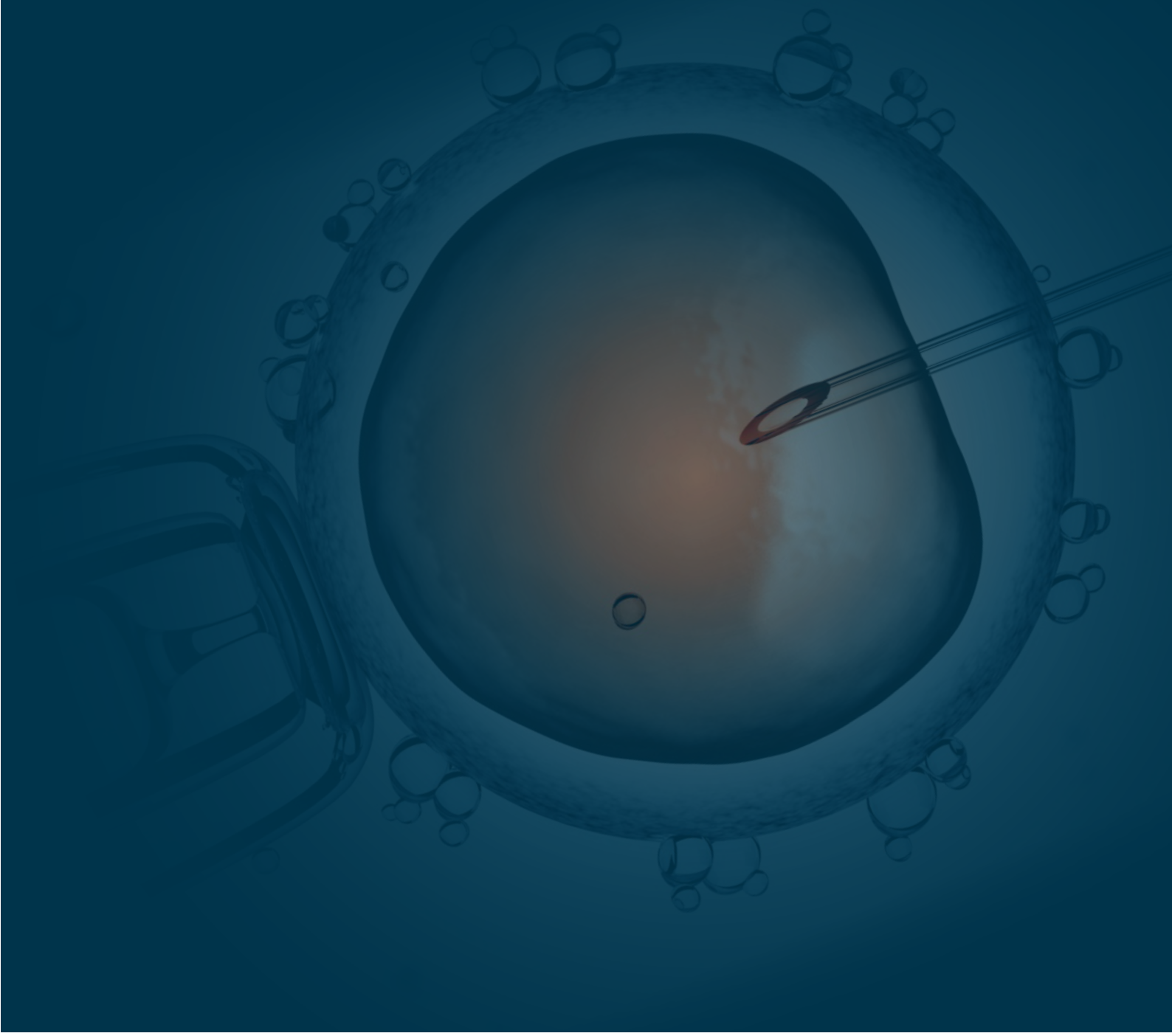
ANNUAL WORK REPORT

TRENDS AND FIGURES OF FERTILITY TREATMENTS IN MALTA FOR 2015



EMBRYO PROTECTION AUTHORITY

Putting Patients First

MAY 2016

ANNUAL WORK REPORT

TRENDS AND FIGURES OF FERTILITY TREATMENTS IN MALTA FOR 2015

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

May 2016

EMBRYO PROTECTION AUTHORITY

PUTTING PATIENTS FIRST

ANNUAL WORK REPORT FOR 2015

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1. BACKGROUND

1.1. The Embryo Protection Authority (EPA)

The Embryo Protection Authority is a legal entity – the sole Regulator of all Assisted Reproductive Technologies (ART) performed at both 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.

All decisions taken by the Embryo Protection Authority are taken in the best interest of the couples and of the child who may be conceived out of any assisted reproductive technology procedure undergone.

1.3. Our Principles – Working closely with Stakeholders

The Authority works closely with all the stakeholders in the Fertility field. It listens to the Service Providers, whilst at the same time ensures that the highest level of standards are being kept by all as specified in the laws governing the fertility sector.

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

Laws and Regulations governing the Fertility Sector:

- Embryo Protection Act 2012 (Cap 524), and
- Embryo Protection Authority Regulations, LN32 of 2015

1.4. 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.

1.5. Human Resources

Ms Simone Attard has been appointed Director/Executive Head by the Minister for Energy and Health with effect from 1st February 2015 as per Legal Notice 32/2015, with responsibility of the Executive Conduct, Administration and Organization of the Authority. The Authority has also employed a Deputy

Head and an Executive Officer as was necessary for the due and efficient execution of its functions. Necessary arrangements are being made so that the Authority will strengthen its Inspectorate function through the employment of two new inspectors.

1.6. Board Members & Meetings

The legal representation of the Authority is vested in its Chairman, Hon. Judge Philip Sciberras. The other appointed members include Dr. Patrick Sammut, Ms. Mariella Meachen, and Ms. Pauline Baldacchino. Since Ms. Simone Attard's appointment as Director/Executive Head, 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 2015, the meetings of the Authority have been called once a month, and in all sittings quorum was achieved. The Director/Executive Head attended all the meetings of the Authority, as per Ln32 of 2015. Attendance by members to these Board meetings was as stated hereunder:

Designation	Name	Attended	Excused
Chairperson	Judge Philip Sciberras	10	2
Member	Dr. Patrick Sammut	10	2
Member	Ms. Mariella Meachen	11	1
Member	Ms. Pauline Baldacchino	9	3
Director	Ms. Simone Attard	12	0

During 2015, seven (7) meetings with Representatives from *the Obstetrics and Gynaecology Association* and the *Paediatric Association of Malta* have been called in order to discuss requests for additional fertilization of oocytes. These requests are made by the clinicians treating the couple. [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].

1.7. 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

1.8. 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 MDH Hospital. 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.

The Authority is represented on this ART Prioritization Committee by its Director/Executive Head Ms Simone Attard and by Dr. Patrick Sammut, Board member. In light of the fact that new cases are registered at Mater Dei Hospital every week, this Committee meets on a monthly basis to decide which of these couples requires prioritization for treatment.

1.9. Consultation on IVF Legislation

An Inter-Ministerial IVF Review Working Committee has been set up by the 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 Director/Executive Head, 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 report has been submitted to the Parliamentary Secretary for Health and will be presented to Cabinet in due course.

1.10. 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 Protocols which the Authority is entitled to enforce. In 2015 the Authority, together with the Superintendency of Public Health (SPH), carried out two separate inspections at Mater Dei Hospital and St. James Assisted Conception Unit respectively. These inspections were 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.

1.11. Other work by the Authority

Apart from the normal processing of all applications for treatment, requests for additional fertilizations, and the cryopreservation of gametes (a detailed report to follow), the Authority was in continuous communication with the Ministry for Energy and 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 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.

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), has been requested to both licensed Clinics storing gametes. This exercise served to ensure that traceability of gametes was being properly documented.

Together with the SPH, the EPA is striving 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.

Finally, pursuant to the new EPA Regulations 2015, the Authority is taking the necessary measures towards becoming fully autonomous.

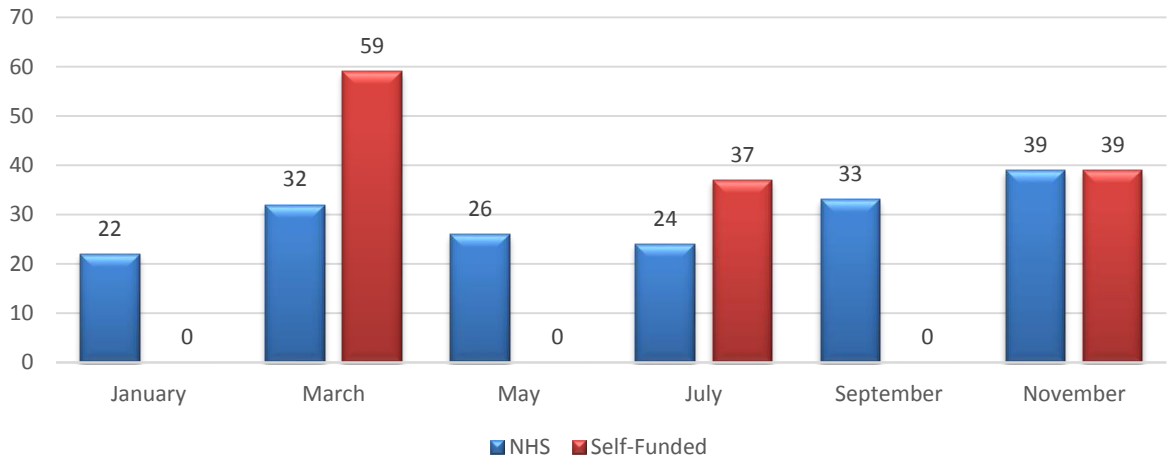
FERTILITY TREATMENTS IN MALTA FOR 2015 – TRENDS AND FIGURES

In line with LN32 of 2015, Clinics in both the Private and Public sector are duty-bound to provide the Embryo Protection 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 2015, the Authority has received a total of 311 applications from Clinics/Hospitals in both Private and Public Sector. All the applications have been approved by the Board and thus, 311 IVF/ICSI procedures have been carried out. One hundred seventy six (176) procedures over six (6) bimonthly cycles have been performed at Mater Dei Hospital while another 135 procedures were performed in the Private Sector over three (3) cycles (Figure 1).

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



The number of IVF procedures carried out in Malta in 2015 increased by 82.9% over the previous year which may be mainly attributed to the fact that the ART Clinic at Mater Dei Hospital has started offering infertile couples IVF/ICSI procedures free of charge as of January 2015. Couples eligible for IVF/ICSI procedures on the NHS are those suffering from primary infertility and secondary infertility (couples who have children from previous relationships, but not from current relationships). Out of the 311 cycles which were performed in 2015, 282 met the NHS eligibility criteria, but only 176 of these were performed on the NHS. The other cycles were performed at the private licensed clinics despite eligibility to be carried out on the NHS.

2.1. First Time/Repeated Cycles

Out of the 311 cycles carried out, 52.4% of couples were undergoing the IVF/ICSI procedure for the first time. There were 28.6% of couples who were undergoing IVF/ICSI for the second time, 12.9% of couples for the 3rd time, 4.2% of the couples were undergoing their fourth attempt, while 1.9% of couples had undergone five or more cycles (Figures 2, 3).

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

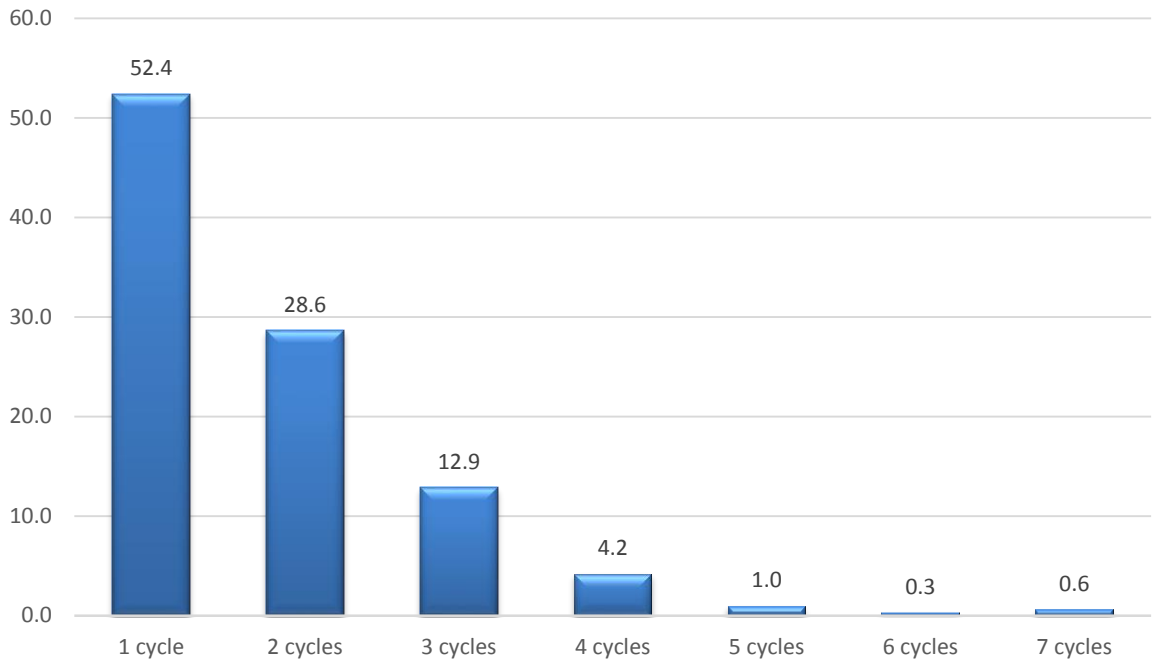
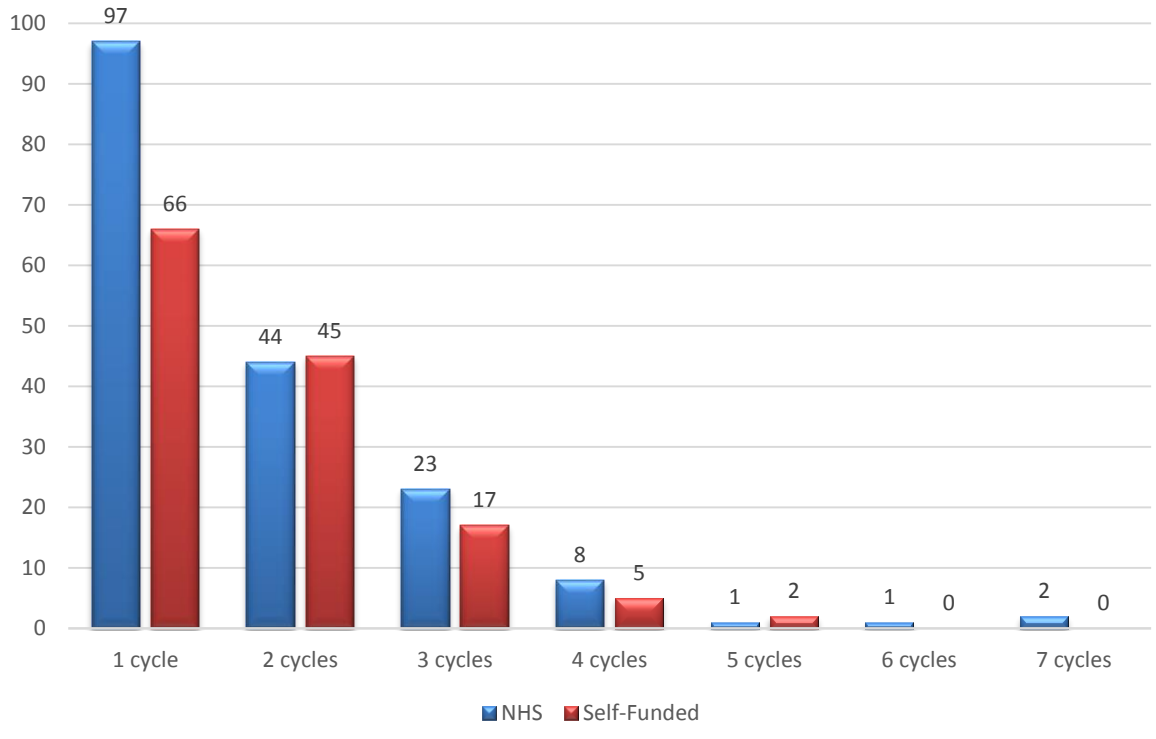
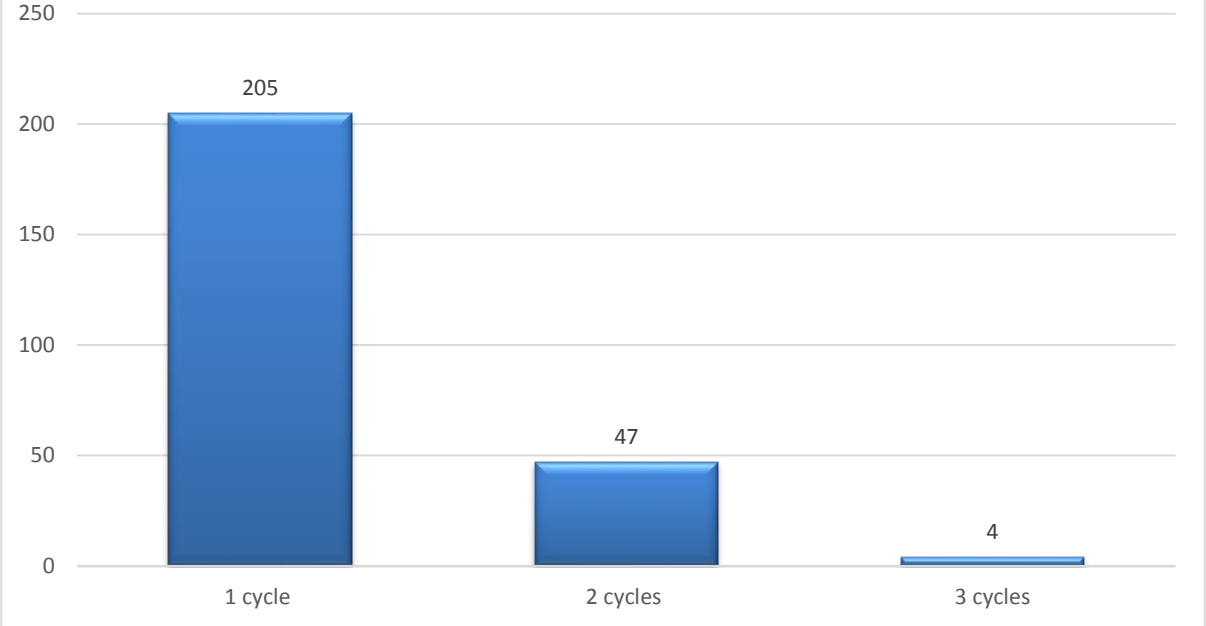


