

## Reproductive Medicine & Surgery

Reproductive Medicine and Surgery direct services are provided by specialists at the National Maternity Hospital (NMH), Merrion Fertility Clinic (MFC), and St Michaels Hospital (SMH). Multidisciplinary input from areas of special expertise in NMH supports the planning and delivery of care in complex cases; Feto-maternal medicine, Pathology, Laboratory Medicine, Genetics, Radiology, Microbiology, Anaesthesia, Early pregnancy Assessment Unit, Perinatal Mental Health, Dietetics and others, are regularly involved in patient care pathways. This feature of best practice was recognised and reflected in the HSE plans to include reproductive medicine services in the new NMH collocated at the SVUH site. The increasingly complex nature of clinical fertility presentations is reflected in the ever-broadening referral basis: (e.g. adolescents, adult spina bifida, cystic fibrosis, organ transplant etc) and continued to influence clinical services development during 2017.

MFC currently remains the only Assisted Reproduction Treatment (ART) service in the country which is not-for-profit. Synergistic collaboration between NMH, MFC and SMH minimises the financial burden for patients who need assisted conception by combining the available public resources with efficiencies in the clinic, which is on-site of the hospital. Adherence to evidence-based medicine is an underlying principle of the clinic which has a strong research and academic profile. Two Clinical Research Fellow posts exist for higher training in Reproductive Medicine & Surgery, with both fellows undertaking higher degrees under the supervision of Professor Wingfield.

Dedicated hospital clinics for Infertility, Endometriosis, and Recurrent Miscarriage continued throughout 2017 with an expansion in numbers attending. Outpatient hysteroscopy procedures were provided to an increased number of patients compared to 2016; the consequent reduction in need for hysteroscopy under general anaesthetic reduced pressure on operating theatre.

Minimal access surgery was provided for an increasing complexity of cases with more level 3, 4 and 5 laparoscopic procedures\* undertaken (see table A). The first laparoscopic oocyte retrieval took place in NMH in collaboration with embryology services from MFC. The care of Gender Dysphoria patients took a comprehensive approach giving consideration to fertility cryopreservation (egg and sperm freezing at MFC) ahead of removal of reproductive organs (TLHBSO at NMH).

The success rates of ART treatments at MFC remained excellent: overall high clinical pregnancy rates per embryo transfer were maintained and the lowest ever multiple pregnancy rate of 4.5% was achieved. These results endorse the elective single embryo transfer policy, as well as the quality of medical, nursing and embryology care. Livebirth rates are the best marker of ART success and results for IVF and ICSI cycles performed in 2016 (delivering in 2016/2017) are very high. Approximately one third of all couples completing IVF/ICSI cycles had a livebirth. The efficacy of IVF/ICSI is more profoundly observed in couples where the female partner was aged less than 35; the livebirth rate after one completed fresh cycle of treatment in this group was almost 54.3%. Results from IUI and FET (frozen embryo transfer) cycles showed an increase from previous years. When controlled for age, the data reassuringly show that pregnancy is possible for the majority of patients attending the fertility services.

Female fertility preservation with oocyte vitrification (OV) aka "egg freezing", commenced in 2016 and numbers increased through 2017. OV is provided for medical indications and individual circumstances where ovarian reserve is at risk. Counselling is an important aspect of the service. MFC's objective is to expand child and adult onco-fertility services (with female and male gamete cryopreservation) in collaboration with national cancer services.

## Hospital Clinics

### *Endometriosis & Infertility*

Outpatient clinics remained busy in 2017 with a total of 810 consults; 262 first visits and 548 return appointments. Standard investigations including hormone profile and semen assessment are organized prior to the first appointment reducing the need for repeat clinic attendance so that treatment, including referral for ART, is instituted quickly.

