Reproductive Medicine & Surgery

Reproductive Medicine and Surgery services are provided by specialists at the National Maternity Hospital (NMH), Merrion Fertility Clinic (MFC), and St. Michael's Hospital (SMH). Multidisciplinary input from areas of special expertise in the NMH and St Vincent's University Hospital (SVUH) supports the planning and delivery of care in complex cases. It is envisaged that this collaboration will increase at the new NMH co-located at the SVUH site. Merrion Fertility Clinic remains the only Assisted Reproduction Treatment (ART) service in Ireland which is not-for-profit and affiliated with a major national teaching hospital. Adherence to evidence-based medicine is an underlying principle of the service.

New Developments 2019

A. Referral and appointment pathway for public fertility clinic
In 2018 we noted a very poor attendance rate at the public infertility clinics, possibly exacerbated by the long wait time for an appointment (DNA rate 32%). In 2019, the referral and appointment pathway was reorganised with a significant improvement in efficiency and patient care. From March 2019, all referred patients were initially asked to complete and return a lifestyle and medical history questionnaire and to have blood tests and a semen analysis performed at the hospital. An outpatient appointment slot was scheduled ***only*** when the completed questionnaire and test results had been received. Disappointingly, only 36% (62 of 174) of those referred completed the questionnaires and preliminary tests. However, once they did this, all patients and couples received an appointment within 4 months of initial referral and within 2 months of completing their tests. The DNA rate was reduced to 3%.

B. Irish Cancer Society Grant to develop Fertility Preservation in Children and Young Adults
In August 2018, in conjunction with Children's Health Ireland (CHI) at Crumlin, MFC set up and funded a structured sperm cryopreservation service for post-pubertal adolescent males due to undergo gonadotoxic treatment or surgery. This service was consolidated in 2019. For post-pubertal adolescent and young adult females, oocyte vitrification is used for fertility preservation. This procedure is significantly more expensive than sperm cryopreservation. In 2019, MFC was successful in securing grant funding from the Irish Cancer Society to develop and provide fertility preservation for children, adolescents and young adults. The project will provide supports and services to three main groups: 1) adolescents and young adults facing a cancer diagnosis; 2) female survivors of childhood cancers who will be invited to have a fertility consultation, and referred for further treatment or investigation where fertility treatments may still be an option; 3) children who have yet to reach adolescence will benefit from the development of fertility preservation protocols (gonadal tissue cryopreservation) previously not available in Ireland. The three-year project (2020-2022) will enable MFC to offer fertility preservation services to young cancer patients and survivors entirely free of cost to the user, in what is designed to provide a forerunner for a new national fertility preservation programme for children, adolescents and young adults.

Hospital Clinics
Dedicated hospital clinics for reproductive medicine, encompassing infertility, endometriosis, PCOS etc continued throughout 2019 with a total of 169 first visits and 248 return appointments. Ninety five women/couples were seen at the recurring miscarriage and 2nd trimester loss clinics.

Reproductive Surgery

The Reproductive Medicine team has four Consultants, operating a weekly shared theatre list at the NMH and a fortnightly list at St Michael's Hospital. The majority of cases (98.5%) are minimal access procedures. Careful selection criteria are used for laparoscopy (history and ultrasound criteria) and this is reflected in the fact that the majority of laparoscopies were operative with proven pathology, and appropriate surgery was performed the same day. The level of complexity of these endoscopic procedures is increasing, and data are collected prospectively on this aspect using the agreed guidelines*.

Table 1: Reproductive surgery under GA and Outpatient Hysteroscopy

Reproductive Surgery under GA 2019	NMH	SMH
Laparoscopic Surgery *	**n=56**	**n=20**
Level 1 (basic procedures)	8	3
Level 2 (minor procedures)	19	13
Level 3 (intermediate procedures)	24	4
Level 4 (major procedures)	5	0
Laparotomies	**n=5**	**n=0**
Open myomectomy	4	
Open ovarian cystectomy	1	
Art Procedures		
Surgical sperm retrieval under GA	1	0
Oocyte retrieval	0	0
Ovarian tissue cryopreservation	0	0
Hysteroscopy under GA	**n=48**	**n=14**
Diagnostic	17	6
Operative		
Adhesiolysis for Asherman's, Resection of septum, Retrieval/ insertion of IUS, Removal RPOC	31	8
Endometrial ablation	2	0
Out-Patient Hysteroscopy 2019	**n=211**	**n=11**
Abnormal uterine bleeding	110	2
Cancers diagnosed	2/158 (1%)	0
Recurring Miscarriage / fertility	101	5
Truclear polypectomy	29	4
Retrieval of Mirena	15	0
Other	27	0
Onward referral for GA hysteroscopy	36	0

