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National Institute for Clinical Excellence

Fertility: assessment and treatment for people with fertility problems

Clinical Guideline 11

February 2004

Developed by the National Collaborating Centre for Women's and Children's Health

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Fertility: assessment and treatment for people with fertility problems

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A version for people who want to understand what NICE has told the NHS, called *Assessment and treatment for people with fertility problems: Understanding NICE guidance – Information for people with fertility problems, their partners and the public* is available from the NICE website or from the NHS Response Line (quote reference number N0466 for a version in English and N0467 for a version in English and Welsh).

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This guidance is written in the following context.
This guidance represents the view of the Institute, which was arrived at after careful consideration of the evidence available. Health professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of health professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

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Intra-uterine insemination

3. Couples with mild male factor fertility problems, unexplained fertility problems or minimal to mild endometriosis should be offered up to six cycles of intra-uterine insemination because this increases the chance of pregnancy.

In vitro fertilisation treatment

4. Couples in which the woman is aged 23–39 years at the time of treatment and who have an identified cause for their fertility problems (such as azoospermia or bilateral tubal occlusion) or who have infertility of at least 3 years' duration should be offered up to three stimulated cycles of in vitro fertilisation treatment.

5. Human menopausal gonadotrophin, urinary follicle-stimulating hormone and recombinant follicle-stimulating hormone are equally effective in achieving a live birth when used following pituitary down-regulation as part of in vitro fertilisation treatment. Consideration should be given to minimising cost when prescribing.

continued

Key priorities for implementation *continued*

6. Couples should be informed that the chance of multiple pregnancy following in vitro fertilisation treatment depends on the number of embryos transferred per cycle of treatment. To balance the chance of a live birth and the risk of multiple pregnancy and its consequences, no more than two embryos should be transferred during any one cycle of in vitro fertilisation treatment.

7. Embryos not transferred during a stimulated in vitro fertilisation treatment cycle may be suitable for freezing. If two or more embryos are frozen then they should be transferred before the next stimulated treatment cycle because this will minimise ovulation induction and egg collection, both of which carry risks for the woman and use more resources.

The following guidance is evidence based. The grading scheme used for the recommendations (A, B, C, D or good practice point [GPP]) is described in Appendix A; a summary of the evidence on which the guidance is based is provided in the full guideline (see Section 5).

1 Guidance

1.1 Initial advice to people concerned about delays in conception

1.1.1 Natural conception

1.1.1.1 People who are concerned about their fertility should be informed that about 84% of couples in the general population will conceive within 1 year if 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 92%). **D**

1.1.1.2 People who are concerned about their fertility should be informed that female fertility declines with age, but that the effect of age on male fertility is less clear. With regular unprotected sexual intercourse, 94% of fertile women aged 35 years, and 77% of those aged 38 years, will conceive after 3 years of trying. **C**

1.1.2 Frequency and timing of sexual intercourse

1.1.2.1 People who are concerned about their fertility should be informed that sexual intercourse every 2 to 3 days optimises the chance of pregnancy. Timing intercourse to coincide with ovulation causes stress and is not recommended. **C**

1.1.3 Alcohol

1.1.3.1 Women who are trying to become pregnant should be informed that drinking no more than one or two units of alcohol once or twice per week and avoiding episodes of intoxication reduces the risk of harming a developing fetus. **D**

1.1.3.2 Men should be informed that alcohol consumption within the Department of Health's recommendations of three to four units per day for men is unlikely to affect their fertility. **GPP**

1.1.3.3 Men should be informed that excessive alcohol intake is detrimental to semen quality. **B**

1.1.4 Smoking

1.1.4.1 Women who smoke should be informed that this is likely to reduce their fertility. **B**

1.1.4.2 Women who smoke should be offered referral to a smoking cessation programme to support their efforts in stopping smoking. **A**

1.1.4.3 Women should be informed that passive smoking is likely to affect their chance of conceiving. **B**

1.1.4.4 Men who smoke should be informed that there is an association between smoking and reduced semen quality (although the impact of this on male fertility is uncertain), and that stopping smoking will improve their general health. **GPP**

1.1.5 Caffeinated beverages

1.1.5.1 People who are concerned about their fertility should be informed that there is no consistent evidence of an association between consumption of caffeinated beverages (tea, coffee and colas) and fertility problems. **B**

1.1.6 Body weight

1.1.6.1 Women who have a body mass index of more than 29 should be informed that they are likely to take longer to conceive. **B**

1.1.6.2 Women who have a body mass index of more than 29 and who are not ovulating should be informed that losing weight is likely to increase their chance of conception. **B**

1.1.6.3 Women should be informed that participating in a group programme involving exercise and dietary advice leads to more pregnancies than weight loss advice alone. **A**

1.1.6.4 Men who have a body mass index of more than 29 should be informed that they are likely to have reduced fertility. **C**

1.1.6.5 Women who have a body mass index of less than 19 and who have irregular menstruation or are not menstruating should be advised that increasing body weight is likely to improve their chance of conception. **B**

1.1.7 Tight underwear for men

1.1.7.1 Men should be informed that there is an association between elevated scrotal temperature and reduced semen quality, but that it is uncertain whether wearing loose-fitting underwear improves fertility. **B**

1.1.8 Occupation

1.1.8.1 Some occupations involve exposure to hazards that can reduce male or female fertility, and therefore a specific enquiry about occupation should be made to people who are concerned about their fertility and appropriate advice should be offered. **B**

