

Reproductive Medicine

eproductive medicine services, including assisted reproduction services, were facilitated and provided by specialists at The National Maternity Hospital (NMH), Merrion Fertility Clinic (MFC), St. Michael's Hospital (SMH) and our satellite clinic in Galway.

A. Public Fertility Hub

The Fertility Hub is a publicly funded service for fertility work-up and investigation at The National Maternity Hospital. Funded by the HSE as part of the new infertility model of care, the NMH hub is led by Dr David Crosby, Consultant Obstetrician & Gynaecologist, Ms Michelle Barry, CNS Fertility Specialist and Ms Catherine Dunne, Fertility Administrator. Ovulation induction services were initiated in September 2022, with plans to develop this further to include all areas of assisted reproductive technology (ART), including IVF. Outcome data from the NMH Fertility hub will be presented in the 2023 Annual Report. Reproductive Surgery activity is outlined in Table 1.

B. Activity levels at Merrion Fertility Clinic continue to increase

Referrals to Merrion Fertility Clinic increased by 42% from 2020 to 2021. This rate increased by an additional 6% into 2022. Oocyte vitrification cycles, preserving female fertility, increased by 43% in 2022, following an increase of 143% from 2020 to 2021. The number of IVF / ICSI treatment cycles also increased dramatically from 2020 to 2021, the increased activity level was maintained in 2022. Other services such as diagnostic semen analysis and surgical sperm retrieval remained stable (Table 2: Five year activity levels).

C. Telehealth and patient e-learning digital platform

Video patient consultations and telemedicine continued throughout 2022, in line with mitigation strategies and enhanced infection control. In-person consultations are anticipated to resume in early 2023.

D. CHKS accreditation

In September 2022, Merrion Fertility Clinic were accredited by CHKS. This accreditation is awarded to healthcare organisations whose processes and standards meet internationally recognised best practice, legislation and regulatory requirements.

E. Hysterosalpingo-contrast-sonography (HyCoSy) scanning

In September 2022, a weekly HyCoSy scanning clinic

for patients was introduced by MFC Clinical Lead, Dr Renato Bauman. This is a specialist scan where dye is injected into the fallopian tubes to investigate tubal or uterine anomalies. The HyCoSy scan can be used as an alternative to hysterosalpingogram (HSG) in many patients who require tubal patency testing.

F. The Childhood Cancer Fertility Project (MFC and Irish Cancer Society)

The Childhood Cancer Fertility Project was launched jointly with the Irish Cancer Society (ICS) in August 2020. MFC was successful in securing grant funding from the ICS for a three-year project (2020-2023) to develop and provide fertility preservation for children, adolescents, and young adults. A sperm and egg freezing service for post-pubertal adolescents about to undergo gonadotoxic treatment is now well established and the post-treatment assessment and treatment clinic established for survivors of childhood cancer was extended in 2022 to include young women up to the age of 26 years.

G. Assisted Human Reproduction Legislation and Funding

Legislation regarding assisted human reproduction (AHR) has been drafted by the Department of Health, with the aim of providing regulations around the provision of assisted reproduction in Ireland. As of December 2022, the proposed AHR Bill (29 of 2022) has been presented to the Oireachtas and is at the third stage. In 2022, the Minister for Health also committed €10 million towards state-funded assisted reproductive treatments, such as IVF. This funding is anticipated to begin in late 2023.

Clinical Activity

Clinic appointments

Dedicated NMH clinics for reproductive medicine, encompassing infertility, endometriosis, PCOS etc in 2022 reported a total of 266 first visits, 188 return appointments and 191 telephone consultations. 49 women/couples were seen at the recurring miscarriage clinic, as well as 32 telemedicine consultations, while 21 women/couple were seen at the mid-trimester miscarriage clinic, with 5 telemedicine consultations. At Merrion Fertility Clinic, in 2022 there were 1,081 new consultations and 1,654 return consults. A breakdown of Reproductive Surgery performed in The NMH can be seen in Table 1.

Assisted Reproduction, Merrion Fertility Clinic

Five year activity levels for assisted reproduction at the Merrion Fertility Clinic can be seen in Table 2.

Conscious sedation was provided by Consultant Anaesthetists for all oocyte retrievals and surgical sperm retrievals.

Clinical pregnancy rates increased in 2022 across all age groups (Chart 1. 2022 Clinical Pregnancy Rates by Maternal Age). Clinical pregnancy is defined as per ESHRE (European Society for Human Reproduction and Embryology) i.e. fetal heart, fetal pole or a clear pregnancy sac are seen on ultrasound at 6 to 8 weeks gestation. Biochemical pregnancies (positive pregnancy test only) are not included but ectopic pregnancies and miscarriages are. The rate per embryo transfer for ages up to 39 years sits between 44% and 45%. This falls to 36.4% in the 40-41 age group, and to 28.1% in the 42-43 year old age group.

