Reproductive Medicine & Surgery

Medical and Surgical services for patients with Fertility needs are provided by specialists at the National Maternity Hospital (NMH), Merrion Fertility Clinic (MFC), and St Michaels Hospital (SMH). Complex cases can benefit from NMH multidisciplinary teams; Feto-matermal medicine, Pathology, Laboratory Medicine, Genetics, Radiology, Microbiology, Anaesthesia, EPAU, Perinatal Mental Health, Dietetics and others, are often involved in patient care pathways. This model of best practice will continue to be supported in the ongoing plans for the new NMH collocated at the SVUH site. Synergies between the main hospital and Merrion Fertility Clinic continue to serve the interests of the ever-expanding population of patients with complex fertility needs.

MFC currently remains the only Assisted Reproduction Treatment (ART) service in the country which is not-for-profit. 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 the site of the NMH. 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 2018.

Minimal access surgery continued to be busy throughout 2018 with day case procedures under anaesthesia and in the awake ('outpatient') state. Ongoing care for patients with Gender Dysphoria was provided with some patients choosing to avail of fertility preservation ahead of gender-reassigning surgery.

The success rates of ART treatments at MFC remained very satisfactory: overall high clinical pregnancy rates per embryo transfer were maintained, and the lowest ever multiple pregnancy rate of 4.2% was achieved. These results endorse the elective single embryo transfer policy, as well and 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 2017 (delivering in 2017/2018) are very high. Almost 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 45%.

Results from IUI and FET (frozen embryo transfer) cycles again 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 and 2018. 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 this child and adult onco-fertility services (with female and male gamete cryopreservation) in collaboration with national cancer services.

Hospital Clinics

Endometriosis & Infertility

Outpatient clinics continued to be in demand throughout 2018; overall numbers of consults were lower than 2017 due to the key personnel maternity leave: a total of 681 consults; 208 first visits and 473 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 & 2nd Trimester Loss

This clinic, run by Dr Cathy Allen and Bereavement 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 O&G gain experience in this service. Extra clinics initiated in 2017 (3 times per month) facilitated the investigation and management of an increased number of patients in 2018; 121 women/couples were seen at the recurrent miscarriage & 2nd 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 1st 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

The Specialist Midwifery team undertook a research project into Bereavement Care Education and Training for Midwifery students, and developed a one-day interactive Training Workshop in Bereavement Care.

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.

Outpatient hysteroscopy (OPH) services had a slightly lower number of patients in 2018 compared with the previous year. 471 patients were seen at the clinic (501 in 2017). 33 (12%) women required a further hysteroscopy under GA. Two gynaecological malignancies were diagnosed in patients referred for abnormal uterine bleeding (1%).

Reproductive Surgery

Since mid-July 2015 the Reproductive Medicine team has three Consultants, operating a weekly shared theatre list. The majority of cases are minimal access procedures. Careful selection criteria for laparoscopy (history and ultrasound) are applied so that many laparoscopies are operative with proven pathology. 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*.

Reproductive Surgery under GA	NMH	SMH
Laparoscopic Surgery *	**n=75**	**n=26**
Level 1 (basic procedures)	17	8
Level 2 (minor procedures)	27	9
Level 3 (intermediate procedures)	27**	9
Level 4 (major procedures)	4	0
***includes one laparoscopic OCR*		
Laparotomies	**n=4**	**n=0**
Open myomectomy	2	0
Open ovarian cystectomy	2	0
Surgical sperm retrieval under GA	**1**	**0**
Hysteroscopy under GA	**n=85**	**n=16**
Diagnostic	18	12
Operative *Adhesiolysis for Asherman's, Resection of septum, Retrieval/ insertion of IUS, Removal RPOC*	73	4
Endometrial ablation	6	0
Outpatient Hysperoscopy	**n= 278**	
Abnormal uterine bleeding	158	
Cancers diagnosed	2/158 (1%)	
Recurring Miscarriage / fertility	60	
Truclear polypectomy	18	
Retrieval of Mirena	15	
Other	27	
Onward referral for GA hysteroscopy	33	

**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.

Additional Services

Transgender Reproductive Services

Under the care of Dr F Martyn, transgender patients are seen in the gynaecology outpatient clinc 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 publically. 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 2018. 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: 66% (117/178) of completed cycles achieve a positive pregnancy test, 34% (61/178) tested negative. Of the positive pregnancy tests, 33 (28%) 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 to 19% (16/84).

