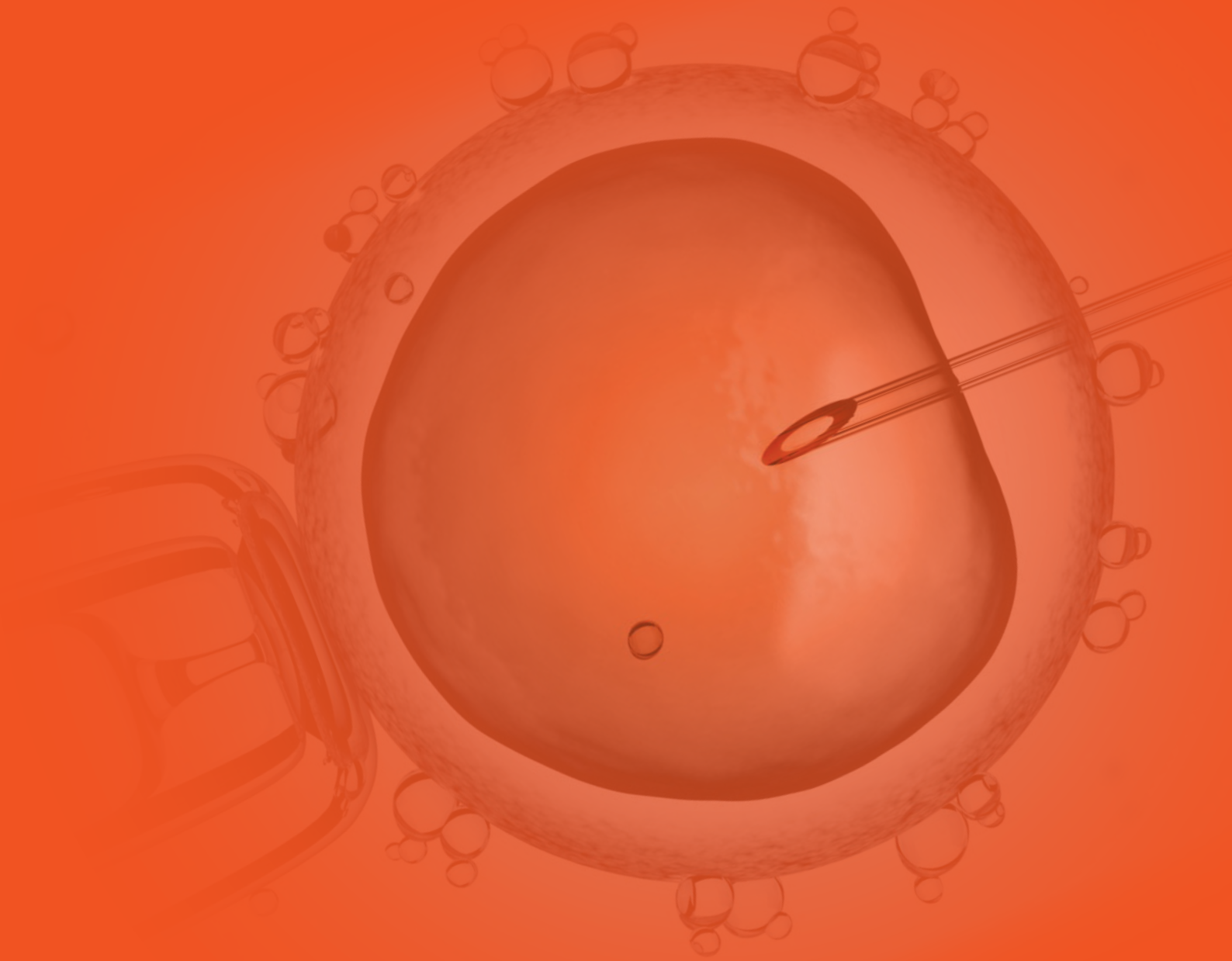
ANNUAL WORK REPORT

TRENDS AND FIGURES OF FERTILITY TREATMENTS IN MALTA FOR 2018



EMBRYO PROTECTION AUTHORITY
Putting Patients First

FEBRUARY 2019

ANNUAL WORK REPORT

TRENDS AND FIGURES

OF FERTILITY TREATMENTS

IN MALTA FOR 2018

EMBRYO PROTECTION AUTHORITY

Putting Patients First

Presented to Deputy Prime Minister and Minister for Health Hon. Chris Fearne

As per Embryo Protection Act 2012, Chapter 524,
Embryo Protection (Amendment) Act, 2018

and

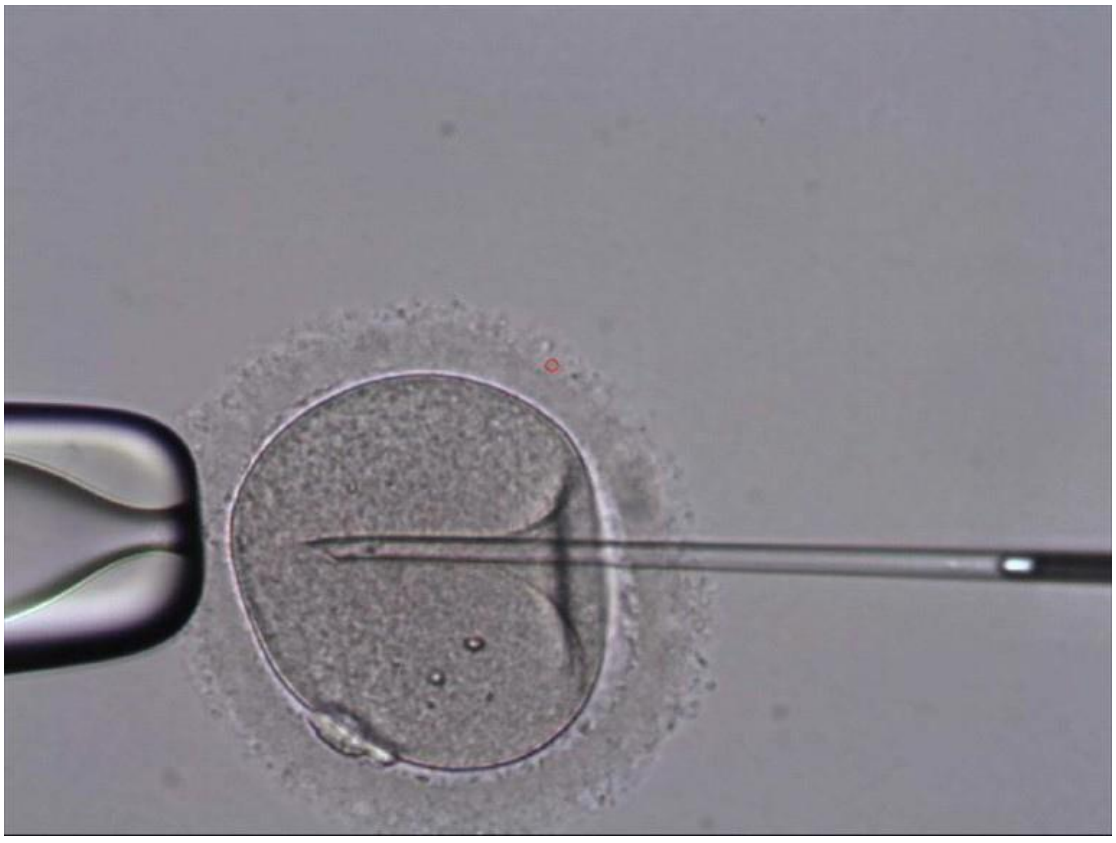
Embryo Protection Authority Regulations, LN32 of 2015

February 2019

EMBRYO PROTECTION AUTHORITY

PUTTING PATIENTS FIRST

ANNUAL WORK REPORT FOR 2018



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1. BACKGROUND

1.1. The Embryo Protection Authority (EPA)

The Embryo Protection Authority is a body corporate having a distinct legal personality and is the sole Regulator of all Assisted Reproductive Technologies (ART) performed at both the public and private licensed clinics/hospitals in Malta. It has been established as per the Embryo Protection Act 2012, (Chapter 524) which covers the use and storage of sperm, oocytes (eggs), and embryos for human application. The Act has been amended through the Embryo Protection (Amendment), 2018. The new Amendment Act was enacted on the 21st June 2018 and came into force on the 1st October 2018 as per Legal Notice LN 313/2018.

The Protocol for Additional Fertilisation Requests (AFR) was established in writing by the Authority compiling all criteria and methodology for the application to grant more than two oocytes to be fertilised and consequently permission for embryo cryopreservation. The AFR Protocol was presented to the Parliamentary Health Committee on the 13th September 2018 and was unanimously approved on same day.

The Authority sets the standards and determines the policy framework (Protocol) while providing information to stakeholders, the general public, and to the prospective parent / parents seeking treatment.

1.2. Our Principles – PATIENTS FIRST

The Embryo Protection Authority treats all prospective parent / parents referred by the licensed Clinics with dignity and respect, and all information provided to the Authority in confidence remains highly confidential and disclosed only in the circumstances permitted by law, as per the Data Protection Act.

All decisions taken by the Embryo Protection Authority are taken in the best interest of the prospective parent/parents and of the child/children who may be conceived out of any assisted reproductive technology procedure undertaken.

1.3. Our Principles – Working closely with Stakeholders

The Authority ensures that the highest levels of standards are being kept as specified in the laws governing the fertility sector by working closely with all stakeholders in the Fertility field.

The Authority also performs its functions consistently and fairly with all clinics as per the established Laws and Regulations.

1.4. The Legal Framework

A number of laws and regulations make up the regulatory framework which covers the Assisted Reproductive Technology (ART) activities held in Malta.

1. *The 'Enabling' Act*:

The Embryo Protection Act 2012 – Chapter 524 of the Laws of Malta is the 'Parent' Act governing the Fertility Sector. The Bill was passed through Parliament and provides for the protection of human embryos through the establishment of the regulatory Authority (The Embryo Protection Authority).

2. *The 'Amended' Act.*

The Embryo Protection (Amendment) Act, 2018 of the laws of Malta is the amended 'parent' Act with the ultimate purpose to make all the regulated processes with the Fertility Sector, more accessible and equitable to all those who need them. This Amended Act amended the definition of prospective parent, allowed embryo cryopreservation and third party donation.

3. *Regulations*:

The Embryo Protection Authority Regulations 2015 – (L.N.32 of 2015 – Chapter 524) have been published by Legal Notice 32/2015 following assent by the then Parliamentary Secretary responsible for Health. It grants the Authority its legal personality and representation, and outlines the executive administration and organisation of its affairs.

4. *The 'Protocol' and 'Additional Fertilisation Request Protocol'*

The Protocol which was published by the Authority in 2013 is intended as a means of assisting licensed Clinics to comply with their legal obligations whilst also serving as a useful reference for patients and professionals working in the

fertility sector. During 2018, work was performed to issue an amended Protocol to reflect the requirement changes stemming from the Embryo Protection (Amendment) Act, 2018.

The Protocol for Additional Fertilisation Requests (AFR) was established in writing by the Authority compiling all criteria and methodology for the application to grant more than two oocytes to be fertilised and consequently permission for embryo cryopreservation. The AFR Protocol was presented to the Parliamentary Health Committee on the 13th September 2018 and was unanimously approved on same day.

Professionals working in the fertility sector are also bound to follow Directive 2004/23/EC which sets standards for donation, procurement, testing, processing, preservation, storage, and distribution of human tissues and cells.

1.5. Functions of the EPA

- To ensure that high standards of ethics are maintained by all medical practitioners, paramedics, and other personnel involved in procedures of medically assisted procreation;

- To request and obtain, in cases of reasonable suspicion that the provisions of the Embryo Protection Act are not being followed, information and copies, in any form, of documents required by the Commission Directive 2004/23/EC of the European Parliament and of the Council of 31 March, 2004 on setting standards of quality and

safety for the donation, procurement, testing, processing, preservation, storage, and distribution of human tissues and cells to ensure traceability of human cells;

- To carry out inspections in order to ensure that the standards of best practice are being respected and implemented and that all information and documentation required under Article 18 of the Embryo Protection Act is being kept appropriately, and for this purpose to access clinics and any other places as necessary;

- To maintain a statement of the general principles which, in its opinion, should be followed in:

  a. Carrying out its activities under the Embryo Protection Act; and
  b. Carrying out its functions in relation to such activities under the Embryo Protection Act.

- To ensure, in relation to activities under the Embryo Protection Act, compliance with:

  a. The obligations and requirements imposed by or under the Embryo Protection Act;
  b. The codes of practice established under paragraph (a) of the Embryo Protection Act.

- To perform such other functions as may, from time to time, be prescribed by regulations made under the Embryo Protection Act.

1.6. Human Resources

During 2018, to further strengthen its corporate structure, the Authority engaged an Administrative Officer through a public call in June. During September interviews were held for the engagement of a clerk and an Assistant Director, both posts were duly filled by year end.

The Authority strives to ensure that its employees have the skills and competences to match the organizational requirements in order to guarantee optimal executive performance. The Executive Director, the Administrative Officer and the Infertility Inspector as well as the clerk received regular training throughout the year.

The Executive Director and the Infertility Inspector have successfully completed training and passed their examination on Good practices in Blood Components and Medicinal Products referring to GPG and GMP, Quality Management and Inspection Criteria for blood establishments. This training was offered by the European Blood Inspection Academy (EuBIS) and is also applicable to ART establishments.

In December, the Executive Director attended an Interactive Workshop on 'Transgender Fertility Preservation: Implications, Legalities and Creating a future family'. This Workshop was organised by the British Infertility Counsellors Association (BICA), and took place in London, United Kingdom.

The Executive Director, during 2018 has also successfully completed her Campus training with the University of Oxford on Bioethics, with her main focus being Reproductive Ethics. Although this study was fully self-funded by Mrs Attard, it is definitely an asset to the Authority.

The Administrative Officer has attended to training on Data Protection Awareness in preparation of the new General Data Protection Regulations that came into force. The Administrative Officer as well as the Clerk attended to Mental Health Awareness Sessions offered by the Employee Support Programme within the People and Standards Division.

Last June, the Executive Director attended a two day meeting held in Brussels for the EU Competent Authorities on Substances of Human Origin Expert Group which was convened to discuss the Transposition of Tissue and Cells Directives, and the Evaluation of the Tissue and Cell Legislation for better regulation. Discussions were also held as recommended by the European Centre for Disease Prevention and Control (ECDC) on the request for Assessment of the associated risks with the non-partner donor testing currently being applied by Denmark, largest supplier on non-partner sperm, discussions were also held on the issue of permanently block sperm following the identification of potentially serious genetic disease or hereditary genes for such diseases in a donor.

Update on the Joint Action ARTHIQS - Good practices on donation, collection, testing, processing, storage and distribution of gametes for Assisted Reproductive Technologies and of haematopoietic stem cells for

transplantation. Update on the Joint Action VISTART – Vigilance and Inspection for the Safety of Transfusion, Assisted Reproduction and Transplantation. The issues of Surveillance and Vigilance, as well as Digital Data in Substances of Human Origin were also discussed.

International Updates from the Council of Europe on Tissue and Cell Activity Data Reporting and Updates on the Implementation of Coding and Import Legislation were also presented for discussion.

The Ministry for Health had assigned new premises to the Authority in 2016, and to date all staff including senior executive staff, are all still housed in this one-room office in St Luke's Hospital. The Authority looks forward to the re-location of its offices to another premises from where it would be able to perform its regulatory duties.

1.7. Board Members and Executive Administration

The legal representation of the Authority is vested in its Chairman, Hon. Judge Emeritus Philip Sciberras UOM. Vice-Chairperson Ms. Josephine Abdilla MBA *Henley,* DIP Mang. *Henley.* The other appointed members include Dr. Patrick Sammut MD MRCPCH MSc., Ms. Mariella Meachen B. Psych (Hons) MA (Psychotherapy) R.N., Profs. Victor Grech MD PhD. PhD FRCPCH FRCP, and Ms. Sarah Camilleri Dip Economic and Political Studies.

Ms Moira Gialanze the Administrative Officer was appointed to also serve as the Authority Board's Secretary with effect from April 2018.

In exercise of the powers conferred by Article 6 (2) of the Embryo Protection Authority Regulations, 2015 (L.N. 32 of 2015), the Hon Minister for Health, after consultation with the Embryo Protection Authority had appointed Ms. Simone Attard PGrad Cert, PGrad Dip Systemic Practice (Tavistock and Portman NHS Trust UK)., MBICA., as Executive Director of the Embryo Protection Authority to serve for a second term of three years up to 31st January 2021.

During 2018, eight Authority board meetings have been called and in all sittings quorum was achieved. Attendance of the members and the Executive Director to these Board meetings were as stated hereunder:

Designation	Name	Attended	Excused
Chairperson	Judge Philip Sciberras	8	0
Vice Chairperson	Ms Josephine Abdilla	8	0
Member	Dr. Patrick Sammut	6	2
Member	Profs. Victor Grech	5	3
Member	Ms. Mariella Meachen	7	1
Member	Ms. Sarah Camilleri	7	1
Executive Director	Ms. Simone Attard	8	0

Eight meetings with Representatives from *the Obstetrics and Gynaecology Association* and the *Paediatric Association of Malta* have been called in order to discuss requests for the additional fertilization of oocytes. These requests are made by the clinicians treating the parent / parents. [Article 6 of the Embryo Protection Act gives the power to the Authority, in consultation with the aforementioned Associations, to approve the fertilization of three oocytes instead of the two currently permitted by law up to September 2018. With the introduction of the Amendment Law as of 1st October the approval was being granted to fertilize maximum five oocytes instead of the two allowed by the Amendment Act].

After the changes coming into effect on the 1st October 2018 and the approval of the Additional Fertilisation Request Protocol by the Parliamentary Health Committee the two members of the Paediatric Association of Malta offered their resignation from attending to the Authority meetings, to date although requests have been made by the Authority, the Association has not yet appointed other members to represent the Paediatrics on the Board.

On the other hand the two members representing the Obstetrics and Gynaecology Association who also offered their resignation from attending the Authority meetings where replaced by a new Member appointed by the Association.

1.8. Annual Remuneration to Board Members

The members of the Board are not fully employed by the Embryo Protection Authority but receive annual remuneration for their services, remuneration capping for 2018 was as listed hereunder, however board members were only paid for sessions they attended to. The remuneration for 2019 will be paid in accordance with the new framework for the categorization, classification and remuneration of Boards and Committees.

Designation	Name	Annual Remuneration (Euros)
Chairperson	Judge Philip Sciberras	13,954
Vice Chairperson	Ms Josephine Abdilla	6,000
Member	Dr. Patrick Sammut	3,494
Member	Profs. Victor Grech	3.494
Member	Ms. Mariella Meachen	3,494
Member	Ms. Pauline Baldacchino	3,494

1.9. The Authority as a Regulator

As the sole regulator of all Assisted Reproductive Technologies (ART) performed at both public and private licensed clinics/hospitals in Malta, the Authority strives to ensure compliance with the obligations and requirements imposed by or under the Embryo Protection Act and Protocol.

Throughout 2018, several requests applications for fertilisation of oocytes for couples undergoing cycles at the licensed clinics were reviewed. All the cases

presented were discussed and decisions of approval or non-approval were unanimously taken accordingly. Also several requests for sperm and oocyte retrieval and cryopreservation only where received by the Authority. These where approved or rejected subject to all virology tests being in order. Details of these approvals are given in detail in the second part of this Annual Report.

In 2018, The Authority received a request regarding a couple suffering from severe oligospermia and testicular failure, where the woman was still under age. The urologist requested permission so that this couple will undergo IVF because of their specific case as it would be useless to have the sperm cryopreserved for several years until the woman reaches the age of 25, as the only way for the couple to become pregnant was through IVF. The Authority discussed this case and unanimously agreed to grant permission to this couple to undergo IVF. The ART prioritisation Committee was informed of this decision to prioritise couple according to the Authority Board's decision. Couple has been prioritised, however cycle was still not carried out by end of December 2018.

In March 2017, the Authority was informed by the Attorney General's Office that one couple had instituted a constitutional application at the Civil Court against the Attorney General and the Embryo Protection Authority. The Chairperson and Executive Director gave evidence in this case. On Friday 28, September 2018, the court decreed that no violation of the applicant's fundamental human rights had occurred. The couple have filed an appeal to this decision. The Authority was still awaiting a Court decision on this appeal.

In January 2017, the Authority was notified of an incident that involved a multi-chamber incubator which contained 18 embryos still in incubation. The Authority was informed that the embryologists, on entering the ART Laboratory in the morning, had found the multi-chamber incubator switched off. This Serious Adverse Event (SAE) was immediately reported to the Authority who requested that: (a) all prospective parents involved are informed on individual basis of the situation with all the possible risks and outcome of embryo transfer, (b) all professionals involved in process must draw up a detailed report of the incident. The Authority also requested the Department of Health to initiate an Internal Investigation / Inquiry to determine the exact cause of the Incident. Later on, in the same day Minister for Health Hon. Chris Fearne, informed that an Independent Inquiry had been ordered.

On the 16th April 2018, the Authority was given a copy of the independent inquiry held, as well as a copy of the Ministerial Statement made in Parliament by the Deputy Prime Minister and Minister for Health Hon. Chris Fearne. The conclusions established that the regular procedure held every month wherein the electricity system transfers automatically to the generator had nothing to do with the incident as was previously reported in the media. This was due to the fact that the incubator was on a UPS system. The Inquiry report also established that the incubator was not faulty and was functioning well even during checks made by the engineers in the Inquiry process. In view of the testimony given, there was no burden of proof as to why the incubator was left on standby and by whom. Hon Fearne in his Ministerial Statement informed that none of the couples involved in the incident had a resultant

pregnancy from that cycle, however three out of the nine couples had subsequently given birth to a child through other IVF cycles carried out.

In February 2018, one incident was reported involving admission of one patient in hospital for observation and investigation due to Ovarian Hyperstimulation Syndrome (OHSS). Patient was admitted to hospital post oocyte retrieval and after fertilisation of oocytes had already taken place, thus patient was not fit for embryos transfer. The Authority immediately received a request from the MDH ART Clinic for the freezing of three embryos which due to a *force majeur* not predictable at the time of fertilization, could not be transferred on the day of the planned embryo transfer. The request was immediately approved by the Authority. The three embryos were later transferred back into the prospective mother when she was fit to undergo embryo transfer later on in 2018.

In September 2018, still under the provisions of the old Act, the Authority received a request for the freezing of two embryos which due to a *force majeur* not predictable at the time of fertilization, could not be transferred on the day of the planned embryo transfer as the mother had developed a medical condition after the oocytes retrieval and fertilisation of oocytes. The request was immediately approved by the Authority. The two embryos are still in storage until the prospective mother is fit to undergo embryo transfer.

Way Back in October 2016, the Authority had received a request for the freezing of two embryos which due to a *force majeur* not predictable at the time of fertilization, could not be transferred on the day of the planned embryo transfer as the mother was very unwell. Approval was granted for the cryopreservation of these embryos, which had been reported in Annual Reports of 2016 and 2017 that they were still in storage. During 2018, these two embryos were transferred back into the prospective mother as she was fit to undergo embryo transfer.

The Authority has received three requests from the licensed clinics to grant permission for oocyte retrieval and cryopreservation only, from three women aged between 28 and 40, who wanted to preserve their fertility. All three permissions were granted on the medical grounds, two patients made this request prior to starting chemotherapy, the other patient prior to undergoing a gynaecological intervention. Out of the three permission granted, all three had successful oocyte retrieval and cryopreservation.

In the last quarter of 2018, the Authority received a request for transfer of cryopreserved gametes from Malta to Cyprus. The Authority informed the licensed clinic that permission will only be granted if the clinic abides by all regulations in place that cover the transfer of gametes between countries. The Authority requested the necessary information to be furnished to the Authority.

1.10. Changes to the Embryo Protection Act and introduction of the Embryo Protection Amendment Act

On the 11th April 2018, Deputy Prime Minister and Minister for Health Hon. Chris Fearne presented the Proposed Bill for amendments to the EPA Act for first reading in Parliament. This was the culmination of extensive fieldwork and input by the Authority's Executive Director, Ms. Simone Attard, as expert in the field. Her input was continuously throughout the Second reading in Parliament attending to all sessions held in Plenary. During the Committee Stage Mrs Attard answered to questions raised by members of Parliament sitting on the Committee as well as queries made by stakeholders and the general public that were allowed to intervene at this stage of Parliamentary discussion.

To this effect an Authority Board Meeting was conveyed so as to explain to members of the Authority Board, the main Changes to the EPA ACT and the Additional Fertilisation Permissions to be Granted by the Embryo Protection Authority, the changes included;

a. The definition of prospective parent / parents has been extended to not only include heterosexual couples, but this is now extended to all prospective parents who have reached aged of majority irrespective of gender or sexual orientation, thus from 1st October 2019 to also include same sex couples and single women.

b. The minimum age for the female prospective parent lowered to 18 from 25 while the maximum age was to remain the same i.e. 42 years if using own oocytes. If the female prospective parent was opting for donated oocytes, age

threshold was to be increased to 48. Women who use their own oocytes and opt out of embryo cryopreservation and who had their oocytes retrieved after age 35 will have a maximum age of 42. However all women who opt to have resultant cryopreserved embryos, age was to be increased to 48 to have embryos transferred only.

c. Number of cycles – Women opting not to have embryos cryopreserved will be entitled to current number of cycles offered on the NHS. Women/couples who have embryos cryopreserved will be given enough cycles so they can make use of the cryopreserved embryos with two transferred in each cycle. This measure will also apply if the previous IVF was successful and have a child in the same relationship.

d. Prospective parents who up to the date of coming into force of the Amendment Act, had cryopreserved embryos abroad are entitled to transfer the embryos two at a time to Malta and be used in a cycle, not for storage only.

e. If prospective parent/s do not opt to cryopreserve embryos, only two oocytes can be fertilised and transferred in each cycle. No permission to be requested by the licensed clinics to the Authority to fertilise 3 oocytes as allowed in Parent Act.

f. Prospective parent/s who consent to embryo cryopreservation and potential embryo donation, will still be allowed to fertilise two eggs but a request to the EPA Authority can be made to fertilise up to a maximum of 5 oocytes in each cycle. If prospective parent/s have cryopreserved embryos from previous ART cycles no request to fertilise further eggs in subsequent cycle can be made until the cryopreserved embryos are utilised. A separate protocol/criteria for this clause to be prepared which will get prior approval from Parliamentary Health Committee prior to this article coming into force.

g. Donation of sperm, oocytes and embryos will be allowed. Donors of gametes both male and female have to be 18 up to 35 years of age. No post humous retrieval of oocytes or sperm can be made. However where gametes were donated prior to the donors death and s/he had consented to use after death these can still be donated. Donation of gametes to be a single donation providing offspring or siblings to one prospective parent/s only.

h. Anonymous donation as was proposed in Bill, has been removed instead the Finland model will be used where donor and recipient will never know identity of each other, however child born of donation (either gamete or embryo) can enquire with the EPA Authority once attaining majority (18) to have medical records and identity records of the donor. The Authority is obliged to give the medical records beforehand of the donor only in cases of medical emergencies. The Authority is also obliged to inform the recipients or the child on attaining majority if it comes to her knowledge of any serious ailments of the donor after the donation had been made. Records of donation have to be kept for 110 years.

i. Donations to be totally altruistic no compensation to be paid for sperm donation, oocytes donors will be reimbursed with the stimulation expenses.

j. EPA Authority to prepare information (booklets etc) for the children born from donated gametes/embryos and also other information for the persons who wish to donate gametes, prior to giving consent for donation.

k. All clinics to keep registers for each separate procedure (IUI, IVF, ICSI) and of all cryopreservation whether of gametes or embryos and of any embryo donation or adoption. All registers shall be confidential and sent to the EPA Authority immediately.

l. Government is proposing that all couples who were registered with the MDH ART Clinic and made use of all their cycles but had no live birth prior to this ACT coming into force will be given another chance within age parameters, if from this extra cycle cryopreserved embryos will result than additional cycles will be given until all embryos are transferred.

m. The EPA Authority will take for adoption purposes those cryopreserved embryos in the following situations:

- Death of the mother
- If the female prospective parent exceeds the maximum age of 48 and still has cryopreserved embryos.
- If prospective parent/s do not renew the cryopreservation contract with the licensed clinic (contract to be prior approved by EPA Authority to be for 5 years which can be renewed for further periods of 5 years each).
- The prospective parent refuses to have the embryo implanted in the womb.
- Prospective parents Jointly decide that their family is now complete and wish to give their embryos for adoption this can be done prior to age 48.

n. Process of adoption of embryos to be made through the Adoption Board under the Adoptions Administration Act and EPA Authority.

o. IVF special vacation leave to be extended also to oocytes donors.

p. Surrogacy has been removed completely from the proposed Bill, this is to be presented in a separate Bill to Parliament.

The new Amendment Act was enacted on the 21st June 2018 and came into force on the 1st October 2018 as per Legal Notice LN 313/2018.

The Protocol for Additional Fertilisation Requests (AFR) was established in writing by the Authority compiling all criteria and methodology for the application to grant more than two oocytes up to a maximum of five oocytes to be fertilised and consequently permission for embryo cryopreservation. The AFR Protocol was presented to the Parliamentary Health Committee on the 13th September 2018 and was unanimously approved on same day.

The MDH ART Clinic started offering additional fertilisations up to maximum five oocytes and embryo cryopreservation as from the October 2018 cycle.

St James Assisted Conception Unit informed the Authority that they will not be offering embryo cryopreservation in the October 2018 cycles, thus additional fertilisation were not approved by the Authority and all couples had permission to fertilise two oocytes only.

1.11. ART Prioritization Committee

The Ministry for Health considers the fact that parent / parents requiring IVF cannot be waitlisted on a *first come-first served* basis. To this effect, the Ministry appointed an ART (Assisted Reproductive Technology) Prioritization Committee with the aim of objectively ranking in order of precedence the couples who are seeking assistance at the ART Clinic at Mater Dei Hospital (MDH). Each clinical case is considered individually and priority of treatment is given to couples where female age is an issue, since delays in providing an opportunity for treatment may make the couple ineligible for future treatment.

Other factors, such as AMH levels, semen parameters, paternal age, duration of infertility, previous failed IVF/ICSI attempts, recurrent miscarriages, etc., are also taken into account. During 2018 the Authority was represented on this Committee by its Executive Director Ms. Simone Attard and by Profs. Victor Grech as member.

In view of the fact that new cases are registered at Mater Dei Hospital every week, this Committee met on a monthly basis to decide which of these couples requires prioritization for treatment. Four reports were consequently issued showing a total of 216 couples that had been reviewed by the ART Prioritisation Committee during 2018. Four couples were deemed ineligible for the prioritisation process.

1.12. Inspections

The Authority, from time to time makes the necessary inspections so as to ensure that there are no infringements of the provisions of the Act or the Regulations, or of the Protocol which the Authority is entitled to enforce. These inspections are held in order to make certain that the standards of best practice are being respected and implemented, that the documented system which ensures the identification of all gametes and embryos from procurement to use is in place, and that the storage and consignment of gametes from one centre to another is verified against Standards of Practice (SOPs) and third party agreements, as required in the EU Directive.

In 2018, inspections together with the Superintendent of Public Health (SPH) were carried out at the Assisted Conception Unit in St James Hospital. These were in conformity with the legislative requirements for periodic re-inspection before renewing the licence. The inspection at the Assisted Conception Unit in St James Hospital was observed by the Infertility Inspector of EPA. During same inspection a separate meeting was held with the Lab Director to explain the various new consent forms to be filed by the licensed clinic to conform with the changes in the Act. During the inspection, various deficiencies were noted. The Authority thus advised the Superintendent Public Health to refrain from issuing a full licence, but rather issue a temporary licence until all deficiencies where rectified. To this effect, the Assisted Conception Unit in St James Hospital was issued with a renewal licence valid only for six months up till 30th June 2019. No inspection for renewal of licence was made at the MDH ART Clinic as licence is valid up to 30th June 2019.

1.13. Other work by the Authority

Apart from the normal processing of all applications for treatment, requests for additional fertilizations, and the storage of gametes (a detailed report is given in the second part of this report), the Authority was in continuous communication with the Ministry for Health in order to provide the relevant information in answer to the several Parliamentary Questions (PQs) repeatedly made on the ART procedures offered on the NHS, and the Eligibility Criteria as established in the Embryo Protection Authority's Protocol.

