Clinical Commissioning Policy: Assisted Conception

Agreed: 2014
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Contents

Policy Statement

NHS England will commission assisted reproduction techniques (IVF/ICSI) in accordance with the criteria outlined in this document and the recommendations of NICE Clinical guideline 156 (2013).

In creating this policy, NHS England has reviewed this clinical condition and the options for its treatment. It has considered the place of this treatment in current clinical practice, whether scientific research has shown the treatment to be of benefit to patients, (including how any benefit is balanced against possible risks) and whether its use represents the best use of NHS resources.

This policy document outlines the arrangements for funding of this treatment for the Armed Forces population in England.

Equality Statement

Throughout the production of this document, due regard has been given to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited in under the Equality Act 2010) and those who do not share it.

Plain Language Summary

This policy sets out the assessment and treatment pathway for Armed Forces' couples with fertility problems and is based on the NICE Clinical Guideline 156 (2013).

This policy only applies to Armed Forces' couples that have fertility problems; need particular treatment or help to get pregnant; or are preparing for cancer treatment that might affect fertility, where there is a wish to preserve fertility.

Around one in seven heterosexual couples in the UK[1] seek advice at some time in their lives about difficulties in getting pregnant. The time it takes to conceive naturally varies and age can be an important factor: both women's and (to a lesser extent) men's fertility gradually declines as they get older.

A woman may have fertility problems because her ovaries do not produce eggs regularly, or because her fallopian tubes are damaged or blocked and the sperm cannot reach her eggs. In men, a fertility problem is usually because of low numbers or poor quality of sperm. For up to a quarter of people, no reason can be found for their fertility problems. This is known as unexplained infertility.

Assisted reproduction is the name given to treatments that can help a woman get pregnant without the need for sexual intercourse. There are a variety of treatments, and what is suitable for each individual will depend on their particular circumstances.

[1] NICE CG 156 p.5

The options include:

- intrauterine insemination (IUI)
- in vitro fertilisation (IVF)
- IVF with intracytoplasmic sperm injection (ICSI)
- the use of donor sperm (donor insemination) or eggs (egg donation).

Certain forms of assisted reproduction (IUI, IVF, ICSI, donor insemination and egg donation) are regulated by law and their use is controlled by the Human Fertilisation and Embryology Authority (HFEA).

IVF

If IVF is a possible treatment, the woman's doctor should first discuss with her the risks and benefits of IVF treatment, in line with the Code of Practice produced by the HFEA.

Women aged under 40 years
If the woman is aged under 40, they should be offered three (3) full cycles of IVF if:

- they have been trying to get pregnant through regular unprotected sexual intercourse for a total of two (2) years **or;**
- they are using artificial insemination to conceive and have not become pregnant after 12 cycles – at least six (6) of these cycles should have been using intrauterine insemination.

However, if tests show that there appears to be no chance of the woman conceiving naturally, and that IVF is the only treatment that is likely to help, they should be referred straightaway for IVF.

Any previous cycles of IVF a woman has had (regardless how they were funded) will count towards the three (3) cycles the woman should be offered by the NHS. This is because the chances of having a baby fall with the number of unsuccessful cycles of IVF.

The woman's doctor should also take into account how the woman has responded to any previous IVF treatment and what the outcome was when deciding how effective and safe further IVF would be for that individual.

If a woman turns 40 during a cycle of IVF, they can finish the current full cycle but should not be offered further cycles. They will still be able to have any frozen embryos transferred from their most recent episode of ovarian stimulation since these count as part of the same full cycle.

Women aged 40–42 years
If the woman is aged 40–42 years, they should be offered one (1) full cycle of IVF if **all** of the following apply:

- they have been trying to get pregnant through regular unprotected sexual intercourse for a total of two (2) years **or** have not become pregnant after 12

cycles of artificial insemination (at least six (6) of these cycles should have been through intrauterine insemination);
- they have never had IVF treatment before;
- their fertility tests show that their ovaries would respond normally to fertility drugs;
- the woman and their doctor have discussed the risks of fertility treatment and pregnancy in women aged 40 years or older.

If a woman's tests show that there appears to be no chance of them conceiving naturally, and that IVF is the only treatment that is likely to help, they should be referred straightaway for IVF.

Intracytoplasmic sperm injection ICSI

For some men, their sperm are not capable of fertilising eggs in the usual way. If this is the case, they and their partner may be offered a procedure called intracytoplasmic sperm injection (ICSI), in which a single sperm is injected directly into an egg.

A man should only be offered ICSI if:
- there are few sperm in their semen or they are of poor quality, **or;**
- there are no sperm in their semen (either because of a blockage or another cause) but there are sperm in their testes which can be recovered surgically, **or;**
- they have already tried IVF but there was poor or no fertilisation of the eggs.

In these situations, ICSI increases the chance of fertilising eggs compared with IVF used on its own. However, it does not make any difference as to whether this will lead to a successful pregnancy.

If a man is unable to ejaculate, it is possible to obtain their sperm using surgical sperm recovery. They should be offered the chance to freeze some of their sperm for possible use at a later date.

Before a man considers ICSI, their doctor should offer both the man and their partner appropriate tests and discuss the results and their implications with them both.

1 Introduction

This policy outlines the pathway and criteria for access to assisted reproduction techniques such as IVF and ICSI for Armed Forces' couples. This policy is based on the NICE Clinical guideline 156 (2013).

It is estimated that infertility affects one in seven heterosexual couples in the UK. Since the original NICE guideline on fertility published in 2004, there has been a small increase in the prevalence of fertility problems, and a greater proportion of people now seeking help for such problems.

The main causes of infertility in the UK are (percent figures indicate approximate prevalence):

- unexplained infertility (no identified male or female cause) (25 percent)
- ovulatory disorders (25 percent)
- tubal damage (20 percent)
- factors in the male causing infertility (30 percent)
- uterine or peritoneal disorders (10 percent).

In about 40 percent of cases disorders are found in both the man and the woman. Uterine or endometrial factors, gamete or embryo defects, and pelvic conditions such as endometriosis may also play a role.

Given the range of causes of fertility problems, the provision of appropriate investigations is critical. These investigations include semen analysis; assessment of ovulation, tubal damage and uterine abnormalities; and screening for infections such as *Chlamydia trachomatis* and susceptibility to rubella.

Once a diagnosis has been established, treatment falls into three main types:

- medical treatment to restore fertility (for example, the use of drugs for ovulation induction);
- surgical treatment to restore fertility (for example, laparoscopy for ablation of endometriosis);
- assisted reproduction techniques (ART) – any treatment that deals with means of conception other than vaginal intercourse. It frequently involves the handling of gametes or embryos.

2 Definitions

Abandoned cycle with IVF / ICSI
Prior to egg retrieval, usually due to a lack of response (where less than three (3) mature follicles are present) or excessive response to gonadotrophins; failure of fertilisation. An abandoned cycle counts towards the number of commissioned cycles.

Assisted hatching
An in vitro procedure in which the zona pellucida of an embryo is either thinned or perforated by chemical, mechanical or laser methods to assist separation of the blastocyst.

Assisted reproduction
The collective name for treatments designed to lead to conception by means other than sexual intercourse. Assisted reproduction techniques include intrauterine insemination (IUI), in vitro fertilisation (IVF), intracytoplasmic sperm injection (ICSI) and donor insemination (DI). The term 'assisted reproduction technology' (ART) is the term sometimes used to collectively describe these procedures and interventions.

Blastocyst
An embryo, five or six days after fertilisation, with an inner cell mass, outer layer of trophectoderm and a fluid-filled blastocoele cavity.

