

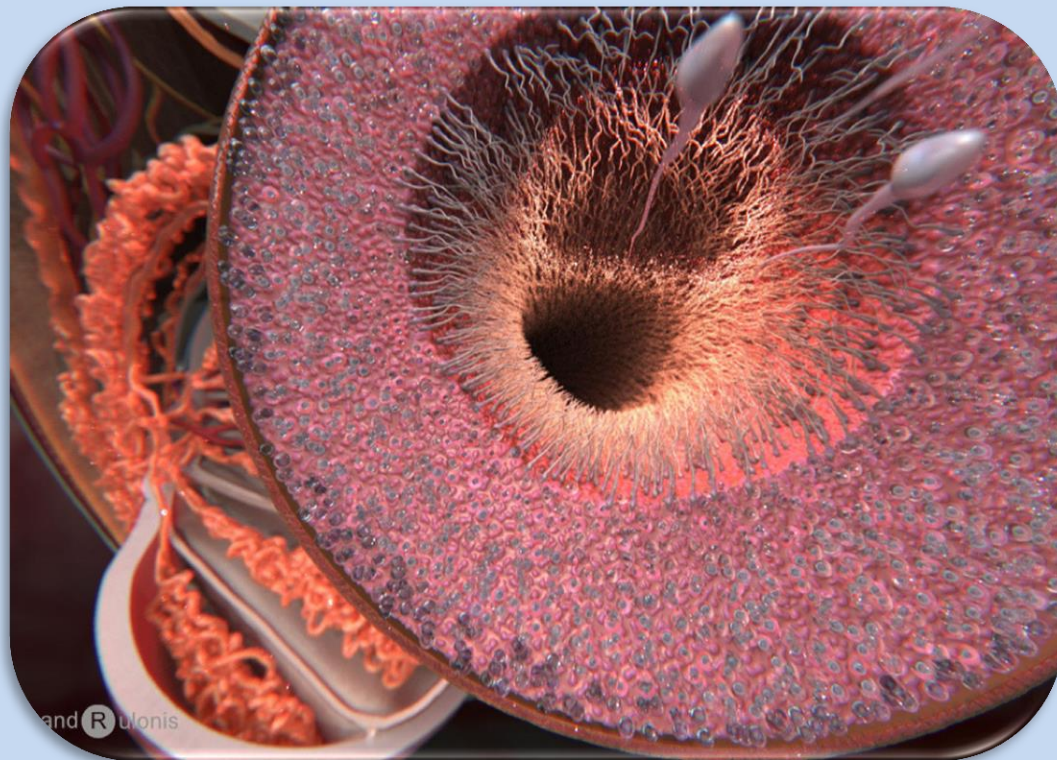


FERTILITY[®]
MEDICAL GROUP

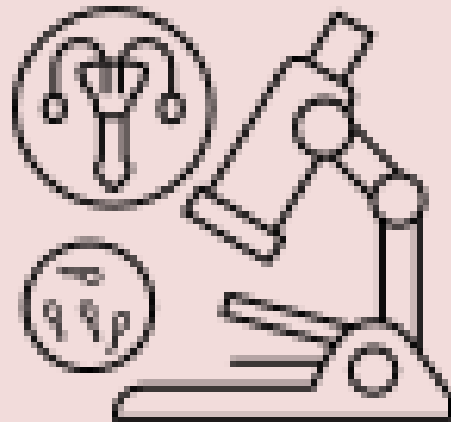
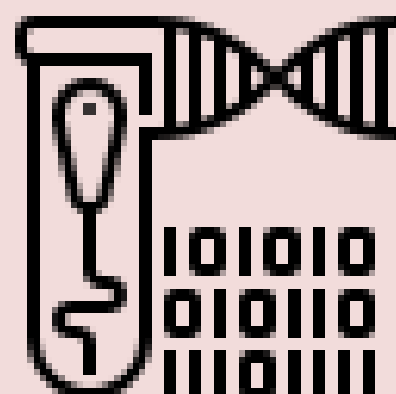
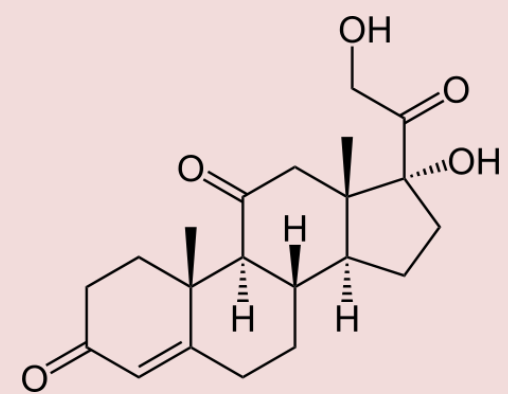
PATERNAL AGEING IMPACTS BLASTULATION AND THE OUTCOMES OF PREGNANCY AT DIFFERENT LEVELS OF MATERNAL AGE: A CLUSTERING ANALYSIS OF 21,960 INJECTED OOCYTES AND 3837 ICSI CYCLES

Amanda Setti, Daniela Paes de Almeida Ferreira Braga, Patrícia Guilherme, Livia Vingris, Assumpto Iaconelli Jr., Edson Borges Jr.