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 have also returned to 2016 levels while FET cycles have continued to grow. This is reflective of changing practice in ART. As stated in the introduction, pregnancy rates remain excellent while 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)
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
2018	1459	151	407	301

There were seven cases of surgical sperm retrieval carried out in 2018.
A breakdown of IVF and ICSI cycles is given, along with details of cancelled cycles 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: 2018 Numbers of IVF/ICSI and FET cycles.

2018	IVF/ICSI	IVF	ICSI	FET
Cycles Started	461	217	244	379
Cycles Cancelled	55	34	21	78
Oocyte Retrievals / Cycles Thawed	406	183	223	301
Embryo Transfers	338	150	188	301
Clinical Pregnancies	144	58	86	109

Table 5: 2018 Numbers of IVF and ICSI cycles by Maternal Age						
2018	**All Ages**	**Under 35**	**35-37**	**38-39**	**40-41**	**42-44**
Cycles Started	461	136	122	105	73	25
Oocyte Collections	406	116	106	94	66	24
Embryo Transfer	338	96	89	78	56	19
Clinical Pregnancies	144	43	41	28	26	6
Average Eggs Collected	9.1	10.3	9.3	9	8	5.3

Pregnancy rates for IVF, ICSI and FET
Clinical pregnancy rates remained excellent across all groups during 2018.

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 2018 with the exception of livebirth rates which relate to treatment started in 2017. This is due to the fact that not all 2018 pregnancies are complete at time of going to press.

The clinical pregnancy rate following IVF/ICSI treatment across all age groups in 2018 was 42.6% per embryo transfer (Table 6 and Chart 1). This rose to 46.1% in the 35 to 37 year old group. The five year clinical pregnancy rates are presented (Chart 2). Overall 72% of MFC patients had a single embryo transfer in 2018. This is a 2% increase from 2017 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 52.5% on the fresh cycle (Chart 3). This is 10% higher than the clinical pregnancy rate in the overall patient population. Clinical pregnancy rates of patients who undergo a double embryo transfer were 1.5% 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 36.6. In 2018, 21. % of all cycles started were in women aged 40 or more. This represents a slight drop of almost 1% from the prevalence of this group in 2017.

Table 6: Clinical pregnancy rates (CPR) for IVF and ICSI cycles in 2018						
2018	**All Ages**	**Under 35**	**35-37**	**38-39**	**40-41**	**42-44**
CPR per Cycle Started	31.2	31.6	33.6	26.7	35.6	24.0
CPR per Oocyte Collection	35.5	37.1	38.7	29.8	39.4	25.0
CPR per ET	42.6	44.8	46.1	35.9	46.4	31.6

