

FRESH VERSUS FROZEN EMBRYO TRANSFER OVERVIEW



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DISCLOSURES

Celmatix: sponsored research



Overview

- Definitions
- Fresh versus FET
- Fresh versus freeze-only transfer – example studies
- Cryopreservation in cancer patients



Definitions

- **Fresh transfer:** cycles where embryo(s) are transferred during the same cycle as ovarian stimulation is performed
- **Frozen embryo transfer (FET):** cycles where embryo(s) are transferred in a subsequent natural or medicated cycle, after being frozen following an ovarian stimulation cycle
 - **Freeze-only transfer (subset of FET):** cycles where all embryos are electively frozen and transferred in a later natural or medicated cycle (also used terms: elective FET, freeze-all)

Note: FETs may include transfer of supernumerary embryos (after the best embryos from the cohort are already transferred in a prior fresh or FET cycle), which makes freeze-only transfers a stronger direct comparison with fresh transfer



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- Definitions

- Fresh versus frozen transfer

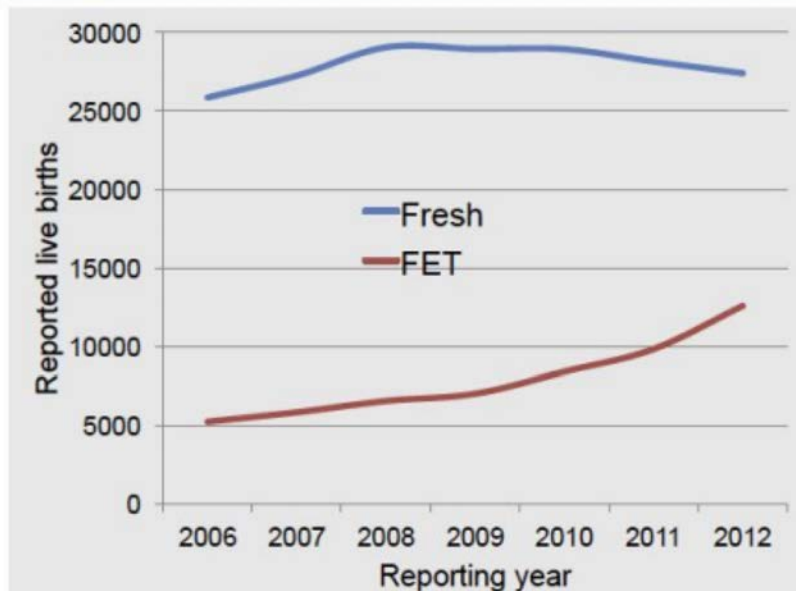
- Fresh versus freeze-only transfer – example studies

- Cryopreservation in cancer patients



Rate of FET increase in the United States

FIGURE 3



Trends in estimated numbers of live births with fresh transfer and FET. These estimates were calculated by multiplying the reported numbers of cycles and the respective birth rates on SART's national report, and summing across age groups.

Shapiro. Cryopreservation of embryo cohorts. *Fertil Steril* 2014.

- **FET is on the rise**, increasing 82.5% from 2006-2012, compared to 3.1% for fresh cycles during this time¹
- Reasons for this FET increase include advances in vitrification, preimplantation genetic screening, and increased awareness of freeze-only protocols



Fresh versus frozen transfer – maternal and fetal risks

- **Frozen embryo transfer may be associated with better maternal and fetal outcomes in some parameters, including lower risk of preterm delivery, placental complications, perinatal mortality¹⁻⁴**
- However, some adverse outcomes may have increased likelihood with FET, including macrosomia and placenta accreta

1. Fertility Sterility 102.1 (2014): 3-9.
2. Fertility Sterility 2012;98:368-77 e1-9.
3. Human Reproduction Update 2013;19:87-104.
4. Fertility Sterility 2012;97:1338-42.

Comparison of fresh transfer and FET with respect to maternal and fetal risks.

Reduced risks in FET

OHSS
LBW (<2,500 g)
SGA
Preterm LBW
Preterm delivery (<37 wk)
Placenta previa
Placental abruption
Antepartum hemorrhage
Perinatal mortality

Increased risk with FET

Placenta accreta
Macrosomia (>4,500 g)
Large for gestational age
Cesarean section delivery

Risks without a clear difference

Implantation failure^a
Ectopic pregnancy^a
Pre-eclampsia
Very low birth weight (<1,500 g)
Very preterm delivery (<32 wk)
Neonatal intensive care unit admission
Congenital abnormalities

^a May depend on the FET protocol, patient population, and cycle parameters.

Shapiro. Cryopreservation of embryo cohorts. Fertil Steril 2014.

