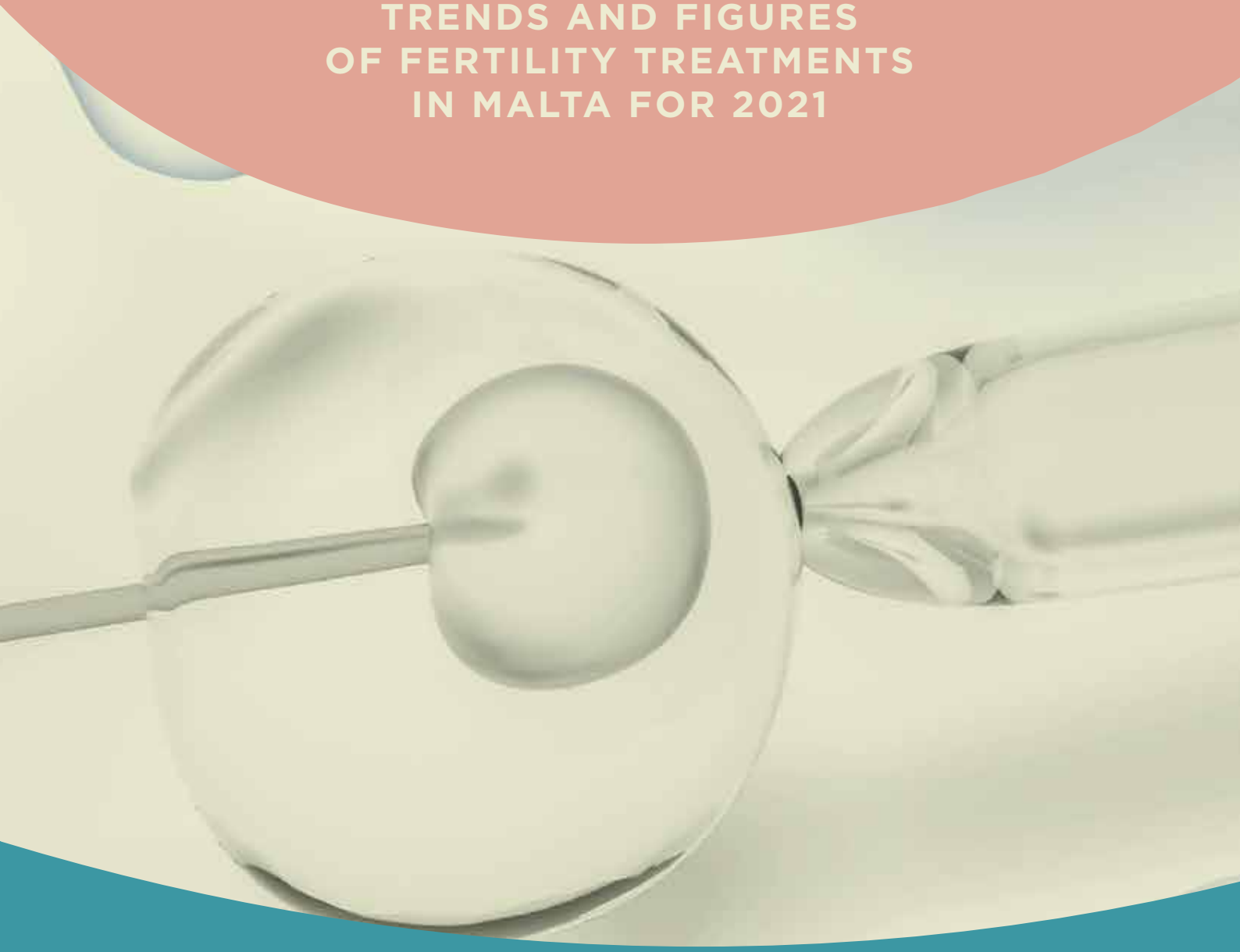
EMBRYO PROTECTION AUTHORITY

ANNUAL WORK REPORT

TRENDS AND FIGURES OF FERTILITY TREATMENTS IN MALTA FOR 2021



PUTTING PATIENTS FIRST

FEBRUARY 2022

ANNUAL WORK REPORT

TRENDS AND FIGURES
OF FERTILITY TREATMENTS
IN MALTA FOR 2021

EMBRYO PROTECTION AUTHORITY

Putting Patients First

Presented to Deputy Prime Minister and Minister for Health

Hon Christopher Fearne

As per Embryo Protection Act 2012, Chapter 524,

Embryo Protection (Amendment) Act, 2019

and

Embryo Protection Authority Regulations, LN32 of 2015 and LN343 of 2020

February 2022

EMBRYO PROTECTION AUTHORITY

PUTTING PATIENTS FIRST

ANNUAL WORK REPORT FOR 2021

Dedicated to all prospective parents who have embarked this long and winding journey of Assisted Reproduction.

The Authority will continue to strive to see that the highest standards are offered in Malta, so that you may achieve your dream.

This is one of the many Testimonials we received from prospective parents undergoing treatment in Malta in 2021. This specific one is being reproduced, as it shows how with our dedicated work, we are touching the lives and making a difference in the lives of those who seek our help.

"Thank you very much for all your work. You have changed my life and as I embark in a new role as a pregnant woman and soon to be mum. Know that you are very instrumental in my life, and I can't thank you enough. May you continue to be a blessing to other women as you have been to me. I will continuously pray for your health and God's wisdom to bless the work you do".

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Chief Executive Officer's foreword

Welcome

2021 was another year which brought with it challenges as well as achievements. This year the balance scale was more tilted to the positive side, as I will explain later.

This year was another year in which Covid-19 has impacted the clinics who offer ART services, the patients undergoing treatment as well as the work of the Embryo Protection Authority. The Authority reacted immediately to the re-emergence of the pandemic and following the decision of the Superintendence of Public Health to cease all non-urgent treatment again in 2021, we worked with the professional bodies to define a set of working protocols that would allow clinics to offer treatment in a Covid safe manner.

The Authority put in place a review process and requested clinics to submit a plan for the way forward in offering services, to ensure that plans were robust enough so that patients and clinics staff could be kept safe. Fertility clinics suspended and stopped all Intra-Uterine Inseminations, stimulations for ICSI/IVF were also stopped, however all other activities that didn't require anaesthesia were continued with most services going online.

The pandemic had a big impact on the Authority, whilst most of the public sector moved to work from home, our dedicated Staff were working extraordinarily long hours for weeks in a row, to suspend and ensure a safe reopening of the fertility sector; and to offer the much-needed support to patients through our helpline which was available 24/7.

As an Authority we also showed empathy by extending the maximum age of all women who were going to reach their maximum age of 43 years by the end of June 2021. This was the second extension granted by the Authority during the pandemic so no one would miss the chance of undergoing fertility treatment and thus miss the chance of becoming a parent, the Authority issued a six-month extension to these women. With this measure more women were granted this extension to undergo procedures in both the private and public tissue establishments.

Later, in the last quarter of the year 2021, the Authority was informed that the embryologists and other staff of the MDH ART Clinic were in quarantine thus the suspension of theatre procedures by the MDH ART Clinic, although general theatre procedures had not been cancelled yet.

The Authority resolved to grant three women who were going to reach their maximum age by end of year 2021, an extension of 3 months on their maximum age. This will give ample time to the clinic for things to turn to a better situation and for procedures to proceed.

The suspension of services had an immediate impact on the financial position of the Authority, as a major part of the income of the EPA comes from the fees, we levy on the sector that are dependent on the number of cycles performed. This shortfall in income was then partially compensated by fees the Authority charges clinics for embryo cryopreservations carried out.

Our priority was always to keep patients and clinic staff safe, but we also had to consider guidance from the professional international societies and government advice about the COVID-19 pandemic.

Through these struggles, 2021 was still another busy and successful year of daily miracles for the Embryo Protection Authority. We are proud that since our inception in 2013 to date **415 babies** have been born through ART Technologies, some of these babies were born as a result of the amendments to the Embryo Protection Act in 2018 which were then implemented by the licenced clinics in the following years. We are proud that this year the Take-Home Baby Rate has increased by **5.69%** over previous year.

As with previous years, the Authority was invited to raise awareness on the various media and take part in the public debates that arose on the subjects mainly on the implications of embryo freezing and embryo adoption as well as the introduction of direct and non-direct third-party donation and other new services in the pipeline.

During 2021, we saw the introduction and the full functioning of our new electronic exchange IT programme which is now linking all clinics who perform all medically assisted procreation techniques including intrauterine inseminations with the Authority. This has facilitated the recording of data, storage of data, approvals of the treatments to be performed and real time statistics to help us report on the state of the fertility sector both to the patients, the general public and Maltese Authorities.

2021, was also the year in which finally after years of hard work, the Authority moved into its own premises. Offices which are now to the calibre of a Regulating Authority

and in which our staff can work with dignity. A place which has been upgraded to all the latest technologies included a vault for the safe keeping of donor identification records and registers as required by law.

During this year, and after the move to the new premises, the Authority engaged more human resources. Current staff also successfully completed the training they were undergoing.

The cherry on the cake, was achieved in December wherein the Authority staff were nominated in two categories in the most prestigious awards 'Premju Nazzjonali Haddiema tas-Sena 2021'. In this month the Maltese Regulatory Authority and Malta achieved international recognition from the 'European Atlas of Fertility Treatment Policies, composed of the EU Commission, ESHRE (European Society for Human Reproduction and Embryology) and Fertility Europe. We classified in the 'Very Good' category together with England, Sweden, Spain, Finland, and Denmark. Classification was held in terms of the Laws of the Country, Regulation, Non-Anonymous Donation, Access to service and national funding as well as psychological support.

I take this opportunity to thank my very limited but very supportive staff at the EPA, who have proved to be the EPA's most valuable asset once again. Thanks to their professionalism with which they regard their work and the sector we regulate and through continuous round the clock work, we managed to obtain so many achievements, delivered in a timely manner against very tight resources available to the Authority. All the statistical information can be found in this report in the Trends and Figures section.

Looking forward to 2022, which will see the introduction of third-party donations of oocytes from abroad thus opening the services to a wider range of patients. Introducing also necessary changes to the Embryo Protection Act, to offer more high standard services to our prospective patients. 2022 will also bring about the opening of a new Tissue Establishment, offering more services to our patients.

We will continue to strive to see that the many strides we have made in this sector since the inception of the Authority in 2013 will continue to flourish.

We also promise that we will continue to be the voice of our patients by introducing a new Strategy for 2022-2025, which unfortunately had to be delayed due to the pandemic. This will also coincide to mark our 10-year anniversary working in this sector, that will focus on what we want to achieve in this field and how we will work together with all stakeholders towards achieving it.

Ms Simone Attard

Chief Executive Officer

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 Independent Regulator of all Assisted Reproductive Technologies (ART) performed at both the public and private licensed clinics/hospitals in Malta. It has been established as per the Embryo Protection Act 2012, (Chapter 524) which covers the use and storage of sperm, oocytes (eggs), and embryos for human application.

The Act has been amended through the Embryo Protection (Amendment), 2018. The new Amendment Act was enacted on the 21st of June 2018 and came into force on the 1st of October 2018 as per Legal Notice LN 313/2019.

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

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

At the Authority, we aim to ensure that everyone who receives treatment at a fertility clinic in Malta, and everyone born as a result of treatment undergone in Malta, receives high quality and high standard care with dignity and respect. We do this by regulating, monitoring, and inspecting fertility clinics and providing free, clear, and impartial guidance and information about fertility treatment, the clinics providing them, and oocyte, sperm, and embryo donation where applicable.

1.2. Our Principles – PATIENTS FIRST

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

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

1.3. Our Principles – Working closely with Stakeholders

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

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

1.4. The Legal Framework

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

1. *The 'Enabling' Act*:

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

2. *The 'Amended' Act:*

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

3. *The Regulations*:

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

The Embryo Protection Authority (Amendment) Regulations 2020 have been published by Legal Notice 343/2020 and came into force on the 21st of August 2020 following the assent of the Minister responsible for Health with the concurrence of the Minister responsible for Justice.

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

The Protocol which was published by the Authority in 2013 is intended as a means of assisting licensed Clinics to comply with their legal obligations whilst also serving as a useful reference for patients and professionals working in the fertility sector. During 2018, work was performed to issue an amended Protocol to reflect the requirement changes stemming from the Embryo Protection (Amendment) Act, 2018. The Updated version of the Protocol was tabled in Parliament during 2019.

The Protocol for Additional Fertilisation Requests (AFR) was established in writing by the Authority compiling all criteria and methodology for the application to grant more than two oocytes to be fertilised with a set maximum of five oocytes and consequently permission for embryo cryopreservation. The AFR Protocol was presented to the Parliamentary Health Committee on the 13th of September 2018 and was unanimously approved on same day. During 2020 tissue establishments making additional fertility requests had to strictly abide by this Protocol for their application to be approved by the Board.

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 31st of 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. Board Members and Executive Administration

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

Dr Patrick Sammut has offered his resignation in January 2020, however, to date he has not been replaced.

Ms Moira Gialanze the Administrative Officer was appointed to also serve as the Authority Board's Secretary with effect from April 2019.

In exercise of the powers conferred by Article 6 (2) of the Embryo Protection Authority Regulations, 2015 (L.N. 32 of 2015), the Hon Minister for Health, after consultation with the Embryo Protection Authority had appointed Ms. Simone Attard RRCouns., PGrad Cert, PGrad Dip Systemic Practice (Tavistock and Portman NHS Trust UK)., MBICA., GHZ., OLJ., as Executive Director of the Embryo Protection Authority to serve for a second term of three years up to 31st January 2021. Following the publication of the Legal Notice 343/2020 Ms Simone Attard was appointed as Chief Executive Officer on the 21st of August 2020 to serve for a third term as Head of the Authority for three years up to 20th of August 2023.

During 2021, twelve Authority board meetings have been called and, in all sittings, quorum was achieved. Meetings up to August 2021 were held in several boardrooms at Mater Dei Hospital, as of September 2021 board meetings were held at the new Authority premises. All meetings were held with physical attendance but precautions to follow the COVID 19 measures were in place. Attendance of the board members and the CEO to these Board meetings were as stated hereunder:

Designation	**Name**	**Attended**	**Excused**
Chairperson	Judge Philip Sciberras	11	1
Vice Chairperson	Ms. Josephine Abdilla	12	0
Member	Dr. Patrick Sammut	0	0
Member	Profs. Victor Grech	9	3
Member	Ms. Mariella Meachen	12	0
Member	Ms. Sarah Camilleri	11	1
Chief Executive Officer	Ms. Simone Attard	12	0

During the twelve meetings, two representatives from *the Obstetrics and Gynaecology Association* were invited to attend the meetings in order to discuss requests for the additional fertilization of oocytes. These requests are made by the clinicians treating the prospective parent / parents to the Embryo Protection Authority to approve the fertilization of a maximum of five oocytes instead of the two currently permitted by law.

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

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, remuneration capping for 2021 in line with the new framework for the categorization, classification and remuneration of Boards and Committees stood as follows: Chairperson €13,954, Vice Chairperson €6,000, and members €5,176- respectively.

However, in line with good governance, board members were only paid for sessions they attended to, and if sessions were held in the mornings a vacation leave form from their full-time job had to be presented for payment to be affected. The remuneration for 2021 paid to each member is as listed overleaf.

Designation	Name	Annual Remuneration (Euros)
Chairperson	Judge Philip Sciberras	12,782.88
Vice Chairperson	Ms. Josephine Abdilla	5,825
Member	Dr. Patrick Sammut	0
Member	Profs. Victor Grech	3,881.70
Member	Ms. Mariella Meachen	5,175.60
Member	Ms. Sarah Camilleri	4,744.30

1.8. 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.

During 2019, the issue of having two competent Authorities that the clinics must report to, was raised by one of the clinics. To iron out these misunderstandings a meeting was held between the licencing Authority (SPH) and the Regulator (EPA) together with their legal representatives as well as the Chief Medical Officer to put in writing the different roles of the Authorities as well as when and to whom the clinics must report to. Unfortunately, although this meeting was very fruitful and to this effect a letter was circulated to clinics with the defined roles and responsibilities and reporting obligations of each Authority, during 2021, there still were instances when one of the clinics did not adhere to the established agreement between both Authorities and totally ignored the EPA as an Authority from which authorisation prior to procedure is to be sought. To this effect we are hereby again listing the separate roles and responsibilities of each Authority.

All reporting as regards to issuing of Licences and renewals of same, is to be made solely with the Licensing Authority, i.e., SPH. Same applies to quality and safety of general public health.

There are instances where the reporting is to be made by the Clinics to **both** Authorities simultaneously. Thus, reporting of serious adverse events (SAE) and serious adverse reaction events (SARE), as well as all quality and safety issues relating to quality and safety of gametes and embryos during processes and storage are to be reported to both SPH and EPA.

Alterations to premises and equipment are to be reported to **both Authorities.** Henceforth, all requests for permissions are to be submitted before the actual activities are embarked upon.

Reporting of activities that need to reach solely EPA, supported by EPA forms and documentation including testing results, should include but are not limited to:

- Request for permission to cryopreserve gametes in oncology cases
- Request for permission to cryopreserve gametes in fertility preservation
- Request for permission to cryopreserve gametes by transgender persons prior to starting hormone therapy treatment
- Request for permission to discard gametes
- Request for permission to transfer gametes/embryos between licenced centres in Malta
- Request for permission to transfer gametes/embryos from a Malta Centre to abroad and from abroad to a Malta Centre
- Request for ART Procedures (IUI, IVF, ICSI) as well as procedures making use of thaw and transfer of cryopreserved embryos and storage of gametes for patients undergoing an ART cycle
- Request for Additional Fertilisation of oocytes (up to a maximum of 5 oocytes) to be made in line with the EPA Protocol as approved by the Parliament Health Committee
- Request for Embryo Cryopreservation and potential Embryo Donation
- Request for Use of Third-Party Donation and duly inform immediately every donation made with full identity details of the donor.
- Prior Authorisation by the Authority for the donation of cryopreserved Embryos
- Prior Authorisation by the Authority of the Agreement between the prospective parent or prospective parents and the licensee to regulate the cryopreservation of embryos.

- Prior authorisation by the Authority to be granted to a prospective parent or prospective parents who prior to the coming into force of the Amendment Act, had cryopreserved embryos in tissue establishments abroad to bring two cryopreserved embryos to be transferred locally into the prospective parent or prospective parents for each cycle

- Outcomes of all procedures and storage carried out.

- To provide the Authority with all documentation and data in regard to reporting obligation of the Authority to the House of Representatives

- To pass on information to the Authority without delay of all confidential registers held by the licensee with full details of every medically assisted procreation procedure, germ line cell donation, cryopreservation of germ line cells and cryopreservation of embryos.
- Any other documentation that the Authority as Regulator may request in terms of the Embryo Protection Act
- Payment of all procedure and storage fees

Breaches in reporting duties with regards to the EPA may lead to prosecution by the Authority in accordance with the Embryo Protection Act.

As Regulator, the Authority took an active role in the COVID 19 pandemic, and again, the Authority considered issuing an extension to the women who were to undergo treatment and were nearing reaching their maximum age. Thus so no one would miss the chance of undergoing fertility treatment and thus miss the chance of becoming a parent, the Authority issued a second six-month extension to the women who would be reaching the age of 43 by end of June 2021. With this measure more

women were granted this extension to undergo procedures in both the private and public tissue establishments.

The Authority was also very much in touch with the Maltese Licenced clinics and was providing them with the latest news and updates from ESHRE, ECDC and other institutions on the experience of maintaining safe and sufficient supply of substances of human origin (SoHO) gained during the COVID-19 pandemic and through recent scientific developments in understanding the evolution of the disease. The documents provided reassess the risk posed by COVID-19 and revises management options for the safe and sustainable supply of SoHO. It also includes information relating to the safety of staff in SoHO establishments and recipients of SoHO products. The aim of this active role by the Authority was to assist the tissue establishments in responding to the threat posed by the pandemic.

The Authority has proceeded with caution in its decisions to suspend or postpone treatments in order not to continue creating emotional suffering to those who had already started their treatment, in fact the Authority was offering counselling services to the patients through a special dedicated telephone line. The Authority also requested tissue establishments to forward their plan on how activities will continue after new measures were announced in March 2021. It was agreed that all genetic, urology and counselling sessions are to be held online. Clinics were to stop new stimulations for IVF/ICSI and IUI's until new measures are announced. All other activities that did not need anaesthesia involvement were to continue.

Throughout 2021, several requests of applications for fertilisation of oocytes for couples undergoing cycles at the licensed clinics were reviewed. All the cases

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

The Authority has received eight (8) requests in 2021, which is more than double to the requests received in 2020, from the licensed clinics to grant permission for oocyte retrieval and cryopreservation only and or embryo cryopreservation for eight women aged between 20 and 42, who wanted to preserve their fertility.

Six permissions were granted to six women aged between 22 and 38 years of age on medical grounds who made this request prior to starting chemotherapy for oncology diagnosis. Three of these women opted to cryopreserve oocytes only and not proceed with embryo cryopreservation. One other woman opted for embryo cryopreservation only, while the other two women chose to cryopreserve both their supernumerary oocytes as well as their embryos.

Another approval was granted to a female prior to starting the process to transitioning into a male, this patient opted for cryopreservation of oocytes.

The other woman requested to cryopreserve her oocytes at the private facility for social freezing reasons, to use her oocytes at a later stage in life, this was also granted permission by the Authority.

Out of the eight approvals granted, all eight women had successful oocyte retrieval, seven had successful oocyte cryopreservation and three women successfully cryopreserved embryos for future use after ending chemotherapy.

The Authority also received a total of 86 requests from the licenced tissue establishments to grant permission for sperm cryopreservation, 84 at MDH ART Clinic and 2 at the private clinic. All 86 requests were granted permission to cryopreservation sperm. In several cases, sperm was obtained through nine testicular aspiration/extraction (TESA/TESE).

The 86 requests were made for males aged between 17 years and 62 years. Eighty-two (82) males vitrified their sperm, whilst four (4) males who requested sperm cryopreservation did not vitrify sperm.

Twenty-five (25) requests were made by males, aged between 20 years and 44 years requesting Fertility preservation following oncology diagnosis prior to starting chemotherapy.

Another seven (7) males aged between 17 years and 28 years made requests for cryopreservation of sperm prior to starting to receive hormone therapy to transition from male to female.

The other fifty-four (54) requests were made by males who had Urology referrals with the main reason for referral being decrease in male fertility parameters and azoospermia.

In the first quarter of 2021, the Authority received a request for the transfer of cryopreserved embryos from the United Kingdom to Malta. The Maltese patient had cryopreserved these embryos prior to coming into force of the changes to the Embryo Protection Act and thus was eligible to transfer two embryos to Malta. The Authority recommended to the Superintendent of Public Health to issue an on-off importation approval on named patient bases so this transfer could be affected.

Once approval was granted from the SPH, the Authority approved the transfer, in March 2021 of the cryopreserved embryos to be cryopreserved in the public clinic in Malta. Eventually two cryopreserved embryos were imported to Malta in June 2021.

In 2021, the Authority also received three further requests for the transfer of cryopreserved gametes, vials of sperm, from the United Kingdom, France, and Italy to Malta. The Authority issued, one off approvals for the transfers of the cryopreserved gametes. Two of these approvals were to be cryopreserved in the public clinic and one in the private clinic in Malta. To date these transfers have not yet been finalised.

In the last quarter of 2021, the Authority received a request from a patient to transfer her cryopreserved oocytes from the private local clinic to a clinic in Spain. The Authority requested the local clinic to establish the necessary documentation for the distribution of gametes to another country for which an approval will be issued once all documentation is in place.

In 2021, after the establishing of a third-party agreement for the distribution of donor third party sperm from abroad, a country within the European Union, by the MDH ART Clinic, the Authority received twenty-nine (29) requests for the transfer of donor sperm to Malta. Twenty-six (26) requests were approved by the Authority; however, three (3) requests were rejected as they did not meet the requirements of the Maltese Legislation. Out of the 26 approvals granted, by end of year 2021 the distribution of sperm of 24 donors had already been made to Malta and a total of ninety-six (96) donor sperm vials had been cryopreserved in the public tissue establishment to be used in procedures requiring the use of third-party donor sperm.

During 2021, the Authority also received requests for transfer of gametes and embryos between the Maltese Licenced Tissue establishments. Four (4) requests were received for the transfer of embryos from the St James Conception Unit to the MDH ART Clinic. The Authority approved all four requests for embryo movement and a total of ten (10) embryos were shifted from the private to the public clinic.

Another seven (7) requests for transfer of gametes were received by the Authority to transfer sperm and oocytes between the Maltese Licenced Clinics. Six (6) of the requests were to transfer gametes from the St James Conception Unit to the MDH. ART Clinic. The Authority approved all six requests which included the transfer of seven (7) vials of sperm of two males, and four requests for the transfer of oocytes of four women, transferring 21 oocytes in total.

The Authority also approved the only one request received to transfer sperm from MDH ART Clinic to St James Conception Unit. A total of three sperm vials were shifted from the public clinic and cryopreserved for future use at the private clinic.

1.9. Human Resources

During 2021, to further strengthen its corporate structure, the Authority engaged in issuing calls to fill the vacated post of Assistant Director, although several interviews were held the post was still not filled up till the end of the year. The main struggle to this is that this position holds a definite contract. In the last quarter of 2021 negotiations were held with the Industrial Relationship Unit, to amend the Authority's structure through a legal notice to enable other positions on an indefinite contract to be amended or adjusted. The necessary amendments came into force by the publication of Legal Notice 343/2020.

The Authority structure has been amended to also include the position of Manager which although several interviews were held the post was still not filled up till the end of the year.

New positions of Infertility Inspectors were amended and filled during 2021. New positions of Senior Executives and clerks were also created in the new structure that will come into place in 2022. The total number of employees directly employed with the Authority now stands at seven (7) employees, two other employees are on secondment with the Authority

1.9.1 Training of Staff

The Authority strives to ensure that its employees have the skills and competences to match the organizational requirements to guarantee optimal executive performance. All the staff receive regular training throughout the year including training for the wellbeing of the staff themselves. Staff also attend for sessions on Online Awareness Session on Health Relationship and Practical Skills for Managing Stress organised by the People Support and Well Being Directorate. All staff underwent training in General Data Protection Regulation (GDPR). Other employees attended Health and Safety training, training courses on Accountability and Good Governance as well as ECDL Standard IT Security course. Staff also received detailed training in IT Service Management ITIL 4 and obtained certification of same.

At the Authority, our patients are very dear to our hearts, thus patients who have received bad news or diagnosis need special care. In 2021 the Authority chose to participate in the training offered by the Positive Parenting Taskforce set to implement the Positive Parenting Strategy for the Maltese Islands. The breaking bad news sessions focused on several different situations and focused on 'Understanding and being sensitive to the needs of parents of young children when receiving negative news and/or diagnoses' it also gave insight on 'Breaking the news prior to birth when there is a disability or a condition incompatible with life'. The themes of 'Acknowledging the needs of parents with disability when accessing treatment' as well as 'Working with the context in the aftermath of bad news breakup: liaising with services, community and peers to sustain inclusion for all' were also explored.

In February 2021, the Chief Executive Officer attended a Campus Symposium online on 'Counselling and the provision of information in third party reproduction and surrogacy: best practice in the face of new challenges.' This Symposium was organised by the European Society for Human Reproduction and Embryology (ESHRE) and was attended virtually.

EPA staff in February 2021, attended for a very informative session on 'Airborne Awareness: The Impact of Air Purification system, towards improved patient care in IVF, Health Care and long-term Care. This training was held virtually online.

In April 2021, two training workshops were attended virtually by EPA staff, these focused on 'Breaking Bad News' and 'The fate of the Embryo'. Both workshops were organised by the European Society for Human Reproduction and Embryology (ESHRE).

In May 2021, EPA was represented by Mrs Attard who attended virtually the British Infertility Counselling Association (BICA) annual conference. During the conference discussions were held on the challenges and developments in patient support during the pandemic, the framework of understanding loss and grief, donor conception registries, oncology prior to fertility treatment, male fertility as well as training on surrogacy support.

In May 2021, three other interactive training workshops were attended by EPA Staff virtually. The online courses were organised by the European Society for Human Reproduction and Embryology (ESHRE) and focused on 'SARS COV 2 and assisted reproduction in 2021', 'Quality Management in Assisted Reproductive Technologies – an update' and the last workshop was on 'Supporting patients' decisions for fertility preservation.

During the month of June, Authority personnel attended a training workshop virtually, this training gave a detailed explanation of the EURO GTPII Methodology on 'Good practices for evaluating, quality, safety and efficacy of novel tissue and cellular therapies and products.' This workshop was organised by the European Society for Human Reproduction and Embryology (ESHRE).

In July 2021, officials of the Authority virtually attended for the European Society for Human Reproduction and Embryology (ESHRE) 37th Annual General Meeting held online, including a Pre-Congress Course. The Pre-Congress course focused entirely on Ethics in In-Vitro Fertilisation. The following three-day conference included a scientific programme on various topics ranging from genetics, psychosocial support, surgery, diet and lifestyle and the new technologies trends of oocyte and embryo freezing as well as add-ons to assisted reproduction techniques.

Between the months of June and October 2021, the Authority's CEO completed her 'Advanced training Course on Common approaches to the preparation process authorisation (PPA) in the blood, tissue, cells and Medical Assisted Reproduction Sectors'. This advanced training course was co-funded by the EU Health Programme and organised by the Medical University of Warsaw in collaboration with the Italian National Transplant Centre and the Italian National Blood Centre.

The Authority is proud that our CEO, Mrs Attard has passed the final exam with flying colours, and is now one of only sixteen (16) personnel qualified on this subject in all, of the EU countries. This not only augurs well to Mrs Attard herself, but this is definitely an achievement for the Authority and the Maltese Fertility Sector, as we are more than sure that she will use this knowledge for the best interest of our patients.

Between September and October 2021, the Council of Europe in Strasbourg through the European Directorate for the Quality of Medicines and Healthcare (EDQM) organised the 'First European Course on Biovigilance for Tissues and Cells'. This course was attended virtually by the Authority staff who participated in the live sessions held.

EPA officials also attended an informative session organised by the Superintendence of Public Health in November 2021 on 'Establishing a National Platform to address Social Determinants of Health – Health in all policies.'

1.9.2. EU Meetings and other international meetings attended by Staff

In January 2021, the Embryo Protection Authority as the Maltese Competent Authority on Medical Assisted Reproduction (MAR) was invited to attend to a meeting on the EU Health Programme. During this meeting The EU4Health Work programme for 2022 was discussed and adopted to be published later in the year. This health programme included also issues and actions on Substances of Human Origin.

A Joint Action is to follow-up, pilot, and take-up the GAPP approach in the EU national competent authorities, with direct grants to Member States' authorities: piloting a new model approach for assessing and authorising novel Blood, Tissues and Cells (BTC) preparation processes.

During the meeting discussions were also held on the procurement to support cooperation between the national authorities and professional sector associations in the blood, tissue and cells and organs sectors, focusing on: Central IT modules that facilitate coordination amongst NCAs; Further IT support; and the Exploring a possible larger role for hospital blood banks in the Blood Tissue and Cells framework.

In February 2021, the CEO attended a meeting held virtually for the EU Competent Authorities on Substances of Human Origin Expert Group which was convened mainly to discuss the COVID 19 situation. The meeting was attended by officials of Authorities in Member States as well as the representatives of the European Centre for Disease Prevention and Control (ECDC), the World Health Organisation (WHO), the Council of Europe (EDQM) were present as observers and the Consumer, Health and Food Executive Agency (CHAFEA).

The meeting focused on Covid-19 issues relevant for the tissues and cells field in particular, surveillance, the impact of COVID-19 on donation programmes, testing protocols, inspection, and authorisation issues.

The European Centre for Disease Prevention and Control (ECDC) updated the participants on the current situation regarding the SARS-CoV-2 pandemic in the EU and worldwide, showing the most recent distribution of COVID-19 cases and deaths. In response to the pandemic, ECDC published several risk assessments on the topic and two specific documents on the safety of SoHo and the risk mitigation measures recommended. No reports of COVID-19 transmissions through SoHo have been reported so far, although the risk should not be excluded.

According to ECDC, EU/EEA countries should continue precautionary actions to mitigate the potential risks to the viral safety of Substances of Human Origin (SoHO) and to manage the sufficiency of the national SoHO supply. Measures should be proportionate to the evolution of the pandemic and consistent with governmental and public health advice.

Furthermore, it updated on how to contain the spread of the virus, so it is crucial that SoHO establishments remain vigilant and maintain precautionary measures. The EU meeting also focused on the Commission activities on COVID-19 and the surveillance as well as the epidemiological state of play COVID and other CD (ECDC).

Another Main point on the Agenda was the Revision for the EU legal Framework, wherein discussions were held on the Process – state of play and planning, Updated safety/quality guidelines for recipients, donors and offspring, Options in and feedback from the Inception Impact Assessment, Consultation questions, and Inputs from expert bodies. Other issues discussed were Oversight, Measures in and feedback from the Inception Impact Assessment, as well as Issues arising in the Inspection Expert Sub-group and Issues arising in the Vigilance Expert Sub-group. Other matters discussed were Innovation as well as Supply sufficiency. The issue of Datasets for tissues and cells was discussed, as not all member states were collecting the same data.

In March 2021, the Authority was invited to attend the Council on General Affairs and Policies of the Hague Conference on the Private International Law (HCCH). The HCCH is The World Organisation for Cross-Border Cooperation in Civil and Commercial Matters. The Authority accepted the invitation and was represented by its Chief Executive Officer, Ms Simone Attard.

The Council on General Affairs and Policy (CGAP) met online from the 1st to the 5th of March 2021, with attendance from 68 HCCH Members, 5 non-Member States and other Observers from 8 intergovernmental organisations and 10 international non-governmental organisations. The Council discussed several topics amongst which were the family, parentage, surrogacy, family arrangements, adoptions, and International family and child protection laws.

In May 2021, the Authority Head attended a regular meeting held virtually for the EU Competent Authorities on Substances of Human Origin Expert Group which was convened to discuss the issue of Regulating for Sufficiency – tissues and cells. The meeting was attended by officials of Authorities in member States as well as the representatives of the European Centre for Disease Prevention and Control (ECDC) and the Council of Europe (EDQM).

Present also for the meeting were key tissue and cell professional stakeholders, donor, and patient representatives, amongst whom were present the European Association of Tissue and Cell Banks, European Eye Bank Association, European Society for Blood and Marrow Transplantation, World Marrow Donors Association, European Society for Human Reproduction and Embryology, Fertility Europe, European Hospital and Healthcare Federation and the Standing Committee of European Doctors.

The workshop meeting explored legislative measures that might support member states in safeguarding sufficiency of supply. This includes rules regarding activity reporting for improved monitoring of supply. Proposals and recommendations for mandatory reporting from an EDQM project (tissues and cells) were evaluated.

Participants also discussed potential EU-level measures to increase collection and provide guidance on utilization, indication, or use, while strengthening the Member State measures to control the flow of substances, monitor their volumes, and report these at the EU-level.

In June 2021, the Authority Head attended another meeting held virtually for the EU Competent Authorities on Substances of Human Origin Expert Group which was convened to discuss the Blood, Tissue and Cells impact assessment and revision process – debrief from stakeholder consultations and workshops. The meeting was attended by officials of Authorities in member States as well as the representatives of the European Centre for Disease Prevention and Control (ECDC) and the Council of Europe (EDQM).

During this meeting, the member states discussed the Impact of Covid-19 on the BTC Evaluation Results, Keeping technical rules up to date, Protecting donors and children born from gamete and embryo donors, Strengthening oversight – increasing inter-MS confidence and BTC exchange, Facilitating access to innovative BTC that are safe and effective as well as Regulating for sufficiency.

Also, during this meeting, Ethical principles on voluntary and unpaid donations were also discussed by the stakeholders. The Authority had submitted prior to this meeting, the consultation survey with its recommendations for changes necessary to the BTC directive, as well as the Regulating point of care of BTC processing.

Also in June 2021, the Authority received an invitation to attend to the first meeting held between the EU Commission Expert Subgroup on inspections in the Blood, Tissues and Cells Sector (IES) and PICS - The Expert Circle on Human Blood, Tissues, Cells and Advanced Therapy Medicinal Products (ATMPs). This joint virtual meeting was to discuss the Distant Assessment (DA) and Remote Virtual Inspections (RVI).

The meeting kicked off with an introduction and welcome address by the European Commission (SoHO Team) – Mr Stefaan Van der Spiegel, Ms Béatrice Marquez Garrido and Ms Deirdre Fehily, This was followed by a presentation from PIC/S by Ms Marisa Delbò, and a presentation by the Centro Nazionale Sangue delivered by Mr Vincenzo De Angelis. The webinar followed by a presentation of the PIC/S on the approach to the topic as well as by a presentation by the European Medicines Authority on Distant Assessment Guidance & experience. In the afternoon presentations were held on the IES RVI Guidance Document and experiences from inspectors who have already performed DA/RVI from different sectors. The meeting concluded with a final discussion on the limitations and challenges of the Distant Assessment and the Remote Virtual Inspections.

1.10. Authority Premises

The Ministry for Health had assigned premises to the Authority in 2016, and all staff including senior executive staff, were all housed in this one-room office in St Luke's Hospital. The size of this office limited the Authority to invest in the recruiting of the much-needed human resources. This one room office also posed a challenge to work in considering the measures taken re the COVID 19 pandemic.

In this regard a call for tenders was issued on the 30th of June 2020 for the relocation of the Authority into a larger premises, this tender was not awarded. Several meetings were held by the Authority in conjunction with FMS and CPSU to draft a new tender document which has been published having a closing date of submission in February 2021. After an evaluation process the tender was awarded for office space including furniture in Luqa and would be ready to occupy within 60 days.

The Authority relocated to its new offices on the 11th of September 2021 and all services were up and running smoothly by the following Monday the 13th of September. The new premises now houses a main reception area, two inspector offices, CEO office, six other offices to house Assistant Director, Managers, IT staff, Accounts Staff, and administration. The premises also has a large boardroom, IT room complete with server, a fire resistant and alarmed vault room to store all sensitive documentation, an archive store, and a private room for one-to-one meetings with patients. The premises also includes facilities for staff with a fully equipped kitchenette, pantry, two bathrooms and parking spaces in a garage underlying the office.

The premises were inaugurated by the Hon Deputy Prime Minister and Minister for Health Mr Chris Fearne on the 22nd of December 2021. In her speech the Authority's CEO, Mrs Attard emphasised that now the Authority had its own Offices which are now to the calibre of a Regulating Authority and in which the staff can work with dignity. These new offices would enable staff to be able to perform its regulatory duties and be able to house the new staff which is crucial to employ due to the increase in the Authority work and implementation of new services.

1.11. New Corporate Branding

As the Authority has evolved during the nine years of its establishment, the management thought of re-branding the corporate identity of the Authority. This was done to establish the key messages that will effectively communicate our Authority's values and mission statement. The artwork produced and its creative content were required to communicate such messages to our stakeholders, prospective parents, and society at large.

The new artwork reflects the corporate identity of the Embryo Protection Authority and includes a logo which represents the Authority's objectives. The logo features an embryo carried by a prospective parent. This represents the work of the Authority, firstly that of offering the best services to the prospective parent/s involved in the process and that of the Authority's structure giving a feeling of protection to all involved in the process.

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

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

The new Amendment Act was enacted on the 21st of June 2018 and came into force on the 1st of October 2018 as per Legal Notice LN 313/2019.

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

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

St James Assisted Conception Unit informed the Authority that they will not be offering embryo cryopreservation in the October 2018 cycles, thus additional fertilisations were not approved by the Authority and all couples had permission to fertilise two oocytes only. However, in the first quarter of 2019, the Responsible Person of the St James Assisted Conception Unit informed the Authority in writing that now the Clinic will start offering embryo cryopreservation to the couples who will be undergoing their cycles as of February 2019.

Following the introduction of the new amended law, clinics had to sign contracts with prospective parents who opted to cryopreserve their embryos as per required by the terms of the law. Both licenced tissue establishments are now providing the contracts to the Authority. The Authority has noted that whilst the private tissue establishment contracts are signed by the patients and representative of the Tissue Establishment, the Public MDH ART Clinic contracts are signed by the patients and by the Chief Medical Officer and not by the Tissue Establishment itself.

Pursuant to changes coming into force, donations of third-party gametes were allowed by law for all prospective parents as defined by law as any person regardless of gender or sexual orientation, who has attained the age of majority and is a receiver or user of the medically assisted procreation techniques. Thus, these services are provided to single women, heterosexual couples, and lesbian couples.

After the introduction of the changes in law, St James Conception Unit has informed the Authority that they do not wish to perform any cycles using donated oocytes, sperm, or embryos and that they will not seek to be licenced to provide such services or the distribution or importation of third-party gametes from abroad to store in Malta.

On the other hand, the Public MDH ART clinic has sought permission from the Authority to start offering third party donations as allowed by law, those being of Known Direct Donations and donations through the distribution of sperm and oocytes from abroad.

After several meetings held between the Authority, legal representatives, the office of the Chief Medical Officer and the MDH ART Clinic personnel, the necessary documentation was drafted for the approval of the Authority to grant permission for Known Direct (local) Donation of non-partner gametes (sperm and oocytes).

The Embryo Protection Authority granted its approval for same services and in 2019 the Superintendent of Public Health issued a licence for Known Direct (local) donations for both sperm and oocytes to MDH ART Clinic. However, to date no

requests have been made by the MDH ART Clinic for direct donation neither through IUI nor IVF.

For the distribution of donor gametes from abroad to be brought to Malta a third-party agreement had to be reached between the ART Clinic and the foreign tissue establishment. The Authority was involved in quite a number of meetings with the legal representatives, office of the Chief Medical Officer, the Licence Holders, and representatives of the ART Clinic together with the foreign tissue establishment for the distribution of third party (non-partner) donor sperm to Malta. Following submission of the necessary documentation that was certified as being in line with Maltese Embryo Protection Act Legislation, the Authority issued its approval for the distribution of sperm from a sperm bank in a European Union Member State.

Subsequently the Superintendent of Public Health issued a Licence to the MDH ART Clinic in May 2020 for the non-partner sperm distribution from abroad, to be used in open donations. These procedures will be regulated with identity release of donor identifying information to the child on reaching age of majority if s/he only requests it. These third-party sperm donations can be used in both IUI and IVF procedures.

Distribution of third-party donor oocytes from abroad is still not approved by the Authority as no third-party agreement has been reached by the MDH ART Clinic with a foreign tissue establishment yet.

The Embryo Protection Authority was presented with a draft third party agreement by MDH ART Clinic with an EU tissue establishment. The Authority brought to the attention of the Clinic that this was not in line with Maltese Legislation. Several meetings were held to this effect with the MDH ART Clinic personnel, the Chief Medical Officer, the Licence holders, and legal representatives to explain why this draft agreement was not in line with Maltese Legislation and needed amendments.

The Authority's position was final and that it could not approve this agreement as the foreign tissue establishment could not provide all the required donor documentation to the Embryo Protection Authority as well as the term of donor record keeping was not in line with Maltese Legislation. Thus, amendments need to be made for the Authority to approve and Superintendence of Public Health to issue licence for the distribution of donor oocytes from abroad.

In 2021, several meetings were also held by the Authority with the Chief Medical Officer's office as well as the State Advocate office on other necessary changes to the Embryo Protection Act for the introduction of a new service of altruistic surrogacy and other necessary changes to law to allow for the smooth distribution of third-party donor gametes from abroad to Maltese Tissue Establishments.

In the meetings held regarding the possible introduction of altruistic surrogacy, meetings were held with the Clinical Chairperson as well as other clinicians from the Obstetrics and Gynaecology Department, who together with the Chief Medical Officers office discussed and amended the very basic bill that was prepared by the CMO's office.

Other meetings included several other stakeholders such as the Ministry for Health lawyers and Identity Malta to discuss in detail the registration of the birth resulting from surrogacy. Other stakeholders involved in the meetings included the Chief Executive Officer of the Foundation for Social Welfare Services, the Operations Director, the International Relations Director, and the Director of Child Protection of the same foundation.

All meetings were attended by the Chief Medical Officer, a representative of the State Advocate's office and the CEO of the Embryo Protection Authority. A draft bill was prepared for further discussion and implementation in 2022.

Following the changes to the Embryo Protection Act, the Superintendence of Public Health received an application for the licencing of a new tissue establishment in Malta that will offer Assisted Reproduction Technology services. This application was forwarded to the Authority for its approval.

The application was in the process of being assessed by both the SPH and EPA following the submission of a robust quality system, standard operating procedures, and third-party agreements as well as other validation reports. Meetings were held internally between the SPH and EPA personnel, and another meeting was held between both Authorities and the proposed licence holder, Responsible Person and Quality Manager of the new Tissue Establishment.

It is envisaged that a joint inspection between SPH and EPA will be held in the first months of 2022 to assess the recommendation of a new licence.

Pursuant to the Introduction of the new concept of Embryo adoption the Authority started discussions together with the Social Care Standards Authority (SCSA), to start working on the standards and protocols to regulate this procedure. However, during said meetings and during the National Adoption Conference organised by SCSA to which the Authority was invited to attend, it was made very clear that the remit of the Adoptions Administration Act Board was solely on born children to be adopted and not embryos. Moreover, there are divergencies in the laws of both Authorities, as while the adopted embryo will be automatically recognised as the child of the prospective parents, prospective adoptive parents of children adopted would have to make a court request. A meeting was also held with representatives of the Foundation for Social Welfare Services to explain to them the provisions of the law.

Several meetings were held with the Social Care Standards Authority (SCSA) and the office of the State Advocate on this issue of embryo adoption, it was agreed that a bill is presented to Parliament that will amend the current Adoption Administration Act to provide the necessary legal framework to facilitate embryo adoption. The main change to the principal Act, Chapter 495 is that the Adoption Administration Board will make recommendations to the Embryo Protection Authority regarding the eligibility and suitability of prospective parent or parents relative to adoption of an embryo as provided in sub-article (3) of article 4 of the Embryo Protection Act.

This bill has been already reviewed by the Legislation Unit of the Ministry for Justice, Equality and Governance and will be presented by SCSA to the Minister for the Family, Children's Rights and Social Solidarity to table at the House of Representatives for discussion. To date this bill has not yet been tabled in Parliament for the regulation of Embryo Adoption.

