

Social oocyte cryopreservation: pros and cons

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Disclosure

- Nothing to disclose.



[앵커&리포트] "출산은 미래에"..냉동 난자 여성 급증

KBS | 김학재

입력 16.02.26. 21:57 (수정 16.02.26. 21:57)

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가 가

<앵커 멘트>

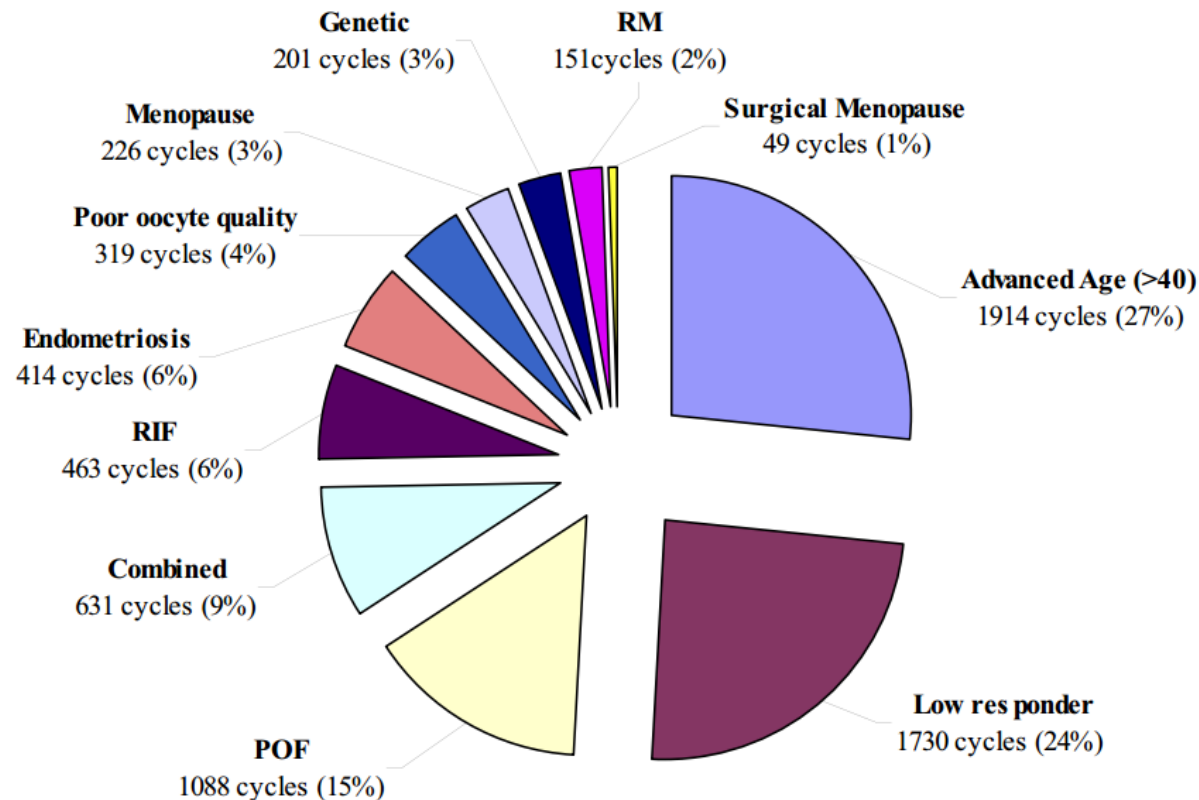
세계보건기구 WHO는 산모 나이가 만 35살을 넘으면 '고령 출산'으로 보고 있는데요.

결혼 연령이 늦어지면서 지난 10년 사이 우리나라의 고령 출산이 2배 이상 증

Social egg freezing: Is this a real trend?

FIGURE 1

Indications for oocyte donation (cycles with embryo transfer = 7,186). POF = premature ovarian failure, RIF = recurrent IVF failure, RM = recurrent miscarriage.



Budak. Evolution of a large oocyte donation program over a 10-year period. Fertil Steril 2007.

Social egg freezing: Trend changes

- Oocyte freezing for fertility preservation without a medical indication should not be encouraged. (*Shenfield et al., 2004, ESHRE Task Force on Ethics and Law 7*)
- Oocyte cryopreservation to improve prospects of future child bearing should also be available for non-medical reasons. (*2012, ESHRE Task Force*)

Social egg freezing: Trend changes

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

There is good evidence that fertilization and pregnancy rates are similar to IVF/ICSI with fresh oocytes when vitrified/warmed oocytes are used as part of IVF/ICSI for young women. Although data are limited, no increase in chromosomal abnormalities, birth defects, and developmental deficits has been reported in the offspring born from cryopreserved oocytes when compared to pregnancies from conventional IVF/ICSI and the general population. Evidence indicates that oocyte vitrification and warming should no longer be considered experimental. This document replaces the document last published in 2008 titled, "Ovarian Tissue and Oocyte Cryopreservation," Fertil Steril 2008;90:S241-6. (Fertil Steril® 2013;99:37-43. ©2013 by American Society for Reproductive Medicine.)

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Social egg freezing: Emerging trend

Efficacy

Safety



Social egg freezing: Efficacy

Summary of randomized controlled trials comparing fresh versus vitrified oocytes.

	Cobo 2008 (24)	Cobo 2010 (26)	Rienzi 2010 (25)	Parmegiani 2011 (19)
Patient population	Oocyte donors	Oocyte donors	Infertile patients <43 years of age requiring ICSI with >6 mature oocytes	Infertile patients <42 years of age requiring ICSI with >5 mature oocytes
No. patients	30 vitrification 30 fresh	295 vitrification 289 fresh	40 vitrification 40 fresh	31 vitrification 31 fresh
Mean age at retrieval	26	26	35	35
No. oocytes	231 vitrification 219 fresh	3286 vitrification 3185 fresh	124 vitrification 120 fresh	168 vitrification NA fresh
No. oocytes per retrieval	18.2	11	13	NA
Survival	96.9%	92.5%	96.8%	89.9%
Fertilization rate	76.3 vitrification 82.2 fresh	74% vitrification 73% fresh	79.2% vitrification 83.3% fresh	71% vitrification 72.6% fresh
No. transferred vitrification vs. fresh	3.8 vitrification 3.9 fresh	1.7 vitrification 1.7 fresh	2.3 vitrification 2.5 fresh	2.5 vitrification 2.6 fresh
Day of transfer	3	3	2	2-3
Implantation rate	40.8% vitrification 100% fresh	39.9% vitrification 40.9% fresh	20.4% vitrification 21.7% fresh	17.1% vitrification NA fresh
CPR/transfer vitrification vs. fresh	60.8% (23 vitrification transfers) 100% (1 fresh transfer)	55.4% vitrification 55.6% fresh	38.5% vitrification 43.5% fresh	35.5% vitrification 13.3% fresh
CPR/oocyte thawed	6.1%	4.5%	12%	6.5%

Note: All used vitrification with Cryotop, 15% EG + 15% DMSO + 0.5M sucrose. CPR = clinical pregnancy rate.

