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# RACIAL DIFFERENCE IN ART SUCCESS

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# Racial difference in IVF

Fertility rate decline is across the board and observed similar drop in Europe, USA and china. It is estimated that 15-20% of couples desiring a family may have fertility issues. This puts a demand on ART and indeed that world wide numbers of IVF procedure has been increasing in the last decade. This might also be a result of increased awareness and facilities. But demand and supply often goes hand to hand.

There is an awareness of racial and ethnic differences in achieving ART pregnancies.



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# Racial difference and Fertility

Puberty timing – black earlier than white

Menopause – Asian, black and Hispanic earlier

ART results – white > Hispanic

> black/Asian

Missoner et al, Fertil Steril. 2011

Luboosky et al, Hum Reprod. 2003

Fujimoto et al, Fertil Steril. 2010

Seifer et al, Fertil Steril. 2010

Baker et al, Fertil Steril. 2010



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Noted that black American has one third less live birth rate than white. They have lower implantation rates and higher spontaneous abortion. Other confounding factors are less access to ART, presence of leiomyoma, endometriosis and pelvic infection.

? Social class and environment?

Seifer et al, Fertil Steril.. 2008



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There were large population studies based on UK HEFA and US SART and CDC data but either contain scanty data on Chinese (0.01% of sample) or just grouped under minority ethnic or Asian. Other more dedicated reports also had not further separate Asian to specific racial groups - thus collectively demonstrated a difference but not specific. Is there a significance? Because not only there is a genetic difference, but environment of life style may play a part in IVF – response to stimulation, sperm condition, embryo qualities and endometrium, to name a few.



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Many other reports also demonstrated the difference in ART success between different racial/ethnic groups:

Asians vs non-Hispanic whites

But no subgrouping Asians so included Indians, Chinese, Japanese, Koreans etc

Purcell et al, Fertil Steril. 2007

Fujimoto et al, FertilSteril. 2008

# AMH – Racial differences

- Age 27-43, black, Hispanic 25% less than white

Seifer et al, Fertil Steril 2009

- AFC and AMH – both as ovarian ageing indices seems to have a genetic component as yet not clarified

Rosen et al, Menopausal 2010

- Genes affecting AFC also positively affecting AMH

Schula-Hereta et al, Hum Genetics. 2012

- FMR1 genes (CGG repeats) showed differences

African black highest AMH, lowest FSH but declines fast

Asians low AMH, ovarian reserve, but declines slowly

Seifer et al, Fertil Steril. 2009

Gleicher et al, Reprod Biol Endocrinol 2012



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# Vitamin D

Increasing focus as it may control 10% of our genes. In fertility it affects oocyte development, fertility treatment as well as uterine function in endometrial receptivity (immune modulator)

Differs from skin colour and race -> darker skin tone less response to UV and so need less Vitamin D.

Racial difference showed according to race, and latitude they live in.

No study on Chinese vs Caucasian



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# Vitamin D and AMH

Positively correlated

Significant difference between white and black

Not related to BMI.

Vit D up regulate genes which affects AMH production in granulosa cells.