1.1.9 Prescribed, over-the-counter and recreational drug use

1.1.9.1 A number of prescription, over-the-counter and recreational drugs interfere with male and female fertility, and therefore a specific enquiry about these should be made to people who are concerned about their fertility and appropriate advice should be offered. **B**

1.1.10 Complementary therapy

1.1.10.1 People who are concerned about their fertility should be informed that the effectiveness of complementary therapies for fertility problems has not been properly evaluated and that further research is needed before such interventions can be recommended. **GPP**

1.1.11 Folic acid supplementation

1.1.11.1 Women intending to become pregnant should be informed that dietary supplementation with folic acid before conception and up to 12 weeks' gestation reduces the risk of having a baby with neural tube defects. The recommended dose is 0.4 mg per day. For women who have previously had an infant with a neural tube defect or who are receiving antiepileptic medication, a higher dose of 5 mg per day is recommended. **A**

1.1.12 Susceptibility to rubella

1.1.12.1 Women who are concerned about their fertility should be offered rubella susceptibility screening so that those who are susceptible to rubella can be offered rubella vaccination. Women who are susceptible to rubella should be offered rubella vaccination and advised not to become pregnant for at least 1 month following vaccination. **D**

1.1.13 Cervical cancer screening

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

1.2 Defining infertility, assessment and referral

1.2.1 Defining infertility[1]

1.2.1.1 Infertility should be defined as failure to conceive after regular unprotected sexual intercourse for 2 years in the absence of known reproductive pathology. **D**

[1] This guideline does not include the management of people who are outside this definition, such as the initial management of those with sexual dysfunction, couples who are using contraception (for example, where one partner has been sterilised) and couples outside the reproductive age range.

1.2.2 Assessment and referral

1.2.2.1 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. **GPP**

1.2.2.2 The environment in which investigation of fertility problems takes place should enable people to discuss sensitive issues such as sexual abuse. **GPP**

1.2.2.3 People who have not conceived after 1 year of regular unprotected sexual intercourse should be offered further clinical investigation including semen analysis and/or assessment of ovulation. **GPP**

1.2.2.4 Where there is a history of predisposing factors (such as amenorrhoea, oligomenorrhoea, pelvic inflammatory disease or undescended testes), or where a woman is aged 35 years or over, earlier investigation should be offered. **GPP**

1.2.2.5 Where there is a known reason for infertility (such as prior treatment for cancer), early specialist referral should be offered. **GPP**

1.2.2.6 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. **GPP**

1.3 Principles of care

1.3.1 Information giving and couple-centred management

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

1.3.1.2 People should have the opportunity to make informed decisions regarding their care and treatment via access to evidence-based information. These choices should be recognised as an integral part of the decision-making process. Verbal information should be supplemented with written information or audio-visual media. **C**

1.3.1.3 Information regarding care and treatment options should be provided in a form that is accessible to people who have additional needs, such as people with physical, cognitive or sensory disabilities, and people who do not speak or read English. **GPP**

1.3.2 Psychological effects of fertility problems

1.3.2.1 Couples should be informed that stress in the male and/or female partner can affect the couple's relationship, and is likely to reduce libido and frequency of intercourse which can contribute to fertility problems. **C**

1.3.2.2 People who experience fertility problems should be informed that they may find it helpful to contact a fertility support group. **GPP**

1.3.2.3 People who experience fertility problems should be offered counselling because fertility problems themselves, and the investigation and treatment of fertility problems, can cause psychological stress. **C**

1.3.2.4 Counselling should be offered before, during and after investigation and treatment, irrespective of the outcome of these procedures. **GPP**

1.3.2.5 Counselling should be provided by someone who is not directly involved in the management of the couple's fertility problems. **GPP**

1.3.3 Specialist and generalist care

1.3.3.1 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 patient satisfaction. **D**

1.4 Investigation of fertility problems and management strategies

1.4.1 Semen analysis

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

- volume: 2.0 ml or more
- liquefaction time: within 60 minutes
- pH: 7.2 or more
- sperm concentration: 20 million spermatozoa per ml or more
- total sperm number: 40 million spermatozoa per ejaculate or more
- motility: 50% or more motile (grades a* and b**) or 25% or more with progressive motility (grade a) within 60 minutes of ejaculation
- vitality: 75% or more live
- white blood cells: fewer than 1 million per ml
- morphology: 15% or 30%***

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

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

* Grade a: rapid progressive motility (sperm moving swiftly, usually in a straight line).
** Grade b: slow or sluggish progressive motility (sperm may be less linear in their progression).
*** Currently being reassessed by the World Health Organization. In the interim, the proportion of normal forms accepted by laboratories in the UK is either the earlier World Health Organization lower limit of 30% or 15% based on strict morphological criteria.

1.4.1.4 Repeat confirmatory tests should ideally be undertaken 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. **GPP**

1.4.2 Assessing ovulation

1.4.2.1 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. **B**

1.4.2.2 Women with regular menstrual cycles and more than 1 year's infertility can 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. **B**

1.4.2.3 Women with prolonged irregular menstrual cycles should be offered a blood test to measure serum progesterone. Depending on 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. **GPP**

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

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

1.4.2.6 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. **C**

1.4.2.7 Tests of ovarian reserve currently have limited sensitivity and specificity in predicting fertility. However, women who have high levels of gonadotrophins should be informed that they are likely to have reduced fertility. **C**

1.4.2.8 Women should be informed that the value of assessing ovarian reserve using Inhibin B is uncertain and is therefore not recommended. **C**

1.4.2.9 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. **C**

1.4.2.10 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. **B**

1.4.3 Screening for *Chlamydia trachomatis*

1.4.3.1 Before undergoing uterine instrumentation women should be offered screening for *Chlamydia trachomatis* using an appropriately sensitive technique. **B**

1.4.3.2 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. **C**

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

1.4.4 Assessing tubal damage

The results of semen analysis and assessment of ovulation should be known before a test for tubal patency is performed.

