NGICNS
National Gender Identity Clinical Network for Scotland

NHS National Services Scotland

Endocrine and Fertility Preservation guidance

Contents

Introduction

This guidance relates to the provision of feminising and masculinising gender affirming hormone treatment for transgender, non binary and gender diverse (TGD) people. It updates and replaces the previous NGICNS guidance on 'Endocrine Management of Adult Transgender Patients', first published 11 August 2015 and revised 7 July 2016 and 18 October 2018.

It has been structured with three main sections; masculinising gender affirming treatment, feminising gender affirming treatment and fertility preservation, followed by appendices covering medical conditions and endocrine treatments, off licence prescribing, and Gamete storage for use by 3rd party reproduction.

The guidance development group convened by National Services Division (listed in an appendix 6) had diverse professional and lived experience. While previous versions of this and other guidelines as well as primary research were used in developing this document, it is recognised that the evidence base remains incomplete and that there is variation in acceptable practice, which will therefore evolve over time. In this document we have aimed to outline what is currently considered best practice for safe and effective care as applicable within NHS Scotland for endocrine management and fertility preservation in this field.

1. Masculinising gender affirming hormone treatment

This guidance makes no assumptions about an individual's gender identity but provides information with regard to masculinising hormone treatment.

This guidance relates to people originally assigned female at birth, wishing masculinising hormone treatment who are aged 16 years and over and have completed puberty.

Masculinisation is achieved by commencing testosterone treatment.

1.1. Baseline assessment

The aim of the baseline assessment is for the person who is starting testosterone to have a discussion with an appropriately experienced professional about the risks and benefits of starting testosterone treatment, to enable an informed choice to be made about starting testosterone treatment.

The baseline assessment should cover the following areas:

1) Medical review and family history
2) Likely effects of commencing testosterone treatment
3) Potential risks of starting testosterone treatment
4) Advice on the impact on fertility, contraception and pregnancy
5) Treatment options
6) Agreeing a starting dose and titration regime
7) Maintenance doses
8) Ongoing monitoring requirements.
9) Consent

1.2. Medical review and family history

There are almost no absolute contraindications to starting testosterone treatment. There needs to be a review of medical and family history so the person considering treatment can understand the potential risks and ongoing monitoring required if testosterone treatment is started.

- Medical and family history are taken. Conditions that are of particular relevance regarding testosterone treatment are below highlighted below, more details are available in Appendix 1

    - Cardiovascular disease
    - Cardiovascular risk (Assess cardiovascular risk using a recognised tool e.g. qrisk3 or ASSIGN)
    - Polycythaemia
    - Hypertension
    - Diabetes
    - Liver disease
    - Breast disease
    - Abnormal vaginal or menstrual bleeding, and prolonged amenorrhoea

- Check Baseline FBC and lipid profile.
- Baseline liver function
- Baseline hormonal profile particularly if history of amenorrhea/irregular periods (LH, FSH, estradiol, testosterone, prolactin).
- BMI: high BMI is not a contraindication for hormone treatment. However, people with high BMI should be should be counselled re. the additional risk of a higher BMI, offered weight-loss assistance and informed clearly that there are BMI limits for most NHS funded surgical procedures

1.3. Likely effects of commencing testosterone treatment

Table 1 shows the effects and expected time course of testosterone treatment.

These changes should be discussed with the person considering starting testosterone treatment. Testosterone treatment has a systemic (whole body) effect, so it is not possible to be selective about which effects occur and which do not.

It should be advised that the degree of change is highly variable for person to person, as can be seen in the variation across the general population e.g. amount of facial body hair / body build. These differences are dependent on not just testosterone levels but other factors such as genetics, exercise and build.

Androgen dependant balding or male pattern hair loss is genetically determined. This genetic potential will be revealed by starting testosterone treatment. There are

limited effective treatments for male pattern balding. Any advice and treatments would be as per the general population.

It should be advised that some of these changes (notably voice change and facial hair) are likely to be permanent and will not completely resolve on stopping hormone treatment.

Periods will usually restart if testosterone is stopped (although menopause will occur at the normal age).

Testosterone will not alter height, once final height has been achieved.

Aggression is not usually seen in people given physiological (normal range) testosterone treatment. Aggression can be seen in people taking excessive testosterone treatment but this is not the aim of masculinising hormone treatment. Mood and other aspects of mental health usually improve as the effects of testosterone develop.

Table 1

Effect	Expected Onset	Expected Maximum Effect
Skin oiliness/acne	1-6 months	1-2 years
Deepened voice	3-12 months	1-2 years
Facial/body hair growth	3-6 months	3-5years
Scalp hair loss	>12 months	variable
Increased muscle mass/strength	6-12 months	2-5 years
Body fat redistribution	3-6 months	2-5 years
Cessation of menses	2-6 months	n/a
Clitoral Enlargement	3-6 months	1-2 years
Vaginal atrophy	3-6 months	1-2 years

Source: Adapted from Hembree et al (2009). Effects also dependant on genetics, exercise, build.

1.4. Potential risks of starting testosterone treatment

See Appendix 1: Medical conditions and testosterone for full details

Testosterone treatment has been shown to increase cardiovascular risk in some studies.

Testosterone treatment can also be associated with an increased haematocrit which will increase cardiovascular risk and may worsen cardiovascular disease. Risk of polycythaemia can be reduced by addressing other risk factors such as smoking and obesity.

Men have an increased risk of diabetes. Screening and treatment should be as general population

Oral testosterone is not recommended as it is associated with impaired liver function and liver tumours. There is no evidence that transdermal or IM preparations affect liver function/ cause liver tumours. Impaired liver function/liver disease should be investigated and managed as per general population.

Testosterone has been associated with male breast cancer but there is no evidence of increased risk of breast cancer in this group. For people with breast tissue breast screening should be performed as per guidelines.

Testosterone treatment will usually cause cessation of periods. There is currently insufficient evidence to suggest routine ultrasound scanning to assess endometrial thickness for people on testosterone, however people with new or abnormal bleeding on testosterone should be investigated as per standard guidelines.

1.5. Advice on the impact on fertility, contraception and pregnancy

Fertility

People should be made aware that hormonal preparations impair fertility. Prior to starting testosterone, future fertility options need to be explored. Should the person wish to preserve their fertility then referral to the local fertility clinic or fertility preservation team should be made, ideally prior to starting full dose testosterone treatment. Please see Fertility Preservation section for more details.

Contraception

Although most people on full dose testosterone treatment will not have periods, testosterone is not a reliable contraceptive and if required, contraception should be used. People can use their preferred method but oestrogen-containing contraceptives are less popular, and concomitant use with testosterone should be avoided because of the thrombosis risk. Progestogen-only contraceptives or intrauterine methods (IUS or IUD) may be more acceptable.