Evidence also suggests that FETs may result in better transfer outcomes-1st meta-analysis

Fresh embryo transfer versus frozen embryo transfer in in vitro fertilization cycles: a systematic review and meta-analysis

Matheus Roque, M.D.,^{a,c} Karinna Lattes, M.D.,^{a,d} Sandra Serra, M.Sc.,^{a,d} Ivan Solà, B.Psych.,^{e,f,g} Selmo Geber, Ph.D.,^{c,h} Ramón Carreras, Ph.D.,^b and Miguel Angel Checa, Ph.D.^{b,d}

Meta-analysis of 3 studies (total 263 events) found that:

- FET resulted in a **statistically significant increase in the ongoing pregnancy rate (RR 1.32, 95% CI 1.10–)** and **clinical pregnancy rate (RR 1.31, 95% CI 1.10–1.56)** compared to fresh transfer
- Fresh group showed a higher miscarriage rate compared with the FET group, but this difference did not reach statistical significance (33 events; RR 0.83, 95% CI 0.43–1.60)



Evidence that FETs may result in better transfer outcomes (continued)

Characteristics of the clinical trial included in the review.

Study ID	Patients (Fresh/FET)	Age, y (Fresh/FET)	Duration of trial	Day of embryo transfer	Outcome
Aflatoonian et al. (24)	374 (187/187) High responders	28.1 ± 3.5/27.3 ± 4.4	February 2007– February 2009	Day 2	Ongoing pregnancy Implantation Clinical pregnancy Miscarriage rate
Shapiro et al. (13)	137 (67/70) Normal responders	32.9 ± 3.7/33.0 ± 3.8	October 2007– October 2010	Day 5 (blastocyst)	Ongoing pregnancy Implantation Clinical pregnancy Early pregnancy loss
Shapiro et al. (25)	122 (62/60) High responders	31.4 ± 3.7/30.6 ± 3.7	July 2007–July 2010	Day 5 (blastocyst)	Ongoing pregnancy Implantation Clinical pregnancy Early pregnancy loss

Roque. Elective frozen-thawed embryo transfer. Fertil Steril 2013.

- In conclusion, the meta-analysis suggests that there is **evidence of moderate quality that the implantation, clinical, and ongoing pregnancy rates of ART cycles may be improved by performing FET compared with fresh embryo transfer**
- These results may be explained by improved embryo endometrium synchrony achieved with endometrium preparation cycles instead of controlled ovarian stimulation cycles



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Freeze-only versus fresh transfer

- **Freeze-only literature more limited:** two randomized controlled trials (RCTs) until recently, several small trials, and retrospective matched cohort study all suggested **improved pregnancy outcomes with freeze-only transfer**⁶⁻¹⁰
- RCT of 179 patients with fresh versus freeze-only transfer in euploid embryos found **increased ongoing pregnancy and live birth rates in freeze-only, but no significant difference in implantation rates**¹¹

6. Fertility Sterility 2011;96:344-8.

8. NEJM 2016;375:523-33.

9. Fertility Sterility 2015;103:1190-3.

10.. Reproductive Biomedicine Online 2014;29:286-90.

11. Fertility Sterility 107.3 (2017): 723-730.



Freeze-only versus fresh transfer (continued)

- Few other studies have investigated frozen transfer of PGS-screened embryos but have not compared fresh vs frozen/freeze-only transfer directly¹²⁻¹³
- Two large retrospective studies from Stanford and Celmatix **have reported benefits of freeze-only transfer for both non-PGS and PGS embryos**¹⁴⁻¹⁵

12. Molecular Human Reproduction 2005;11:195-205.

13. Human Reproduction 2011;26:1813-25.

14. Fertility Sterility 108, no. 2 (2017): 254-261.

15. ASRM 2017



Freeze-only versus fresh transfer (continued)

- Previous studies have suggested that frozen transfer may be associated with better pregnancy outcomes due to **supraphysiologic hormone levels in controlled ovarian stimulation affecting genes involved in implantation, placentation, endometrial angiogenesis, and endometrial maturation**¹⁶⁻²⁷

16. Biology Reproduction 2010;82:679-86.

17. RBMO 2011;22:263-71.

18. Human Reproduction 2009;24:1436-45.

19. Human Reproduction 2009;24:1330-8.

20. Human Reproduction 2010;25:265-7

21. Fertility Sterility 2011;95:548-53.

22. Human Reproduction 2013;28:6-9.

23. Fertility Sterility 1999;71:1040-7.

24. JCEM 2004;89:5742-52.

25. Fertility Sterility 1997;67:521-6.

26. Fertility Sterility 2002;78:1025-9.

27. Human Reproduction Update 2007;13:343-55.



Freeze-only versus fresh transfer RCT

Evidence of impaired endometrial receptivity after ovarian stimulation for in vitro fertilization: a prospective randomized trial comparing fresh and frozen-thawed embryo transfer in normal responders

Bruce S. Shapiro, M.D., Ph.D.,^{a,b} Said T. Daneshmand, M.D.,^{a,b} Forest C. Garner, M.Sc.,^{a,b} Martha Aguirre, Ph.D.,^a Cynthia Hudson, M.S.,^a and Shyni Thomas, B.Sc.^a

