Edinburgh Fertility Centre

A Guide for Prospective Patients

Your guide to your treatment

This document is distributed by the Edinburgh Fertility Centre for the benefit of all patients undergoing treatment licensed by the Human Fertilisation and Embryology Authority (HFEA).

Contents

Introduction

The Edinburgh Fertility Centre is dedicated to the provision of highly specialised treatment to individuals and couples with fertility problems. We offer both NHS and self-funding treatment.

We are regulated and licensed by the Human Fertilisation and Embryology Authority (HFEA). They are the Government regulator responsible for making sure fertility clinics and research centres comply with the law and are there to safeguard both patients and the children born as a result of fertility treatment.

The journey through fertility treatment can be a stressful one. We aim to support you by offering guidance and counselling throughout your care. We are committed to the provision of a high quality and evidence based clinical care in a caring and friendly environment, sensitive to your needs.

The purpose of this booklet is to provide information on various aspects of your treatment. Additional information will be provided as your treatment progresses. Further information including our patient journey video can be found on our website https://services.nhslothian.scot/edinburghfertilitycentre/.

You can also scan this code using the camera on your phone to visit our website.

On the HFEA website there is also a very helpful document you may wish to read prior to your doctor's consultation called **'Getting started – your guide to fertility treatment'.**
Go to www.hfea.gov.uk, click on **'Patients'** and then **'getting started'**

Before Treatment

Treatments available

In-vitro fertilisation (IVF) was originally developed to overcome the problem of fallopian tube blockage but it is also indicated for the treatment of certain couples with long-standing unexplained infertility, endometriosis and male factor infertility. The technique involves removal of eggs (oocytes) from the ovaries, fertilisation with sperm in the laboratory to create embryos, which can then be transferred directly into the womb (uterus) in a procedure known as embryo transfer. Intracytoplasmic Sperm Injection (ICSI) is offered to couples with male factor infertility after investigation and assessment, if clinically appropriate.

In a natural menstrual cycle women produce only one (or at most two) eggs, but during the IVF cycle of treatment, the woman is given a course of drug treatment, to stimulate the development of several eggs. These eggs can be collected, frozen and stored for use in the future or put together with sperm (this can be partner sperm or donor sperm) to create embryos. We aim to replace one embryo (or in specific circumstances, a maximum of two embryos) into the womb during any one treatment, and any other good quality embryos can be frozen and replaced in the womb during later treatment cycles.

You may be undergoing treatment to create and store eggs or embryos for future use. If this is the case, some parts of the process outlined below will be deferred until you wish to use the eggs or embryos.

If you are having assisted conception treatment as part of pre-implantation genetic testing, you will be given additional information about the process of embryo testing and genetic analysis.

Entering the treatment programme

The majority of individuals/ couples entering the assisted conception programme will already have undergone full investigations and discussion of treatment options in the Fertility Clinic of the Royal Infirmary of Edinburgh. For those who have attended other clinics, it is necessary to have a letter of referral from a fertility specialist with a summary of all investigations and treatment carried out. With your permission, we may have to write to your general practitioner[s] and other medical practitioners involved in your care, requesting any relevant information prior to treatment, and informing your general practitioner of your proposed treatment.

You will be given an initial appointment at the Assisted Conception Unit (ACU) clinic, prior to your appointment with a doctor, where you will have the following tests; AMH blood test, height, weight, blood pressure and Carbon Monoxide test. At your medical appointment you will receive detailed information about the treatments, risks involved and further visits. If you are self-funding your treatment, all fees are required to be paid before the treatment can start. You may be offered an ultrasound scan and blood tests at this appointment.

You should have had an up-to-date cervical smear test. If you have not had a recent smear, please visit your GP to arrange this before your treatment starts. Please inform our staff if your recent cervical smear was abnormal.

AMH blood test

When you are seen at the Centre, we will take a blood test to measure your anti-mullerian hormone (AMH). AMH is produced by the medium sized immature follicles (sacs of fluid containing potential eggs) in the ovaries and is a measure of ovarian reserve. It gives an indication of how your ovaries (or ovary) are likely to respond to the drugs in an IVF cycle (and how many eggs you are likely to get).

Women with an AMH of less than 7.0 pmol/l are less likely to respond to ovarian stimulation. A low AMH level suggests that you are likely to produce few eggs in an IVF cycle (sometimes none) and therefore, the chance of having a baby from IVF treatment is reduced. It shows us that your risk of ovarian hyperstimulation syndrome is low and so we can push your ovaries as hard as we can. Having a low AMH level does not reduce the chance of having a baby naturally, provided you have patent (open) fallopian tubes, a normal uterus, a normal sexual relationship, and your partner's semen analysis was normal. We are aware that a low AMH result may come as a shock to some patients, and we encourage patients to phone us if they have any queries. The AMH result will be discussed with you prior to your treatment and the drugs used in your treatment are tailored to your egg reserve.

What does treatment involve?

In-Vitro Fertilisation (IVF) is the medical term for the "test tube baby" technique. It literally means that the egg and the sperm meet and fertilise in a glass dish. This technique was originally designed to help woman with damaged tubes, as the egg and sperm are prevented from meeting by tubal blockage. However, it has now been found to be of use in other circumstances such as selected cases of male infertility, endometriosis and in unexplained infertility. If you require a more specialised treatment such as intracytoplasmic sperm injection (ICSI), you will be given an additional information leaflet. The basic treatment regime is identical to that for IVF.

Not all parts of the process may be relevant to you at this time. Information about other forms of treatment can be discussed at the clinic and written information may be available. During your treatment you will be given an individualised treatment plan in writing.

Treatment stages

Pre-treatment

Before starting your drugs, you will need a scan to check to see if your ovaries are accessible and that there are no ovarian cysts. We may also want to check to see if the neck of the womb allows a fine plastic catheter to go through (a “mock embryo transfer”). Please use a barrier method of contraception (condom/cap) from the first day of onset of your period in the month before your treatment cycle and throughout your treatment, unless there is absolutely no chance of spontaneous conception. We sometimes give pre-treatment with a combined oral contraceptive pill (COCP) to programme the timing of your hormone changes. If you have had problems on a COCP in the past or you have a medical condition that means that you should not use it (such as migraines), please let us know.