Pregnancy

Testosterone treatment needs to be stopped prior to conception and should not be restarted until after delivery.

There is a risk of foetal abnormality when a pregnancy is conceived while on testosterone treatment. Testosterone needs to be stopped prior to conception. The time required for testosterone levels to reduce to pre-treatment levels varies widely depending on the preparation. Expert advice should be sought in advance of conception, or in the event of unintended pregnancy.

Testosterone can usually be restarted soon after delivery, depending on the individual's thrombosis risk and decision/options regarding breast feeding.

1.6. Treatment options

Masculinising hormone treatment is achieved by commencing testosterone.

Recommended testosterone preparations are either transdermal preparations or intramuscular (IM) injections.

Oral testosterone is not recommended due to poor bioavailability resulting in low blood levels, and adverse effects on the liver.

Most testosterone preparations, with the exception of Sustanon, do not have a marketing authorisation for use as a gender affirming treatment See Appendix 2 for guidance on prescribing medication "off licence", i.e. outside the conditions of the marketing authorisation.

1.7. Agreeing a starting dose and titration regime

Gradual introduction of testosterone is recommended. This is usually achieved with transdermal preparations such as gels. Different brands of gel have different concentrations and care should be taken when switching between brands. **Testosterone gel should therefore be prescribed by brand name.**

Table 2: recommended starting doses/titration and usual maintenance doses for some testosterone gels.

Brand	Type	Concentration	Amount per metered dose or sachet/tube	Starting dose	Titration	Usual maintenance dose
Tostran ®	Pump	20mg/g	10mg in 0.5g press	2 presses (20mg)	Increase by 1 press a month	4-6 presses
Testogel ® pump	Pump	16.2mg/g	20.25mg in 1.25g press	1 press (20.25mg)	Increase to 2 presses after 2 months	2-3 presses
Testogel ® sachet*	Sachet	16.2mg/g	40.5mg per 2.5g sachet	½ sachet (20.25mg)/day or one sachet 40.25mg) on alternate days	Increase to 1 sachet daily after 2 months	1 sachet
Testim®	Tube	10mg/g	50mg per 5g tube	½ tube (25mg)/day or one sachet 50mg) on alternate days	Increase to 1 tube daily after 2 months	1 tube
Testavan®	Pump	20mg/g	23mg in 1.15g press	1 press (23mg)	Increase to 2 presses after 2 months	2-3 presses

* Testogel® 50mg sachet discontinued

If transdermal gel is not suitable, an alternative is Sustanon (a mixture of testosterone decanoate, isocaproate, phenylpropionate and propionate). As Sustanon contains arachnis oil it should be avoided if there is a history of peanut or soya allergy. Use of testosterone enantate (starting dose 125mg i.e. 3 weekly) is appropriate if Sustanon is not suitable. It is shorter acting and, although generically named, significantly more expensive than Sustanon. Sustanon and testosterone enantate can be injected into the vastus lateralis (thigh) muscle so can be self-administered after appropriate instruction.

Testosterone undecanoate (Nebido) is a long acting testosterone and is therefore not routinely recommended as an initial therapy. It can be considered if other options are not appropriate, however, the long duration with rapid onset of adult male testosterone levels should be discussed with the individual. Nebido contains castor oil. It is only suitable for injection into the gluteal (buttock) muscle because of its 4ml volume. It should be injected slowly over 2 minutes by an appropriately qualified person.

Once established on testosterone, menses will usually stop. If there is a desire to stop periods more quickly GnRH analogues can be prescribed. These are not usually not required in the long term and are typically stopped after 6 months but can be continued longer if required. Options include Leuprorelin/Triptorelin 3.75mg 4 weekly, 11.25mg 12 weekly or 22.5mg six monthly by IM injection, Goserelin 3.6mg implant subcutaneously 4 weekly or 10.8 mg implant 12 weekly.

1.8. Maintenance doses

Testosterone gel can be continued long term, alternatively, testosterone undecanoate (Nebido) can be considered after 4-6 months of testosterone treatment.

Testosterone undecanoate is usually started as follows:

Starting doses:
1g week 0,
1g week 6,
1g week 18 (ie 12 weeks after 2nd injection) then continued every 12-16 weeks.

Trough testosterone and FBC should be checked prior to 4th injection, with the interval between injections adjusted to maintain trough testosterone no greater than mid age adjusted male range, and haematocrit in normal male range. Loading intervals can be adjusted if there are concerns about haematocrit, e.g. week 0, 2nd week 8, third week 20.

1.9. Ongoing monitoring requirements

Testosterone levels and haematocrit should be monitored every 4-6 months while dose is titrated and then annually once the individual is established on a dose.

Testosterone levels

Testosterone levels should be checked:

- 2-6h after gel application
- Just prior to injection (trough level)

In people on testosterone supplementation there is no need for blood samples to be taken while fasted or early morning.

Local age adjusted male ranges should be used when measuring testosterone levels.

Target Testosterone levels:

- 2-6h after gel: no higher than the age adjusted male range
- For trough levels prior to IM injection: lower to mid age adjusted range.

Target testosterone levels should be clearly communicated by GIC to primary care. Beware of spuriously high levels from contamination of the injection site with gel. Consider repeating the test, especially if the haematocrit level does not correspond.

Effects of testosterone treatment are dependent on other factors in addition to achieved testosterone levels e.g. genetics/body size and aiming for higher or lower testosterone levels may not alter the achieved effects.

Haematocrit

Aim for haematocrit ideally less than 0.5 but within the normal male range. The dose of testosterone should be reduced if haematocrit is elevated. Changing from injectable testosterone preparations to transdermal may be beneficial. **Seek urgent advice if haematocrit >0.6**. See Appendix1 for more details

1.10. Consent

If the person wishes to commence testosterone consent should be obtained using information in the consent form and this decision documented in medical records and shared with GP.

1.11. Ongoing care

1) Annual blood monitoring as above for testosterone levels and haematocrit.

2) Screening - more details are contained in the monitoring and screening section.

   - Cervical screening should continue as for female guidelines if cervical tissue is present, however, sensitive discussion of this should take into account the patient's dysphoria
   - Breast screening should also follow female guidelines if mastectomy/chest reconstruction has not been performed (surgeon should confirm if all breast tissue has been removed)

   - Cardiovascular risk should be assessed as per the general population. Risk calculations should use male gender. Cardiovascular risk factors should be treated as per the general population. Trans men will be invited for abdominal aortic aneurysm (AAA) screening at age 65 years if they are recorded as male in their NHS record. They have a lower risk of AAA than natal males but they can decide whether they wish to take part in AAA screening.