Chart 1: Clinical Pregnancy Rates by Maternal Age

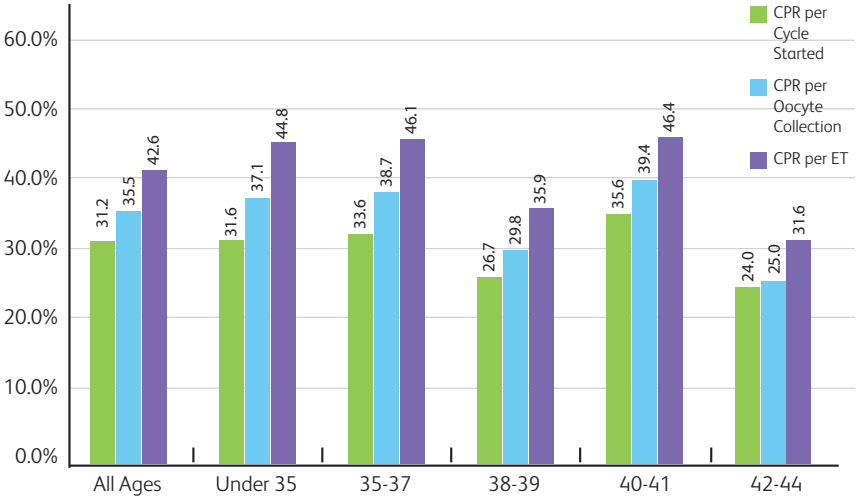


Chart 2: 5 Year Clinical Pregnancy Rates per Transfer for IVF / ICSI Cycles

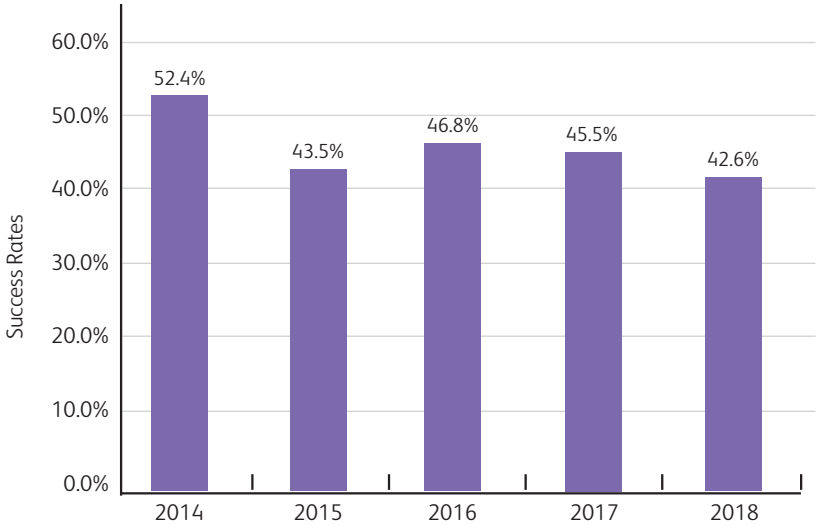
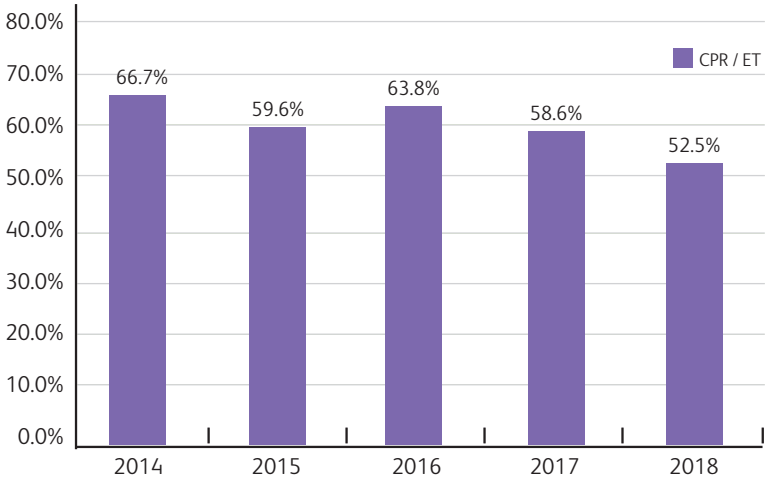


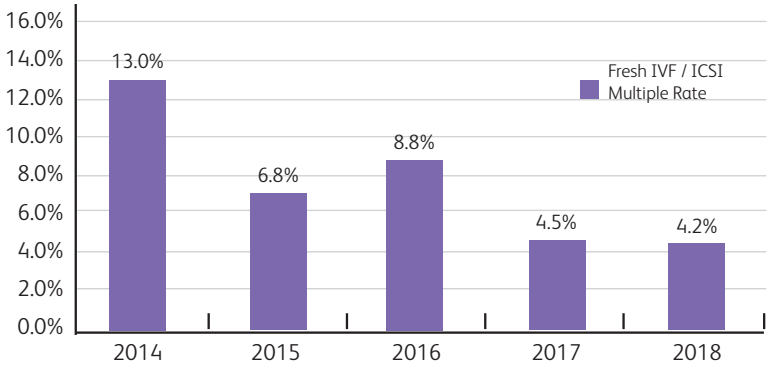
Chart 3: 5 Year CPR / ET for eSET Patients



Multiple Pregnancy (IVF, ICSI)

The overall multiple pregnancy rate for 2018 was 4.2% (Chart 4). MFC has made substantial progress over the last 5 years in reducing the multiple pregnancy rate.