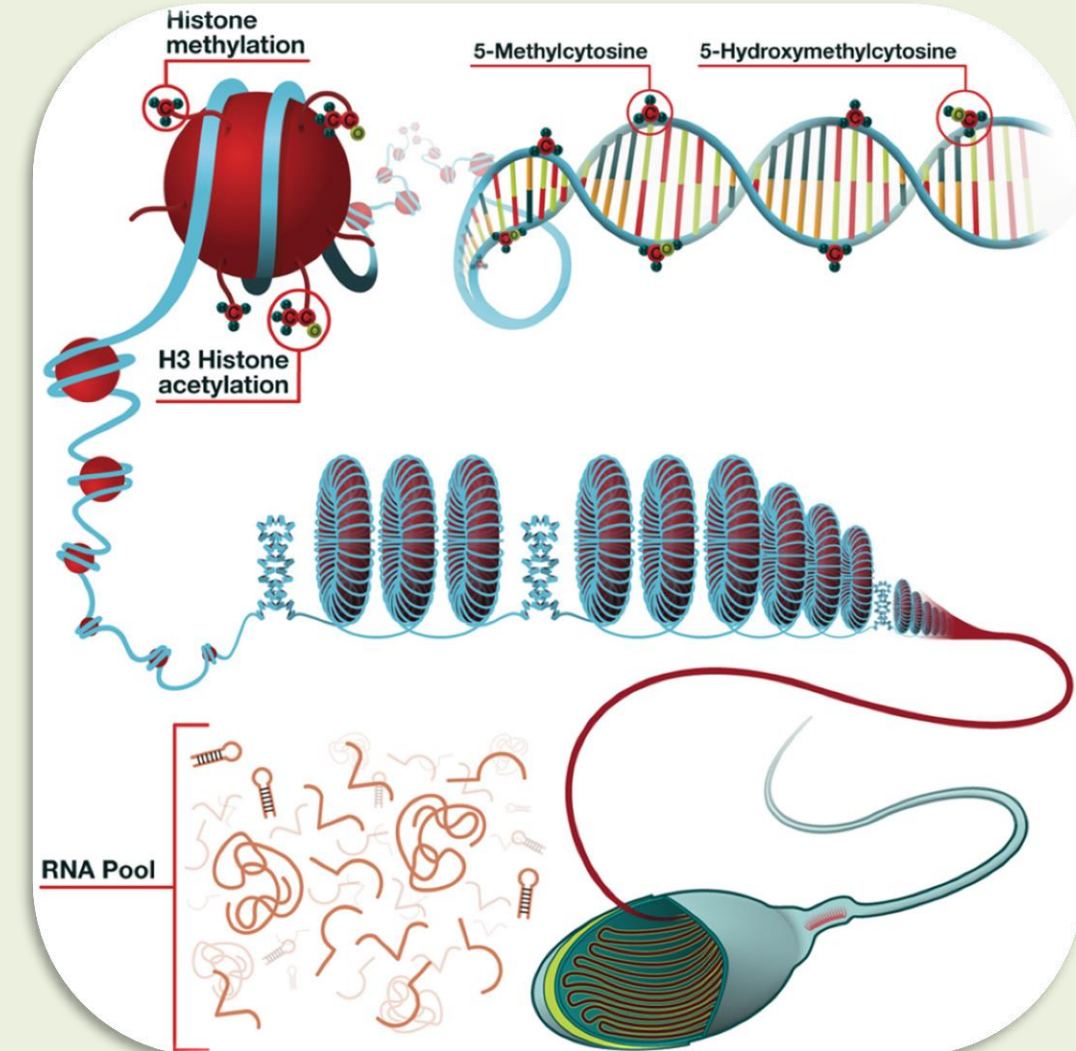
INTRODUCTION



Spermatogenesis

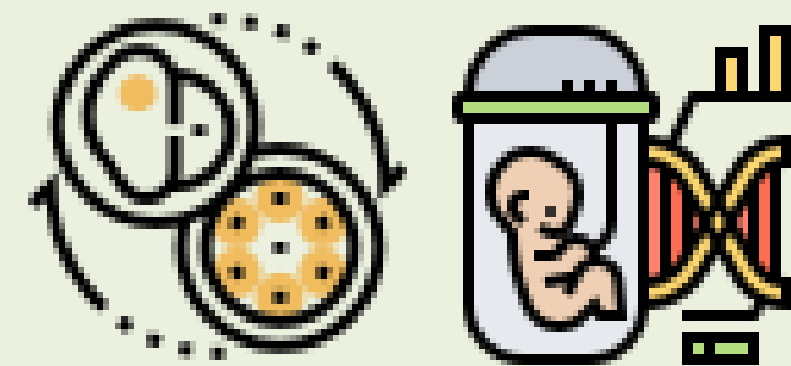


Testosterone Sperm DNA Semen quality



Sperm epigenome

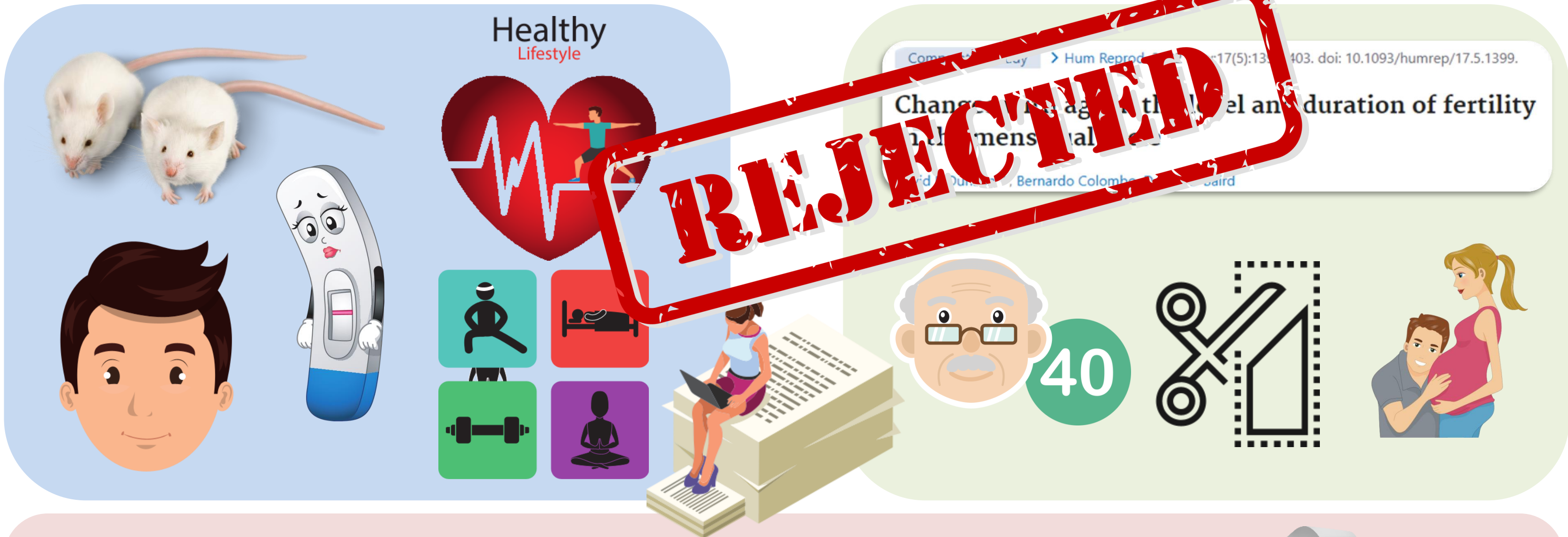

Embryo development



Offspring disease

INTRODUCTION

Healthy Lifestyle



REJECTED

Changes in age at the onset of menopause and duration of fertility

Compendium > Hum Reprod 17(5):1399-1403. doi: 10.1093/humrep/17.5.1399.