1.4.4.1 Women who are not known to have co-morbidities (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. **B**

1.4.4.2 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 co-morbidities. **A**

1.4.4.3 Women who are thought to have co-morbidities should be offered laparoscopy and dye so that tubal and other pelvic pathology can be assessed at the same time. **B**

1.4.5 Assessing uterine abnormalities

1.4.5.1 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. **B**

1.4.6 Post-coital testing of cervical mucus

1.4.6.1 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. **A**

1.5 Medical and surgical management of male factor fertility problems

1.5.1 Medical management

1.5.1.1 Men with hypogonadotrophic hypogonadism should be offered gonadotrophin drugs because these are effective in improving fertility. **B**

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

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

1.5.1.4 Men with leukocytes 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. **A**

1.5.2 Surgical management

1.5.2.1 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 in vitro fertilisation. **C**

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

1.5.3 Management of ejaculatory failure

1.5.3.1 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. **C**

1.6 Ovulation induction

Classification of ovulatory disorders

Anovulation and oligo-ovulation are ovulatory disorders that are estimated to cause 21% of female fertility problems. The World Health Organization classifies ovulation disorders into three groups.

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

1.6.1 Anti-oestrogens

1.6.1.1 Women with World Health Organization Group II ovulation disorders (hypothalamic pituitary dysfunction) such as polycystic ovary syndrome should be offered treatment with clomifene citrate (or tamoxifen) as the first line of treatment for up to 12 months because it is likely to induce ovulation. **A**

1.6.1.2 Women should be informed of the risk of multiple pregnancies associated with both clomifene citrate and tamoxifen. **B**

1.6.1.3 Women with unexplained fertility problems should be informed that clomifene citrate treatment increases the chance of pregnancy, but that this needs to be balanced by the possible risks of treatment, especially multiple pregnancy. **A**

1.6.1.4 Women undergoing treatment with clomifene citrate should be offered ultrasound monitoring during at least the first cycle of treatment to ensure that they receive a dose that minimises the risk of multiple pregnancy. **GPP**

1.6.2 Metformin

Metformin is not currently licensed for the treatment of ovulatory disorders in the UK.

1.6.2.1 Anovulatory women with polycystic ovary syndrome who have not responded to clomifene citrate and who have a body mass index of more than 25 should be offered metformin combined with clomifene citrate because this increases ovulation and pregnancy rates. **A**

1.6.2.2 Women prescribed metformin should be informed of the side effects associated with its use (such as nausea, vomiting and other gastrointestinal disturbances). **GPP**

1.6.3 Ovarian drilling

1.6.3.1 Women with polycystic ovary syndrome who have not responded to clomifene citrate should be offered laparoscopic ovarian drilling because it is as effective as gonadotrophin treatment and is not associated with an increased risk of multiple pregnancy. **A**

1.6.4 Gonadotrophin use in ovulation induction therapy for ovulatory disorders

1.6.4.1 Women with World Health Organization Group II ovulation disorders such as polycystic ovary syndrome who do not ovulate with clomifene citrate (or tamoxifen) can be offered treatment with gonadotrophins. Human menopausal gonadotrophin, urinary follicle-stimulating hormone and recombinant follicle-stimulating hormone are equally effective in achieving pregnancy and consideration should be given to minimising cost when prescribing. **A**

1.6.4.2 Women with World Health Organization Group II ovulation disorders such as polycystic ovary syndrome who ovulate with clomifene citrate but have not become pregnant after 6 months of treatment should be offered clomifene citrate-stimulated intra-uterine insemination. **A**

1.6.5 Gonadotrophin use during in vitro fertilisation treatment

1.6.5.1 Human menopausal gonadotrophin, urinary follicle-stimulating hormone and recombinant follicle-stimulating hormone are equally effective in achieving a live birth when used following pituitary down-regulation as part of in vitro fertilisation treatment. Consideration should be given to minimising cost when prescribing. **A**

1.6.6 Gonadotrophin-releasing hormone analogues in ovulation induction therapy

1.6.6.1 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. **A**

1.6.7 Gonadotrophin-releasing hormone analogues during in vitro fertilisation treatment

1.6.7.1 For pituitary down-regulation as part of in vitro fertilisation treatment, using gonadotrophin-releasing hormone agonist in addition to gonadotrophin stimulation facilitates cycle control and results in higher pregnancy rates than the use of gonadotrophins alone. The routine use of gonadotrophin-releasing hormone agonist in long protocols during in vitro fertilisation is therefore recommended. **A**

1.6.7.2 The use of gonadotrophin-releasing hormone antagonists is associated with reduced pregnancy rates and is therefore not recommended outside a research context. **A**

1.6.8 Growth hormone as an adjunct to ovulation induction therapy

1.6.8.1 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. **A**

1.6.9 Pulsatile gonadotrophin-releasing hormone

1.6.9.1 Women with World Health Organization Group I ovulation disorders (hypothalamic pituitary failure, characterised by hypothalamic amenorrhoea or hypogonadotrophic hypogonadism) should be offered pulsatile administration of gonadotrophin-releasing hormone or gonadotrophins with luteinising hormone activity because these are effective in inducing ovulation. **B**

