

## NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

### Interventional procedures consultation document

# Removal, preservation and reimplantation of ovarian tissue to restore fertility after gonadotoxic treatment

Some treatments for cancer or other medical conditions can damage the ovaries (gonadotoxic treatment). This can lead to early menopause and infertility. This procedure is done before planned gonadotoxic treatment, under a general anaesthetic. An ovary or part of an ovary is removed, usually using keyhole surgery, and then frozen and stored. After the gonadotoxic treatment is complete and when a pregnancy is planned, the ovarian tissue is thawed and reimplanted into the body. The aim is to restore ovarian function and fertility.

NICE is looking at removal, preservation and reimplantation of ovarian tissue to restore fertility after gonadotoxic treatment.

NICE's interventional procedures advisory committee met to consider the evidence and the opinions of professional experts with knowledge of the procedure.

This document contains the [draft guidance for consultation](#). Your views are welcome, particularly:

- comments on the draft recommendations
- information about factual inaccuracies
- additional relevant evidence, with references if possible.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

**This is not NICE's final guidance on this procedure. The draft guidance may change after this consultation.**

After consultation ends, the committee will:

- meet again to consider the consultation comments, review the evidence and make appropriate changes to the draft guidance

- prepare a second draft, which will go through a [resolution process](#) before the final guidance is agreed.

Please note that we reserve the right to summarise and edit comments received during consultation or not to publish them at all if, in the reasonable opinion of NICE, there are a lot of comments or if publishing the comments would be unlawful or otherwise inappropriate.

Closing date for comments: 20 March 2023

Target date for publication of guidance: July 2023

## 1 Draft recommendations

- 1.1 Removal, preservation and reimplantation of ovarian tissue to restore fertility after gonadotoxic treatment may be used if standard arrangements are in place for clinical governance, consent and audit. Find out [what standard arrangements mean on the NICE interventional procedures guidance page](#).
- 1.2 Healthcare organisations should:
- Ensure systems are in place that support clinicians to collect and report data on outcomes and safety for everyone having this procedure.
  - Regularly review data on outcomes and safety for this procedure.
- 1.3 For auditing the outcomes of this procedure, the main efficacy and safety outcomes identified in this guidance can be entered into [NICE's interventional procedure outcomes audit tool](#) (for use at local discretion).
- 1.4 Patient selection should be done by a multidisciplinary team experienced in the procedure, ideally using nationally agreed criteria.

### Why the committee made these recommendations

For people who need treatment that is likely to damage the ovaries and cause infertility, standard techniques for preserving fertility include egg or embryo freezing. But for some people, such as those who have not reached puberty, these options are not suitable. For these people, removal, preservation and reimplantation of ovarian tissue may offer the only chance of becoming pregnant in the future.

Evidence suggests that people who have had the procedure can become pregnant and have successful live births. The evidence did not raise any major safety concerns.

## **2 The condition, current treatments and procedure**

### **The condition**

- 2.1 Some treatments for cancer or other medical conditions can damage the ovaries (gonadotoxic treatment). This can lead to early menopause and infertility.

### **Current treatments**

- 2.2 There are a number of pharmacologic and surgical strategies that aim to reduce the risk of infertility after gonadotoxic treatment, including ovarian transposition, ovarian suppression, and fertility-sparing surgery.
- 2.3 For people who are going to have treatments that may damage their ovaries, cryopreservation of oocytes or embryos before the treatment begins are options for preserving fertility. These both involve ovarian stimulation, which may lead to a delay in treatment. Embryo cryopreservation also requires sperm from a partner or donor.

### **The procedure**

- 2.4 Before starting gonadotoxic treatments, ovarian tissue is removed surgically through laparoscopy, mini-laparotomy, or laparotomy. Usually, at least half of one ovary is removed and the other ovary is left in place to act as a site for future orthotopic autotransplantation. After histological examination of a portion to exclude malignancy, most of the excised ovarian tissue is frozen for future autotransplantation.

- 2.5 When indicated, the frozen cortical ovarian tissue is thawed and transplanted back to the same person. It can be placed into pelvic sites such as the remaining ovary, ovarian fossa, or broad ligament (orthotopic autotransplantation) through laparoscopy or mini-laparotomy. Alternatively, it can be placed into extra-pelvic sites such as the subcutaneous space of the abdominal wall or forearm (heterotopic autotransplantation). In this case, the follicle and oocyte develop outside the usual environment, so subsequent ovarian stimulation, egg collection, and in vitro fertilisation are needed to achieve pregnancy. Another technique involves the vascular grafting and anastomosis of a frozen-thawed whole ovary through mini-laparotomy or laparotomy.
- 2.6 Future pregnancies may require assisted reproduction technologies, although the procedure can offer the possibility of natural conception.
- 2.7 Ovarian stimulation is not needed before removal of ovarian tissue for autotransplantation and gonadotoxic treatment can start immediately afterwards. It may be the only fertility preservation option suitable before puberty or for people with oestrogen-sensitive malignancies.

### **3 Committee considerations**

#### **The evidence**

- 3.1 NICE did a rapid review of the published literature on the efficacy and safety of this procedure. This comprised a comprehensive literature search and detailed review of the evidence from 6 sources, which was discussed by the committee. The evidence included 3 systematic reviews, 1 retrospective cohort study, 1 multicentre case series and 1 registry analysis. It is presented in the [summary of key evidence section in the interventional](#)

[procedures overview](#). Other relevant literature is in table 5 of the overview.

- 3.2 The professional experts and the committee considered the key efficacy outcomes to be: return of endocrine function, pregnancy, live birth rate, long-term outcomes of children born using this procedure.
- 3.3 The professional experts and the committee considered the key safety outcomes to be: transmission of original malignancy through reimplanted ovarian tissue.
- 3.4 Patient commentary was sought but none was received.

### **Committee comments**

- 3.5 The committee encourages formation of a registry to collect details of patient selection, including original malignancy and age (both at harvesting of ovarian tissue and at reimplantation), details of the procedure used for harvesting and reimplantation, including the amount of tissue removed and reimplanted, live birth rates and longer-term outcomes.
- 3.6 The committee noted that preservation of ovarian tissue for this procedure is regulated by the Human Tissue Authority (HTA). Only ovarian tissue that has been stored under HTA regulations can be reimplanted.
- 3.7 The committee was informed that this procedure is not currently used for people with leukaemia in the UK, but there is ongoing research in this area.
- 3.8 The committee was informed that this procedure is not usually used when egg harvesting is an option.
- 3.9 This guidance covers the use of this procedure to restore fertility and not to reduce symptoms of the menopause. NICE has

produced separate guidance on [removal, preservation and subsequent reimplantation of ovarian tissue to prevent symptoms from the menopause](#) (interventional procedures guidance 738).

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Chair, interventional procedures advisory committee

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