Cancelled cycle
An IVF cycle in which ovarian stimulation or monitoring has been carried out with the intention to treat but the woman does not proceed to follicular aspiration or, in the case of a thawed embryo, to embryo transfer.

Clinical pregnancy
A pregnancy diagnosed by ultrasonographic visualisation of one or more gestational sacs or definitive clinical signs of pregnancy. It includes ectopic pregnancy. Note: Multiple gestational sacs are counted as one clinical pregnancy.

Clinician
A healthcare professional providing patient care, for example a doctor, nurse/midwife or physiotherapist.

Completed Cycle with IVF / ICSI
One (1) episode of ovarian stimulation, egg recovery, fertilisation and transfer of any resultant fresh and frozen embryo(s)

Couple
Two people in a partnership, irrespective of gender and sexual orientation, who wish to have a baby but are having difficulty conceiving and are having investigations and possible treatment for infertility.

Cryopreservation
The freezing and storage of embryos, sperm or eggs for future use in IVF treatment cycles. The technique of controlled rate slow freezing is well established; vitrification is a newer ultra-rapid freezing process.

Donor insemination
The placement of donor sperm into the vagina, cervix or womb.

Embryo
The product of the division of the zygote to the end of the embryonic stage, eight weeks after fertilization.

Embryo transfer
The procedure in which one or more embryos are placed in the uterus or Fallopian tube.

Expectant management
This is a formal approach that encourages conception through unprotected vaginal intercourse. It involves supportively offering an individual and/or couple information and advice about the regularity and timing of intercourse and any lifestyle changes which might improve their chances of conceiving. This approach does not involve any active clinical or therapeutic interventions.

Fertilisation
The penetration of the ovum by the spermatozoon and combination of their genetic material resulting in the formation of a zygote.

Full cycle
This term is used to define a full IVF treatment, comprising of one (1) episode of ovarian stimulation and the transfer of any resultant fresh embryo(s). Where an excess of embryos is available following a fresh cycle, these embryos may be frozen for future use. Once thawed, these embryos may be transferred to the patient as a frozen cycle and be included within the 'full cycle'.

All frozen embryos from a previous cycle should be used before a further IVF cycle is initiated.

Storage of frozen embryos will be routinely funded for one (1) year unless the provider has agreed an alternative as part of a pathway agreement.

Any costs relating to the continued storage of embryos beyond this will ordinarily be the responsibility of the couple.

Gamete intrafallopian transfer
A procedure in which eggs are retrieved from a woman, mixed with sperm and immediately replaced in one or other of the woman's fallopian tubes so that they fertilise inside the body.

Gonadotrophins
Hormones that stimulate the ovaries.

Infertility
In practice infertility is defined as the period of time people have been trying to conceive without success after which formal investigation is justified and possible treatment implemented.

Implantation
The attachment and subsequent penetration by the zona-free blastocyst (usually in

the endometrium) that starts five to seven days after fertilisation.

Intra-cervical insemination
Clinical delivery of sperm into the cervical os.

Intracytoplasmic sperm injection
A variation of in vitro fertilisation in which a single sperm is injected into the inner cellular structure of an egg.

Intrauterine insemination
Clinical delivery of sperm into the uterine cavity.

In vitro fertilisation
A technique whereby eggs are collected from a woman and fertilised with a man's sperm outside the body. Usually, one or two resulting embryos are then transferred to the womb with the aim of starting a pregnancy.

Mild male factor infertility
The term 'mild' male factor infertility is used extensively in practice and in the literature. However, no formally recognised definition of what this means is currently available. Therefore, where the term 'mild' male factor infertility is applied in this guideline, it is defined as meaning: two or more semen analyses that have one or more variables which fall below the 5th centile as defined by WHO, 2010[2], and where the effect on the chance of pregnancy occurring naturally through vaginal intercourse within a period of 24 months would then be similar to people with unexplained infertility or mild endometriosis.

Natural cycle IVF
An IVF procedure in which one or more oocytes are collected from the ovaries during a spontaneous menstrual cycle without any drug use.

Oocyte donation
The process by which a fertile woman donates her eggs to be used in the treatment of others or for research.

Ovarian Hyper-Stimulation Syndrome (OHSS)
An exaggerated systemic response to ovarian stimulation characterised by a wide spectrum of clinical and laboratory manifestations. It is classified as mild, moderate or severe according to the degree of abdominal distension, ovarian enlargement and respiratory, haemodynamic and metabolic complications.

Ovulation induction
Stimulation of the ovary to achieve growth and development of immature ovarian follicles (ideally monofollicular development) to reverse anovulation or oligo-ovulation.

[2] WHO laboratory manual for the examination and processing of human semen, 2010

Unsuccessful cycle of IVF/ ICSI
Includes failure of fertilisation, failure of cleavage of embryos, failure to conceive following transfer of embryos.

An unsuccessful cycle counts towards the number of commissioned cycles.

3 Aim and objectives

This policy document aims to specify the conditions under which assisted reproduction techniques (IVF/ICSI) will be routinely commissioned by NHS England as a means of making it possible for Armed Forces' couples to conceive a child.

The objectives are to:

- reduce the variation in access to assisted reproduction techniques (IVF/ICSI) for Armed Forces' couples;
- ensure that assisted reproduction techniques are commissioned for those patients for which there is acceptable evidence of clinical benefit and cost-effectiveness;
- promote the cost-effective use of healthcare resources.

4 Epidemiology and needs assessment

According to the recent NICE clinical guideline on Fertility [3] infertility affects one in seven heterosexual couples in the UK. NICE indicates that the following are the main causes of infertility in the UK (percentage figure indicates approximate prevalence)

- Unexplained infertility – no identified male or female cause (25 percent)
- Ovulatory disorders (25 percent)
- Tubal damage (20 percent)
- Factors in the male causing infertility (30 percent)
- Uterine or peritoneal disorders (10 percent)

In about 40% of cases disorders are found in both the male and female.

A typical clinical commissioning group (CCG) is estimated to see 230 consultant referrals per 250,000 population.

The Armed Forces population is smaller than this at 169,379[4] but NHS England has commissioning responsibility for not just those in Service, estimated at approximately 140,000, but also their partners, many of whom will not be registered with a Defence Medical Services practice making population estimates difficult to construct. The latest Tri-Service Families Continuous Attitude Survey estimates

[3] NICE Clinical guideline 156, Fertility, issued February 2013, http://www.guidance.nice.org.uk/cg156
[4] Securing Excellence in Commissioning for the armed forces and their families http://www.england.nhs.uk/wp-content/uploads/2013/03/armed-forces-commissioning.pdf

that there are just over 57,000 service personnel recorded as being married or in a civil partnership[5].

5 Evidence base

The evidence base for the use of assisted conception techniques and their long term safety is given in the full NICE clinical guideline156 (2013).

Long-term health outcomes of ovulation induction and ovarian stimulation[6]
No direct association has been found between ovulation induction or ovarian stimulation and invasive cancer **and** no association has been found in the short- to medium-term between these treatments and adverse outcomes (including cancer) in children born from ovulation induction.

Information about long-term health outcomes in women and children is still awaited.

Long-term health outcomes and safety of IVF[7]
The absolute risks of long-term adverse outcomes of IVF treatment, with or without ICSI, are low; a small increased risk of borderline ovarian tumours cannot be excluded.

The absolute risks of long-term adverse outcomes in children born as result of IVF are low.

6 Rationale behind the policy statement

This policy has been based on the NICE clinical guideline 156 and sets the mandatory access criteria for the Armed Forces' couple including lifestyle choices which may impact on a person's ability to conceive.

