



Clinical Ethics of Assisted Reproductive Technology

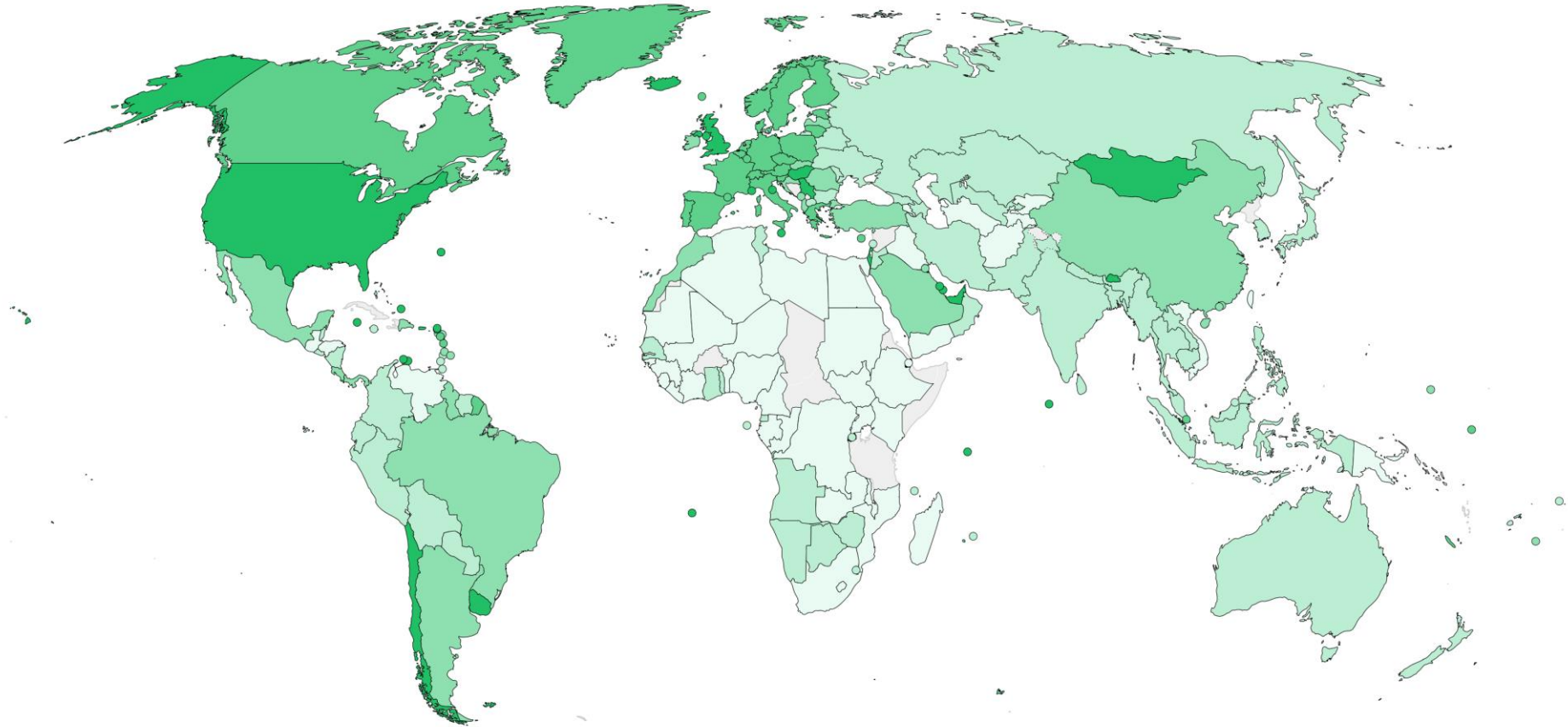
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World Map of Vaccinations

More than 1.63 billion doses have been administered—enough to fully vaccinate 10.7% of the global population

no data 1 10 20 30% of population covered



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and the trials:

Would we have had the COVID-19 vaccine today?

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Would we be having vaccine roll-out in such a coordinated fashion across the whole world today?

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If an individual person, patient, client doesn't *want* to take the COVID-19 vaccine today?

Can we make them?

If many patient volunteers hadn't contributed to the science, and the trials:

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Research: creating new, generalizable knowledge

If public health professionals and governments across the world hadn't cooperated to manage vaccine flow:

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Public Health: common good

If an individual person, patient, client doesn't *want* to take the COVID-19 vaccine today?

Can we make them?

Individual good: Clinical Ethics: Doctor—patient relationship

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How does the patient come to see us?

Does the patient come to see us:

Individual good: Clinical Ethics: Doctor—patient relationship

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Does the patient come to see us:

By Car? **X**

By MRT? **X**

By Foot? **X**

Individual good: Clinical Ethics: Doctor—patient relationship

How does the patient come to see us?

By Trust

1. Nonmaleficence

First, do no harm; *primum non nocere*

2. Beneficence

3. Autonomy

4. Justice incl. Distributive Justice

Others:

Confidentiality, Fidelity, Veracity, Social Responsibility

41-year-old woman

Primary infertility for 11 years

Low ovarian reserve

Going for IVF

Only 1 blastocyst obtained

PGT-A reveals it's Trisomy 21

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Patient requests to have this embryo transferred

What would you do?

