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Does the Freeze-all strategy improves the cumulative live birth rate and the time to become pregnant in IVF cycles?

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Objectives

- **Benefit of the Freeze all strategy in hyper-responders** with a decrease in risk of OHSS and an increase in live birth rate. (Evans et al.,2014; Roque et al.,2013; Chen et al.,2016)

Is there an increase in live birth rate while using the freeze all strategy for the overall IVF population?

Many recent studies : Different conclusions..

Objectives

Human Reproduction Update, Vol.25, No.1 pp. 2–14, 2019
Advanced Access publication on November 2, 2018 doi:10.1093/humupd/dmy033

human reproduction update

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 2018:** Roque et.al ; 11 studies including 5379 patients
- LBR between 2 subgroups: eFET and fresh ET
- **LBR FA group > fresh ET** (46% versus 42.7%, P= 0.04)
- BUT: after analysing the sub-groups of patients this **is true for hyper-responders** but no difference in LBR for normo-responders

Objectives

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transfer of Fresh versus Frozen Embryos in Ovulatory Women

Yuhua Shi, M.D., Ph.D., Yun Sun, M.D., Ph.D., Cuifang Hao, M.D., Ph.D., Heping Zhang, Ph.D., Daimin Wei, M.D., Ph.D., Yunshan Zhang, M.D., Yimin Zhu, M.D., Ph.D., Xiaohui Deng, M.D., Xiujuan Qi, M.D., Hong Li, M.D., Xiang Ma, M.D., Ph.D., Haiqin Ren, M.D., Yaqin Wang, M.D., Ph.D., Dan Zhang, M.D., Ph.D., Bo Wang, M.S., Fenghua Liu, M.D., Qiongfang Wu, M.D., Ze Wang, M.S., Haiyan Bai, Ph.D., Yuan Li, M.D., Ph.D., Yi Zhou, M.D., Mei Sun, M.D., Ph.D., Hong Liu, M.D., Ph.D., Jing Li, M.S., Lin Zhang, M.S., Xiaoli Chen, M.D., Ph.D., Songying Zhang, M.D., Ph.D., Xiaoxi Sun, M.D., Ph.D., Richard S. Legro, M.D., and Zi-Jiang Chen, M.D., Ph.D.

- **Prospective multicentric randomised trial**, 2018: Shi et.al
- 2157 ovulatory women
- 2 groups: FA with FET and fresh ET
- **No difference in LBR** between the 2 groups

Objectives

Human Reproduction, pp. 1–6, 2018
doi:10.1093/humrep/dey044

human reproduction

ORIGINAL ARTICLE *Reproductive epidemiology*

Live birth rates in the first complete IVF cycle among 20 687 women using a freeze-all strategy

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- **Retrospective study** including **20 687 women**: Zhu et al. 2018
- **CLBR after the first complete IVF cycle : 50.74%**
- BUT: No control group

Objectives

Is there an increase in live birth rate while using the freeze all strategy for the overall IVF population?

Contradictive results from the recent studies

Retrospective monocentric study comparing the **cumulative live birth rate** (CLBR) of patients having undergone the **freeze all** strategy (FA) compared to a **control group** (C)

Design and methods

Monocentric retrospective study from **January 2008 to December 2018**

Freeze all group (FA)
Patients who had an OPU with **all** their **embryos cryopreserved** which were transferred in subsequent cycles

- PCOs (75%)
- Inadequate endometrium (15.5%)
- Prog > 1.5 ng/ml (2.3%)
- Others (11.2%)

Control group (C)
Patients who had an OPU with the transfer of fresh embyos and **at least one frozen embryo (FE)**

First end point = **Cumulative live birth rate (CLBR)**

- **One IVF cycle**
- Logistic regression analysis **for the CLBR** to identify **confounding variables**
- Analysis were made for different subgroups according to the BELRAP criteria and to the confounding factors selected by the LR.