Merhi et al, Fertil Steril. 2012

Coney et al, Int. Gynecol. Obstet. 2012

Mally et al, Endocrinology 2009



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# Racial differences

AMH

AFC

Response to FSH: Higher E, less follicles

Higher E, more follicles less eggs

Higher incidence of PCO

Higher incidence of poor response

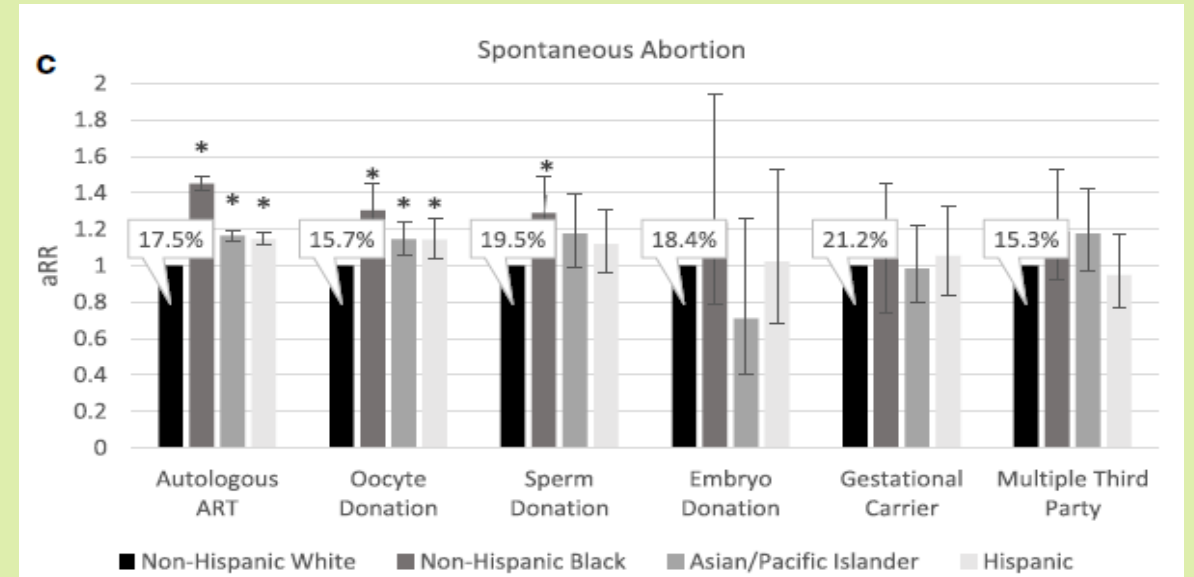
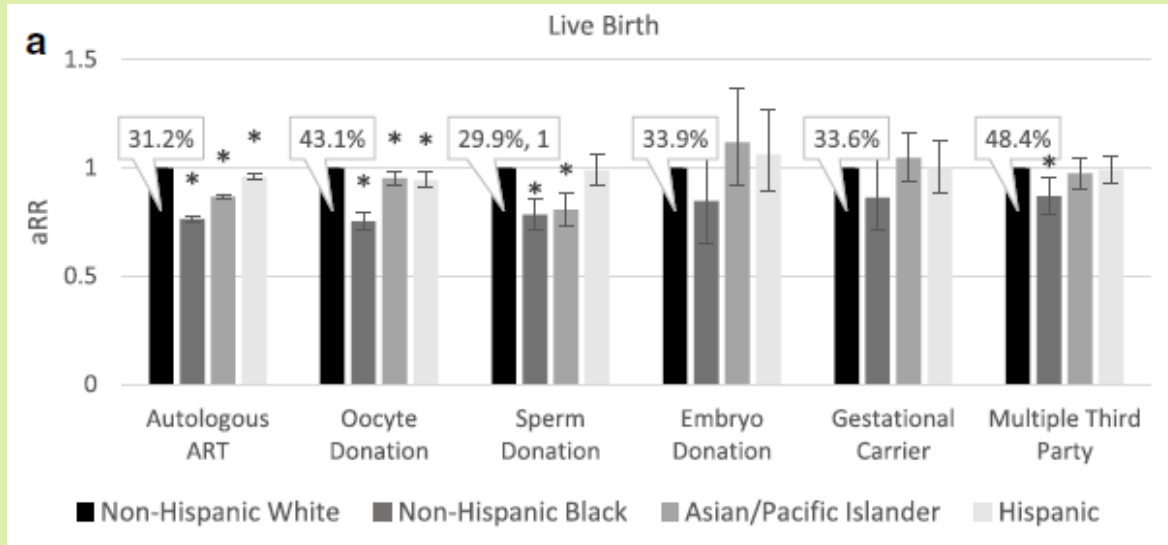


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Adjusted relative risk for live birth rates (a), pregnancy rates (c) for each ART modality, stratified by race and ethnicity of the intended mother. Non-Hispanic White women were the reference group for all comparisons, data is adjusted for age of the intended mother and oocyte donor. A generalized estimating equation (GEE) model was used to controlled for patients with multiple cycles. Bars represent 95% confidence intervals. Percentages indicate live birth rates for each treatment modality among Non-Hispanic White women. \* indicates P-value < 0.05