Practice Committee. Oocyte cryopreservation. Fertil Steril 2013.

Obstetric and perinatal outcome of babies born from vitrified oocytes

Ana Cobo, Ph.D., Vicente Serra, M.D., Nicolás Garrido, Ph.D., Inés Olmo, M.D., Antonio Pellicer, M.D., and José Remohí, M.D.

● Instituto Valenciano de Infertilidad, Universidad de Valencia, Valencia, Spain.

Objective: To assess outcomes after oocyte vitrification on obstetric and perinatal outcomes compared with those achieved with fresh oocytes.

Design: Retrospective cohort study.

Setting: Private university-affiliated IVF center.

Patient(s): Children born after use of vitrified oocytes (1,027 from 804 pregnancies) and fresh oocytes (1,224 from 996 pregnancies). Singleton and multiples pregnancies from own and donated ova were included.

Intervention(s): Oocyte vitrification by the Cryotop method.

Main Outcome Measure(s): Pregnancy, delivery, and neonatal outcomes.

Result(s): Vitrification had no clinically relevant adverse effects on obstetric and perinatal outcomes after adjusting for potential confounders. No differences were found between the vitrified and fresh oocyte groups in the rate of obstetric problems (including diabetes, pregnancy-induced hypertension, preterm birth, anemia, and cholestasis), gestational age at delivery, birth weight, Apgar scores, birth defects, admission to neonatal intensive care unit (ICU), perinatal mortality, and puerperal problems. Only a greater number of invasive procedures (adjusted odds ratio 2.12; 95% confidence interval 1.41–3.20), and a reduced occurrence of urinary tract infection (adjusted odds ratio 0.51; 95% confidence interval 0.28–0.91), were observed in the vitrified oocytes group.

Conclusion(s): Although our data, the largest series to date, suggest that oocyte vitrification does not increase adverse obstetric and perinatal outcomes in children conceived with vitrified oocytes, further studies with larger samples are required to reinforce our conclusions. (Fertil Steril® 2014;102:1006–15. ©2014 by American Society for Reproductive Medicine.)

Key Words: Assisted reproduction, oocyte vitrification, perinatal outcome, pregnancy problems

Discuss: You can discuss this article with its authors and with other ASRM members at <http://fertstertforum.com/coboa-obstetric-perinatal-babies-vitrified-oocytes/>



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Comparative analysis of fetal and neonatal outcomes of pregnancies from fresh and cryopreserved/thawed oocytes in the same group of patients

Paolo Emanuele Levi Setti, M.D.,^a Elena Albani, Biol.Sc.,^a Emanuela Morengi, Ph.D.,^b Giovanna Morreale, Biol.Sc.,^a Luisa Delle Piane, M.D.,^a Giulia Scaravelli, Ph.D.,^c and Pasquale Patrizio, M.D., M.B.E., H.C.L.D.^d

^a Department of Gynecology, Division of Gynecology and Reproductive Medicine and ^b Biostatistics Unit, Humanitas Clinical and Research Institute, Milan; ^c ART Italian National Register, National Center for Epidemiology, Surveillance and Health Promotion, National Health Institute, Rome, Italy; and ^d Department of Obstetrics, Gynecology and Reproductive Sciences, Yale University, School of Medicine, New Haven, Connecticut

Objective: To analyze the fetal and neonatal outcomes of pregnancies achieved with fresh and/or frozen oocytes in the same group of patients.

Design: Observational study and comparative analysis.

Setting: Research unit of an academic medical center.

Patient(s): A group of 855 women with cryopreserved oocytes and their resulting 954 assisted reproductive technology clinical pregnancies were enrolled and followed up during the same time period and in the same clinical setting; the outcomes of 197 pregnancies from frozen/thawed oocytes were compared with 757 obtained from fresh sibling oocyte cycles.

Intervention(s): None.

Main Outcome Measure(s): Pregnancies were followed until delivery, and neonatal data (up to 28 days after delivery) were collected.

Result(s): No significant differences were found between the use of fresh and frozen oocytes in the rates of therapeutic abortions for fetal anomaly (1.5% vs. 0.8%) and ectopic pregnancies (3.6% vs. 2.9%), but a significantly higher rate of spontaneous abortions at ≤ 12 weeks (17.6% vs. 26.9%) was observed in the frozen/thawed oocytes group. No statistical differences were found in major anomalies at birth (2.8% vs. 4.6%). Despite no difference in gestational age at delivery, the mean birth weights were significantly lower with fresh oocyte pregnancies, both in singleton ($2,725 \pm 727$ g) and twins ($2,128 \pm 555$ g), than with frozen-thawed oocytes ($3,231 \pm 615$ g and $2,418 \pm 492$ g, respectively). However, the analysis of the 63 patients who obtained pregnancies both in fresh and thawed cycles (138 pregnancies) showed no differences in the abortion rate and in the mean birth weight.

Conclusion(s): These results provide strong support to the notion that fetal and perinatal complications and congenital anomalies do not differ between pregnancies from frozen-thawed and fresh oocytes. The significantly lower mean birth weight observed with pregnancies from fresh oocytes supports similar observations reported for pregnancies from embryo cryopreservation and requires further prospective studies. (Fertil Steril® 2013;100: 396–401. ©2013 by American Society for Reproductive Medicine.)



Use your smartphone

Social egg freezing: there are more than these.

Efficacy

Safety

**Medical
needs**

Ethics

**Cost-
effective
ness**

Question 1: Medical needs

Is it necessary?