Following a meeting held with the Malta College for Obstetric and Gynaecologists as in line with Article 22 of the Act every medical practitioner is to keep a register of all medically assisted procedures, including intra-uterine inseminations and forward these registers to the Authority without delay. To date eleven clinics have registered with the Authority although we are of the knowledge that much more practitioners perform this procedure prior to referring patients for IVF.

1.13. ART Prioritization Committee

The Ministry for Health considers the fact that parent / parents requiring IVF cannot be waitlisted on a *first come-first served* basis. To this effect, the Ministry appointed an ART (Assisted Reproductive Technology) Prioritization Committee with the aim of objectively ranking in order of precedence the couples who are seeking assistance at the ART Clinic at Mater Dei Hospital (MDH). Each clinical case is considered individually, and priority of treatment is given to couples where female age is an issue, since delays in providing an opportunity for treatment may make the couple ineligible for future treatment. Other factors, such as AMH levels, semen parameters, paternal age, duration of infertility, previous failed IVF/ICSI attempts, recurrent miscarriages, etc., are also considered. During 2021 the Authority was represented on this Committee by its Chief Executive Officer Ms. Simone Attard and by Profs. Victor Grech as member.

During 2021, the prioritisation Committee revised the criteria for prioritisation of prospective parents and introduced new prioritisation criteria for prospective parent /parents making use of third party donated sperm.

Since new cases are registered at Mater Dei Hospital every week, this Committee met on a monthly basis, with an unforeseen delay between meetings due to COVID 19, to decide which of these couples requires prioritization for treatment. A total of eight sittings were held during 2021.

Eight reports were consequently issued showing a total 247 prospective parent/s files that had been reviewed by the ART Prioritisation Committee during 2021, this saw an increase over the 155 files that were reviewed in 2020. The majority of the files reviewed came from two hundred and eleven heterosexual couples who were going treatment with their own gametes. The other thirty-six files reviewed came from prospective parent/ parents who were going to undergo treatment with the use of third-party donor sperm. These thirty-six applications were filed by fifteen (15) heterosexual couples, eight (8) from same sex female couples and thirteen (13) applications were filed by single women.

Two hundred and forty prospective parent/parents were prioritised as they met the necessary criteria for prioritisation. Five prospective parent/s were deemed ineligible for the prioritisation process as the files presented by the MDH ART Clinic had missing documentation, thus the Committee requested that these files will be prioritised in following sessions when all documents are in order.

One other couple were not prioritised as the Committee requested that the couple should undergo counselling sessions prior to proceeding with treatment and another couple was not prioritised as the Committee requested legal guidance on the status of the couple prior to prioritising, as one of the partners in a same sex female relationship was still married to a foreign male.

1.14. Inspections

The Authority, from time to time makes the necessary inspections 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 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 2021, due to COVID19 measures in place, no physical inspections together with the Superintendence of Public Health (SPH) were carried out at the tissue establishments. These were in conformity with the legislative requirements for periodic re-inspection before renewing the licence as both tissue establishments have a valid licence in place, with that of the Public MDH ART Clinic valid up to 30th April 2022 and that of St James Conception Unit valid up to 19th November 2021.

With regards to St James Conception Unit, a variation in licence was requested by the Tissue Establishment, following a meeting held between the Embryo Protection Authority CEO and the Responsible Person and Licence Holder of the Tissue Establishment. In August 2021, patients had informed the Authority that their forthcoming cycle was suspended with no prior notice. A new licence was issued by SPH to St James Conception Unit with changes in activities and is valid up to 19th November 2023.

Re the inspections due as new services were going to be introduced that of non-partner third party donations, at the MDH ART Clinic, the Authority held virtual online meetings with the stakeholders and in collaboration between both Entities that of SPH and EPA.

1.15 Incidents, investigations and actions taken

In the first quarter of 2021, the Authority received a request from a patient who wished to transfer her embryos from MDH ART Clinic to the private tissue establishment as she was undergoing treatment there. The Authority verified her request, however we noticed that the Consultant in charge of this patient had already lodged a request so that the patient undergoes treatment at MDH ART Clinic. The Authority informed patient about this, however the patient kept insisting that she was to undergo treatment at the private facility. When the Authority contacted the personnel who had inputted the request on the system, the personnel informed the Authority that rightfully so, the patient was right as she was to undergo treatment at the private facility, however she was instructed to register her through MDH ART Clinic.

The Authority took this incident very seriously and wrote to the Chief Medical Officer under whose responsibility falls the MDH ART Clinic, and the Responsible Person of the MDH ART Clinic, informing them that a private undergoing treatment at St James Hospital has been registered through the ART Clinic at Mater Dei, thus now showing as a patient of Mater Dei and for which a request for treatment and AFT was lodged for the Authority Board Approval.

The Authority insisted with the Responsible Person to make sure that only patients who will be undergoing treatment at MDH ART Clinic are registered through the EEART system of the MDH ART Clinic. Any other private patients not undergoing treatment at MDH are to be registered by the respective private feeder clinic.

In 2021, the Authority received an email from the MDH ART Clinic requesting an urgent approval for a patient which was to undergo an embryo transfer the next day, without the necessary request or approval granted through EEART. The Authority informed the MDH ART Clinic that it is unacceptable that the clinic has scheduled patient for transfer for the following without EPA approval, with request for approval just filed in the morning when patient has started treatment days ago.

The Authority requested the Responsible Person of the MDH ART Clinic to take the necessary steps to avoid this happening again and with Clinic filing request on time, whilst the Authority reserves the right to take the necessary action on this episode.

The Responsible Person of the MDH ART Clinic replied to the Authority insisting that he is in agreement with the Authority and that it is unacceptable to schedule a patient for treatment without the final_EPA approval. He explained that the most senior officer on duty had regrettably not submitted the request to the Authority on time. The Responsible Person assured the Authority that more controls will be implemented immediately to ensure no repeats of the sort and that they take seriously compliance to their regulatory obligations.

In the second quarter of 2021, the Authority received a complaint from a patient that informed the Authority that he had received a call from the private tissue establishment, St James Conception Unit to confirm the number of embryos to be thawed prior to embryo transfer. Patient who was very agitated informed the Authority that his embryos were only to be transferred from the facility to another tissue establishment in Malta and not thawed.

The Authority contacted St James Conception Unit to check out this incident and the private facility filed an incident report on the EEART system in which it was explained that in accordance with standard operating practice, prior to initiating the embryo thawing process, the clinic calls the patient to confirm the process as well as the number of embryos to be thawed.

In this case, there was a slight and genuine oversight in that the contact number contacted was incorrect. No personal details were divulged during the brief telephone conversation. The Authority requested the clinic to take the necessary preventative action so that this incident will not re-occur, and the patient was re-assured that the embryos were still in storage awaiting transfer to the other facility.

In September 2021, an incident was lodged on the EEART system by the MDH ART Clinic that confirmation was received from the regular microbiological monitoring that in a localised spot inside one of the incubators there was a presence of an airborne microbe. The likelihood of this having a negative impact on the culture or the patient is very remote, however, the outcomes of procedures are going to be followed up and a full report will be provided to the Authority and SPH at the earliest.

In the report received from the MDH ART Clinic it resulted that this non-conformance did not affect any other part of the laboratory since no similar or other growth were found in other places and this was a first-time occurrence. The report concluded that the incubator cannot prevent the influx of airborne microbe as the door must be opened frequently during routine use.

The potential root cause is increased activity and hence increasing the risk of potential airborne growth in between and during the clinical activities and laboratory activities. Additional advice was requested from the Head of the Infection control department who concluded that these are sporadic occurrences with very low counts would suggest it is not a significant contamination.

Prevention action was put in place by MDH ART Clinic to sterilise shelves more often, running UV Mode when activity rises, communication among the embryologists and adding a warning to the staff about the hygiene and aseptic techniques rules to be always followed in the lab during processing and while using any consumables or materials.

In September 2021, the Authority received an application for IVF Leave approval from the People Management Department after the receipt of an application by patient which included a declaration for IVF leave purposes that the patient and her partner will be undergoing IVF at MDH ART Clinic with a cycle starting in October 2021.

The Authority noted that patient was not yet registered on the EEART system and no request for IVF or AFR had been made to the Authority and to this effect no IVF was approved to start in October. The Authority requested the MDH ART

Clinic to verify and get back as the Authority needed to approve or decline an internal administration process.

The MDH ART Clinic informed the Authority that patient was undergoing treatment abroad. The Authority then informed the MDH ART Clinic to provide an explanation to why if patient is undergoing IVF abroad, why was a certification from the MDH ART Clinic issued that she is going to undergo IVF at MDH, just few days before.

The Authority informed the Clinic to refrain from issuing further declarations if patients are not officially approved to undergo IVFs at MDH. The Responsible Person at the MDH ART Clinic was also informed to put in place preventive measure, so that this instance does not repeat itself.

In the last quarter of 2021, the Authority was informed that a couple who had an embryo cryopreserved at day 3 were requesting further culture of the embryo to day 5 following thawing before transfer into the woman. The Authority informed the clinic that a decision by the Authority Board will be provided following receipt of the hereunder requested documentation and namely

An Amended Standard Operating Procedure showing that culture of embryos prior to cryopreservation can be held either up to day 3 or up to day 5, as per prior discussion and agreement with prospective parent/s. A new SOP clearly indicating that after the thawing process embryos can either be transferred immediately or else, they can be thawed, cultured up to day 5 and then transferred following request by prospective parent/s and following receipt of implications counselling.

An SOP for implications Counselling by the Infertility counsellors wherein prospective parents are well counselled prior to thawing process, on the implications that the decision to further culture embryos may bring as opposed to thaw and transfer. An amended SOP re request to EPA board for approval for the thaw and transfer of cryopreserved embryos. New amended SOP must clearly indicate if request is being made to thaw and transfer or request is being made for thaw, further culture for another 2 days and then transfer.

The Authority also requested that with immediate effect the Authority will also require that all report sheets of the disposal of non-viable embryos (irrespective if from a fresh or a thaw cycle) are uploaded on the EEART system together with the IVF report. Clinic was also reminded that EPA Act only allows the transfer of maximum of two embryos and that discarding, and research of embryos is not allowed.

After several requests by the Authority to the MDH ART Clinic to submit the requested documentation, we were informed that the MDH ART Clinic will not be proceeding with this request as the couple had retracted their decision to extend culture and were happy to transfer the thawed day 3 embryo.

In the last quarter of 2021, the Authority received a request from ART Clinic MDH on the EEART system for board approval of a couple in a relationship where the male was still legally married to another woman. The Authority has sought the advice of the office of the State Advocate prior to approval or rejection of this request.

The Authority was advised that authorizing this procedure to go on may raise issues of public policy and could be in violation thereof. Article 2(1) of the Civil Code states

that '*The Law promotes the unity and stability of the family*.' Furthermore, sub-article 2 of the same article states that the spouses owe to one another a duty of fidelity. From the information provided the male mentioned does not appear to be in the process of dissolving his existing marriage, nor does he appear to have any intention of doing so. Therefore, by approving such procedure, the State authorities could be seen as aiding extra-marital relationships and jeopardizing the unity and stability of the male's family with his existing wife and child(ren), in violation of the mentioned laws.

On these grounds the Authority rejected the MDH ART Clinic's request for treatment advised that patient is informed accordingly by the MDH ART Clinic. Moreover, the Authority insisted with the Responsible person of the MDH ART Clinic to take the necessary action so that when patients are taken in for their first intake at the ART clinic the above is taken into consideration.

In October 2021, the Authority Board Secretary underwent an exercise to identify files of patients at the MDH ART Clinic that had been approved by the Board in the previous years' however, the Authority noted that although these files were prioritized and approved, procedures were still showing on the EEART as pending to undergo treatment. The Authority requested an explanation from the MDH ART Clinic to this issue.

The Responsible person sent a reply informing the board members that thirty seven (37) patients that the board had approved to do an IVF Cycle were never done and a reason was provided for each patient. The reasons given were that one patient had done the IVF Abroad, another patient became pregnant spontaneously. Two other patients had dropped out as they had a medical condition, another two patients were

not answering the calls of the MDH ART Clinic. Another three patients showed interest in doing the procedure in the coming days and three other patients had opted to go for treatment with a donor instead of use of autologous gametes in the coming child. Nine other patients had chosen to close their file including four of which had already a child through other options. Six patients had informed the ART Clinic that they are not interested anymore to continue with treatment and the remaining then patients were not interested to undergo the treatment at this point that were postponing for later but still wanted their file to remain open.

The Authority informed the MDH ART Clinic that this exercise will be performed on a yearly basis so that the Authority will have a full picture of all the approvals granted and the drop out of patients after approval.

In November 2021, the Authority received a notification of a near miss on the Incident Reporting Platform from MDH ART Clinic. The clinic had received a report from the supplying foreign donor sperm bank, that a mentioned donor, whose gametes had been distributed to Malta was under investigation following the diagnosis of a genetic disorder in a child born from his donation in another country.

Further genetic testing was to be done on the donor by the supplying foreign sperm bank to identify the root cause. The mentioned sperm sampled from this donor were received at the MDH ART Clinic in August of 2021, however had not yet been used by the prospective parent as she had not yet started the treatment process at the MDH ART Clinic.

As sperm from this donor should not be used for treatment the four sperm vials received in Malta were removed from released storage and were transferred to a Quarantine Storage until further update from the supplying foreign bank to transfer them back to them. The Authority has also taken the necessary measures to block this donor on the EEART platform.

In December 2021, the Authority Board Secretary notified the ART Clinic regarding missing embryo Cryopreservation agreements and informed them that the MDH ART Clinic is obliged by Article 7 of the Embryo Protection Act to draw up these agreements with prospective parents, prior to cryopreservation.

'Embryos which cannot be transferred into the prospective parent within a treatment cycle shall be cryo-preserved in licensed tissue establishments for future use by that prospective parent: Provided that the cryo-preservation of embryos shall be regulated by an agreement between the prospective parent or prospective parents and the licensee subject to the prior authorisation of the Authority and shall have a maximum term of validity of five years renewable up to a maximum permissible age for the transfer thereof into the prospective parent in terms of the Protocol'

Seventeen embryo cryopreservation agreements were still pending, four of which were for cryopreservation of embryos carried out way back in October 2021.

The Authority gave a deadline up to a definite date in February for the agreements to be provided, sixteen agreements were provided, and one was still pending as patient was in quarantine and could not sign. However, after a decision taken in the

next Authority board meeting, it was resolved that breaching Articles of the Act is a criminal offence, and that other instances of breach of this article or any other article of the EPA Act, will have to be reported to higher Authorities for further investigation.

During 2021, the Authority received several complaints from patients who had undergone or were in the process of undergoing treatment at the public tissue establishments. Most of the complaints were mainly on the long waiting list and the waiting time to undergo the procedure on the NHS, when we all know that time for these patients is a ticking bomb. Other complaints received were that patients wished to be seen directly by the consultants however sometimes were seen by their seniors or other doctors. Another complaint received was that patients wished to have a more personalised protocol. One other patient complained that while ART Clinic MDH had informed her that she could not undergo and IVF cycle due to a needed medical intervention which could not be done at MDH, the patient had the intervention carried out at a private facility and then went abroad at her own expense and had a successful pickup and embryo transfer abroad. Patient complained that no one had guided her if she could have been sent internally through tissue establishments.

One particular patient complained that she had undergone IVF treatment at both the public and private facilities, however whilst at the private facility all bloodwork and necessary paperwork were completed in two or three visits with the Consultant, at the MDH ART Clinic these were spread on several outpatient visits, with some of the visits merely being called just to sign necessary consents and paperwork. Patient complained that this not only meant loss of time but also the reason why patients had longer waiting list time at MDH ART Clinic.

During one of the Board meetings of the Authority, the Board secretary informed the members that from requests received to be approved by board, it was evident that MDH ART Clinic were calling patients not as per listed in the Prioritisation lists which the ART Prioritisation Committee lists in order of precedence.

The Board was also informed that a particular patient from the latest report issued prior to the Board meeting had scored not to high was called prior to other patients in the previous reports and prior to all the patients that scored before her in the same report she was prioritised in. The Board resolved that a letter is to be sent by Hon Judge Sciberras as Chairperson of the Authority on behalf of the Board to Dr Denis Vella Baldacchino, the then CMO responsible for the MDH ART Clinic, and copied in were Permanent Secretary Mr Joseph Rapa and Profs Yves Muscat Baron as the Clinical Chairperson.

The Permanent Secretary informed the Authority that this issue was raised with the new Chief Medical Officer Dr Walter Busuttil, and an investigative board will be appointed to investigate the matter and report back to CMO and Permanent Secretary, who will then report outcome to the Authority. This board of investigation was still undergoing the process by end of 2021 and the Authority still awaits outcome of same.

In the last quarter of 2020, the Authority was also notified that a complaint had been filed by a couple with the Ombudsman Officer against the MDH ART Clinic, in relation to the conduct, treatment received, action and/or inaction of the ART Clinic personnel regarding the couple's treatment procedure. The couple are requesting redress and the Ombudsman to conduct an investigation.

The file is currently being processed by the Ombudsman's office and during 2021 communication was made with the Authority by the Ombudsman's office on same case. The Authority still awaits outcome of same.

1.16 Other work by the Authority

Apart from the normal processing of all applications for treatment, requests for additional fertilizations, and the storage of gametes (a detailed report is given in the second part of this report), the Authority was in continuous communication with the Ministry for Health in order to provide the relevant information in answer to the several Parliamentary Questions (PQs) repeatedly made on the ART procedures offered on the NHS, and the Eligibility Criteria as established in the Embryo Protection Authority's Protocol. The CEO was also in constant contact with the Chief Medical Officer's office to advice on other matters and especially on the amendments required to the NHS eligibility criteria, which came into effect in 2020 through DH68/2020 and amended again in 2021.

Authority personnel have also attended several Conferences online to keep abreast with the changes being held in the various sectors. Such as the Social Determinants of Health Conference and the CRPD Conference. The Authority also attended the LGBTIQ+ conference, wherein the Authority gave its contribution on the important role it plays in providing cryopreservation of gametes to patients prior to receiving hormonal treatment. Attendance was also made to the Conference organised by the Primary Health Care.

The Authority's Chief Execute Officer attends monthly the Ministry Management Board meetings called by the Permanent Secretary of Health which discuss the various Health matters.

Together with the office of the Chief Medical Officer work was also ongoing on the changes needed to the Entitlement Criteria of patients applying for services on the NHS, these needed to be updated to include Intra-Uterine Insemination (IUI) and non-partner third party donation now also to be in line with the new Maltese Legislation. A lot of input was also made by the Authority on the changes and documentation needed to now cater for the introduction of direct and non-direct third-party donation.

Another joint venture held with the office of the Chief Medical officer and Mater Dei Hospital Finance office as well as the Cross Border Committee was the establishing of all individual services and the breakdown of every ART procedure into segments to enable the issue of the proper costings for each part of the procedure. This would be later used for the re-imbursement of costs incurred by patients who would apply through the cross-border committee for funding.

Several meetings were also held in 2021, in conjunction with the Chief Medical Officer's audit office, Mater Dei, Obstetrics and Gynae Department, Central Procurement and Supplies Unit, Directorate for Pharmaceutical Affairs, Permanent Secretary as well as with the Hon Deputy Prime Minister and Minister for Health re the introduction of free stimulation medication for the patients undergoing the process at the MDH ART Clinic as announced in the Health Budget.

Several meetings were also held with the Chief Medical Officer's office, firstly with the outgoing CMO and with the newly appointed CMO re the way forward for the ART Services carried out at the MDH ART Clinic. These meetings were held in conjunction with the CEO of Mater Dei, the Managing Director of CPSU and the Licence Holder of the MDH ART Clinic.

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

In February 2019, the contract was awarded to a software company that immediately started on the Software Development Procedure, the detailed analysis and design phase as well as the system customisation of the application that satisfy the functional, technical, and business requirements have all been completed by end of year 2019. A prototype was made available by first quarter of 2020 for user testing and any re-work necessary on the system. Final implementation of the system and issuing of software licences as well as data migration was ready by end of 2020.

This high-end software system for the Electronic Exchange and filing of Assisted Reproductive Technologies (EEART) that meets the current and future requirements of the Embryo Protection Authority to link the said Regulatory Authority with all ART Registered Clinics both public and Private.

This project of €100K+ investment provided from local funds under the Ministry for Health, included the development of tailor-made software according to the Maltese Legislation regulating the ART Sector and will be handling all applications for treatment, approvals for additional fertilisation, oocyte and sperm collection, fertilisations, embryo transfers, gamete and embryo storage, pregnancies and life births, and embryo adoption, all to be filed online.

It will also provide for the handling of Intra-Uterine insemination procedures, as well as the cryopreservation and storage of gametes and embryos for patients prior to receiving oncology treatment for preservation of fertility for future use. The system provides also for the movement of gametes and embryos between tissue establishments in Malta as well as the distribution of gametes and embryos to and from foreign clinics.

This system also features, as required by the EPA Act, the keeping of registers of all assisted reproductive procedures carried out in Malta. It also supports the encryption of donor identity data which will be held at the Authority and will only be released if the donor conceived child requests this information on attaining age of majority.

This project now enables real time statistics on the events being held in the ART field in Malta. It is currently installed at two Tissue Establishments and two ART Storage banks as well as ten clinics registered with the Authority. It also supports the possibility of including other clinics who will opt to offer ART services in the future.

Prior to launching of this project all staff at the Embryo Protection Authority as well as the staff at all the clinics were provided with adequate training and a user manual of the EEART system. The user manuals are updated from time to time with every new upgrade to the system and are sent to all the stakeholders.

On the launch of the EEART system, and its go-live in January 2021, the CEO of the Authority Ms Simone Attard, thanked her staff, a very small team, who worked literally round the clock to make this project possible and inputted over 6000 transactions in the system, so that all the procedures which were manually documented since the Authority was established in 2013, are now also accessible through the EEART system.

The Embryo Protection Authority, through its Chief Executive Officer, during 2021 was also in continuous discussion with the Ministry for the Family and Social Solidarity and the Ministry for Social Dialogue, Consumer Affairs and Civil Liberties, to update the Legal Notice that was issued on the 31st of May 2017, granting Special Leave for Medically Assisted Procreation to now be in line with the New Amendment Act. Amendments were necessary to now include also single women and same-sex couples.

The changes came into force by Legal Notice 263/2020. These changes were further enhanced and now also included in the Public Service Manual and all applications for leave are being approved in line with these legal notices.

The Embryo Protection Authority, through its Chief Executive Officer, during 2021 also attended to meetings organised between the Ministry for Health and the Ministry for the Family and Social Solidarity and the Ministry for Social Dialogue, Consumer Affairs and Civil Liberties, regarding the implementation of Policies on the Rights of the Child. During these meetings the Additional Protocols of the Oviedo Convention were also discussed amongst which those concerning the Protection of Human Rights and Dignity.

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

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

During 2021, the Authority was also requested to give its feedback regarding the launch of the Transgender Medical Services and to assist the transgender clinic in any clarifications they may require. An online meeting was held with the transgender clinic on way forward.

This issue was being brought to the attention of the Authority as prior to transgender persons starting hormone therapy, a request will be made to EPA Authority to authorise cryopreservation of gametes to preserve fertility.

The Chief Executive Officer attended several meetings and gave constructive input on the subject. This contribution was acknowledged by the 'Sexual Orientation, Gender Identity, Gender Expression and Sex Characteristics' (SOGIGESC) Unit within the Human Rights and Integration Directorate, during their Annual Conference. This was also highlighted in the LGBTIQ Equality Strategy and Action Plan 2019 - 2022 Annual Report for September 2020 to September 2021 wherein it was mentioned that the EPA Authority had revised its protocol in line with SOGIGESC. In 2021, several enquires were made to the Authority for cryopreservation of gametes prior to transitioning process and receiving of hormone therapy.

One of the functions of the EPA is to see that all prospective parents receive clinical counselling. During 2021, the Chief Executive Officer, who is also a warranted Infertility Counsellor, was invited to give several sessions and information to Maltese Counsellors, family therapists and other professionals working in the family field about the changes in the Embryo Protection Act and the implications counselling that now needs to be offered to all accessing treatment.

In 2021, the British Infertility Counsellors Association (BICA) Accredited by the Counselling and Psychotherapy Central Awarding Body (CPCAB) which is the only Awarding Body to specialise in Counselling, invited the Chief Executive Officer to contribute to the Journal of Fertility Counselling.

Previous articles were also published in the summer edition of the Journal detailing the journey from the initial contribution by Mrs Attard to the Maltese Parliament way back in 2004 to the introduction of the Principal Embryo Protection Act and the latest Amendments to the Act were highlighted as well as the way forward. These publications, and the way Malta has progressed in this sector were always well received by our counterparts in other European Countries.

Since the Authority processes personal data, in 2017 it took the necessary measures to be in conformity with the Data Protection Act, and duly registered its operations with the Commissioner for Data Protection and appointed a Data Protection Officer to take care of Data Protection issues. To this effect with the introduction of the New Amendment Act, the Authority underwent the exercise of Data Protection Impact Assessment for all new processes that were being introduced.

The Authority's website was launched on the Ministry for Health's portal, though continuous collaboration with the Information Management Unit of the Ministry for Health in 2017. The website contains the Authority's Mission Statement, details about the Entity's Corporate Identity, Board Members and Executive Administration together with an Organisation Chart. All publications of the Authority have also been uploaded and these include: The Act and Legal Notices, EU Directives, Authority's Protocol, and all Annual Reports issued to date. During 2020, the website was being continuously amended and uploaded with the new changes that came into effect. The website can be accessed on www.epa.gov.mt .

During 2021, the Authority received an invitation to hold a meeting with the New Commissioner for the Rights of Persons with Disability, this meeting was called following the mention in the media of changes to the Embryo Protection Act that will include Surrogacy and Pre-Implantation Genetic Diagnosis.

This meeting was attended by the Chief Executive Officer on behalf of EPA, the Commissioner Ms Samantha Pace Gasan, Ms Solange Bonello, Mr Bernard Busuttil and Ms Rhoda Garland on behalf of the Commission. During this meeting access to Assisted Reproduction Techniques by persons with a disability was also discussed.

During the whole calendar year, the Authority was invited by various media stations to attend to various programmes both televised on different tv stations especially on the National Television station TVM, the Authority was also invited to attend radio programmes aired on various radio stations. In these programmes the Authority was invited to inform re the procedures being carried out due to the Covid 19 situation, as well as the general work of the Authority and following the Annual publication of the Authority report and other achievements of the Authority.

1.17 National and International Recognitions

In September 2021, the Deputy Prime Minister and Minister for Health Hon Chris Fearne presented the Authority Chief Executive Officer, with the 'Heroes of the Pandemic' commemorative coin. A National token of appreciation for the commendable work in difficult time and trying circumstances as well as selfless effort and dedication during the Pandemic.

All EPA staff worked continuously round the clock to provide support to patients, a coin will also be provided to all staff in the first quarter of 2022.

In October 2021, the Authority received the good news that the Authority was nominated in two categories in the prestigious awards of the 'Premju Nazzjonali Haddiema tas-sena 2021'. The Worker of the Year National Awards 2021 are about showcasing best practice and, as of this year focused on improving the personal and professional development of the worker on the workplace and in the community.

The aims of these awards are to give recognition to the challenges of work life, setting and environment; to promote best practice and celebrate success; improve understanding of the range of work and an appreciation of quality work; celebrate and promote sustainability and social responsibility.

In December 2021 our hard-working Chief Executive Officer Ms Simone Attard was presented with certificates of recognition for her achievements as she was nominated in both the National Worker of the Year Award, 2021 and the Head of Entity Award, 2021. On the night, all the Authority personnel congratulated Ms Attard and felt proud of forming part of the team led by this hard-working lady who never tires to provide sterling work and bring about changes to the fertility sector.

In December 2021, the Embryo Protection Authority, as the Maltese Competent Authority on Medical Assisted Reproduction, also received International Recognition.

This recognition was awarded by the 'European Atlas of Fertility Treatment Policies' which is composed of the European Commission, ESHRE (European Society for Human Reproduction and Embryology) and Fertility Europe (a patient Association).

This international recognition classified Malta with a score of 'Very Good' obtaining 71% and placed in the second-best category together with United Kingdom, Sweden, Spain, Finland, and Denmark. Malta was classified in a better position than other countries who have been offering these fertility services for many years, amongst which are Germany, Italy, Austria, Cyprus, and Ireland. Classification was made on Legislation, Regulation, Registers held, Non-Anonymous Donation, Access to service and funding as well as the offer of psychological support. This international recognition is a way of celebration to the hard work of the Authority, and to what it has achieved in the last nine years and is also a push to complete to work hard to achieve more for your prospective parents.

1.18 Annual submissions and debate in Parliament

Pursuant to the EPA Regulations of 2015, the Authority is taking the necessary measures towards becoming fully autonomous and to this effect in July 2021 sent a letter to all Tissue Establishment Licence Holders and to the Heads of IUI Centres.

In this letter it was explained that changes to Article 29 of the Protocol were being made so that in line with moving forward so that the Authority will become totally autonomous it is envisaged that fees from the sector – Clinics and Tissue Establishment will cover the majority of the costs of Regulation.

It is the vision of the Authority that when, in the coming years, the number of cycles increase from various Tissue Establishments, these will fully fund the cost of Regulation and at that point the Authority becomes fully autonomous and will not depend on funding from the Central Government.

The Deputy Prime Minister and Minister for Health, Hon. Chris Fearne on the 15th of March 2021, laid on the Table of the House of Representatives, the Embryo Protection Authority's Audited Accounts for 2020 and Financial Estimates for 2021, together with the Authority's Annual Report for 2020. A Parliamentary debate on the Authority's finances and work was held in one sitting on Wednesday 30th of June 2021 in the morning and a vote taken in plenary on same day Wednesday 30th of June 2021 in the evening.

FERTILITY TREATMENTS IN MALTA FOR 2021 – 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, 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 Licence Holders of the Clinics as at 28th February 2021.

Article 22 of the Embryo Protection Act, which came into force on 1st October 2018 also requires that all medical practitioners keep a register with full details of all medical assisted procreation procedures, including also Intra Uterine Inseminations and pass this information without delay to the Authority.

Information about our data

These are official statistics of treatments carried out between 1st January 2021 and 31st December 2021 as recorded by the Tissue Establishments and Clinics themselves on the EEART platform. The Embryo Protection Act made it a legal requirement for every fertility clinic in the Maltese Islands to submit information on all fertility treatments and children born as a result to the Embryo Protection Act activities. The Embryo Protection Authority, as also required by the Act, holds a Register of these treatments since 2013, which is the largest database of fertility treatment on the Maltese Islands comprising all activities held in the Public and

Private fertility clinics. This Register also holds detailed information on partner intrauterine insemination (IUI) and activities using donor gametes. As an Authority we produce this statistical release on an annual basis. As Regulator and the holder of the statutory Register of fertility treatments, we take our responsibilities for information management and security most seriously and have a low tolerance for information risks. We have taken all the necessary measures in keeping secure the information we hold, particularly sensitive personal patient and donor data. It is our highest priority, and this principle has framed our approach to the implementation of more digital projects for backup and recovery plans in 2022.

Accuracy and reliability

We report on cycle level information rather than patient level information. We however also include a section on the number of patients doing multiple cycles. For a typical cycle, clinics will initially report patient registration, cycle-related information and early outcomes including pregnancies in line with the Authority Protocol, once the birth is registered clinics will subsequently report the outcome of cycles for which they reported a pregnancy, if a miscarriage takes place, this is also reported to the Authority.

The Register undergoes regular validation – this was last completed in December 2021. Treatment cycles performed on or before 31 December 2021 have been verified along with their pregnancy status. Live births have been verified for treatments that took place in early 2021. Other subsequent live births occurring in 2022 for cycles carried out in 2021 are registered as Expected live births in this Report. The Actual live births for the full year 2021 will be included in the report of the following year.

2. CYCLES PERFORMED

2.1. Cycles, Intra Uterine Inseminations and Cryopreservations Approved by the Embryo Protection Authority Board

With the introduction of the amendments to the law, embryo cryopreservation was now possible to be carried out as part of the cycle if the prospective parent/s opted for it together with embryo donation if necessary. Prospective parent/s could still opt for the request to fertilise two oocytes only and have them transferred without embryo cryopreservation. As new types of cycles where being introduced during 2021, we are hereby providing the definitions for the terminology being used in this year's Annual Report.

A **Cycle** refers to all treatments that are conducted at a fertility clinic. **Oocyte cryopreservation cycle** is a treatment where prospective parent/s have all their oocytes collected and cryopreserved for future use due to medical reasons or for other social reasons. **Fresh oocytes treatment cycle** is a treatment cycle in which fresh oocytes are collected and are injected with sperm which may result in a fresh embryo which is transferred during IVF. IVF treatments in this report include ICSI. **Thaw oocyte treatment cycle** is a treatment cycle where prospective parents use their cryopreserved oocytes in an IVF treatment cycle. **Cryopreserved / Thaw embryo treatment cycle** is a treatment cycle in which a frozen embryo or embryos are transferred during IVF. Maltese Legislation allows only for the maximum of two embryos (irrespective of fresh or cryopreserved embryos) to be transferred in each treatment cycle. **Embryo 'freeze all' cycle** is a cycle in which all created embryos are cryopreserved due to the patient either having a risk of OHSS or else some other medical reason which at the time of the cycle the embryos cannot be transferred into

the woman. **Sperm Cryopreservation** refers to cryopreserved sperm which can be produced through a fresh ejaculate or else surgically extracted. **Intra-Uterine Insemination (IUI)** is a treatment cycle where sperm is injected into the women's uterus.

For the first time in the Annual report, we are not only reporting the use of partner sperm in IUI's or IVF/ ICSI but have now also included the use of donor sperm in such treatments. Moreover, the term prospective parents this year includes both heterosexual couples, same-sex female couples and single women.

Throughout 2021, although with all the restrictions of the pandemic, the Authority has received and a total of **Nine hundred and four applications (904),** which is a record number of requests considering the Four hundred and eighty-three (483) applications received in 2020 and, the five hundred and thirteen (513) applications recorded for 2019. These approvals were issued for different procedures carried out by clinics in both the private and public sector. These were divided into **six (6)** approvals for **Oocyte cryopreservation cycle** where oocytes were retrieved and cryopreserved only on prior approval by the Authority due to medical reasons prior to receiving oncology treatment so no IVF procedure was carried out following the retrieval. Another **one (1)** approval was granted for **Oocyte cryopreservation cycle** for the preservation of oocytes to a female prior to receiving hormonal treatment prior to transitioning to a male. Another **one (1)** approval was issued to the private tissue establishment for **Oocyte cryopreservation cycle** for social freezing reasons. These requests were made by **seven women**. Another **two hundred and twenty-nine (229) applications** were approved for **Fresh oocytes treatment cycles** by **224 heterosexual couples and one single women** as there were couples who had more than one approval for Fresh oocytes treatment cycles in the same year. An increase of applications was registered over the previous year.

Only **four (4) applications** were filed, and approvals were granted for **Thaw oocyte treatment cycles** carried out by **four (4) heterosexual couples.** All these applications for thaw cycles came from the private facility as MDH ART Clinic did not undergo any oocyte thawing processes. **One hundred and seventeen (114)** approvals were issued for **Intra Uterine Inseminations** using partner sperm to **70 heterosexual couples.**

Twenty-six (26) applications, out of the **29 applications filed,** were approved for **the distribution of donor sperm from abroad. Two** further applications were approved to undergo **a fresh oocytes treatment cycles using donor sperm by one single women.** And **ten (10)** approvals were issued for **Intra Uterine Inseminations** using **donor sperm** to **8 heterosexual couples and two single women.**

A total of **One hundred and sixty (160)** approvals were issued for **Cryopreserved / Thaw embryo treatment cycles** in which a frozen embryo or embryos were transferred, here again an increase was registered over 2020 were only sixty-nine requests had been made. **Ninety-six (96) sperm cryopreservation** were approved for **96 males.** There were **two hundred and five (205)** requests for **Additional fertilisations,** all the requests were approved by Board.

Ten (10) approvals were granted to **four (4) heterosexual couples** to transfer oocytes between Maltese Tissue establishments, **three (3)** approvals were further granted to **three (3) heterosexual couple** to transfer sperm between Maltese Tissue establishments, whilst **four (4)** approval was issued to **four heterosexual couples** to transfer embryos from the public to the private tissue establishment.

Another **three (3)** approvals were granted to transfer sperm from abroad to Malta. This approval was issued to **three single males. One (1)** approval was issued for **the transfer of embryos from UK to Malta to one heterosexual couple.** Whilst a **One (1)** request was made for the **transfer of oocytes from Malta to abroad by one single women.**

Thirty-eight requests were received and approved from prospective parents who wished to discard their **frozen oocytes and sperm stored** both at the public and private facility.

Thus during 2021, the Embryo Protection Authority approved 904 procedures for heterosexual couples, single women, and males. An increase in all sectors over 2020.

2.2. Intrauterine Inseminations

Since the Authority was established in 2013, this is the third year in which the Authority is presenting statistics of Intra Uterine Inseminations carried out in Malta, as prior to the coming into force of the amendments to the Act, only IVF/ICSI procedures were required to be registered with the Embryo Protection Authority.

Intra Uterine Insemination (IUI) is a type of fertility treatment in which the better-quality sperms are separated from sperm that are of lower quality, non-motile or of abnormal morphology. These sperm are then injected directly into the uterus. This procedure may be performed using partner's sperm or donor sperm (known as donor insemination).

IUI may be used in the treatment of prospective parents who need donated sperm but have no female fertility problems, including single women and same sex couples. It may also be used by heterosexual couples who have a male factor infertility and thus need donated sperm. IUI may also be used by heterosexual couples who have unexplained infertility as a first step prior to moving on to IVF, however as it is less invasive and less successful, normally several cycles are performed.

Up to 31st December 2020, only IUI's with partner sperm were being performed, as although the public tissue establishment had a licence to process, distribute and make use of transfer of donor sperm no procedures were reported to the Authority. Local direct non-partner donation was also allowed at MDH however again no IUI's were reported using direct donated non-partner sperm.

As the law came into force in 2018, one private clinic registered with the Authority to perform IUI's with partner sperm. During 2019, seven other clinics, six in the private sector and one in the public sector registered with the Authority to perform IUI's with partner sperm, and during 2020 another three registered with the Authority. In 2021 one other private clinic registered with the Authority bringing the total to twelve clinics that are registered to perform IUI's with partner sperm.

In May 2020 MDH ART Clinic was licenced to perform IUI's with donor sperm also.

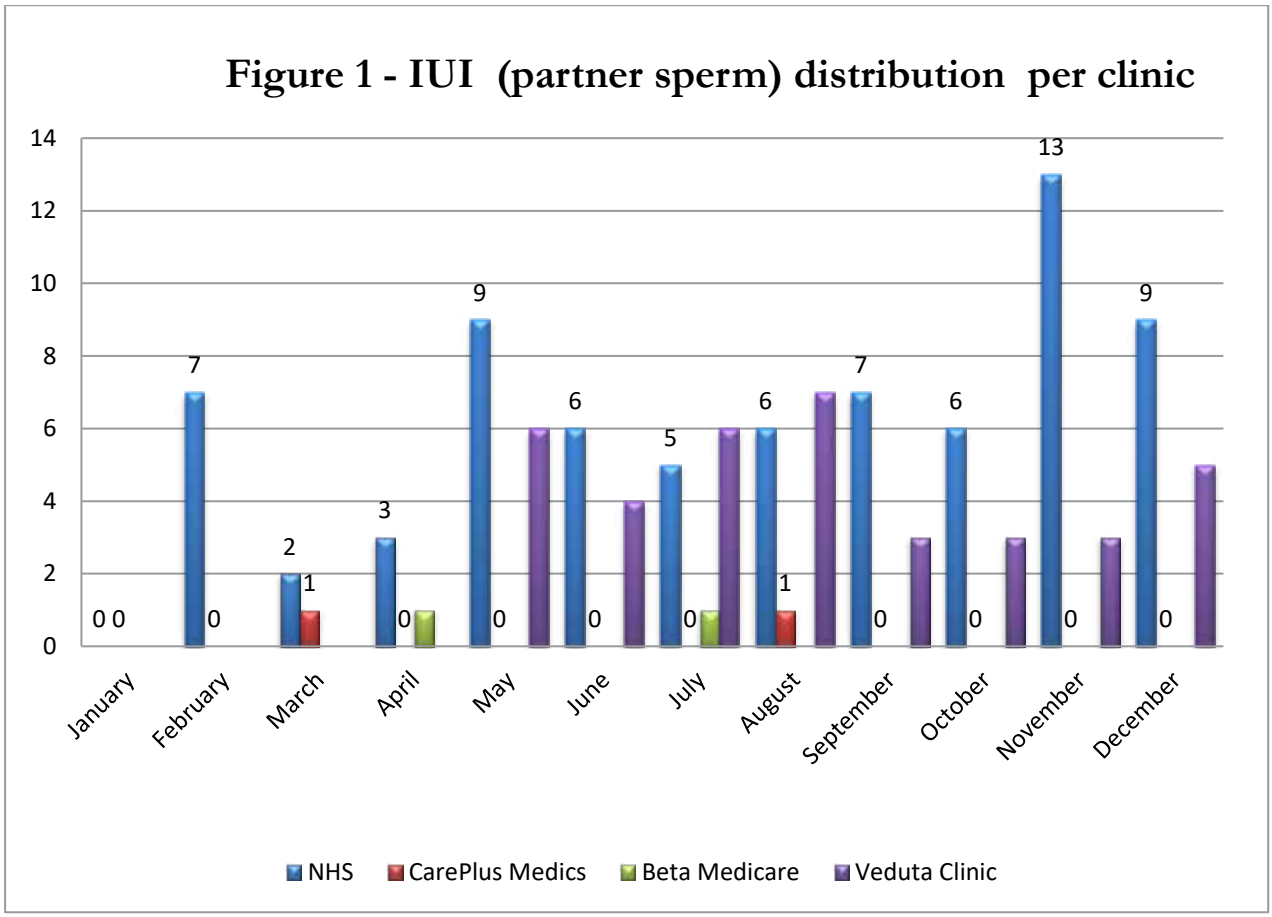
Due to the pandemic, out of the twelve clinics registered with the Authority, eight clinics informed the Authority that they had suspended treatment with IUI and thus had nothing to report for 2021. Thus, IUI reporting is for four clinics, three in the private sector and one at the public facility registered with the Authority.

2.2.1 Intra Uterine Inseminations with partner sperm

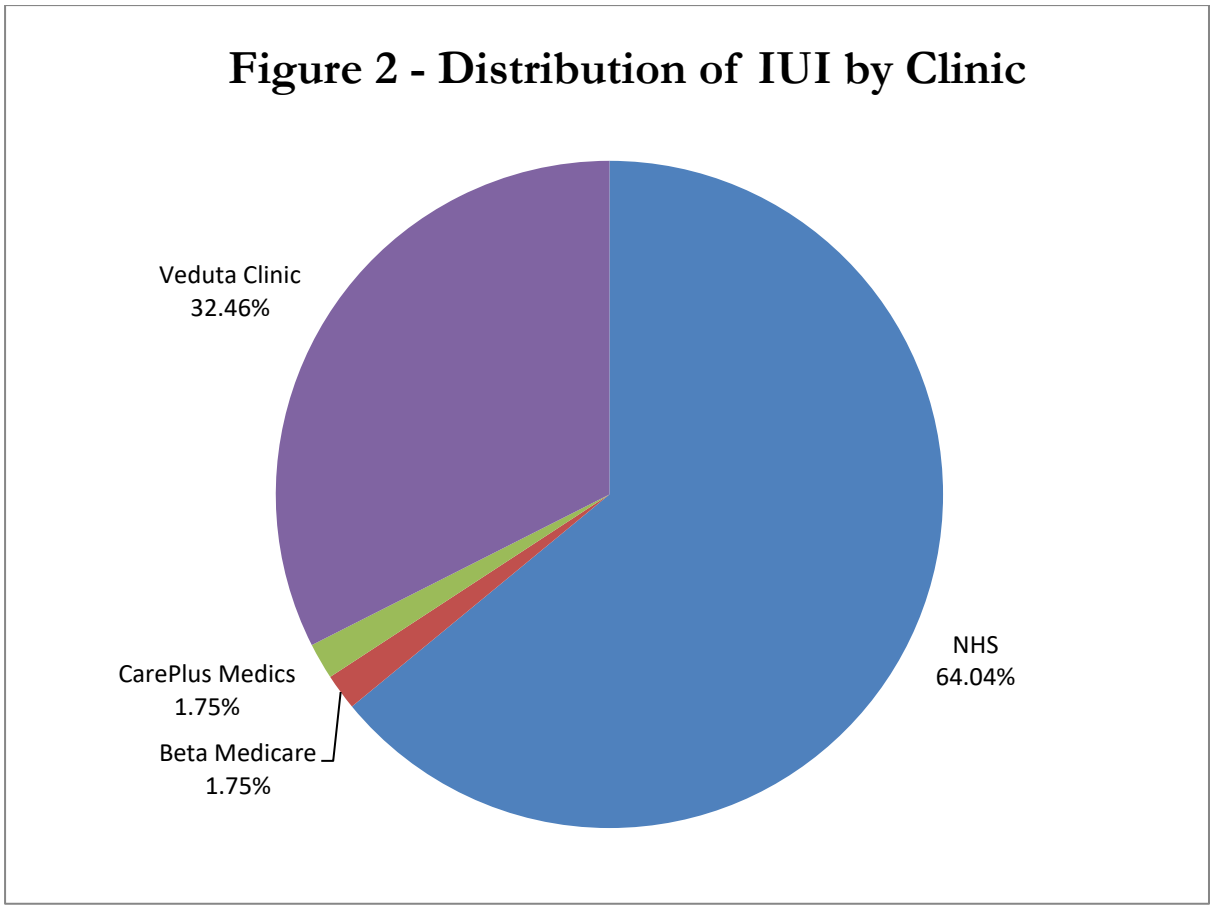
A total of 114 Intra Uterine Inseminations have been reported to the Authority as carried out up to end of 2021.

Seventy-three (73) IUIs or 64.04% of total IUIs were carried out at the MDH ART Clinic, followed by thirty-seven (37) IUIs or 32.46% of total IUIs were carried out at Veduta Clinic, whilst the remaining four (4) IUIs were carried out at Beta Medicare and CarePlus Medics Clinic. It is to be noted that whilst at MDH ART Clinic IUI

procedures were carried out throughout between February and December 2021, the private clinics offered their services to the patients between March and December 2021. (Figures 1 and 2).