Downregulation

This is the name given to the process of using medication to shut down the natural menstrual cycle to prevent release of the eggs. We have two types of medication that we use for downregulation – Ganirelix (GnRH antagonist) and Buserelin or Prostap (GnRH agonist). We will recommend what we think is best for you based on your egg reserve though if you prefer an antagonist protocol please ask for this. Using the antagonist protocol minimises the risk of ovarian hyperstimulation syndrome.

Before any stimulation injections are given, you will have another scan - this scan is carried out on a Thursday and is Day 1 of your treatment. This scan is done vaginally, is painless and requires an **empty** bladder. This first scan is to check that you have responded to the Buserelin and that the ovaries are inactive. The lining of your womb (endometrium) is measured to confirm that you have responded to Buserelin/ Prostap.

Stimulation

If the first scan is satisfactory, you will start your daily injections of stimulation drugs (gonadotrophins). If the first scan shows that you are not ready to start treatment, this will be postponed for up to 2 weeks or under exceptional circumstances longer. Nearly all of our patients, after training by our staff, are able to give themselves the injections.

Daily gonadotrophin injections are used to stimulate the development of several follicles containing eggs within the ovaries. This phase usually takes 10-14 days but for some women can be longer or shorter. Downregulation medication must be continued during this time. The drugs used for stimulating your ovaries are hormones called LH and FSH and different drug preparations have different combinations of LH and FSH. Both LH and FSH are natural hormones found in women.

Monitoring

It is important to monitor the results of drug treatment in order to decide on the timing of the egg collection. The developing follicles containing the eggs can be seen very easily by ultrasound scanning which is carried out by inserting a small probe into the vagina.

Scans are performed regularly (approximately two or three times a week) once stimulation medication has been commenced. Further information about the progress of treatment may also be obtained by hormone measurements performed on a blood sample taken (towards the end of the treatment) at each visit. Once the follicles have reached a certain size, (preferably three follicles of 17 mm diameter) your egg collection procedure will be scheduled.

Trigger

Once the follicles are large enough you will be booked for an egg recovery. Until then, the daily injections are continued and scans are repeated. You will need to take a single trigger injection 36 hours prior to your egg collection to stimulate the final maturation of the eggs. There are two types of trigger injection – Ovitrelle (human chorionic gonadotrophin) and Buserelin. Buserelin can only be used in antagonist cycles and its effect may need to be

checked with a blood test the following day. Once a buserelin trigger has been given, we cannot do a fresh embryo transfer. We therefore need to freeze the embryos and the embryo transfer is done in a thaw cycle of treatment.

Egg collection

The egg collection procedure is performed using the vaginal probe which has a fine needle attached. This is then passed into each ovary and the fluid from the follicles is removed. Not all the follicles seen on the scan will contain an egg. We normally obtain an egg from about 70% - 80% of the follicles. There is a possibility that if there are a small number of follicles, we may not be able to retrieve any egg(s).

We will ask you to have nothing to eat from 12 midnight. You may have a glass of still water before 0700 hrs, but **do not** drink milk or any fizzy drinks or chew chewing gum. Your operation will be **cancelled** if you do not follow these instructions as it would not be safe to administer an anaesthetic. You will be given an injection containing a pain killer (Fentanyl) and then a sedative (propofol). An antibiotic injection is given before we commence egg recovery. You will feel drowsy during the procedure and may feel some discomfort. Following your egg collection, you will be transferred to a six-bedded recovery area. We are unable to provide single recovery rooms. We need to observe you in the recovery room for at about 3 hours before being allowed home. Light refreshments are provided. There is a small possibility you may have to stay overnight for observation after your operation.

It is necessary to avoid driving or any tasks requiring precision for 24 hours after the procedure. Therefore, you will need your partner or other nominated person to take you home. Egg collection procedures are performed in the mornings between 9.00 am and 12.00 noon. Most couples can leave the Centre 2-3 hours after the egg collection procedure.

After your egg collection, you may experience some lower abdominal discomfort and a bloated feeling, and this may be associated with feeling sick. You may also have slight vaginal bleeding, and this is less than the bleeding you experience when you have a period. It is important to drink plenty of fluids and you may take paracetamol for pain relief. Please contact us on 0131 242 2450 if you feel unwell or have pain. ***IF YOU ARE ALLERGIC TO ANY ANTIBIOTICS OR ANY DRUGS, PLEASE INFORM US*.**

Sperm collection and preparation

A sample of your semen is required about an hour before egg collection (unless a frozen specimen is used). You are advised to ejaculate 2 days prior to the egg recovery procedure to maximise the number of sperm in the ejaculate. Your specimen is prepared in culture medium, and a washed sample of sperms is added to the eggs. In some circumstances, it may be necessary to ask you to produce a second semen sample on the day of egg collection. For this reason, you should be easily contactable by telephone during this time. On rare occasions the sperm sample on the day is very different from previous ones and we therefore need to discuss changing the treatment plan (e.g. ICSI rather than IVF or vice versa).

Hyperstimulation

Occasionally, if the ovaries are very sensitive to drug stimulation and produce too many eggs or high levels of hormones, a condition we call "ovarian hyperstimulation syndrome" may develop. The ovaries become very swollen and painful and fluid may leak from your circulation into the abdomen causing extreme distension. To minimise this risk, we ask you to drink plenty of fluid and to report to us if you feel or are sick or if your abdomen is very bloated or painful after your egg recovery. If we think you are at risk of developing this complication, the cycle may have to be cancelled. In other circumstances, we may advise against the replacement of embryos and instead freeze the embryos, so that they can be replaced later. Occasionally, hospital admission is necessary, this occurs in around 1 in 100 women.

Cancelled cycles

In some cases, an IVF cycle has to be abandoned, for example if there is an inadequate or over response to the drugs used for superovulation or if a complicating factor arises after drug treatment has commenced. If your cycle is cancelled before the 'egg collection' and you are self-funding your treatment, depending on the circumstances, there will usually be a refund of a proportion of the fees paid.

If your treatment is funded by the NHS and your treatment is cancelled due to poor response or no eggs are collected, you will not receive further NHS funded IVF/ICSI treatment using your own eggs. If your cycle is cancelled prior to the 'egg recovery' for other reasons, for example, risk of ovarian hyperstimulation (over response), the cancelled cycle will not be counted.