### *Recurring Miscarriage & 2<sup>nd</sup> Trimester Loss*

This clinic is run by Dr Cathy Allen, Clinical Midwife Specialists Brenda Casey and Sarah Cullen, is supported by the gynaecology nursing and administrative staff, as well as associated clinical, pathology services. Clinical Fellows in Reproductive Medicine as well as trainees in Obstetrics & Gynaecology gain experience in this service. Increase in demand necessitated extra clinics so in 2017 the frequency of clinics increased to 3 times per month. In 2017, 91 women/couples were seen at the recurrent miscarriage and 2<sup>nd</sup> trimester loss clinics.

The initial contact for care of patients with Recurrent Miscarriage (RM) is with the Midwife Specialists, and usually occurs in the hospital at the time of initial diagnosis. Patient distress in such circumstances is well recognised, and the prompt access to the RM clinic signals the beginning of ongoing support. Agreed management protocols and comprehensive investigations are followed so that results are available for patient follow-up as quickly as possible. Clear management plans for subsequent pregnancies in these patients are now immediately accessible electronically to doctors and midwives when new pregnancies are diagnosed. Access to weekly pregnancy surveillance in the 1<sup>st</sup> trimester is arranged for RM patients. Approximately 51% of patients attended with a subsequent pregnancy(ies), and 50% of all patients have had a successful outcome.

Patient Information Booklets for RM were redesigned. The Bereavement Counselling office was upgraded and redecorated so that ongoing patient support now takes place in this tranquil room. This project was made possible by the NMH Foundation. The development of a dedicated database for RM patients was completed in association with the ICT department of the hospital and an audit of the service was completed. (*accepted for publication 2018*).

Sarah Cullen was awarded Masters' thesis based on patient's experience of 2<sup>nd</sup> trimester miscarriage, and Brenda Casey was awarded a Masters focusing on Bereavement Support.

### *Outpatient Hysteroscopy*

The outpatient hysteroscopy (OPH) clinics, in close collaboration with the Ultrasound department, are conducted on a weekly basis in the Gynaecology Outpatient Department. Indications include post-menopausal bleeding (PMB), fertility issues and for removal of intrauterine devices.

The OPH service continued to expand in 2017. 501 patients were seen at the clinic in 2017 (371 in 2016). 351 outpatient hysteroscopies were performed (284 in 2016). 42 (12%) women required a further hysteroscopy under GA. Five gynaecological malignancies were diagnosed in patients referred for abnormal uterine bleeding (3%). An additional 7 OPH procedures were performed at SMH.

## Reproductive Surgery

Since mid-July 2015 the Reproductive Medicine team has three Consultants, operating a weekly shared theatre list. 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 has been observed to be increasing, and data will be collected prospectively on this aspect using the agreed guidelines\*.

	NMH	SMH
<b>Laparoscopic Surgery *</b>	<b>n=83</b>	<b>n=39</b>
Level 1 (basic procedures)	2	14
Level 2 (minor procedures)	56	19
Level 3 (intermediate procedures)	20	6
Level 4 (major procedures)	5	0
<b>Laparotomies</b>	<b>n= 8</b>	<b>n=0</b>
Open myomectomy	5	
Open oophorectomy	1	
Total abdominal hysterectomy	1	
Surgical sperm retrieval	1	
<b>Outpatient Hysteroscopy</b>	<b>n=351</b>	<b>n=7</b>
PMB	109	
Abnormal uterine bleeding	66	
Cancers diagnosed	5/175 (3%)	
Recurring Miscarriage / fertility	85	
Truclear polypectomy	42	
Retrieval of Mirena	41	
Other	50	
Onward referral for GA hysteroscopy	42/351 (12%)	
<b>Hysteroscopy under GA</b>	<b>n= 121</b>	<b>n= 32</b>
Diagnostic	63	8
Operative	58	24
polypectomy	27	11
myomectomy	14	0
Adhesiolysis for Asherman's	2	0
Resection of septum	3	0
Retrieval/ insertion of IUS	15	12
Endometrial ablation	3	0
Removal RPOC	0	1

\*ESGE categorisation for laparoscopic surgery

Level 1, basic procedures

Level 2, minor procedures : eg cauterly 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.