- **RCT of blastocyst transfer:** 53 fresh patients and 50 freeze-only
- All were first-time IVF patients aged <41 years, with cycle day 3 FSH <10 mIU/mL and 8-15 antral follicles.
- **Clinical pregnancy rate per transfer was 84.0% in the freeze-only (significantly greater than 54.7% in the fresh group)**
- Implantation rates were 70.8% and 38.9%, respectively, and ongoing pregnancy rates per transfer (at 10 weeks' gestation) were 78.0% and 50.9%, respectively
- Attributable risk percentage of implantation failure due to reduced endometrial receptivity in the fresh group was 64.7%.



ORIGINAL ARTICLE

Fresh versus Frozen Embryos for Infertility in the Polycystic Ovary Syndrome

Z.-J. Chen, Y. Shi, Y. Sun, B. Zhang, X. Liang, Y. Cao, J. Yang, J. Liu, D. Wei,
N. Weng, L. Tian, C. Hao, D. Yang, F. Zhou, J. Shi, Y. Xu, J. Li, J. Yan, Y. Qin,
H. Zhao, H. Zhang, and R.S. Legro

- 1508 women with PCOS undergoing first IVF cycle randomized to either fresh or freeze-only transfer of day 3 embryos
- Freeze-only transfer resulted in a **higher frequency of live birth after the first transfer than did fresh-embryo transfer** (49.3% vs. 42.0%), RR 1.17 (95% CI 1.05 to 1.31; P=0.004)
- Freeze-only transfer also had a **lower frequency of pregnancy loss (22.0% vs. 32.7%)** RR 0.67 (95% CI, 0.54 to 0.83; P<0.001), **and of the ovarian hyperstimulation syndrome** (1.3% vs. 7.1%), RR 0.19 (95% CI, 0.10 to 0.37; P<0.001)
- However, FET was associated with **higher frequency of preeclampsia** (4.4% vs. 1.4%), RR 3.12 (95% CI, 1.26 to 7.73; P=0.009)
- No significant between-group differences in rates of other pregnancy and neonatal complications.



Freezing of all embryos in in vitro fertilization is beneficial in high responders, but not intermediate and low responders: an analysis of 82,935 cycles from the Society for Assisted Reproductive Technology registry

Kelly S. Acharya, M.D.,^a Chaitanya R. Acharya, Ph.D., P.S.M.,^b Katherine Bishop, M.D.,^a Benjamin Harris, M.D.,^a Douglas Raburn, Ph.D.,^a and Suheil J. Muasher, M.D.^a

- Analysis of 82,935 SART cycles (69,102 patients had their first fresh transfer, and 13,833 had a first FET)²⁸
- **High responders were found to have a higher CPR and LBR in the FET cycles compared with the fresh ET cycles (61.5 vs. 57.4%; 52.0 vs. 48.9%)**
- In intermediate responders, both CPR and LBR were higher after fresh ET compared with FET (49.6% vs. 44.2%; 41.2 vs. 35.3%)
- Similarly, in low responders, CPR and LBR were higher after fresh compared with FET (33.2% vs. 15.9%; 25.9% vs. 11.5%).
- Conclusion: A freeze-all strategy is beneficial in high responders but not in intermediate or low responders, thus refuting the idea that freeze-all cycles are preferable for all patients.



Optimal euploid embryo transfer strategy, fresh versus frozen, after preimplantation genetic screening with next generation sequencing: a randomized controlled trial

Alison Coates, B.Sc.,^{a,e} Allen Kung, B.S.,^{c,e} Emily Mounts, M.S.,^a John Hesla, M.D.,^a Brandon Bankowski, M.D.,^a Elizabeth Barbieri, M.D.,^a Baris Ata, M.D.,^d Jacques Cohen, Ph.D.,^b and Santiago Munné, Ph.D.^b

- RCT of 179 patients randomized to **freeze-only versus fresh transfer of euploid blastocysts**
- Implantation rate per embryo transferred showed an improvement in the frozen group compared with the fresh group, but not significantly (75% vs. 67%).
- **Ongoing pregnancy rates (80% vs. 61%) and live birth rates (77% vs. 59%) were significantly higher in the frozen group compared with the fresh group.**



Freeze-only versus fresh embryo transfer in a multicenter matched cohort study: contribution of progesterone and maternal age to success rates

Ange Wang, M.D.,^a Anthony Santistevan, M.S.,^b Karen Hunter Cohn, Ph.D.,^b Alan Copperman, M.D.,^{c,d} John Nulsen, M.D.,^{e,f} Brad T. Miller, M.D.,^g Eric Widra, M.D.,^h Lynn M. Westphal, M.D.,^a and Piraye Yurttas Beim, Ph.D.^b

