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The need to revisit KPIs in cryopreservation: concerns and considerations

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Declarations-No Conflict of Interest

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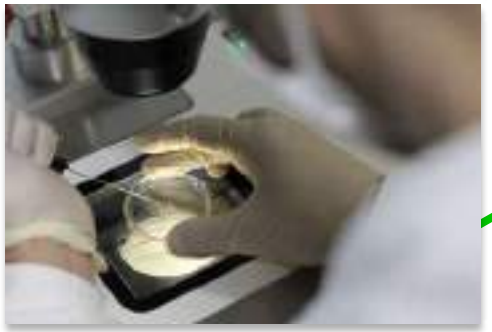
International Fertility Education Initiative

Oocyte Retrieval



Cumulous Cell Removal

Oocyte Insemination

Fertilization

Cleavage Assessment

Assisted

Embryo Transfer

Blastocyst Assessment

Warming

Vitrification

Trophectoderm Biopsy

Adapted from Professors Bormann and Dimitric

Cryopreservation in Europe … On the rise

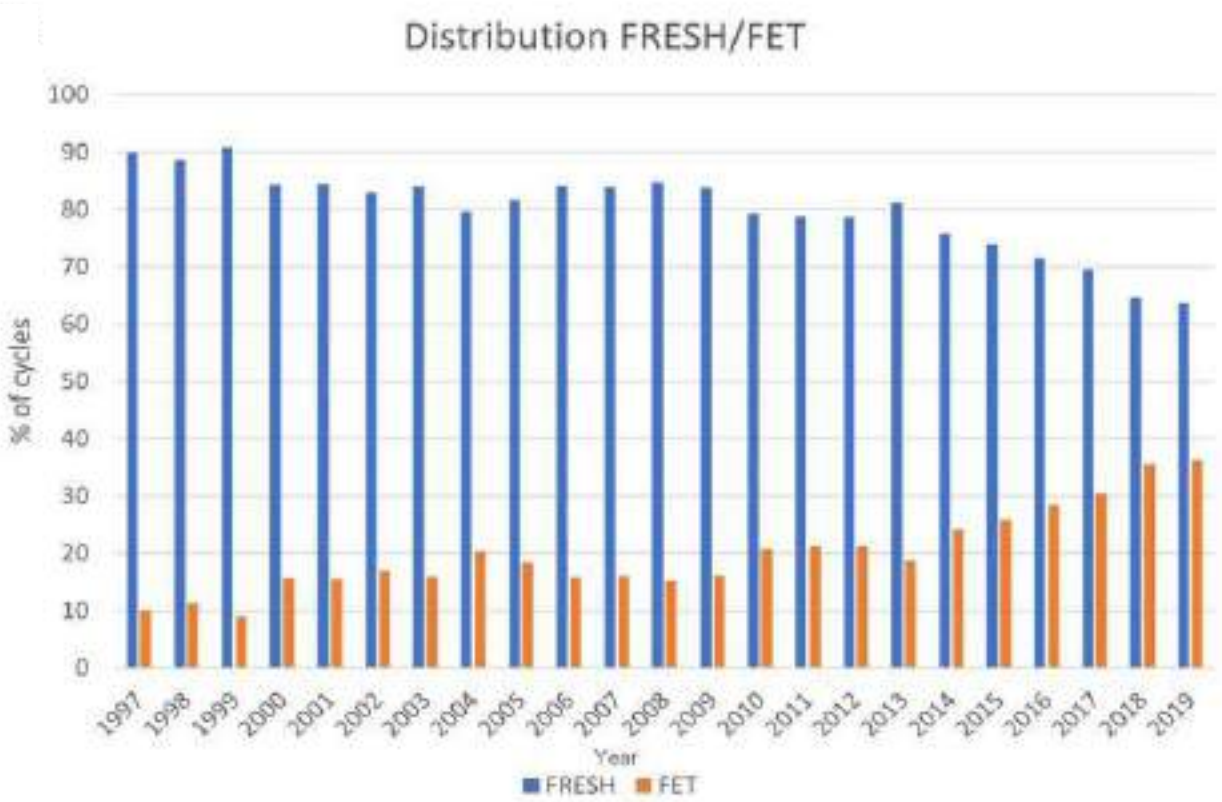
Hum Reprod. 2023 Dec 4;38(12):2321-2338. doi: 10.1093/humrep/dead197.

ART in Europe, 2019: results generated from European registries by ESHRE†

European IVF Monitoring Consortium (EIM) for the European Society of Human Reproduction and Embryology (ESHRE):
Jesper Smeenk [1], Christine Wyns [2], Christian De Geyter [3], Markus Kupka [4], Christina Bergh [5], Irene Cuevas Saiz [6], Diane De Neubourg [7], Karel Rezabek [8], Andreas Tandler-Schneider [9], Ionna Rugescu [10], Veerle Goossens [11]

Collaborators, Affiliations + expand

PMID: 37947771 PMCID: PMC10694409 DOI: 10.1093/humrep/dead197



Country	FET Thawings FET	FET Pregnancies per thawing (%)	FET Deliveries per thawing (%)
Albania	73	37.4	30.5
Armenia	2143	38.0	32.8
Austria	3485	39.1	
Belarus	1326	37.7	26.3
Belgium	14 597	28.6	19.9
Bosnia-Herzegovina, Federation part.	71	22.5	15.5
Bulgaria	1832	40.2	33.9
Czech Republic	16 174	31.0	18.9
Denmark			
Estonia	1142	30.2	22.3
Finland			
France	45 312	25.4	21.2
Germany	30 436	28.6	20.5
Greece	5667	44.9	28.3
Hungary	1616	34.3	18.3
Iceland	377	42.4	33.2
Ireland	814	42.5	32.2
Italy	21 296	31.0	20.2
Kazakhstan	4860	46.0	35.0
Latvia	661	44.9	30.6
Lithuania	387	48.3	7.5
Luxembourg	0		
Malta	23	39.1	30.4
Moldova	415	33.7	24.8
Montenegro	75	41.3	38.7
North Macedonia	408	46.1	39.9
Norway	6516	28.0	23.2
Poland	12 875	37.5	25.6
Portugal	3125	37.0	25.6
Russia	50 864	42.2	27.0
Serbia	965	24.1	15.3
Slovakia			
Slovenia	1721	35.6	26.7
Spain	55 957	37.5	26.5
Sweden			
Switzerland	5134	34.4	24.8
The Netherlands			
Turkey	8433	49.5	39.1
Ukraine	31 848	50.1	41.4
UK	24 581		
All	309 311	32.3	22.7

70.200 deliveries

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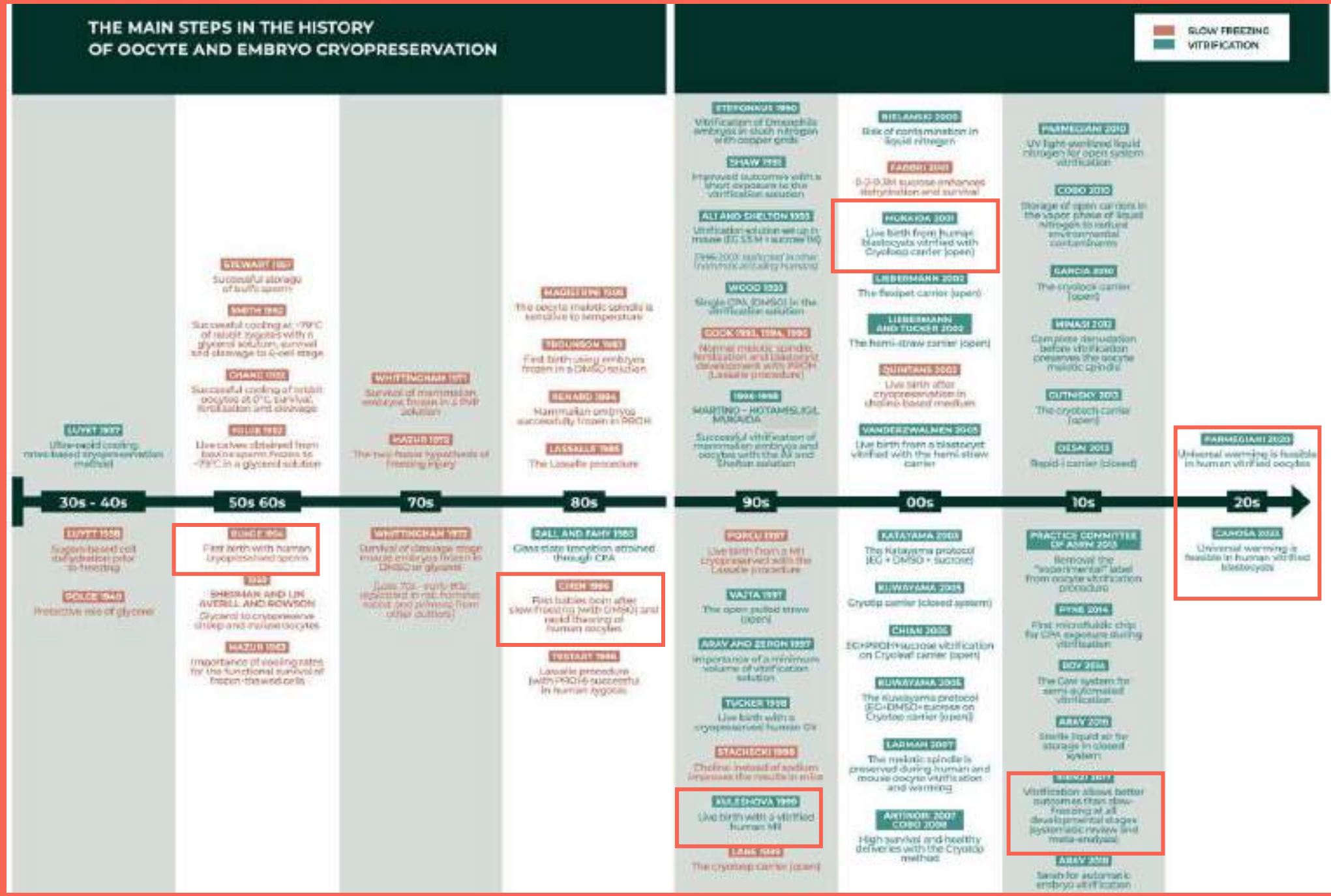

Oocyte and embryo cryopreservation in assisted reproductive technology: past achievements and current challenges Casciani, Valentina et al. Fertility and Sterility, Volume 120, Issue 3, 506 - 520