**Additional Services**

*Transgender Reproductive Services*

Under the care of Dr F Martyn, transgender patients are seen in the gynaecology outpatient clinic where surgery and fertility preservation are discussed. Female to male patients are offered oocyte vitrification and male to female, sperm freezing. Like all ART services, these treatments are not available publicly. Surgery (TAH and BSO) is now performed laparoscopically in the majority of cases.

**Oocyte Donation Satellite Service**

Collaboration with selected donor egg IVF clinics in Spain and Czech Republic continued to grow in 2017. Through MFC, satellite services are provided for suitable patients easing the burden of travel and providing high quality counselling and support, medical investigations therapies that adhere to best-practice standards. Early pregnancy assessment, support medications, and clinical summaries for subsequent obstetric care are provided by MFC.

As in previous years, the success rate is high: 65% (91/139) of completed cycles achieve a positive pregnancy test, 35% (48/139) tested negative. Of the positive pregnancy tests, 15 (16%) were non-continuing. Counselling of patients and more single embryo transfers by our partner clinics has been successful in reducing the proportion of multiple pregnancies.

**Assisted Reproduction – Merrion Fertility Clinic**

Merrion Fertility Clinic continues to provide a full range of Assisted Reproduction services for those attending the National Maternity Hospital. Demand for semen analysis remains high. Numbers of ovulation induction and IUI treatments have fallen from 2016 levels, and are now more reflective of previous years (Table 3). Numbers of IVF/ICSI cycles continue to grow, as stated in the introduction, pregnancy rates are excellent and multiple pregnancy rates remain low.

Table 3: 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)
2007	998	243	271	107
2008	1046	255	296	112
2009	1120	264	321	102
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

**GYNAECOLOGY & COLPOSCOPY**

There were eight cases of surgical sperm retrieval carried out in 2017. A breakdown of IVF and ICSI cycles is given, along with details of cancellation rates and pregnancy numbers (Table 4). The variation in outcomes by maternal age is also presented (Table 5). Conscious sedation was provided by Consultant Anaesthetists for all oocyte retrievals and surgical sperm retrievals.

Table 4: Numbers of IVF, ICSI and FET cycles				
	IVF/ICSI	IVF	ICSI	FET
Cycles Started	512	251	261	308
Cycles Cancelled	58	27	31	40
Oocyte Retrievals / Cycles Thawed	454	224	230	268
Embryo Transfers	393	191	202	263
Clinical Pregnancies	179	95	84	90
Cycles Started	413**	188	225	261
Cycles Cancelled	34**	21	13	43
Oocyte Retrievals / Cycles Thawed	379	167	212	218
Embryo Transfers	338	144	194	204
Clinical Pregnancies	147	69	78*	68

Table 5: Numbers of IVF and ICSI cycles by maternal age						
2017	All Ages	Under 35	35-37	38-39	40-41	42-44'
Cycles Started	512	98	182	120	85	26
Oocyte Collections	454	88	157	105	78	25
Embryo Transfer	393	70	142	90	70	20
Clinical Pregnancies	179	38	65	43	29	4
Average Eggs Collected	8.5	9.5	9.4	7.8	7.5	5.1

\*One 45 year old patient was treated in 2017. She had an ICSI cycle which resulted in the transfer of 2 embryos but did not result in a pregnancy.

**Pregnancy rates for IVF, ICSI and FET**

Clinical pregnancy rates remained excellent across all groups during 2017. 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 are. All data reported relates to treatment started in 2017 with the exception of livebirth rates which relate to treatment started in 2016. This is due to the fact that not all 2017 pregnancies are complete at time of going to press.

