Impact Of Calling Mosaicism For A Less Stringent Threshold On Clinical Pregnancies In More Than 6000 PGT-A Cycles

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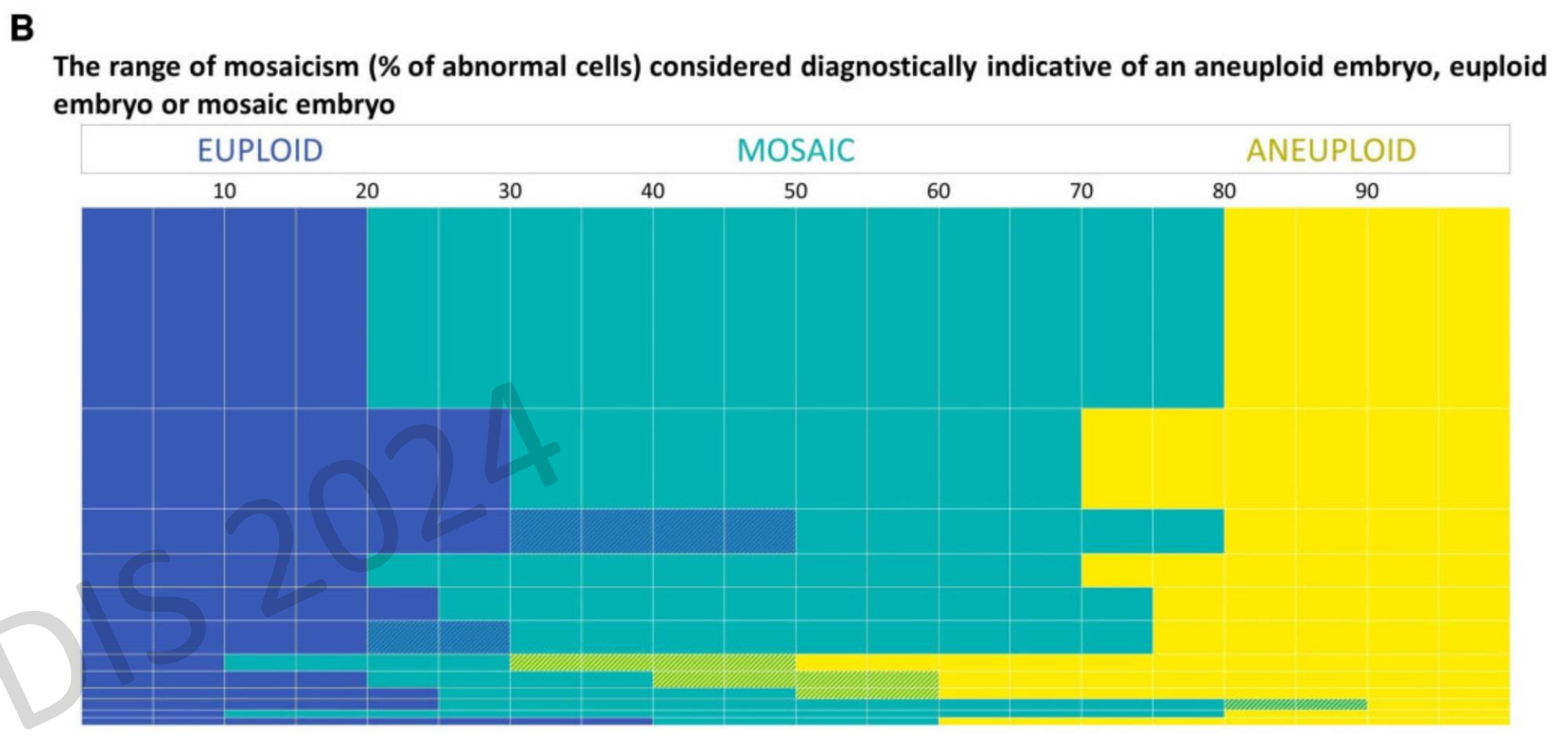
Is there a consensus for the range of mosaicism?