Further information on NHS Scotland's screening programmes can be found here

3) Ongoing medical care

Testosterone treatment will not alter management of other health conditions and people should be investigated and referred through standard pathways. If there are concerns about the ongoing safety of continuing testosterone refer back to local GIC or endocrine services.

4) Vaginal Atrophy

Vaginal atrophy can occur with testosterone therapy. If required this can be managed with topical vaginal oestrogen. Systemic (whole body effects) are minimised by using the lowest effective dose to control symptoms. Treatment is continued for as long as needed to relieve symptoms, for example vaginal pessaries 10micrograms daily for 2 weeks then reduced to 10micrograms twice weekly.

5) Considerations later in life

Although a number of studies have shown a fall in testosterone levels with age, this is most likely due to high prevalence of other conditions such as obesity and long term health conditions, rather than a normal physiological response. This age related fall is not seen in healthy populations. Testosterone treatment can therefore be continued lifelong if desired. Dose may need to be adjusted depending on other health conditions.

1.12. Stopping testosterone treatment

Any individual making the decision to stop testosterone treatment should be adequately informed of the risks and benefits. Stopping treatment completely is rarely required purely on medical grounds. An individual may decide that the benefits do not outweigh the potential risk or they may feel that the desired effects have been achieved. This is absolutely the person's choice and options should be discussed with an appropriately experienced professional.

Stopping treatment may lead to deterioration in mental health. Irrespective of the reason for stopping, individuals should be offered review while they adjust, and psychological support if required.

Testosterone treatment should be stopped temporarily during pregnancy.

The long term effects of stopping testosterone will depend on whether gender reassignment surgery (GRS) has been performed.

No Gender Reassignment Surgery

Stopping testosterone in people who have not had GRS will usually result in a return to menstrual cycles and return pretreatment levels of oestrogen and progesterone as testosterone levels fall. In people on longer acting testosterone treatment such as testosterone undecanoate (Nebido) this may take 6 months. In people who are post-menopausal oestrogen levels will remain low. People may experience symptoms of sex hormone deficiency

such as flushing and loss of libido. Low dose sex hormone in the form of either oestradiol or testosterone can be used temporarily to relieve symptoms but may delay return of endogenous hormone levels.

GRS with oophorectomy

If GRS including oophorectomy has been performed stopping testosterone will result in deficiency of sex hormones. Long periods of sex hormone deficiency can be associated with long term health effects notably osteoporosis. Sex hormone (oestrogen usually or low dose testosterone) replacement would usually be recommended up to the natural age of menopause (usually around 50-55years) to protect bone health.

2. Feminising gender affirming hormone treatment

2.1. Introduction

This guidance makes no assumptions about an individual's gender identity but provides information with regard to feminising hormone treatment.

This guidance relates to people originally assigned male at birth wishing feminising hormone treatment who are over the age of 16 and who have completed puberty.

Feminisation is achieved by commencing oestrogen and, if needed, use of GnRH analogues for suppression of the reproductive axis.

2.2. Baseline assessment

The aim of the baseline assessment is for the person who is starting feminising gender affirming hormone treatment to have a discussion with an appropriately experienced professional about the risks and benefits of starting endocrine treatment. By the end of the review they should be able to make an informed choice about starting endocrine treatment.

The baseline assessment should cover the following areas:

1. Medical review and family history
2. Higher risk groups including individuals over the age of 40
3. Likely effects of commencing hormone treatment
4. Potential risks of starting hormone treatment
5. Advice re. the impact on fertility and contraception
6. Treatment options
7. Agreeing a starting dose and titration regime
8. Maintenance doses
9. Ongoing monitoring requirements
10. Consent

2.3. Medical review and family history

There are almost no absolute contraindications to starting feminising gender affirming hormone treatment. There needs to be a review of medical and family history so there can be a tailored discussion so the person considering hormone treatment can understand the potential risks and ongoing monitoring required if hormone treatment is started.

- Medical and family history are taken. Conditions that are of particular relevance regarding hormone treatment are (see **Appendix 3**):
    - Cardiovascular disease
    - Cardiovascular risk (Assess cardiovascular risk using a recognised tool e.g. qrisk3 or ASSIGN)
    - Prostate disease
    - Hypertension
    - Diabetes
    - Liver disease
    - Breast disease
    - Migraine
    - Thromboembolic disease

- Baseline hormonal profile (LH, FSH, estradiol, testosterone, prolactin).
- Where clinically indicated check:
    - Baseline FBC, lipid profile and HbA1c.
    - BP
    - BMI: high BMI is not a contraindication for hormone treatment. However, people with high BMI should be should be counselled re the additional risk with a higher BMI (in particular relating to the risk of VTE), offered weight-loss assistance and clearly informed there are BMI limits for some surgery

2.4. Higher risk groups including individuals over the age of 40

For individuals starting hormone treatment after the age of 40 or with additional risk factors or QRISK3 score >5-10% careful discussion about risks and benefits is needed including realistic discussion about the physical changes that can be expected with starting feminising hormone treatment at this age. Transdermal preparations are recommended for individuals over 40 and in patients with cardiovascular risk factors, high BMI, liver disease.

2.5. Likely effects of commencing feminising gender affirming hormone treatment

Table 3 shows the effects and expected time course of feminising gender affirming hormones.

These changes should be discussed with the person considering starting hormone treatment. Hormone treatment has a systemic (whole body) effect so it is not possible to be selective about which effects occur and which do not.

It should be advised that the degree of change is highly variable from person to person, as can be seen in the variation seen across the general population, for example in breast size / physical build. These differences are dependent on other factors such as genetics and not just hormone levels.

Some of these changes (notably breast development) are likely to be permanent and not completely resolve on stopping hormone treatment.

Table 3: Expected effects from feminising hormone treatment

Effect	Expected Onset	Expected Maximum Effect
Body fat redistribution	3-6 months	2-5 years
Decreased muscle mass/strength	3-6 months	1-2 years
Softening of the skin/decreased oiliness	3-6 months	unknown
Decreased libido	1-3 months	1-2 years
Decreased spontaneous erections	1-3 months	3-6 months
Erectile dysfunction	variable	variable
Breast growth	3-6 months	2-5 years
Decreased testicular volume	3-6 months	2-3 years
Decreased sperm production	Variable	variable
Thinning and slowed growth or facial and body hair	6-12 months	>3 years
Scalp hair loss	No regrowth, loss stops 1-3 months	1-2 years

Source: Adapted from Hembree et al (2009). Effects also dependant on genetics, exercise, build.

