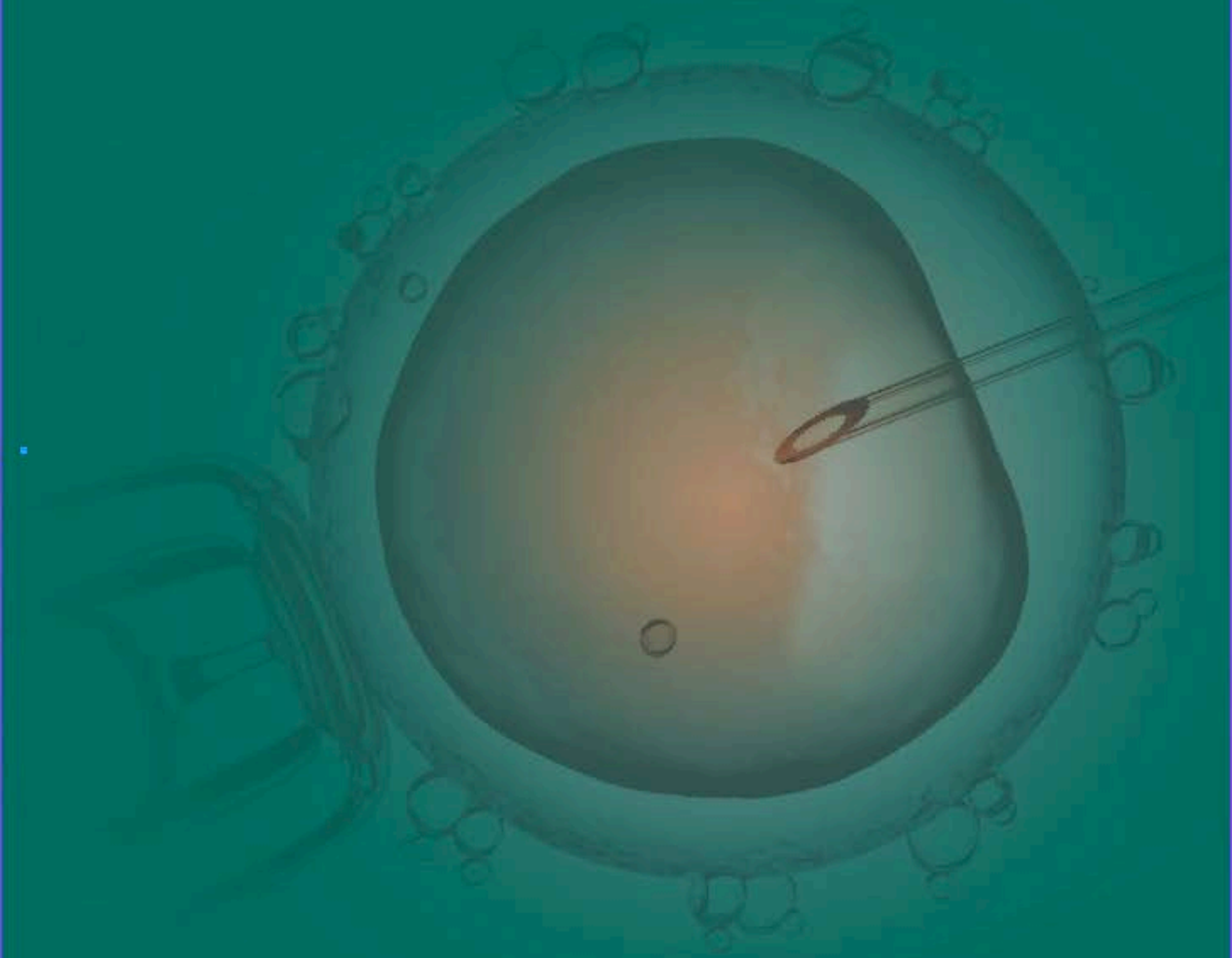
ANNUAL WORK REPORT

TRENDS AND FIGURES OF FERTILITY TREATMENTS IN MALTA FOR 2016



EMBRYO PROTECTION AUTHORITY
Putting Patients First

MARCH 2017

ANNUAL WORK REPORT

TRENDS AND FIGURES

OF FERTILITY TREATMENTS

IN MALTA FOR 2016

EMBRYO PROTECTION AUTHORITY

Putting Patients First

Presented to Minister for Health Hon. Chris Fearne

As per Embryo Protection Act 2012

and

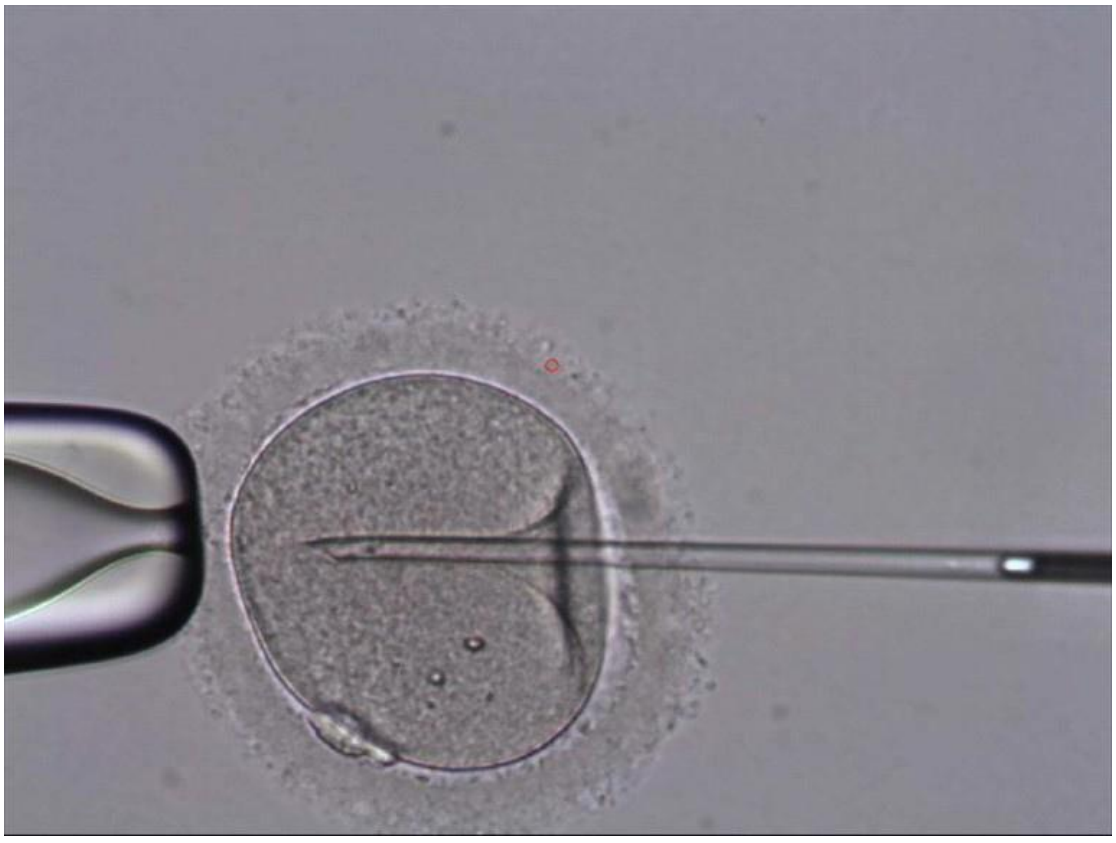
Embryo Protection Authority Regulations, LN32 of 2015

March 2017

EMBRYO PROTECTION AUTHORITY

PUTTING PATIENTS FIRST

ANNUAL WORK REPORT FOR 2016



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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 which covers the use and storage of sperm, oocytes (eggs), and embryos for human application. The Authority sets the standards and determines the policy framework (Protocol) while providing information to stakeholders, the general public, and to couples seeking treatment.

1.2. Our Principles – PATIENTS FIRST

The Embryo Protection Authority treats all couples 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 couples 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. *Regulations*:

The Embryo Protection Authority Regulations 2015 – (L.N.32 of 2015 – Chapter 524) have been published by Legal Notice 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.

3. *The 'Protocol' and European Tissues and Cells Directive*:

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.

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 2016, the Authority started receiving the services of a driver/messenger who is engaged with the Foundation for Medical Services and seconded to EPA. His salary is paid in full by the Authority. There were no further appointments in 2016.

Necessary arrangements are also being made so that the Authority will strengthen its inspectorate function through the engagement of two inspectors to be jointly shared with the Superintendency of Public Health. Additionally, an agreement has been reached with PACBU with regards to salaries for all staff presently engaged or to be engaged up to 2018, as per Directive 7 for Public Sector Entities.

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, Deputy Head, and the Administrative Officer received regular training throughout the year. The Executive Director and Deputy Head are in the process of completing the Public Management Toolkit which is being offered by the Institute for Public Services (IPS). In addition, the Executive Director is currently receiving training on EU Fund Management which will be completed in the first quarter of 2017. The Executive Officer has attended various courses offered by the IPS.

Last June, the Executive Director attended a meeting held in Brussels for the EU Competent Authorities on Substances of Human Origin Expert Group which was convened to discuss European Updates and necessary changes in the directives related to ART Technologies.

She was also present for a workshop on Third Party Reproduction and Psychosocial Issues of Fertility held in Vienna. The workshop was organised by

the European Society for Human Reproduction and Embryology (ESHRE) and topics discussed included the openness and secrecy of donor conception and working with lesbian couples and single women wishing to undergo fertility treatments.

In July, the Deputy Head of the Authority attended the ESHRE Annual Conference held in Helsinki, including a Pre-Congress course. The Pre-Congress course focused entirely on the genetics and epigenetics behind male subfertility and reproductive disease. The topics covered during the 3-day conference included genetics, surgery, psychology, diet/lifestyle, and effects of maternal obesity on pregnancy outcomes.

The Executive Director successfully completed a training course on the EU Tissues and Cells Product Compendium. The Vigilance and Inspection for Safety of Transfusion, Assisted Reproduction, and Transplantation (VISTART) training focused on the new EU Directive on the Implementation of the Single European Code (SEC) for Tissues and Cells, which was transposed in the Maltese Legislation in October 2016 and which would lead to better traceability of gametes. The Executive Director held meetings with the respective licensed clinics so as to introduce the new system to both Lab Managers and Embryologists.

The Ministry for Health has assigned new premises to the Authority. In 2017, after the necessary refurbishment works have been completed, EPA shall relocate to its new offices at the ex-CPSU building in Pieta.

1.7. Board Members & Meetings

The legal representation of the Authority is vested in its Chairman, Hon. Judge Emeritus Philip Sciberras UOM. The other appointed members include Dr. Patrick Sammut MD MRCPCH MSc., Ms. Mariella Meachen B. Psych (Hons) MA (Psychotherapy) R.N., and Ms. Pauline Baldacchino MSc. (Psych) B.A. (Hons) B.A. PGCE PGDip Couns. PGDip Psych. MBPsS.

Since Ms. Simone Attard's appointment as Executive Director, the Vice-Chairperson's seat has remained vacant. All the members of the Board have been appointed on the 17th May 2013, as per Article 3 of the Embryo Protection Act.

During 2016, ten meetings have been called and in all sittings quorum was achieved. Attendance by members and Executive Director to these Board meetings was as stated hereunder:

Designation	Name	Attended	Excused
Chairperson	Judge Philip Sciberras	10	0
Member	Dr. Patrick Sammut	8	2
Member	Ms. Mariella Meachen	10	0
Member	Ms. Pauline Baldacchino	7	3
Director	Ms. Simone Attard	9	1

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 couples. [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].

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, as listed hereunder:

Designation	Name	Annual Remuneration (Euros)
Chairperson	Judge Philip Sciberras	13,954
Member	Dr. Patrick Sammut	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 2016, the Authority has received various requests from the Clinics to grant permission to specific couples to undergo the IVF/ICSI procedure despite the female patient being of an age which falls outside the bracket specified in the Protocol. All the requests were turned down as they constituted a serious breach of the Protocol. With reference to age limits as specified by the Protocol, one couple filed a judicial letter against the Authority which was then rebutted by the Ministry for Health's Legal Advisor through another judicial letter.

Throughout 2016, the Authority was also notified of four separate incidents which occurred at the licensed Clinics. The first one occurred late in 2015 and an investigation was carried out in January 2016. The incident involved transfers of gametes between the private licensed clinic and the ART Clinic at Mater Dei Hospital and both clinics were found to be in serious breach of the Protocol and EU Directive and were fined accordingly.

The second incident involved the cracking of a sperm-containing conical tube in the centrifuge. A risk assessment was performed by the Clinic in question.

The third incident involved admission of a patient in hospital for observation and investigation due to mild/moderate Ovarian Hyperstimulation Syndrome, two days post-embryo transfer. Incident was resolved as per Stimulatory Treatment Protocol.

The last incident involved 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. The request was immediately approved by the Authority. Embryos are still in storage until the prospective mother is fit to undergo embryo transfer.

In December 2016, the Authority was notified that a couple, who attended infertility counselling and were due to undergo the procedure in the following month, appeared to have relational issues. In view of the fact that the welfare of the child who might have been conceived out of the IVF/ICSI procedure could not be guaranteed, the Authority referred the couple for further counselling before their application could be reconsidered.

In 2016, the Authority gave permission to a couple and assisted them in transferring their gametes to another European country. Following consultations amongst the respective Competent Authorities, necessary procedures, in line with the EU Directive, were followed to ascertain that gametes were indeed being transferred to another licensed clinic and their safe transportation could be guaranteed.

The Authority has received two requests from the licensed private clinic to grant permission for oocyte retrieval from two women aged 40 and 42 respectively, who wanted to preserve their fertility. Permission was granted on the grounds that these women were already in a relationship, but no oocyte retrieval was then performed due to medical reasons.

1.10. ART Prioritization Committee

The Ministry for Health considers the fact that couples 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 2016, The ART Prioritization Committee was re-composed. The Authority is represented on this Committee by its Executive Director Ms Simone Attard and by Dr. Patrick Sammut, member, who were both re-appointed to serve on this Committee.

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, and 4 reports were consequently issued.

1.11. Consultation on IVF Legislation

An Inter-Ministerial IVF Review Working Committee had been set up by the then Health Parliamentary Secretariat in order to review the current legislation within the context of outcomes of current regulations, new local legislation involving various sectors of the Maltese community, and recent judgments of the European Court of Human Rights. The Committee is made up of professionals from the Ministry for Energy and Health, the Ministry for Social Dialogue, Consumer Affairs and Civil Liberties, and the Ministry for Justice, Culture and Local Government. The Authority is represented on this Committee by its Executive Director, Ms Simone Attard.

As part of this review process, the Committee had invited the general public and all stakeholders concerned to submit their suggestions towards the evaluation of the IVF legal framework. The final updated report has been presented to the Minister for Health and also to the Bio-Ethics Committee for their consideration and feedback. The report will eventually be presented to Cabinet and will consequently be put up for discussion in the House of Representatives.

1.12. Inspections

The Authority, together with the Superintendency of Public Health (SPH), 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 2016, the Superintendency of Public Health carried out an inspection at the ART Clinic in Mater Dei Hospital. This was in conformity with the legislative requirements for periodic re-inspection before renewing the licence. The ART Clinic's license was up for renewal in early January 2017. This inspection was observed by the Deputy Head of the Authority.

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 to follow), 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.

The Embryo Protection Authority, through its Executive Director, 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, regarding the introduction of new Budgetary Measures related to Assisted Reproductive Technologies so as to ensure compliance with the Authority's Protocol.

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 cyropreservations (July 2013), is kept by the Authority. This serves to ensure that storage of gametes is being properly documented so as to guarantee 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.

In view of the fact that the Authority processes personal data, in 2016 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.

Pursuant to the EPA Regulations of 2015, the Authority is taking the necessary measures towards becoming fully autonomous. A parliamentary debate on the Authority's finances was held late in 2016 where the Minister for Health laid on the Table of the House EPA's Audited Accounts for 2015 and Financial Estimates for 2016.