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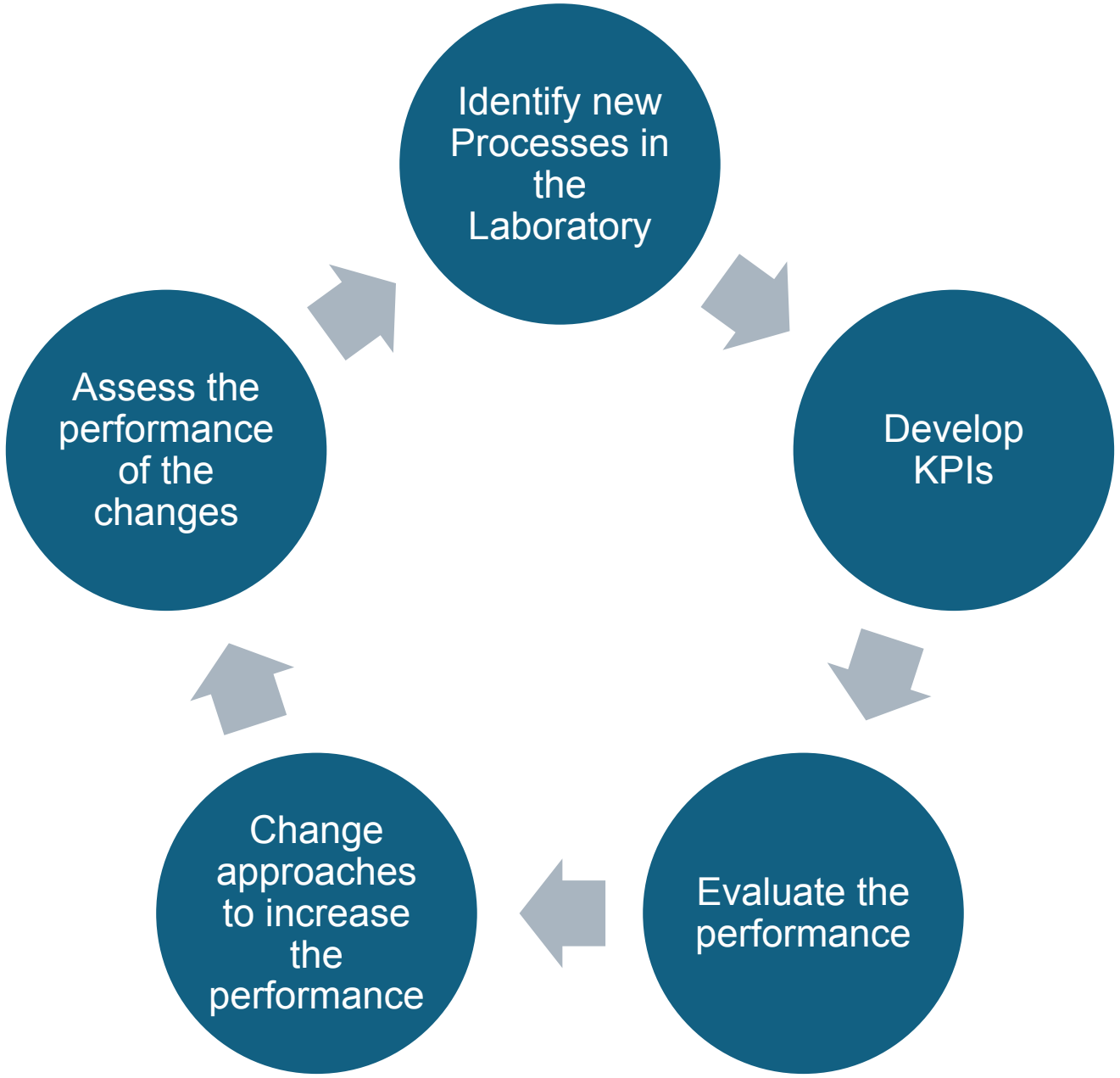
What are the KPIs

- Key Performance Indicators (KPIs) are employed to evaluate and measure our performance
- KPIs are not static but a dynamic process
- Positive reinforcement cycle



> Reprod Biomed Online. 2012 Aug;25(2):146-67. doi: 10.1016/j.rbmo.2012.05.006. Epub 2012 May 29.

The Alpha consensus meeting on cryopreservation key performance indicators and benchmarks: proceedings of an expert meeting

Alpha Scientists In Reproductive Medicine

Oocyte

KPI			Competence	Benchmark
O1	Morphological survival	Freezing	≥50%	75%
		Vitrification	70%	85% (95% for donors <30 years)
O2	Fertilization rate	No more than 10% (absolute; i.e. 10 percentage points) lower than that for the comparable population of fresh oocytes at the centre		
O3	Embryo development rate	Freezing	No more than 10–30% (relative) lower than that for the comparable population of fresh embryos at the centre	The same as for the comparable population of fresh embryos at the centre
		Vitrification	The same as for the comparable population of fresh embryos at the centre	
O4	Implantation rate	No more than 10–30% (relative) lower than that for the comparable population of fresh embryos at the centre		

Cleavage stage embryo

KPI			Competence	Benchmark
E1	Morphological survival: fully intact	Freezing	40%	55%
		Vitrification	70%	85%
E2	Morphological survival: ≥50% intact	Freezing	60%	85%
		Vitrification	85%	95%
E3	Post-thaw development (including implantation rate) for fully intact embryos		≤10% (relative) lower than that for the comparable population of fresh embryos at the centre	The same as for the comparable population of fresh embryos at the centre

Blastocyst

KPI			Competence	Benchmark
B1	Survival rate	Freezing	70%	85%
		Vitrification	80%	95%
B2	Transfer rate	Freezing	70%	85%
		Vitrification	80%	95%
B3	Implantation rate		≤10% (relative) lower than that for the comparable population of fresh embryos at the centre	The same as for the comparable population of fresh embryos at the centre

Table IV KPIs for the ART laboratory.

KPI	Calculation	Competency value (%)	Benchmark value (%)
ICSI damage rate	$\frac{\text{no. damaged or degenerated}}{\text{all oocytes injected}} \times 100$	≤10	≤5
ICSI normal fertilization rate	$\frac{\text{no. oocytes with 2PN and 2PB}}{\text{no. MII oocytes injected}} \times 100$	≥65	≥80
IVF normal fertilization rate	$\frac{\text{no. oocytes with 2PN and 2PB}}{\text{no. COCs inseminated}} \times 100$	≥60	≥75
Failed fertilization rate (IVF)	$\frac{\text{no. cycles with no evidence of fertilization}}{\text{no. of stimulated IVF cycles}} \times 100$	<5	
Cleavage rate	$\frac{\text{no. cleaved embryos Day 2}}{\text{no. 2PN/2PB oocytes on Day 1}} \times 100$	≥95	≥99
Day 2 Embryo development rate	$\frac{\text{no. 4-cell embryos on Day 2}}{\text{no. normally fertilized oocytes}^{a}} \times 100$	≥50	≥80
Day 3 Embryo development rate	$\frac{\text{no. eight cell embryos on Day 3}}{\text{no. normally fertilized oocytes}^{a}} \times 100$	≥45	≥70
Blastocyst development rate	$\frac{\text{no. blastocysts Day 5}}{\text{no. normally fertilized oocytes}^{a}} \times 100$	≥40	≥60
Successful biopsy rate	$\frac{\text{no. biopsies with DNA detected}}{\text{no. biopsies performed}} \times 100$	≥90	≥95
Blastocyst cryosurvival rate	$\frac{\text{no. blastocysts appearing intact}}{\text{no. blastocysts warmed}} \times 100$	≥90	≥99
Implantation rate (cleavage-stage)[b]	$\frac{\text{no. sacs seen on ultrasound}^{c}}{\text{no. embryos transferred}} \times 100$	≥25	≥35
Implantation rate (blastocyst-stage)[b]	$\frac{\text{no. sacs seen on ultrasound}^{c}}{\text{no. blastocysts transferred}} \times 100$	≥35	≥60

- In ESHRE's KPIs (Vienna Consensus) only blastocyst cryosurvival rate was included as a KPI
- The cryosurvival was evaluated according to morphological appearance
- **Would that introduce a certain degree of relativity?**

The Vienna consensus: report of an expert meeting on the development of art laboratory performance indicators[‡]

ESHRE Special Interest Group of Embryology, Alpha Scientists in Reproductive Medicine
Author Notes

Human Reproduction Open, Volume 2017, Issue 2, 2017, hox011,
https://doi.org/10.1093/hropen/hox011
Published: 04 August 2017 **Article history**

Even in 2023, looks still matter…

J Assist Reprod Genet. 2023 Apr 24;40(6):1479–1494. doi: 10.1007/s10815-023-02792-1

Clinical and laboratory key performance indicators in IVF: A consensus between the Italian Society of Fertility and Sterility and Reproductive Medicine (SIFES-MR) and the Italian Society of Embryology, Reproduction and Research (SIERR)

Alberto Vaiarelli [1,5,*], Carlotta Zacà [2,*], Valentina Spadoni [2], Danilo Cimadomo [1], Alessandro Conforti [3], Carlo Alviggi [4], Roberto Palermo [5], Carlo Bulletti [6,7], Lucia De Santis [8], Valerio Pisaturo [9], Vincenzo Vigiliano [10], Giulia Scaravelli [10], Filippo Maria Ubaldi [1], Andrea Borini [2]

Table 2 List of PIs identified by SIFES-MR and SIERR panel of experts with medium agreement (40–80%). Competence and benchmark values were proposed for each KPI, along with a suggested frequency for their analysis

PERFORMANCE INDICATORS	*Reference population*	*Competence value*	*Benchmark value*	*Suggested frequency of analysis*
1. IVF fertilization rate	All patients (*except for SMF*)	≥60%	≥75%	Monthly or 100 cycles
2. Oocytes cryo-survival rate	All patients	≥70%	≥85%	Monthly or 100 cycles
3. Embryo cryo-survival rate: > 50% blastomeres survived AND 3. Embryo cryo-survival rate: all blastomeres survived	All patients	≥80% ≥70%	≥95% ≥85%	Monthly or 100 cycles
4. Blastocyst cryo-survival rate	All patients	≥90%	≥99%	Monthly or 100 cycles
5. Successful biopsy rate	All patients	≥95%	≥97%	Monthly or 100 cycles
6. Follicular output rate (FORT)	All patients	≥40%	≥80%	Monthly or 100 cycles
7. Cumulative live birth rate (CLBR)	a) ≤34 years b) 35–39 years c) ≥40 years	a) ≥30% b) ≥20% c) ≥5%	a) ≥40% b) ≥30% c) ≥10%	Yearly

2. Oocyte cryo-survival rate

- **Definition:** Proportion of morphologically intact oocytes at the time of ICSI after thawing-warming.

3. Embryo cryo-survival

- **Definition:** Survival was defined as the proportion of thawed-warmed viable embryos with at least 50% blastomeres intact and with all blastomeres intact.

4. Blastocyst cryo-survival

- **Definition:** Blastocyst cryo-survival was defined as at least 75% of cells intact after thawing-warming

- Is morphologically assessed “survival” enough?
- How is the threshold of “at least 50% or 75% intactness decided on?”
- What does survival mean?
- Does intactness =survival?

Anything else worthwhile reporting on?

Table 3. Embryo kinetics of development according to the type of cycle (fresh donations and donations with the use of vitrified oocytes).

Timing (h)	Group	n	Mean (h)	95% CI	P value
t2	Fresh	9,935	27.7	27.6–27.8	<.01
	Vitrified	3,793	28.7	28.5–28.9	
t3	Fresh	9,746	37.8	37.6–37.9	<.01
	Vitrified	3,697	38.9	38.5–38.9	
t4	Fresh	9,546	40.2	40.1–40.3	<.01
	Vitrified	3,585	41.4	41.2–41.7	
t5	Fresh	8,789	50.5	50.3–50.7	<.01
	Vitrified	3,141	51.7	51.4–52.1	
tM	Fresh	2,594	86.6	86.1–87.1	<.01
	Vitrified	779	88.5	87.5–89.4	
tB	Fresh	1,938	103.4	103–103.9	.016
	Vitrified	580	104.5	103.7–105.4	
tEB	Fresh	1,045	114.4	113.8–114.9	.466
	Vitrified	325	114.8	113.7–115.9	
tHB	Fresh	164	114.9	113.4–116.4	.196
	Vitrified	59	116.9	113.8–120	
cc2	Fresh	9,746	10.2	10.1–10.3	.901
	Vitrified	3,697	10.2	10.0–10.4	
s2	Fresh	9,546	2.6	2.5–2.6	<.01
	Vitrified	3,585	2.9	2.7–3.1	

What about time?