2.6. Fertility and contraception

Fertility

Prior to the initiation of feminising gender affirming hormone treatment the individual should be made aware that hormonal preparations impair fertility. Prior to starting

feminising treatment, future fertility options need to be explored. Should the person wish to preserve their fertility then referral to the local fertility clinic/fertility preservation team should be made, ideally prior to starting full dose hormone treatment. See Fertility Preservation for more details.

2.7. Contraception

Hormone treatment is not reliable contraception and if required contraception should be used.

2.8. Treatment options

Feminising gender affirming hormone treatment is achieved by giving oral or transdermal estradiol preparations often in combination with GnRH suppression of the reproductive axis. Estradiol is introduced gradually and slowly titrated to avoid adverse reactions and subsequently a GnRH analogue added if needed.

Most preparations used do not have specific marketing authorisation for use as a gender affirming treatment. See Appendix 2 for guidance in prescribing medication out-with their marketing authorisation. Advice regarding hormone treatment is in line with guidance for prescribing out with marketing authorisation sometimes referred to as “off licence”.

2.9. Starting doses and dose titration

The option for oral or transdermal oestradiol preparations should be discussed at the initial visit highlighting the more favourable risk profile associated with transdermal preparations. Transdermal preparations should be favoured for individuals over 40 and in patients with cardiovascular risk factors, high BMI, liver disease taking in account individual preference.

Gradual introduction of estradiol alone is recommended as detailed in the table below.

For higher risk individuals, it is recommended that a low dose of a transdermal preparation is started with more gradual dose titration than detailed in the table below. For example an initial starting dose of a 25mcg estradiol patch used twice a week with titration to a 50mcg patch after 2 months and no further initial dose titration until review. Individual circumstances and preferences should be taken into consideration when deciding on initial dosing regimens.

Review at 4 months with monitoring of estradiol and testosterone levels. Aim for estradiol concentrations of 200-600 pmol/l (based on mid follicular range). Usually levels in the middle of this range are acceptable for feminisation and general health. Timing of blood sampling should be considered when interpreting levels. Pharmacokinetic data are often not readily available for estradiol preparations and there is evidence that levels 24 hours after an oral preparation can fall to baseline and

blood sampling soon after gel application especially from the arm used for application can lead to spurious high levels. It is suggested that estradiol levels should be taken 48hours after a patch has been applied. When discussing levels and dose adjustments an individual's preferences and wellbeing should be considered.

At the 4 month review estradiol dose can be adjusted and a GnRH analogue added as needed if serum testosterone concentrations are outwith female range and depending on an individual's preference.

Table 4: Recommended starting doses/titration and usual maintenance doses for estradiol preparations

Preparation	Starting dose	titration	Usual maintenance dose
Oral estradiol	1 mg	Increase by 1mg/month to initial maximum dose of 4mg	2-6mg
Estradiol patch 25mcg patch changed twice weekly	25mcg patch changed twice weekly	After 1 month change to a 50mcg patch changed twice weekly, after a further 1-2 months change to a 75mcg patch changed twice weekly	50mcg – 200mcg patch changed twice weekly
Oestrogel	1 measure a day	Start with 1 measure a day and titrate up by 1 measure a month for the first 4 months	2 - 4 measures a day
Sandrena gel	1mg	Start with 1mg and titrate by 500mcg a month to initial maximum dose of 3mg	1 – 3mg daily
Lenzetto transdermal spray	1.5mg (1 spray)	Start with 1 spray and increase by 1 spray a month for the first 4 months	2-4 sprays daily

Oral and transdermal estradiol prescribing can be generic. Advice on dose alternatives can be found in Appendix 4.

2.10. Androgen suppression

Androgen suppression is recommended for individuals who do not suppress androgen levels with oestrogen alone. This occurs in approximately 1 in 3 patients after 3-6 months. Standard practice would be GnRH suppression of the reproductive axis using GnRH analogues. Examples include:

- Leuprorelin/triptorelin 3.75mg 4 weekly,11.25mg 12 weekly or 22.5mg triptorelin 6 monthly by IM injection OR
- Goserelin 3.6mg implant subcutaneously 4 weekly or 10.8 mg implant 12 weekly

Other agents

- Cyproterone acetate would not usually be used as a long-term treatment due to concerns relating to liver toxicity and increased risk of meningioma. There is evidence that 10mg daily is sufficient for suppression, but only 50mg tablets are available.
- Finasteride 5mg daily and spironolactone (50 -100mg daily) are not recommended as they are less effective in androgen suppression and associated with other side effects.

2.11. Typical maintenance estradiol regimes

- Maintenance dose is determined by estradiol levels. Target levels usually not higher than 600pmol/l (based on mid follicular range).
- Transdermal estradiol patches twice weekly (usual maximum dose 200mcg changed twice weekly) OR
- Oral estradiol (usual maximum dose 6mg daily) OR
- Estradiol gel approx. 4 measures a day
- If there are availability issues, it is acceptable to switch to other equivalent prescriptions. Generic prescribing is recommended.

Currently, progesterone (or synthetic progestogens) is of no proven benefit in this patient group and is not recommended due to potential associated risks. This approach would be consistent with female sex hormone treatment for any individual without a uterus.

2.12. Monitoring of hormone treatment

Monitoring of hormone treatment should be done on a 3-4 monthly basis whilst doses are titrated and within the first 2 years on gender affirming treatment. This will include:

- Serum estradiol (aiming for levels not higher than 600 pmol/l).
- Testosterone
- LFTs
- Routine monitoring of prolactin is not necessary unless there are relevant symptoms such as galactorrhoea, new headaches or visual disturbance.

2.13. Annual monitoring

When an individual is established on feminising gender affirming hormone treatment a minimum of 2-yearly review is recommended. This could include:

- Blood pressure, height, weight and lipid profile
- Cardiovascular risk assessment using ASSIGN or QRISK 3 at baseline and then at age 40yrs. Cardiovascular risk should be managed as per standard female guidance.
- Estrogen dose and route may need to be adjusted if there are concerns regarding risk of venous thrombo-embolism (VTE) or cardiovascular disease, or abnormal LFTs. Transdermal preparations are associated with lower risk and should be considered for people with higher cardiovascular risk (e.g. QRISK3 5-10%). Strong recommendation for transdermal preparations for women with a high cardiovascular risk (e.g QRISK3>10%) and all women over the age of 50.

Considerations later in life

- Feminising hormone treatment can be continued lifelong if desired and if the benefits outweigh the risks. The dose/route may be adjusted depending on risk factors
- For trans women who have undergone orchiectomy discontinuing feminising endocrine therapy later in life (over age 50 years) could be considered. The expected effects of this might be similar to the menopause.
- Withdrawal of feminising endocrine therapy in trans women who retain their gonads would result in a return of virilisation.