- Retrospective matched cohort study of **13 academic and private fertility centers** in the United States
- **Propensity score analysis identified 2,910 matched blastocyst transfer cycles (1,455 fresh, 1,455 freeze-only)**
- For fresh cycles, luteal support was initiated after retrieval and embryos were transferred into the uterus at the blastocyst stage
- For freeze-only cycles, embryos were cryopreserved according to established practice protocols at each clinic
 - In a subsequent cycle, patients underwent blastocyst FET in either a natural or medicated cycle (using estrogen and progesterone supplementation)



METHODS

- Cohorts were matched on the following measures:
 - **Patient characteristics:** maternal age, clinic, gravidity, parity, diagnosis, body mass index
 - **Ovarian reserve:** antral follicle count, basal follicle stimulating hormone/luteinizing hormone/estradiol,
 - **Cycle characteristics:** progesterone (P) at trigger, eggs retrieved, embryo cohort size, and embryos transferred
- Generalized estimating equations modeling was used to compute the odds ratios (ORs) of ongoing pregnancy
- Receiver operating curve (ROC) analysis was used to determine cutoffs for maternal age and P at trigger



Baseline characteristics

- All characteristics were similar between the fresh and freeze-only groups after matching, as seen in Table 1

TABLE 1

Baseline characteristics of fresh and freeze-only cohorts after propensity score matching.

Metric	Fresh	Freeze-only	P value
N	1,455	1,455	–
Age (y)	34.1 (4.0)	34.1 (4.3)	.98
BMI	24.8 (4.8)	25.0 (5.1)	.21
Parity	0.2 (0.6)	0.2 (0.6)	.58
Gravidity	0.7 (1.2)	0.7 (1.2)	.78
Basal AFC	17.8 (9.4)	17.9 (9.5)	.78
Day 3			
FSH	6.7 (2.1)	6.9 (2.1)	.11
E ₂	51.5 (22.8)	51.4 (22.5)	.91
LH	7.3 (4.1)	7.4 (4.5)	.57
Gonadotropin dose	2,536.5 (1,698.7)	2,563.8 (1,589.9)	.66
P at trigger	1.5 (1.1)	1.5 (1.0)	.19
Oocytes retrieved	20.8 (10.3)	21.2 (11.4)	.37
No. of usable embryos	5.6 (3.9)	5.7 (3.9)	.57
Endometrial thickness (mm)	10.2 (2.2)	10.0 (2.3)	.46
No. of embryos transferred	1.5 (0.5)	1.5 (0.5)	.76
% ICSI	93.7%	91.6%	.94
Clinic distribution ^a	–	–	.82
Diagnosis			
DOR	8.5%	7.8%	.59
Endometriosis	6.0%	5.7%	.81
Idiopathic	4.3%	3.6%	.45
Male factor	20.8%	18.7%	.16
None provided	3.2%	3.3%	.1
Other	18.8%	19.7%	.57
Ovulatory dysfunction	13.3%	15.0%	.2
PCOS	6.3%	6.3%	.1
Tubal	17.9%	19.0%	.5
Uterine	1.0%	0.9%	.85

Note: Mean (± standard deviation) is shown for continuous variables, and percentages are shown for dichotomous variables. AFC = antral follicle count; BMI = body mass index; DOR = diminished ovarian reserve; FSH = follicle-stimulating hormone; E₂ = estradiol; LH = luteinizing hormone; P = progesterone; PCOS = polycystic ovary syndrome.

^a P value is the result of a chi-square test for the difference in distribution of clinics between protocols.

Wang. Freeze-only versus fresh transfer cycle success. *Fertil Steril* 2017.

Pregnancy outcomes

TABLE 2

Pregnancy outcomes in matched data.

Outcome	Fresh	Freeze-only	Odds ratio (Freeze-only vs. Fresh)	P value
Ongoing pregnancy rate	45.3% (42.7%, 47.9%)	52.0% (49.4%, 54.6%)	1.31 (1.13, 1.51)	<.001
Implantation rate	42.0% (39.5%, 44.5%)	46.8% (44.2%, 49.4%)	1.21 (1.05, 1.41)	<.01

Note: Values in parentheses are 95% confidence interval.

Wang. Freeze-only versus fresh transfer cycle success. *Fertil Steril* 2017.

TABLE 3

Ongoing pregnancy rates comparison between freeze-only and fresh cycles by progesterone and age strata in matched data.

P at trigger	Age (y)	Fresh		Freeze-only		Odds ratio (Freeze-only vs. Fresh)	P value
		n	OPR (%)	n	OPR (%)		
≤1	≤35	302	56.4 (51.6, 61.2)	284	54.6 (49.7, 59.5)	0.93 (0.70, 1.23)	.61
	>35	203	45.1 (39.8, 50.5)	198	48.9 (43.5, 54.3)	1.17 (0.86, 1.58)	.33
>1	≤35	576	46.1 (42.3, 49.9)	578	54.1 (50.3, 57.9)	1.38 (1.11, 1.71)	<.01
	>35	374	35.2 (31.0, 39.5)	395	48.4 (44.0, 52.8)	1.73 (1.34, 2.24)	<.0001

Note: Values in parentheses are 95% confidence interval. OPR = ongoing pregnancy rates; P = progesterone.