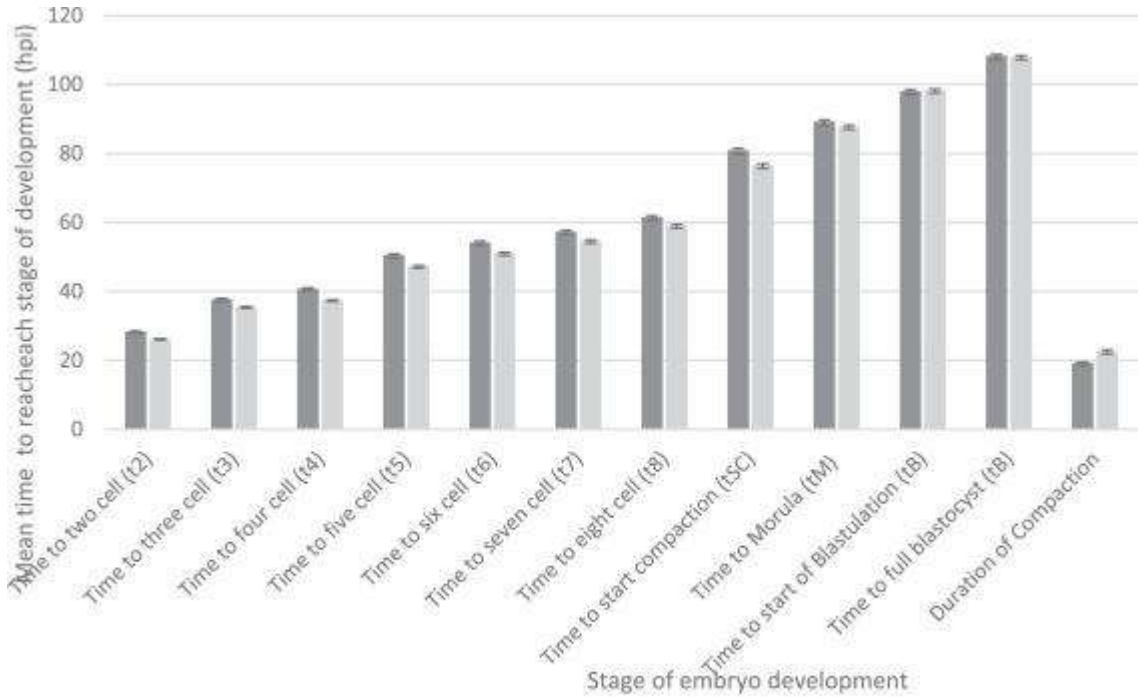
Observational Study > Fertil Steril. 2017 Sep;108(3):491-497.e3.
doi: 10.1016/j.fertnstert.2017.06.024.

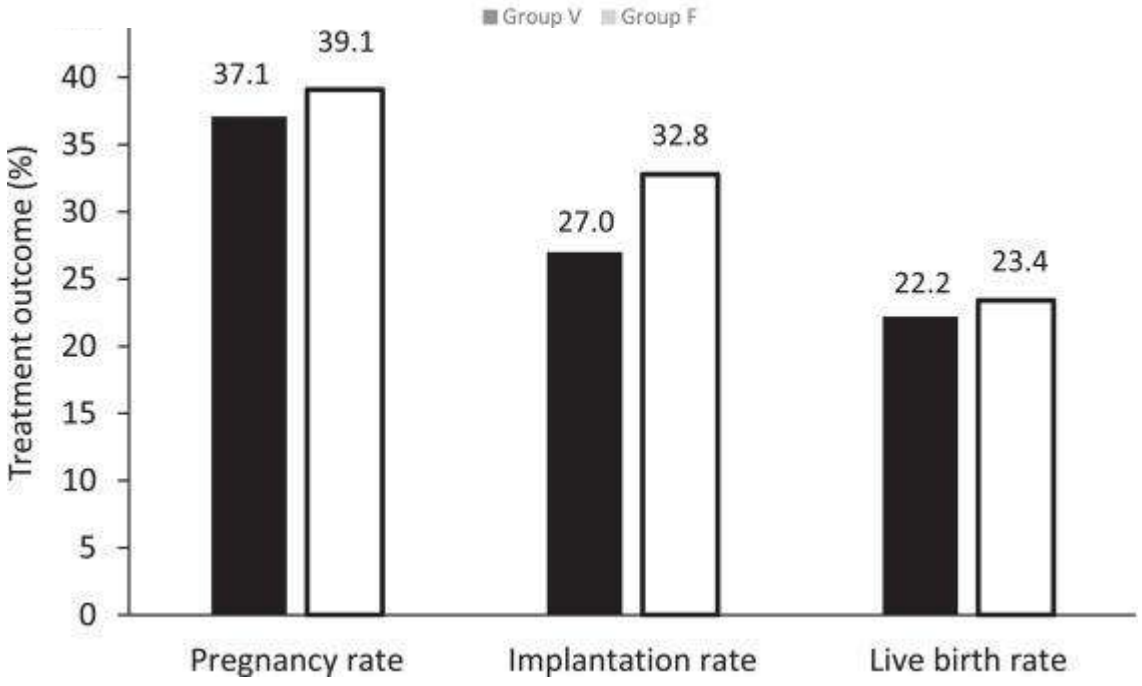
Effect of oocyte vitrification on embryo quality: time-lapse analysis and morphokinetic evaluation

Ana Cobo [1], Alla Coello [2], Jose Remohí [2], Jose Serrano [2], Jose María de Los Santos [2], Marcos Meseguer [2]

Until Blastocyst formation, embryos deriving from frozen oocytes seem to develop slower than embryos derived from fresh oocytes.

More recent data





Multicenter Study > Reprod Biomed Online. 2023 Jul;47(1):51-60.
doi: 10.1016/j.rbmo.2023.02.011. Epub 2023 Mar 1.

A comparison of the morphokinetic profiles of embryos developed from vitrified versus fresh oocytes

Kathryn Montgomery [1], Susan Montgomery [2], Alison Campbell [3], Deborah Mary Nash [1]

Similar results to previous data indicating slower rates up to compaction.

However, time to blastocyst formation was similar between embryos deriving from fresh and frozen oocytes.

No statistically significant difference on live-birth rates. Some difference in implantation rates

Very recent data

J Assist Reprod Genet. 2024 Mar;41(3):643-648. doi: 10.1007/s10815-023-03016-2. Epub 2024 Jan 11.

Similar pregnancy outcomes from fresh and frozen donor oocytes transferred to gestational carriers: a SART database analysis isolating the effects of oocyte vitrification

Jacqueline Klose [1], Channing Kuoks [2], Alexandra Purdue-Smithe [3], Elizabeth DeVilbiss [4], Sunni L Mumford [5], Rachel Weinerman [6]

Outcome	Fresh donor oocyte and gestational carrier (*n* = 1119)	Frozen donor oocyte and gestational carrier (*n* = 165)	RR (95% CI)	aRR (95% CI)*
Pregnancy Outcomes, *n* (%)				
Live birth	534 (47.7)	76 (46.1)	0.97 (0.81, 1.15)	0.89 (0.70, 1.13)
Clinical pregnancy	611 (54.6)	90 (54.5)	1.00 (0.86, 1.16)	1.01 (0.82, 1.24)
Biochemical pregnancy loss	66 (5.9)	17 (10.3)	1.75 (1.05, 2.9)	1.00 (0.46, 2.19)
Clinical pregnancy loss	132 (11.8)	29 (17.6)	1.49 (1.03, 2.15)	1.13 (0.65, 1.97)
Birthweight, *n* (%)				
Low birthweight (< 2500 g)	190 (26.6)	22 (23.7)	0.92 (0.63, 1.35)	0.85 (0.52, 1.39)
Normal birthweight (≥ 2500 g and ≤ 3999 g)	480 (67.2)	62 (66.7)	Ref	Ref
High birthweight (> 4000 g)	44 (6.2)	9 (9.7)	1.51 (0.77, 2.96)	0.50 (0.14, 1.88)
Pregnancy plurality, *n* (%)				
Singleton	341 (63.9)	58 (76.3)	Ref	Ref
Multiple	193 (36.1)	18 (23.7)	0.66 (0.43, 1)	0.77 (0.47, 1.29)

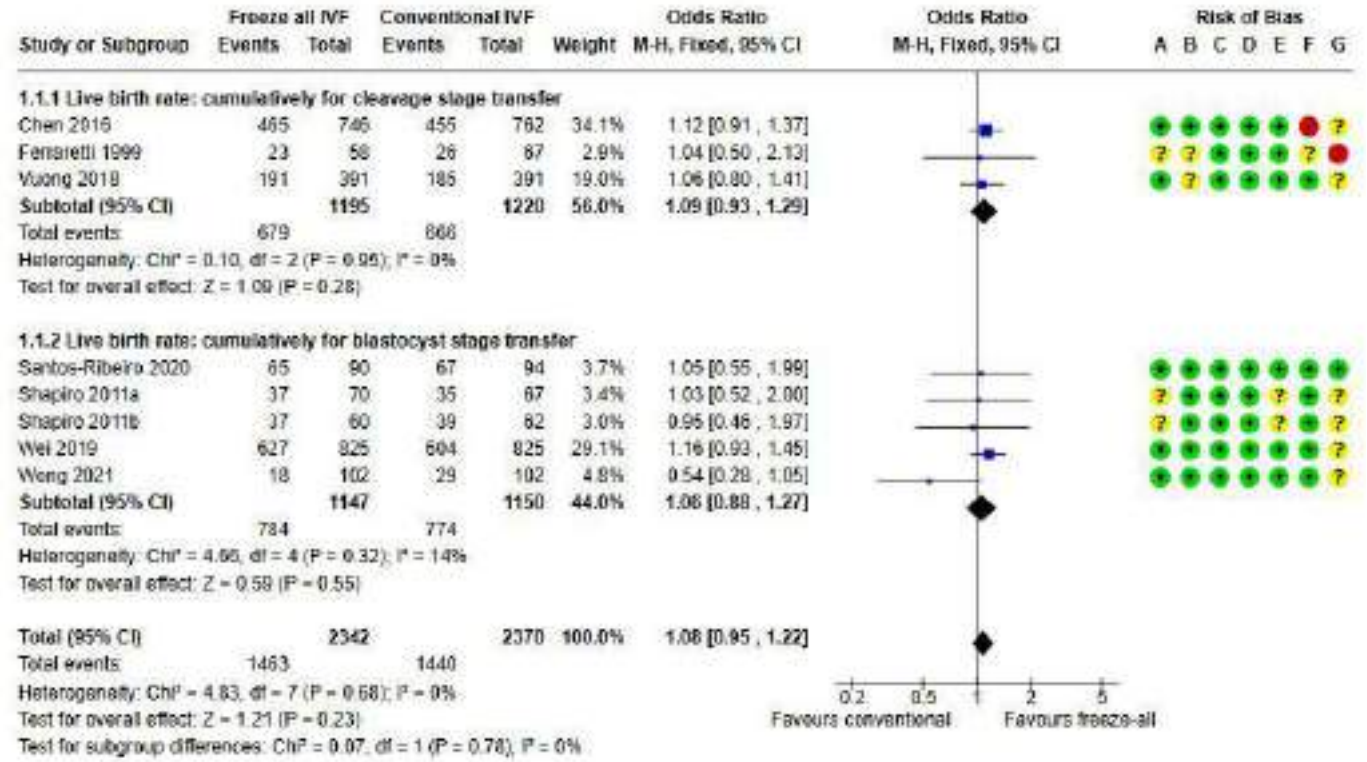
*Use of frozen **oocytes** in gestational carriers provided **similar clinical outcomes** with fresh oocytes in gestational carriers which may serve as a KPI*

