

Supplementary data SI. Survey questions.

DEMOGRAPHICS

- COUNTRY
- Private/Public/Academic
- SET-UP
 - o ART centre without PGT centre (PGT is outsourced)
 - o ART/PGT centre (in house PGT)
 - o PGT centre (not linked to an ART centre)
 - o Other set-up
- Estimated nr of cycles
 - o ART
 - o PGT-A
 - o PGT-M
 - o PGT-SR
- Indications for which PGT is performed
 - o PGT-A
 - o PGT-M
 - o PGT-SR
 - o PGT-M/PGT-A (combined)
 - o PGT-SR/PGT-A (combined)
- Does your centre have accreditation?
 - o Yes, accreditation for the ART centre
 - o Yes, accreditation for the PGT centre
 - o Yes, accreditation for the ART centre and for the PGT centre
 - o No

Biopsy and PGT

- What type of biopsy do you perform? (per indication)
- Which method do you use for zona breaching?
- If you perform blastocyst/trophectoderm biopsy, what is the optimal number of cells that you aim to obtain in a TE biopsy?
- On which day(s) do you perform blastocyst/trophectoderm biopsy?

PGT Technologies

- Which technologies (with the capacity to provide information on aneuploidy) are used in your centre for the different PGT options?
- Have you, in your centre, validated the technology you are using?
- Have you, in your centre, validated the technology specifically for the detection of chromosomal mosaicism?
- Report the range of mosaicism (% of abnormal cells) that you consider diagnostically indicative of aneuploid, euploid and mosaic embryo

REPORT

- Which of the following information is included in the PGT report?
 - o Whole chromosome aneuploidies
 - o Segmental aneuploidies
 - o Whole chromosome mosaicism
 - o Segmental mosaicism
- If segmental aneuploidies are reported, is there a specification in the report with regards to the minimal size of segmental aneuploidies that can be detected?
- If Mosaicism is reported, does the report also include the degree of mosaicism?
- Does the genetic report include a recommendation and/or prioritization (i.e. a priority order for transfer is indicated in the report based on the results of the analysis) of embryos for transfer?
 - o Yes, recommendation
 - o Yes, prioritization/ranking
 - o Yes, both recommendation and prioritization/ranking
 - o No
- In making a recommendation for embryo transfer, are mosaic embryos included? If yes, are specific criteria considered for prioritization of mosaic embryos?

Embryo transfer policy

- Please indicate for which type of PGT there is a written embryo transfer (ET) policy in your centre, and whether it includes management of mosaic embryos
- Indicate your preferred embryo transfer (ET) strategy for PGT cycles
 - o Fresh ET
 - o Vitrified/warmed ET (freeze-all policy)
- What is your preferred strategy for PGT cycles with regard to the number of embryos to transfer?
 - o Single ET
 - o Double ET
 - o Multiple ET
 - o Other (please specify)
- Have you ever transferred a mosaic embryo
 - o Yes, and would consider doing so again
 - o Yes, but would not in the future
 - o No, but we would consider it
 - o No, and this would never be considered
 - o Mosaicism is not reported by policy in our centre, thus no transfer has ever been performed for this reason

