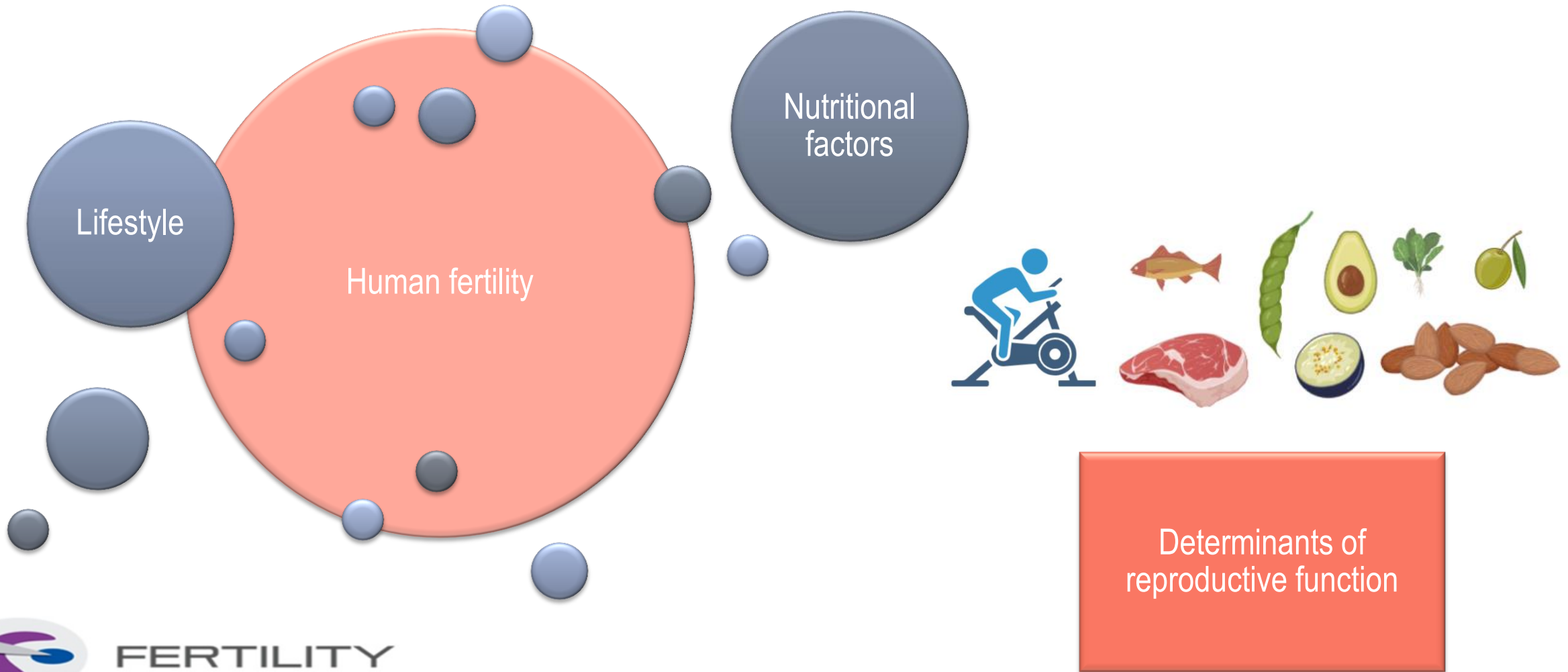# REDUCED OOCYTE QUALITY JUSTIFIES POOR ICSI OUTCOMES AMONG SMOKERS AND SUGAR CONSUMERS
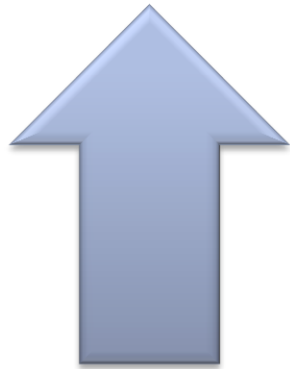
Gabriela Halpern [1], Amanda Setti [1,2], Daniela Paes de Almeida Ferreira Braga [1,2], Assumpto Iaconelli Jr. [1,2], Edson Borges Jr. [1,2]
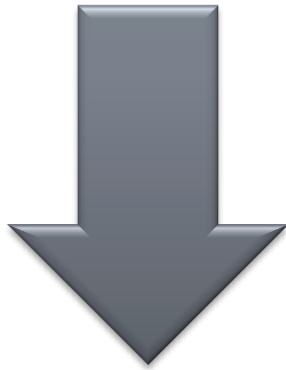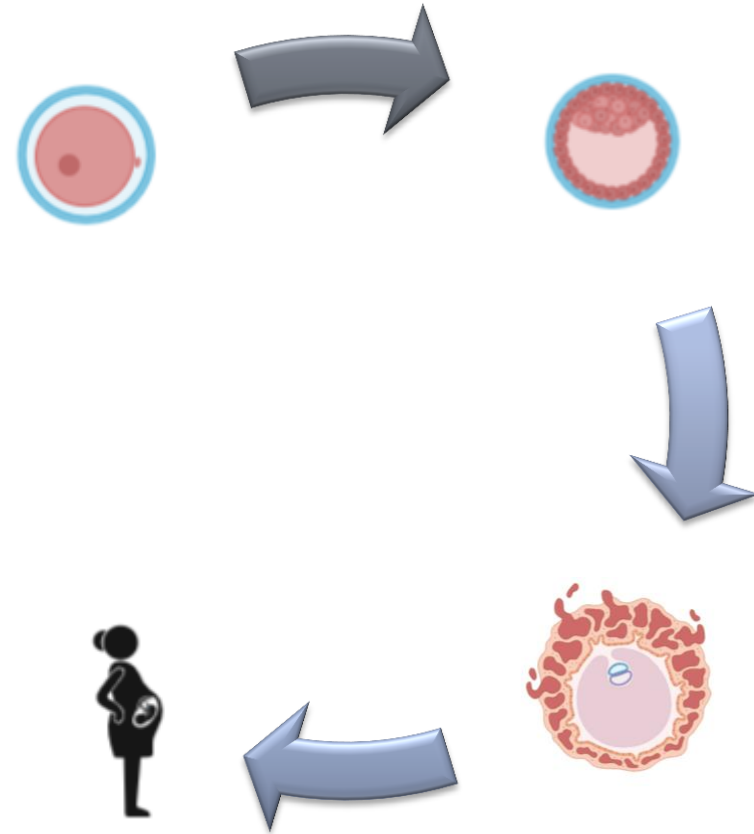
INTRODUCTION