Cochrane Database of Systematic Reviews · Review · Intervention

Fresh versus frozen embryo transfers in assisted reproduction

Tjitske Zaat, Miriam Zagers, Femke Mol, Mariëtte Goddijn, Madelon van Wely, Sebastiaan Mastenbroek
Authors' declarations of interest

Version published: 04 February 2021 Version history
https://doi.org/10.1002/14651858.CD011184.pub3

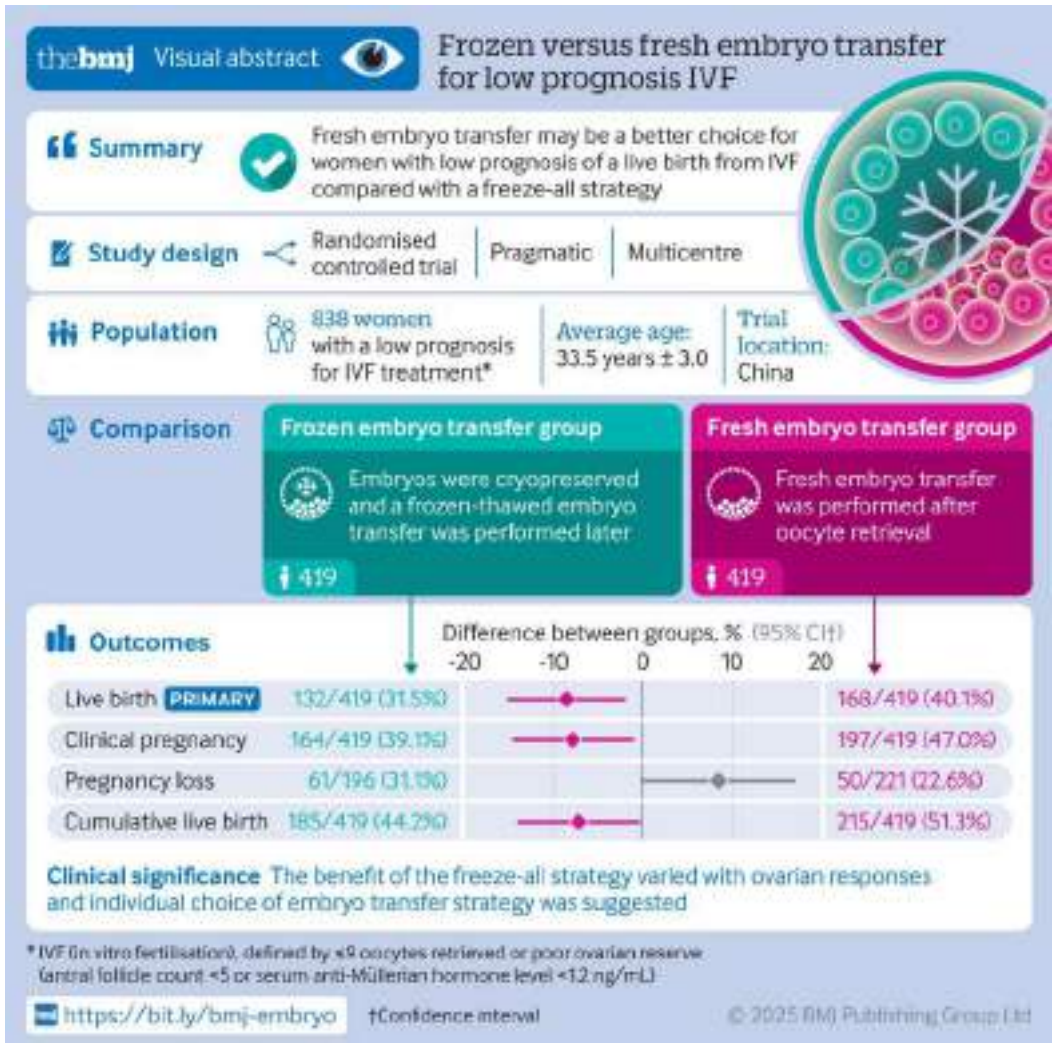


The jury is still out there regarding **embryo** cryopreservation effect on LBR

Randomised Controlled Trial · BMJ 2025 Jan 29;388:e081474. doi: 10.1136/bmj-2024-081474

Frozen versus fresh embryo transfer in women with low prognosis for in vitro fertilisation treatment: pragmatic, multicentre, randomised controlled trial

Demin Wei, Yun Sun, Hen Zhao, Jianhao Yan, Hong Zhou, Fei Gong, Aijun Zhang, Ze Wang, Lei Jin, Hongchu Bao, Shuyan Zhao, Zhuoni Xiao, Yingying Qin, Ling Gong, Linlin Cui, Yan Sheng, Mei Sun, Peihao Liu, Lingling Ding, Hong Liu, Kellang Wu, Yan Li, Yao Lu, Bufeng Xu, Bei Xu, Luqing Zhang, Heping Zhang, Richard S Legro, Zi-Kang Chen



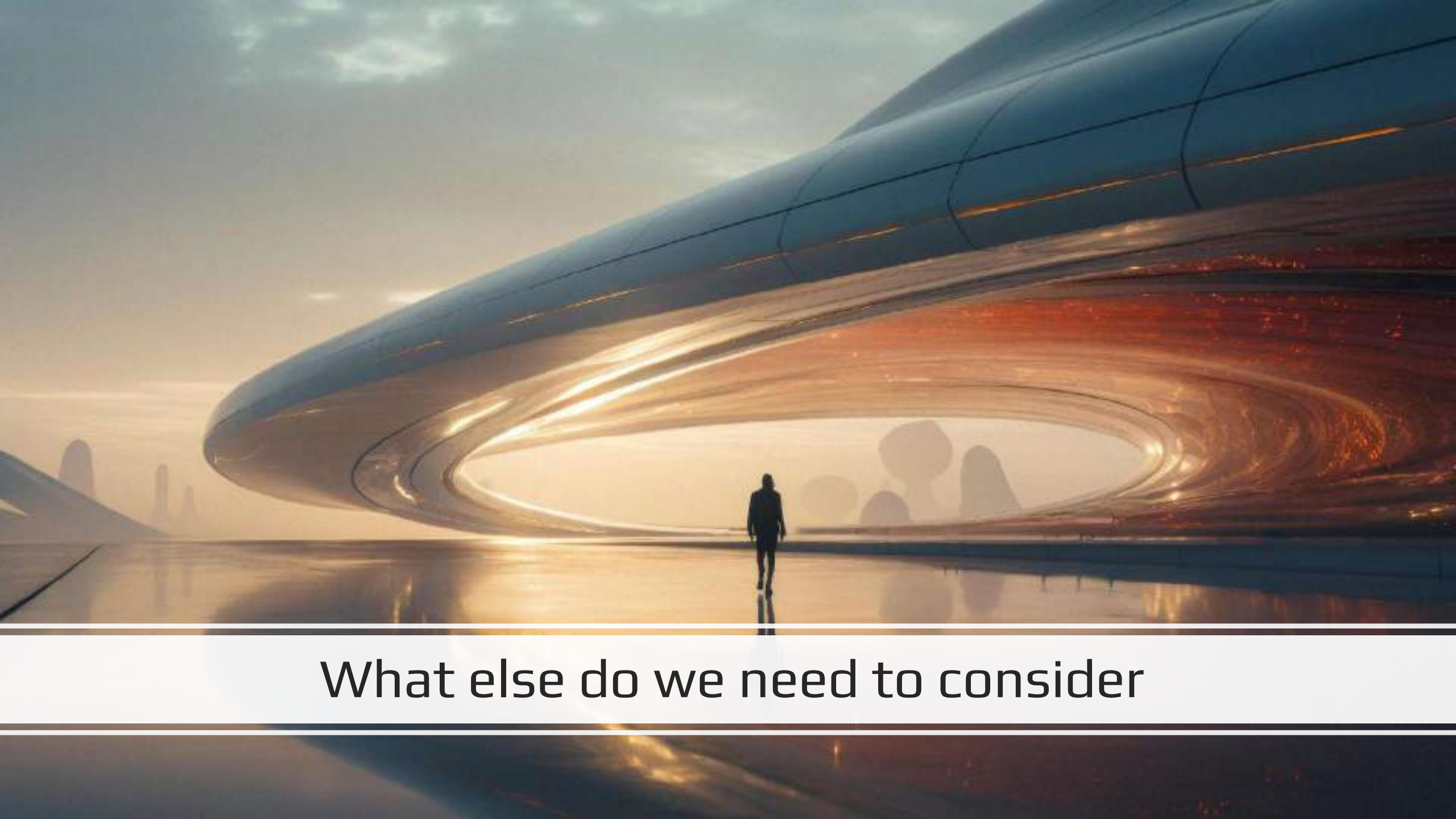
Summary I

No statistically significant difference in live-birth rates comparing fresh and frozen oocytes

Vitrified oocytes seem to develop slower at least up to compaction stage

Embryo vitrification in general population seem to result to similar clinical outcomes compared to fresh embryos.

This may not be the case for all subpopulations – especially poor prognosis women. Should we consider different KPIs for different populations?