**ESGE categorisation for laparoscopic surgery*
Level 1, basic procedures Level 2, minor procedures : eg cautery of minor endometriosis, ovarian drilling, cyst aspiration, simple adhesiolysis
Level 3, intermediate procedures: eg oophorectomy, cystectomy of cysts <8cm, salpingostomy, stage 3 endometriosis
Level 4, major procedures: eg hysterectomy, management of cysts >8cm, stage 4 endometriosis.

Assisted Reproduction – Merrion Fertility Clinic: 2019 at a glance	
454	egg collections
393	embryo transfers
43.7%	clinical pregnancy rate per embryo transfer
5.6%	multiple pregnancy rate
8.5	average number of eggs collected
76%	cumulative clinical pregnancy rate (eSET fresh cycle and 1st frozen embryo transfer cycle)
3	peer-reviewed papers in medical and scientific journals
15	presentations at medical and scientific conferences

Activity levels and treatment success rates are detailed in the following tables and Figures. All pregnancy rates listed are clinical pregnancy rates as per ESHRE (European Society for Human Reproduction and Embryology) i.e. cases where a fetal heart or a 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. All data reported relates to treatment started in 2019 with the exception of livebirth rates which relate to treatment started in 2018. This is due to the fact that not all 2019 pregnancies are complete at time of going to press.

The mean age of women undergoing fresh IVF/ICSI cycles was 36.8 years. In 2019, 21% of all cycles started were in women aged 40 or more, consistent with the rates in previous years.

Six cases of surgical sperm retrieval (SSR) were carried out in 2019. Conscious sedation was provided by Consultant Anaesthetists for all oocyte retrievals and surgical sperm retrievals.

Table 2: Ten year overall activity levels (numbers)				
Year	**Semen analyses**	**Ovulation induction and IUI (completed)**	**IVF/ICSI (completed to oocyte retrieval)**	**Frozen embryo transfer cycles (completed to embryo transfer)**
2010	1262	326	324	151
2011	1277	251	390	162
2012	1281	143	401	142
2013	1296	143	399	167
2014	1254	204	430	169
2015	1375	161	379	204
2016	1375	223	401	260
2017	1398	157	454	263
2018	1459	151	407	301
2019	1412	161	399	334

Table 3: Numbers of IVF, ICSI and FET cycles				
2019	**IVF/ICSI**	**IVF**	**ICSI**	**FET**
Cycles Started	434	185	249	392
Cycles Cancelled	35	13	22	55
Oocyte Retrievals / Cycles Thawed	399	172	227	337
Embryo Transfers	327	139	188	334
Clinical Pregnancies	143	60	83	128

Table 4: Numbers of IVF and ICSI cycles by maternal age						
2019	**All Ages**	**Under 35**	**35-37**	**38-39**	**40-41**	**42-44**
Cycles Started	434	107	124	112	66	25
Oocyte Collections	399	101	115	100	61	22
Embryo Transfer	327	76	94	88	54	15
Clinical Pregnancies	143	35	51	38	16	3
Average Eggs Collected	9.1	11	9.8	8	7.7	5.9

Clinical pregnancy rates remained excellent across all groups during 2019.The clinical pregnancy rate following IVF/ICSI treatment across all age groups was 43.7% per embryo transfer (Table 5, Figures 1 and 2), rising to 50.6% in those aged 37 and under.