*Shapiro et al. Reproductive Biology and Endocrinology (2017)*

# Data Caucasian vs Chinese



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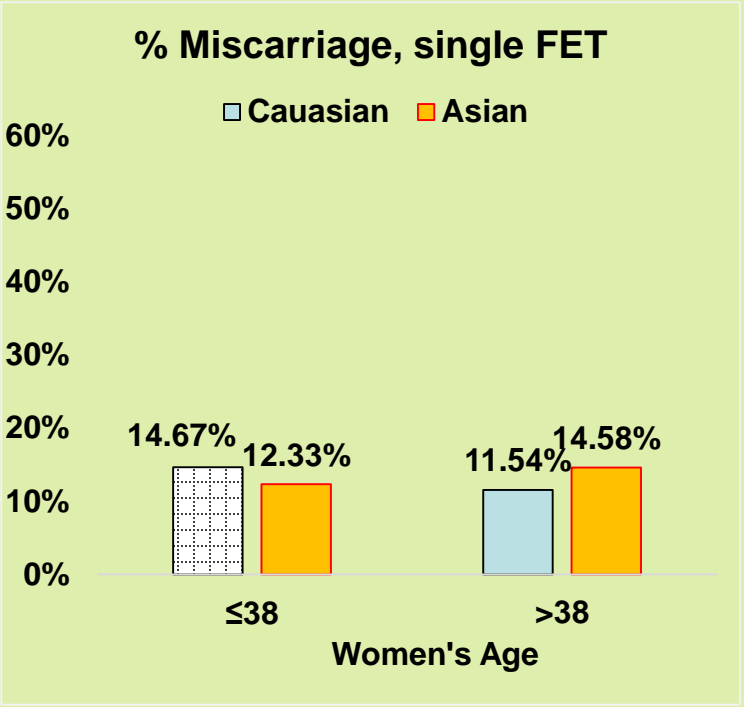
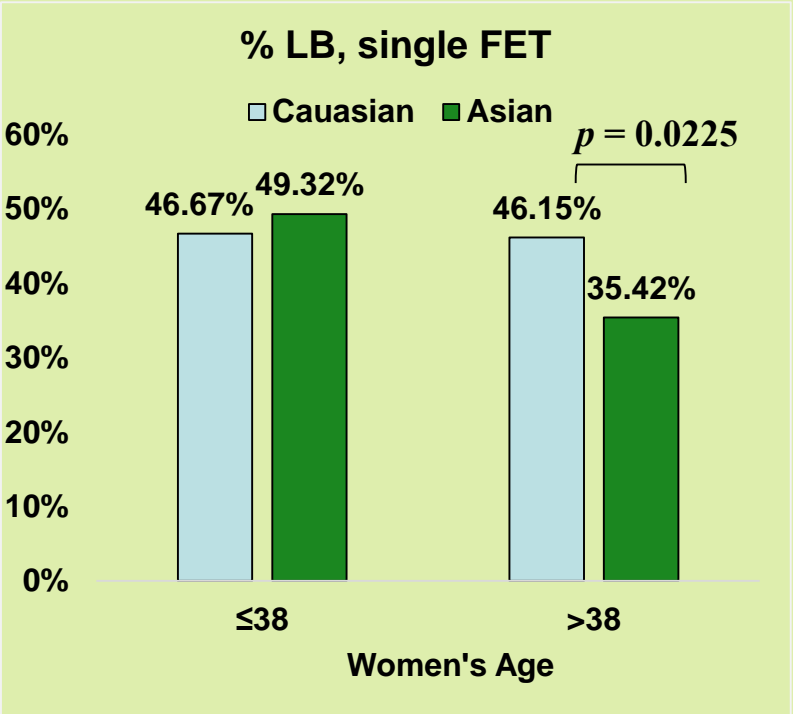
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- Reporting a single center experience 2015-2019
- A retrospective look but is actually a prospective study
- Same stimulation protocol – to achieve enough oocytes
- Same embryology laboratory
- All single blastocyst transfer under US using Wallace
- Representing a homogenous data set
- Four groups: Caucasian/Caucasian; Chinese/Chinese; Caucasian/Chinese; Chinese/Caucasian

# Differences in assisted reproduction treatment (ART) outcomes between Chinese and Caucasian women in a private *in vitro* fertilization (IVF) clinic of Hong Kong