Hypothesis

Oocyte dimorphisms

Reproductive outcomes

FERTILITY

OBJECTIVE

To investigate the impact of maternal lifestyle factors and nutritional habits on oocyte morphology and on the outcomes of ICSI cycles

FERTILITY

MATERIAL AND METHODS

Prospective cohort study

Private-university affiliated IVF center

561 couples, 1st ICSI cycle

Jan/2015 – Dec/2018

D5 ET

> 4 and ≤ 20 retrieved oocytes

> 5 x 10^6 spermatozoa / mL

Questionnaire

- Smoking habit
- Alcoholic beverages
- Refined sugar
- Artificial sweetener
- Soft drinks
- Legumes and vegetables
- Fruits
- Milk and dairy
- White and red meats
- Exercise frequency

FERTILITY

MATERIAL AND METHODS

Oocyte dimorphisms

- Centrally located cytoplasmic granulation (CLCG)
- Dark cytoplasm (DC)
- Vacuoles
- Smooth endoplasmic reticulum (SER)
- Large perivitelline space (PVS)
- PVS granularity
- Fragmented polar body (PB)
- Zona pellucida (ZP) abnormalities
- Shape abnormalities
- Membrane resistance (MR) abnormalities

non-resistant membrane

resistant membrane

MATERIAL AND METHODS

Data analysis

Multivariate regression analysis, adjusted for maternal age and BMI

Lifestyle and nutritional factors: independent variables

Incidence of oocyte dimorphisms and ICSI outcomes: dependent variables

FERTILITY

RESULTS - Influence of lifestyle and nutrition on the incidence of oocyte dimorphisms