Table 5: Clinical pregnancy rates (%) for IVF and ICSI cycles						
2019	**All Ages**	**Under 35**	**35-37**	**38-39**	**40-41**	**42-44**
CPR per Cycle Started	32.9	32.7	41.1	33.9	24.2	12.0
CPR per Oocyte Collection	35.8	34.7	44.3	38.0	26.2	13.6
CPR per ET	43.7	46.1	54.3	43.2	29.6	20.0

Figure 1: 2019 Clinical Pregnancy Rates by Maternal Age

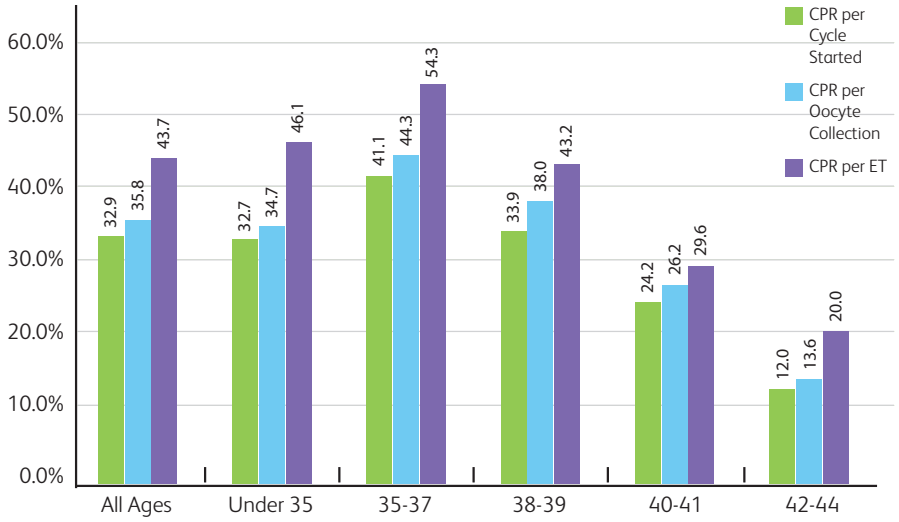
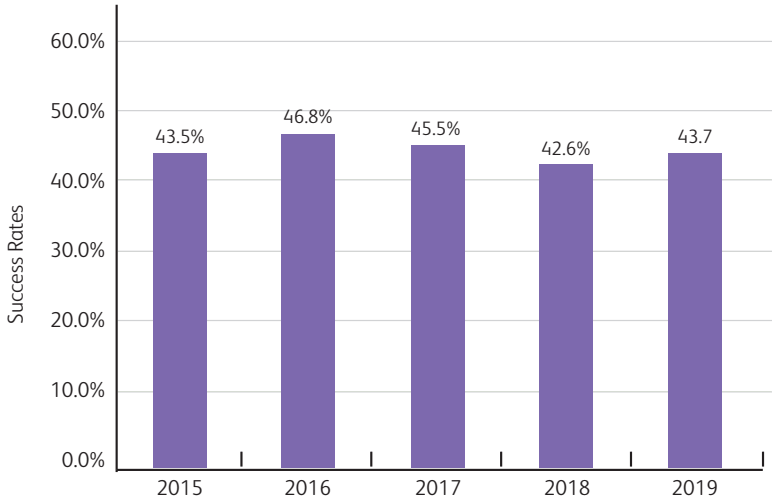


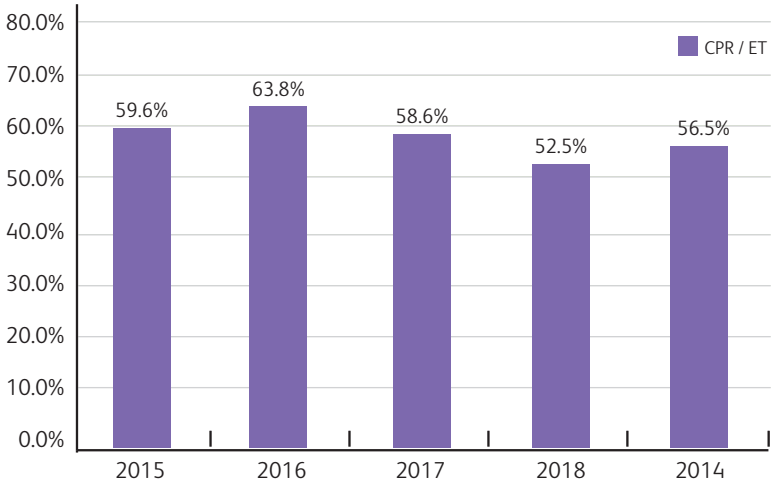
Figure 2: 5 Year Clinical Pregnancy Rates per Transfer for IVF / ICSI Cycles