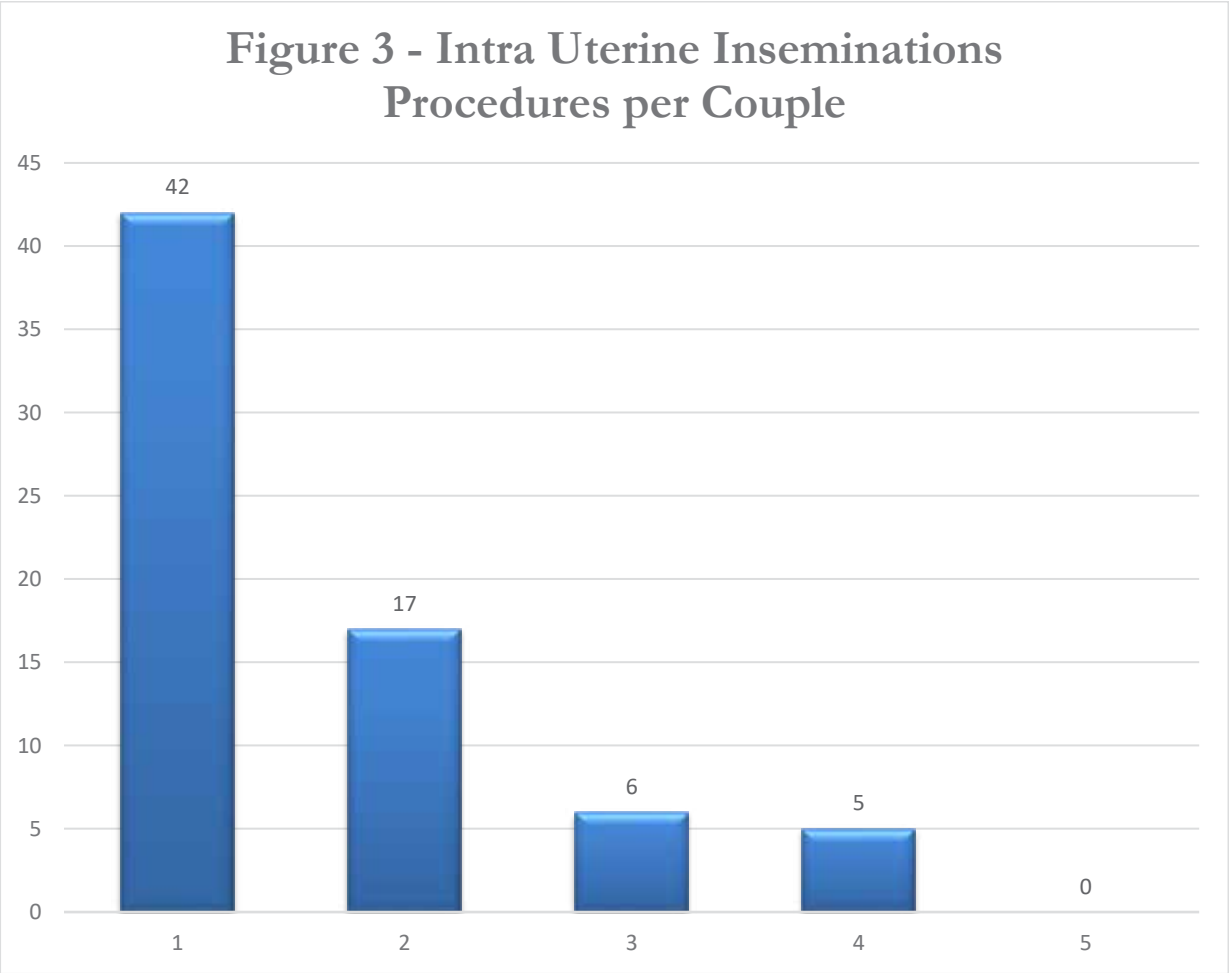
The 114 IUI's were carried out by 70 heterosexual couples using partner sperm. The procedures were undertaken by women aged between 25 and 43 years which is a shorter bracket when compared to ages of year 2020, that ranged from 18 to 48 years, whilst the male partners were aged between 26 and 60 years, same parameters as last year.



The majority of couples forty-two (42) had undergone one session of IUI during 2021, followed by seventeen (17) couples who underwent two sessions in the same year at. Six (6) couples were reported as having 3 IUIs during 2021 Five (5) couples were reported as undergoing 4 sessions of IUIs in one calendar year. From records filed on the EEART, there were patients who did IUI's at both the private and the public clinics in the same calendar year.

Contrary to what was reported in 2020, this year the majority of IUIs 64.04%, were carried out at the public facility, while all private facilities together carried out 35.96% of all IUIs. This contrasts with figures of 2020 were the majority of IUIs 60.68%

were carried out in the private facilities whilst only 39.32% were carried out in the public facility.



It is well known that Intra Uterine Insemination procedures are less successful than the more invasive IVF/ICSI procedures. In fact, out of the 114 cycles carried out, only four (4) pregnancies were reported, all at the MDH ART Clinic and no pregnancies were reported from the private facility. One woman suffered a miscarriage, thus only three women have remained pregnant. One of the women gave birth to a boy in 2022 and the other 2 women are still expecting to give birth to singletons.

Thus, from data submitted to the Authority for 2021, **take-home baby rate for IUI's using partner sperm is only of 2.63%** which is a drop of 1.57% from the 4.27% figure reported in 2020 and the 4.62% reported in 2019. (Figure 4).

Figure 4 - Intra Uterine Inseminations with partner sperm - Take-home baby Rate

2.2.2 Intra Uterine Inseminations with donor sperm

Use of third-party donation was allowed in Legislation in 2018, and Superintendent of Public Health issued a Licence to the MDH ART Clinic in May 2020 for the non-partner sperm distribution from abroad, to be used in open donations in Malta. However, it was only during 2021, that this activity started to be practiced at the MDH ART Clinic in September 2021.

The Authority in 2021 approved the use of twenty-six (26) donors, whose sperm would be used in Malta in one prospective parent/s only, after verifying that they are in line with Maltese Legislation. Nine (9) intra-uterine inseminations with donor sperm were held in 2021, by six (6) prospective parent/s.

Four (4) heterosexual couples, three of which underwent the IUI process with donor sperm twice during 2021 and two (2) single women benefited from the first introduction of IUI with donor sperm.

Out of the 9 procedures carried out, one (1) heterosexual couple and one (1) single woman became pregnant on their first attempt of IUI with donor sperm and are both expecting singletons.

Thus, from data submitted to the Authority for 2021, **take-home baby rate for IUI's using donor sperm is of 22.22%, which is nearly ten times higher than the 2.63% success rate resulting from use of partner sperm.** (Figure 5).

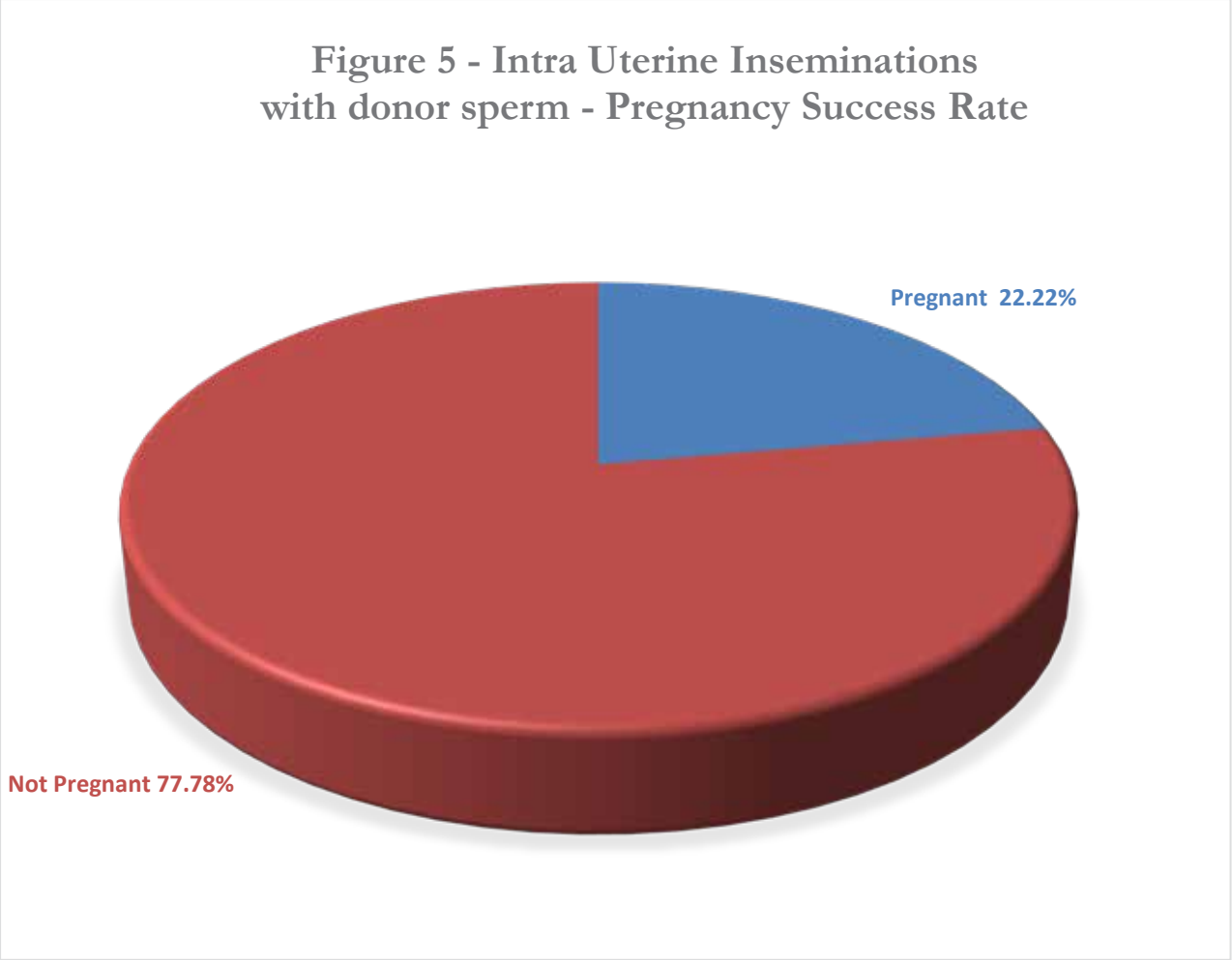
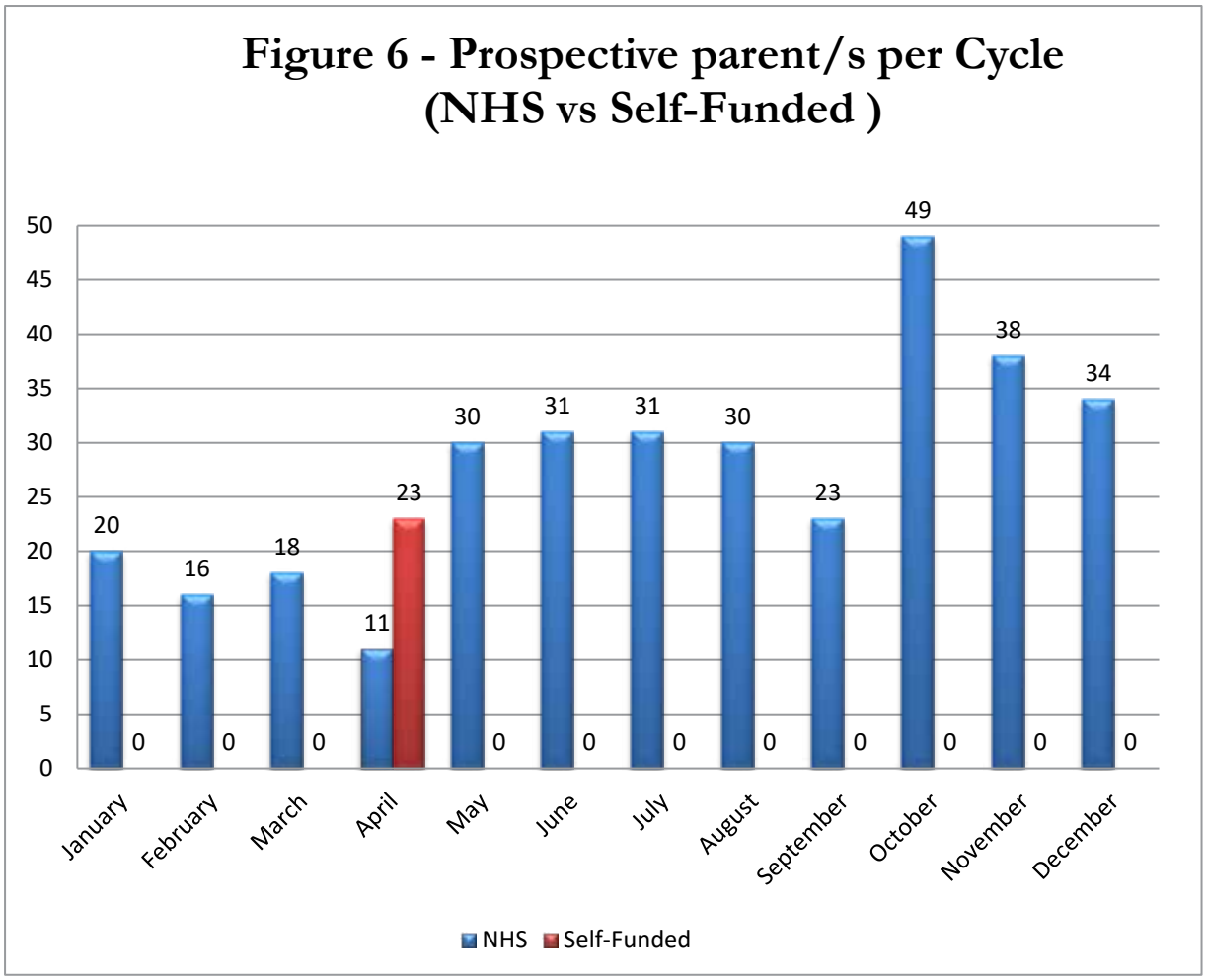


Figure 5 - Intra Uterine Inseminations
with donor sperm - Pregnancy Success Rate
Pregnant 22.22%
Not Pregnant 77.78%

2.3. Cycles and Treatment Cycles carried out by the Tissue Establishments. (IVF/ ICSI and Cryopreserved Embryo Treatment Cycles)

Three hundred and thirty-one (331) procedures (not treatment cycles) have been carried out at the ART clinic in Mater Dei Hospital (MDH), and twenty-three (23) procedures were performed in the private sector at the Assisted Conception Unit in St James Hospital, thus a total of 354 procedures were carried out in Malta in 2021 compared to the 214 carried out in 2020. (Figure 6).



These 354 procedures were carried by 353 heterosexual prospective parents and by one single woman who made use of donor sperm for her ICSI cycle.

The number of ART procedures carried out in Malta in 2021 increased by 65.42% over the previous year, which is mainly attributed to the fact that in 2020 less procedures were carried out at the MDH clinic as the clinic had stopped activity due to Covid-19 measures in place. The private clinic registered a decrease of 11 procedures, over the procedures carried out in the private clinic in the previous year. Again in 2021, the private facility did only one batch of procedures, same as 2020, which differs to previous years when a minimum of three batches used to be held in one calendar year.

One also must point out that the 23 procedures carried out at the private facility are now being held by three feeder clinics a decrease of one feeder clinic over 2020. As of 2015 at the St James Conception Unit procedures of patients of St James Hospital and patients of St Claire's Medical Services were being carried out. In 2020 the addition of procedures of patients of Veduta Clinic and Melody Clinic were added to the St James Conception Unit. It is to be noted that in 2021, Melody Clinic did not perform any procedures.

Out of the twenty-three (23) procedures carried out in 2021 at the private clinic, one case was prior approved to be a 'freeze all oocytes cycle' for social reasons. One other case was reported as a risk of Ovarian Hyperstimulation (OHSS) after fertilisation of the oocytes were carried out thus all embryos had to be cryopreserved. Thus, twenty-one (21) procedures could lead to a treatment cycle. Two of the 21 procedures carried out did not have a successful fertilisation, thus only nineteen (19) cycles resulted in a completed treatment cycle from which a pregnancy could result.

On the other hand, at the MDH ART Clinic from the three hundred and thirty-one (331) procedures carried out, six were prior approved 'freeze all oocytes/ embryo cycle' oncology cases, another cycle was for fertility preservation prior to transitioning from female to male, which was approved for freeze all, thus three hundred and twenty-four cycles (324) could lead to a treatment cycle. However, four of the procedures carried out did not have any oocytes for collection, another two had immature oocytes whilst another three of the procedures carried out did not have a successful fertilisation, thus only three hundred and fifteen (315) cycles resulted in a completed treatment cycle from which a pregnancy could result. One hundred and forty-one (141) of these cycles were thawed embryo transfer cycles

Out of the remaining one hundred and seventy-four (174) fresh oocyte cycles carried out, the Embryologists of the MDH ART Clinic, reported on the EEART system that in one hundred and forty (140) cycles, or 80.46% of cases, all embryos created had to be cryopreserved. The Embryologist reported that seventy-seven (77) of these cycles or 55% of all freeze all embryo cycles were a result of a risk of Ovarian Hyperstimulation (OHSS) after fertilisation of the oocytes were carried out, this was followed by forty (40) cycles or 28.57% due to High Oestradiol levels. Another sixteen (16) cases were due to various medical reasons amongst which were polyps, liquid found in uterine cavity and uterine treatment necessary between fertilisation and embryo transfer date. Six (6) other cases were abandoned and required a freeze all embryo cycle due to High Progesterone levels. There was one request by patient to postpone cycle and freeze all embryos.

Thus, from the 174 fresh oocyte cycles, only thirty-four underwent fresh embryos transfer. This led to the fact that at MDH ART Clinic only one hundred and seventy-five (175) out of the 331 cycles resulted in completed treatment cycle from which a pregnancy could result.

2.4. First Time/Repeated Cycles

Out of the 346 cycles carried out, patients reported a range of up to eight attempts of IVF/ICSI. The majority, 67.63% of prospective parents (233 couples and one single woman) were undergoing the IVF/ICSI procedure for the first time. There were 21.10% of couples (73 couples) who were undergoing the cycle for the second time, 6.94% of couples (24 couples) for the third time, 2.6% of couples (9 couples) were undergoing their fourth attempt. Three (3) other couples, 0.86% were undergoing their fifth attempt, whilst one couple their sixth attempt, another couple had undergone their seventh attempt and another couple had undergone their eight cycles.

These figures are in line with the number of attempts, couples are ready to go through to achieve a pregnancy as reported for 2020 but show an increase over those reported for 2019 which had shown couples going for a maximum of six attempts. One also notes a considerable increase of 20.23% in couples undergoing their first attempt over last year's figures.

Noteworthy is also the fact that there was a considerable decrease of 7.3% of couples undergoing their second attempt at an IVF cycle. (Figures 7 and 8).

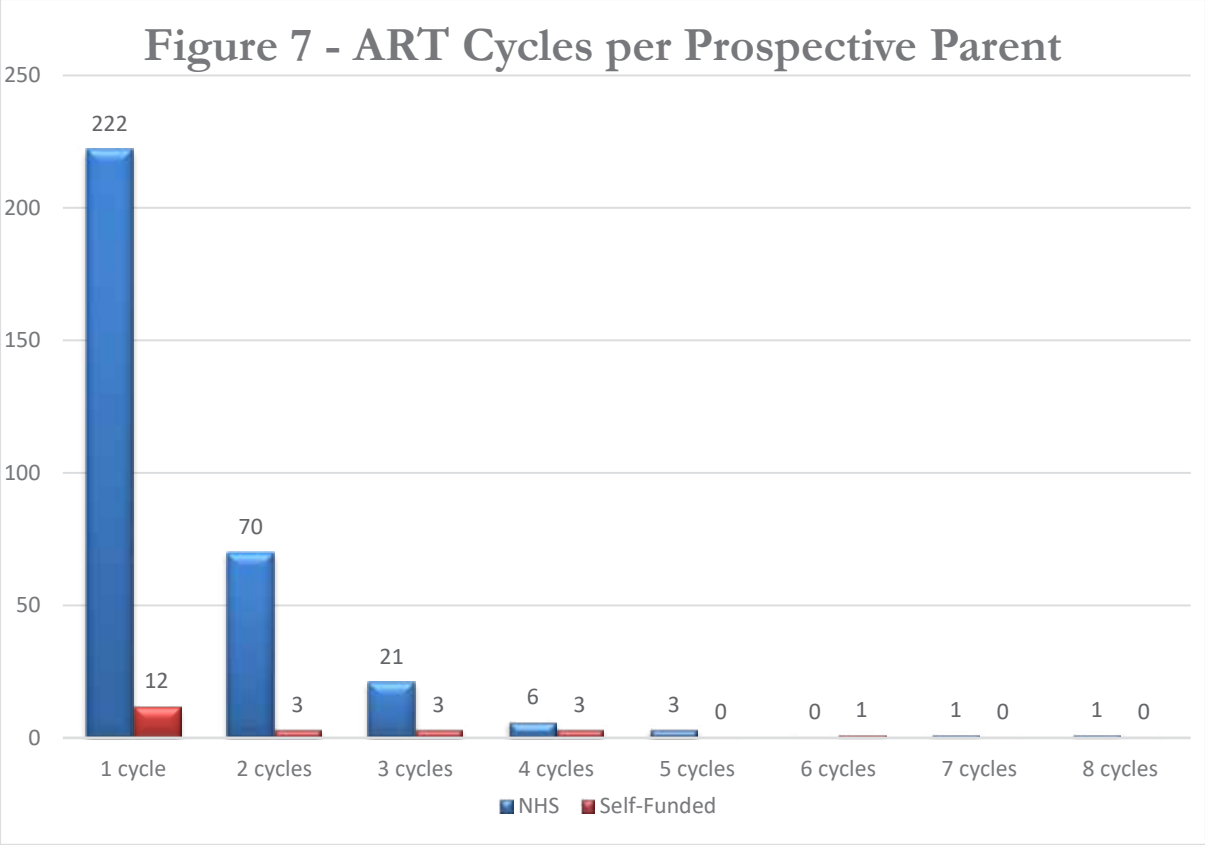


Figure 7 - ART Cycles per Prospective Parent
250
200
150
100
50
0
222
12
70
3
21
3
6
3
3
0
0
1
1
0
1
0
1 cycle
2 cycles
3 cycles
4 cycles
5 cycles
6 cycles
7 cycles
8 cycles
NHS
Self-Funded

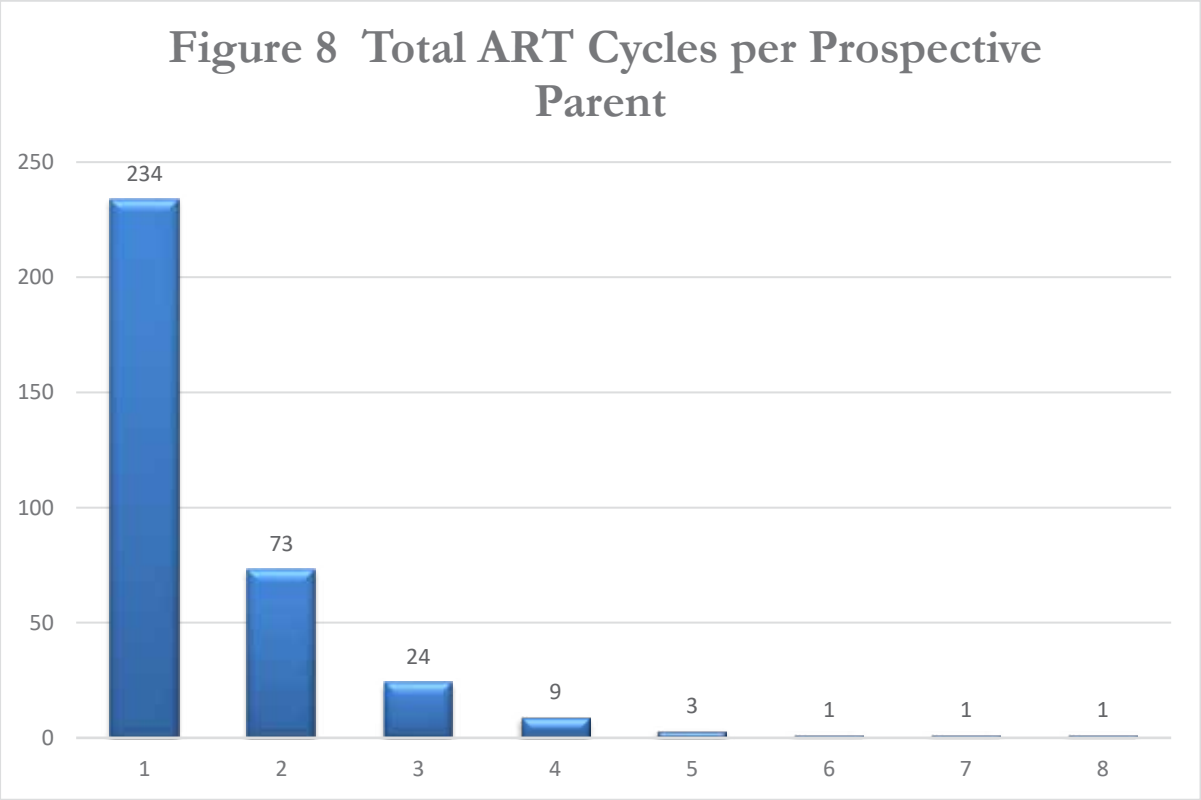


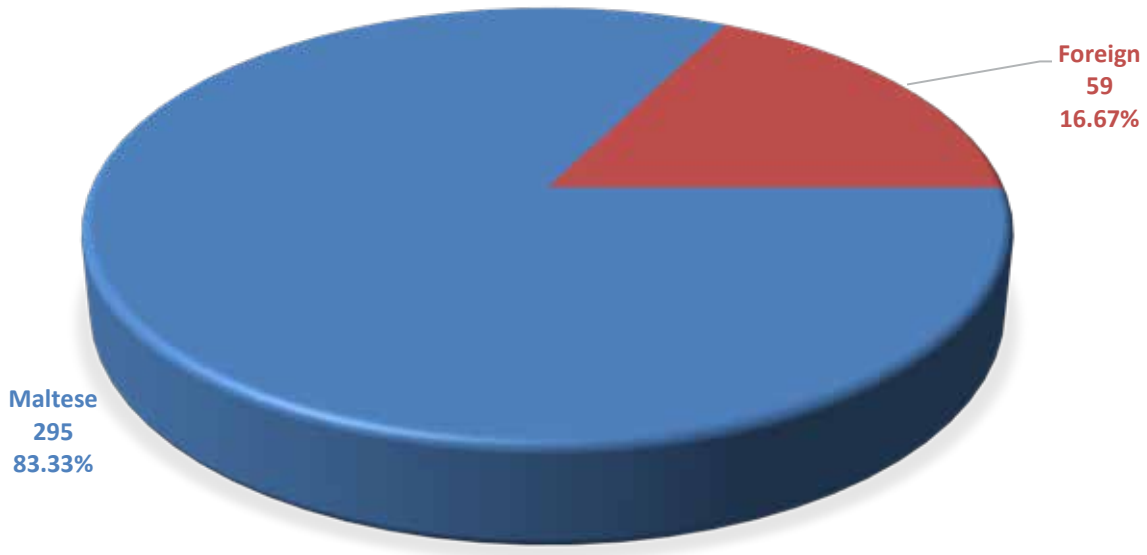
Figure 8 Total ART Cycles per Prospective Parent
250
200
150
100
50
0
234
73
24
9
3
1
1
1
1
2
3
4
5
6
7
8

3. DEMOGRAPHICS

3.1. Nationality

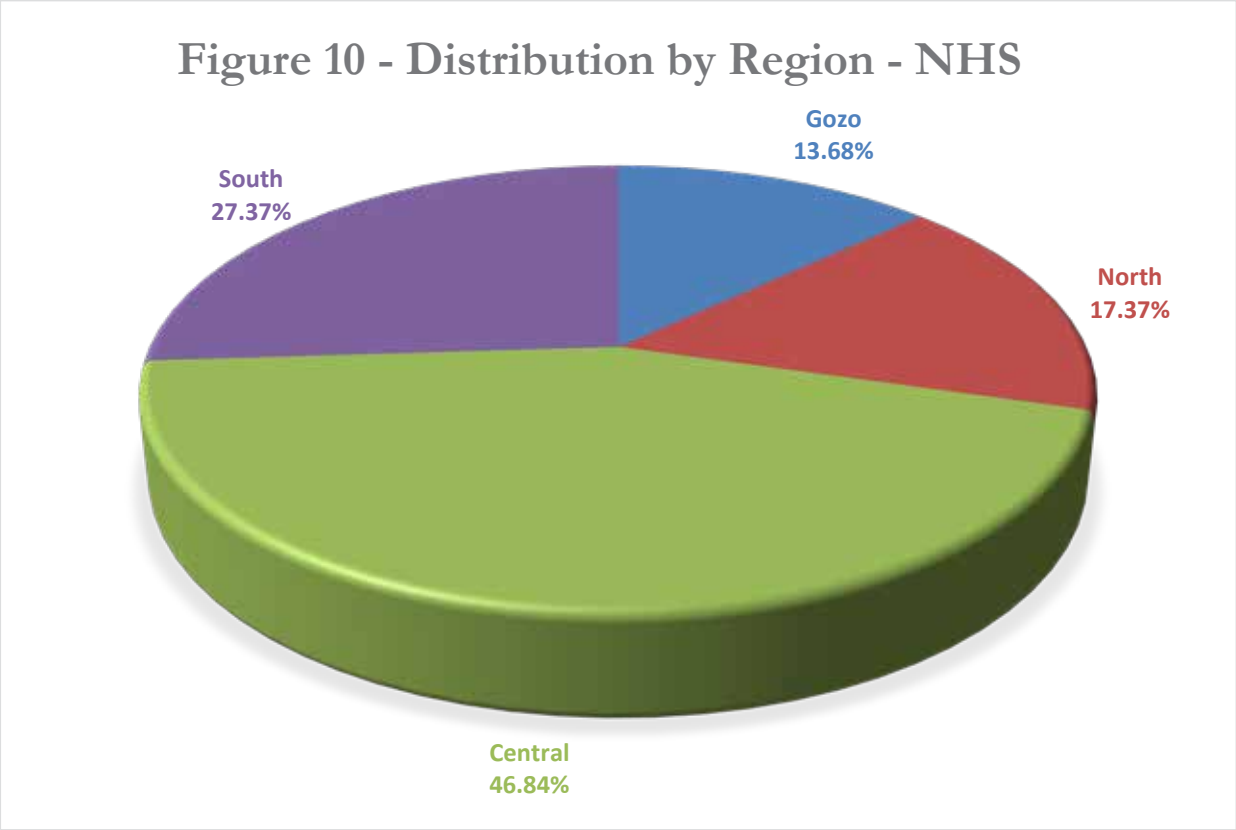
Out of the 354 cycles performed this year, all were undertaken by Maltese Residents of different nationality. There were no foreign couples (non-Residents) who came to Malta specifically to perform the IVF/ICSI procedure in the private sector. This is in line with last year, it was in 2019 the last time wherein the private sector had reported Medical Tourism procedures in the Fertility sector. During this year the Maltese Residents seeking ART treatment registered an increase in foreign nationals living and working in Malta up to 59 couples when compared to the 37 couples of last year. Foreign Nationals ranged from countries such as Philippines, Romania, England, Italy, Ukraine, Serbia, India, Poland, Pakistan, Syria, Tunisia, Russia, Brazil, Argentina, Greece, Denmark, Canada, Albania, Ireland, France, Uzbekistan, Sudan, Nigeria, and USA amongst others. These amounted to 16.67% of cycles carried out in 2021. (Figure 9).

Figure 9 - Maltese and Foreign Residents



3.2. Regions

As reported in previous years, the overall majority of couples 48.08% (100 couples) who had undergone fresh oocytes cycles of IVF/ICSI procedures in 2021 reside in Central Malta, followed by 26.44% (55 couples) who reside in Southern areas of Malta, 16.82% (35 couples) reside in the Northern part of the island, while the remaining 8.65% (18 couples) reside in Gozo. These figures show a decrease in couples from Gozo and couples from the Southern part over last year's figures. This was reflected in an increase by the couples residing in the Central and Northern part of the island (Figures 10, 11 and 12).



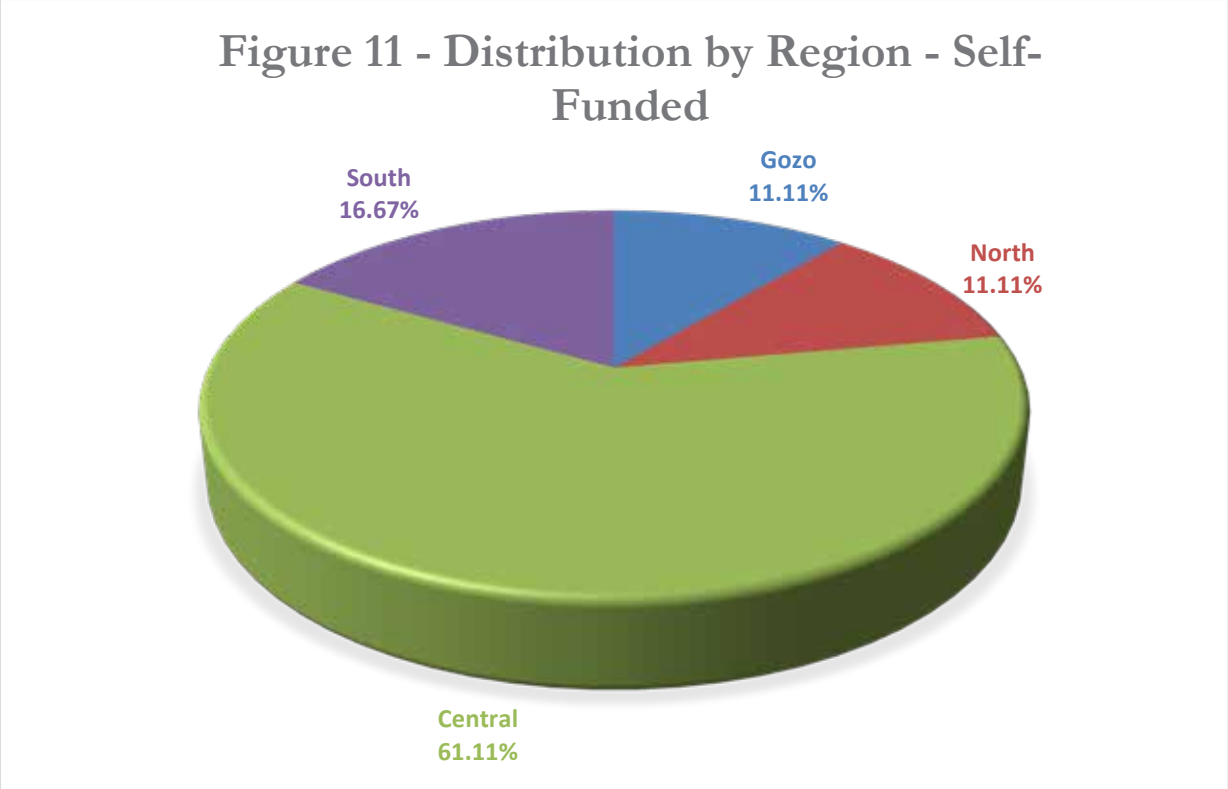


Figure 11 - Distribution by Region - Self-Funded
South
16.67%
Gozo
11.11%
North
11.11%
Central
61.11%

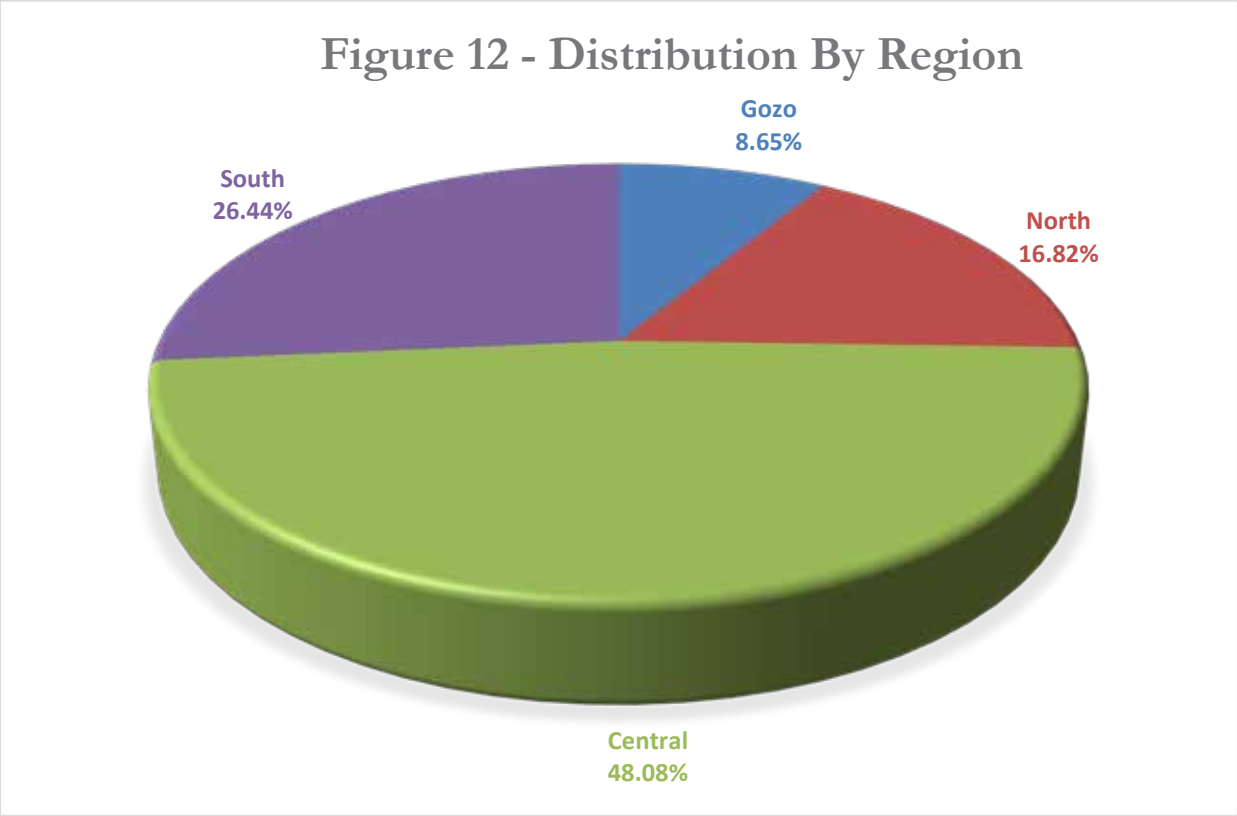


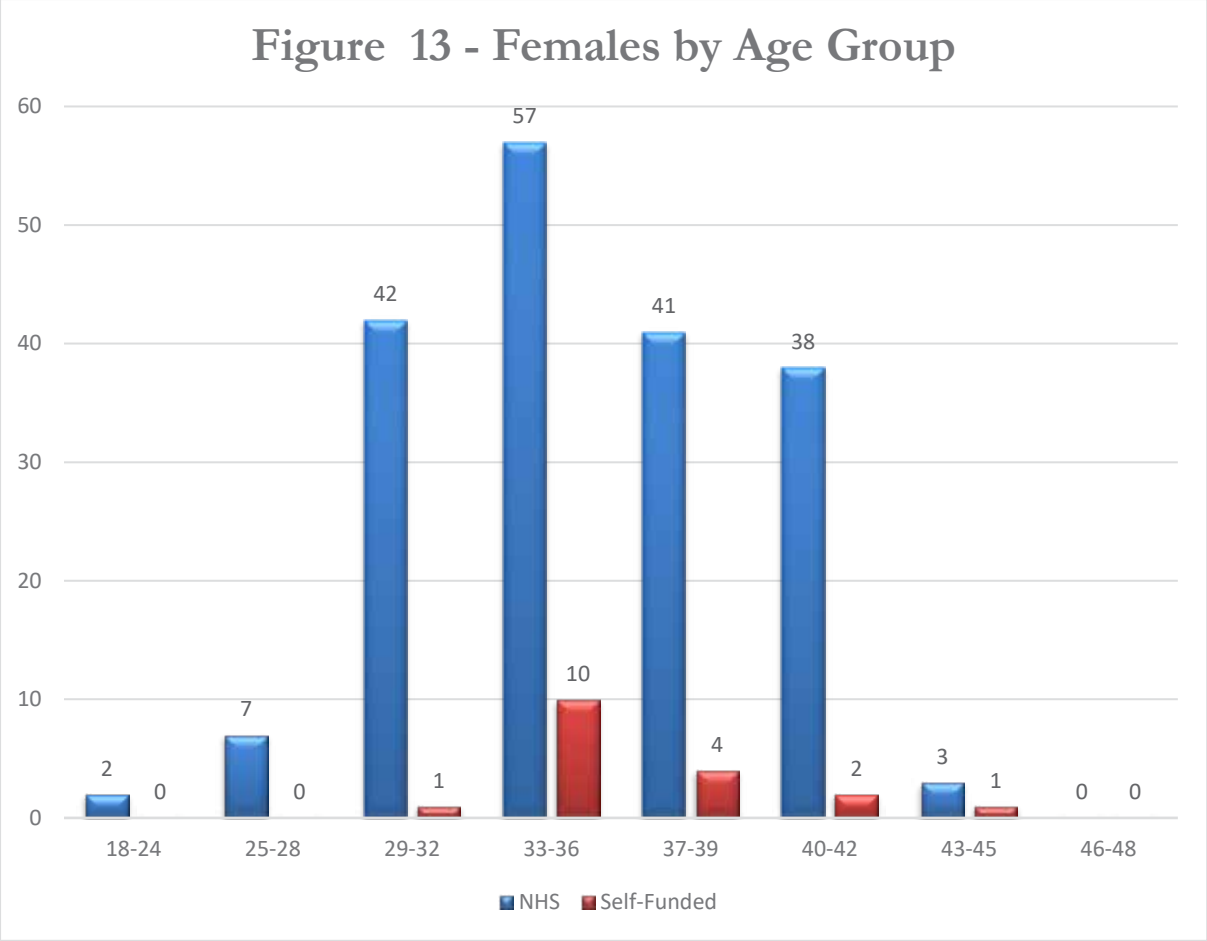
Figure 12 - Distribution By Region
Gozo
8.65%
South
26.44%
North
16.82%
Central
48.08%

3.3. Maternal Age

In line with the Embryo Protection Authority's Protocol as amended in 2018, in Malta, women falling within the stipulated age bracket of 18 and 48 are eligible to undergo ART Treatment, the extension of maximum age from 42 to 48 years is applicable to women who make use of donated oocytes, women who have previously cryopreserved embryos and are undergoing an Embryo Cryopreservation / Thaw Cycle and women who had previously cryopreserved their oocytes prior to reaching age 36.

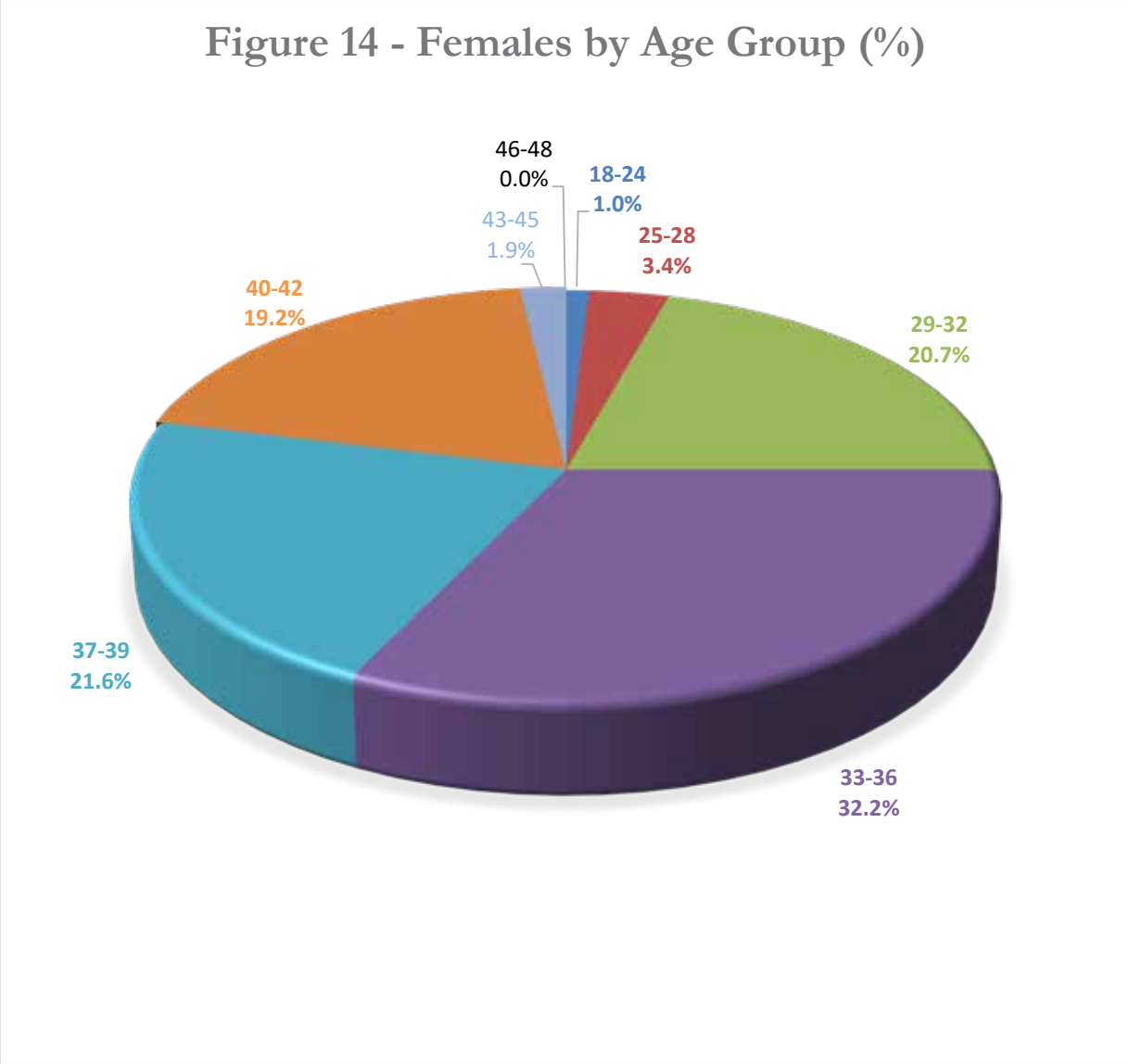
Throughout 2021, all IVF/ICSI procedures except one (1) were carried out using own gametes and embryos, the other lady was to use donor sperm. All women who had embryo cryopreservation cycles were still much younger than the maximum age of 48. During 2021, two women aged between 18 and 24 made use of the services, in 2020 the youngest women was 25 years of age.

