

## National Institute for Health and Care Excellence

### IP1804 Removal, preservation and subsequent reimplantation of ovarian tissue to prevent symptoms from the menopause

IPAC date: 14<sup>th</sup> July 2022

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response
				Please respond to all comments
1	Consultee 1 British Fertility Society	General	<p>Many thanks for the requesting the British Fertility Society for their comments on this consultation document:</p> <p>There is no good evidence to show that this procedure will prevent menopausal symptoms or 'delay the menopause'</p> <p>Given what we know about tissue/graft survival it is likely that multiple surgeries would be required</p> <p>There is a significant loss of ovarian follicles during freeze-thaw-regraft process (loss of about 40% of follicles) which impacts ovarian reserve. Efficacy therefore depends on age at the time of storage. Also, it is known that grafts taken after the age of 38 are not likely to restore fertility. This would mean removing ovarian tissue in young women which might accelerate the menopause for some young women.</p> <p>There are multiple pharmacological and non-pharmacological ways to prevent menopausal symptoms that could avoid multiple surgeries (at</p>	<p>Thank you for your comments.</p> <p>Consultee agrees with the draft recommendations.</p> <p>The committee considered these comments and decided no change to the guidance was necessary.</p> <p>The committee noted the BFS guideline (2018) on fertility preservation. However, the BFS guideline discusses ovarian tissue cryopreservation in the context of fertility preservation for medical reasons. This guidance only considers the use of this procedure specifically to prevent menopause symptoms in otherwise healthy people. It does not cover the use of this procedure to preserve fertility or to prevent menopausal symptoms or premature menopause from iatrogenic (such as cancer treatment) or non-iatrogenic (such as hereditary or disease) causes.</p>

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			<p>least two) which carry both surgical and anaesthetic risks.</p> <p>Hormone replacement therapy is effective for the management of menopausal symptoms and is available on the NHS in the primary and secondary care.</p> <p>NICE would be better placed evaluating the same technology for the restoration of fertility- some good evidence already</p> <p>Please note the conclusion from the current BFS guideline (2018): “OTC (Ovarian Tissue Cryopreservation) is still not an established treatment and as such, should only be offered by units with relevant clinical and laboratory expertise, protocols and HTA licensing or associated with an established unit using a third-party arrangement. NHS trusts also require local governance requirements to be satisfied before a new procedural technique is introduced.”</p> <p>In the British Fertility Society’s opinion, it is inappropriate to undertake this procedure currently outside a research setting.</p>	
2	<p>Consultee 2</p> <p>British Menopause Society</p>	General	<p>"The British Menopause Society welcomes the Interventional Procedures Advisory Committee’s (IPAC) decision to review this procedure and to assess aspects related to its safety and efficacy.</p> <p>We have included the British Menopause Society’s comments below:</p>	<p>Thank you for your comments.</p> <p>Consultee agrees with the draft recommendations. Consultee suggests several aspects of the procedure that need clinical investigation.</p>

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			<p>1. This procedure is intended to delay the menopause by offering women cryopreservation of their ovarian tissue with the intention of subsequently replacing the ovarian tissue to provide hormones to counteract the adverse effects of the menopause.</p> <p>2. The British Menopause Society recommends that this procedure should be initially assessed in controlled clinical research trials to evaluate its safety and feasibility before it could be considered as a potential option in clinical practice.</p> <p>3. The procedure in principle is not new and has now been used for a number of years in young women at risk of losing their ovarian function as a result of cancer treatment. The focus in such cases is replacing the women's eggs to restore fertility. There have been to date more than 150 children born as a result of this technique and many of the reports have indicated that the ovarian tissue grafts result in hormonal activity.</p> <p>4. There are a number of aspects that need to be further assessed before considering this technique in standard clinical practice that is intended to delay the menopause including long-term efficacy data.</p> <p>This is particularly relevant as research on the use</p>	<p>The committee considered these comments and decided no change to the guidance was necessary.</p>

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			<p>of this technique in infertility has shown that re-implanted samples do not always function and the duration of tissue activity / viability is variable. Studies have suggested that the functional longevity of tissue highly variable with some reports showing ovarian function up to 10 years whilst others have reported this up 1–2 years.</p> <p>In addition, the duration of tissue activity has been reported to vary with:</p> <ul style="list-style-type: none"> <li>-Age.</li> <li>-Ovarian reserve.</li> <li>-Amount of tissue being transplanted.</li> </ul> <p style="padding-left: 40px;">This requires further clinical studies to assess.</p> <p>5. There is a need to assess the long-term safety of this procedure. The biopsies are obtained through a surgical procedure that while safe and commonly performed can be associated with potential surgical risks and requires a general anaesthetic. In addition, the potential impact of removing ovarian tissue on long-term ovarian function including future fertility, especially in women who do not have a clear indication to do so, requires further assessment and evaluation.</p> <p>6. Assessment of the impact of extending reproductive years in terms of contraceptive needs in women who do not desire a pregnancy is required as well as the risks of pregnancy, including the increased maternal and fetal risks in</p>	

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			<p>this age group.</p> <p>7. There is also a need to assess the theoretical unknown risk of ovarian cancer that may be associated with re-implanting ovarian tissue and the potential risk of breast cancer with delayed menopause.</p> <p>8. The procedure should also be compared against the standard more controllable ways of managing the menopause that are currently used including HRT. The latter has been well studied and its safety has been demonstrated in numerous studies over many years.</p> <p>9. There is a need to carry out a benefit / risk assessment of this procedure to assess the potential role this procedure may offer in clinical practice.</p> <p>10. These is a need to assess the optimal heterotopic site for re-implantation of the ovarian tissue.</p> <p>11. Assessment of the role of this intervention in women who underwent hysterectomy who do not need progesterone.</p> <p>12. Assessment of the risk of insufficient hormone production and whether the endometrium is adequately protected by progesterone secreted by ovarian tissue grafted to a heterotopic site.</p>	

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			<p>13. Ethical implications as well as the medical aspects require assessment before introducing this procedure in clinical practice.</p> <p>██████████ On behalf of the BMS Board of Trustees and Medical Advisory Council."</p>	
3	<p>Consultee 3</p> <p>BPAS Fertility</p> <p>Fertility clinic</p>	General	<p>BPAS Fertility support these NICE recommendations. The reimplantation of ovarian tissue with the aim of delaying menopause is novel and unsupported by professional societies or the necessary research.</p> <p>The removal, preservation and subsequent reimplantation of ovarian tissue within the context of fertility preservation can assist patients who wish to resume ovulation and endocrine function and removes the need for hormone replacement therapy. However efficacy is very dependent on the age of the person at the time of storage of tissue and there is still limited data on endocrine outcomes.</p> <p>We strongly agree that there is not enough research to support this procedure being used for the purpose of preventing symptoms of the menopause and believe the potential complications associated with laparoscopy pose an unnecessary risk for the healthy women that could potentially be persuaded to undergo this procedure for the purpose of menopause symptom treatment. Clinics should not be allowed</p>	<p>Thank you for your comments.</p> <p>Consultee agrees with the draft recommendations.</p> <p>The committee considered these comments and decided no change to the guidance was necessary.</p>

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			to offer or advertise reimplantation of ovarian tissue for the treatment of menopause symptoms. Clients should be provided with evidence-based information regarding treatment of symptoms for the menopause.	

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