Reduction or withdrawal of feminising endocrine therapy later in life must involve discussion with the individual, taking into account their wishes, preferences, understanding and acceptance of risk.

2.14. Surgery

- Individual guidance regarding cessation and restarting of hormone treatment should always be sought from the surgical team.
- For gender related surgery, surgeons currently recommend that estrogen treatment should be ceased 6 weeks prior to surgery, and resumed 3 weeks after surgery if there are no complications.
- Androgen suppression is not required after orchidectomy.

2.15. Consent

If the person wishes to commence feminising gender affirming hormone treatment consent should be obtained using information in the consent form and this decision documented in medical records and shared with the GP.

2.16. Stopping hormone treatment

Any individual making the decision to stop testosterone treatment should be adequately informed of the risks and benefits. Stopping treatment completely is rarely required purely on medical grounds. An individual may decide that the benefits do not outweigh the potential risk or they may feel that the desired effects have been

achieved. This is absolutely the person's choice and options should be discussed with an appropriately experienced professional.

Stopping treatment may lead to deterioration in mental health. Irrespective of the reason for stopping, individuals should be offered review and psychological support if required.

2.17. Hormone therapy for non-binary individuals

Some individuals seek limited effects from hormones or a mix of masculine and feminine characteristics. It is important to have a clear discussion regarding expectations and unknowns. It is not possible to select in advance an exact hormone regimen that will predictably allow an individual to arrive at a specified configuration of characteristics. Individual genetic and physiologic variation can result in wide variations in both blood levels and response to therapy between different individuals using the same route and dose. The best approach in these cases is to start with low doses and advance slowly, titrating to effect. The use of GnRH analogues without use of adequate sex hormone replacement would not be recommended.

3. Provision of Fertility Preservation in NHS Scotland

The purpose of this document is to set out the principles of provision and criteria for accessing NHS funded fertility preservation for TGD people. This document considers only fertility preservation through gamete/ovarian tissue cryopreservation for those who are pubertal or adult.

Fertility preservation is relevant to TGD individuals. Fertility preservation is a relatively new speciality with an emerging evidence base. The recommendations below are therefore based largely on national and international guidelines (e.g. WPATH and the European Society for Human Reproduction and Embryology [ESHRE]), and taking into account the current provision of assisted reproduction services in NHS Scotland.

The over-riding principles of access to NHS funded fertility preservation are that:

- A specific, imminent and significant risk to the patient's fertility is identified. Quantifying that risk is difficult and may be uncertain at the time of referral, but where it is clinically judged to be low (estimated on available evidence to be <30%), FP will not be offered.
- A pathway of medical intervention exists that has the potential to successfully address the risk to the patient's fertility
- There is a route to achieving a successful pregnancy and birth of a child for that patient in the future

- Any clinical risks to the patient from the required intervention (and where relevant, of subsequent pregnancy) are identified
- Long-term survival of the patient is expected, with the ability to be able to use their stored gametes.

It is important that all relevant patients are offered a consultation with an appropriately trained medical/paramedical member of staff, and that there is provision of information on the full range of methods for fertility preservation that might be appropriate for that individual. In general, this discussion will take place at the referring clinic (ie the gender identity clinic [GIC]) with referral to assisted reproduction only where the patient is keen to proceed to a fertility preservation procedure, and access criteria are met. It is recognised that the details of relevant procedures are likely to be outwith the knowledge of staff at the GIC, but such staff should have sufficient knowledge to be able to provide initial information, and signpost patients to further information.

3.1. Referral pathways and initial assessment considerations

Pathways for referral need to be developed locally that ensure timely receipt of referral from relevant clinical services. A template referral form should be used by the referring GIC (consultant or specialist nurse) giving an outline of the diagnosis and proposed treatment, other relevant medical issues, and documenting completion of any relevant initial tests.

In many cases the decision to proceed to fertility preservation can be made simply and quickly. However, for more complex cases, discussion by a review group with multi-disciplinary expertise from all four Scottish Fertility Centres has now been established and should be used to help with decisions to ensure that these are consistent between the centres. Record keeping will allow past decisions to be recalled. Documentation of the key issues raised by the case, the decision made and the outcome will be recorded to allow reference to previous decisions.

There are four NHS Fertility Centres in Scotland that provide fertility preservation for those patients that require this treatment. Travel costs for patients where required will be met.

3.2. Specific issues regarding TGD individuals

1. Referral pathways: only patients who have been assessed and referred by the GIC as suitable for gender reassignment will be considered. Initial discussion of fertility preservation will be provided by the GIC prior to referral, when early information provision about the effect of gender reassignment on fertility and fertility options will be provided. The HFEA has developed specific information related to this (https://www.hfea.gov.uk/treatments/fertility-preservation/information-for-trans-and-non-binary-people-seeking-fertility-treatment/).
2. An appointment with the fertility clinic counsellor should be arranged initially.
3. Discussion will include consideration how the gametes will be used in the future as well as just storage, although it is recognised that there may be considerable

uncertainty about potential use when patients are just about to start on hormones or other treatment and options must be kept open. Options may include surrogacy or stopping gender affirming hormone treatment.

4. The effect of trans-endocrine treatment on fertility is considered reversible, however it is likely that many people would not want to stop treatment once initiated for the several months that would be required. Guidance on the appropriate pathway for people already taking gender-affirming hormone treatment is given in the next section.
5. Clinics need to be sensitive to dysphoria and should provide gender-neutral signage whenever possible. Transvaginal egg recovery is a central part of the process of egg storage. Transabdominal egg recovery is only appropriate where the ovaries are physically not accessible transvaginally.
6. Some people may later choose or require surrogacy. This may not be known at the time of gamete storage and has issues for whether subsequent use will count as 'gamete donation' and thus what clinical activities/tests are required. Please see Appendix 2 for details of how to approach this.

3.3. TGD patients already taking gender-affirming hormone treatment

While it is preferable for TGD people to store eggs or sperm before starting gender-affirming hormone treatment, sometimes this is not possible, and consideration must be given to how best to manage that situation. In some cases, it may be considered more appropriate to defer gamete storage (perhaps for years) despite imminently starting gender affirming hormone treatment, to allow continuing consideration of the wish for such storage. Gamete storage can be considered at any time up until surgical removal of the gonads.

3.4. For egg cryopreservation

The procedures required prior to oocyte cryopreservation, such as hormonal ovarian stimulation and transvaginal ultrasound (TVS), have a negative impact on gender dysphoria; successful management requires sensitivity and awareness of these issues, eg offering transabdominal ultrasound monitoring (Armound et al 2017).

