

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Guideline scope

Fertility problems (update)

This guideline will update and replace the NICE guideline on fertility problems: assessment and treatment (CG156).

The guideline will be developed using the methods and processes outlined in [developing NICE guidelines: the manual](#).

This guideline will also be used to update the [NICE quality standard for fertility problems](#).

1 Purpose of the guideline

The purpose of this guideline is to make recommendations on the management of health-related fertility problems, which include diseases of the reproductive system and any other health problems that reduce or limit the ability to have children, including the need for fertility preservation. As part of this, it will include criteria for what constitutes sufficient evidence of health-related fertility problems to access further services, such as referral for in vitro fertilisation (IVF). There are known complexities around access and funding in this area – in particular where some people may have had to self-fund initial treatments to demonstrate a health-related fertility problem in order to access further care. As part of the [Women's Health Strategy for England](#), the Department for Health and Social Care has committed to removing non-clinical access criteria for fertility treatment, and the requirement for self-funding for initial treatments, particularly in relation to female same-sex couples.

This guideline will not make recommendations on funding arrangements to demonstrate a health-related fertility problem.

1 ***Why the update is needed***

2 New evidence that could affect recommendations was identified through the
3 surveillance and scoping process. Topic experts and stakeholders advised
4 NICE on areas that should be updated or new areas that should be added.

5 ***Why the guideline is needed***

6 **Key facts and figures**

7 It is estimated that 1 in 6 couples in the UK need specialist help to conceive
8 after trying for more than 2 years ([Hull et al. 1985](#), [Templeton et al. 1990](#)).
9 90% of fertility treatment is for heterosexual couples, 6.4% of treatments are
10 for same-sex couples and 3.2% are for single people ([HFEA, 2018](#)).

11 The main causes of fertility problems are female factors such as ovulatory
12 disorders (21%), tubal damage (14%) and endometriosis (6%) ([Hull et al.](#)
13 [1985](#)). Male factors account for 26% of fertility problems and are mainly due to
14 issues with sperm production or sperm delivery, including poor quality semen,
15 testicular problems, ejaculation disorders, or hypogonadism, although in up to
16 70% of male factor cases the cause may be unknown ([Babakhanzadeh et al.](#)
17 [2020](#)). It is common to find both female and male factor fertility problems. In
18 about 25% of cases, investigations do not reveal a defined cause of fertility
19 problems; this is called unexplained fertility problems ([NHS, 2022](#)).

20 **Current practice**

21 In England, decisions about providing and accessing fertility services within
22 the NHS are made locally by Integrated Care Boards. The existing NICE
23 guidance has not been uniformly implemented. There is a lot of variation
24 between different geographical areas, both in relation to who gets access to
25 fertility services and how much is offered (for example the number of
26 treatment cycles). Almost 59,000 people received IVF cycles in the UK in
27 2019 ([HFEA 2021a](#)) but most of these were not NHS funded. In addition, the
28 [Human Fertilisation and Embryology Authority \(HFEA\)](#) has documented
29 disparities in the outcomes of fertility treatments between different ethnic
30 groups, although reasons for these are uncertain ([HFEA 2021b](#)).

Preserving fertility is also an increasingly common part of fertility services' work. Requests can come from people starting cancer treatment and those with specific health conditions or about to undergo interventions which have a significant risk of reducing fertility.

This guideline update aims to provide an evidence-based resource for healthcare professionals:

- recognising the range of clinical situations where investigations and treatment are needed for health-related fertility problems and
- the variety of settings where these may take place, including HFEA-licensed private clinics providing NHS funded care.

2 Who the guideline is for

This guideline is for:

- commissioners of NHS fertility services
- providers of NHS commissioned fertility services, including HFEA-licensed private clinics
- people using fertility services, their families and carers, and the public.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the [Welsh Government](#), [Scottish Government](#), and [Northern Ireland Executive](#).