Results

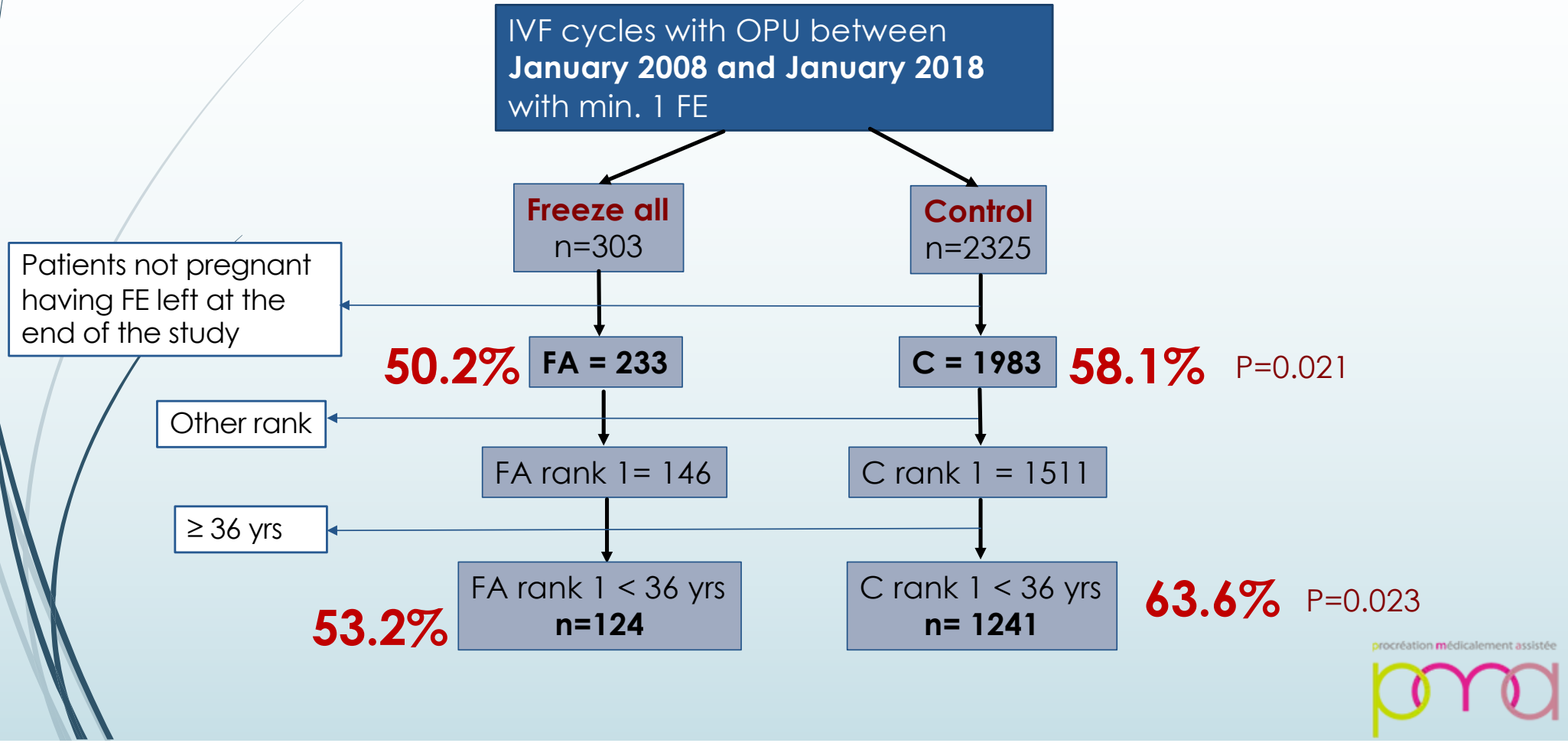
❑ **First end point**:

- **Cumulative live birth rate (CLBR)** → *Live birth rate for one patient after one OPU until the first live birth or after having used all the FE from this OPU*

❑ **Second end points:**

- Cumulative clinical pregnancy rate
- Cumulative misscariage rate
- Number of embryos transferred
- **Time to become pregnant**
- Number of frozen embryos
- Number of frozen embryos left
- CLBR compared to the number of oocytes retrieved
- OHSS rate