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> Fertil Steril. 2006 May;85(5):1420-4. doi: 10.1016/j.fertnstert.2005.11.040. Epub 2006 Apr 17.

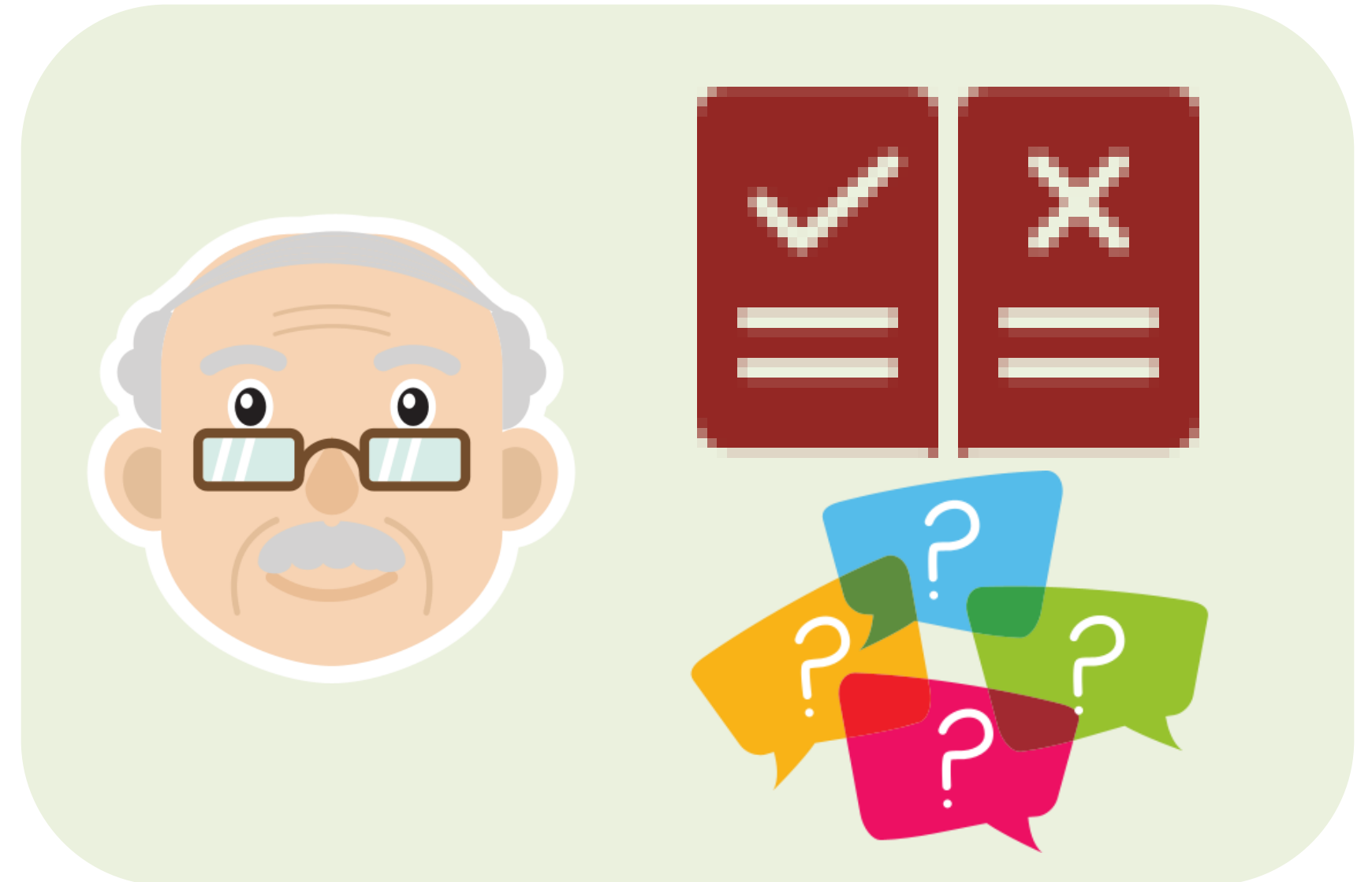
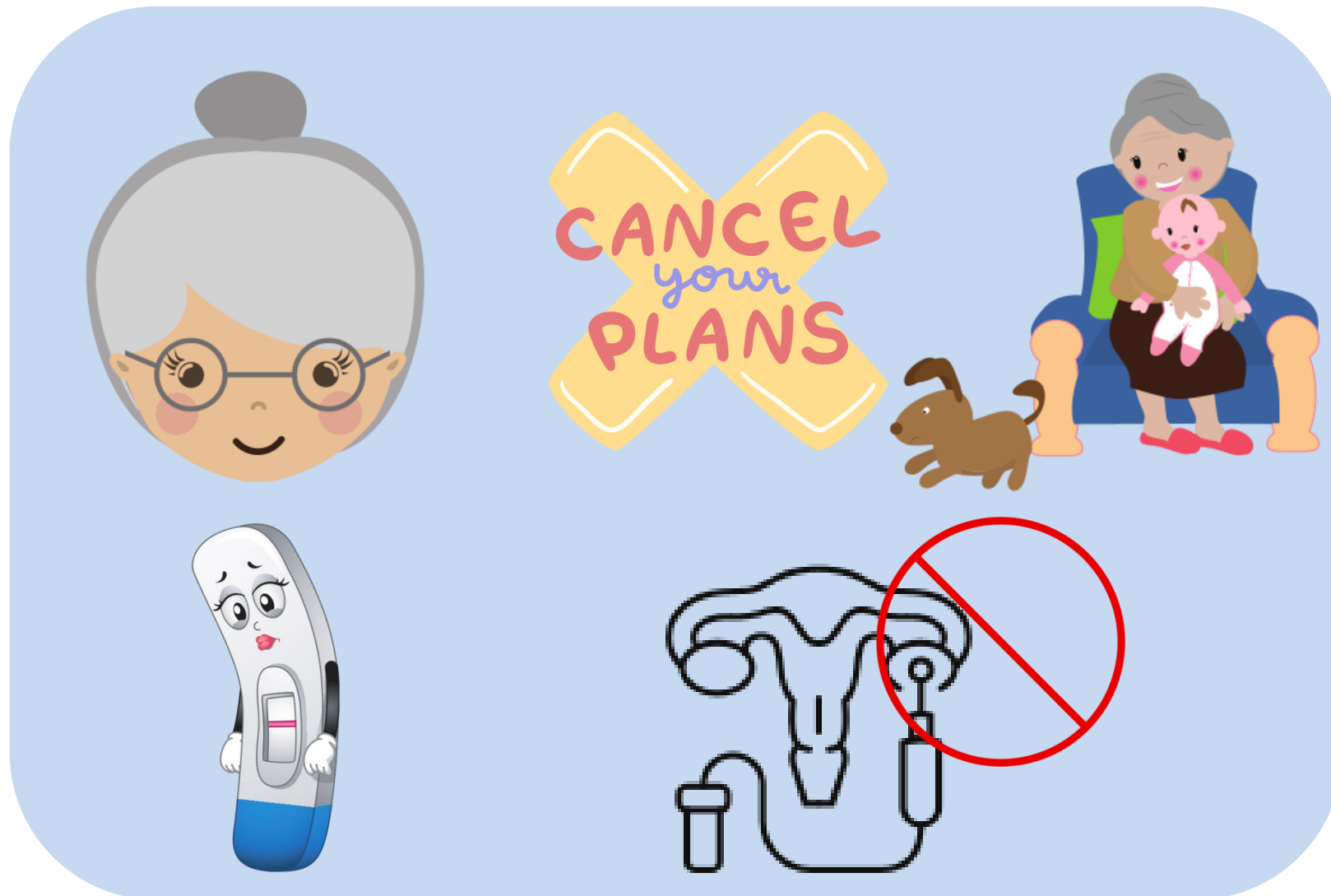
Fathers over 40 and increased failure to conceive: the lessons of in vitro fertilization in France