Work was also ongoing about the new IT solution that will link all licensed clinics to the Authority. The Authority sought and obtained permission from the Central Procurement and Supplies Unit to outsource the preparation process of the tender documents for the issuance of the second tender for the procurement and implementation of a new IT system based on the Technical Specifications Report prepared in 2017 that will link the Authority with all licensed clinics both private and public so all documentation can be filed on-line thus enabling the Authority to have real time data. The Authority followed closely developments and subsequently awaited publication of such document by the Contracts Department. Publication was made in the last quarter of 2018.

The Embryo Protection Authority, through its Executive Director, during 2018 was also in continuous discussion with the Ministry for the Family and Social Solidarity and the Ministry for Social Dialogue, Consumer Affairs and Civil Liberties, to update the Legal Notice was issued on the 31st May 2017, granting Special Leave for Medically Assisted Procreation to now be in line with the New Amendment Act.

In addition to the monitoring of ART services given to patients by the licensed Clinics, the Authority also supervises the storage of gametes. A Gamete Storage Inventory (Dewar mapping) which stretches back to the date of first cryopreservations (July 2013), is kept by the Authority. This serves to ensure that storage of gametes is being properly documented so as to guarantee full traceability.

Together with the SPH, the EPA strives to make sure that each licensed Clinic adopts a Quality Management System that is in line with the EU Directives and Human Tissues and Cells Local Legislations related to the ART services.

During 2018, the Authority was also requested to give its feedback regarding the launch of the Consultation on Transgender Medical Services. This was being brought to the attention of the Authority as prior to transgender persons starting hormone therapy, a request will be made to EPA Authority to authorise cryopreservation of gametes to preserve fertility. The Executive Director attended to several meetings on the subject.

One of the functions of the EPA is to see that all prospective parents receive clinical counselling. On the 18th October 2018, the Authority was informed that the British Infertility Counsellors Association (BICA) Course for Counsellors working in IVF licensed clinics, as requested by EPA Protocol, was awarded Accreditation by the Counselling and Psycho Therapy Central Awarding Body (CPCAB) which is the only Awarding Body to specialise in Counselling.

In view of the fact that the Authority processes personal data, in 2017 it took the necessary measures to be in conformity with the Data Protection Act, and duly registered its operations with the Commissioner for Data Protection and also appointed a Data Protection Officer to take care of Data Protection issues. To this effect with the introduction of the New Amendment Act, the Authority

underwent the exercise of Data Protection Impact Assessment for all new processes that were being introduced.

The Authority's website was launched on the Ministry for Health's portal, though continuous collaboration with the Information Management Unit of the Ministry for Health in 2017. The website contains the Authority's Mission Statement, details about the Entity's Corporate Identity, Board Members and Executive Administration together with an Organisation Chart. All publications of the Authority have also been uploaded and these include: The Act and Legal Notices, EU Directives, Authority's Protocol and all Annual Reports issued to date. During 2018, the website was being continuously amended and uploaded with the new changes that came into effect. The website can be accessed on www.epa.gov.mt .

Pursuant to the EPA Regulations of 2015, the Authority is taking the necessary measures towards becoming fully autonomous.

The Deputy Prime Minister and Minister for Health, Hon. Chris Fearne on the 13th March 2018, laid on the Table of the House of Representatives EPA's Audited Accounts for 2017 and Financial Estimates for 2018, together with the Authority's Annual Report for 2017. A Parliamentary debate on the Authority's finances was held in one sitting on the 4th of June 2018.

FERTILITY TREATMENTS IN MALTA FOR 2018 – TRENDS AND FIGURES

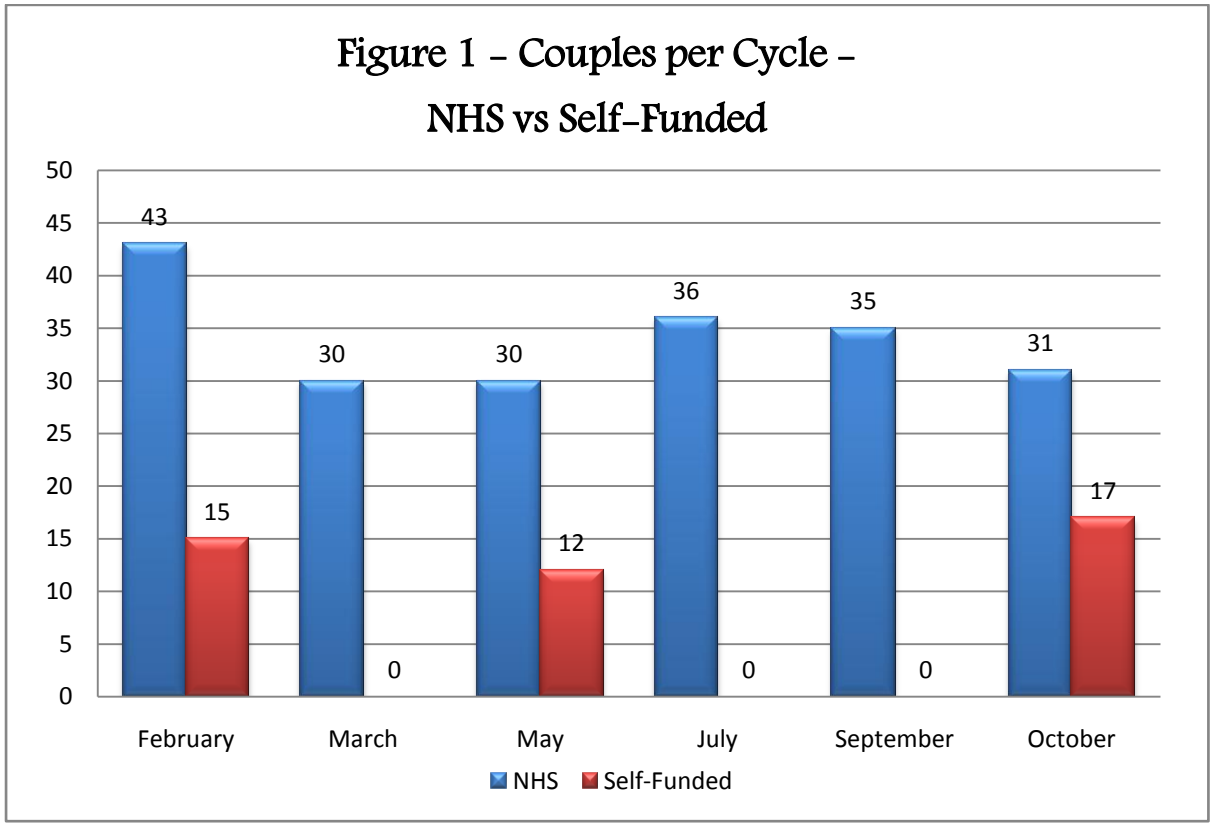
In line with LN32 of 2015 and the Embryo Protection Authority's Protocol which has been prepared in accordance with the Embryo Protection Act 2012, clinics in both the private and public sector are bound to provide the Authority with accurate data about their activities. This data is held on the Authority's Register of ART Procedures and the accuracy of this report is based on the information provided by the Clinics as at 31st January 2019.

2. CYCLES PERFORMED

Throughout 2018, the Authority has received a total of 249 applications from clinics in both the private and public sector. All applications have been approved and thus 249 cycles were carried out, these were divided into 3 patients having a cycle where oocytes were retrieved and cryopreserved only on prior approval by the Authority due to medical reasons so no IVF procedure was carried out, the other 246 underwent an IVF/ICSI procedure, two of which underwent embryo transfer only of embryos that were cryopreserved under force-majeure.

Two hundred and five (205) procedures have been carried out at the ART clinic in Mater Dei Hospital (MDH), and forty four (44) cycles were performed

in the private sector at the Assisted Conception Unit in St James Hospital (Figure 1).



The number of ART procedures carried out in Malta in 2018 decreased by 19.42% over the previous year, which is mainly attributed to the fact that less procedures were being carried out at both licensed clinics. There was a major drop of 41.33% in procedures carried out in the private clinic.

2.1. First Time/Repeated Cycles

Out of the 246 cycles carried out, 50.4% of couples (124 couples) were undergoing the IVF/ICSI procedure for the first time. There were 29.7% of couples (73 couples) who were undergoing IVF/ICSI for the second time,

12.6% of couples (31 couples) for the third time, 4.1% of couples (10 couples) were undergoing their fourth attempt, 1.6% of couples (4 couples) were undergoing their fifth attempt, while the remaining 1.6% of couples (4 couples) had undergone their sixth attempt (Figures 2 and 3).

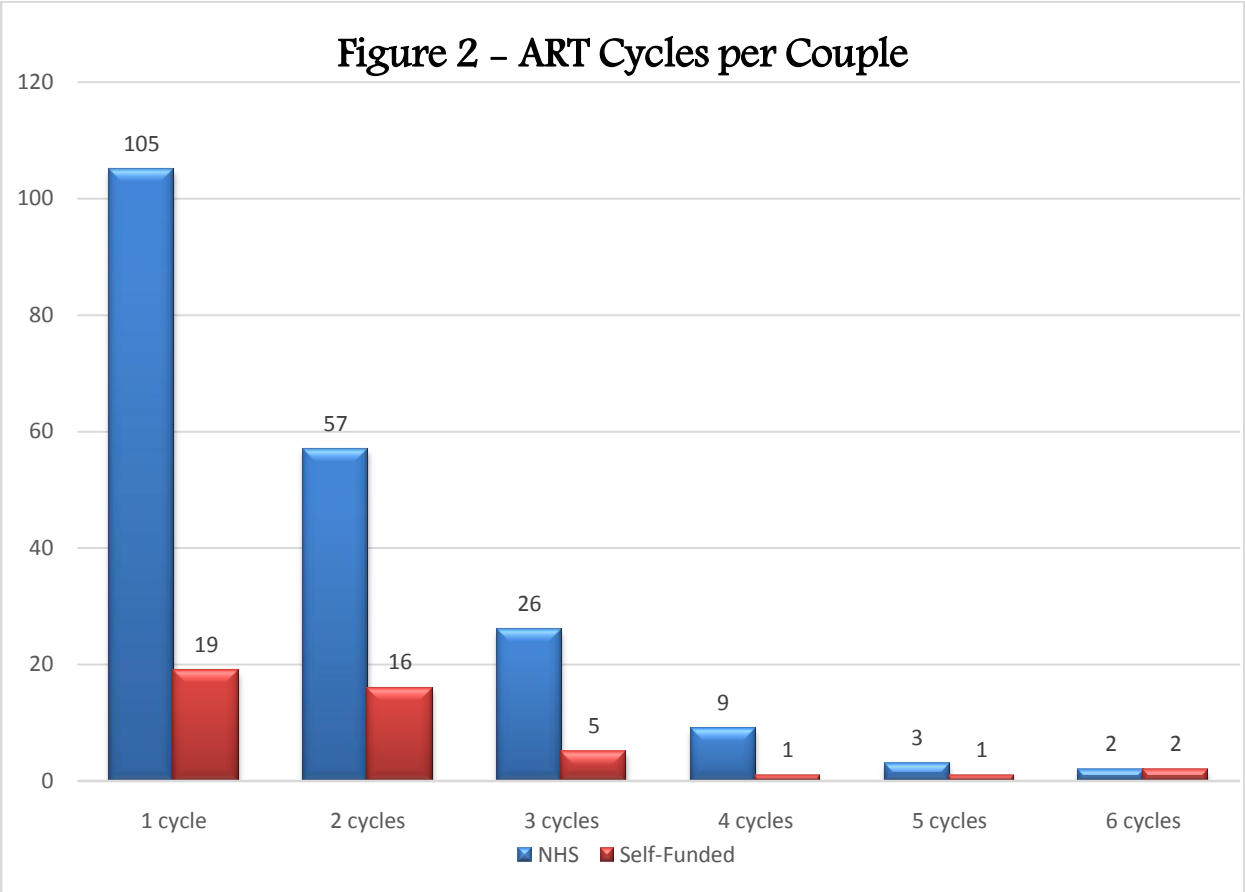
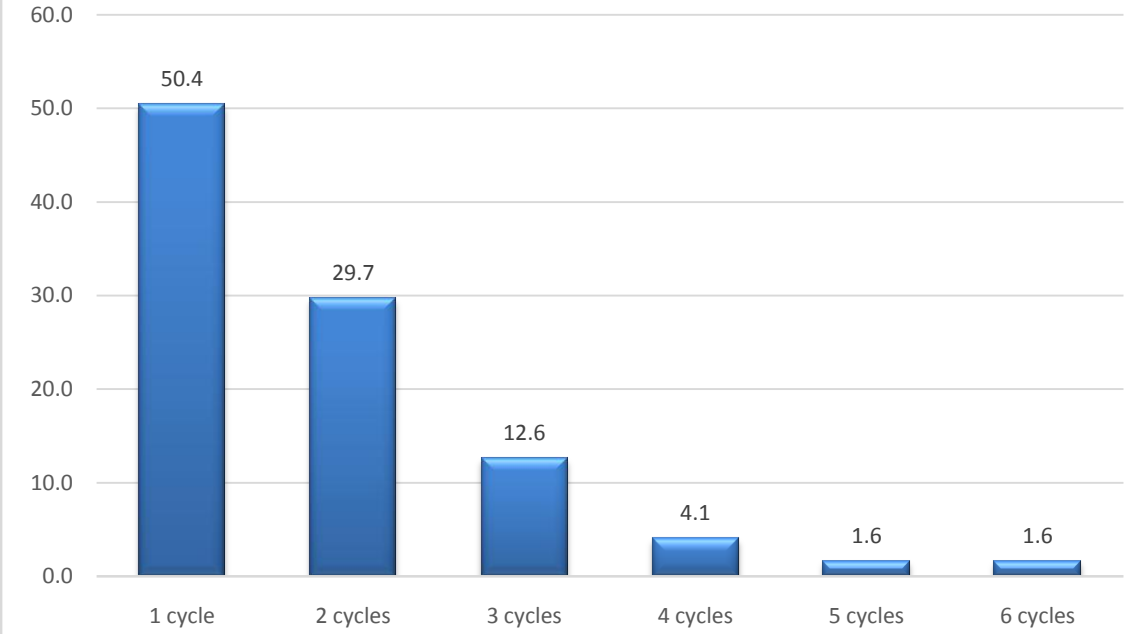
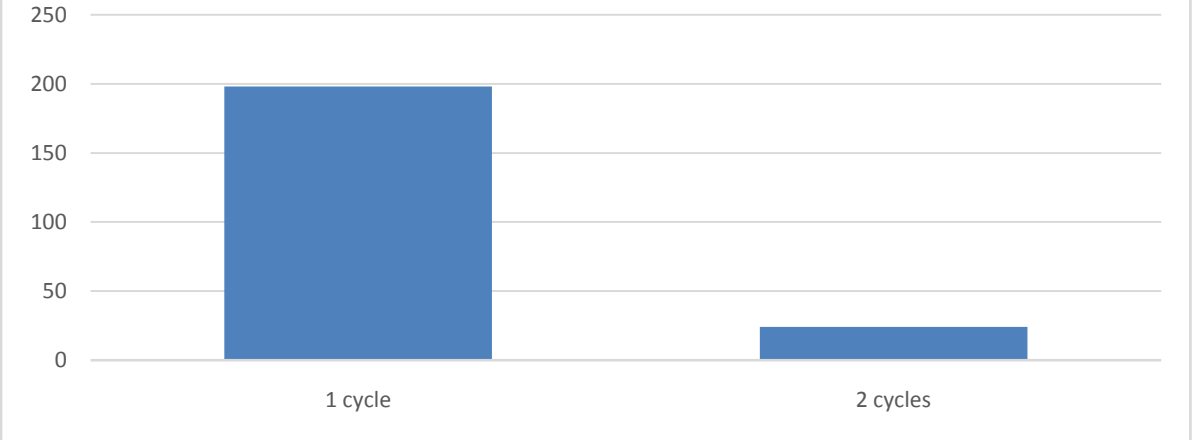


Figure 3 – ART Cycles per Couple (% of total couples)



During the same calendar year in 2018, there were 198 couples who had undergone a single cycle and 24 couples who had undergone 2 cycles during the same calendar year. Thus, these 246 procedures were undertaken by 222 couples (Figure 4).

Figure 4 – Cycles per Couple in same Calendar Year



3. DEMOGRAPHICS

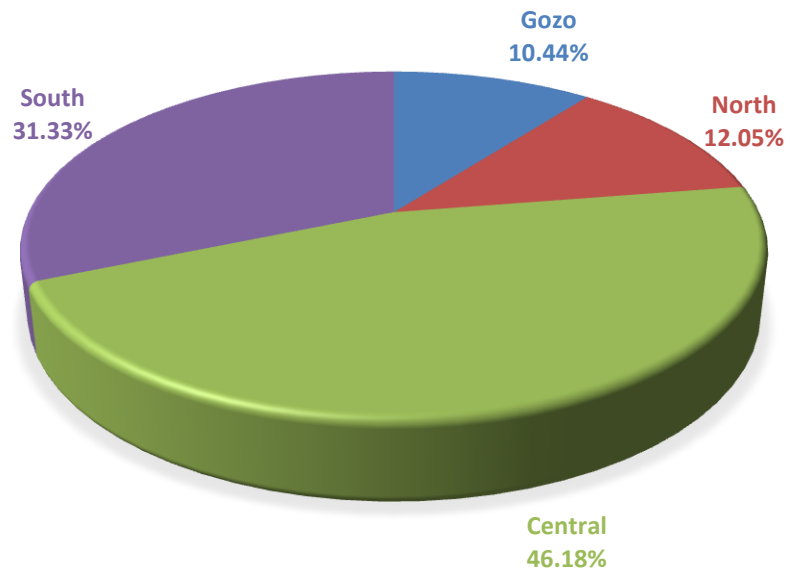
3.1. Nationality

All of the 246 cycles performed this year were undertaken by Maltese Residents. There were no foreign couples (non-Residents) who came to Malta specifically to perform the IVF/ICSI procedure in the private sector. This is consistent with last year wherein the private sector had reported no Medical Tourism in the Fertility sector.

3.2. Regions

As reported in previous years, the overall majority of couples 46.18% (115 couples) who had undergone IVF/ICSI procedures in 2018 reside in Central Malta, followed by 31.33% (78 couples) who reside in Southern areas of Malta, 12.05% (30 couples) reside in the Northern part of the island, while the remaining 10.44% (23 couples) reside in Gozo. These figures show a slight decrease in couples from the Southern part over last year's figures, this was reflected in an increase by the couples residing in the Northern part and from Gozo (Figure 5).

Figure 5 – Distribution By Region – Overall



Worth nothing is the fact that when it comes to self-funded treatments, the majority of couples 40.91%, still come from the Central areas of Malta followed by 22.73% of couples who reside in the Southern part of the island, however both the Gozitan couples 18.18% and the couples residing in the Northern part of Malta also 18.18% chose to self-fund their treatment. This contrasts with the 8.78% of Gozitan couples and 10.73% of the couples residing in the Northern part of Malta that chose to undergo their treatment on the NHS (Figures 6, 7 and 8).

Figure 6 – Distribution by Region – NHS

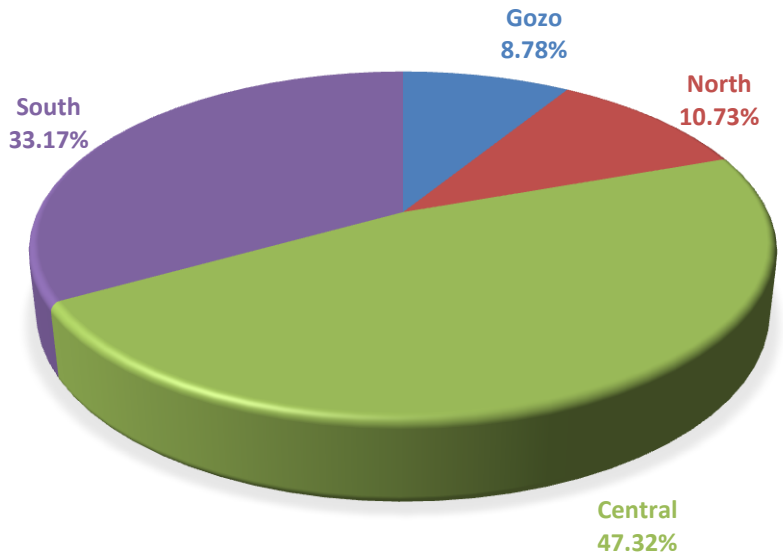
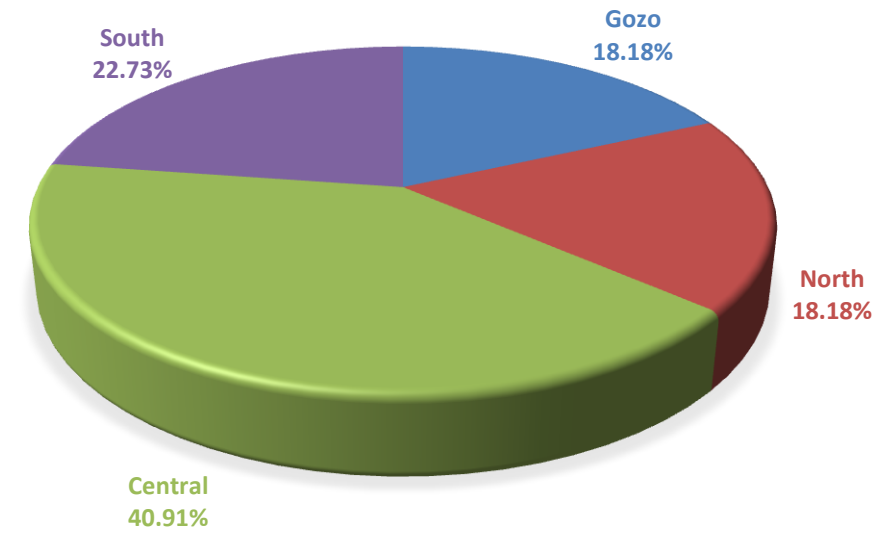
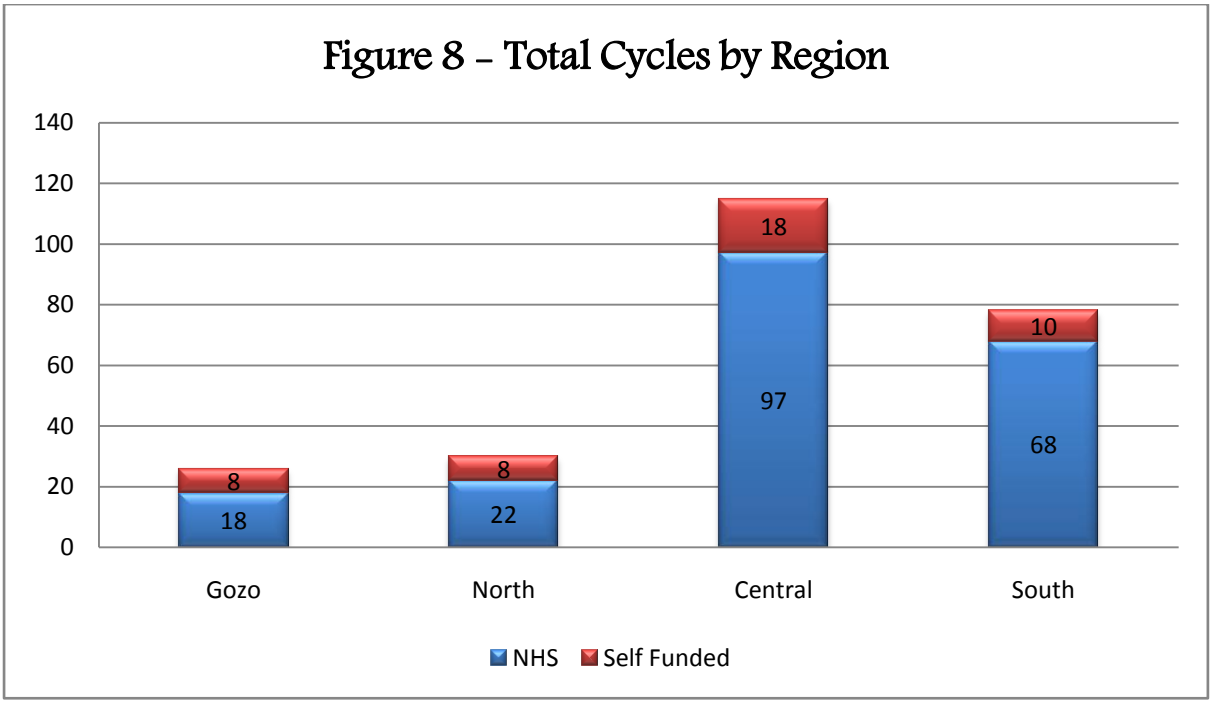


Figure 7 – Distribution by Region – Self-Funded





In 2018, only 15% of couples (19 couples) suffering from primary infertility who were undergoing their *first-ever* IVF/ICSI attempt, opted to self-fund their treatment, despite being eligible for treatment on the NHS (Figure 9). Figures 10 to 13 show the couples' funding preference per region.

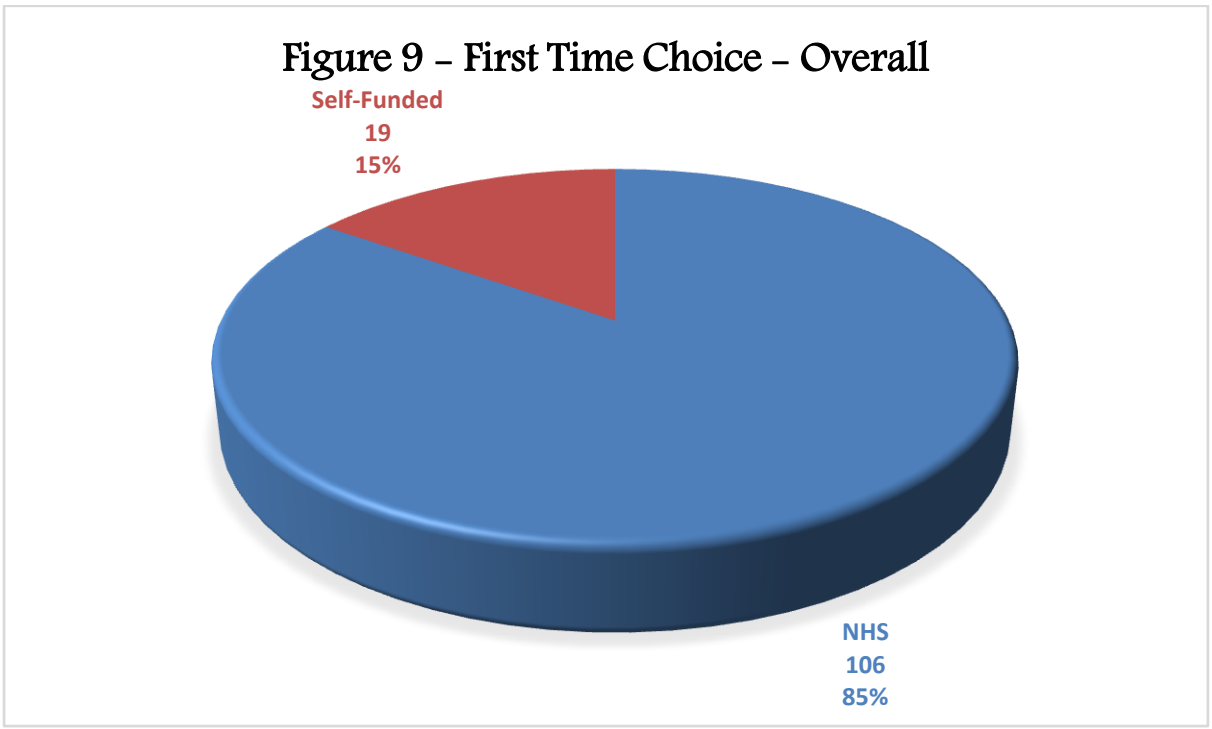


Figure 10 – First Time Choice – Gozo

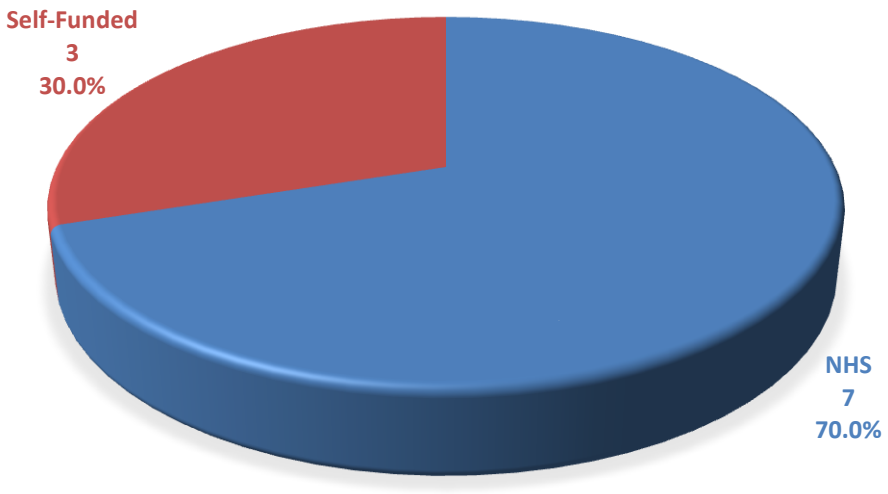


Figure 11 – First Time Choice – North

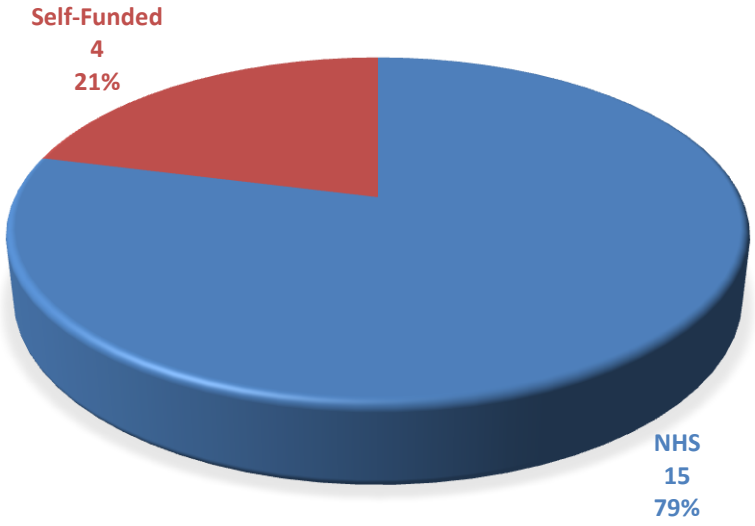


Figure 12 – First Time Choice – Central

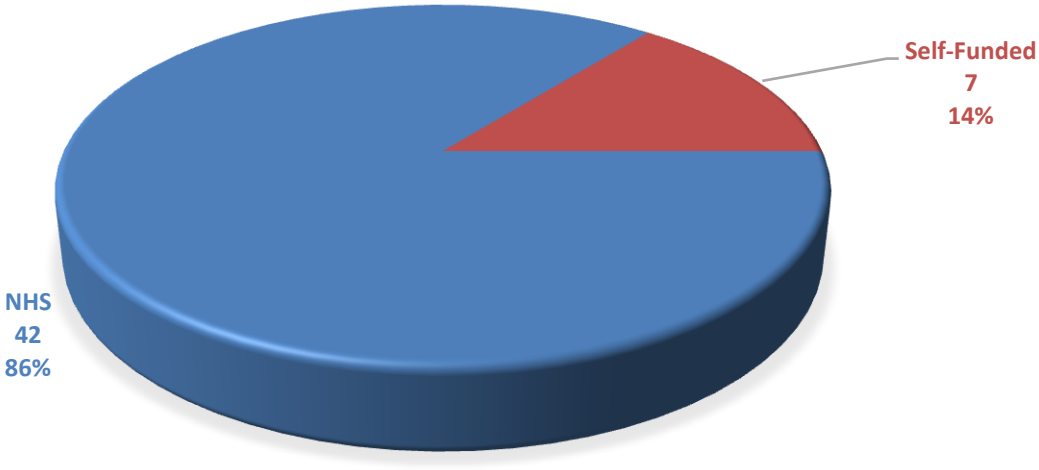
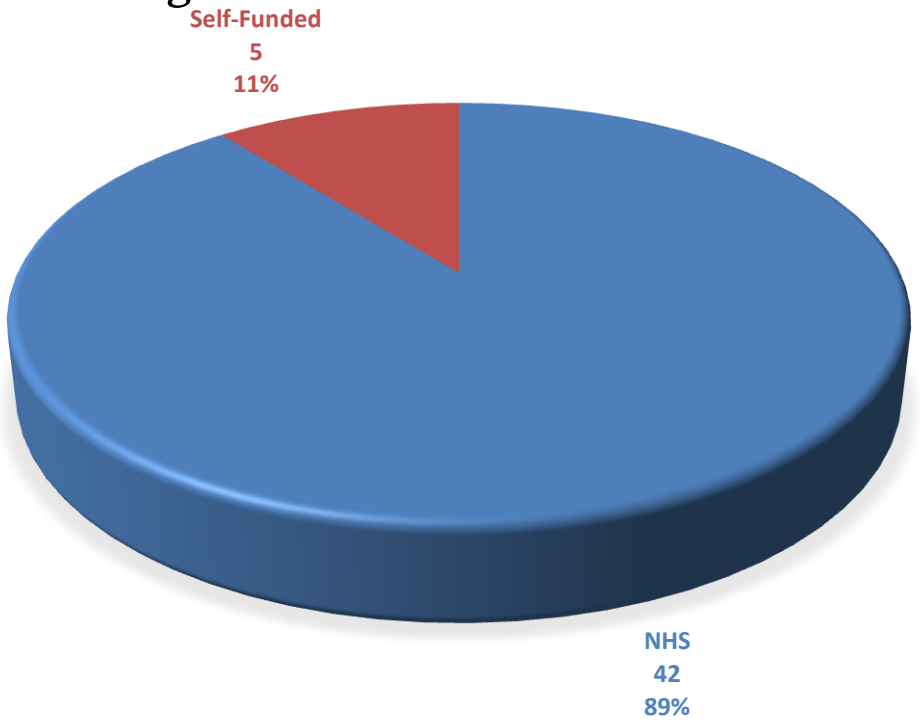