Equality considerations

NICE has carried out [an equality impact assessment](#) [add hyperlink in final version] during scoping. The assessment:

- lists equality issues identified, and how they have been addressed
- explains why any groups are excluded from the scope.

3 What the guideline will cover

3.1 *Who is the focus?*

Groups that will be covered in the update

- People with health-related fertility problems
- People who may require interventions to preserve fertility because of high risk of fertility problems due to clinical conditions or medical or surgical interventions

In this guideline, people with health-related fertility problems are those who have a known health-related impediment to fertility, or those who do not achieve a pregnancy:

- after 12 months of regular unprotected sexual intercourse or
- after 6 cycles of artificial insemination.

The guideline will be applicable to all people seeking assessment and treatment of health-related fertility problems who meet these criteria, irrespective of their sexual orientation, partnership status or gender reassignment. This includes single people, people in heterosexual relationships, people in same sex relationships, people who are non-binary, undergoing or have undergone gender transition and people using a surrogate.

3.2 *Settings*

Settings that will be covered

All settings where NHS-commissioned health-related fertility advice or treatment is provided including primary, secondary and tertiary settings, and HFEA-licensed private clinics.

3.3 *Activities, services or aspects of care*

Key areas that will be covered in the update

We will look at evidence in the areas below when developing this update. The guideline may be developed in a staggered approach in which sections 1 to 4 are developed and published one at a time, not necessarily in the order they appear below.

1 Male factor fertility problems

1.1 Investigations for male factor fertility problems

1.2 Treatments for male factor fertility problems

1.3 Surgical sperm retrieval

2 Female factor fertility problems

2.1 Investigations for female factor fertility problems

2.2 Treatments for female factor fertility problems

3 Assisted reproduction techniques (ART)

3.1 Predictive factors and models for the success of assisted reproduction techniques (ART) to inform recommendations on criteria for access to treatments

3.2 Ovarian stimulation and intrauterine insemination (IUI) for unexplained fertility problems

3.3 Intrauterine insemination (IUI)

3.4 Intracytoplasmic sperm injection (ICSI) in non-male factor fertility problems

3.5 Fertility treatment add-ons

3.6 Embryo transfer strategies

3.7 Frozen embryo transfer

3.8 Safety of assisted reproductive technologies (ART) for people with fertility problems and their children conceived through ART

4 Preservation of fertility

4.1 Effectiveness and safety of fertility preservation

Areas that will not be covered in the guideline

1 The management of recurrent miscarriage

1 2 The medical and surgical management of endometriosis

2 **Proposed outline for the guideline**

3 The table below outlines all the areas that will be included in the guideline. It
4 sets out what NICE plans to do for each area in this update.

5 Recommendations in areas that are being retained from the existing guideline
6 may be edited to ensure that they meet current editorial standards, and reflect
7 the current policy and practice context.

Area in the guideline	What NICE plans to do
1.1 Principles of care	<p>No evidence reviews: retain recommendations from sections 1.1.1 'Providing information', 1.1.2 'Psychological effects of fertility problems' and 1.1.3 'Generalist and specialist care' of the existing guideline, as appropriate.</p> <p>The guideline may cross-refer to information resources from the HFEA.</p>
1.2 Initial advice to people concerned about delays in conception	<p>No evidence reviews: retain recommendations from section 1.2 'Initial advice to people concerned about delays in conception' of the existing guideline, as appropriate.</p> <p>The guideline may cross-refer to existing NICE guidance, as appropriate, such as:</p> <ul style="list-style-type: none"> • Maternal and child nutrition: nutrition in pregnant women, and nutrition in women and children up to 5 years (2008, update in progress, publication expected November 2023; relevant areas: preconception care in relation to folic acid supplementation) • Weight Management: preventing, assessing and managing overweight and obesity (update in development, publication expected June 2023) • Tobacco: preventing uptake, promoting quitting and treating dependence (2021).