Elise de La Rochebrochard¹, Jacques de Mouzon, François Thépot, Patrick Thonneau, French National IVF Registry (FIVNAT) Association



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INTRODUCTION

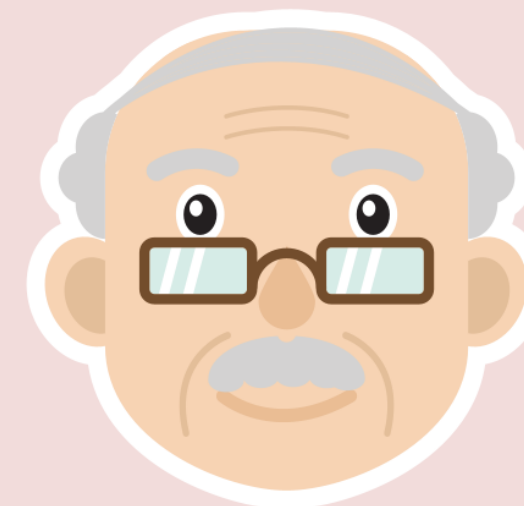


> Mol Reprod Dev. 2018 Mar;85(3):271-280. doi: 10.1002/mrd.22963. Epub 2018 Mar 1.

Paternal age: Negative impact on sperm genome decays and IVF outcomes after 40 years

Ismail Kaarouch¹, Nouzha Bouamoud¹, Aicha Madkour¹, Nouredine Louanjli²,
Brahim Saadani³, Said Assou⁴, Smahane Aboulmaouahib², Saaid Amzazi¹, Henri Copin⁵,
Moncef Benkhalifa⁶, Omar Sefrioui⁷

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OBJECTIVE

To investigate if the effect of paternal age on embryo development and clinical outcomes differs at different values of maternal age, thus creating a rationale for the data to reach physicians, patients, and public health recommendations.

MATERIAL AND METHODS

Study design

Cross-sectional study

January 2014 –
October 2020

Private university-affiliated IVF center

1st attempt

3837 ICSI couples /
cycles

21960 injected oocytes

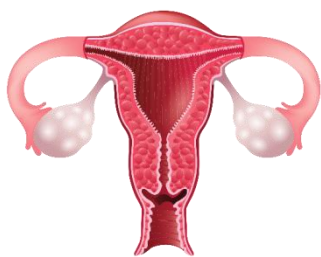
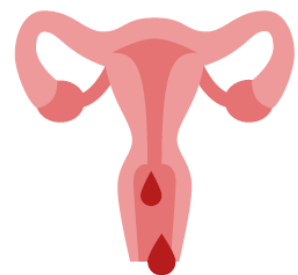
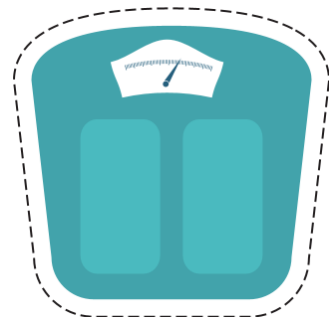
Culture until D5

Maternal and paternal ages

Embryo development
Pregnancy outcomes

MATERIAL AND METHODS

Eligibility criteria



Inclusion



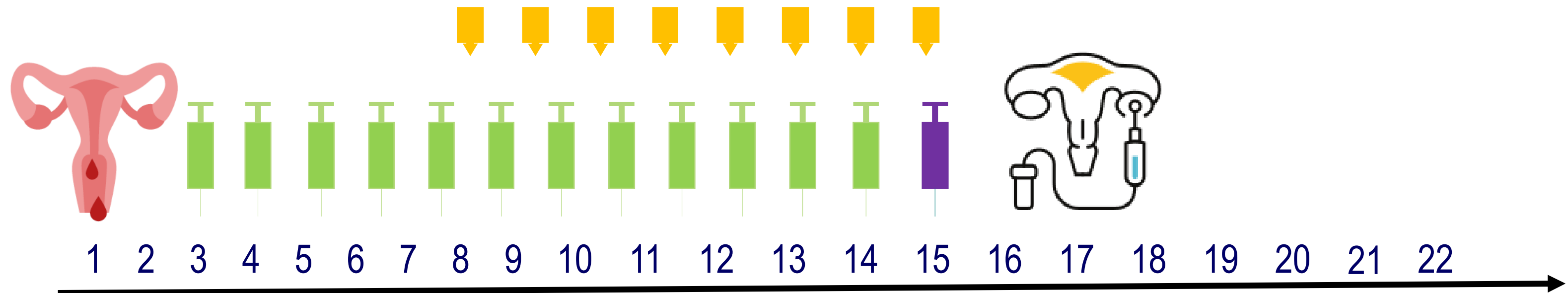
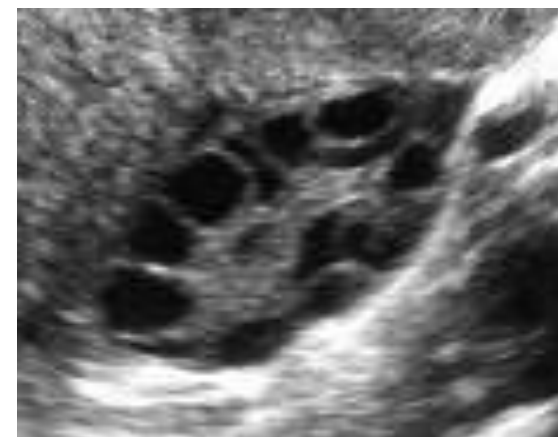
- ☐ Women 18-45 y-old
- ☐ Regular cycles 24-35d
- ☐ BMI 17.5-29.9 kg/m²
- ☐ Normal uterus / ovaries
- ☐ 1st ICSI cycle
- ☐ Female or male factor, unexplained infertility
- ☐ Fresh ejaculatd sperm
- ☐ Male ≥ 18 y-old, healthy