	Centrally located cytoplasmic granulation (CLCG)	Dark cytoplasm (DC)	Vacuole	Smooth endoplasmic reticulum (SER)	Perivitelline space (PVS) granularity	Fragmented polar body (PB)	Zona pellucida (ZP)	Shape	Membrane
Cigarette smoking	B: 41.2 CI: -13.1 – 95.5 p: 0.137	B: 2.1 CI: 1.0 – 3.3 p<0.001	B: 10.5 CI: -23.7 – 44.7 p: 0.548	B: 14.0 CI: 6.3 – 21.7 p<0.001	B: -15.8 CI: -42.4 – 10.9 p: 0.247	B: 32.4 CI: 7.9 – 57.0 p: 0.011	B: 14.9 CI: 3.9 – 25.9 p: 0.009	B: 14.2 CI: 4.6 – 23.8 p: 0.004	B: 28.3 CI: 9.9 – 46.6 p: 0.02
Alcoholic beverages	B: 8.84 CI: -12.2 – 29.8 p: 0.409	B: 2.14 CI: 1.3 – 3.0 p<0.001	B: -6.6 CI: -19.3 – 6.0 p: 0.302	B: 12.6 CI: 0.6 – 25.8 p: 0.040	B: 5.2 CI: -4.7 – 15.1 p: 0.307	B: 36.2 CI: 12.7 – 59.7 p: 0.003	B: 8.4 CI: 4.5 – 12.3 p<0.001	B: 1.0 CI: -3.0 – 5.0 p: 0.635	B: 0.6 CI: -2.1 – 3.2 p: 0.685
Refined sugar	B: 19.5 CI: 0.5 – 38.4 p: 0.044	B: 1.5 CI: 0.4 – 2.6 p: 0.008	B: -38.6 CI: -94.6 – 17.4 p: 0.177	B: -3.4 CI: -11.8 – 4.9 p: 0.420	B: 21.6 CI: 2.6 – 40.6 p: 0.027	B: 72.3 CI: 44.6 – 100.0 p<0.001	B: 3.7 CI: -10.9 – 18.3 p: 0.622	B: 1.5 CI: -0.3 – 3.3 p: 0.105	B: -1.7 CI: -4.2 – 0.8 p: 0.193
Artificial sweetener	B: 19.7 CI: 4.7 – 34.7 p: 0.010	B: 4.5 CI: 2.7 – 6.3 p<0.001	B: 1.6 CI: -76.1 – 79.3 p: 0.968	B: 22.1 CI: -35.9 – 80.1 p: 0.455	B: 44.0 CI: 3.8 – 84.2 p: 0.032	B: 89.1 CI: 30.6 – 147.6 p: 0.003	B: -4.9 CI: -35.8 – 25.9 p: 0.754	B: 1.3 CI: 0.3 – 2.6 p: 0.044	B: 21.6 CI: 14.1 – 29.1 p<0.001
Milk and dairy	B: -29.3 CI: -80.6 – 21.9 p: 0.262	B: -0.8 CI: -3.2 – 1.6 p: 0.504	B: 19.1 CI: -73.1 – 111.3 p: 0.685	B: 5.2 CI: -5.5 – 15.9 p: 0.341	B: 40.2 CI: -20.4 – 100.8 p: 0.194	B: -26.4 CI: -51.2 - -1.5 p: 0.038	B: - 24.4 CI: -48.5 - -0.328 p: 0.047	B: -12.4 CI: -15.4 - -9.4 p: 0.004	B: -5.3 CI: -10.2 - -0.5 p: 0.03
Legumes and vegetables	B: -79,4 CI: -132.4 - -26.4 p: 0.003	B: -2.8 CI: -4.4 - -1.2 p: 0.001	B: -76.3 CI: -162.9 – -0.2 p: 0.047	B: -24.0 CI: -38.2 - -9.8 p: 0.001	B: -21.6 CI: -78.5 – 35.3 p: 0.457	B: 11.3 CI: -31.5 – 54.1 p: 0.605	B: 14.4 CI: -8.1 – 37.0 p: 0.210	B: 2.0 CI: -1.2 – 5.2 p: 0.220	B: -26.2 CI: -42.2 - -10.1 p: 0.001
Fish	B: - 3.6 CI: -32.2 – 25.0 p: 0.806	B: -0.7 CI: -4.6 - -3.2 p: 0.741	B: 37.5 CI: -22.2 – 97.1 p: 0.218	B: 4.6 CI: -2.6 – 11.8 p: 0.215	B: -16.7 CI: -55.9 – 22.5 p: 0.404	B: -11.8 CI: -45.2 – 21.6 p: 0.489	B: -4.8 CI: -20.4 – 10.7 p: 0.544	B: -0.7 CI: -2.7 – 1.2 p: 0.447	B: -8.7 CI: -16.4 - -1.0 p: 0.027
Physical activity	B: -0.1 CI: -44.8 – 44.6 p: 0.996	B: -3.5 CI: -4.8 - -2.1 p: <0.001	B: -24.2 CI: -95.2 – 46.7 p: 0.504	B: 6.0 CI: -5.5 – 17.4 p: 0.306	B: 9.4 CI: -37.2 – 56.0 p: 0.693	B: -35.2 CI: -70.4 - -0.1 p: 0.049	B: 3.9 CI: -14.6 – 22.4 p: 0.680	B: 1.9 CI: -4.1 – 7.9 p: 0.530	B: 9.3 CI: -4.7 – 23.4 p: 0.194