7 Criteria for commissioning

Mandatory Criteria for the Couple

GP	At least one partner (A) is registered with a Defence Medical Services practice in England
Relationship	The other partner (B) is either (i) the spouse or civil partner of A or (ii) A and B are cohabiting as partners in a substantial and exclusive relationship where either B is financially dependent on A or A & B are financially interdependent
Woman's age	Under 43 years of age at the time of treatment
Woman's BMI[8]	More than 19 kg/m^2 and less than 30 kg/m^2
Man's BMI[9]	Less than 30 kg/m^2

[5] http://www.dasa.mod.uk/publications/other/surveys/tri_service_families_continuous_attitude_survey/2013/2013-main-report.pdf?PublishTime=09:30:00, page 14
[6] NICE CG156, 1.17.1
[7] NICE CG156, 1.17.2
[8] NICE CG156 recommendation 1.2.6 & 1.2.7
[9] NICE CG156 recommendation 1.2.6.4

Welfare of the child	The welfare of any resulting children is paramount. In order to take into account the welfare of the child, the clinician should consider factors which are likely to cause serious physical, psychological or medical harm, either to the child to be born or to any existing children of the family. This is a requirement of the licencing body, Human Fertilisation and Embryology Authority (HFEA).
Family structure	There should be no living children from this relationship including adopted children but excluding fostered children. There should be no children from previous relationships. There is an explicit and recorded assessment that the social circumstances of the family unit have been considered within the context of the assessment of the welfare of the child.
Smoker[10]	Both partners should be confirmed non-smokers.
Consent	Written consent to treatment is required from both partners.
Previous history	Neither partner has been sterilised.

8 Patient pathway

This pathway summarises the recommendation points within the NICE clinical guideline 156.

1. Principles of care[11]

Couples who experience problems in conceiving should be seen together because both partners are affected by decisions surrounding investigation and treatment.

People who experience fertility problems should be treated by a specialist team because this is likely to improve the effectiveness and efficiency of treatment and is known to improve people's satisfaction with treatment.

2. Initial advice to people concerned about delays in conception

Chance of conception[12]

People who are concerned about their fertility should be informed that over 80 percent of couples in the general population will conceive within one (1) year if:

- the woman is aged under 40 years **and;**
- they do not use contraception and have regular sexual intercourse.
- Of those who do not conceive in the first year, about half will do so in the second year (cumulative pregnancy rate over 90 percent).

[10] NICE CG156 recommendation 1.2.4
[11] NICE CG156 full guideline recommendations 1, 9
[12] NICE CG156 full guideline recommendations section 5.2

People who are using artificial insemination to conceive and who are concerned about their fertility should be informed that :

- over 50 percent of women aged under 40 years will conceive within six (6) cycles of intrauterine insemination (IUI);
- of those who do not conceive within six (6) cycles of intrauterine insemination, about half will do so with a further six (6) cycles (cumulative pregnancy rate over 75 percent).

People who are using artificial insemination to conceive, and who are concerned about their fertility, should be informed that using fresh sperm is associated with higher conception rates than frozen–thawed sperm. However, intrauterine insemination, even using frozen–thawed sperm, is associated with higher conception rates than intra-cervical insemination.

Table : Cumulative probability of conceiving a clinical pregnancy by number of cycles of insemination[13]

Woman's age	**ICI using thawed semen (Schwartz et al. 1982)**		**Woman's age**	**ICI using fresh semen (van Noord-Zaadstra, 1991)**		**Woman's age**	**IUI using thawed semen (HFEA data & personal communication)**	
	6 cycles	12 cycles		6 cycles	12 cycles		6 cycles	12 cycles
<30	50%	70%	<31	58%	76%	-		
30-34	43%	62%	31-35	50%	71%	<35	63%	86%
>34	33%	54%	>35	39%	55%	35-39	50%	75%
ICI = intra-cervical insemination IUI = intrauterine insemination								

Inform people who are concerned about their fertility that female fertility and (to a lesser extent) male fertility decline with age.

Discuss chances of conception with people concerned about their fertility who are:

- having sexual intercourse **or;**
- using artificial insemination.

Table – cumulative probability of conceiving a clinical pregnancy by number of menstrual cycles[14]

Age (years)	**Pregnant after 1 year (12 cycles) %**	**Pregnant after 2 years (24 cycles) %**
19-26	92	98
27-29	87	95
30-34	86	94
35-39	82	90

Frequency and timing of sexual intercourse or artificial insemination[15]
People who are concerned about their fertility should be informed that vaginal sexual intercourse every two (2) to three (3) days optimises the chance of

[13] NICE CG156, p. 56
[14] NICE CG156, table 1, p56
[15] NICE CG156 full guideline recommendations section 5.3

pregnancy.

People who are using artificial insemination to conceive should have their insemination timed around ovulation.

Lifestyle Advice[16]
Lifestyle advice in relation to fertility should be given in relation to:

- Alcohol
- Smoking
- Caffeinated beverages
- Obesity
- Low body weight
- Tight underwear
- Prescribed, over-the-counter and recreational drug use
- Complementary therapy
- Folic acid supplementation
- Occupation – evidence suggestive of a harmful effect on the human reproductive system has been recognised for specific agents such as heat, X-rays, metals and pesticides, whereas for many other agents the association is only suspected and needs further evaluation.[17]

3. Defining infertility[18]

People who are concerned about delays in conception should be offered an initial assessment. A specific enquiry about lifestyle and sexual history should be taken to identify people who are less likely to conceive.

An initial consultation should be offered, to discuss the options for attempting conception to people who are unable to, or would find it very difficult to, have vaginal intercourse.

Healthcare professionals should define infertility in practice as the period of time people have been trying to conceive without success after which formal investigation is justified and possible treatment implemented.

A woman of reproductive age, who has not conceived after **one (1) year** of unprotected vaginal sexual intercourse, in the absence of any known cause of infertility, should be offered further clinical assessment and investigation along with her partner.

A woman of reproductive age who is using artificial insemination to conceive (with either partner or donor sperm) should be offered further clinical assessment and investigation if she has not conceived after **six (6) cycles of treatment**, in the absence of any known cause of infertility. Where this is using partner sperm, the referral for clinical assessment and investigation should include her partner.

[16] NICE CG156 full guideline recommendations sections 5.4-5.11
[17] NICE CG156 full guideline recommendation 31
[18] NICE CG156 full guideline recommendations section 5.13

Offer an earlier referral for specialist consultation to discuss the options for attempting conception, further assessment and appropriate treatment where:

- the woman is aged 36 years or over; there is a known clinical cause of infertility; or a history of predisposing factors for infertility.

Where treatment is planned that may result in infertility (such as treatment for cancer), early fertility specialist referral should be offered.

People who are concerned about their fertility, and who are known to have chronic viral infections such as hepatitis B, hepatitis C or HIV, should be referred to centres that have appropriate expertise and facilities to provide safe risk-reduction investigation and treatment.

4. Investigation of fertility problems and management strategies

Semen analysis[19]

The results of semen analysis conducted as part of an initial assessment should be compared with the following World Health Organization reference values:

- semen volume: 1.5 ml or more
- pH: 7.2 or more
- sperm concentration: 15 million spermatozoa per ml or more
- total sperm number: 39 million spermatozoa per ejaculate or more
- total motility (percentage of progressive motility and non-progressive motility): 40 percent or more motile or 32 percent or more with progressive motility
- vitality: 58 percent or more live spermatozoa
- sperm morphology (percentage of normal forms): 4 percent or more.