The clinical pregnancy rate following IVF/ICSI treatment across all age groups in 2017 was 45.5% per embryo transfer (Chart 2). This rose to 54.3% in those aged under 35 (Table 6 and Chart 1). Overall 69.7% of MFC patients had a single embryo transfer in 2017. This is a 5% increase from 2016 and reflects MFC's strong single embryo transfer policy. Of this group, a subset of good prognosis patients had an elective single embryo transfer, meaning they had a good quality embryo to transfer and at least one other to freeze. This group had a clinical pregnancy rate of 58.6% on the fresh cycle (see below and Chart 3).

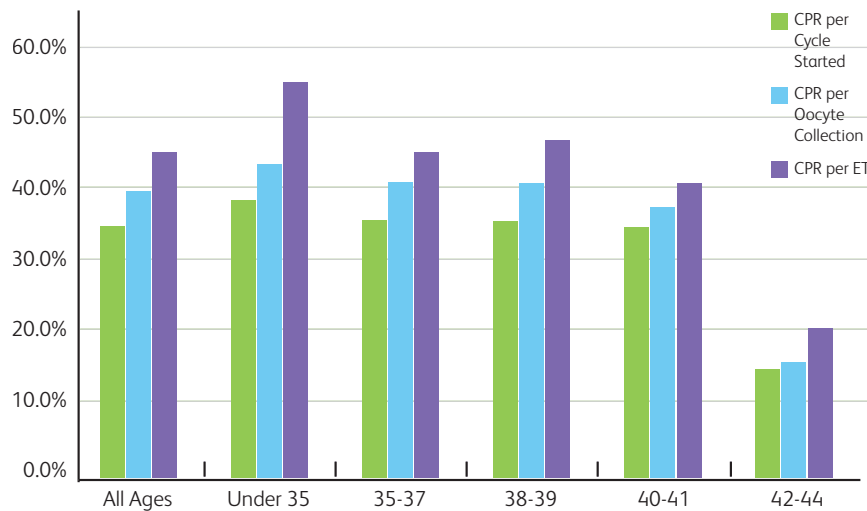
Clinical pregnancy rates of patients who undergo a double embryo transfer were approximately 8% less than those who have a single embryo transfer. This figure reflects the promotion of single embryo transfer unless embryo quality is compromised, necessitating a second embryo to be transferred to maintain a reasonable chance on establishing a pregnancy.

The mean age of women undergoing fresh IVF/ICSI cycles was 36.9. In 2017, 21.8% of all cycles started were in women aged 40 or more. This is an increase of 4% from 17.7% in 2016.

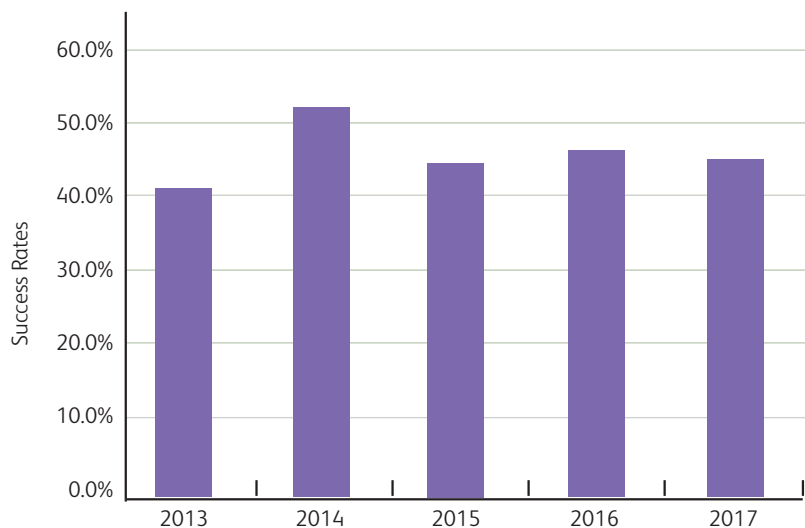
**Table 6: Clinical pregnancy rates for IVF and ICSI cycles in 2017**