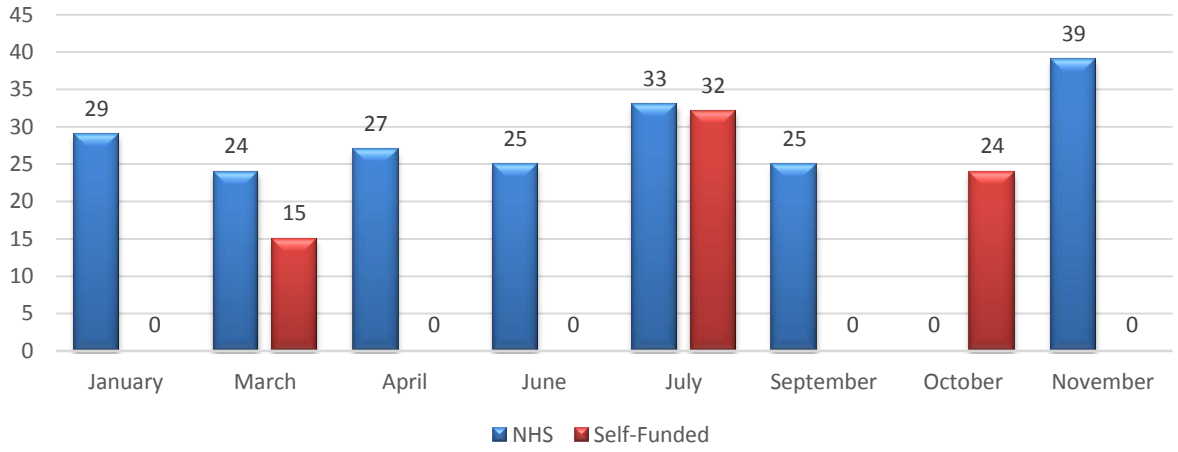
FERTILITY TREATMENTS IN MALTA FOR 2016 – TRENDS AND FIGURES

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.

2. CYCLES PERFORMED

Throughout 2016, the Authority has received a total of 273 applications from clinics in both the private and public sector. All applications have been approved and thus 273 cycles were carried out. Two hundred and two (202) procedures have been carried out at the ART clinic in Mater Dei Hospital (MDH), and seventy one cycles were performed in the private sector (Figure 1).

FIGURE 1 – COUPLES PER CYCLE
(NHS vs. SELF-FUNDED)



The number of IVF/ICSI procedures carried out in Malta in 2016 decreased by 13.9% over the previous year, which is mainly attributed to the fact that there has been a drop of 47.4% in procedures carried out in the private sector. Conversely, procedures carried out at the ART Clinic in Mater Dei Hospital increased by 14.8%.

2.1. First Time/Repeated Cycles

Out of the 273 cycles carried out, 49.8% of couples were undergoing the IVF/ICSI procedure for the first time. There were 28.2% of couples who were undergoing IVF/ICSI for the second time, 13.9% of couples for the third time, 6.2% of couples were undergoing their fourth attempt, while the remaining 1.9% of couples had undergone five or more cycles (Figures 2, 3).

FIGURE 2 – ART CYCLES PER COUPLE (% OF TOTAL COUPLES)

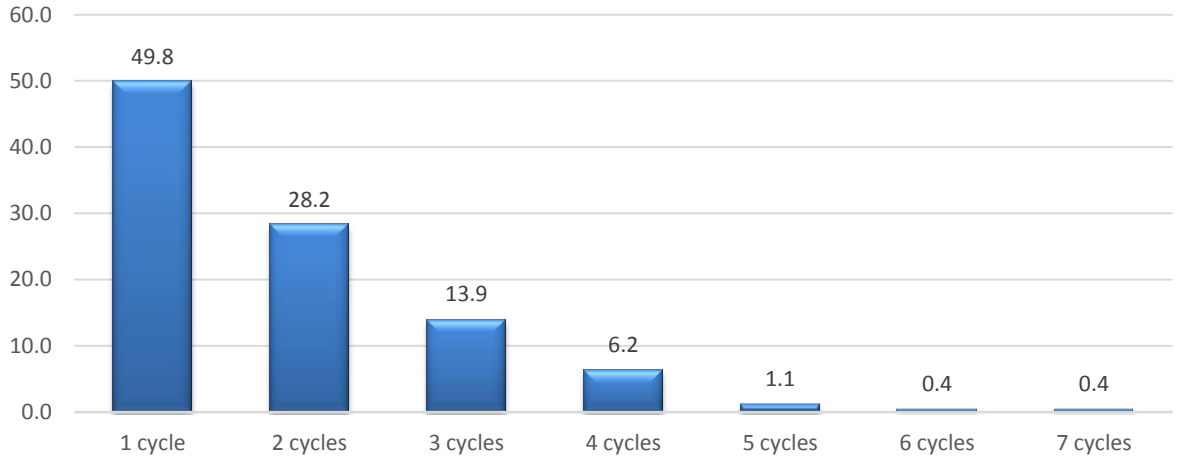
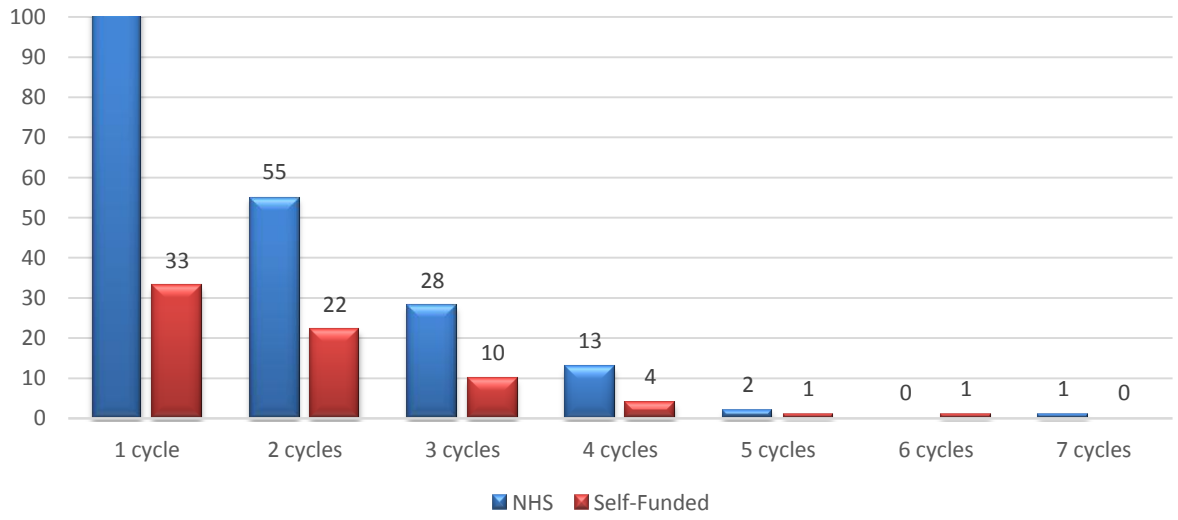
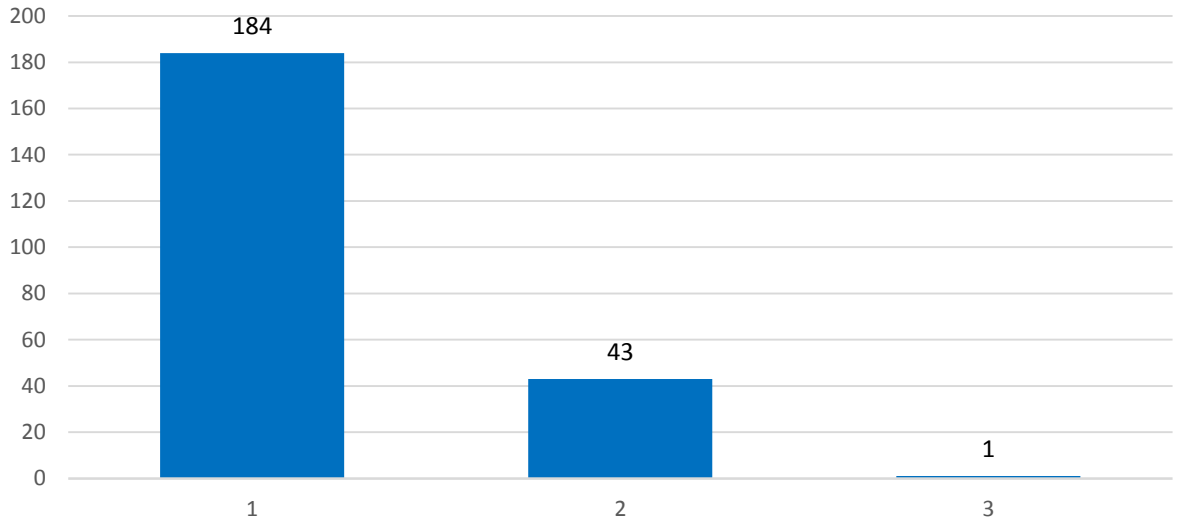


FIGURE 3 – ART CYCLES PER COUPLE (QTY)



During the same calendar year, there were 184 couples who had undergone a single cycle, 43 couples who had undergone 2 cycles, and a single couple who had undergone three cycles. Thus, these 273 IVF/ICSI procedures were undertaken by 228 couples (Figure 4).

FIGURE 4 – CYCLES PER COUPLE



3. DEMOGRAPHICS

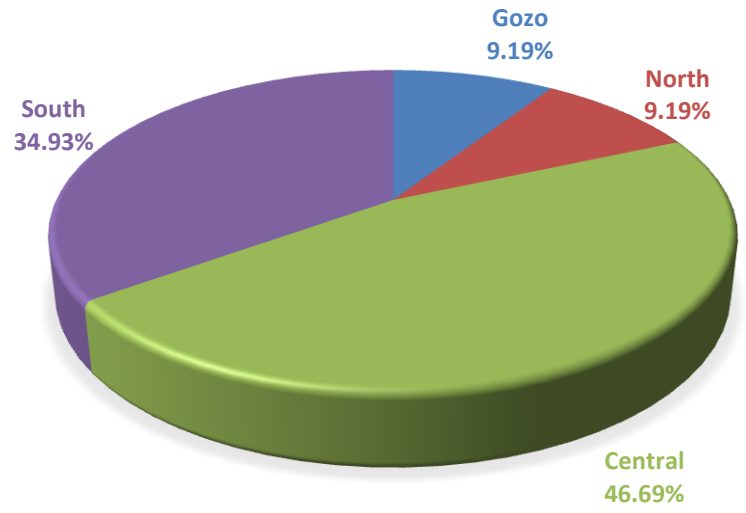
3.1. Nationality

All of the 273 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. There has been a marked decrease in Medical Tourism in the Fertility sector when compared to 2015 and 2014, where the number of non-residents undertaking IVF/ICSI procedures amounted to 5 and 13 respectively.

3.2. Regions

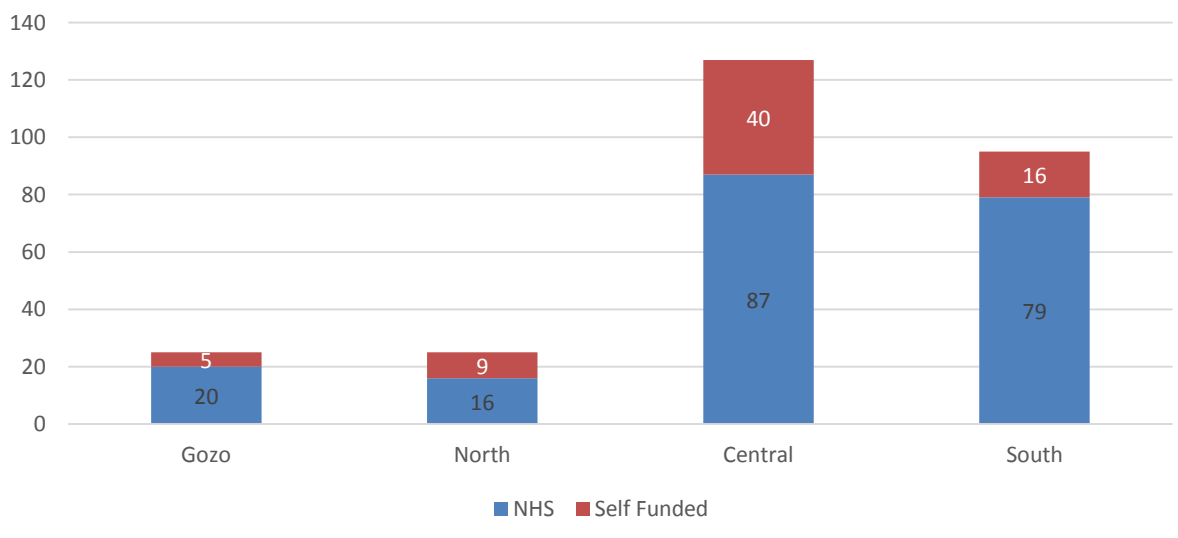
Over 9% of couples who had undergone IVF/ICSI procedures reside in Gozo, another 9.19% reside in the Northern part of the island, 46.69% reside in the Central part, while the remaining 34.93% were couples who reside in Southern areas of Malta (Figure 5).

FIGURE 5 – DISTRIBUTION BY REGION – OVERALL



Worth mentioning is the fact that unlike in 2015, where 66.66% of the Gozitan couples chose to self-fund their treatment, in contrast, last year 80% of them chose to undergo the procedure at the ART Clinic in MDH (Figure 6).

FIGURE 6 – TOTAL CYCLES BY REGION



Worth noting also is the fact that in 2016, only 18% of couples suffering from primary infertility who were undergoing their *first-ever* IVF/ICSI attempt, opted to self-fund their treatment, as opposed to 2015 where almost twice the number (34%) of first-timers self-funded their treatment, despite being eligible for treatment on the NHS (Figure 7). Figures 8 to 11 show the couples' funding preference per region.

FIGURE 7 – FIRST TIME CHOICE – OVERALL

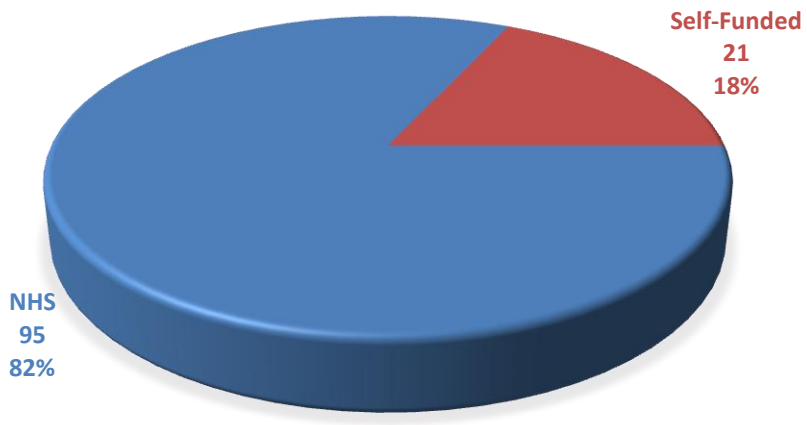


FIGURE 8 – FIRST TIME CHOICE – NORTH

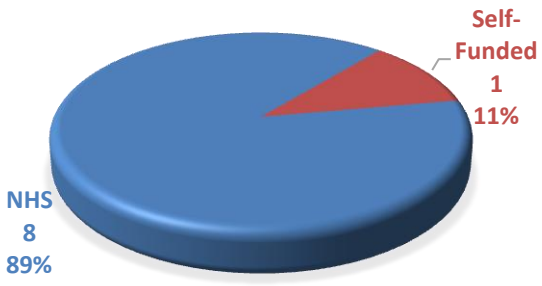


FIGURE 9 – FIRST TIME CHOICE – CENTRAL

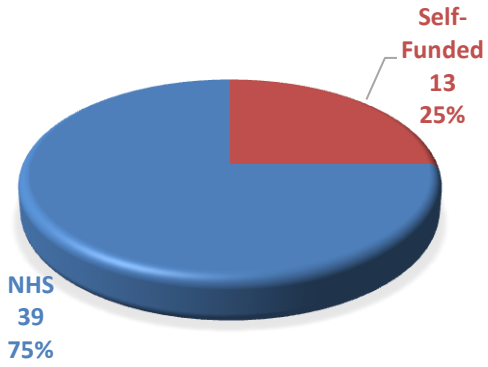


FIGURE 10 – FIRST TIME CHOICE – SOUTH

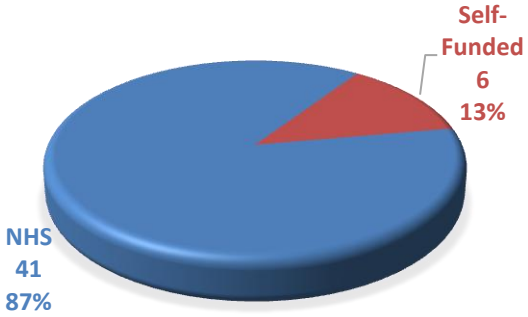
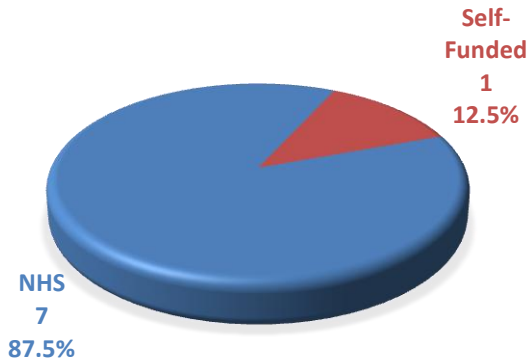


FIGURE 11 – FIRST TIME CHOICE – GOZO



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. Throughout 2016, there has been a distribution of procedures across all age brackets, as can be noted from the chart hereunder (Figure 12).