Screening for antisperm antibodies should not be offered because there is no evidence of effective treatment to improve fertility.

If the result of the first semen analysis is abnormal, a repeat confirmatory test should be offered.

Repeat confirmatory tests should ideally be undertaken three (3) months after the initial analysis to allow time for the cycle of spermatozoa formation to be completed. However, if a gross spermatozoa deficiency (azoospermia or severe oligozoospermia) has been detected the repeat test should be undertaken as soon as possible

Post-coital testing of cervical mucus[20]

The routine use of post-coital testing of cervical mucus in the investigation of fertility problems is not recommended because it has no predictive value on pregnancy rate.

[19] NICE CG156 full guideline recommendations section 6.2
[20] NICE CG156 full guideline recommendations section 6.2

Ovarian reserve testing[21]

Use a woman's age as an initial predictor of her overall chance of success through natural conception or with in vitro fertilisation (IVF).

Use one of the following measures to predict the likely ovarian response to gonadotrophin stimulation in IVF:

- total antral follicle count of less than or equal to 4 for a low response and greater than 16 for a high response
- anti-Müllerian hormone of less than or equal to 5.4 pmol/l for a low response and greater than or equal to 25.0 pmol/l for a high response
- follicle-stimulating hormone greater than 8.9 IU/l for a low response and less than 4 IU/l for a high response

Do not use any of the following tests individually to predict any outcome of fertility treatment:

- ovarian volume
- ovarian blood flow
- inhibin B
- oestradiol (E2).

Regularity of menstrual cycles[22]

Women who are concerned about their fertility should be asked about the frequency and regularity of their menstrual cycles. Women with regular monthly menstrual cycles should be informed that they are likely to be ovulating.

Women who are undergoing investigations for infertility should be offered a blood test to measure serum progesterone in the mid-luteal phase of their cycle (day 21 of a 28-day cycle) to confirm ovulation even if they have regular menstrual cycles.

Women with prolonged irregular menstrual cycles should be offered a blood test to measure serum progesterone. Depending upon the timing of menstrual periods, this test may need to be conducted later in the cycle (for example day 28 of a 35-day cycle) and repeated weekly thereafter until the next menstrual cycle starts.

The use of basal body temperature charts to confirm ovulation does not reliably predict ovulation and is not recommended.

Women with irregular menstrual cycles should be offered a blood test to measure serum gonadotrophins (follicle-stimulating hormone and luteinising hormone).

Prolactin measurement[23]

Women who are concerned about their fertility should not be offered a blood test to measure prolactin. This test should only be offered to women who have an ovulatory disorder, galactorrhoea or a pituitary tumour.

[21] NICE CG156 full guideline recommendations section 6.3
[22] NICE CG156 full guideline recommendations section 6.3
[23] NICE CG156 full guideline recommendations section 6.3

Thyroid function tests[24]
Women with possible fertility problems are no more likely than the general population to have thyroid disease and the routine measurement of thyroid function should not be offered. Estimation of thyroid function should be confined to women with symptoms of thyroid disease.

Endometrial biopsy[25]
Women should not be offered an endometrial biopsy to evaluate the luteal phase as part of the investigation of fertility problems because there is no evidence that medical treatment of luteal phase defect improves pregnancy rates.

Investigation of suspected tubal and uterine abnormalities[26]
Women who are not known to have comorbidities (such as pelvic inflammatory disease, previous ectopic pregnancy or endometriosis) should be offered hysterosalpingography (HSG) to screen for tubal occlusion because this is a reliable test for ruling out tubal occlusion, and it is less invasive and makes more efficient use of resources than laparoscopy.

Where appropriate expertise is available, screening for tubal occlusion using hysterosalpingo-contrast-ultrasonography should be considered because it is an effective alternative to hysterosalpingography for women who are not known to have comorbidities.

Women who are thought to have comorbidities should be offered laparoscopy and dye so that tubal and other pelvic pathology can be assessed at the same time.

Women should not be offered hysteroscopy on its own as part of the initial investigation unless clinically indicated because the effectiveness of surgical treatment of uterine abnormalities on improving pregnancy rates has not been established.

Testing for viral status[27]
People undergoing IVF treatment should be offered testing for HIV, hepatitis B and hepatitis C. People found to test positive for one or more of HIV, hepatitis B, or hepatitis C should be offered specialist advice and counselling and appropriate clinical management.

Viral transmission[28]
For couples where the man is HIV positive, any decision about fertility management should be the result of discussions between the couple, a fertility specialist and an HIV specialist.

Advise couples where the man is HIV positive that the risk of HIV transmission to

[24] NICE CG156 full guideline recommendations section 6.3
[25] NICE CG156 full guideline recommendations section 6.3
[26] NICE CG156 full guideline recommendations section 6.4
[27] NICE CG156 full guideline recommendations section 6.5
[28] NICE CG156 full guideline recommendations section 6.5

the female partner is negligible through unprotected sexual intercourse when all of the following criteria are met:

- the man is compliant with highly active antiretroviral therapy (HAART)
- the man has had a plasma viral load of less than 50 copies/ml for more than 6 months
- there are no other infections present
- unprotected intercourse is limited to the time of ovulation.

Advise couples that if all the above criteria are met, sperm washing may not further reduce the risk of infection and may reduce the likelihood of pregnancy.

For couples where the man is HIV positive and either he is not compliant with HAART or his plasma viral load is 50 copies/ml or greater, offer sperm washing. Inform couples that sperm washing reduces, but does not eliminate, the risk of HIV transmission.

If couples who meet all the criteria still perceive an unacceptable risk of HIV transmission after discussion with their HIV specialist, consider sperm washing.

Inform couples that there is insufficient evidence to recommend that HIV negative women use pre-exposure prophylaxis, when all the conditions are met.

For partners of people with hepatitis B, offer vaccination before starting fertility Treatment.

Do not offer sperm washing as part of fertility treatment for men with hepatitis B.

For couples where the man has hepatitis C, any decision about fertility management should be the result of discussions between the couple, a fertility specialist and a hepatitis specialist.

Advise couples who want to conceive and where the man has hepatitis C that the risk of transmission through unprotected sexual intercourse is thought to be low.

Men with hepatitis C should discuss treatment options to eradicate the hepatitis C with their appropriate specialist before conception is considered.

Susceptibility to rubella[29]
Women who are concerned about their fertility should be offered testing for their rubella status so that those who are susceptible to rubella can be offered vaccination. Women who are susceptible to rubella should be offered vaccination and advised not to become pregnant for at least one month following vaccination.

Cervical cancer screening[30]
To avoid delay in fertility treatment, a specific enquiry about the timing and result of the most recent cervical smear test should be made to women who are concerned

[29] NICE CG156 full guideline recommendations section 6.5
[30] NICE CG156 full guideline recommendations section 6.5

about their fertility. Cervical screening should be offered in accordance with the national cervical screening programme guidance.

Screening for *Chlamydia trachomatis*[31]
Before undergoing uterine instrumentation, women should be offered screening for *Chlamydia trachomatis* using an appropriately sensitive technique.

If the result of a test for *Chlamydia trachomatis* is positive, women and their sexual partners should be referred for appropriate management with treatment and contact tracing.

Prophylactic antibiotics should be considered before uterine instrumentation if screening has not been carried out.

5. Medical and surgical management of male factor fertility problems

Medical management (male factor infertility)[32]
Men with hypogonadotrophic hypogonadism should be offered gonadotrophin drugs because these are effective in improving fertility.

Men with idiopathic semen abnormalities should not be offered antioestrogens, gonadotrophins, androgens, bromocriptine or kinin-enhancing drugs because they have not been shown to be effective.