What else do we need to consider

What about

Post-warming time

Day of blastocyst vitrification

Physiology

Blastocyst Post-Thaw Culture

D5

Outcome	Short culture	Long culture	p Value
	(n = 384)	(n = 384)	
Implantation rate, n/N (%)	287/486 (59.1)	306/483 (63.4)	0.170
Clinical pregnancy rate, n/N (%)	245/384 (63.8)	257/384 (66.9)	0.363
Abortion rate, n/N (%)	29/245 (11.8)	37/257 (14.4)	0.396
Live birth rate, n/N (%)	216/384 (56.3)	220/384 (57.3)	0.771

D6

Outcome	Short culture	Long culture	p Value
	(n = 544)	(n = 327)	
Implantation rate, n/N (%)	356/781 (45.6)	173/487 (35.5)	<0.001
Clinical pregnancy rate, n/N (%)	308/544 (56.6)	148/327 (45.3)	0.001
Abortion rate, n/N (%)	44/308 (14.3)	32/148 (21.6)	0.049
Live birth rate, n/N (%)	264/544 (48.5)	116/327 (35.5)	<0.001

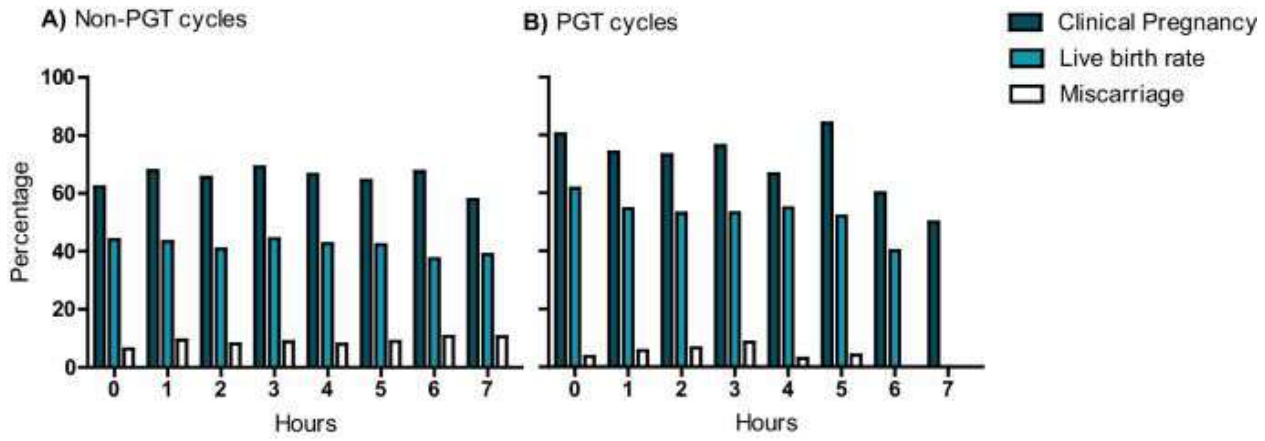
Syst Biol Reprod Med. 2023 Feb;69(1):64-74. doi: 10.1080/19396368.2022.2121191. Epub 2022 Sep 29.

Influence of post-thaw culture duration on pregnancy outcomes in frozen blastocyst transfer cycles

Hui Li [1], Shaowei Cao [1], Hui Ding [1], Li Dong [1], Chun Zhao [1], Jianping Zhang [1], Jing Lu [1], Xiuling Li [1], Rufeng Ling [1]

Short: 0-6
Long: over 7h
The difference between short and long culture is present only for D6 embryos (extended culture worse outcomes)

The JARG study shows post thaw culture between 0-7 hours no difference



J Assist Reprod Genet. 2024 Jun;41(6):1539-1547. doi: 10.1007/s10815-024-03115-8. Epub 2024 Apr 20.

Effect of time post warming to embryo transfer on human blastocyst metabolism and pregnancy outcome

Goli Ardestani [1], Marion Martins [2,3], Olcay Ocali [2], Tim H Sanchez [4], Coleyn Gulliford [4], C Brent Barrett [2], Danny Sakkas [2]

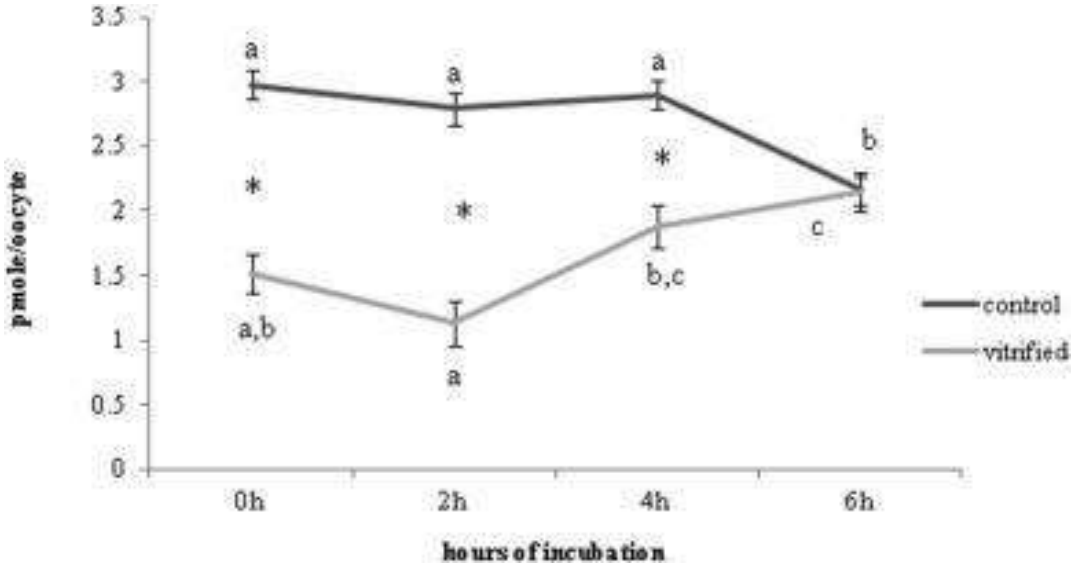
Looking at oocyte data

Theriogenology

A recovery time after warming restores mitochondrial function and improves developmental competence of vitrified ovine oocytes

Sara Succu [a, ✉], Sergio Domenico Gaspa [a], Elisa Sanna [a], Angela Zinellu [b], Ciriaco Carru [b], Cristian Porcu [a], Salvatore Nottola [a], Fiammetta Berlinguer [a], Giovanni Giuseppe Leoni [a]

Quantification of ATP intracellular content



Mitochondrial function as measured by ATP content seems to be similar to fresh oocytes following 6 hours.

Theriogenology

Recovery of spindle morphology and mitochondrial function through extended culture after vitrification-warming of bovine oocytes

Emilio Gutierrez-Castillo [a], Fabian A. Diaz [a], Sydney A. Talbot [a], Kenneth R. Bondioli [a, ✉]

Table2. Experiment 1: effect of post-warming extended culture on the meiotic spindle of vitrified bovine oocytes.

Treatment	N	Mat. Rate %	Microtubule Distribution		Chromosomal Arrangement	
			Normal	Abnormal	Normal	Abnormal
Control	41	73.17[a]	25 (83.3%)	5 (16.7%)[a]	26 (86.7%)	4 (13.3%)[a]
Vit.+EC	35	83.33[a]	22 (73.3%)	8 (26.7%)[a]	25 (83.3%)	5 (16.7%)[ab]
Vit. Control	34	76.47[a]	11 (42.3%)	15 (57.7%)[b]	16 (61.5%)	10 (38.5%)[b]

Similarly Extended Culture (6h vs 2h) seems to ameliorate the effects of vitrification completely on microtubule distribution and partially on chromosomal arrangement

*Research on oocyte extended culture is mainly performed in animal models

Day of Blastocyst freezing-Does it matter? -Yes

› Curr Med Sci. 2023 Apr;43(2):297-303. doi: 10.1007/s11596-023-2699-4. Epub 2023 Mar 17.

Pregnancy Outcomes for Day 5 Versus Day 6 Single Frozen-thawed Blastocyst Transfer with Different Qualities of Embryos: A Large Matched-cohort Study

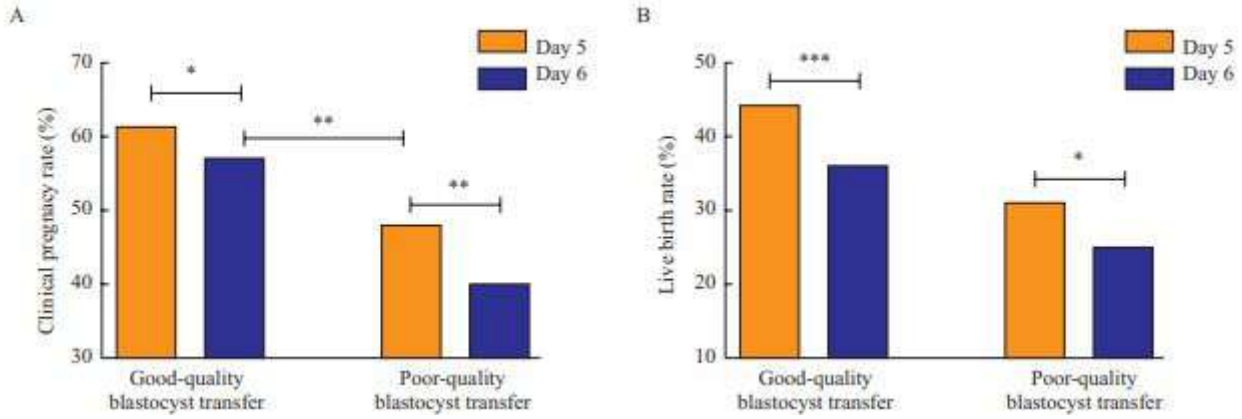
Qiong Yu [1], Hui He [1], Xin-Ling Ren [1], Shi-Fu Hu [2], Lei Jin [3]

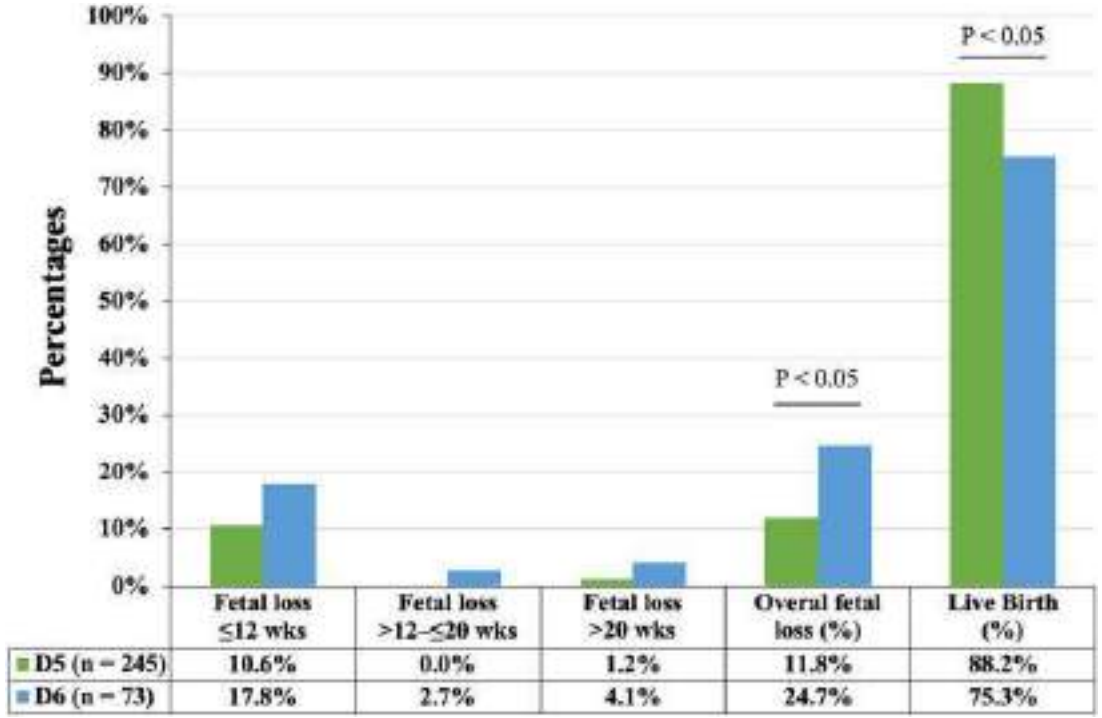
Increased incidence of live births in implanted day 5 versus day 6 blastocysts following single embryo transfers with PGT-A

Chien-Hong Chen, Chun-I Lee, Chun-Chia Huang, Hsiu-Hui Chen, Chih-Ying Cheng, En-Hui Cheng, Pin-Yao Lin, Chung-I Chen, Tsung-Hsien Lee ✉ & Maw-Sheng Lee ✉

Scientific Reports 13, Article number: 12725 (2023) | Cite this article

D5 seems to provide better results
Different KPIs needed or freeze only on D5?