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

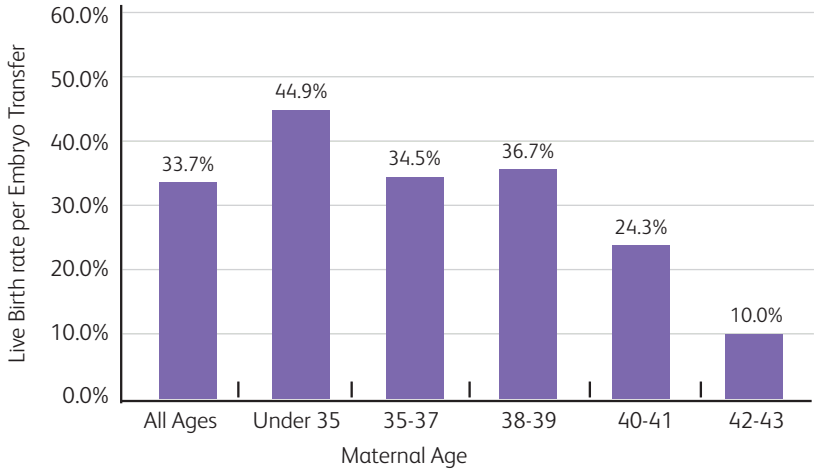


Livebirth Rate

Livebirth rates are presented with a one year lag to account for gestation period and follow up. We are therefore presenting 2017 live birth rates. Rates achieved for the under 35 group were noteworthy (Table 7 and Chart 5).

Table 7: Livebirth Rate IVF/ICSI for 2017						
	All Ages	**Under 35**	**35-37**	**38-39**	**40-41**	**42-44**
LBs	132	31	49	33	17	2
LBR per OCR	29.1%	35.6%	31.2%	31.4%	21.8%	8.0%
LBR per ET	33.7%	44.9%	34.5%	36.7%	24.3%	10.0%

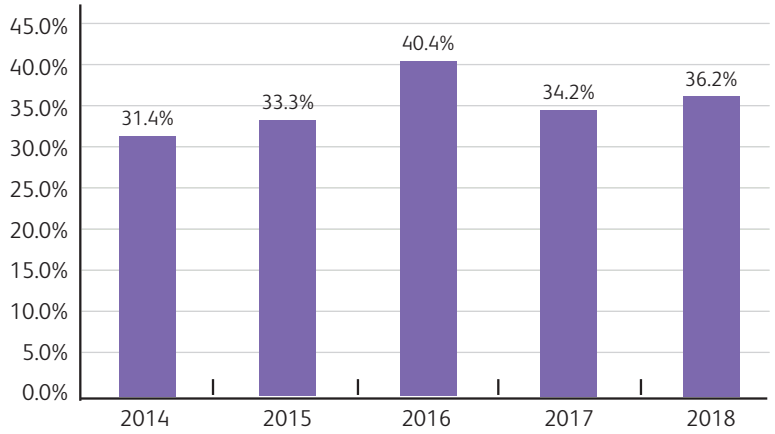
Chart 5: Live Birth Rate per Embryo Transfer 2017 by Maternal Age



Frozen Embryo Transfer

The number of FET cycles carried out in 2018 was 301. This figure has grown year on year since 2014 and represents almost double the numbers of frozen embryos transfers carried out in 2018 compared with 2014. Clinical pregnancy rates have increased 2% from 2017 and stand at 36.2% per embryo transfer. (Chart 6)