1.6.9.2 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. **A**

1.6.10 Dopamine agonists

1.6.10.1 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. **A**

1.6.11 Monitoring ovulation induction during gonadotrophin therapy

1.6.11.1 Women who are offered ovulation induction with gonadotrophins should be informed about the risk of multiple pregnancy and ovarian hyperstimulation before starting treatment. **C**

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

1.6.12 Other risks and side effects associated with ovulation induction agents

1.6.12.1 Women who are offered ovulation induction should be informed that a possible association between ovulation induction therapy and ovarian cancer remains uncertain. Practitioners should confine the use of ovulation induction agents to the lowest effective dose and duration of use. **C**

1.7 Tubal and uterine surgery

1.7.1 Tubal microsurgery and laparoscopic tubal surgery

1.7.1.1 For women with mild tubal disease tubal surgery may be more effective than no treatment. In centres where appropriate expertise is available it may be considered as a treatment option. **D**

1.7.2 Tubal catheterisation or cannulation

1.7.2.1 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. **B**

1.7.3 Uterine surgery

1.7.3.1 Women with amenorrhoea who are found to have intra-uterine adhesions should be offered hysteroscopic adhesiolysis because this is likely to restore menstruation and improve the chance of pregnancy. **C**

1.8 Medical and surgical management of endometriosis

1.8.1 Medical management (ovarian suppression)

1.8.1.1 Medical treatment of minimal and mild endometriosis does not enhance fertility in subfertile women and should not be offered. **A**

1.8.2 Surgical ablation

1.8.2.1 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. **A**

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

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

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

1.9 Intra-uterine insemination

1.9.1 Couples with mild male factor fertility problems, unexplained fertility problems or minimal to mild endometriosis should be offered up to six cycles of intra-uterine insemination because this increases the chance of pregnancy. **A**

1.9.2 Where intra-uterine insemination is used to manage male factor fertility problems, ovarian stimulation should not be offered because it is no more clinically effective than unstimulated intra-uterine insemination and it carries a risk of multiple pregnancy. **A**

1.9.3 Where intra-uterine insemination is used to manage unexplained fertility problems, both stimulated and unstimulated intra-uterine insemination are more effective than no treatment. However, ovarian stimulation should not be offered, even though it is associated with higher pregnancy rates than unstimulated intra-uterine insemination, because it carries a risk of multiple pregnancy. **A**

1.9.4 Where intra-uterine insemination is used to manage minimal or mild endometriosis, couples should be informed that ovarian stimulation increases pregnancy rates compared with no treatment, but that the effectiveness of unstimulated intra-uterine insemination is uncertain. **A**

1.9.5 Where intra-uterine insemination is undertaken, single rather than double insemination should be offered. **A**

1.9.6 Where intra-uterine insemination is used to manage unexplained fertility problems, fallopian sperm perfusion for insemination (a large-volume solution, 4 ml) should be offered because it improves pregnancy rates compared with standard insemination techniques. **A**

1.10 Factors affecting the outcome of in vitro fertilisation treatment

1.10.1 Surgery for hydrosalpinges before in vitro fertilisation treatment

1.10.1.1 Women with hydrosalpinges should be offered salpingectomy, preferably by laparoscopy, before in vitro fertilisation treatment because this improves the chance of a live birth. **A**

1.10.2 Female age

1.10.2.1 Women should be informed that the chance of a live birth following in vitro fertilisation treatment varies with female age and that the optimal female age range for in vitro fertilisation treatment is 23–39 years. Chances of a live birth per treatment cycle are: **C**

- greater than 20% for women aged 23–35 years
- 15% for women aged 36–38 years
- 10% for women aged 39 years
- 6% for women aged 40 years or older.

The effectiveness of in vitro fertilisation treatment in women younger than 23 years is uncertain because very few women in this age range have in vitro fertilisation treatment.

1.10.3 Number of embryos to be transferred and multiple pregnancy

1.10.3.1 Couples should be informed that the chance of multiple pregnancy following in vitro fertilisation treatment depends on the number of embryos transferred per cycle of treatment. To balance the chance of a live birth and the risk of multiple pregnancy and its consequences, no more than two embryos should be transferred during any one cycle of in vitro fertilisation treatment. **C**

1.10.4 Number of previous treatment cycles

1.10.4.1 Couples should be informed that the chance of a live birth following in vitro fertilisation treatment is consistent for the first three cycles of treatment, but that the effectiveness after three cycles is less certain. **C**

1.10.5 Pregnancy history

1.10.5.1 Women should be informed that in vitro fertilisation treatment is more effective in women who have previously been pregnant and/or had a live birth. **C**

1.10.6 Alcohol, smoking and caffeine consumption

1.10.6.1 Couples should be informed that the consumption of more than one unit of alcohol per day reduces the effectiveness of assisted reproduction procedures, including in vitro fertilisation treatment. **C**

1.10.6.2 Couples should be informed that maternal and paternal smoking can adversely affect the success rates of assisted reproduction procedures, including in vitro fertilisation treatment. **C**

1.10.6.3 Couples should be informed that caffeine consumption has adverse effects on the success rates of assisted reproduction procedures, including in vitro fertilisation treatment. **C**

1.10.7 Body weight

1.10.7.1 Women should be informed that female body mass index should ideally be in the range 19–30 before commencing assisted reproduction, and that a female body mass index outside this range is likely to reduce the success of assisted reproduction procedures. **B**