RESULTS

Comparison of oocyte dimorphisms' incidence amongst non-smoker and smokers, according to self-reported frequency

Outcomes	Smoking habit				p-value
	Non-smoker (n= 407)	Up to 5 cigarettes/day (n= 66)	Between 5 and 10 cigarettes/day (n= 50)	More than 10 cigarettes/day (n= 38)	
DC	0.0 ± 0.0 [a]	0.0 ± 0.0 [a]	1.5 ± 0.1 [b]	2.5 ± 0.2 [c]	<0.001
Fragmented PB	14.4 ± 0.8 [a]	28.4 ± 0.3 [b]	34.1 ± 1.0 [c]	50.0 ± 7.1 [c]	<0.001
ZP abnormality	0.0 ± 0.0 [a]	4.4 ± 0.1 [b]	3.9 ± 0.3 [b]	9.7 ± 0.4 [c]	<0.001
MR abnormality	0.0 ± 0.0 [a]	1.3 ± 0.2 [b]	2.1 ± 0.2 [c]	3.5 ± 0.1 [d]	<0.001

DC: dark cytoplasm, PB: polar body, ZP: zona pellucida, MR: membrane resistance.

FERTILITY

RESULTS

Comparison of oocyte dimorphisms' incidence amongst refined sugar's non-consumers and consumers, according to self-reported frequency

Outcomes	Refined sugar consumption				
	Non-consumer (n= 77)	Up to 2x/week (n= 236)	Between 3x and 6x/week (n= 47)	More than 6x/week (n=201)	p-value
CLCG	0.0 ± 0.0 [a]	1.9 ± 0.2 [b]	7.5 ± 0.2 [c]	8.6 ± 0.2 [d]	<0.001
DC	0.0 ± 0.0 [a]	0.6 ± 0.1 [b]	2.9 ± 0.1 [c]	2.9 ± 0.4 [c]	<0.001
Fragmented PB	21.9 ± 0.7 [a]	27.1 ± 0.5 [b]	31.1 ± 0.4 [c]	33.9 ± 1.9 [c]	<0.001

CLCG: centrally located cytoplasmic granulation, DC: dark cytoplasm, PB: polar body.

Regular chocolate, sweet desserts, candies, pastries, regular soft drinks, or addition of refined sugar to beverages or any other food item