Chart 6: 5 Year FET Cycles CPR per ET



Oocyte Vitrification

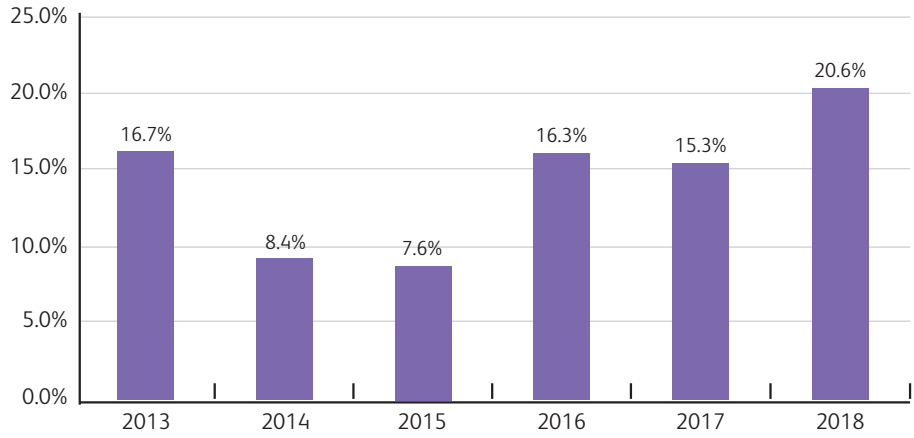
Merrion Fertility began vitrifying unfertilised oocytes in late 2016. A total of three cases were carried out that year. The number of cases carried out in 2018 remains small at 40, but is twice the number of cycles carried out in 2017 and indicates significant growth in the service. The average number of oocytes frozen for patients is 9.6. This figure increases to 12.5 when under 35 year olds are considered alone. Oocytes must have reached a minimum point of development, metaphase I, at time of collection before they are suitable to freeze.

2018	All Ages	Under 35	35-37	38-39	40-41
Cycles Started	43	11	19	12	1
Oocyte Collections	40	11	18	10	1
Average No. collected	11.6	14.6	11.5	9.4	3
Average No. Vitrified	9.6	12.5	9.3	7.6	3
Mean Age	35.5	30.5	36.5	38.5	41

IUI (intrauterine insemination)

Following disappointing results in 2014/2015 a review of patient eligibility for IUI and IUI treatment protocols was carried out. This resulted in a marked improvement in pregnancy rates in 2016. 2018 has seen a continuation of this trend with clinical pregnancy rates standing at 20.6% per IUI. (Chart 7).

Chart 7: 5 Year IUI CPR per IUI



Publications:

O'Brien Y, Kelleher C, Wingfield M. "So what happens next?" exploring the psychological and emotional impact of anti-Mullerian hormone testing. *J Psychosom Obstet Gynaecol.* 2018 Nov 29:1-9.

O'Doherty AM, O'Brien YM, Browne JA, Wingfield M, O'Shea LC. Expression of granulosa cell microRNAs, AVEN and ATRX are associated with human blastocyst development. *Mol Reprod Dev.* 2018 Nov;85(11):836-848.

Crosby D, O'Brien Y, Glover L, Martyn F, Wingfield M. Influence of body mass index on the relationship between endometrial thickness and pregnancy outcome in single blastocyst frozen embryo transfer cycles. *Hum Fertil (Camb).* 2018 Sep 17:1-6.

Lee JS, Wang RX, Alexeev EE, Lanis JM, Battista KD, Glover LE, Colgan SP. Hypoxanthine is a checkpoint stress metabolite in colonic epithelial energy modulation and barrier function. *J Biol Chem.* 2018 Apr 20;293(16):6039-6051.

Crosby DA, Glover LE, Martyn F, Wingfield M. CA125 measured during menstruation can be misleading. *Ir Med J*. 2018 Apr 19;111(4):738.

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Nguyen N, Fernando SD, Biette KA, Hammer JA, Capocelli KE, Kitzenberg DA, Glover LE, Colgan SP, Furuta GT, Masterson JC. TGF-β1 alters esophageal epithelial barrier function by attenuation of claudin-7 in eosinophilic esophagitis. *Mucosal Immunol.* 2018 Mar;11(2):415-426.