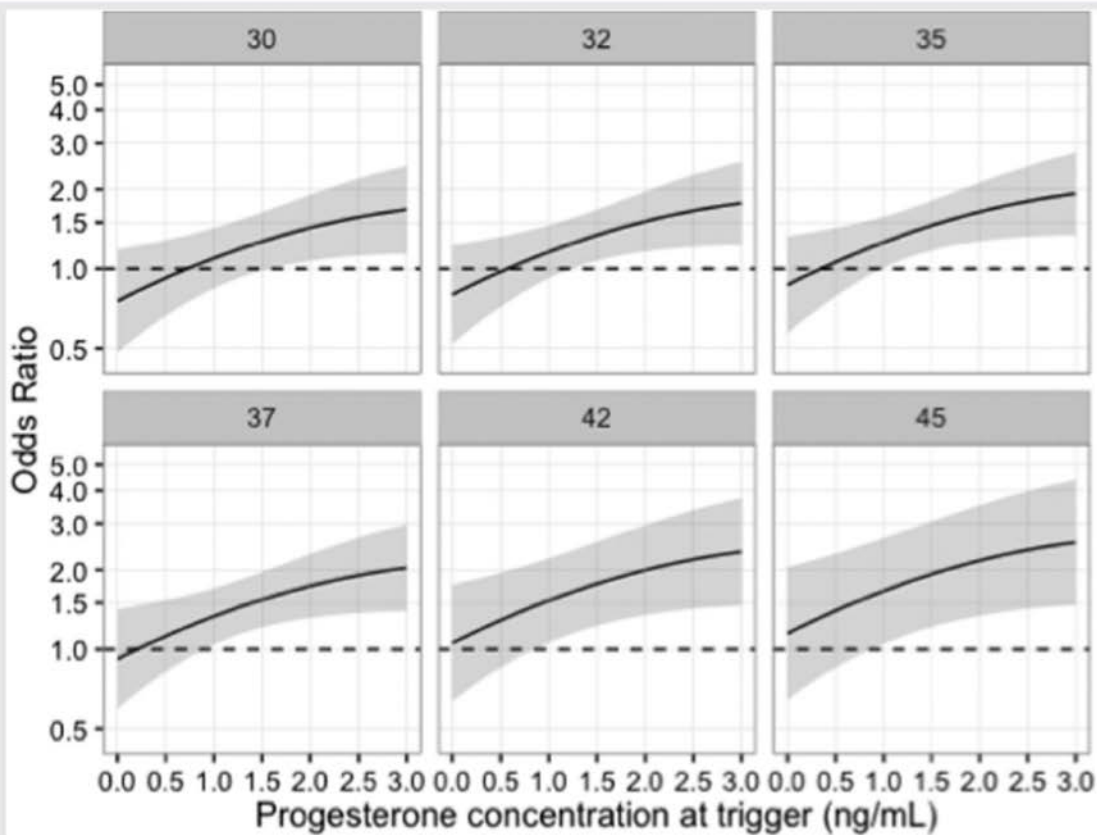
Wang. Freeze-only versus fresh transfer cycle success. *Fertil Steril* 2017.

- Freeze-only was only beneficial for P > 1 at trigger



SENSITIVITY ANALYSIS BY MATERNAL AGE AND PROGESTERONE AT TRIGGER

FIGURE 1



Effect of patient age and progesterone (P) concentration at trigger on determining the odds ratio (OR) for ongoing pregnancy for freeze-only versus fresh cycles. Patient age and P concentration at trigger modify the OR for achieving ongoing pregnancy between a freeze-only versus a fresh cycle. The 95% pointwise confidence intervals are shown in gray. The y-axes are on the natural logarithmic scale. Each panel represents the effect of P on the OR at the indicated age (labeled at the top of the panel).

Wang. Freeze-only versus fresh transfer cycle success. *Fertil Steril* 2017.