MATERIAL AND METHODS

Controlled ovarian stimulation

- GnRH Antagonist
- Recombinant FSH
- Recombinant hCG

E2



MATERIAL AND METHODS

Embryo culture





Conventional culture



MATERIAL AND METHODS

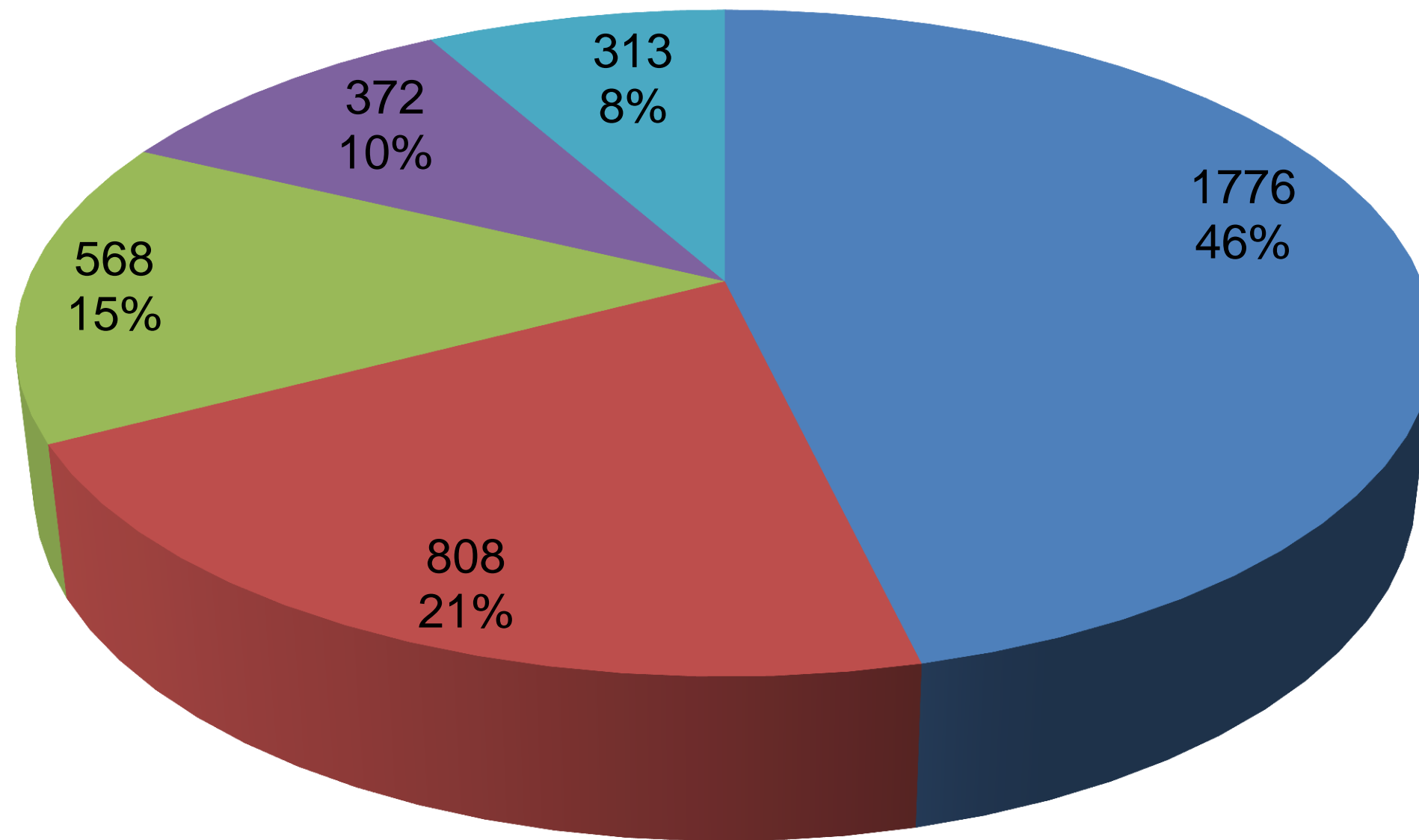
Data analysis and statistics

Post hoc power analysis	 GPower 3.1		α 5%	 IBM SPSS Statistics		GMM	GzLM
	21960 zygotes	3315 cycles with ET	Main effects: maternal and paternal ages (interaction term)			Single observation/couple	
	Effect sizes: blastulation and pregnancy		Embryo quality and blastulation			Pregnancy outcomes	
	Superior to 99%						
	Random effect – correlation between embryos within the same cycle						
Regression coefficient (B)			OR with 95% CI		p-values (5%)		

RESULTS

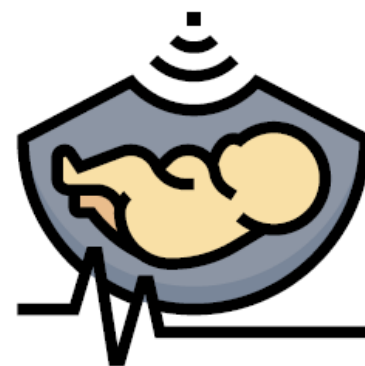
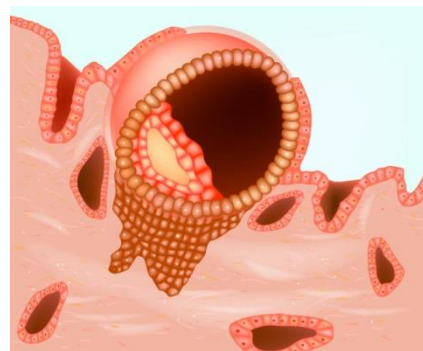
Factors of infertility