FIGURE 3 – ART CYCLES PER COUPLE (QTY)



Out of a total of 311 procedures performed in 2015, there were 205 couples who had undergone a single cycle, 47 couples who had undergone 2, and 4 couples who had a third cycle performed during the same calendar year. Thus, these 311 IVF/ICSI procedures were undergone by 256 couples (Figure 4).

FIGURE 4 – COUPLES vs. CYCLES



3. DEMOGRAPHICS

3.1. Nationality

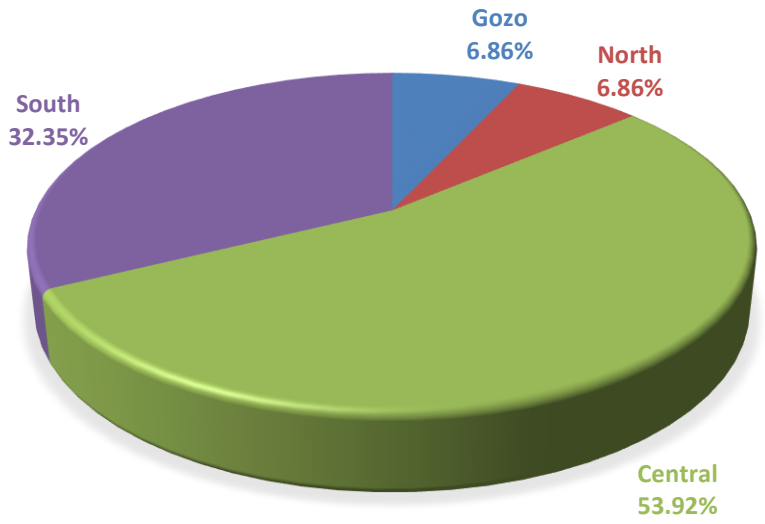
Out of the 311 IVF/ICSI cycles performed this year, 306 (98.4%) were undertaken by Maltese Residents while the remaining 5 (1.6%) were undertaken by foreign couples (non-Residents) who came to Malta specifically to perform the IVF/ICSI procedure at a private clinic. There has been a marked

decrease in Medical Tourism in the IVF sector when compared to 2014, where the number of foreign couples undergoing IVF/ICSI amounted to 13.

3.2. Regions

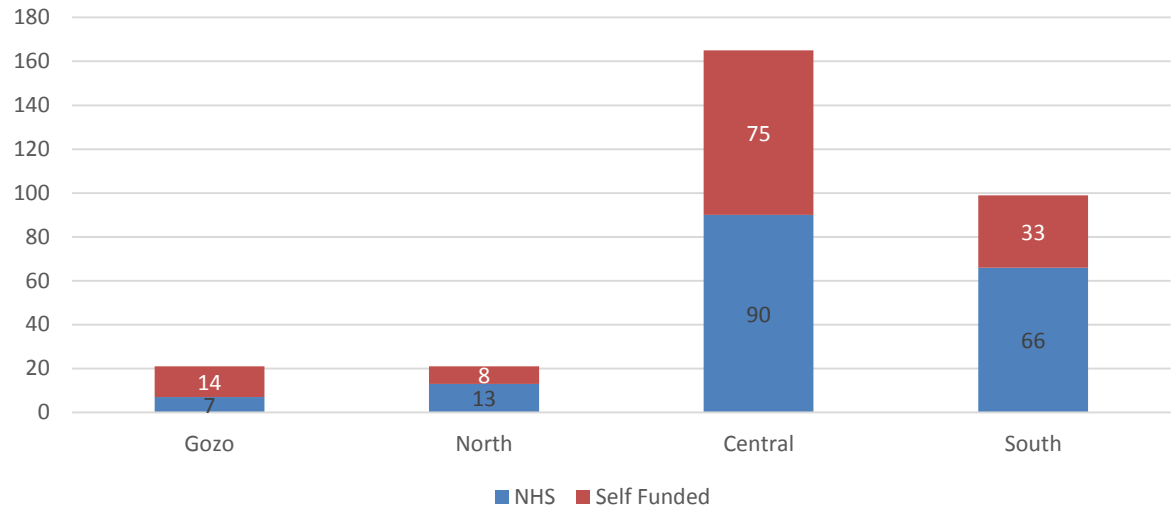
Out of the 306 IVF/ICSI cycles performed by Maltese residents, 6.86% were by couples residing in Gozo, 6.86% were by couples residing in the Northern part of the island, 53.92% by couples residing in the Central part, while the remaining 32.35% were by couples who reside in Southern areas of Malta (Figure 5).

FIGURE 5 – DISTRIBUTION BY REGION – OVERALL



It's interesting to note that out of the 21 Gozitan couples undergoing IVF/ICSI procedures, 14 (66.66%) choose to self-fund their treatment. In contrast, there were 66 couples out of the 99 (66.66%) coming from the Southern part of the island who chose to undergo the procedure at the ART Clinic in Mater Dei Hospital rather than self-fund their treatment (Figure 6).

FIGURE 6 – TOTAL CYCLES BY REGION



Worth noting also is that 34% of those undergoing their *first ever* IVF/ICSI attempt, still opted to self-fund the treatment, even though they were eligible to do it on the NHS (Figure 7). Thirty four percent (34%) of couples from both the Central and Southern part of the island, and 27% from the Northern part of the island chose to undergo their first IVF cycle at a private clinic (Figures 8-10). Half the Gozitan couples (50%) who were eligible for IVF/ICSI treatment on the NHS, still opted to self-fund their first IVF/ICSI attempt (Figure 11).

FIGURE 7 – FIRST TIME CHOICE – OVERALL

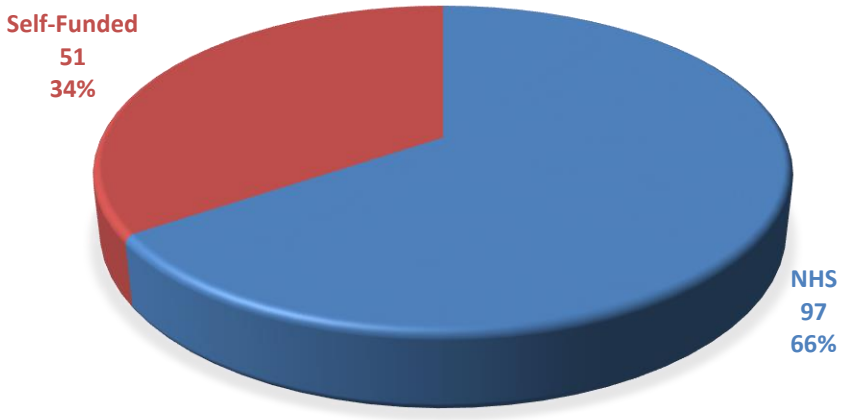


FIGURE 8 – FIRST TIME CHOICE – NORTH

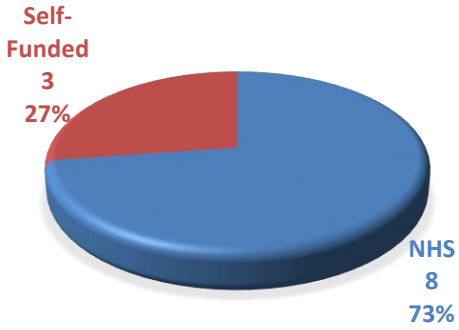


FIGURE 9 –FIRST TIME CHOICE – CENTRAL

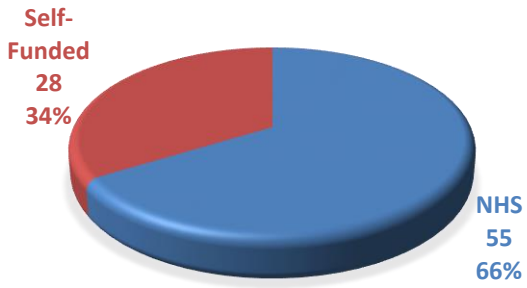


FIGURE 10 – FIRST TIME CHOICE – SOUTH

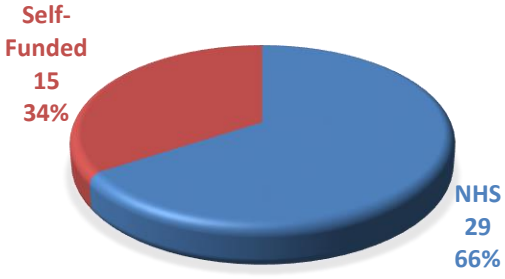
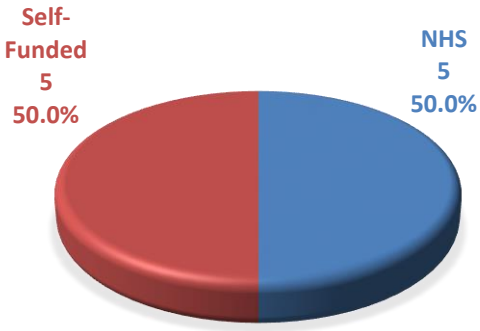


FIGURE 11 – FIRST TIME CHOICE – GOZO



3.3. Maternal Age

In line with Embryo Protection Act of 2012, in Malta only women within the stipulated age bracket of 25 and 42 are eligible to undergo IVF/ICSI procedures. Throughout 2015, there has been a distribution of procedures across all age brackets, as can be seen from the chart hereunder (Figure 12).

FIGURE 12 – FEMALES BY AGE GROUP (QTY)

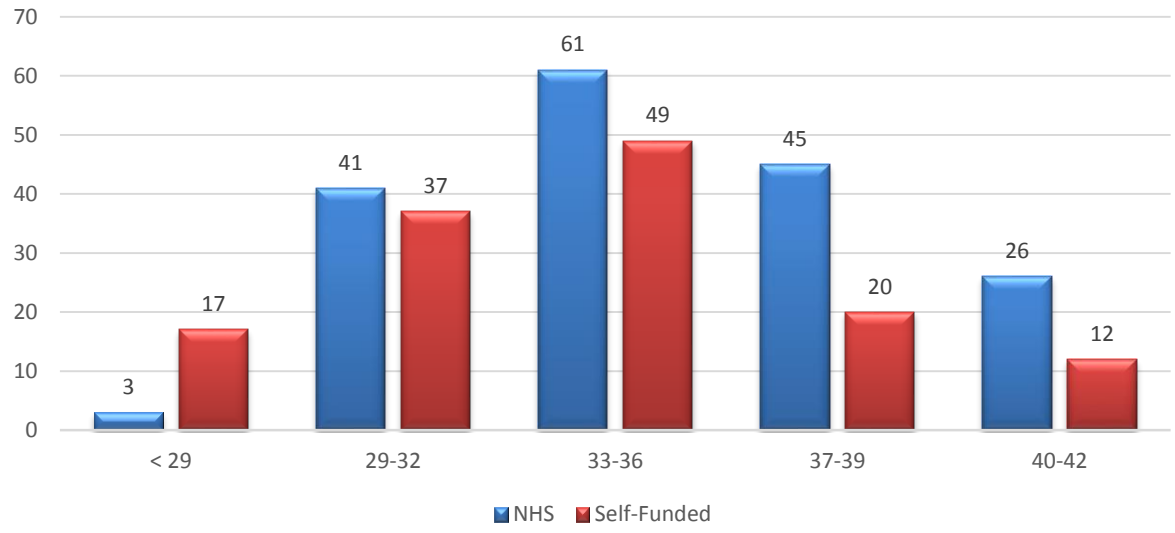
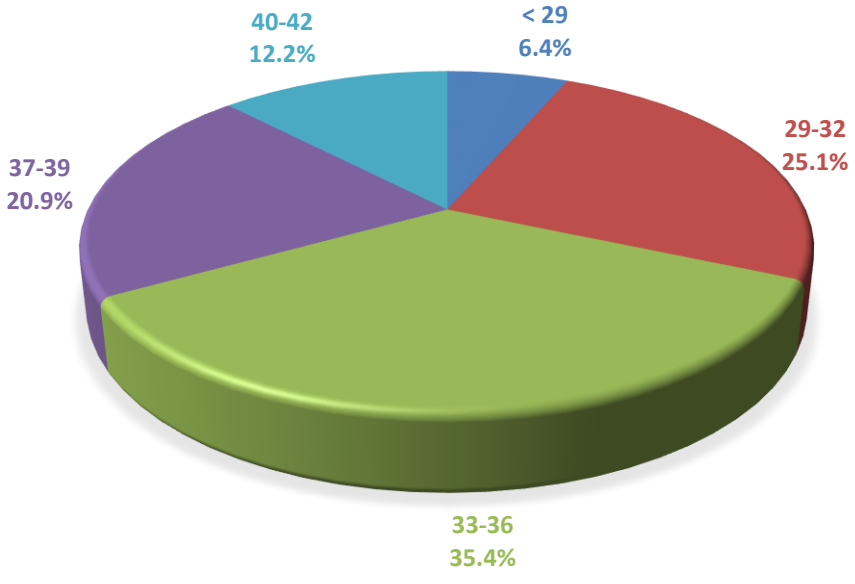


FIGURE 13 – FEMALES BY AGE GROUP (%)



As in 2014, the largest number (35.4%) of female patients undergoing IVF/ICSI procedures this year was aged between 33 and 36. The second largest age group was that for female patients aged between 29-32 years (25.1%), while 20.9% of female patients were in the 37-39 year old bracket. There were 12.2% of female patients aged between 40-42 years, while the remaining 6.4% were under the age of 29. The smallest number of couples referred for IVF/ICSI procedures were those where the female is less than 29 years old (Figure 13), which is in line with international figures, whereby couples are expected to wait and try out other ART procedures before resorting to powerful reproductive techniques such as IVF/ICSI. This year, the Board considered the request of a 24 year old woman who wished to undergo an IVF/ICSI procedure. Permission was granted on medical grounds.