Transfer of mosaic embryos

- How do you deal with mosaic embryos in a cycle where NO euploid embryos are available for transfer? (Preferred option - Option - Never an option)
 - o Rebiopsy
 - o Transfer/store of a single embryo (with ranking)
 - o Transfer/store of 2 embryos (with ranking)
 - o Transfer/store of a single embryo (without ranking)
 - o Transfer/store of 2 embryos (without ranking)
 - o Discard/ Give to research
- How do you deal with mosaic embryos in a cycle where euploid embryos are available for transfer? (Preferred option - Option - Never an option)
 - o Rebiopsy
 - o Transfer/store of a single embryo (with ranking)
 - o Transfer/store of a single embryo (without ranking)
 - o Transfer/store of 2 (both euploid) embryos (with ranking)
 - o Transfer/store of 2 (both euploid) embryos (without ranking)
 - o Transfer/store of 2 (both mosaic) embryos (with ranking)
 - o Transfer/store of 2 (both mosaic) embryos (without ranking)
 - o Transfer/store of 2 (euploid plus mosaic) embryos (with ranking)
 - o Transfer/store of 2 (euploid plus mosaic) embryos (without ranking)
 - o Discard/ Give to research
- When are patients counselled about the potential outcomes of a PGT cycle?
 - o Before the cycle is initiated, with discussion of mosaic embryos
 - o Before the cycle is initiated, without discussion of mosaic embryos
 - o Between PGT diagnosis and embryo transfer
 - o Other (please specify)
- When are patients counselled about the potential detection and/or transfer of mosaic embryos ?
 - o Before the cycle is initiated
 - o Between PGT diagnosis and embryo transfer
- How is informed consent (IC) covered for the transfer of mosaic embryos:
 - o It is included in the general informed consent for the PGT cycle
 - o It is covered in a separate specific informed consent
 - o Other (please specify)
- Do you recommend prenatal diagnosis after transfer of a mosaic embryo?

Prenatal testing

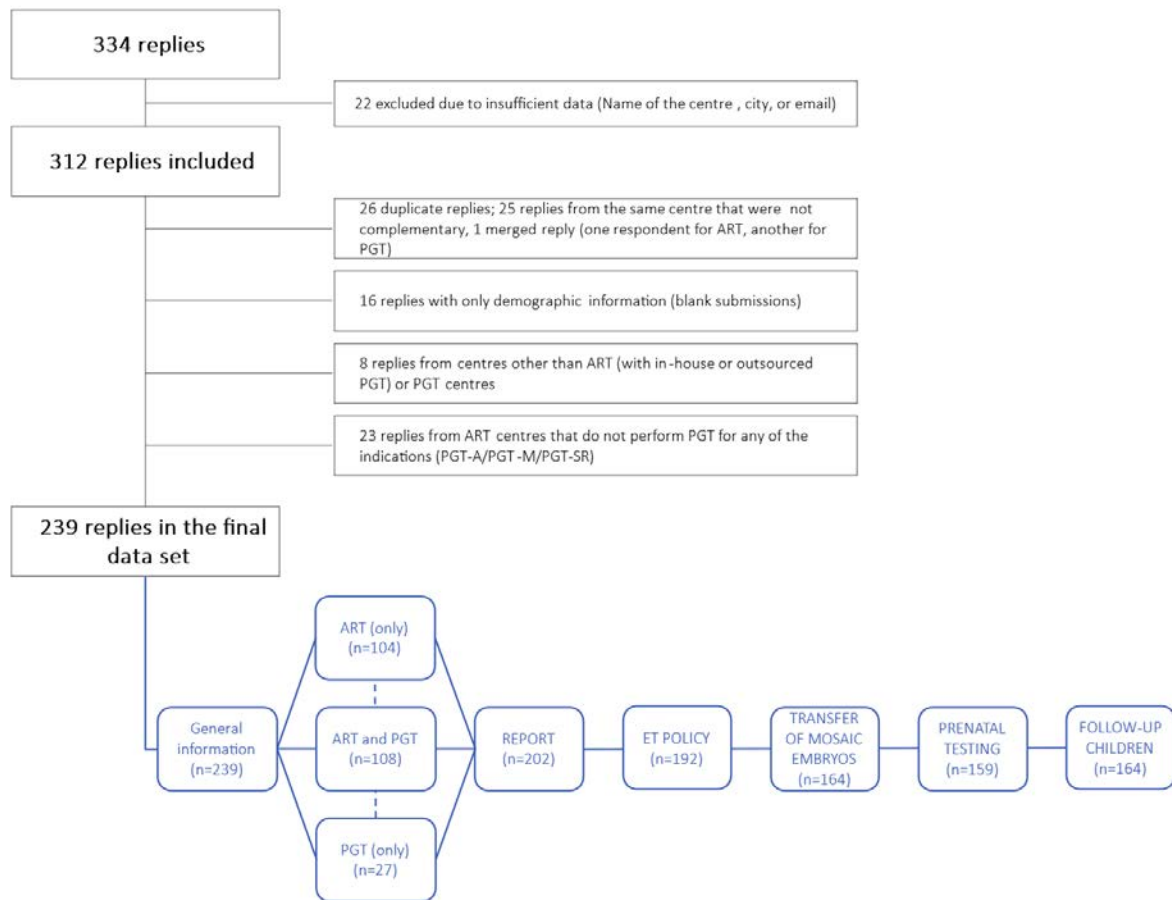
- What do you recommend for prenatal diagnosis after transfer of a mosaic embryo?
 - o Non-invasive prenatal test (NIPT)
 - o Chorionic villus sampling (CVS)
 - o Amniocentesis