Area in the guideline	What NICE plans to do
1.3 Investigations of fertility problems and management strategies	<p>No evidence reviews and retain recommendations from section 1.3 'Investigations of fertility problems and management strategies' of the existing guideline on the following topics:</p> <ul style="list-style-type: none"> 1.3.1 'Semen analysis' 1.3.2 'Post-coital testing of cervical mucus' 1.3.4 'Regularity of menstrual cycles' 1.3.5 'Prolactin measurement' 1.3.8 'Investigation of suspected tubal and uterine abnormalities' (but will consider editorial amendment to include ultrasound as an investigation technique) 1.3.9 'Testing for viral status' 1.3.10 'Viral transmission' (but will consider cross-reference to updated British HIV association guidelines on Sexual and Reproductive Health). 1.3.11 'Susceptibility to rubella' 1.3.12 'Cervical cancer screening' 1.3.13 'Screening for Chlamydia trachomatis'. <p>Recommendation in section 1.3.7 'Endometrial biopsy' will be stood down because it is not part of current clinical practice (subject to committee's review).</p> <p>Review evidence and update existing recommendations in section 1.3 'Investigations of fertility problems and management strategies' as needed and add new recommendations, as appropriate, on:</p> <ul style="list-style-type: none"> 1.3.3 'Ovarian reserve testing' 1.3.6 'Thyroid function tests' 1.3.8.4 hysteroscopy • endometrial receptivity testing (new area in the guideline). <p>Review evidence and add new recommendations on the following topics (new areas in the guideline), as appropriate:</p> <ul style="list-style-type: none"> • hormone profile • testicular biopsy • imaging studies • genetic studies. <p>For reference limits of semen characteristics, the guideline may also cross-refer to other sources and update existing recommendations in line with these, for example, the WHO laboratory manual for the examination and processing of human semen.</p> <p>The guideline may cross-refer to recommendation 1.1.2 in the NICE guideline on coeliac disease: recognition, assessment and management (2015).</p>

Area in the guideline	What NICE plans to do
1.4 Medical and surgical management of male factor fertility problems	<p>Review evidence and update existing recommendations in section 1.4.1 'Medical management (male factor infertility)' and 1.4.3 'Management of ejaculatory failure' as needed and add new recommendations, as appropriate, on:</p> <ul style="list-style-type: none"> • hormone treatment • treatments for ejaculatory failure. <p>Review evidence and update existing recommendations in section 1.4.2 'Surgical management (male factor infertility)' as needed and add new recommendations, as appropriate, on:</p> <ul style="list-style-type: none"> • surgical interventions for obstructions • treatments for varicocele. <p>The guideline may cross-refer to guidance from other developers, such as the European Association of Urologist (EAU) Guidelines on sexual and reproductive health, chapter 10: male infertility (2022).</p>
1.5 Ovulation disorders	<p>Review evidence and update existing recommendations in section 1.5 'Ovulation disorders' as needed and add new recommendations, as appropriate, on:</p> <ul style="list-style-type: none"> • ovulation induction strategies for ovulation disorders • cabergoline for fertility problems associated with hyperprolactinaemic amenorrhoea.
1.6 Tubal and uterine surgery	<p>Review evidence and update existing recommendations in section 1.6 'Tubal and uterine surgery' as needed and add new recommendations, as appropriate, on surgical interventions including tubal surgery and uterine surgery.</p> <p>The guideline will cross-refer to section surgical management if fertility is a priority in the NICE guidance on endometriosis: diagnosis and management (2017).</p>
1.7 Medical and surgical management of endometriosis	<p>This section of the guideline has been stood down as it has been superseded by the NICE guideline on endometriosis, and it will be removed.</p>
1.8 Unexplained fertility	<p>Review evidence and update existing recommendations in section 1.8 'Unexplained infertility' as needed and add new recommendations, as appropriate, on treatments for unexplained fertility problems including ovarian stimulation.</p>