3.4. Paternal Age

As with the female patients, the largest number of male patients (33.8%) undergoing procedures was aged between 33 and 36 years, while 21.2% were aged between 40 and 45. Following closely at 20.3% were males in 37-39 year old bracket, while 12.9% of male patients were aged between 29 and 32. There were 8.3% of males who were 46 years and over, while the remaining 3.5% of males were under the age of 29. (Figures 14, 15)

FIGURE14 – MALES BY AGE GROUP (QTY)

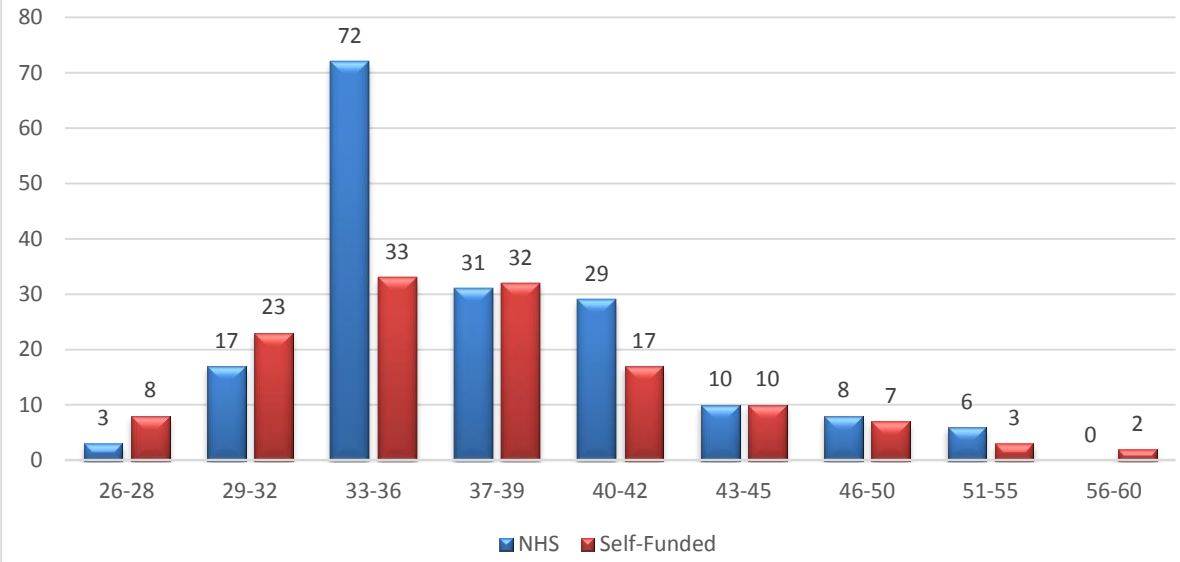
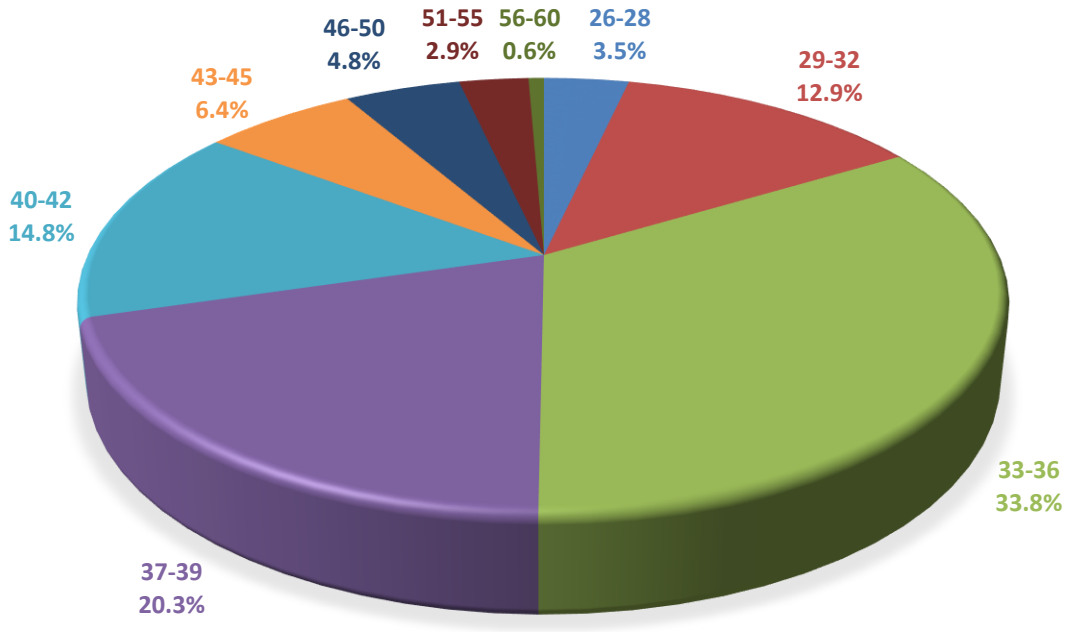


FIGURE 15 – MALES BY AGE GROUP (%)

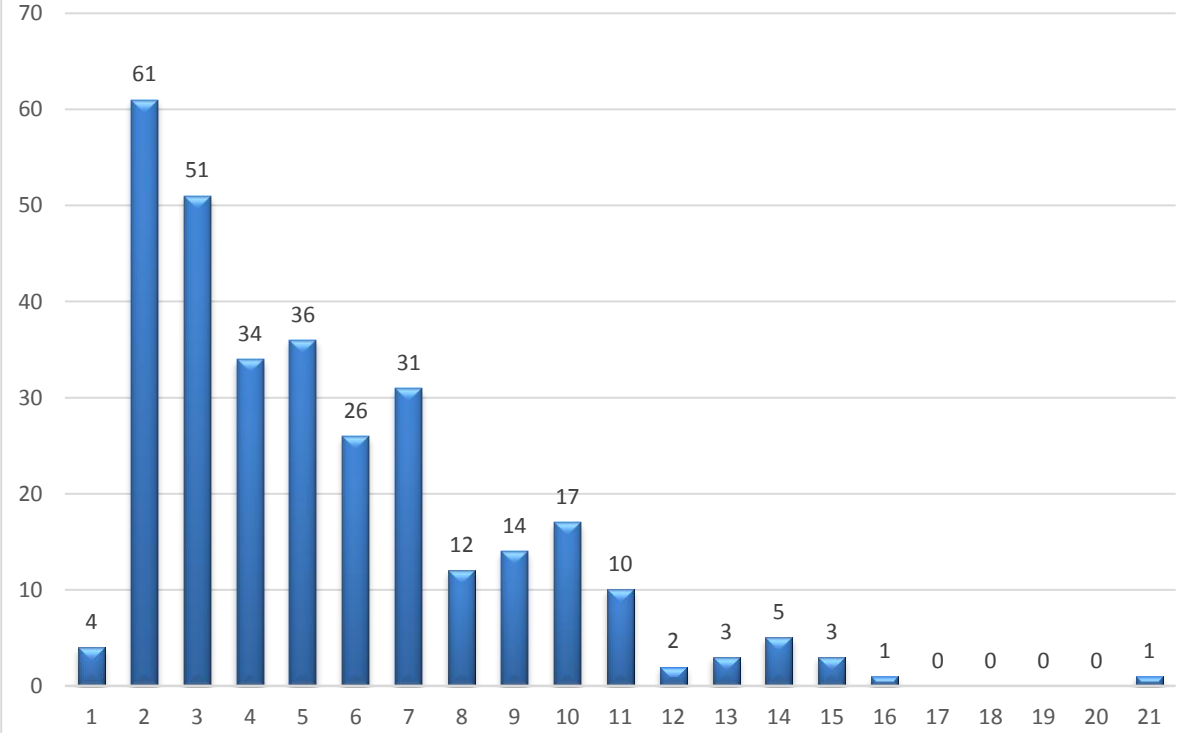


4. INFERTILITY

4.1. Duration of Infertility

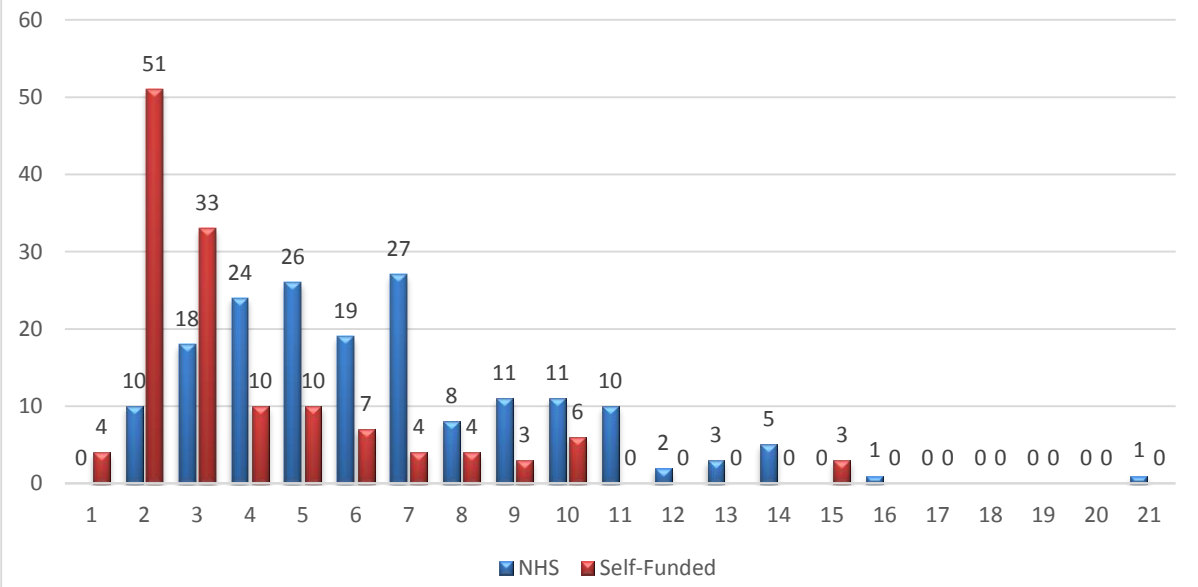
There was a surprising amount of variability in the reported duration of infertility between couples undergoing procedures in both the private and public sector, with the minimum reported duration period being that of one (1) year stretching up to a maximum of 21 years. Sixty-one (61) couples appear to have been infertile for 2 years, 51 couples for 3 years, 34 couples for 4 years, 36 couples for 5 years, while 125 couples (or 40%) have been infertile for 6 years or more (Figure 16).

FIGURE 16 – DURATION OF INFERTILITY (YRS)



To be eligible for treatment on the NHS, a couple must report being infertile for at least two years. The largest number of couples undergoing procedures on the NHS (54.5%) had reported being infertile for 4 to 7 years while the largest number of couples (65%) who self-funded their procedures have reported less than three years of infertility (Figure17). In contrast, the average reported duration of infertility for patients undergoing IVF/ICSI procedures in the private sector in 2014 was that of 3-4 years. The 4 couples who have reported infertility duration of one year self-funded their treatment.

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



The attributing factor in the prolonged duration of infertility reported by couples undergoing procedures at Mater Dei Hospital *vis-a-vis* those self-funded their treatment appears to be due to the fact that since January 2015, IVF/ICSI procedures were being offered at Mater Dei Hospital free of charge. Hence those couples who were never in a position to self-fund their treatment were now able to undergo the IVF/ICSI procedure for the first time.

4.2. Classification of Infertility

The vast majority of patients (90.03%) undergoing IVF/ICSI procedures suffered from Primary Infertility. The government only offers IVF/ICSI procedures on the NHS to patients suffering from primary infertility or from secondary infertility where either partner has children from a previous relationship. Out of the 176 cycles carried out at Mater Dei Hospital, only 2 couples reported suffering from Secondary Infertility. The majority of couples (106) undergoing IVF/ICSI procedures at private clinics suffered from Primary Infertility. Twenty six (26) couples already had children from the same relationship, while another 3 couples suffered from secondary infertility (previous relationships) (Table 1).

Table 1. Classification of Infertility

Classification of Infertility	NHS	Self-Funded	Total
Primary	174	106	280
Secondary- Same Relationship	0	26	26
Secondary- Previous Relationship-Female	2	2	4
Secondary- Previous Relationship-Male	0	1	1
Total	176	135	311

4.3. Infertility Factors

The Authority gathers data on what the contributing factor of infertility for each couple is. These factors are split up into four: Female factor only, Male factor only, Male and Female factor, or Idiopathic (unexplained) infertility (Figures 18, 19).

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

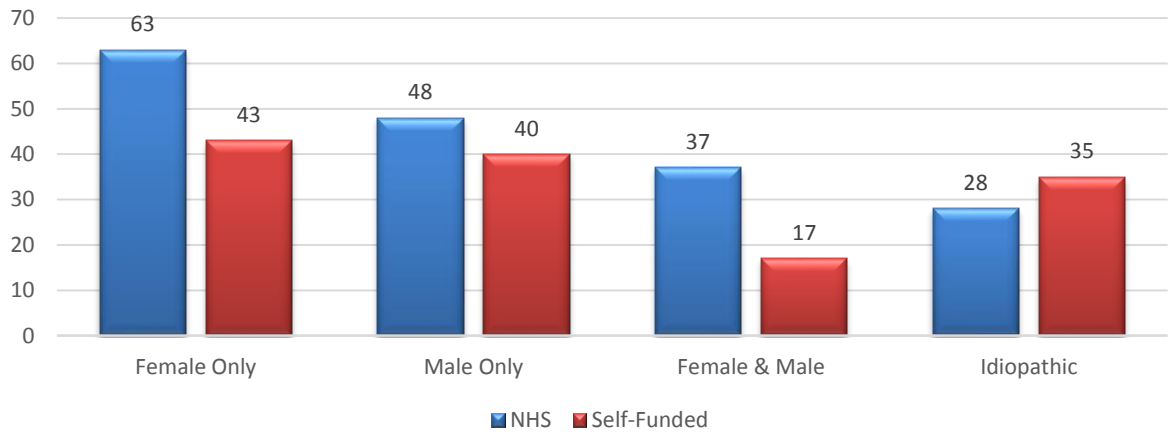
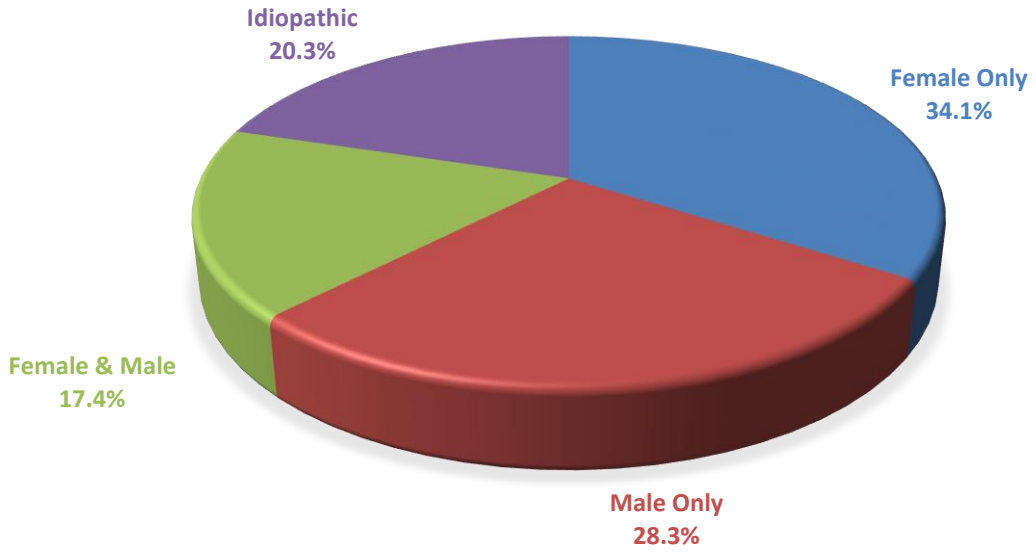


FIGURE 19 – INFERTILITY FACTORS (%)



As portrayed in Figures 18 and 19, the largest group of couples (34.1%) undergoing IVF/ICSI procedures in 2015 were those suffering from Female factor infertility only. Followed closely at 28.3% was Male factor infertility only, another 17.4% suffering from Male and Female factor infertility, while the remaining 20.3% of couples suffered from idiopathic infertility.

From those couples suffering from female factor infertility only and male factor infertility only, the largest group (30% and 32.4% respectively) were in the 33-36 year old bracket (Figures 20, 21).