Men should be informed that the significance of antisperm antibodies is unclear and the effectiveness of systemic corticosteroids is uncertain.

Men with leucocytes in their semen should not be offered antibiotic treatment unless there is an identified infection because there is no evidence that this improves pregnancy rates.

Surgical management (male factor infertility)[33]
Where appropriate expertise is available, men with obstructive azoospermia should be offered surgical correction of epididymal blockage because it is likely to restore patency of the duct and improve fertility. Surgical correction should be considered as an alternative to surgical sperm recovery and IVF.

Men should not be offered surgery for varicoceles as a form of fertility treatment because it does not improve pregnancy rates.

Management of ejaculatory failure[34]
Treatment of ejaculatory failure can restore fertility without the need for invasive methods of sperm retrieval or the use of assisted reproduction procedures. However, further evaluation of different treatment options is needed.

[31] NICE CG156 full guideline recommendations section 6.5
[32] NICE CG156 full guideline recommendations section 7.2
[33] NICE CG156 full guideline recommendations section 7.3
[34] NICE CG156 full guideline recommendations section 7.4

6. Ovulation disorders

Classification of ovulatory disorders
The World Health Organization (WHO) classifies ovulation disorders into three groups:

Group I:	hypothalamic pituitary failure (hypothalamic amenorrhoea or hypogonadotrophic hypogonadism).
Group II:	hypothalamic-pituitary-ovarian dysfunction (predominately polycystic ovary syndrome).
Group III:	ovarian failure.

WHO Group I ovulation disorders[35]
Advise women with WHO Group I anovulatory infertility that they can improve their chance of regular ovulation, conception and an uncomplicated pregnancy by:

- increasing their body weight, if they have a BMI of less than 19, **and/or**
- moderating their exercise levels if they undertake high levels of exercise.

Offer women with WHO Group I ovulation disorders pulsatile administration of gonadotrophin-releasing hormone or gonadotrophins with luteinising hormone activity to induce ovulation.

WHO Group II ovulation disorders[36]
In women with WHO Group II ovulation disorders receiving first-line treatment for ovarian stimulation:

Advise women with WHO Group II anovulatory infertility who have a BMI of 30 or over to lose weight. Inform them that this alone may restore ovulation, improve their response to ovulation induction agents, and have a positive impact on pregnancy outcomes.

Offer women with WHO Group II anovulatory infertility one of the following treatments, taking into account potential adverse effects, ease and mode of use, the woman's BMI, and monitoring needed:

- clomifene citrate **or**
- metformin **or**
- a combination of the above.

For women who are taking clomifene citrate, offer ultrasound monitoring during at least the first cycle of treatment to ensure that they are taking a dose that minimises the risk of multiple pregnancy.

For women who are taking clomifene citrate, do not continue treatment for longer than six (6) months.

Women prescribed metformin[37]should be informed of the side effects associated

[35] NICE CG156 full guideline recommendations section 8.2
[36] NICE CG156 full guideline recommendations section 8.3

with its use (such as nausea, vomiting and other gastrointestinal disturbances).

In women with WHO Group II ovulation disorders who are known to be resistant to clomifene citrate:

For women with WHO Group II ovulation disorders who are known to be resistant to clomifene citrate, consider one of the following second-line treatments, depending on clinical circumstances and the woman's preference:

- laparoscopic ovarian drilling **or;**
- combined treatment with clomifene citrate and metformin if not already offered as first-line treatment **or;**
- gonadotrophins.

Women with polycystic ovary syndrome who are being treated with gonadotrophins should not be offered treatment with gonadotrophin-releasing hormone agonist concomitantly because it does not improve pregnancy rates, and it is associated with an increased risk of ovarian hyperstimulation.

The use of adjuvant growth hormone treatment with gonadotrophin-releasing hormone agonist and/or human menopausal gonadotrophin during ovulation induction in women with polycystic ovary syndrome who do not respond to clomifene citrate is not recommended because it does not improve pregnancy rates.

The effectiveness of pulsatile gonadotrophin-releasing hormone in women with clomifene citrate-resistant polycystic ovary syndrome is uncertain and is therefore not recommended outside a research context.

Hyperprolactinaemic amenorrhoea – dopamine agonists[38]
Women with ovulatory disorders due to hyperprolactinaemia should be offered treatment with dopamine agonists such as bromocriptine. Consideration should be given to safety for use in pregnancy and minimising cost when prescribing.

Monitoring ovulation induction during gonadotrophin therapy[39]
Women who are offered ovulation induction with gonadotrophins should be informed about the risk of multiple pregnancy and ovarian hyperstimulation before starting treatment.

Ovarian ultrasound monitoring to measure follicular size and number should be an integral part of gonadotrophin therapy to reduce the risk of multiple pregnancy and ovarian hyperstimulation.

7. Tubal and uterine surgery

Tubal microsurgery and laparoscopic tubal surgery[40]
For women with mild tubal disease, tubal surgery may be more effective than no

[37] See NICE CG156 page 45 note 8
[38] NICE CG156 full guideline recommendations section 8.4
[39] NICE CG156 full guideline recommendations section 8.5
[40] NICE CG156 full guideline recommendations section 9.2

treatment. In centres where appropriate expertise is available it may be considered as a treatment option.

Tubal catheterisation or cannulation[41]
For women with proximal tubal obstruction, selective salpingography plus tubal catheterisation, or hysteroscopic tubal cannulation, may be treatment options because these treatments improve the chance of pregnancy.

Surgery for hydrosalpinges before in vitro fertilisation treatment[42]
Women with hydrosalpinges should be offered salpingectomy, preferably by laparoscopy, before IVF treatment because this improves the chance of a live birth.

Uterine surgery[43]
Women with amenorrhoea who are found to have intrauterine adhesions should be offered hysteroscopic adhesiolysis because this is likely to restore menstruation and improve the chance of pregnancy.

8. Medical and surgical management of endometriosis

Medical management (ovarian suppression) of endometriosis[44]
Medical treatment of minimal and mild endometriosis diagnosed as the cause of infertility in women does not enhance fertility and should not be offered.

Surgical ablation[45]
Women with minimal or mild endometriosis who undergo laparoscopy should be offered surgical ablation or resection of endometriosis plus laparoscopic adhesiolysis because this improves the chance of pregnancy.

Women with ovarian endometriomas should be offered laparoscopic cystectomy because this improves the chance of pregnancy.

Women with moderate or severe endometriosis should be offered surgical treatment because it improves the chance of pregnancy.

Post-operative medical treatment does not improve pregnancy rates in women with moderate to severe endometriosis and is not recommended.

9. Unexplained infertility

Ovarian stimulation for unexplained infertility[46]
Do not offer oral ovarian stimulation agents (such as clomifene citrate, anastrozole or letrozole) to women with unexplained infertility.

Inform women with unexplained infertility that clomifene citrate as a standalone

[41] NICE CG156 full guideline recommendations section 9.3
[42] NICE CG156 full guideline recommendations section 9.4
[43] NICE CG156 full guideline recommendations section 9.5
[44] NICE CG156 full guideline recommendations section 10.2
[45] NICE CG156 full guideline recommendations section 10.3
[46] NICE CG156 full guideline recommendations section 11.2

treatment does not increase the chances of a pregnancy or a live birth.

Advise women with unexplained infertility who are having regular unprotected sexual intercourse to try to conceive for a total of two (2) years (this can include up to one (1) year before their fertility investigations) before IVF will be considered.

Offer IVF treatment to women with unexplained infertility who have not conceived after two (2) years (this can include up to one (1) year before their fertility investigations) of regular unprotected sexual intercourse.