Fertilisation

Once collected, the eggs are kept in the incubator until later in the day. If you are undergoing conventional IVF, the sperm and eggs are placed together then returned to the incubator for approximately 18 hours. In ICSI treatment, sperm are individually injected into each mature egg prior to incubation. If you would like more detailed information about ICSI, please see our ICSI information sheet.

The following day, the eggs are inspected microscopically for the signs of normal fertilisation. Usually, the fertilisation rate is between 60% - 70%. This may be lower if a problem has been previously identified. In approximately 5% of cases, low or no fertilisation will occur unexpectedly. Failed fertilisation is more likely to occur when there are less than three eggs.

An embryologist will phone you in the morning of the day after your egg collection procedure to tell you what fertilisation has taken place and to make arrangements for your embryo transfer (if applicable).

Failed fertilisation

Failure of any of the eggs to fertilise ('failed fertilisation') occurs in less than 5% of cases. This news can be a devastating as there is no possibility of an embryo transfer. The reasons for this failed fertilisation include problems with sperm being able to penetrate the egg, very few eggs retrieved or poor sperm/egg quality and, rarely, bacterial contamination from the vagina/semen infecting the culture.

Our staff will conduct a thorough investigation of the reason(s) for failed fertilisation and the findings will be discussed with you.

Unfortunately, if you are self-funding your treatment, there is no refund if failed fertilisation occurs. If your treatment is funded by the NHS and you have less than three eggs collected, this will still count as one of your rounds/cycles of treatment. A round/cycle of treatment is defined as a change to 'stimulation' of your ovaries using drugs (gonadotrophin) and any transfer of frozen embryos resulting from the round/cycle. If you have 2 or less eggs collected, you will not be eligible for further NHS funded IVF/ICSI treatment.

Embryo culture
All embryos are cultured in a time lapse incubator called an Embryoscope. This technology allows our embryologists to continuously monitor embryo development in a stable culture environment. The Embryoscope also allows our embryologists to take the pattern of embryo development into account when they choose the best embryo to replace. We do not use a computerised algorithm for embryo selection. An embryologist will phone you on most days to let you know how the embryo/s are developing and to plan your embryo transfer.

Embryo transfer
This usually takes place 5 days after egg collection. On the day of embryo transfer, you will be asked to come to the Centre 15 minutes before your procedure. This procedure is very simple, feels similar to having a smear taken and usually only takes a few minutes. You may eat and drink normally prior to this procedure. During the transfer, a fine catheter containing your embryo(s) is passed through the cervix (neck of your womb) directly into your womb. The embryo transfer is carried out using an ultrasound scan to confirm that the catheter is in your womb and therefore, we advise that you should have a full bladder during the procedure. It is necessary to insert a speculum into the vagina in order to see the cervix clearly. You do not require any anaesthetic drugs and you may go straight home after the procedure. Please refrain from use of perfume of aftershave when attending the Centre as strong scents may affect the embryos in the laboratory.

We will, in most cases, transfer one embryo to minimise the risk of multiple pregnancy. In certain cases where the embryo quality is suboptimal and the woman does not have any risk factors for preterm birth, we may consider transferring a maximum of 2 embryos following a detailed discussion. If for any reason, an embryo appears abnormal, it will not be replaced. If more than one embryo is replaced, the chance of success is increased although it will also increase the chance of a twin or rarely triplet pregnancy. If you wish more information concerning multiple pregnancy, please look at the HFEA (www.hfea.gov.uk) and RCOG websites (www.rcog.org.uk).

We routinely use Embryoglue for our fresh embryo transfers. This is an embryo transfer medium that contains hyaluronan which is found naturally in the womb lining and may help the embryo to implant. Please be aware that this may increase the risk of multiple pregnancy, particularly if two embryos are replaced.

Following embryo transfer
Additional hormone treatment is given for the first 12 days. This is progesterone, the hormone normally produced by the ovaries to sustain an early pregnancy. This may be given as vaginal pessaries or gel. A blood test is arranged two weeks after the egg collection to look for the early signs of pregnancy. This test is done even if your period has already started. If you conceive from treatment, we advise that you complete the course of progesterone that you have been given. There is no good evidence that using progesterone for more than 15 days will increase the chance of a successful pregnancy in a fresh cycle of treatment.

Freezing
Any of your remaining embryos of good quality may be frozen and stored, provided that you have given consent for storage. They will be available for thawing and replacement in subsequent cycles. Any remaining embryos not suitable for freezing will be allowed to perish by day 6 – unless you have consented to their use for research or training.

If you are not eligible for NHS treatment, you will be charged an annual storage fee for the initial freezing and subsequent storage of eggs, sperm and embryos. A separate fee will be charged for the thawing and replacement of embryos or fertilisation of your eggs for your treatment. The storage fee is payable after 12 months from the date of storage. Please see our website for the current price list. If you have frozen embryos stored with us, please let us know ***IMMEDIATELY*** of any change in your address or personal circumstances. It is advisable that you let us have your e-mail address/mobile telephone so that we can contact

you regarding extension of storage of your frozen embryos. Embryos can only remain in storage if your consent(s) are valid. You can consent to up to 10 years of storage at a time and for up to 55 years in total.

Detection of Pregnancy
If treatment is unsuccessful, a period should be expected approximately 2 weeks after egg retrieval. You will have a blood test for pregnancy about 2 weeks after your operation. If the pregnancy test is positive, you will have an appointment for a scan 3 weeks later. After your scan we will discharge you to maternity services for your obstetric care. As none of the details of your treatment will be available to your obstetric team, please take your discharge letter from us with you to your first appointment with your midwife.

Our clinic has to report to the Human Fertilisation and Embryology Authority (HFEA) the outcome of your treatment. It is therefore very important that you attend our clinic for a pregnancy test following your treatment and that if your treatment is successful, you return the pregnancy outcome form to us. If your pregnancy test is negative and you wish to have another attempt, this can be discussed at a clinic appointment.