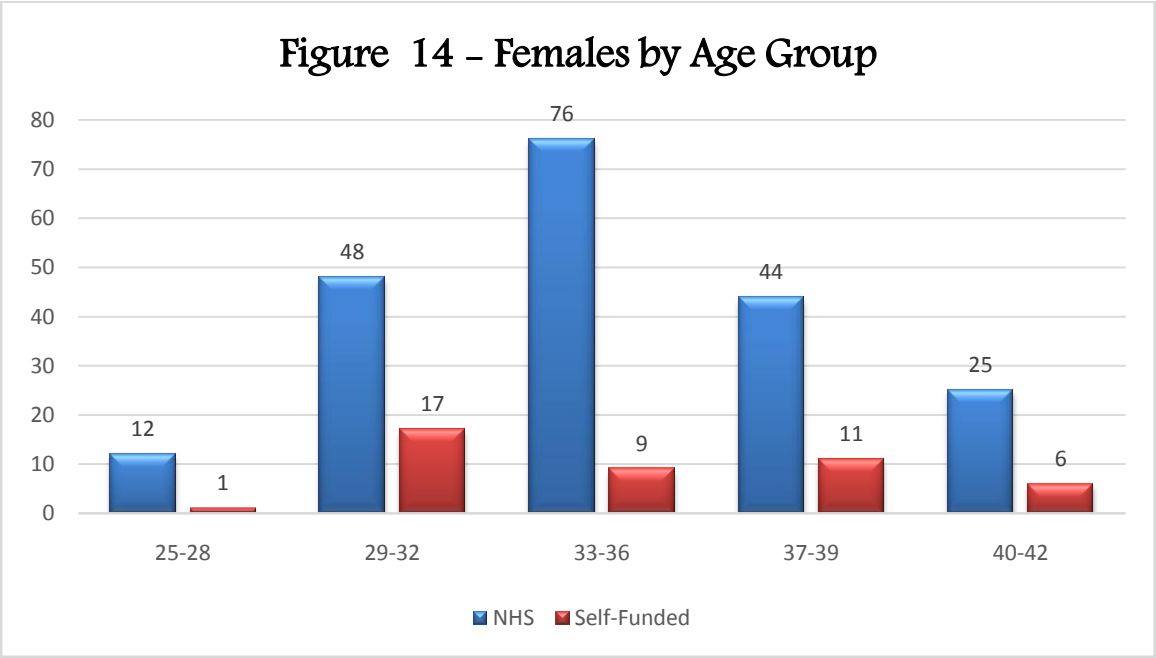
Figure 13 – First Time Choice – South



3.3. Maternal Age

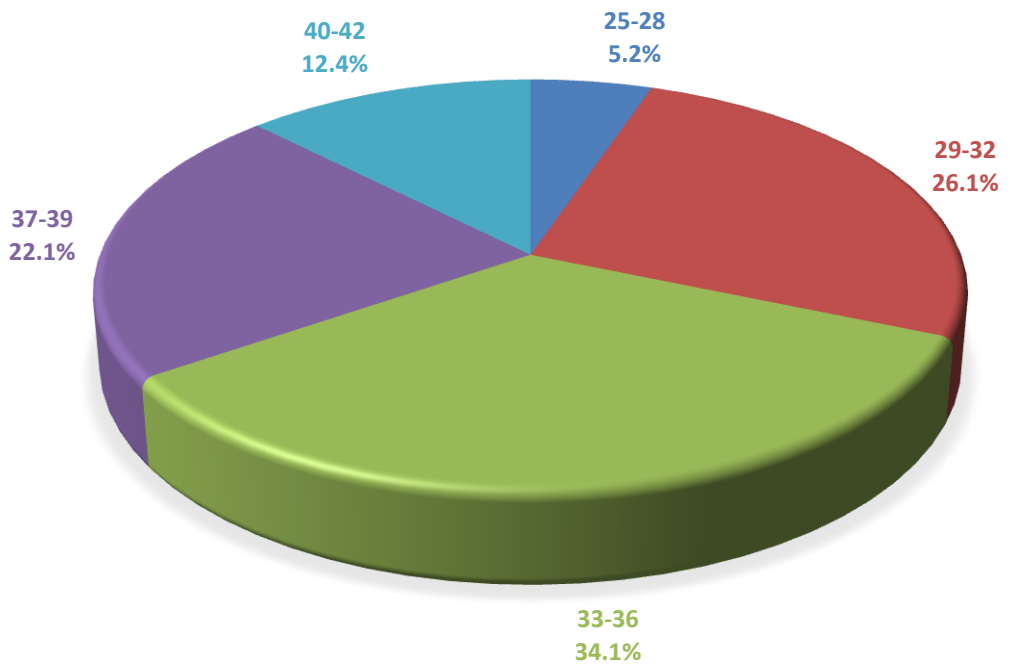
In line with the Embryo Protection Authority's Protocol, in Malta, only women falling within the stipulated age bracket of 25 and 42 are eligible for IVF/ICSI procedures, if not making use of donated oocytes. Throughout 2018, all procedures were carried out using own gametes. There has been a distribution of procedures across all age brackets, as can be noted from the chart hereunder (Figure 14).

Figure 14 – Females by Age Group



As for the past four years, the largest number of female patients, 85 females (34.1%) undertaking IVF/ICSI procedures throughout 2018 was aged between 33 and 36. The second largest age group was for female patients aged 29-32, 65 females (26.1%), while 55 females (22.1%) were in the 37-39 year old bracket. There were 31 female patients (12.4%) aged 40-42, while the remaining 13 female patients (5.2%) were aged between 25 and 18 years. (Figure 15).

Figure 15 – Females by Age Group (%)

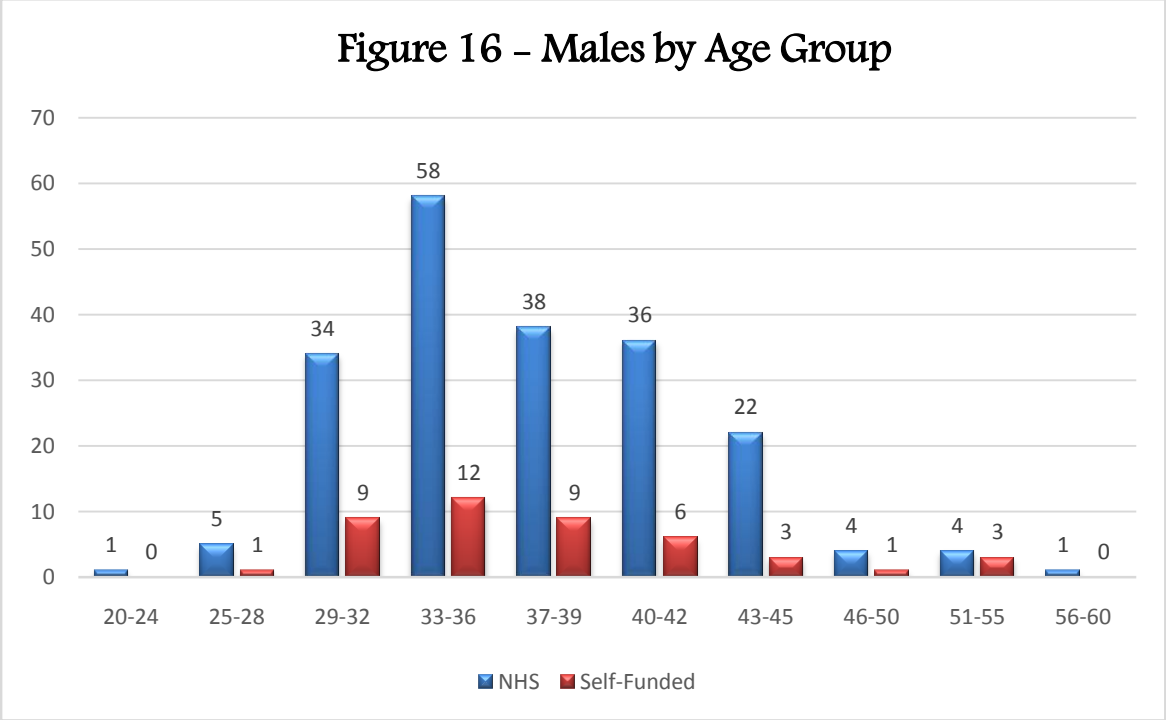


Noteworthy is the fact that in 2018 there has been a drop of 3.6% in the age group of females aged between 33 and 36 years and a slight drop in the age group of women aged between 37 and 39.

Conversely the age group of women aged between 40 and 42 registered an increase of 2.9%. The other age groups registered a slight increase in females who had undergone IVF/ ICSI procedure.

3.4. Paternal Age

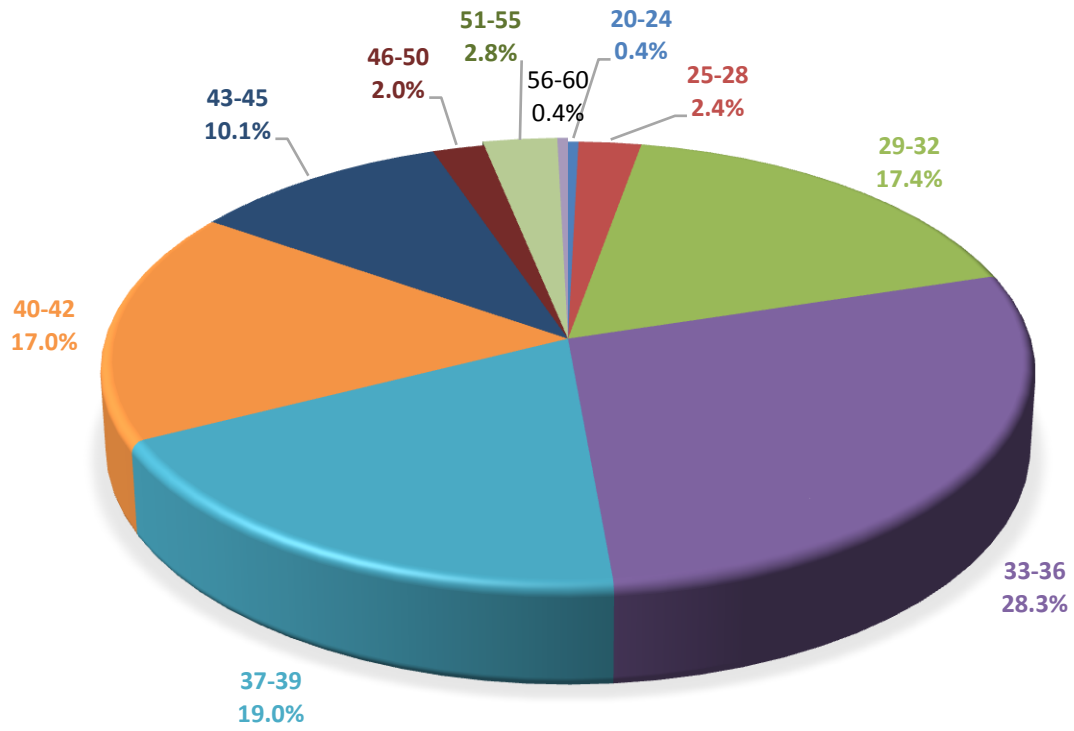
As with the female patients, the largest number of male patients, 70 males (28.3%) undergoing procedures was in the 33-36 year old bracket, while 47 males (19%) were aged between 37 and 39. The third largest age group (17.4%) consisted of 43 males aged 29-32. Following closely at (17%) were 42 males in the 40-42 year old bracket. The male age group of males aged between 43-45 years was the fifth largest age group with 25 males (10.1%) while 13 patients (5.2%) of male patients were aged 46 years and over. The remaining 7 males (2.8%) of males were under the age of 29. (Figures 16 and 17).



Noteworthy is the fact that while in 2017 the oldest male was in the 51-55 age bracket, in 2018 the oldest male was in the 56-60 age bracket. In 2018 there was an increase in the age group of males aged more than 51 years. It is

also good to note that whilst the youngest male undergoing IVF/ICSI procedure last year was 25years old, in 2018 the youngest male is reported to be only 24 years old.

Figure 17 – Males by Age Group (%)

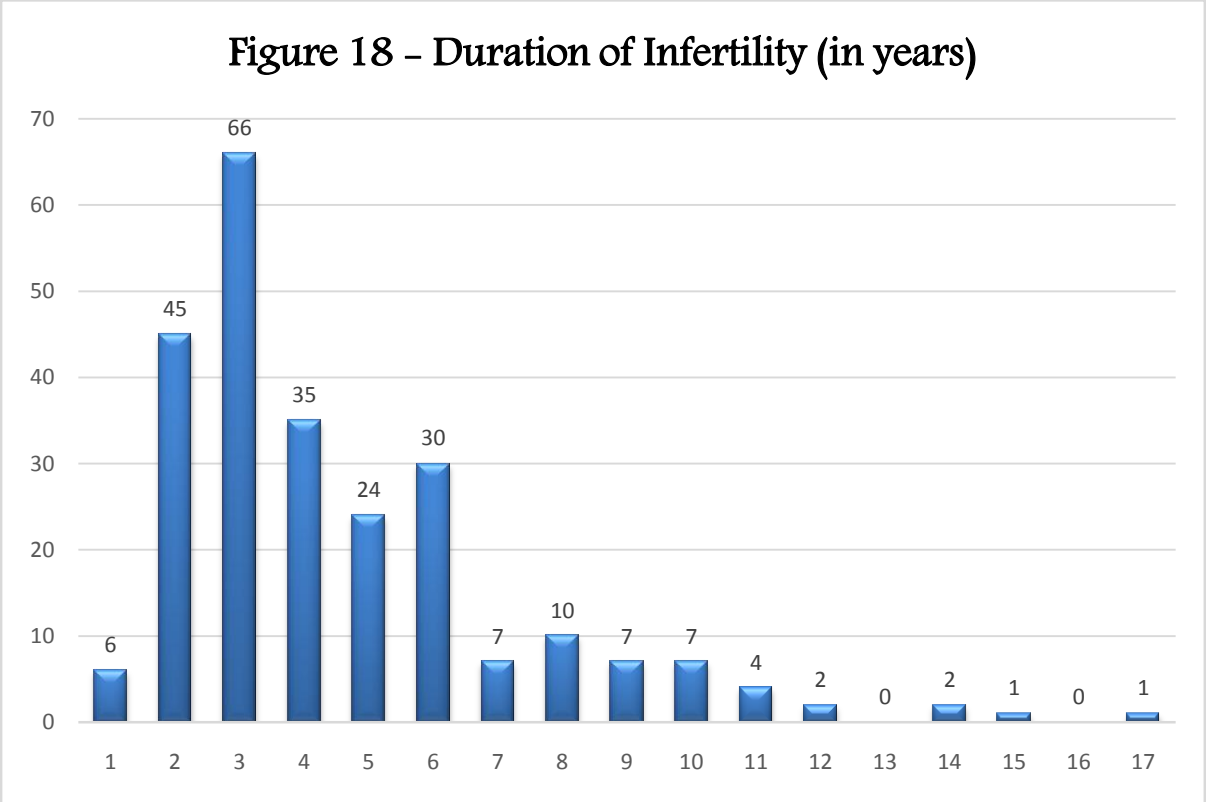


4. INFERTILITY

4.1. Duration of Infertility

There was a significant amount of variability in the reported duration of infertility amid couples undertaking procedures in 2018, with the minimum reported duration being that of one year, up to a maximum of 17 years. Noteworthy to note is that in 2017, the maximum duration was reported to be 14 years. All the six (6) couples who reported to be infertile for one year only, had undergone treatment at the private sector and self-funded their treatment. Forty five (45) couples reported to be infertile for two years, sixty six (66) couples for 3 years, thirty five (35) couples for 4 years, twenty four (24) couples for 5 years, while sixty one (61) couples reported to be infertile between 6 and 10 years. Only ten (10) couples who had undergone treatment reported being infertile between 11 and 17 years. (Figure 18).

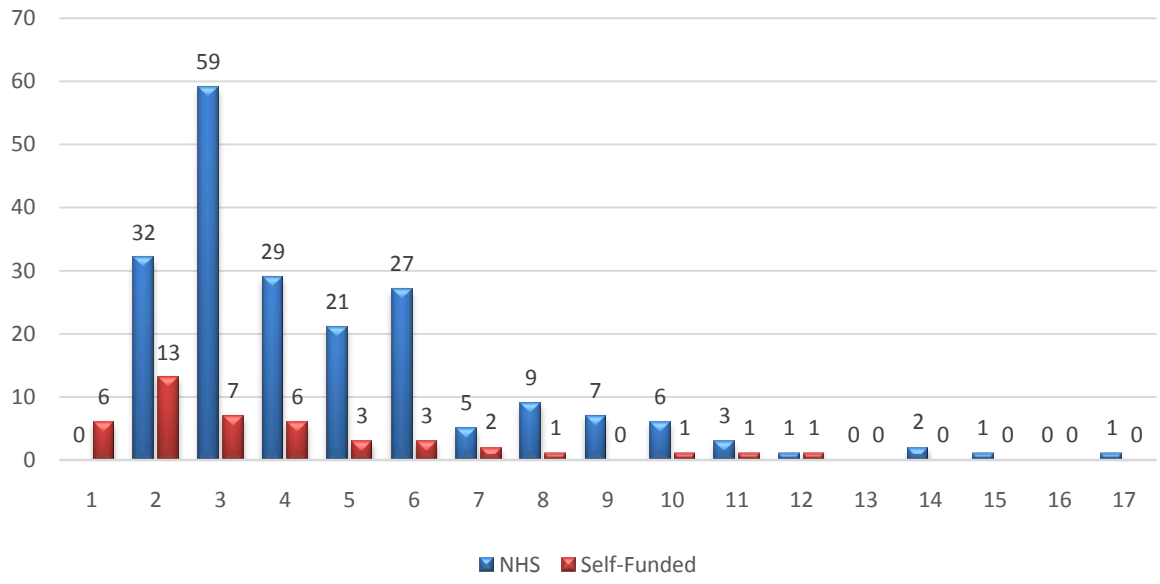
Figure 18 – Duration of Infertility (in years)



To be eligible for treatment on the NHS, a couple must declare being infertile for at least two years. In fact, 13.6% of couples who self-funded their treatment declared less than 2 years of infertility. The majority of couples (59.1%) self-funding their treatment have reportedly been infertile for 2 to 4 years, while the remaining 27.3% have been infertile for 5 years or more.

Similarly, the majority of couples (59.1%) who applied to undergo IVF/ICSI treatment on the NHS declared being infertile for 2-4 years. Forty eight (48) couples, or 23.7%, have declared being infertile for 5-6 years, while the remaining thirty five (35) couples (17.2%) have been infertile between seven and seventeen years. (Figure 19).

Figure 19 - Duration of Infertility (in years)
NHS vs Self Funded



Noteworthy is the fact that 141 couples (69.46%) of total couples undergoing treatment on the NHS reported to have been infertile for 5 years. This shows an increase of 1.77% over the previous year, wherein 67.69% of the couples had been reported in 2017. This may be explained by the fact that since the service has been offered for free by the Government, it is much easier for couples to resort to IVF/ICSI earlier, at a younger age. In the figures quoted above the two women undergoing oocytes retrieval only, prior to receiving chemotherapy have not been included.

4.2. Classification of Infertility

IVF/ICSI procedures are offered free of charge by the Government to couples who have no children (Primary Infertility), or to those who have children from a previous relationship (Secondary Infertility). The majority of couples, 226 couples (91.5%) who have applied for IVF/ICSI treatment in both the NHS and private sector in 2018 suffered from Primary Infertility, an increase of 8.6% over 2017. Noteworthy is the fact that 14 couples who reported secondary infertility, as they already had a child from the same relationship, self-funded their treatment, as they were not eligible on the NHS, these represent 5.67% of couples undergoing treatment in 2018. (Table 1).

Table 1. Classification of Infertility

Classification of Infertility	NHS	Self-Funded	Total	%
Primary	197	29	226	91.50%
Secondary- Same Relationship	0	14	14	5.67%
Secondary- Previous Relationship-Female	6	1	7	2.83%
Secondary- Previous Relationship-Male	0	0	0	0.00%
Total	203	44	247	

4.3. Indication for Infertility Factors

The Authority gathers data on what the contributing factor of infertility for each couple is. These consist of Female factor only, Male factor only, Female and Male factor, and Idiopathic (unexplained) infertility.

As shown in Figures 20 and 21, the majority of couples (32.8%) undertaking IVF/ICSI procedures suffered from Female factor only infertility. These were followed by couples (29.1%) suffering from Female and Male factor and followed by the couples (24.3%) suffering from Male factor only while the remaining 13.8% suffered from idiopathic infertility.

These figures contrast considerably with those reported in 2017, as the majority of couples in 2017 was reported by the Female and Male factor group, followed by the Female factor only infertility group.

Noteworthy to bring to attention is the fact that in 2018, there was a drastic drop of 27.5% in the group of patients who reported Female and Male factor infertility over the figures reported in 2017. On the other hand in 2018 there was an increase of 6.2% in the Male factor only group and an increase of 9.2% in the idiopathic infertility group over the figures reported in 2017. The major increase reported in 2018, was in the Female factor only group with an increase of 12.1% over figures reported in 2017.

Figure 20 – Indication for Infertility Factors

NHS – Self funded

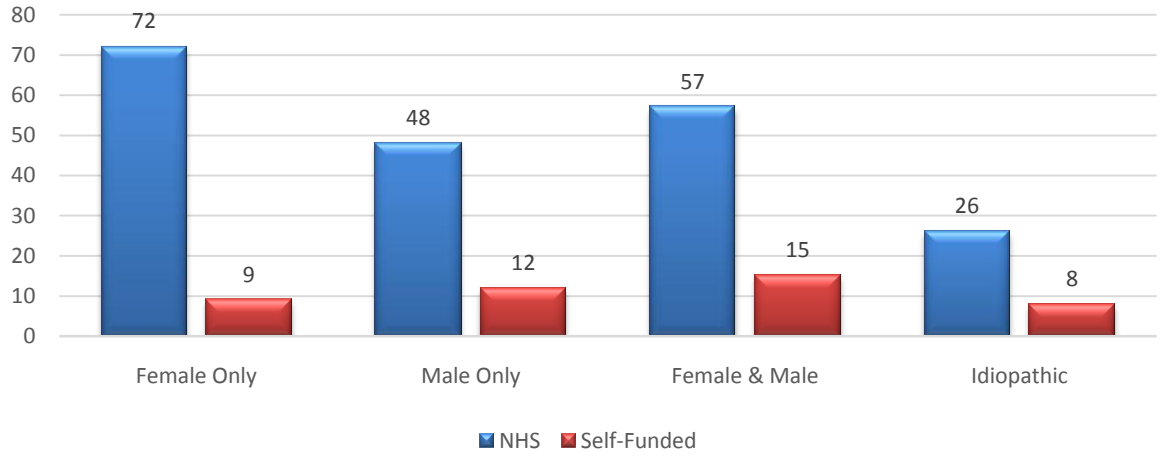
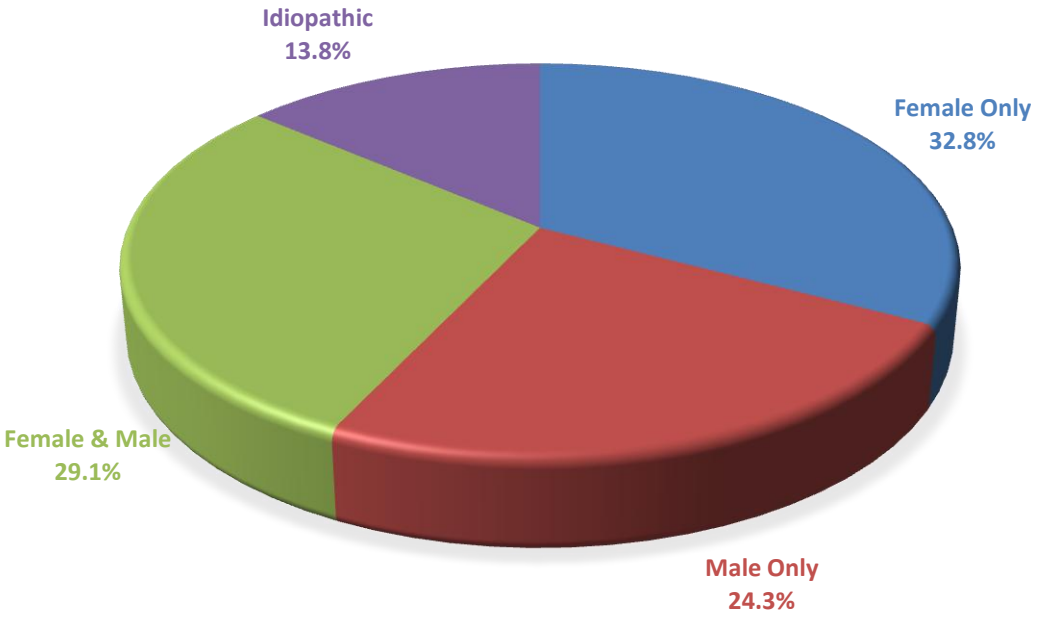


Figure 21 – Indication for Fertility Factors (%)



From those couples suffering from Female factor infertility, the largest group (38.6%) were in the 33-36 year old bracket, this age bracket has been registering increase over the years. The 2018 figures show an increase of 2.4% over figures reported in 2017 and a 6.8% increase over figures reported in 2016. (Figures 22 and 23).

Figure 22 – Female Infertility by Age Group

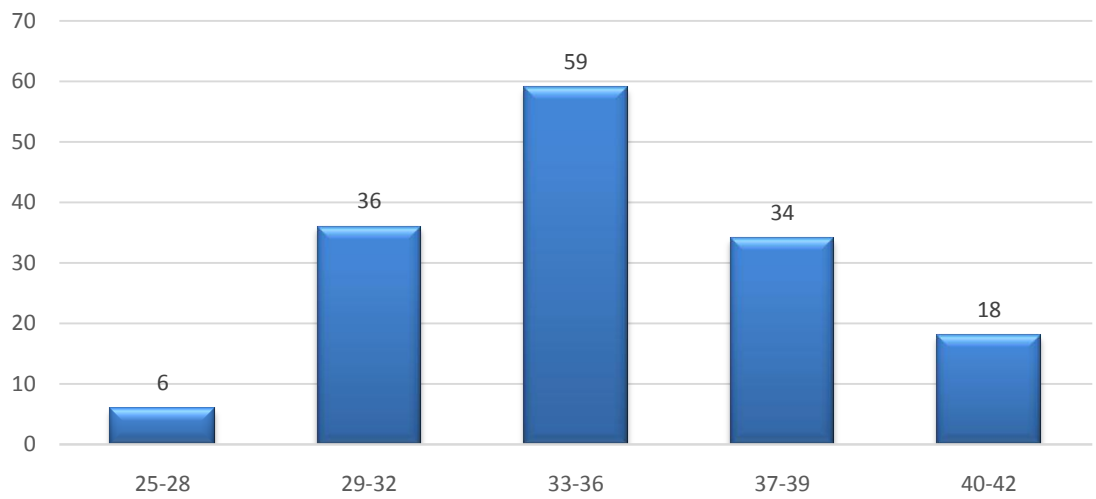
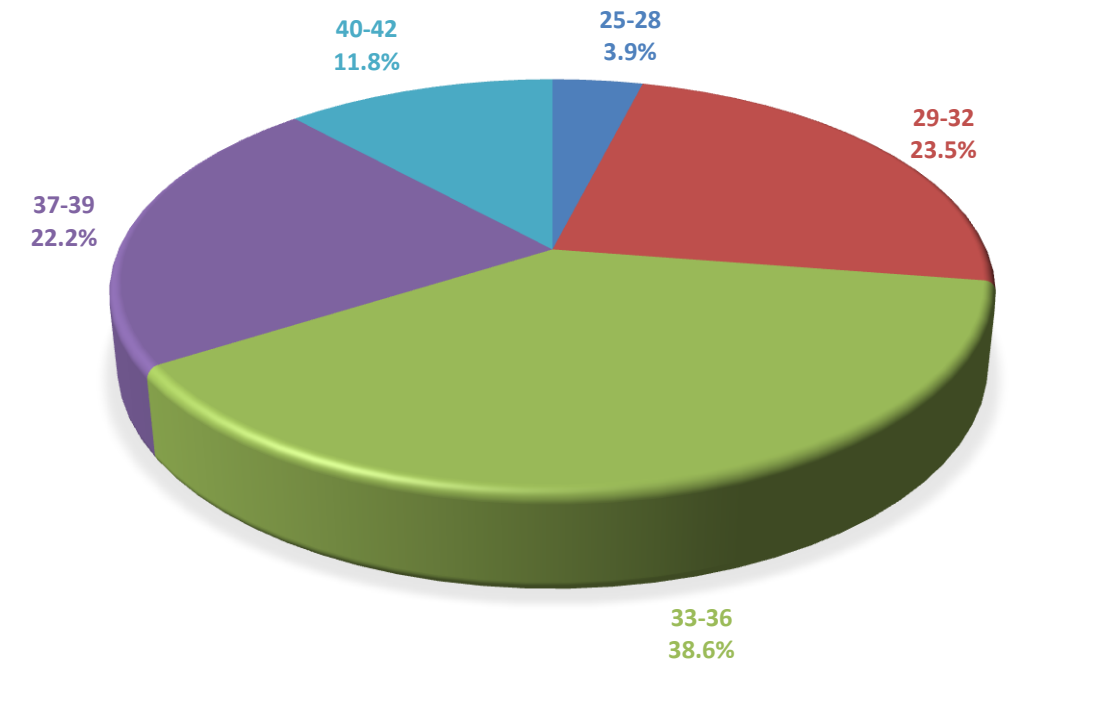


Figure 23 – Female Infertility by Age Group (%)



From those couples suffering from Male factor infertility, the largest group (31.8%) were also reported in the 33-36 year old bracket, followed by males in the 29-32 year old bracket. (Figures 24 and 25).

