

**THRESHOLD POLICY – T40
CRYOPRESERVATION OF SPERM, OOCYTES AND EMBRYOS IN PATIENTS WHOSE
TREATMENT POSES A RISK TO THEIR FERTILITY**

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1. Policy Summary

- 1.1 This policy aims to provide clear criteria for clinicians, commissioners and managers on access to and funding for cryopreservation of sperm, oocytes and embryos in patients faced with infertility as a complication of their NHS-funded treatment.
- 1.2 This policy states eligibility for fertility cryopreservation for patients receiving NHS-funded cytotoxic treatments that can cause permanent infertility, provided they meet the access criteria set out in the policy. Cancer patients undergoing chemotherapy and/or radiotherapy are recognised as the main candidates in this context but this policy applies to all patients receiving such cytotoxic treatments, regardless of the underlying condition (malignant or non-malignant).
- 1.3 Loss of fertility may also arise as a consequence of treatments other than cytotoxic therapy, these scenarios are variable and will be considered on an individual basis by the CCGs' individual funding request (IFR) panel.

2. Eligibility Criteria

- 2.1 All patients whose treatment poses a threat to their fertility must have the opportunity to discuss fertility, regardless of their eligibility for gamete or embryo cryopreservation.
- 2.2 The CCG will fund cryopreservation of sperm, oocytes and embryos for patients undergoing forthcoming cytotoxic treatments that are likely to cause permanent infertility, regardless of the underlying condition requiring treatment
 - a) The degree of gonadal damage from chemotherapy and irradiation is dependent on several factors that will be personalized to the patient's individual circumstances and treatment plan e.g. age, drugs used, route of administration, dose etc. It is beyond the scope of this policy to second guess all such scenarios, instead, when considering cryopreservation for people before starting chemotherapy or radiotherapy, clinicians are signposted to the guidance set out in *'The Effects of Cancer Treatment on Reproductive Functions'*².

- b) The patient should meet the access criteria stated in this policy.
- c) Oocyte or embryo cryopreservation should be offered to women only if:
 - They are well enough to undergo ovarian stimulation and egg collection
 - This will not worsen their condition
 - Enough time is available before the start of their treatment

2.3 Any other clinical scenario where fertility may be permanently lost as a result of NHS funded treatment should be considered on an individual basis by the CCGs' IFR panel.

2.4 Access Criteria

- a) Age:
 - There is no *lower* age limit for gamete or embryo cryopreservation as long as it is clinically appropriate.
 - For women: Cryopreservation of oocytes and embryos in females is available to those less than 42 years of age.
 - For men: Cryopreservation of sperm in men is available to those less than 55 years of age.
 - These limits are chosen in line NICE CG 156 and the existing CCG fertility policy (T39).
- b) Residency:
 - For cancer patients: Patients must be registered with a GP practice that is part of Ipswich and East Suffolk or West Suffolk CCG at the point at which referral for access to cryopreservation storage is made.
 - For patients with non-malignant conditions: Patients must be registered with a GP practice that is part of Ipswich and East Suffolk or West Suffolk CCG at the time of diagnosis of the condition.
- c) Previous Sterilisation:
 - Patients are ineligible for CCG funded cryopreservation to preserve fertility if previous sterilisation has taken place, even if it has been reversed.
- d) Existing Congenital Disorder Causing Infertility:
 - Patients who are infertile due to an existing congenital disorder will not be eligible.
- e) Social Freezing:
 - Patients wishing to have gametes frozen for non-medical or non-surgical reasons, such as for social reasons, will not be eligible.

f) Written Consent:

- Patient must provide written consent to treatment and gamete storage.

2.5 CCG Funding for Subsequent Use of Stored Material

This policy is for cryopreservation only and has no bearing on access to NHS-funded IVF treatment. Whilst the CCG's eligibility criteria used in conventional infertility treatment do not apply in the case of access to fertility cryopreservation in cancer patients, patients should be informed that the CCG will fund assisted conception using stored material in line with the CCG fertility policy at the time of use. The treating clinician should make this clear to the patient at the time of the storage in order not to raise undue expectation and to avoid future disappointment.

2.6 CCG Funding for Storage of Material:

- a) Patients entering the cryopreservation pathway under the age of 23 years will have their treatment and ongoing storage fully funded by the CCGs until they reach their 23rd birthday. At the point which the patient reaches their 23rd birthday, funding will be available for a further 5 years from this date. The combined funded storage period up to age 28 (23 + 5) gives those youngest patients entering the cryopreservation pathway the opportunity to reach an age of maturity approaching the UK averages at which men and women have children. In 2012, for first births the standardised average age of mothers was 28.1 years³.