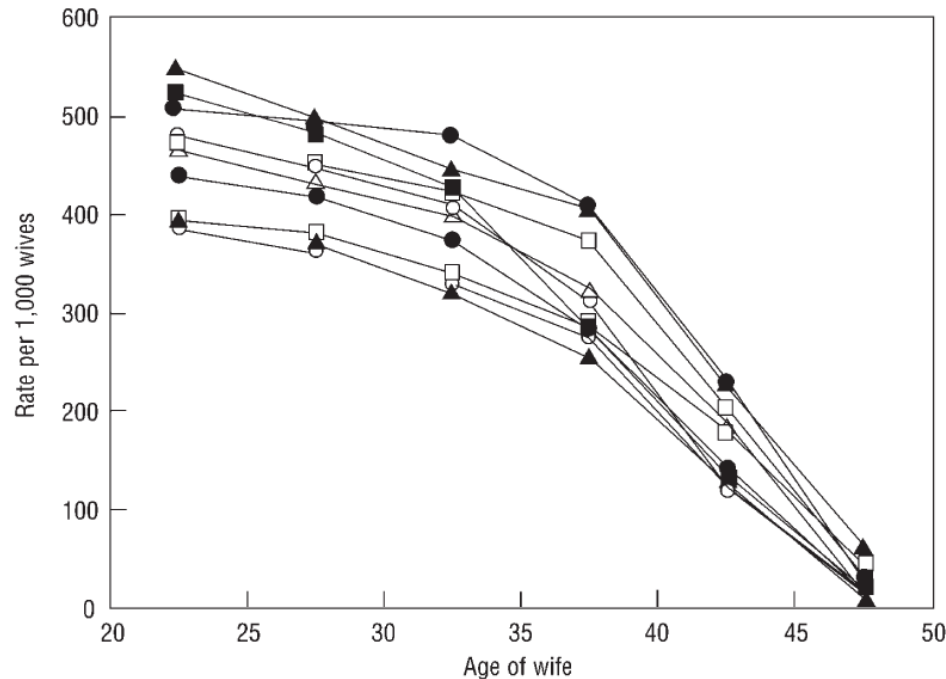


Fig. 1. Marital fertility rates by 5-year age groups. The ten populations (in descending order at age 20–24 years) are Hutterites, marriages in 1921–1930 (▲); Geneva bourgeoisie, husbands born in 1600–1649 (■); Canada, marriages in 1700–1730 (●); Normandy marriages in 1760–90 (○); Hutterites, marriages before 1921 (□); Tunis, marriages of Europeans 1840–1859 (△); Normandy, marriages in 1674–1742 (●); Norway, marriages in 1874–1876 (□); Iran, village marriages in 1940–1950 (▲); Geneva bourgeoisie, husbands born before 1600 (○). From Menken J, Trussell J, Larsen U. Age and fertility. *Science* 1986;233:1389–94. Reprinted with permission from AAAS. ⇐

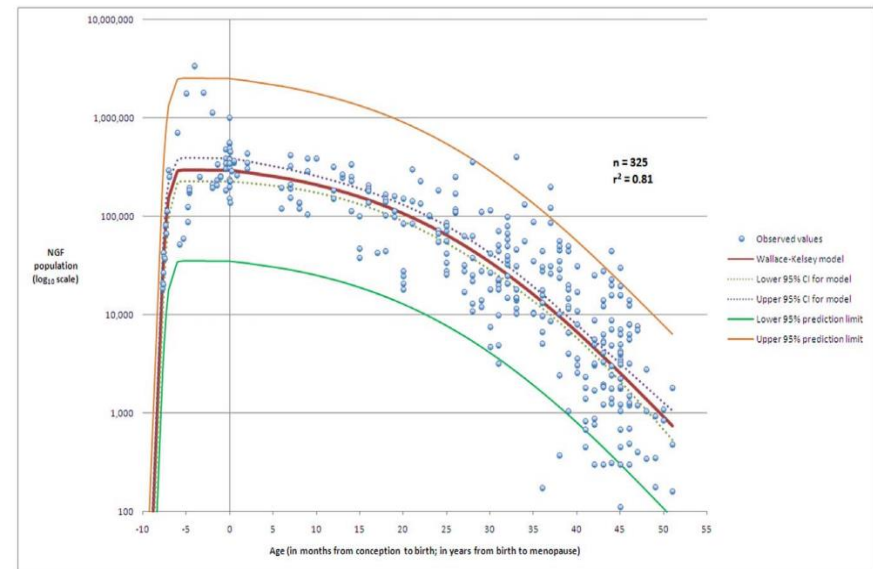
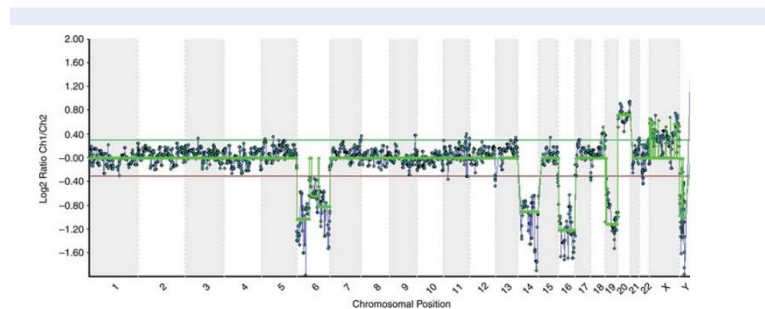


Figure 1. The model that best fits the histological data. The best model for the establishment of the NGF population after conception, and the subsequent decline until age at menopause is described by an ADC model with parameters $a = 5.56$ (95% CI 5.38–5.74), $b = 25.6$ (95% CI 24.9–26.4), $c = 52.7$ (95% CI 51.1–54.2), $d = 0.074$ (95% CI 0.062–0.085), and $e = 24.5$ (95% CI 20.4–28.6). Our model has correlation coefficient $r^2 = 0.81$, fit standard error = 0.46 and F-value = 364. The figure shows the dataset ($n = 325$), the model, the 95% prediction limits of the model, and the 95% confidence interval for the model. The horizontal axis denotes age in months up to birth at age zero, and age in years from birth to 51 years.

Question 1: Medical needs

Is it necessary?

- 77% oocytes are aneuploid at 40 y.



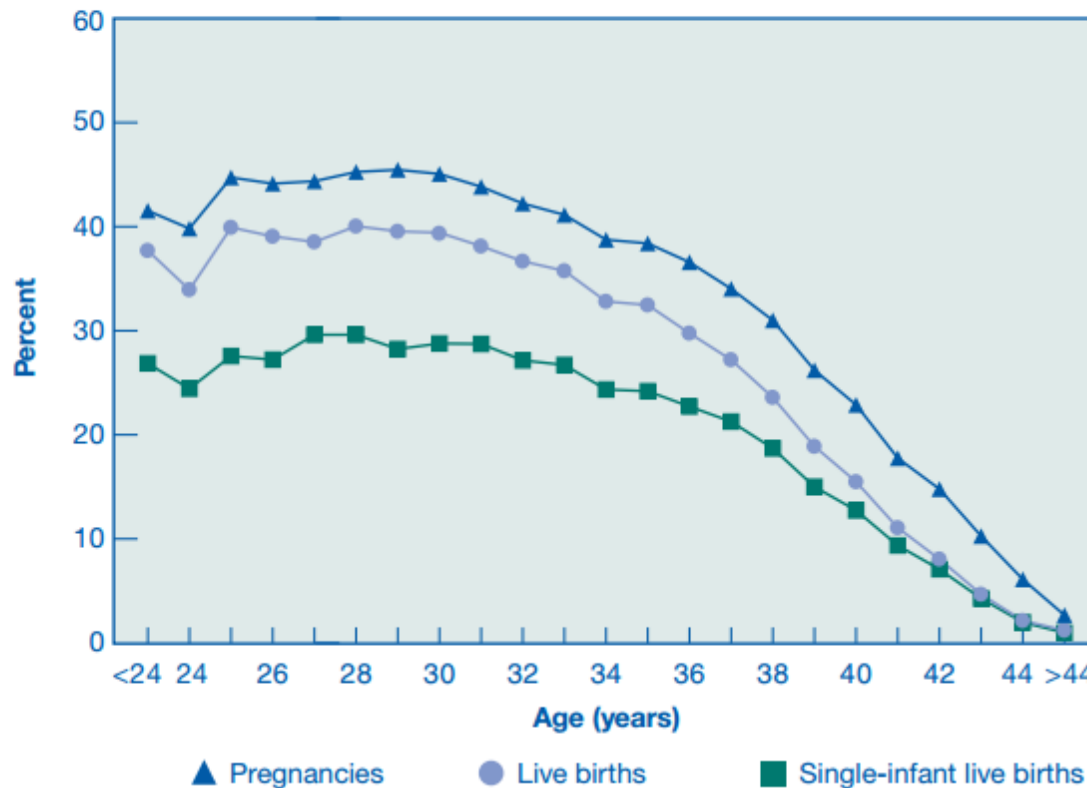
car body II with losses of chromosomes 6, 14, 16, 19 and gain of chromosome 20.