Figure 2.



ESHRE Working Group on Chromosomal Mosaicism, ESHRE Survey Results, 2022. doi.org/10.1093/hropen/hoac044

Our Center’s Mosaicism Approach Until 2021

- Mosaicism was reported over 20% euploid-mosaic cut-off (EMC)
- Overall mosaicism ratio : 13.4%
- 20% of the mosaics were lower than 30% mosaicism
- Pregnancy outcomes for mosaics lower than 30% level were similar with euploids
  - Ongoing Pregnancy, Euploid vs <30% mosaic
    - 59.2% vs 57.1% (p=0.76)
- Other factors also counted for:
  - `Safe` outcomes
  - Avoid `unnecessary` new cycles
  - Stress factor and decision-making process for couples with mosaic embryos

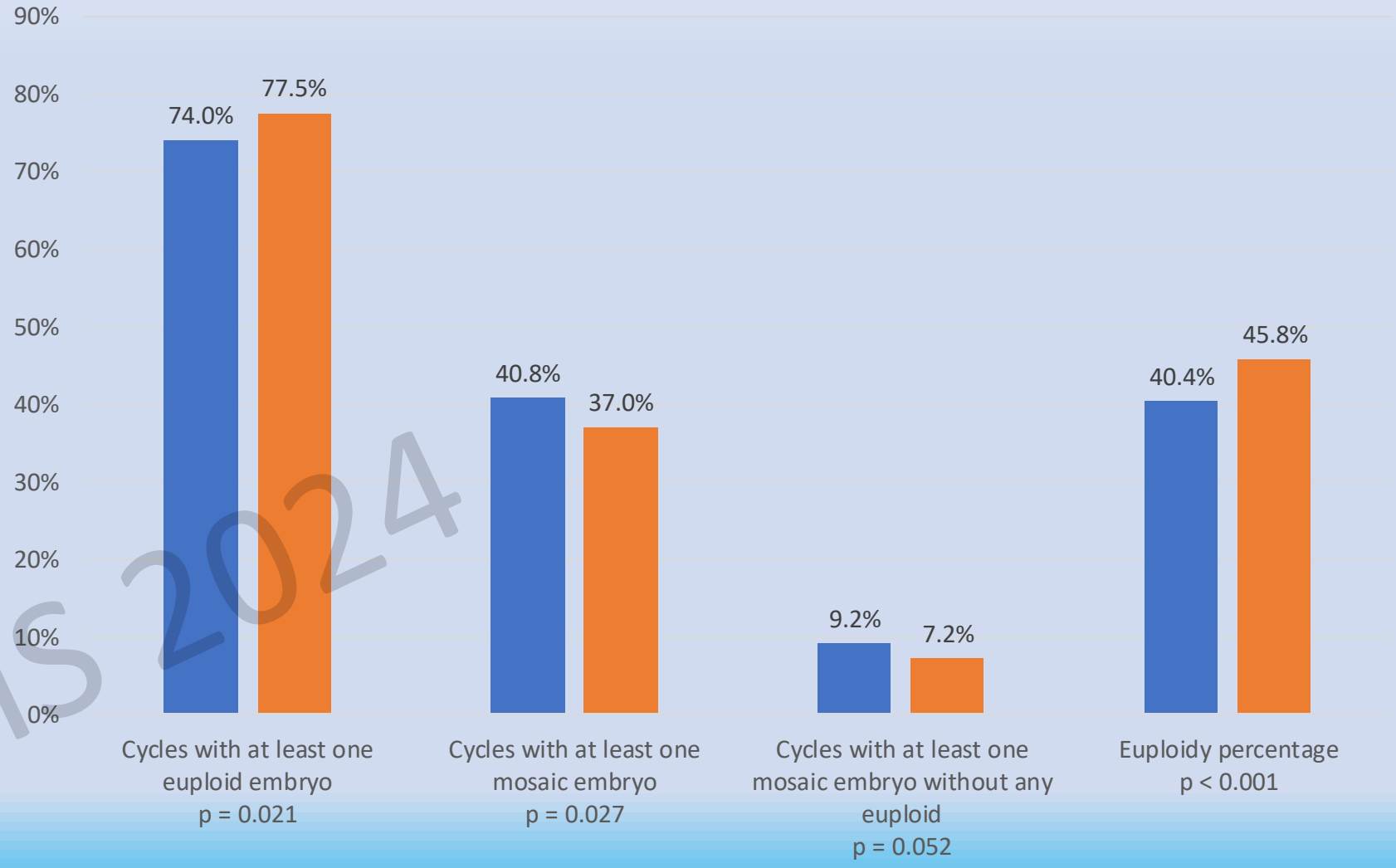
Materials and Methods

- January 2017 to October 2022
- 6063 PGT-A cycles, 18425 trophectoderm biopsies analyzed with NGS (ReproSeq, Thermo Fisher)

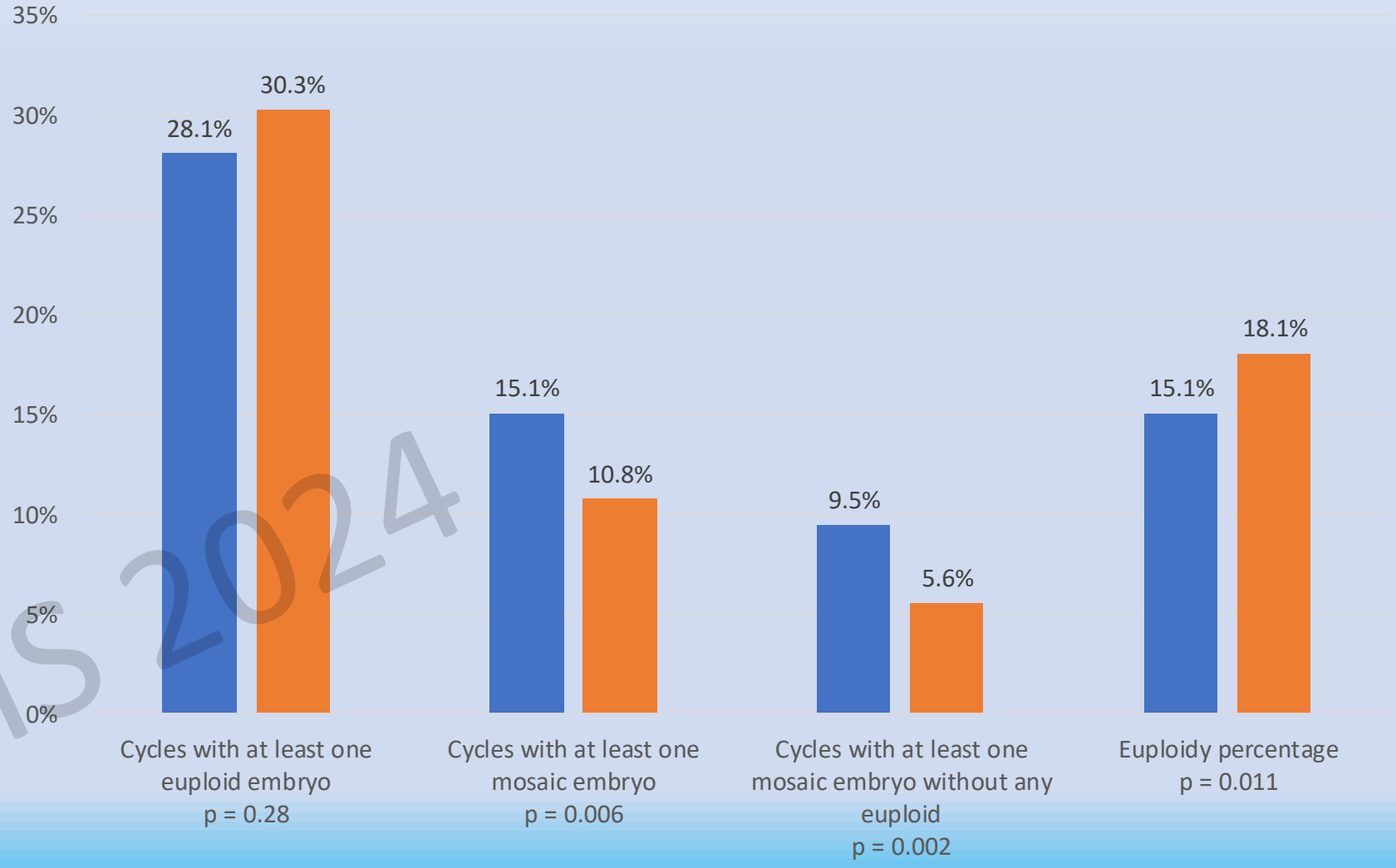
Euploid – Mosaic Cut-off (EMC)	Start date	End Date	Number of biopsies	Mean Female age *
20%	January 2017	December 2020	12751	36.7 ± 5.1
30%	January 2021	October 2022	5674	35.9 ± 5.2

