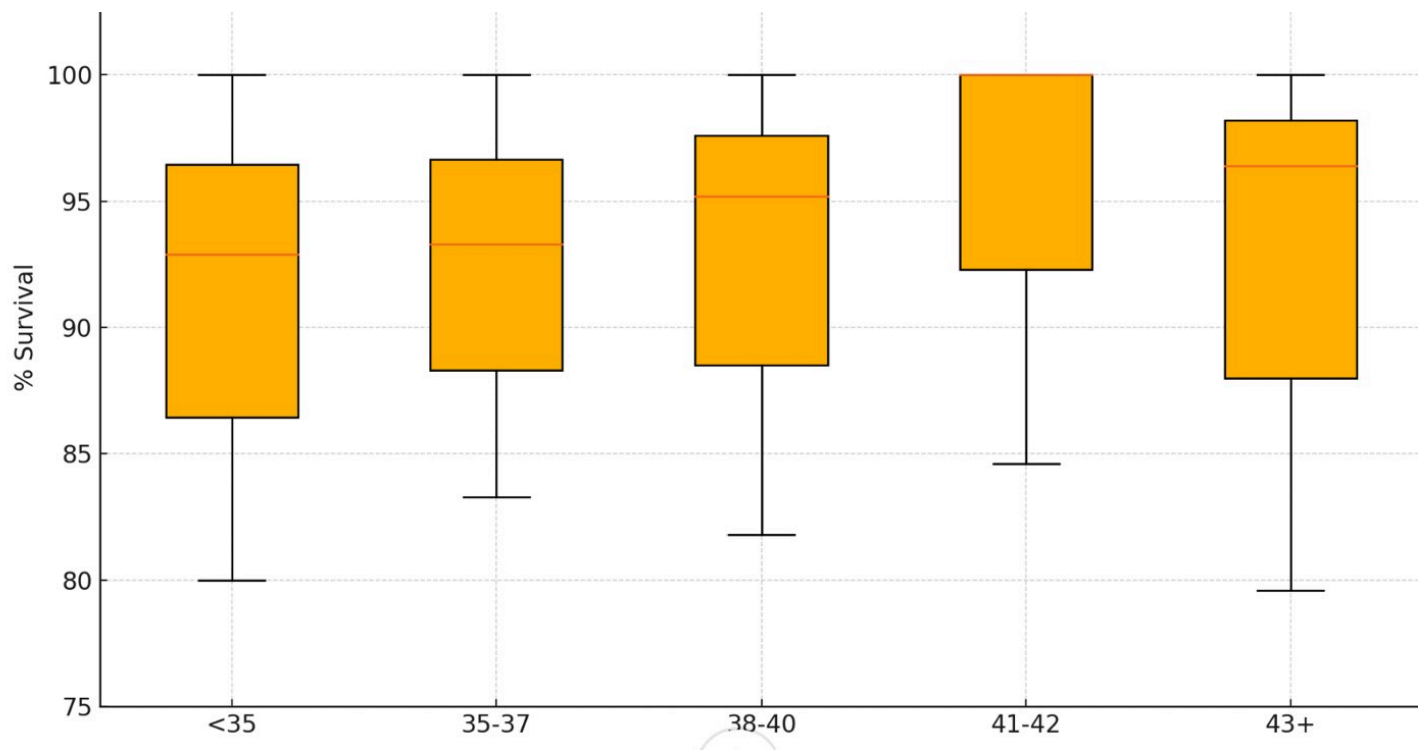


Figure 2

Median Survival by Age Group