1.10.8 Clinical effectiveness and referral for in vitro fertilisation treatment

1.10.8.1 Couples in which the woman is aged 23–39 years at the time of treatment and who have an identified cause for their fertility problems (such as azoospermia or bilateral tubal occlusion) or who have infertility of at least 3 years' duration should be offered up to three stimulated cycles of in vitro fertilisation treatment. **GPP**

1.10.8.2 Embryos not transferred during a stimulated in vitro fertilisation treatment cycle may be suitable for freezing. If two or more embryos are frozen then they should be transferred before the next stimulated treatment cycle because this will minimise ovulation induction and egg collection, both of which carry risks for the woman and use more resources. **GPP**

1.10.9 Gamete intrafallopian transfer and zygote intrafallopian transfer

1.10.9.1 There is insufficient evidence to recommend the use of gamete intrafallopian transfer or zygote intrafallopian transfer in preference to in vitro fertilisation in couples with unexplained fertility problems or male factor fertility problems. **A**

1.11 Procedures used during in vitro fertilisation treatment

The Human Fertilisation and Embryology Act 1990 (HFE Act) requires that any fertility clinic in the UK offering licensed treatment services, such as in vitro fertilisation or use of donated gametes, must take account of the welfare of the potential child (including the determination of who will have parental responsibility for the child), and of any other existing children who may be affected by the birth, before treatment. Details on the issues of assessment of people seeking treatment, confidentiality, information, consent and counselling are referred to the Human Fertilisation and Embryology (HFEA) Code of Practice.

1.11.1 Medical assessment and screening

1.11.1.1 People undergoing in vitro fertilisation treatment should be offered screening for HIV, hepatitis B virus and hepatitis C virus; people found to test positive should be managed and counselled appropriately. **B**

1.11.2 Management of couples with viral infections

1.11.2.1 In considering the decision to provide fertility treatment for couples with HIV, hepatitis B or hepatitis C infections the implications of these infections for potential children should be taken into account. **D**

1.11.3 Ovulation induction during in vitro fertilisation treatment

Sections 1.6.5 to 1.6.8 also relate to ovulation induction during in vitro fertilisation treatment.

1.11.3.1 Natural cycle in vitro fertilisation has lower pregnancy rates per cycle of treatment than clomifene citrate-stimulated and gonadotrophin-stimulated in vitro fertilisation and is therefore not recommended, except in the rare circumstances where gonadotrophin use is contraindicated. **A**

1.11.3.2 For women who have regular ovulatory cycles, the likelihood of a live birth after replacement of frozen-thawed embryos is similar whether the embryos are replaced during natural or stimulated cycles. **B**

1.11.3.3 The use of adjuvant growth hormone with gonadotrophins during in vitro fertilisation cycles does not improve pregnancy rates and is therefore not recommended. **A**

1.11.4 Oocyte maturation – human chorionic gonadotrophin

1.11.4.1 Couples should be informed that, in effecting oocyte maturation, recombinant human chorionic gonadotrophin achieves similar results to urinary human chorionic gonadotrophin in terms of pregnancy rates and incidence of ovarian hyperstimulation syndrome. Consideration should be given to minimising cost when prescribing. **A**

1.11.5 Monitoring of stimulated cycles

1.11.5.1 Ultrasound monitoring of ovarian response should form an integral part of the in vitro fertilisation treatment cycle. **C**

1.11.5.2 Monitoring oestrogen levels during ovulation induction as part of in vitro fertilisation treatment is not recommended as a means of improving in vitro fertilisation treatment success rates because it does not give additional information with regard to live birth rates or pregnancy rates compared with ultrasound monitoring. **A**

1.11.6 Ovarian hyperstimulation syndrome

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

1.11.6.2 Women who have a significant risk of developing ovarian hyperstimulation syndrome should not be offered oocyte maturation (or luteal support) using human chorionic gonadotrophin. **A**

1.11.7 Oocyte retrieval

1.11.7.1 Women undergoing transvaginal retrieval of oocytes should be offered conscious sedation because it is a safe and acceptable method of providing analgesia. **A**

1.11.7.2 The safe practice of administering sedative drugs published by the Academy of Medical Royal Colleges should be followed. **D**

1.11.7.3 Women who have developed at least three 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. **A**

1.11.8 Assisted hatching

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

1.11.9 Embryo transfer techniques

1.11.9.1 Women undergoing in vitro fertilisation treatment should be offered ultrasound-guided embryo transfer because this improves pregnancy rates. **A**

1.11.9.2 Embryo transfers on day 2 or 3 and day 5 or 6 appear to be equally effective in terms of increased pregnancy and live birth rates per cycle started. **B**

1.11.9.3 Replacement of embryos into a uterine cavity with an endometrium of less than 5 mm thickness is unlikely to result in a pregnancy and is therefore not recommended. **B**

1.11.9.4 Women should be informed that bed rest of more than 20 minutes' duration following embryo transfer does not improve the outcome of in vitro fertilisation treatment. **A**

1.11.10 Luteal support

1.11.10.1 Women who are undergoing in vitro fertilisation treatment using gonadotrophin-releasing hormone agonists for pituitary down-regulation should be informed that luteal support using human chorionic gonadotrophin or progesterone improves pregnancy rates. **A**

1.11.10.2 The routine use of human chorionic gonadotrophin for luteal support is not recommended because of the increased likelihood of ovarian hyperstimulation syndrome. **A**

1.12 Intracytoplasmic sperm injection

1.12.1 Indications for intracytoplasmic sperm injection

1.12.1.1 The recognised indications for treatment by intracytoplasmic sperm injection include: **B**

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

In addition, treatment by intracytoplasmic sperm injection should be considered for couples in whom a previous in vitro fertilisation treatment cycle has resulted in failed or very poor fertilisation.