FIGURE 12 – FEMALES BY AGE GROUP (QTY)

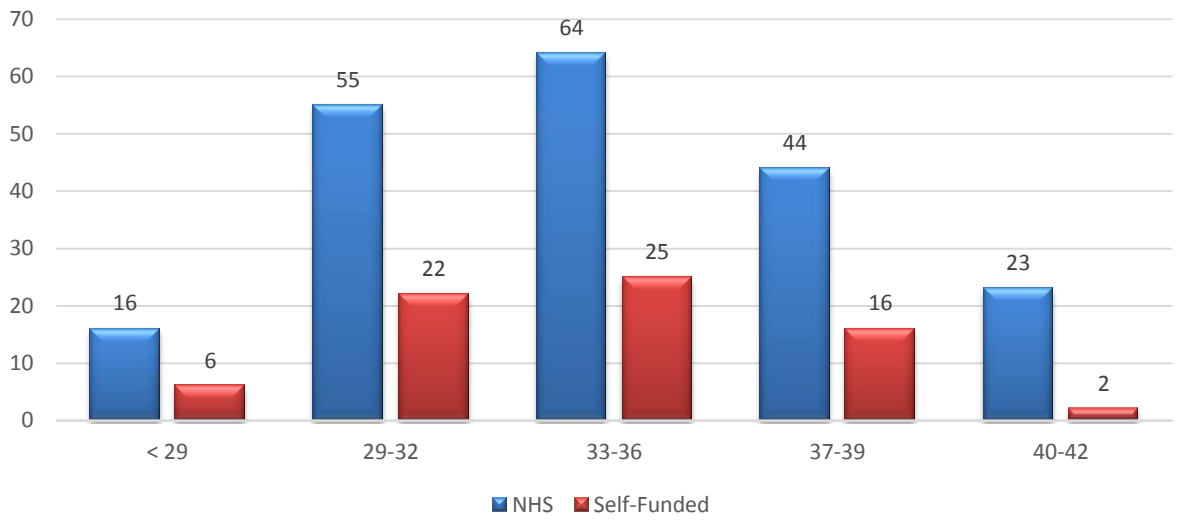
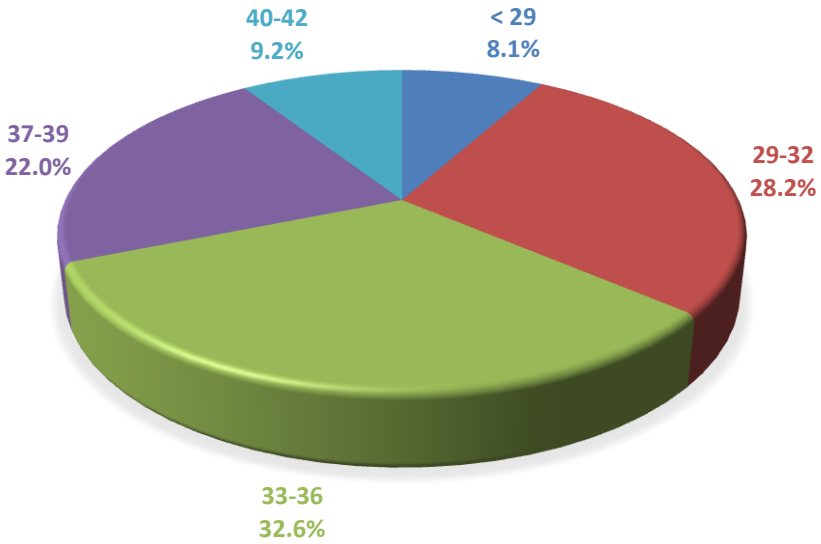


FIGURE 13 – FEMALES BY AGE GROUP (%)



As for the past two years, the largest number of female patients (32.6%) undertaking IVF/ICSI procedures throughout 2016 was aged between 33 and 36. The second largest age group was for female patients aged 29-32 (28.2%), while 22% of females were in the 37-39 year old bracket. There were 9.2% of female patients aged 40-42, while the remaining 8.1% were under the age of 29 (Figure 13). Noteworthy is the fact that last year there has been a drop of 3% in females aged 40-42 who had undergone IVF/ICSI, when compared to 2015. Conversely, a rise of 1.7% was registered for patients aged 29 or less. It would appear that couples may be resorting to powerful reproductive techniques such as IVF/ICSI at a younger age. If this were the case, the likelihood of a successful cycle outcome would increase given that it is a proven fact that fertility decreases with age.

3.4. Paternal Age

As with the female patients, the largest number of male patients (35.9%) undergoing procedures was in the 33-36 year old bracket, while 24.2% were aged between 37 and 39. The third largest age group (18.3%) consisted of males aged 40-45. Following closely at 15.4% were males in the 29-32 year old bracket, while 4.5% of male patients were 46 years and over. The remaining 1.8% of males was under the age of 29 (Figure 14, 15).

FIGURE 14 – MALES BY AGE GROUP (QTY)

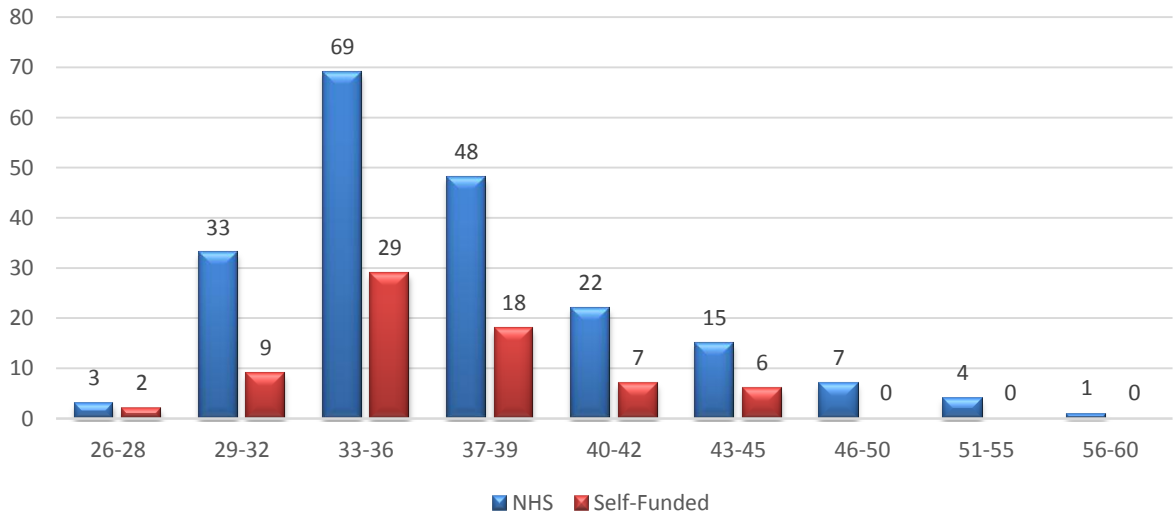
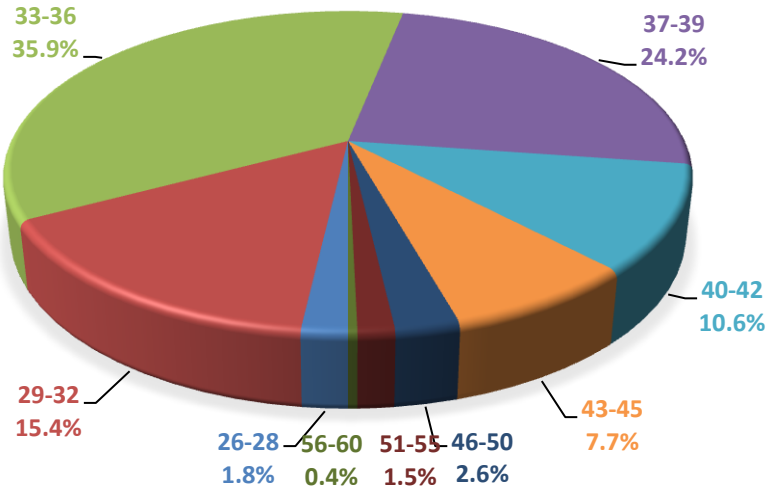


FIGURE 15 – MALES BY AGE GROUP (% TOTAL)

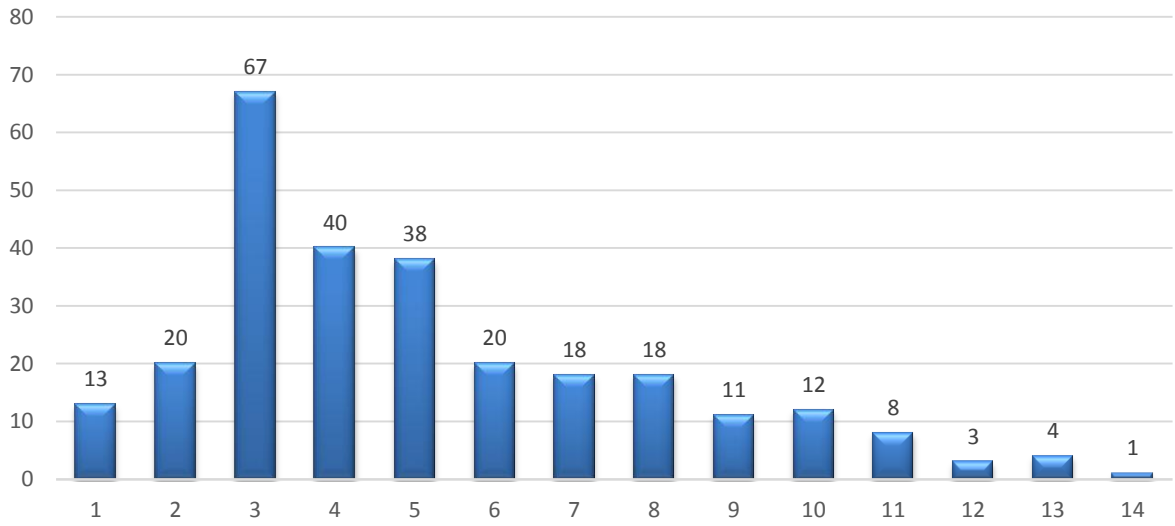


4. INFERTILITY

4.1. Duration of Infertility

There was a significant amount of variability in the reported duration of infertility amid couples undertaking procedures in 2016, with the minimum reported duration being that of one (1) year, up to a maximum of 14 years. Thirty three (33) couples appear to have been infertile for two years or less, 67 couples for 3 years, 40 couples for 4 years, 38 couples for 5 years, while 95 couples, or 34.8% of the total couples who applied for IVF/ICSI procedures, have been infertile for more than 6 years (Figure 16).

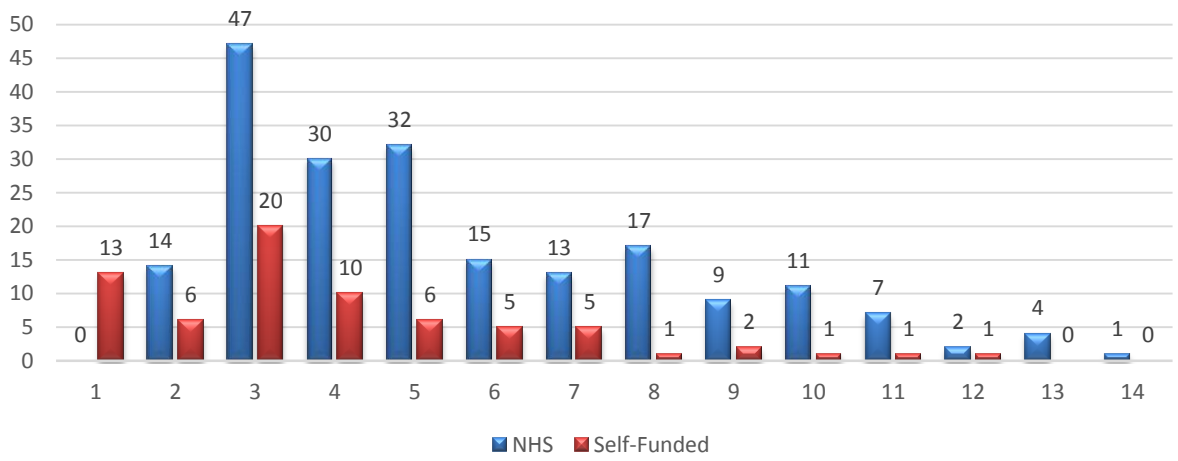
FIGURE 16 – DURATION OF INFERTILITY (YRS)



To be eligible for treatment on the NHS, a couple must declare being infertile for at least two years. In fact, 18.3% of couples who self-funded their treatment declared less than 2 years of infertility. The majority of couples

(50.7%) self-funding their treatment have reportedly been infertile for 2 to 4 years, while the remaining 31.0% have been infertile for 5 years or more. Similarly, the majority of couples (45%) who applied to undergo IVF/ICSI treatment on the NHS declared being infertile for 2-4 years. Forty seven (47) couples, or 23.3%, have declared being infertile for 5-6 years, while the remaining 64 couples (31.7%) have been infertile for seven years or more (Figure 17).

FIGURE 17 – DURATION OF INFERTILITY (YRS)
NHS vs. SELF-FUNDED



While the majority of couples (65%) undergoing treatment in 2015 on the NHS have declared being infertile for between 4 to 7 years, this year only 44.6% of couples declared 4-7 years of infertility. This may be explained by the fact that since the service is now being offered for free by the Government, it is easier for couples to resort to IVF/ICSI earlier, at a younger age, as already pointed out in Section 3.3.

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 (89.01%) who have applied for IVF/ICSI treatment suffered from Primary Infertility (Table 1).

Table 1. Classification of Infertility

Classification of Infertility	NHS	Self-Funded	Total	%
Primary	189	54	243	89.01%
Secondary- Same Relationship	0	16	16	5.86%
Secondary- Previous Relationship-Female	7	0	7	2.56%
Secondary- Previous Relationship-Male	6	1	7	2.56%
Total	202	71	273	

4.3. 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 18 and 19, the majority of couples undertaking IVF/ICSI procedures suffered from male and female factor infertility. There were equal amounts of couples suffering from female factor only and male factor only (24.5%, 24.5% respectively), while the remaining 5.1% suffered from idiopathic infertility. These figures vary significantly when compared to last year's (Female only – 34.1%; Male only – 28.3%; Female and Male – 17.4%; Idiopathic: 20.3%). A plausible explanation for this would be that fertility investigations are becoming more and more comprehensive and hence, the cause of infertility may be more easily resolved.

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FIGURE 18 – INFERTILITY FACTORS (QTY)
NHS vs. SELF-FUNDED

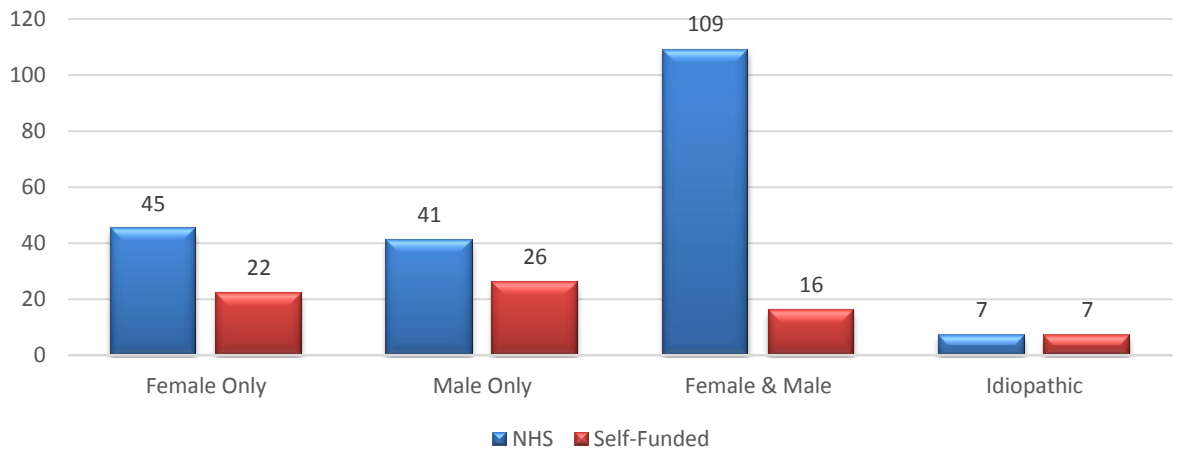
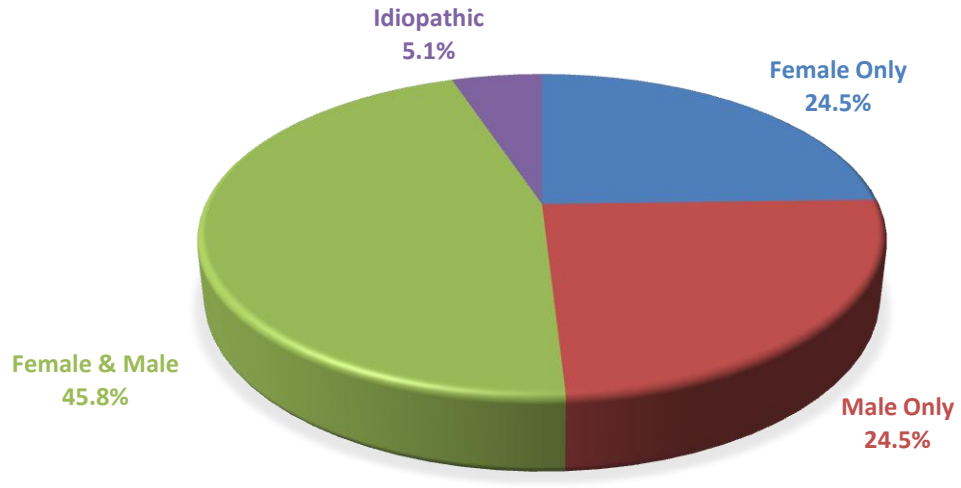


FIGURE 19 – INFERTILITY FACTORS (%)



From those couples suffering from female factor infertility only and male factory infertility only, the largest group (31.8% and 33.9% respectively) were in the 33-36 year old bracket (Figures 20 and 21).