	Fetal loss ≤12 wks	Fetal loss >12–≤20 wks	Fetal loss >20 wks	Overal fetal loss (%)	Live Birth (%)
D5 (n = 245)	10.6%	0.0%	1.2%	11.8%	88.2%
D6 (n = 73)	17.8%	2.7%	4.1%	24.7%	75.3%

Cryopreservation on D5 provides enhanced CPR and LBR compared to D6 both in good and in poor quality embryos– and in PGT-A tested embryos

Do we see everything? Are things really as they appear…or can looks be deceiving?

Do we see everything?

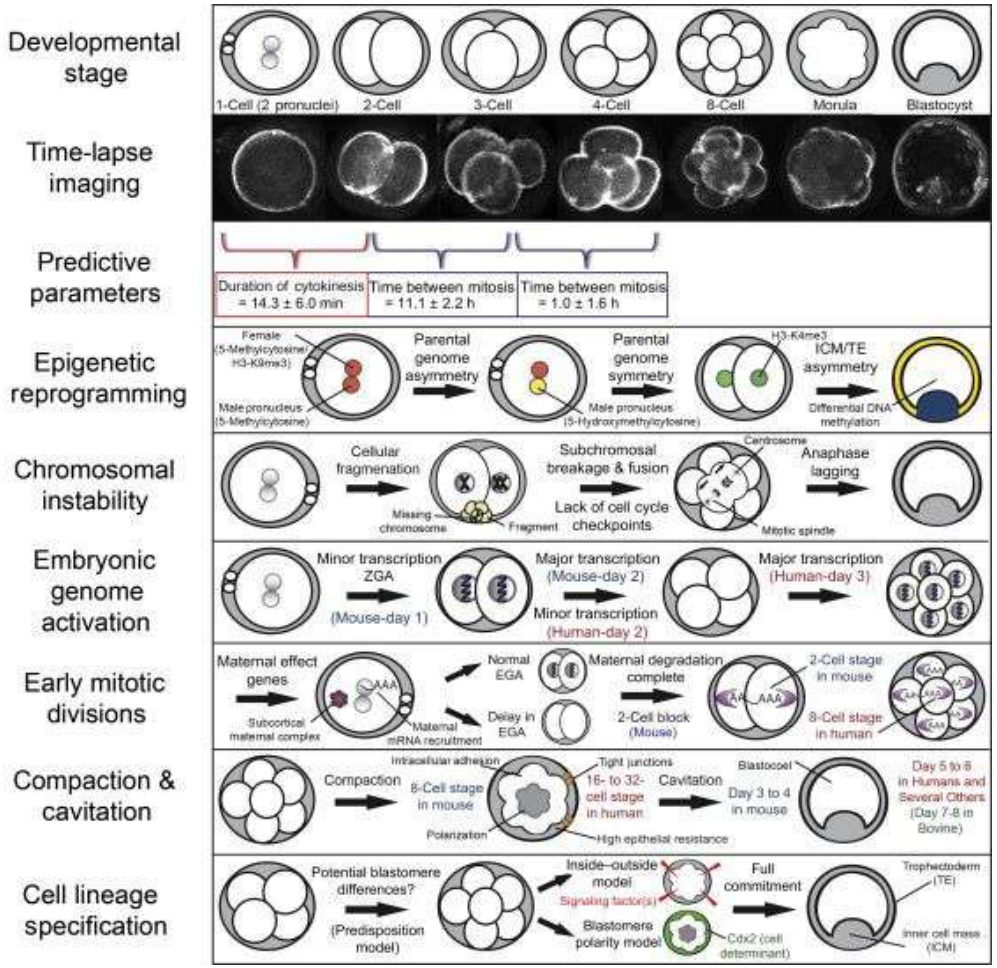
Reviews and Hypotheses

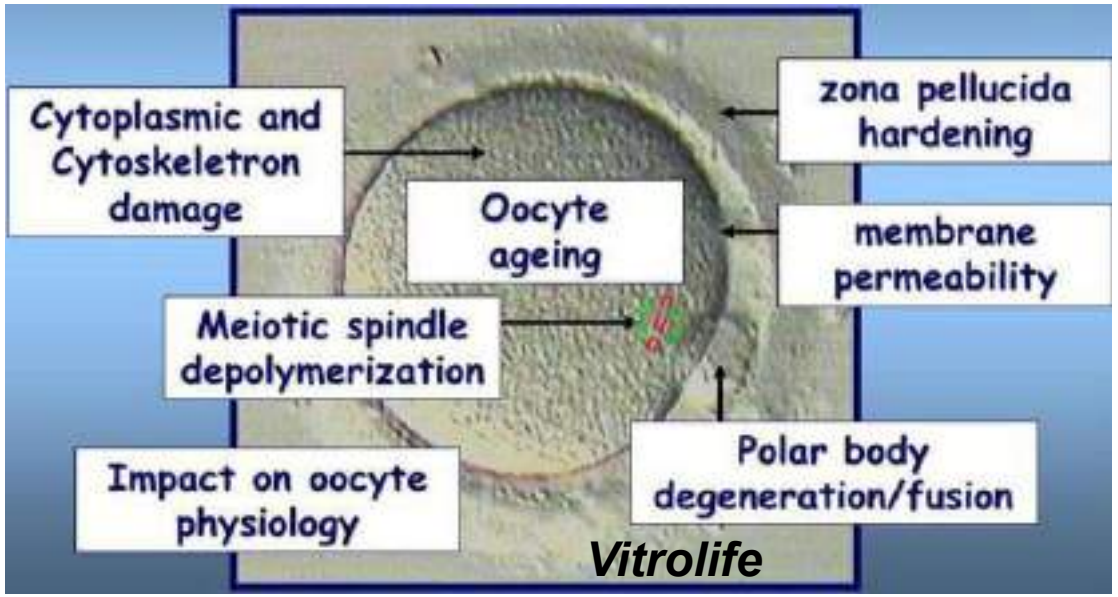
Mammalian pre-implantation chromosomal instability: species comparison, evolutionary considerations, and pathological correlations

Lucia Carbone & Shawn L. Chavez

Pages 321-335 | Received 29 Mar 2015, Accepted 10 Jun 2015, Published online: 14 Sep 2015

Cite this article https://doi.org/10.3109/19396368.2015.1079406



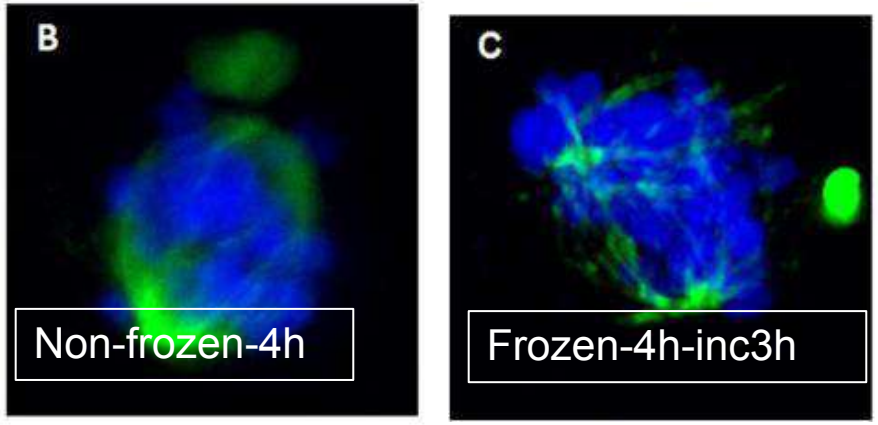


Cryobiology. 2021 Jun:100:110-116. doi: 10.1016/j.cryobiol.2021.03.001. Epub 2021 Mar 5.

Important parameters affecting quality of vitrified donor oocytes

Olga Teplá [1], Zinovij Topurko [2], Jaromír Mašata [3], Simona Jirsová [4], Michaela Frolíková [5], Kateřina Komrsková [6], Adela Minks [7], Jaroslav Turánek [8], Anna Lynnyk [9], Irena Kratochvílová [10]

*In 3D reconstructions, the average **volume of the chromosomes from the vitrified oocytes** was more than **1.8 times greater** than the average volume of the chromosomes from the never-frozen oocytes.*