1.12.2 Genetic issues and counselling

1.12.2.1 Before considering treatment by intracytoplasmic sperm injection, couples should undergo appropriate investigations, both to establish a diagnosis and to enable informed discussion about the implications of treatment. **C**

1.12.2.2 Before treatment by intracytoplasmic sperm injection, consideration should be given to relevant genetic issues. **B**

1.12.2.3 Where a specific genetic defect associated with male infertility is known or suspected couples should be offered appropriate genetic counselling and testing. **B**

1.12.2.4 Where the indication for intracytoplasmic sperm injection is a severe deficit of semen quality or non-obstructive azoospermia, the man's karyotype should be established. **B**

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

1.12.2.6 Testing for Y chromosome microdeletions should not be regarded as a routine investigation before intracytoplasmic sperm injection. 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. **C**

1.12.3 Intracytoplasmic sperm injection versus in vitro fertilisation

1.12.3.1 Couples should be informed that intracytoplasmic sperm injection improves fertilisation rates compared to in vitro fertilisation alone, but once fertilisation is achieved the pregnancy rate is no better than with in vitro fertilisation. **A**

1.12.4 Sperm recovery

1.12.4.1 Surgical sperm recovery before intracytoplasmic sperm injection may be performed using several different techniques depending on the pathology and wishes of the patient. In all cases, facilities for cryopreservation of spermatozoa should be available. **C**

1.13 Donor insemination

1.13.1 Indications for donor insemination

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

- obstructive azoospermia
- non-obstructive azoospermia
- infectious disease in the male partner (such as HIV)
- severe rhesus isoimmunisation
- severe deficits in semen quality in couples who do not wish to undergo intracytoplasmic sperm injection.

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

1.13.2 Information and counselling

1.13.2.1 Couples should be offered information about the relative merits of intracytoplasmic sperm injection and donor insemination in a context that allows equal access to both treatment options. **C**

1.13.2.2 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. **C**

1.13.3 Screening of sperm donors

1.13.3.1 Units undertaking semen donor recruitment and the cryopreservation of donor spermatozoa for treatment purposes should follow the current guidelines issued by the British Andrology Society describing the selection and screening of donors. **C**

1.13.3.2 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. **GPP**

1.13.4 Assessment of the female partner

1.13.4.1 Before starting treatment by donor insemination 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. **C**

1.13.4.2 Women with no risk factors in their history should be offered tubal assessment after three cycles if treatment has been unsuccessful. **GPP**

1.13.5 Intra-uterine insemination versus intra-cervical insemination

1.13.5.1 Couples using donor sperm should be offered intra-uterine insemination in preference to intra-cervical insemination because it improves pregnancy rates. **A**

1.13.6 Unstimulated versus stimulated donor insemination

1.13.6.1 Women who are ovulating regularly should be offered a minimum of six cycles of donor insemination without ovarian stimulation to reduce the risk of multiple pregnancy and its consequences. **GPP**

1.13.7 Timing of donor insemination

1.13.7.1 Couples should be informed that timing of insemination using either urinary luteinising hormone or basal body temperature changes is equally effective in donor cycles. However, using urinary luteinising hormone detection reduces the number of clinic visits per cycle. **C**

1.13.8 Maximum number of cycles

1.13.8.1 Couples should be offered other treatment options after six unsuccessful cycles of donor insemination. **GPP**

1.14 Oocyte donation

1.14.1 Indications for oocyte donation

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

- premature ovarian failure
- gonadal dysgenesis including Turner syndrome
- bilateral oophorectomy
- ovarian failure following chemotherapy or radiotherapy
- certain cases of in vitro fertilisation 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.

1.14.2 Screening of oocyte donors

1.14.2.1 Before donation is undertaken, oocyte donors should be screened for both infectious and genetic diseases in accordance with guidance issued by the Human Fertilisation and Embryology Authority. **D**

1.14.3 Oocyte donation and egg sharing

1.14.3.1 Oocyte donors should be offered information regarding the potential risks of ovarian stimulation and oocyte collection. Section 1.6.12 refers to risks and side effects associated with ovarian stimulation. **C**

1.14.3.2 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. **GPP**

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

1.15 Applications of cryopreservation in cancer treatment

1.15.1 Before commencing chemotherapy or radiotherapy likely to affect fertility, or management of post-treatment fertility problems, the procedures recommended by the Royal College of Physicians and the Royal College of Radiologists should be followed. **D**

1.15.2 Men and adolescent boys preparing for medical treatment that is likely to make them infertile should be offered semen cryostorage because the effectiveness of this procedure has been established. **B**

1.15.3 Local protocols should exist to ensure that health professionals are aware of the value of semen cryostorage in these circumstances, so that they deal with the situation sensitively and effectively. **C**

1.15.4 Women preparing for medical treatment that is likely to make them infertile should be offered oocyte or embryo cryostorage as appropriate if they are well enough to undergo ovarian stimulation and egg collection, provided that this will not worsen their condition and that sufficient time is available. **C**

1.15.5 Women preparing for medical treatment that is likely to make them infertile should be informed that oocyte cryostorage has very limited success, and that cryopreservation of ovarian tissue is still in an early stage of development. **D**