■ Male factor ■ Tubal factor ■ Unexplained infertility ■ Endometriosis ■ PCOS



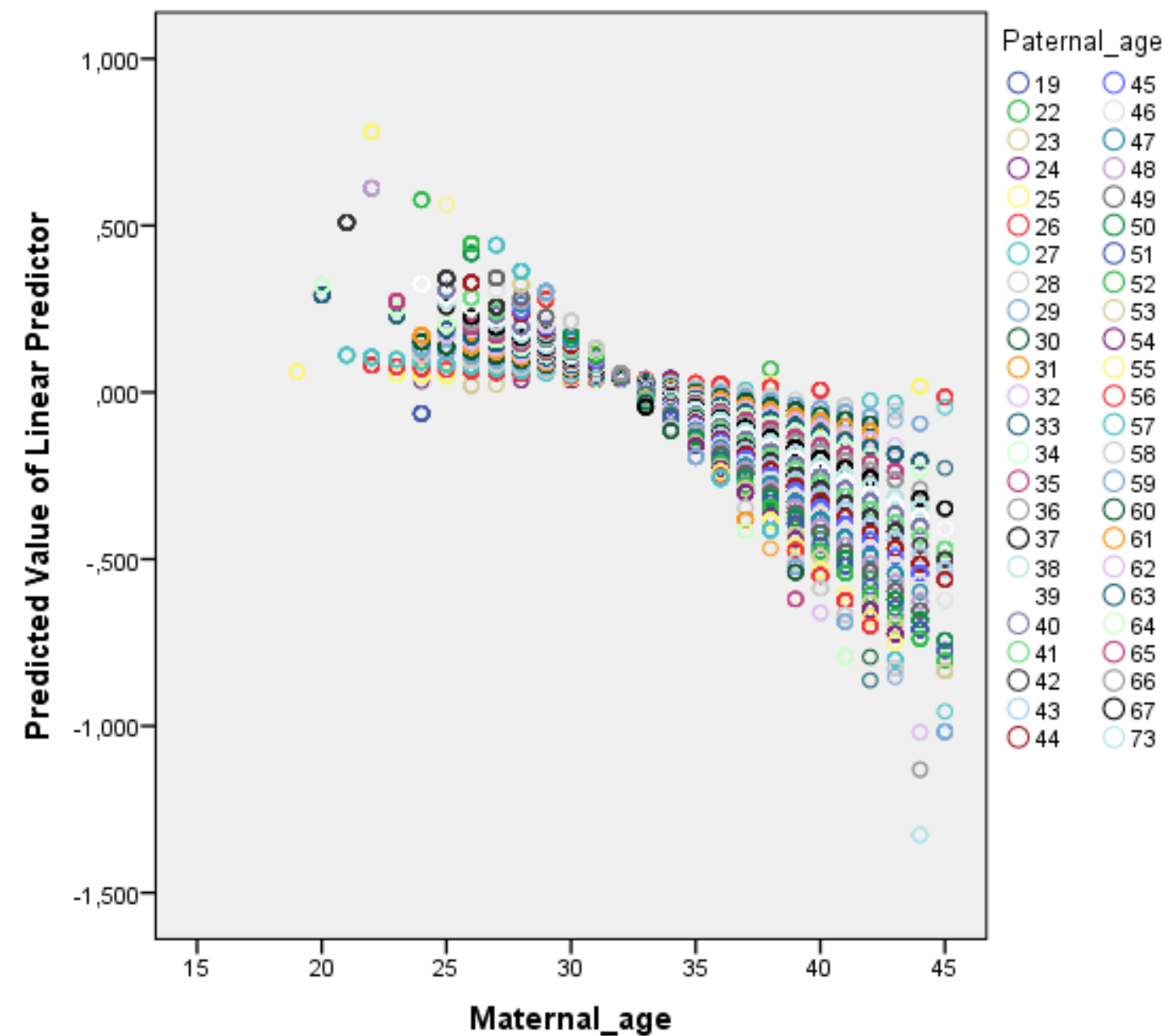
RESULTS

Variable	Value (n=3837)
Female age (y-old)	35.3 ± 4.5
Female BMI	24.2 ± 3.9
Male age (y-old)	38.0 ± 6.4