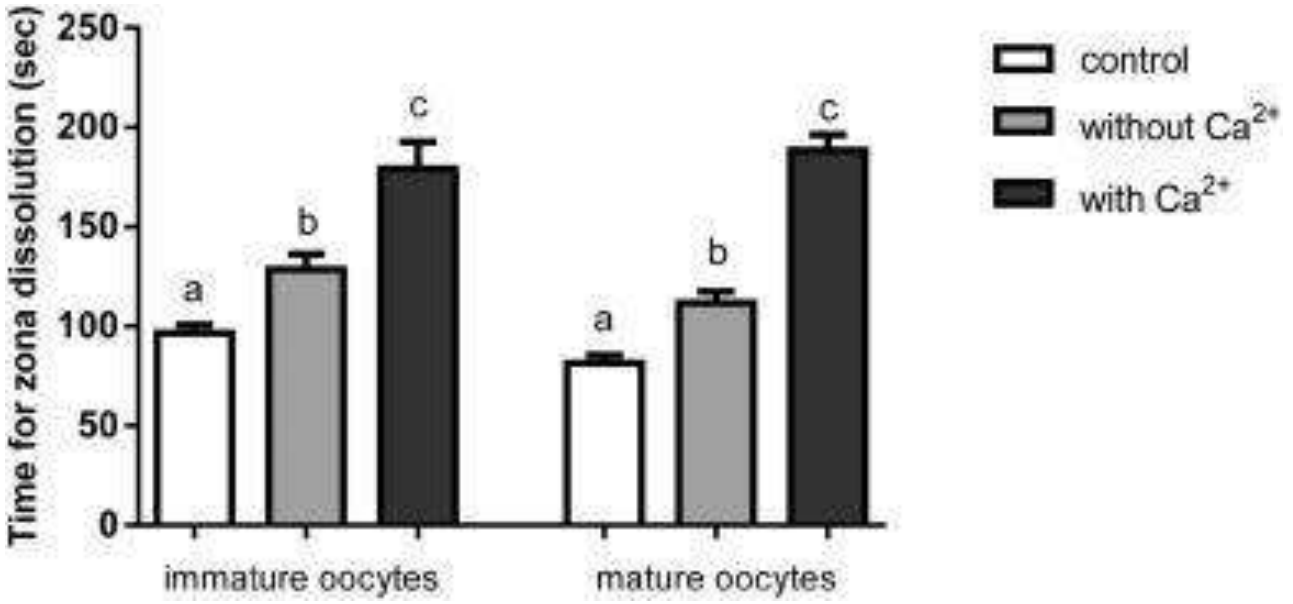


We need to understand more and better

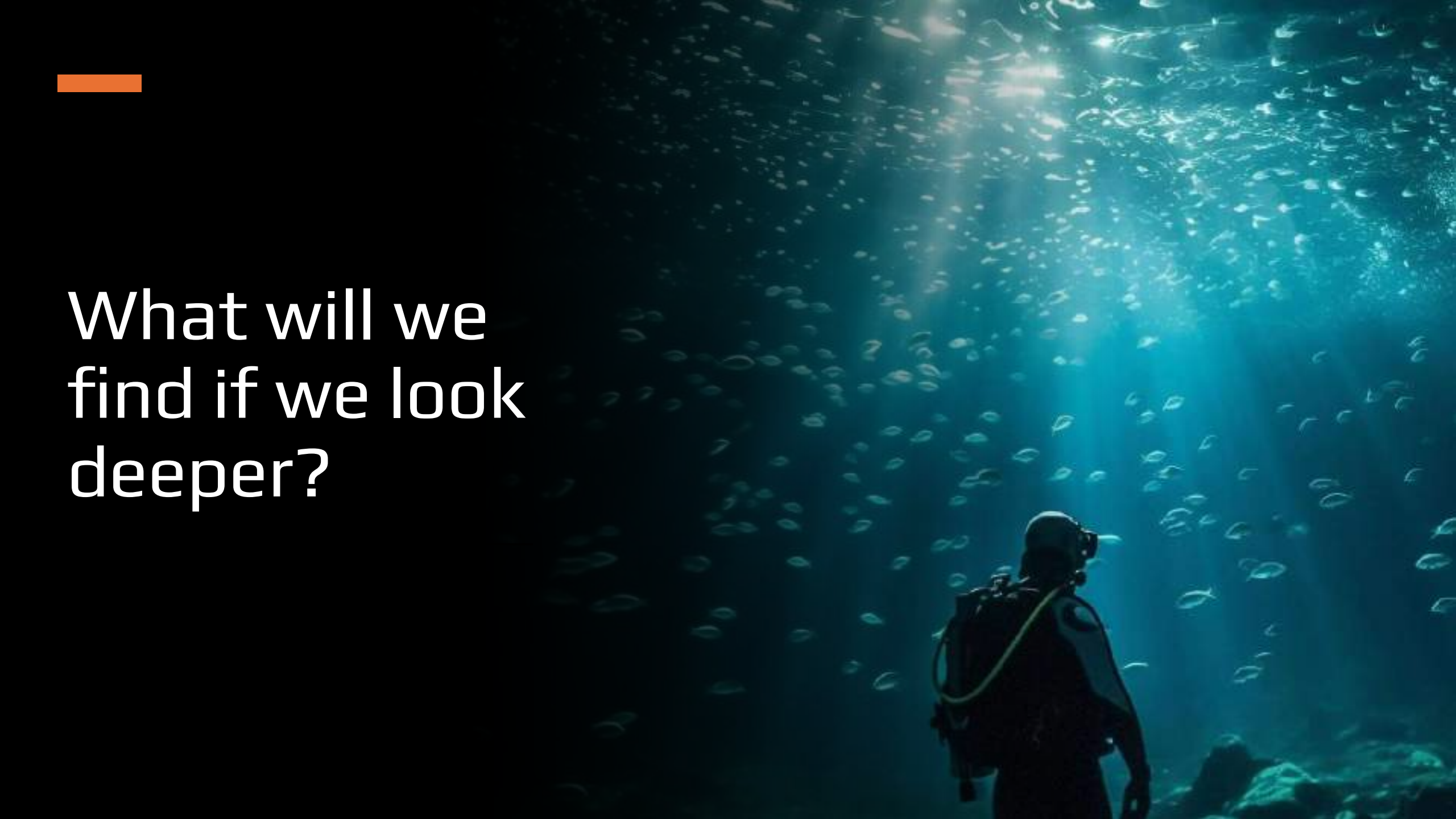
Cryobiology. 2017 Jun:76:18-23. doi: 10.1016/j.cryobiol.2017.05.001. Epub 2017 May 6.

Effect of vitrification on the zona pellucida hardening and follistatin and cathepsin B genes expression and developmental competence of in vitro matured bovine oocytes

Teresa Wiesak [1], Marta Wasielak [2], Aleksandra Złotkowska [3], Robert Milewski [4]



What will we find if we look deeper?



RNA integrity and differential expression

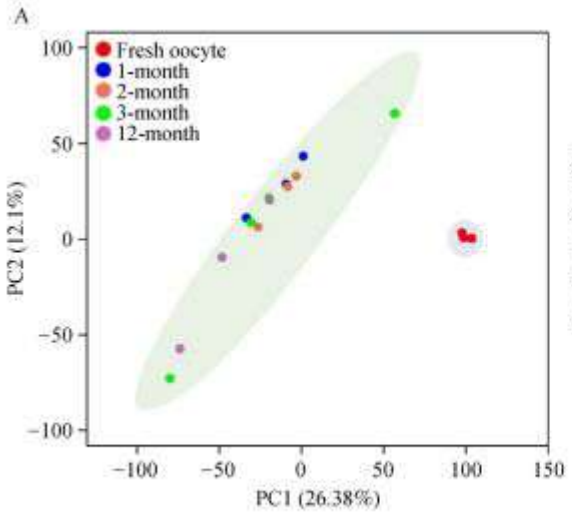
› Front Med. 2021 Feb;15(1):144-154. doi: 10.1007/s11684-020-0792-7. Epub 2020 Sep 2.

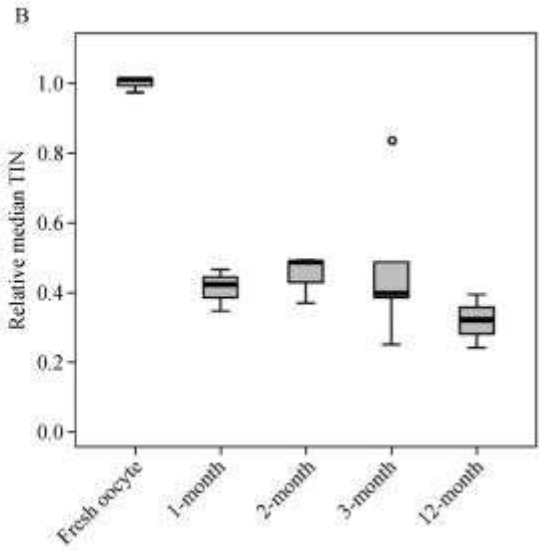
Effects of vitrification and cryostorage duration on single-cell RNA-Seq profiling of vitrified-thawed human metaphase II oocytes

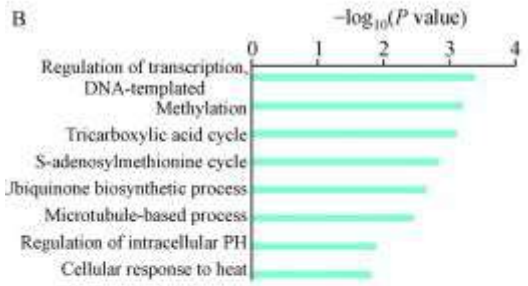
Ying Huo [*1,2,3,4], Peng Yuan [*1,3,4], Qingyuan Qin [*1,3,4], Zhiqiang Yan [1,3,4,5], Liying Yan [1,3,4,6], Ping Liu [1,3,4], Rong Li [1,3,4,6], Jie Yan [7,8,9], Jie Qiao [1,3,4,5,6]

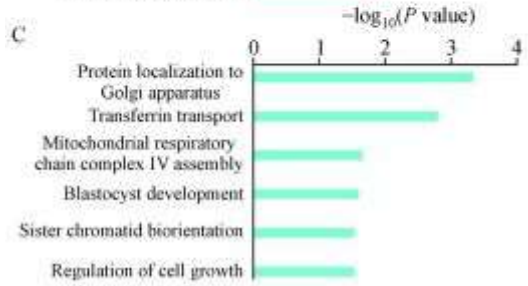
Affiliations + expand

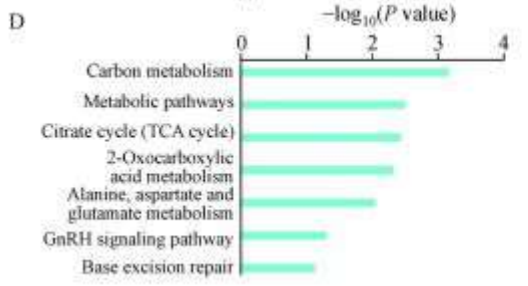
PMID: 32876878 DOI: 10.1007/s11684-020-0792-7

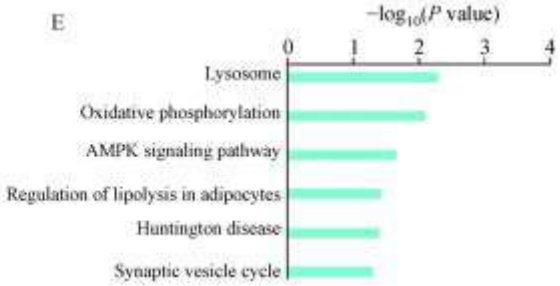




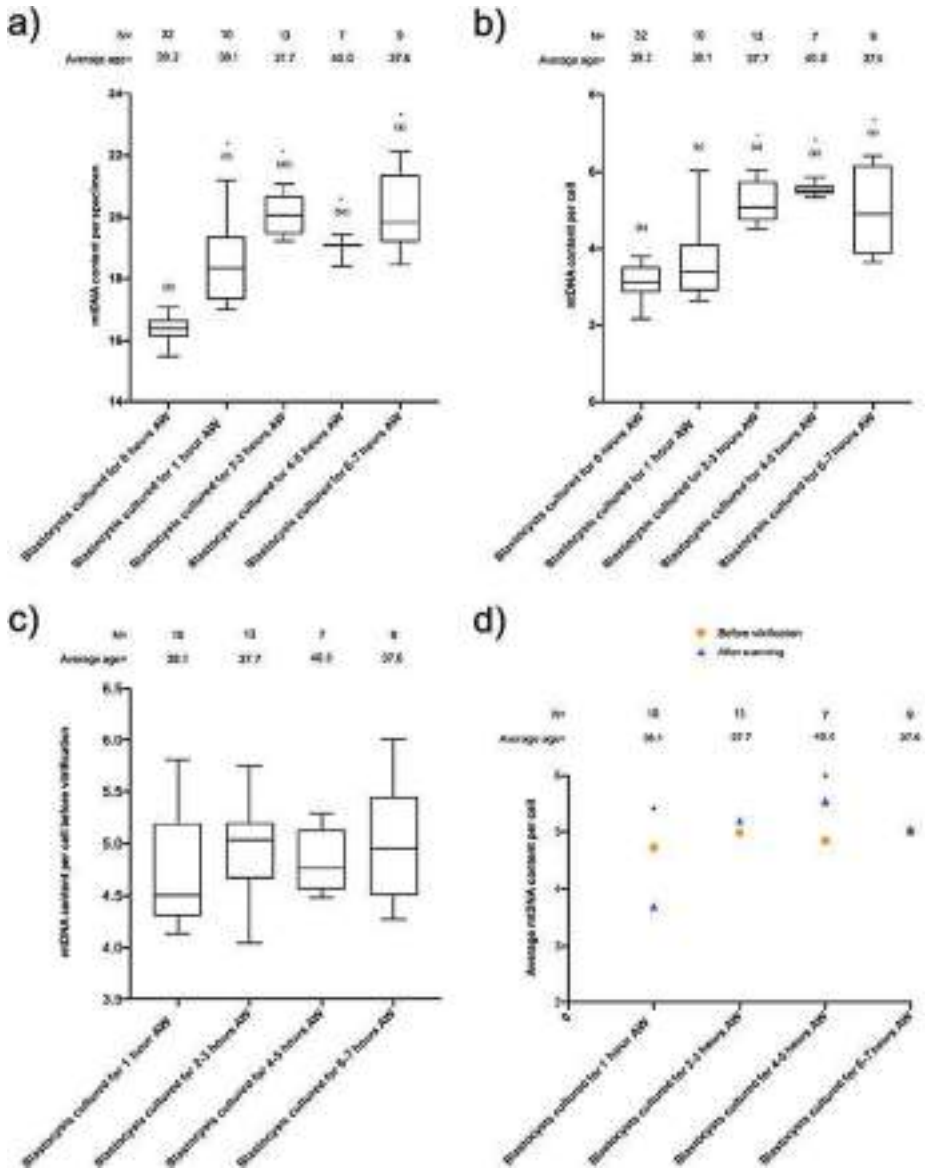








- *The RNA integrity in vitrified oocytes was lower compared to fresh oocytes.*
- *No difference was observed between vitrified oocytes in RNA integrity during the 1st year of cryopreservation*
- ***A number of DEGs were observed leading to different biological processes***