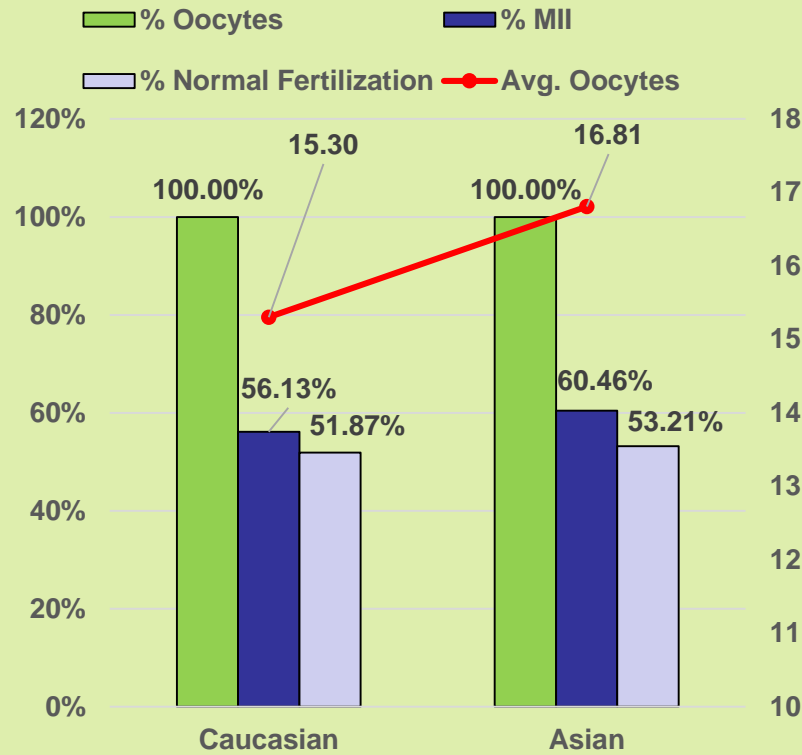
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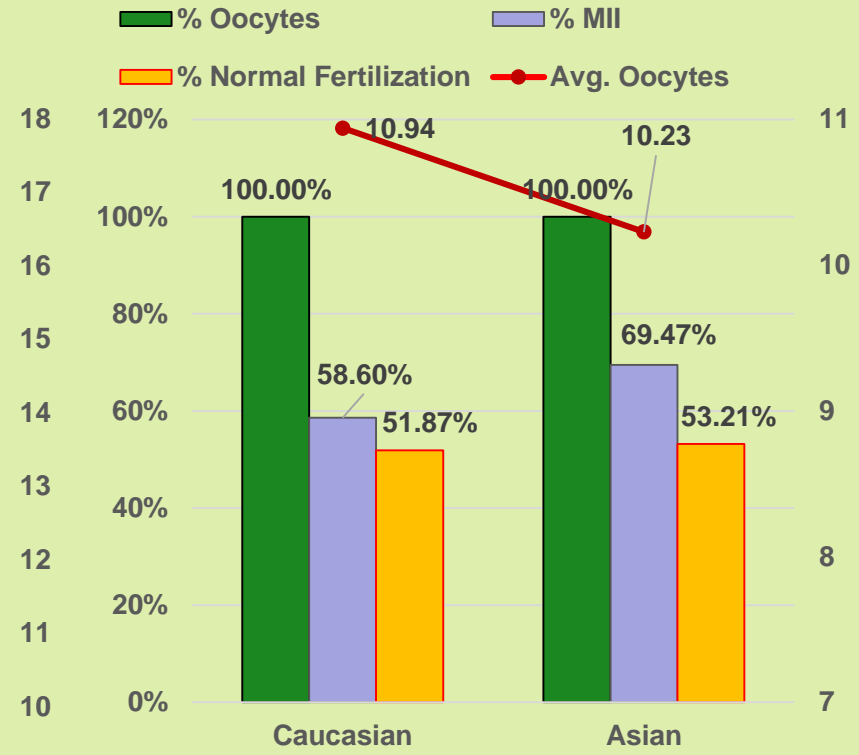
Age groups	≤38		>38		
	Races	Caucasian	Asian	Caucasian	Asian
Total numbers of single embryo transferred		75	219	26	96
Total day-3 embryo transferred		6	14	5	14
Total day-5 embryo transferred		65	172	17	69
Total day-6 embryo transferred		4	32	4	13