Results: CLBR

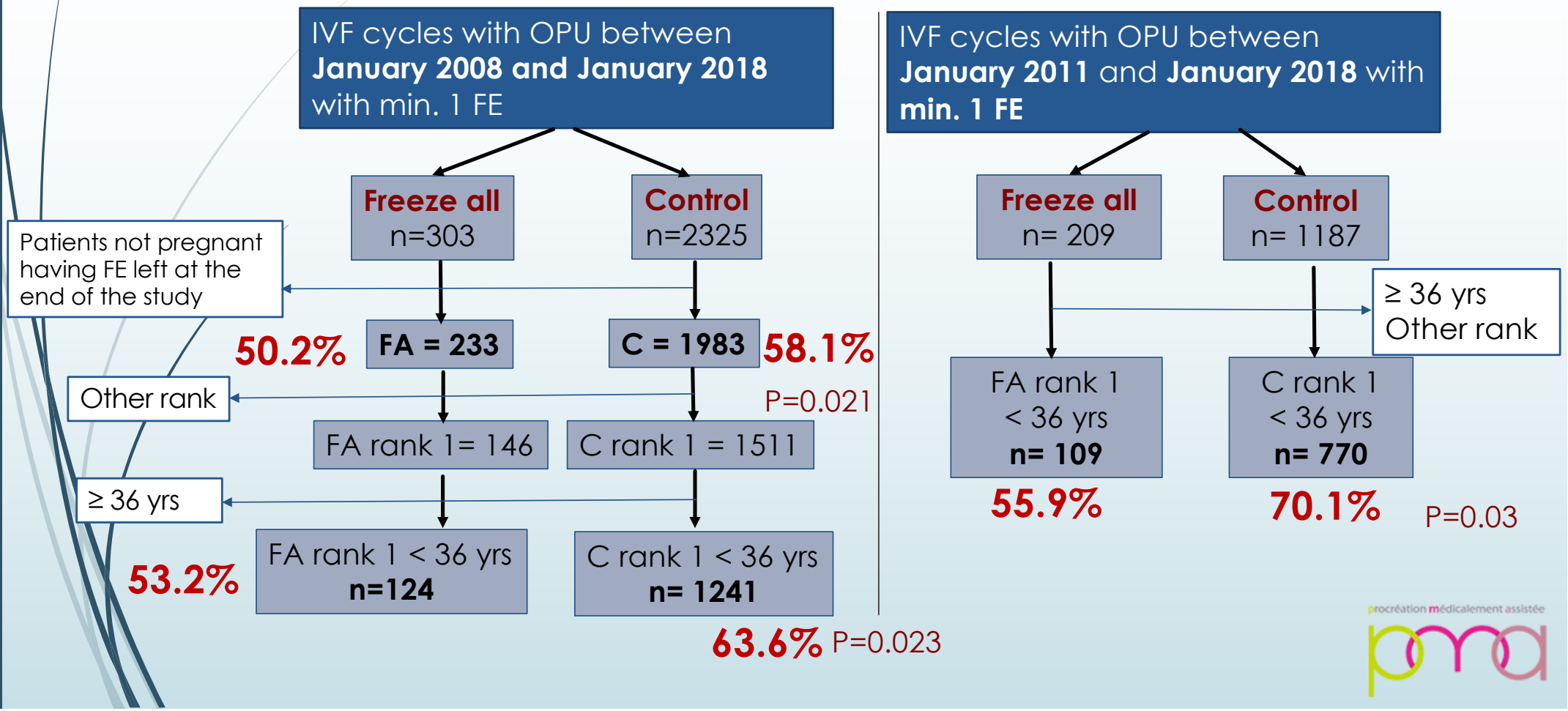


Results

Logistic regression analysis for the CLBR

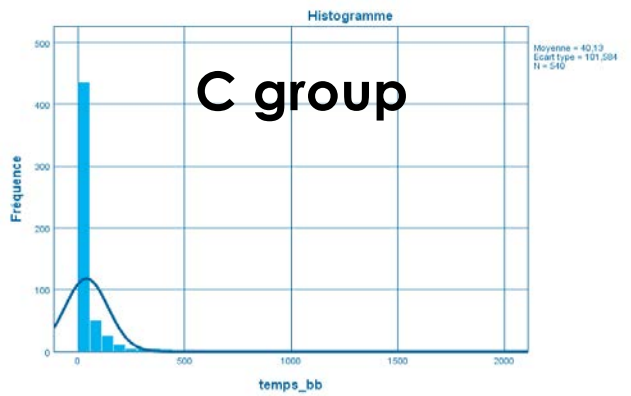
	OR	IC 95%	P value
Group	2,247	1,532-3,295	**0,000**
Age (yrs)	0,905	0,879-0,931	**0,000**
Rank	0,726	0,541-0,973	**0,032**
Primary/secondary infertility patient	1,249	0,941-1,658	0,123
Primary/secondary infertility partner	1,178	0,892-1,555	0,248
BMI (Kg/m²)	0,998	0,972-1,024	0,863
Tobacco patient	0,695	0,513-0,941	**0,019**
Tobacco partner	1,422	1,087-1,861	**0,010**
Infertility diagnosis patient	1,072	0,943-1,217	0,287
Infertility diagnosis partner	0,969	0,781-1,203	0,778
Number of oocytes retrieved	0,990	0,954-1,026	0,573
Number of embryos obtained	1,229	1,157-1,306	**0,000**
Total number of transfers	0,483	0,425-0,549	**0,000**
Average number of transfers	1,127	0,811-1,565	0,477
Date OPU after 2011	1,915	1,461-2,510	**0,000**