10. Intrauterine insemination

Intrauterine insemination[47]
Consider unstimulated intrauterine insemination as a treatment option in the following groups as an alternative to vaginal sexual intercourse:

- people who are unable to, or would find it very difficult to, have vaginal intercourse because of a clinically diagnosed physical disability or psychosexual problem who are using partner or donor sperm;
- people with conditions that require specific consideration in relation to methods of conception (for example, after sperm washing where the man is HIV positive);
- people in same-sex relationships.

For those people who have not conceived after six (6) cycles of donor or partner insemination, despite evidence of normal ovulation, tubal patency and semen analysis, offer a further six (6) cycles of un-stimulated intrauterine insemination before IVF is considered

For people with unexplained infertility, mild endometriosis or 'mild male factor infertility', who are having regular unprotected sexual intercourse:

- do not routinely offer intrauterine insemination, either with or without ovarian stimulation (exceptional circumstances include, for example, when people have social, cultural or religious objections to IVF)
- advise them to try to conceive for a total of two (2 years (this can include up to one (1) year before their fertility investigations) before IVF will be considered.

11. Prediction of IVF success[48]

Female age
Inform women that the chance of a live birth following IVF treatment falls with rising female age
Number of previous treatment cycles
Inform people that the overall chance of a live birth following IVF treatment falls as the number of unsuccessful cycles increases.

[47] NICE CG156 full guideline recommendations section 12.2
[48] NICE CG156 full guideline recommendations section 13.2

Previous pregnancy history
People should be informed that IVF treatment is more effective in women who have previously been pregnant and/or had a live birth.
Body mass index
Women should be informed that female BMI should ideally be in the range 19–30 before commencing assisted reproduction, and that a female BMI outside this range is likely to reduce the success of assisted reproduction procedures.
Lifestyle factors
People should be informed that the consumption of more than one (1) unit of alcohol per day reduces the effectiveness of assisted reproduction procedures, including IVF.

People should be informed that maternal and paternal smoking can adversely affect the success rates of assisted reproduction procedures, including IVF treatment.

People should be informed that maternal caffeine consumption has adverse effects on the success rates of assisted reproduction procedures, including IVF treatment.

12. Access criteria for IVF[49]

Criteria for referral for IVF
When considering IVF as a treatment option for people with fertility problems, discuss the risks and benefits of IVF in accordance with the current Human Fertilisation and Embryology Authority (HFEA) Code of Practice.[50]

Inform people that normally a full cycle of IVF treatment, with or without intracytoplasmic sperm injection (ICSI), should comprise one (1) episode of ovarian stimulation and the transfer of any resultant fresh embryo(s).

Where an excess of embryos is available following a fresh cycle, these embryos may be frozen for future use. Once thawed, these embryos may be transferred to the patient as a frozen cycle and be included within the 'full cycle'.

All frozen embryos from a previous cycle should be used before a further IVF cycle is initiated.

Storage of frozen embryos will be routinely funded for one (1) year unless the provider has agreed an alternative as part of a pathway agreement.

Any costs relating to the continued storage of embryos beyond this will ordinarily be the responsibility of the couple.

Patients should be counselled by the clinician and infertility counsellor to this effect.

In women aged under 40 years, who have not conceived after two (2) years of regular unprotected intercourse or 12 cycles of artificial insemination (where six (6) or more are by intrauterine insemination), offer three (3) full cycles of IVF, with or without ICSI. If the woman reaches the age of 40 during treatment, complete the

[49] NICE CG156 full guideline recommendations section 14.5
[50] http://www.hfea.gov.uk/code.html

current full cycle but do not offer further full cycles.

In women aged 40–42 years, who have not conceived after two (2) years of regular unprotected intercourse or 12 cycles of artificial insemination (where six (6) or more are by intrauterine insemination), offer one (1) full cycle of IVF, with or without ICSI, provided the following three (3) criteria are fulfilled:

- they have never previously had IVF treatment;
- there is no evidence of low ovarian reserve[51];
- there has been a discussion of the additional implications of IVF and pregnancy at this age.

Where investigations show there is no chance of pregnancy with expectant management and where IVF is the only effective treatment, refer the woman directly to a specialist team for IVF treatment.

In women aged under 40 years, any previous full IVF cycle, whether self or state-funded[52]-, should count towards the total of three (3) full cycles that should be offered by the NHS.

Take into account the outcome of previous IVF treatment when assessing the likely effectiveness and safety of any further IVF treatment.

A cancelled IVF cycle is defined as one where an egg collection procedure is not undertaken. However, cancelled cycles due to low ovarian reserve should be taken into account when considering suitability for further IVF treatment.

An abandoned cycle is defined as prior to egg retrieval, usually due to lack of response (where less than three (3) mature follicles are present) or excessive response to gonadotrophins; failure of fertilisation.

An abandoned cycle counts towards the number of commissioned cycles.

13. Procedures used during IVF treatment

Pre-treatment in IVF[53]
Advise women that using pre-treatment (with either the oral contraceptive pill or a progestogen) as part of IVF does not affect the chances of having a live birth.

Consider pre-treatment in order to schedule IVF treatment for women who are not undergoing long down-regulation protocols.

Down regulation and other regimens to avoid premature luteinising hormone surges in IVF [54]
Use regimens to avoid premature luteinising hormone surges in gonadotrophin-

[51] Cross reference recommendation 50 (full guideline) / 1.3.3.2 summary guideline
[52] i.e. regardless of who has paid for any previous cycles they count towards the total of three (3) cycles
[53] NICE CG156 full guideline recommendations section 15.2
[54] NICE CG156 full guideline recommendations section 15.3

stimulated IVF treatment cycles.

Use either gonadotrophin-releasing hormone agonist down-regulation or gonadotrophin-releasing hormone antagonists as part of gonadotrophin-stimulated IVF treatment cycles.

Only offer gonadotrophin-releasing hormone agonists to women who have a low risk of ovarian hyperstimulation syndrome.

When using gonadotrophin-releasing hormone agonists as part of IVF treatment, use a long down-regulation protocol.

Controlled ovarian stimulation in IVF[55]
Use ovarian stimulation as part of IVF treatment.

Use either urinary or recombinant gonadotrophins for ovarian stimulation as part of IVF treatment.

When using gonadotrophins for ovarian stimulation in IVF treatment:

- use an individualised starting dose of follicle-stimulating hormone, based on factors that predict success, such as:
    - age
    - BMI
    - presence of polycystic ovaries
    - ovarian reserve
- do not use a dosage of follicle-stimulating hormone of more than 450 IU/day.

Offer women ultrasound monitoring (with or without oestradiol levels) for efficacy and safety throughout ovarian stimulation.

Inform women that clomifene citrate-stimulated and gonadotrophin-stimulated IVF cycles have higher pregnancy rates per cycle than 'natural cycle' IVF.

Do not offer women 'natural cycle' IVF treatment.

Do not use growth hormone or dehydroepiandrosterone (DHEA) as adjuvant treatment in IVF protocols.

Triggering ovulation in IVF[56]
Offer women human chorionic gonadotrophin (urinary or recombinant) to trigger ovulation in IVF treatment.

Offer ultrasound monitoring of ovarian response as an integral part of the IVF treatment cycle.

Clinics providing ovarian stimulation with gonadotrophins should have protocols in place for preventing, diagnosing and managing ovarian hyperstimulation syndrome.