FIGURE 20 – FEMALE INFERTILITY BY AGE GROUP (%)

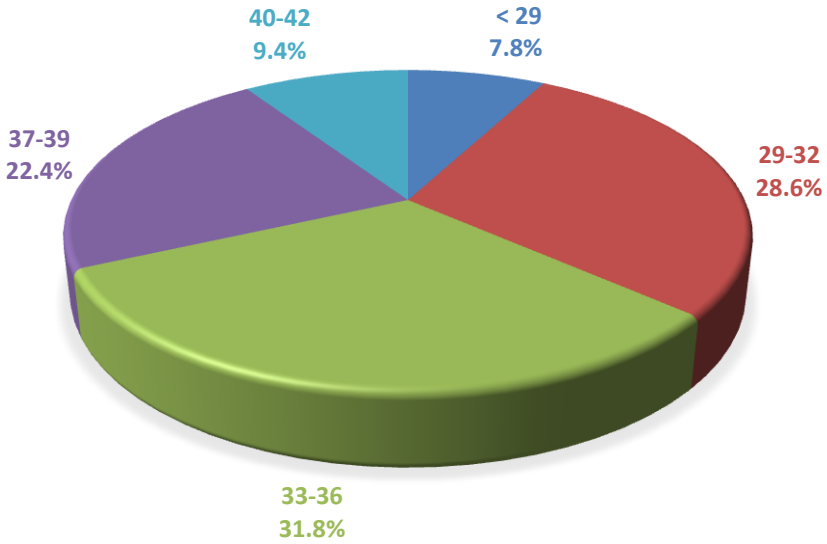
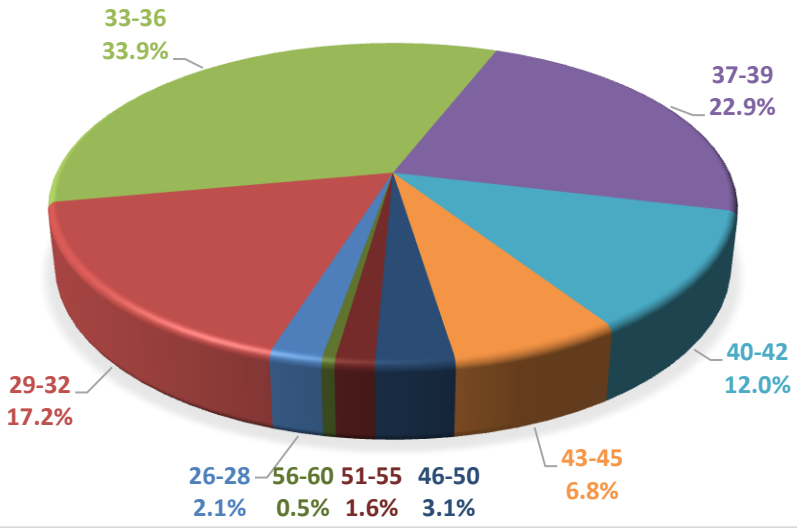


FIGURE 21 – MALE INFERTILITY BY AGE GROUP (%)



5. TYPE OF CYCLE

5.1. Fresh vs. Thawed

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 (or three in cases approved by the Authority). All embryos created will have to be transferred since vitrification (freezing) of embryos is forbidden. Thus, oocyte selection and vitrification are routine practice at the local ART clinics. Couples may opt for Fresh or Thawed cycles, or a combination of Fresh and Thawed. 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, like in the case of oncology patients.

Table 2. Type of Cycle

Fresh/Frozen	NHS	Self-Funded	Total	% of Total
Fresh	153	40	193	70.70%
Thawed	48	31	79	28.94%
Combined	1	0	1	0.37%
Total	**202**	**71**	**273**	

From a total of 273 procedures carried out, 193 (70.7%) were Fresh cycles; while another 79 (28.94%) were Thawed cycles. One couple (0.37%) opted for

a combined cycle whereby both fresh and thawed oocytes were utilized for the procedure. The majority of cycles (75.7%) carried out at the ART Clinic in Mater Dei Hospital were Fresh cycles and 23.7% were Thawed. In contrast, 56.3% of cycles carried out in the Private clinics were Fresh, and the remaining 43.7% were Thawed cycles (Table 2).

5.2. Additional Fertilization Requests (AFRs)

The Authority receives a significant number of requests by representative clinicians to consider the fertilization of three 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.

Throughout 2016, a total of 172 requests were received by the Authority. The majority of requests (84.3%) came from the ART Clinic at MDH, where 37.9% of them were not approved. In contrast, only 22.2% of the AFR requests made by private clinics have not been approved (Figure 22). Out of the total requests received, 64.5% were approved while the remaining 35.5% were not approved (Figure 23).

FIGURE 22 – AFR REQUESTS (QTY)

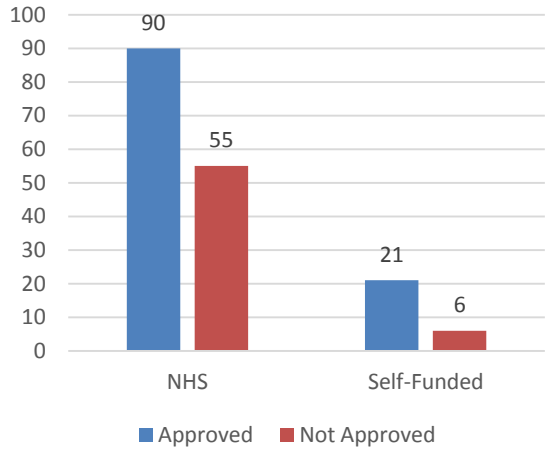
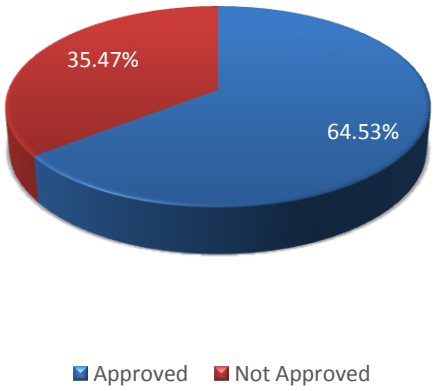


FIGURE 23 – AFR APPROVAL RATE (%)



6. GAMETES

6.1. Transfer of Gametes

Throughout 2016, there were 4 female patients who had their oocytes transferred from MDH to the licensed private Clinic. In turn, gametes of 6 patients, 4 females and 2 males, have been transferred from the private clinic to MDH. It appears that not all gametes have been transferred for immediate utilization.

6.2. 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 different follicles, inducing a controlled ovulation and maturation of oocytes so as to increase the chances of achieving a pregnancy during treatment.

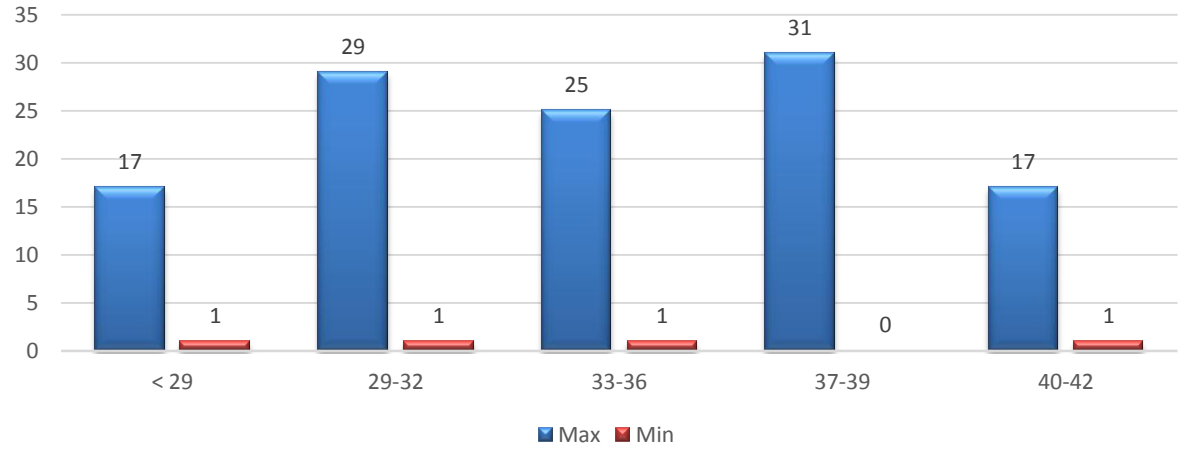
From the 193 Fresh cycles carried out in 2016, a total of 1630 oocytes have been collected, for an average of 8.45 oocytes per patient. The maximum

number of oocytes collected from a single patient was 31. The patient was a 38 year old undergoing treatment at MDH. Conversely, there were 3 patients, aged 37-39, who produced zero (0) oocytes. The largest number of oocytes collected, for an average of 10.31 oocytes per patient, was from females in the 29-32 year old bracket. An average of 9.44 oocytes was collected from patients under the age of 29, while from females aged 33-36, an average of 8.31 oocytes were collected. Not surprisingly, less oocytes were collected from women aged 37-39 and 40-42, for an average of 6.56 and 5.88 oocytes respectively (Table 3, Figure 24).

Table 3. Oocytes Collected by Age Group

Age	No. of Females	Total Oocytes Collected	Average	Max	Min
< 29	16	151	9.44	17	1
29-32	59	608	10.31	29	1
33-36	62	515	8.31	25	1
37-39	39	256	6.56	31	0
40-42	17	100	5.88	17	1
OVERALL	193	1630	8.45		

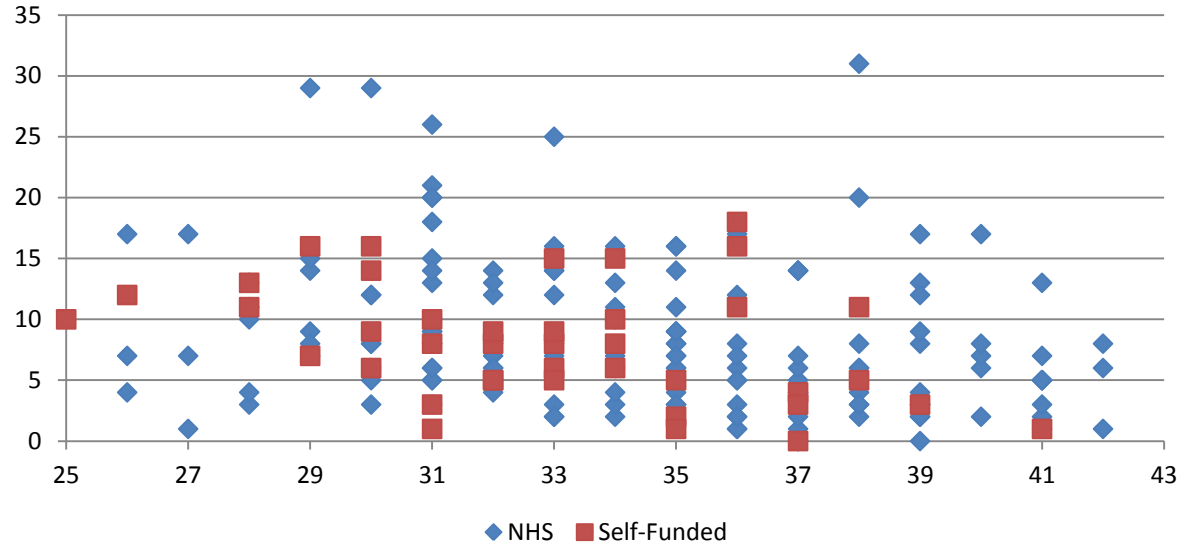
FIGURE 24 – MAX. & MIN. OOCYTES COLLECTED – FRESH CYCLES BY AGE GROUP



When taking into account the number of oocytes collected from the total number of female patients undergoing a Fresh cycle, it would appear that the quantity of oocytes collected per cycle relative to the age of the female patient is higher at MDH (Figure 25).

FIGURE 25 – OOCYTES COLLECTED

NHS vs. SELF –FUNDED



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 aged 37 or under, and whose serum AMH values were ≤1µg/l, was performed. To avoid distorted results from this analysis, an age and serum AMH values cut-off range were set based on the fact that women approaching menopause would normally have low AMH levels in any case.

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.

Table 4. Oocytes collected for AMH ≤1µg/l (Age ≤37)

AMH ≤1µg/l Occurrences	Min Oocytes Collected	Max Oocytes Collected	Total Oocytes Collected	Average Oocytes Collected	Occurrences with 3 oocytes or more
21	0	7	68	3.24	10

There were 22 female patients aged 37 or under with a serum AMH concentration of ≤1µg/l, 21 of whom had undergone a Fresh cycle. The total amount of oocytes collected from these 21 patients was 68, with the maximum number of oocytes collected being 7 and the minimum 0 (zero). The average number of oocytes collected was 3.24 per patient and there were 10 females who had 3 or more oocytes collected (Table 4).

6.3. Oocytes Discarded

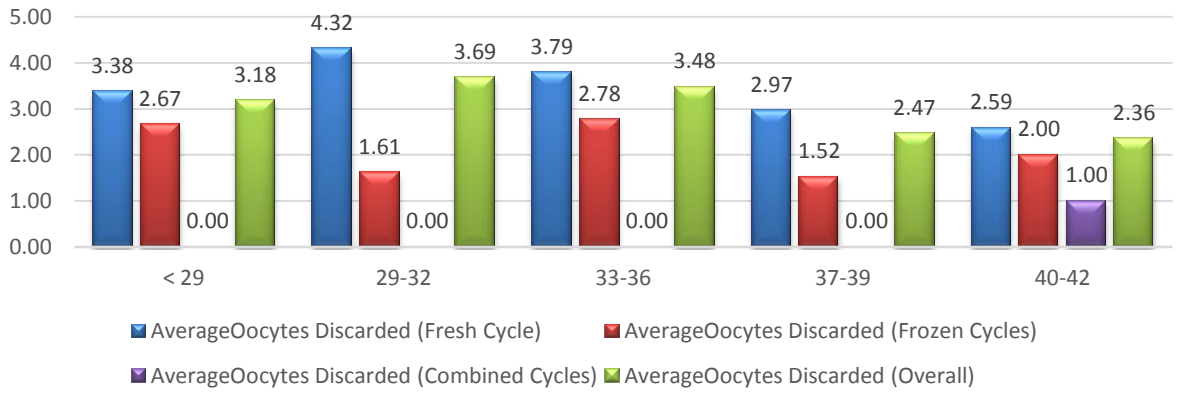
Oocytes obtained following ovarian stimulation should meet certain criteria in order to be considered suitable for IVF/ICSI. An appraisal is usually done by Embryologists to classify these oocytes, and those which are not deemed suitable for immediate fertilization or vitrification are discarded.

A total of 871 oocytes have been discarded in 2016. Seven hundred and five (705) oocytes (80.9%), or 43% from the total oocytes collected, were discarded following the egg retrieval process (Fresh cycle), for an average of 3.65 discarded oocytes per Fresh cycle. The remaining166 oocytes (19.1%) failed to survive the thawing process, for an average of 2.1 oocytes discarded per Thawed cycle (Table 5).