- o Other (please specify)
- Please explain your strategy for prenatal diagnosis or give an example

Follow-up of children

- Have you obtained live births following transfer of mosaic embryos?
- Do you perform follow-up of children born following PGT in general?
 - o Yes and follow-up is successful in most cases
 - o Yes, but many patients are lost to follow-up
 - o No
- Do you perform a specific follow-up of pregnancies (including ultrasound scans, obtaining prenatal diagnosis results, or other) and children born following transfer of a mosaic embryo?
 - o Yes and follow-up is successful in most cases
 - o Yes, but many patients are lost to follow-up
 - o No

Supplementary data SII. Flowchart from raw replies to the replies included in the final dataset, and the number of replies per section.

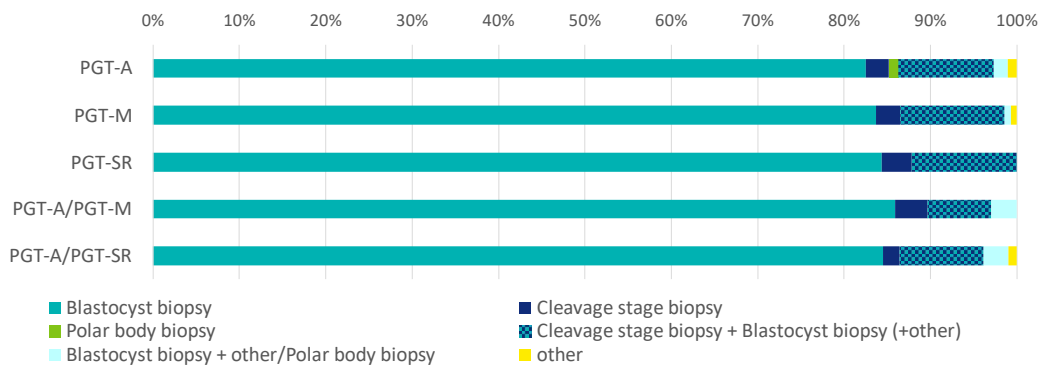


PGT: preimplantation genetic testing, PGT-A: PGT for aneuploidy, PGT-M: PGT for monogenic/single gene defects, PGT-SR: PGT for chromosomal structural rearrangements, ET: embryo transfer.

Supplementary data SIII. Data on biopsy and PGT.

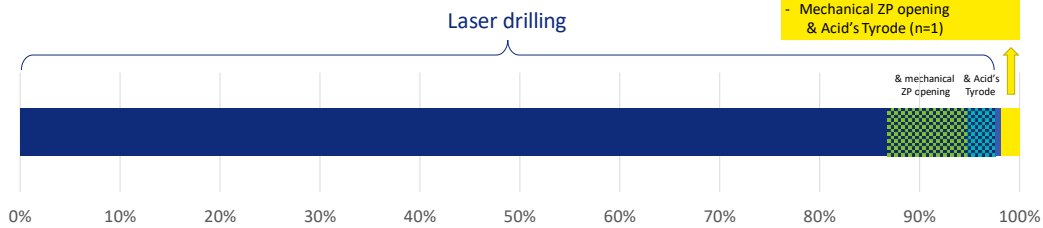
A

Type of biopsy, corresponding to the indications for which PGT is performed (n=212)