The mean age of women

The mean age of women undergoing fresh IVF/ICSI cycles at Merrion Fertility Clinic fell slightly to 37.1 years in 2022. The percentage of those starting cycles of treatment at 40 or older was 27.5%, representing a slight drop from the 30.1% of patients 40 years and older starting treatment cycles in 2021.

Elective single embryo transfer (eSET)

Merrion Fertility Clinic has continued to uphold a strong ethos of single embryo transfer. In 2022, 70% of all transfers were single embryo transfers, with a clinical pregnancy rate of 3% higher than the overall clinical pregnancy rate for the clinic. A further subset of these patients had additional embryos to freeze. Patients in this group, the "elective" single embryo transfer group, eSET, made up 42% of all transfers, and had a clinical pregnancy rate of 55%, 13% higher than the clinic average. Following on from this policy, the multiple pregnancy rate at Merrion Fertility Clinic remains low at 6.6% overall.

Frozen embryo transfer (FET) cycles.

Many patients undergoing Assisted Human Reproduction (AHR) will have a transfer of an embryo that has been cryopreserved for a period of time. In some cases this is following the birth of a child from a fresh transfer, following a negative outcome from a fresh transfer or possibly they were not in a position to have a transfer following their fresh collection. In 2021, we saw a significant increase in the clinical pregnancy rate following frozen embryo transfer. This

was maintained through 2022 and now stands at 52.9%. This is higher than the clinical pregnancy rate for fresh transfers. This can be explained in part by the fact that only good or top quality embryos are frozen, where fresh transfers can include fair quality embryos.

Intrauterine Insemination (IUI): The number of partner IUIs carried out at Merrion Fertility Clinic in 2022 remained stable from 2022, with a clinical pregnancy rate of 7.5%. This figure rose to 16% where donor sperm was used.

Donor sperm treatments

Merrion Fertility Clinic commenced a donor sperm service in 2018. The service has been growing since and now makes up approximately 6% of IVF/ICSI treatment cycles.

Livebirth rates

Livebirth rates are the best marker of success in assisted human reproduction. Live birth rates for patients who had a fresh transfer in 2021 are 26%. When considering patients who had a transfer of a frozen embryo the rate rose to 36%. This is an increase of 10% on the rate recorded for live birth following a frozen embryo transfer in 2020. Livebirth rates following IUI was 12% for treatment carried out in 2021.

Female fertility preservation.

As indicated in Table 2, the number of oocyte vitrification cycles provided by Merrion Fertility Clinic has increased rapidly since its introduction. A small number of patients have returned to use their oocytes and the clinical pregnancy rate for 2022 was 50%.

Child, Adolescent and Young Adult (CAYA) Fertility Preservation Services

AYA Males: Seventeen adolescent males (<18 years) were referred to MFC in 2022 for sperm cryopreservation services before undergoing gonadotoxic treatment or surgery for cancer (16 patients) or autoimmune disease (1 patient). Diagnoses included: glioma, Hodgkin's lymphoma, Burkitt's lymphoma, osteosarcoma, acute myeloid leukaemia (AML) and rhabdomyosarcoma. Of these 17 boys, 17 attended the clinic, 12 produced a semen sample and all 12 had sperm of suitable quality for freezing (mean of 8 straws frozen per patient).

AYA Females: Seven adolescent females (<18 years) were referred to MFC in 2022 for oocyte vitrification before undergoing gonadotoxic cancer therapy.

Oncology diagnoses included osteosarcoma, Hodgkin's lymphoma and Ewing's sarcoma. All seven of these young women had a successful egg freezing cycle within a mean of 14 days (range 9-30 days) from first visit to the clinic, with a mean of 15 oocytes per patient cryopreserved for future use.

Female survivors of CAYA cancer, who had previously received gonadotoxic treatment as part of their cancer therapy, are also eligible for fertility assessment and oocyte vitrification through the Childhood Cancer Fertility Project. Five female survivors attended MFC in 2022 for an initial fertility consultation, while eight young women attended for a follow-up fertility consultation and ovarian reserve testing. Four female survivors (mean age 24 years) had a successful oocyte vitrification cycle, with a mean of 6 oocytes cryopreserved for future use.

