Europe needs registries to protect the intended parents, third-party donors and children born from Medically Assisted Reproduction

Position paper – January 2022

Infertility affects approximately 25 million citizens in Europe.[1] Already in 2008, the European Parliament pointed out that infertility was on the rise, the occurring prevalence being approximately 15% of the population at that time.[2] As far as possible, every human being has the right to decide the timing and the number of their children. Infertility can negate the realisation of these essential human rights and addressing it is of major importance.[3] Infertility leads to a decline in many quality-of-life metrics for both men and women. The result can be an increased prevalence of depression, shame, feelings of guilt and inadequacy and social isolation.[4] Moreover, infertility does not only negatively affect the individuals suffering from it, but it also has an impact on their families and communities.

While there is no cure for many specific causes of infertility, fertility treatments can help a large proportion of patients who seek treatment to become parents.[5] Medically Assisted Reproduction (MAR) treatments range in complexity from Intrauterine Insemination (IUI) and In Vitro Fertilisation (IVF) to fertility preservation, Preimplantation Genetic Testing, gamete and embryo donation and surrogacy.[6] IVF is the most iconic MAR procedure and involves the fusion of an egg with a spermatozoon in the laboratory. It can be performed with the couples' own egg and sperm, or with gametes from a third-party donor. It is estimated that more than 10 million babies resulted from MAR techniques so far.[7] The annual MAR delivery rates are steadily rising and now comprise 2–6% of the total number of births in European countries.[8]

Current data collection may underestimate the risks and overestimate the effectiveness of MAR strategies and treatments. More accurate data can be derived from mandatory, transnational and harmonised data collection. Such data collection could monitor the effectiveness of (emerging) MAR treatments and identify the risks of MAR, which is essential for information provision to those involved in MAR, as well as for the development of strategies for risk reduction or prevention.

CURRENT DATA COLLECTION PRACTICES AND IDENTIFIED ISSUES

MAR professionals have been continuously raising awareness to enhance safety and quality assurance in clinical and laboratory procedures. Even if the risks for the intended parents, third-party donors and children born from MAR are limited, there is a need for establishing detailed registries both to monitor the safety of treatments as well as to document their effectiveness, especially in what concerns innovations in MAR.

The current situation in Europe indicates the absence or insufficient development of MAR registries, which is related to several issues, such as:

- Different national data registries functioning with different aims and collecting different parameters and outcomes. In some countries, data collection is scarce or absent.
- High complexity of monitoring MAR treatments due to a fragmented political and legal landscape throughout Europe countries.
- Cross-border care, which is associated with additional challenges with regard to monitoring and data registration. Many cross-border cases are likely not even included in the current registries.

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[1] *A policy audit on fertility: Analysis of 9 countries, March 2017; Fertility Europe and ESHRE*
[2] *European Parliament's Resolution on the demographic future of Europe, February 2008*
[3] *WHO Factsheet on Infertility, September 2020*
[4] *AMA backs global health experts in calling infertility a disease, June 2017*
[5] *Assisted reproduction and COVID-19: A joint statement of ASRM, ESHRE and IFFS; September 2020*
[6] *Idem 1*
[7] *Calhaz-Jorge C, et al. Survey on ART and IUI: legislation, regulation, funding and registries in European countries. Human Reproduction Open, 2020; hoz044.*
[8] *Berntsen S, et al. The health of children conceived by ART: 'the chicken or the egg? Human Reproduction Update, 2019;25(2):137–58*

The European Society of Human Reproduction and Embryology (ESHRE) understands that health authorities and/or professional societies of some European Union (EU) countries have already developed specific software systems to collect data from their respective institutions offering MAR treatments. **Therefore, a future centralized EU data collection system must use a software that can be linked to the software of the national authorities and/or professional societies.** Confidentiality and privacy protection must be safeguarded, and traceability of submitted data should be organised in full compliance with EU General Data Protection Regulation 2016/679 and national data protection legislation.[9]

Registries for MAR data collection are of great importance as they are a unique way to monitor MAR activities and developments, to foster vigilance and to support corrective (technical, regulatory, political) measures. Therefore, ESHRE proposes the following recommendations:

1. DATA COLLECTION SHOULD BE FURTHER EXPANDED TO IMPROVE PROTECTION OF THE INTENDED PARENTS, THIRD-PARTY DONORS, AND CHILDREN BORN FROM MAR

For the protection of the intended parents, third-party donors and children born from MAR, data registries should include a **predefined list of parameters**, with standardised definitions, for each MAR treatment cycle. These parameters should be selected to monitor efficacy and safety, but also to answer emerging questions.

For the protection of the intended parents in MAR, mandatory reporting should include:

- Adverse reactions/outcomes related to the treatment, including complications from ovarian stimulation, such as ovarian hyperstimulation syndrome.
- Treatment outcome (e.g., implantation, pregnancy, live birth) to enable research on the efficacy and effectiveness of MAR treatments and their variants.

For the protection of third-party donors in MAR, mandatory reporting should include:

- Adverse reactions/outcomes related to the donation procedure, including unanticipated results from medical and genetic screening, and complications from ovarian stimulation, such as ovarian hyperstimulation syndrome.
- The health status of the donor and complications after the donation, including psychosocial implications of donation, specifically in cases of adverse outcomes.