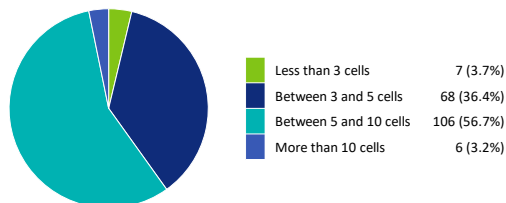
B

Zona Pellucida breaching method (n=212)



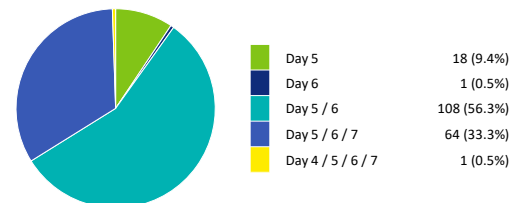
C

Blastocyst biopsy; number of cells biopsied (n=187)



D

Blastocyst biopsy; Timing of biopsy (n=192)



A. Biopsy stage corresponding to the indications for PGT (multiple choice question, data represented as percentages). **B.** Zona Pellucida breaching method (multiple choice question, data represented as percentages). **C.** Optimal number of cells that centres aim to collect in blastocyst biopsy (open question, replies categorised, data represented as number and percentage). **D.** Day at which blastocyst biopsy is performed (single reply, data represented as number and percentage)

PGT: preimplantation genetic testing, PGT-A: PGT for aneuploidy, PGT-M: PGT for monogenic/single gene defects, PGT-SR: PGT for chromosomal structural rearrangements, ZP: Zona Pellucida.

Supplementary data SIV. Data on the different PGT techniques applied per PGT indication in the responding centres.

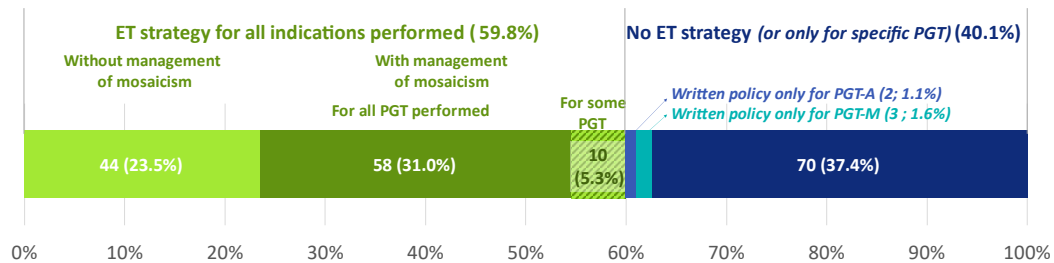
A. The number of centres that perform the listed PGT techniques, categorised per indication for which PGT is performed at the centre (multiple choice question, data represented as number of centres). **B.** The number of centres indicating that they perform 1 technique, 2 techniques or more than 2 techniques, categorised per indication.

PGT: preimplantation genetic testing, PGT-A: PGT for aneuploidy, PGT-M: PGT for monogenic/single gene defects, PGT-SR: PGT for chromosomal structural rearrangements, aCGH: Array comparative genomic hybridization, SNP: Single nucleotide polymorphism, qPCR: quantitative polymerase chain reaction, FISH: Fluorescent in-situ hybridization

Supplementary data SV. Data on the availability of a written policy for embryo transfer, the preferred embryo transfer strategy, and the preferred number of embryos transferred.