Treatment Add-ons

Add-ons are optional extras that some clinics offer on top of your normal fertility treatment. They are sometimes emerging techniques that may have shown some promising results in initial studies, or they may have been around for a number of years but haven't necessarily been proven to improve pregnancy or birth rates. To make it easier to identify which add-ons have been shown to be effective, the HFEA have developed a traffic light rating system (https://www.hfea.gov.uk/treatments/treatment-add-ons).

We do not charge for any add-ons. Any that we use, are part of routine practice and we do not charge extra for these. These include time-lapse imaging and EmbryoGlue which are detailed above. There is insufficient evidence at this time to indicate that the use of EmbryoGlue or an Embryoscope would significantly increase the effectiveness of treatment. Similarly, there is little evidence to suggest any longer-term risks to patients and conceived children using these methods.

The Centre only offers procedures based on robust clinical evidence. We cannot prescribe or facilitate add-ons for you that have been advised by other clinicians, such as in the private sector, that we would not recommend ourselves.

What are the Chances of Success with IVF/ICSI?

Several factors affect the chances of success, including the actual cause of the fertility problem and the response of the woman to the drug treatment. There is a drop in pregnancy rate for women who commence treatment after the age of 35. For women over 40, the chance of success is more significantly reduced. Even if the initial pregnancy test is positive, there is still a considerable risk of early miscarriage.

The aim of an elective single embryo transfer is to reduce the chance of multiple pregnancies in women up to the age of 37. In line with the HFEA directive and health board eligibility criteria, we are now offering elective single embryo transfer for good prognosis patients. If your treatment cycle is funded by the NHS, an elective single embryo transfer will be our aim in your fresh and frozen treatment cycles. This may be reviewed if your response to stimulation is poor or if the embryos are not optimal quality, but this will be discussed with you. The overall single embryo transfer rate for our centre is over 90%, and our multiple birth rate is around 2% which is well below the HFEA target of less than 10%. Our success rates can be seen on our website (www.nhslothian.scot.nhs.uk/edinburghivf), as well on the HFEA website. The HFEA publishes statistics for each clinic (www.hfea.gov.uk) with the main focus on presentation of success rate on the live birth rate per embryo transferred. You can also compare clinic data using the HFEA website however, the HFEA have state that "information on success rates is of limited value in comparing centres and choosing where to seek treatment".

Multiple pregnancies (twins and triplets) can result from IVF and these are associated with a higher chance of complications than a pregnancy with a single baby.

Frozen embryo replacement
Good quality embryos which are not transferred are frozen using a fast-freezing method known as vitrification and the survival rate of these embryos is >90%. Previously, embryos were frozen using a different method ("slow" freezing) which is not as efficient, so embryos still in storage which were frozen using slow freezing prior to 2012 may not have such a good survival rate (50-70%). If you wish to specify extra conditions for storing or using your gametes/embryos, please discuss this with a member of our staff who will guide you.

The freezing process is technically difficult, so we cannot rule out the possibility that embryos may be damaged or lost during the freezing or thawing procedure. The possibility of this happening is rare but the loss or damage of an embryo during the freeze/thaw process is a recognised complication of cryopreservation.

The main factor which determines the success rate of a frozen embryo transfer is the age of the woman at the time the embryos were frozen. The success rate for frozen embryo replacement in our unit is shown on our website (www.nhslothian.scot.nhs.uk/edinburghivf).

If you are having treatment as a couple, the HFEA requires that we check the consent from both partners in every cycle to ensure that both of you wish to have the treatment.

Unsuccessful treatment
Unfortunately, it is still the case that many of our treatment cycles are not successful and this can cause profound disappointment and distress. If you have an unsuccessful cycle of treatment and you would like to discuss this in detail please request an appointment with a doctor. Our nurses and counsellors are also available to offer you any additional support that you may need.

Risks of IVF/ICSI

Like all medical treatments, fertility treatment carries some risks and your doctor will discuss these with you before you go ahead. Risks can include reactions to fertility drugs that may be prescribed, and also the risks associated with any pregnancy. Other risks, of which some are not yet fully understood, relate to the children born as a result of the treatment. We understand that if you experience any of these outcomes it may be very distressing and uncomfortable. Our team of dedicated staff will be available to you at every step of your journey to guide and support you through your choices.

Drug reaction

What it is:	A mild reaction to fertility drugs.
Symptoms:	Hot flushes, feeling down or irritable, headaches and restlessness.
What to do:	Contact our clinic if you have any unexpected reaction to treatment.

The risks of the egg collection include the risk of drugs administered during conscious sedation, rare risk of damage to bowel, bladder or blood vessel at the time of egg collection and risk of serious pelvic infection after egg collection (affects 1 : 1000 women) and overstimulation of ovaries (see below).

Miscarriage

What it is: When a pregnancy in the womb has died or not developed. Unfortunately this is not less common after fertility treatment and occurs in around 1 in 3 pregnancies depending on a woman's age. This is most common in the first 12 weeks of pregnancy.

Symptoms: Bleeding, pain, loss of pregnancy symptoms (but can have no symptoms).

What to do: Contact us if you have concerns and we will arrange further tests (blood tests or scans) depending on how far on in pregnancy you are. We arrange a scan routinely at around seven weeks to check for the baby's heartbeat.

Ectopic pregnancy

What it is: When an embryo implants outside the uterus. The most common site is in the fallopian tube. Occasionally an ectopic pregnancy can develop in the ovary. The chances of an ectopic pregnancy seem to be higher in women having IVF, especially if they already have problems affecting their tubes.

Symptoms: The first symptom is usually a one-sided low abdominal pain, followed by vaginal bleeding or dark brown or red vaginal discharge. As the pregnancy continues, the pain increases.

The major risk is that the ectopic pregnancy will rupture through the tube causing internal bleeding. This can cause severe abdominal pain and pain in your shoulders.

What to do: We will arrange a pregnancy blood test to check for the pregnancy hormone, human chorionic gonadotrophin or 'hCG'. We will also arrange a scan around seven weeks to check for the baby's heartbeat and to make sure it is growing properly in the uterus. This can be brought forward to six weeks to check the location of the pregnancy if needed.

If you have stomach/abdominal pain or vaginal bleeding in early pregnancy please contact us (or RIE ward 210 if out-of-hours). Alternatively, please contact NHS 24, your GP surgery or attend A&E if necessary.