Would you do accede to her request to
replace the blastocyst?

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Only 2 blastocysts obtained

Single Embryo transfer performed

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Single Embryo transfer performed

At 11 weeks, NIPT suggested Trisomy 21

At 12 weeks, NT 3.0 mm

At 16 weeks, Amniocentesis done

At 18 weeks, confirmed Trisomy 21

At 18 weeks+, Midtrimester termination of pregnancy performed

What would you have done?

Would you have recommended blastocyst
PGT-A?

Singapore fertility rates have been falling progressively

Women are having their children later in life

IVF and ART rates are rising

Today, we have the technology to replace only Euploid embryos

Overall outcomes of PGT-A

Good prognosis cohort

- PGT-A likely improves reproductive outcomes, especially in reducing multiple preg rates

Recurrent implantation failure

- Aneuploidy is likely to be a principal factor in RIF; PGT- A may improve implantation rates

RPL cohort

- Data remains limited; may lead to reduced miscarriage rates

AMA cohort

- **If a euploid embryo is found there is a clear benefit in AMA patients**

PGT-A for good prognosis cohorts: STAR Trial

Author, year	PGT-A technique	Control	Results	Limitations
Munne, 2019	NGS and D5 biopsy, SET 'STAR Trial'	Morphology assessment	<p>NO sig diff in continuing preg rates when comparing per-embryo transfer and intention to treat analysis</p> <ul style="list-style-type: none"> Per embryo: 50% [137/274] versus 46% [143/313] Per cycle: 41.8% vs 43.5% 	<p>Excluded women >40yo, >1 miscarriage, >2 previous failed ET</p> <p>Multi-centre, multi-national: each clinic was allowed to follow their own protocol and genetics labs used their own criteria to identify aneuploidy A large range of outcomes e.g. 38-100% for euploid embryos</p> <p>No embryos for transfer</p> <ul style="list-style-type: none"> - 42 women excluded as no euploid embryo found - If mosaicism found (16.8% of the tested embryos) they were also excluded from transfer

PGT-A for Advanced Maternal Age

*Improved outcomes if
there is a euploid embryo
available for selection*

3 RCTs focused on AMA (>35yo)

- 2 were global, multicentre trials;
aCGH was performed on cleavage stage or polar body
biopsies
- Mean age of trial participants 38-40 yo

Increased implantation rate

- Rubio et al: 44% vs 24.8%, $p < 0.005$
- Verpoest et al: 38% vs 32%, $p = 0.36$

Decreased miscarriage rate

- Rubio et al: 2.7% vs 39%, $p = 0.0007$
- Schoolcraft et al 0% vs 20%, $p < 0.05$

Higher or similar live birth rates

- Rubio, ITTA: 31.9% vs 18.6%, $p = 0.0031$
- Verpoest 30% vs 22%, $p = 0.15$

Rubio C, et al. Fertil Steril 2017;107:1122–9

Verpoest W, et al. Hum Reprod 2018;33:1767–76

Schoolcraft WB, et al. Fertil Steril 2012;98 Suppl 3:S1

PGT-A for Advanced Maternal Age

- Rubio et al demonstrated higher delivery and live birth rates after both 1st transfer of a euploid embryo (64.7% vs 27.4%, $p < 0.001$) and per patient (44% vs 24.8%, $p < 0.005$).
- Ubaldi et al. show that <50% (43.6%) of PGT-A cycles had a euploid embryo available for transfer.
- Griffin et al. (ESTEEM trial) demonstrated nearly identical live birth rates in a year when ALL randomised women were considered
 - But, comparing known euploid embryos vs unknown ploidy status → higher Live Birth Rate in euploid embryos

Parliament: Do more to help couples trying for a baby through IVF, says Louis Ng



Nee Soon GRC MP Louis Ng suggested extending IVF subsidies to support couples trying to conceive through the process. PHOTO: ST FILE

Parliament: Do more to help couples trying for a baby through IVF, says Louis Ng



	Today	Enhanced
Government co-funding for intra-uterine insemination (IUI)	Not applicable	Up to \$1,000 per cycle for three cycles of IUI
Government co-funding for assisted reproduction technology (ART) treatments	Up to six cycles for women who are below 40 years at the start of the ART cycle	Up to two out of the existing six co-funded ART cycles for women aged 40 and above (As long as they have attempted assisted reproduction or IUI procedures before age 40)
Maximum age limit for ART treatments	45 years old	Age limit removed
Maximum number of ART treatment cycles a woman can undergo	≤ 40 years: 10 > 40 years: 5	Limit removed

Undergoing PGD may increase the likelihood of a successful pregnancy by ensuring the implanted embryo is free from such genetic defects and lower the overall costs as fewer IVF cycles would then be needed, argued Mr Ng, in making his case for extending subsidies to such screenings and letting couples use their MediSave to pay the balance.

Nee Soon GRC to support couples trying for a baby through IVF, says Louis Ng. ST FILE

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PGD (PGT-M, SR)

Mendelian, Structural Rearrangements



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PGD (PGT-M, SR) → PGT-A

Aneuploidy

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Thank you