Area in the guideline	What NICE plans to do
1.9 Intrauterine insemination	Review evidence and update existing recommendations in section 1.9 'Intrauterine insemination' as needed and add new recommendations, as appropriate, on treatments for unexplained fertility problems including intrauterine insemination (IUI).
1.10 Prediction of IVF success	<p>Review evidence and update existing recommendations in section 1.10 'Prediction of IVF success' as needed and add new recommendations as appropriate.</p> <p>Predictive factors and models for the success of assisted reproduction techniques (ART) to inform recommendations on criteria for access to treatments</p>
1.11 Access criteria for IVF	<p>Review evidence and update existing recommendations in section 1.11 'Access criteria for IVF' as needed and add new recommendations as appropriate.</p> <p>Predictive factors and models for the success of assisted reproduction techniques (ART) to inform recommendations on criteria for access to treatments</p>

Area in the guideline	What NICE plans to do
1.12 Procedures used during IVF treatment	<p>The guideline may cross-refer to guidance from other developers, such as the European Society of Human Reproduction and Embryology (ESHRE) guideline on ovarian stimulation for IVF/ICSI (2019). No evidence reviews: the recommendations in the following sections will be stood down, as appropriate:</p> <p>1.12.1 'Pre-treatment in IVF'</p> <p>1.12.2 'Down regulation and other regimens to avoid premature luteinising hormone surges in IVF'</p> <p>1.12.3 'Controlled ovarian stimulation in IVF'</p> <p>1.12.4 'Triggering ovulation in IVF'</p> <p>1.12.7 'Luteal phase support after IVF'</p> <p>Review evidence and update existing recommendations in section 1.12.5 'Oocyte and sperm retrieval in IVF' on sperm retrieval as appropriate.</p> <p>Review evidence and update existing recommendations in section 1.12.6 'Embryo transfer strategies' as needed and add new recommendations as appropriate.</p> <p>No evidence reviews and recommendations in section 1.12.8 'Gamete intrafallopian transfer and zygote intrafallopian transfer' will be stood down because they are not part of current clinical practice (subject to committee's review).</p> <p>Frozen embryo transfer: Review evidence; new area in guideline</p>
1.13 Intracytoplasmic sperm injection	Review evidence and update existing recommendations in section 1.13 'Intracytoplasmic sperm injection' as needed and add new recommendations as appropriate.
Fertility treatment add-ons	Review evidence: new area in the guideline.
1.14 Donor insemination	No evidence reviews and retain recommendations in section 1.14 'Donor insemination', as appropriate.
1.15 Oocyte donation	No evidence reviews and retain recommendations in section 1.15 'Oocyte donation', as appropriate.
1.16 People with cancer who wish to preserve fertility	Review evidence on fertility preservation for populations beyond those with cancer and update existing recommendations in section 1.16 'People with cancer who wish to preserve fertility' as needed and add new recommendations as appropriate.

Area in the guideline	What NICE plans to do
1.17 Long-term safety of assisted reproductive technologies (ART) for people with fertility problems and their children	Review evidence and update existing recommendations in section 1.17 'Long-term safety of assisted reproductive technologies for women with infertility and their children' as needed and add new recommendations as appropriate.

1

2 **Related NICE guidance**3 ***Published***

- 4 • [Ectopic pregnancy and miscarriage: diagnosis and initial management](#)
5 (2019) NICE guideline NG126
- 6 • [Tobacco: preventing uptake, promoting quitting and treating dependence](#)
7 (2021) NICE Guideline NG209
- 8 • [Endometriosis: diagnosis and management](#) (2017) NICE guideline NG73
- 9 • [Menopause: diagnosis and management](#) (2015) NICE guideline NG23
10 (currently being updated, publication date TBC)
- 11 • [Coeliac disease: recognition, assessment and management](#) (2015) NICE
12 guideline NG20
- 13 • [Hysteroscopic metroplasty of a uterine septum for primary infertility](#) (2015)
14 Interventional procedure guidance IPG509
- 15 • [Ovarian cancer: recognition and initial management](#) (2011) NICE guideline
16 CG122
- 17 • [Weight management before, during and after pregnancy](#) (2010) NICE
18 guideline PH27 (recommendations on weight management before
19 pregnancy are being incorporated to a guideline being developed on [weight](#)
20 [management: preventing, assessing and managing overweight and](#)
21 [obesity](#), publication expected June 2023)
- 22 • [Maternal and child nutrition: nutrition in pregnant women, and nutrition in](#)
23 [women and children up to 5 years](#) (2008) NICE guideline PH11 ([update in](#)
24 [progress](#), publication expected November 2023)
- 25 • [Uterine artery embolisation for fibroids](#) (2010) Interventional procedure
26 guidance IPG367
- 27 • [Fallopian tube recanalisation by guidewire](#) (2004) Interventional procedure
28 guidance IPG71