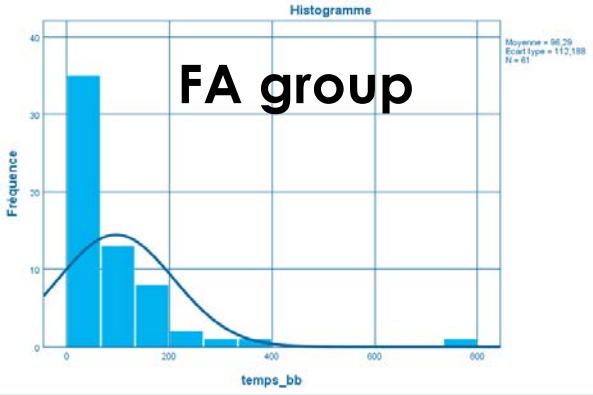
Results: CLBR



Results: time to become pregnant

Definition: Time **between OPU** and the **transfer** that will give the live birth





- The time to become pregnant is significatively lower in the C group
- **Median 5 days** (average 40 d) **C** vs **median 61 days** (average 96 d) **FA** (P=0.00)
- C group= good responders (min. 1 FE after the fresh transfer)
- FET is done min. 1 month after OPU and sometimes later if OHSS

Conclusion

- Cumulative live birth rate **(CLBR) C group > FA group** for the different populations

	Freeze all	control	P
CLBR tot. Pop.	50.2%	58.1%	0.021
CLBR rank 1 < 36 yrs	53.2%	63.6 %	0.023
CLBR rank 1 < 36 yrs ≥ 2011	**55.9%**	70.1%	0.03

BUT…

- **CLBR excellent** for the control group and so significatively better than the FA group.
- **CLBR of 55.9% is still a very good rate for the FA population** as its the best found in the littérature
- We possibly selected **« good responders » in the C group**(min. 1 FE in addition to the fresh embryos precedently transfered **and cumulative rates**
- Period selected by the LR underlines the **superiority of vitrification** compared to slow freezing used before

Strenghts and Weaknesses

❑ Weaknesses:

- **Retrospective** study
- **Long period of time with changes** in the freezing techniques and in our transfer politics during the study
- **Heterogeneous FA group** with mostly hy- responders (75%)

❑ Strenghts:

- **« Real life study »**
- **Included a large number of patients**
- **Results compared with a control group** (patients who had an OPU with the transfer of fresh embyos and at least one FE)
- First end point: **Cumulative live birth rate**(CLBR), better than analysing the live birth rate after one transfer

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Thank you for your attention

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Results

❑ Average number of embryos transferred

- ➢ **Rank 1, < 36yrs, > 2008**
  - **1.26** FA vs **1.23** C **(P=0.37)**

- ➢ **Rank1, < 36 yrs , > 2011**
  - **1,25** FA vs **1,16** C **(P=0,007)**
  - Not Clinically significant

Average number of embryos transferred FA > C (not clinically significant))

- **Belgian law : First transfer and < 36 yrs: 1 fresh embryo but 2 frozen embryos**
- Since 2011 CHC: blastocystes vitrification
- To minimise the amount of multiple pregnancies we encourage the transfer of 1FE < 35 yrs since 2014 (Raick D et al.,2014)
- Not enough cases for a new study.. But theses results could be different
- Not a problem for the study because **CLBR in favour of C group even if the number of embryos transferred is superior in the FA group**