It may seem to be better to leave blastocysts for 6 hours prior to ET

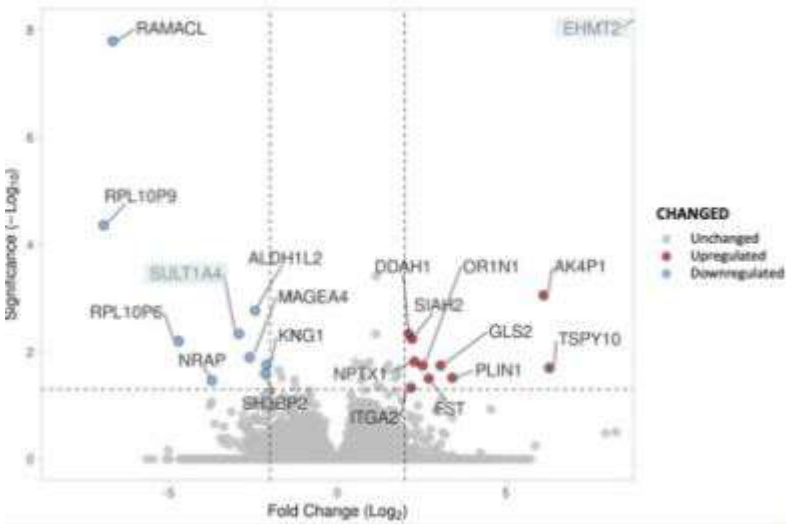
J Assist Reprod Genet. 2023 Oct 6;40(11):2577-2589. doi: 10.1007/s10815-023-02952-3

The effect of vitrification on blastocyst mitochondrial DNA dynamics and gene expression profiles

Marta Pérez Sánchez [1], María Luisa Pardiñas [1], Antonio Díez Juan [2], Alicia Quiñonero [1], Francisco Domínguez [1], Angel Martín [1], Carmina Vidal [3], Diana Beltrán [4], Amparo Milsud [4], Amparo Mercader [4], Antonio Pellicer [5], Ana Cobo [4], María José de los Santos [4,✉]

*mtDNA content of the blastocyst is lower during the first hour post-thaw, then increases sharply and seems to be at pre-vitrification levels at about **6-hours post thaw**.*

Over 100 DEGs were observed between 0h post-thaw and 4-5 hours post-thaw, affecting 186 biological processes.



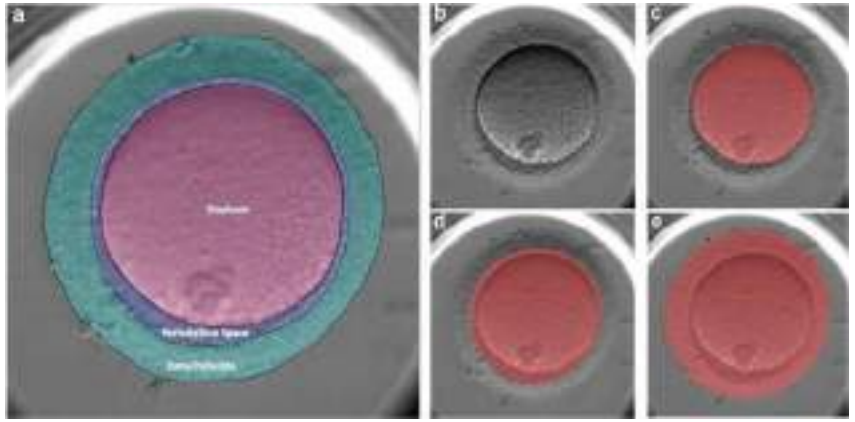
Summary II

An extended post-thaw time (around 6h) may be beneficial for blastocysts.

Blastocyst vitrification seems to lead to improved results when performed on D5 versus D6 (diff KPIs?)

Vitrification seems to result to differential gene expression both in oocytes and in embryos (FU)

What about AI

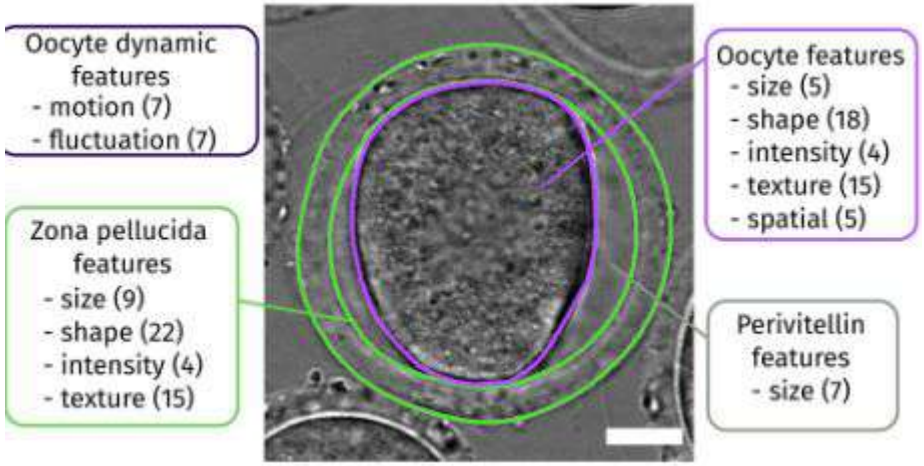


Article | Open access | Published: 08 May 2024

Segmentation of mature human oocytes provides interpretable and improved blastocyst outcome predictions by a machine learning model

Julián Fjeldstad ✉, Weikai Qi, Nadia Siddique, Natalie Mercuri, Dan Nayot & Alex Krivoi

Scientific Reports 14, Article number: 10569 (2024) | Cite this article



- Morphology may not be uninformative but the way we evaluate it may be.
- AI may provide a new perspective.
- Should we consider AI to be introduced in KPIs?
- No before it is tested and validated

© 2022. Published by The Company of Biologists Ltd | Journal of Cell Science (2022) 135, jcs260281. doi:10.1242/jcs.260281

TOOLS AND RESOURCES

An interpretable and versatile machine learning approach for oocyte phenotyping

Gaelle Letort[1,*], Adrien Eichmuller[1], Christelle Da Silva[1], Elvira Nikalayevich[1], Flora Crozet[1], Jeremy Salle[3], Nicolas Minc[2], Elsa Labrune[3,4,5], Jean-Philippe Wolf[6,7], Marie-Emilie Terret[1] and Marie-Hélène Verlhac[1]

How long is it safe to cryopreserve an embryo?
Different KPIs for different cryo times?

"Open Debate"

Storage time does not influence pregnancy and neonatal outcomes for first single vitrified high-quality blastocyst transfer cycle

Cryostorage duration does not affect pregnancy and neonatal outcomes: a retrospective single-centre cohort study of vitrified-warmed blastocysts

The effect of extended cryo-storage following vitrification on embryo competence: a systematic review and meta-analysis

The Impact of Embryo Storage Time on Pregnancy and Perinatal Outcomes and the Time Limit of Vitrification: A Retrospective Cohort Study

Does duration of cryostorage affect survival rate, pregnancy, and neonatal outcomes? Large-scale single-center study of slush nitrogen (SN_2) vitrified-warmed blastocysts

Prolonged Cryopreservation Negatively Affects Embryo Transfer Outcomes Following the Elective Freeze-All Strategy: A Multicenter Retrospective Study

The effect of storage time after vitrification on pregnancy and neonatal outcomes among 24 698 patients following the first embryo transfer cycles

Pregnancy and neonatal outcomes after long-term vitrification of blastocysts among 6,900 patients after their last live birth

The association between embryo storage time and treatment success in women undergoing freeze-all embryo transfer

Impact of prolonged embryo storage on reproductive and neonatal outcomes: a systematic review and meta-analysis

Take-home messages

With vitrification on the rise, It is high time to revisit KPIs

In the era of precision medicine and artificial intelligence KPIs can no longer be based on morphology and clinical outcomes

Addition of molecular data and AI could be considered in the future. Further interdisciplinary research on molecular effects and time.

Clinical outcomes are important; however, the molecular content may affect the health status of the neonate in the long-term.

Is the research that we do enough?

- **Multi-disciplinary**: people from different disciplines working together, each drawing on their disciplinary knowledge.
- **Cross-disciplinary**: viewing one discipline from the perspective of another.
- **Inter-disciplinary**: **integrating knowledge and methods from different disciplines, using a real synthesis of approaches**

Interdisciplinary Approach *... Medical Doctor, Clinical Embryologist, Experimental Biologist, Computational Biologist, Product Developer, Marketing, Software Developer, Surgical Robotics, Biomedical Engineer, Computer Vision Engineer, Robotics Engineer, Mechatronics Engineer...*

An ounce of prevention is worth a pound of cure.

~ Benjamin Franklin

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Advanced Course

Clinical Embryology and Physiology of Preimplantation Embryo

Programme of Teaching Module 6

"Understanding the Embryo and Culture Systems: Mapping of state-of-the-art Equipment and Protocols"

Submodule	Lecture-Speakers	Date-Time
6.1	Physiology and development of the preimplantation embryo ***Mara Simopoulou***	**2/3/2022** 6:00 p.m - 7:00 p.m
6.2	The pyramid of successful implantation ***Laura Rienzi***	**2/3/2022** 7:00 p.m - 8:00 p.m
6.3	Metabolism of the preimplantation embryo ***Roger Sturmey***	**9/3/2022** 5:00 p.m - 6:00 p.m
6.4	Culture media in IVF ***Dean Morbeck***	**9/3/2022** 6:00 p.m - 7:00 p.m
6.5	Embryo culture incubators ***Jason E. Swain***	**16/3/2022** 5:00 p.m - 6:00 p.m
6.6	Time-lapse imaging technology in the IVF laboratory ***Marcos Meseguer***	**16/3/2022** 6:00 p.m - 7:00 p.m
6.7	Troubleshooting in embryo culture ***Eros Nikitas***	**23/2/2022** 5:00 p.m - 6:00 p.m
6.8	Embryo culture and Evidence Based Clinical Practice ***David Gardner***	**30/3/2022** 8:00 a.m - 9:00 a.m

Thank You!

Contact details

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