Age considerations in the management of recurring miscarriage.
Crosby D, Cullen S, Allen C.
Irish Journal of Medical Science, Jun 2018

Doherty, J., Coughlan, B., Casey, B., Sheehy, L., Brosnan, M., Barry, T., McMahon, A. and Cullen, S. (2018) Student midwives' education needs and their experiences of attending a bereavement education workshop. British Journal of Midwifery, 26(8):523-531
https://doi.org/10.12968/bjom.2018.26.8.523

Doherty, J, Cullen, S., Casey, B., Sheehy, L., Brosnan, M., Barry, T., McMahon, A. and Coughlan, B. (2018) Bereavement care education and training in clinical practice: supporting the development of confidence in student midwives. Midwifery. 66, 1-9
https://doi.org/10.1016/j.midw.2018.06.026

Posters/Presentations

Fertility 2018: Liverpool Jan 4-6, 2018
Follicular fluid Anti-Mullerian Hormone and Progesterone and oocyte developmental competence
O'Brien Y, Wingfield M, O'Shea LC

Fertility Preservation in a Transgender Population
O'Brien Y, Wingfield M

IDENTIFCATION OF WHOLE TRANSCRIPTOMIC CHANGES IN MID-LUTEAL ENDOMETRIUM ASSOCIATED WITH SUCCESSFUL IMPLANTATION IN ASSISTED REPRODUCTIVE TECHNOLOGY
DA Crosby, LE Glover, E Brennan, F Martyn, B Loftus, C O'Farrelly, F McAuliffe, DJ Brennan, M Wingfield

Irish Fertility Society 12th Annual Scientific Meeting: "Assisted Human Reproduction Policies and Practice in Ireland", Dublin May 11-12, 2018:
Endometrial injury in nulliparous women may increase success rates in ART
DA Crosby, LE Glover, E Brennan, F Martyn, B Loftus, C O'Farrelly, F McAuliffe, DJ Brennan, M Wingfield

Dysregulation of metabolic pathways in endometrium of women with unexplained infertility affects embryo implantation
DA Crosby, LE Glover, E Brennan, F Martyn, B Loftus, C O'Farrelly, F McAuliffe, DJ Brennan, M Wingfield

American Society for Reproductive Medicine (ASRM): Denver Oct 6-10, 2018
DYSREGULATION OF METABOLIC PATHWAYS IN ENDOMETRIUM OF WOMEN WITH UNEXPLAINED INFERTILITY AFFECTS EMBRYO IMPLANTATION AND SUBSEQUENT PREGNANCY
DA Crosby, LE Glover, EP Brennan, P Cormican, P Downey, E Mooney, C O'Farrelly, B Loftus, FM McAuliffe, DJ Brennan, M Wingfield

Junior Obs Gynae Society (JOGS) annual meeting: Royal College of Physicians Ireland, Nov 23, 2018:
The First Case of Oophorectomy for Fertility Presentation in Ireland
L Hartigan, J Cullinane, F Martyn, V Broderick, M Wingfield
Best Case Report (1st place awarded)

DYSREGULATION OF METABOLIC PATHWAYS IN ENDOMETRIUM OF WOMEN WITH UNEXPLAINED INFERTILITY AFFECTS EMBRYO IMPLANTATION IN ASSISTED REPRODUCTIVE TECHNOLOGY
DA Crosby, LE Glover, EP Brennan, P Cormican, P Downey, E Mooney, C O'Farrelly, B Loftus, FM McAuliffe, DJ Brennan, M Wingfield
Best Oral Presentation (2nd place awarded)

Age considerations in the management of recurring miscarriage.
Crosby D, Cullen S, Allen C.
Irish Journal of Medical Science, Jun 2018

Doherty, J., Coughlan, B., Casey, B., Sheehy, L., Brosnan, M., Barry, T., McMahon, A. and Cullen, S. (2018) Student midwives' education needs and their experiences of attending a bereavement education workshop. British Journal of Midwifery, 26(8):523-531
https://doi.org/10.12968/bjom.2018.26.8.523

Doherty, J, Cullen, S., Casey, B., Sheehy, L., Brosnan, M., Barry, T., McMahon, A. and Coughlan, B. (2018) Bereavement care education and training in clinical practice: supporting the development of confidence in student midwives. Midwifery. 66, 1-9 https://doi.org/10.1016/j.midw.2018.06.026