In development

- [Maternal and child nutrition](#) NICE guideline. Publication expected November 2023.
- [Ovarian cancer: Identifying and managing genetic and familial risk](#) NICE guideline. Publication expected March 2024.

NICE guidance about the experience of people using NHS services

NICE has produced the following guidance on the experience of people using the NHS. This guideline will not include additional recommendations on these topics unless there are specific issues related to fertility:

- [Shared decision making](#) (2021) NICE guideline NG197
- [Medicines optimisation](#) (2015) NICE guideline NG5
- [Patient experience in adult NHS services](#) (2012) NICE guideline CG138
- [Medicines adherence](#) (2009) NICE guideline CG76

3.4 Economic aspects

We will take economic aspects into account when making recommendations. We will develop an economic plan that states for each review question (or key area in the scope) whether economic considerations are relevant, and if so whether this is an area that should be prioritised for economic modelling and analysis. We will review the economic evidence and carry out economic analyses, using an NHS and personal social services (PSS) perspective, as appropriate.

3.5 Key issues and draft questions

While writing this scope, we have identified the following key issues where review of evidence is needed and draft review questions related to them.

1 Male factor fertility problems

1.1 Investigations for male factor fertility problems

1.1.1 What is the prevalence of diagnostic abnormalities in males with fertility problems when using the following techniques:

- hormone profile,

- 1 • testicular biopsy,
- 2 • imaging studies,
- 3 • genetic studies (karyotype, Y chromosome microdeletions, cystic
- 4 fibrosis)?

5 1.2 Treatments for male factor fertility problems

6 1.2.1 What is the effectiveness of hormone treatment in male factor
7 fertility problems?

8 1.2.2 What is the effectiveness of treatments for ejaculatory failure?

9 1.2.3 What is the effectiveness of surgical interventions for different
10 types of fertility problems associated with obstruction?

11 1.2.4 What is the effectiveness of treatments for fertility problems
12 associated with varicocele (including radiological embolisation and
13 surgery)?

14 1.3 Surgical sperm retrieval

15 1.3.1 What is the effectiveness of surgical sperm retrieval (SSR)
16 techniques in males with:

- 17 • non obstructive azoospermia,
- 18 • obstructive azoospermia?

19 2 Female factor fertility problems

20 2.1 Investigations for female factor fertility problems

21 2.1.1 What is the accuracy of ovarian reserve testing in predicting:

- 22 • the outcome of fertility treatment,
- 23 • the likelihood of spontaneous conception?

24 2.1.2 What is the effectiveness of treating hypothyroidism identified
25 through screening in improving outcomes in women with fertility
26 problems?

27 2.1.3 What is the effectiveness of hysteroscopy in improving outcomes
28 for women with fertility problems?

29 2.1.4 What is the value of endometrial receptivity (ERA) testing in
30 improving the chance of live birth in women undergoing in vitro
31 fertilisation (IVF)?