- Risk of being childless

<30 y	6%
<35 y	14%
40 y	35%

Figure 14

Percentages of ART Cycles Using Fresh Nondonor Eggs or Embryos That Resulted in Pregnancies, Live Births, and Single-Infant Live Births, by Age of Woman,* 2014



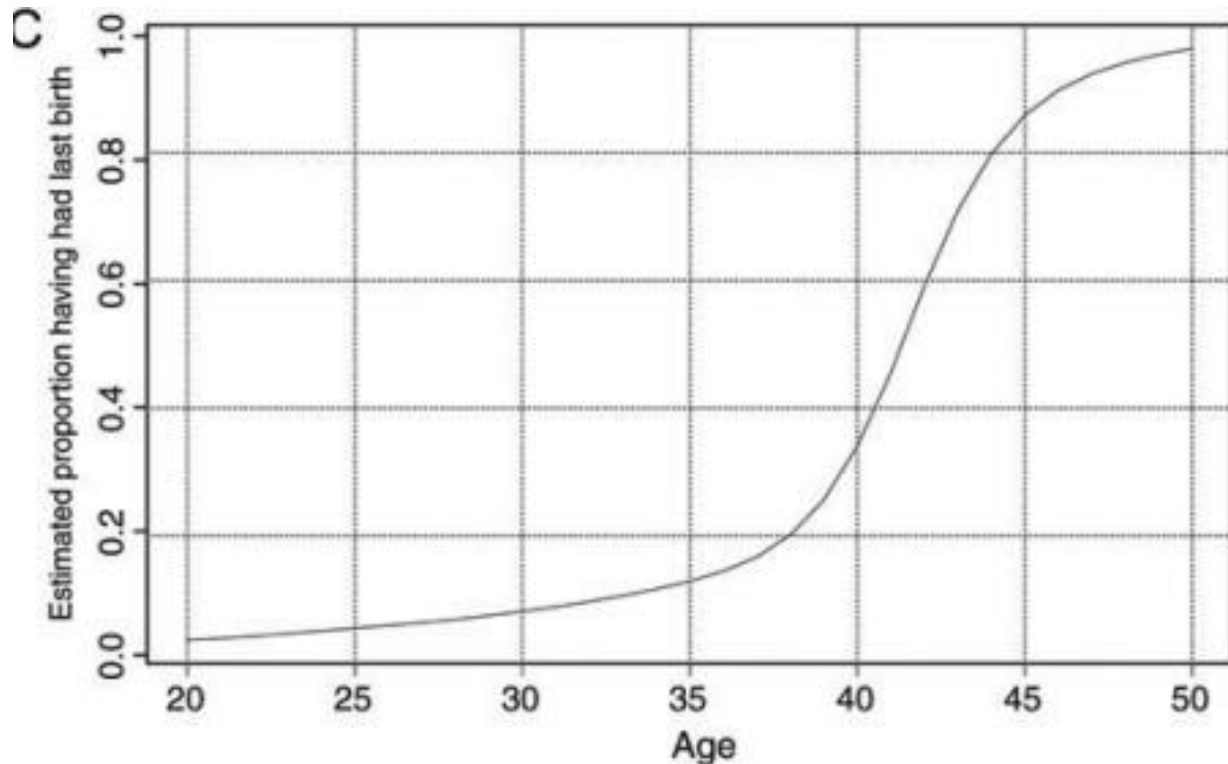
* For consistency, all percentages are based on cycles started.

Social egg freezing: Medical needs

human
reproduction

ORIGINAL ARTICLE *Reproductive epidemiology*

Too old to have children? Lessons from natural fertility populations



Social egg freezing: Medical needs

PROS

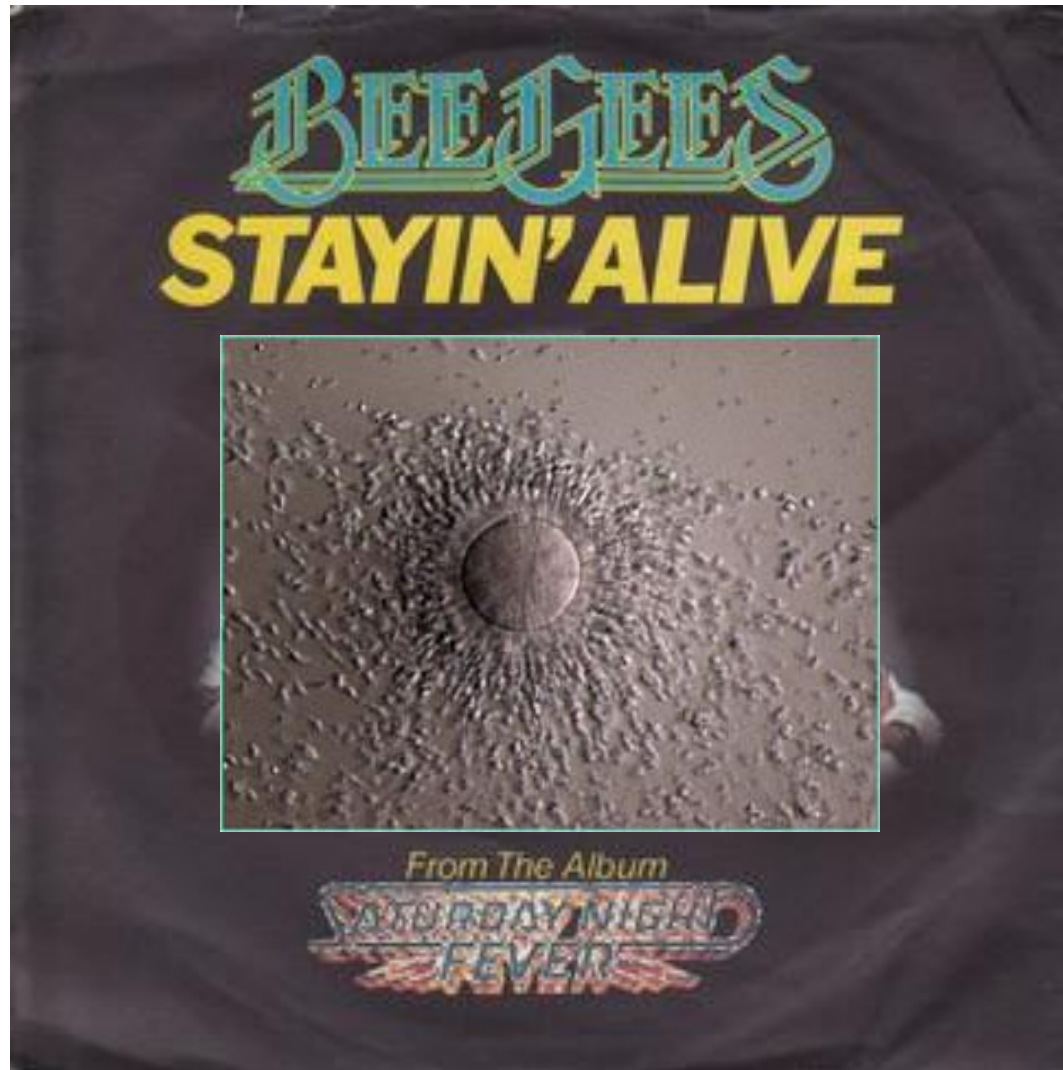
To some extent, a helpful solution of age-related fertility decline.