Patients may be on testosterone, and some also on GnRH agonists. Thus they will be hypogonadotrophic - much like people on long-term agonists eg for endometriosis. Importantly, intrafollicular testosterone concentrations are 100-200 nmol/l (Kristensen et al 2018), thus serum testosterone concentrations are not relevant to the huge concentrations that the oocyte is exposed to during normal development. Successful ovarian stimulation and oocyte storage have been reported without prior cessation of testosterone treatment, though only in a single individual at present (Cho et al., 2020), and most of the literature is on trans men who have stopped testosterone treatment for some months prior to ovarian stimulation.

Options for ovarian stimulation:

1. Lower testosterone dosage while maintaining some gender-affirming effect can be achieved by using testosterone gel at eg 25mg/day for 2-3 months before ovarian stimulation. This is likely to allow at least partial recovery of

gonadotrophin section and ovarian activity, which may have a positive effect on the response to ovarian stimulation.
2. If the person is established on GnRHa, continue as per long-cycle conventional stimulation
3. Letrozole may be added during ovarian stimulation to minimise the rise in estradiol levels.

There seems no justification to require patients to stop gender affirming hormone treatment before starting ovarian stimulation. This is the practice in other centres with substantial experience of this.

3.5. For sperm cryopreservation

Patients may be on long-term GnRH agonists and estradiol treatment. They will be markedly hypogonadotrophic, and spermatogenesis will be suppressed (though not always completely). There is also some evidence that even before endocrine treatment is started, trans women are more likely to show oligospermia (Li et al 2018), possibly due to tucking: this practice should be specifically enquired about, as its effect on spermatogenesis is fully reversible.

Patients started on GnRH agonists at the time of puberty may never have initiated or fully established spermatogenesis: it is likely that a very prolonged period of stopping treatment will be necessary for establishment of spermatogenesis.

The procedures for sperm cryopreservation may have a negative impact on gender dysphoria; successful management requires sensitivity and awareness of these issues.

Options

4. Assess sperm production at presentation. If there are sperm present, store them. More than one semen sample may be needed to ensure an adequate number of sperm are stored.
5. If there is severe oligo/azoospermia, discuss stopping endocrine treatment. It may take many months for spermatogenesis to be restored, and stopping treatment may not be acceptable to some patients.
6. If they do accept to stop treatment, it seems reasonable to offer a repeat assessment at 3-6 months and at intervals thereafter, until sufficient sperm can be stored.

3.6. Access criteria

The principle for these is that they should largely be in line with nationally agreed access criteria for assisted reproduction, while recognising the special circumstances surrounding fertility preservation. All NHS patients will be assessed using the same equitable criteria for treatment and storage.

1. For those storing eggs/embryos, BMI needs to be under 35. This differs from IVF criteria (due to time constraints).

2. Upper cut off age for oocyte/embryo/ovarian tissue fertility preservation should be 41.
3. There is a need for an upper age limit for those storing sperm, although this is based on less clear grounds. The group considered that 53 years is an appropriate age limit for those storing sperm because of increasing risk to offspring with paternal age.
4. The individual proposing to store gametes will have no biological children, or not be a legal parent.
5. Previous sterilisation will preclude access.
6. Smoking would not preclude access to storage; however where there is time, patients should be strongly encouraged to stop smoking.
7. Being in a stable relationship is not a relevant criterion for access (or ongoing storage)
8. If they are in a relationship, whether the partner meets IVF access criteria (eg BMI) is not relevant.

It is essential that patients recognise that full IVF access criteria will apply when it comes to using stored material for assisted conception in an NHS setting.

3.7. Treatment to be offered

Egg/embryo storage: one cycle of ovarian stimulation will be offered. When it is considered that the ovarian stimulation regimen did not result in an optimal response for that patient, a second stimulation may be considered. The number of eggs stored is not the basis for whether a second cycle is offered.

Sperm storage: this may involve the storage of sperm obtained from more than one ejaculate or a surgical sperm extraction procedure. Centres may offer storage of up to 3 ejaculates, but this may be limited by the time available and may not be necessary if the sample quality is high.

3.8. Information provision

Patients should be provided with verbal and written information at all stages, ie both in the referring clinic and in the assisted reproduction clinic. The use of Near Me in conjunction with the “Language Line” telephone interpretation service and “face to face” language or British Sign Language (BSL) interpreters may be appropriate for non-English speaking people.

Patient information leaflets in line with this guidance are available (Appendix), for sperm and egg storage. Information is available from the HFEA website (including information specific for TGD people):
https://www.hfea.gov.uk/treatments/fertility-preservation/

3.9. Counselling

Access to a specialist fertility Counsellor will be offered to patients prior to their giving consent to treatment (on, among other things, the implications of taking the proposed steps) and following fertility preservation.

The HFEA Code of Practice states that fertility centres should provide a suitable opportunity for counselling after the individual or couple has received oral and written information about the services to be provided and before they consent to treatment, donation, or to the storage or use of gametes or embryos. The HFEA also state that the centre should provide proper counselling throughout the treatment, donation or storage processes, and afterwards if requested.

3.10. Ongoing NHS storage of gametes

Current HFEA regulations use duration of storage rather than age. The main upper age limit for NHS IVF treatment in Scotland is a female age of 40 however Scotland follows the NICE guidance which allows for women aged 40 to 42 to have one cycle of NHS IVF treatment if they meet certain criteria, therefore gametes in storage after that age cannot be used for NHS treatment.

1. The above access criteria specify the cut off age for starting storage of gametes should be 41 for egg/embryo storage and 53 for sperm storage, at time of storage (ie fertility preservation treatment to be initiated before 42nd/ 54th birthday).
2. Patients should have a 5 year follow up initiated by the fertility clinic that provided storage (with further assessment as required) to assess whether it is appropriate to continue NHS funded storage.,
3. Not being in a stable relationship is not a relevant criterion for either initiating storage, or for ongoing storage.
4. Young patients may need to store gametes for a very long time.
5. If at follow up review the patient is not eligible (e.g. now has children, or age >42 for oocyte storage or 55 for sperm storage, i.e up to 43rd/56th birthday) then ongoing NHS funded storage will not be provided. A review appointment offers the opportunity for discussion/assessment (potentially also with an appointment with the fertility clinic counsellor) without denying ongoing storage, which may need to be at the patient's own expense.
6. It is considered that a normal semen analysis indicates likely fertility, and certainly shows the presence of sperm which could potentially be used in assisted conception. If at the 5 year appointment or thereafter the patient is shown to have a normal semen analysis, there should be a discussion regarding disposal of stored sperm; or alternatively, ongoing storage will need to be at the patient's expense. If however the sperm count is found to be low then ongoing storage will be provided. If the patient does not provide a semen

sample, further storage at NHS expense will not be provided, and the stored samples will be disposed of or with further storage at the patient's expense.