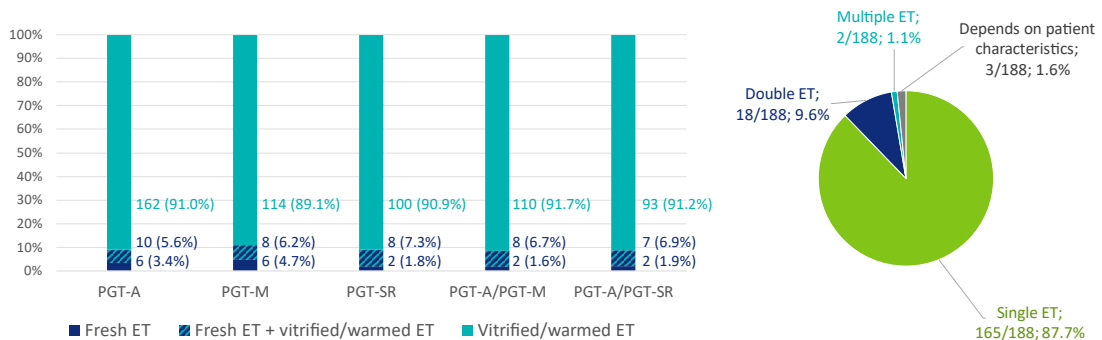
A

Availability of a written embryo transfer strategy corresponding to the indications for which PGT is performed



B

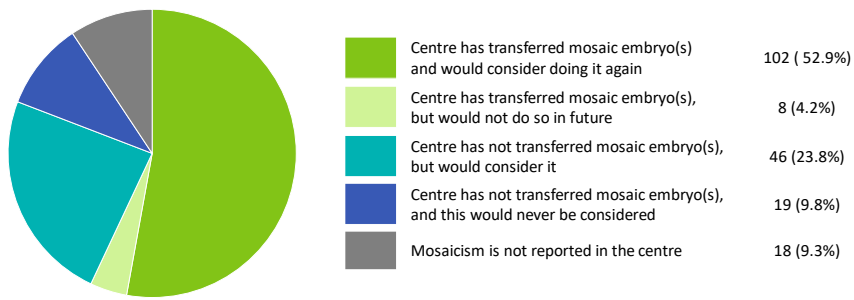
Preferred embryo transfer strategy for PGT cycles



All data are represented as numbers and percentages. **A.** The availability of a written embryo strategy is visualised. When the ET strategy includes management of mosaicism, respondents indicated that this is available for all PGT that are performed at the centre, or for some but not all PGT indications. **B.** The preferred ET strategy (fresh, fresh or vitrified/warmed, vitrified/warmed), and the preferred number of embryos transferred.

PGT: preimplantation genetic testing, PGT-A: PGT for aneuploidy, PGT-M: PGT for monogenic/single gene defects, PGT-SR: PGT for chromosomal structural rearrangements. *ET, embryo transfer*

Supplementary data SVI. Experience of the centres with the transfer of mosaic embryo(s).

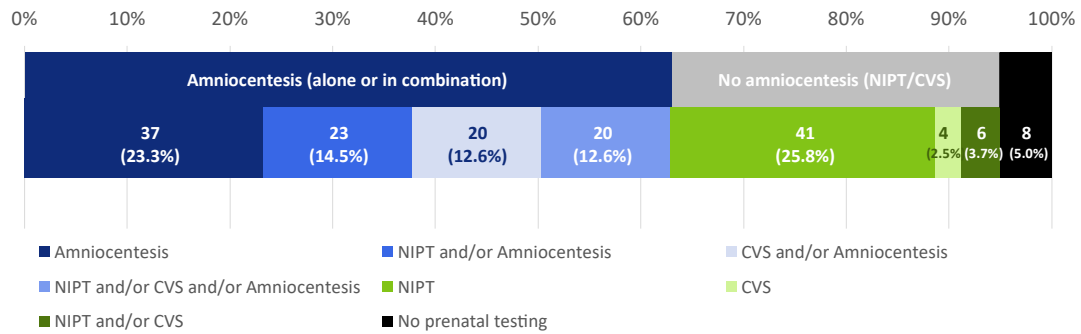


Data represented on whether embryo transfer of a mosaic embryo has been performed in the past, and would be performed in the future (single reply, data represented as number and percentage)

Supplementary data SVII. Overview of the replies to the survey related to prenatal testing and follow-up of children.