Figure 24 – Male Infertility by Age Group

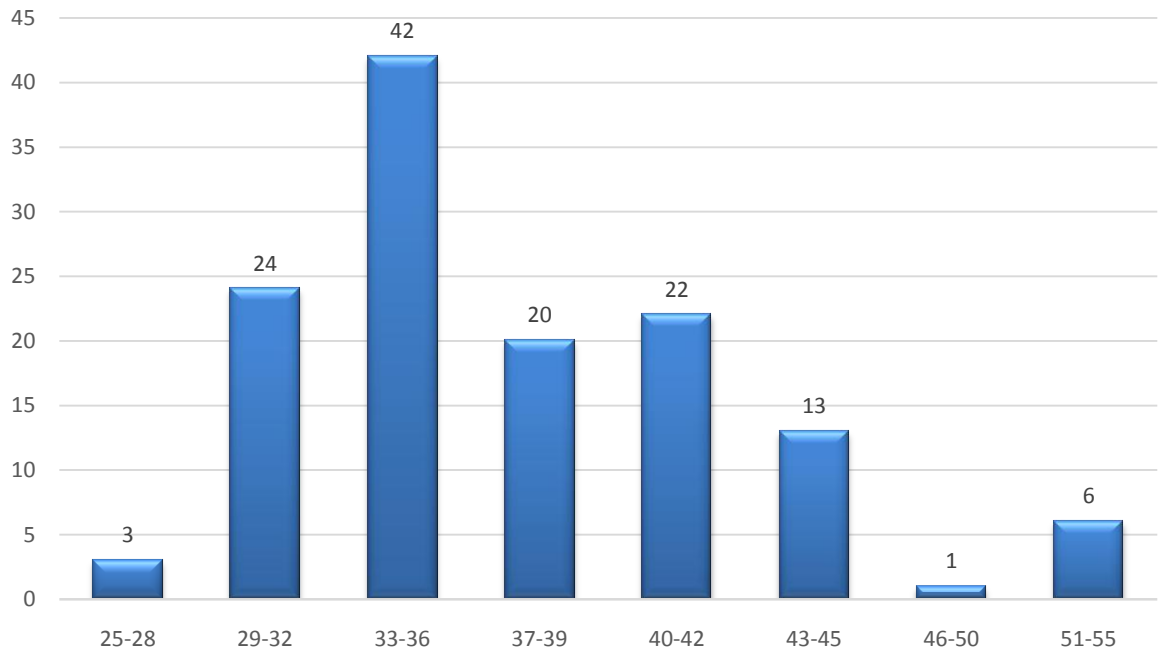
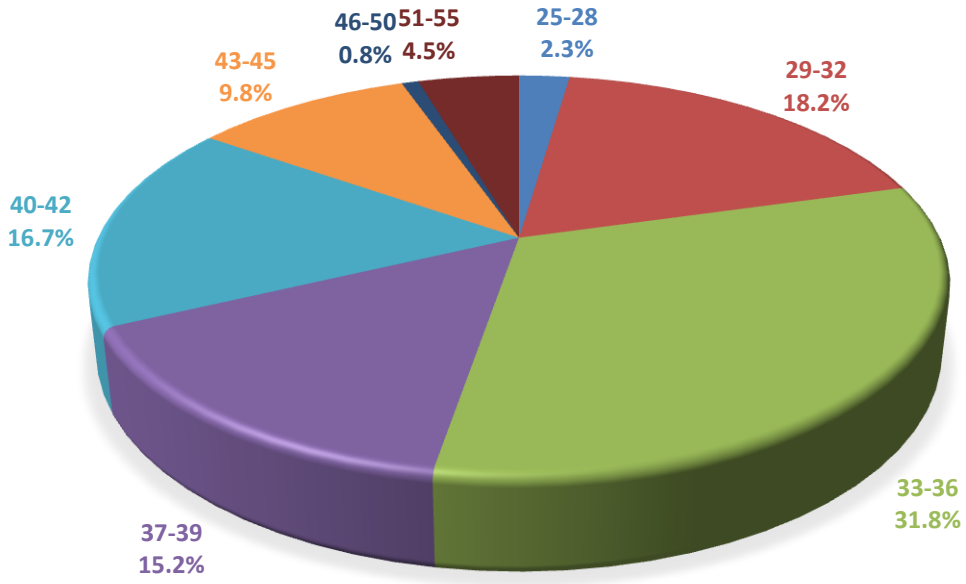


Figure 25 – Male Infertility by Age Group (%)



5. Lifestyle Indicators

5.1. Body Mass Index

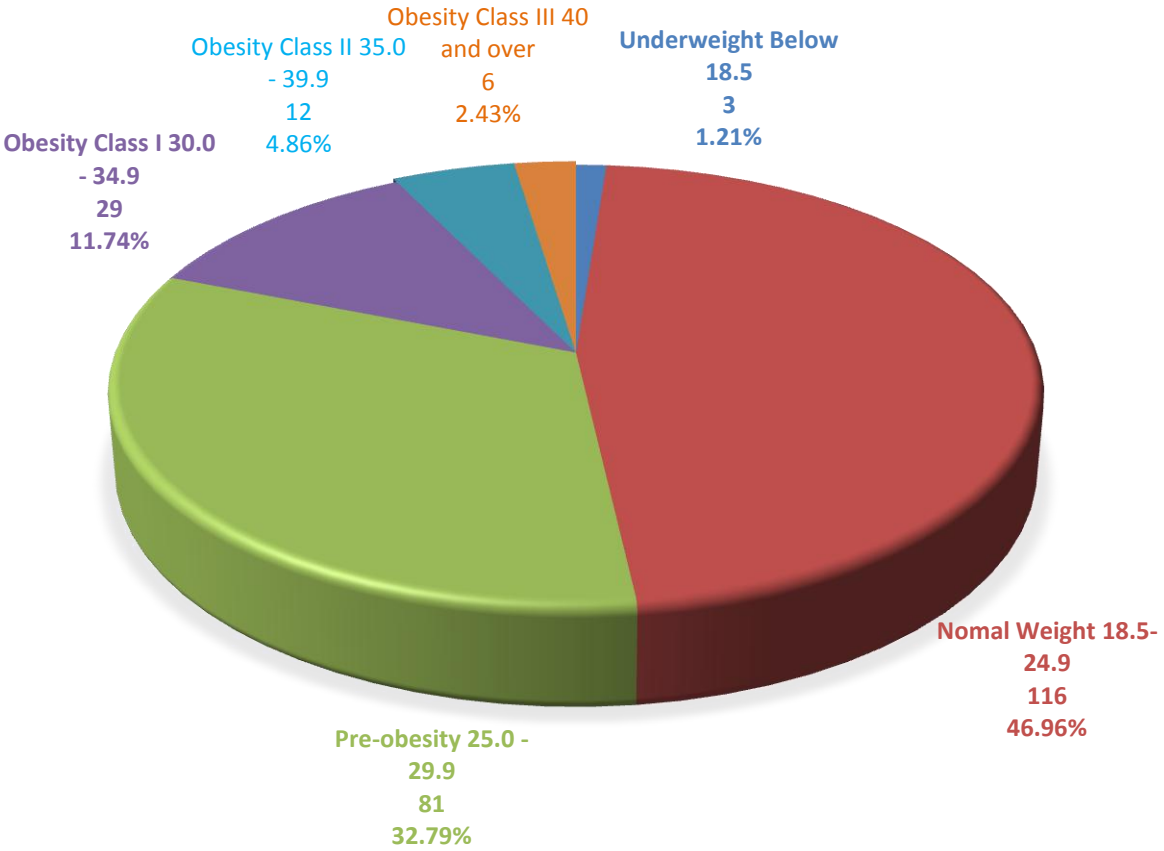
For the very first time since issuing its Annual Report, this year the Authority is presenting a picture of the body Mass Index (BMI) of the Females resorting for Assisted Reproduction Treatments in Malta. Classifications reported are based on the World Health Organisation Classifications, thus women having a BMI below 18.5 are classified as underweight, women with a BMI between 18.5 and 24.9 as normal weight, women with a BMI of 25 to 29.9 as pre-obesity (overweight). Women are classified as Obesity Class I if reporting a BMI of 30 to 34.9, Obesity Class II with a BMI of 35 to 39.9. Women with a BMI above 40 are classified as Obesity Class III.

In 2018, the BMI's of females reported ranged from as low as 17.2 with the maximum BMI reported to be 47.1, average of BMI of women who resorted to IVF/ICSI was of 31.37, thus being classified as in the range of Obesity Class I.

3 females or (1.21%) of females undergoing ART treatment in Malta through IVF/ICSI were reported to be underweight, 116 females (46.96%) were of normal weight while the remaining 128 females or 51.82% were classified in the overweight and obese classifications. Noteworthy to bring to attention is the fact that 19.03% of all females resorting to ART treatments were classified as Obese. (Figure 26).

The Authority felt that this study needed to be presented in this year's annual report to give a holistic picture of the females undergoing ART treatments. As will be reported later in the miscarriages section, 20% of the females who were pregnant in the Obesity class I suffered a miscarriage, this miscarriage rate increased to 33.3% in women who were pregnant in Obesity class II. The only woman who was pregnant from the Obesity Class III suffered a miscarriage, thus the incidence here was reported as 100%.

Figures 26 – Body Mass Index of Females



6. TYPE OF CYCLE

6.1. Fresh vs Thawed

Couples may opt for Fresh collection of oocytes or Thawed cycles using vitrified oocytes, or a combination of Fresh and Thawed. Oocyte selection and vitrification are routine practice at the local ART clinics. Given that vitrification technology holds great promise in terms of gamete survival, pregnancy rates, and live births, data gathered on the outcomes from Thawed cycles is of high relevance. This is especially true in light of gamete vitrification techniques being employed for fertility preservation, as in the cases of oncology patients.

From a total of 249 procedures carried out, 218 (87.55%) were Fresh procedures with collection of oocytes; while another 29 (11.65%) were Thawed oocytes cycles. None of the couples, in 2018, opted for a combined cycle whereby both fresh and thawed oocytes would have been utilized for the procedure. During 2018, two couples (0.8%) had undergone embryo transfer only of embryos that were cryopreserved previously through the force majeur permission granted by the Authority. (Table 2).

Table 2. Type of Procedure

Procedure	NHS	Self-Funded	Total	% of Total
Fresh oocytes	180	35	215	86.35%
Thawed oocytes	20	9	29	11.65%
Prior approval for a freeze all oocytes cycle	3	0	3	1.20%
Thawed embryos	2	0	2	0.80%
Total	205	44	249	

Noteworthy is the fact that there has been a continuous increase in the option of undergoing a fresh collection of eggs cycle. During 2018, there was an 11.56% increase in fresh oocytes collection cycles when compared to last year 2017, and an increase of 16.85% over 2016. A considerable drop of 12.36% was registered in the couples opting to undergo a thawed cycle in 2018 when compared to 2017, and a drop of 17.29% over figures reported in 2016.

The majority of cycles (89.27%) carried out at the ART Clinic in Mater Dei Hospital were Fresh oocytes collection cycles, 9.75% were Thawed oocytes cycles, whilst only 0.98% of cycles were thawed embryo cycles. In the self-funded cycles the majority of cycles (79.55%) were Fresh oocytes collection cycles, and the remaining 20.45% were Thawed oocytes cycles. No embryo transfer only cycles were carried out that were self-funded in 2018.

6.2. Additional Fertilization Requests (AFRs)

Pursuant to the introduction of the Embryo Protection Act of 2012, the maximum number of oocytes which may be injected in any one cycle is two oocytes, or three oocytes in cases approved by the Authority under the Principal Act). All embryos created had to be transferred since vitrification (freezing) of embryos was forbidden by law under the Principal Act.

With the introduction of the Embryo Protection (Amendment) Act, 2018, all prospective parents will have two oocytes which may be injected in any one cycle however as approved in the AFR Protocol presented to the Parliamentary Health Committee, the Authority can now approve up to a maximum of five oocytes to be injected in any one cycle, provided that the couples have consented for embryo vitrification and potential embryo donation. Prospective parents who do not consent to embryo vitrification will only be allowed to inject two oocytes in any one cycle.

The Authority receives a significant number of requests from the licensed establishment clinicians to consider the fertilization of additional oocytes for specific couples, instead of the two permitted by law. These requests are analysed and discussed between the Members of the Authority together with Representatives from the Obstetrics and Gynaecology Association and the Paediatric Association of Malta, as per Article 6 of the Embryo Protection Act. Requests are considered on a case by case basis and matched against established criteria. These criteria include the age of the female patient undergoing treatment, together with the number of failed IVF/ICSI cycles that the couple had already undergone as well as the indication of infertility.

Throughout 2018, a total of 137 requests were received by the Authority. The majority of requests, 130 requests (94.89%) came from the ART Clinic at MDH, 27 of these requests were for the maximum injection of 5 oocytes under the Amendment Act, all of the 27 requests were approved. A total of 24 requests (18.46%) made by the ART Clinic at MDH were not approved.

In contrast, while the minority of requests, 7 requests only (5.11%) of the AFR requests were made by private clinics, 2 requests amounting to 28.57% have not been approved (Figures 27 and 28).

Out of the total requests received, 81.02% were approved while the remaining 18.98% were not approved (Figure 29). The approval rate is 12.54% higher than the figures reported in 2017 and 16.49% higher than the figures quoted in 2016.

Figure 27 – AFR Requests

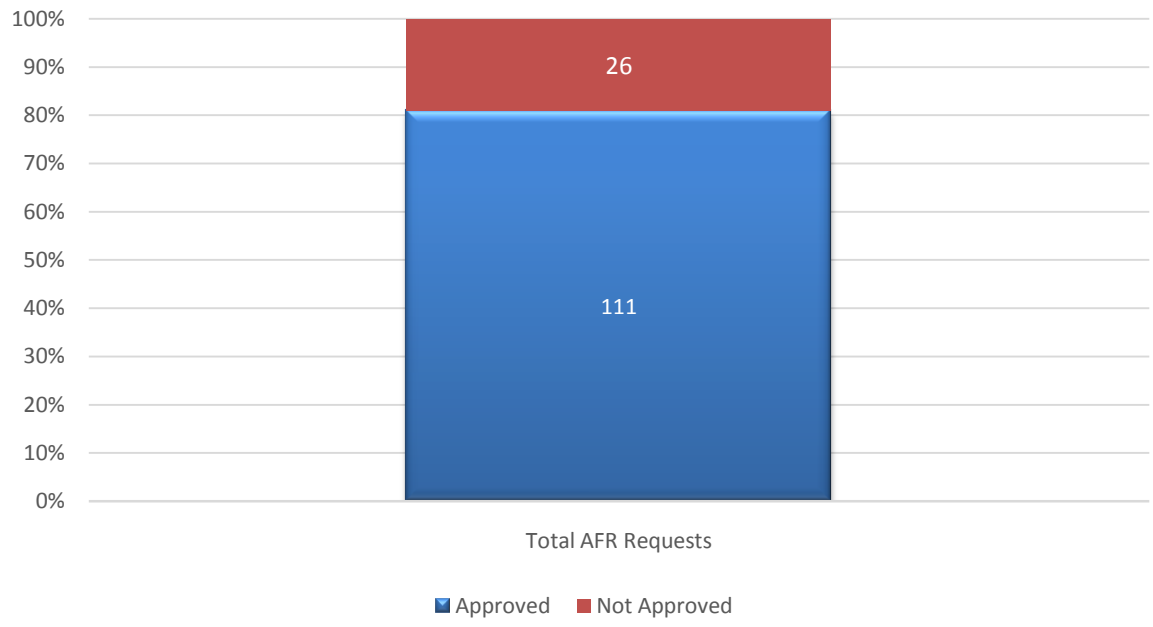


Figure 28 – AFR Requests NHS vs Self-Funded

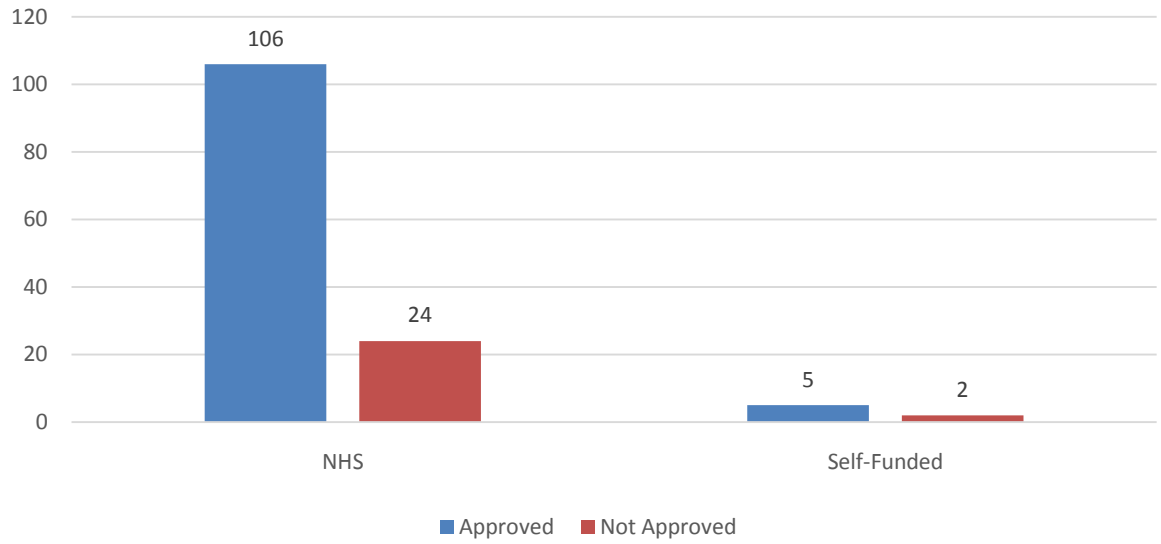
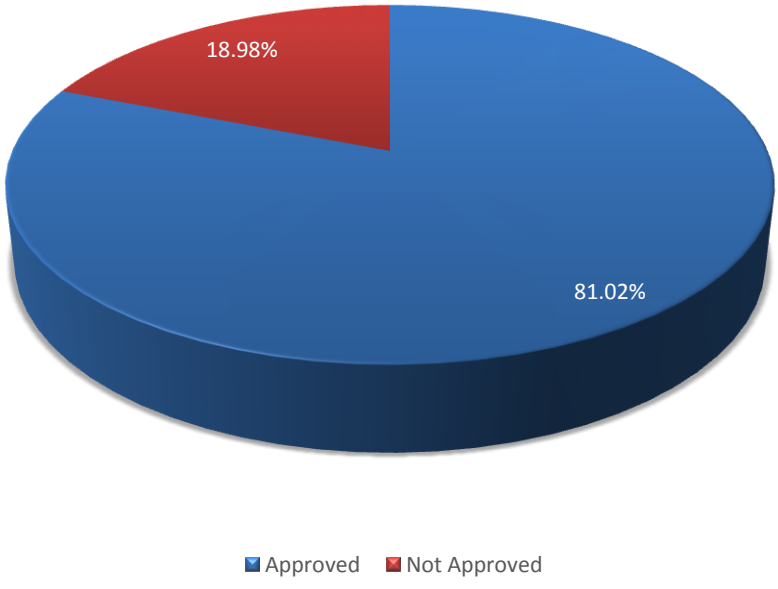


Figure 29 – AFR Approval Rate (%)



7. GAMETES

7.1. Transfer of Gametes

Throughout 2018, there were only 3 female patients who had their oocytes transferred from MDH to the licensed private Clinic. In turn, no gametes have been transferred from the private clinic to MDH.

7.2. Collection of Oocytes

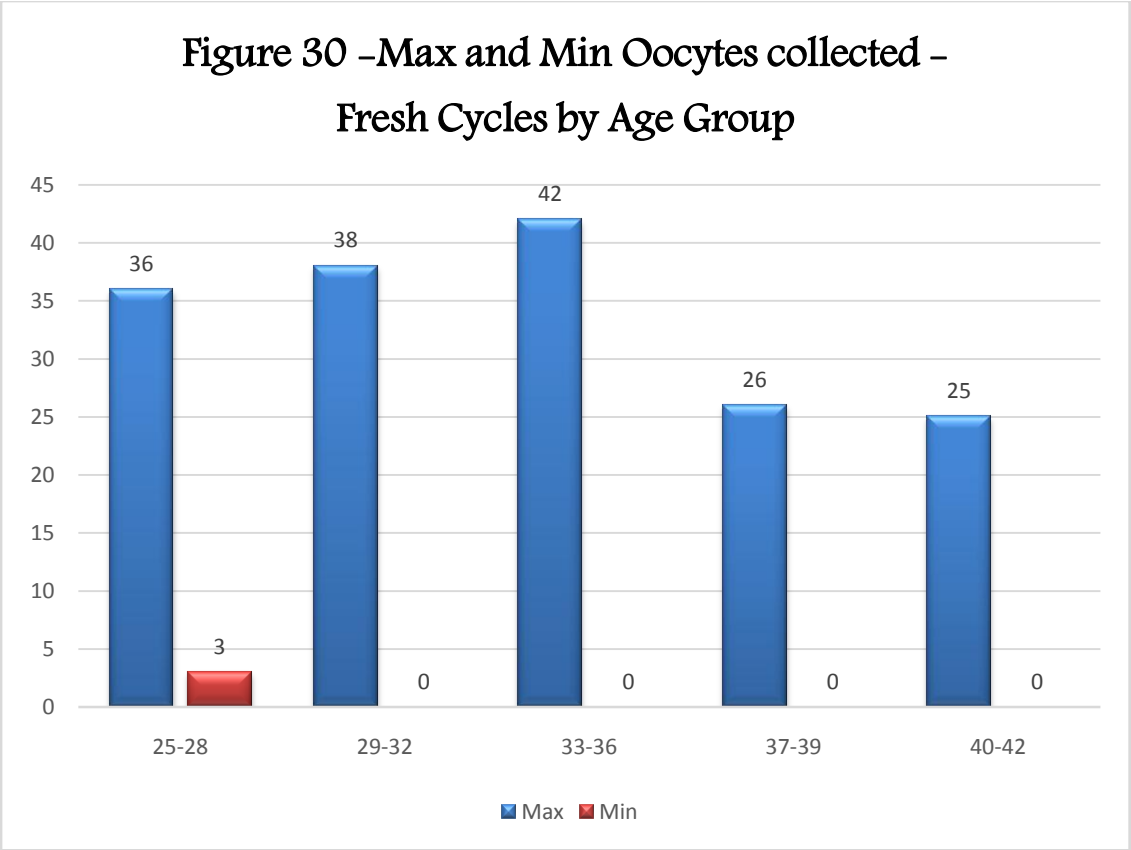
The number of oocytes a female has remaining for the future, better known as 'ovarian reserve' is closely related to a woman's age but can vary considerably at any age. Oocyte quality is also associated with female age and the better the quality, the higher the probability for pregnancy since embryo quality is dependent on the quality of the oocytes. The number of oocytes attained through ART procedures such as IVF/ICSI strongly influences the chance for success.

During a Long Protocol IVF cycle, the female patient goes through down-regulation and ovarian stimulation phases that prepare her for treatment. The purpose of the Ovarian Stimulation phase is to stimulate the ovary into producing several follicles, inducing a controlled ovulation and maturation of oocytes so as to increase the chances of achieving a pregnancy during treatment.

From the 218 Fresh cycles carried out in 2018, a total of 2095 oocytes have been collected, for an average of 9.61 oocytes per patient. The maximum number of oocytes collected from a single patient was 42 oocytes from a female aged 36 years, this was followed by 38 oocytes collected from a female aged 32 years and 36 oocytes from a female aged 27 years. All three patients had undergone treatment at MDH.

Conversely, there were 9 patients, aged between 29 and 42 years, undergoing treatment who produced zero (0) oocytes. Three of these patients had self-funded their treatment whilst the other 6 had undergone treatment at MDH (Figure 30).

Figure 30 –Max and Min Oocytes collected – Fresh Cycles by Age Group



As expected, the largest number of average oocytes collected from one single patient, for an average of 15.33 oocyte per patient, was from females aged between 25 and 28, these were closely followed by 11.54 oocytes per patient, from females in the 29-32 year old bracket. An average of 10.27 oocytes was collected from patients aged 33-36. Not surprisingly, less oocytes were collected from women aged 37-39 and 40-42, for an average of 7.40 and 6.00 oocytes respectively (Table 3).

Table 3. Oocytes Collected by Age Group

Age	No of Females	Total Oocytes Collected	Average	Max	Min
25-28	9	138	15.33	36	3
29-32	54	623	11.54	38	0
33-36	79	811	10.27	42	0
37-39	48	355	7.40	26	0
40-42	28	168	6.00	25	0
OVERALL	218	2095	9.61		

When taking into account the number of oocytes collected from the total number of female patients undergoing a Fresh cycle, it appears that the quantity of oocytes collected per cycle relative to the age of the female patient is higher at MDH in all age groups when compared to self-funded patients. The average oocytes collected per patient at MDH is 10.31 compared to the 5.37 at the private establishment (Table 4).

Table 4. Oocytes Collected by Age Group – NHS vs Self-Funded

	NHS			Self-Funded		
Age	No of Females	Total Oocytes Collected	Average	No of Females	Total Oocytes Collected	Average
25-28	9	138	15.33	0	0	0.00
29-32	43	532	12.37	11	91	8.27
33-36	70	755	10.79	9	56	6.22
37-39	39	308	7.90	9	47	5.22
40-42	22	153	6.95	6	15	2.50
OVERALL	183	1886	10.31	35	209	5.97

As pointed out already, women are born with a lifetime reserve of oocytes, and with age, the quantity and their quality gradually decrease. The cells in developing follicles secrete a chemical substance named Anti-Mullerian Hormone (AMH) and the levels of this particular hormone in a woman's blood, is normally a good indicator of her ovarian reserve. With increasing age, serum AMH levels decrease. Women suffering from polycystic ovaries tend to have high serum AMH concentrations while women close to menopause normally have low levels.

Clinicians generally refer to the AMH test results to get some insight into the remaining amount of oocytes their patient has got. This is especially important since low AMH values could possibly suggest a poor response to IVF, while high values may denote an over-response to the IVF medication.

Unfortunately, AMH levels do not tell us much about the quality of a woman's oocytes or her ability to get pregnant.

An analysis of the quantity of oocytes collected for women undergoing treatment and whose serum AMH values were ≤1µg/l, was performed. Due to the fact that a significant number of AMH test results were older than 6 months, on the day of oocyte retrieval the actual serum AMH values of the patient might have been less than the reported value. Hence the accuracy of all the AMH-related analysis in this report cannot be guaranteed. The data in the chart may however be of significance to clinicians dealing with patients with poor ovarian reserve, with respect to possibilities and expectations.

Throughout 2018, there were 53 female patients with a serum AMH concentration of ≤1µg/l, who had undergone a Fresh cycle. The total amount of oocytes collected from these 53 patients was 202, with the maximum number of oocytes collected being 12 and the minimum 0 (zero). The average number of oocytes collected was 3.81 per patient and there were 35 females who had 3 or more oocytes collected. All nine patients who had no oocytes to collect had an AMH of less than 1. (Table 5).

Table 5. Oocytes collected for AMH ≤1µg/l

AMH <= 1 Occurances	Min Oocytes Collected	Max Oocytes Collected	Total Oocytes Collected	Average Oocytes Collected	Occurances with 3 oocytes or more
53	0	12	202	3.81	35

7.3. Oocytes Discarded

Oocytes obtained following ovarian stimulation should meet certain criteria in order to be considered suitable for IVF/ICSI. An appraisal is usually done by Embryologists to classify these oocytes, and those which are not deemed suitable for immediate fertilization or vitrification are discarded.

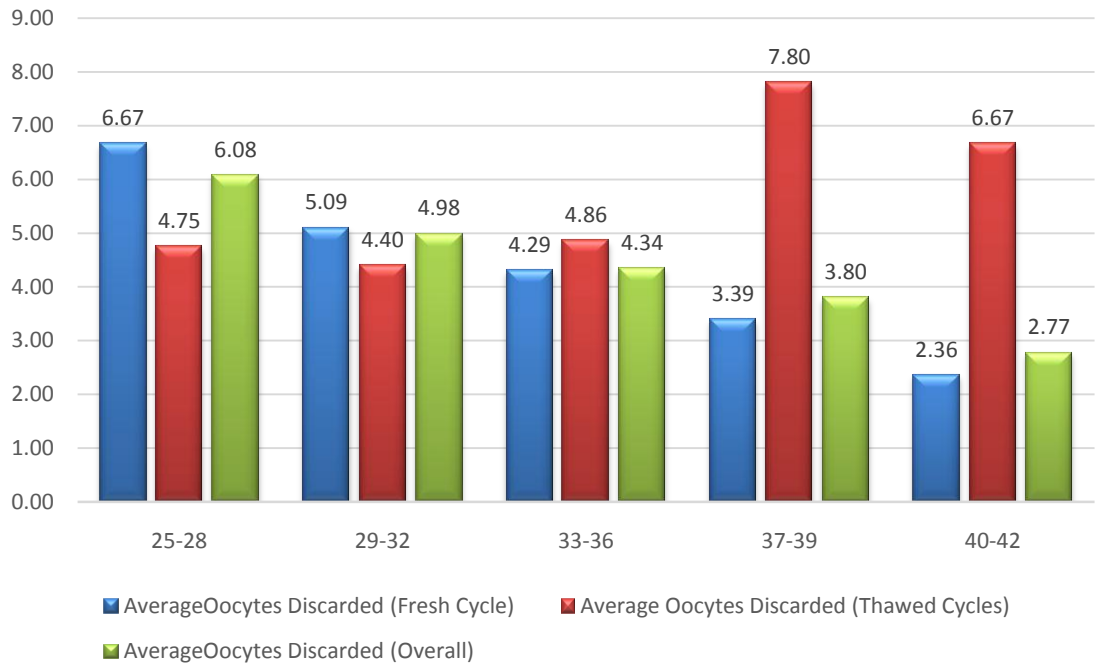
A total of 1058 oocytes have been discarded in 2018. Nine hundred and two (902) oocytes (85.26% of all discarded oocytes), or 43.05% from the total oocytes collected, were discarded following the egg retrieval process (Fresh cycle), for an average of 4.14 discarded oocytes per Fresh cycle. The remaining 156 oocytes (14.74% of all discarded oocytes) failed to survive the thawing process, for an average of 5.38 oocytes discarded per Thawed cycle (Table 6).

Table 6. Oocytes Discarded

Age	No of Females (Fresh Cycle)	Total Oocytes Discarded (Fresh Cycle)	Average Oocytes Discarded (Fresh Cycle)	No of Females (Thawed Cycles)	Total Oocytes Discarded (Thawed Cycles)	Average Oocytes Discarded (Thawed Cycles)	No of Females (Overall)	Total Oocytes Discarded (Overall)	Average Oocytes Discarded (Overall)
25-28	9	60	6.67	4	19	4.75	13	79	6.08
29-32	54	275	5.09	10	44	4.40	64	319	4.98
33-36	79	335	4.24	7	34	4.86	86	369	4.29
37-39	48	166	3.46	5	39	7.80	53	205	3.87
40-42	28	66	2.36	3	20	6.67	31	86	2.77
OVERALL	218	902	4.14	29	156	5.38	247	1058	4.28

In 2018, same as reported in 2017, the largest number of oocytes discarded is from women in the 33-36 year old bracket which incidentally was the group from which the largest number of oocytes had been collected (Figure 31).

Figure 31 – Average Oocytes Discarded by Age Group (Fresh vs Thawed vs Overall)



7.4. Fresh vs Thawed Sperm

Out of the 246 cycles carried out in 2018, thawed sperm has been utilized in 3 cycles only, or 1.22%, of the procedures undergone. Fresh sperm, ejaculated or in some instances obtained through testicular extraction/aspiration, has been used in the remaining procedures which have been carried out.

7.5. Storage of Gametes and Embryos

Pursuant to the introduction of the Embryo Protection Act of 2012, licensed clinics were allowed to store gametes (oocytes and sperm). Storage of gametes started as of July 2013 in the private licensed clinic, while storage from Government-funded cycles started in January 2014. Storage at the MDH facility started as of January 2015. Up to 1st October 2018, embryo cryopreservation was only allowed in exceptional cases as approved by the Authority. With the introduction of the Embryo Protection Amendment Act of 2018, embryo cryopreservation was made available to all prospective parents with prior approval of additional fertilisations from the Authority.

7.5.1. Storage of Oocytes

Out of the 218 females who had oocytes retrieved in 2018, only 102 (46.79%) had enough oocytes to store. A total of 116 couples had no oocytes left to vitrify (Table 7). This is in line with figures registered in 2017 where more couples had oocytes to discard than couples who had oocytes to store.

Table 7 – Fresh Cycles with NO Oocyte Vitrification

	NHS			Self-Funded			Total		
Age	No of Cycles	Total Cycles with NO Oocytes to Vitrify	% of cycles with no Oocytes to Vitrify	No of Cycles	Total Cycles with NO Oocytes to Vitrify	% of cycles with no Oocytes to Vitrify	No of Cycles	Total Cycles with NO Oocytes to Vitrify	% of cycles with no Oocytes to Vitrify
25-28	9	2	22.2%	0	0	0.0%	9	2	22.2%
29-32	43	13	30.2%	11	3	27.3%	54	16	29.6%
33-36	70	36	51.4%	9	4	44.4%	79	40	50.6%
37-39	39	30	76.9%	9	4	44.4%	48	34	70.8%
40-42	22	19	86.4%	6	5	83.3%	28	24	85.7%
OVERALL	183	100	54.6%	35	16	45.7%	218	116	53.2%

The total number of oocytes vitrified from Fresh cycles carried out in 2018 was 707, for an average of 6.93 oocytes per couple. The maximum number of oocytes vitrified from a single cycle was 24 at MDH ART Clinic.