Four women who made use of the six months extension granted by the Authority in lieu of the Covid-19 measures were aged 43 when undergoing their procedure. There has been a distribution of procedures across all age brackets, as can be noted from the chart hereunder (Figure 13).



As for the past seven years, the largest number of female patients, 67 females (32.2%) undertaking procedures throughout 2021 were aged between 33 and 36. The second largest age group as per previous years, was for female patients aged 37-39, where 45 females (21.6%), while 43 females (20.7%) followed closely in the 29–32-year-old bracket. These were followed by 40 female patients (19.2%%) aged between 40-42.

Seven female patients (3.4%) were aged between 25 and 28 years. And two patients were aged between 18 and 24 years. Four patients who benefited from the Covid-19 extension were 43 years. (Figure 14).

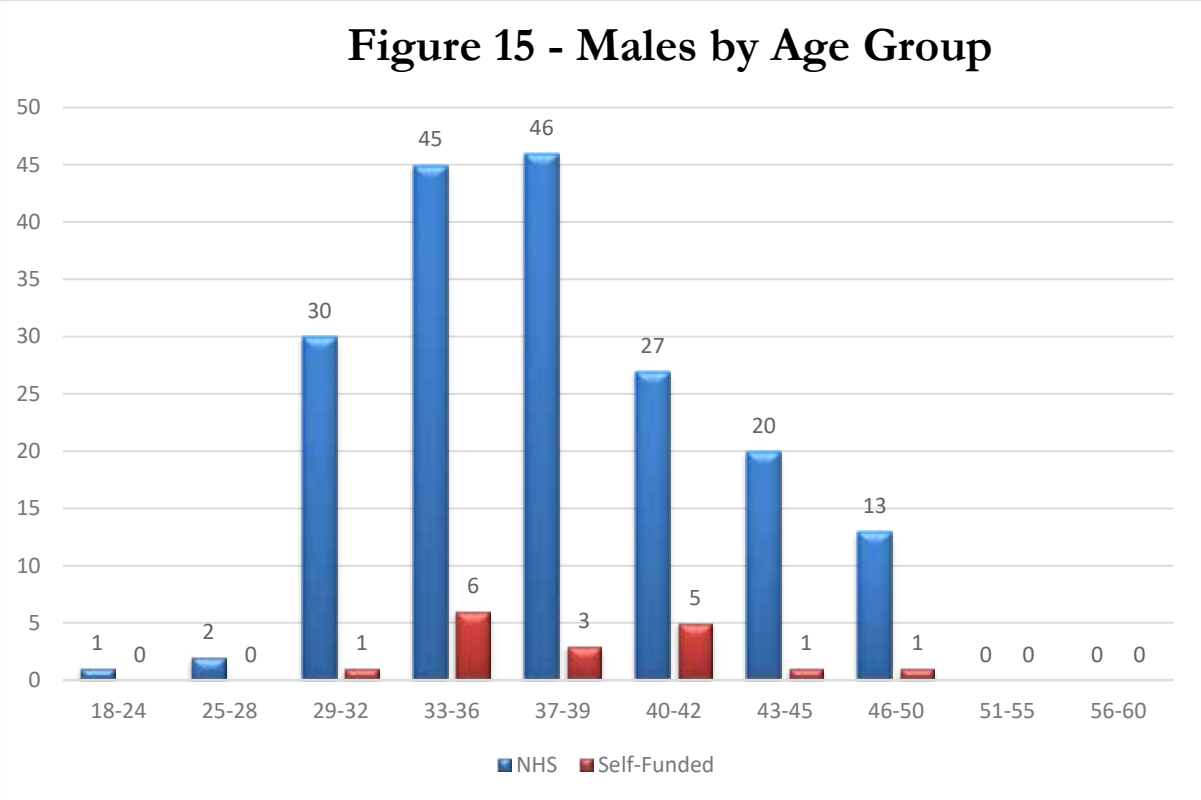


Noteworthy is the fact that in 2021 there has been a drop of 2.7% in the age group of females aged between 25 and 28 years, this drop was also reported in 2020 and a drop of 1% in the age group of women aged between 33 and 36.

Conversely, the group of women aged between 18 and 24 years registered an increase of 1% over 2020. An increase of 1.1%. was also noted in the age bracket of 29 to 32 years over the previous year. An increase of 1.4% was registered by women aged 43 years due to the Covid-19 extensions granted by the Authority.

3.4. Paternal Age

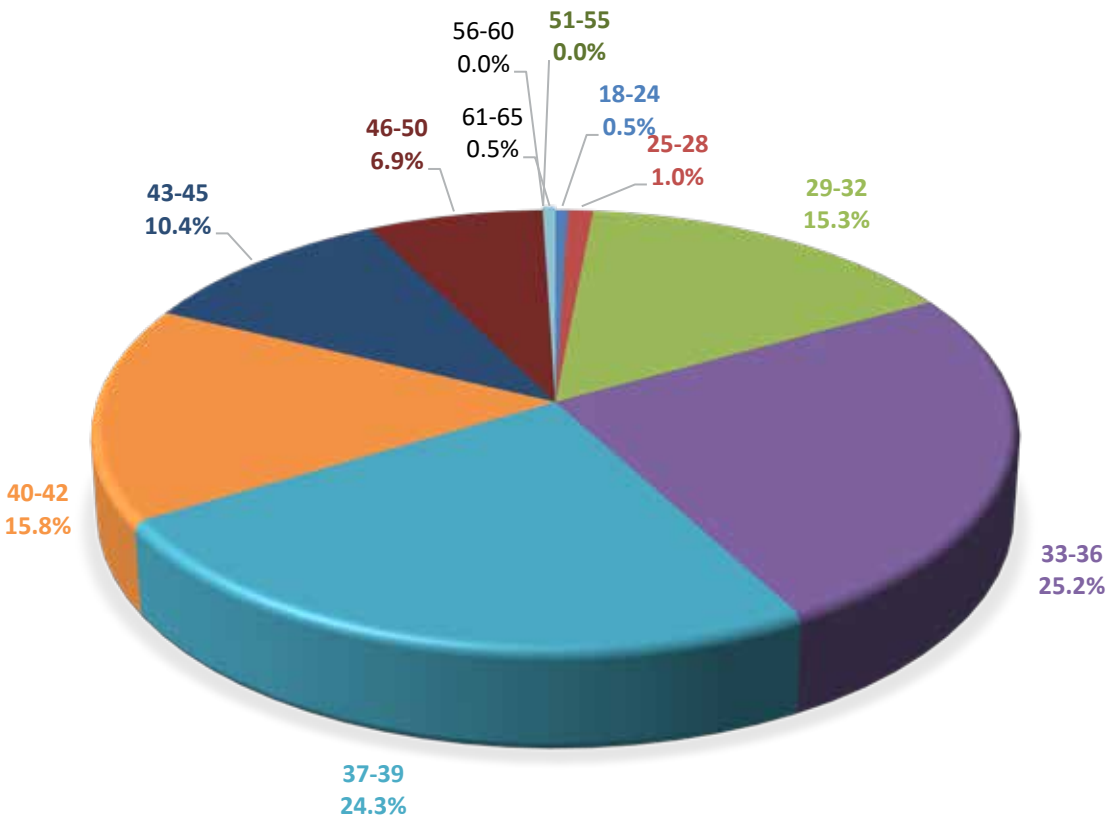
As with the female patients, the largest number of male patients, which amount to 51 males (25.2%) undergoing procedures was in the 33–36-year-old bracket, while 49 males (24.3%) were aged between 37 and 39. The third largest age group (15.8%) consisted of 32 males in the 40- to 42-year-old bracket. The age group of males aged between 29-32 years was the fourth largest age group with 31 males (15.3%), 21 other males were reported to be in the 43 to 45 age brackets, while 15 patients (7.4%) of male patients were aged 46 years and over. The remaining 3 males (1.5%) were under the age of 29. (Figures 15 and 16).



Noteworthy is the fact that while in 2017 the oldest male was in the 51-55 age bracket, in 2019 and 2020 the oldest male was in the 56-60 age bracket, with the oldest male being 58 years undergoing a cycle at the public facility. In 2021 the oldest male was registered to be 61 years. In 2021 there was a significant increase of 6.3% in the age group of males aged between 40 and 42 and an increase of 3.1% in the age group between 46 and 50 years. All males over 50 years of age were registered in the public tissue establishment.

There was also a decrease of 3.3% in the age group of males less than 29 years. Same as in 2019 and 2020, this year the youngest male is reported to be 24 years old.

Figure 16 - Males by Age Group (%)



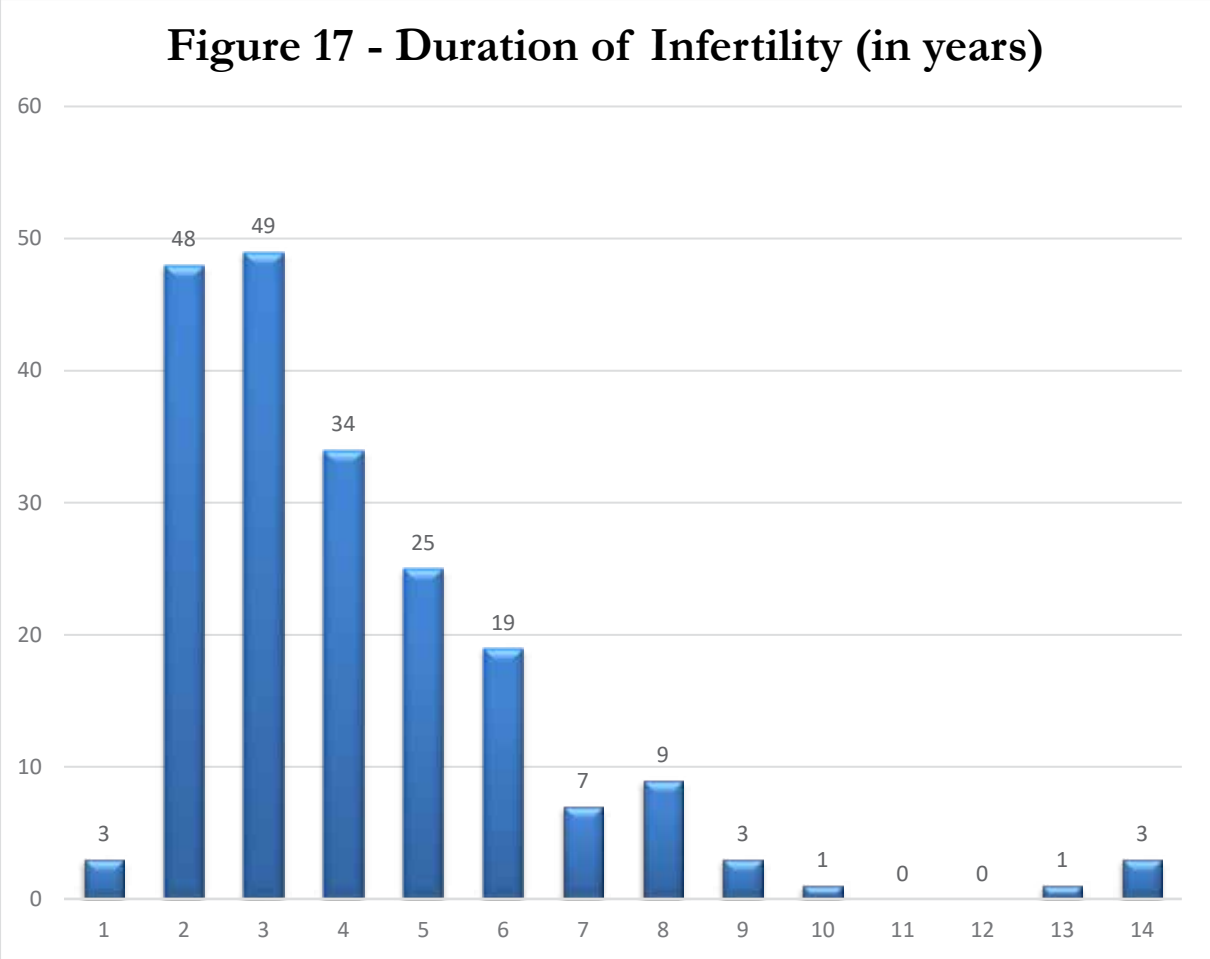
4. INFERTILITY

4.1. Duration of Infertility

There was a significant amount of variability in the reported duration of infertility amid couples undertaking procedures in 2021 which is in line with reporting of 2020, with the minimum reported duration being that of one year up to a maximum of 14 years. Noteworthy to point out is that in 2018 and 2019, the maximum duration was reported to be 17 and 15 years respectively.

Noteworthy is the fact that patients seeking treatment at the private facility reported a maximum infertility duration of up to ten years, whilst all those patients with a duration of 11 years and over sought to receive treatment at the MDH ART Clinic.

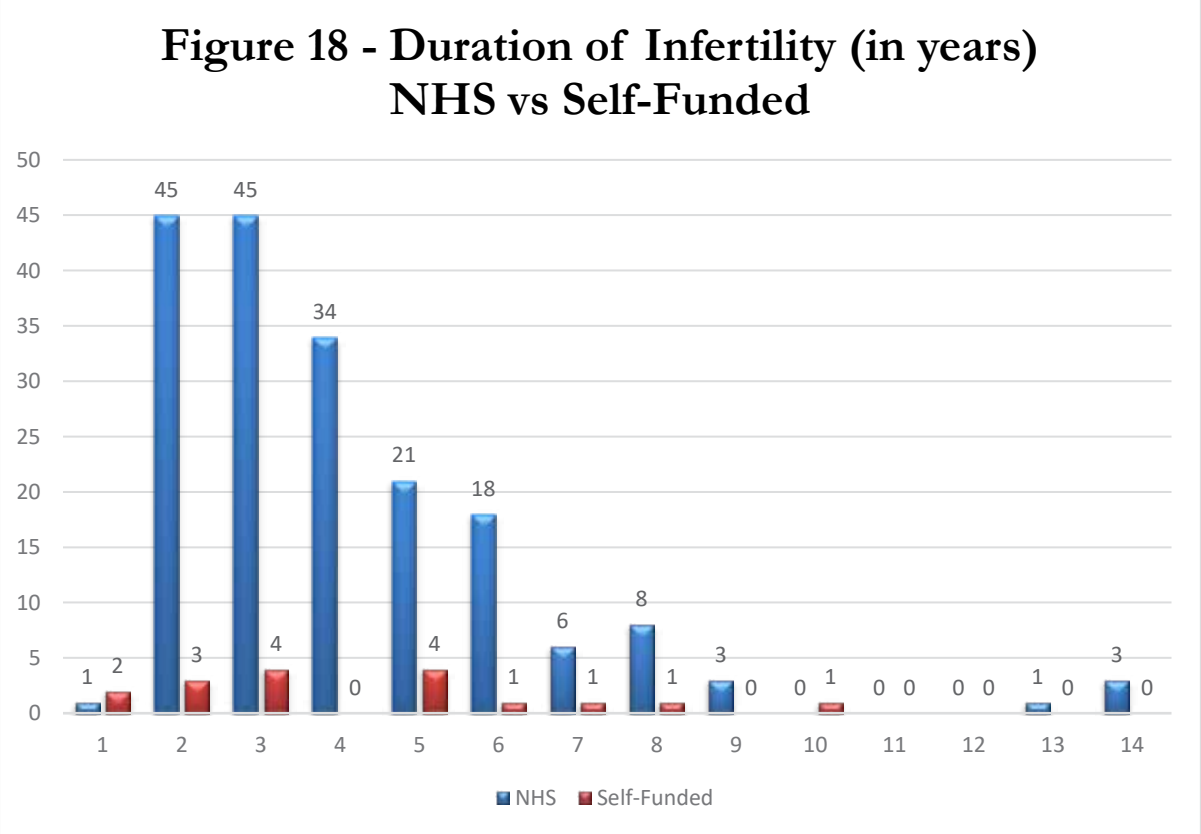
Three (3) couples reported to be infertile for one year only, two had undergone treatment at the private sector and self-funded their treatment, whilst one had procedure done at the public facility. Forty-eight (48) couples reported to be infertile for two years, forty-nine (49) couples for 3 years, thirty-four (34) couples for 4 years, twenty-five (25) couples for 5 years, while thirty-nine (39) couples reported to be infertile between 6 and 10 years. Only four (4) couples, less than half the amount reported in 2020, all undergoing treatment at the MDH ART Clinic reported being infertile between 11 and 14 years. (Figure 17).



To be eligible for treatment on the NHS, a couple must declare being infertile for at least two years if there is no exceptional case to receive treatment before. In fact, 11.11% of couples who self-funded their treatment declared less than 2 years of infertility, same as in 2020 and 2019. Most couples (44.44%) self-funding their treatment have reportedly been infertile for 5 years or more with a substantial increase of 20.20% on the previous year. The remaining 38.89% of couples have been infertile for 2 to 4 years, in this duration bracket there has been a decrease of 27.78%, which is reflected in the increase in the five years or more bracket. In the figures quoted above the women who underwent retrieval for social reasons is not included.

Contrary to the self-funded treatments, the majority of couples (67.03%) who applied to undergo IVF/ICSI treatment on the NHS declared being infertile for 2-4 years, registering a 10.29% increase over the previous year. Thirty-nine (39) couples, or (21.08%), have declared being infertile for 5-6 years, an increase of 1.42% over last year. Twenty-one (21) couples (11.35%), a decrease of 12.25% over 2020, have been infertile between seven and fourteen years.

Noteworthy is the fact that 146 couples (78.92%) of total couples undergoing treatment on the NHS reported to have been infertile for up to 5 years. This shows an increase of 10.38% over the previous year, wherein 68.54% of the couples had been reported in 2020. In the figures quoted above the women undergoing oocytes retrieval only, prior to receiving chemotherapy and hormone therapy have not been included. (Figure 18).



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).

With the introduction of changes to the Embryo Protection Act in 2018, couples who had cryopreserved embryos stored in tissue establishments in Malta were also added to the NHS entitlement criteria to undergo other treatment cycles that make use of their cryopreserved embryos, irrespective if they already have previous children from the same relationship or not.

The Authority during 2021, had brought up the issue that the NHS criteria as issued by the Chief Medical Officer's office, which allowed women who underwent IVF procedures and had a live birth but did not have frozen embryos, to be entitled to have other cycles if they presented themselves at the clinic with a new partner due to various reasons of separation from the partner, they had undergone IVF with.

The Authority had raised the issue that the entitlement criteria might be discriminating against the stability of the family, as if the same woman mentioned above had remained in her relationship she would not have been entitled for other cycles. Thus, whilst newly formed families (different partners) were being given the chance, those family units who remained stable were being denied this opportunity.

The Authority also pointed out that this change did not require change in legislation, but it only required change in entitlement criteria issued by the CMO's office, thus it was much easier to be introduced.

Most couples, 188 couples (93.07%) who have applied for IVF/ICSI treatment in both the NHS and private sector in 2021 suffered from Primary Infertility, an increase of 3.97% over 2020. Noteworthy is the fact that four (4) couples who reported secondary infertility, as they already had a child from the same relationship, self-funded their treatment, as they were not eligible on the NHS, these represent 1.98% of couples undergoing treatment in 2021. The total of couples who reported secondary infertility in 2021 has decreased to 14 couples or 6.93% of couples undergoing treatment, a decrease of 3.90% over 2020. (Table 1).

Table 1. Classification of Infertility

Classification of Infertility	NHS	Self-Funded	Total	%
Primary	178	10	188	93.07%
Secondary - Child from Same Relationship	0	4	4	1.98%
Secondary - Female has child from Previous Relationship	7	3	10	4.95%
Secondary - Male has child from Previous Relationship	0	0	0	0.00%
Secondary - Both Partners had children from Previous Relationship	0	0	0	0.00%
Total	185	17	202	100.00%

4.3. Indication for Infertility Factors

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

The majority of couples who sought treatment in 2021 (37.2%) who were undertaking IVF/ICSI procedures suffered from Female factor only infertility. These were followed by couples (28.6%) suffering from Male factor only and followed by the couples (15.8%) suffering from Female and Male factor while the remaining 18.4% reported that they were facing idiopathic infertility.

Noteworthy to bring to attention is the fact that in 2021, there was a significant increase of 8.4% in the group of patients who reported unexplained or idiopathic infertility, over the figures reported in 2020.

There was also reported a decrease in the other classifications of infertility, the group of couples who suffered from Female only infertility registered a drop of 3.6%, the group of couples who suffered from Male only infertility also registered a drop of 3.6%, while the couples suffering from Female and Male infertility had a slight drop of 1.2% over figures reported in 2020. These drops are then reflected in the increase of 8.4% in the couples with idiopathic infertility. (Figures 19 and 20).

Figure 19 - Indication for Infertility Factors NHS - Self-Funded

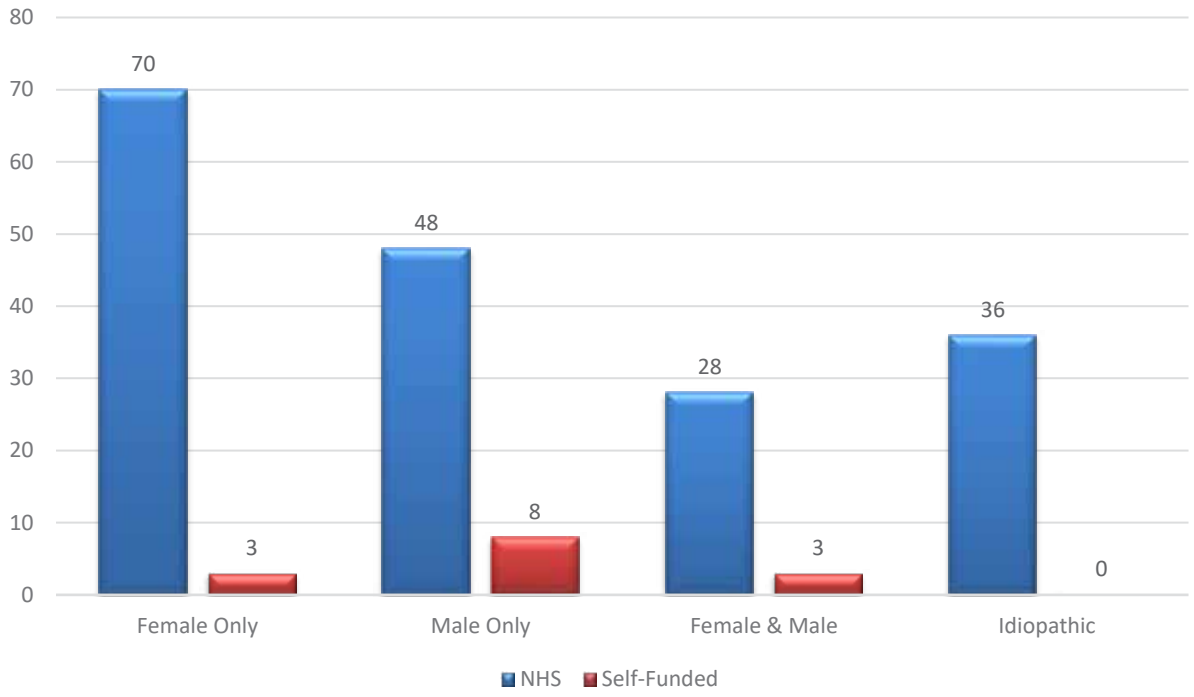
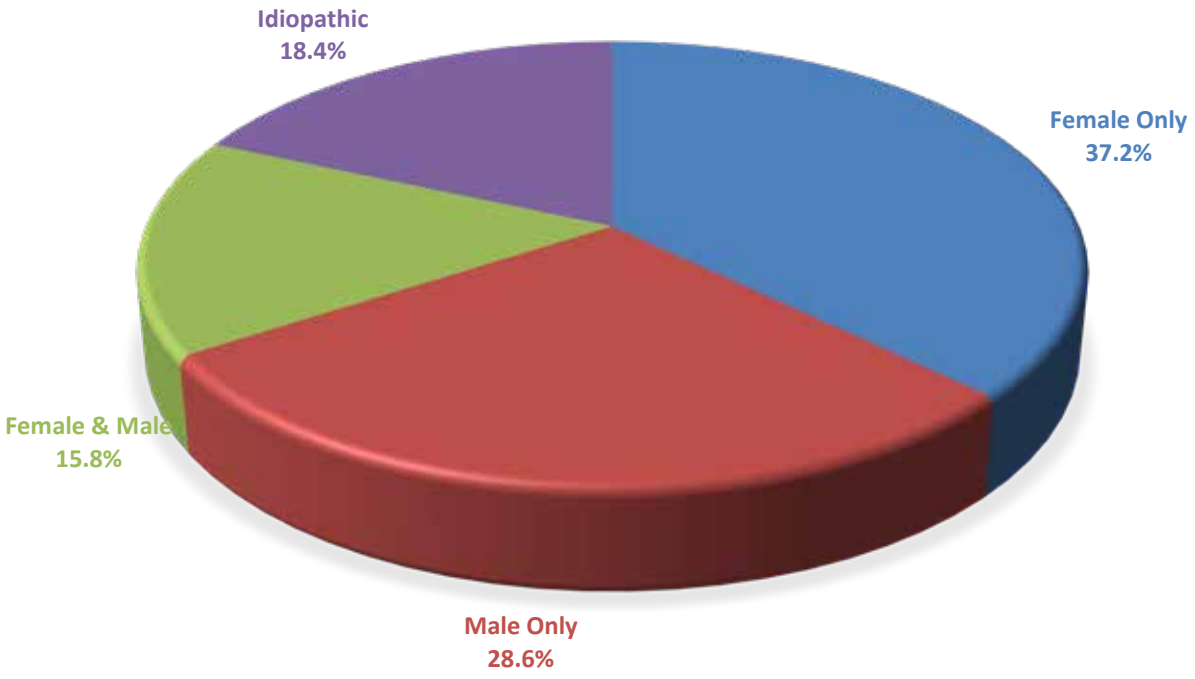
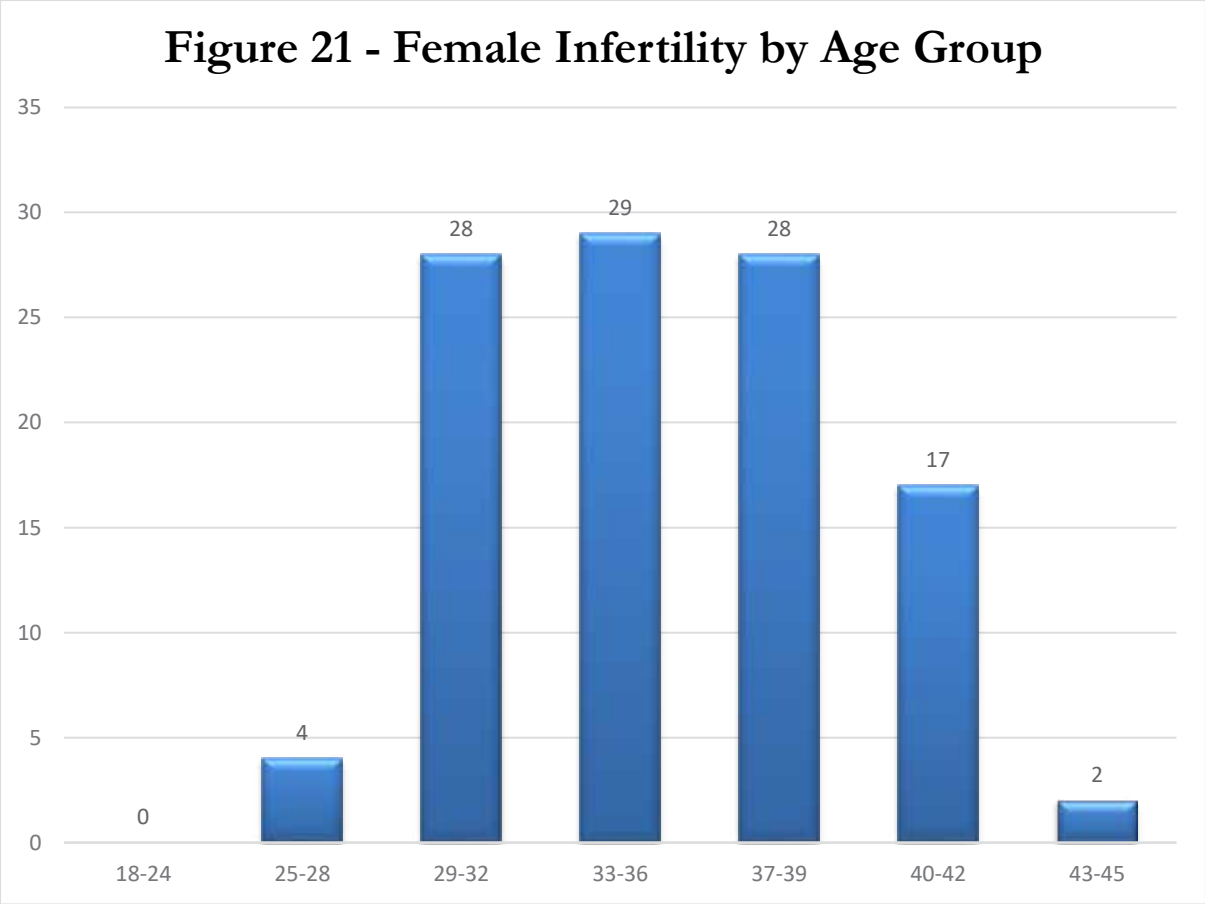


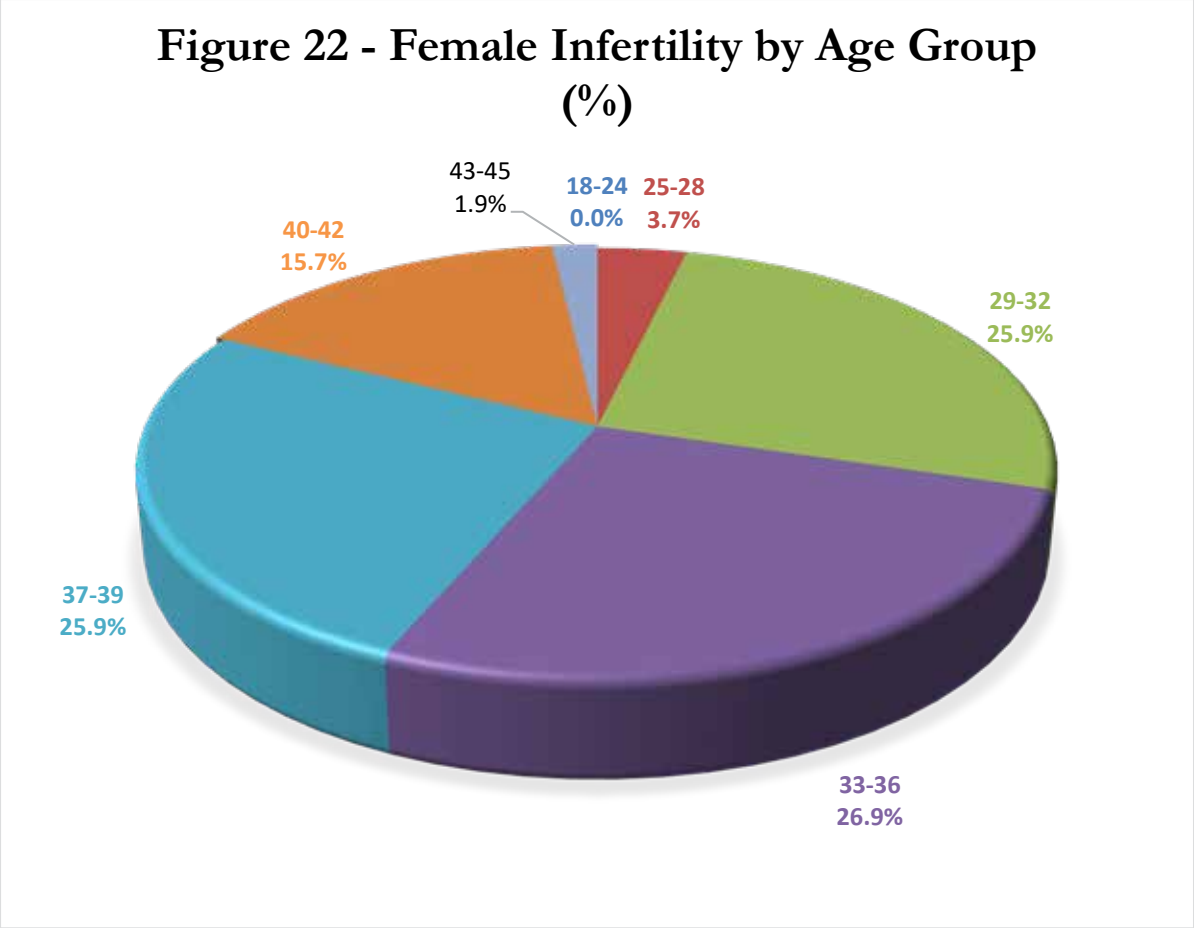
Figure 20 - Indication for Infertility Factors (%)



From those couples diagnosed with Female factor infertility, the largest group (26.9%) were in the 33–36-year-old bracket, this age bracket has registered a drop of 7.50% of the figures of last year. This is followed by the age group of 37–39-year-old females at 25.9%. This age group has registered an increase of 5.40% over figures reported for 2020.

An increase of 7% was registered in females aged between 29 and 32 years who registered 25.9% compared to the 18.9% of 2020. The age group bracket of females between 40-42 years registered a decrease of 5.6% from 21.3% to 15.7%. (Figures 21 and 22).





From those couples suffering from Male factor infertility, the largest group (29.80%) were reported in the 37–39-year-old bracket with a very significant increase of 14.60% over previous year figures, this age group has been registering increase year over year. This is followed by males in the 33 to 36 age brackets at 22.30%. A significant increase of 5.5% was registered in the males aged between 46-50.

A slight increase was also seen in Male Factor infertility where the male partner of the couple is between 29 to 32 years of age, this has increased by 2.1% from 18.1% reported last year to 20.2% for 2021. (Figures 23 and 24).

Figure 23 - Male Infertility by Age Group

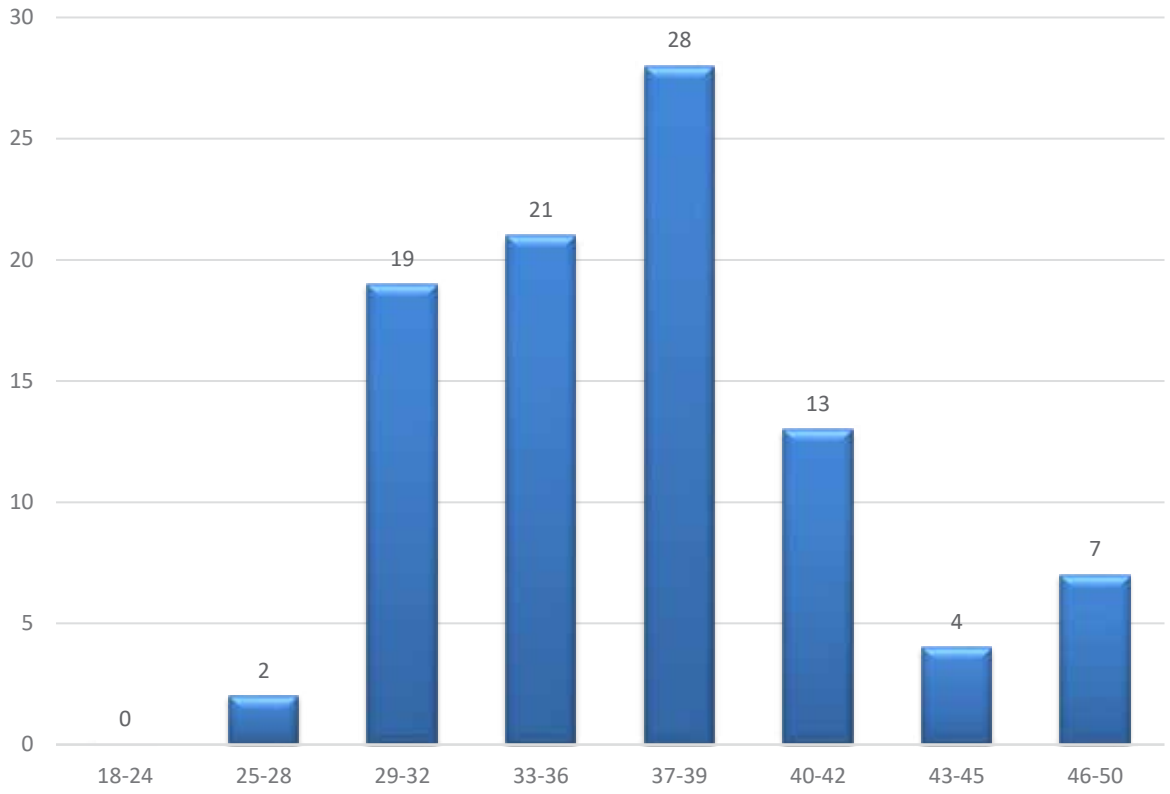
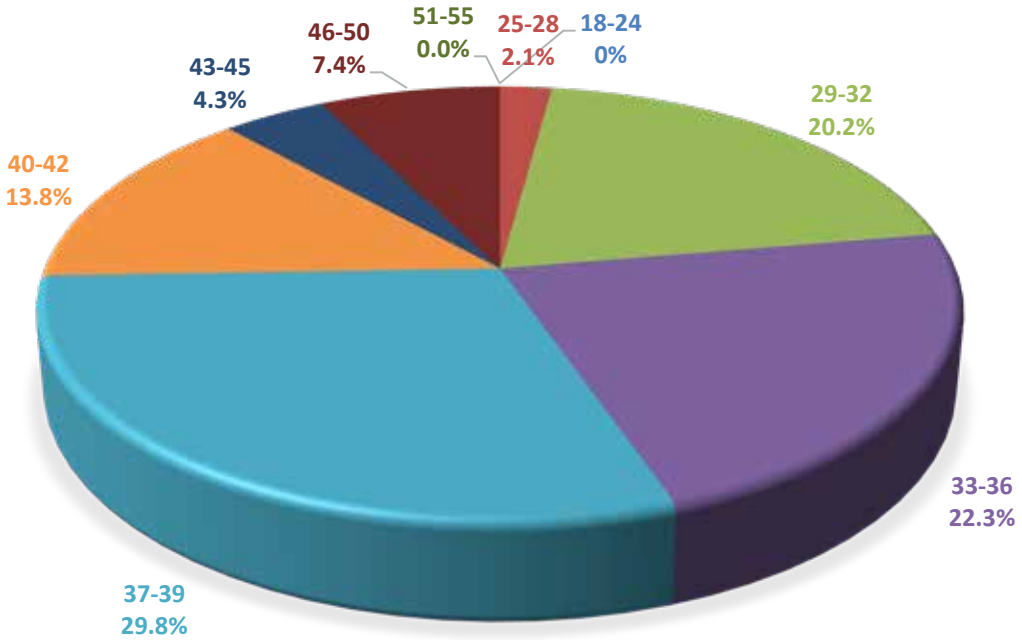


Figure 24 - Male Infertility by Age Group (%)



5. LIFESTYLE INDICATORS

5.1. Body Mass Index

For the fourth time since issuing its Annual Report, the Authority is presenting a picture of the Body Mass Index (BMI) of the Females resorting for Assisted Reproduction Treatments in Malta. It is the Authority's intention that in the coming months it will introduce a fertility education campaign aiming to raise awareness regarding the different factors effecting fertility with BMI being also in mind and to promote a healthy lifestyle that could help in achieving a pregnancy.

Classifications reported are based on the World Health Organisation Classifications, thus women having a BMI below 18.5 are classified as underweight, women with a BMI between 18.5 and 24.9 as normal weight, women with a BMI of 25 to 29.9 as pre-obesity (overweight). Women are classified as Obesity Class I if reporting a BMI of 30 to 34.9, Obesity Class II with a BMI of 35 to 39.9. Women with a BMI above 40 are classified as Obesity Class III.

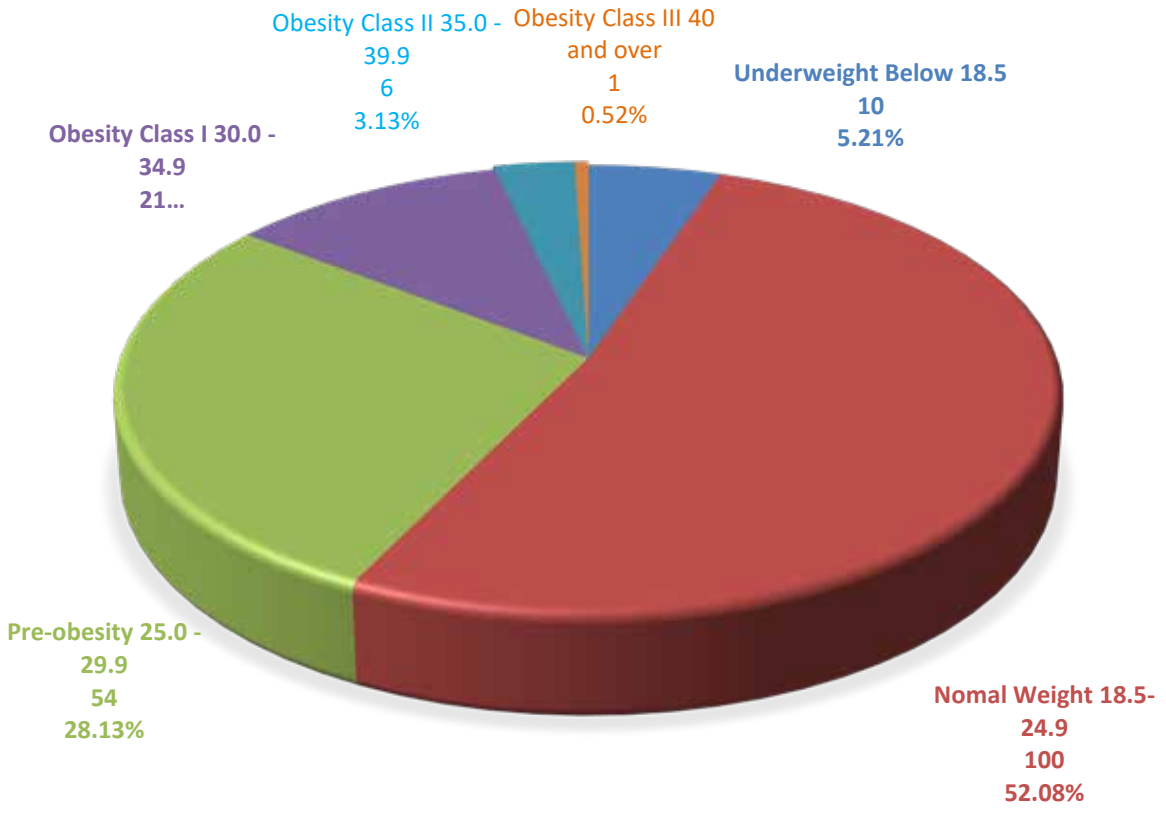
In 2021, the BMIs of females reported ranged from as low as 17.7 with the maximum BMI reported to be 44.5, average of BMI of women who resorted to IVF/ICSI was of 25.2 a slight decrease of 0.4 over average of last year, thus being classified as in the range of pre-obesity (overweight) range.

10 females or (5.20%) of females undergoing ART treatment in Malta through IVF/ICSI were reported to be underweight this shows an increase of 1.83% over 2020, 100 females (52.08%) were of normal weight, an increase of 5.93% over figures in 2020, while the remaining 62 females or 32.29% were classified in the overweight

and obese classifications. Noteworthy to bring to attention is the fact that 14.58% of all females resorting to ART treatments were classified as Obese. (Figure 25).

The Authority felt that this study needed to be presented in this year's annual report to give a holistic picture of the females undergoing ART treatments. As will be reported later in the pregnancy and miscarriages sections, the only female who was pregnant in the underweight class, miscarried same also applies to women in Obesity Class II and Obesity class III where the three pregnancies reported in these BMI classes, also miscarried.

Figure 25 - Body Mass Index of Females



6. TYPE OF CYCLE

6.1. Fresh vs Thawed

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

Since the coming into effect of the changes to the Embryo Protection Act in 2018, patients who have made use of cryopreservation of embryos, will have to undergo embryo transfers of the cryopreserved embryos before creating new embryos through fresh cycles.

From a total of 354 procedures carried out, 196 (55.37%) were Fresh procedures with collection of oocytes; while another 4 (1.13%) were Thawed oocytes cycles, two of which were carried out at the St James Conception Unit. MDH ART Clinic also performed two thawed oocytes procedures during this calendar year. None of the prospective parents in 2021 opted for a combined cycle whereby both fresh and thawed oocytes would have been utilized for the procedure.

During 2021, one hundred and forty-six (146) couples (41.24%), had undergone embryo transfer only procedures in both licenced facilities, of embryos that were cryopreserved previously through the permission granted by the Authority after they had requested additional fertilisation with the possibility of cryopreservation of embryos (Table 2).

Table 2. Type of Procedure

Procedure	NHS	Self-Funded	Total	% of Total
Fresh oocytes	181	15	196	55.37%
Thawed oocytes	2	2	4	1.13%
Prior approval for a freeze all oocytes/embryos cycle	7	1	8	2,26%
Thawed embryos	141	5	146	41.24%
Total	**331**	**23**	**354**	

Noteworthy is the fact that there has been a major drop in the procedures requiring a fresh collection of eggs cycle. During 2021, there was a 12.86% decrease in fresh oocytes collection cycles when compared to last year 2020. A slight drop of 0.27% was registered in the couples opting to undergo a thawed oocyte cycle in 2021 when compared to 2020, however we note that cycles being undertaken at the Maltese Clinics do not promote oocyte vitrification, and the Authority notes that these cases have diminished considerably.