CONS

Over-treatment of future uncertain infertility

Question 2:

Can/may we do this (ethics)?



Social egg freezing: Ethics from a *medical* view

- Medical technique used for a non-health-related preference
- ➔ Fertility preservation for women who fear natural fertility loss vs. abortion and donor insemination for single or lesbian women



Hippocratic core of medical ethics:
medicine understood as preventing and curing disease

Social egg freezing: Ethics from a *social* view

We may look for a medical solution for a social problem.



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trying to climb the ladder while being an at-least-half-present mother.

By telling their female staff to hold off on having babies, these companies are demanding their employees put them before everything else, before their families, before their health. Rather than saying, “have your children in your own time and we’ll support you with well-paid parental leave and subsidised childcare”, they’re saying, “work really hard through your most fertile years and then when you may not be able to have kids anymore, you can give it a shot with the eggs we froze for you as a perk”.

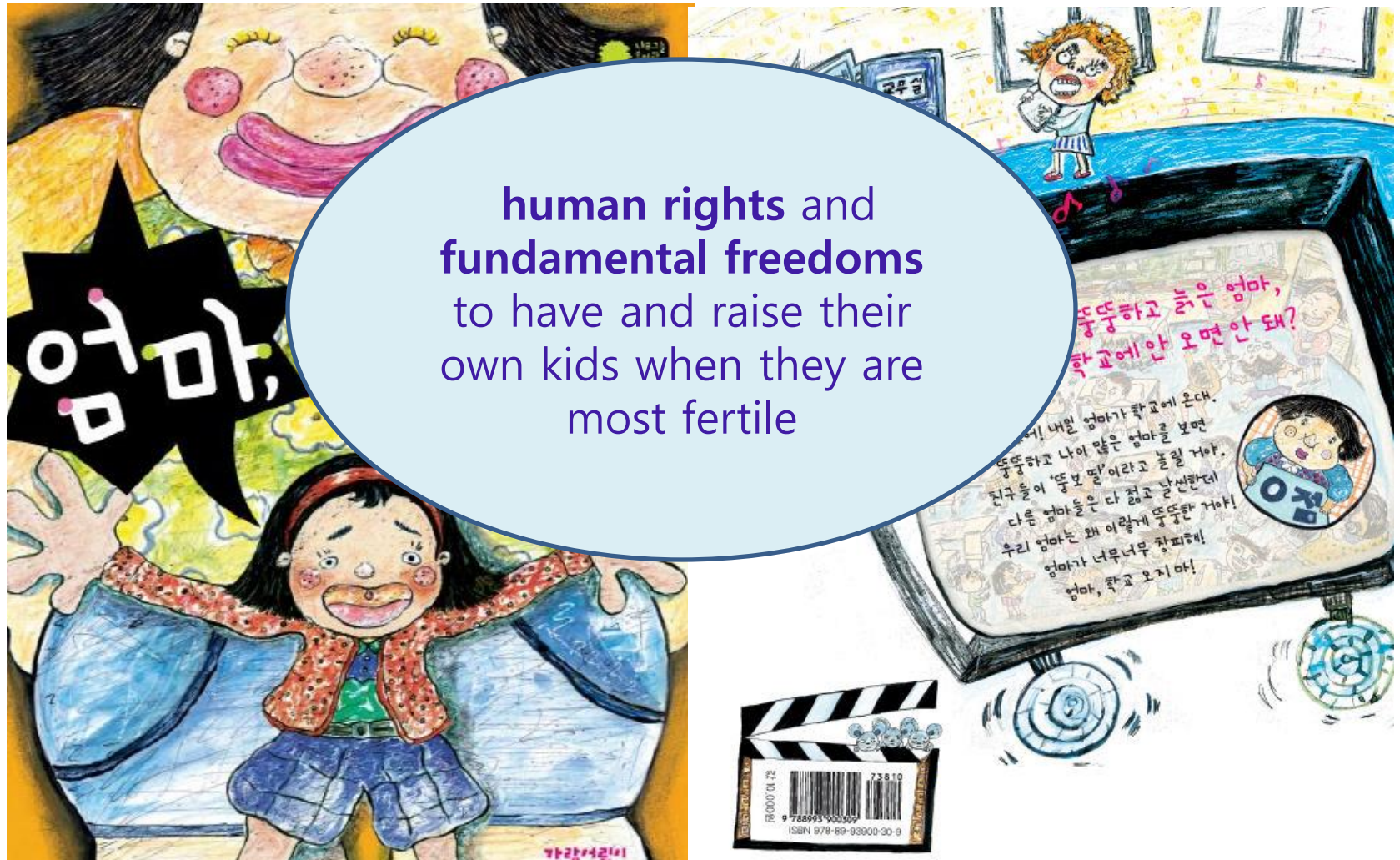
Apparently, Apple’s head of HR asked staff what benefits they’d most appreciate. What a strange list of tickbox options that would have been: shorter working week, more flexibility, better pay, egg freezing. Who was picking the latter? Probably not the women at Apple who already have children and are trying to make a career work around them. Wouldn’t creche facilities or childcare supplements have been more helpful? This isn’t a benefit created to make life better for working women, it’s a threat. Have children at the wrong time and accept that your career is over.

I’m sure there are some women for whom this benefit will be a bonus they’re pleased about. I wonder how many are booking appointments at the fertility clinic not because they want to focus on spreadsheets but because they simply haven’t yet found the right partner. But if being a working mother is hard, being a single working mother is even harder.