Table 5. Oocytes Discarded

Age	No of Females (Fresh Cycle)	TotalOocytes Discarded (Fresh Cycle)	AverageOocytes Discarded (Fresh Cycle)	No of Females (Frozen Cycles)	TotalOocytes Discarded (Frozen Cycles)	AverageOocytes Discarded (Frozen Cycles)	No of Females (Combined Cycles)	TotalOocytes Discarded (Combined Cycles)	AverageOocytes Discarded (Combined Cycles)	No of Females (Overall)	TotalOocytes Discarded (Overall)	AverageOocytes Discarded (Overall)
< 29	16	54	3.38	6	16	2.67	0	0	0.00	22	70	3.18
29-32	59	255	4.32	18	29	1.61	0	0	0.00	77	284	3.69
33-36	62	235	3.79	27	75	2.78	0	0	0.00	89	310	3.48
37-39	39	116	2.97	21	32	1.52	0	0	0.00	60	148	2.47
40-42	17	44	2.59	7	14	2.00	1	1	1.00	25	59	2.36
OVERALL	**193**	**704**	**3.65**	**79**	**166**	**2.10**	**1**	**1**	**1.00**	**273**	**871**	**3.19**

FIGURE 26 – AVERAGE OOCYTES DISCARDED BY AGE GROUP (FRESH vs. THAWED vs. COMBINED vs. OVERALL)



As in 2015, the largest number of oocytes discarded was from women in the 29-32 year old bracket, which incidentally was the group from which the largest number of oocytes had been collected (Figure 26).

6.4. Fresh vs. Thawed Sperm

Out of the 273 cycles carried out last year, thawed sperm has been utilized in 9, or 3.4%, of the IVF/ICSI procedures undergone. Fresh sperm, ejaculated or in some instances obtained through testicular extraction/aspiration, has been used in the remaining IVF/ICSI procedures which have been carried out.

6.5. Storage of Gametes

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.

6.5.1. Storage of Oocytes

Out of the 194 couples who had oocytes retrieved (193 Fresh + 1 Combined Cycles), only 100 (51.5%) had enough oocytes to store. A total of 94 couples had no oocytes left to vitrify (Table 6).

Table 6 – Fresh Cycles with NO Oocyte Vitrification

Age	NHS			SELF-FUNDED			TOTAL		
	No of Cycles	Total Cycles with NO Oocytes to Vitrify	% of cycles with no Oocytes to Vitrify	No of Females	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
< 29	12	5	41.7%	4	0	0.0%	16	5	31.3%
29-32	45	18	40.0%	14	3	21.4%	59	21	35.6%
33-36	47	26	55.3%	15	4	26.7%	62	30	48.4%
37-39	33	21	63.6%	6	3	50.0%	39	24	61.5%
40-42	17	13	76.5%	1	1	100.0%	18	14	77.8%
OVERALL	**154**	**83**	**53.9%**	**40**	**11**	**27.5%**	**194**	**94**	**48.5%**

The total number of oocytes vitrified from Fresh cycles carried out in 2016 was 536, for an average of 5.36 oocytes per couple. The maximum number of oocytes vitrified from a single cycle was 20 (Table 7).

Table 7. Vitrification of Oocytes

NHS					Self-Funded					TOTAL				
No of Cycles	Total Oocytes Vitrified	Average per Cycle	Max	Min	No of Cycles	Total Oocytes Vitrified	Average per Cycle	Max	Min	No of Cycles	Total Oocytes Vitrified	Average per Cycle	Max	Min
70	401	5.73	20	0	30	135	4.50	12	0	100	536	5.36	20	0

The maximum number of oocytes thawed from Frozen cycles was 10, while the minimum number of oocytes thawed was 2.

6.5.2. Storage of Sperm

There has been an increase in sperm storage throughout 2016. A total of 73 patients, 61 at MDH and 12 at the private clinic, vitrified their sperm. In a number of cases, sperm was obtained through testicular aspiration/extraction (TESA/TESE).

Fertility preservation following oncology or urology referrals was the main reason these male patients had their sperm vitrified. Twenty nine (29) of the male patients who stored their sperm proceeded with an IVF/ICSI cycle in the same calendar year, but only 9 of them used thawed sperm for the procedures.

6.5.3. '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 (OHS) 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.

In 2016, the Authority was notified that there were 5 patients undergoing cycles at MDH who had a 'freeze-all' cycle.

6.5.4. Embryo Freezing

In Malta, permission for vitrification 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 2016, there has been a single request from Clinicians at the ART Clinic in

MDH for the vitrification of two embryos which, at the time of publication, were still in storage.

6.6. End of Storage

Last year 4 patients, 3 females and 1 male, have requested to have their gametes discarded. All the patients had their gametes stored at the licensed private clinic.

7. IVF/ICSI PROCEDURES

7.1. Cycles Started

In addition to the 273 cycles which have been performed throughout the year, licensed clinics have also reported a total of 18 cycles which were abandoned prior to oocyte retrieval. 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.

7.2. Type of Procedure – IVF vs. ICSI

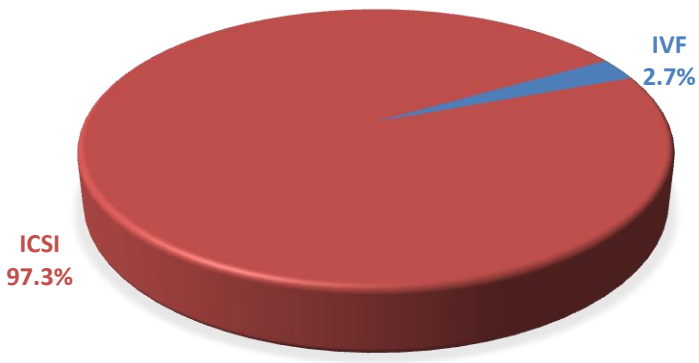
In 2016, from a total of 273 cycles started, no procedure was carried out for 11 couples. This was due to the fact that there were 4 couples who had no oocytes retrieved, another 2 couples who had oocytes collected but which had to be discarded as they were of poor quality, while the remaining 5 couples had to opt for a 'Freeze-all' cycle (Table 8).

Table 8. Type of ART Procedure

Type of ART	NHS	Self-Funded	Total
IVF	7	0	7
ICSI	187	68	255
NIL	8	3	11
TOTAL	202	71	273

Out of the 262 procedures carried out, 255, or 97.3%, were *intra-cytoplasmic sperm injection* (ICSI) (Figure 27). 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 27 – IVF VS. ICSI
(% OF PROCEDURES) – OVERALL



Only seven out of the 194 procedures carried out at MDH were IVF, while the licensed private clinic opted for an '*All-ICSI*' approach (Figure 28, 29).

FIGURE 28 – IVF VS. ICSI (% OF PROCEDURES) – NHS

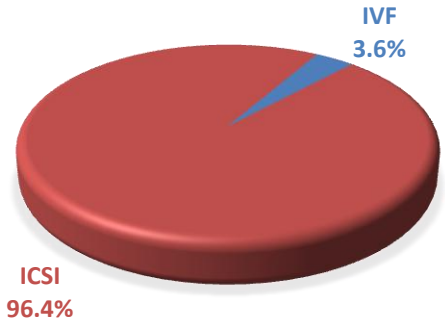
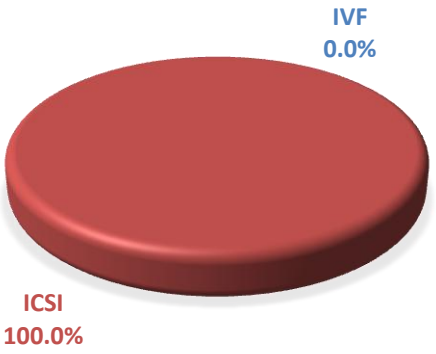


FIGURE 29 – IVF VS. ICSI (% OF PROCEDURES) – SELF-FUNDED



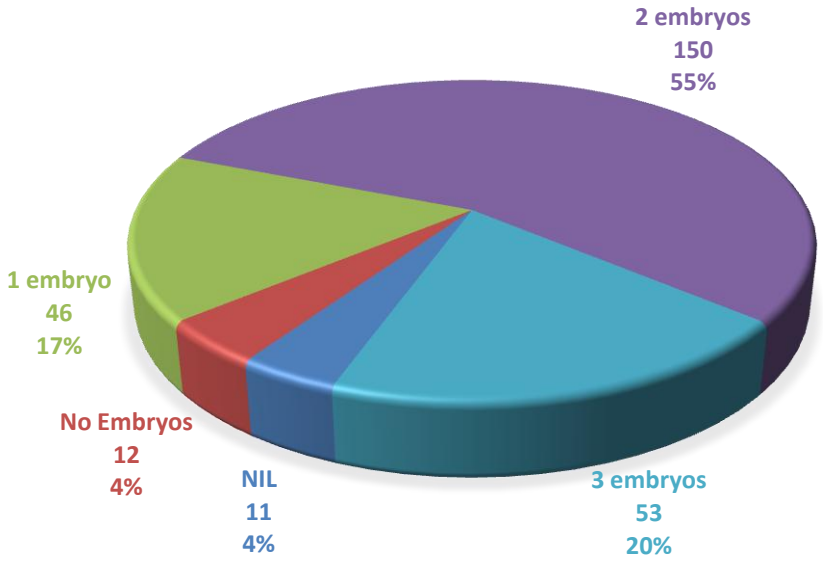
7.3. Embryo Transfers

Out of the 273 cycles carried out, there were a total of 23 couples who had no Embryo Transfer effected. As outlined earlier, there were 11 couples, or 4.03%, who for various reasons had no IVF/ICSI procedures performed. The other 12 couples (4.4%) had no embryos to transfer as the oocytes they had injected failed to fertilize.

Out of the 250 couples who had viable embryos to transfer, 46 of them (17%) had a single embryo transferred. Fifty five percent (55%) of couples, or 150, had 2 embryos transferred, while the remaining 53 couples, or 20%, had 3 embryos transferred (Figure 30).

The couple who had their 2 embryos vitrified owing to grave and certified *force majeur* not predictable at the time of fertilization is not being accounted for when presenting statistics related to embryo transfers.

FIGURE 30 –EMBRYOS TRANSFERRED PER CYCLE



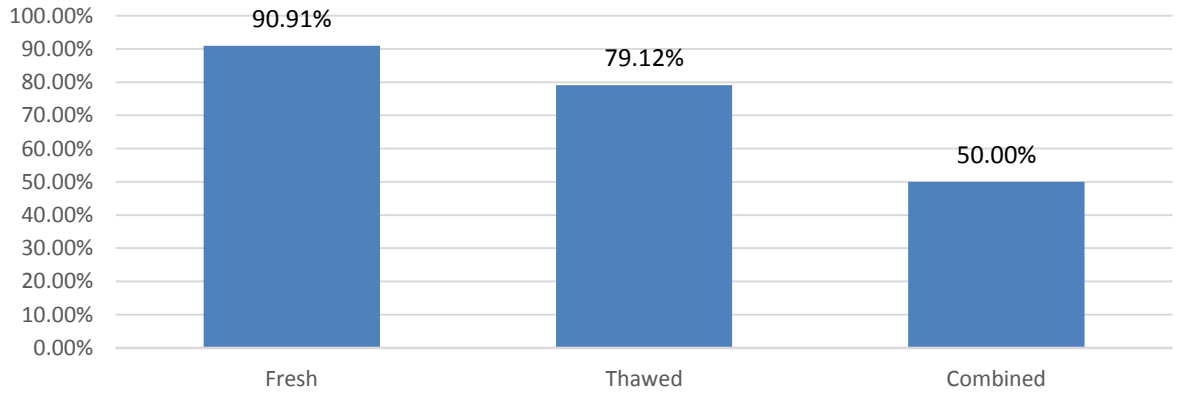
7.4. Embryo Transfers per Type of Cycle

Out of the 396 fresh oocytes injected, 360 (91.91%) resulting embryos were transferred. In contrast, only 144 embryos, or 79.12%, out of the 182 thawed oocytes injected have been transferred. The couple undergoing a Combined cycle had a single embryo transfer (Table 9, Figure 31).

Table 9. Embryos Transferred per Type of Cycle (%)

Type of Cycle	Oocytes Injected	Embryos Transferred	Transferred %
Fresh	396	360	90.91%
Thawed	182	144	79.12%
Combined	2	1	50.00%

FIGURE 31 – % EMBRYOS TRANSFERRED FROM INJECTED OOCYTES – FRESH vs. THAWED vs. COMBINED



There were 3.3% of couples undergoing a Fresh cycle who had no embryos for transfer, 13.8% had a single embryo transfer, 63.5% had two (2) embryos transferred, while the remaining 19.3% had three (3) embryos transferred. 7.6% of couples undergoing a Thawed cycle had no embryos for transfer,

25.3% had a single embryo transfer, and 44.3% had 2 embryos transferred, while the remaining 22.8% had 3 embryos transferred (Table 10).

Table 10. Number of Embryos Transferred per Type of Cycle

Transferred Embryos	FRESH				THAWED				COMBINED				TOTAL			
	NHS	Self-Funded	Total	%	NHS	Self-Funded	Total	%	NHS	Self-Funded	Total	%	NHS	Self-Funded	Total	%
0	5	1	6	3.3%	4	2	6	7.6%	0	0	0	0.0%	9	3	12	4.6%
1	20	5	25	13.8%	9	11	20	25.3%	1	0	1	100.0%	30	16	46	17.6%
2	88	27	115	63.5%	22	13	35	44.3%	0	0	0	0.0%	110	40	150	57.5%
3	31	4	35	19.3%	13	5	18	22.8%	0	0	0	0.0%	44	9	53	20.3%
Total	144	37	181		48	31	79		1	0	1		193	68	261	

7.5. Embryos Transferred per Approved AFR

Out of a total of 111 couples who had their Additional Fertilization Request (AFR) approved, there were 103 who had an IVF/ICSI procedure carried out. Only 51.5% of these 103 couples had three embryos transferred despite having approval for the fertilization of a third oocyte (Figure 32, 33).

FIGURE 32 – EMBRYOS TRANSFERRED PER CASE OF APPROVED AFR

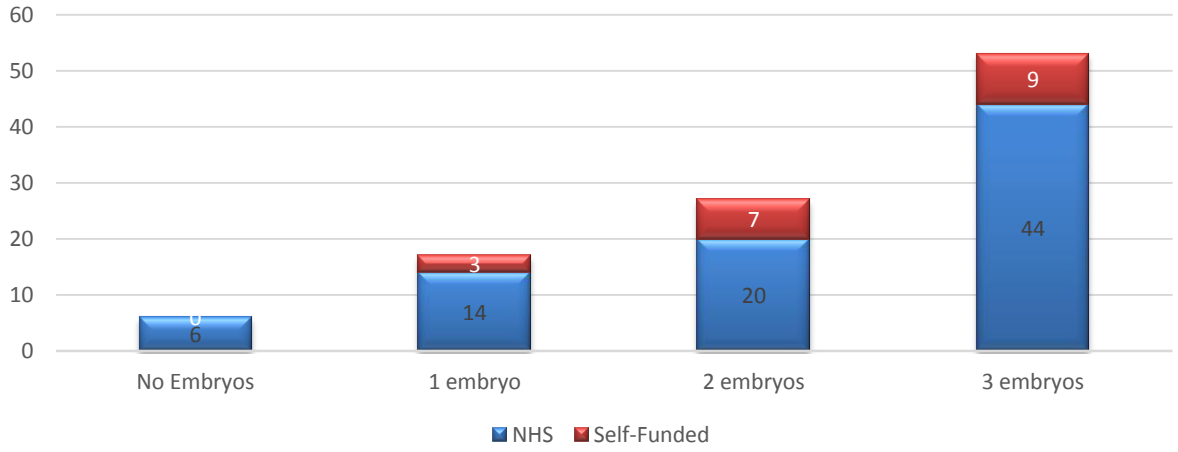
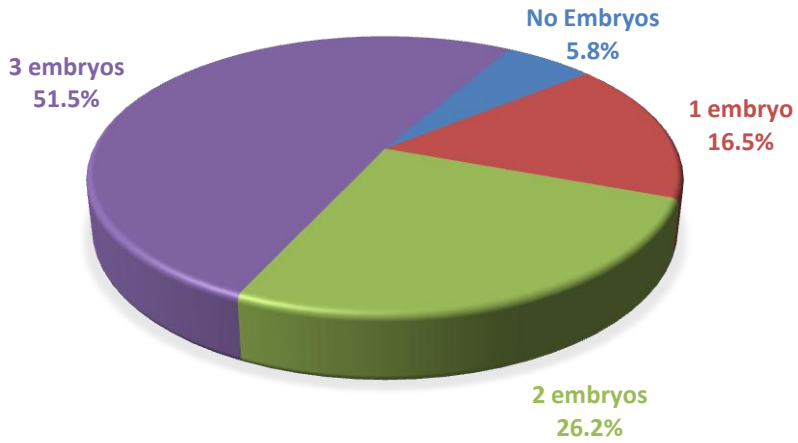


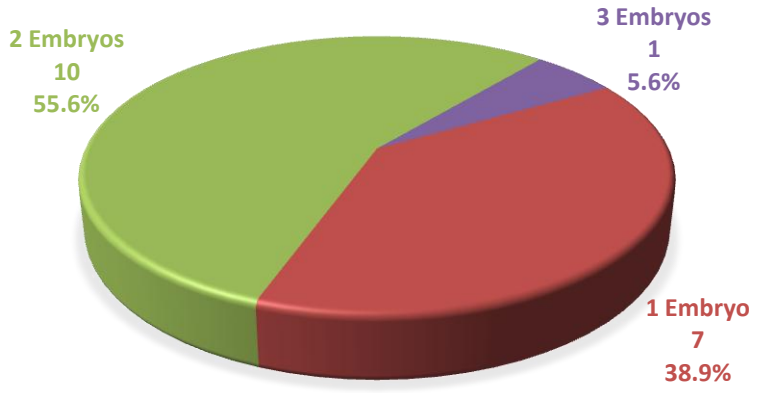
FIGURE 33 – EMBRYOS TRANSFER DISTRIBUTION (% OF APPROVED AFR)



7.6. Embryos transferred per AMH ≤1µg/l

As outlined already in Section 6.2., there was a total of 22 women aged 37 or under, with a serum AMH concentration of ≤1µg/l. Only 17 of these women had an embryo transfer effected. Seven, or 38.9%, had a single embryo transfer; 10, or 55.6%, had 2 embryos transferred, while the remaining couple had 3 embryos transferred (Figure 34).