32 2.2 Treatments for female factor fertility problems

- 1 2.2.1 What is the effectiveness of ovulation induction strategies in
- 2 women with ovulation disorders (WHO groups I, II, III)?
- 3 2.2.2. What is the effectiveness of cabergoline for fertility problems
- 4 associated with hyperprolactinaemic amenorrhoea?
- 5 2.2.3 What is the effectiveness of surgical interventions including tubal
- 6 surgery and uterine surgery as treatment for fertility problems?
- 7 3 Assisted reproduction techniques (ART)
- 8 3.1 Predictive factors and models for the success of assisted reproduction
- 9 techniques (ART) to inform recommendations on criteria for access to
- 10 treatments
- 11 3.1.1 What factors or models predict success in fertility treatment using:
- 12 • intrauterine insemination (IUI),
- 13 • IVF with or without intracytoplasmic sperm injection (ICSI)?
- 14 3.2 Ovarian stimulation and intrauterine insemination (IUI) for unexplained
- 15 fertility problems
- 16 3.2.1 What is the effectiveness of ovarian stimulation or intrauterine
- 17 insemination (IUI), with or without ovarian stimulation, for unexplained
- 18 fertility problems?
- 19 3.3 Intrauterine insemination (IUI)
- 20 3.3.1 What is the effectiveness of intrauterine insemination (IUI)
- 21 compared with expectant management in people with mild endometriosis
- 22 or mild male factor fertility problems?
- 23 3.4 Intracytoplasmic sperm injection (ICSI) in non-male factor fertility problems
- 24 3.4.1 What is the effectiveness of intracytoplasmic sperm injection (ICSI)
- 25 versus standard in vitro fertilisation (IVF) in non-male factor fertility
- 26 problems?
- 27 3.5 Fertility treatment add-ons
- 28 3.5.1 What is the effectiveness of the following fertility treatment add-
- 29 ons:
- 30 • pre-implantation genetic testing for aneuploidy (PGT-A),
- 31 • timelapse imaging,
- 32 • intracytoplasmic morphologic sperm injection (IMSI),
- 33 • physiological intracytoplasmic sperm injection (PICS),

- 1 • immunological tests and treatments,
- 2 • endometrial scratch?

3 3.6 Embryo transfer strategies

4 3.6.1 What is the effectiveness and safety of different embryo or
5 blastocyst transfer strategies in relation to both:

- 6 • number of embryos (single versus double),
- 7 • timing of transfer (cleavage versus blastocyst stage)?

8 3.7 Frozen embryo transfer

9 3.7.1 What is the effectiveness and safety of different regimens of frozen
10 embryo transfer?

11 3.8 Safety of assisted reproductive technologies (ART) for people with fertility
12 problems and their children conceived through ART

13 3.8.1 What is the effect of ART on obstetric risk in women undergoing
14 fertility treatment?

15 3.8.2 What is the long-term safety of in vitro fertilisation (IVF) with or
16 without intracytoplasmic sperm injection (ICSI) in women with fertility
17 problems and their children conceived through ART?

18 4 Preservation of fertility

19 4.1 Effectiveness and safety of fertility preservation

20 4.1.1 What is the effectiveness and safety of fertility preservation for
21 children and adults undergoing treatment for cancer and other conditions
22 or situations which are likely to impair their fertility?

23 **3.6 Main outcomes**

24 The main outcomes that may be considered when searching for and
25 assessing the evidence are:

- 26 • live births
- 27 • gestational age
- 28 • birth weight
- 29 • patient satisfaction
- 30 • anxiety or depression
- 31 • multiple births
- 32 • fetal abnormalities

- adverse pregnancy outcome (ectopic pregnancy, miscarriage, fetal growth restriction, macrosomia, spontaneous preterm delivery, perinatal death, pre-eclampsia, and gestational diabetes)
- safety and long-term effects of specific fertility treatments
- health-related quality of life

4 NICE quality standards

4.1 NICE quality standards

NICE quality standards that may need to be revised or updated when this guideline is published

- [Fertility problems](#) (2014) NICE quality standard 73

5 Further information

The guideline is expected to be published in November 2024.

You can follow progress of the [guideline](#). Our website has information about how [NICE guidelines](#) are developed.

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