Single embryo transfer: 72% of MFC patients had a single embryo transfer in 2019, reflecting the clinic's strong single embryo transfer policy (Figure 3). Of this group, a subset of good prognosis patients had an elective single embryo transfer (eSET), meaning they had a good quality embryo to transfer and at least one other to freeze. This group comprised 42.2% of all embryo transfers and, across all age groups, had a clinical pregnancy rate of 56.5% on the fresh cycle (Figure 3). Of those eSET patients who did not conceive on their fresh cycle, 36.2% conceived on their first frozen embryo transfer (FET), bringing the cumulative pregnancy rate in this group to 76% (following one fresh transfer and a FET if the fresh was unsuccessful).

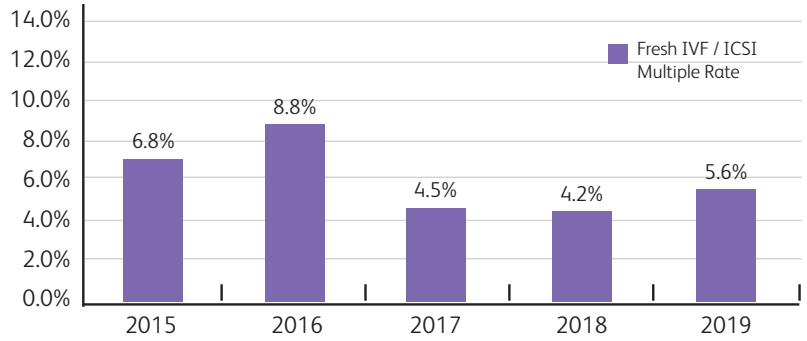
The clinical pregnancy rate per ET of patients who underwent a double embryo transfer was 43.5%. This figure reflects the promotion of single embryo transfer unless embryo quality is compromised, necessitating a second embryo to be transferred to maintain a reasonable chance of establishing a pregnancy.

Figure 3: 5 Year CPR/ET for eSET Patients



Multiple pregnancy: The multiple pregnancy rate following a fresh embryo transfer was 5.6%, a rate which is very low by international standards (Figure 4). All of these multiple pregnancies were twins and occurred following double embryo transfer (20% multiples vs 0% in SET group).

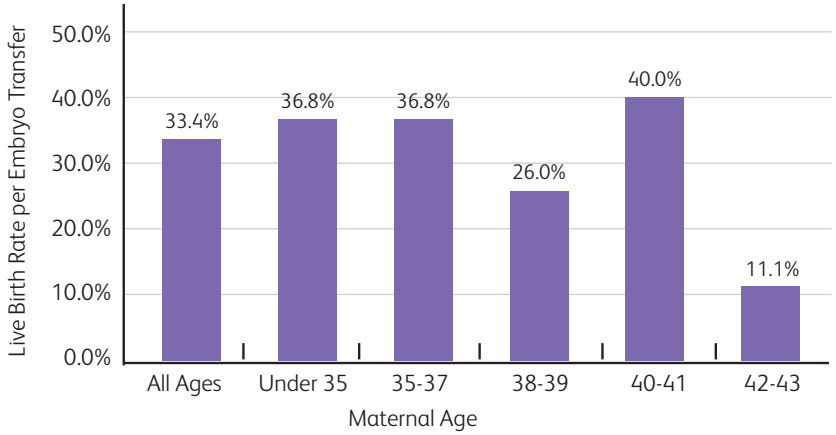
Figure 4: 5 Year Fresh IVF / ICSI Multiple Pregnancy Rate



Livebirth rates are the best marker of ART success and livebirth rates per embryo transfer for fresh IVF and ICSI cycles performed in 2018 (delivering in 2018/2019) are excellent by international norms (Table 6, Figure 5). Approximately one third of all couples completing IVF/ICSI cycles had a livebirth. The livebirth rate per embryo transfer for frozen embryo cycles performed in all age groups in 2018 was 26.6% and that for IUI per completed cycle was 14.7%

Table 6: Livebirth Rate IVF/ICSI for 2018						
	All Ages	**Under 35**	**35-37**	**38-39**	**40-41**	**42-44**
LBs	111	35	32	20	22	2
LBR per OCR	27.8%	30.4%	30.8%	21.7%	33.8%	8.7%
LBR per ET	33.4%	36.8%	36.8%	26.0%	40.0%	11.1%

Figure 5: Live Birth Rate per Embryo Transfer 2018 by Maternal Age



Frozen embryo transfer (FET) cycles (Figure 6): The number of FET cycles is increasing in line with the elective single embryo policy and also the increased numbers of 'freeze all cycles' where embryo transfer is deferred in order to avoid ovarian hyperstimulation syndrome. This is extremely successful and no patient developed OHSS requiring hospital admission in 2019. In 2019, 334 FET cycles were completed with a clinical pregnancy rate of 38.3% per transfer.