FIGURE 34 – EMBRYOS TRANSFERRED FOR AMH ≤ 1UG/L (AGE ≤37)



8. CYCLE OUTCOMES

In 2016, for a cycle that had resulted in a twin pregnancy, the woman, a 40 year old, miscarried one of the dizygotic (fraternal) twins around gestational week 10, but went on to deliver the other twin. In view of the fact that for the purpose of this report each ART cycle is considered as a single event based on its final outcome, as a result, the outcome from this particular cycle was that of a single birth. Hence, for statistical purposes, this case is being reported as a Live Birth event. As a consequence, the miscarriage is not being accounted for in the relative tables and figures.

8.1. Pregnancies

Out of the 273 cycles carried out in 2016, there were 47 reported pregnancies from Fresh cycles and 17 from Thawed cycles. The couple undergoing a Combined cycle failed to get pregnant. **The resulting 64 pregnancies account for 23.4% of all cycles started**, which is 4.9% less than the pregnancy rate for 2015 (Table 11).

Table 11. Cycle Outcome

Type	Outcome	NHS	Self-Funded	Total	% Outcome by Type	% Outcome	% Outcome of Pregnancies
Fresh	Not Pregnant	114	32	146	75.6%	75.6%	
Fresh	Miscarriage	5	0	5	2.6%	24.4%	10.6%
Fresh	Live Birth	5	3	8	4.1%		17.0%
Fresh	Expected	29	5	34	17.6%		72.3%
Thawed	Not Pregnant	35	27	62	78.5%	78.5%	
Thawed	Miscarriage	2	0	2	2.5%	21.5%	11.8%
Thawed	Live Birth	5	1	6	7.6%		35.3%
Thawed	Expected	6	3	9	11.4%		52.9%
Combined	Not Pregnant	1	0	1	100.0%	100.0%	
Combined	Miscarriage	0	0	0	0.0%	0.0%	0.0%
Combined	Live Birth	0	0	0	0.0%		0.0%
Combined	Expected	0	0	0	0.0%		0.0%

8.2. Cycle Outcomes – Fresh vs. Thawed

Forty seven (47) couples, or 24.4% of those undergoing Fresh cycles managed to get pregnant. Out of these 47 pregnancies, 5 couples miscarried, 8 had a live birth, while the remaining 34 couples (17.6%) are still expecting (Figure 35, 37). Out of the17 couples who got pregnant from Thawed cycles, 2 miscarried, 6 had a live birth, while the remaining 9 couples are still expecting (Figure 36, 38). **As a result, in 2016 the pregnancy rate for Fresh cycles was 2.9% higher than for Thawed Cycles** (Table 11).

FIGURE 35 – OUTCOME FROM FRESH CYCLES (QTY)

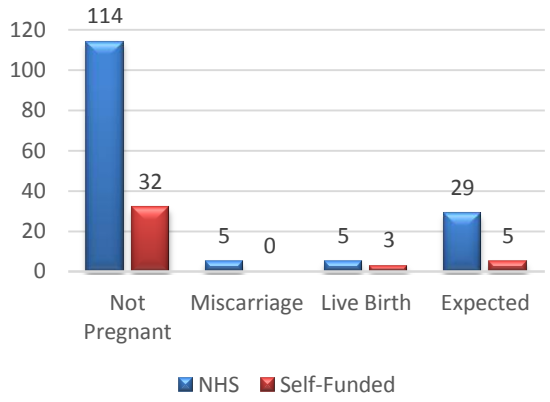


FIGURE 36 – OUTCOME FROM THAWED CYCLES (QTY)

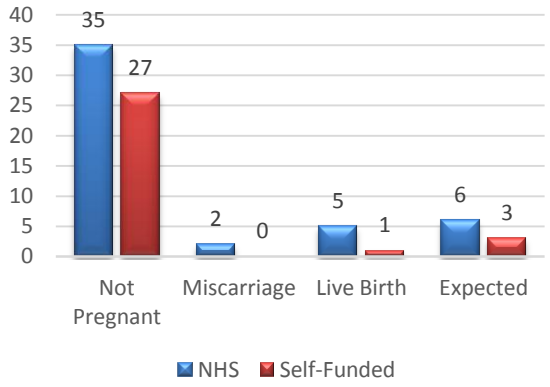


FIGURE 37 – % OUTCOME FROM FRESH CYCLES (NHS + SELF-FUNDED)

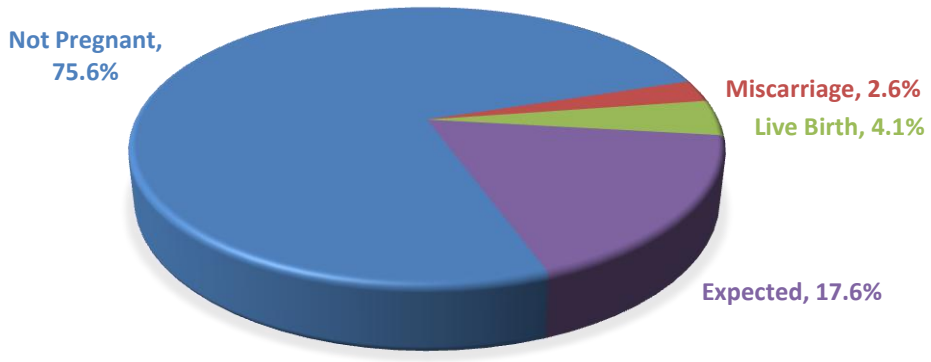
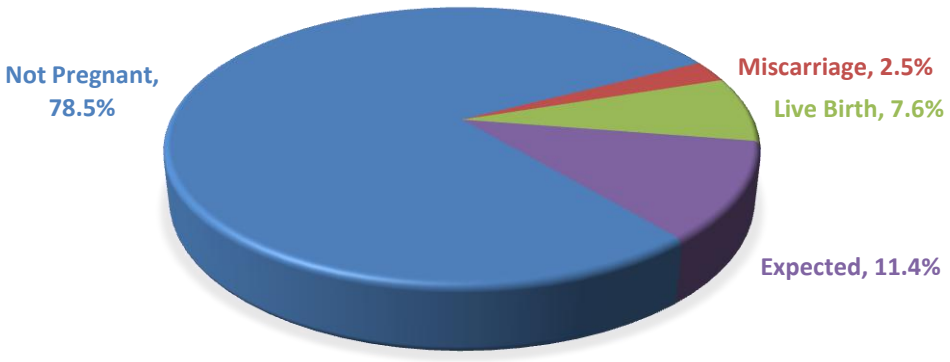


FIGURE 38 – % OUTCOME FROM THAWED CYCLES (NHS + SELF-FUNDED)



8.3. Cycle Outcomes – NHS vs. Self-Funded

The pregnancy rate reported by the private clinics for both Fresh and Thawed cycles was 5.5% lower than that reported by the ART Clinic at MDH. However, while 7 couples who had their IVF/ICSI procedure carried out at MDH miscarried, the private clinics reported no miscarriages. The sum of live and expected births from Fresh cycles carried out at MDH was 22.3%, while that for private clinics was 20% (Figure 39). In contrast, the sum of live and expected births from Thawed cycles was 10% higher for couples undergoing procedures at MDH when compared to private clinics (Figure 40).

FIGURE 39 – FRESH CYCLES– % OUTCOME
NHS vs. SELF–FUNDED

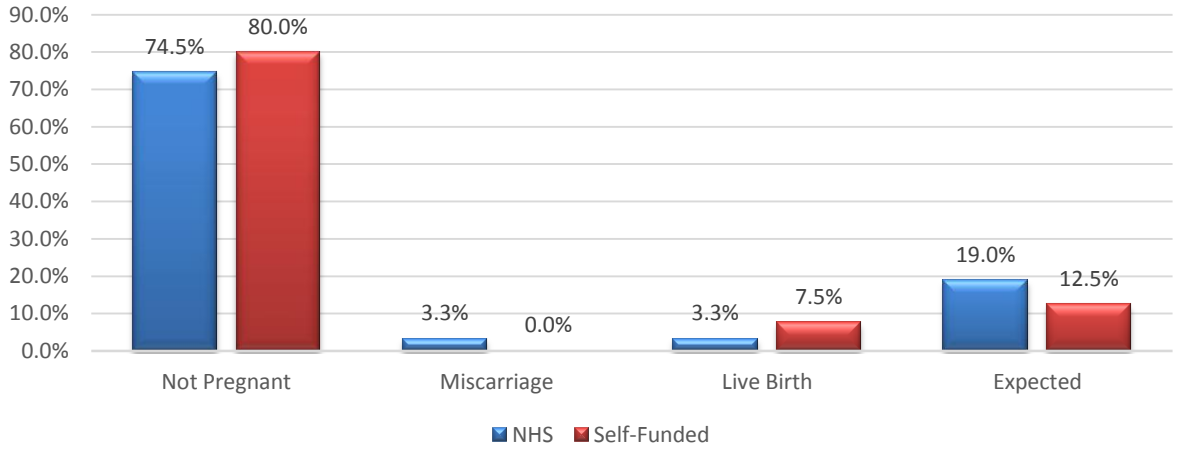
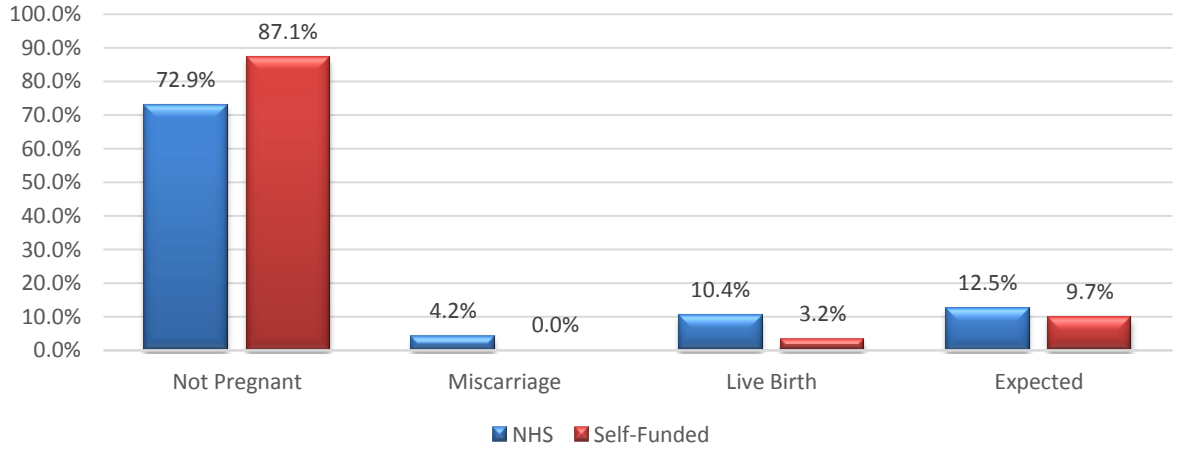


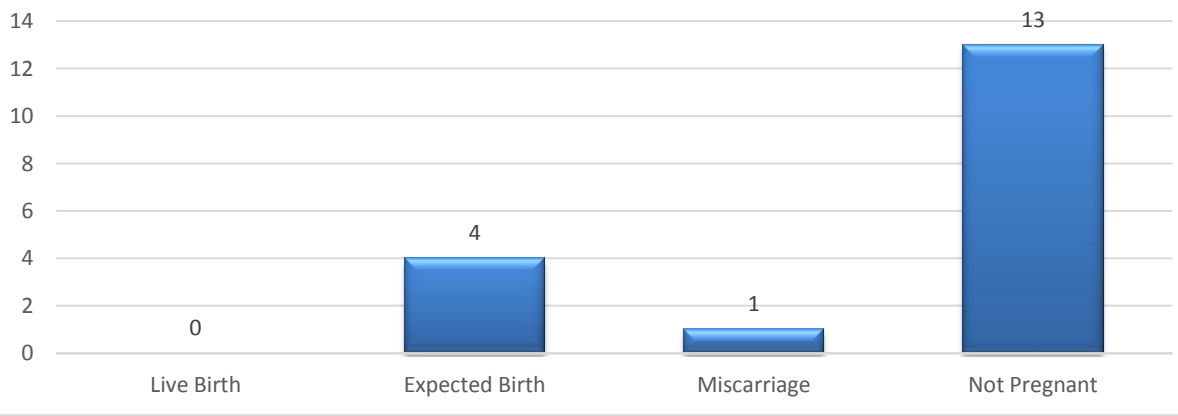
FIGURE 40 – THAWED CYCLES– % OUTCOME
NHS vs. SELF–FUNDED



8.4. Cycle outcome for AMH ≤1µg/l

Out of the 22 females aged 37 or under with a low serum AMH concentration of ≤1µg/l, 4 had no viable oocytes for fertilization. Thirteen out of the remaining 18 did not fall pregnant, 1 miscarried, and the remaining 4 are expecting (Figure 41). The pregnancy rate for women with low serum AMH concentrations was that of 22.7%, which is hence comparable to the overall pregnancy rate of 23.4% of all cycles started.

FIGURE 41- CYCLE OUTCOME FOR AMH ≤ 1UG/L (AGE ≤37)



8.5. Pregnancy by Age

Pregnancies were reported across all age groups. The highest number of pregnancies reported was for women in the 29-32 year old bracket (Figure 42). However, the pregnancy rate as percentage of cycles per age group was highest for women aged 28 or younger, at 40.9% (Figure 43). Thus, it would appear that in 2016, maternal age was the most important predictive factor for an IVF/ICSI procedure to result in a pregnancy.