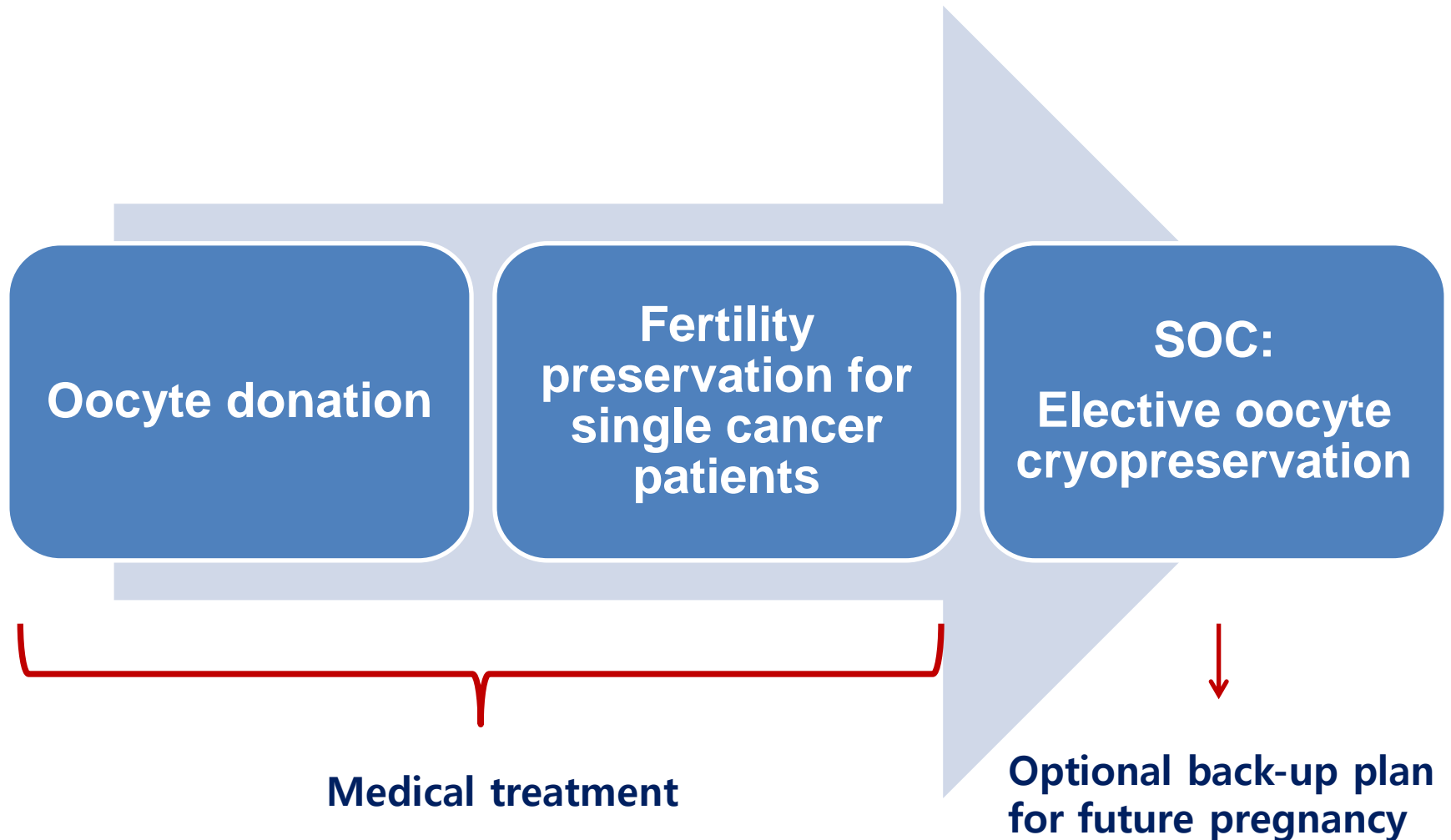
When are we going to wake up and realise that great employees want to be able to blend their work life with their home life, rather than another opportunity to focus entirely on their career? If you’re an ambitious woman or man you know that sometimes work is going to come before family. But wouldn’t it be nice if in

Social egg freezing: Ethics

When is one too **old** to have a baby?



As an additional indication of infertility *free from ethical challenges?*



Growing medical rationale

Let's take a little tweak

- As a treatment of age-related fertility decline



☎ 진행자 > 난자냉동 보관방법이 궁극적으로 난임에도 긍정적인 효과를 줄 수 있을까요?

☎ 김자연 > 네, 그렇게 보여집니다. 왜냐하면 전체 난임 중에서 난소기능 저하로 인한 난임이 상당히 많은 부분을 차지 하고 난소기능 저하의 대부분이 고령으로 인한 난소기능 저하거든요. 그런 측면에서 본다면 난자 냉동으로 미리 건강한 난자를 열려놓는다면 고령으로 인한 난소저하 난임은 어느 정도 조금 도움을 받을 수 있겠죠.

Social egg freezing: Ethics

PROS

Enhanced reproductive freedom

Reduced time pressure

Reduction of future regrets and self-blame for not taking advantage of current technology

CONS

Reduced focus on necessary societal changes

Not offering a foolproof way to optimize career success and family planning

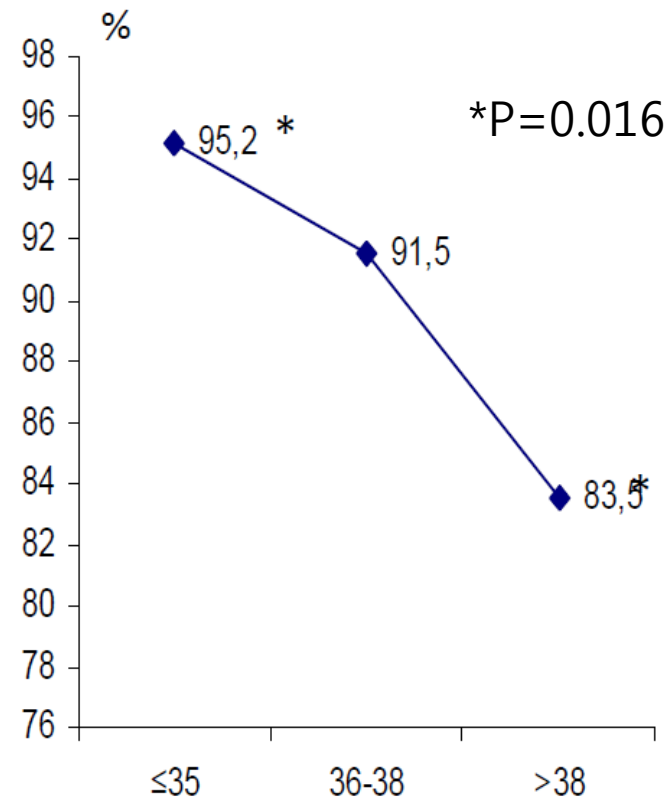
Question 3:

Does it deserve? (cost-effectiveness)

Survival after thawing per age

Group	N° Patients	MII oocytes (mean ± SD)
≤35	50	605 (12,5 ± 1,8) ^a
36-38	33	428 (9,1 ± 3,0) ^b
>38	47	252 (3,7 ± 3,9) ^c

a≠b≠c (p<0,05)