For the protection of children born from MAR, mandatory reporting should include:

- Adverse reactions/outcomes: serious adverse events, malformations, diseases, diagnosed genetic conditions.
- Established minimal clinical data sets pertaining to growth, development and metabolism of the child.

Whenever possible, linking of MAR registries with other (existing) registries should be explored. For example linking the MAR data registry with paediatric registries (diabetes, malignancy) would facilitate long-term follow-up of the health status of the child and the impact of specific MAR interventions (such as cryopreservation techniques)[10]. Linking with health registries, such as hospital diagnosis codes and drug prescription registries, could help in the follow-up of the intended parents and in the long-term follow-up of the third-party donor and of the complications after the donation.

[9 & 10] *Idem 8*

2. DATA COLLECTION SHOULD BE MADE MANDATORY AND INCLUDED IN THE REVISED EU LEGISLATION ON BLOOD, TISSUES AND CELLS

The growing number of MAR treatments, the higher variability in treatment modalities and the rising contribution to births over the last 20 years point towards an increasing impact of MAR on epidemiological data. High levels of completeness in data reporting have been reached, but inconsistencies and inaccuracies still remain and need to be identified and corrected. The revised EU blood, tissues and cells directive should foresee requirements for mandatory reporting of all MAR treatments, including cross-border treatments, for follow-up and protection of the intended parents, third-party donors, and the children born from MAR.

3. DATA COLLECTION AND REGISTRIES SHOULD BE COORDINATED AT EU LEVEL TO ACCOMMODATE FOR CROSS-BORDER ACTIVITY

Some people affected by infertility seek cross-border treatment due to certain limitations in access to MAR treatments in their own countries (e.g. legislation, affordability, cultural or religious barriers). In this context, the current concept of surveillance in MAR through national or supranational registries presents some shortcomings. The more appropriate cumulative approach of MAR surveillance requires more continuous recording systems in which the various therapeutic steps and their outcome for each couple or individual can be linked together over prolonged periods of time, in different institutions and across borders. It is therefore crucial to establish an EU-wide data collection system based on individual patients and/or couples to monitor their path through different treatments and medical institutions prospectively.[11] This data collection system should apply a single code for all the intended parents and third-party donors (i.e., the same unique code in all Member States) to allow registration and protection of the intended parents and third-party donors across Member States and across consecutive treatments.

4. MAR REGISTRIES SHOULD BE A REFERENCE RESOURCE FOR PROFESSIONALS, PROFESSIONAL SOCIETIES AND OTHER STAKEHOLDERS

Ideally, the MAR registry should be able to provide an answer to different questions and objectives, e.g. qualitative data for monitoring activity and trends in MAR, data to facilitate quality management in MAR centres, and data to support guidelines and good practice.

To allow the MAR registry to be a reference resource, detailed, cycle-by-cycle data should be collected.

[11] *De Geyter Ch, et al. 20 years of the European IVF-monitoring Consortium registry: what have we learned? A comparison with registries from two other regions. Human Reproduction, 2020;35(12):2832–49* and *De Geyter Ch, et al. Data collection systems in ART must follow the pace of change in clinical practice. Human Reproduction, 2016;31(10):2160–3*

CALL TO ACTION

An improved EU legal basis on MAR surveillance would have multiple benefits:

- **It would facilitate data collection and ensure full coverage data;**
- **It would help ensuring traceability of data, third-party donors and offspring; and**
- **It would allow translation of data towards good practice recommendations.**

To protect the intended parents, third-party donors and children born from MAR, an EU MAR Registry should be developed.

→ EU and national health legislation should include requirements for mandatory reporting of all MAR treatments, including cross-border treatments, for follow-up and protection of the intended parents, third-party donors and children born from MAR.

→ The European Commission should identify the right initiatives for the development of an EU cycle-by-cycle MAR Registry, ensuring the collected data can provide answers to questions about uptake and safety of specific MAR interventions and MAR policies.

→ The revised EU Directive on Blood, Tissues and Cells should include provisions for mandatory reporting and cross-border data exchange, respecting the applicable data protection legislation in Member States and at EU level.

→ ESHRE's established data collection of MAR treatments by the European IVF Monitoring Consortium (EIM) can form a good basis of the future EU MAR Registry. Since its creation in 1997, EIM has been publishing annual reports covering the European activities in MAR from 1997 to 2017, including a survey describing the trends over 15 years of ART in Europe. EIM currently manages the largest register worldwide, dealing with MAR data reported by 40 European countries.[12]

→ Professional societies, such as ESHRE, as well as European bodies such as European Center for Disease Prevention and Control (ECDC) and European Directorate for the Quality of Medicines & HealthCare (EDQM) should collaborate to provide guidance on serious adverse events reporting and follow-up actions

We firmly believe that not only professional societies should be interested in such an accurate, far-reaching and transgenerational healthcare monitoring system in MAR, but also the European institutions, the national authorities and the lay public awaiting for higher transparency on MAR therapies.

ABOUT ESHRE

ESHRE is a European non-profit organisation with international membership, whose main mission is to promote the study and research of reproductive science and medicine as well as the treatment of infertility. Established in 1984, the Society now comprises more than 8.000 members and has become the leading Society in reproductive science and medicine worldwide. Our members are medical professionals, scientists and researchers working in reproductive science, reproductive medicine and embryology.

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[12] *Wyns C, et al. ART in Europe, 2016: results generated from European registries by ESHRE. Human Reproduction Open, 2020; 2020 (3), hoaa032*