The maximum number of oocytes thawed for one single female from Frozen cycles was 24 at MDH ART Clinic, 21 oocytes of which were discarded, while the minimum number of oocytes thawed was 4.

7.5.2. Storage of Sperm

There has been a continuous request for sperm storage throughout 2018. A total of 82 patients requested to have their sperm cryopreserved, 80 at MDH and 2 at the private clinic. In a number of cases, sperm was obtained through testicular aspiration/extraction (TESA/TESE). Seventy four (74) males vitrified their sperm, only eight males who requested sperm cryopreservation did not vitrify sperm.

Twenty three (23) males requested Fertility preservation following oncology diagnosis prior to starting chemotherapy. The other fifty nine (59) males had Urology referrals with the main reason for referral being decrease in male fertility parameters. Twenty three (23) of the male patients who stored their sperm proceeded with an IVF/ICSI cycle in the same calendar year, but only 3 of them used thawed sperm for the procedures (Table 8).

Table 8 – Storage of Sperm

Sperm Type	NHS	Self-Funded	Total	%
Vitrified	23	0	23	9.43%
Not Vitrified	177	44	221	90.57%
Total	200	44	244	

All the male patients that vitrified their sperm and proceeded to undergo an IVF/ICSI procedure were all undergoing their cycle at MDH (Figure 32). Out of all the procedures carried out it only accounts to 9.43% of all cycles, the remaining 221 males (90.57%) did not vitrify any sperm (Figure 33).

Figure 32 – Vitrified vs Non-Vitrified Sperm (NHS vs Self-Funded)

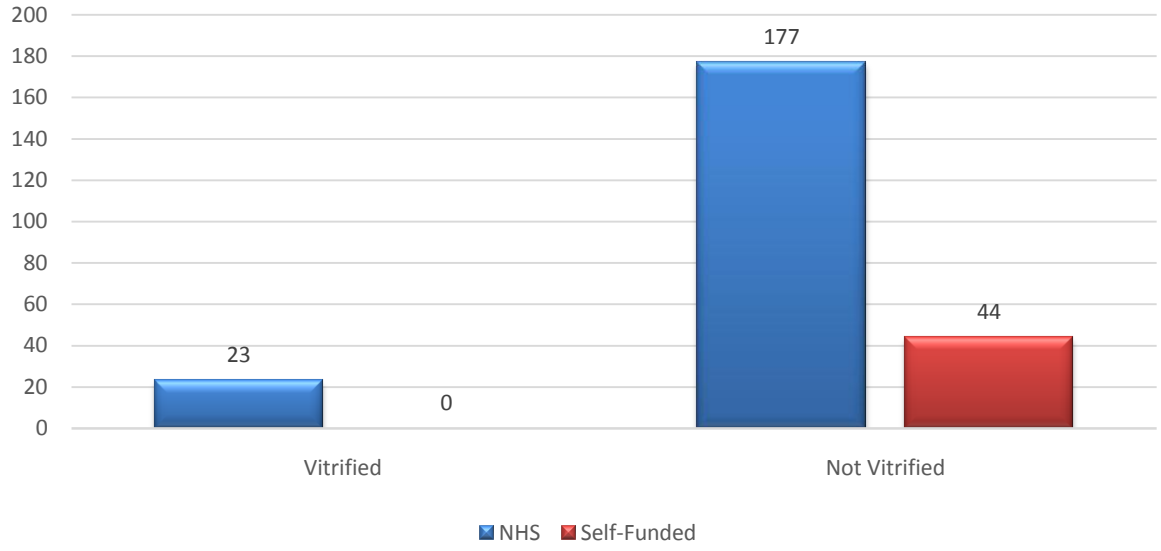
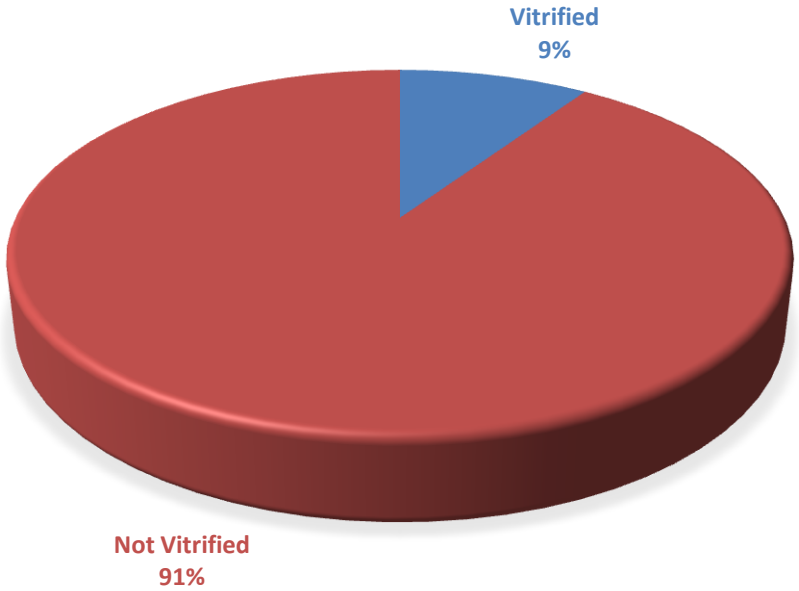


Figure 33 – Vitrified vs Non-Vitrified Sperm (% of All Cases)



7.5.3. 'Freeze-All' Cycles

In exceptional circumstances, clinicians may decide to proceed with oocyte retrieval but freeze all the oocytes for later fertilization. This is usually the case when uterine pathologies or a risk of Ovarian Hyperstimulation (OHSS) has been identified. It may also be the case that while the oocytes were being retrieved, the male partner had no viable sperm in the sample provided; or else no sperm was found during a TESA procedure, and hence fertilization couldn't take place. During this calendar year there were also patients who were given prior approval by the Authority to proceed with a freeze-all cycle, as per detailed in Section 1.9 above.

In 2018, apart from the three women who were granted prior approval to proceed with a 'freeze-all cycle', the Authority was notified that there were 3 patients undergoing cycles at MDH who had a 'freeze-all' cycle, while at the private clinic there was 1 patients who had a 'freeze-all' cycles. Thus a total of 7 patients had a 'freeze-all' cycle and did not proceed with the fertilization process.

7.5.4. Embryo Cryopreservation

In Malta, under the Principal Act up to 30th September 2018 permission for cryopreservation of embryos can only be granted by the Embryo Protection Authority as per Article 7 of the Law, in the event that transfer of the fertilized embryos in the womb is not possible owing to grave and certified *force majeur* not predicted at the moment of fertilization. In 2018, two requests were made by the MDH ART Clinic for vitrification of embryos. Permission was granted by the Authority and five embryos in total were cryopreserved in 2018. Thus

the total of embryos cryopreserved under the exceptional cases clause between 2013 and 2018 amounted to 7 embryos. Only two embryos vitrified in 2018, at the ART Clinic in MDH under this exceptional cases clause are still in storage.

With effect from 1st October 2018 and the introduction of the Embryo Protection Amendment Act, prospective parents undergoing ART treatment could opt to have additional fertilisation, two embryos transferred in one cycle and the resultant embryos cryopreserved for future use. The Authority received 27 requests from MDH ART Clinic which were all accepted, out of these only 10 prospective parents had resultant embryos to cryopreserve, subsequently 16 embryos have been cryopreserved for future use. Only two of the prospective parents who have cryopreserved embryos are expecting to give birth.

7.6. End of Storage

During 2018, 19 requests were received by the Authority from patients to have their gametes discarded, all gametes were stored at the Assisted Conception Unit at St James Hospital. 14 female patients have requested to have their oocytes discarded, 13 requests were approved, while one request is still pending as the clinic was requested to supply further information re discrepancy in number of oocytes held. Thus a total of 65 oocytes were approved by the Authority to undergo the discarding process. The other five requests were from male patients requesting to discard fifteen vials of sperm, approval for same was granted by the Authority.

7.7. Total Storage

As at 31st December 2018, the total amount of oocytes stored at the licensed clinics stood at a total of 1748 oocytes with the majority stored at MDH, whilst the total number of sperm vials was of 891, again the majority stored at MDH. The eighteen embryos cryopreserved are all stored at the ART Clinic in Mater Dei Hospital (Table 9).

Table 9 – Total Storage

Type of Storage	NHS	Self-Funded	Total
Oocytes	1315	433	1748
Sperm	820	71	891
Embryos	18	0	18

8. IVF/ICSI PROCEDURES

8.1. Cycles Started

In addition to the cycles which have been performed throughout the year, licensed clinics have also reported a total of 32 cycles which were abandoned prior to oocyte retrieval. Twenty one (21) couples abandoned their cycle at the ART Clinic in MDH, while another eleven couples (11) who were going to self-fund their treatment abandoned their cycle. The majority of cycles were abandoned due to poor response to the stimulation treatment the female patients received. Other couples abandoned their cycle on medical grounds.

Noteworthy is the fact that one couple reported abandoning the cycle due to achieving a natural pregnancy, one other couple abandoned the cycle as the female could not withstand treatment and another two couples dropped out due to personal reasons.

8.2. Type of Procedure – IVF vs ICSI

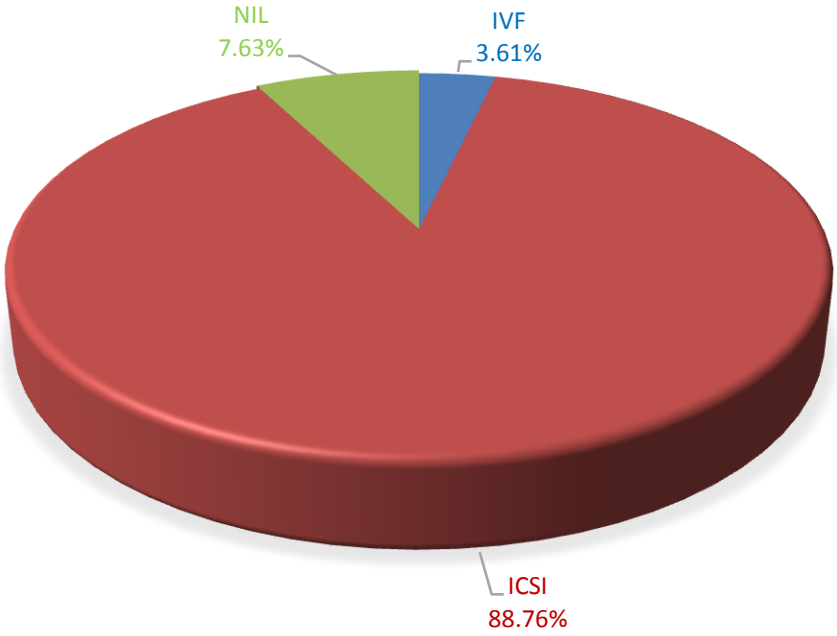
In 2018, from a total of 249 cycles started, no IVF/ICSI procedure was carried out for 19 couples. This was due to the fact that there were 9 couples who had no oocytes retrieved, another couple who had oocytes collected but which had to be all discarded as they were of poor quality, the 7 couples that had to opt for a 'Freeze-all' cycle and the two couples that had an embryo transfer only. (Table 10).

Table 10. Type of ART Procedure

Type of ART	NHS	Self-Funded	Total	Total %
IVF	9	0	9	3.61%
ICSI	181	40	221	88.76%
NIL	15	4	19	7.63%
Total	205	44	249	

Out of the 230 procedures carried out, 221 or (88.76%), were *intra-cytoplasmic sperm injection* (ICSI). In contrast to conventional *in vitro* fertilization (IVF), where a single egg is incubated in the presence of a significant number of sperm, in ICSI, the embryologist selects a single sperm to be injected directly into an egg (Figure 34).

Figure 34 – IVF vs ICSI (% of Procedures) – Overall



Only nine out of the 190 procedures carried out at MDH were IVF, while the licensed private clinic opted for an '*All-ICSI*' approach (Figures 35 and 36).

Figure 35 – IVF vs ICSI (% of Procedures) – NHS

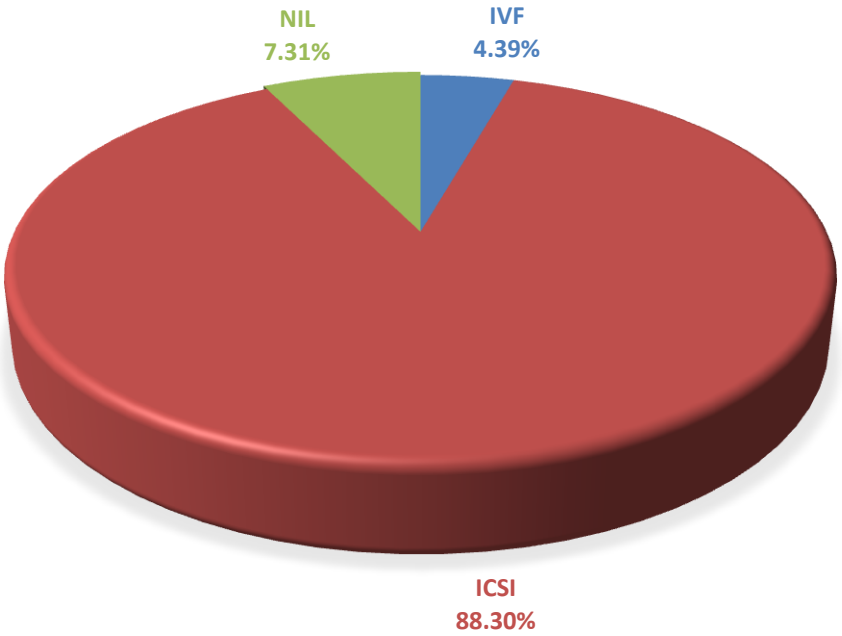
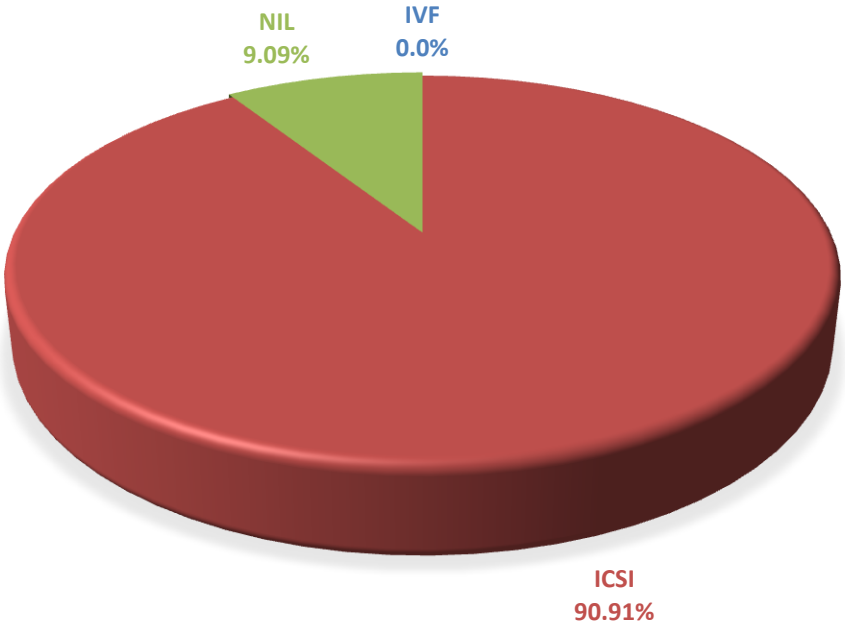


Figure 36 – IVF vs ICSI (% oF Procedures) – Self-Funded



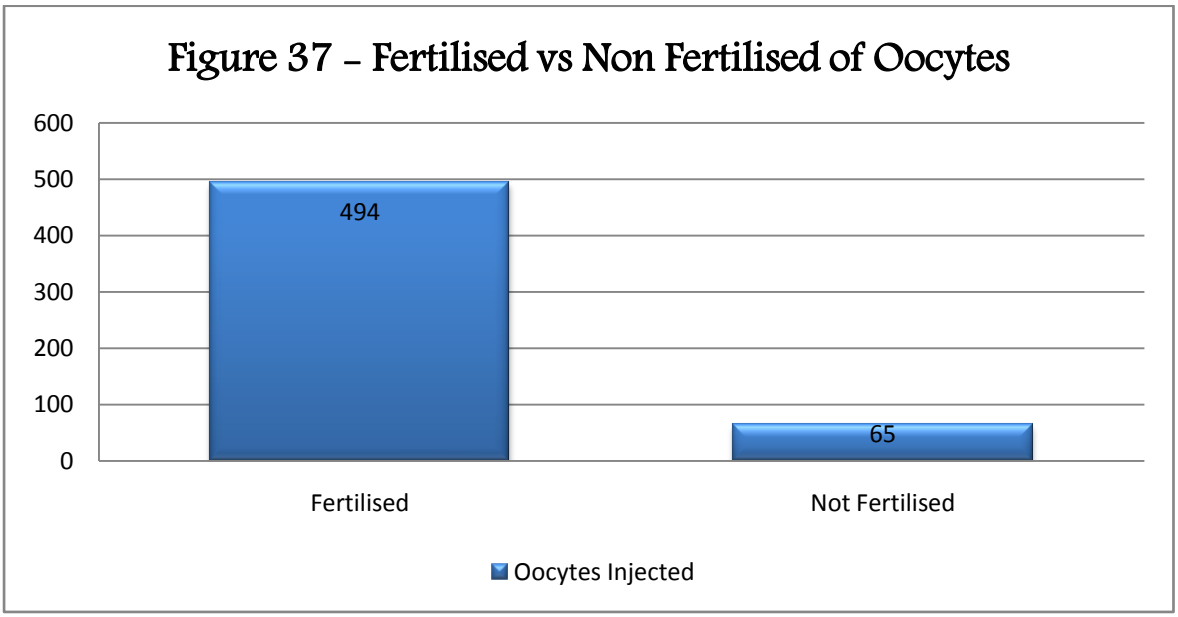
8.3. Oocytes Injected and Fertilisation

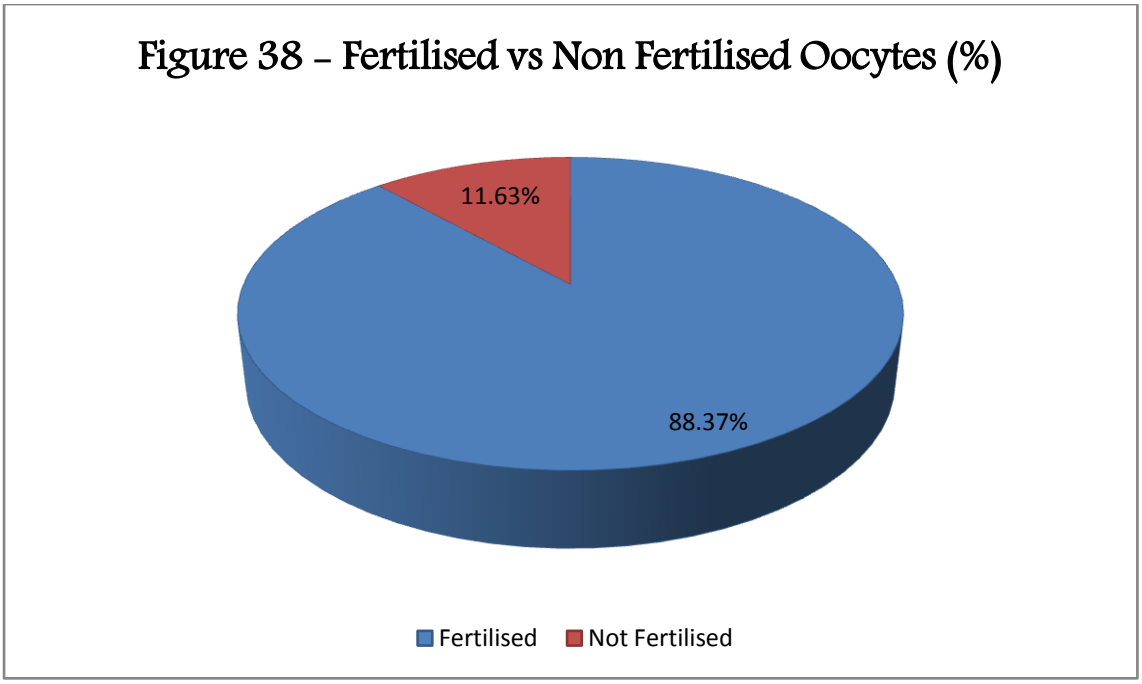
Throughout 2018, a total of 559 oocytes were injected, the majority 486 oocytes or 86.94% of the total oocytes injected were from fresh cycles, the remaining 73 oocytes or 13.06% of the total injected oocytes where from thawed cycles (Table 11).

Table 11. Oocytes Injected

Type of Cycle	Oocytes Injected	%
Fresh	486	86.94%
Thawed	73	13.06%
Total	559	

Out of the total 559 injected oocytes, there were 494 oocytes that reached fertilisation stage while 65 oocytes did not fertilise (Figure 37). Thus fertilisation rate is of 88.37% of all oocytes injected, an increase of 1.64% over figures reported in 2017. (Figure 38).

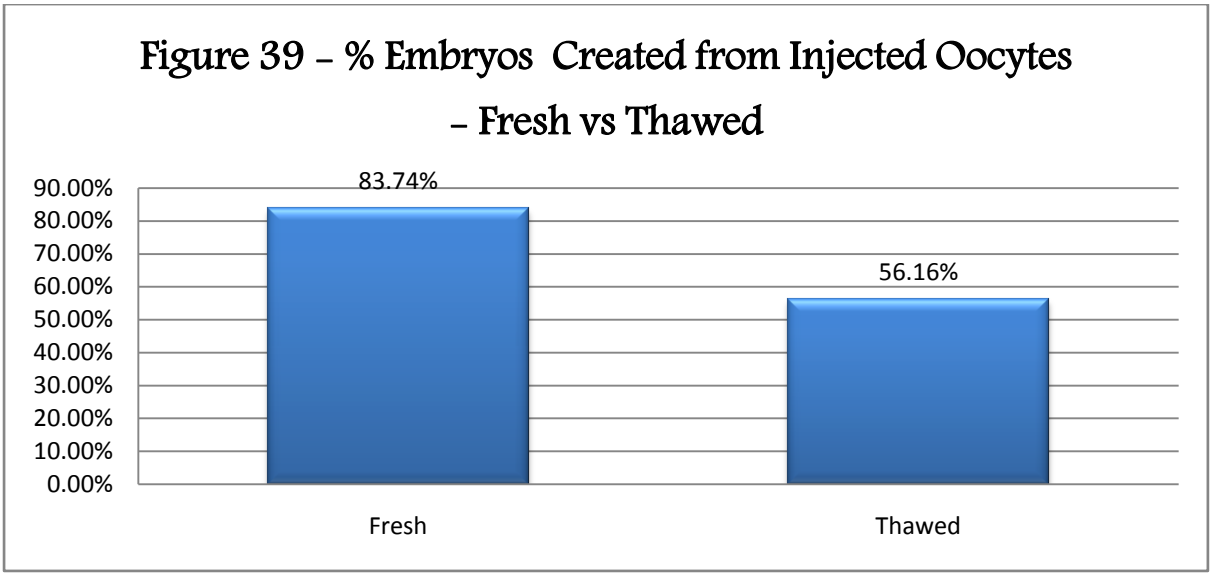




Out of the 494 fertilised oocytes, embryologists report that 46 oocytes had arrested during the incubation phase, 43 of these oocytes were from fresh cycles whilst 3 arrested oocytes were from thawed cycles. This resulted in the creation of 448 embryos, 407 from fresh oocytes and 41 from thawed oocytes. (Table 12 & Figure 39). Eighteen embryos were cryopreserved, two embryos which were cryopreserved in 2016 were removed from storage for transfer, thus a total of 432 were eventually transferred.

Table 12. Embryos Created

Type of Cycle	Oocytes Injected	Embryos Created	Transferred %
Fresh	486	407	83.74%
Thawed	73	41	56.16%
Total	559	448	

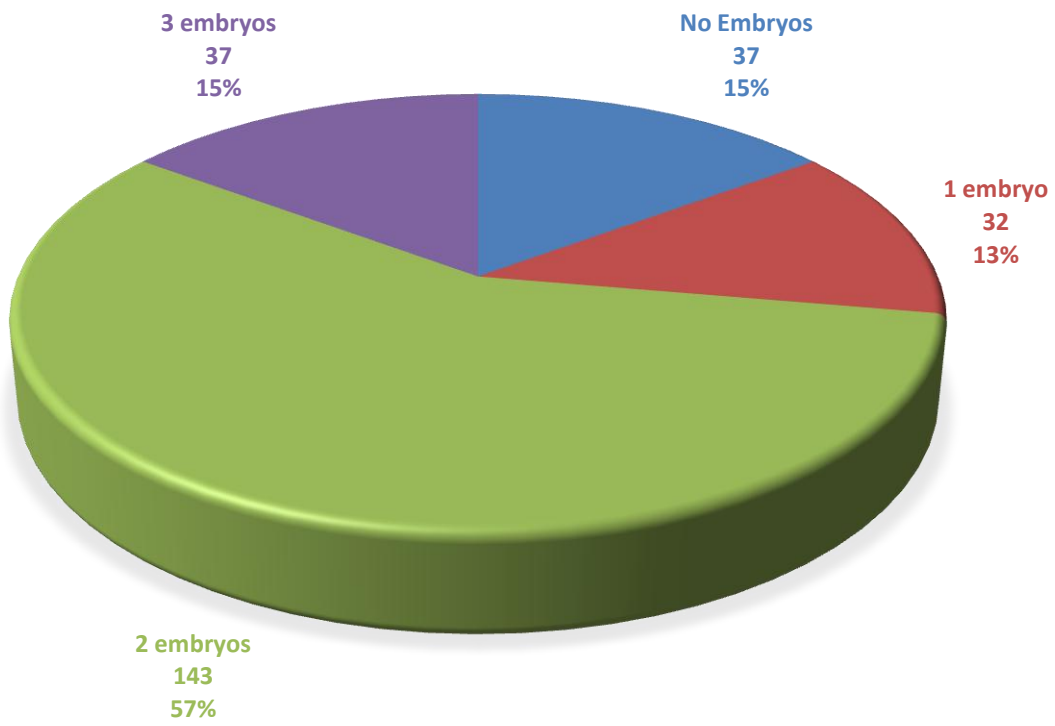


8.4. Embryo Transfers

Out of the 249 cycles carried out, 432 embryos were transferred. There were a total of 37 couples or 14.86% who had no Embryo Transfer affected. As outlined earlier, there were 19 couples who for various reasons had no IVF/ICSI procedures performed. The other 18 couples had no embryos to transfer as the oocytes they had injected failed to fertilize.

Out of the 212 couples who had viable embryos to transfer, 32 of them (12.85%) had a single embryo transferred. One hundred and forty three (57.43%) couples, had 2 embryos transferred, while the remaining 37 couples, or 14.86%, had 3 embryos transferred (Figure 40).

Figure 40 – Embryos Transferred per Cycle

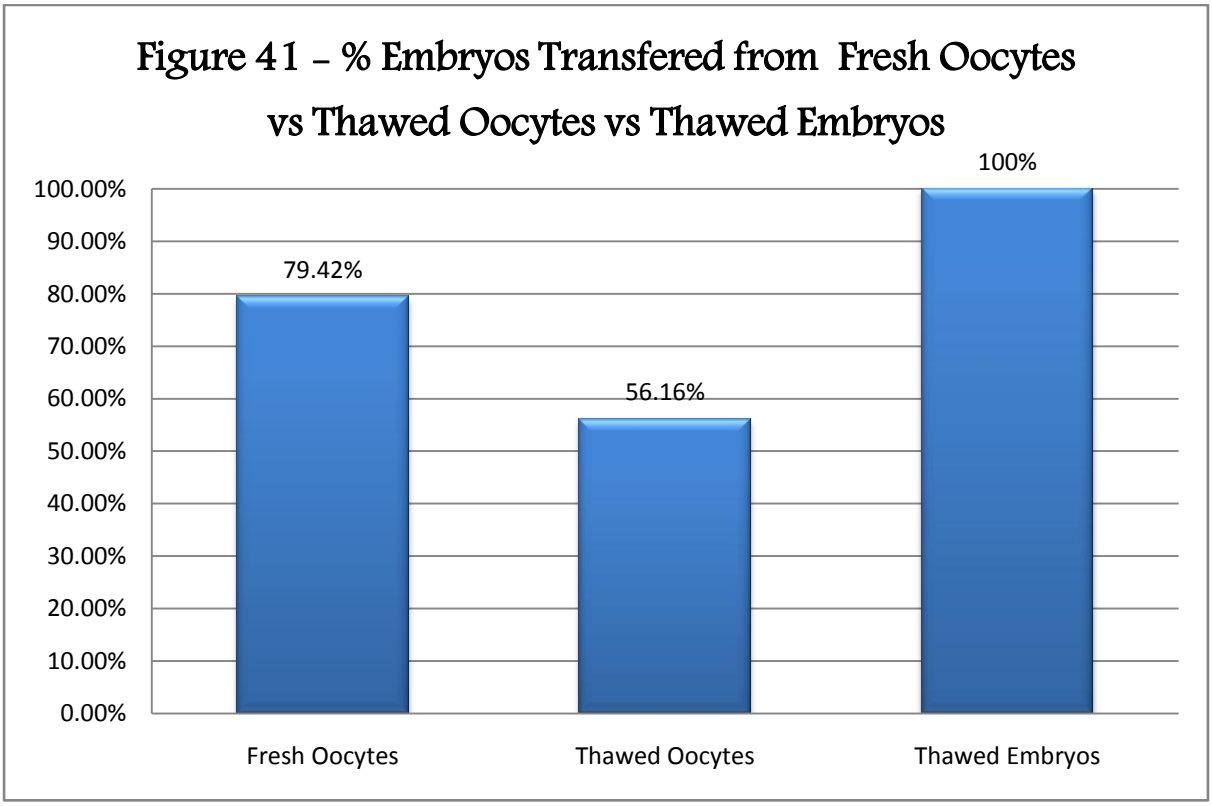


8.5. Embryo Transfers per Type of Cycle

Out of the 486 fresh oocytes injected, 386 (79.42%) resulting embryos were transferred and 41 embryos, or 56.16%, out of the 73 thawed oocytes injected have been transferred. This contrasts well with the figures reported in 2017, as there is a drop of 28.35% in embryos resulting from thawed injected oocytes. registered an increase of 5.39% over last year. Noteworthy is the fact that all 5 embryos thawed were viable to be transferred. (Table 13 and Figure 41).

Table 13. Embryos Transferred per Type of Cycle (%)

Type of Cycle	Oocytes Injected	Embryos Transferred	Transferred %
Fresh Oocytes	486	386	79.42%
Thawed Oocytes	73	41	56.16%
Thawed Embryos	5	5	100.00%
Total		432	



8.6. Embryos Transferred per Approved AFR

Out of a total of 111 couples who had their Additional Fertilization Request (AFR) approved, 102 had an IVF/ICSI procedure carried out. Only 37.25% of these couples, 38 in No, had three embryos transferred despite having approval for the fertilization of a third oocyte (Figures 42 and 43).