FIGURE 20 – FEMALE INFERTILITY BY AGE GROUP (%)

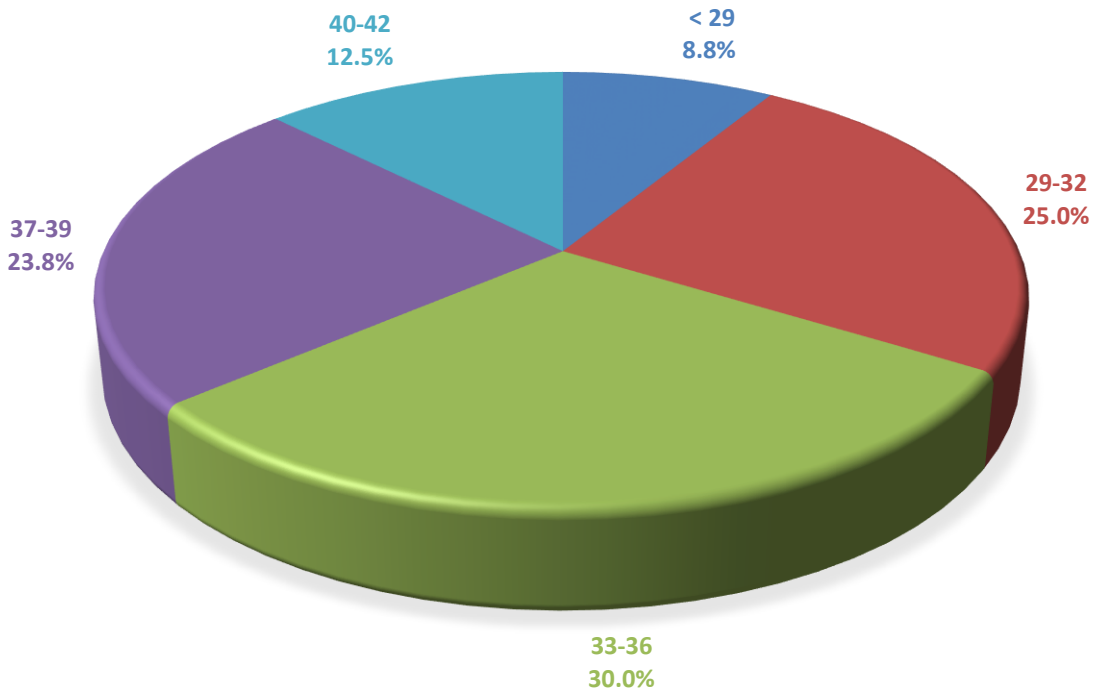
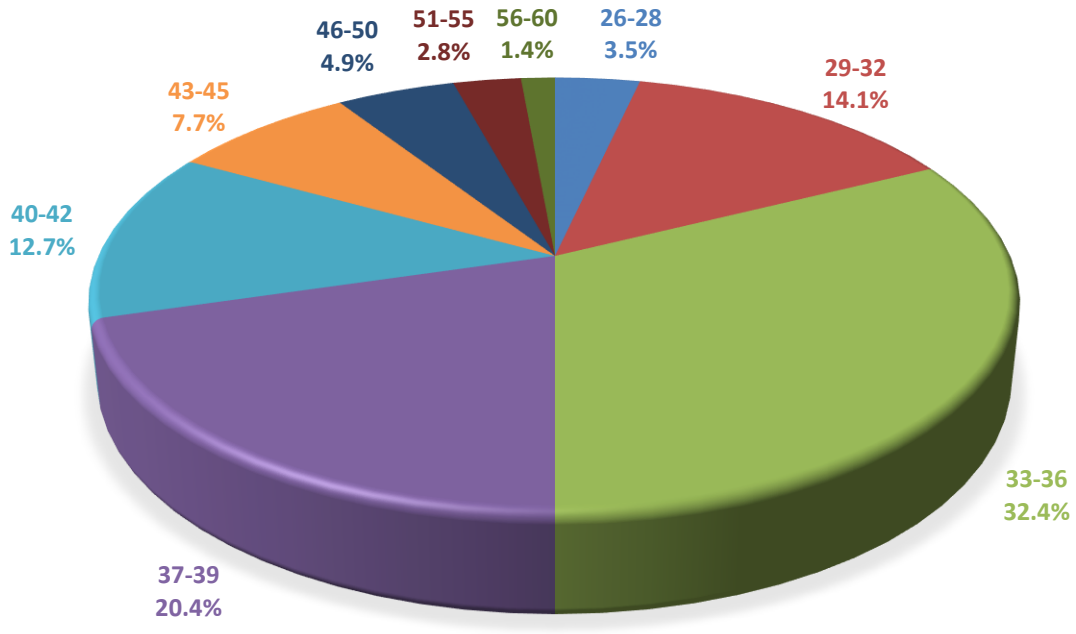


FIGURE 21 – MALE INFERTILITY BY AGE GROUP (%)



5. TYPE OF CYCLE

5.1. Fresh vs. Thawed

Pursuant to the introduction of the Embryo Protection Act in 2013, the maximum number of oocytes which may be injected in any one cycle is two (three oocytes in cases approved by the Authority), and all embryos created will have to be transferred since embryo cryopreservation is forbidden. Thus, oocyte selection and cryopreservation are the routine practice in Malta's ART clinics. Couples are allowed to opt for Fresh or Thawed/Frozen cycles, or a combination of Fresh and Thawed. Given that oocyte cryopreservation still denotes a huge challenge in Assisted Reproductive Techniques, data gathered on the outcomes from Thawed cycles is of utmost importance, especially in light of the gamete cryopreservation technique being applied for fertility preservation (e.g. in the case of oncology patients).

Table 2. Type of Cycle

Fresh/Thawed/Combined	NHS	Self-Funded	Total	% of Total
Fresh	144	86	230	73.95%
Thawed	31	49	80	25.72%
Combined	1	0	1	0.32%
Total	176	135	311	

Out of 311 procedures carried out, 230 (73.95%) were Fresh cycles; while another 80 (25.72%) were Thawed cycles. One couple (0.32%) opted for a combined cycle, whereby both Fresh and Thawed gametes were utilized. 62.9% of the Fresh cycles were carried out at Mater Dei Hospital while the remaining 37.1% were held at private Clinics. In contrast, there were more Thawed cycles carried out in the private sector (61.7%) than in the public sector (38.3%). This appears to be mainly due to the fact that the ART clinic at Mater Dei Hospital started offering IVF/ICSI procedures in January 2015, while the private clinics have been cryopreserving gametes since 2013.

5.2. Additional Fertilization Requests (AFRs)

The Authority ceaselessly receives requests by representative clinicians in both the private and public sector to consider the fertilization of three oocytes for specific couples, instead of the two permitted by law. These requests are analysed and discussed by the EPA Board members together with Representatives from *the Obstetrics and Gynaecology Association* and the *Paediatric Association of Malta,* as per Article 6 of the Embryo Protection Act. Such requests are considered on a case by case basis and matched against established criteria which include the age of the female patient undergoing treatment, together with the number of failed cycles which the couple had already undergone.

There have been 234 Additional Fertilization Requests (AFRs) altogether in 2015. The majority of requests (74%) came from the ART clinic at Mater Dei Hospital while the remaining 26% came from the private clinics. Out of the total 234 requests made, 57.3% were approved, while the remaining 42.7% were not on the basis that the couples on behalf of whom the requests have been made, did not meet the established criteria. Out of the 174 requests made

by the ART Clinic at Mater Dei Hospital, only 52% were approved, while 73% of the requests made by the private Clinics have been approved (Figures 22, 23).

FIGURE 22 – AFR REQUESTS (QTY)

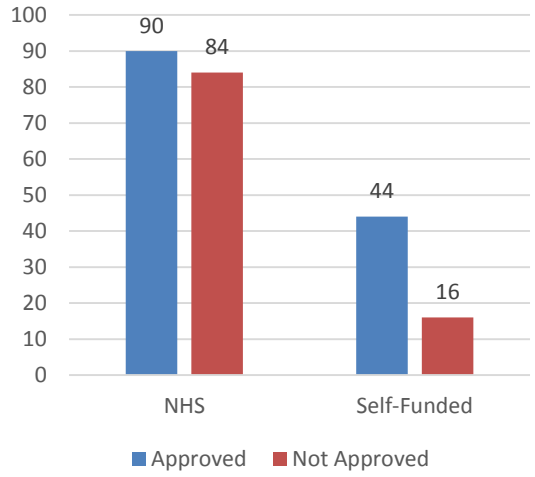
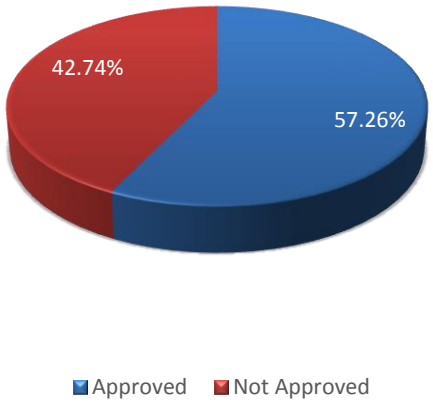


FIGURE 23 – AFR APPROVAL RATE (%)



Two AFR requests have been declined due to late submission of documentation by the licensed Clinics. In such cases, besides informing the Clinics about the Authority's decision that their requests have been declined due to non-adherence to EPA's Protocol, the couples involved were also informed in writing that due to late submission of documentation by Clinics, their requests could not be considered.

6. GAMETES

6.1. Transfer of Gametes

Aside from offering IVF/ICSI procedures free of charge, the Government also gives couples the opportunity to store their gametes for free. Since the ART Clinic at Mater Dei Hospital started running in January 2015, there was a total of 28 patients (25 females and 3 males), who transferred their gametes from the licensed private Clinic storing gametes to Mater Dei Hospital. It appears that not all of these gametes have been transferred for immediate utilization. A number of couples chose to transfer their gametes to the ART Clinic at Mater Dei Hospital so as to avail themselves of free storage.

6.2. Collection of Gametes

Egg quantity, or 'ovarian reserve', refers to the number of eggs a female has remaining for the future. Egg quantity is closely related to a woman's age, but it can vary considerably at any age. The quality of the eggs is also highly related to a woman's age and the better the quality of the eggs, the higher the probability for pregnancy, as embryo quality is dependent on the quality of the eggs. The number of oocytes attained with IVF strongly influences the chance for success.

During a Long Protocol IVF cycle, a woman goes through down regulation and ovarian stimulation phases that prepare her for the IVF treatment. The objective of the Ovarian Stimulation phase is to stimulate the ovary into producing different follicles, inducing a controlled ovulation and maturation

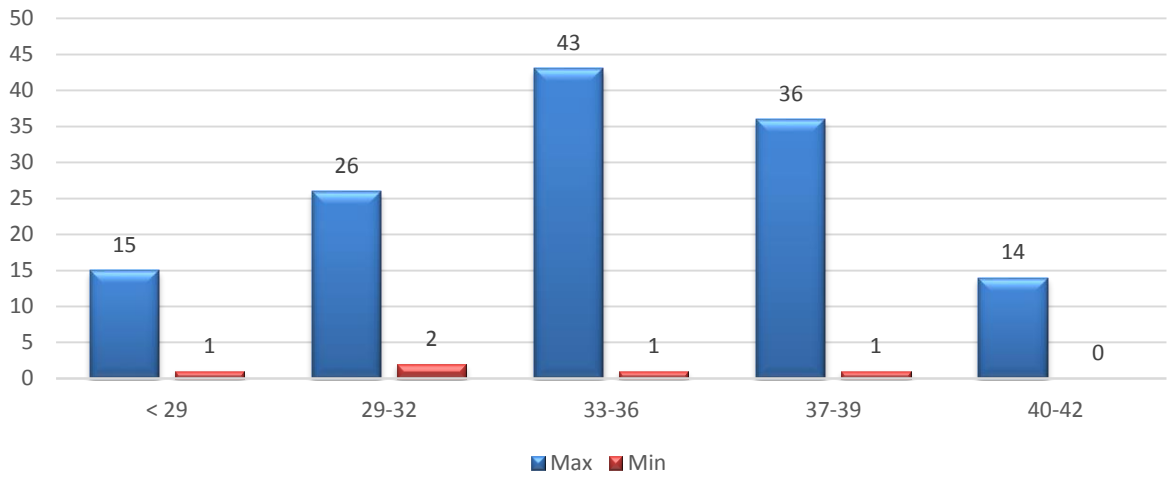
of oocytes (eggs) so as to increase the chances of achieving a pregnancy during treatment.

Out of the 230 Fresh cycles carried out in 2015, a total of 1926 oocytes have been collected, with an average of 8.37 oocytes collected per female. The maximum amount of oocytes collected from a single female patient was 43. This patient was aged 33 and was undergoing IVF/ICSI treatment at Mater Dei Hospital. Conversely, there were 2 patients aged between 40 and 42 who produced zero (0) oocytes. The highest number of oocytes collected, with an average of 10.62 oocytes, was from female patients aged between 29 and 32. An average of 8.57 oocytes was collected from patients under the age of 29, while female patients in the 33 to 36 year old bracket had an average of 8.21 oocytes collected. An average of 7.4 oocytes per patient was collected from patients aged between 37-39 while, not surprisingly, only an average of 5.36 oocytes was collected from women over the age of 40 (Table 3, Figure 24).

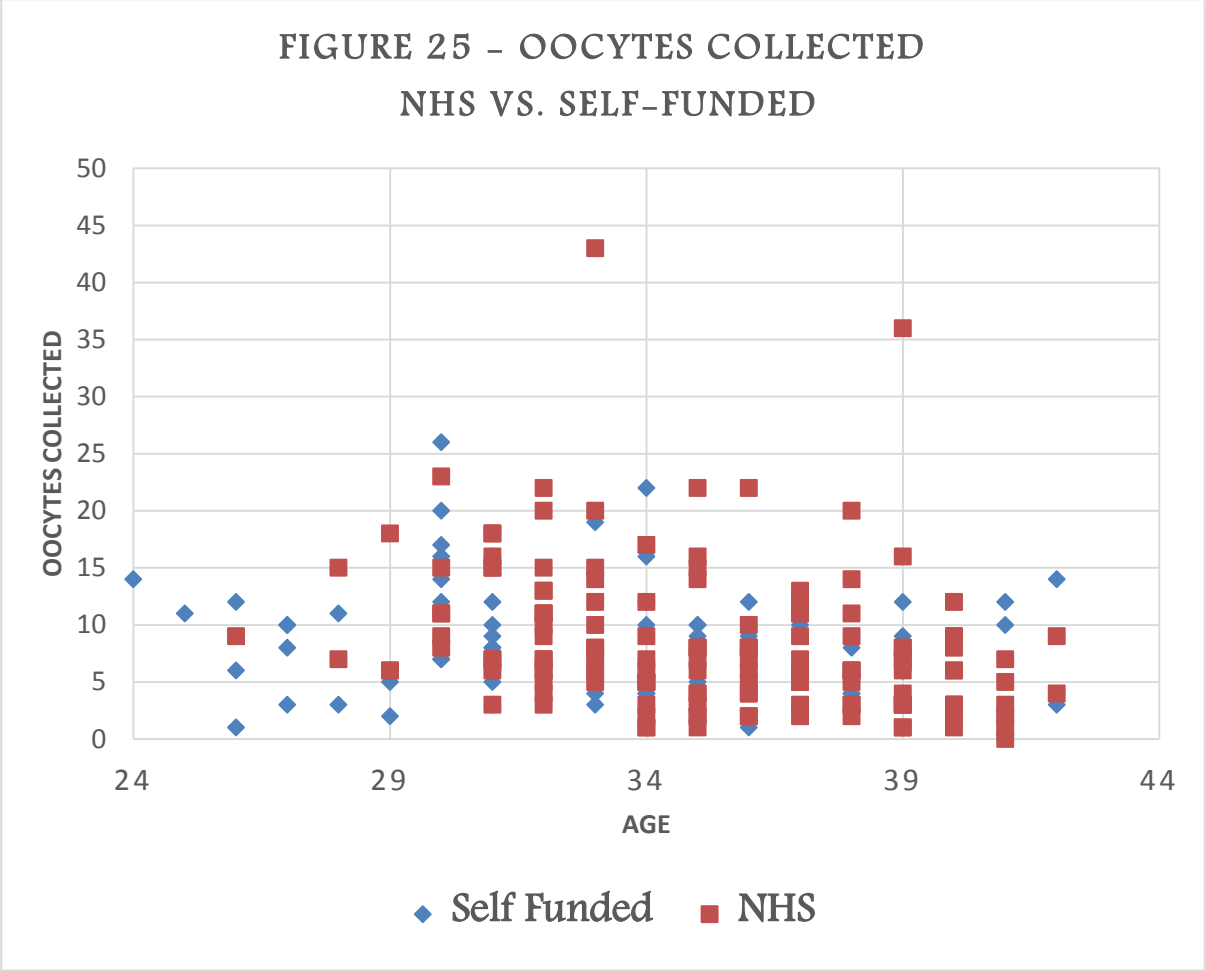
Table 3. Oocytes Collected - Females by Age Group

Age	No of Females	Total Oocytes Collected	Average	Max	Min
< 29	14	120	8.57	15	1
29-32	60	637	10.62	26	2
33-36	81	665	8.21	43	1
37-39	50	370	7.40	36	1
40-42	25	134	5.36	14	0
OVERALL	230	1926	8.37		

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



The maximum number of oocytes collected in both private and public sector was similar for female patients in the following three age groups: <29; 29-32; 40-42. However, there was a surprising amount of variability in the maximum number of oocytes collected from women aged between 33 and 36 and those aged between 37 and 39 (Figure 25).