[55] NICE CG156 full guideline recommendations section 15.4
[56] NICE CG156 full guideline recommendations section 15.5

Oocyte and sperm retrieval in IVF[57]
Women undergoing transvaginal retrieval of oocytes should be offered conscious sedation because it is a safe and acceptable method of providing analgesia. The safe practice of administering sedative drugs published by the Academy of Medical Royal Colleges should be followed.

Women who have developed at least three (3) follicles before oocyte retrieval should not be offered follicle flushing because this procedure does not increase the numbers of oocytes retrieved or pregnancy rates, and it increases the duration of oocyte retrieval and associated pain.

Surgical sperm recovery before ICSI may be performed using several different techniques depending on the pathology and wishes of the man. In all cases, facilities for cryopreservation of spermatozoa should be available.

Assisted hatching is not recommended because it has not been shown to improve pregnancy rates.

Embryo transfer strategies in IVF[58]
Women undergoing IVF treatment should be offered ultrasound-guided embryo transfer because this improves pregnancy rates.

Replacement of embryos into a uterine cavity with an endometrium of less than 5mm thickness is unlikely to result in a pregnancy and is therefore not recommended.
Women should be informed that bed rest of more than 20 minutes' duration following embryo transfer does not improve the outcome of IVF treatment.

Evaluate embryo quality, at both cleavage and blastocyst stages, according to the Association of Clinical Embryologists (ACE) and UK National External Quality Assessment Service (UK NEQAS) for Reproductive Science Embryo and Blastocyst Grading schematic.

When considering the number of fresh or frozen embryos to transfer in IVF treatment:

- For women aged under 37 years:
  - in the first full IVF cycle use single embryo transfer;
  - in the second full IVF cycle use single embryo transfer if one (1) or more top-quality embryos are available. Consider using two (2) embryos if no top-quality embryos are available.
  - In the third full IVF cycle transfer no more than two (2) embryos

[57] NICE CG156 full guideline recommendations section 15.6
[58] NICE CG156 full guideline recommendations section 15.7

- For women aged 37–39 years:
  - In the first and second full IVF cycles use single embryo transfer if there are one (1) or more top-quality embryos. Consider double embryo transfer if there are no top-quality embryos.
  - In the third full IVF cycle transfer no more than two (2) embryos.

- For women aged 40–42 years consider double embryo transfer.

- For women undergoing IVF treatment with donor eggs, use an embryo transfer strategy that is based on the age of the donor.

- No more than two (2) embryos should be transferred during any one (1) cycle of IVF treatment.

- Where a top-quality blastocyst is available, use single embryo transfer.

- When considering double embryo transfer, advise people of the risks of multiple pregnancy associated with this strategy.

- Offer cryopreservation to store any remaining good-quality embryos after embryo transfer.

- Advise women who have regular ovulatory cycles that the likelihood of a live birth after replacement of frozen–thawed embryos is similar for embryos replaced during natural cycles and hormone-supplemented cycles.

Luteal phase support after IVF[59]
Offer women progesterone for luteal phase support after IVF treatment.

Do not routinely offer women human chorionic gonadotrophin for luteal phase support after IVF treatment because of the increased likelihood of ovarian hyperstimulation syndrome.

Inform women undergoing IVF treatment that the evidence does not support continuing any form of treatment for luteal phase support beyond 8 weeks' gestation.

Gamete intrafallopian transfer and zygote intrafallopian transfer[60]
There is insufficient evidence to recommend the use of gamete intrafallopian transfer or zygote intrafallopian transfer in preference to IVF in couples with unexplained fertility problems or male factor fertility problems.

[59] NICE CG156 full guideline recommendations section 15.8
[60] NICE CG156 full guideline recommendations section 15.9

14. Intracytoplasmic sperm injection

Indications for intracytoplasmic sperm injection[61]

The recognised indications for treatment by ICSI include:

- severe deficits in semen quality
- obstructive azoospermia
- non-obstructive azoospermia.

In addition, treatment by ICSI should be considered for couples in whom a previous IVF treatment cycle has resulted in failed or very poor fertilisation.

Genetic issues and counselling[62]

Before considering treatment by ICSI, people should undergo appropriate investigations, both to establish a diagnosis and to enable informed discussion about the implications of treatment.

Before treatment by ICSI consideration should be given to relevant genetic issues. Where a specific genetic defect associated with male infertility is known or suspected, couples should be offered appropriate genetic counselling and testing.

Where the indication for ICSI is a severe deficit of semen quality, or non-obstructive azoospermia, the man's karyotype should be established.

Men who are undergoing karyotype testing should be offered genetic counselling regarding the genetic abnormalities that may be detected.

Testing for Y chromosome microdeletions should not be regarded as a routine investigation before ICSI. However, it is likely that a significant proportion of male infertility results from abnormalities of genes on the Y chromosome involved in the regulation of spermatogenesis, and couples should be informed of this.

Intracytoplasmic sperm injection versus IVF[63]

Couples should be informed that ICSI improves fertilisation rates compared to IVF alone, but once fertilisation is achieved the pregnancy rate is no better than with IVF.

15. Donor insemination

Indications for donor insemination[64]

The use of donor insemination is considered effective in managing fertility problems associated with the following conditions:

- obstructive azoospermia
- non-obstructive azoospermia
- severe deficits in semen quality in couples who do not wish to undergo ICSI.

[61] NICE CG156 full guideline recommendations section 16.2
[62] NICE CG156 full guideline recommendations section 16.3
[63] NICE CG156 full guideline recommendations section 16.4
[64] NICE CG156 full guideline recommendations section 17.2

Donor insemination should be considered in conditions such as:

- where there is a high risk of transmitting a genetic disorder to the offspring
- where there is a high risk of transmitting infectious disease to the offspring or woman from the man severe rhesus isoimmunisation.

Information and counselling[65]

Couples should be offered information about the relative merits of ICSI and donor insemination in a context that allows equal access to both treatment options.

Couples considering donor insemination should be offered counselling from someone who is independent of the treatment unit regarding all the physical and psychological implications of treatment for themselves and potential children.

Screening of sperm donors[66]

Units undertaking semen donor recruitment and the cryopreservation of donor spermatozoa for treatment purposes should follow the 'UK guidelines for the medical and laboratory screening of sperm, egg and embryo donors' (2008) describing the selection and screening of donors.

All potential semen donors should be offered counselling from someone who is independent of the treatment unit regarding the implications for themselves and their genetic children, including any potential children resulting from donated semen.

Assessments to offer the woman[67]

Before starting treatment by donor insemination (for obstructive or non-obstructive azoospermia, severe semen quality deficit or high risk of transmitting genetic or infectious diseases) it is important to confirm that the woman is ovulating. Women with a history that is suggestive of tubal damage should be offered tubal assessment before treatment.

Women with no risk factors in their history should be offered tubal assessment after three (3) cycles if treatment by donor insemination (for obstructive or non-obstructive azoospermia, severe semen quality deficit or high risk of transmitting genetic or infectious diseases) has been unsuccessful

Intrauterine insemination versus intracervical insemination[68]

Couples using donor sperm should be offered intrauterine insemination in preference to intracervical insemination because it improves pregnancy rates.

Unstimulated versus stimulated donor insemination[69]

Women who are ovulating regularly should be offered a minimum of six (6) cycles of donor insemination (for obstructive or non-obstructive azoospermia, severe semen quality deficit or high risk of transmitting genetic or infectious diseases) without ovarian stimulation to reduce the risk of multiple pregnancy and its consequences.

