

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of removal, preservation and subsequent reimplantation of ovarian tissue to prevent symptoms from the menopause

Reduced oestrogen levels after the menopause can cause symptoms such as hot flushes, altered mood and fatigue, and can weaken the bones (osteoporosis) and increase the risk of heart disease and stroke. In this procedure, under general anaesthesia, a small piece of ovarian tissue is removed before the menopause using keyhole surgery (laparoscopic). This is then frozen and stored. When menopause starts, the tissue is thawed and transplanted under the skin of the armpit, abdomen, or forearm. The aim is for the transplanted ovarian tissue to produce oestrogen to prevent menopause symptoms.

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Introduction

The National Institute for Health and Care Excellence (NICE) prepared this interventional procedure overview to help members of the interventional procedures advisory committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and professional opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in December 2021.

Procedure name

- Removal, preservation and subsequent reimplantation of ovarian tissue to prevent symptoms from the menopause.

Professional societies

- Royal College of Obstetricians and Gynaecologists
- Faculty of Sexual and Reproductive Healthcare
- British Fertility Society
- British Menopause Society

Description of the procedure

Indications and current treatment

Menopause occurs with the final menstrual period and is usually diagnosed clinically after 12 months of amenorrhoea. It usually happens when someone is between 45 and 55, although around 1% of people have early (premature) menopause before 40.

As oestrogen levels reduce, most people have some symptoms, which can affect quality of life. Most commonly, these are hot flushes and night sweats. Other symptoms are mood changes, memory and concentration loss, vaginal dryness, a lack of interest in sex, headaches, and joint and muscle stiffness. Menopause can also increase the risk of osteoporosis and cardiovascular disease.

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Symptoms can be treated with pharmacological hormone replacement therapy (HRT). For someone with a uterus, HRT usually consists of an oestrogen and a progestogen. For someone who has had their uterus removed, it is usually oestrogen only. HRT aims to replace the hormones that are no longer produced by the ovaries because of menopause. Non-hormonal treatments can also be used.

What the procedure involves

The level of reproductive hormones and ovarian reserve is assessed first. If this is adequate, one-third to one-half of the outer cortex of 1 ovary is removed laparoscopically under general anaesthesia and cryopreserved in thin slices. When menopause starts, a slice of the ovarian tissue is thawed and regrafted under the skin in a heterotopic site (for example, the forearm or axilla) with the aim of restoring normal ovarian endocrine function. The transplantation process is reversible and may be repeated to maintain endocrine function. The aim is to prevent the symptoms associated with the menopause.

This overview does not consider evidence for this procedure in women who are at risk of infertility or early menopause from iatrogenic (such as cancer treatment) or non-iatrogenic (such as hereditary) causes. Nor does it consider evidence for the preservation or restoration of fertility in menopausal women. It only considers the evidence on the use of this procedure in healthy women who wish to delay the symptoms associated with the menopause (such as the symptoms detailed in the previous section).

Efficacy summary

No relevant studies were identified.

Safety summary

No relevant studies were identified.

Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, professional experts are asked about anecdotal adverse events (events that they have heard about) and about theoretical adverse events (events that they think might possibly occur, even if they have never happened).

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For this procedure, the professional expert noted that there is no data for this procedure in healthy women. Therefore, this overview considers that all adverse events that the professional expert listed were theoretical:

- surgical complications during laparoscopy: infection, bleeding, venous thromboembolism, damage to bowel or bladder or blood vessels which may require further surgery
- anaesthetic complications
- risk of unintended pregnancy (depending on the graft site) and need for contraception
- restoration of menstrual periods (some women may consider this an unwanted outcome)
- procedure failure.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to removal, preservation and subsequent reimplantation of ovarian tissue to prevent symptoms from the menopause. The following databases were searched, covering the period from their start to 19 October 2021: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the internet were also searched. No language restriction was applied to the searches (see the [literature search strategy](#)). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The [inclusion criteria](#) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	<p>Clinical studies were included. Emphasis was placed on identifying good quality studies.</p> <p>Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study.</p> <p>Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.</p>
Patient	Otherwise healthy women who wish to avoid symptoms from the menopause.
Intervention/test	Removal, preservation, and reimplantation of ovarian tissue.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

No relevant studies were identified.

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Validity and generalisability of the studies

- No relevant studies were identified.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure.

NICE guidelines

- Menopause: diagnosis and management. NICE guideline 23. Available from: <https://www.nice.org.uk/guidance/ng23>

Additional information considered by IPAC

Professional experts' opinions

Expert advice was sought from consultants who have been nominated or ratified by their professional Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by professional experts, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate.

Two professional expert questionnaires for removal, preservation and subsequent reimplantation of ovarian tissue to prevent symptoms from the menopause were submitted and can be found on the [NICE website](#).

Patient commentators' opinions

NICE's Public Involvement Programme will send questionnaires to NHS trusts for distribution to patients who had the procedure (or their carers). When NICE has received the completed questionnaires, these will be discussed by the committee.

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Company engagement

Not relevant for this procedure.

Issues for consideration by IPAC

- There was no evidence identified for the use of this procedure in the proposed indication.

References

No relevant studies were identified.

Literature search strategy

Appendix: Overview Search history

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	19/10/2021	Issue 10 of 12, October 2021
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	19/10/2021	Issue 10 of 12, October 2021
International HTA database	19/10/2021	-
MEDLINE (Ovid)	19/10/2021	1946 to October 15, 2021
MEDLINE In-Process (Ovid) & MEDLINE ePubs ahead of print (Ovid)	19/10/2021	October 15, 2021
EMBASE (Ovid)	19/10/2021	1974 to 2021 October 18
Embase Conference (Ovid)	19/10/2021	1974 to 2021 October 18

Trial sources searched

- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

Websites searched

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- General internet search

MEDLINE search strategy

The MEDLINE search strategy was translated for use in the other sources.

- 1 MENOPAUSE/ or MENOPAUSE, PREMATURE/ or PERIMENOPAUSE/ or POSTMENOPAUSE/
- 2 CLIMACTERIC/
- 3 (menopaus* or postmenopaus* or perimenopaus* or climacteri*).tw.
- 4 "change of life".tw.

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5 PRIMARY OVARIAN INSUFFICIENCY/
6 ((primary or prematur* or gonadotrop* or hypergonadotrop* or resist*) adj4 ovar*
adj4 (insuffic* or fail* or incompet* or syndrom*)).tw.
7 ((earl* or prematur*) adj4 menopaus*).tw.
8 (POI or POF).tw.
9 or/1-8
10 Cryopreservation/
11 Tissue Preservation/
12 Tissue Transplantation/ or Transplants/
13 (ovar* adj4 tissue* adj4 (transplant* or graft* or preserv* or reimplant* or re-
implant* or freez* or frozen or cryopreserv* or cryofixat* or "cryonic suspen*")).tw.
14 (OTC or OTT or OTCT).tw.
15 or/10-14
16 9 and 15
17 animals/ not humans/
18 16 not 17

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Appendix

There were no additional papers identified.