7. Regular menstrual cycles or biochemical tests of ovarian function should not be used as grounds for disposal or charging for ongoing storage of oocytes, where other criteria for access to NHS treatment are still met.
8. A patient contract is considered the best way of combining these aspects of duration of storage, the need to reassess eligibility, and self-funding of further storage. This needs to be completed at the time of storage.

3.11. Data Collection

It is important that information regarding use of NHS resources is collected, and this will become a valuable and robust data set informing future service development. Information to be collected includes:

1. Number and source of referrals
2. Number of patients proceeding to fertility preservation; their characteristics (e.g. age, diagnosis) and FP results (e.g. no of eggs)
3. Ultimately, data on usage/other outcomes.

ISD have developed a data capture form which has been circulated to all centres to start using immediately, with the opportunity for revision to improve functionality. Centres will send completed forms to ISD monthly to align with their IVF returns. ISD will collate data at quarterly intervals. Centralised storage by SNBTS will allow collection of these data with sample storage: this is being developed.

3.12. Funding options considered

The Fertility Scotland Strategic Plan has been approved by NHS National Services Division. Fertility Preservation is included in this plan.

Appendix 1: Medical conditions and testosterone

Cardiovascular disease and cardiovascular risk

Testosterone treatment has been shown to increase cardiovascular risk in some studies. Testosterone treatment can also be associated with an increased haematocrit which will increase cardiovascular risk and may worsen cardiovascular disease. In most population studies men have increased cardiovascular risk compared to women. Reasons for this are not fully understood but will partly relate to genetics and hormones.

People starting testosterone treatment should have a discussion about cardiovascular disease and have their cardiovascular risk calculated using a risk calculator such as QRISK3 or assign. Generally risk should be assessed using male gender.

There are no large studies assessing testosterone treatment in people specifically taking testosterone as a gender affirming treatment. Advice is extrapolated from population studies and testosterone treatment studies. Established cardiovascular disease and cardiovascular risk factors should be treated as per general population.

Polycythaemia/raised haematocrit

- Testosterone will increase FBC production and therefore haematocrit. Increased haematocrit is associated with increased cardiovascular risk.
- Haematocrit should be monitored for people on testosterone.
- When assessing FBC and Haematocrit, local male ranges should be used. A haematocrit should be measured 4-6 months after every dose titration and then yearly for people on a stable dose
- Risk of polycythaemia can be reduced by addressing other risk factors such as smoking and obesity.
- Aim for haematocrit of ≤ 0.5
- If HCT >0.5 first step is to reduce dose of testosterone either by increasing interval between injections or reducing dose of gel.
- For some people it may not be possible to achieve acceptable testosterone levels while maintaining a HCT <0.5. In this situation can accept a HCT of >0.5 but in normal range (most labs <0.52) providing the person has been counselled about risk of increased haematocrit.
- Other cardiovascular risk factors should be treated
- Seek guidance if haematocrit is significant elevated as urgent venesection may be required.

Hypertension

- BP should be monitored and treated as per general population using standard risk calculators to determine targets.

Diabetes

- Men have an increased risk of diabetes. Screening and treatment should be as general population

Liver disease

- Oral testosterone has been associated with impaired liver function and liver tumours. Oral testosterone is not recommended. There is no evidence that transdermal or IM preparations affect liver function/ cause liver tumours. Impaired liver function/liver disease should be investigated and managed as per general population. There may be a need to adjust the dose of testosterone.

Breast disease

- Testosterone has been associated with male breast cancer. There is no evidence of increased risk of breast cancer in this group. For people with breast tissue breast screening should be performed as per guidelines. Breast screening is not required after mastectomy or chest reconstruction. Breast lumps should be investigated as per general population

Abnormal PV or menstrual bleeding, and prolonged amenorrhoea

Testosterone treatment will usually cause cessation of periods. Studies have looked at endometrium in people on testosterone with both atrophic and hypertrophic endometrium being found on biopsy. There is currently insufficient evidence to suggest routine ultrasound scanning to assess endometrial thickness for people on testosterone, however people with new bleeding developing on full dose testosterone, or who have abnormal bleeding should be investigated as per standard guidelines.

Benign Intracranial Hypertension

Testosterone has been associated with Benign Intracranial Hypertension. Obesity and polycystic ovary syndrome also appear to be risk factors. Testosterone may be stopped at least until intracranial pressure, papilloedema and visual disturbance improve. Testosterone treatment may be restarted with the agreement of neurology and endocrinology specialists. The preparation or dose may need to be adjusted to minimise the risk of recurrence. Testosterone may need to be stopped or reduced, and this should be discussed with individual.

Appendix 2: Marketing authorisation and “off label” use

A marketing authorisation (MA), previously called a product licence, is granted by a regulatory body to a pharmaceutical company for a specific medicinal product. It specifies the terms of use, including the indications, doses, routes and patient populations for which it can be marketed

Although there is no official definition, generally ‘off-label’ describes the use of a medicinal product beyond the specifications of its MA, e.g. for an indication or in a dose, route or patient population not covered by the MA.

Most of the testosterone preparations described in this guidance do not currently have marketing authorisation for masculinising gender affirming hormone treatment. The GMC has specific guidance for prescribing unauthorised medicinal product, with key points below.

The General Medical Council (GMC) recommends that when prescribing off-label or prescribing an unauthorised medicinal product, doctors should:

- be satisfied that such use would better serve the patient’s needs than an authorised alternative (if one exists)
- be satisfied that there is sufficient evidence/experience of using the medicinal product to show its safety and efficacy, seeking the necessary information from appropriate sources
- record in the patient's clinical notes the medicinal product prescribed and, when not following common practice, the reasons for the choice
- take responsibility for prescribing the medicinal product and for overseeing the patient’s care, including monitoring the clinical effects, or arrange for another suitable doctor to do so.

The guidance given regarding testosterone treatment is in line with this GMC guidance.

Appendix 3: Medical conditions and estrogen

Venous thromboembolism

Venous thromboembolism is the most important potential complication of oestrogen treatment. A 20-fold increase in venous thromboembolic disease was reported in a large cohort study. However this increase may have been associated with the use of ethinyl estradiol which is now not standard practice. The same results are not replicated in large cohort studies with trans women on relatively high doses of estradiol (E2) where only single cases of VTE were observed.

Osteoporosis

Estrogen preserves bone mineral density in people who continue on estrogen and antiandrogen therapies.