Birth defects

The risk of birth defects in the general population is low: 2% of children in Europe are born with birth defects. Although some research suggests that fertility treatment may be associated with an increased incidence of birth defects, this risk remains low.

Some research suggests that assisted reproductive techniques are associated with longer-term health issues in the children born. Whether there is a direct link is yet to be conclusively agreed, as it is possible that the association is due to other factors. These could relate to underlying subfertility in the patients.

Research into the area is ongoing and, in order to make sure patients understand the risks of fertility treatment, the HFEA keep research of this kind under review. The HFEA also aids researchers seeking to conduct studies that link fertility treatment data held by the HFEA to other health data sets in order to explore the effects on health. A key study of 106,013 children born after assisted conception, one of the largest of its kind, found no increased risk of cancer in ART children.

You should be aware that where studies report, for example, a doubling of risk or cases of a health complication (e.g., from 0.1 to 0.2%) this may not necessarily equate to a significant clinical risk, and you should discuss any concerns with their clinician.

There are no documented long term side effects of fertility treatment. Some patients/couples worry that fertility treatment will 'use up' their eggs and cause premature ovarian failure but there is no evidence to support this.

Psychological effects

Some patients/couples may experience negative psychological effects of undergoing fertility treatment. Despite the stressful consequences of infertility and IVF, it is important to note that research has shown that the vast majority of patients adjust well emotionally. Further, there seems to be no long-term impact on the marital relationship and individual functioning. In fact, some research has shown that the crisis of infertility may actually improve marital communication and emotional intimacy. Couples may learn coping skills and communication patterns that provide life-long benefit. Those individuals who do develop uncomfortable anxiety or depression symptoms should consult with a mental health professional who has knowledge and experience with infertility. Free counselling is available in the centre and we can also help you to access other sources of support such as local support groups.

Ovarian hyperstimulation

Despite careful monitoring, ovarian hyperstimulation can occur. This occurs after administration of an injection to trigger ovulation or in a woman who conceives within 1 – 2 weeks after embryo transfer. It is due to the ovaries growing too many follicles leading to excessive production of hormones.

A woman may have mild, moderate or severe ovarian hyperstimulation. Mild – moderate ovarian hyperstimulation occurs in approximately 5% of cases and 1 – 2% of women may have severe hyperstimulation syndrome. Ovarian hyperstimulation is unlikely to occur in women more than 40 years old. Patients with ovarian hyperstimulation may experience abdominal pain/swelling, nausea, vomiting or shortness of breath. If you develop the condition, you may require a daily blood thinning injection (low molecular weight heparin) after egg collection and occasionally hospital admission is necessary. Mild to moderate hyperstimulation is managed with scans and blood tests as an outpatient. It is advisable that you do not plan to go on holidays abroad during or immediately after embryo replacement as you may need to be seen on a regular basis in the Clinic. Fatality from severe ovarian hyperstimulation occurs in less than 1 in 100,000 treatment cycles.

Ovarian tumours

In the past it had been suggested that fertility drugs may be associated with an increase in the risk of ovarian cancer and borderline ovarian tumours. This has been looked at in many epidemiological studies and, reassuringly, no significant association has been identified.

Multiple births and their risks

Couples having NHS IVF/ICSI treatment will have an elective single embryo transfer. This is a national strategy to help reduce the risks to mother and baby of a twin pregnancy.

If a self-funding couple wishes to have two embryos transferred, they will be asked to sign a disclaimer form to confirm they are fully aware of all the risks of a twin pregnancy. Two is the maximum number of embryos we are permitted to transfer and we individualise our care. A woman with pre-existing medical/genetic conditions may not be suitable for transfer of two embryos.

We have been able to demonstrate that in a select group of women who are under the age of 35, non-smokers, have a good ovarian reserve and normal body mass index, the clinical pregnancy rate is up to 50% for an elective single embryo transfer.

The prospect of twins or triplets may seem attractive but there are many serious risks involved in multiple births. Multiple births can lead to a much higher risk of complications during pregnancy, premature birth and low birth weight, disability and death of infants at or within 28 days of birth (known as neonatal death). Low birth weight babies are more likely to suffer from serious life-long health problems such as cerebral palsy. Research has shown that the average birth weight is 2.5kgs for twins and 1.8kg for triplets compared to the average birth weight of 3.3kg for single babies.

In comparison to single births, the risk of stillbirth and neonatal death is greater in multiple births. For single births from IVF treatment, the rate of stillbirth and neonatal death is 8.8 per thousand birth events. The rate is 46.8 for twin births and 82.6 for triplet births.

In addition, a multiple birth can create enormous strains for the parents, including financial difficulties, emotional and physical exhaustion. In some instances, the joy of parenthood may be greatly reduced by these problems.

It is still possible to have an identical twin pregnancy from a single embryo transfer (from one embryo splitting) and the chance of this is approximately 2:100. There is a risk of having a triplet pregnancy from having two embryos transferred and the chance of this is around 1:700.

Please visit the HFEA website for more information on the risks associated with multiple pregnancies.

Increased maternal age

Unlike men who make a new batch of sperm every 3 months, women are born with a finite number of eggs. These eggs gradually undergo an ageing process and are “used up” until the fall in numbers becomes critical and this results ultimately in the menopause at an average age of 51. A reduction in the quality of eggs precedes this and may result in a reduced chance of a successful pregnancy. This is reflected not only in a lower general fertility rate but a significantly reduced chance of success of procedures such as assisted conception.

Clearly, there are exceptions to the overall trend. There are many women over 40 who have successful pregnancies. If you are over 40 and unable to become pregnant by natural means with no known identifiable cause of infertility, the likely cause is a reduction in the quality and number of your eggs. This problem is not overcome by IVF/ICSI treatment.

Unfortunately, there is no reliable test to assess the quality of eggs. Women who are 40 years or over and conceive naturally, or from IVF treatment using their own eggs, have a higher chance of miscarriage because of the effects of ageing on the genetic material in the eggs. The chance of miscarriage is around 50% in women over 40.