FERTILITY

RESULTS - Influence of lifestyle and nutrition on the outcomes of ICSI

Predictor variables	Retrieved oocytes	Mature oocyte rate	Fertilization rate	Blastocyst development	High-quality blastocysts	Implantation rate	Pregnancy rate	Miscarriage rate
Cigarette smoking	B: -0.7 CI: -1.1 - -0.3 p<0.001	B: 3.9 CI: -19.1 – 27.0 p: 0.734	B: -11.8 CI: -23.2 - -0.3 p: 0.044	B: -79.8 CI: -141.0 - -18.6 p: 0.011	B: -31.0 CI: -77.6 – -15.6 p<0.001	B: -0.8 CI: -1.1 - -0.5 p<0.001	OR: 0.8 CI: 0.7 – 0.9 p: 0.007	OR: 2.5 CI: 1.8 – 5.6 p: 0.013
Alcoholic beverages	B: -1.5 CI: -2.0 - -1.2 p<0.001	B: -1.1 CI: -9.3 – 7.0 p: 0.783	B: -2.5 CI: -11.1 – 6.1 p: 0.575	B: 2.7 CI: -5.8 – 11.1 p: 0.536	B: -3.7 CI: -17.9 – 10.4 p: 0.605	B: -0.2 CI: -0.2 - -0.1 p<0.001	OR: 0.5 CI: 0.09 – 3.1 p: 0.484	OR: 1.8 CI: 0.3 – 9.5 p: 0.479
Refined sugar	B: -9.0 CI: -12.8 - -5.3 p<0.001	B: -7.2 CI: -18.6 – 4.2 p: 0.215	B: -25.7 CI: -46.0 - -5.3 p: 0.013	B: -32.9 CI: -63.5 - -2.4 p: 0.035	B: -17.8 CI: -58.1 – 22.5 p: 0.387	B: -0.9 CI: -1.0 - -0.8 p<0.001	OR: 0.07 CI: 0.006 - 0.9 p: 0.045	OR: 2.0 CI: 0.1 – 36.3 p: 0.639
Artificial sweetener	B: -22.7 CI: -29.2 - -16.2 p<0.001	B: -0.2 CI: -1.4 – 0.9 p: 0.698	B: -36.2 CI: -70.2 - -2.2 p: 0.037	B: 8.7 CI: -3.6 – 21.2 p: 0.167	B: -12.7 CI: -56.3 – 30.9 p: 0.567	B: -0.3 CI: -0.4 - -0.1 p<0.001	OR: 0.6 CI: 0.2 – 1.5 p: 0.252	OR: 17.1 CI: 0.2 – 1216.4 p: 0.191
Fruits	B: 7.5 CI: 2.9 – 12.1 p: 0.001	B: -17.7 CI: -56.9 – 21.5 p: 0.375	B: -3.2 CI: -30.4 – 24.0 p: 0.818	B: -20.7 CI: -65.3 – 23.8 p: 0.362	B: -14.7 CI: -47.1 – 17.6 p: 0.372	B: -1.2 CI: -17.0 – 14.6 p: 0.885	OR: 0.8 CI: 0.5 – 1.4 p: 0.507	OR: 0.2 CI: 0.04 – 1.5 p: 0.123
Legumes and vegetables	B: 11.8 CI: 5.4 – 18.1 p<0.001	B: 56.4 CI: 14.0 – 98.7 p: 0.009	B: 9.2 CI: -25.1 – 43.6 p: 0.598	B: 27.6 CI: -22.1 – 77.3 p: 0.277	B: 18.6 CI: -19.3 – 56.5 p: 0.336	B: 12.4 CI: 2.7 – 22.1 p: 0.013	OR: 2.4 CI: 1.1 – 5.2 p: 0.028	OR: 0.7 CI: 0.2 – 1.8 p: 0.423
Physical activity	B: 10.2 CI: 5.4 – 15.0 p<0.001	B: -5.1 CI: -39.1 – 28.8 p: 0.767	B: 8.5 CI: -16.7 – 33.7 p: 0.510	B: 44.03 CI: 25.89 - -6.7 p: 0.089	B: 18.2 CI: -1.1 – 37.5 p: 0.064	B: 0.03 CI: -0.07 – 0.1 p: 0.528	OR: 1.9 CI: 0.6 – 5.9 p: 0.282	OR: 1.1 CI: 0.1 – 9.9 p: 0.916

FERTILITY

RESULTS

Comparison of ICSI outcomes amongst non-smoker and smokers, according to self-reported frequency

Outcomes	Smoking habit				
	Non-smoker (n= 407)	Up to 5 cigarettes/day (n= 66)	Between 5 and 10 cigarettes/day (n= 50)	More than 10 cigarettes/day (n= 38)	p-value
Fertilization rate	83.7 ± 1.9 [a]	74.6 ± 0.5 [b]	71.5 ± 1.4 [b]	60.0 ± 0.7 [c]	<0.001
Implantation rate	33.3 ± 3.3 [a]	20.1 ± 0.2 [b]	17.5 ± 0.5 [c]	15.1 ± 0.6 [d]	<0.001

FERTILITY

RESULTS

Comparison of ICSI outcomes amongst refined sugar's non-consumers and consumers, according to self-reported frequency

Outcomes	Refined sugar consumption				
	Non-consumer (n= 77)	Up to 2x/week (n= 236)	Between 3x and 6x/week (n= 47)	More than 6x/week (n=201)	p-value
Fertilization rate	80.4 ± 1.4 [a]	78.3 ± 0.8 [a]	71.9 ± 3.0 [b]	61.1 ± 0.7 [b]	<0.001
Implantation rate	25.7 ± 0.6 [a]	18.7 ± 0.3 [b]	20.0 ± 1.0 [b]	15.3 ± 0.3 [c]	<0.001

