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2 **Guideline scope**

3 **Fertility problems (update)**

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

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

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

10 **1 Purpose of the guideline**

11 The purpose of this guideline is to make recommendations on the
12 management of health-related fertility problems, which would include both
13 diseases of the reproductive system and any other physical or mental health
14 problems that reduce or limit the ability to have children. As part of this, it may
15 include criteria for what constitutes sufficient evidence of health-related fertility
16 problems to access further services, such as referral for IVF. There are known
17 complexities around access and funding in this area – in particular where
18 some people may have had to self-fund initial treatments to demonstrate a
19 health-related fertility problem in order to access further care. As part of the
20 [Women's Health Strategy for England](#), the DHSC has committed to removing
21 non-clinical access criteria for fertility treatment, and the requirement for self-
22 funding for initial treatments, particularly in relation to female same-sex
23 couples.

24 This guideline will not make recommendations on funding arrangements for
25 the initial tests or procedures 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 whether areas should be updated or new areas added.

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

6 **Key facts and figures**

7 In this guideline, the term 'health-related fertility problems' covers failure to
8 achieve a pregnancy:

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

11 It is estimated that 1 in 6 heterosexual couples in the UK need specialist help
12 to conceive after trying for more than 2 years ([Hull et al. 1985](#), [Templeton et
13 al. 1990](#)). The main causes of female fertility problems are ovulatory disorders
14 (21%), tubal damage (14%) and endometriosis (6%). Male factors account for
15 26% of fertility problems. They are either due to issues with sperm production
16 or sperm delivery. It is common to find both female and male factor fertility
17 problems. In about 25% of cases, investigations do not reveal a defined cause
18 of fertility problems; this is called unexplained fertility problems.

19 **Current practice**

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

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

5 This guideline update aims to provide an evidence-based resource for
6 healthcare professionals, recognising the range of clinical situations where
7 investigations and treatment are needed for health-related fertility problems
8 and the variety of settings where these may take place, including HFEA-
9 licensed private clinics providing NHS funded care.

10 **2 Who the guideline is for**

11 This guideline is for:

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

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

19 ***Equality considerations***

20 NICE has carried out [an equality impact assessment](#) during scoping. The
21 assessment:

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

24 **3 What the guideline will cover**

25 **3.1 Who is the focus?**

26 **Groups that will be covered in the update**

- 27 • People with health-related fertility problems

- 1 • People who may require interventions to preserve fertility because of high
2 risk of fertility problems due to clinical conditions or medical or surgical
3 interventions

4 **3.2 Settings**

5 **Settings that will be covered**

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

9 **3.3 Activities, services or aspects of care**

10 **Key areas that will be covered in the update**

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

15 1 Male factor fertility problems

16 1.1 Investigations for male factor fertility problems

17 1.2 Treatments for male factor fertility problems

18 1.3 Surgical sperm retrieval

19 2 Female factor fertility problems

20 2.1 Investigations for female factor fertility problems

21 2.2 Treatments for female factor fertility problems

22 3 Assisted reproduction techniques (ART)

23 3.1 Predictive factors and models for the success of assisted
24 reproduction techniques (ART) to inform recommendations on criteria for
25 access to treatments

26 3.2 Ovarian stimulation and intrauterine insemination (IUI) for
27 unexplained fertility problems

28 3.3 Intrauterine insemination (IUI)

29 3.4 Intracytoplasmic sperm injection (ICSI) in non-male factor fertility
30 problems

- 1 3.5 Fertility treatment add-ons
- 2 3.6 Embryo transfer
- 3 3.7 Frozen embryo transfer
- 4 3.8 Long-term safety of assisted reproductive technologies (ART) for
- 5 people with fertility problems and their children conceived through ART
- 6 4 Preservation of fertility
- 7 4.1 Effectiveness and safety of fertility preservation

8 **Areas that will not be covered in the guideline**

- 9 1 The management of recurrent miscarriage

10 **Proposed outline for the guideline**

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

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

Area in the guideline	What NICE plans to do
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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).

<p>1.3 Investigations of fertility problems and management strategies</p>	<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> <p>1.3.1 'Semen analysis'</p> <p>1.3.2 'Post-coital testing of cervical mucus'</p> <p>1.3.4 'Regularity of menstrual cycles'</p> <p>1.3.5 'Prolactin measurement'</p> <p>1.3.8 'Investigation of suspected tubal and uterine abnormalities'</p> <p>1.3.9 'Testing for viral status'</p> <p>1.3.10 'Viral transmission'.</p> <p>1.3.11 'Susceptibility to rubella'</p> <p>1.3.12 'Cervical cancer screening'</p> <p>1.3.13 'Screening for Chlamydia trachomatis'.</p> <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> <p>1.3.3 'Ovarian reserve testing'</p> <p>1.3.6 'Thyroid function tests'</p> <p>1.3.8.4 hysteroscopy</p> <ul style="list-style-type: none"> • 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>
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	<p>The guideline may cross-refer to recommendation 1.1.2 in the NICE guideline on coeliac disease: recognition, assessment and management (2015).</p>
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>

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>

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).</p> <p>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.

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.
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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

1 ***In development***

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

6 **NICE guidance about the experience of people using NHS services**

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

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

14 **3.4 Economic aspects**

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

22 In the case of fertility treatment, NICE's preferred quality adjusted life years
23 (QALY) approach may not be suitable. For example, a baby who might be
24 conceived as a result of assisted reproduction will experience no loss in
25 health-related quality of life if conception does not occur. In the previous
26 guideline, the psychological impact of fertility problems on parents wishing to
27 conceive was used to inform a QALY framework for economic analysis.