Figure 42 – Embryos Transfered per case of Approved AFR

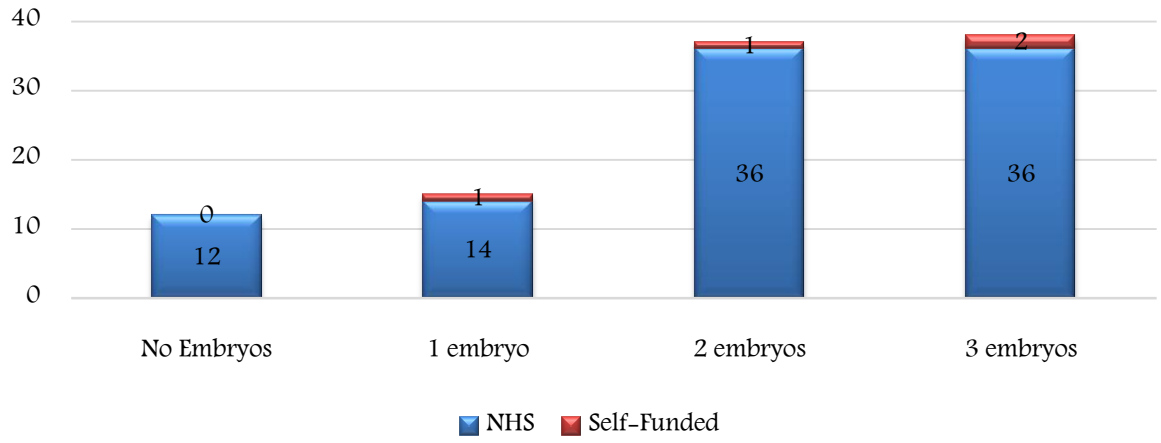
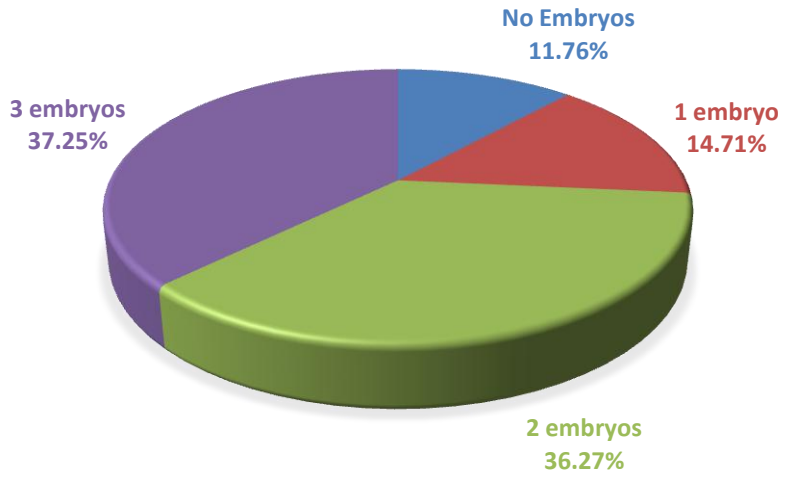


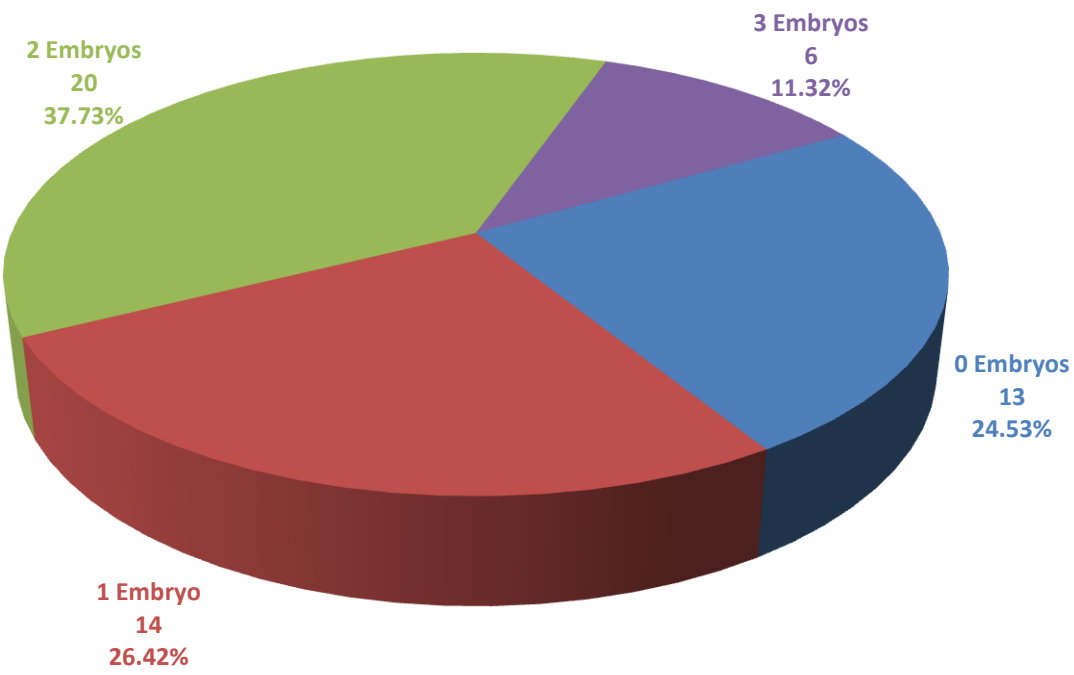
Figure 43 – Embryos Transfer Distribution (% of approved AFR)



8.7. Embryos transferred per AMH ≤1µg/l

As outlined already in Section 7.2, there was a total of 53 women with a serum AMH concentration of ≤1µg/l. Only 40 of these women had an embryo transfer affected as thirteen women (24.53%) did not have any embryos to transfer. Fourteen women, or 26.42%, had a single embryo transfer; 20, or 37.73%, had 2 embryos transferred, while the remaining six couples had 3 embryos transferred (Figure 44).

Figure 44 – Embryos Transferred for AMH ≤ 1ug/L



9. CYCLE OUTCOMES

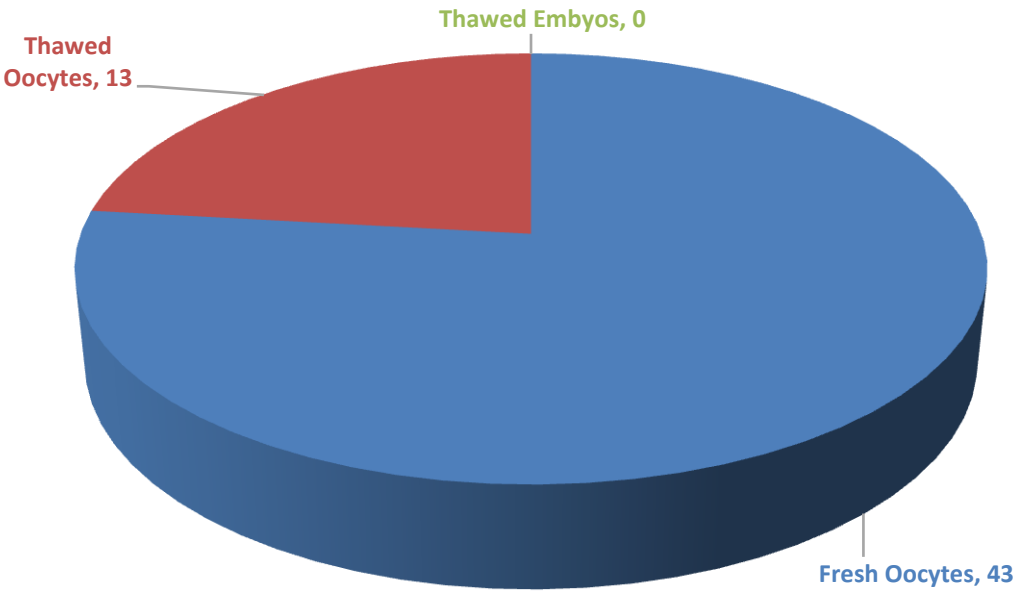
9.1. Pregnancies

Out of the 246 cycles (deducted the 3 cycles which had prior approval for freeze all), carried out in 2018, there were 43 reported pregnancies from Fresh cycles and 13 from Thawed cycles. **The resulting 56 pregnancies account for 22.76% of all cycles started**, which is 1.05% **higher** than the pregnancy rate for 2017(Figure 45 & Table 14).

Table 14. Cycle Outcome

Type	Outcome	NHS	Self-Funded	Total	% Outcome by Type	% Outcome	% Outcome of Pregnancies
Fresh Oocytes	Not Pregnant	141	24	165	76.0%	76.0%	
Fresh Oocytes	Miscarriage	7	2	9	4.1%	24.0%	17.3%
Fresh Oocytes	Live Birth	14	4	18	8.3%		34.6%
Fresh Oocytes	Expected	20	5	25	11.5%		48.1%
Thawed Oocytes	Not Pregnant	16	7	23	85.2%	85.2%	
Thawed Oocytes	Miscarriage	1	0	1	3.7%	14.8%	25.0%
Thawed Oocytes	Live Birth	0	1	1	3.7%		25.0%
Thawed Oocytes	Expected	1	1	2	7.4%		50.0%
Thawed Embryos	Not Pregnant	2	0	2	100.0%	100.0%	
Thawed Embryos	Miscarriage	0	0	0	0.0%	0.0%	0.0%
Thawed Embryos	Live Birth	0	0	0	0.0%		0.0%
Thawed Embryos	Expected	0	0	0	0.0%		0.0%

Figure 45 – Outcome – Fresh Cycles vs Thawed Cycles (NHS + Self-Funded)



9.2. Cycle Outcomes – Fresh vs Thawed

Fifty two (52) couples, or 24.0% of those undergoing Fresh cycles managed to get pregnant. Out of these 52 pregnancies, 9 couples miscarried, 18 had a live birth, while the remaining 25 couples (11.5%) are still expecting (Figures 46 and 47). Four (4) couples, or 14.8% of those undergoing a Thawed cycle got pregnant. Out of these four pregnancies, 1 miscarried, 1 had a live birth, while the remaining 2 couples are still expecting (Figures 48 and 49). The only two couples that underwent embryo transfer did not have a successful cycle (Figure 50).

As a result, in 2018 the pregnancy rate for Fresh cycles was 9.2% higher than for Thawed Cycles (Table 14).

Figure 46 – Outcome of Fresh Cycle (Qty)

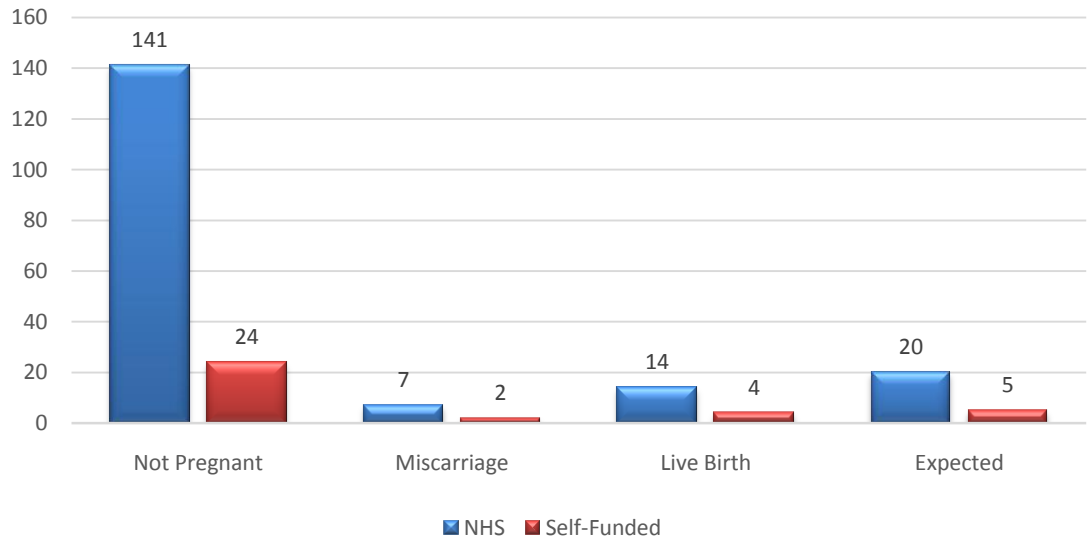


Figure 47 – % Outcome – Fresh Cycles (NHS + Self-Funded)

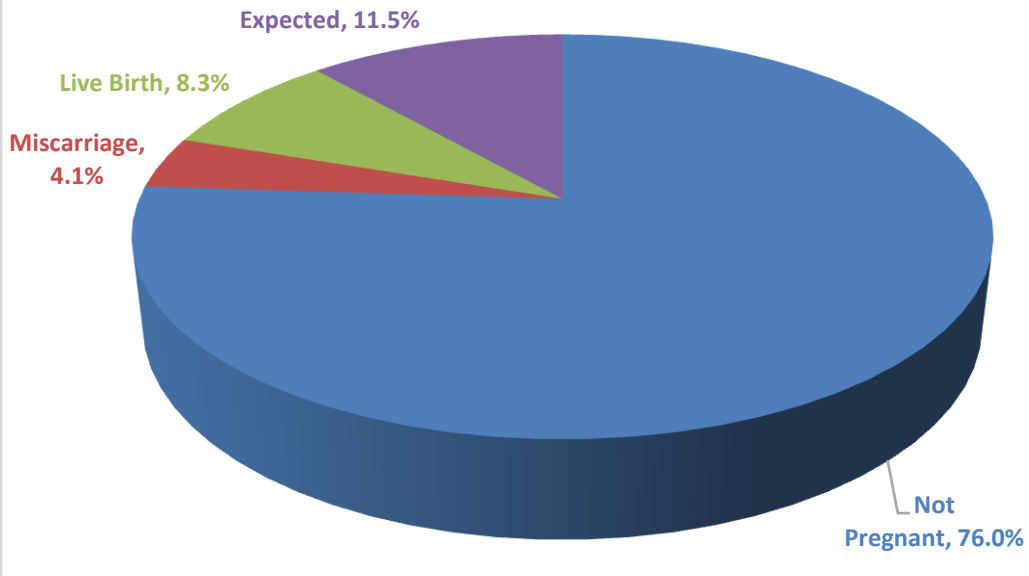


Figure 48 – Outcome of Thawed Oocytes Cycle

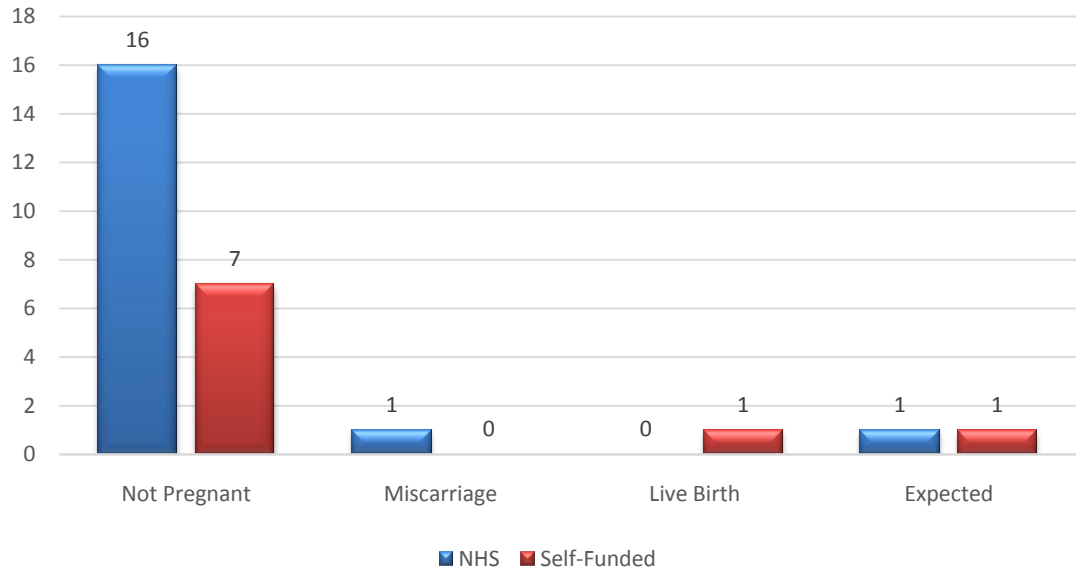
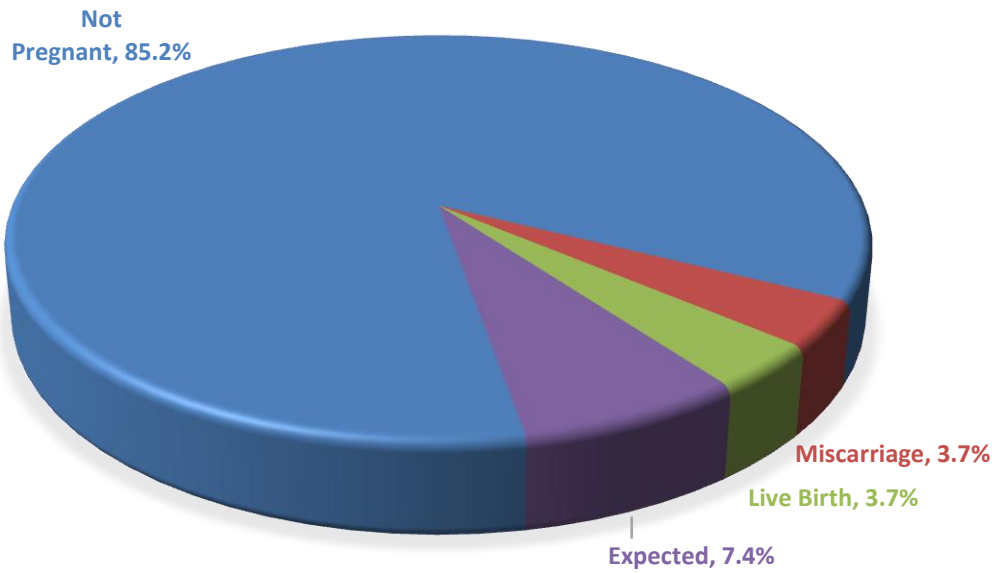
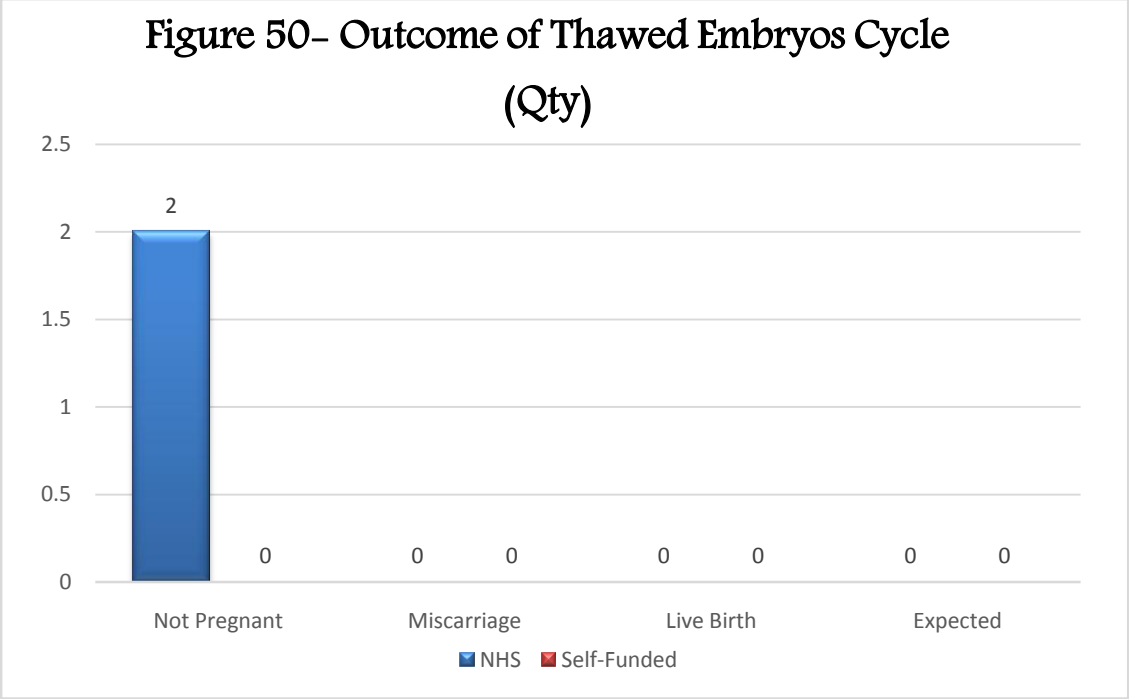


Figure 49 – % Outcome – Thawed Oocytes Cycles (NHS + Self-Funded)





9.3. Cycle Outcomes – NHS vs Self-Funded

The pregnancy rate in 2018, reported by the private clinics for thawed oocytes cycles was 11% higher than that reported by the ART Clinic at MDH. Same applies to the pregnancy rate reported by the private clinics for fresh oocytes cycles which was 8.9% higher than that reported by the ART Clinic at MDH. This contrasts well with figures reported in 2017, as MDH ART Clinic had a 3.4% higher pregnancy rate from thawed oocytes cycles.

The sum of live and expected births from Fresh cycles carried out at MDH was 18.7%, while that for private clinics was 25.7% (Figure 51), this was also due to the fact that MDH reported 7 miscarriages whilst the private clinics reported only 2 miscarriages. Same also applies to the sum of live and expected births from Thawed oocytes cycles carried out at MDH which was reported as 5.6% while that for the private clinics was 22.2%, only 1

miscarriage was reported by MDH, while the private clinics reported no miscarriages from thawed cycles (Figure 52). There are no live or expected births from cycles carried out with thawed embryo transfers (Figure 53).

Figure 51 – Fresh Cycles – % Outcome (NHS vs Self-Funded)

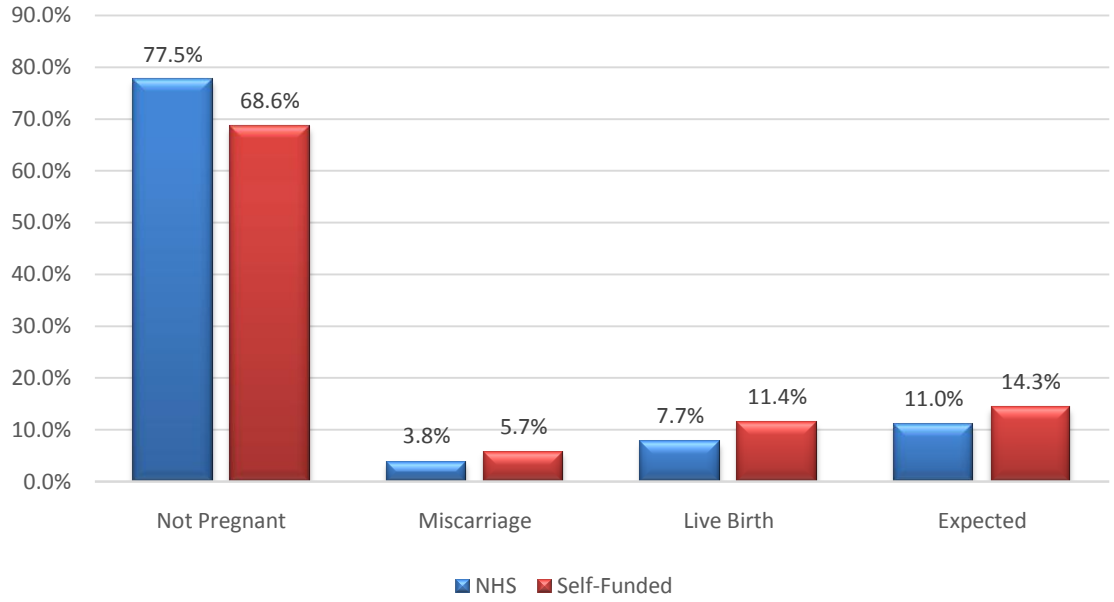


Figure 52 – Thawed Oocytes Cycles – %Outcome (NHS vs Self-Funded)

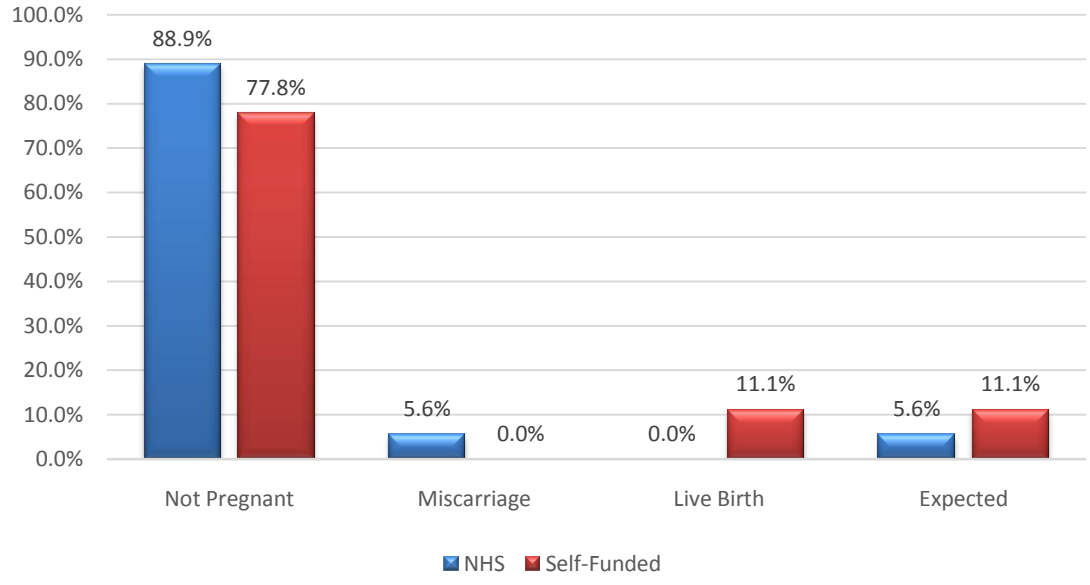
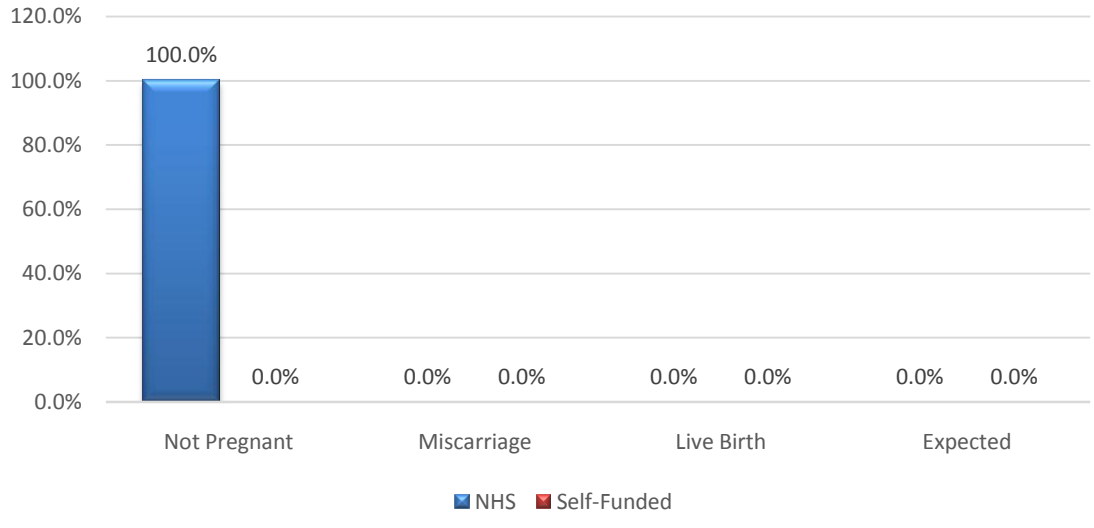


Figure 53 – Thawed Embryos Cycles – % Outcome (NHS vs Self-Funded)



9.4. Pregnancies by Age

In 2018, pregnancies were reported across all age groups. The highest number of pregnancies reported was for women in the 33-36 year old bracket, this is in line with figures reported in 2017 (Figure 54). This was however not reflected in the pregnancy rate as percentage of cycles per age group which was highest for women aged 25-28, at 46.2% (Figure 55).

This contrasts well with the pregnancy rate as percentage cycles per age group reported in 2017 wherein the highest group was in couples where the female was between 33 to 36 years of age. It would appear that in 2018, maternal age was one of the most important predictive factor for an IVF/ICSI procedure to result in a pregnancy.

Figure 54 – Pregnancy by Age Group

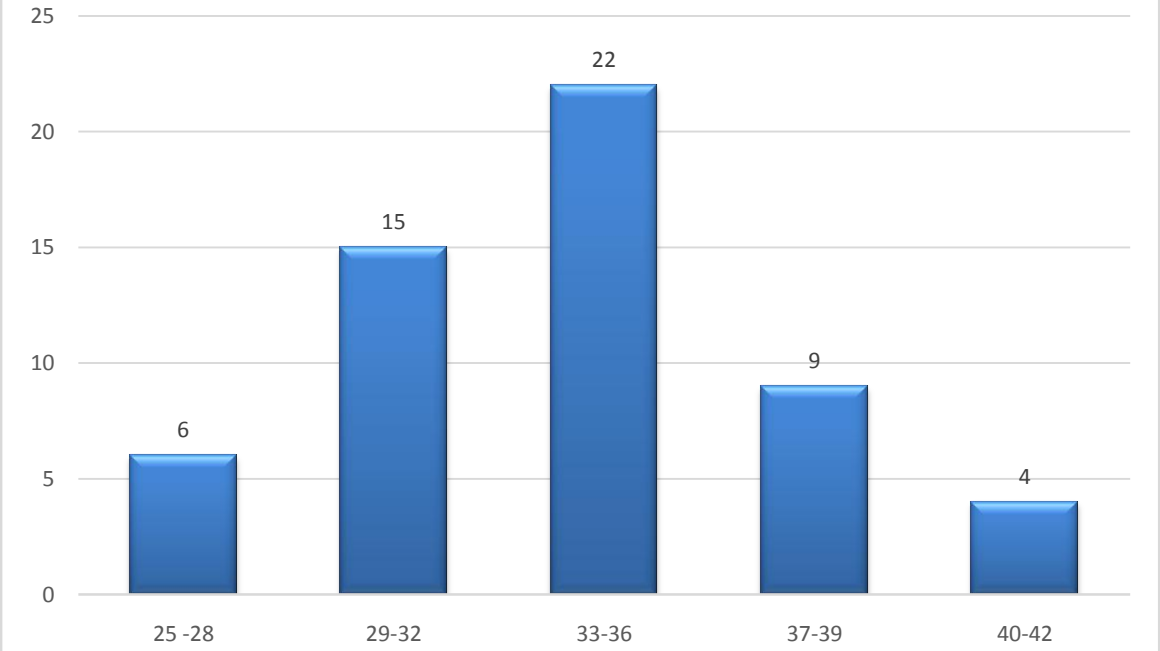
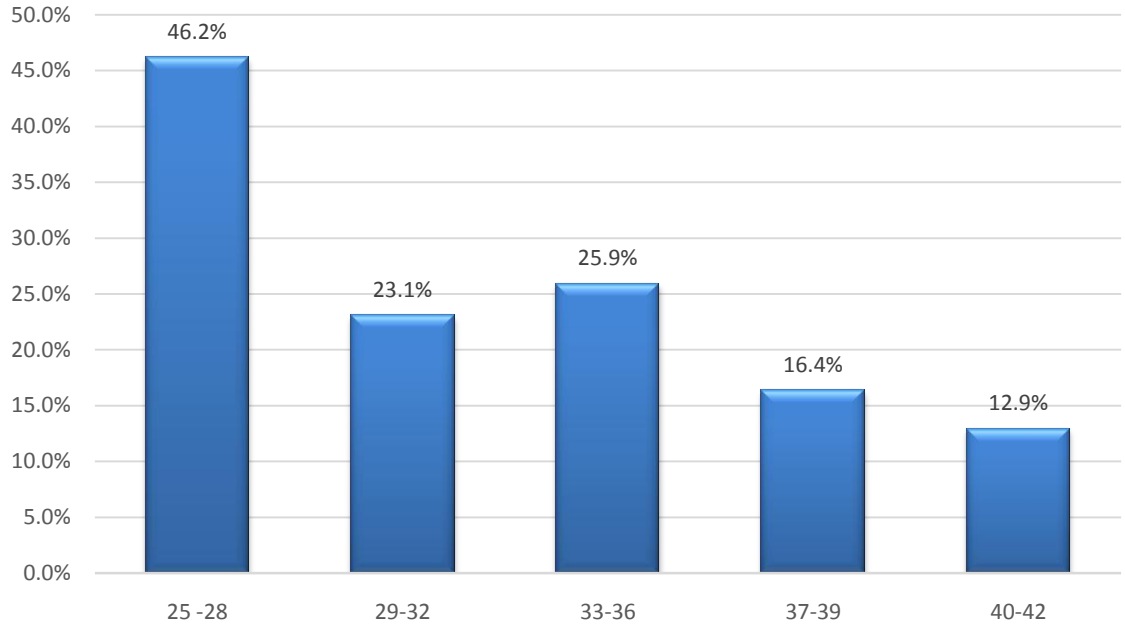


Figure 55 – Pregnancy Rate as % of Cycles per Age Group



9.5. Pregnancy Rate per Embryos Transferred

From a total of 212 couples who had an embryo transfer effected, there were 56 resulting pregnancies, or 26.42%, an increase of 1.98% when compared to the previous year.