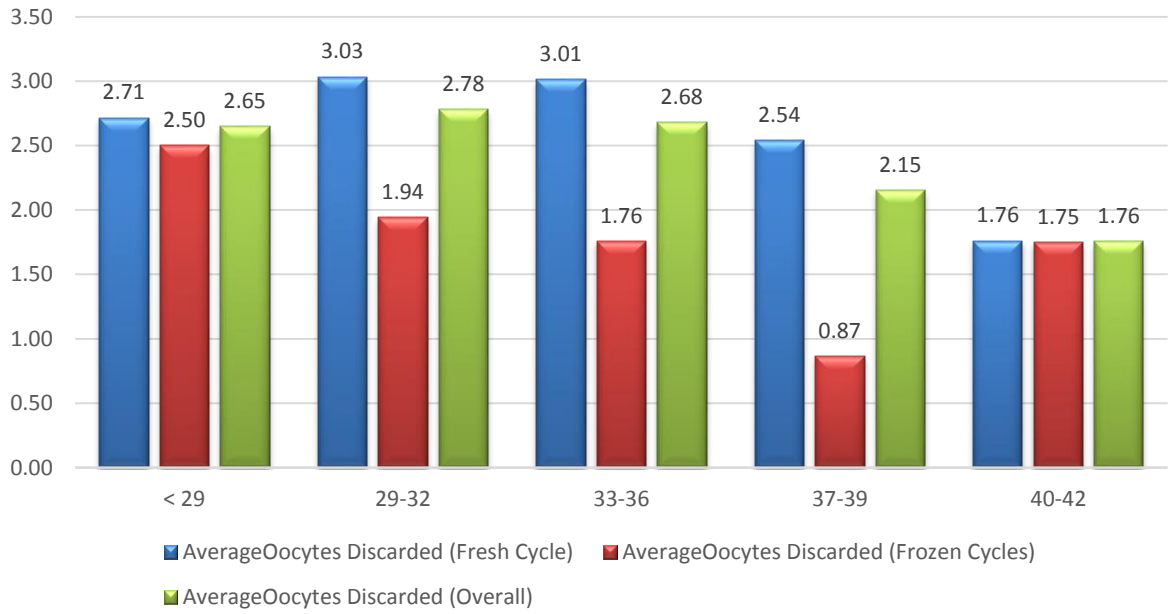
All sperm utilized for IVF/ICSI procedures appears to have been fresh.

6.3. Oocytes Discarded

The oocytes which are obtained following ovarian stimulation should meet various characteristics in order to be considered suitable for IVF/ICSI. An appraisal is usually done to classify these oocytes and those which are not deemed suitable for immediate fertilization or cryopreservation are discarded.

Out of 311 cycles carried out in 2015, a total of 770 oocytes have been discarded. Six hundred thirty five (635) oocytes (82.5%), or 33% from the total oocytes collected, were discarded following the egg retrieval process (Fresh cycle), for an average of 2.76 discarded oocytes per Fresh cycle. The remaining 135 oocytes (17.5%) did not survive the thawing process, averaging 1.69 oocytes discarded per Thawed/Frozen cycle (Figure 26).

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



The highest number of oocytes discarded was from women aged 29-32, which incidentally was the group from which the largest average number of oocytes had been collected.

6.4. Cryopreservation of Gametes

Pursuant to the Embryo Protection Act of 2012, clinics in Malta were allowed to cryopreserve gametes (oocytes and sperm). Cryopreservation in the Private Clinics started as of July 2013. Cryopreservation from Government-funded cycles started as of January 2014.

6.4.1. Oocyte Cryopreservation

Throughout 2015, only 135 out of the 229 couples (59%) undergoing Fresh cycles cryopreserved their oocytes. The total number of oocytes vitrified throughout cycles carried out this year was 797, for an average of 5.86 oocytes per couple. Forty one percent (41%) of couples undergoing Fresh cycles had no oocytes to vitrify (Table 4).

Table 4 –Fresh Cycles with NO Oocyte Cryopreservation

Age	NHS			Self-Funded			Total		
	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	Total No. of Cycles	Total Cycles with NO Oocytes to Vitrify	% of cycles with no Oocytes to Vitrify
< 29	3	0	0.0%	11	4	36.4%	14	4	28.6%
29-32	35	6	17.1%	25	5	20.0%	60	11	18.3%
33-36	50	26	52.0%	31	11	35.5%	81	37	45.7%
37-39	37	22	59.5%	13	4	30.8%	50	26	52.0%
40-42	19	13	68.4%	6	3	50.0%	25	16	64.0%
TOTAL	**144**	**67**	**46.5%**	**86**	**27**	**31.4%**	**230**	**94**	**40.9%**

The maximum number of oocytes vitrified from a single cycle was 29, while there were 94 couples undergoing Fresh cycles who had no oocytes left to store.

Out of a total of 136 Fresh cycles carried out where there were oocytes left to store, a total of 797 oocytes were vitrified, for an average of 5.86 per couple (Table 5).

Table 5. Cryopreservation 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
77	512	6.65	29	0	59	285	4.83	16	0	136	797	5.86	29	0

The maximum number of oocytes thawed from Frozen cycles was 13 while the minimum number of thawed oocytes was 2.

In 2015, there was a single patient who cryopreserved her oocytes on medical grounds so as to preserve her fertility.

6.4.2. Sperm Cryopreservation

In 2015, there were 32 patients who cryopreserved their sperm on medical grounds. A number of these males had undergone an IVF/ICSI procedure following Testicular Sperm Aspiration (TESA).

No cryopreserved sperm at the ART Clinic at Mater Dei Hospital and at St. James Assisted Reproduction Unit appears to have been thawed to be utilized for IVF/ICSI procedures carried out in 2015.

6.4.3. Embryo Cryopreservation

There have been no requests for the cryopreservation of embryos from Clinicians/Responsible Persons of Licensed Clinics this year. In Malta, permission for cryopreservation of embryos can only be granted by the Embryo Protection Authority as per Article 7 of the Law, where the transfer of the fertilized embryos in the womb is not possible owing to grave and certified *force majeur* not predictable at the moment of fertilization.

6.5. End of Storage

In 2015, there were only 2 female patients who have requested their oocytes to be discarded. These patients had their oocytes stored at the private licensed Clinic. No male patients have made requests for their sperm to be discarded.

7. IVF/ICSI PROCEDURES

7.1. Cycles Started

Beside the 311 cycles which have been performed in Malta throughout the year, Clinics have also reported a total of 14 cycles which were abandoned prior to oocyte retrieval. Eleven of these patients (79%) had to abandon the cycle as their ovaries did not respond well to the stimulation treatment they were receiving. The remaining three patients abandoned the cycle for medical reasons.

7.2. Embryo Transfers

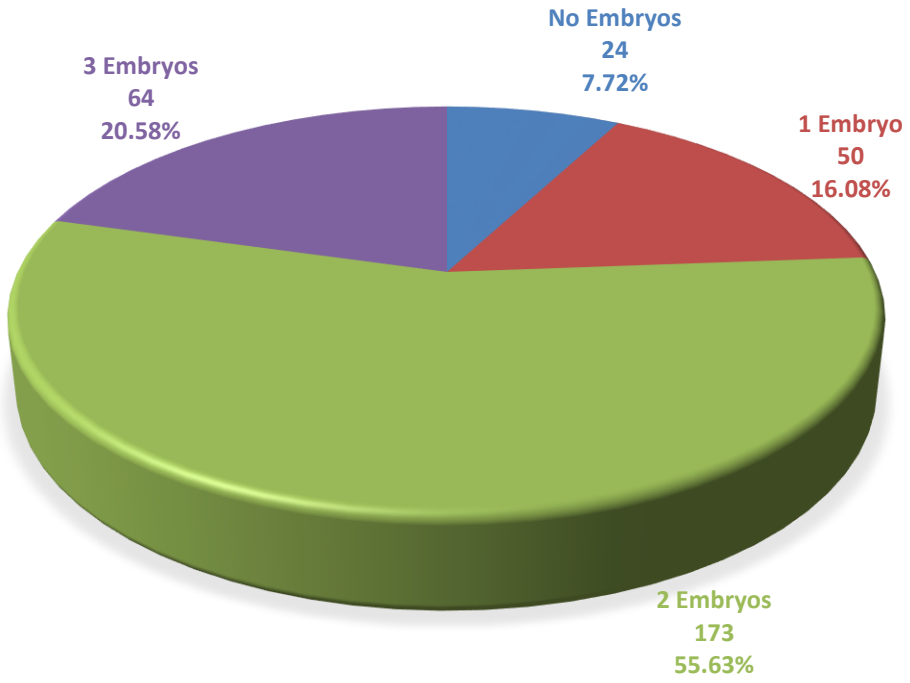
Out of the 311 cycles carried out, there were a total of 24 couples (7.72%), 16 from the ART Clinic at Mater Dei Hospital and 8 from private Clinics, who had no viable embryos to transfer. A number of reasons may explain why couples have no embryo transfer effected. One reason might be that there were no oocytes to collect, or the oocytes collected were of poor quality and had to be discarded. It may also be the case that while the eggs were being retrieved, the male partner had no viable sperm in the sample provided, so the oocytes collected would have had to be cryopreserved for future use. Cryopreserved oocytes may not always survive the thawing process and such oocytes have to be discarded. Another possible reason might be that the oocytes fail to fertilize, or fertilize but the embryo stops developing properly.

When a risk of Ovarian Hyperstimulation (OHS) has been identified, no embryo transfer might be effected, as clinicians may decide to proceed with egg retrieval but freeze all the oocytes for later fertilization, since pregnancy

appears to worsen the condition. In 2015, the Embryo Protection Authority was notified that there have been a number of patients from the April cycle carried out at Mater Dei Hospital who were admitted for treatment of Ovarian Hyperstimulation Syndrome (OHSS). Upon notification, the Authority's Board requested the Clinical Director at Mater Dei Hospital's ART Clinic to provide EPA with a copy of the medical protocols used during down-regulation and stimulation phases, together with a report on those patients who were admitted for treatment with OHSS, complete with their medical records showing the severity of the condition. A full report was provided to the Embryo Protection Authority by the ART Clinic's Medical Director, whereby he declared that there were 4 reported cases of OHSS, with one patient having to go for a '*freeze all* cycle'.

Out of the 287 couples who had viable embryos for transfer, 50 of them, or 16.08%, had a single embryo transfer (SET). The vast majority of couples (173 couples, or 55.63%) had 2 embryos transferred, while the remaining 64 couples (or 20.58%), had 3 embryos transferred (Figure 27).

FIGURE 27 – EMBRYOS TRANSFERRED PER CYCLE



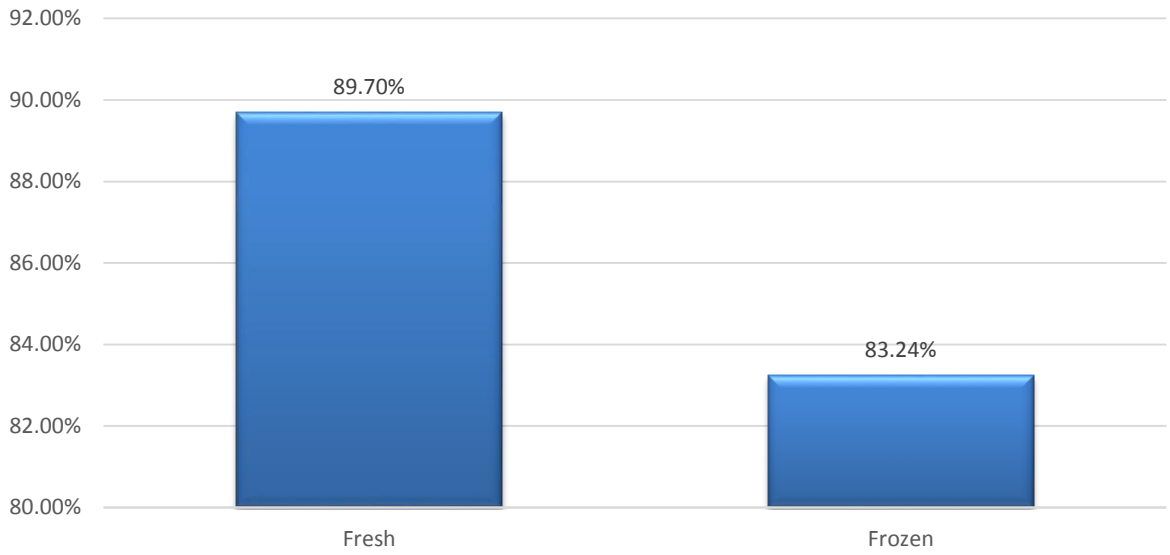
7.3. Embryo Transfers from Fresh/Thawed Cycles

There were 495 injected fresh oocytes (Fresh cycle) out of which only 444 embryos have been transferred (89.7%). Out of the 173 thawed oocytes injected (Thawed/Frozen cycle), 144 embryos were transferred (83.2%). Hence, in 2015, there were 6.5% more embryos transferred from fresh oocytes over injected thawed oocytes (Table 6, Figure 28).

Table 6. Embryos transferred from Fresh vs. Thawed Cycles

Fresh / Thawed	Oocytes Injected	Embryos Transferred	Transferred %
Fresh	495	444	89.70%
Thawed	173	144	83.24%

FIGURE 28 – EMBRYOS TRANSFERRED FROM INJECTED OOCYTES (%) – FRESH vs. THAWED



There were 0.11% more cycles with zero (0) embryos transferred from injected thawed oocytes when compared to fresh oocytes. Single embryo transfers were 8.59% higher in Thawed *vis-a-vis* Fresh cycles, while there were higher percentages of two and three embryos transferred from Fresh over the Thawed cycles (4.46% and 4.24% respectively) (Table 7).

Table. 7 – Number of Embryos Transferred per Fresh vs. Thawed Cycles

Transferred Embryos	FRESH CYCLES				FROZEN CYCLES				TOTAL			
	NHS	Self-Funded	Total Fresh	%	NHS	Self-Funded	Total Frozen	%	NHS	Self-Funded	Total Overall	Total %
0	13	4	17	**7.39%**	2	4	6	**7.50%**	15	8	23	**7.42%**
1	23	9	32	**13.91%**	5	13	18	**22.50%**	28	22	50	**16.13%**
2	74	57	131	**56.96%**	13	29	42	**52.50%**	87	86	173	**55.81%**
3	34	16	50	**21.74%**	11	3	14	**17.50%**	45	19	64	**20.65%**
Total	**144**	**86**	**230**		**31**	**49**	**80**		**175**	**135**	**310**	

It's interesting to note that although there have been a total of 134 approved requests on behalf of couples for the fertilization of three oocytes, only 47.01% of these couples managed to have three embryos transferred, 26.12% had 2 embryos transferred, 17.16% had just a single embryo transferred, while 9.7% of these couples had no viable embryos for transfer (Figures 29, 30).

FIGURE 29 – EMBRYOS TRANSFERRED PER CASE OF APPROVED AFR

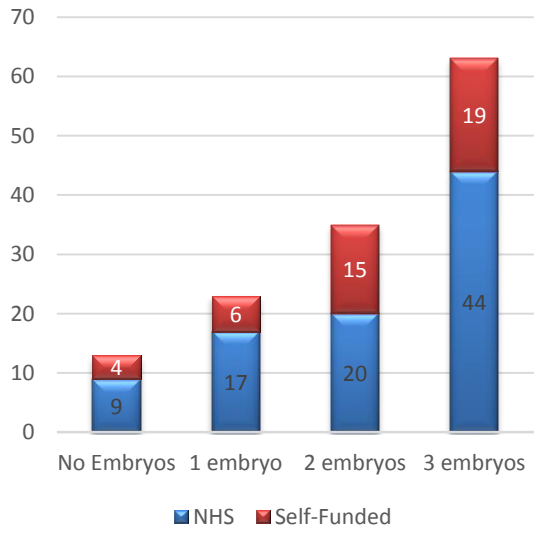
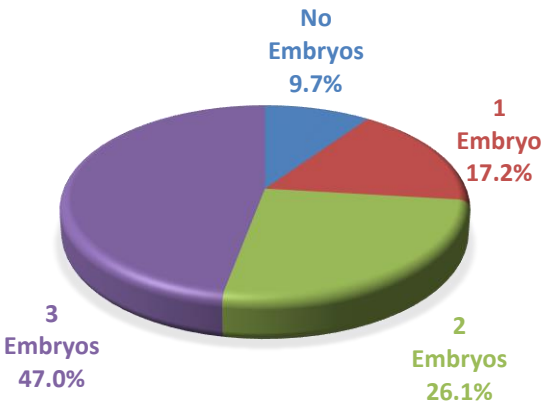


FIGURE 30 – EMBRYO TRANSFER DISTRIBUTION (% OF APPROVED AFR)



8. RESULTS

8.1. Pregnancies

The outcome from the 311 procedures carried out last year was 71 pregnancies from Fresh cycles and 17 from Thawed cycles. The only couple undergoing a Combined cycle did not get pregnant. This gives us a total of 88 pregnancies out of all cycles started, or 28.3%, a 0.52% drop from the pregnancy rate in 2014 (Table 8).