Breast cancer

A few cases of breast cancer in trans women have been reported in the literature. In a large Dutch cohort of 1800 trans women followed for a mean of 15 yr only one case of breast cancer was found. The Women's Health Initiative study reported that women taking conjugated equine estrogen without progesterone for 7 yr did not have an increased risk of breast cancer as compared with women taking placebo. Women with primary hypogonadism (XO) treated with estrogen replacement exhibited a significantly decreased incidence of breast cancer as compared with national standardized incidence ratios. These studies suggest that estrogen treatment does not increase the risk of breast cancer in the short-term. Long-term studies are required to determine the actual risk. Monthly breast checks and breast screening as per people assigned female is recommended.

Prostate cancer

Prostate cancer is very rare, especially with androgen deprivation treatment but an awareness of prostate disease should be retained by trans women and clinicians.

Prolactinoma

Estrogen treatment can increase the growth of pituitary lactrotroph cells and result in hyperprolactinaemia. Given that prolactinomas have been reported only in a few case reports the risk of prolactinoma is likely to be very low. Prolactin should be checked at baseline and during titration of oestradiol doses and in individuals presenting with headache, visual disturbance or galactorrhoea. Prolactin persistently >1000mU/l should be investigated as per standard guidance including pituitary MRI.

Cardiovascular disease

A prospective study of trans women found favourable changes in lipid parameters. However. There was also increased weight, blood pressure, and markers of insulin resistance. The largest cohort of trans women (with a mean age of 41 yr) followed for a mean of 10 yr showed no increase in cardiovascular mortality despite a 32% rate

of tobacco use. Thus, there is limited evidence to determine whether estrogen is protective or detrimental in trans women.

Appendix 4: Preparations and dose alternatives

The following tables are helpful for writing prescriptions and switching hormone treatment. Information on starting, titrating and maintenance doses is available in the main sections of this document.

Preparation	Alternative to 2mg oral estadiol daily
Oral estradiol (e.g Elleste Solo 2mg, Zumenon 2mg or Progynova 2mg)	2mg daily
Estradiol patches (e.g. Estraderm MX, Estradot, Evorel)	50 microgram/24hour patch used twice weekly
Oestrogel	1 pump twice a day
Sandrena gel	1mg sachet daily
Lenzetto transdermal spray	3 sprays daily

Testosterone Gel Preparations and Doses per Pack

Brand name	Container	Concent-ration	Metered dose	Pack size	Metered doses per pack
Tostran ®	canister	20mg/g	10mg in 0.5g	60g	120
Testogel ®	pump	16.2mg/g	20.25mg in 1.25g	88g	60
Testogel ®	sachet	16.2mg/g	40.5mg in 2.5g sachet	30 x 2.5g	N/A
Testavan ®	pump	20mg/g	23mg in 1.15g (1.25ml)	85.5g	56
Testim®	tube	10mg/g	5g tube	30 x 5g	N/A

Estradiol Preparations used for Feminising Gender Affirming Treatment and Approximate Equivalent Doses*

Estradiol Preparation	Commonly Prescribed Strengths**	Number of doses per pack	Level of Dose		
			Starting/ Low Dose	Medium Dose	Higher Dose
Oral tablet	1mg 2mg	84 tablets	1mg daily	2mg daily	3-4mg daily

Patch	25 mcg 50mcg 75mcg 100mcg	8 patches	25mcg twice weekly	50-75mcg twice weekly	100-150mcg twice weekly
Gel Pump (Oestrogel® 0.06%)	0.75mg per 1.25g press	64 doses per 80g pump	1 press daily	2 presses daily	3-4 presses daily
Gel sachet (Sandrena®)	0.5mg 1mg	28 sachets	1mg daily	1.5mg daily	2-3mg daily
Spray (Lenzetto®)	1.53mg per spray	56 sprays per pack	1 spray daily	3 sprays daily	4 sprays daily

* This information is provided as a practical guide based on a combination of pharmacokinetics, clinical trials and clinical experience. Levels of dose are approximate as there is wide inter- and intra-individual variation between the clinical response to different preparations and estradiol serum levels. Higher doses may be required for some individuals.

**Other strengths of patch and of conjugated oral oestrogen are available.

Appendix 5: Gamete storage for use by 3rd party reproduction

Some patients undergoing gamete storage may subsequently require 3rd party reproduction (donation and surrogacy). For this, they are considered to be gamete donors, requiring additional screening tests, as specified in the current HFEA Code of practice that the donor is tested for cystic fibrosis, karyotype, cytomegalovirus, syphilis and gonorrhoea and blood group (in addition to standard viral testing) and completes a questionnaire regarding risk of genetic disease.

The need for surrogacy will often be unclear at the time of gamete storage. Options would therefore be to (i) treat all as potential donors, (ii) treat selected individuals as potential donors, or (iii) treat none as potential donors and undertake additional screening at the time of use.

Considerations include:

- Unnecessary investigations at storage, with cost and inconvenience considerations.
- Infection tests changing between storage and use: these tests therefore need to be undertaken at storage for optimum validity.
- Tests that will not change are CF, karyotype, blood group: these could therefore be undertaken at time of use.
- Questionnaire: important for identification of recent travel/infection risk.

All individuals undergoing gamete storage should be assessed as to the potential need for 3rd party reproduction, recognising that the individual's situation in the years to come is difficult to predict. This applies equally to those storing sperm and eggs, and it is important to recognise that this possibility should be discussed (and recorded) with all patients proceeding to fertility preservation procedures. If there is considered to be a possibility of needing 3rd party reproduction, the following approach should be taken:

- Infection-related tests should be done at the time of gamete storage, with medical/behavioural/social questionnaire
- Karyotype, blood group and CF screening should be done at time of gamete use, not at the time of gamete storage.
- Genetic questionnaire: to be completed at the time of gamete use.

Not doing these tests at time of storage will not preclude later use in donation, except where infection tests are positive at time of potential donation and would have been negative at time of storage (but were not done).

Appendix 6

Development Group membership

[redacted]

Acknowledgements

The individual needs of people accessing gender identity healthcare was at the heart of this work. We engaged widely with people using or interested in accessing services and also with professional organisations.

Individuals with lived experience were asked if they would like to provide subsequent information to the by participating in 1-2-1 interviews. These individuals' added suggestions and revisions, in addition to those supplied through the web form surveys.

NHS National Services Division would like to thank everyone who was involved in the working groups and who responded to our requests for feedback.

If you have any further queries, please contact the team at [redacted]

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HFEA information specific to transgender individuals https://www.hfea.gov.uk/treatments/fertility-preservation/information-for-trans-and-non-binary-people-seeking-fertility-treatment/