- Sensitivity analysis of ongoing pregnancy shows that at higher P concentration, **trend toward increasing benefit of freeze-only cycles with advancing age**



Largest study on freeze-only versus fresh transfer of **euploid** embryos (prelim data)

- Retrospective matched cohort study of **13 academic and private fertility centers** in the United States
- Propensity score analysis identified **1,642 matched blastocyst transfer cycles** (821 fresh, 821 freeze-only) that had undergone 24-chromosome PGS
- For fresh cycles, luteal support was initiated after retrieval and embryos were transferred into the uterus at the blastocyst stage
- For freeze-only cycles, embryos were cryopreserved according to established practice protocols at each clinic
 - In a subsequent cycle, patients underwent blastocyst FET in either a natural or medicated cycle (using estrogen and progesterone supplementation)



BASELINE CHARACTERISTICS

Table 1. Baseline characteristics after propensity score matching [Mean (Stdev)]

Metric	Fresh	Freeze-only	p-value
Maternal age	35.5 (4.3)	35.7 (4.1)	0.33
BMI	24.4 (4.8)	24.4 (4.8)	0.9
Gravidity	0.9 (1.4)	0.9 (1.4)	0.65
Parity	0.2 (0.5)	0.2 (0.5)	0.49
Basal antral follicle count	15.7 (8.6)	15.5 (8.2)	0.56
Day 3 LH	5 (3.2)	5.1 (3.6)	0.48
Day 3 FSH	6.3 (2.7)	6.4 (2.7)	0.43
Day 3 E2	48.4 (23.8)	48.5 (22.8)	0.91
Oocytes retrieved	17.6 (8.6)	17.1 (9.3)	0.21
Embryo cohort size	4.4 (3.2)	4.7 (3)	0.07
Embryos transferred	1.4 (0.5)	1.3 (0.5)	0.1
Progesterone at surge	1 (0.5)	1 (0.6)	0.65
Diagnosis			
DOR	9.30%	10%	0.68
Endometriosis	2.10%	1.30%	0.34
Idiopathic	11.40%	12.50%	0.54
Male factor	13.80%	13.40%	0.89
None provided	6.20%	5.70%	0.75
Other	30.80%	28.40%	0.3
Ovulatory dysfunction	9.40%	10%	0.74
PCOS	4.80%	4.80%	1
Tubal	3.90%	4.80%	0.47
Uterine	8.40%	9.10%	0.66
Clinic	--	--	0.018*
ICSI	95%	97%	0.026
Gonadotropin dose (FSH)	3671(1720)	3857(1847)	0.048
N	821	821	--

- All matched categories had no significant differences
- Gonadotropin dose and ICSI usage were slightly higher in freeze-only groups (not matched)

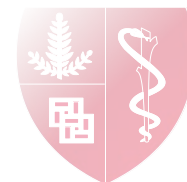


PREGNANCY OUTCOMES

Table 2. Freeze-only versus fresh transfer among euploid embryos

	Freeze-only	Fresh	OR Freeze-only/Fresh (95% CI)
Ongoing Pregnancy	53.1%	42.6%	1.52 (1.25, 1.85), p-value <0.0001
Implantation rate	50.8%	42.7%	1.38 (1.15, 1.66), p-value <0.001

After transfer of euploid embryos, **implantation and ongoing pregnancy rates were significantly higher in the freeze-only cohort than in the matched fresh cohort** ($p < 0.001$ and $p < 0.0001$, respectively)



PREGNANCY OUTCOMES - STRATIFIED

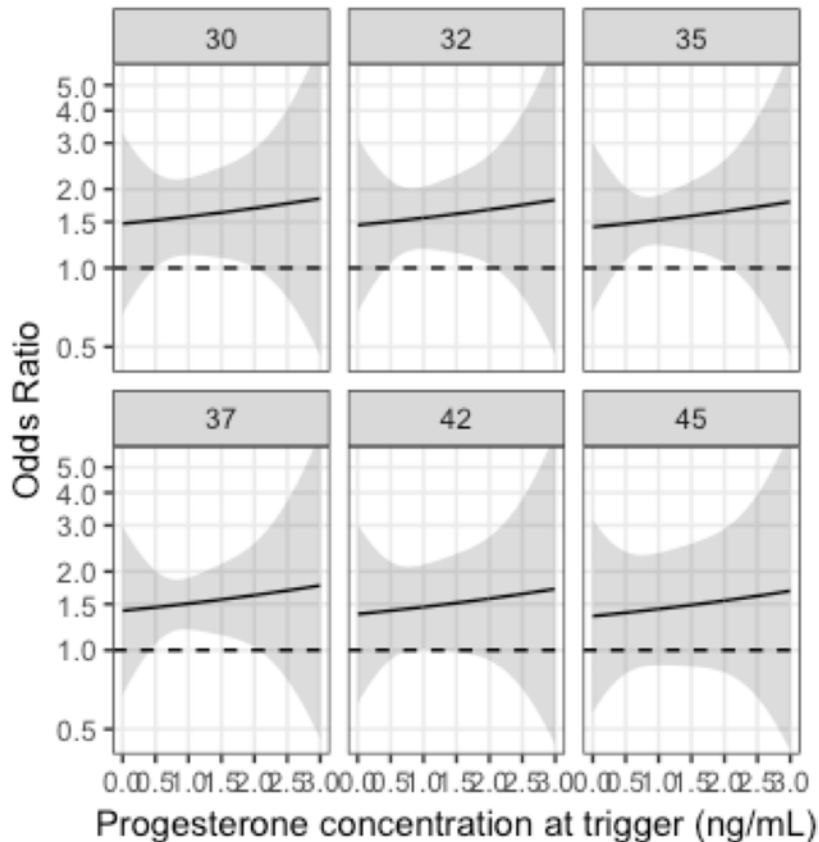
Table 3. Freeze-only versus fresh ongoing pregnancy rate stratified by maternal age and progesterone