Table 8 – Cycle Outcome

Type	Outcome	NHS	Self-Funded	Total	% Outcome by Type	% Outcome	% Outcome of Pregnancies
Fresh	Not Pregnant	95	64	159	69.1%	69.1%	
	Miscarriage	19	4	23	10.0%	30.9%	32.4%
	Live Birth	13	9	22	9.6%		31.0%
	Expected	17	9	26	11.3%		36.6%
Thawed	Not Pregnant	24	39	63	78.8%	78.8%	
	Miscarriage	3	3	6	7.5%	21.3%	35.3%
	Live Birth	2	1	3	3.8%		17.6%
	Expected	2	6	8	10.0%		47.1%
Combined	Not Pregnant	1	0	1	100.0%		
	Miscarriage	0	0	0	0.0%		
	Live Birth	0	0	0	0.0%		
	Expected	0	0	0	0.0%		

8.2. Cycle Outcomes – Fresh vs. Thawed

From the 230 Fresh cycles carried out, only 71 couples **(30.9%)** got pregnant. Out of these 71 pregnancies, 32.4% miscarried, 31% had a live birth, while the remaining 36.6% are still expecting (Figures 31, 33). Out of the 80 Thawed cycles performed, only 17 couples **(21.3%)** got pregnant, 35.3% miscarried, 17.6% had a live birth, while the remaining 47.1% are still expecting (Figures 32, 34). These results are in contrast with those for 2014, where the pregnancy rate from Thawed cycles was 2.86% higher than for Fresh. **In 2015, the pregnancy rate for Fresh cycles was 9.6% higher than for Thawed.**

FIGURE 31 – OUTCOME FROM FRESH CYCLES (QTY)

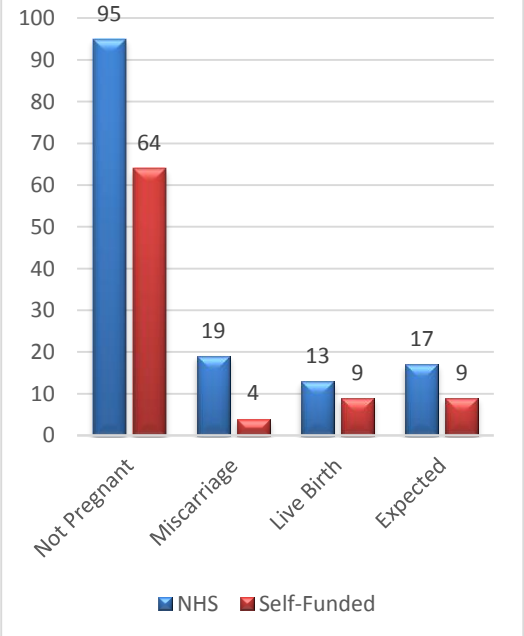


FIGURE 32 – OUTCOME FROM THAWED CYCLES (QTY)

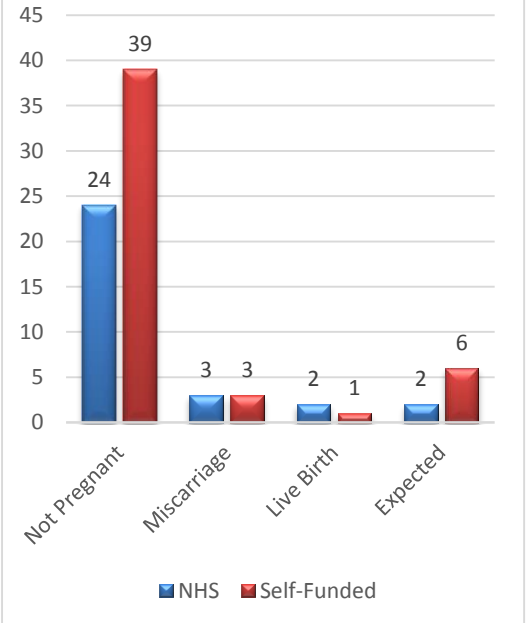


FIGURE 33 – OUTCOME FROM FRESH CYCLES (%) – NHS + SELF-FUNDED

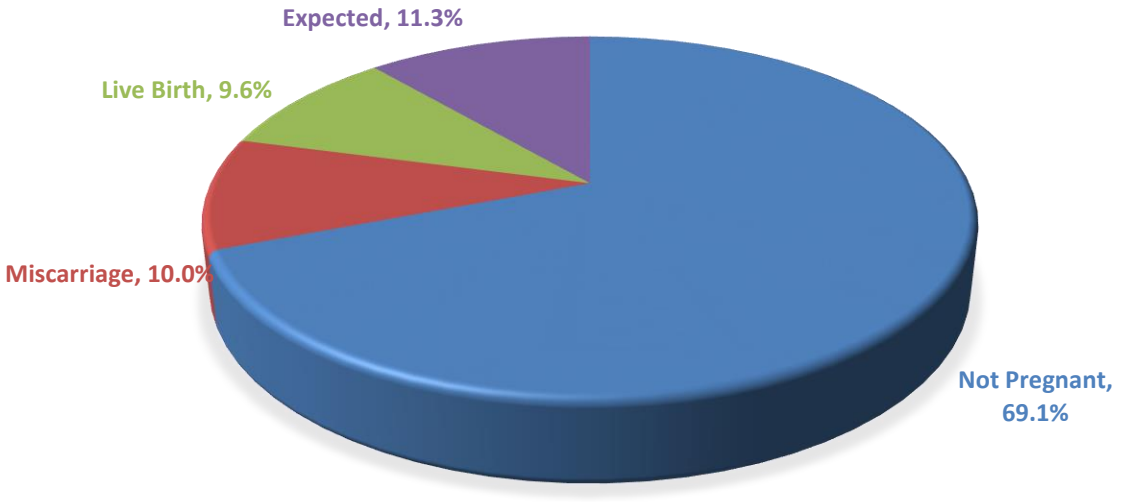
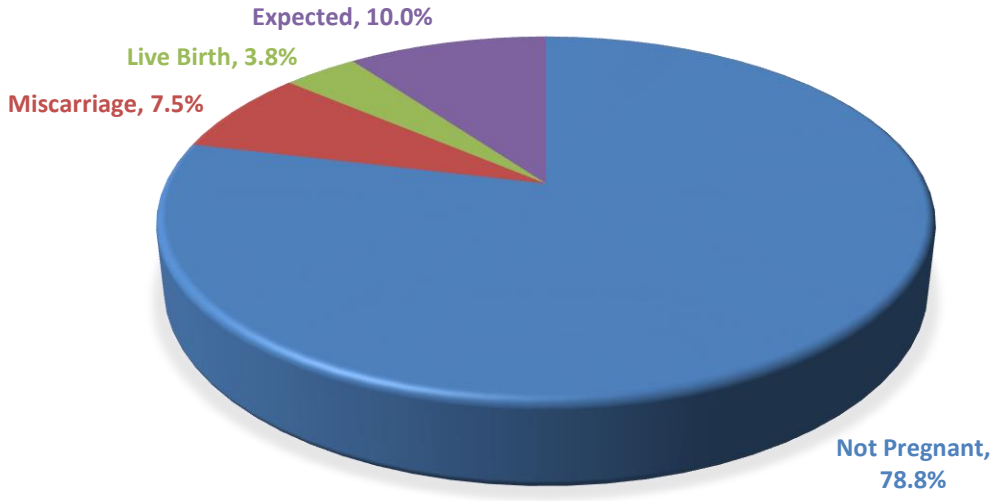


FIGURE 34 – OUTCOME FROM THAWED CYCLES (%) – NHS + SELF-FUNDED



8.3. Cycle Outcomes – NHS vs. Self-Funded

The pregnancy rate reported by the private clinics for both Fresh and Thawed cycles was significantly lower than that reported by the ART Clinic at Mater Dei Hospital. However, the reported miscarriages were also significantly less than the number reported by Mater Dei Hospital's ART Clinic. The percentage of live births and expectancies from Fresh cycles reported by the private and public sectors were comparable, whereas for Thawed cycles, to-date, there were fewer reported births and a higher expectancy rate for the private Clinics *vis-a-vis* the public Clinic (Figures 35, 36).

FIGURE 35 – % OUTCOME – NHS vs. SELF-FUNDED

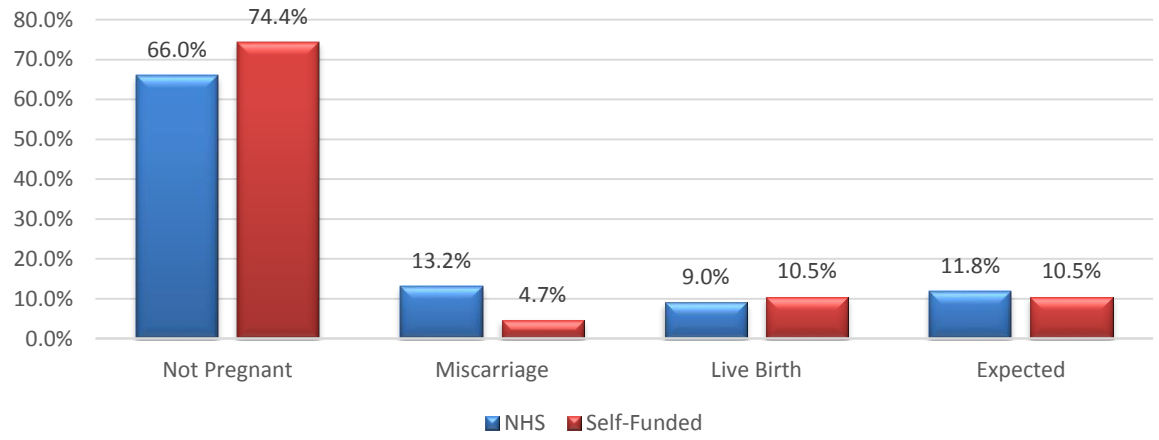
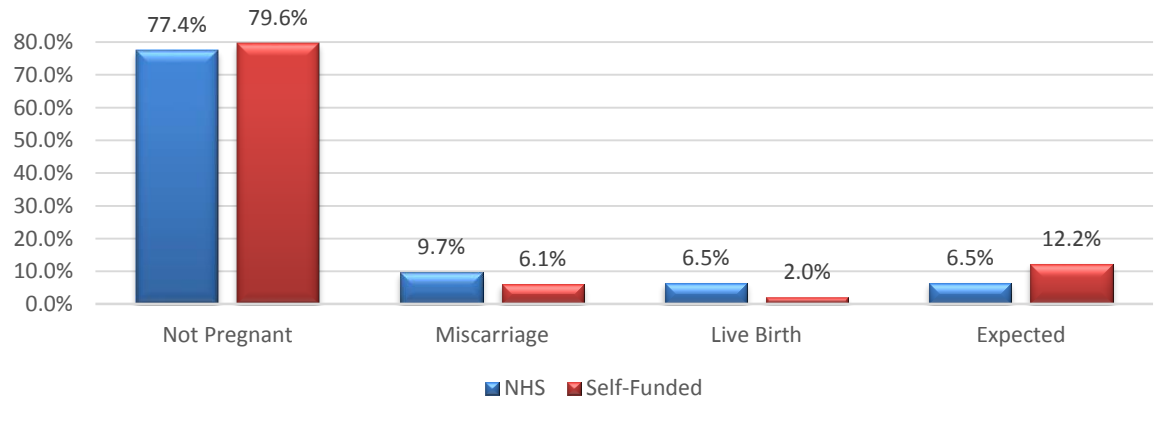


FIGURE 36 – THAWED CYCLES – % OUTCOME
NHS vs. SELF-FUNDED



8.4. Pregnancy by Age

Pregnancies were reported across all age groups. There were 35.9% of women aged between 29 and 32, 32.3% of women in the 37-39 year old bracket, and 30% of the females under the age of 29, for whom a pregnancy was reported. Unlike the previous year, where 44.9% of women who got pregnant were aged between 33 and 36, only 25.5% of women in this age group got pregnant this year. As might be expected, the number of pregnant women aged between 40 and 42 was only 13.2% (Figures 37, 38).

FIGURE 37 – PREGNANCY BY AGE GROUP (QTY)

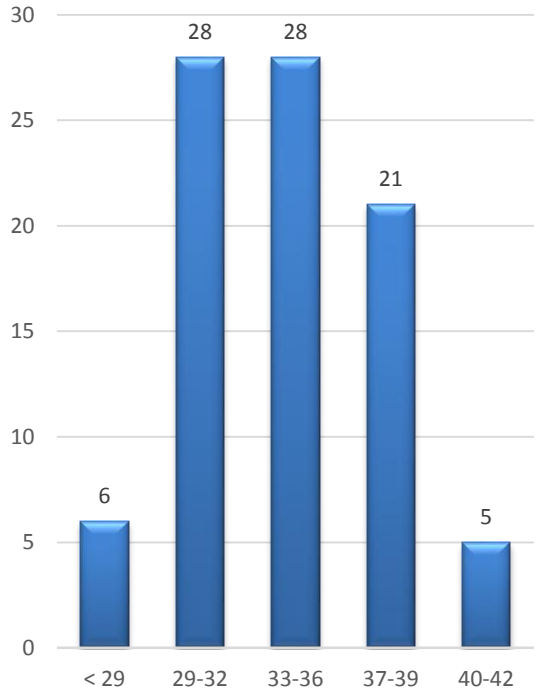
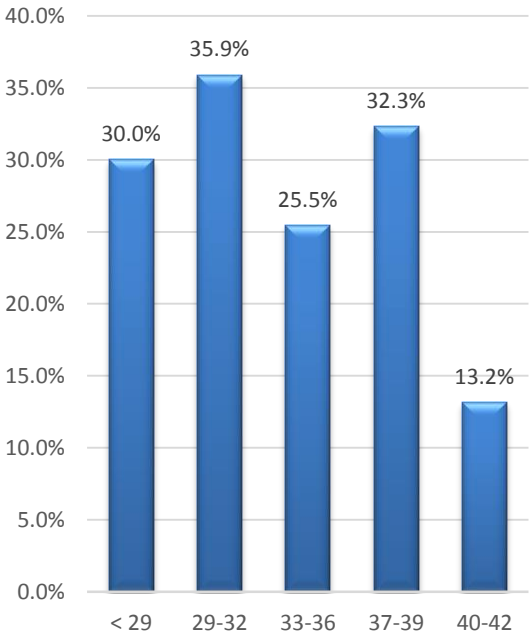


FIGURE 38 – PREGNANCY RATE AS % OF CYCLES PER AGE GROUP



8.5. Pregnancy Rate per Embryos Transferred

Out of the 287 couples who had embryos transferred, there were 88 resulting pregnancies, or 30.66% – 0.16% less than in 2014. The couples who were most successful at achieving a pregnancy were those who had 3 embryos transferred (43.75%). Fifty six (56) couples, or 32.37%, who had 2 embryos transferred achieved a pregnancy while the success rate from single embryo transfers (SET) was only of 8% (Table 9).