FIGURE 42 – PREGNANCY BY AGE GROUP (QTY)

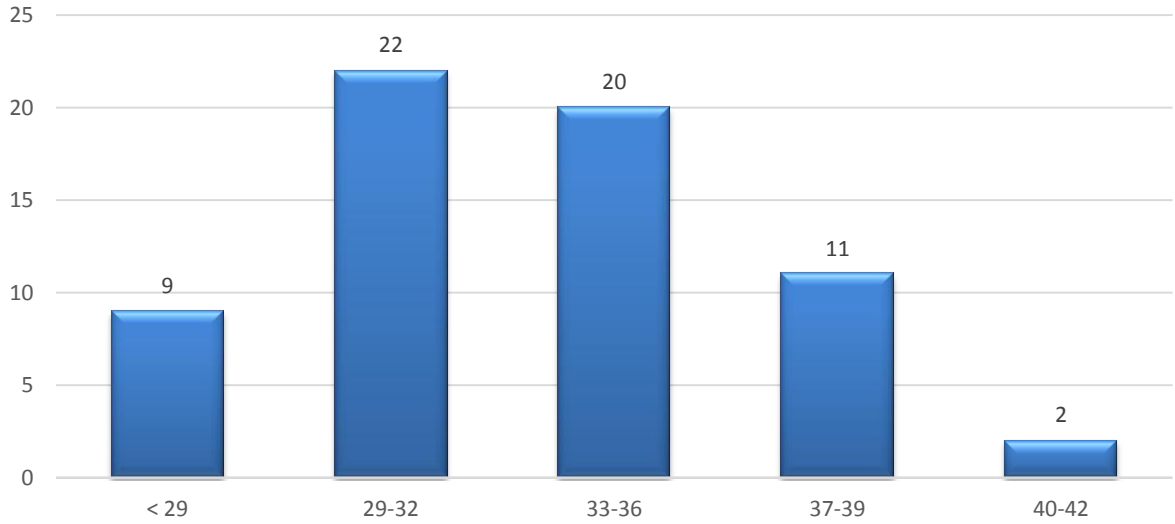
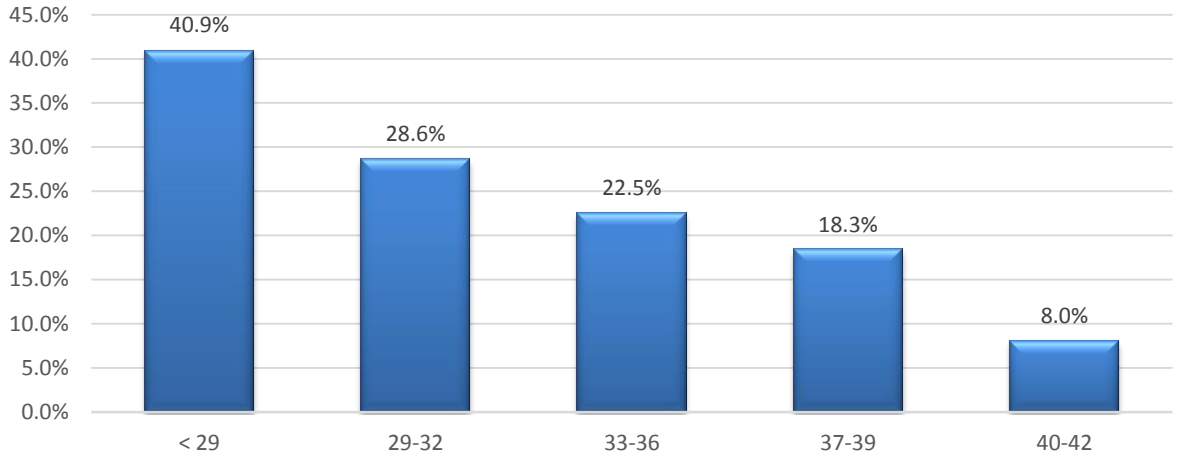


FIGURE 43 – PREGNANCY RATE AS % OF CYCLES PER AGE GROUP



8.6. Pregnancy Rate per Embryos Transferred

From a total of 249 couples who had an embryo transfer effected, there were 64 resulting pregnancies, or 25.7%, a drop of 4.96% when compared to the previous year. The couples who were most successful at achieving a pregnancy were those who had 2 embryos transferred (28.67%), followed by those couples who had 3 embryos transferred (24.53%). The remaining 17.39% achieved a pregnancy through a single embryo transfer (Table 12).

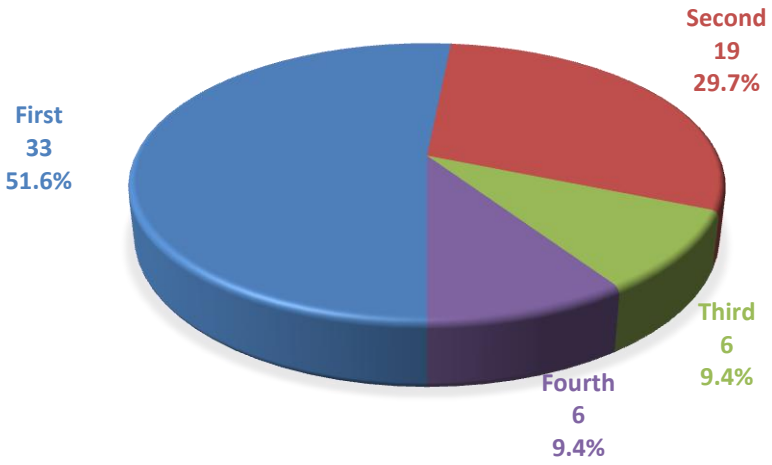
Table 12. Pregnancy Rate per Embryos Transferred

Transferred Embryos	Total IVF/ICSI Procedures	Total Pregnancies	% Pregnancies
0	12	0	0.00%
1	46	8	17.39%
2	150	43	28.67%
3	53	13	24.53%
Total	261	64	24.52%
Total procedures with Embryo transfer	**249**	**64**	**25.70%**

8.7. Pregnancy Distribution per ART Cycle Attempts

Thirty three (33) couples (or 51.6%) out of the 64 who got pregnant from cycles carried out in 2016, achieved a pregnancy on their 1st IVF/ICSI attempt, 19 couples (29.7%) on their 2nd attempt, 6 couples (9.4%) on their 3rd attempt, and the remaining 6 couples (9.4%) on their 4th attempt (Figure 44).

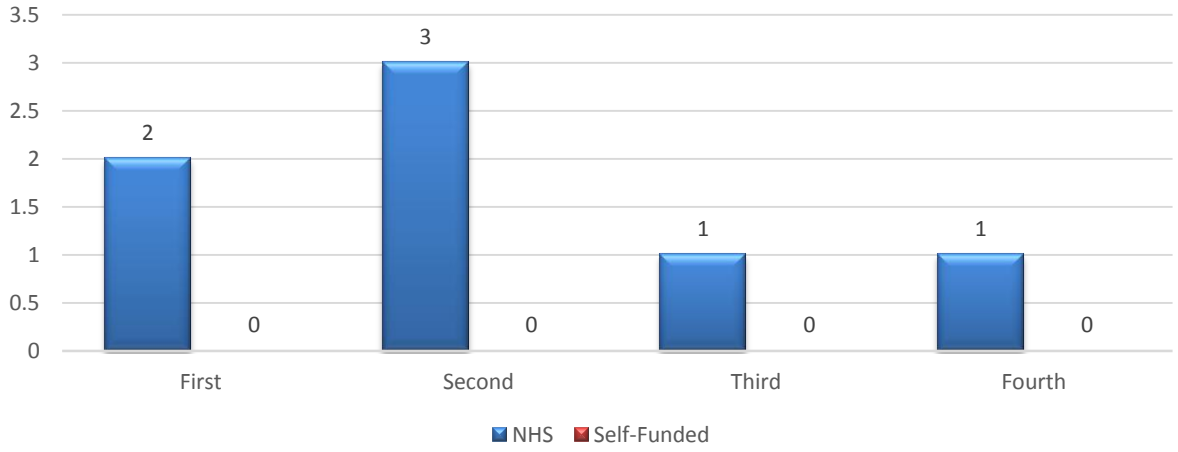
FIGURE 44 – PREGNANCY DISTRIBUTION PER ART CYCLE ATTEMPTS (%)



8.8. Miscarriages per ART Cycle

In 2016, a total of 7 miscarriages were reported, all from cycles carried out at MDH. The private clinics reported no miscarriages. Two (2) of the couples who got pregnant on their first IVF/ICSI attempt miscarried. There were 3 couples who miscarried after a successful 2nd IVF/ICSI attempt. One couple miscarried after getting pregnant from a 3rd attempt, while the remaining couple lost a pregnancy after a successful 4th attempt (Figure 45).

FIGURE 45 – MISCARRIAGES PER ART CYCLE
NHS vs. SELF-FUNDED



8.9. Miscarriages by Age

Miscarriages were only reported for women aged 29 and over. There were 2 reported miscarriages for women aged 29-32, 3 miscarriages for women in the 33-36 year old bracket, and one miscarriage was reported for a woman aged 37-39. One of the 2 women aged 40-42 who got pregnant, miscarried (Figure 46, 47).

FIGURE 46 – MISCARRIAGES BY AGE GROUP (QTY)

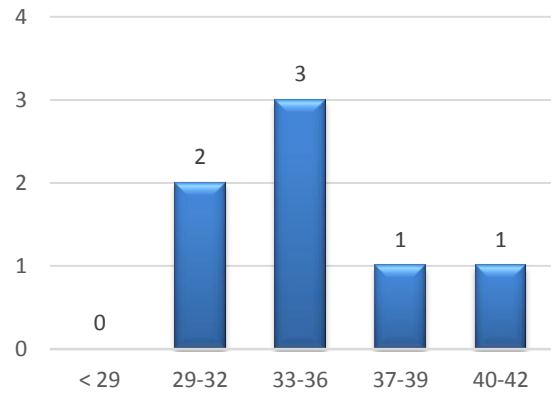
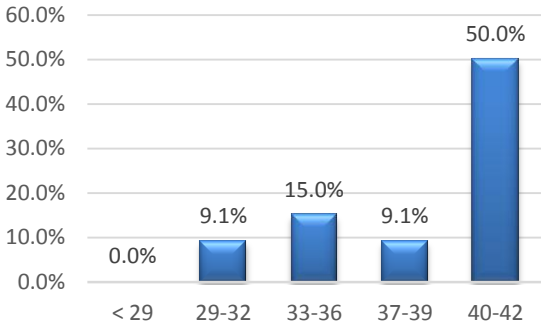


FIGURE 47 – MISCARRIAGES AS % OF PREGNANCIES IN AGE GROUP



8.10. Miscarriages by Gestational Age

The ART Clinic at MDH reported 2 miscarriages for women who were in their 2nd to 3rd week gestation. One (1) woman miscarried at 4 weeks; another miscarried at 6 weeks, while the remaining 3 women miscarried around the 8th week (Figure 48, 49).

FIGURE 48 – MISCARRIAGE DISTRIBUTION BY GESTATIONAL AGE (QTY)

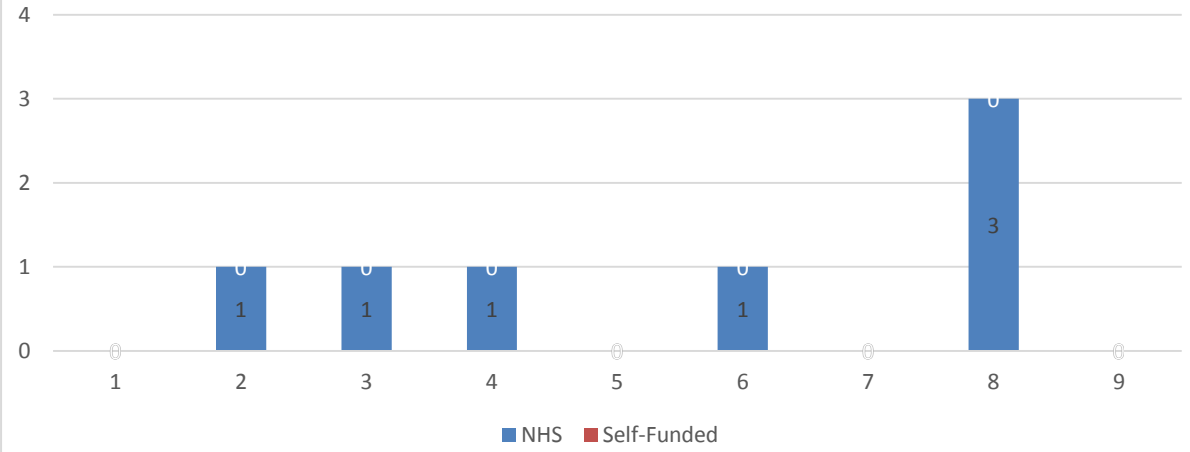
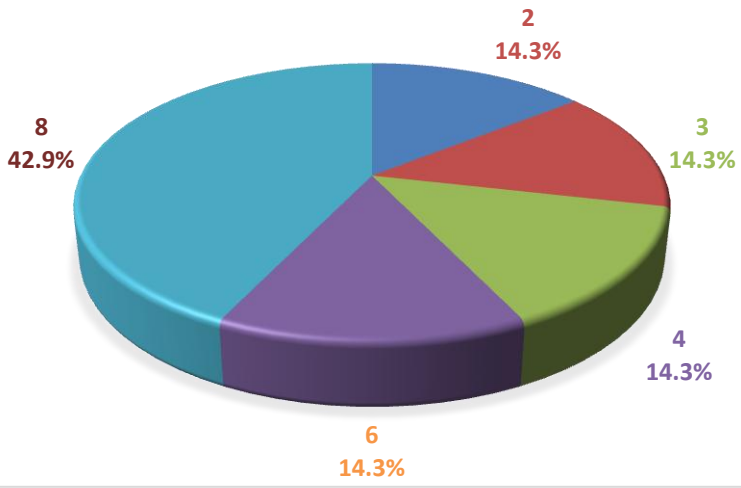


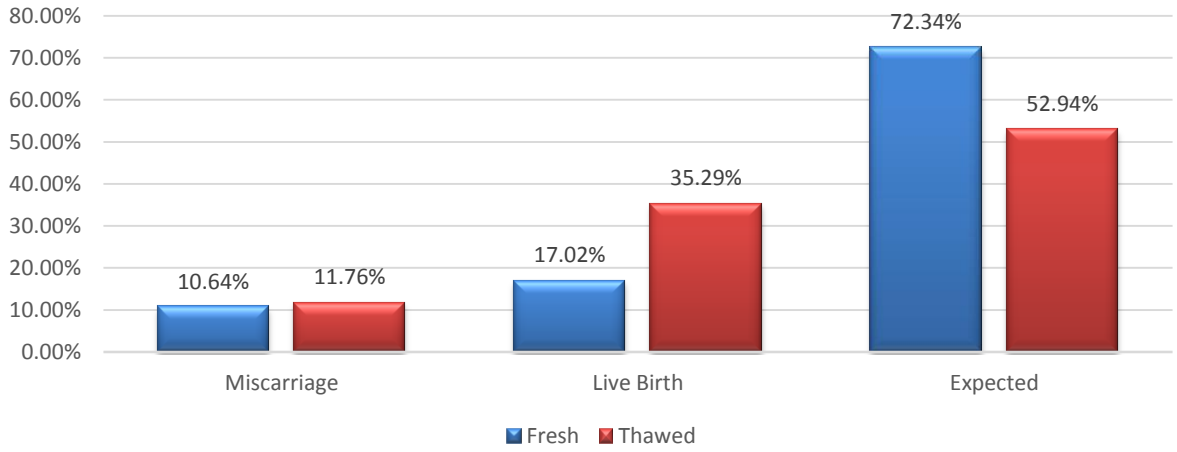
FIGURE 49 – MISCARRIAGE DISTRIBUTION BY GESTATIONAL AGE (%)



8.11. Miscarriages from Fresh vs. Thawed Cycles

Five (5) couples, or 10.64%, miscarried after achieving a pregnancy from a Fresh cycle and 2 couples (11.76%), miscarried after a successful Thawed cycle (Figure 50, Table 11).

FIGURE 50 – PREGNANCY OUTCOME %
FRESH vs THAWED



9. BIRTH EVENTS

9.1. Births from July – November 2015 Cycles

Forty four (44) babies, 23 females and 21 males, were born as a result of cycles performed between July and November 2015 (Figure 51). Hence, a total of 72 babies, 37 females and 35 males, were born out of the 311 procedures carried out throughout 2015 (Figure 52). Anomaly was observed in 2 of these babies, while no information was provided on the condition of a set of twins conceived during the November 2015 cycle.

FIGURE 51 – JUL–NOV '15 LIVE BIRTHS
MALES vs. FEMALES

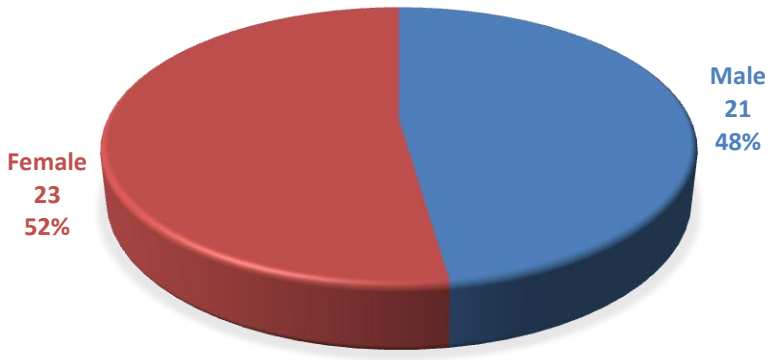
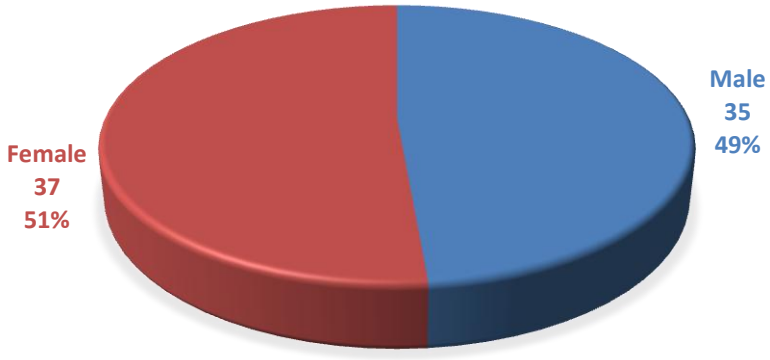


FIGURE 52 – 2015 LIVE BIRTHS

MALES vs. FEMALES



Fifty nine (59) babies, or 82%, were born out of Fresh cycles and 13 babies were born out of Thawed cycles (Figure 53). Fifty seven percent (57%) of the babies born out of procedures carried out in 2015 were from procedures carried out at MDH, while the remaining 43% were from procedures carried out at the private clinics (Figure 54).