1.15.6 People preparing for medical treatment that is likely to make them infertile should be offered counselling from someone who is independent of the treatment unit to help them cope with the stress and the potential physical and psychological implications for themselves, their partners and any potential children resulting from cryostorage of gametes and/or embryos. **GPP**

1.15.7 Where cryostorage of gametes and/or embryos is to be undertaken because of medical treatment that is likely to make people infertile, this should occur before such treatment begins. **GPP**

1.16 Follow-up of children born as a result of assisted reproduction

1.16.1 Couples contemplating assisted reproduction should be given up-to-date information about the health of children born as a result of assisted reproduction. Current research is broadly reassuring about the health and welfare of children born as a result of assisted reproduction. **C**

2 Notes on the scope of the guidance

All NICE guidelines are developed in accordance with a scope document that defines what the guideline will and will not cover. The scope of this guideline was established at the start of the development of this guideline, following a period of consultation; it is available from www.nice.org.uk/Docref.asp?d=26649

The guideline offers best practice advice on the care of people in the reproductive age group who perceive problems in conceiving and is relevant to primary, secondary and tertiary healthcare professionals who have direct contact with and make management decisions concerning the care of infertile and subfertile people.

The guideline addresses optimal lower and upper age ranges for treatment and offers advice on the management of people with a known condition or reason for their fertility problems, for example, prior treatment for cancer, HIV or a genetic condition. It includes recommendations on the diagnostic, medical and surgical management of people throughout all stages of their care in primary, secondary and tertiary care settings.

The guideline does not include the primary prevention of infertility, the management of pregnancies after fertility treatment, pre-implantation genetic diagnosis, the management of multiple births, or the management and treatment of conditions found during the investigation of subfertility that are not directly related to the problem. The management of co-morbidities is covered only where they relate to the treatment of subfertility. The guideline does not address laboratory standards or social criteria for treatment (for example, whether it is single women or same-sex couples who are seeking treatment, or whether either partner in a couple already has children).

The link to the costing template on this page is incorrect. To view the costing template, go to http://guidance.nice.org.uk/CG11/CostingTemplate/xls/English

3 Implementation in the NHS

3.1 Resource implications

Information on the cost impact of this guideline is available on the NICE website and includes a template for local health communities to use ~~(www.nice.org.uk/CGcosttemplate)~~. In light of this information, local health communities should review their existing practice for assessment and treatment for people with fertility problems against this guideline as they develop their Local Delivery Plans. The review should consider the resources required to implement the recommendations set out in Section 1, the people and processes involved and the timeline over which full implementation is envisaged. It is in the interests of people with fertility problems, and their partners, that the implementation timeline is as rapid as possible.

3.2 In general

Relevant local clinical guidelines, care pathways and protocols should be reviewed in the light of this guidance and revised accordingly. The following guidance is referred to in the recommendations set out in Section 1.

Academy of Medical Royal Colleges (2001) Implementing and ensuring safe sedation for healthcare procedures in adults: report of an Intercollegiate Working Party chaired by the Royal College of Anaesthetists (see www.aomrc.org.uk).

British Andrology Society (1999). British Andrology Society guidelines for the screening of semen donors for donor insemination. *Human Reproduction* **14**, 1823–26 (see www.britishandrology.org.uk).

Human Fertilisation and Embryology Authority (2004). Code of Practice, 6th edition (see www.hfea.gov.uk).

Royal College of Physicians and Royal College of Radiologists (1998). Management of gonadal toxicity resulting from the treatment of adult cancer: report of a working party of the Joint Council for Clinical Oncology. Joint Council for Clinical Oncology (see www.rcplondon.ac.uk).

3.3 Audit

Suggested audit criteria are listed in Appendix D. These can be used as the basis for local clinical audit, at the discretion of those in practice.

4 Research recommendations

Despite an abundance of scientific literature which addresses the management of people with fertility problems, there is a scarcity of robust evidence to answer important research questions, due to the serious limitations inherent in the design of these studies. Future research should focus on improved methodology including case definition, outcome measures, randomisation, power calculation, analysis, follow up and resource use based on the UK population. The research recommendations below have been identified for this NICE guideline, not as the most important research recommendations, but as those that are most representative of the full range of recommendations. In each case, the clinical and cost effectiveness of interventions need further evaluation.The Guideline Development Group's full set of research recommendations is detailed in the full guideline produced by the National Collaborating Centre for Women's and Children's Health (see Section 5).

4.1 Further research to assess the long-term psychological impact of investigation and treatment of people who perceive problems with their fertility, both in people who subsequently achieve a live birth and people who do not.

4.2 Further research to assess the long-term health effects of ovulation induction agents on women who have undergone ovulation induction therapy for their fertility problems.

4.3 Research to define semen quality criteria for assisted reproduction to be effective in the management of male infertility.

4.4 Further research to determine the relative effectiveness of intra-uterine insemination and in vitro fertilisation in couples with unexplained fertility problems.

4.5 Further research to improve embryo selection to facilitate single embryo transfers.

4.6 Long-term longitudinal follow-up of children resulting from assisted reproduction. This research should focus on physical, genetic, psychological and social development, and it should be coordinated on a national basis.

5 Full guideline

The National Institute for Clinical Excellence commissioned the development of this guidance from the National Collaborating Centre for Women's and Children's Health. The Centre established a Guideline Development Group, which reviewed the evidence and developed the recommendations. The full guideline, *Fertility: assessment and treatment for people with fertility problems*, is published by the National Collaborating Centre for Women's and Children's Health; it is available on its website (www.rcog.org.uk/mainpages.asp?PageID=117), the NICE website (www.nice.org.uk) and on the website of the National Electronic Library for Health (www.nelh.nhs.uk).