Age	P4	OR Freeze-only/ Fresh (95% CI)	P-value
<=36	<=1	1.59 (1.16, 2.18)	<0.01
>36	<=1	1.45 (1.04, 2.01)	0.03
<=36	>1	1.60 (1.12, 2.27)	<0.01
>36	>1	1.45 (1.01, 2.09)	0.04

Odds of ongoing pregnancy after freeze-only transfer were significantly higher than fresh transfer for all stratifications of maternal age and P at trigger (cutoff values of maternal age = 36 years and P = 1 ng/mL determined by ROC analysis).



PROGESTERONE AND MATERNAL AGE SENSITIVITY ANALYSIS – ODDS RATIO FREEZE-ONLY/FRESH



- Sensitivity analysis of ongoing pregnancy shows **no significant trend regardless of progesterone at trigger or maternal age** (unlike prior study for non-PGS embryos)
- However, there may be a non-significant trend towards more benefit at higher levels of progesterone
- Freeze-only transfer with euploid embryos was associated with **significantly higher ongoing pregnancy and implantation rates than fresh transfer, regardless of progesterone level at trigger or maternal age**



STRENGTHS AND LIMITATIONS OF FREEZE-ONLY RETROSPECTIVE MATCHED COHORT STUDIES

- **Strengths**
 - Large sample size
 - Multicenter data set
 - Detailed information on potential confounders to create matched cohorts
 - Stratification by maternal age and progesterone at trigger
 - Wide group of diagnoses to make findings generalizable to multiple patient groups
- **Limitations**
 - Retrospective
 - Different clinics, laboratory assays, laboratory procedures, and PGS companies used
 - Lack of live birth data and perinatal outcomes



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Ovarian stimulation and in-vitro fertilization outcomes of cancer patients undergoing fertility preservation compared to age matched controls: a 17-year experience

Eden R. Cardozo • Alexcis P. Thomson •
Anatte E. Karmon • Kristy A. Dickinson •
Diane L. Wright • Mary E. Sabatini

- Literature on oncofertility outcomes is limited
- Study from 1997-2014 of 63 cancer patients, 57 cryopreserved embryos, and 21(36.8%) returned for frozen embryo transfer (comparison: age-matched controls undergoing fresh transfer, with 23 returning for frozen embryo transfer) found that outcomes were comparable between groups²⁹
- No difference between cancer patients and controls on gonadotropin dose, number of oocytes retrieved , and number of 2pn embryos obtained
- **Cumulative pregnancy rate per transfer for cancer patients compared to controls was 37 vs. 43 % respectively (p = 0.49) and cumulative live birth rate per transfer was 30 vs. 32 % respectively (p = 0.85).** Cancer patients had a higher likelihood of live birth resulting in twins (44 vs. 14 %; p = 0.035).



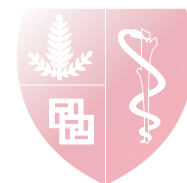
Hot off the Press!

- Fresh versus elective frozen embryo transfer in IVF/ICSI cycles: a systematic review and meta-analysis of reproductive outcomes

Matheus Roque  ^{1,2,*†}, Thor Haahr  ^{3,†}, Selmo Geber^{2,4}, Sandro C. Esteves  ^{3,5,6}, and Peter Humaidan^{3,5}

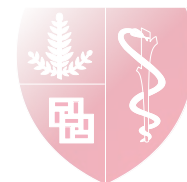
Meta-analysis of 11 RCTs (5379 patients) found that:

- FET resulted in a **statistically significant increase in live birth rate in hyper-responders** (RR 1.16, 95% CI 1.05–1.28) compared to fresh transfer
- No difference was found in normo-responders (RR 1.04, 95% CI 0.97–1.11)
- Risk of pre-eclampsia increased with FET (RR 1.79, 95% CI=1.03-3.09)
- No differences noted in ectopic pregnancy, miscarriage, preterm birth, congenital anomalies, or mean birthweight (low quality evidence; heterogeneity substantial)