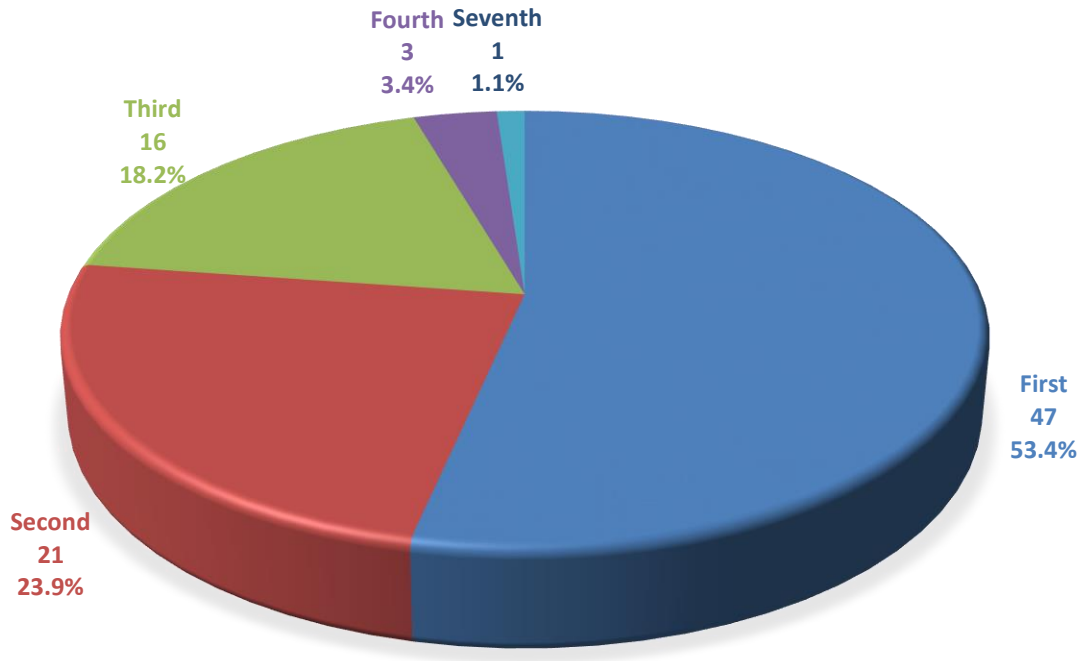
Table 9. Pregnancy Rate per Embryos Transferred

Transferred Embryos	Total Cycles	Total Pregnancies	% Pregnancies
0	24	0	0.00%
1	50	4	8.00%
2	173	56	32.37%
3	64	28	43.75%
Total	311	88	28.30%
Total Cycles with Embryo Transfer	**287**	**88**	**30.66%**

8.6. Pregnancy Rate per ART Cycle Attempts

Out of a total of 88 pregnancies reported in 2015, 47 couples (or 53.4%) achieved a pregnancy on their 1st attempt, 21 couples (23.9%) on their 2nd attempt, 16 couples (18.2%) on their 3rd attempt, 3 couples (3.4%) on their 4th attempt, while there were no couples who got pregnant on their 5th and 6th attempt. A single couple achieved a pregnancy on their 7th attempt (Figure 39).

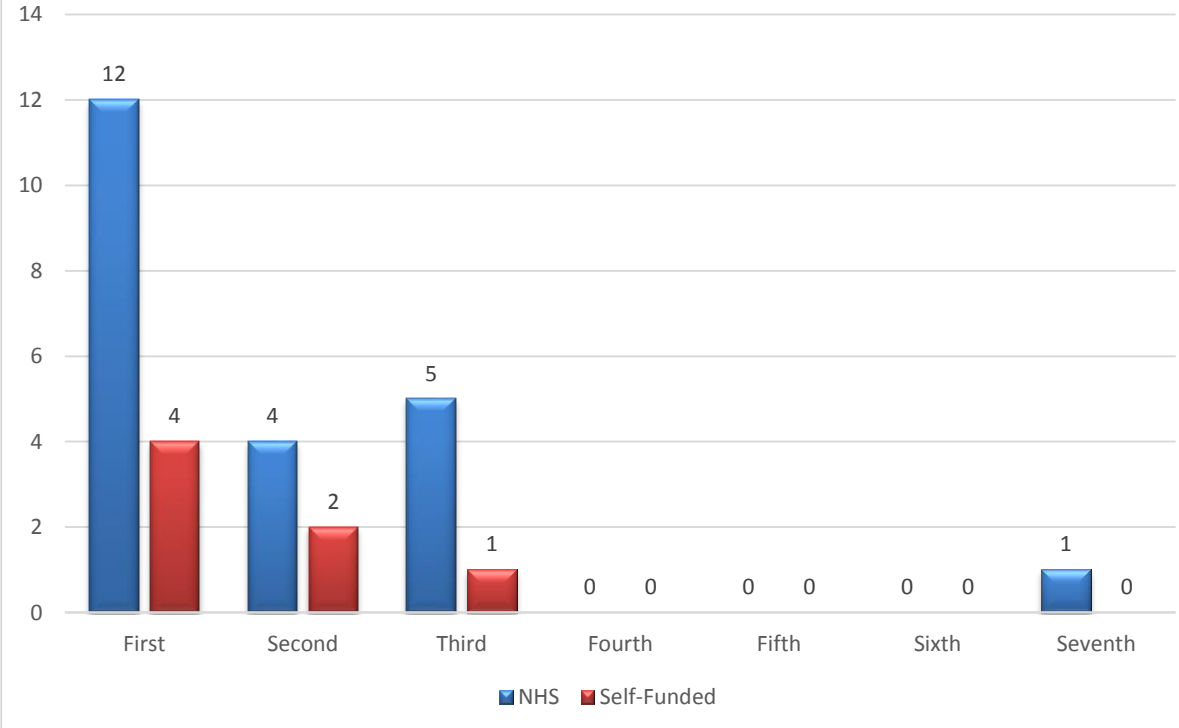
FIGURE 39 – PREGNANCY DISTRIBUTION BY ART CYCLE ATTEMPTS



8.7. Miscarriages per ART Cycle

Out of the 88 couples who achieved a pregnancy, 29 of them miscarried. Private clinics reported fewer miscarriages than the ART Clinic at Mater Dei Hospital. Sixteen couples out of the 29 who miscarried (55%), miscarried on their first IVF attempt. Six couples (20.7%) miscarried on their 2nd attempt; another 6 couples miscarried on their 3rd attempt, while the remaining couple miscarried on their 7th IVF attempt (Figure 40).

FIGURE 40 – MISCARRIAGES PER ART CYCLE (QTY)
NHS vs. SELF-FUNDED



8.8. Miscarriages by Age

Miscarriages were only reported for women over the age of 29. There were 10 reported miscarriages for women aged between 29 and 32 and another 10 for women in the 33-36 year old bracket. Six miscarriages were reported for women aged between 36 and 39, while another 3 were reported for women in the 40-42 year old bracket. Sixty percent (60%) of women aged between 40 and 42 for whom a pregnancy was reported, miscarried. There were no reported miscarriages for women under the age of 29 (Figures 41, 42).

FIGURE 41 – MISCARRIAGES BY AGE GROUP (QTY)

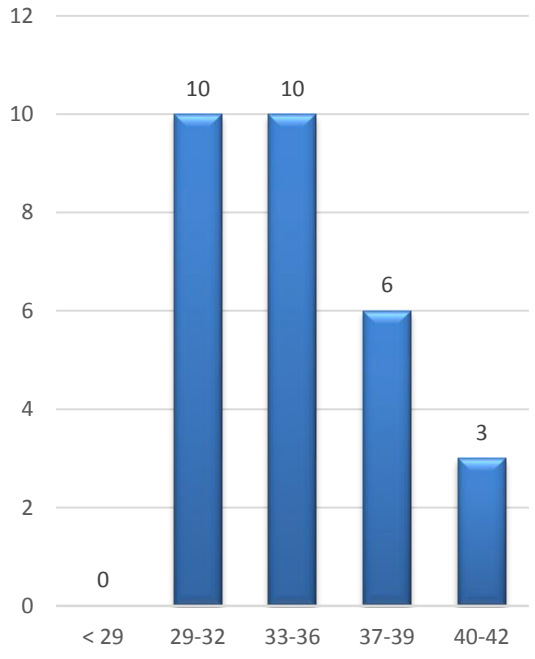
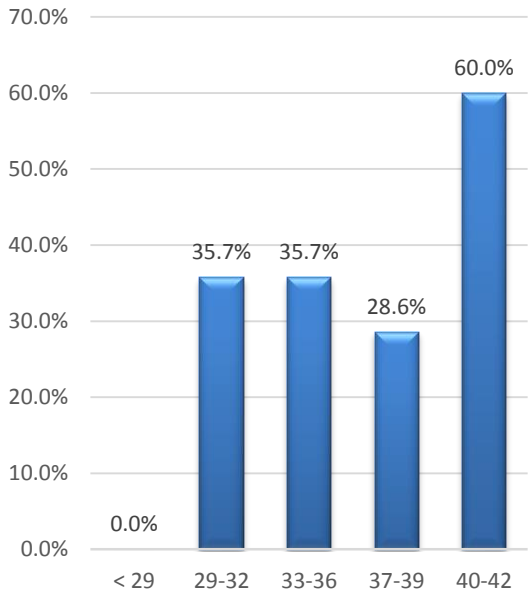


FIGURE 42 – MISCARRIAGES AS % OF PREGNANCIES IN AGE GROUP



8.9. Miscarriages by Gestational Age

The ART Clinic at Mater Dei Hospital reported 10 miscarriages for women in their 2nd to 3rd week of gestation (often referred to as 'biochemical pregnancies'). There were a total of 6 reported miscarriages at Week 5 of gestation, 9 miscarriages at 6 to 9 weeks gestation, and 4 miscarriages for women in their 10th to 18th week of gestation (Figures 43, 44).

FIGURE 43 - MISCARRIAGE DISTRIBUTION BY GESTATIONAL AGE (QTY)

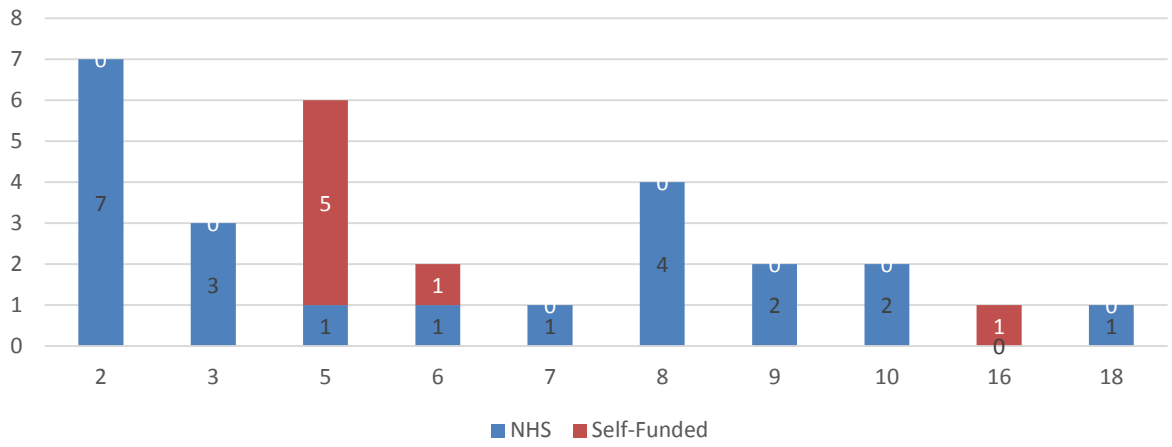
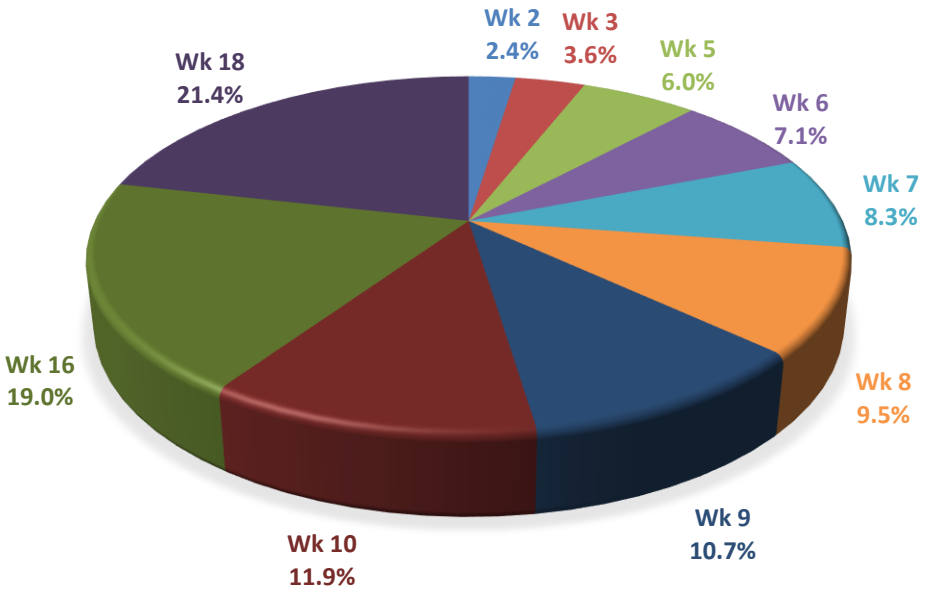


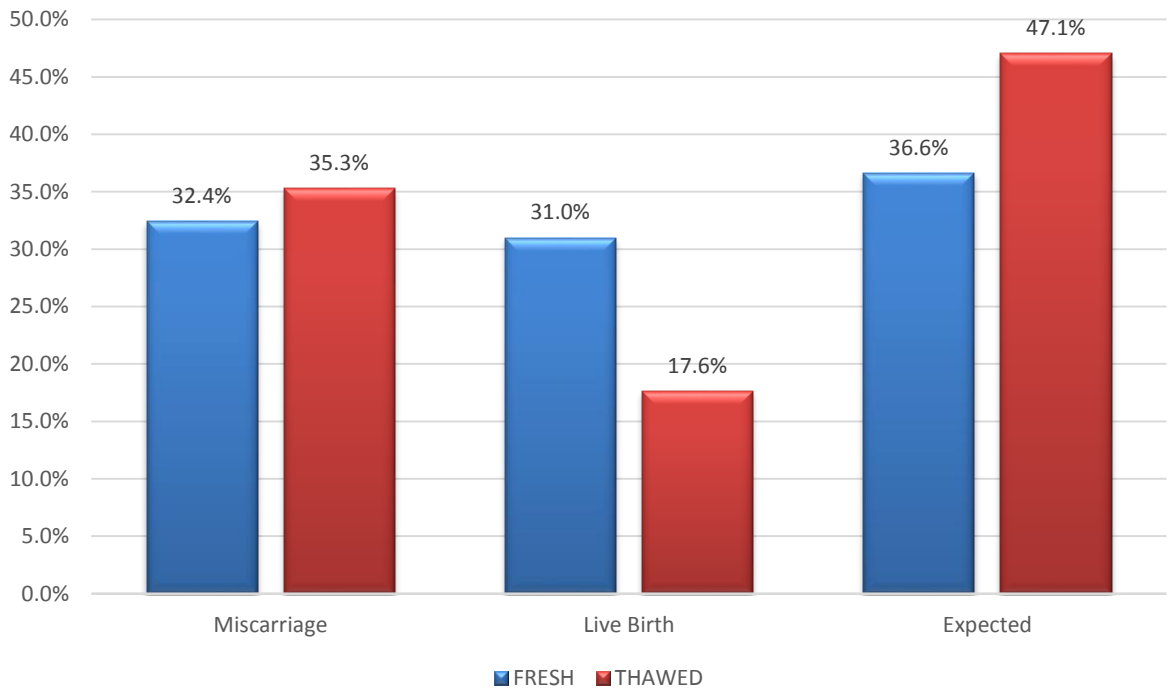
FIGURE 44 – MISCARRIAGE DISTRIBUTION BY GESTATIONAL AGE (%)



8.10. Miscarriages from Fresh vs. Thawed

There were 23 couples (32.4%) who miscarried after achieving pregnancy from a Fresh cycle and 6 couples (35.3%) who miscarried after achieving pregnancy from a Thawed cycle (Figure 45).