FERTILITY

COMMENTS

Background – Maternal smoking habit

human reproduction update

Effects of cigarette smoking upon clinical outcomes of assisted reproduction: a meta-analysis

A.L. Waylen[1,6], M. Metwally[2], G.L. Jones[3], A.J. Wilkinson[4], and W.L. Ledger[5]

↓ Clinical pregnancy and live birth rates / ↑ miscarriage rates

human reproduction update

Effects of cigarette smoking on reproduction

C. Dechanet[1,*], T. Anahory[1], J.C. Mathieu Daude[2], X. Quantin[3], L. Reyftmann[1], S. Hamamah[1], B. Hedon[1], and H. Dechaud[1]

Negative effects on folliculogenesis, embryo transportation, endometrial receptivity, uterine blood flow

DOSE-DEPENDENT

FERTILITY

COMMENTS

Background – Maternal nutrition

The Influence of Diet on Fertility and the Implications for Public Health Nutrition in the United States

RESEARCH   **Open Access**

Mediterranean diet improves embryo yield in IVF: a prospective cohort study

Hongmei Sun[†], Yihua Lin[†], Dongxia Lin, Change Zou, Xiangli Zou, Lan Fu, Fanhua Meng and Weiping Qian[*]
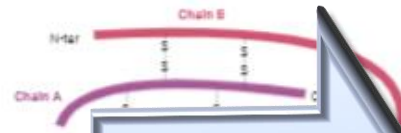
FERTILITY

COMMENTS

Background – Maternal nutrition

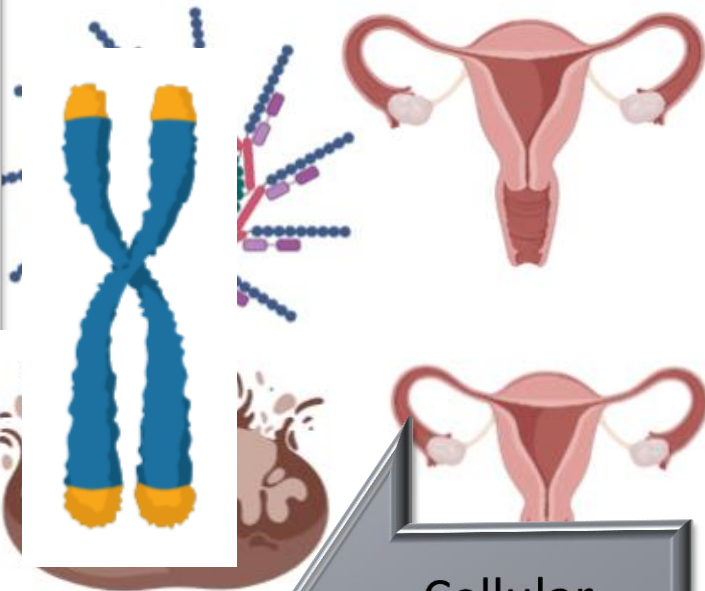Telomere length as a marker of cellular ageing is associated with prevalence and progression of metabolic syndrome

Shortening of telomeres

Cellular ageing

Maternal Glucose Concentration Influences Fetal Growth, Gestation, and Pregnancy Complications