CONCLUSIONS

- **Most studies on frozen versus fresh transfer have reported benefits of frozen transfer**
 - However, some maternal or neonatal outcomes may be more beneficial in fresh cycles
- Studies on freeze-only transfer are more limited but **most have suggested benefits of freeze-only transfer compared to fresh transfer, though they may be beneficial for only certain populations (primarily high responders)**
 - Further prospective studies and RCTs should investigate this question, including stratifications by maternal age, progesterone levels, and specific transfer protocols (natural vs medicated)
- Given advances in vitrification, evidence suggesting benefits of freeze-only, and the increasing use of PGS, **there has been a shift towards freeze-only cycles**
 - Other freeze-only advantages include decreased risk of OHSS
 - Disadvantages of freeze-only include increased cost and time, and possible loss of embryos during freeze-thaw



CONCLUSIONS (continued)

- These findings are encouraging in the oncofertility population, **as frozen transfers are often necessitated for these patients**
 - However, majority of cryopreservation cycles now for oncofertility are oocyte cryopreservation in which more study is needed (versus embryo cryopreservation)
 - Literature on oncofertility in general is limited
 - Studies are also needed on frozen transfer in cancer patients versus patients with other etiologies of infertility



REFERENCES

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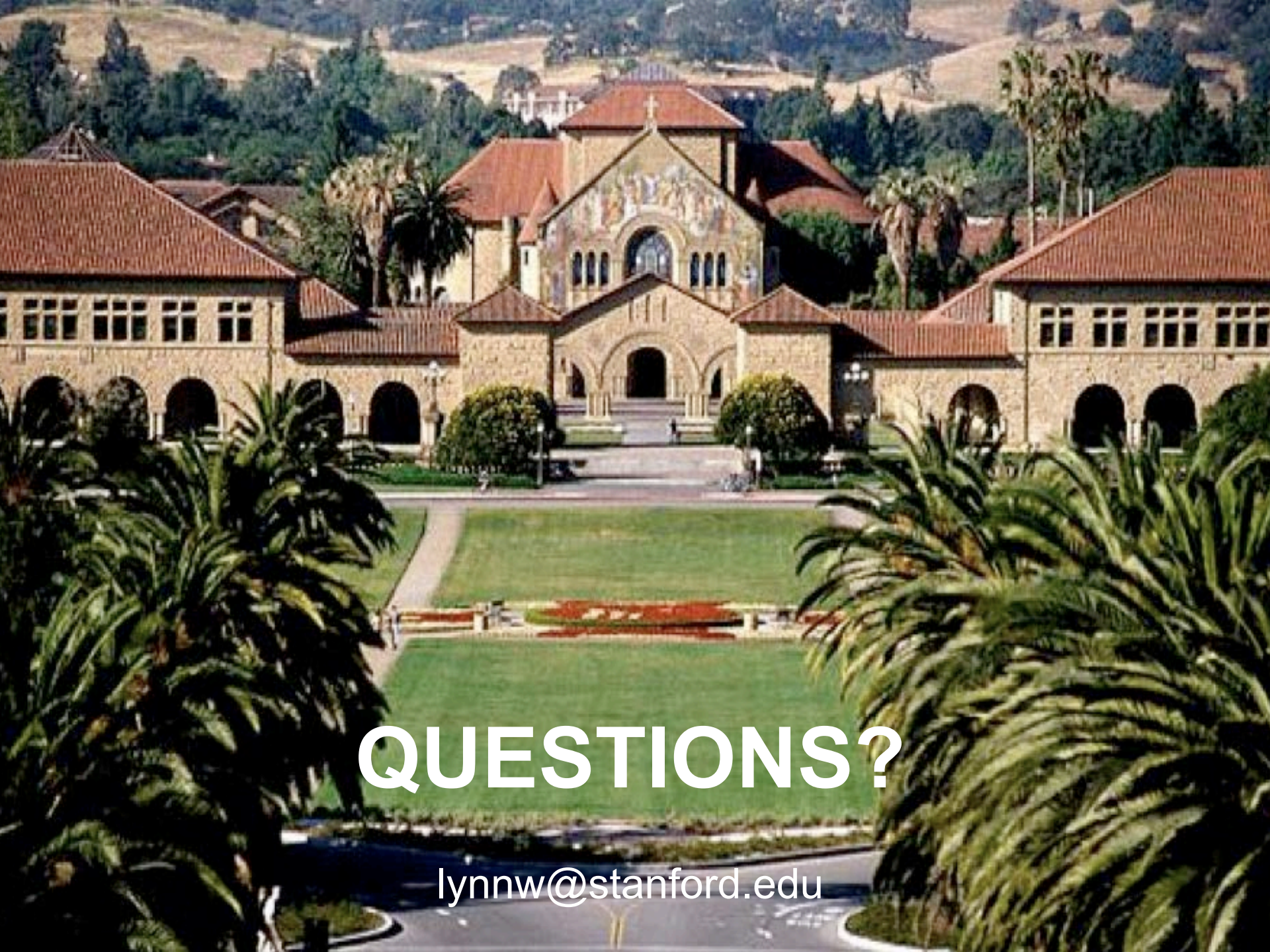
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QUESTIONS?

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