# Oocyte retrieval between Chinese and Caucasian women

≤38



>38



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Age groups	≤38		>38	
	Caucasian	Asian	Caucasian	Asian
Races				
Number of Cycle	112	303	85	343
Avg. Oocytes	15.30	16.81	10.94	10.23
Avg. MII	8.59	10.16	6.41	7.10
Avg. 2PN	7.94	8.94	5.47	5.19
Avg. usable embryos	4	4	3	3
% MII	56.13%	60.46%	58.60%	69.47%
% Normal Fertilization (2PN/MII)	92.41%	88.01%	85.32%	73.00%

# Caucasian vs. Chinese Patients

Age groups	≤38		>38	
	Caucasian	Asian	Caucasian	Asian
Races				
Number of Cycle ID	112	303	85	343
Avg. Age	35.37	34.84	41.39	42.01
Avg BMI (kg/m <sup>2</sup> )	21.95	21.44	21.35	21.59
Avg. AMH (ng/mL)	1.90	2.57	1.25	1.47
Avg. Vit.D (ng/mL) P <0.001	<b>29.10</b>	<b>20.94</b>	<b>26.29</b>	<b>22.07</b>
Avg. FSH D3 (mIU/mL) P <0.001	6.97	7.16	8.63	7.54
Avg. LH D3 (mIU/mL)	5.30	4.37	3.87	3.58
Avg. AFC	8.43	9.06	6.79	6.66



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# Caucasian vs. Chinese Patients

Age groups	≤38		>38	
Races	Caucasian	Asian	Caucasian	Asian
Number of Cycle ID	112	303	85	343
Avg. Age	35.37	34.84	41.39	42.01
Avg. Total use of FSH (IU)	3759.46	3470.76	4054.41	3979.73
Avg. Peak E2 (pg/mL)	2148.19	3126.16	1778.95	2032.73
Avg. Progesterone (ng/mL)	1.14	1.69	1.28	1.18
Avg. Endometrial Thickness (mm)	9.97	10.95	9.46	10.17
Live Birth Rate				
Chi square p <0.05 in red	46.67%	49.32%	46.15%	35.42%



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# Caucasian-Chinese couples vs. Chinese-Caucasian couples

Groups (Husband-Wife)	Caucasian-Chinese		Chinese-Caucasian	
Live Birth Count/ Total # of FET	48	156	10	22
Avg. Wife Age	38.53		36.64	
Live Birth Rate $p = 0.169$	30.77% (*P<0.01)		45.45%	



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# Melbourne Study – 10 years experience

2072 Caucasian, 522 Asian

IVF success (CPR) Caucasian > Asian

No specific groups of Asian based on race and ethnicity

After controlling for age and years fertility

# oocytes

# embryos

Differences not significant

Conclusion: Asian delay treatment

Kan et al, J Obstet Gynecol Research 2015(6)946



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Does chromosome play and part in IVF success and ethnicity?

2328 cases in 4 groups:

African, Caucasian, East Asia, Central/South east Asia

No difference in aneuploidy occurrence

Fransiak et al, Human Reprod 2016

# Environmental Factors

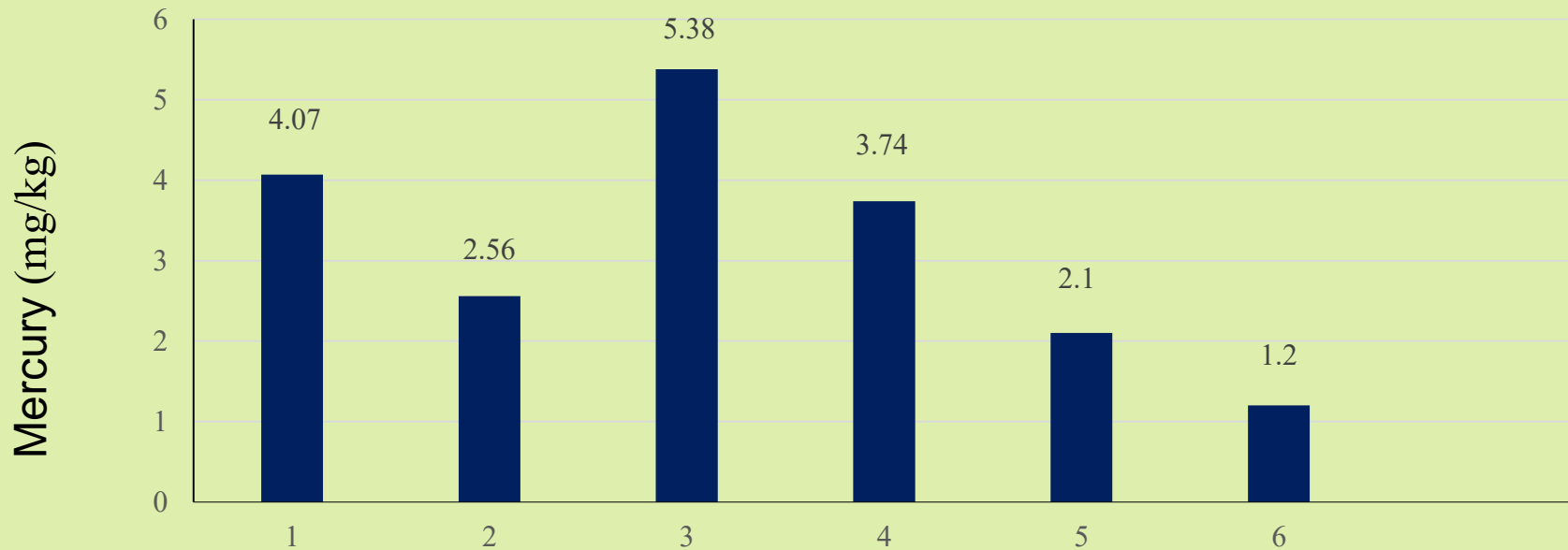
- One big difference between Caucasian and Chinese in Hong Kong may be environment as well as food intake. Southern Chinese are brought up mainly on a seafood diet, plus the propensity to favour “scavengers” – shrimps, crabs and other shell fishes. These are known to be high especially in heavy metals – Mercury, Cadmium, lead, to name a few. Can this be the reason for fertility and IVF success difference? Difference in microbiome, for example?



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# Mercury Concentration in Human Hair



1 = Hg in Hong Kong residents that consume 4 or more meals of fish per week

2 = Hg in Hong Kong residents that consume less than 4 meals of fish per week

3 = Hg in Hong Kong subfertile males that consume 4 or more meals of fish per week

4 = Hg in Hong Kong subfertile males that consume less than 4 meals of fish per week

5 = Hg in hair from over 200 people from coastal areas of Finland (Salonen et al. 1995)

6 = Hg in hair from over 200 people chosen at random from Europe (WHO 1990)

Mercury concentrations in the hair of European, Scandinavian and Hong Kong residents. Vertical bars represent one standard deviation about the mean.



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## Relative risk of male subfertility by hair mercury levels

Mercury Levels (ppm)	Fertile / subfertile	RR <sup>a</sup> (95% C.I.)	RR <sup>b</sup> (95% C.I.)
Low (0.02-1.96)	16/12	1.00	1.00
Medium (2.0-3.69)	16/15	1.78 (1.14-2.78)	1.94 (1.60-2.35)
High (3.70-25.28)	17/53	1.77 (1.14-2.75)	1.95 (1.61-2.37)
Trend <i>P</i> -value		1.0114	<0.0005

<sup>a</sup>Crude relative risk.

<sup>b</sup>Adjusted by exact age.

## Mercury in hair samples from 16 Hong Kong vegetarians

	<i>n</i>	Mean Hg	S.D.	S.E.
Hong Kong vegetarians	16	0.38	0.49	0.115

# Summary

- We report our data on a single center, single protocol prospective IVF treatment 2015-2019
- The patients were separated into race groups for analysis
- No social or other accessibility confounding factors
- We noted that there was a marked difference between Caucasians and Chinese especially as they age, although there were no differences in most parameters
- But there was no difference at younger age



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# Summary

- The only difference noted was aging Chinese seemed to do a lot worse than Caucasians.
- Mixed marriages showed similar trend, but numbers too small
- Chinese has lower Vitamin D levels, and on the whole has higher heavy metal “damage”
- Thus, apart from genetic reasons as proposed, there may be environment and life style reasons
- The exact reasons calls for more and larger single racial group analysis, and likely multicenter studies, perhaps using mixed marriages (and infant outcome?) for comparison.
- Racial IVF success difference remains an enigma



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# Acknowledgement



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The Hong Kong IVF Clinic

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