You may be aware that in women 40 years or over, there is a slightly higher chance of Down’s Syndrome. The risk of having a baby with Down’s syndrome varies from 1% in a 37 year old woman and up to 5% in a 45 year old woman. If you fall pregnant, you may wish to discuss with your Community Midwife or your Obstetrician regarding the accuracy of screening tests (blood test and nuchal translucency ultrasound scan at around 12 weeks of pregnancy), and diagnostic tests (NIPT, chorionic villous sampling from 11 weeks and amniocentesis from 15 weeks). There is a small risk of miscarriage (1% in amniocentesis and up to 4% in chorionic villous sampling) for both procedures.

The live birth rate for women varies from 10% to 15% in their early forties to around 1%-2% when the woman is 45. There is a small risk of a twin pregnancy even with a single embryo transfer. Our policy is to transfer a maximum of two embryos to reduce the risk of triplet pregnancy.

As women get older, both mothers and babies face an increased risk of pregnancy-related complications and health problems. These are due to changes in the reproductive system and the increased likelihood of general health problems that comes with age. Pregnant women who are more than 45 years old are much more likely to experience pregnancy complications such as gestational diabetes, gestational hypertensive disorders, Caesarean delivery, preterm birth and ITU admission, than younger women. For this reason, the age cut-off for treatment in our unit is generally 45 years although, in some circumstances, we can do frozen embryo transfers up to and including the age of 47.

Risks to children conceived from treatment

What are the risks of IVF?

Babies conceived by IVF may be at slightly increased risk of birth defects. The risk of birth defects in children conceived naturally is 2-3% whereas the risk of birth defects in children conceived by IVF is estimated to be 2.6-3.9% (http://www.asrm.org).

What are the risks of intracytoplasmic sperm injection (ICSI)?

Intracytoplasmic sperm injection (ICSI) was introduced in 1992 and there is still research into the long-term consequences of this treatment type.

The risks that have so far been associated with ICSI are:

- Certain genetic and developmental defects in a very small number of children born using this treatment. However, problems that have been linked with ICSI may have been caused by the underlying infertility, rather than the technique itself.
- Young men conceived as a result of ICSI have been shown to have lower semen quality than those who have been conceived spontaneously.
- An increased risk of miscarriage because the technique uses sperm that may not otherwise have been able to fertilise an egg.
- A low sperm count caused by genetic problems could be passed on to a male child. Men with low sperm count or no sperm in their ejaculate may be tested for cystic fibrosis genes and for chromosome abnormalities. You may want to discuss the full implications of taking these tests with our clinician(s) or the clinic's counsellor before going ahead.

What are the risks of using donated sperm, eggs or embryos?

If you use donated gametes or embryos, we minimise the risks as much as possible. Donors must answer a series of questions designed to ensure that they are suitable. The donors' family histories for inherited diseases are checked.

All donors go through stringent screening checks to ensure they are not carrying infections, such as HIV, Hepatitis B and C, cytomegalovirus (CMV), syphilis and gonorrhoea. Donated sperm and eggs (if not used fresh) is quarantined for three to six months whilst the donor is being screened.

There are limits on the numbers of families created by each donor where donor gametes are used. Please be aware that although we carry out comprehensive screening, it is not possible to screen for every disease.

If you are considering using donated sperm, eggs or embryos you will be given further information about these issues.

Consents to your treatment

Your consent forms are a legal requirement and the clinic needs to make sure that you understand and agree to, everything the treatment will involve. We encourage couples to discuss these matters together and make joint decisions on the issues which affect them both. We recognize the difficulty you may have with the nature of these conversations.

It is important that you fully understand the implications of any treatment you agree to. Your clinic will help you do this by:

- Providing information about your treatment and procedures, and discussing the risks and benefits with you
- giving you time and opportunity to consider your options and ask questions
- offering you emotional support and professional counselling
- providing you with clear information about the costs of treatment when applicable

When you (and your partner) undergo treatment in our Centre, you will be given sufficient time to reflect on your decision regarding your treatment before we obtain your consent(s). You will be given sufficient time to consider donation of your eggs/embryos or storage of eggs/sperm/embryos before we obtain your consent(s). You may vary or withdraw your consent at any time during your treatment/donation.

Visit ***www.hfea.gov.uk*** for more information and guidance.

HFEA consent forms

Consent to Disclosure

In your information pack, received prior to attending your clinic appointment, you will find a 'Consent to Disclosure' form.

All patients/couples having fertility treatment are required to complete this form.

The clinic or the HFEA may want to use or share your information, to allow us to;

- contact your GP for your medical history (or in case of emergency)
- help the HFEA and our Centre improve the quality of our services
- contact you for medical or other research.

In a couple, if both parties differ in their consent, their identifying details regarding their treatment cannot be provided to researchers. If you wish to have clarification, please discuss this with us.

Contact with your GP

Our centre is required by the HFEA to be satisfied that we know of no reason why either of you might not be suitable for treatment. Your GP may be asked to provide relevant factual information, medical or otherwise, about you that might have implications for the health or welfare of any resulting child.

When you are ready to proceed, you should discuss the consent form with a member of our staff. Once you are satisfied with our explanation, please complete the form. It is useful for your GP to be aware of your treatment with us in case any medical complications arise. We will need you to complete the consent form to contact your GP. If you decide not to give your consent, for whatever reason, and if this was felt necessary by the Centre, this information will be taken into account when deciding whether or not to offer treatment.

Treatment consent forms (WT and MT)

These consent for treatment forms should be completed by patient/partner for the use and storage of eggs, sperm and embryos. You will also have to decide what will happen to stored eggs/sperm/embryos if you or you/your partner die (posthumous use) or lose the ability to decide for yourself (become mentally incapacitated). If you are having treatment to store eggs you will be asked to complete a gamete storage (GS) form instead. Please keep copies of your consent forms so that you know what you have consented to and when your consent to storage expires.

Storage period

If you have any embryo(s) or gametes in storage please note that the storage period starts on the date of storage and that you have given us consent to store for the duration specified on your treatment consent forms (WT +/- MT) or gamete storage (GS) form. We have a legal obligation to review consent to storage forms at regular intervals and to thaw/ discard embryos if we do not have valid consent to continue storage. In order to contact you to check your wishes with regard to continued storage of your embryo(s) it is very important we have up to date details (address, telephone number(s)). We will attempt to contact you in advance of the date your consent expires.