Figure 6: 5 Year FET Cycles CPR per ET

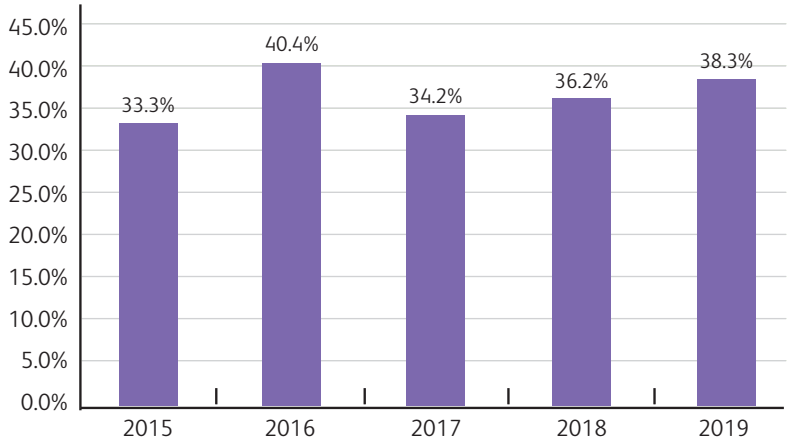


Table 7: Livebirth Rate Frozen Embryo Transfer (FET) for 2018	
Cycles started	379
Embryo Transfers	301
Live Births	80
LBR / cycle started	21.1%
LBR / ET	26.6%

Oocyte vitrification/egg freezing: Merrion Fertility Clinic began vitrifying oocytes (freezing eggs) in late 2016. A total of three cases were carried out that year. The number of cases carried out in 2019 was 49, increased from 40 cases the previous year. The average number of oocytes frozen per patients was ten.

Table 8: Oocyte Vitrification 2019					
2019	**All Ages**	**Under 35**	**35-37**	**38-39**	**40-41**
Cycles Started	52	13	22	14	2
Oocyte Collections	49	13	19	14	2
Average no. collected	11.5	12.6	12.8	9.5	9.5
Average no. vitrified	10.4	10.8	12.5	8.1	9
Mean Age	35.6	30.3	36.2	38.3	40.5

Intrauterine Insemination (IUI): Pregnancy rates with intrauterine insemination in 2019 were 10.6%, a decrease from the previous year (Figure 7). However the number of cycles is small (72) so this drop is not likely to be statistically significant.

Figure 7: 5 year IUI CPR per IUI

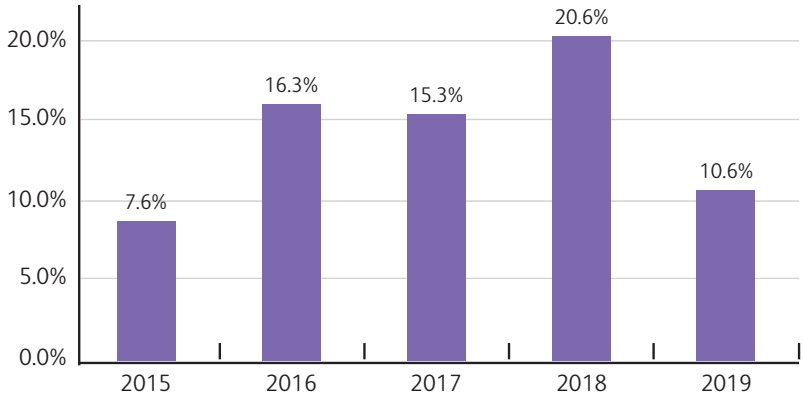


Table 9: Livebirth Rate IUI for 2018	
Cycles started	85
Inseminations	68
Live Births	10
LBR / cycle started	11.8%
LBR / insemination	14.7%

Donor Sperm treatments: Merrion Fertility Clinic commenced a donor sperm service in 2018. Sperm is sourced from 2 approved banks in Denmark. This is an essential treatment for single women, lesbian couples and heterosexual couples with severe male factor infertility, not suitable for ICSI. This is a growing and successful service. As expected, treatment success rates are higher than for those using own gametes, but the numbers are relatively low.