Background – Maternal nutrition

RBM ONLINE
ELSEVIER

Article

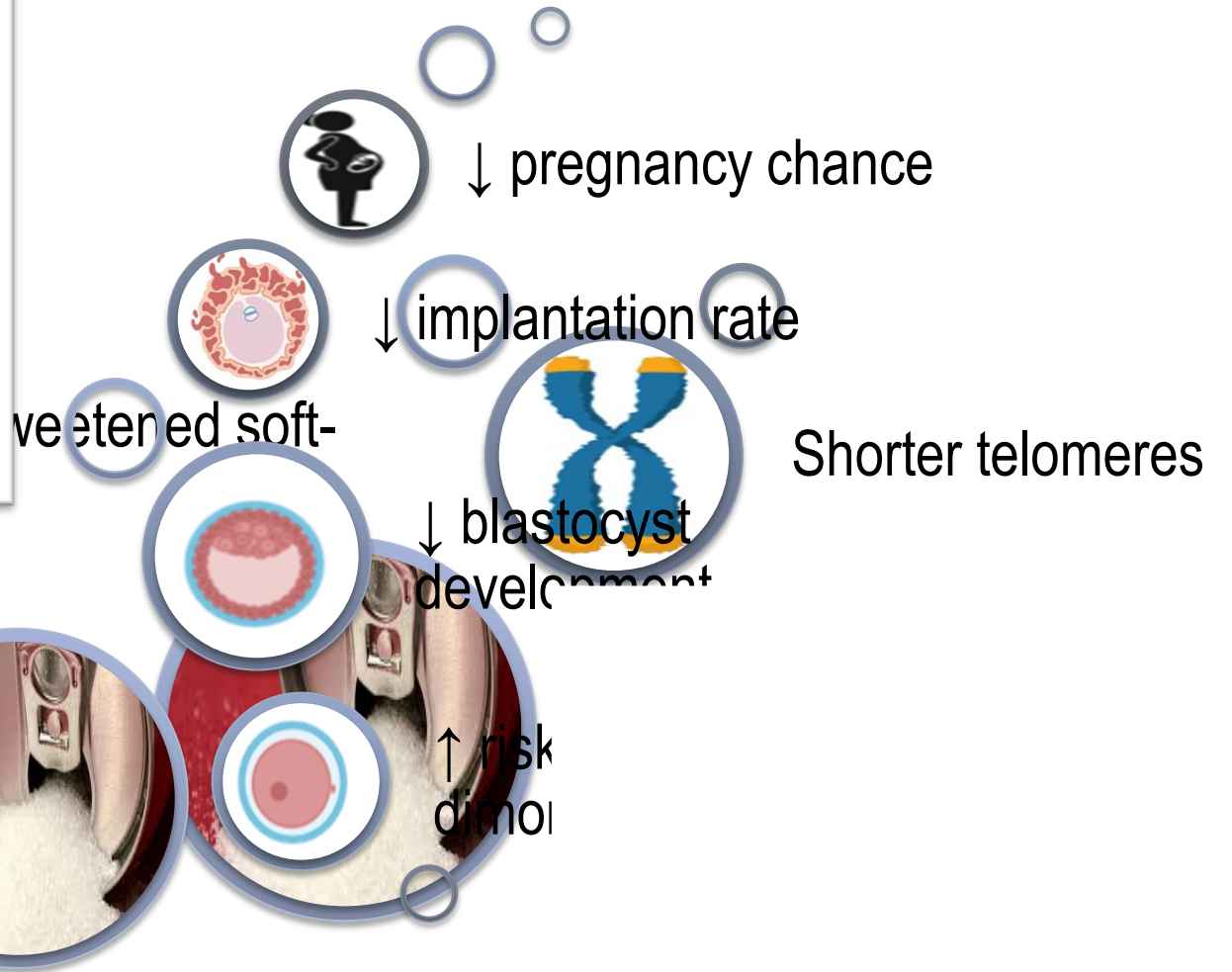**Is there an association between artificial sweetener consumption and assisted reproduction outcomes?**

Amanda Souza Setti [a,b], Daniela Paes de Almeida Ferreira Braga [a,b], Gabriela Halpern [a], Rita de Cássia S Figueira [a], Assumpto Iaconelli Jr [a], Edson Borges Jr [a,b,*]

Telomeres and human reproduction

Keri Horan Kalmbach, M.S.,[a] Danielle Mota Fontes Antunes, M.S.,[a,b] Roberta Caetano Dracxler, M.D.,[a,c] Taylor Warner Knier, B.A.,[a] Michelle Louise Seth-Smith, B.S.,[a] Fang Wang, Ph.D.,[a] Lin Liu, Ph.D.,[d] and David Lawrence Keefe, M.D.[a]

[a] Department of Obstetrics and Gynecology, New York University, Langone Medical Center, New York City, New York; [b] Graduate Program in Pathology, Fluminense Federal University, Rio de Janeiro, and CAPES Foundation, Ministry of Education of Brazil, Brasilia, Brazil; [c] São Paulo University, São Paulo, Brazil; and [d] College of Life Sciences, Nankai University, Tianjin, People's Republic of China

FERTILITY

↓ pregnancy chance

↓ implantation rate

sweetened soft-

Shorter telomeres

↓ blastocyst development

↑ risk dimor

CONCLUSION

Maternal lifestyle factors and nutritional habits appear to reduce oocyte quality and the outcomes of ICSI

FERTILITY

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