28 **3.5 Key issues and draft questions**

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

1 1 Male factor fertility problems

2 1.1 Investigations for male factor fertility problems

3 1.1.1 What is the prevalence of diagnostic abnormalities in males with
4 fertility problems using the following techniques:

- 5 • hormone profile,
- 6 • testicular biopsy,
- 7 • imaging studies,
- 8 • genetic studies (karyotype, y chromosome microdeletions, cystic
9 fibrosis)?

10 1.2 Treatments for male factor fertility problems

11 1.2.1 What is the effectiveness of hormone treatment in male factor
12 fertility problems?

13 1.2.2 What is the effectiveness of treatments for ejaculatory failure?

14 1.2.3 What is the effectiveness of surgical interventions for different
15 types of fertility problems associated with obstruction?

16 1.2.4 What is the effectiveness of treatments for fertility problems
17 associated with varicocele (including radiological embolisation and
18 surgery)?

19 1.3 Surgical sperm retrieval

20 1.3.1 What is the effectiveness of surgical sperm retrieval (SSR)
21 techniques in males with:

- 22 • non obstructive azoospermia,
- 23 • obstructive azoospermia?

24 2 Female factor fertility problems

25 2.1 Investigations for female factor fertility problems

26 2.1.1 What is the accuracy of ovarian reserve testing in predicting:

- 27 • the outcome of fertility treatment,
- 28 • the likelihood of spontaneous conception?

29 2.1.2 What is the effectiveness of treating hypothyroidism identified
30 through screening in improving outcomes in women with fertility
31 problems?

32 2.1.3 What is the effectiveness of hysteroscopy in improving outcomes
33 for women with fertility problems?

- 1 2.1.4 What is the value of endometrial receptivity (ERA) testing in
2 improving the chance of live birth in women undergoing in vitro
3 fertilisation (IVF)?
- 4 2.2 Treatments for female factor fertility problems
- 5 2.2.1 What is the effectiveness of ovulation induction strategies in
6 women with ovulation disorders (WHO group I, II, III)?
- 7 2.2.2. What is the effectiveness of cabergoline for fertility problems
8 associated with hyperprolactinaemic amenorrhoea?
- 9 2.2.3 What is the effectiveness of surgical interventions including tubal
10 surgery and uterine surgery as treatment for fertility problems?
- 11 3 Assisted reproduction techniques (ART)
- 12 3.1 Predictive factors and models for the success of assisted reproduction
13 techniques (ART) to inform recommendations on criteria for access to
14 treatments
- 15 3.1.1 What factors or models predict success in fertility treatment using:
- 16 • intrauterine insemination (IUI),
17 • IVF with or without intracytoplasmic sperm injection (ICSI)?
- 18 3.2 Ovarian stimulation and intrauterine insemination (IUI) for unexplained
19 fertility problems
- 20 3.2.1 What is the effectiveness of ovarian stimulation or intrauterine
21 insemination (IUI), with or without ovarian stimulation, for unexplained
22 fertility problems?
- 23 3.3 Intrauterine insemination (IUI)
- 24 3.3.1 What is the effectiveness of intrauterine insemination (IUI)
25 compared with expectant management in people with mild endometriosis
26 or mild male factor fertility problems?
- 27 3.4 Intracytoplasmic sperm injection (ICSI) in non-male factor fertility problems
- 28 3.4.1 What is the effectiveness of intracytoplasmic sperm injection (ICSI)
29 versus standard in vitro fertilisation (IVF) in non-male factor fertility
30 problems?
- 31 3.5 Fertility treatment add-ons
- 32 3.5.1 What is the effectiveness of the following fertility treatment add-
33 ons:

- 1 • pre-implantation genetic testing for aneuploidy (PGT-A),
- 2 • timelapse imaging,
- 3 • intracytoplasmic morphologic sperm injection (IMSI),
- 4 • physiological intracytoplasmic sperm injection (PICSI),
- 5 • immunological tests and treatments,
- 6 • endometrial scratch?

7 3.6 Embryo transfer

8 3.6.1 What is the effectiveness and safety of different embryo or
9 blastocyst transfer strategies in relation to both:

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

12 3.7 Frozen embryo transfer

13 3.7.1 What is the effectiveness and safety of different regimens of frozen
14 embryo transfer?

15 3.8 Long-term safety of assisted reproductive technologies (ART) for people
16 with fertility problems and their children conceived through ART

17 3.8.1 What is the long-term safety of in vitro fertilisation (IVF) with or
18 without intracytoplasmic sperm injection (ICSI) in women with fertility
19 problems and their children conceived through ART?

20 4 Preservation of fertility

21 4.1 Effectiveness and safety of fertility preservation

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

25 **3.6 Main outcomes**

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

- 28 • Live births
- 29 • Gestational age
- 30 • Birth weight
- 31 • Patient satisfaction
- 32 • Anxiety or depression

- 1 • Multiple births
- 2 • Fetal abnormalities
- 3 • Adverse pregnancy outcome (ectopic pregnancy, miscarriage, fetal growth
- 4 restriction, macrosomia, spontaneous preterm delivery, perinatal death,
- 5 pre-eclampsia, and gestational diabetes)
- 6 • Safety and long-term effects of specific fertility treatments
- 7 • Health-related quality of life

8 **4 NICE quality standards**

9 **4.1 NICE quality standards**

10 **NICE quality standards that may need to be revised or updated when**

11 **this guideline is published**

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

13 **5 Further information**

This is the draft scope for consultation with registered stakeholders. The consultation dates are 19th August to 16th September 2022.

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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