A major increase of 12.27% was registered in thawed embryo cycles which were now being carried out in both licenced facilities.

Most cycles (56.80%) carried out at the ART Clinic in Mater Dei Hospital were Fresh oocytes collection cycles, which were undertaken by heterosexual couples and one single women making use of donor sperm. 42.60% of cycles were thawed embryo cycles all undertaken by heterosexual couples. Only 0.60% thawed oocytes cycles were carried out on the NHS.

In the self-funded cycles, the majority of cycles (69.56%) were Fresh oocytes collection cycles, 9.70% were Thawed oocytes cycles, whilst the remaining 21.74% of cycles were thawed embryo transfer that were self-funded in 2021. All the cycles that were performed at the private facility St James Conception Unit were undertaken by heterosexual couples, as the facility had opted out to apply for a licence to undergo procedures with third party donation.

6.2. Additional Fertilization Requests (AFRs)

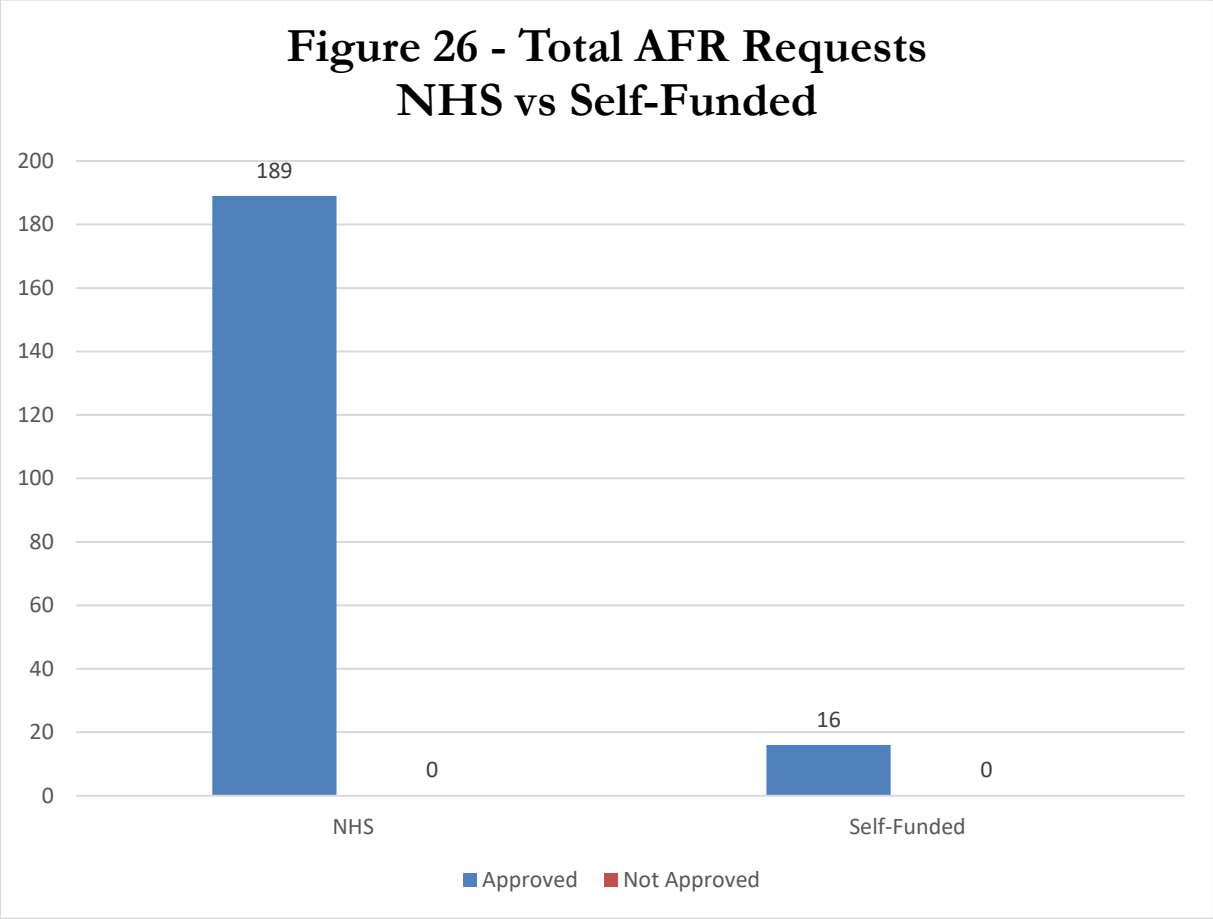
Pursuant to the introduction of the Embryo Protection Act of 2012, the maximum number of oocytes which may be injected in any one cycle is two oocytes, or three oocytes in cases approved by the Authority under the Principal Act. All embryos created had to be transferred since vitrification (freezing)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

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

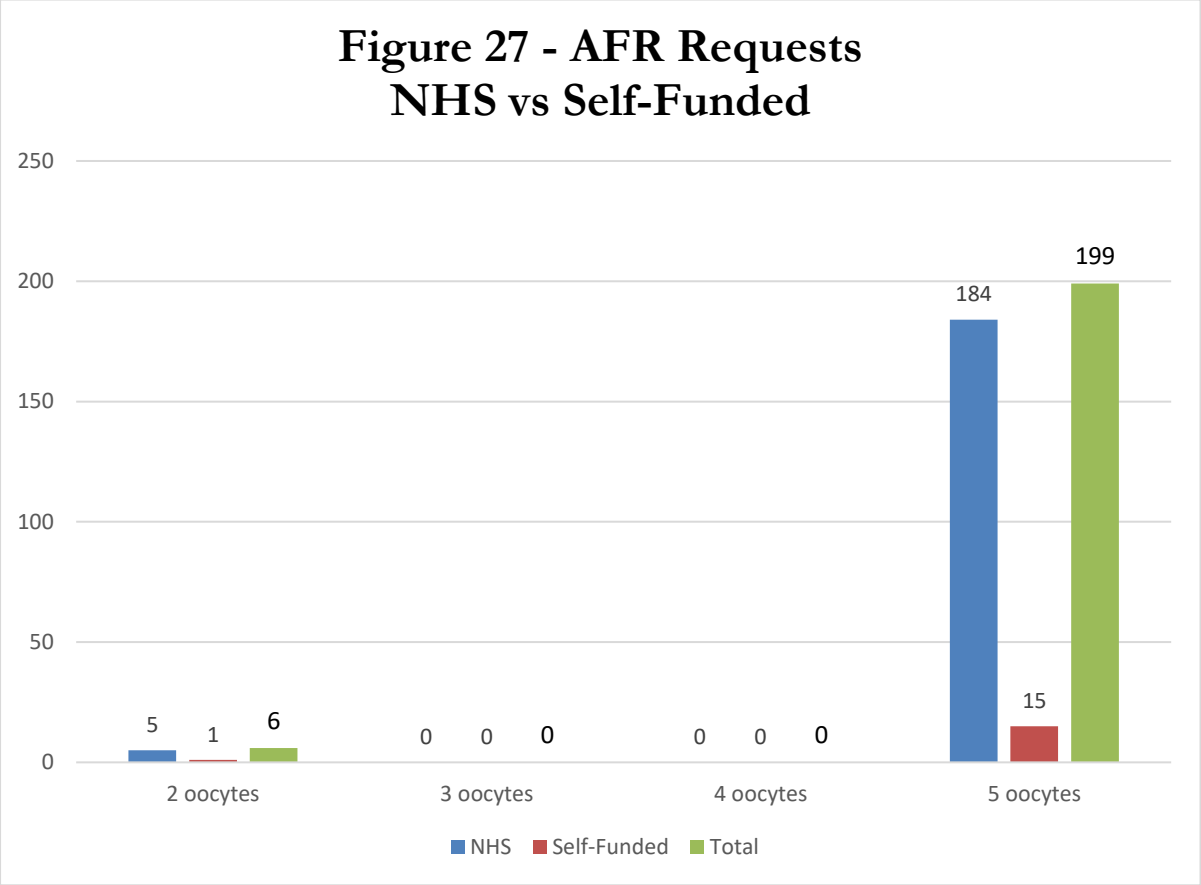
The Authority receives a significant number of requests from the licensed establishment clinicians to consider the fertilization of additional oocytes for specific couples, instead of the two permitted by law. These requests are analysed and discussed between the Members of the Authority together with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

Throughout 2021, a total of 205 requests were received by the Authority, an increase of 56 requests from the requested that were received by the Authority in 2020. Most requests, 189 requests (92.20%) came from the ART Clinic at MDH, 184 of these requests were for the maximum injection of 5 oocytes under the Amendment Act, all the 184 requests were approved. The remaining 5 requests made by the ART Clinic at MDH were for patients who opted to follow the principal Act and thus fertilise only two oocytes.

The remaining of requests, 16 requests only (7.80%) of the AFR requests were made by private clinics, 15 of these requests were for the maximum injection of 5 oocytes under the Amendment Act, all the 15 requests were approved. The remaining 1 request made by the St James Conception Unit was for prospective parents who opted to follow the principal Act and thus fertilise only two oocytes. (Figures 26 and 27).



During 2021, all requests for fertilisations were approved by the Board. These approvals were issued both for the prospective parents who opted to follow the Principal Act and fertilise only two oocytes a well as the requests made for additional fertilisations up to a maximum of five oocytes.



The number of patients who chose to undergo a procedure following the Principal Act and thus fertilise only two oocytes and not opt for additional fertilisations thus not cryopreserving embryos, were only six prospective parents. This registered a considerable drop of 9.15% to the requests made in 2020. Thus 2.93% chose not to go for additional fertilisation whilst 97.07% requested the Authority for additional fertilisation approvals.

7. GAMETES

7.1. Transfer of Gametes and Embryos

7.1.1 Transfer of Gametes and Embryos between Local Clinics

Throughout 2021, seven (7) requests for transfer of gametes were received by the Authority to transfer sperm and oocytes between the Maltese Licenced Clinics. Six (6) prospective parents requested transfer of gametes from the St James Conception Unit to the MDH ART Clinic. Consequently, gamete movement transfer of seven (7) vials of sperm of two males, and gamete movement of 21 oocytes of four women were made.

Only one request was made by a male prospective parent to transfer his cryopreserved sperm from MDH ART Clinic to St James Conception Unit. A total of three sperm vials were shifted from the public clinic and cryopreserved for future use at the private clinic.

In 2021, the Authority also received requests for transfer of embryos between the Maltese Licenced Tissue establishments from four heterosexual couples who had their embryos stored at St James Conception Unit and requested distribution to the MDH ART Clinic. The Authority approved all four requests for embryo movement and a total of ten (10) embryos were shifted from the private to the public tissue establishment.

7.1.2 Transfer of Gametes and Embryos to and from Tissue Establishments Abroad

In 2021, the Authority received a request for the transfer of cryopreserved embryos from the United Kingdom to Malta. The Maltese patient had cryopreserved these embryos prior to coming into force of the changes to the Embryo Protection Act and thus was eligible to transfer two embryos to Malta. Following the necessary Authority and SPH approvals for the transfer to Malta, two cryopreserved embryos were imported to Malta and stored at the MDH ART Clinic.

In 2021, the Authority received twenty-nine (29) requests from the MDH ART Clinic for the transfer of donor sperm to Malta. Twenty-six (26) requests were approved by the Authority; however, three (3) requests were rejected as they did not meet the requirements of the Maltese Legislation. Out of the 26 approvals granted, the distribution of sperm of 24 donors had already been made to Malta and a total of ninety-six (96) donor sperm vials had been cryopreserved in the public tissue establishment to be used in procedures requiring the use of third-party donor sperm.

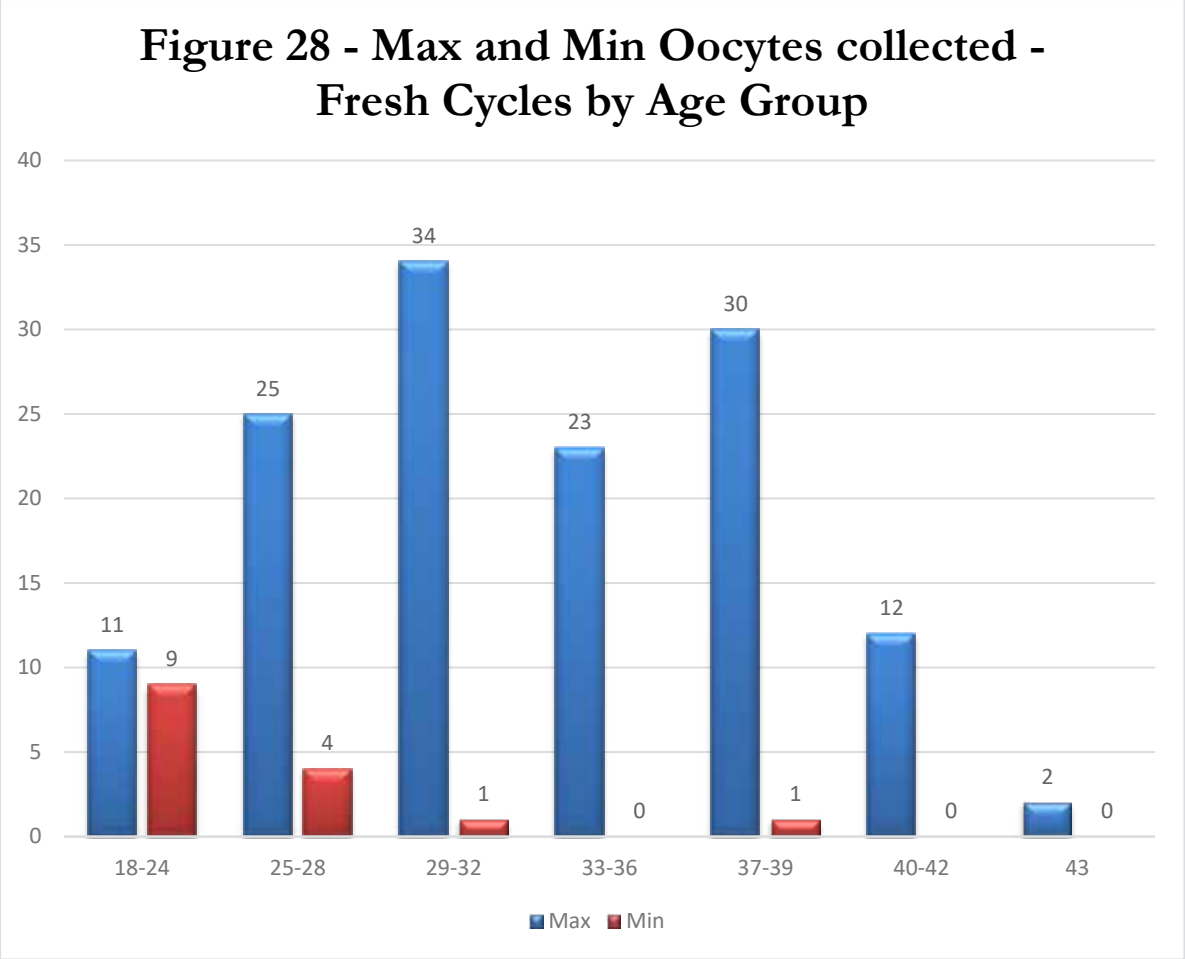
In 2021, the Authority also received requests and issued one off approvals for the transfer of cryopreserved gametes, vials of sperm, from the United Kingdom, France, and Italy to Malta. Two of these approvals were to be cryopreserved in the public clinic and one in the private clinic in Malta. To date these transfers have not yet been finalised. Another request from a patient to transfer her cryopreserved oocytes from the private local clinic to a clinic in Spain was received, The Authority requested the local clinic to establish the necessary documentation for the distribution of gametes to another country for which an approval will be issued once all documentation is in place.

7.2. Collection of Oocytes

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

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

From the 204 Fresh cycles carried out in 2020, a total of 1665 oocytes have been collected, at an average of 8.16 oocytes per patient. The maximum number of oocytes collected from a single patient was 34 oocytes from a female in the 29-32 years age bracket, this was followed by 30 oocytes collected from a female in the 37-39 years bracket and followed by 25 oocytes collected from a female in the 25-28 age bracket. All three patients had undergone treatment at MDH ART Clinic. The maximum number of oocytes collected in the St James Conception Unit was of 18 oocytes collected from a female in the 33-36 age bracket. (Figure 28).



In line with the reporting of previous year, in 2021 the largest number of average oocytes collected from one single patient, for an average of 14 oocyte per patient, was from females aged between 25 and 28, these were closely followed by 10.23 oocytes per patient, from females in the 29–32-year-old bracket. An average of 8.92 oocytes was collected from patients aged 33-36. Not surprisingly, less oocytes were collected from women aged 37-39 and 40-42, for an average of 7.12 and 5.25 oocytes respectively. Noteworthy is the fact that from the three women that were aged 43, who were given extension due to Covid measures, a total of 2 oocytes were collected from one woman only, thus the average oocytes collected per patient is just of 0.67. Thus, statistics clearly show that women over 40, undergoing fresh cycles have a less chance of having a successful outcome if they use their own oocytes. (Table 3).

Table 3. Oocytes Collected by Age Group

Age	No of Females	Total Oocytes Collected	Average	Max	Min
18-24	2	20	10.00	11	9
25-28	7	98	14.00	25	4
29-32	43	440	10.23	34	1
33-36	66	589	8.92	23	0
37-39	43	306	7.12	30	1
40-42	40	210	5.25	12	0
43	3	2	0.67	2	0
OVERALL	204	1665	8.16		

When considering the number of oocytes collected from the total number of female patients undergoing a Fresh cycle, it appears that the quantity of oocytes collected per cycle relative to the age of the female patient is higher at MDH ART Clinic in all age groups except in the 40-42 age bracket, when compared to self-funded patients. The average oocytes collected per patient at MDH ART Clinic is 8.32 compared to the 6.31 at the private establishment (Table 4).

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

	NHS			Self-Funded		
Age	**No of Females**	**Total Oocytes Collected**	**Average**	**No of Females**	**Total Oocytes Collected**	**Average**
18-24	2	20	0.00	0	0	0.00
25-28	7	98	14.00	0	0	0.00
29-32	42	439	10.45	1	1	1.00
33-36	57	519	9.11	9	70	7.78
37-39	40	288	7.20	3	18	6.00
40-42	38	198	5.21	2	12	6.00
43	2	2	1.00	1	0	0.00
OVERALL	**188**	**1564**	**8.32**	**16**	**101**	**6.31**

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 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 number of oocytes their patient has got left. 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 from women undergoing treatment and whose serum AMH values were ≤1μg/l, or less than 7pmol/l was performed. Since a significant number of AMH test results which were provided were older than six 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 both patients themselves and the clinicians dealing with patients with poor ovarian reserve, with respect to possibilities and expectations of outcomes.

Throughout 2021, there were 57 female patients with a serum AMH concentration of ≤1μg/l, or less than 7pmol/l who had undergone a Fresh cycle. The total amount of oocytes collected from these 57 patients was 241, with the maximum number of oocytes collected being 11 compared to the maximum 16 reported in 2020. Whilst in 2020 the minimum oocytes collected were only 1, this year the minimum is 0 as it was reported that there were four (4) women who had no oocytes to collect.

Also, good to note that a further four (4) women, although managed to have a collection of oocytes they did not have a fertilisation. One other woman had all her collected oocytes, discarded as they were immature.

From a total of fifty-seven (57) women only nineteen had an embryo transfer, out of which five had a pregnancy. Two of these women suffered a miscarriage, thus only three women with very low AMH gave birth or were expected to give birth.

The average number of oocytes collected was 4.22 per patient, same as figures reported in 2020, and there were 21 females who had 5 or more oocytes collected. (Table 5).

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

AMH <= 1 Occurrences	Min Oocytes Collected	Max Oocytes Collected	Total Oocytes Collected	Average Oocytes Collected	Occurrences with 5 oocytes or more
57	0	11	241	4.22	21

7.3. Oocytes Discarded

Oocytes obtained following ovarian stimulation should meet certain criteria 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.

From a total of 208 oocytes collections carried out during the calendar year, a total of 629 oocytes have been discarded in 202. Six hundred and nineteen (619) oocytes (98.41% of all discarded oocytes), or 37.18% from the total oocytes collected, were discarded following the egg retrieval process (Fresh cycle), for an average of 3.03 discarded oocytes per Fresh cycle.

The remaining 10 oocytes (1.59% of all discarded oocytes) failed to survive the thawing process, for an average of 2.50 oocytes discarded per Thawed cycle.

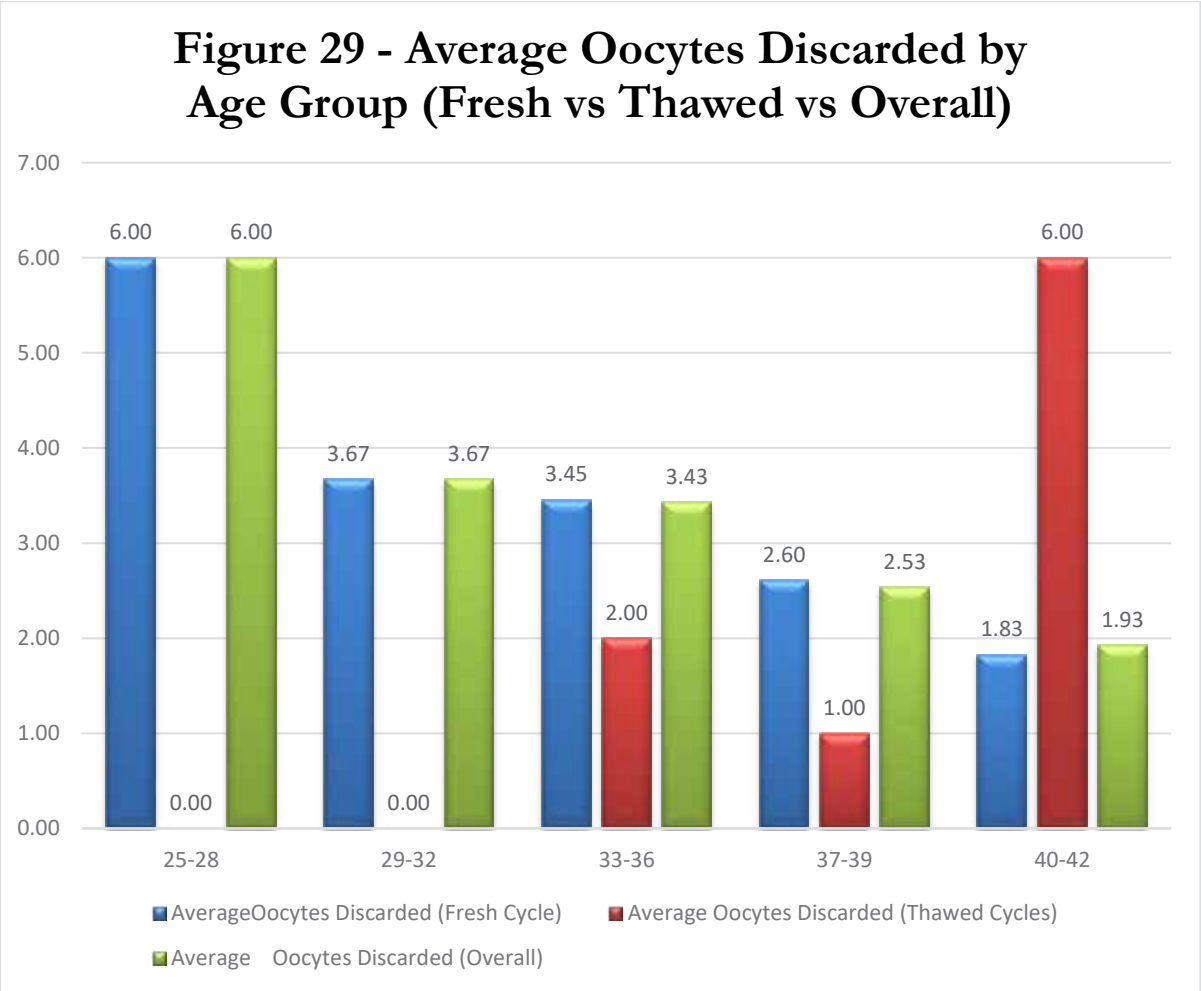
The total average of discarded oocytes for both Fresh and thawed processes was 3.02 per process. (Table 6).

Table 6. Oocytes Discarded

Age	No of Females (Fresh Cycle)	Total Oocytes Discarded (Fresh Cycle)	Average Oocytes Discarded (Fresh Cycle)	No of Females (Frozen Cycles)	Total Oocytes Discarded (Frozen Cycles)	Average Oocytes Discarded (Frozen Cycles)	No of Females (Overall)	Total Oocytes Discarded (Overall)	Average Oocytes Discarded (Overall)
18-24	2	6	3.00	0	0	0.00	2	6	3.00
25-28	7	42	6.00	0	0	0.00	7	42	6.00
29-32	43	158	3.67	0	0	0.00	43	158	3.67
33-36	66	228	3.45	1	2	2.00	67	230	3.43
37-39	43	112	2.60	2	2	1.00	45	114	2.53
40-42	40	73	1.83	1	6	6.00	41	79	1.93
43	3	0	0.00	0	0	0.00	3	0	0.00
OVERALL	**204**	**619**	**3.03**	**4**	**10**	**2.50**	**208**	**629**	**3.02**

In 2021, contrary to figures as reported in 2020, but in line with figures reported in 2019 and 2018, the largest number of oocytes discarded is from women in the 33–36-year age bracket. In 2020, most oocytes were discarded from women in the 29–32-year age groups. Noteworthy is the fact that whilst in 2020 the discarding rate of oocytes stood at 50.14%, during 2021 there was a substantial decrease of 12.36% in oocytes that were discarded resulting in 37.78% of all collected oocytes / thawed oocytes being discarded.

The MDH ART Clinic reported a 37.85% discarding rate from oocytes collected at its centre, whilst the St James Conception Unit reported a discarding rate of 36.63% of total oocytes collected collectively from the three feeder clinics referring patients to its centre. (Figure 29).



Whilst figures of 2020, show a constant average discarding of oocytes per patient for each age group which ranged from 2.91 to 7.31, this year's figures range from 1.00 to 6.00 oocytes discarded per patient, with the most oocytes discarded in the younger age group and the older age group brackets.

7.4. Fresh vs Thawed Sperm

Out of the 204 cycles carried out in 2021 which required the provision of sperm, thawed sperm has been utilized in twenty-five cycles, or 12.25%, of the procedures undergone. This is very high compared to the only 3 cycles that used thawed sperm in 2020 which was only 2.01% of all procedures carried out in that calendar year. Fresh sperm, ejaculated or in some instances obtained through nine testicular extraction/aspiration, has been used in the remaining procedures which have been carried out.

7.5. Storage of Gametes and Embryos

Pursuant to the introduction of the Embryo Protection Act of 2012, licensed clinics were allowed to store gametes (oocytes and sperm). Storage of gametes started as of July 2013 in the private licensed clinic, while storage from Government-funded cycles started in January 2014. Storage at the MDH facility started as of January 2015.

Up to 1st October 2018, embryo cryopreservation was only allowed in exceptional cases as approved by the Authority. With the introduction of the Embryo Protection Amendment Act of 2018, embryo cryopreservation was made available to all prospective parents with prior approval of additional fertilisations from the Authority.

7.5.1. Storage of Oocytes

Out of the 204 females who had oocytes retrieved in 2021, only 47 (23.04%) had enough oocytes to store. This has registered an increase of 1.56% from previous year. A total of 157 couples had no oocytes left to vitrify (Table 7). This is in line with figures registered in 2020, 2019 and 2018 where more prospective parents had oocytes to discard than prospective parents who had oocytes to store.

Table 7 – Fresh Cycles with NO Oocyte Vitrification

	NHS			Self-Funded			Total		
Age	No of Cycles	Total Cycles with NO Oocytes to Vitrify	% of cycles with no Oocytes to Vitrify	No of Cycles	Total Cycles with NO Oocytes to Vitrify	% of cycles with no Oocytes to Vitrify	No of Cycles	Total Cycles with NO Oocytes to Vitrify	% of cycles with no Oocytes to Vitrify
18-24	2	0	0.0%	0	0	0.0%	2	0	0.0%
25-28	7	5	71.4%	0	0	0.0%	7	5	71.4%
29-32	42	25	59.5%	1	1	100.0%	43	26	60.5%
33-36	57	40	70.2%	9	7	77.8%	66	47	71.2%
37-39	40	34	85.0%	3	3	100.0%	43	37	86.0%
40-42	38	38	100.0%	2	1	50.0%	40	39	97.5%
43	2	2	100.0%	1	1	0.0%	3	3	100.0%
OVERALL	188	144	76.6%	16	13	81.3%	204	157	77.0%

The total number of oocytes vitrified from Fresh cycles carried out in 2021 was of 257, this is higher than the 160 oocytes vitrified in 2020 and the 172 vitrified in 2019 and this contrasts well with the 707 oocytes that were cryopreserved in 2018, for an average of 5.46 oocytes per prospective parent. The maximum number of oocytes vitrified from a single cycle was twenty-one (21) and the minimum was two (2) oocytes which both were vitrified at the public facility.

It is noteworthy to point that while three (3) out of the 16 patients who had oocyte collection vitrified oocytes at the St James Conception Unit equivalent to 18.75% of self-funded cycles, at the MDH ART clinic only forty-four (44) women out of the 188 who had oocyte collection had oocytes to vitrify thus 23.40% of cycles had resultant good quality eggs for collection and vitrification.

The maximum number of oocytes thawed for one single female from thawed oocyte cycles was 10 oocytes at MDH ART Clinic while the minimum number of oocytes thawed was 4, two prospective parents who underwent a thawed oocyte cycle carried out at St James Conception Unit and MDH ART Clinic had the minimum of four oocytes thawed.

7.5.2. Storage of Sperm

Eighty-six (86) sperm cryopreservation requests were approved during 2021. A total of eighty-two (82) males vitrified their sperm, the remaining 4 who requested sperm cryopreservation did not vitrify sperm. In nine (9) cases, testicular aspiration/extraction (TESA/TESE) was performed to obtain sperm surgically.

Twenty-five (25) males requested Fertility preservation following oncology diagnosis prior to starting chemotherapy, out of which 24 had a successful cryopreservation.

Another forty-nine (49) males had Urology referrals with the main reason for referral being decrease in male fertility parameters. Forty-six (46) of these males successfully cryopreserved sperm. There has been a continuous request for sperm storage from the Urology Consultants throughout 2021. Only five (5) of the male patients who stored their sperm did this prior to immediately proceeding with an IVF/ICSI or an IUI cycle, all of which successfully cryopreserved sperm. A total of twenty-five males used thawed sperm previously cryopreserved for their procedures.

For the first time since the Authority has issued its annual reports, during 2021, there were seven (7) males who requested cryopreservation of sperm prior to starting their hormonal or surgical transitioning process to females. All seven had successful cryopreservation. (Table 8).

Table 8 – Storage of Sperm

	Cryopreservation Requests	Cryopreserved Sperm	Not Cryopreserved
Oncology Referrals	**25**	**24**	**1**
Urology Referrals	**49**	**46**	**3**
Prior to IVF or IUI Procedures	**5**	**5**	**0**
Transgender	**7**	**7**	**0**
Total	**86**	**82**	**4**

7.5.3. 'Freeze-All' Oocytes Cycles

In exceptional circumstances, clinicians may decide to proceed with oocyte retrieval but freeze all the oocytes for later fertilization. This is usually the case when uterine pathologies or a risk of Ovarian Hyperstimulation (OHSS) has been identified. It may also be the case that while the oocytes were being retrieved, the male partner had no viable sperm in the sample provided; or else no sperm was found during a TESA procedure, and hence fertilization couldn't take place.

During this calendar year there were also patients who were given prior approval by the Authority to proceed with a freeze-all cycle, as detailed in Section 1.8 above.

In 2021, Six permissions were granted to six women aged between 22 and 38 years of age on medical grounds who made their request prior to starting chemotherapy for oncology diagnosis. Three of these women opted to cryopreserve oocytes only and not proceed with embryo cryopreservation. One other woman opted for embryo cryopreservation only, while the other two women chose to cryopreserve both their supernumerary oocytes as well as their embryos. All these women underwent their procedure at the MDH ART Clinic.

Another approval was granted to a female prior to starting the process to transitioning into a male, this patient opted for cryopreservation of oocytes at the MDH ART Clinic.

Another woman requested to cryopreserve her oocytes at the private facility for social freezing reasons, to use her oocytes at a later stage in life, this was also granted permission by the Authority in 2021.

7.5.4. Embryo Cryopreservation

In Malta, under the Principal Act up to 30th September 2018 permission for cryopreservation of embryos could only be granted by the Embryo Protection Authority as per Article 7 of the Law, if transfer of the fertilized embryos in the womb was not possible owing to grave and certified *force majeure* not predicted at the moment of fertilization. The total of embryos cryopreserved under these exceptional cases clause between 2013 and 2018 amounted to 7 embryos.

With effect from 1st October 2018 and the introduction of the Embryo Protection Amendment Act, prospective parents undergoing ART treatment could opt to have additional fertilisation, two embryos transferred in one cycle and the resultant embryos cryopreserved for future use.

During 2021, the Authority received notification of 1 cycle carried out at the St James Conception Unit that all the embryos created were cryopreserved due to a Risk of OHSS.

During same calendar year, the Authority also received notification from MDH ART Clinic Embryologists, as reported on the EEART system that in one hundred and forty (140) cycles, or 80.46% of cases, all embryos created had to be cryopreserved. The Embryologist reported that seventy-seven (77) of these cycles or 55% of all freeze-all embryo cycles were a result of a risk of Ovarian Hyperstimulation (OHSS) after fertilisation of the oocytes were carried out, this was followed by forty (40) cycles or 28.57% due to High Oestradiol levels. Another sixteen (16) cases were due to various medical reasons amongst which were polyps, liquid found in uterine cavity and uterine treatment necessary between fertilisation and embryo transfer date. Six (6) other cases were abandoned and required a freeze all embryo cycle due to High Progesterone levels. There was one request by patient to postpone cycle and freeze all embryos.

Since the introduction of the amendment law in 2018, a total of seven hundred and fifty-two (752) embryos have been cryopreserved for future use, thus bringing total to seven hundred and fifty-nine (759) cryopreserved embryos. Noteworthy is the fact that four hundred and eighteen of which were cryopreserved during the calendar year of 2021.

A total of seven hundred and twenty-six (726) embryos were cryopreserved at MDH ART Clinic whilst only thirty-three (33) were cryopreserved at St James Conception Unit. (Table 9).

Table 9 – Storage of Embryos since 2013

Embryo Storage	NHS	Self-Funded	Total
Exceptional Cases	7	0	7
Oct-18	16	0	16
2019	121	6	127
2020	184	7	191
2021	398	20	418
Total Storage	726	33	759

Out of the total seven hundred and fifty-nine (759) embryos in storage, ten embryos were transferred between the two local licenced clinics. Another two embryos were brought from abroad and stored in Malta. Whilst two hundred and twenty-nine (229) embryos were thawed to be used in embryo transfer procedures carried out in 2021. All embryos thawed survived the thawing process. Thus, the total of embryos cryopreserved as at end of 2021 stood at three hundred and eighty-eight (388), nearly double the embryo storage recorded at end of 202 which stood at 197 embryos. The majority of these embryos three hundred and seventy-six (376) are stored at the MDH ART Clinic and the remaining twelve embryos are stored at the private facility of St James Conception Unit. (Table 10).

Table 10 – Storage of Embryos distribution 2021

Embryo Storage	NHS	Self-Funded	Total
Storage as at 01/01/2021	187	10	197
2021	398	20	418
Total	585	30	615
Transfer between local Clinics	10	-10	0
Transfer from Clinics Abroad	2	0	2
Embryos Used 2021	-221	-8	-229
Storage as at 31/12/2021	376	12	388

7.6. End of Storage

During 2021, thirty-eight requests were received from prospective parents who wished to discard their frozen oocytes and sperm, stored both at the public and private facility.

7.7. Total Storage

As at 31st December 2021, the total amount of oocytes stored at the licensed clinics stood at a total of 2203 oocytes with the majority stored at MDH, whilst the total number of sperm vials was of 1891, again the majority stored at MDH. The three hundred and eighty-eight (388) cryopreserved embryos of which the majority 376, are stored at the ART Clinic in Mater Dei Hospital whilst the remaining twelve (12) embryos are stored at the St James Conception Unit (Table 11).

Table 11 – Total Storage

Type of Storage	NHS	Self-Funded	Total
Oocytes	1730	473	2203
Sperm	1810	81	1891
Embryos	376	12	388

The three hundred and eighty-eight (388) embryos cryopreserved at both centres, belong to 181 prospective parents, 175 of which received treatment at the MDH ART Facility and 6 at the St James Conception Unit.

The embryos stored at the MDH ART Clinic are of 56 prospective parents who have one (1) cryopreserved embryo each, 65 prospective parents who have two (2) cryopreserved embryo each, 31 prospective parents who have three (3) cryopreserved embryos each, 18 prospective parents who have four (4) cryopreserved embryos each, whilst 5 prospective parents have five (5) cryopreserved embryos each.

The embryos stored at the St James Conception Unit are of 1 prospective parent who have one (1) cryopreserved embryo, 4 prospective parents who have two (2) cryopreserved embryo each and one prospective parent who have three (3) embryos stored.

All prospective parents have expressed their willingness to make use of their cryopreserved embryos including the couples that already gave birth through IVF and the couples that are expecting to give birth from cycles carried out. Thus, no embryos are currently available for embryo adoption.

8. IVF/ICSI PROCEDURES

8.1. Cycles Started

In addition to the cycles which have been performed throughout the calendar year, licensed clinics have also reported a total of 39 cycles which were abandoned prior to oocyte retrieval. All thirty-nine (39) couples who abandoned their cycle were going to undergoing treatment either at the MDH ART Clinic or else at the private facility. Many cycles were abandoned due to poor response to the stimulation treatment the female patients received, other cycles were abandoned as the prospective parent got pregnant naturally whilst waiting for their cycle, others abandoned the cycle for medical reasons, whilst others had decided that they do not want to pursue any more in this journey.

8.2. Type of Procedure - IVF vs ICSI

In 2021, from a total of 354 cycles started, no IVF/ICSI procedure was carried out for 16 prospective parents. This was due to the fact that there were eight (8) couples who had either no oocytes to collect or their oocytes did not fertilise or else the oocytes collected had to be all discarded as they were of poor quality, these couples performed their procedures at both the MDH ART Clinic and the St James Conception Unit

Another 6 patients that had to opted for a 'Freeze-all oocyte' or a 'freeze-all embryos' cycle that were prior approved by the Authority, due to oncology reasons, another

one patient chose to go for social freezing at the private facility, while another female stored her oocytes prior to receiving hormonal treatment prior to transitioning. (Table 12).

Table 12. Type of ART Procedures

Type of ART	NHS	Self-Funded	Total	Total %
IVF	0	0	0	0.00%
ICSI	177	15	192	54.24%
Embryo Transfer	141	5	146	41.24%
NIL	13	3	16	4.52%
Total	**331**	**23**	**354**	

Out of the 192 procedures carried out, all (100%) were *intra-cytoplasmic sperm injection* (ICSI). In contrast to conventional *in vitro* fertilization (IVF), where a single egg is incubated in the presence of a significant number of sperm, while in ICSI, the embryologist selects a single sperm to be injected directly into an egg.

This contrast with figures quoted for the early years in regard to procedures carried out at MDH ART Clinic wherein few procedures were reported as IVF's. The licensed private clinic always opted for an '*All-ICSI*' approach.

8.3. Oocytes Injected and Fertilisation

Throughout 2021, a total of 803 oocytes were injected, the majority 789 oocytes or 98.26% of the total oocytes injected were from fresh cycles, the remaining 14 oocytes or 1.74% of the total injected oocytes where from thawed cycles. (Table 13).

Table 13. Oocytes Injected

Type of Cycle	Oocytes Injected	%
Fresh	789	98.26%
Thawed	14	1.74%
Total	803	

Out of the total 803 injected oocytes, there were 651 oocytes that reached fertilisation stage while 152 oocytes did not fertilise (Figure 30).

Thus, fertilisation rate is of 81.07% of all oocytes injected, a decrease of 0.38% over figures reported in 2020. (Figure 31).

Figure 30 - Fertilised vs Non Fertilised of Injected Oocytes

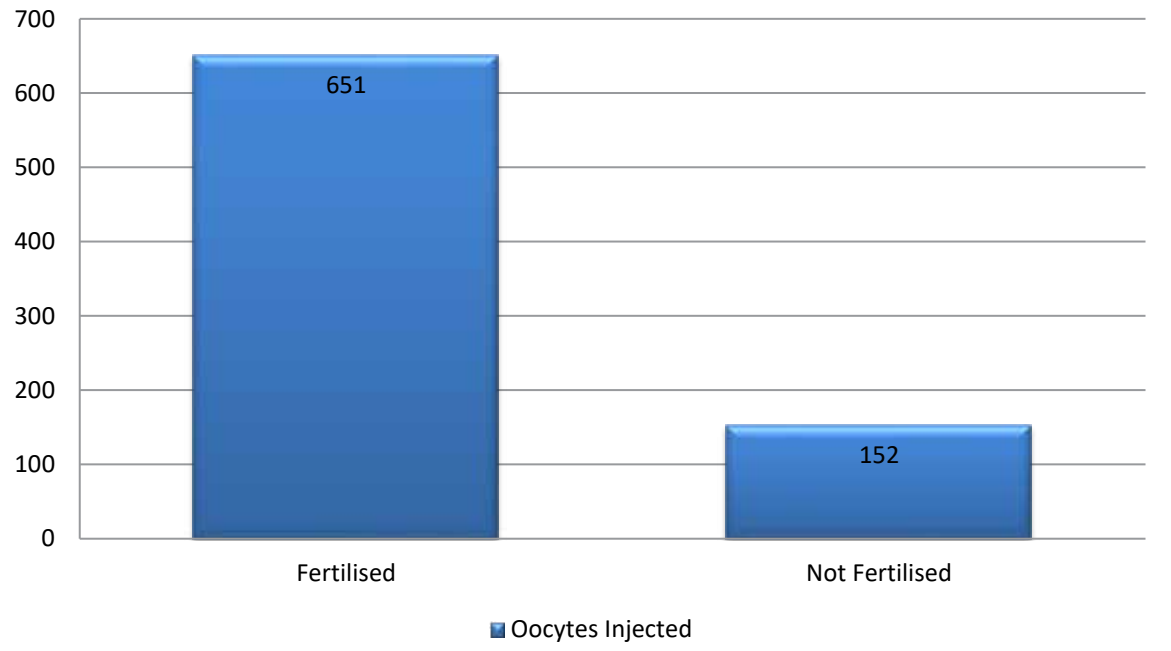
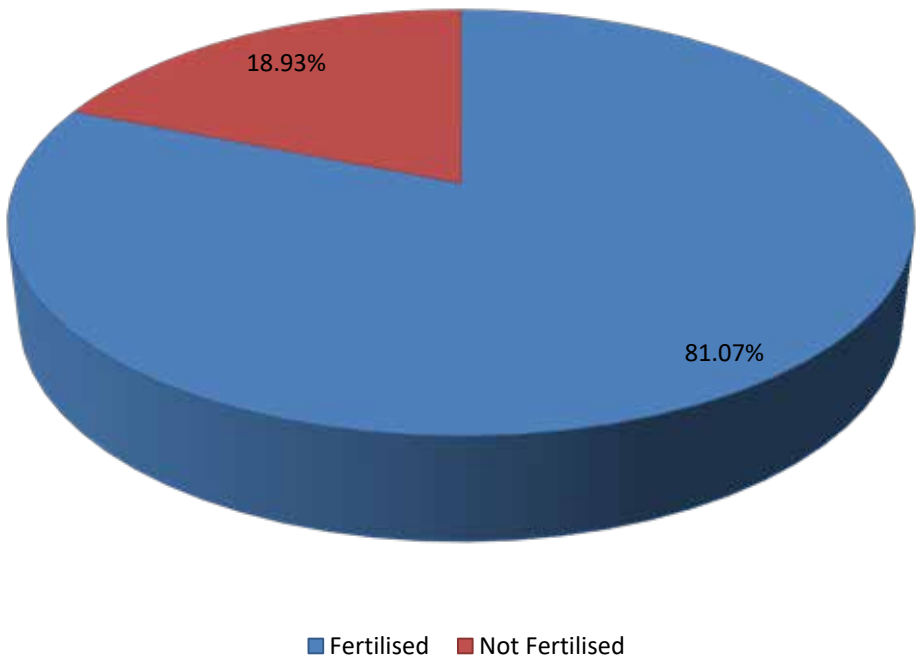


Figure 31 - Fertilised vs Non Fertilised Oocytes (%)

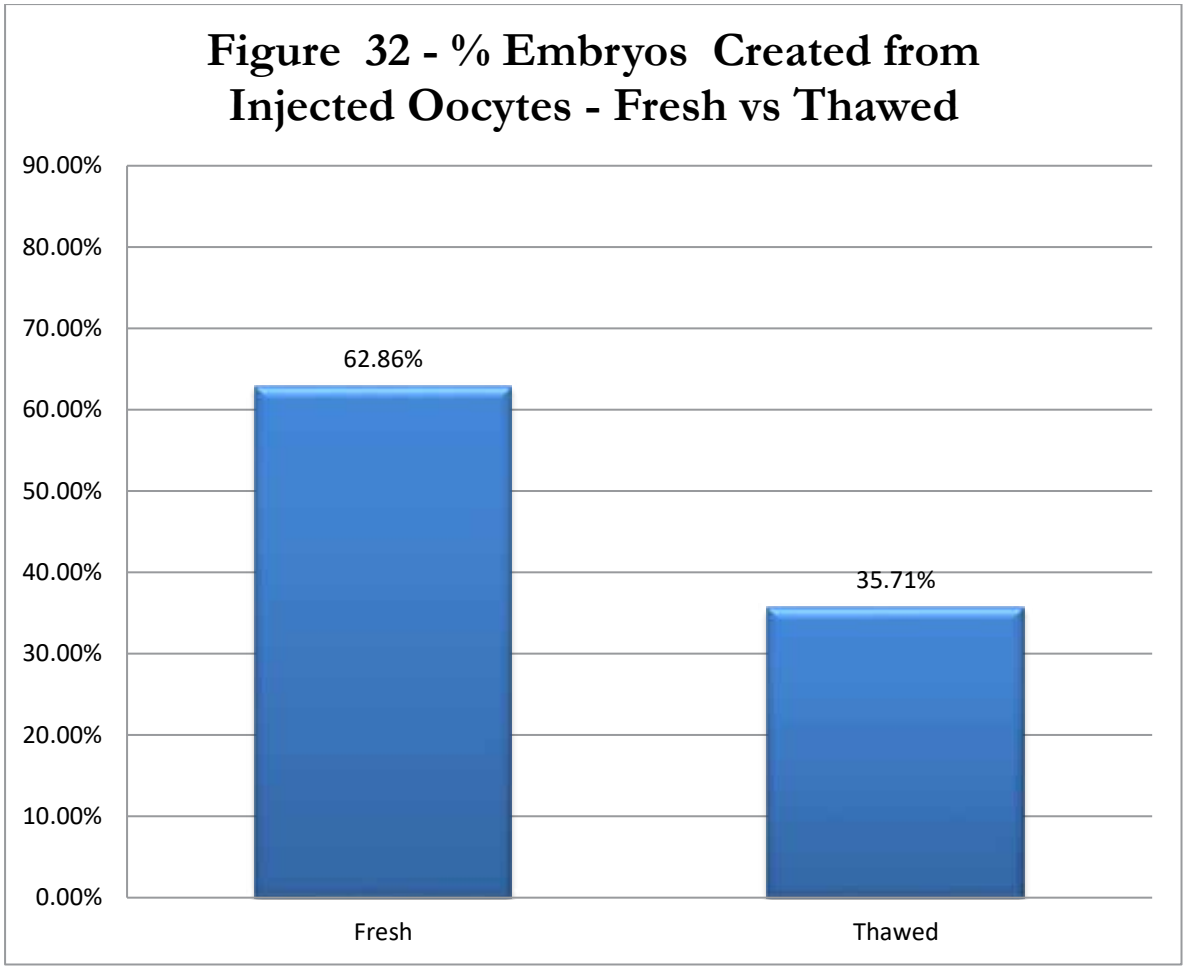


Out of the 651 fertilised oocytes, embryologists reported that a total of 150 embryos had arrested, 149 of these were from fresh oocyte cycles whilst only one arrested embryo was from a thawed oocyte cycle. The majority of these arrested embryos 139 were from cycles at MDH ART Clinic and 11 embryos arrested at the private facility.