	All Ages	Under 35	35-37	38-39	40-41	42-44
CPR per Cycle Started	35.0%	38.8%	35.7%	35.8%	34.1%	15.4%
CPR per Oocyte Collection	39.4%	43.2%	41.4%	41.0%	37.2%	16.0%
CPR per ET	45.5%	54.3%	45.8%	47.8%	41.4%	20.0%

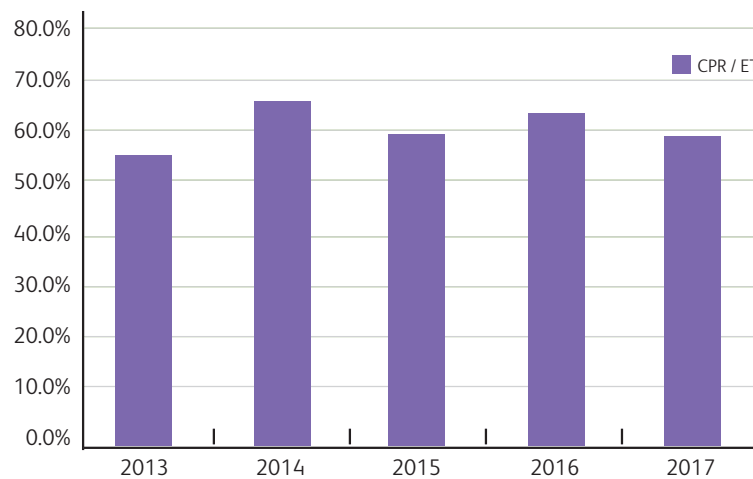
**Chart 1: Clinical Pregnancy Rates by Maternal Age**



**Chart 2: Year Clinical Pregnancy Rates per Transfer for IVF / ICSI Cycles**



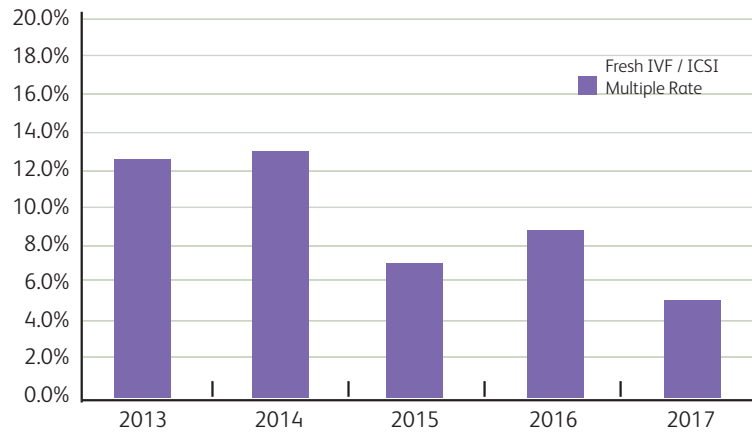
**Chart 3: 5 Year CPR/ET for eSET Patients**



**Multiple pregnancy (IVF, ICSI and FET)**

The overall multiple pregnancy rate for 2017 was 4.5% (Chart 4). All multiples were twins.