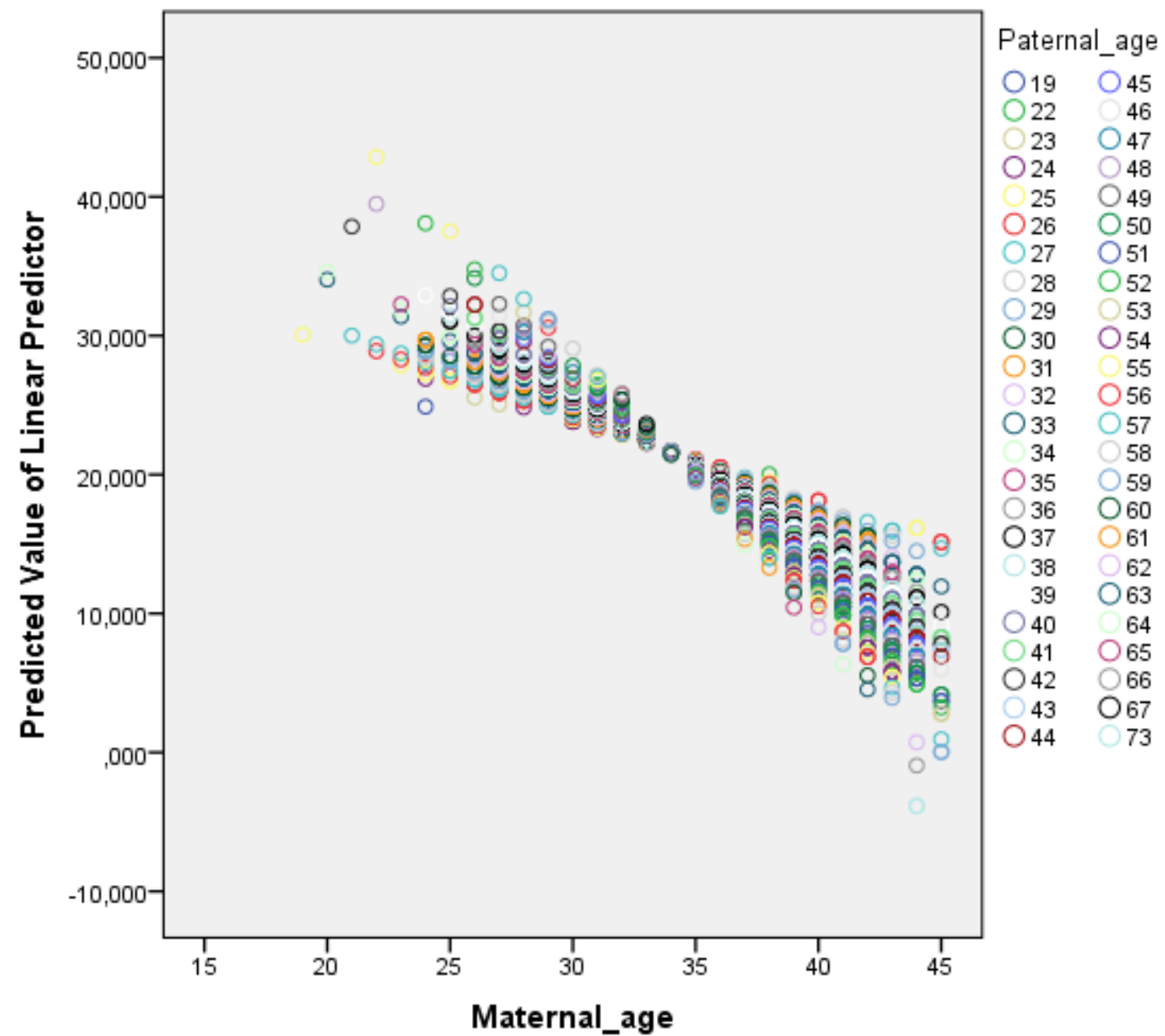
RESULTS

Dependent variable	B	OR	CI	p-value
Blastocyst development	- 0.005	0.995	0.994 – 0.996	< 0.001



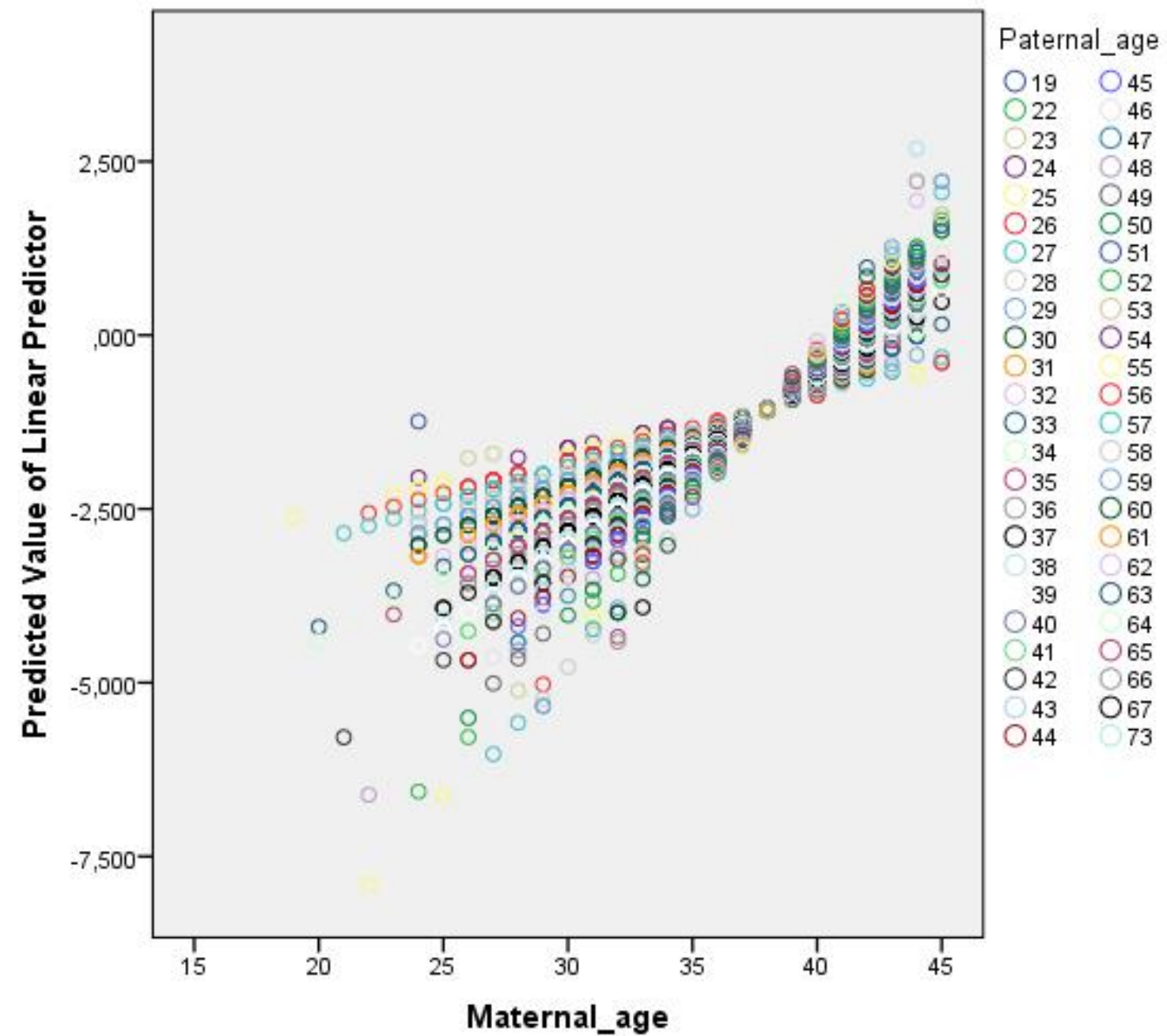
RESULTS

Dependent variable	B	OR	CI	p-value
Implantation rate	- 0.041	0.960	0.947 – 0.973	< 0.001