The couples who were most successful at achieving a pregnancy in 2018, were those who had 3 embryos transferred (35.14%), this contrasts with figures reported in 2017, where the couples that were most successful were those who had 2 embryos transferred. The current calendar year registered an increase of 21.35% over the 13.79% that was reported last year with 3 embryos transferred. These were followed by those couples who had 2

embryos transferred (25.17%). The remaining 21.55% achieved a pregnancy through a single embryo transfer (Table 15).

Noteworthy to note is that there was a significant drop of 8.36% in the pregnancies achieved by 2 embryos transferred and an increase of 15.63% in the pregnancies achieved by one embryo transferred.

Table 15. Pregnancy Rate per Embryos Transferred

Transferred Embryos	Total IVF/ICSI Procedures	Total Pregnancies	% Pregnancies
0	37	0	0.00%
1	32	7	21.88%
2	143	36	25.17%
3	37	13	35.14%
Total	249	56	22.49%
Total procedures with Embryo transfer	**212**	**56**	**26.42%**

9.6. Pregnancy Distribution per ART Cycle Attempts

Twenty six (26) couples (or 21%) out of the 56 who got pregnant from cycles carried out in 2018, achieved a pregnancy on their 1st IVF/ICSI attempt, these were achieved by 21 couples who had undergone their cycle at the ART Clinic at MDH and 5 couples who self-funded their treatment. 18 couples (or 24.1%) achieved a pregnancy on their 2nd attempt, 14 from MDH cycles and 4 from the private clinics cycles. 12 couples (38.7%) on their 3rd attempt, these pregnancies were achieved 8 from cycles on the NHS and 4 that were self-funded (Figures 56, 57 and 58). No pregnancies were reported for the couples who had undergone their 4th, 5th, and 6th attempt.

Figure 56 – NHS Pregnant vs Non-Pregnant Totals per ART Cycle Attempts

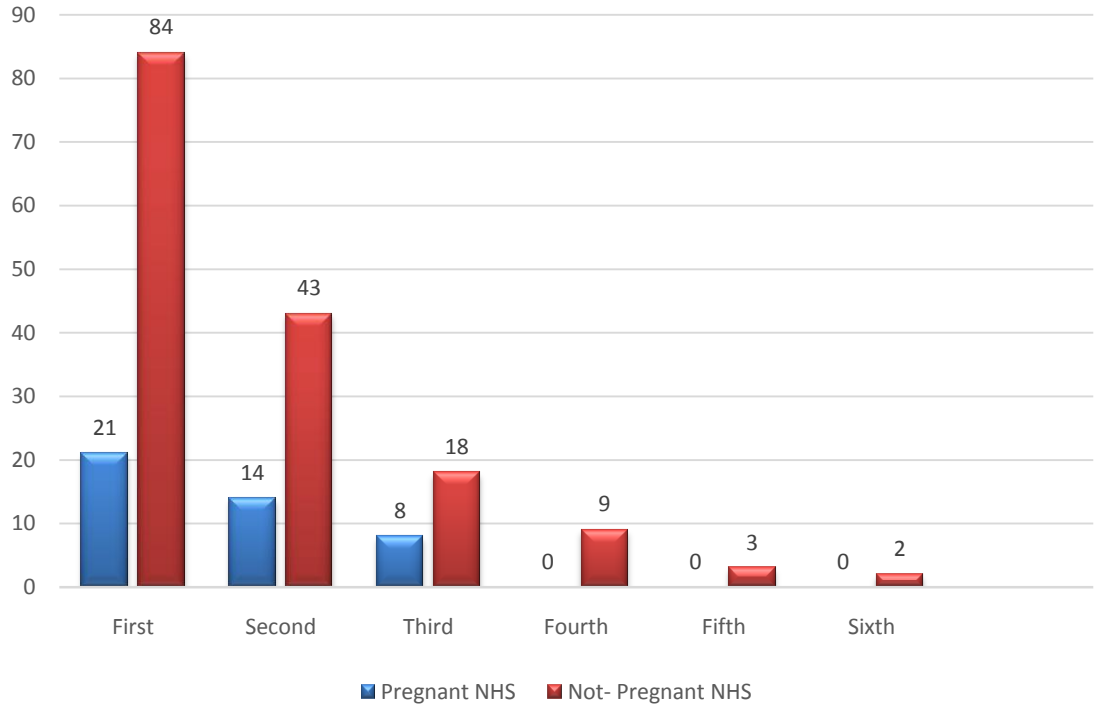


Figure 57– Self-Funded Pregnant vs Non-Pregnant Totals per ART Cycle Attempts

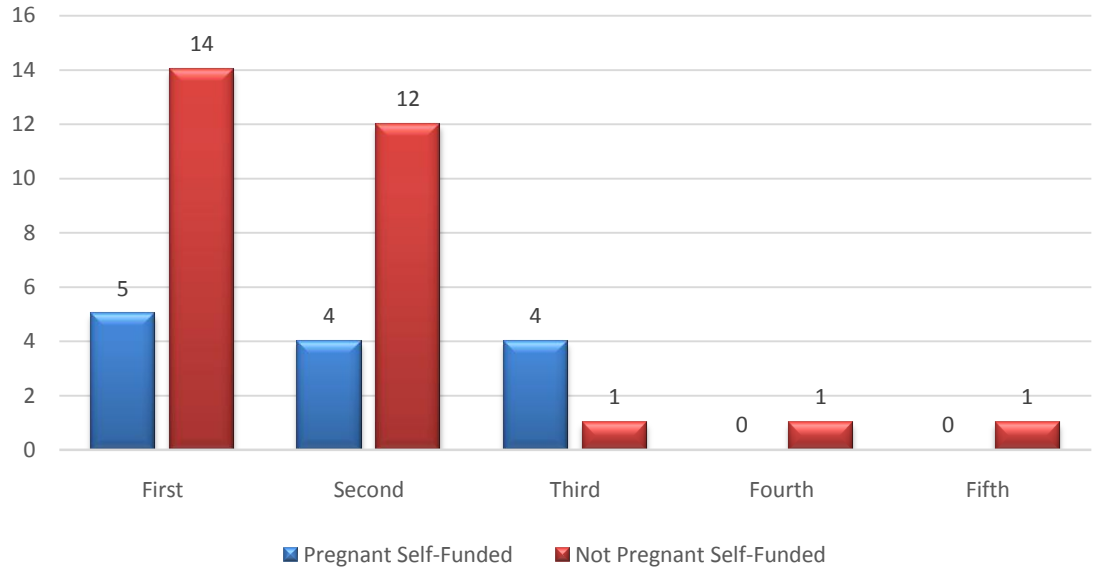
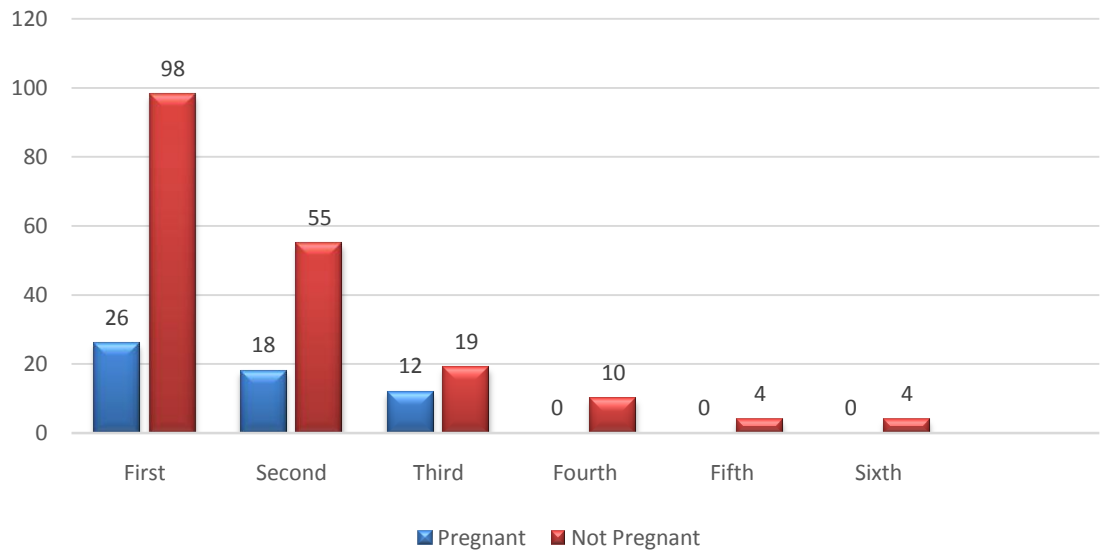


Figure 58 – Total Pregnant vs Non-Pregnant per ART Cycle Attempts



9.7. Miscarriages per ART Cycle

In 2018, a total of 10 miscarriages were reported, 8 from cycles carried out at MDH and 2 from cycles that were self-funded. Five (5) of the couples who got pregnant on their first IVF/ICSI attempt miscarried. There were (4) couples who miscarried after a successful 2nd IVF/ICSI attempt. The other one (1) couple miscarried after getting pregnant from a 3rd attempt (Figures 59 and 60).

Figure 59 – Miscarriage per ART Cycle (NHS vs Self-Funded)

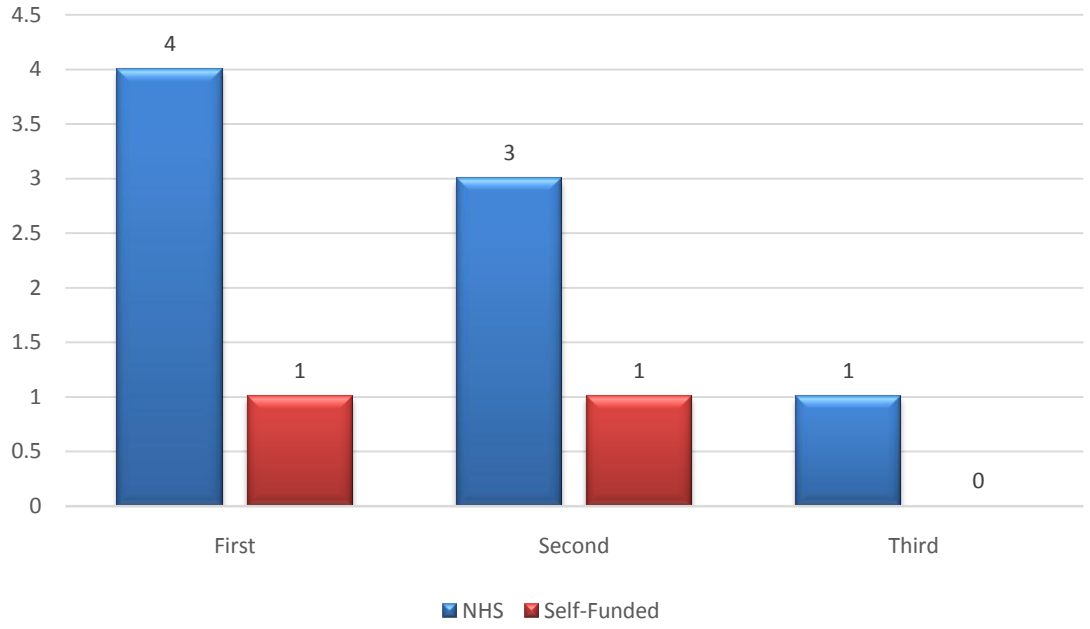
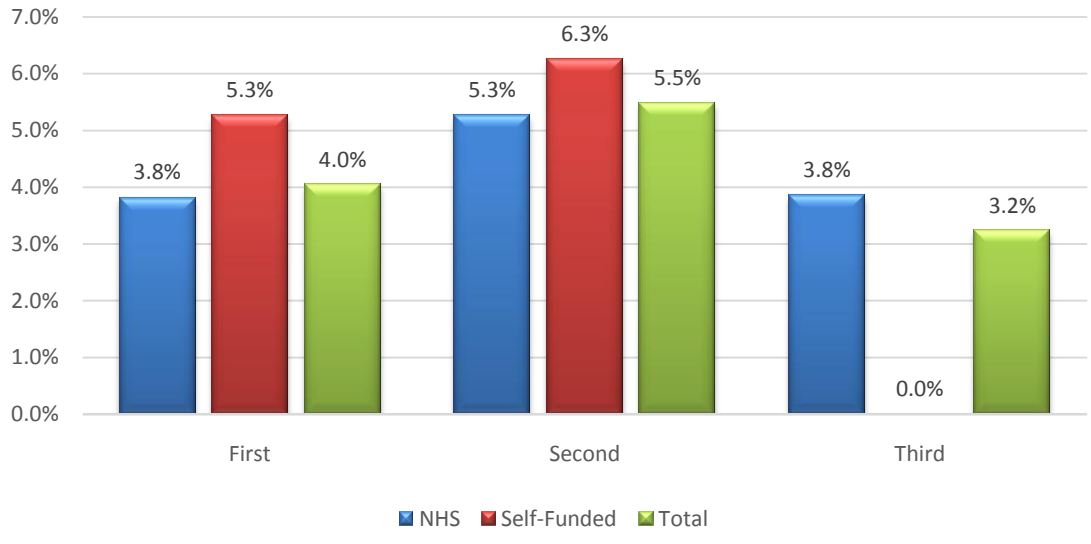


Figure 60 – % Miscarriage per ART Cycle (NHS vs Self-Funded vs Total of all Cycles)



9.8. Miscarriages by Age

Miscarriages were reported for women aged up to age 39. There were 2 reported miscarriages for women aged 25-28, 1 miscarriage for women in the 29-32year old bracket. The majority of miscarriages, 6 in number were reported in the 33-36 year old bracket, and one miscarriage was reported for women aged 37-39. No miscarriages were reported for women aged 40-42 years (Figures 61 and 62).

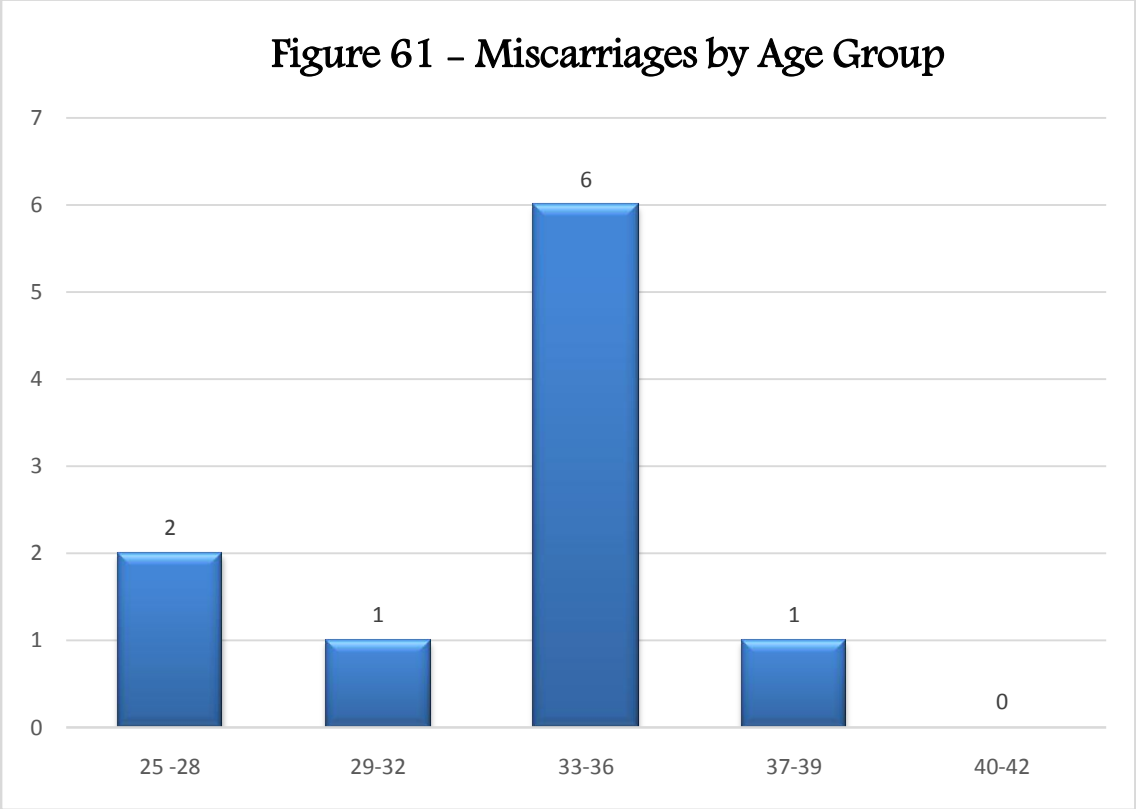
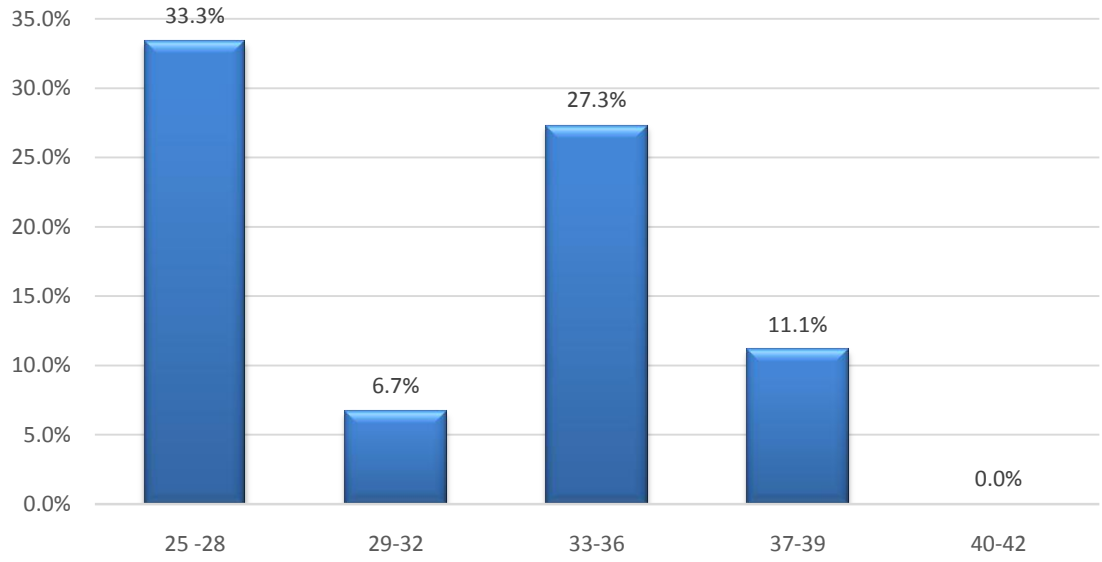


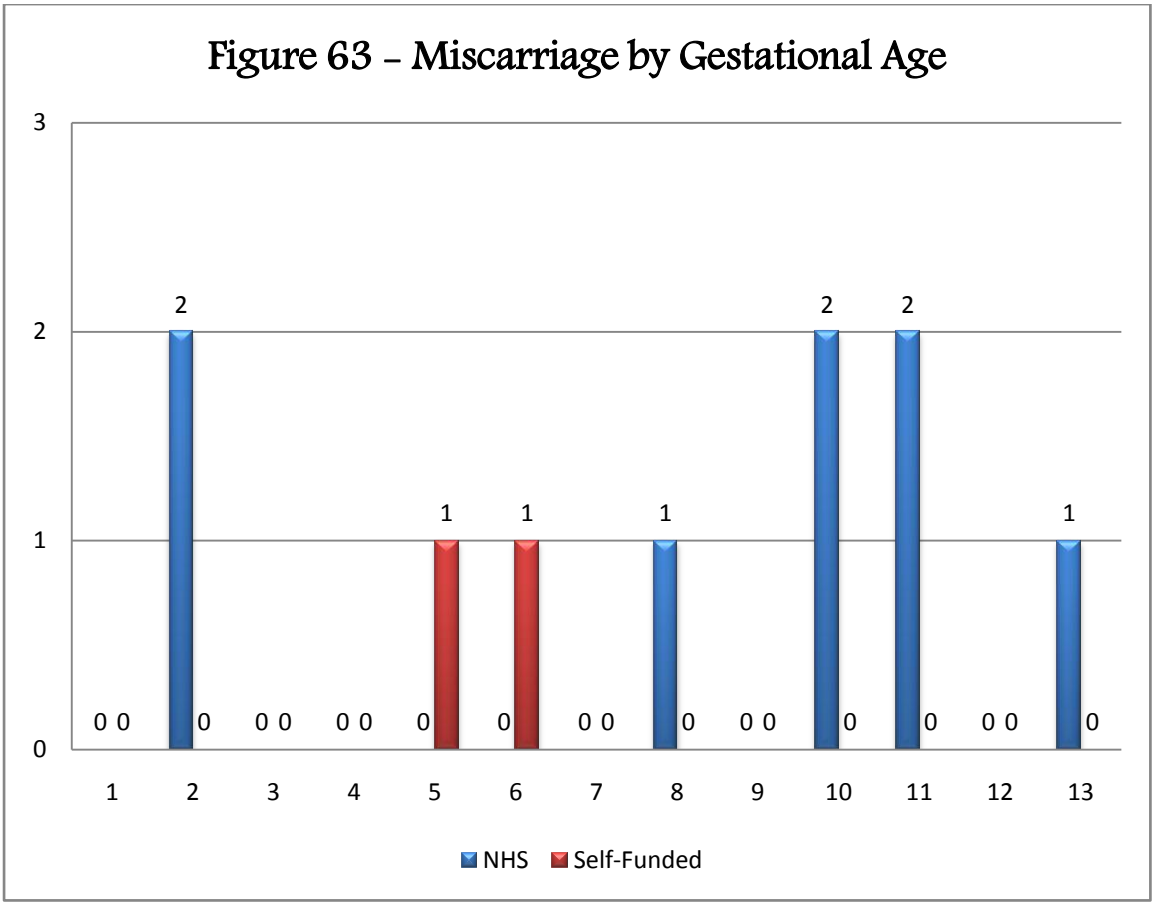
Figure 62 – Miscarriages as % of Pregnancies in Age Group



9.9. Miscarriages by Gestational Age

The 10 miscarriages reported were from two women who were in their 2nd week gestation. One (1) woman miscarried at 5 weeks; another one miscarried at 6 weeks; one miscarried at 8th week while another 2 women miscarried at the 10th week respectively. Two other women miscarried at 11 weeks gestation. The remaining woman miscarried at 13 weeks gestation (Figure 63).

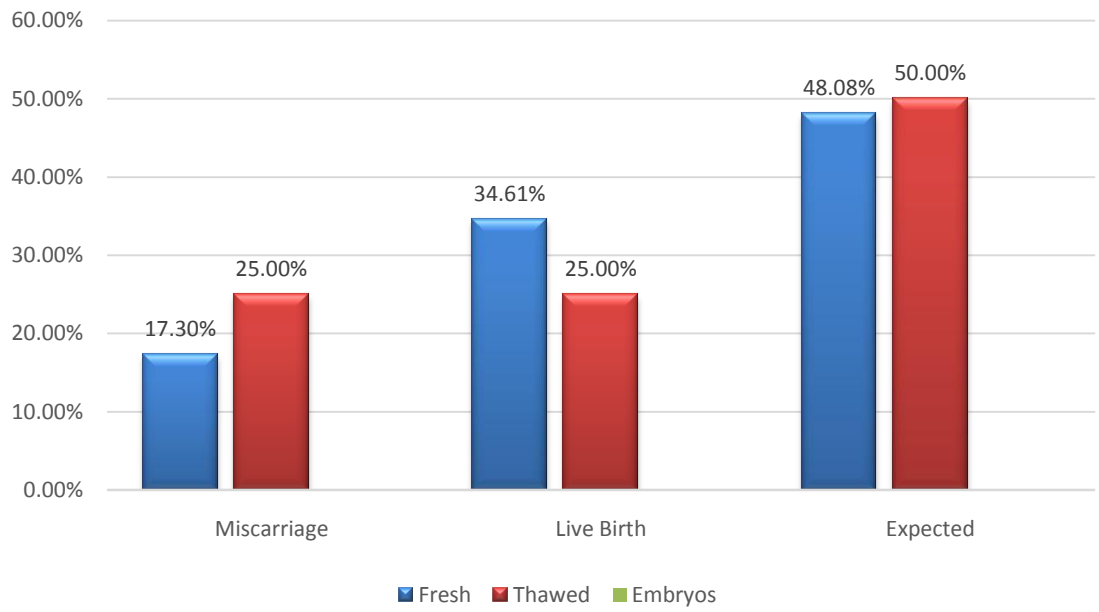
Figure 63 – Miscarriage by Gestational Age



9.10. Miscarriages from Fresh vs Thawed Cycles

Ten (10) couples, or 17.50%, miscarried after achieving a pregnancy from a Fresh cycle and 2 couples (22.20%), miscarried after a successful Thawed cycle (Figure 64, Table 14).

Figure 64 – Pregnancy Outcome %
Fresh vs Thawed Oocytes



10. BIRTH EVENTS

10.1. Births from April – November 2017 Cycles

In 2018, thirty three (33) babies, 17 females and 16 males, were born as a result of cycles performed between April and November 2017 (Figure 65). Hence, a total of 61 babies, 32 females and 29 males, were born out of the 304 procedures carried out throughout 2017 (Figure 66).

Figure 65 – Apr–Nov '17 Live Births
Males vs Females

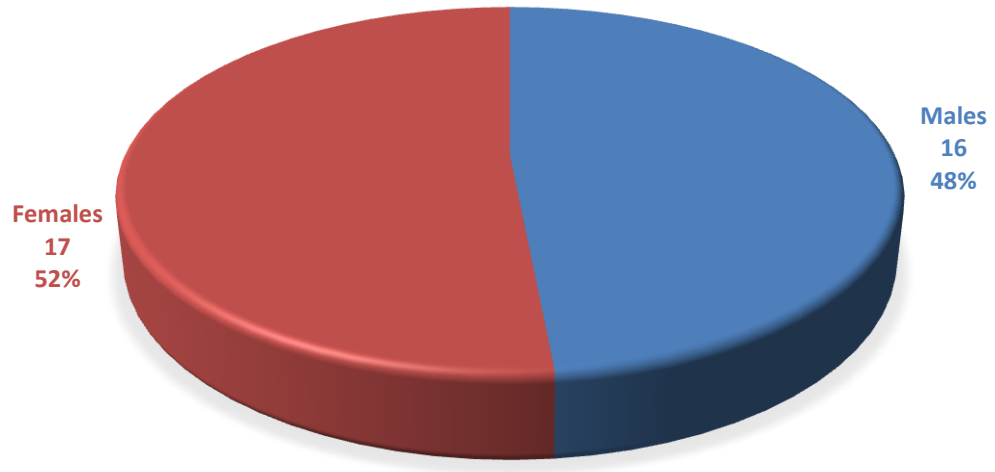
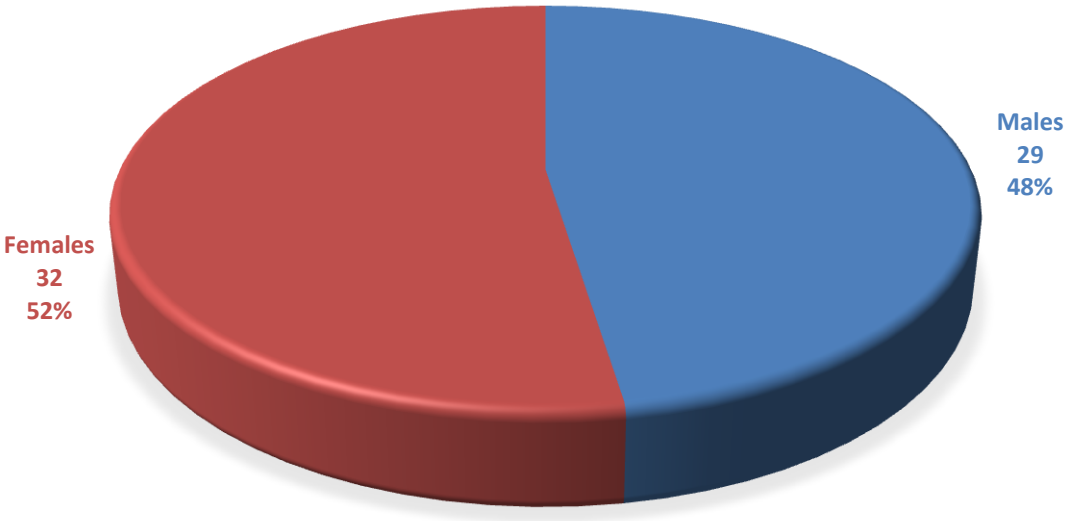


Figure 66 – 2017 Live Births
Males vs Females



Forty four (44) babies, or 86%, were born out of Fresh cycles and 7 babies were born out of Thawed cycles (Figure 67). Thirty seven babies or (73%) of the babies born out of procedures carried out in 2017 were from procedures carried out at MDH, while the remaining 27% were from procedures carried out at the private clinics (Figure 68).

Figure 67 – 2017 Live Births
Fresh vs Thawed

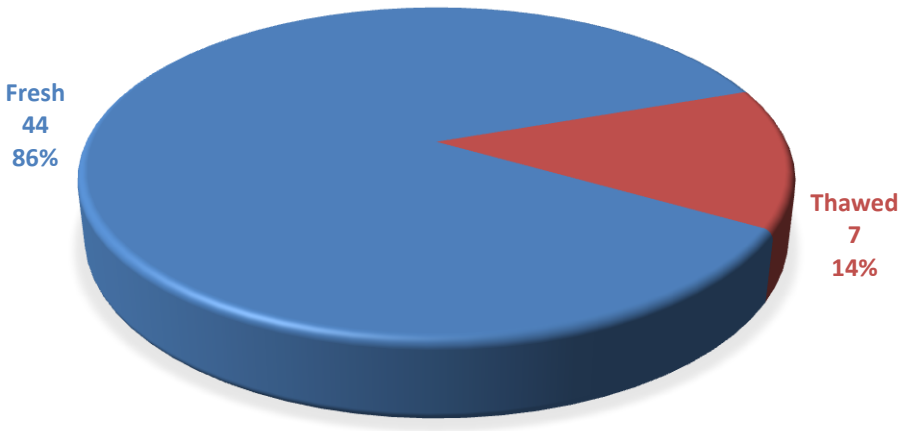
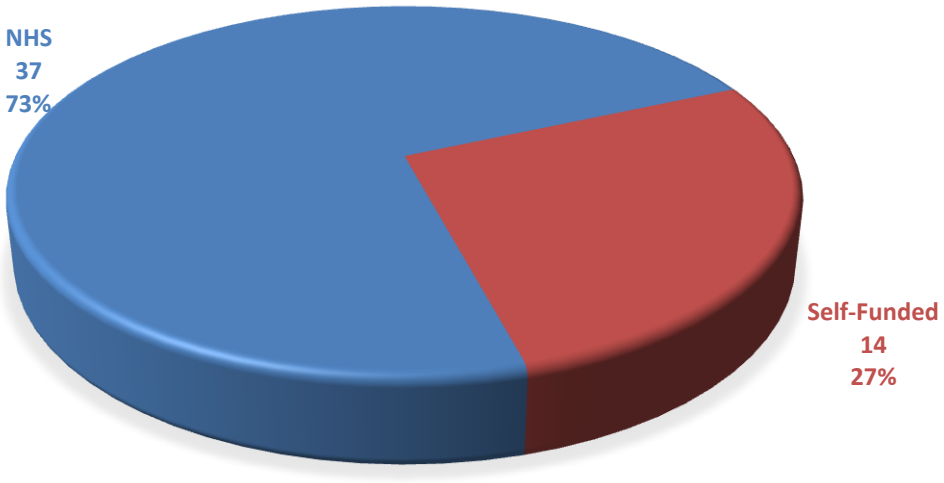
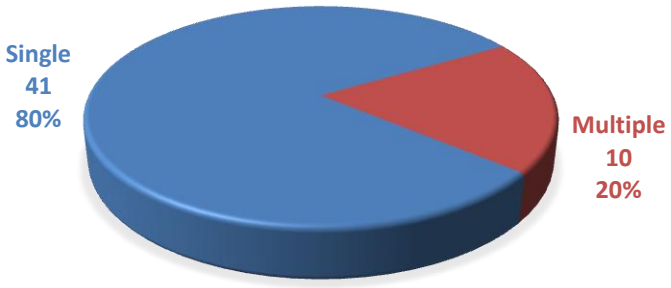


Figure 68 – 2017 Live Births
NHS vs Self-Funded



Out of a total of 51 Live Birth Events in 2017, there were 41 single births and 10 multiple births. The multiple births consisted of ten sets of twins (Figure 69).