FIGURE 53 – 2015 LIVE BIRTHS
FRESH vs. THAWED

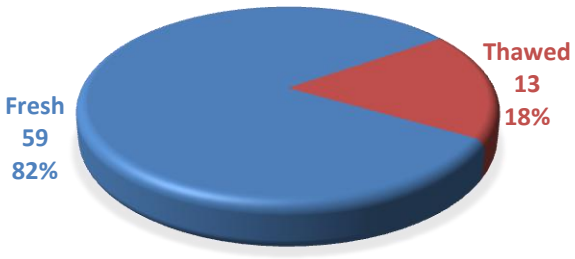
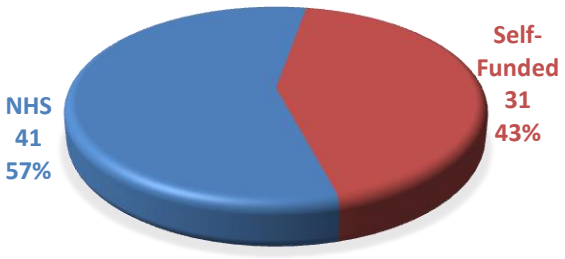
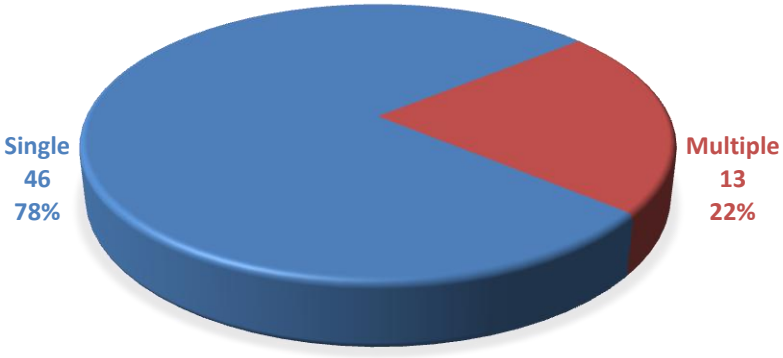


FIGURE 54 – 2015 LIVE BIRTHS
NHS vs. SELF-FUNDED



As shown in Figure 55, out of a total of 59 Live Birth Events, there were 46 single births and 13 multiple births (twins).

FIGURE 55 – 2015 LIVE BIRTH EVENTS –
SINGLES vs. MULTIPLES



In summary, out of a total of 311 cycles carried out in 2015, 222 couples did not achieve a pregnancy, 30 miscarried, and 59 had a live birth, for a **final Take-Home Baby Rate of 18.97%** (Table 13).

Table 13 – % Take-Home Baby Rate 2015

Cycle Outcome	Qty	% of pregnancies	% of total cycles
Live Birth	59	66.29%	**18.97%**
Miscarriage	30	33.71%	9.65%
Not Pregnant	222		71.38%
TOTAL CYCLES 2015	311		100.00%

9.2. Birth Events from 2016 Cycles – Fresh vs. Thawed

The number of babies born out of procedures carried out in January and March 2016 was 14. Eight (8) singletons, 4 males and 4 females, were born from Fresh cycles. The remaining 6 singletons, 5 males and 1 female were born from Thawed cycles (Figure 56, 57). Anomaly was observed in one (1) of the infants.

FIGURE 56 – LIVE BIRTH OCCURENCES UP TO MARCH 2016 CYCLE

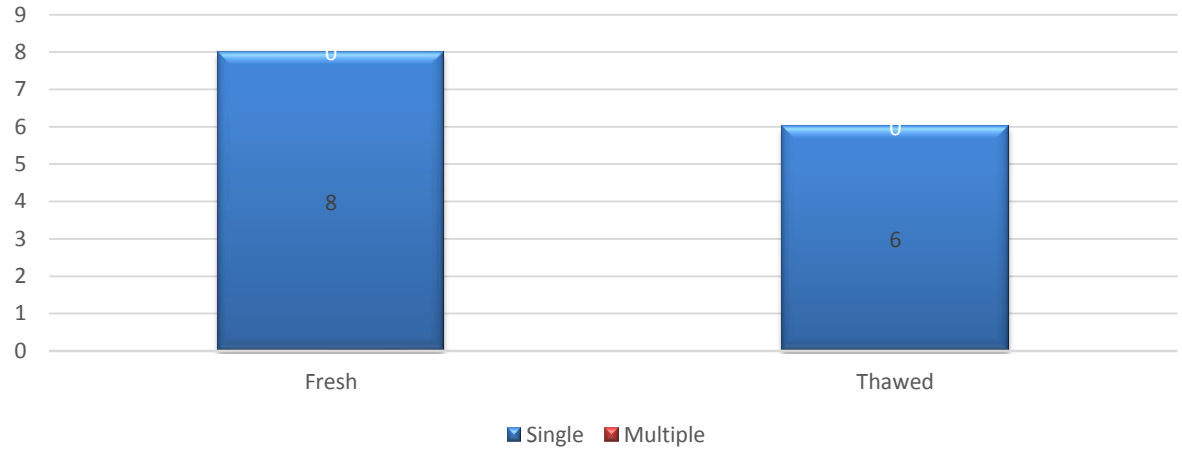
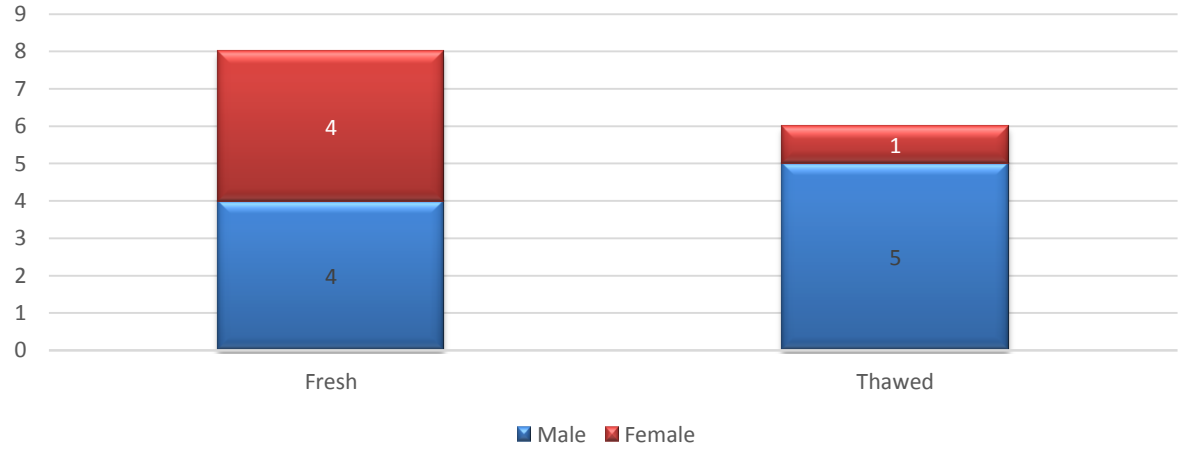


FIGURE 57 – LIVE BIRTHS UP TO MARCH 2016 CYCLES – GENDER OF NEWBORNS

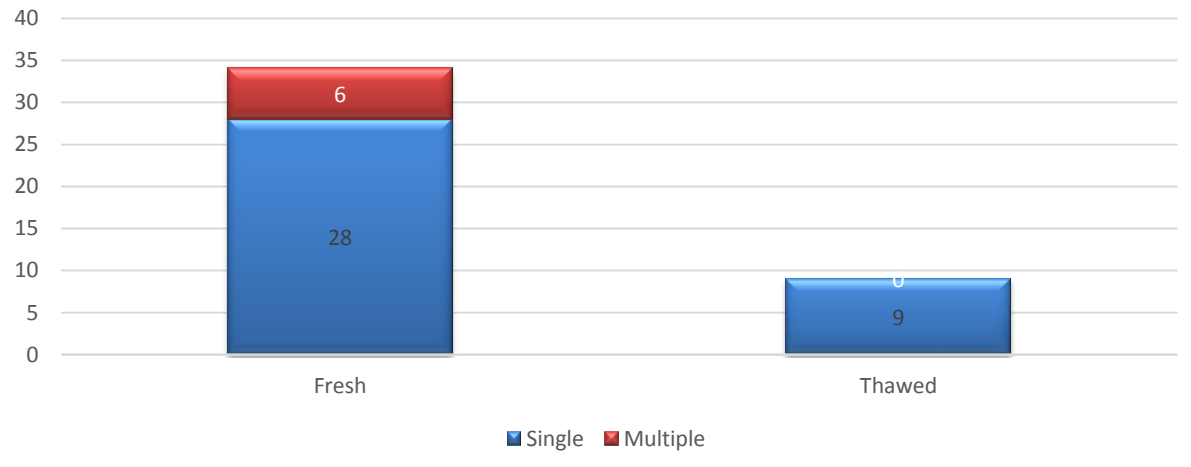


9.2.1. Expected Birth Events from Fresh vs. Thawed

Forty three (43) birth events are expected from cycles carried out between April and November 2016. Twenty eight (28) singletons and 6 multiples are expected from Fresh cycles and 9 singletons are expected from Thawed cycles (Figure 58). The multiple pregnancies reported include 5 sets of twins and 1 set of triplets. The percentage of multiple pregnancies is 2.2% of all cycles started.

Hence, out of the 64 live and expected births from procedures carried out in 2016, 49 babies (76.6%) are from pregnancies achieved through Fresh cycles, and the remaining 23.4% are from pregnancies achieved through Thawed cycles.

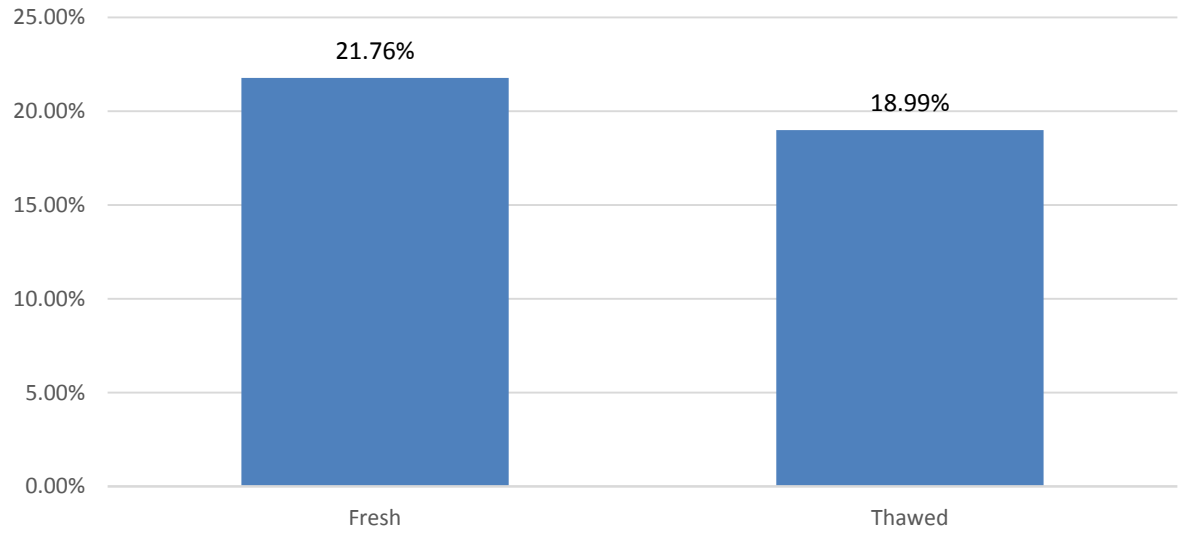
FIGURE 58 – EXPECTED BIRTH EVENTS
(APR – NOV 2016 CYCLES)



9.3. Maximum Success Rate – Fresh vs. Thawed

From the 193 **Fresh** cycles carried out, there are 42 reported birth events (live + expected), for a maximum success rate of **21.76%,** which compares well to last year's 20.87% maximum success rate from fresh cycles. Fifteen (15) birth events (live + expected) are reported from the 79 **Thawed** cycles performed, for a maximum success rate of **18.99%,** which is 5.24% higher than last year's (Figure 59).

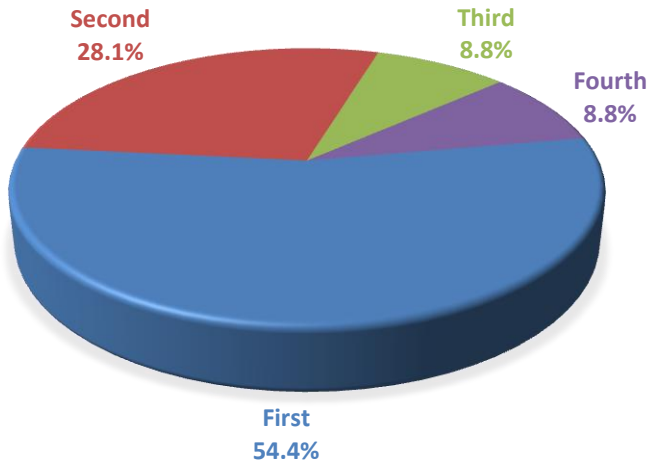
FIGURE 59 – % CYCLES WITH LIVE OR EXPECTED BIRTHS FROM TOTAL CYCLES – FRESH vs. THAWED



9.4. Birth Events per ART Cycle

Out of a total of 43 reported birth events (live + expected) from procedures carried out in 2016, there were 31 birth events (54.4%) from couples undergoing their first IVF/ICSI attempt, 16 birth events from a 2nd attempt, 5 birth events from a 3rd attempt, and 5 more birth events from a 4th attempt (Figure 60).

FIGURE 60 – LIVE & EXPECTED BIRTH EVENTS DISTRIBUTION BY ART CYCLE



9.5. Outcome for Approved AFR

As outlined in Section 7.5 above, there were 8 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 103 couples had an extra oocyte available for fertilization, the rate of Birth Events (Live + Expected) with multiples (0.97%) is lower than the overall rate of Birth Events (Live+ Expected) with multiples which stands at 2.2%. The total Birth Events (Live + Expected) for couples with an approved AFR who had undergone an IVF/ICSI procedure stand at 12.62% (Table 14).

Table 14. 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	103	17	4	13	12	1
% of Procedures undergone from Approved AFR		16.50%	3.88%	12.62%	11.65%	0.97%

These results show that for this population, approval for the fertilization of 3 oocytes instead of 2 was of benefit since, even though an extra oocyte was available for fertilization, these couples still fell short of reaching the overall Maximum Success Rate, which is the sum of the live and expected birth events, as illustrated in Table 15.

9.6. Percentage Maximum Success Rate

In conclusion, from the 64 couples who achieved a pregnancy in 2016, 14 (21.88%) had a live birth, 34 (67.19%) are still expecting, and 7 couples (10.94%) miscarried. Out of a total of 273 cycles carried out, 5.13% of couples had a live birth, 15.75% are still expecting, while 2.56% miscarried. Consequently, the *maximum percentage success rate for 2016 is* **20.88%** (Table 15).

Table 15. % Maximum Success Rate

Pregnancy Outcome	Qty	% of pregnancies	% of total cycles	% Max Success Rate
Live Birth	14	21.88%	5.13%	**20.88%**
Expected	43	67.19%	15.75%	
Miscarriage	7	10.94%	2.56%	

10. Conclusion

The number of IVF/ICSI procedures carried out in Malta in 2016 has decreased by around 12% when compared to 2015. There was an increase in Government-funded cycles and a significant drop in self-funded ones.

ICSI was the preferred procedure of choice in 97.3% of all procedures carried out by the licensed clinics. There were 64 (23.4%) reported pregnancies out of all cycles started – a drop of 4.9% from 2015. 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**, which implies a birth event and is the most meaningful measure of treatment success*, stands at **20.88%**, which is 1.91% higher than last 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.

Judge Philip Sciberras UOM

Chairperson

Ms. Simone Attard

Executive Director