**Chart 4: 5 Year Fresh IVF / ICIS Multiple Pregnancy Rate**

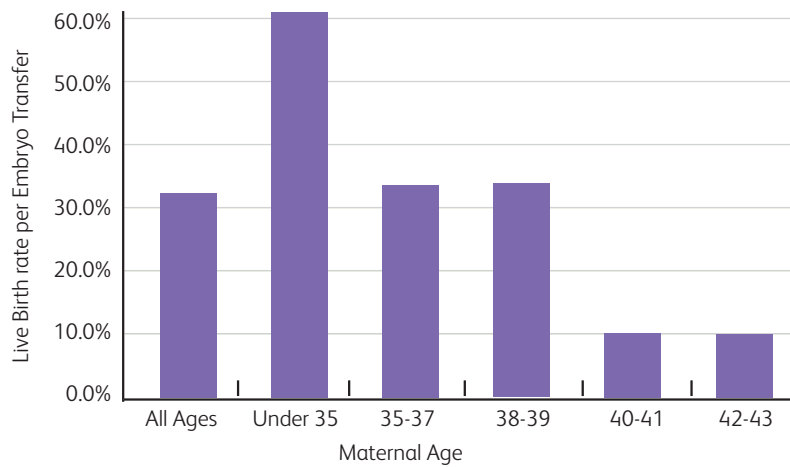


**Livebirth Rate**

Live birth rates are presented with a one year lag to account for gestation period and follow up. We are therefore presenting 2016 live birth rates. Rates achieved for the under 35 group were noteworthy (Table 7 and Chart 5).

Table 7: Livebirth Rate IVF/ICSI for 2016						
	All Ages	Under 35	35-37	38-39	40-41	42-44
LBs	129	43	47	30	7	2
LBR per OCR	28.4%	48.8%	29.9%	28.6%	9.0%	8.0%
LBR per ET	32.8%	61.4%	33.0%	33.3%	10.0%	10.0%

**Chart 5: Live Birth Rate per Embryo Transfer 2015 by Maternal Age**

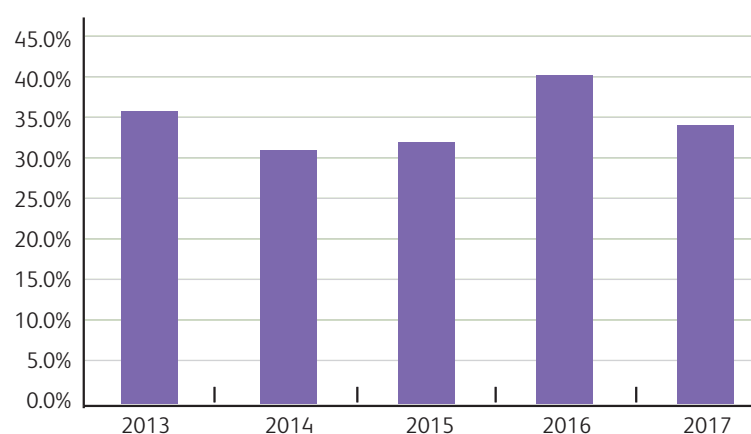




**Frozen Embryo Transfer**

The number of FET cycles carried out in 2017 was 263, this level of activity is on par with 2016. The percentage success has decreased from the previous year but remains above 2014/2015 levels. (Chart 6)

**Chart 6: 5 Year FET Cycles CPR per ET**



**Oocyte Vitrification**

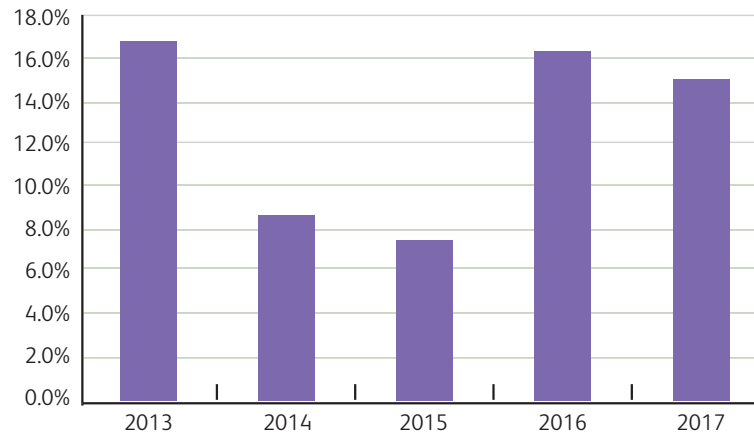
Merrion Fertility began vitrifying unfertilised oocytes in late 2016. A total of three cases were carried out that year. The number of cases carried out in 2017 remains small at 20, with the average number of oocytes frozen for patients being eight. Oocytes must have reached a minimum point of development, metaphase I, at time of collection before they are suitable to freeze.