FIGURE 45 – PROCEDURE OUTCOME % – FRESH vs. THAWED

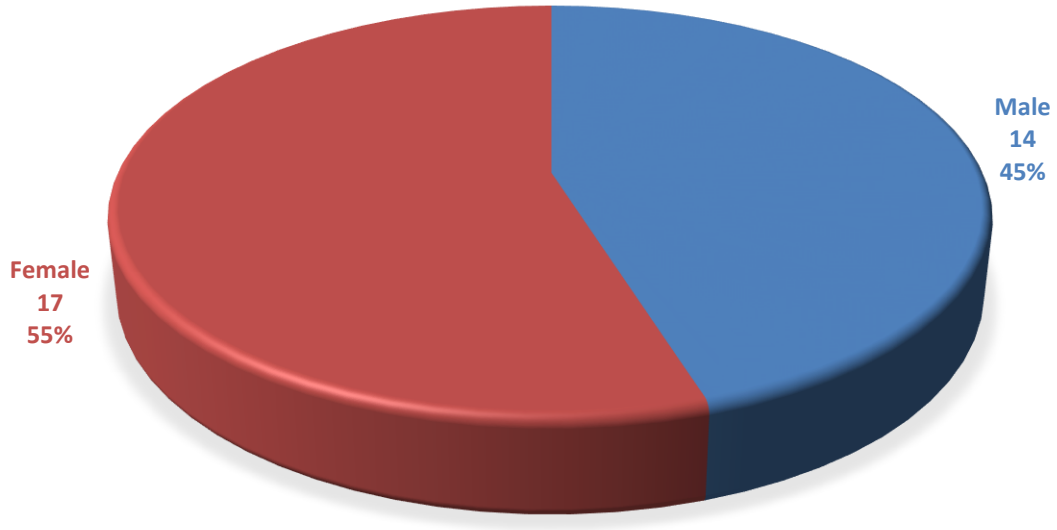


9. BIRTH EVENTS

9.1. Births – July & November 2014 Cycles

Thirty one (31) babies, 19 singletons and 6 sets of twins, were born as a result of cycles carried out in July and November 2014. Six (6) males and 8 females (including 1 stillborn) were born out of the July cycle, while 8 males and 9 females were born from the November cycle (Figure 46).

FIGURE 46 – JUL & NOV '14 –LIVE BIRTHS
(MALES VS. FEMALES)



9.2. Birth Events from 2015 Cycles – Fresh vs. Thawed

The total number of live borns out of IVF/ICSI procedures carried out in January, March, and May 2015 was 28. Nineteen (19) singletons and 3 sets of twins were born from Fresh cycles while 3 singletons were born from Thawed cycles (Figure 47). There were no reported birth events (live and expected) with triplets from ART procedures carried out in 2015.

9.2.1. Gender of Newborns from Fresh vs. Thawed

Thirteen (13) females and 12 males were born from Fresh cycles, while 1 female and 2 males were born from Thawed cycles (Figure 48).

FIGURE 47 – LIVE BIRTH OCCURENCES UP TO MAY '15 CYCLE

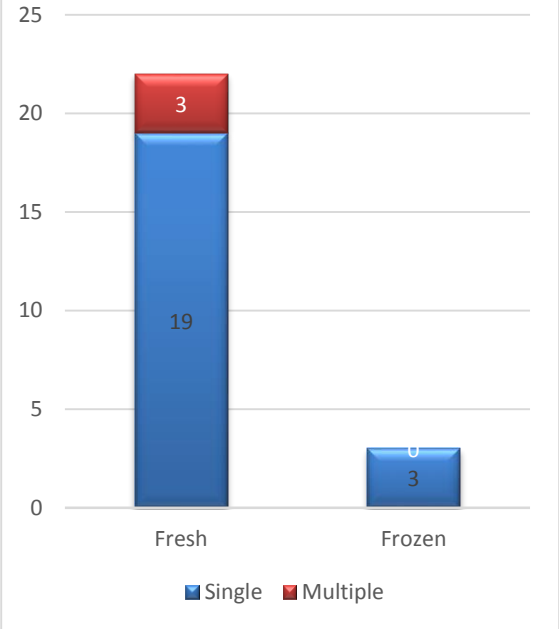
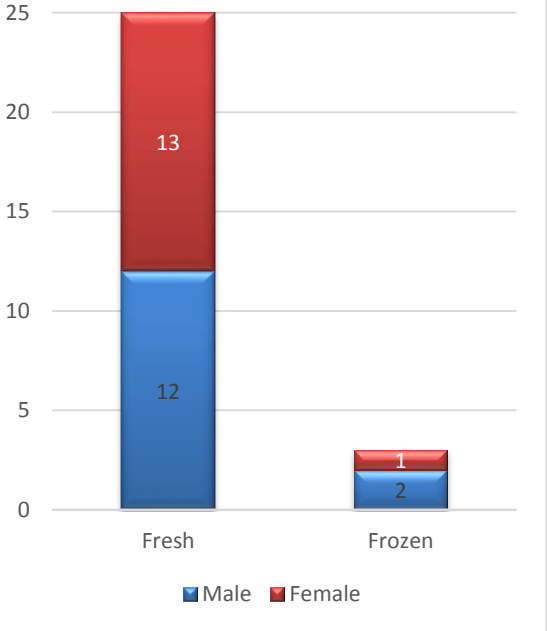


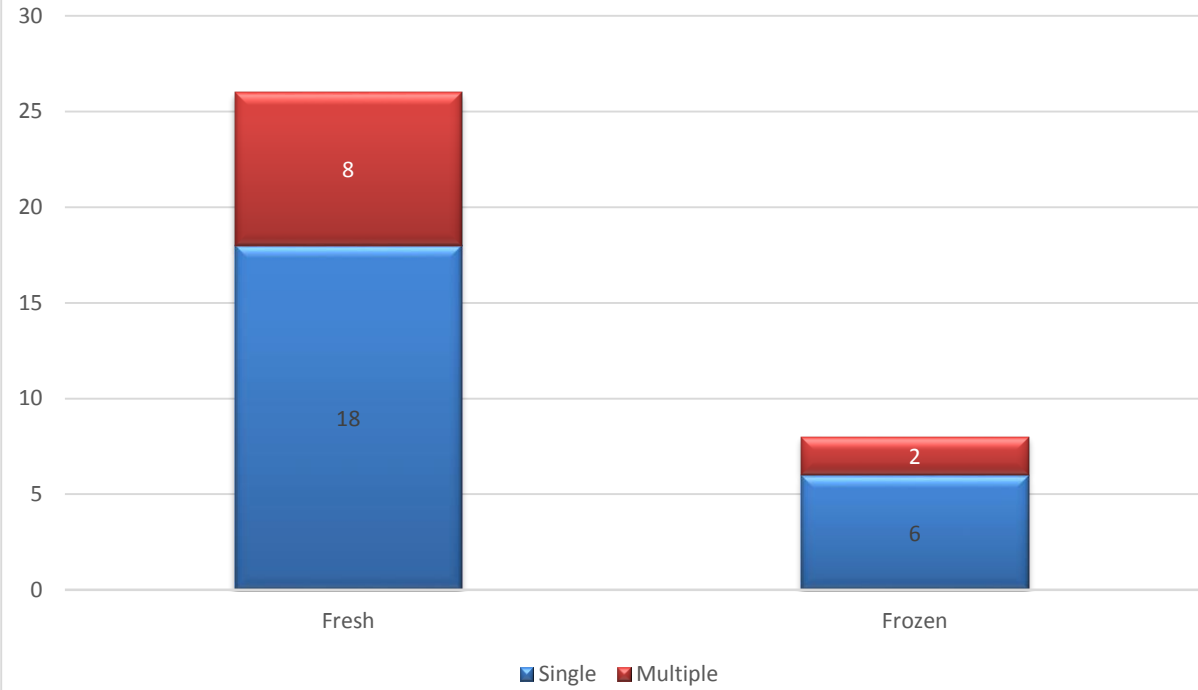
FIGURE 48 – LIVE BIRTHS UP TO MAY '15 – GENDER OF NEWBORNS



9.2.2. Expected Birth Events from Fresh vs. Thawed

Out of the cycles carried out in July, September, and November 2015, there are 34 expected birth events. Eighteen (18) singletons and 8 sets of twins are expected from Fresh cycles while 6 singletons and 2 sets of twins are expected from Thawed cycles, for a total of 44 babies (Figure 49).

FIGURE 49 – EXPECTED BIRTH EVENTS
(JUL '15, SEP '15, NOV '15 CYCLES)

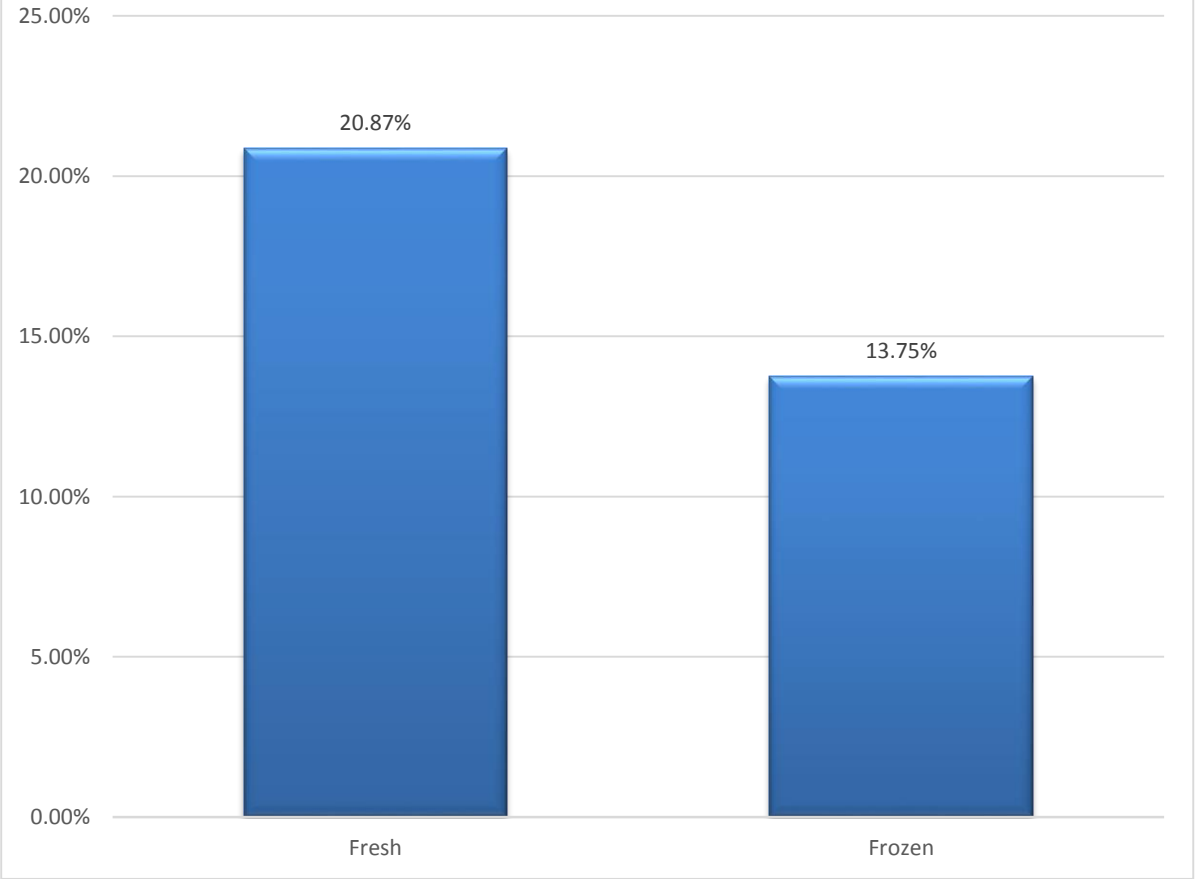


Hence, out of the 72 live and expected births from procedures carried out in 2015, 59 babies, or 81.9%, are from pregnancies achieved through Fresh cycles, and the remaining 18.1% are from pregnancies achieved through Thawed cycles.

9.3. Maximum Success Rate – Fresh vs. Thawed

Out of the 230 Fresh cycles carried out in 2015, there were 48 birth events (live + expected) for a maximum success rate of **20.87%**. There were 11 reported birth events (live + expected) out of the 80 Thawed cycles carried out, for a maximum success rate of **13.75%** (Figure 50).

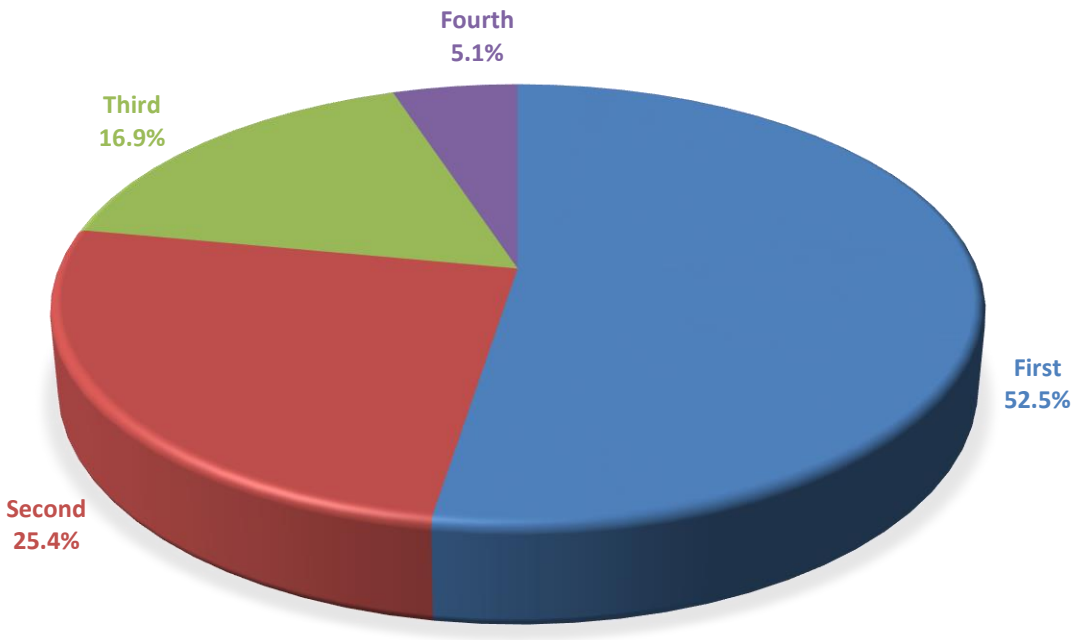
FIGURE 50 – % CYCLES WITH LIVE OR EXPECTED BIRTHS FROM TOTAL CYCLES – FRESH vs. THAWED



9.4. Birth Events per ART Cycle

Out of the 59 reported birth events from procedures carried out in 2015, there were 31 birth events (52.5%) from couples undergoing their first IVF/ICSI attempt, 15 birth events (25.4%) from a 2nd attempt, 10 birth events (16.9%) from a 3rd attempt, and 3 birth events (5.1%) from a 4th attempt (Figure 51).

FIGURE 51 – BIRTH EVENTS DISTRIBUTION BY ART CYCLE



9.5. Take-Home Baby Rate

Finally, out of the 88 couples who achieved a pregnancy, 25 (or 28.4%) had a live birth, 34 (or 38.6%) are still expecting, and 29 couples (33.0%) miscarried. From the 311 cycles carried out in 2015, there were 8% of couples who had a live birth, 10.9% who are still expecting, while 9.3% of couples miscarried, for a maximum percentage *take-home baby rate* of **18.9%** (Table 10).

Table 10 - % Take-Home Baby Rate

Pregnancy Outcome	Qty	% of pregnancies	% of total cycles	Max % Success Rate
Live Birth	**25**	28.4%	**8.0%**	**18.9%**
Expected Birth	**34**	38.6%	**10.9%**	
Miscarriage	**29**	33.0%	**9.3%**	

10. CONCLUSION

The number of IVF/ICSI procedures carried out in Malta has increased considerably over the past years. In 2015 there were 311 cycles performed as compared to the 170 and 100 carried out in 2014 and 2013 respectively. This increase appears to be reflective of the introduction of Government-funded cycles which have been carried out at the ART Clinic in Mater Dei Hospital since January 2015.

There were 88, or 28.3%, reported pregnancies out of all cycles started - a 0.52% drop from 2014. As opposed to last year, cryopreservation was less effective than fresh treatments, with a larger number of Embryo transfers, pregnancies, and birth events (live + expected) reported from Fresh cycles *vis-a-vis* Thawed cycles. The expected take-home baby rate for 2015 is 18.9%.

The Embryo Protection Authority shall keep providing guidance and support to all ART clinics in Malta so as to ensure that they are operating under the highest standards. Moreover, the Embryo Protection Authority has worked closely with the Review Working Group Embryo Protection Act in evaluating the current Embryo Protection Act and has proposed changes to reflect the outcomes of current regulations and recent judgements of the European Court of Human Rights.

As Regulator, the Authority will keep on striving to make Malta one of the best Centres in ART, thus attracting more Medical Tourism to Malta.

Judge Philip Sciberras	Ms. Simone Attard
Chairman	Director/Executive Head

The *Annual Work Report – Trends and Figures of Fertility Treatments in Malta for 2015* has been produced through the collaborative work of the Embryo Protection Authority's Executive Director, Deputy Head, and Executive Officer, and approved by the Chairperson and Members of the Board prior to publishing.