The members of the Guideline Development Group are listed in Appendix B. Information about the independent Guideline Review Panel is given in Appendix C.

The booklet *The Guideline Development Process – Information for the Public and the NHS* has more information about the Institute's guideline development process. It is available from the Institute's website and copies can also be ordered by telephoning 0870 1555 455 (quote reference N0038).

6 Related NICE guidance

There is no related NICE guidance for this topic.

7 Review date

The process of reviewing the evidence is expected to begin 4 years after the date of issue of this guideline. Reviewing may begin earlier than 4 years if significant evidence that affects the guideline recommendations is identified sooner. The updated guideline will be available within 2 years of the start of the review process.

A version of this guideline for people with fertility problems, their partners and the public is available from the NICE website (www.nice.org.uk) or from NHS Response Line (0870 1555 455; quote reference number N0466 for an English version and N0467 for an English and Welsh version).

Appendix A: Grading scheme

The grading scheme and hierarchy of evidence used in this guideline (see Table) is adapted from Eccles and Mason (2001).

Recommendation grade	**Evidence**
A	Directly based on category I evidence
B	Directly based on: • category II evidence, **or** • extrapolated recommendation from category I evidence
C	Directly based on: • category III evidence, **or** • extrapolated recommendation from category I or II evidence
D	Directly based on: • category IV evidence, **or** • extrapolated recommendation from category I, II, or III evidence
Good practice point (GPP)	The view of the Guideline Development Group
Evidence category	**Source**
I	Evidence from: • meta-analysis of randomised controlled trials, **or** • at least one randomised controlled trial
II	Evidence from: • at least one controlled study without randomisation, **or** • at least one other type of quasi-experimental study
III	Evidence from non-experimental descriptive studies, such as comparative studies, correlation studies and case-control studies
IV	Evidence from expert committee reports or opinions and/or clinical experience of respected authorities
Adapted from Eccles M, Mason J (2001) How to develop cost-conscious guidelines. *Health Technology Assessment* **5** (16)	

Appendix B: The Guideline Development Group

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Appendix C: The Guideline Review Panel

The Guideline Review Panel is an independent panel that oversees the development of the guideline and takes responsibility for monitoring its quality. The Panel includes experts on guideline methodology, health professionals and people with experience of the issues affecting patients and carers. The members of the Guideline Review Panel were as follows.

Miss Helen Spiby (Chair)
Senior Lecturer (evidence-based practice in midwifery),
Mother and Infant Research Unit, University of Leeds

Mrs Carol Youngs
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Dr Monica Lakhanpaul
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Mr Vincent Argent
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Dr Jenny Tyrell
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Mrs Christine Oppenheimer
Consultant in Obstetrics and Gynaecology,
Leicester Royal Infirmary, and Honorary Senior Lecturer in
Medical Education, University of Leicester

Appendix D: Technical detail on the criteria for audit

Measures that could be used as a basis for an audit

One or more audits could be carried out on the investigation and management of fertility problems. In vitro fertilisation treatment is one of several assisted reproduction techniques regulated by the HFEA, and all cycles of in vitro fertilisation treatment are registered with the HFEA. Thus, HFEA records would form one potential source of data for monitoring compliance with recommendations relating to in vitro fertilisation treatment (see table overleaf).

Outcomes of treatment (for example, the proportion of cycles of in vitro fertilisation treatment that result in a live birth) as well as offers of treatment could also be used for audit purposes.

Criterion	Standard	Exception	Definition of terms
1. Percentage of women with documented offer of screening for *Chlamydia trachomatis* before undergoing uterine instrumentation	100%	Women currently being treated for *Chlamydia trachomatis*	Screening for *Chlamydia trachomatis* using an appropriately sensitive technique
2. Percentage of women without pelvic inflammatory disease, previous ectopic pregnancy or endometriosis with documented offer of hysterosalpingography (HSG)	100%	Women with pelvic inflammatory disease, previous ectopic pregnancy or endometriosis	
3. Percentage of couples with mild male factor fertility problems, unexplained fertility problems or minimal to mild endometriosis with documented offer of up to six cycles of intra-uterine insemination	100%	Couples with severe male factor fertility problems or moderate to severe endometriosis	

continued

Criterion	Standard	Exception	Definition of terms
4. Number of couples in which the woman is aged 23–39 years at the time of treatment who have an identified cause for their fertility problems or who have infertility of at least 3 years' duration and who have a documented offer of up to three stimulated cycles of in vitro fertilisation treatment	100%	Women aged younger than 23 years or older than 39 years at the time of treatment	Identified causes for fertility problems include azoospermia and bilateral tubal occlusion
5. Number of embryos transferred during any one treatment cycle in women undergoing in vitro fertilisation treatment registered by the Human Fertilisation and Embryology Authority	No more than two embryos transferred in any one cycle	Women not undergoing in vitro fertilisation treatment	

Calculation of compliance

Compliance (%) with each measure described in the table above is calculated as follows.

$$\frac{\text{Number of patients whose care is consistent with the } \textbf{criterion } \textbf{\textit{plus}} \text{ number of patients who meet any } \textbf{exception} \text{ listed}}{\text{Number of patients to whom the } \textbf{measure} \text{ applies}} \times 100$$

Clinicians should review the findings of measurement, identify whether practice can be improved, agree on a plan to achieve any desired improvement and repeat the measurement of actual practice to confirm that the desired improvement is being achieved.

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