	All Ages	Under 35	35-37	38-39	40-41
Cycles Started	23	4	7	11	1
Oocyte Collections	20	3	6	10	1
Average No. collected	9.45	9	10.6	7.8	20
Average No. Vitrified	8	8.6	9.2	6.4	13
Mean Age	36.7	32.8	36.1	38.3	40

**IUI (intrauterine insemination)**

Following disappointing results in 2014/2015 a review of patient eligibility for IUI and IUI treatment protocols was carried out. This has resulted in a marked improvement in pregnancy rates in 2016, with similar results in 2017 (Chart 7).

**Chart 7: 5 Year IUI CPR per IUI**



#### **Publications**

O'Brien Y, Martyn F, Glover LE, Wingfield MB. **What women want? A scoping survey on women's knowledge, attitudes and behaviours towards ovarian reserve testing and egg freezing.** Eur J Obstet Gynecol Reprod Biol. 2017 Oct;217:71-76.

O'Brien YM, Ryan M, Martyn F, Wingfield MB. **A retrospective study of the effect of increasing age on success rates of assisted reproductive technology.** Int J Gynaecol Obstet. 2017 Jul;138(1):42-46.

Martyn F, O'Brien YM, Wingfield M. **Review of clinical indicators, including serum anti-Müllerian hormone levels, for identification of women who should consider egg freezing.** Int J Gynaecol Obstet. 2017 Jul;138(1):37-41.

Wingfield M.

**The Fertility Handbook.** Gill Press, 2017

**Invited Lecture:** Wingfield M

Institute of Obstetricians and Gynaecologists, Public Meeting, Mar 17

**"The Changing Face of Fertility"**

**Presentations**

DA Crosby, N Fee, LE Glover, F Martyn, MB Wingfield. Can we incentivise outpatient hysteroscopy and promote economic efficiency?

Fourth Irish Congress of Obstetrics, Gynaecology & Perinatal Medicine, Kilkenny, December 2017

DA Crosby, L Glover, E Brennan, A Murphy, C Moss, B Loftus, MB Wingfield, DJ Brennan. Identification of whole transcriptomic changes in mid-luteal endometrium associated with successful implantation in assisted reproductive technology. Selected for moderated poster presentation.

UCD Conway Festival of Research and Innovation, Dublin, September 2017.

DA Crosby, YM O'Brien, LE Glover, F Martyn, MB Wingfield.

Influence of body mass index on the relationship between endometrial thickness and pregnancy outcome in single blastocyst frozen embryo transfer cycles.

Irish Fertility Society, Belfast, May 2017.

Glover LE, Crosby DA, U. Thirumalchevam, C Ní Chorca, C O' Farrelly, M Wingfield. Uterine Natural Killer Cell Phenotype: Predicting ART (Assisted Reproductive Technology) success in endometriosis-associated infertility.

Irish Fertility Society, Belfast, May 2017. First Prize for Best Oral Presentation.

Y.O'Brien, F Martyn, L Glover, M Wingfield.

What women want? A scoping survey of women's knowledge attitudes and behaviours towards ovarian reserve testing and egg freezing.

Irish Fertility Society, Belfast, 2017.

O'Doherty AM, O'Brien YM, Browne JA, Wingfield M, O'Shea LC. Identification of microRNAs associated with blastocyst development in human granulosa cells.

Irish Fertility Society, Belfast, 2107.

YM O'Brien, F Martyn, D O'Shea, M Wingfield.

Fertility Preservation in a Transgender Population.

British Fertility Society Annual Meeting, Edinburgh, Jan 2017.

YM O'Brien, M Wingfield, L O'Shea.

Follicular Fluid Anti-Mullerian Hormone and oocyte developmental competence.

British Fertility Society Annual Meeting, Edinburgh, Jan 2017.