This resulted in the creation of a total of 501 embryos, 496 from fresh oocytes and 5 from thawed oocytes. Most of these created embryos, 455 were created from cycles carried out at the MDH ART Clinic whilst the remaining 46 were created from cycles carried out at the St James Conception Unit. (Table 14 & Figure 32).

Table 14. Embryos Created

Type of Cycle	Oocytes Injected	Embryos Created	Created %
Fresh	789	496	**62.86%**
Thawed	14	5	**35.71%**
Total	**803**	**501**	



8.4. Embryo Transfers

The risk of a multiple birth is in large part determined by the number of embryos transferred back during IVF cycle treatment. Nowadays single embryo transfer has become common practice with a maximum of two embryos transferred.

With the introduction of the Principal Act which came into force in 2013, three embryos were allowed to put back if permission was sought from and granted by the Authority in that particular IVF cycle. In 2018, the amendments to the Embryo

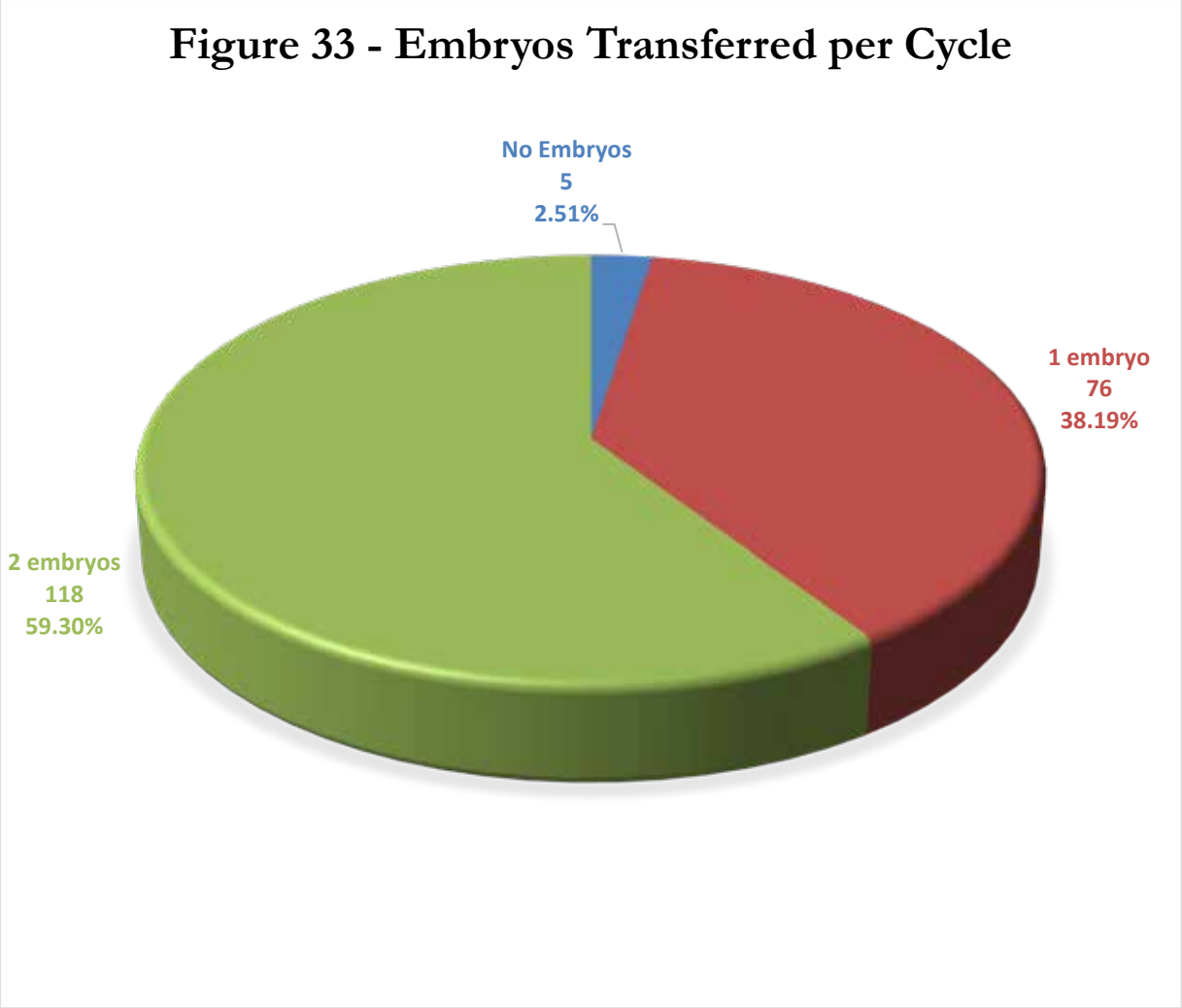
Protection Act came into force banning the use of triple embryos transfers. The combination of coming into effect of these policies and concerted efforts across the fertility sector led to fewer multiple births as a result. This led to restricting the birth of triplets. Multiple births remain a health risk for IVF patients and babies, but the decreasing multiple birth rate means that IVF is a safer treatment.

Out of the 501 fresh embryos created, four hundred and eighteen (418) embryos were cryopreserved, thus only eighty-three (83) embryos were transferred from fresh and thawed oocyte cycles. Another two hundred and twenty-nine (229) embryos from those that were previously cryopreserved were removed from storage for transfer, all of which survived the thawing process. Thus, a total of three hundred and twelve (312) embryos were eventually transferred that could lead to a pregnancy.

There was a total of 5 prospective parents or 2.51% who had no Embryo Transfer affected, as the oocytes they had injected failed to fertilize or else the fertilised oocytes/embryos arrested.

The three hundred and twelve (312) embryos were transferred in 194 treatment cycles that could result in a pregnancy. 175 of these treatment cycles were carried out at MDH ART Clinic whilst 19 treatment cycles were carried out at the private facility.

Out of the 194 couples who had viable embryos to transfer, 76 of them (38.19%) had a single embryo transferred. Whilst the remaining one hundred and eighteen (59.30%) couples, had two embryos transferred, the maximum allowed by law (Figure 33).



8.5. Embryo Transfers per Type of Cycle

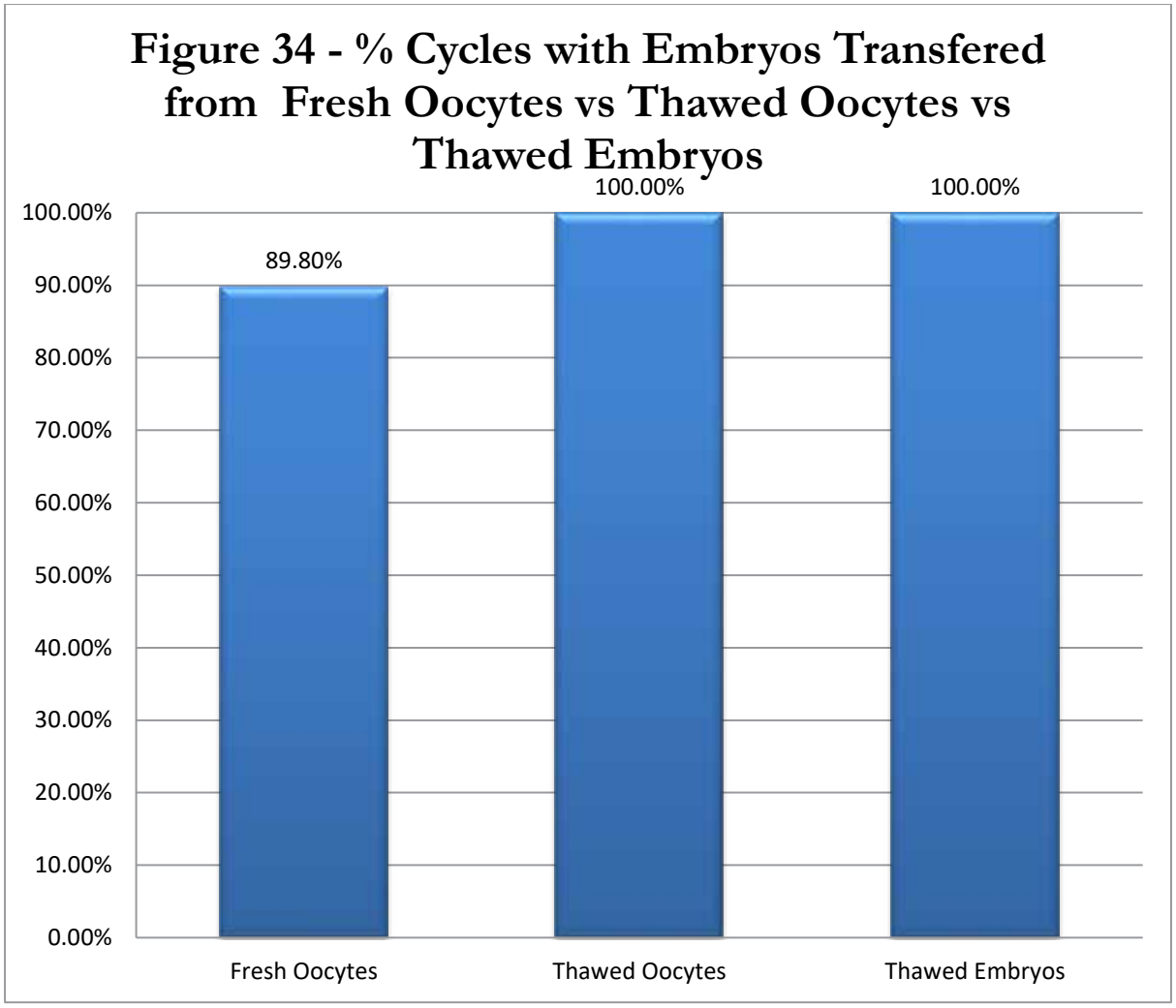
Out of the 194 embryo transfer procedures carried out, 44 were fresh oocytes cycles, whilst 4 where thawed oocyte cycles. The remaining 146, where thawed embryos cycles, 141 of which were carried out at the MDH ART Clinic, and five thawed embryo transfers were carried out at the St James Conception Unit.

The majority of the forty-four (44) fresh oocyte cycles that had an embryo transfer were carried out at MDH ART clinic, 32 in number, whilst the remaining twelve fresh oocyte cycles that had an embryo transfer were carried out at the private facility.

The four (4) thawed oocyte cycles, were carried out two each at the private facility and at the public facility. (Table 15 and Figure 34).

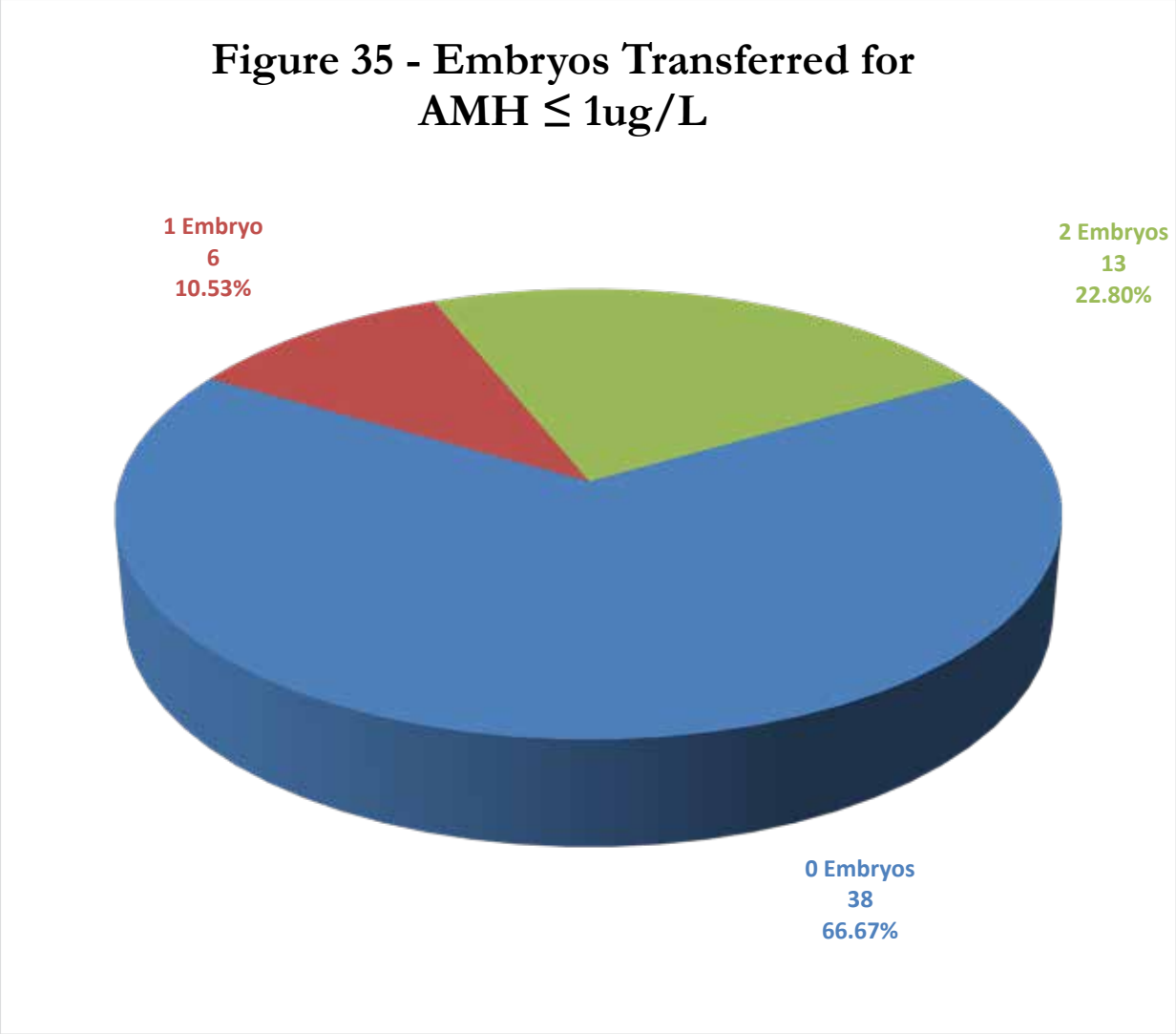
Table 15. Cycles with Embryo Transfer per Type of Cycle (%)

Type of Cycle	Cycles	Cycles with Embryo Transfer	Transferred %
Fresh Oocytes	49	44	**89.80%**
Thawed Oocytes	4	4	**100.00%**
Thawed Embryos	146	146	**100.00%**
Total	**199**	**194**	



8.6. Embryos transferred per AMH ≤1µg/L

As outlined already in Section 7.2, there was a total of 57 women with a serum AMH concentration of ≤1µg/l or less than 7 pmol/l. Only 19 of these women had an embryo/s created and transferred as thirty-eight women (66.67%) did not have any embryos. Six women, 10.53%, had a single embryo created and transferred; 13 women, or 22.80%, had 2 embryos created and transferred. (Figure 35).



Noteworthy is the fact that out of the 19 prospective parents who had an embryo transfer, only five of these women became pregnant. Two of which suffered a miscarriage, thus only three women out of the total of 57 women with a very low AMH level were expected to give birth.

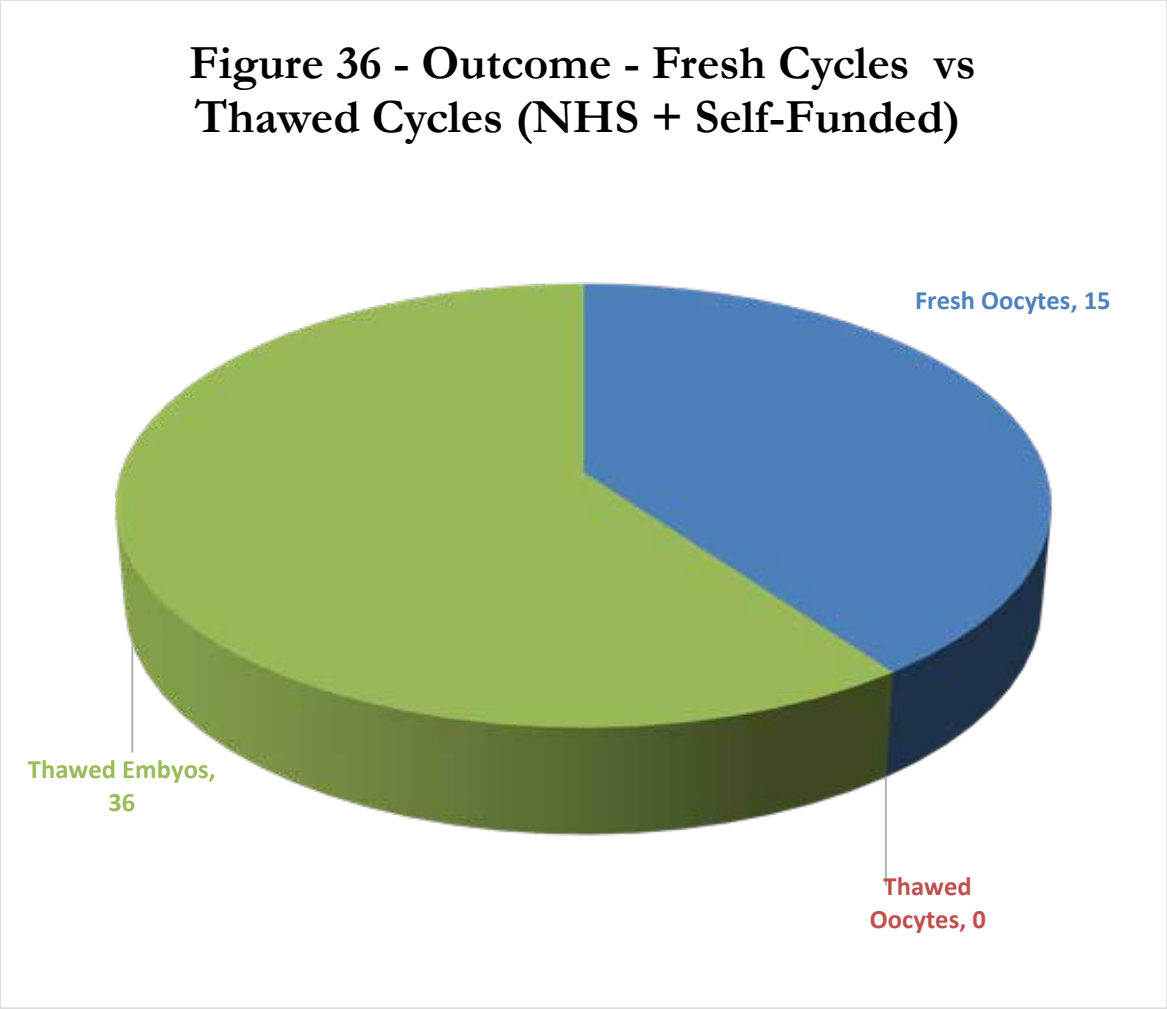
9. TREATMENT CYCLE OUTCOMES

9.1. Pregnancies

Out of the 194 treatment cycles that could lead to a pregnancy, carried out in 2021, there were 15 reported pregnancies from Fresh oocyte cycles, no pregnancies were reported from thawed oocyte cycle and 36 pregnancies from Thawed embryo cycles. **The resulting 51 pregnancies account for 26.29% success** which is **7.91% Higher** than the pregnancy rate for 2020. (Table 16 and Figure 36).

Table 16. Cycle Outcome

Outcome	NHS	Self-Funded	Total	% Outcome by Type	% Outcome	% Outcome of Pregnancies
Not Pregnant	21	8	29	**65.9%**	**65.91%**	
Miscarriage	2	0	2	**4.5%**	**34.09%**	**13.3%**
Live Birth	8	4	12	**27.3%**		**80.0%**
Expected	1	0	1	**2.3%**		**6.7%**
Not Pregnant	2	2	4	**100.0%**	**100.00%**	
Miscarriage	0	0	0	**0.0%**	**0.00%**	**0.0%**
Live Birth	0	0	0	**0.0%**		**0.0%**
Expected	0	0	0	**0.0%**		**0.0%**
Not Pregnant	107	3	110	**75.3%**	**75.34%**	
Miscarriage	7	1	8	**5.5%**	**24.66%**	**22.2%**
Live Birth	12	1	13	**8.9%**		**36.1%**
Expected	15	0	15	**10.3%**		**41.7%**



9.2. Cycle Outcomes – Fresh vs Thawed

Fifteen (15) couples, or **34.09%** of those undergoing Fresh oocyte cycles managed to get pregnant, **with a registered increase in success of 20.20% over figures of 2020** wherein only 13.89% had registered a pregnancy. Out of these 15 pregnancies, 12 couples (80%) had a live birth, 2 couples suffered a miscarriage, while the remaining 1 couple are still expecting to give birth. (Figures 37 and 38).

Figure 37 - Outcome of Fresh Cycles (Qty)

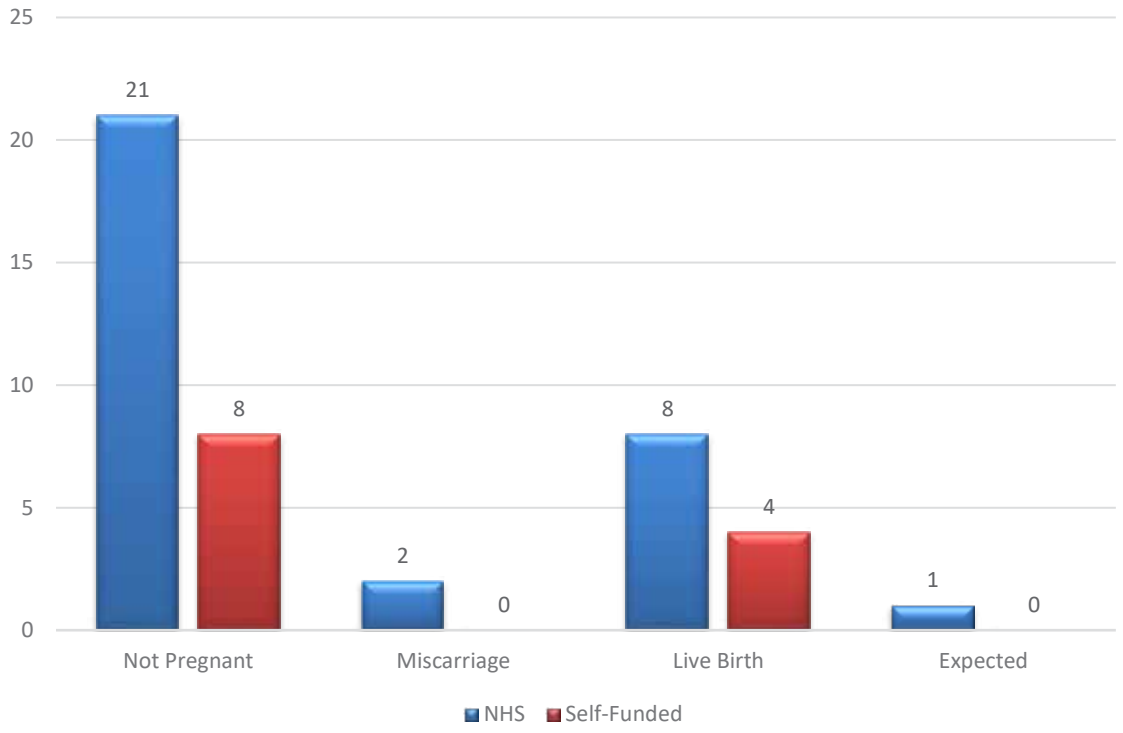
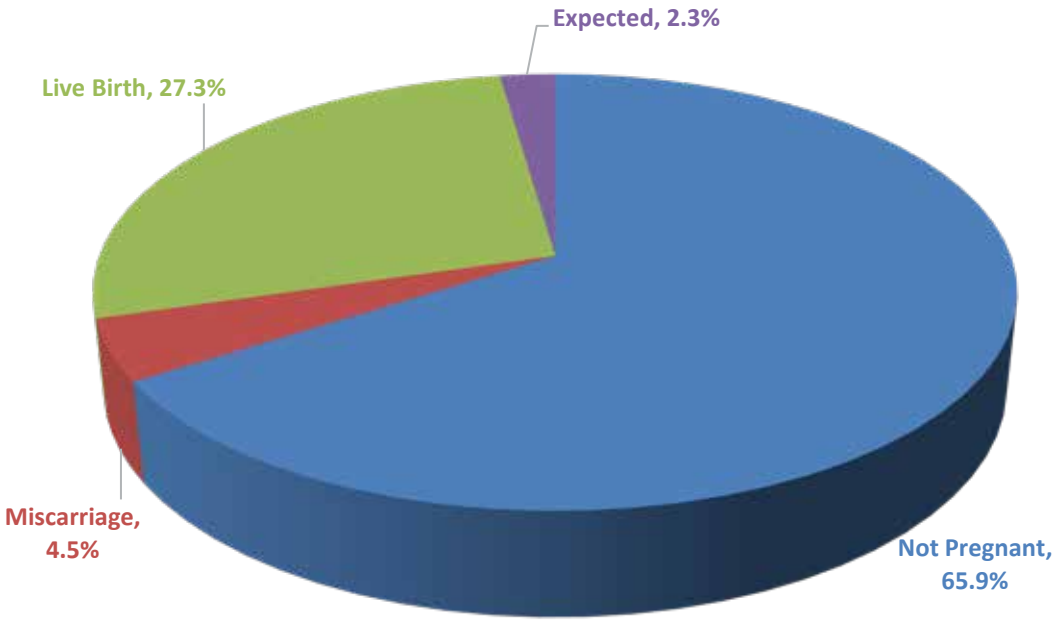
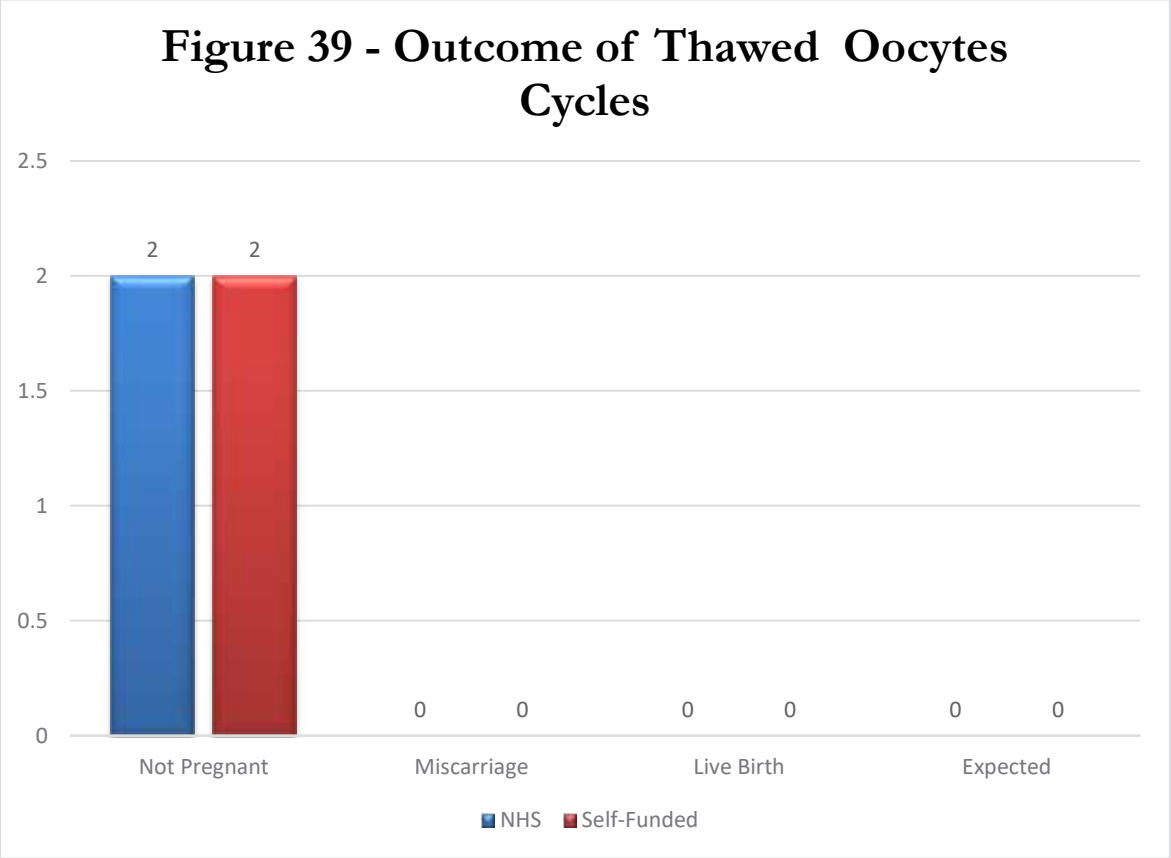


Figure 38 - % Outcome - Fresh Cycles (NHS + Self-Funded)



None of the four couples undergoing a Thawed oocyte cycle at both Tissue establishments got pregnant. This is in line with figures reported in 2020 where the three couples undergoing a thawed oocyte cycle, also did not get pregnant. (Figures 39).



Thirty-six (36) couples that underwent a thawed embryo cycle managed to get pregnant. Out of these 36 pregnancies, 8 couples suffered a miscarriage, 13 couples had a live birth, whilst the remaining 15 couples (41.70%) are still expecting to give birth (Figures 40 and 41).

Figure 40 - Outcome of Thawed Embryos Cycle (Qty)

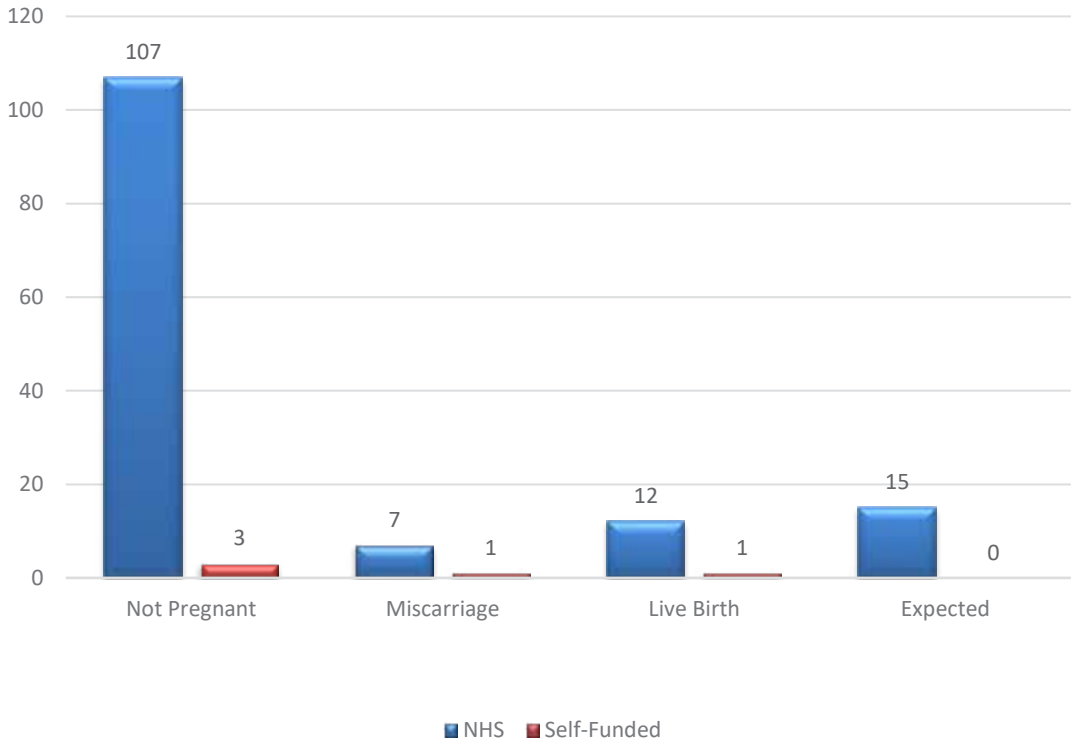
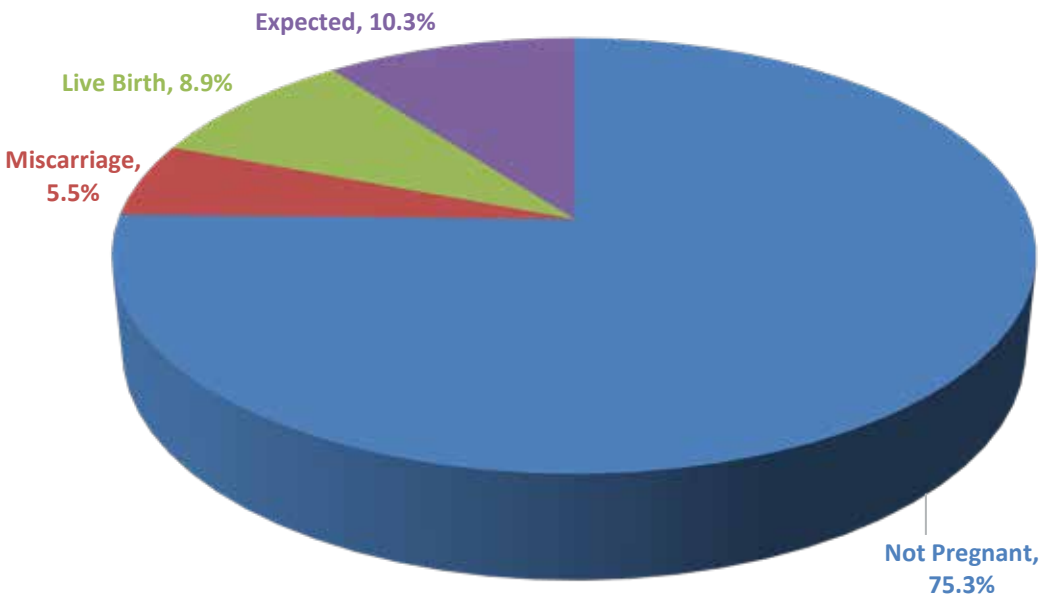


Figure 41 - % Outcome - Thawed Embryo Cycles (NHS + Self-Funded)



Whilst MDH ART Clinic registered a pregnancy rate of **24.13% from thawed Embryo Cycles,** the St James Conception Unit registered a **40% success pregnancy rate. As a result, in 2021 the pregnancy rate for Thawed Embryo Cycles was 24.66%, which registered a slight increase of 0.07% over the figures which were registered for 2020.**

It is noteworthy to point out that during 2021, the pregnancy success rate for Fresh oocyte cycles was 9.43% higher than that of Thawed Embryo Cycles.

Another noteworthy fact to point out is that the miscarriage rate from Thawed Embryo Cycle was 22.2% of pregnancies registered which is 8.9% higher than the miscarriage rate reported form fresh oocyte cycles, which stood at 13.3% of pregnancies. (Table 16)**.**

9.3. Cycle Outcomes – NHS vs Self-Funded

The pregnancy rate reported by the MDH ART Clinic, for fresh oocytes cycles was 1.05% higher than that reported by the St James Conception Unit. This is in line with figures reported in 2020. The sum of live and expected births from Fresh cycles carried out at MDH was 28.13%, a 5.2% less success than that registered for private clinics which was 33.33% (Figure 42). The sum of live and expected births from Thawed oocytes cycles carried out at both centres was nil, as all four procedures carried out did not result in a pregnancy. (Figure 43).

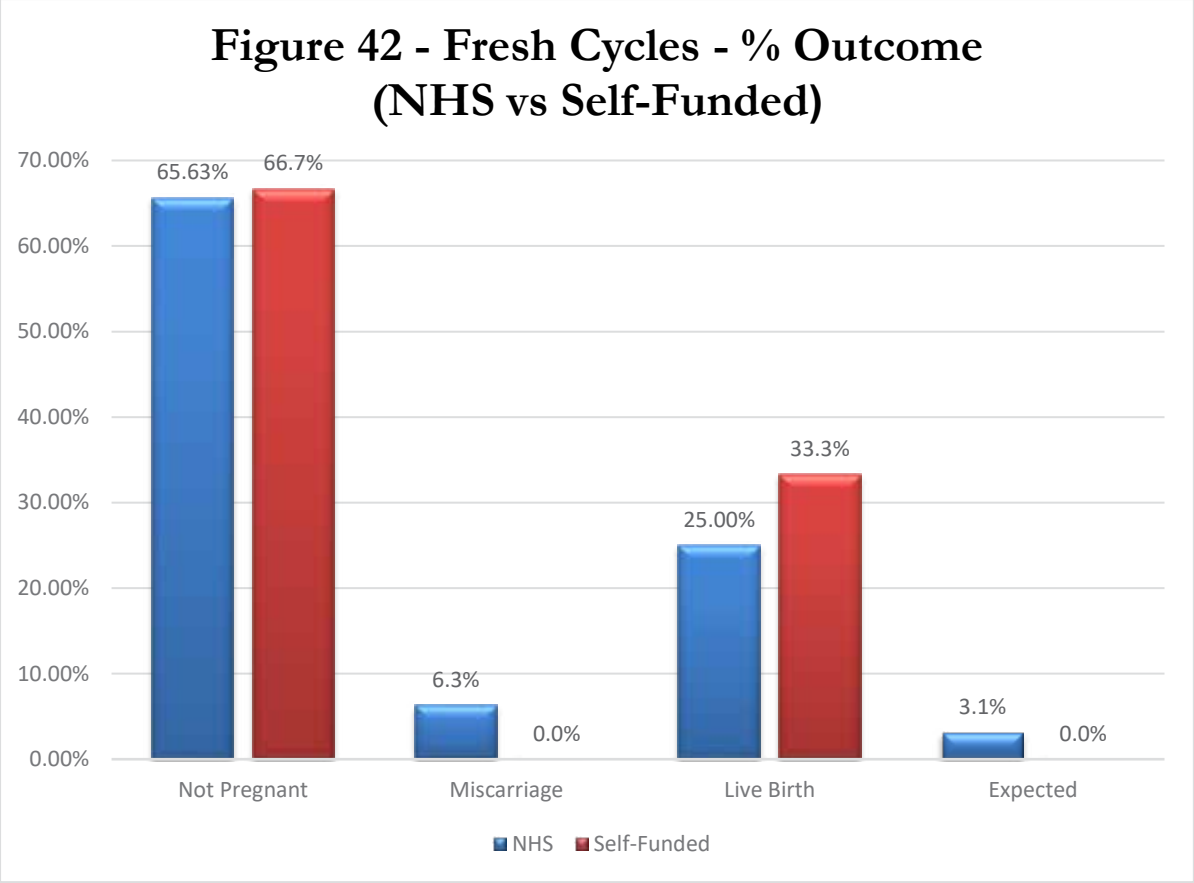


Figure 42 - Fresh Cycles - % Outcome (NHS vs Self-Funded)
70.00%
60.00%
50.00%
40.00%
30.00%
20.00%
10.00%
0.00%
65.63%
66.7%
6.3%
0.0%
25.00%
33.3%
3.1%
0.0%
Not Pregnant
Miscarriage
Live Birth
Expected
NHS
Self-Funded

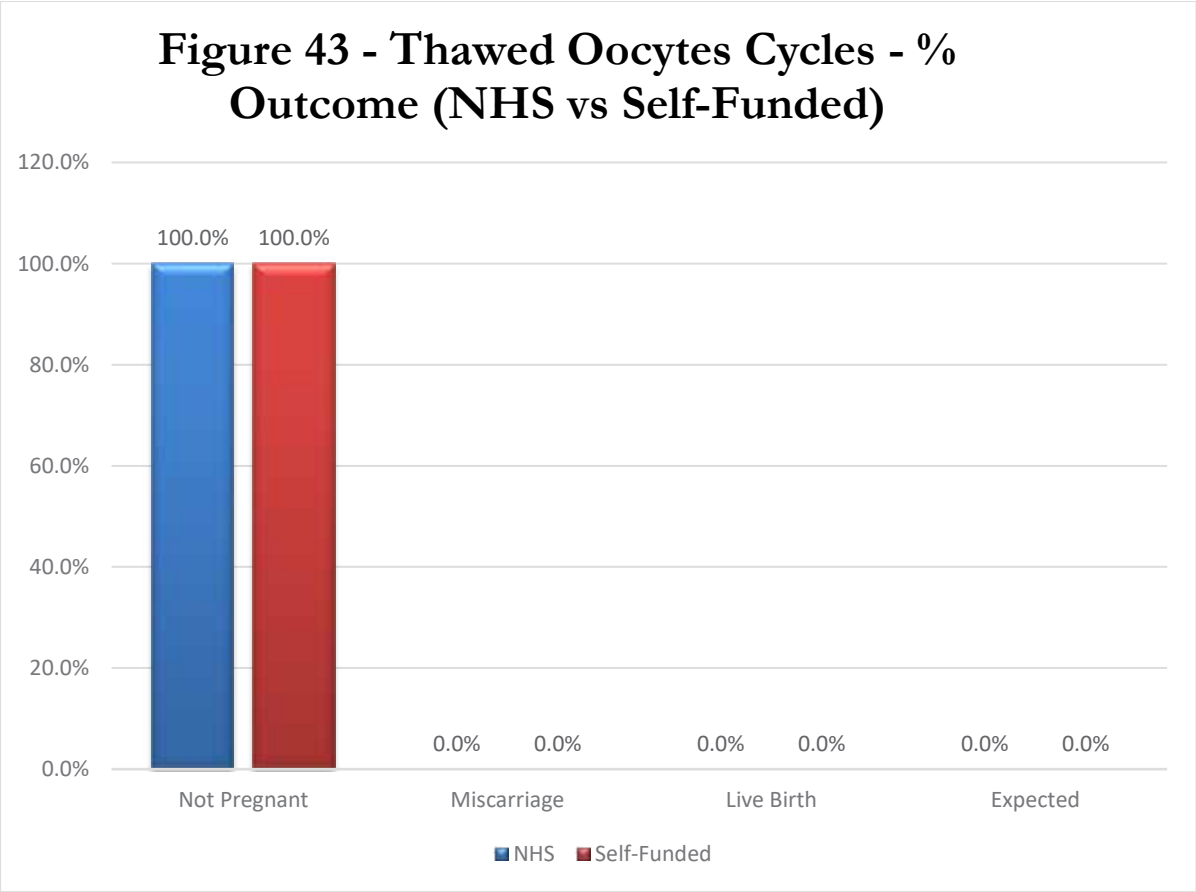
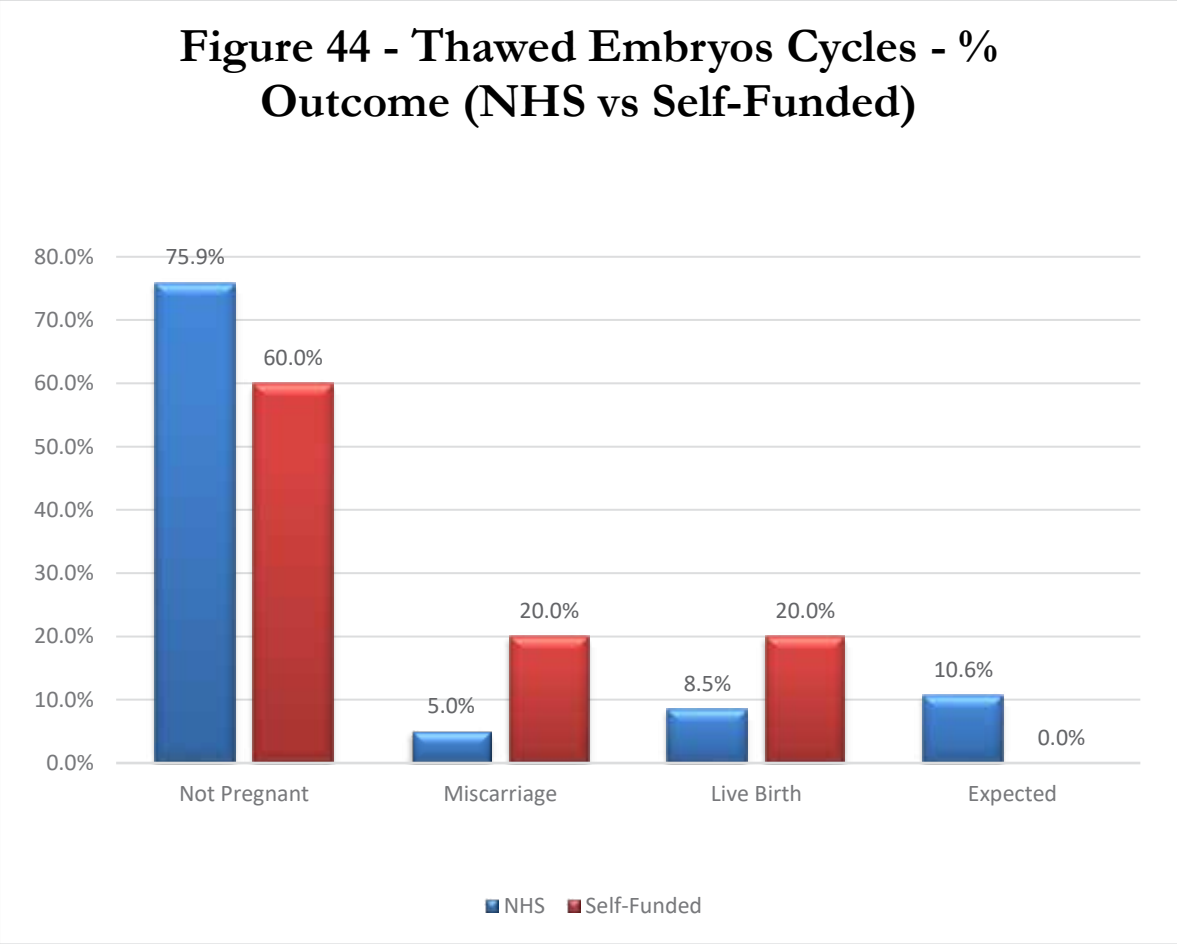


Figure 43 - Thawed Oocytes Cycles - % Outcome (NHS vs Self-Funded)
120.0%
100.0%
80.0%
60.0%
40.0%
20.0%
0.0%
100.0%
100.0%
0.0%
0.0%
0.0%
0.0%
0.0%
0.0%
Not Pregnant
Miscarriage
Live Birth
Expected
NHS
Self-Funded

The sum of live and expected birth rate from cycles carried out with thawed embryo transfers at the MDH ART Clinic was of 19.15%, this was due to the fact that MDH reported 7 miscarriages from the thirty-four pregnancies registered for these cycles. The sum of live and expected birth rate from cycles carried out with thawed embryo transfers at the St James Conception Unit was of 20%, this was due to the fact that SJH reported 1 miscarriage from the pregnancies registered for these cycles. (Figure 44).