Figure 69 – 2017 Live Birth Events – Singles vs Multiples



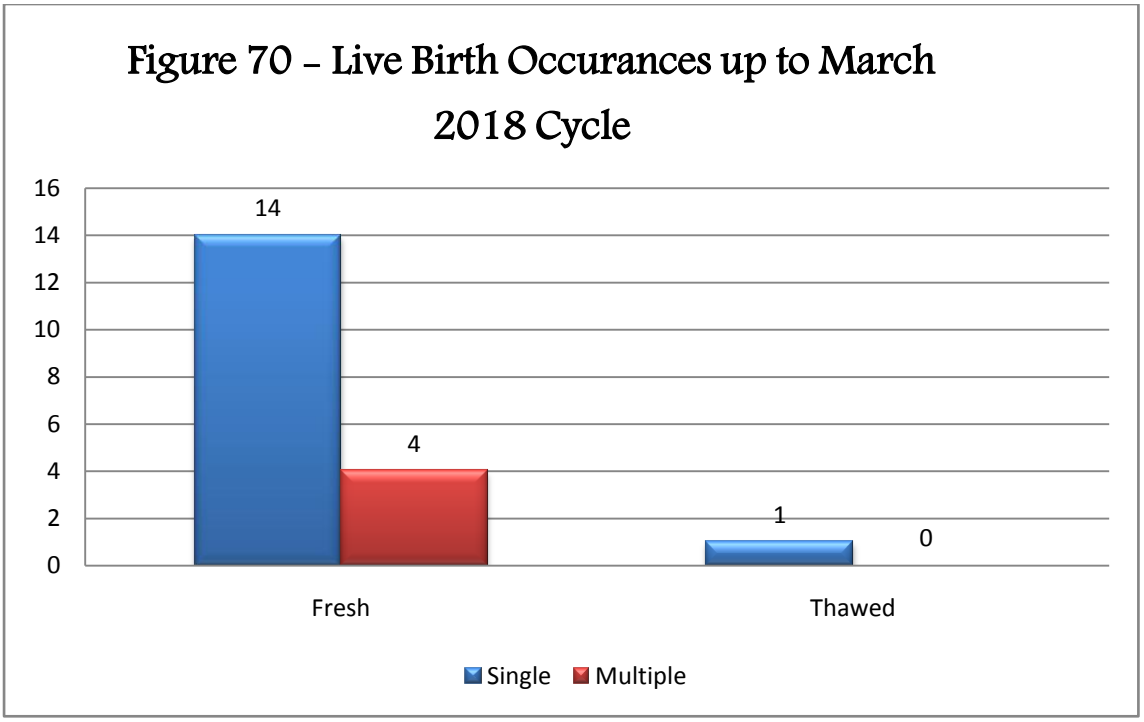
In summary, out of a total of 304 cycles carried out in 2017, 238 couples did not achieve a pregnancy, 15 miscarried, and 51 had a live birth, for a **final Take-Home Baby Rate of 16.78%** (Table 16), **which is a 3.37% decrease than that reported in 2016.**

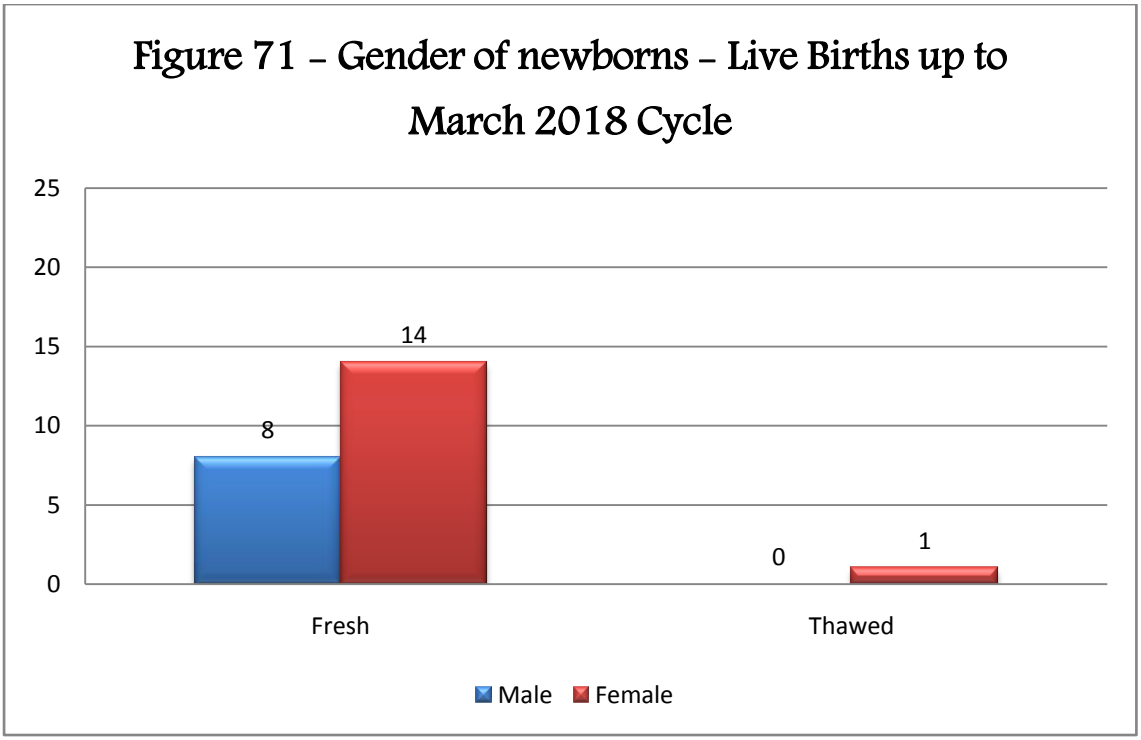
Table 16 – % Take-Home Baby Rate 2017

Cycle Outcome	Qty	% of pregnancies	% of total cycles
Live Birth	51	77.27%	**16.78%**
Miscarriage	15	22.73%	4.93%
Not Pregnant	238		78.29%
TOTAL CYCLES 2017	304		100.00%

10.2. Birth Events from 2018 Cycles – Fresh vs Thawed

The number of babies born out of procedures carried out between January and March 2018 was 23. Fourteen (14) singletons and four multiples were born from Fresh cycles. One singleton was born from Thawed cycles. Babies born were 8 males and 15 females (Figures 70 and 71). No Anomalies were observed in infants born.



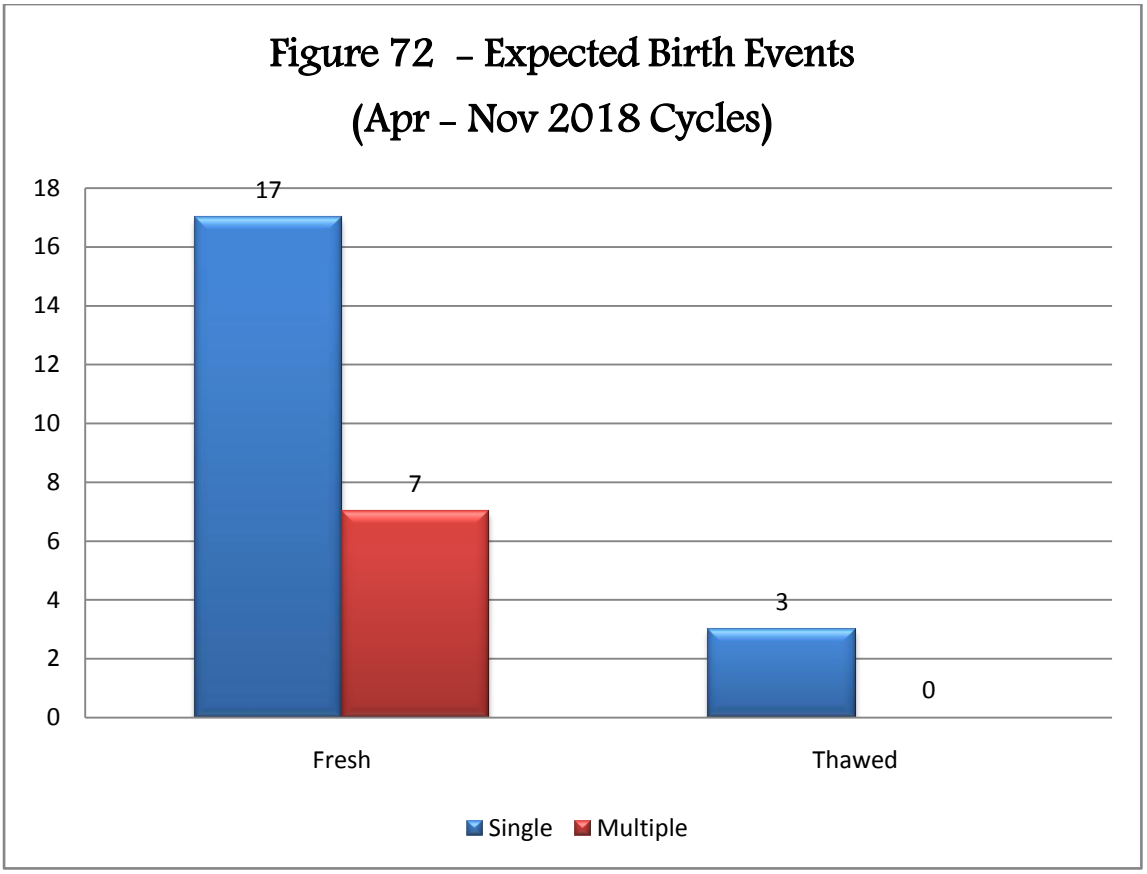


10.2.1. Expected Birth Events from Fresh vs Thawed

Twenty seven (27) birth events are expected from cycles carried out between April and November 2018. Seventeen (17) singletons and 7 multiples (6 sets of twins and one set of triplets) are expected from Fresh cycles and 3 singletons are expected from Thawed cycles (Figure 72). **The percentage of live and expected births from multiple pregnancies in 2018 is 4.47% of all cycles, an increase of 1.18% over 2017.**

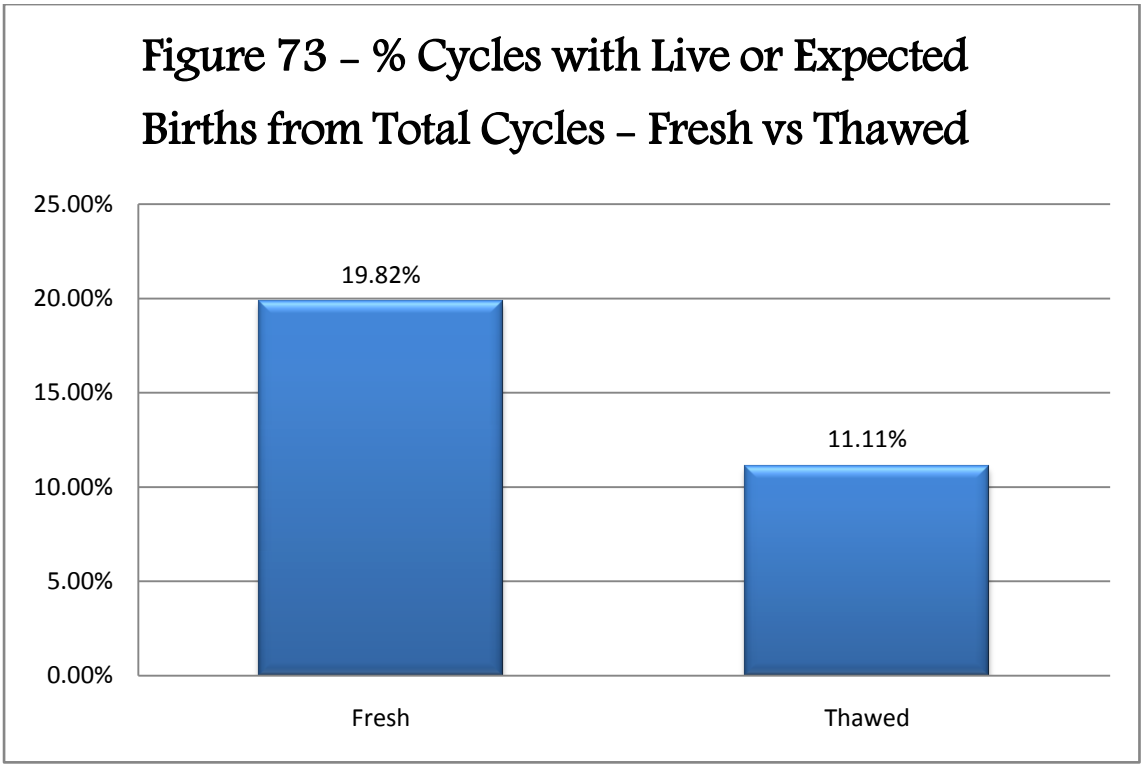
Hence, out of the 46 live and expected births from procedures carried out in 2018, 54 babies are from pregnancies achieved through Fresh cycles, and the remaining 4 babies are from pregnancies achieved through Thawed cycles.

Figure 72 – Expected Birth Events (Apr – Nov 2018 Cycles)



10.3. Maximum Success Rate – Fresh vs Thawed

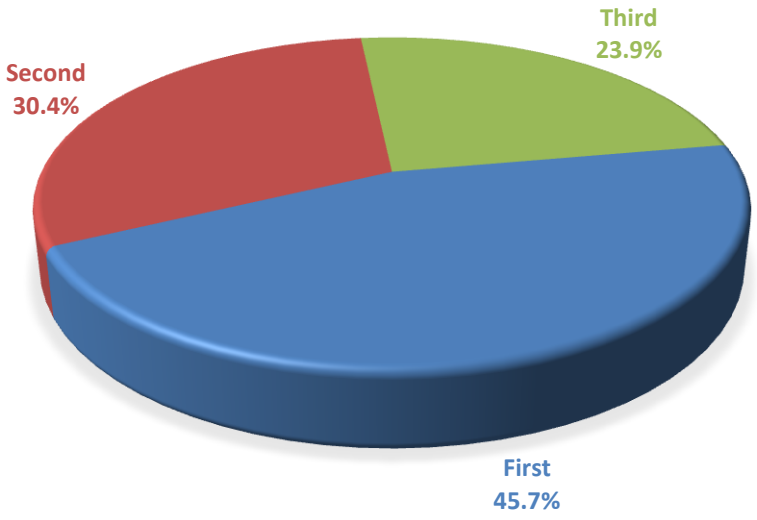
From the **217 Fresh** cycles carried out, there are 43 reported birth events (live + expected), for a maximum success rate of **19.82%**, which is 0.53% lower than last year's 20.35% maximum success rate from fresh cycles. Three (3) birth events (live + expected) are reported from the 27 **Thawed** cycles performed, for a maximum success rate of **11.11%**, which is 1.22% lower than that of 2017 (Figure 73).



10.4. Birth Events per ART Cycle

Out of a total of 46 reported birth events (live + expected) from procedures carried out in 2018, there were 21 birth events (40.35%) from couples undergoing their first IVF/ICSI attempt, 14 birth events (30.43%) from a 2nd attempt and 11 birth events (23.91%) from a 3rd attempt (Figure 74). Noteworthy is the fact that whilst there was a decrease in first time attempts, there was increase in both the 2nd and 3rd attempts with an increase of 4.53% and 16.51% respectively.

Figure 74 – Live & Expected Birth Events Distribution by ART Cycle



The majority of these birth events (live and expected) 35 couples or 76% of couples experiencing a birth event, are from cycles undergone at MDH, the remaining 11 couples had self-funded their treatment (Figures 75 and 76).

Figure 75 –NHS Live Birth & Expected per ART Cycle

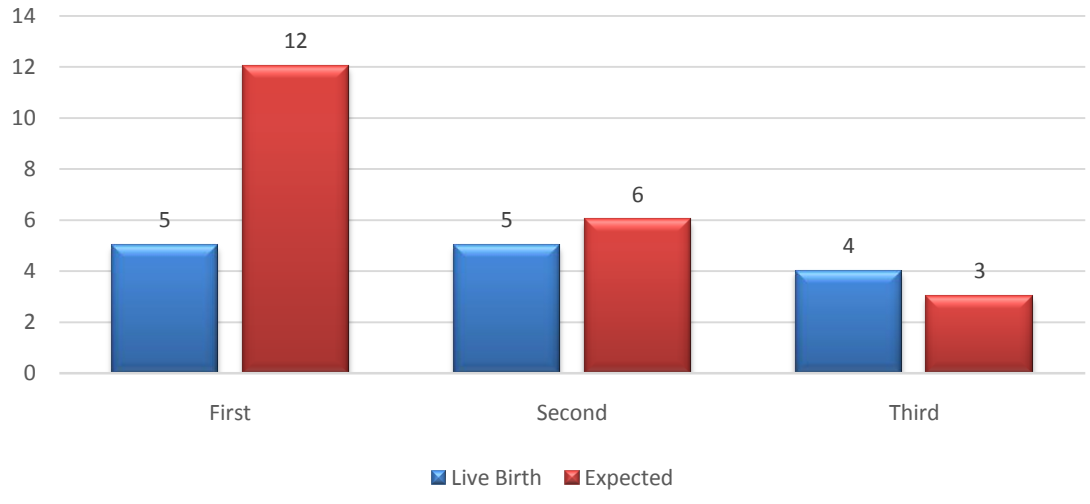
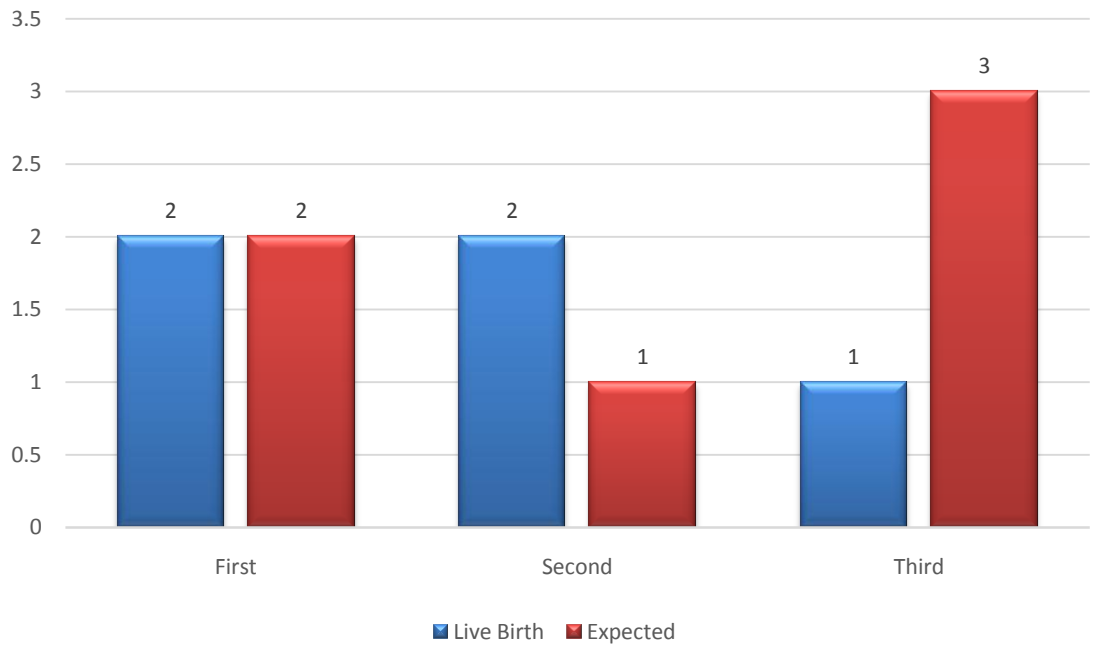


Figure 76 – Self-Funded Live Birth & Expected per ART Cycle



Overall outcome of birth events (live + expected) from all 246 procedures carried out in 2018, show that 16.9% of all couples undergoing their first IVF/ICSI attempt will experience a birth event a drop of 5% from figures reported in 2017. Total of couples undergoing a 2nd attempt have also registered an increase of 4.6% over previous year from 14.6% to 19.2%. A total of 35.5% of all couples undergoing their third attempt will experience a birth event. These figures are encouraging as they show a major increase of 20.9% over the figures reported in 2017 (Figures 77, 78, 79 and 80).

Figure 77 – NHS – % Live Birth & Expected of Cycles per ART Cycle

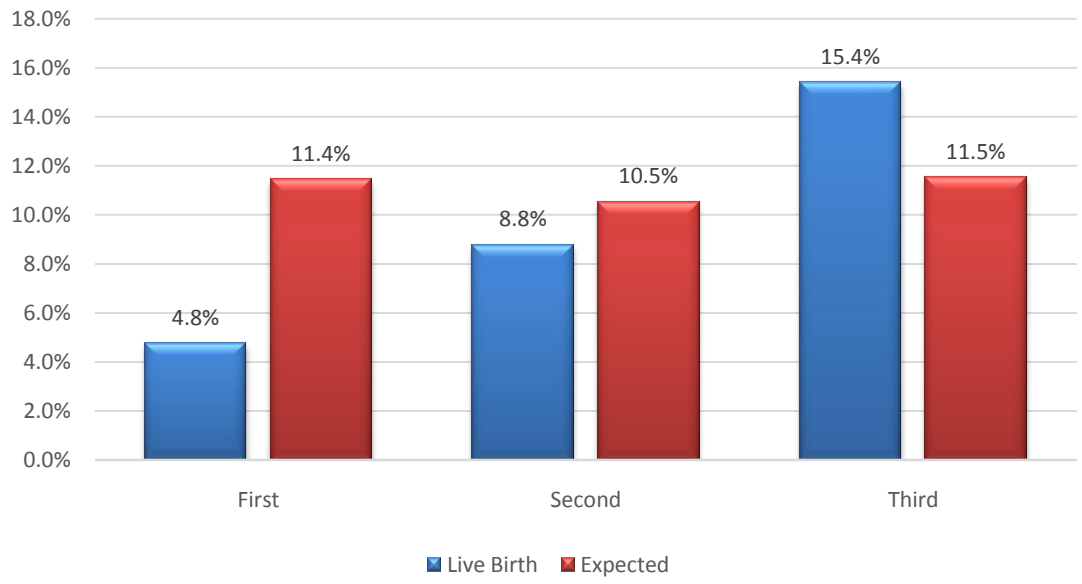


Figure 78 – Self-Funded – % Live Birth & Expected of Cycles per ART Cycle

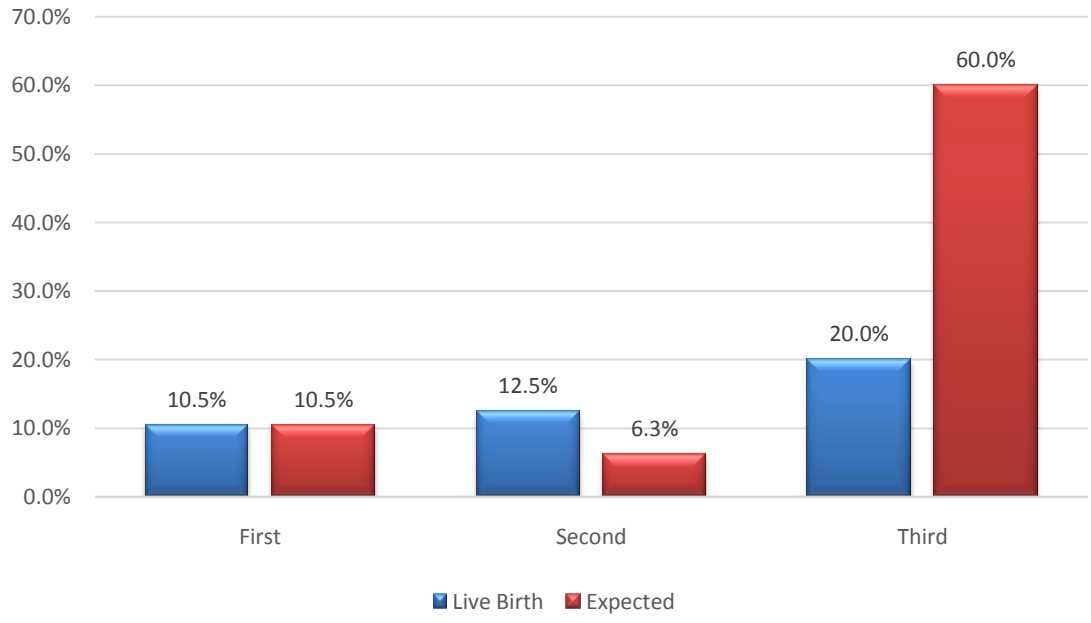


Figure 79 – Overall – % Live Birth & Expected of Cycles per ART Cycle

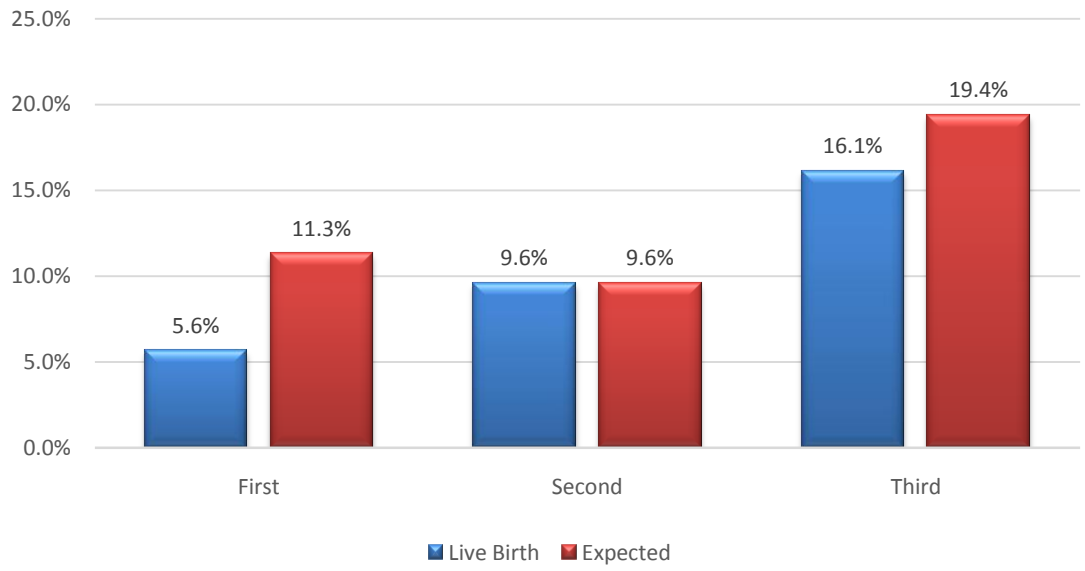
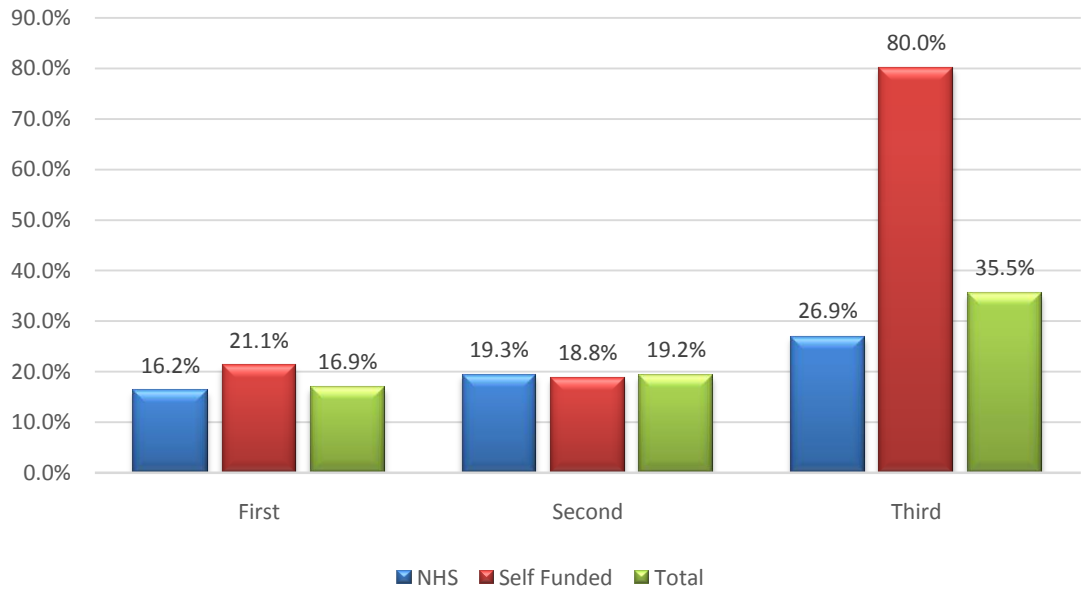


Figure 80 – Max 'Take-Home Baby' Rate – % of Cycles per ART Cycle – NHS vs Self-Funded



10.5. Outcome for Approved AFR

As outlined in Section 8.6 above, there were 9 couples who had their Additional Fertilization Request (AFR) approved but did not manage to undergo the IVF/ICSI procedure.

Notwithstanding the fact that the remaining 102 couples had an extra oocyte available for fertilization, the rate of Birth Events (Live + Expected) with multiples (2.94%) is lower than the overall rate of Birth Events (Live+ Expected) with multiples which stands at 4.47%. The total Birth Events (Live + Expected) for couples with an approved AFR who had undergone an IVF/ICSI procedure stand at 17.64%, an increase of 3.23% over figures reported in 2017 (Table 17).

Table 17. Outcome for Approved AFRs

No of Approved AFR	No of Procedures undergone from Approved AFR	No of Pregnancies	Miscarriages	Expected & Live Birth Events	Singles	Multiples
111	102	23	5	18	15	3
% of Procedures undergone from Approved AFR		22.55%	4.90%	17.64%	14.70 %	2.94%

These results show that for this population, approval for the fertilization of 3 oocytes instead of 2 was of benefit since these couples only fell short 1.3% of reaching the overall Maximum Success Rate, which is the sum of the live and expected birth events, as illustrated in Table 18.

10.6. Percentage Maximum Success Rate – 'Take Home Baby' Rate

In conclusion, from the 56 couples who achieved a pregnancy in 2018, 19 (33.93%) had a live birth, 27 (48.21%) are still expecting, and 10 couples (17.86%) miscarried.

Out of a total of 246 cycles carried out, **7.72%** of couples had a live birth, **10.98%** are still expecting, while **4.07%** miscarried.

Consequently, the maximum percentage success rate, or 'Take Home Baby' rate for calendar year 2018 is 18.70%, resulting in an increase of 1.92% over 2017. (Table 18).

Table 18. % Maximum Success Rate – 'Take Home Baby' Rate 2018

Pregnancy Outcome	Qty	% of pregnancies	% of total cycles	% Max Success – 'Take Home Baby' Rate
Live Birth	19	33.93%	7.72%	
Expected	27	48.21%	10.98%	**18.70%**
Miscarriage	10	17.86%	4.07%	

11. Conclusion

The number of IVF/ICSI procedures carried out in Malta in calendar year 2018, has decreased by 19.42% when compared to 2017. This was due to a decrease in procedures by both licensed clinics and a major drop of 41.33% in self-funded cycles.

ICSI was the preferred procedure of choice in 88.76% of all procedures carried out by the licensed clinics. There were **56** (22.76%) reported pregnancies out of all cycles started – **an increase of 1.05%** over 2017. As with last year, Thawed cycles were less effective than Fresh treatments, with a larger percentage of Embryo transfers, pregnancies, and birth events (live + expected) reported from Fresh cycles *vis-a-vis* Thawed cycles. *The **maximum percentage success rate**, or **'Take Home Baby' rate** which implies a birth event and is the most meaningful measure of treatment success*, stands at **18.70%**, which is **1.92%** higher than previous year.

The Embryo Protection Authority shall keep providing guidance and support to all the licensed ART clinics in Malta so as to ensure that they are operating under the highest standards. Moreover, as the Regulator, the Authority will keep on striving to ensure that local ART Clinics comply with the obligations and requirements imposed by or under the Embryo Protection Act 2012, and the Embryo Protection (Amendment) Act, 2018.

Judge Philip Sciberras UOM
Chairperson

Ms. Simone Attard
Executive Director