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PGT and BEYOND...

Is PGT-A for everyone?

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What is PGT-A for?

PGT-A, in all of its forms, is a molecular assessment of the chromosome complement of an embryo

Results can be used to identify aneuploid embryos which have little or no successful pregnancy potential
Appropriate embryos can be prioritized for subsequent transfer

Such prioritization can improve transfer outcomes relative to other prioritization processes
in terms of pregnancy initiation and implantation potential
continuing pregnancy and ultimately live birth

PGT-A does NOT improve an embryo, it only describes an embryo in terms of its chromosome make up

The Biology underlying PGT-A use

The understanding behind PGT-A is simple enough: aneuploid embryos do not usually lead to successful pregnancy outcomes.

It has been observed that a proportion of embryos generated in an IVF cycle are aneuploid- typically through meiotic non disjunction

The morphology and growth characteristics of an embryo are useful in identifying a potentially useful embryo but such discrimination is limited

Better selection processes improve transfer outcomes

So, what's the problem?

Early approaches to PGT-A were not successful

- the biopsy process appeared to impact on embryo vitality
- the analysis approach was limited and didn't identify the full extent of the chromosome problem

In the last 15 years or so, improved biopsy approaches and more comprehensive chromosome screening resulted in a better overall process.

So, what's the problem??

Some groups reported improved transfer outcomes after such a selection process while other groups found little or no gains with some even suggesting a negative outcome!

There was a misconception that was propagated by many of the positive reports that somehow, PGT-A improved IVF outcomes

this was clearly false since PGT-A can only identify a chromosome makeup and not logically change that makeup. Commercial interests and over eager reporting both played a part in furthering this misconception

The subsequent confusion polarized the IVF clinical world and split groups between a pro PGT-A stance and an anti PGT-A position

So, what was the problem???

Some groups suggested that the positive benefits were only identifiable when the embryo cohort aneuploid rates exceeded a threshold- typically an age-related threshold

below this threshold, improved transfer outcomes were not evident

while above this threshold, most groups identified improvements

Why a threshold?

Age related embryo cohort aneuploidy was identified quickly

younger women had lower cohort aneuploid levels while older women had fewer embryos and many more were aneuploid

So, in good tradition, women were grouped according to an arbitrary age category and made a statistic with related probabilities

So, what's the problem????

This led to suggestions that PGT-A might be considered only when a patient hit an arbitrary statistic

below this statistic, PGT-A should not be considered

above this statistic, you might consider PGT-A but only in some circumstances

Is this logical?

Only superficially, since the underlying biology of transferred aneuploid embryos not being very successful applies to women of all ages.

Failure to show improved transfer outcomes for women of any age group is just a statistical quirk brought about by good embryology, poor embryology, mediocre analysis approaches and inadequate sample sizes

Eh?????

Good embryology more readily identifies a good embryo

the whole field was misled by authors who reported group statistics as representing the same as embryo transfer choice- this was false and was simply revealed by Forman over 10 years ago.

Good embryology enriches the euploid rate amongst chosen embryos

So, good embryology can enhance euploid embryo choice well past the arbitrary age thresholds

Poor embryology will impact on the how well the PGT-A process is performed

Embryos are not super entities- handled poorly, they can lose vitality and implantation potential

Eh??????

Mediocre analysis can impact on final interpretations and ultimately reduce the cycle potential by loss of useful embryos through poor analysis

- Not all approaches are equal in their accuracy
- Not all laboratories are equal in their capabilities (often despite their own beliefs)

Eh????????

Sample sizes

With small differences, larger sample sizes are needed for statistical significance to be gained.

When good embryology identifies euploid embryos to high levels (typically around 80%), then PGT-A can only assist with a marginal gain- with even a small percentage of women having a euploid embryo transferred not achieving a pregnancy, then the apparent gain after PGT-A is even smaller

this necessitates very large group sizes (beyond most of the under-powered studies currently reported)

A second fallacy that permeates the debate is that lack of statistical significance implies no difference!

this is a gross misunderstanding of significance and the actual meaning of a P value

So, is PGT-A for anyone?

The biology underlying PGT-A is indisputable

- Euploid embryo transfers are more successful than aneuploid embryo transfers

Even with younger women

- 20% of first choice embryos are aneuploid (this will rise with subsequent transfers)
- Some younger women only have aneuploid embryos in their cohort (5-8% of young women)

No embryologist can get it right every time

So, is PGT-A for anyone?

The Patient

Every patient has their own dreams, expectations, desires and goals.

Some patients will assess the risk of an untested transfer being an aneuploid as acceptable while others do not consider it acceptable (history, time, emotions, finances, etc)

Patients are not statistics- they are individuals

Patients typically pay for every procedure that is done

failed transfers benefit the clinic financially, not the patient. Transfers of aneuploid embryos are futile transfers, destined for failure

So, PGT-A can benefit any patient wanting a less risky journey to pregnancy

So, is PGT-A for anyone??