- Mean female ages were statistically significantly different
  - Further analysis was performed in age subgroups of ≤38 and >38.

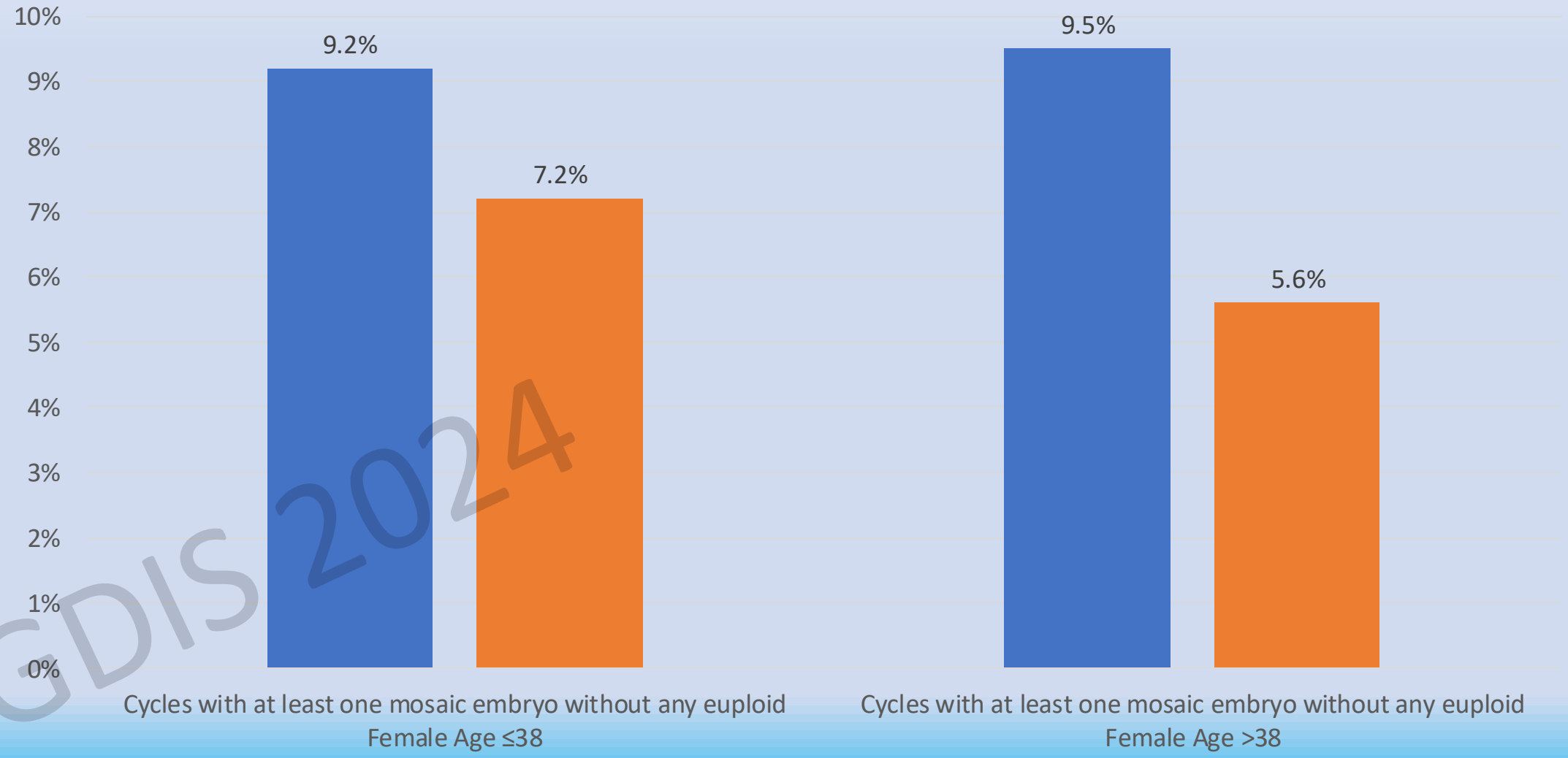
Results – Female Age ≤38



Results – Female Age >38



Cases with only mosaic embryos as transferrable



Pregnancy Outcomes For Euploid Embryo Transfers

- Ongoing clinical pregnancy
  - EMC 20% → 59.1 %
  - EMC 30% → 64.5 %
  - $p<0.01$
- Biochemical pregnancy loss
  - EMC 20% → 9.4 %
  - EMC 30% → 10.4 %
  - $p=0.375$

Detailed Clinical Outcomes for Euploid Embryo Transfers

	EMC 20% Female Age ≤38 n=2147	EMC 30% Female Age ≤38 n=920	EMC 20% Female Age >38 n=649	EMC 30% Female Age >38 n=208
Biochemical Pregnancy	74.9	78.7	73.3	76.9
Biochemical Miscarrage	9.2	10.1	9.9	11.7
Clinical Pregnancy	68	70.3	65.9	67.3
Clinical Miscarriage	12.5	7.0	12.2	8.8
Ongoing Pregnancy	59.5	65.3	57.9	61.3

Pregnancy Outcomes for Mosaic Embryo Transfers

- Ongoing clinical pregnancy
  - EMC 20% → 53.9 %
  - EMC 30% → 60.2 %
  - p=0.54
- Biochemical pregnancy loss
  - EMC 20% → 17.7 %
  - EMC 30% → 8.3 %
  - p=0.09

Detailed Clinical Outcomes for Mosaic Embryo Transfers

	EMC 20% Female Age ≤38 n=130	EMC 30% Female Age ≤38 n=58	EMC 20% Female Age >38 n=97	EMC 30% Female Age >38 n=26
Biochemical Pregnancy	79.2	74.1	62.8	65.4
Biochemical Miscarrage	16.5	9.3	18.3	5.8
Clinical Pregnancy	66.1	67.2	51.0	64.0
Clinical Miscarriage	10.5	7.7	8.1	12.5
Ongoing Pregnancy	59.2	62.0	46.8	56

Conclusions

- Mosaicism is undeniably a true biological phenomenon. However, trophectoderm biopsy methods and NGS are prone to create an artefactual false mosaicism.
  - False mosaicism may be more common in either edges of the spectrum
- Relaxing the mosaicism calling rate by 10% may have added some better-quality blastocysts to the euploid pool giving the opportunity to embryologists of transferring blastocysts with higher implantation potential.
  - Embryo quality may be more important for implantation especially for embryos that are euploid or `low level mosaic`

Thanks

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