The current statutory storage period is up to 55 years, with consent requiring renewal at 10-year intervals. You will consent to store for up to 10 years initially. Extensions must be done before the current consent expires. If at any time you wish to discuss changing your consent form or extending the storage period please contact the Centre for advice. If you are storing embryos, both the sperm and egg providers must provide written consent to extend storage. Please be aware you may be required to pay storage fees if you are a self-funding patient or you no longer meet the NHS Access Criteria.

Changing or withdrawing your consent

If you or your partner withdraws consents for the use of your eggs/sperm/embryos for treatment, we are obliged to follow your individual wishes and cannot offer treatment to you or your partner. In addition, if you and your partner withdraw your consent(s) for storage of your embryos, we cannot store your embryos without a valid consent. There is a 12 month 'cooling off' period where the centre can continue to store your embryos if only one party withdrawals their consent but this 12 month period cannot extend beyond the period consented to in your original forms. If both parties to the treatment withdraw their consent, the centre can remove the embryos from storage earlier than 12 months. If you wish to change or withdraw your consent, you must contact our Clinic as soon as possible and we aim to get back to you within 14 working days. It is important that you contact us if you have not heard from us after 14 working days.

You will be required to complete a 'Withdrawal of Consent' form. Please see HFEA document 'HFEA Consent Form Guidance', www.hfea.gov.uk) if you withdraw your consent. If you wish to change any of your individual consent forms, please speak to a member of the clinic staff. You/your partner will be required to complete new consent forms. It is your responsibility to keep the clinic informed of any changes to your circumstances.

Legal aspects and parental responsibility

Under the terms of the Human Fertilisation and Embryology Act (1990), the HFEA licenses and regulates centres which practice IVF/donor insemination.

Any child born to a married woman following IVF/donor insemination will be legally the child of the husband unless he did not consent to his wife's treatment. If you (and your partner) wish to find out more about the definition of legal parenthood, please look up the HFEA website, www.hfea.gov.uk and search for legal parenthood. The meaning will be clearly defined and if you have any queries, please ask us for clarification.

Unmarried couples are recommended to seek their own legal advice about the partner's rights and responsibilities in relation to the potential child who may be born as a result of the treatment if they have concerns. If you are not clear as to the definition of legal parenthood, we advise that you seek legal advice.

If donor sperm, eggs or embryos are used you will be asked to complete additional HFEA consent forms relating to legal parenthood.

Please note, men wishing to donate embryos originally created for the treatment of their partner and themselves and those wanting to have treatment using these embryos should be aware of the uncertain legal status of the men when the embryo is used to treat single women. Each party should seek independent legal advice and refer to the HFEA's website (www.hfea.gov.uk) for further information on this issue.

Welfare of the child assessment

The Human Fertilisation & Embryology (HFE) Act 1990 requires that any fertility clinic in the UK offering treatment services, such as IVF and the use of donated gametes must take into account the of the welfare of any child born as a result of the treatment, and of any other existing child who may be affected by the birth.

Many factors need to be taken into consideration in this assessment including who would be legally responsible for any child born as a result of treatment, and who will be bringing up the child. The HFEA Act does not exclude any woman from being considered for treatment. People seeking treatment are entitled to a fair and unprejudiced assessment of their situation and needs. This will be done with sensitivity and include the wishes and feelings of those involved.

What may be discussed?
We will need to take a detailed medical and social history of you and your partner. The issues that may be discussed are:

- Your commitment to having and bringing up a child/children
- Your ability to provide a stable and supportive environment for any child produced as a result of treatment.
- Your medical history and the medical histories of your families.
- Your health and consequent future ability to look after or provide for a child's needs.
- Your ages and likely future ability to look after or provide for a child's needs.
- Your ability to meet the needs of any child or children who may be born as a result of treatment, including the implications of any possible multiple births.
- Any risk of harm to the child or children who may be born, including the risk of inherited disorders or transmissible diseases, problems during pregnancy and of neglect or abuse.
- The effect of a new baby or babies upon any existing child/children of your family.

In addition, if your treatment involves the use of donated gametes, the following will be discussed:

- A child's potential need to know about their origins and whether you are prepared for the questions which may arise while the child is growing up.
- The possible attitudes of other members of the family towards the child, and towards their status in your family.
- The implications for the welfare of the child if the donor is personally known within the child's family and social circle.
- An explanation of who will be the legal parents of any child produced as a result of treatment with donated gametes.
- These issues will be discussed in detail at your 'implications counselling' appointment which is a pre-requisite before donor gametes or embryos can be used.

Contact with other agencies
Where necessary, our centre may need to make further inquiries of other relevant individuals, authorities or agencies. Again, your consent will be sought before any such contact is made.

Why treatment may be refused
The Consultant responsible for administering the fertility treatment is responsible for making the final decision about whether treatment will be offered. Treatment may be refused on clinical

grounds, or if the Centre believes that it would not be in the interests of any resulting child or any existing child, to provide treatment. Treatment may also be refused if the Centre is unable to obtain sufficient relevant information or advice to reach a proper conclusion.

If treatment is refused for any reason, an appropriate member of staff at the Centre will explain to you (and your partner where appropriate) the reasons for this will be explained and any other options will be discussed.

Confidentiality, privacy and data protection

Prior to and during your treatment you and your partner must complete the 'Consent to Disclosure' form. This will confirm who we can share information with.

We are required by law to submit data to HFEA relating to the use and outcome of any treatment using of eggs, sperm and embryos. If your treatment is successful, we will ask you to complete an 'Outcome of Pregnancy Form' to share the information with the HFEA. The HFEA use this data to monitor the activity and performance of clinics which is available from the HFEA website.

Our Centre complies with general data protection regulations e.g. when requesting copy a of medical notes. If you agree to disclose information regarding your treatment to your GP or agencies, the information we have relating to you will no longer be covered by the HFE Act 1990 and will be subjected to the general law of confidentiality. For more information on how we manage your data, please visit the NHS Lothian website www.nhslothian.scot/YourRights/DataProtection.