Time and Cost

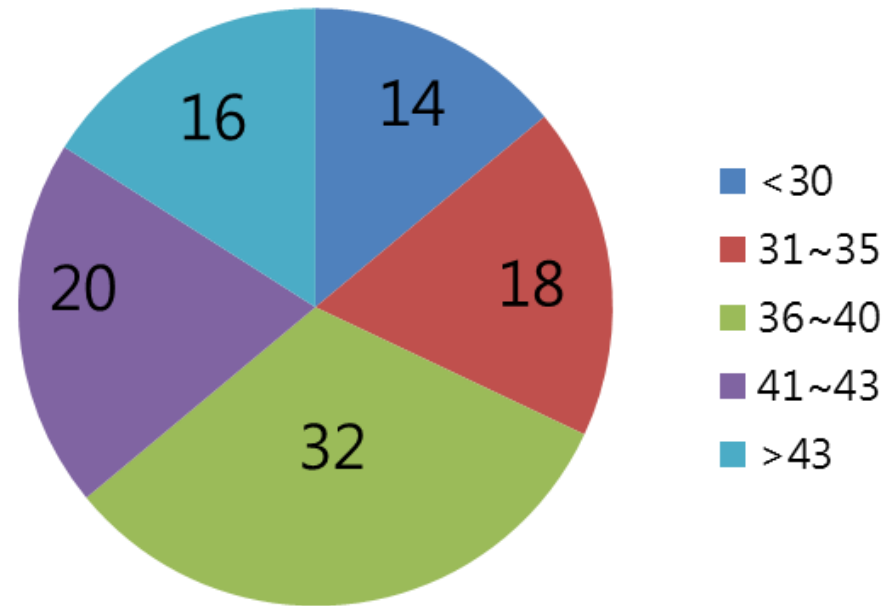
- Optimal timing for elective egg freezing, *Fertil Steril* 2015, Tolga et al.
 - Decision tree model to assess success and cost-effectiveness
 - Greatest improvement in probability of live birth compared with no action (51.6% vs. 21.9%) when performed at age **37 years**



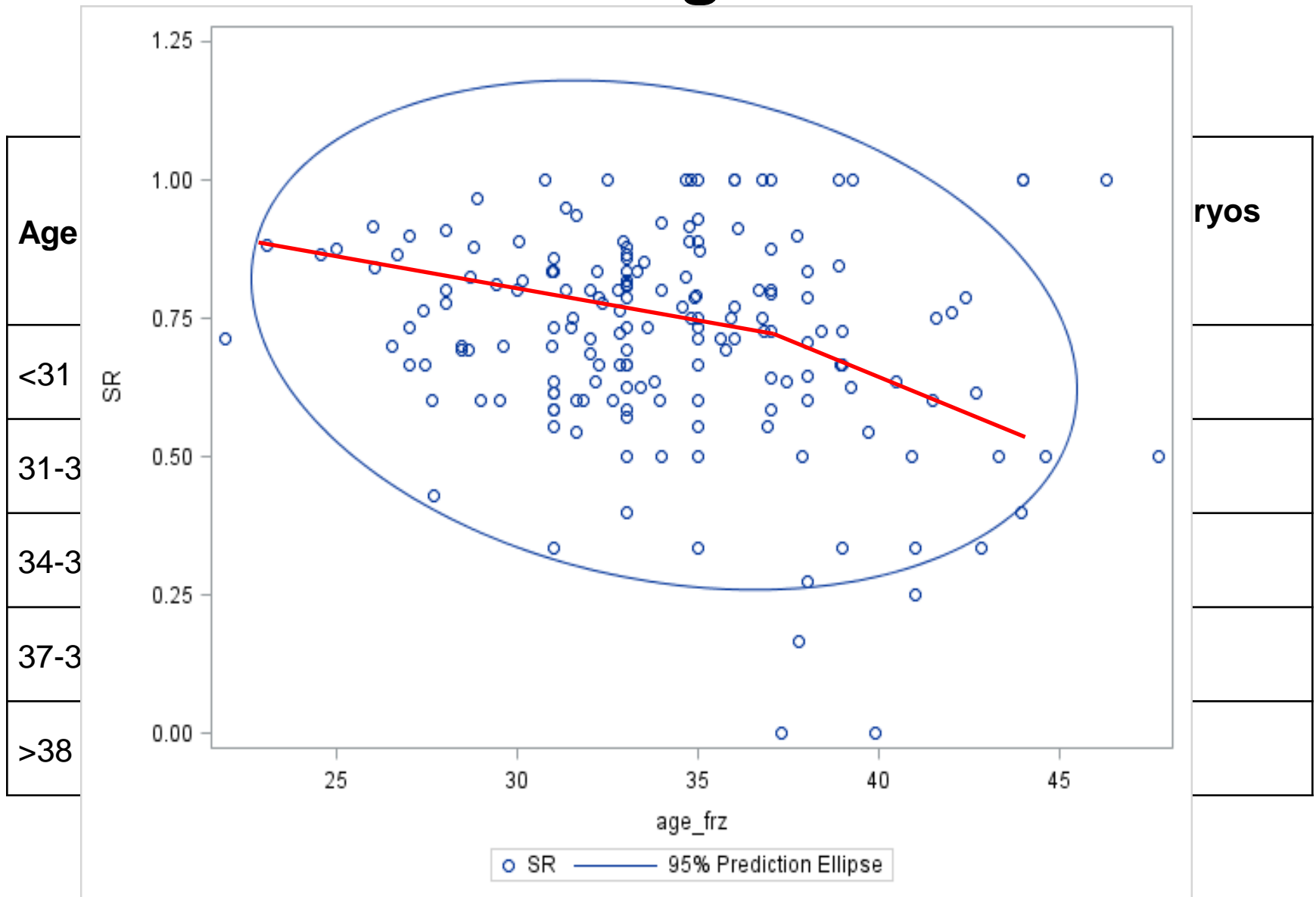
Patients' age

37 oocyte banking

Age



VERY old age women



How many to freeze



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.

메뉴열보기 TopBar 고정 SideBar 펼침 x (조회) 전체닫기 x 모든 화면닫기

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외래기록 x 초음파 x

An Play An Stop 오름 차순 내림 차순 Summary 모두펼침 Summary 모두접힘 서식 닫기 썸네일 보기

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외래기록

■가족관계증명서
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LMP 2015-11-05 # 생리 후 2 일째

Endometrium 0.5 (cm)

Rt. Ovary(cm) Lt. Ovary(cm)

0.6 0.5 0.4

진 • OPU 14, MII 8, GV 6

P -0-
PMP regular (25-28)

For 2nd oocyte cryo: 6 oocytes frozen

AFC> 5
AMH> 0.38, FSH> 18.15

"성공을 대단히 희박하고 거의 불가능하다고 상담함. 그런데도 진행 원함"

op-lab> EKG: incomplete RBBB -> 심장내과 컨설팅: OPU OK

Cervical polypectomy> EM polyp

1. 2nd try: puregon200/100 for 4 days -> FU on 11/11
2. E2

How long can we keep them?

- So far, as long as you want to.

TABLE 1

Survival and clinical outcome according to storage time.