[65] NICE CG156 full guideline recommendations section 17.3
[66] NICE CG156 full guideline recommendations section 17.4
[67] NICE CG156 full guideline recommendations section 17.5
[68] NICE CG156 full guideline recommendations section 17.6
[69] NICE CG156 full guideline recommendations section 17.7

16. Oocyte donation

Indications for oocyte donation[70]

The use of donor oocytes is considered effective in managing fertility problems associated with the following conditions:

- premature ovarian failure
- gonadal dysgenesis including Turner syndrome
- bilateral oophorectomy
- ovarian failure following chemotherapy or radiotherapy
- certain cases of IVF treatment failure.

Oocyte donation should also be considered in certain cases where there is a high risk of transmitting a genetic disorder to the offspring.

Screening of oocyte donors[71]

Before donation is undertaken, oocyte donors should be screened for both infectious and genetic diseases in accordance with the 'UK guidelines for the medical and laboratory screening of sperm, egg and embryo donors' (2008)

Oocyte donation and 'egg sharing' [72]

Oocyte donors should be offered information regarding the potential risks of ovarian stimulation and oocyte collection.

Oocyte recipients and donors should be offered counselling from someone who is independent of the treatment unit regarding the physical and psychological implications of treatment for themselves and their genetic children, including any potential children resulting from donated oocytes.

All people considering participation in an 'egg-sharing' scheme should be counselled about its particular implications.

17. People with cancer who wish to preserve fertility[73]

Cryopreservation of semen, oocytes and embryos

When considering and using cryopreservation for people before starting chemotherapy or radiotherapy that is likely to affect their fertility, follow recommendations in 'The effects of cancer treatment on reproductive functions' (2007)[74]

At diagnosis, the impact of the cancer and its treatment on future fertility should be discussed between the person diagnosed with cancer and their cancer team.

When deciding to offer fertility preservation to people diagnosed with cancer, take

[70] NICE CG156 full guideline recommendations section 18.2
[71] NICE CG156 full guideline recommendations section 18.3
[72] NICE CG156 full guideline recommendations section 18.4
[73] NICE CG156 full guideline recommendations 19.2
[74] Royal College of Physicians, The Royal College of Radiologists, Royal College of Obstetricians and Gynaecologists, (2007) The effects of cancer treatment on reproductive functions: Guidance on Management. Report of a Working Party, London: RCP

into account the following factors:

- diagnosis
- treatment plan
- expected outcome of subsequent fertility treatment
- prognosis of the cancer treatment
- viability of stored/post-thawed material.

For cancer-related fertility preservation, do not apply the eligibility criteria used for conventional infertility treatment.

Do not use a lower age limit for cryopreservation for fertility preservation in people diagnosed with cancer.

Inform people diagnosed with cancer that the eligibility criteria used in conventional infertility treatment do not apply in the case of fertility cryopreservation provided by the NHS. However, those criteria will apply when it comes to using stored material for assisted conception in an NHS setting.

When using cryopreservation to preserve fertility in people diagnosed with cancer, use sperm, embryos or oocyctes.

Offer sperm cryopreservation to men and adolescent boys who are preparing for medical treatment for cancer that is likely to make them infertile.

Use freezing in liquid nitrogen vapour as the preferred cryopreservation technique for sperm.

Offer oocyte or embryo cryopreservation as appropriate to women of reproductive age (including adolescent girls) who are preparing for medical treatment for cancer that is likely to make them infertile if:

- they are well enough to undergo ovarian stimulation and egg collection **and;**
- this will not worsen their condition **and;**
- enough time is available before the start of their cancer treatment.

In cryopreservation of oocytes and embryos, use vitrification instead of controlled-rate freezing if the necessary equipment and expertise is available.

Store cryopreserved material for an initial period of 10 years.

Offer continued storage of cryopreserved sperm, beyond 10 years, to men who remain at risk of significant infertility.

9 Governance arrangements

NHS England expects robust mechanisms will be put in place to support clinical governance to comply with the Human Fertilisation and Embryology Authority (HFEA) Code of Practice[75].

[75] http://www.hfea.gov.uk/code.html

10 Mechanism for funding

Payment is on a cost per case basis requiring prior approval on the form N-SC037 from the appropriate lead area team for Armed Forces health.

- North of England region – North Yorkshire & Humber Area Team: england.nyh-armedforces@nhs.net
- Midlands & East of England region – Derbyshire & Nottinghamshire Area Team: england.midlandsarmedforces@nhs.net
- NHS England South (& London): england.southarmedforces@nhs.net

11 Audit requirements

NHS England expects robust mechanisms will be put in place to support audit requirements to comply with the Human Fertilisation and Embryology Authority (HFEA) Code of Practice[76].

12 Documents which have informed this policy

National Institute for Health and Care Excellence (2013) Fertility, CG 156. London: National Institute for Health and Care Excellence. http://www.guidance.nice.org.uk/cg156

Royal College of Obstetricians and Gynaecologists (2013), Fertility: assessment and treatment for people with fertility problems, London: Royal College of Obstetricians and Gynaecologists. http://guidance.nice.org.uk/CG156

The National Health Service Commissioning Board and Clinical Commissioning Groups (Responsibilities and Standing Rules) Regulations 2012, S.I. 2012/2996 http://www.legislation.gov.uk/uksi/2012/2996/contents/made

NHS England (2013) Clinical Commissioning Policy: Pre-implantation Genetic Diagnosis (PGD) (NHSCB/E01/P/a) http://www.england.nhs.uk/wp-content/uploads/2013/04/e01-p-a.pdf

Ministry of Defence (2011) Armed Forces Covenant: Today and Tomorrow, London: MoD https://www.gov.uk/government/publications/the-armed-forces-covenant

[76] http://www.hfea.gov.uk/code.html

13 Links to other policies

This policy follows the principles set out in the ethical framework that govern the commissioning of NHS healthcare and those policies dealing with the approach to experimental treatments and processes for the management of individual funding requests (IFR).

NHS England (2014) Clinical Commissioning Policy: Pre-implantation Genetic Diagnosis (PGD) (NHSCB/E01/P/a) http://www.england.nhs.uk/wp-content/uploads/2013/04/e01-p-a.pdf

14 Date of review

This policy will be reviewed in April 2016 unless information is received which indicates that the proposed review date should be brought forward or delayed.

15 References

National Institute for Health and Care Excellence (2013) Fertility, CG 156. London: National Institute for Health and Care Excellence. http://www.guidance.nice.org.uk/cg156

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16 Version Control Sheet

Version	Section/Para/Appendix	Version/Description of Amendments	Date	Author/Amended by
1	All	First draft for CPAG approval	11-9-13	AMT
2	All	Grammar	21-10-13	JS
3	Plain language summary	Updated to reflect views of CPAG	21-10-13	AMT
4	8.12 Access Criteria	Updated to reflect views of CPAG	23-10-13	AMT
5	8.13 Embryo Transfer	Update to reflect views of CPAG	23-10-13	AMT
6	Plain Language Summary – Women aged under 40	Update to three cycles (<40)	28-5-14	AMT
7	8.12 Access Criteria	Updated to three cycles (<40)	28-5-14	AMT

Version	Section/Para/Appendix	Version/Description of Amendments	Date	Author/Amended by
8	8.13 Embryo Transfer	Updated to reflect third cycle (<40)	28-5-14	AMT
9	10 mechanism for funding	Added application form reference	28-5-14	AMT
10	Definitions	Added definitions for abandoned, completed and unsuccessful cycles following CPAG approval Amended definition of full cycle	28-8-14	AMT / JK
11	8.12 Access Criteria	Updated to reflect definitions of full, abandoned cycle	28-8-14	AMT / JK
12	All	NHS England Branding	18-09-14	GW
13	All	Review of grammar etc	10-12-14	JN / AMT