Table 10: Clinical Pregnancy Rate (%) for IVF / ICSI cycles using Donor Sperm						
2019	**All Ages**	**< 35**	**35-37**	**38-39**	**40-41**	**42-43**
Cycles started	23	5	3	6	5	4
Oocyte collections	21	5	3	5	4	4
Average eggs collected	9	11.6	10	7.4	10.3	6
Embryo transfers	16	3	3	5	4	1
Clinical pregnancies / ET	50%	66.7%	100%	20%	25%	100%
Multiple rate	12.5%	0%	33.3%	0%	0%	0%

Table 11: Clinical Pregnancy Rate (%) for IUI cycles using Donor Sperm 2019	
Cycles started	28
Inseminations	25
Clinical pregnancies	5
CPR / cycle started	17.9%
CPR / insemination	20%
Multiple rate	0%

Child, Adolescent and Young Adult (CAYA) Fertility Preservation Services:
AYA Males: Ten adolescent males between the ages of 12 and 17 years were referred to MFC in 2019 for sperm cryopreservation services before undergoing gonadotoxic treatment or surgery. Of these, 80% (8 patients) produced a semen sample at MFC for semen and sperm assessment. Of those individuals who produced a sample, 62.5% (5 patients) had sperm of suitable quality for freezing (Table 12).

Table 12: AYA Male Fertility Preservation			
2019	**Sperm to freeze (n=5)**	**No sperm to freeze (n=3)**	**WHO threshold normal**
Age, years (median, range)	14 (12-17)	15 (15-16)	
Sperm concentration (x106/ml)	32 (27-59)	0 (0-0)	15
Motility (%)	37 (16-48)	0 (0-0)	32
Volume (ml)	0.8 (0.25-1.5)	0.8 (0.15-1.4)	1.5
Number of straws frozen	7 (4-8)	0	
Diagnosis (n)			
Hodgkins Lymphoma	2	1	
Acute Myeloid Leukemia	0	1	
Non-Hodgkins Lymphona	0	1	
Sickle Cell Disease	1	0	
Ewings Sarcoma	1	0	
Osteosarcoma	1	0	

AYA Females: One adolescent female who was referred to MFC in 2019 for oocyte vitrification ***before*** undergoing gonadotoxic cancer therapy. This patient had a successful cycle, with 33 oocytes cryopreserved for future use.

Eleven female survivors of CAYA cancer, who had previously received gonadotoxic treatment as part of their cancer therapy, attended MFC in 2019 for a fertility consultation (Table 13).

Table 13: Female CAYA Cancer Survivors Fertility Assessment 2019 (n=11)	
Age at diagnosis (median, range)	13 (11 - 15)
Age at fertility consultation (median, range)	23 (20 - 25)
Anti-Mullerian hormone (mean, range)	18.5 pmol/L (0.3 - 64.3)
Antral follicle count (mean, range)	14 (3 - 30)
Diagnosis	
Soft tissue sarcoma	1
Osteosarcoma	2
Hodgkin's Lymphoma	7
Ewing's sarcoma	1

The Reproductive Medicine department maintains an active and productive research portfolio, collaborating with scientists in Irish academic institutions such as UCD and TCD. MFC employs a full-time Research Officer and two Clinical Research Fellow posts exist for higher training in Reproductive Medicine & Surgery, with both fellows undertaking higher degrees. MFC also hosts PhD and 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 2019, 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:

- Novel biomarkers of oocyte developmental competence (Funding: NMH Medical Fund)
- Gene expression analysis in failed embryo implantation (Funding: WT-SFI-HRB)
- 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)
- Development of improved laboratory tests for sperm quality and function in male infertility Funding: Irish Research Council)
- Knowledge and attitudes towards fertility preservation among healthcare providers.
- Ovarian Reserve in childhood cancer survivors