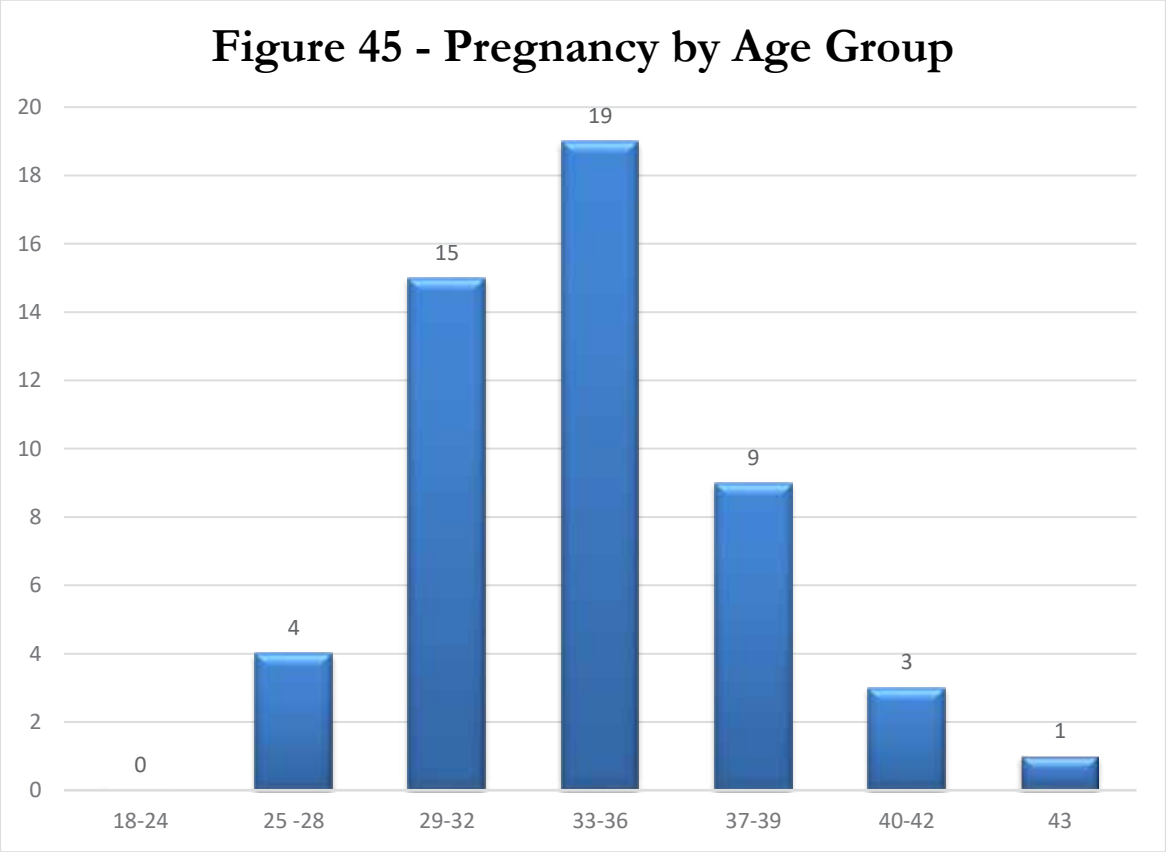


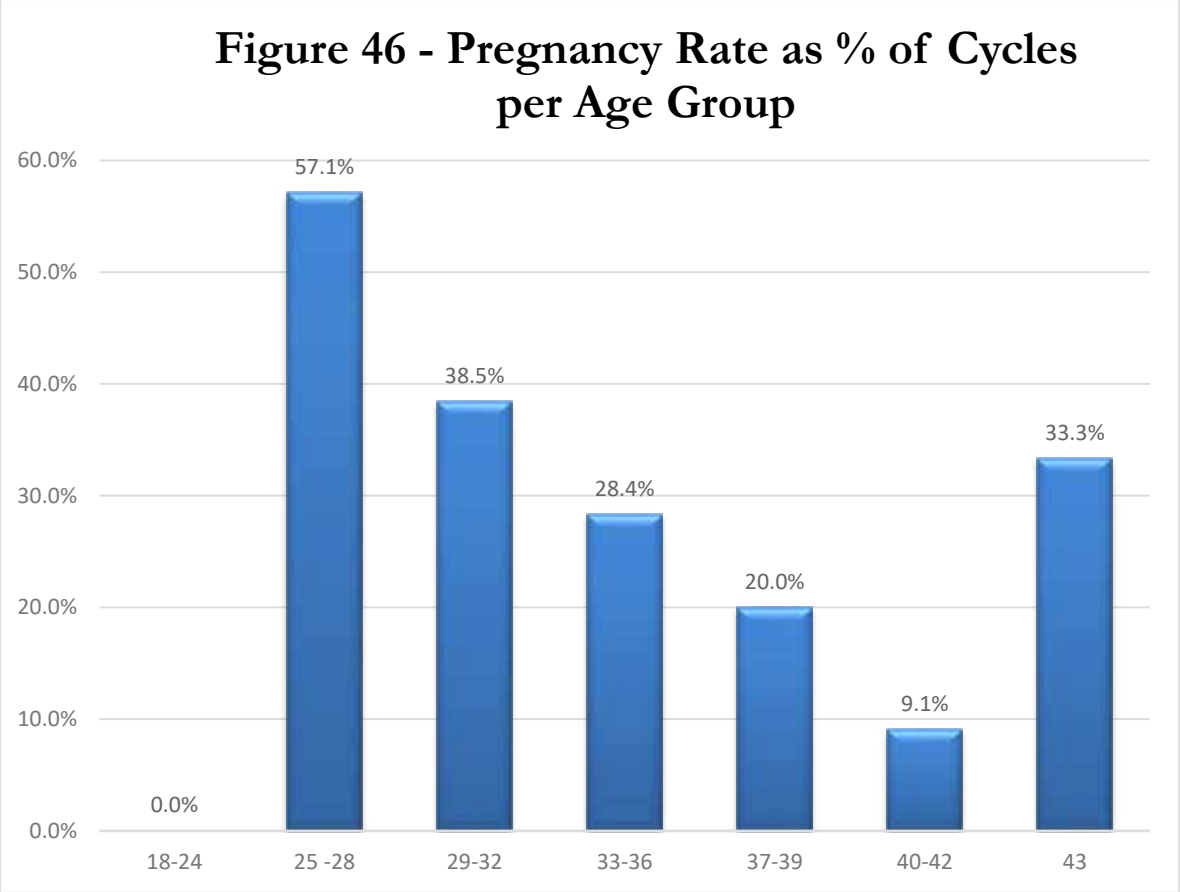
The Overall pregnancy rate for **MDH ART Clinic** was of **25.71%** whilst that of the **St James Conception Unit** incorporating patients from St James Hospital, St Claire's Medial Centre, and Veduta Clinic stood at **31.58%. With the average pregnancy rate for Malta for 2021 being 26.29%, 7.91% Higher** than for the year 2020.

9.4. Pregnancies by Age

In 2021, fifty-one (51) pregnancies were reported across all age groups. The highest number of pregnancies reported was for women in the 33–36-year-old bracket, this is in line with figures reported in the last three years. (Figure 45). This was however not reflected in the pregnancy rate, as percentage of cycles per age group was highest for women aged 25-28 at 57.1% (Figure 46).

This is in line with figures reported in the last years, where the highest pregnancy rate as percentage of cycle was reported in the 25-28 age group. It appears that in 2021 as in 2020 and 2019, maternal age was one of the most important predictive factors for an IVF/ICSI procedure to result in a pregnancy.





9.5. Pregnancy Rate per Embryos Transferred

From a total of 194 prospective parents who had a treatment cycle with the possibility of an embryo transfer effected, there were 51 resulting pregnancies, or 26.29%, an increase of 7.91% when compared to the previous year.

The couples who were most successful at achieving a pregnancy in 2021, were those who had 2 embryos transferred (32.20%), the current calendar year registered an increase of 9.15% over the 23.05% that was reported in 2020 with 2 embryos transferred.

Noteworthy to point is that there was also an increase of 10.66% in the pregnancies achieved by only one embryo transferred, from 6.45% reported during 2020 to 17.11% for 2021. (Table 17).

Table 17. Pregnancy Rate per Embryos Transferred

Transferred Embryos	Total IVF/ICSI Procedures	Total Pregnancies	% Pregnancies
0	5	0	0.00%
1	76	13	17.11%
2	118	38	32.20%
Total	199	51	25.63%
Total procedures with Embryo transfer	**194**	**51**	**26.29%**

9.6. Pregnancy Distribution per ART Cycle Attempts

Thirty-five (35) couples out of the 51 couples who got pregnant from cycles carried out in 2021, achieved a pregnancy on their 1st IVF/ICSI attempt, these were achieved by 31 couples who had undergone their cycle at the ART Clinic at MDH and 4 couples who self-funded their treatment at the St James Conception Unit. Ten (10) couples achieved a pregnancy on their 2nd attempt, 9 couples had treatments at the MDH facility whilst 1 couple had the treatment carried out at the private facility. Four couples on their 3rd attempt, achieved pregnancies from three cycles on the NHS and one was self-funded. Two couples achieved pregnancy on their 4th attempt at the NHS facility. All couples undergoing their 5th, 6th, 7th, or 8th attempt did not achieve a pregnancy. (Figures 47, 48 and 49).

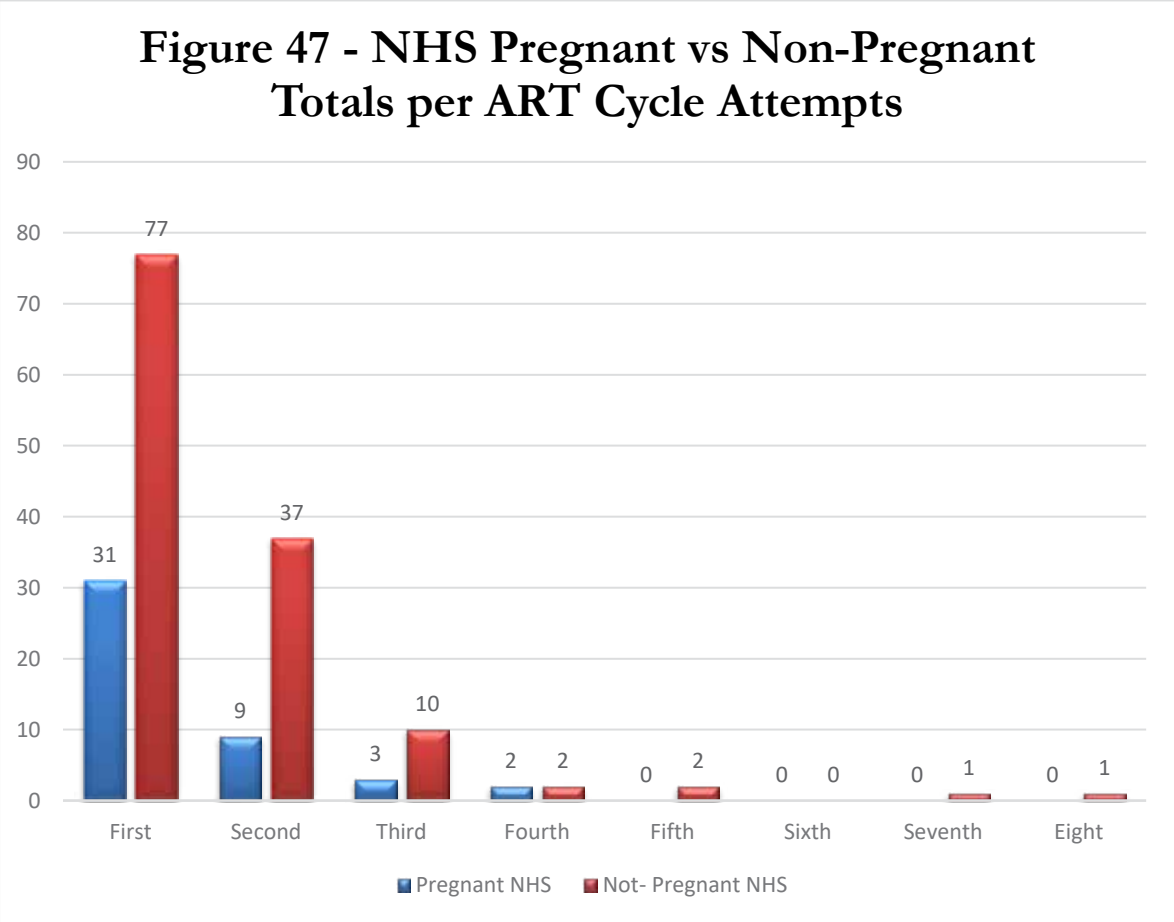


Figure 48 - Self-Funded Pregnant vs Non-Pregnant Totals per ART Cycle Attempts

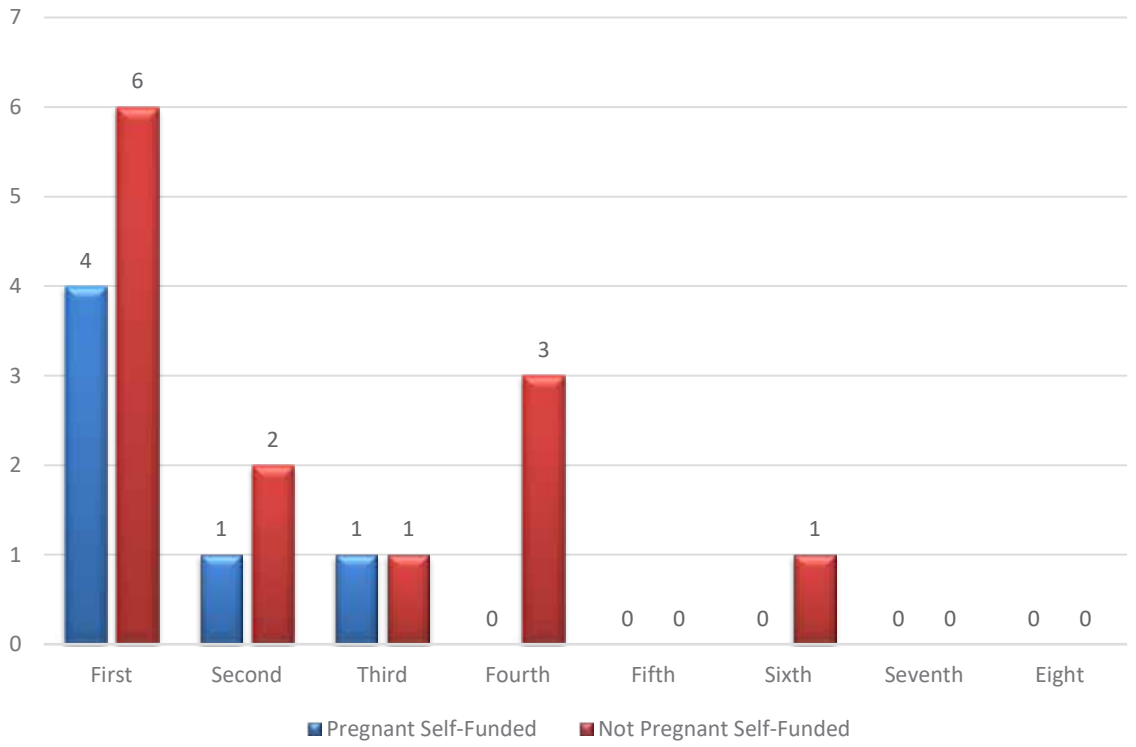
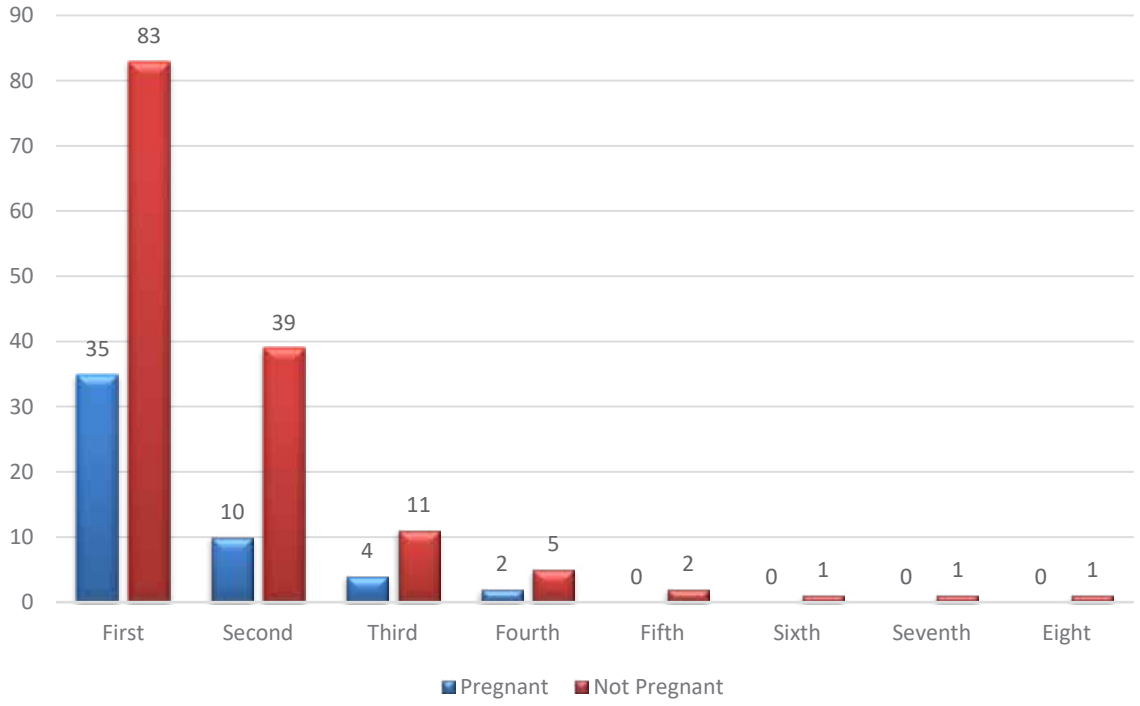
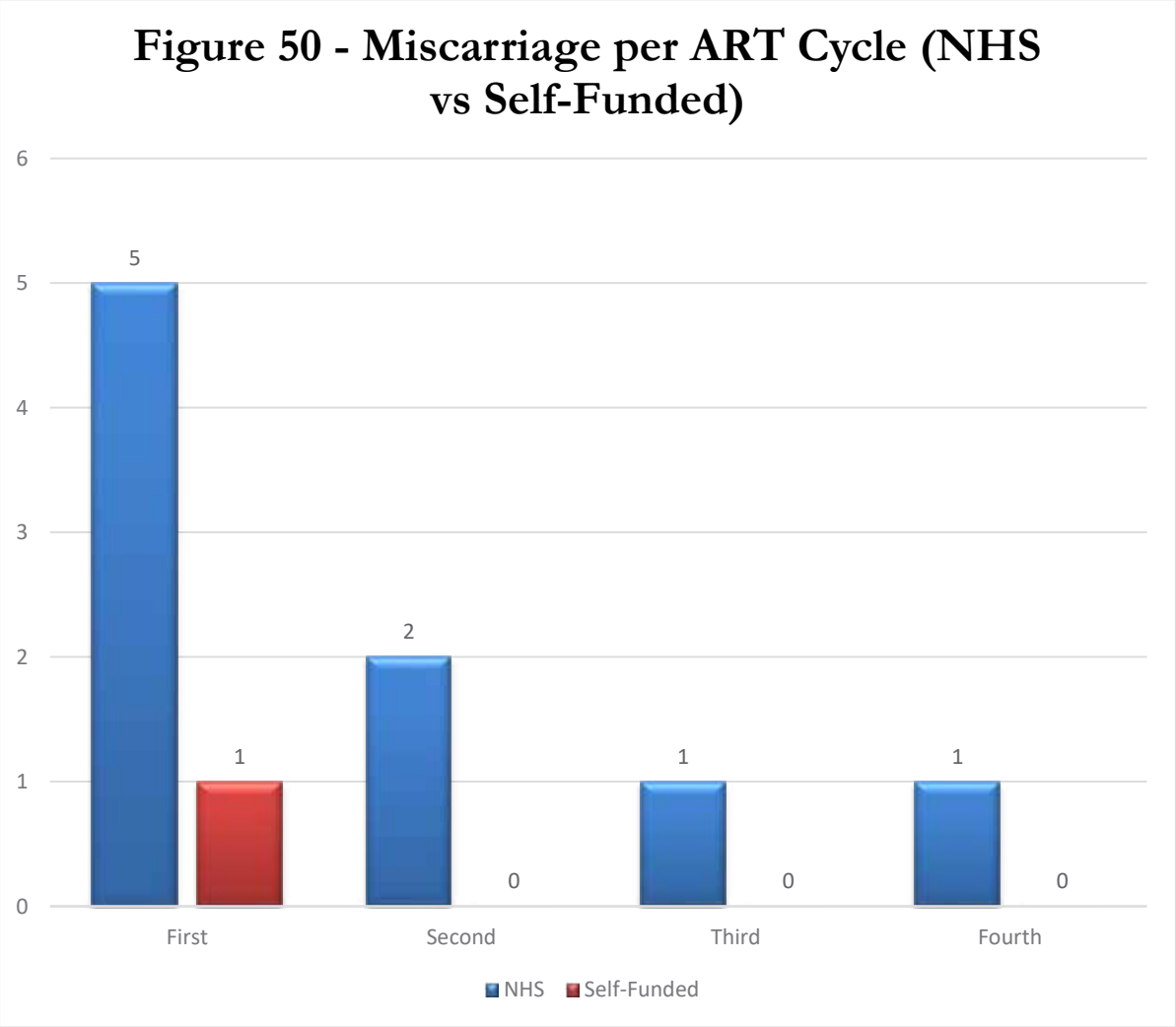


Figure 49 - Total Pregnant vs Non-Pregnant per ART Cycle Attempts



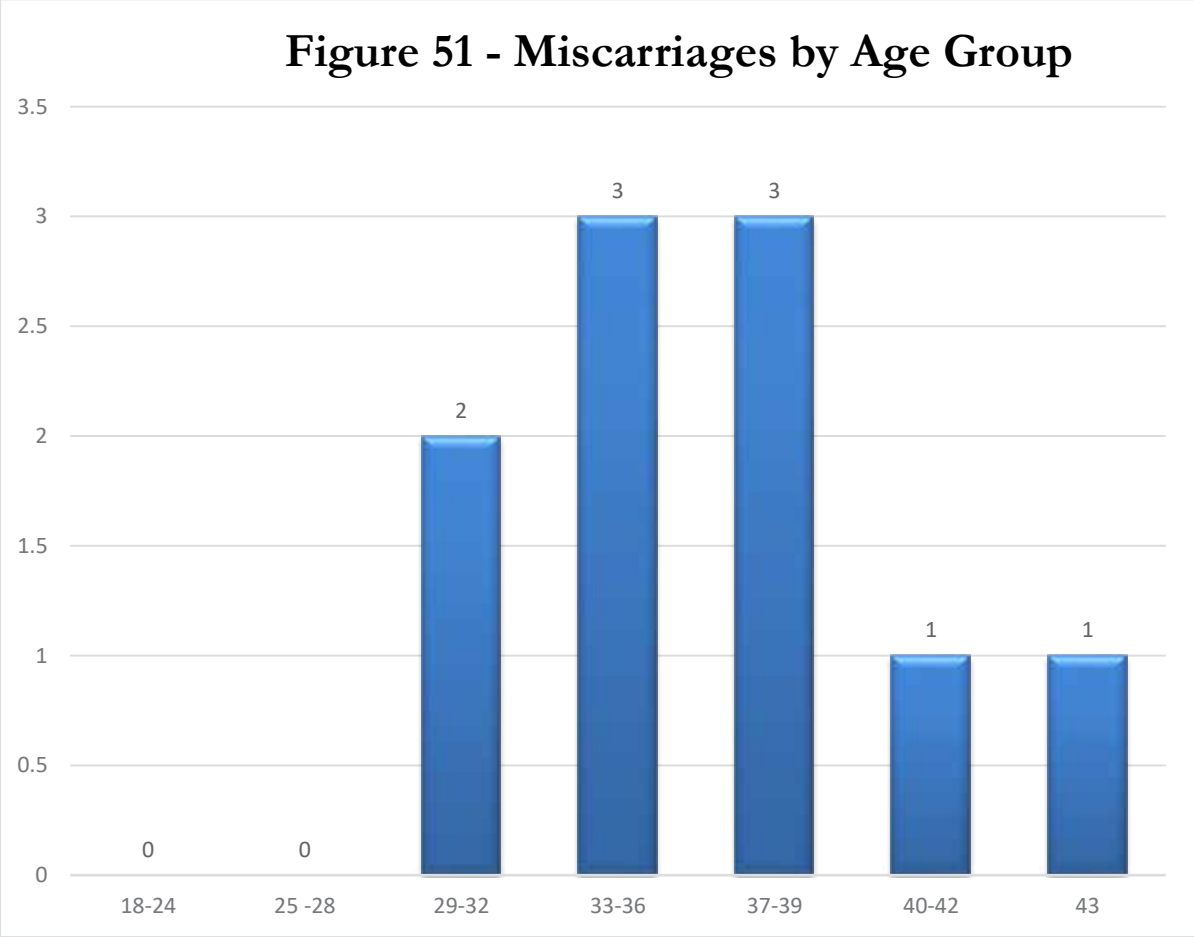
9.7. Miscarriages per ART Cycle

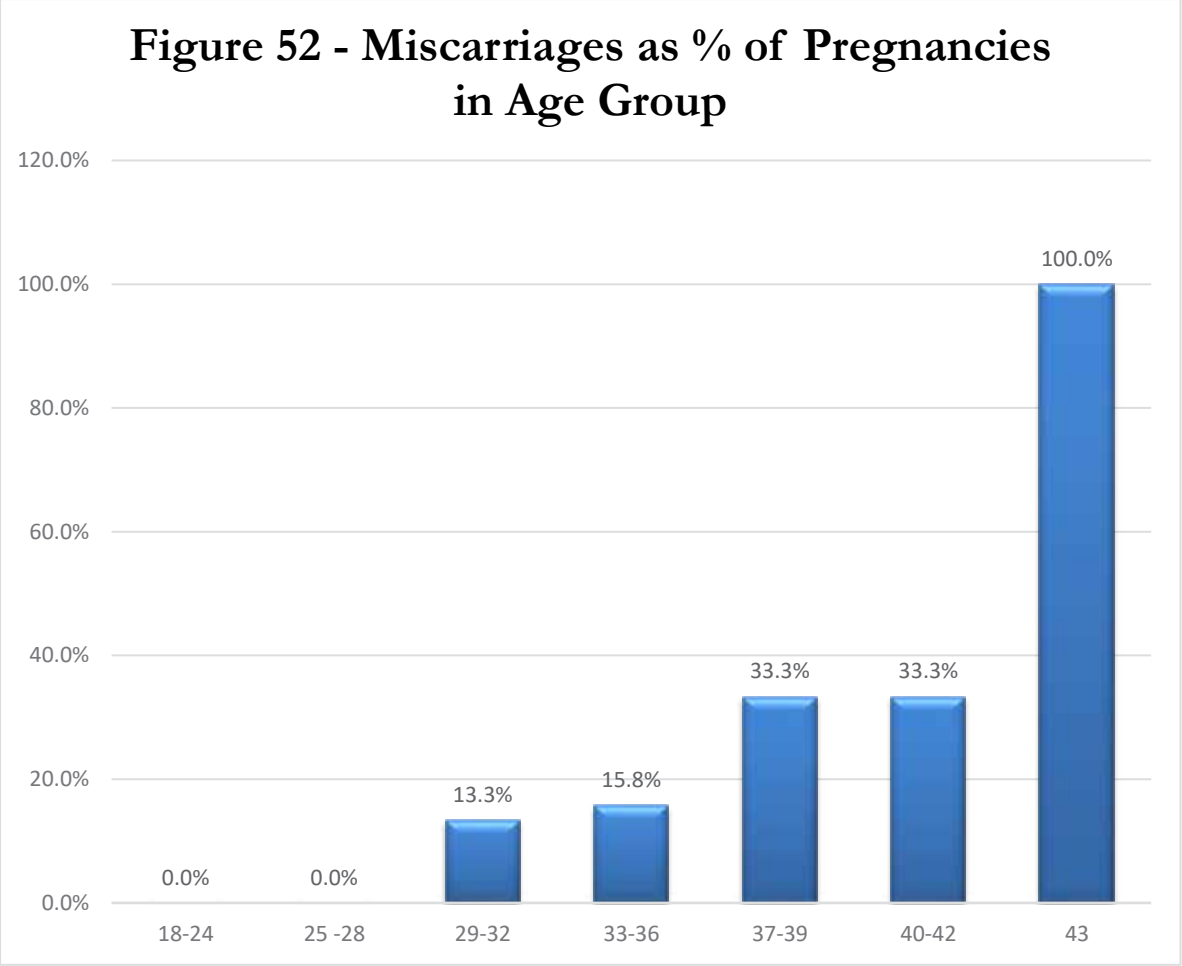
In 2021, a total of 10 miscarriages were reported, nine from cycles carried out at MDH ART Clinic and one from the St James Conception Unit. Six (6) of the couples who got pregnant on their first IVF/ICSI attempt miscarried. There were two (2) couples who miscarried after a successful second IVF/ICSI attempt. Another one (1) couple miscarried after getting pregnant from a 3rd attempt and the remaining one couple miscarried during their 4th attempt. (Figures 50).



9.8. Miscarriages by Age

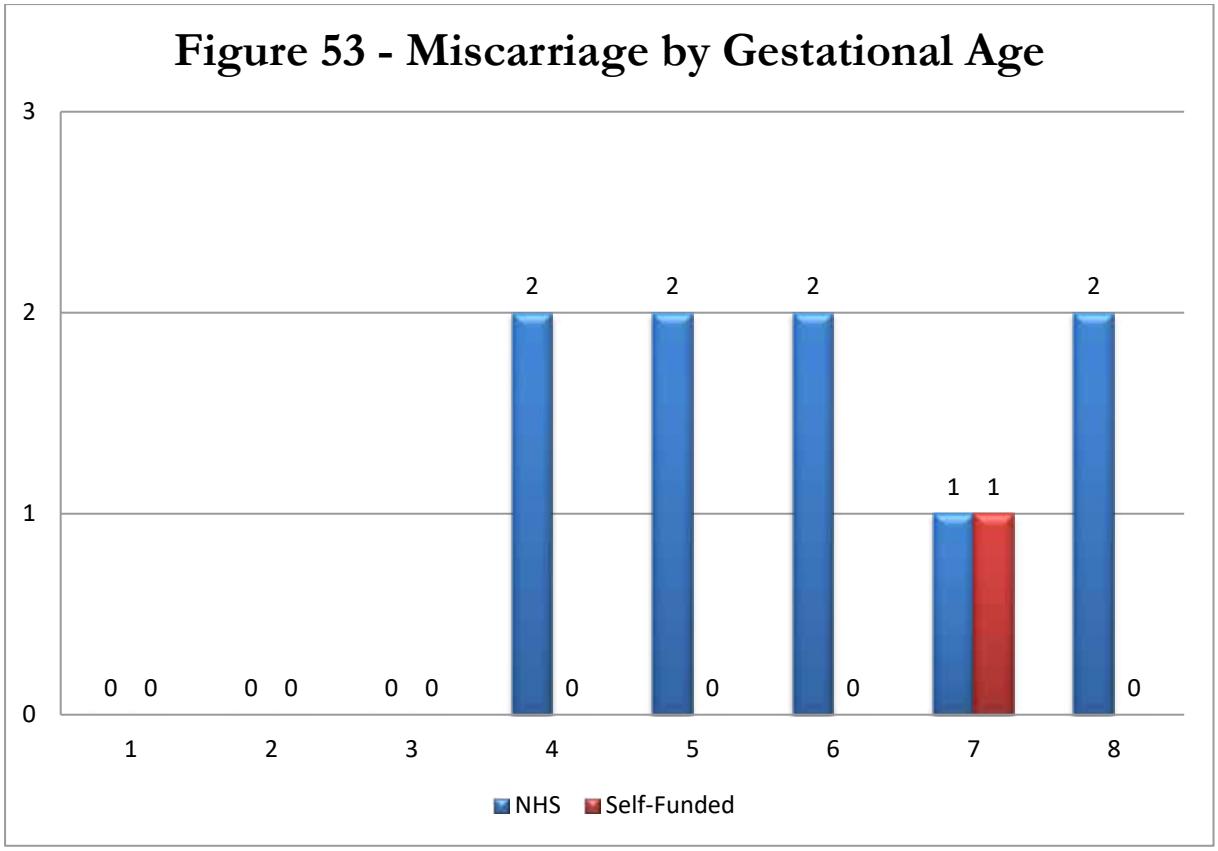
Miscarriages were reported for women aged from 29 up to age 43. There were two (2) reported miscarriage for women in the 29–32-year-old bracket, another three (3) miscarriage was reported in the 33–36-year-old bracket. Three (3) other miscarriage was reported for women aged 37-39. One other miscarriage in the 40–42-year bracket. The only one woman who got pregnant from an extension granted aged 43, miscarried also. (Figures 51 and 52).





9.9. Miscarriages by Gestational Age

The ten miscarriages reported were from two women who were in their 4th week of gestation. Another two women were in their 5th weeks, another two were in their 6th week. Two other women miscarried at 7 weeks gestation, and the last two women miscarried at 8th weeks gestation (Figure 53).



9.10. Miscarriages from Fresh vs Thawed Cycles

Eight (8) couples miscarried after achieving a pregnancy from a thawed embryo cycle carried out seven at the MDH ART Clinic and one at the St James Conception Unit. Two miscarriages were reported from fresh cycles carried out at MDH ART Clinic. No miscarriages were reported from Fresh cycles carried out at the private facility. (Figure 54, Table 16).

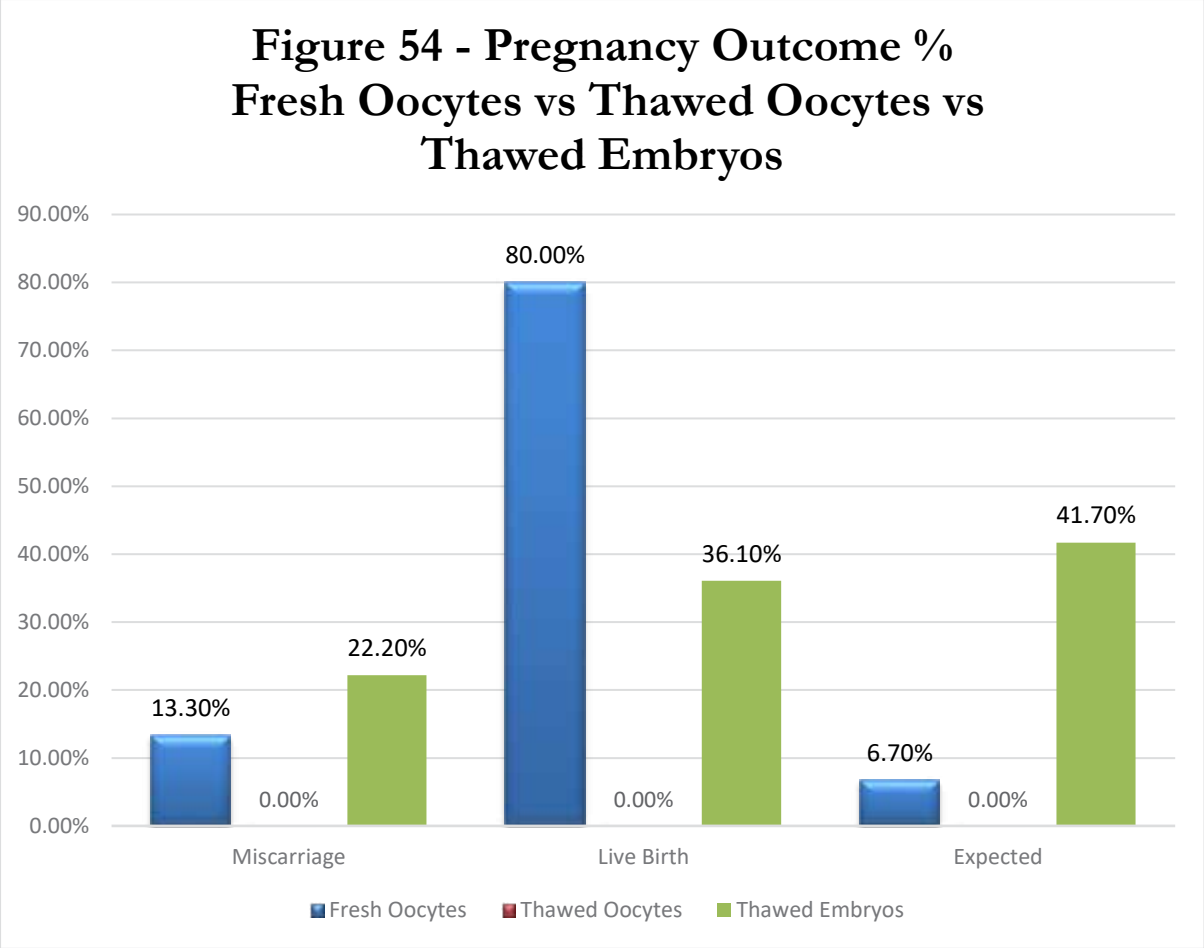


Figure 54 - Pregnancy Outcome %
Fresh Oocytes vs Thawed Oocytes vs
Thawed Embryos
90.00%
80.00%
70.00%
60.00%
50.00%
40.00%
30.00%
20.00%
10.00%
0.00%
13.30%
0.00%
22.20%
80.00%
0.00%
36.10%
6.70%
0.00%
41.70%
Miscarriage
Live Birth
Expected
Fresh Oocytes
Thawed Oocytes
Thawed Embryos

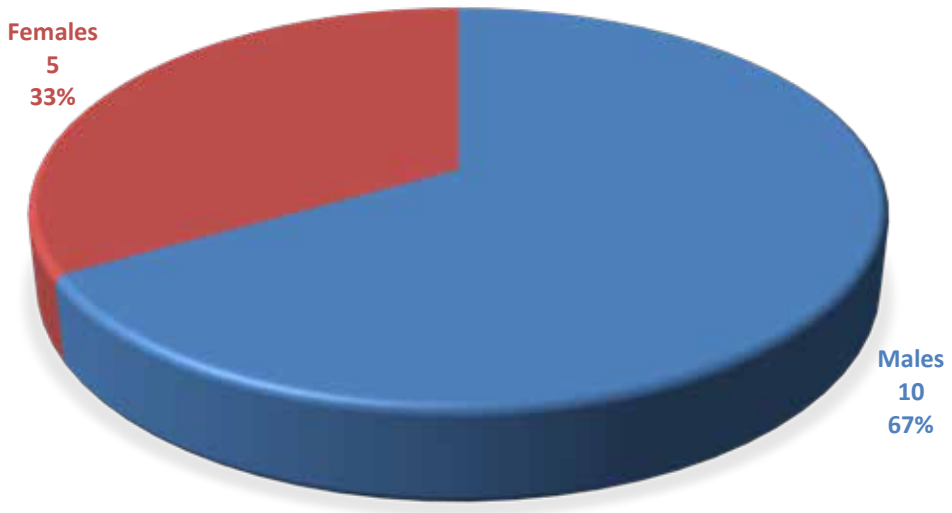
10. BIRTH EVENTS

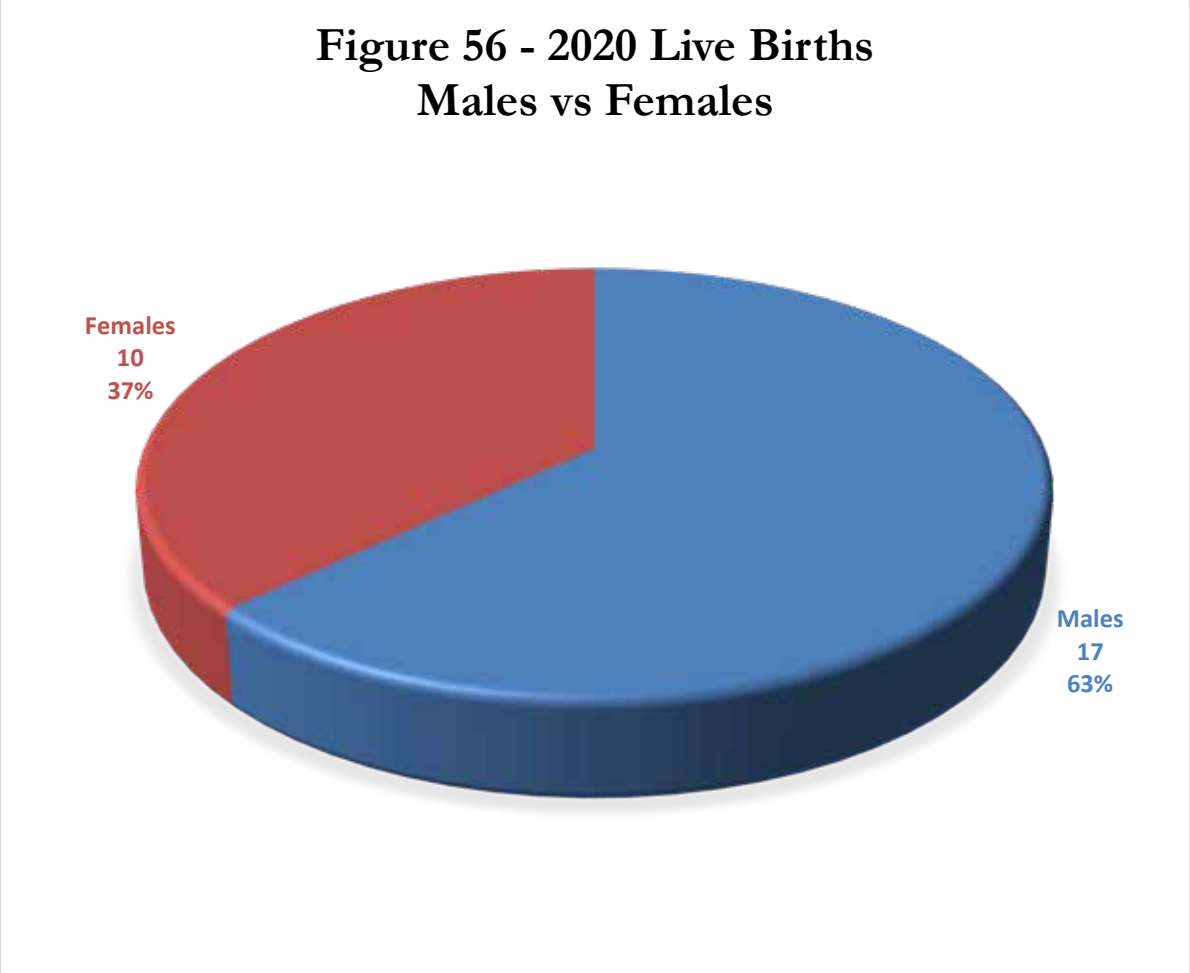
10.1. Births from June - December 2020 Cycles

In 2021, fifteen (15) babies, 5 females and 10 males, were born as a result of ICSI cycles performed between June and December 2020 (Figure 55). Hence a total of 27 babies, 10 females and 17 males, were born out of the 25 pregnancies from procedures carried out throughout 2020. (Figure 56).

Another Girl was born from an IUI procedure carried out at Virtu Clinic whilst a twin expected pregnancy from an IUI at MDH ART Clinic resulted in one baby miscarried and the other was reported as a neonatal death.