The Clinic

Every clinic has a belief in itself and what it is doing

Reality is that clinics are not equal in their activities and poor IVF is possibly a bigger negative than clinics want to acknowledge

“Biopsy doesn’t hurt an embryo” is a mantra that is incorrectly repeated.

Biopsy can hurt an embryo if done poorly or on a weak embryo because of poor embryology or poor timing decisions

Good clinics get good results- poor clinics will often get poor results

Not all clinics should be doing biopsy and PGT-A

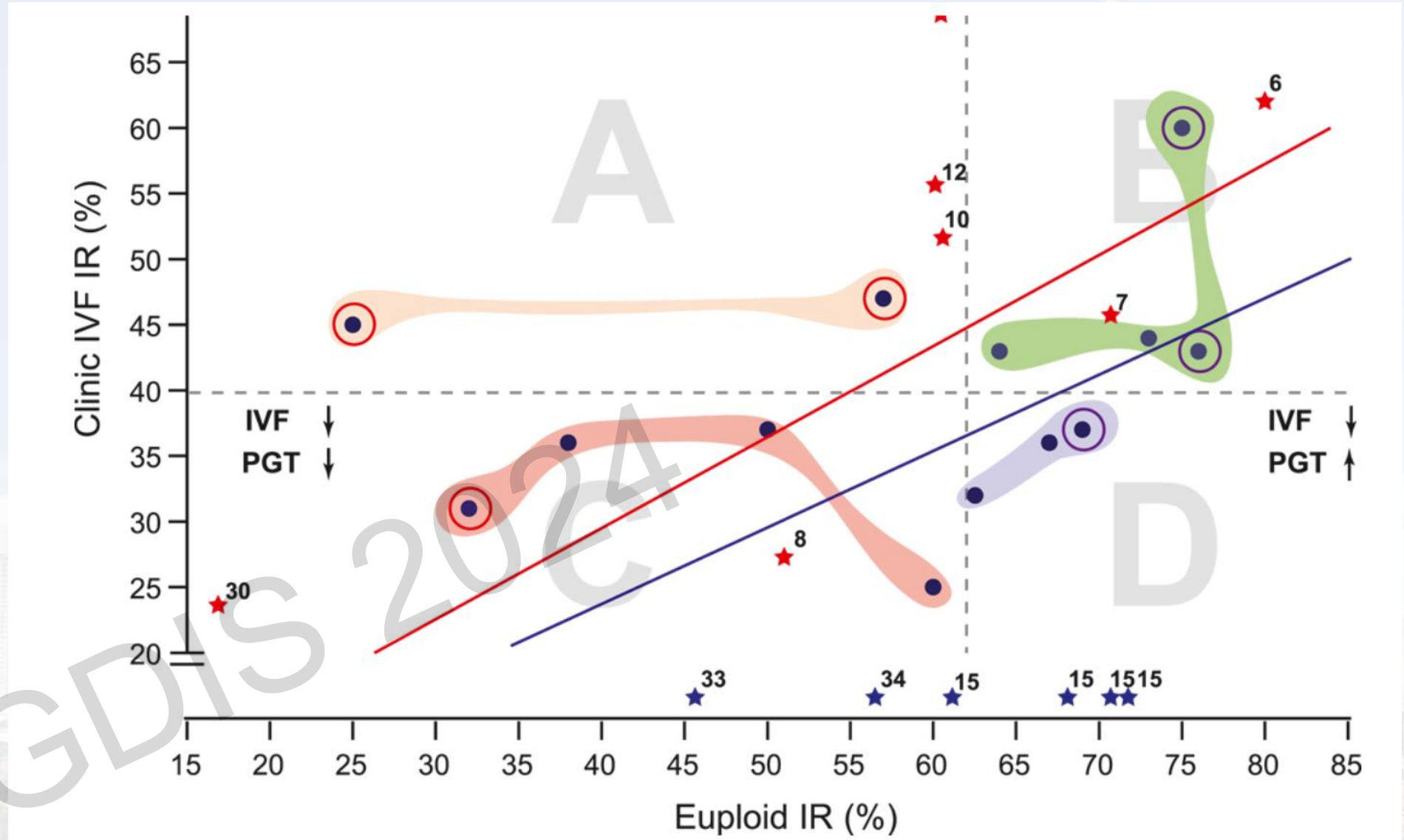

FIGURE 4.

fr Wang et al 2022

So, is PGT-A for anyone???

The laboratory

While some clinics may do analysis internally, there are a number of large commercial service suppliers that do a majority of analysis for clinics offering PGT-A

These groups are not always equal in the quality of what they do and are generally driven by commercial imperatives. Proclamations of validation and quality are sometimes a screen and not genuine. These groups are also subject to pressures brought about by their clients and will relent when pressure comes for an answer.

So, as with clinics, not all laboratories should be offering PGT-A analysis services

So, is PGT-A for anyone????

PGT-A is for every patient who wants it. It is for every patient who wants to reduce the uncertainty just that little bit more

Unfortunately, it is not for every clinic to perform just because they want to offer it. Nor is it appropriate for every laboratory to provide a service, just because they can

THANK YOU