Research

The Reproductive Medicine Department maintains an active and productive research portfolio, collaborating with scientists in Irish academic institutions and other teaching hospitals, and is a member of the UCD Perinatal Research Centre. MFC employs a full-time Head of Research, and two Clinical Research Fellow posts exist for higher training in Reproductive Medicine & Surgery, with both fellows undertaking higher degrees. MFC also hosts and mentors a number of

MSc students.

Research at MFC is aimed at improving knowledge, expertise and care pathways in the field of reproductive medicine. Our studies span a range of topics, from basic mechanistic biology to clinical translational research. In 2022, researchers at MFC also worked closely with collaborators at several of Ireland's leading academic research institutions, including University College Dublin and Trinity College Dublin, on the following research projects:

- Innate immune factors, endometrial receptivity and infertility (Funding: Grant for Fertility Innovation, Merck)
- Endometrial microbiome and infertility (Funding: Grant for Fertility Innovation, Merck)
- Glycome analysis in endometriosis (NIBRT collaboration. Funding: Horizon 2020, Marie Curie International Fellowship)
- Ovarian reserve in childhood cancer survivors
- Impact of the COVID-19 vaccine on male sperm parameters and inflammatory markers.
- Knowledge and attitudes among patients and healthcare providers towards proposed Irish assisted human reproduction (AHR) legislation

Publications are in the Published Research section.

Dr David Crosby, Consultant Obstetrician & Gynaecologist, NMH Reproductive Medicine Department Head and Merrion Fertility Clinic Clinical Director





Tables and Charts

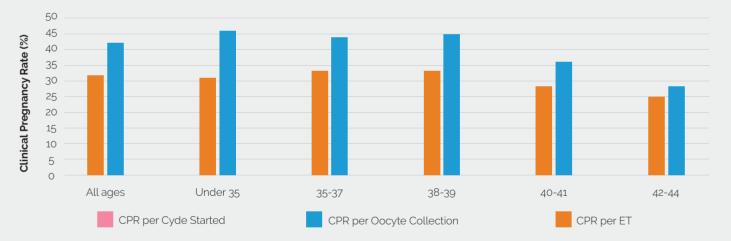
Table 1: Reproductive surgery under General Anaesthetic

| Hysteroscopy – operative and diagnostic | 240 |
|---|-----|
| Operative laparoscopy | 62 |
| Diagnostic laparoscopy | 107 |
| Myomectomy | 6 |
| Total laparoscopic hysterectomy | 5 |

Table 2: Assisted Reproduction, Merrion Fertility Clinic: Five-year activity levels

| Year | Semen analyses | Surgical Sperm Retrievals | IUI (completed) | IVF/ICSI (Completed to oocyte retrieval) | Frozen embryo transfer cycles (Completed to embryo transfer) | Oocyte vitrification Completed to oocyte retrieval) |
|------|----------------|------------------------------|-----------------|--|---|---|
| 2018 | 1459 | 2 | 85 | 407 | 301 | 40 |
| 2019 | 1412 | 6 | 91 | 399 | 334 | 49 |
| 2020 | 1172 | 9 | 60 | 413 | 236 | 46 |
| 2021 | 1426 | 10 | 140 | 609 | 376 | 112 |
| 2022 | 1395 | 9 | 142 | 621 | 367 | 160 |

Chart 1: 2022 Clinical Pregnancy Rates by Maternal Age



PUBLISHED RESEARCH Articles, Editorials, Letters

MERRION FERTILITY CLINIC

Cullen S, Sobczyk K, **Elebert R**, Tarleton D, Casey B, Doyle S, **Crosby D**, **Allen C**. Second-trimester miscarriage: a review of postnatal investigations and subsequent pregnancy outcomes. Ir J Med Sci. 2022 Nov 17. doi: 10.1007/s11845-022-03227-z. Online ahead of print. PMID: 36396810

Schaler L, Glover LE, Wing ield M. COVID-19 Vaccine and Fertility: The Male Perspective. Ir Med J. 2022 Feb 17;115(2):543. PMID: 35418174

Schaler L, Glover LE, Wing ield M. Irish fertility patients' attitudes to pregnancy and risk mitigation strategies during the COVID-19 pandemic. Hum Fertil (Camb). 2022 Mar 7:1-6. doi: 10.1080/14647273.2022.2045518. Online ahead of print. PMID: 35255765

Schaler L, Giblin A, Glover LE, Wing ield M. Assisted human reproduction legislation: Acknowledging the voice of health care professionals. Eur J Obstet Gynecol Reprod Biol. Epub 2022 Nov 9. doi: 10.1016/j. ejogrb.2022.11.007. PMID: 36379181