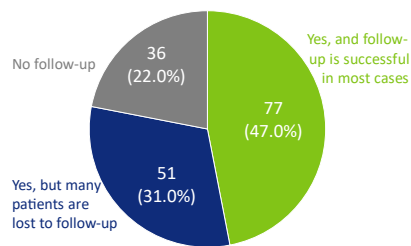
A

Recommended Prenatal testing after transfer of a mosaic embryo



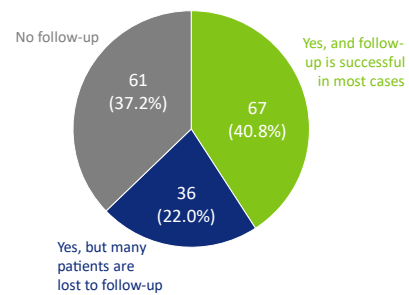
B

Follow-up of pregnancies/children after PGT:



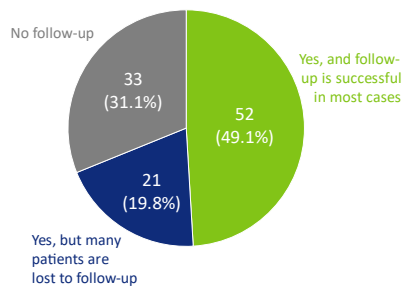
C

Follow-up of pregnancies/children after transfer of a mosaic embryo:



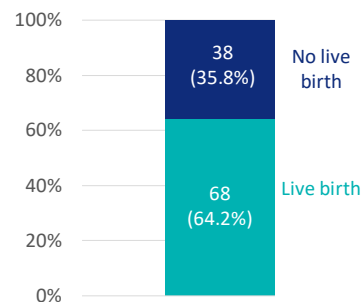
D

Follow-up of pregnancies/children after transfer of a mosaic embryo (subgroup of centres that indicate they have already transferred mosaic embryo(s)):



E

Outcomes of transferred mosaic embryo(s), based on 106 centres that indicate they have already transferred such embryo(s):



A. Whether prenatal testing is recommended and which tests would be recommended after transfer of a mosaic embryo (multiple choice question, different combinations of replies). **B,C and E.** The centres policy with regards to follow-up of PGT cycles (B), PGT cycles with transfer of a mosaic embryo (C), and PGT cycles with transfer of a mosaic embryo from those centres that have already transferred such embryo (D). **E.** Replies to the question “have you obtained live births following transfer of mosaic embryos (yes/no)”. All data are represented as numbers and percentages.

PGT: preimplantation genetic testing, NIPT: non-invasive prenatal test, CVS: chorionic villus sampling.

Supplementary data SVIII. List of experts participating in the stakeholder review.*Representatives of professional organisations*

| Organisation | Country | Representative |
|---|---------|-----------------|
| Fertility Genetics and ARGC | UK | Valerie Shaikly |
| DiNA science | Spain | Diana Campos |
| CARE Fertility UK and Fertility Genetics | UK | Karen Sage |
| Zouves Foundation for Reproductive Medicine | USA | Manuel Viotti |

Individual experts

| Reviewer | Country |
|---|----------------------|
| Paul N Scriven | UK |
| Aşina Bayram | United Arab Emirates |
| Maria José De los Santos | Spain |
| Marco Sbracia | Italy |
| Maximilian Murtinger; Barbara Wirleitner; Maximilian Schuff | Austria |
| Elpida Fragouli | UK |
| Amanda Odell-West | UK |
| Cristina Albanese | Italy |
| Francesca Spinella and Ermanno Greco | Italy |
| Sebastiaan Mastebroek | The Netherlands |
| Cristina Magli | Italy |
| Liborio Stuppia | Italy |