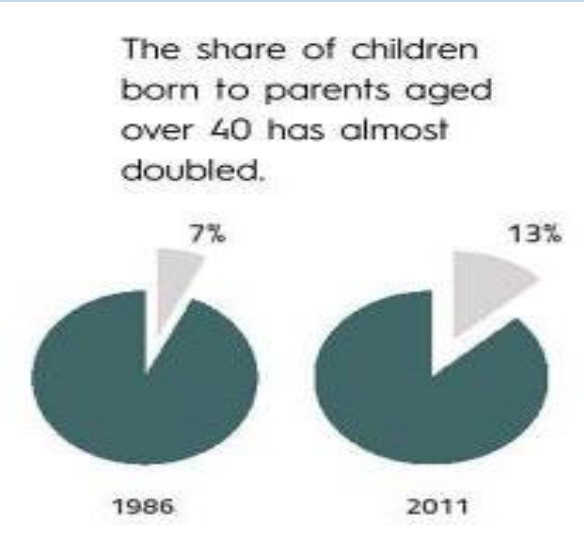


RESULTS

Dependent variable	B	OR	CI	p-value
Miscarriage rate	0.011	1.012	1.005 – 1.018	0.001



WIDER IMPLICATIONS OF THE FINDINGS



Our results underscore the importance of both maternal and paternal ages for blastulation and successful pregnancy

Tests of Model Effects			
Source	Type III		
	Wald Chi-Square	df	Sig.
(Intercept)	25,052	1	,000
Maternal_age	17,146	1	,000
Paternal_age	31,479	1	,000
Maternal_age * Paternal_age	28,319	1	,000

Dependent Variable: LBR
Model: (Intercept), Maternal_age, Paternal_age, Maternal_age * Paternal_age

[Nature](#). Author manuscript; available in PMC 2013 Feb 23.

Published in final edited form as:

[Nature](#). 2012 Aug 23; 488(7412): 471–475.

doi: [10.1038/nature11396](#)

PMCID: PMC3548427

NIHMSID: NIHMS391279

PMID: [22914163](#)

Rate of *de novo* mutations, father's age, and disease risk

[Augustine Kong](#),^{1,*} [Michael L. Frigge](#),¹ [Gisli Masson](#),¹ [Soren Besenbacher](#),^{1,2} [Patrick Sulem](#),¹ [Gisli Magnusson](#),¹ [Sigurjon A. Gudjonsson](#),¹ [Asgeir Sigurdsson](#),¹ [Aslaug Jonasdottir](#),¹ [Adalbjorg Jonasdottir](#),¹ [Wendy Wong](#),³ [Gunnar Sigurdsson](#),¹ [G. Bragi Walters](#),¹ [Stacy Steinberg](#),¹ [Hannes Helgason](#),¹ [Gudmar Thorleifsson](#),¹ [Daniel F. Gudbjartsson](#),¹ [Agnar Helgason](#),^{1,4} [Olafur Th. Magnusson](#),¹ [Unnur Thorsteinsdottir](#),^{1,5} and [Kari Stefansson](#)^{1,5,*}

How old is too old? What about sex equitability? Couples should be aware of the impact of advanced paternal age on reproductive outcomes and offspring health.

CONCLUSION

The slopes of maternal age on blastulation, blastocyst quality, and implantation, pregnancy and miscarriage rates significantly changed (worsened) for every year increase in paternal age.

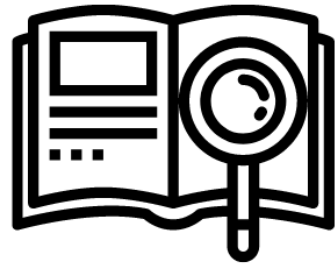
Interim data analysis indicate the same trend for live-birth rate.

STAFF



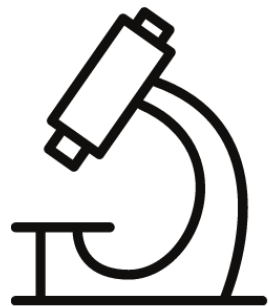
Clinical Board

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Edson Borges Junior



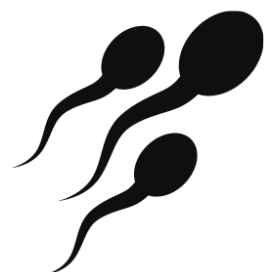
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Tatiana Nunes de Melo



Andrology Laboratory

Rodrigo Rosa Provenza



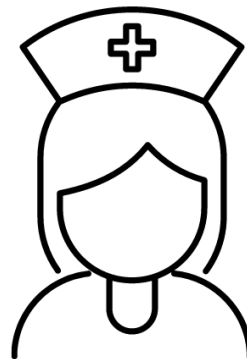
Psychology

Rose Marie Massaro Melamed



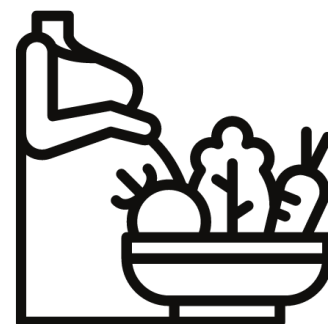
Support

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Katia Rodrigues
Lorrana de Souza Anjos
Lucácio de Souza Anjos
Marcos Vinícius de Sousa
Simone de S. Carvalho
Leonardo S. Lopes



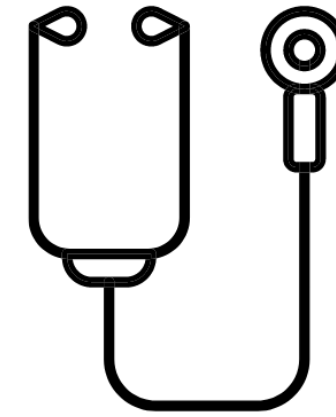
Nursing Team

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Ariele Raiane B. Araujo
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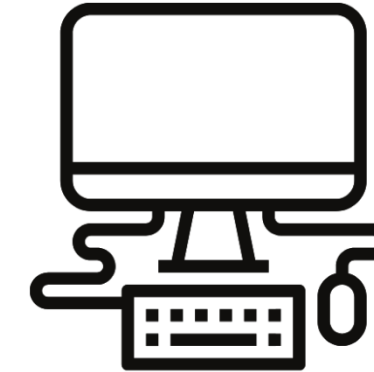
Nutrition

Gabriela Halpern



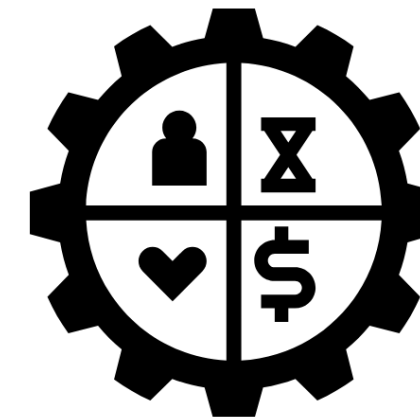
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Paula Ferreiro Vieira



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Marcelo Alexandre Baptista



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Fabiana Garcia



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