Figure 55 - June-December '20 Live Births Males vs Females





Fourteen (14) babies, or 51.55%, were born out of Fresh oocyte cycles. Out of these cycles, four (4) girls and ten boys were born. The other thirteen (13) babies or 48.15%, six girls and seven boys were born from the thawed embryo cycles (Figure 57).

Twenty-six (26) babies or (96.30%) of the babies born out of procedures carried out in 2020 were from procedures carried out at MDH, while the remaining 3.70% were from procedures carried out at the private clinics (Figure 58).

Figure 57 - 2020 Live Births
Fresh Oocytes vs Thawed Oocytes vs Thawed Embryos

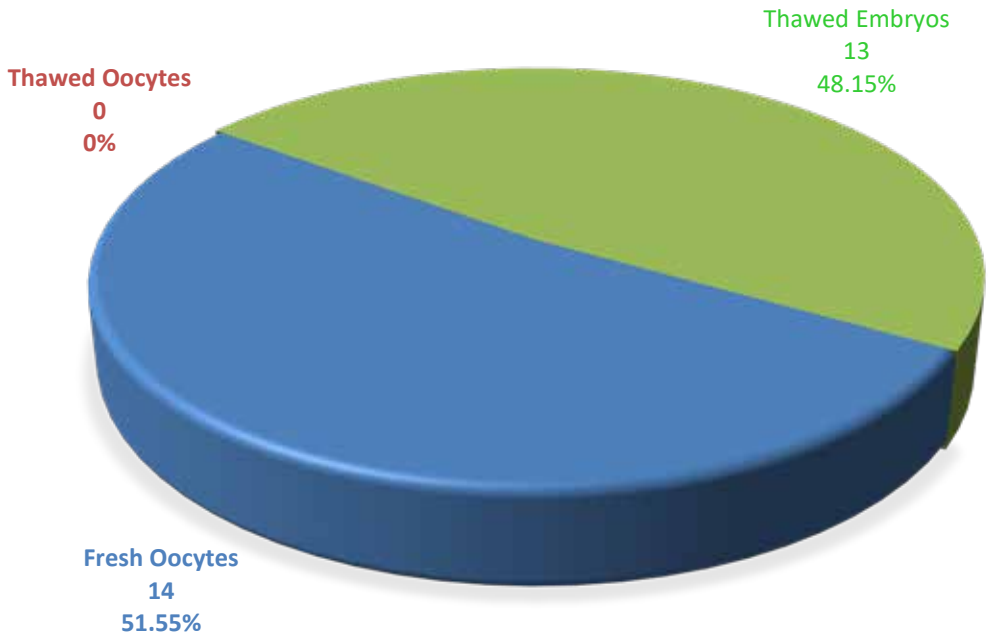
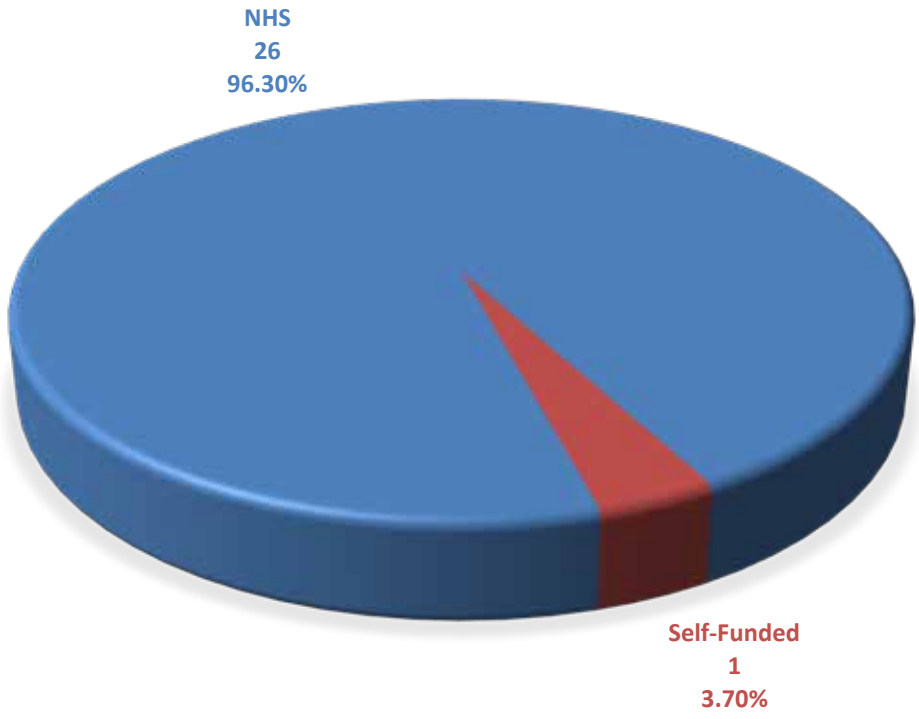


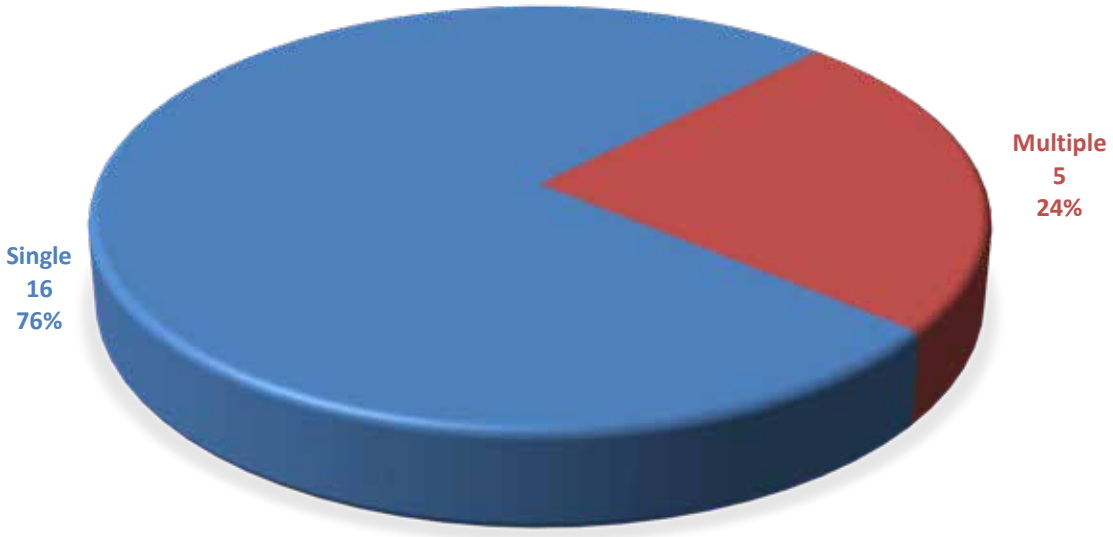
Figure 58 - 2020 Live Births
NHS vs Self-Funded



Out of a total of 25 pregnancies achieved in 2020, four women miscarried thus resulting in 21 live births. No anomalies were recorded in the resulting live births.

Out of the 21 Live Birth Events in 2020, there were 16 single births and 5 multiple births. The multiple births consisted of four sets of twins and one set of triplets. **The percentage of live births from multiple pregnancies in 2020 was of 3.68% of all cycles, an increase of 2.07% over 2019.** (Figure 59).

Figure 59 - 2020 Live Birth Events - Singles vs Multiples



In summary, out of a total of 136 cycles carried out in 2020 that could lead to a pregnancy, 111 couples did not achieve a pregnancy,4 miscarried, and 21 had a live birth, for a **final Take-Home Baby Rate of 15.44%** (Table 18), **which is a 2.30% decrease from that reported in 2019.**

Table 18 - % Take-Home Baby Rate 2020

Cycle Outcome	Qty	% of pregnancies	% of total cycles
Live Birth	21	84.00%	**15.44%**
Miscarriage	4	16.00%	2.94%
Not Pregnant	111		81.62%
TOTAL CYCLES 2020	136		100.00%

10.2. Birth Events from 2021 Cycles – Fresh Oocytes vs Thawed Oocytes vs Thawed Embryos

The number of babies born out of procedures carried out between January and June 2021 was of thirty-one (31) babies. Twenty-one (21) singletons and five multiples being five sets of twins.

Out of the thirty-one (31) babies born, fourteen babies comprising of ten singletons and two sets of twins were born from Fresh oocyte cycles carried out. Six singletons and two sets of twins were born from cycles carried out at the MDH ART Clinic; the other four singletons were born from cycles at the St James Conception Unit.

No baby was born from thawed oocytes cycles. The other seventeen (17) babies born, eleven singletons and threes set of twins were born from thawed embryo cycles. Ten singletons and three sets of twins were born from cycles carried out at the MDH ART Clinic; the other one singleton was born from cycles at the St James Conception Unit. Thus, all multiple births were reported at the MDH ART Clinic.

Babies born were seventeen (17) males and fourteen (14) females. Seven females and seven males were born from fresh oocytes cycles, whilst seven females and ten males were born from thawed embryo cycles. (Figures 60 and 61). No Anomalies were observed in all the infants born.

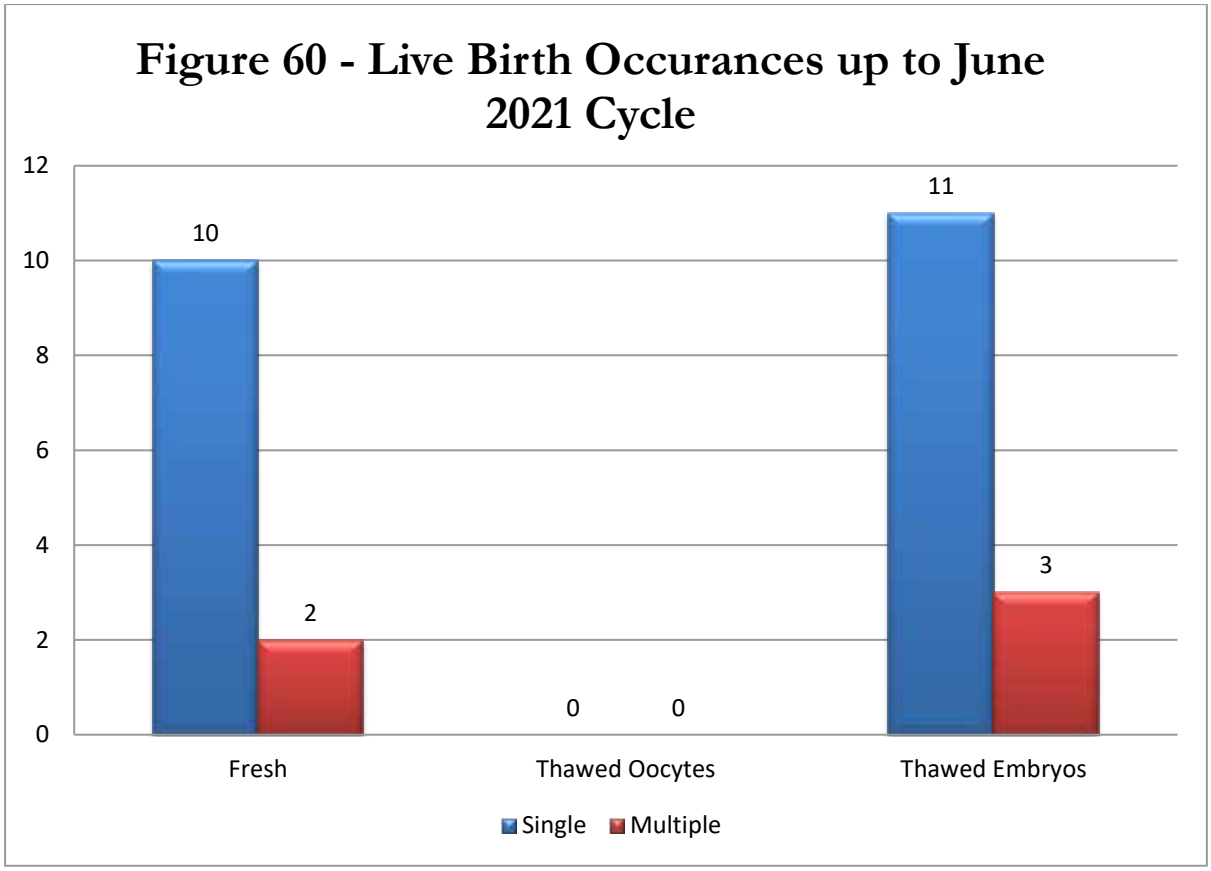


Figure 60 - Live Birth Occurances up to June 2021 Cycle
12
10
8
6
4
2
0
10
2
0
0
11
3
Fresh
Thawed Oocytes
Thawed Embryos
Single
Multiple

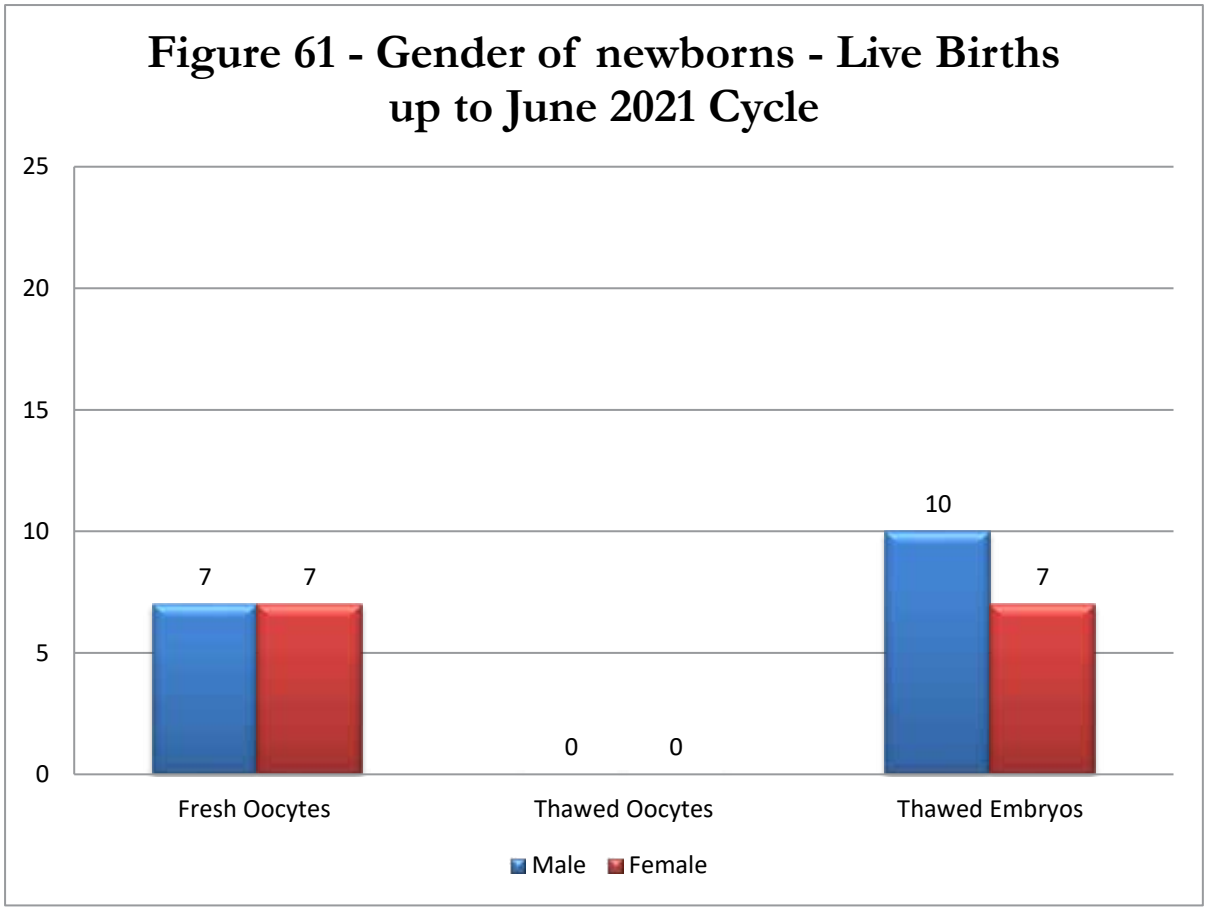
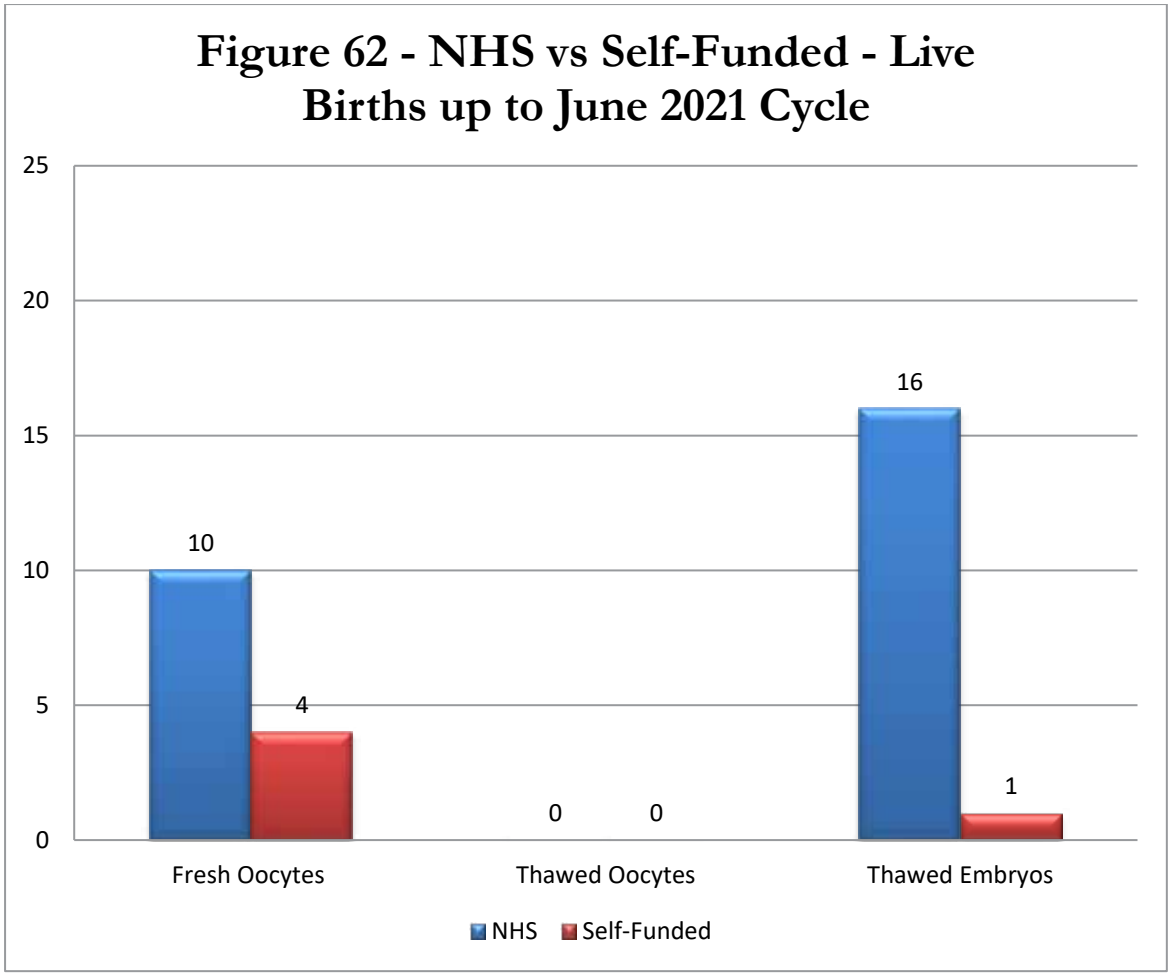


Figure 61 - Gender of newborns - Live Births up to June 2021 Cycle
25
20
15
10
5
0
7
7
0
0
10
7
Fresh Oocytes
Thawed Oocytes
Thawed Embryos
Male
Female

The twenty-six (26) live births events achieved up to June 2021 were reported from procedures done at both facilities. From the fresh cycles four singleton females, two singleton males, and two sets of twins both composed of a female and male were born from MDH ART Clinic. The other four singletons born from fresh cycles were two singleton males and two singleton females born from St James Conception Unit.

From the thawed embryo cycles, ten singletons, 6 male and four females, as well as a set of twin males, and two sets of twins both composed of a feme and male were born from MDH ART Clinic. The other one female singleton was born from St James Conception Unit. (Figure 62).



10.2.1. Expected Birth Events from Fresh Oocytes vs Thawed Oocytes vs Thawed Embryos

Fifteen (15) birth events are expected from cycles carried out between July and December 2021. These expected birth events are expected to give birth to seventeen (17) babies as 13 singleton and 2 sets of twins are expected. All seventeen (17) babies are expected from cycles carried out on the NHS.

One (1) singleton is expected from Fresh oocytes cycles. There are no expected births from thawed oocytes cycles as all treatment cycles were unsuccessful.

Fourteen (14) expected birth events are expected from Thawed embryo cycles carried out at the MDH ART Clinic. Twelve singletons and two multiple births of twins are expected, to give birth to fourteen (14) babies (Figure 63 and Figure 64).

The percentage of live and expected births from multiple pregnancies (7 sets of twins, all from MDH ART Clinic) in 2021 is of 3.61% of all treatment cycles carried out, a decrease of 0.07% from figures reported in 2020.

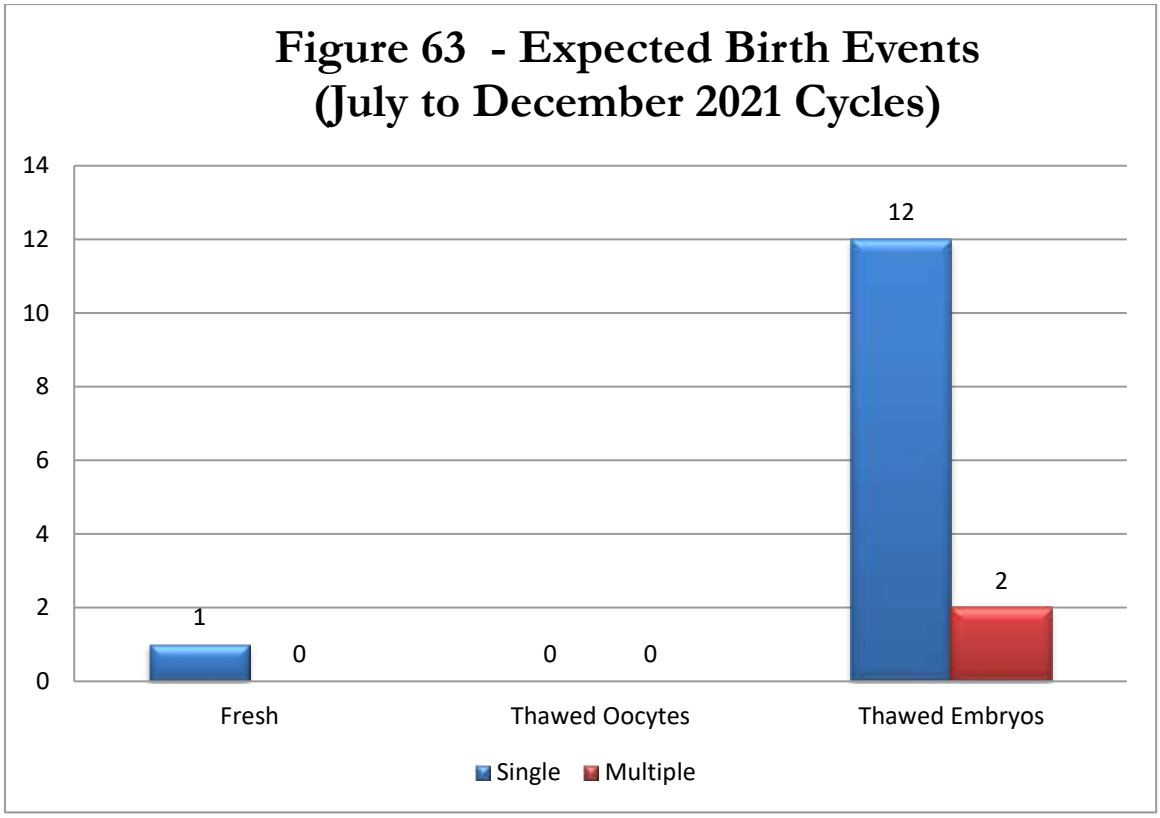


Figure 63 - Expected Birth Events (July to December 2021 Cycles)
14
12
10
8
6
4
2
0
1
0
0
0
12
2
Fresh
Thawed Oocytes
Thawed Embryos
Single
Multiple

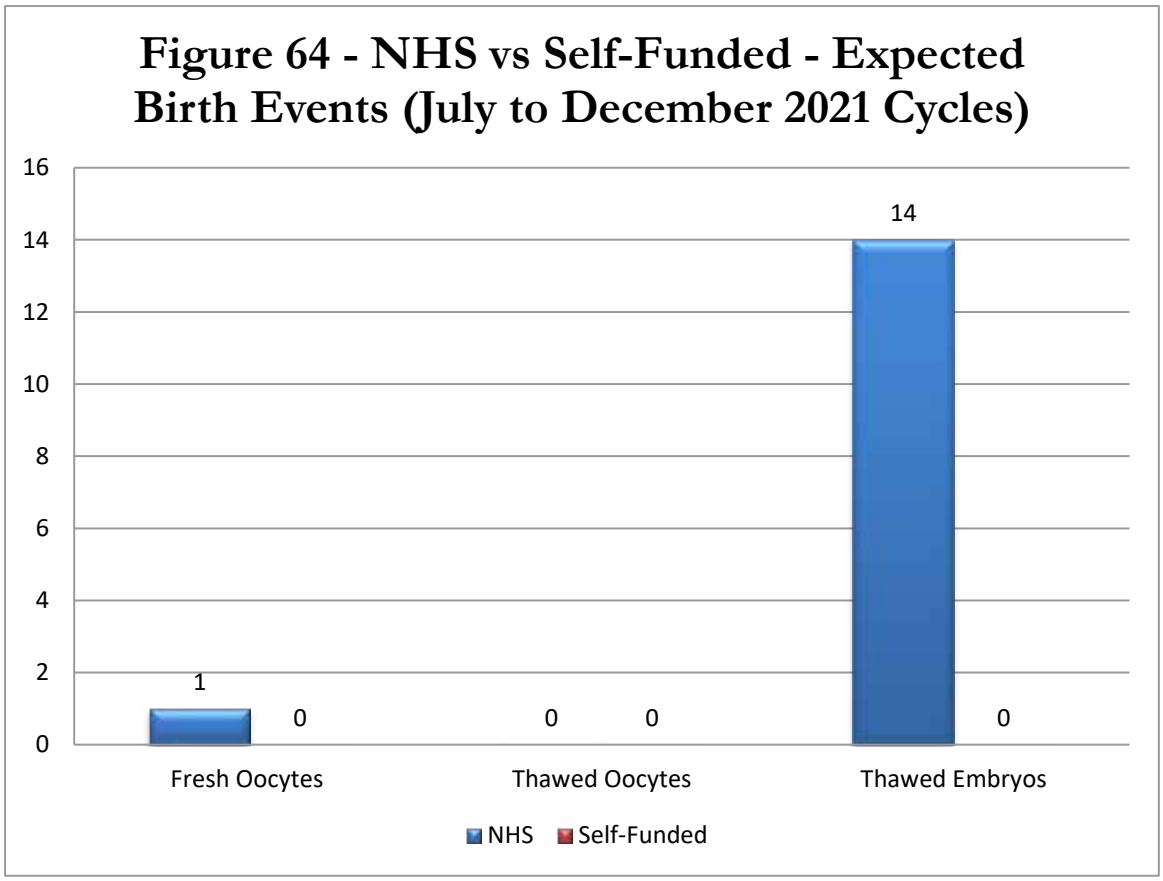


Figure 64 - NHS vs Self-Funded - Expected Birth Events (July to December 2021 Cycles)
16
14
12
10
8
6
4
2
0
1
0
0
0
14
0
Fresh Oocytes
Thawed Oocytes
Thawed Embryos
NHS
Self-Funded

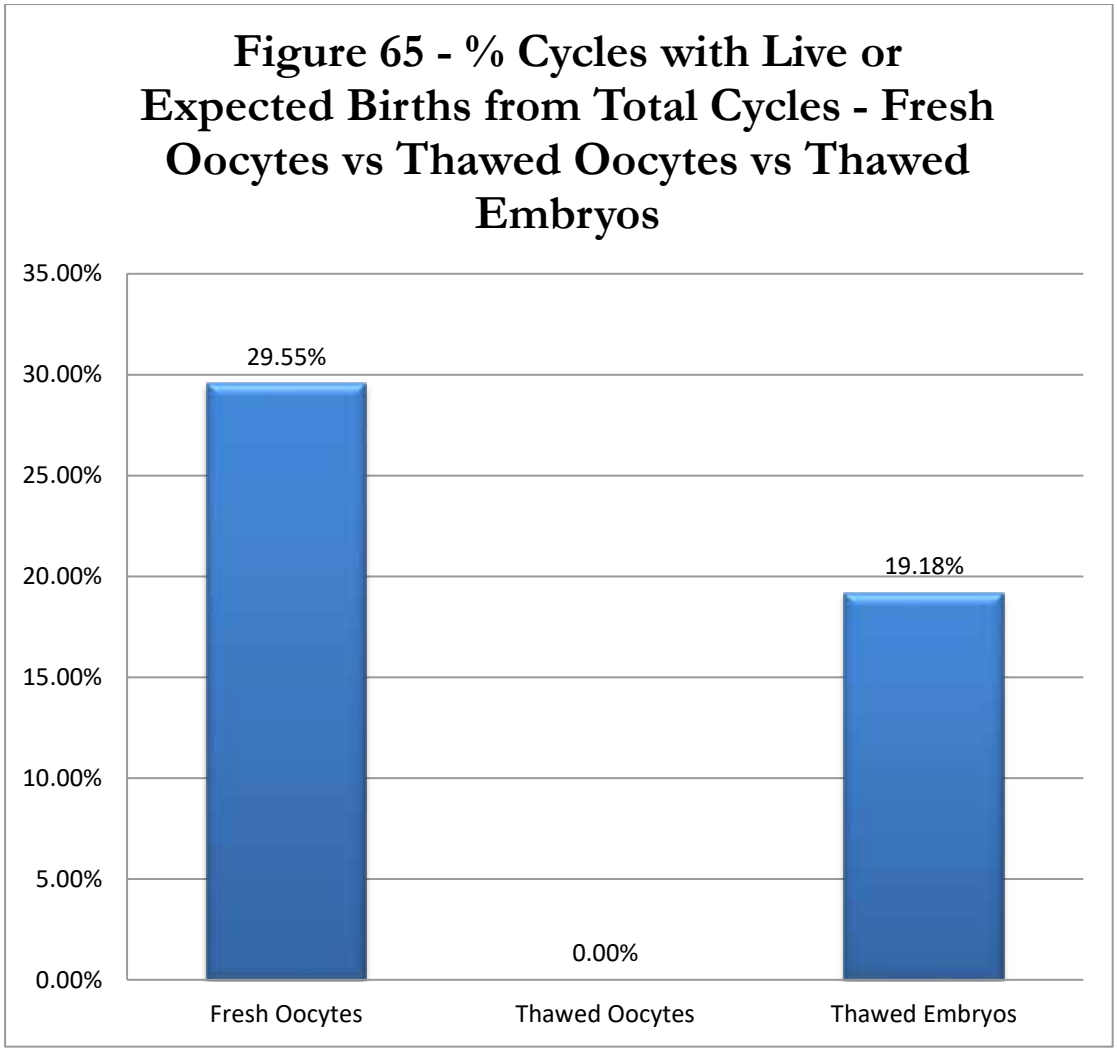
Hence, out of the forty-one (41) live and expected births from ICSI procedures carried out in 2021 **a total of forty-eight (48) babies are to be born**, fifteen (15) babies are from pregnancies achieved through Fresh oocytes cycles and the remaining thirty-three (33) babies are from Thawed embryos cycles.

10.3. Maximum Success Rate – Fresh vs Thawed

From the **44 Fresh Oocytes** cycles carried out, there were **13** reported birth events (live + expected), for a maximum success rate of **29.55%, which is an impressive increase of 15.66%** over last year's 13.89% maximum success rate from fresh cycles**.**

No birth events (live + expected) were reported from the **4 Thawed Oocytes** cycles performed.

Twenty-eight (28) birth events (live + expected) resulted from the **146 Thawed Embryo** Cycles carried out in 2021, for a maximum success rate of **19.18%**, which is 0.49% lower than last year's 19.67% (Figure 65).

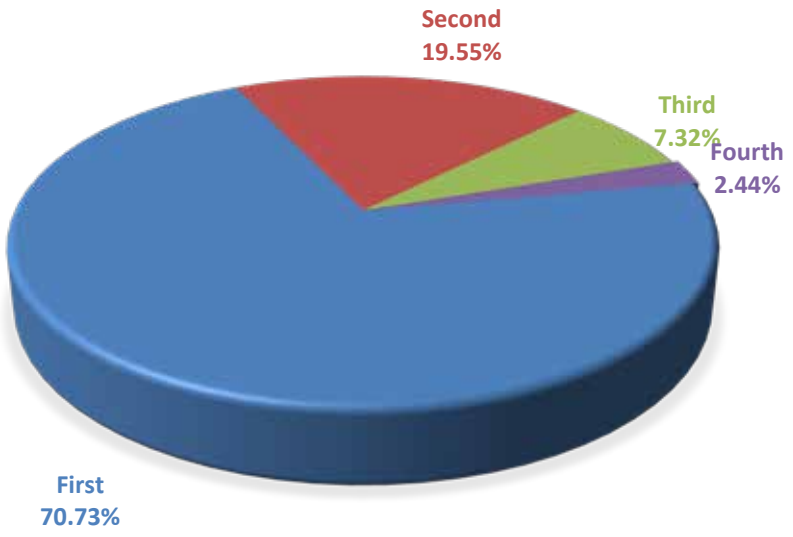


Noteworthy to point out is the fact that while in 2020, the maximum success rate was higher in the Thawed Embryo cycles, which was 5.78% higher than the Fresh Oocytes cycles. During 2021, the Fresh Oocytes cycles reported a success rate of 10.37% higher than the Thawed Embryo cycles.

10.4. Birth Events per ART Cycle

Out of a total of 41 reported birth events (live + expected) from procedures carried out in 2021, there were 29 birth events (70.73%) from couples undergoing their first IVF/ICSI attempt, 8 birth events (19.51%) from a 2nd attempt. Three birth events (7.32%) from couples undergoing their 3rd attempt. One other birth event was from couples undergoing their 4th attempt. Noteworthy is the fact that there was an increase in the first time attempts with a considerable increase of 34.37%. over previous years. It is to be noted that birth events (live + expected) decrease with increase of attempts. During 2021, no birth events were registered for couples undergoing more than 4 attempts. (Figure 66).

Figure 66 - Live & Expected Birth Events Distribution by ART Cycle



The majority of these birth events (live and expected) 36 couples or 87.80% of couples experiencing a birth event, are from cycles undergone at MDH, the remaining 5 couples had self-funded their treatment (Figure 67 and Figure 68).

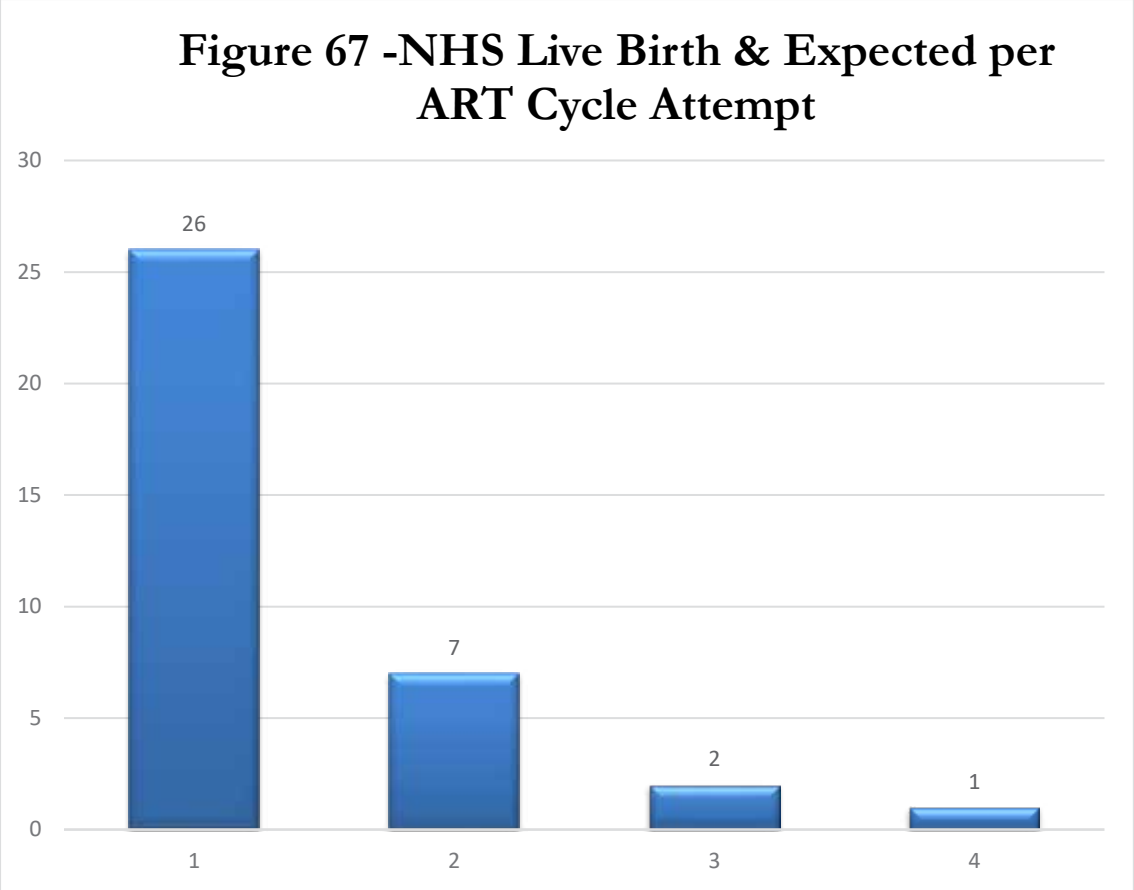


Figure 67 -NHS Live Birth & Expected per ART Cycle Attempt
30
25
20
15
10
5
0
26
7
2
1
1
2
3
4

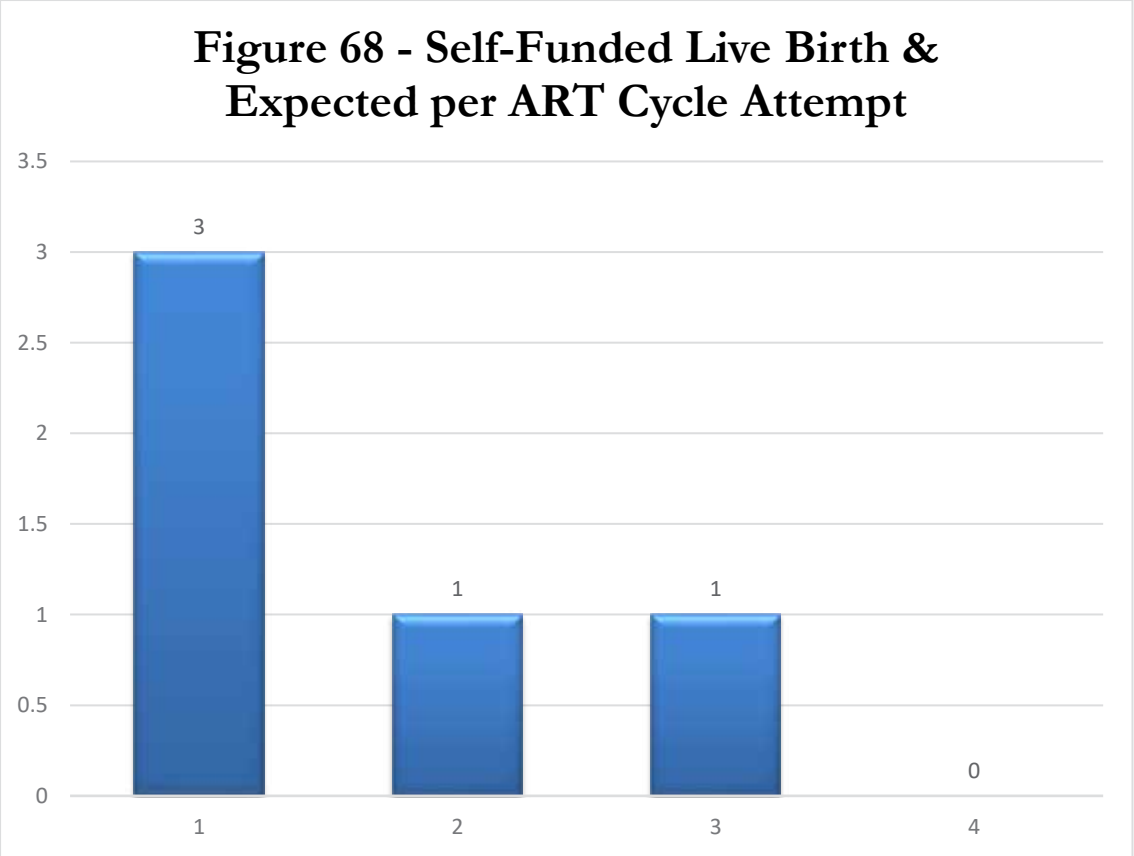


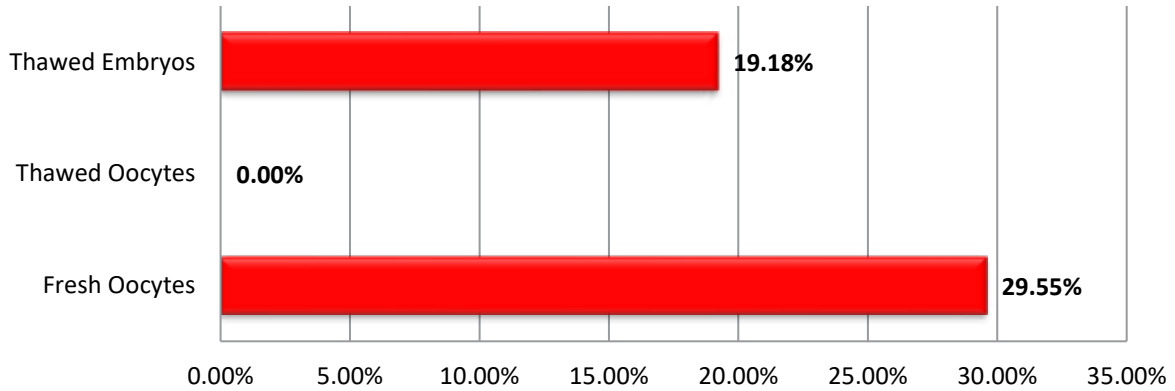
Figure 68 - Self-Funded Live Birth & Expected per ART Cycle Attempt
3.5
3
2.5
2
1.5
1
0.5
0
3
1
1
0
1
2
3
4

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

In conclusion, from the 51 couples who achieved a pregnancy in 2021, 26 (50.98%) had a live birth, 15 (29.41%) are still expecting, and 10 couples (19.61%) miscarried.

These were achieved mainly from Fresh Oocytes cycles (29.55%), followed by Thawed Embryo cycles (19.18%). No successes were registered from Thawed Oocytes Cycles (Figure 69).

Figure 69 - % 'Take Home Baby Rate' - Fresh Oocytes vs Thawed Oocytes vs Thawed Embryos



Out of a total of 194 cycles carried out, **13.40%** of couples had a live birth, **7.73%** are still expecting, while **5.15%** miscarried.

Consequently, the maximum percentage success rate, or 'Take Home Baby' rate for calendar year 2021 is 21.13%, resulting in a good increase of 5.69% over the 'Take-home Baby Rate of 2020. (Table 19).

Table 19. % Maximum Success Rate – 'Take Home Baby' Rate 2021

Pregnancy Outcome	Qty	% of pregnancies	% of total cycles	% Max Success - 'Take Home Baby' Rate
Live Birth	26	50.98%	13.40%	21.13%
Expected	15	29.41%	7.73%	
Miscarriage	10	19.61%	5.15%	

11. Conclusion

The number of ART procedures carried out in Malta in 2020 increased by 65.42% over the previous year, which is mainly attributed to the fact that in 2020 less procedures were carried out at the MDH clinic as the clinic had stopped activity due to Covid-19 measures in place. The private clinic registered a decrease of 11 procedures, over the procedures carried out in the private clinic in the previous year. Again in 2021, the private facility did only one batch of procedures, same as 2020, which differs to previous years when a minimum of three batches used to be held in one calendar year. This increase in activity was still registered notwithstanding the COVID 19 measures in place.

ICSI was the preferred procedure of choice in all procedures carried out by the licensed clinics. There were **51 (26.29%)** reported pregnancies out of the 194 treatment cycles started which is **success of** 7.91**% Higher** than the pregnancy rate for 2020. Thawed oocytes cycles were less effective than Fresh oocytes treatments.

The birth events were achieved mainly from Fresh Oocytes cycles (29.55%), followed by Thawed Embryo cycles (19.18%). No successes were registered from Thawed Oocytes Cycles.

The **maximum percentage success rate**, or '**Take Home Baby' rate** which implies a birth event and is the most meaningful measure of treatment success, stands at **21.13%**, which is **5.69% Higher** than previous year. Considering all the restrictions and measures taken due to the COVID 19 pandemic the increase in success is noteworthy and as an Authority we shall strive together with all stakeholders to increase even more the success rate in the coming years.

The Embryo Protection Authority shall keep providing guidance and support to all the licensed ART clinics, as well as to all IUI registered 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 all local Clinics offering ART services comply with the obligations and requirements imposed by or under the Embryo Protection Act 2012, and the Embryo Protection (Amendment) Act, 2019, as well as the Authority Protocol.

We will continue to strive to see that the many strides we have made in this sector since the inception of the Authority in 2013 will continue to flourish.

We also promise that we will continue to be the voice of our patients by introducing a new Strategy for 2022-2025. This will also coincide to mark our 10-year anniversary working in this sector, that will focus on what we want to achieve in this field and how we will work together with all stakeholders towards achieving it.

Hon Judge Philip Sciberras UOM

Chairperson

Ms. Simone Attard

Chief Executive Officer

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