Storage time, months	No. of WP	No. of surviving oocytes (SR/WP)	95% CI	CPR/WP	95% CI	OPR/WP	95% CI	IR	95% CI
≤6	2,312	24,427 (90.1)	89.7–90.5	1,090 (47.5)	45.5–49.5	902 (39.4)	37.4–41.4	39.7	37.9–41.5
>6 and ≤12	646	6,855 (90.2)	89.4–90.9	296 (45.1)	41.3–48.9	237 (36.1)	32.4–39.8	37.9	35.7–40.1
>12 and ≤18	315	3,495 (91.1)	90.2–92	135 (42.7)	37.3–48.2	117 (37)	31.7–42.3	38.1	35.3–40.9
>18 and ≤24	184	1,938 (94.3)	93.3–95.3	90 (46.4)	39.4–53.4	75 (38.7)	31.9–45.5	38.4	34.3–42.4
>24 and ≤36	123	1,153 (87.5)	85.6–89.5	56 (45.5)	36.7–54.3	40 (32.5)	24.2–40.8	35.6	21.9–41.3
>36 and ≤48	23	160 (88.4)	83.7–93.1	7 (30.4)	11.6–49.2	7 (30.4)	11.6–49.2	36	21.9–50.1
>48 and ≤60	6	45 (91.8)	84.1–99.5	3 (50)	6.2–93.8	3 (50)	10–90.1	100	100–100
>60	1	14 (93.3)		1 (100)		1 (100)		50	–
Total	3,610	38,087 (90.3)		1,678 (46.5)		1,382 (38.3)		39	

Note: Data are expressed as means and proportions with their corresponding 95% CI. No statistical differences were observed while comparing each outcome parameter according to all categories of storage time. SR = survival rate; WP = warming procedures; CPR = clinical pregnancy rate (%).

Cobo. Six years of egg banking for ovum donations. Fertil Steril 2015.

Most of all,

- We don't have the exact pregnancy data in these population.
- Less than 10% women came back to use frozen oocytes.
- No success data using frz eggs in very old women (>39)

Social egg freezing: Cost-effectiveness

PROS

Cost-effective in certain age range women

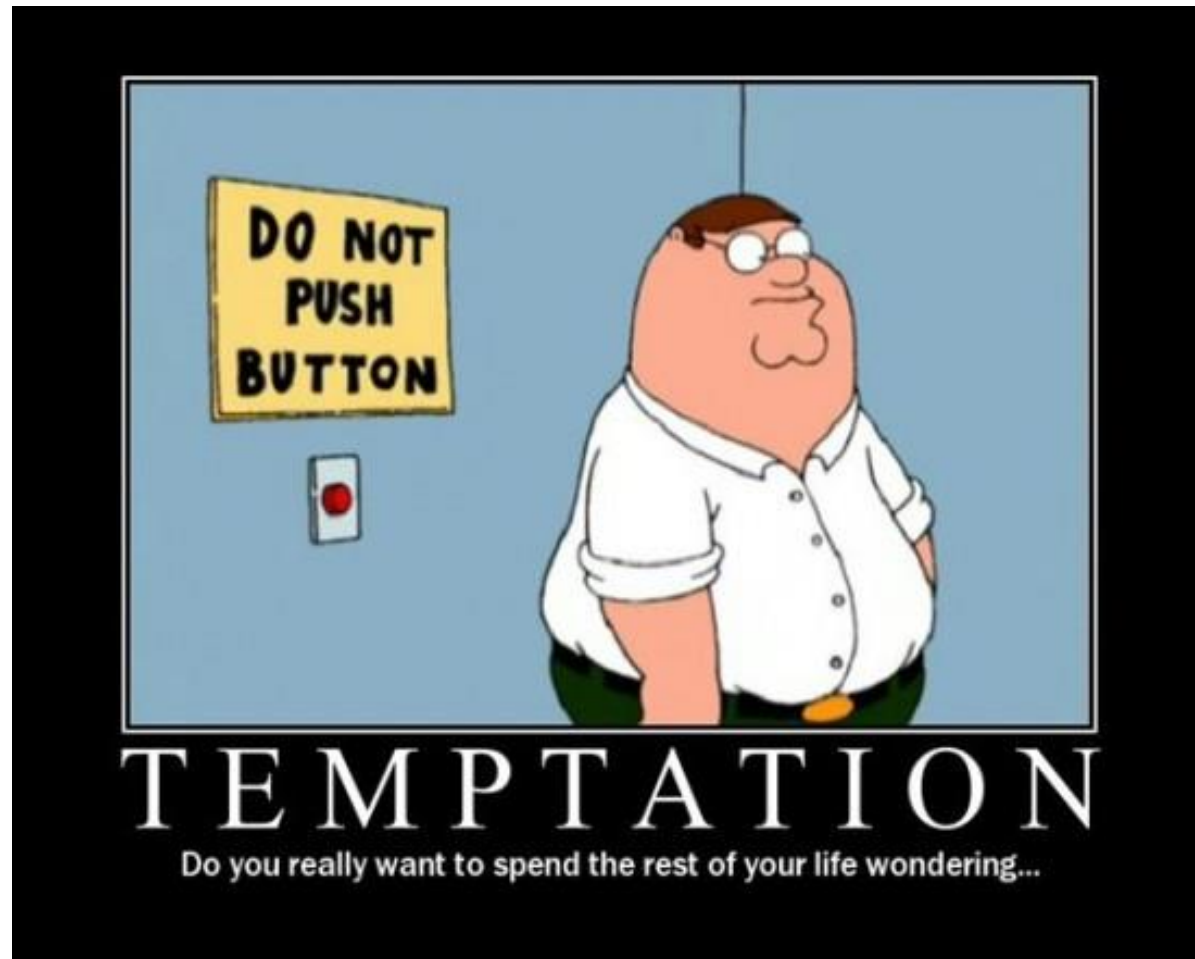
CONS

Cost exploitation preying on women's anxieties

Creating false hope and a false sense of security

Social egg freezing: Ethics

Oops! Did we push the button?



TEMPTATION

Do you really want to spend the rest of your life wondering...

37 oocyte bank

As of Jul-14th-2016

No. of patients who pursued SOC consultation	App.* 52
No. of patients who pursued SOC	48
Patients' mean age who pursued SOC (yr)	37.7
> 1 SOC cycles	11
No. of SOC cycles	59
Mean no. of SOC cycles (per patient)	1.3
Mean no. of oocytes vitrified	9.6

SOC: social oocyte cryopreservation

*: Patients who were given consultation from other physicians may be omitted.

What we should keep in mind.

- We freeze GAMETES, not fertility
- Avoid unrealistic expectation by information based on general data, especially in old age women
- It is our responsibility to inform society about the impact that age has on fertility.

Closing

- Egg freezing does nothing to correct the fundamental social injustice in the workplace, where women are effectively forced to choose between **having a career** and **having a family** — a choice not imposed on men. Better maternity leave, more flexible policies, and better childcare options could transform the workplace, such that career and parenthood would not conflict for women.

Thank You

dr.jykim76@gmail.com