Research

Currently, we are undertaking research projects in collaboration with the world-renowned University Department of Obstetrics and Gynaecology. All such programmes have to be passed by the Ethics Committee which includes lay people as well as by the national Licensing Authority. Couples are ***not*** obliged to take part in research programmes if they do not wish to do so. Full written information will always be given about any research projects that are being undertaken.

Patient Support

We understand that IVF treatment is a stressful experience and we are committed to making your treatment with us as good an experience as is possible. Our staff are available to provide support, information and answer queries during normal working hour and doctor's appointments are available on request.

Counselling

If you and/ or your partner wish to see an independent fertility counsellor at any stage during your treatment or after, if requested, please telephone 0131 242 2460 and we shall arrange an appointment for you.

Our dedicated counsellors have specialist experience in managing couples undergoing treatment in our unit. A separate leaflet explaining the advantages of counselling is available on request. Your meetings are confidential and only recurring 'themes' are discussed in our multidisciplinary meeting.

Lifestyle Changes

For the best chance of success you and/or your partner should:

- stop smoking/vaping and using nicotine replacement therapies. The NHS does not fund IVF/ICSI treatment if you smoke or vape.
- reduce your caffeine consumption (from soft drinks or coffee) because it may affect your chance of success (not more than 200 mg of caffeine/day which is about 2 cups of instant coffee)
- stop drinking alcohol
- maintain a body mass index (BMI) of >18.5 and <30 kg/m2. The NHS does not fund treatment if the intended birth mother does not meet this criterion.

Vitamin supplementation

We advise all women to take folic acid if they are planning a pregnancy to reduce the risk of neural tube defects for example, spina bifida. The usual dose of folic acid is 400 microgram and if you are in a higher risk group (e.g. have epilepsy, diabetes, have a BMI more than 30kg/m², removal of your large bowel, have a family history or have had a child affected by a neural tube defect) we advise that you take 5mg folic acid every day.

For general health reasons it is recommended that everyone in the UK should take Vitamin D supplements (10 micrograms daily). As Vitamin D is particularly important for fertility and pregnancy, we recommend that patients take a Vitamin D supplement.

Safeguarding patients and IVF conceived children

All centres which carry out IVF treatment in the UK must be registered with the Human Fertilisation and Embryology Authority (HFEA). The HFEA Act covers the use and storage of sperm, eggs and embryos for human use as well as all research. Centres are inspected regularly by the HFEA to ensure compliance with the Code of Practice and renew their licence.

The HFEA lay down strict rules about what information is required from patients/couples and how we carry out your treatment: for example Welfare of the Child declaration and witnessing procedures.

NHS-Funded Treatment

The Access Criteria for NHS IVF Treatment in Scotland outlines who is eligible for NHS funded treatment and the number of cycles couples are entitled. Please refer to the information sheet sent to you or on our website (www.nhslothian.scot.nhs.uk/edinburghivf)

Self-Funded Treatment

Your treatment is carried out in an NHS Hospital. Although you are paying for your treatment you should not regard this as “private” treatment as it is not different from what is provided to NHS patients. Please see our website (www.nhslothian.scot.nhs.uk/edinburghivf) for an up-to-date price list.

For new self-funding patients, there is an initial charge which includes consultations with medical / nursing staff and relevant tests. For a full price list (including non-refundable deposits) please see our price list on our website.

Full payment must be received before the Nurse Discussion appointment. If you decide that you do not want to proceed with your treatment, please let us know as soon as possible so that this slot can be offered to another patient.

If a self-funded treatment cycle is cancelled, such as due to poor response or potential ovarian hyperstimulation syndrome, you will be entitled to a partial refund and we will arrange this for you. If you have undergone egg recovery and there is no egg, no fertilisation, or no embryo to transfer, you will not be entitled to a refund. It is important for people who are self-funding to consider the financial implication(s).

Quality Management System

Edinburgh Fertility Centre has a robust quality management system and works to ISO 9001 standards and in 2017, the United Kingdom Accreditation Service (UKAS) granted our diagnostic andrology service with ISO 15189 accreditation. Full details of this accreditation can be found on our “scope of practice” published on the UKAS website (www.ukas.com). The quality management system enables the Edinburgh Fertility Centre to achieve and maintain the highest possible standards of safety and care during your treatment.

The Quality Management System is a regulatory requirement of the HFEA and we are regularly assessed against HFEA standards and European Union Tissue and Cells Directive.

Patient Satisfaction Survey

We regularly monitor and seek to improve to ensure the best possible outcome and care for our patients. To achieve this we carry out internal satisfaction surveys at regular intervals to enable patients to provide us with feedback and this allows us to improve the service and patient experience. The HFEA also collect feedback on clinics via their website (www.hfea.gov.uk) and we would be grateful for any feedback you could provide regarding our centre.

Feedback

We welcome any feedback you can give us on what we are doing well and what we could improve upon. Please ask at reception if you would like to complete feedback card. If you would like to raise a compliment, concern or complaint with the NHS Lothian Patient Experience Team, please see the NHS Lothian website (www.nhslothian.scot/YourRights/ComplimentsConcernsComplaints) for information on how to do this. Complaints are all dealt with as per NHS Lothian policy.

If you wish to make a complaint or any comments about your treatment, please write to or make an appointment with Dr M. Chetty, Consultant in Charge of the Assisted Conception Programme.

Opening Hours

The Centre is open from Monday to Friday 8am to 4.30pm and Saturday 9am to 12pm. We are only open on Sundays for embryo transfers. There are other occasions when the Centre will be closed – such as Christmas Day and New Years Day.

Useful Links

The HFEA website www.hfea.gov.uk is a valuable resource for patients/couples who are thinking about having fertility treatment.

Fertility Network Scotland (www.fertilitynetworkuk.org) is a national charity providing support to those who have experienced fertility problems.

The Fertility Alliance (thefertilityalliance.org.uk) is a national fertility charity offering support and accurate information for anyone who wants to know more about their fertility

☎	0131 242 2450 0131 242 2101 / 4	Edinburgh Fertility Centre: Mon-Fri 8am-4.30pm Outside office hours you may leave a message on the above number or contact Ward 210, New Royal Infirmary of Edinburgh

Please scan this code using the camera on your phone to rate your experience with us on the HFEA website.

***if you are unable to use the QR code above please visit HFEA.gov.uk**