Example: a young person entering the cryopreservation pathway at 15 years of age, would be eligible for 7 years funded storage up to age 23, then an additional five years funded storage up to age 28. Giving them a total funded storage period of potential 12 years.

- b) Patients entering the cryopreservation pathway at age 23 and above will be eligible for five years funded storage or, in females, to the point at which they reach the upper age threshold of 42 years of age and, in men, to the point at which they reach the upper age threshold of 55 years of age, whichever is reached first.

Example: a female entering the cryopreservation pathway at 39 years of age would only be eligible for funded storage up to her 42nd birthday and not to age 44. Vis-à-vis, a man entering the cryopreservation pathway age 52 years of age, would only be eligible for storage up to his 55th birthday and not to age 57.

3. Background to the Condition

- 3.1 Cryopreservation is controlled freezing of biological tissue.¹ In the case of fertility, cryopreservation allows storage of male or female reproductive tissue for future use in conception (via assisted reproductive techniques)². Cryopreservation of sperm is a well-established technique used to maintain an individual's fertility². Embryo cryopreservation is also an established practice and is used following assisted conception techniques such as in-vitro-fertilisation, however in the context of fertility preservation alone, it requires time to obtain and create the sample (ovarian stimulation, oocyte collection and assisted reproduction techniques)^{1,2}. Cryopreservation of eggs is a newer technology, though has been widely used in relation to cancer treatment for a number of years. Again it requires ovarian stimulation and

oocyte collection¹. Cryopreservation of ovarian tissue is also an emerging area of practice, still largely undertaken in a research setting, and this treatment is not supported by this policy at this time².

- 3.2 Cytotoxic therapies cause cell death. Their use in cancer treatment is to kill cancer cells but in doing so they have the potential to kill normal tissue as well. As a result, both systemic and localised (if closely related to reproductive organs) therapy can cause permanent damage to reproductive tissue. The main examples of cytotoxic therapies are chemotherapy drugs and radiotherapy. The document *'The Effects of Cancer Treatment on Reproductive Functions'*² provide further information and explanation on this topic.
- 3.3 Gamete or embryo cryopreservation for patients commencing cancer treatment offers preservation of fertility when the forthcoming cytotoxic treatment is likely to render them infertile. Although cancer predominately affects people after they have completed their families, an important minority are diagnosed at a younger age. Around 11,000 patients in the age group 15-40 years are diagnosed with cancer each year in the UK. ² This represents around 4% of all cases of cancer.² Of particular relevance in this group are patients with breast, cervical and testicular cancers, sarcomas, leukaemias and lymphoma.² The marked success in the treatment of some of these malignancies affecting younger people, and the associated improved survival for an increasing number of patients, means that consideration of the potential impact of the cancer treatment on fertility is one of the issues that should be discussed before that treatment is started.²
- 3.4 Cytotoxic therapy is also used in management of non-malignant conditions. For example, non-malignant haematological disease originating from or involving the bone marrow, such as myeloproliferative disorders and aplastic anaemia, can be successfully treated with a bone marrow transplantation, which includes pre-conditioning regimes with high-dose chemotherapy or radiotherapy.^{3,5} Similarly, autoimmune conditions (such as rheumatoid arthritis, systemic lupus erythematosus (SLE) and multiple sclerosis) may require treatment with cytotoxic agents such as cyclophosphamide.³ These diseases commonly affect women of child-bearing age thus making fertility an important factor to consider.⁴
- 3.5 Fertility may be compromised or lost (temporarily or permanently) as a consequence of medical treatment by mechanisms other than cytotoxic medication or radiation. Examples include urological or other abdominal surgery, long-term use of teratogenic medications and long-term use of virilising hormones. These scenarios are varied and more complex and therefore better addressed on a case-by-case basis.
- 3.6 This policy does *not* address cryopreservation of gametes or embryos obtained following assisted conception as a part of conventional infertility treatment as this is addressed in the relevant policy and pathway on these fertility treatments.

3.7 Table 1. CCG Funding for Stored Material by Age and Duration:

Age Range	Duration of CCG Funding
Men & Women: from age of sexual maturity to 23 years of age	Funded by CCGs up to age 23 years.
Women: 23 years to less than 42 years of age Men: 23 years to less than 55 years of age	Five years funding or up to the upper-age thresholds of 42 years in women and 55 years in men, whichever is reached first.

- 3.8 For men, a clinical review of their testicular function should take place 3 years after material has been stored to check for a full return to spermatogenesis (confirmed when semen analysis results show the patients sperm volume, density, motility, morphology, and pH are within normal value ranges for the patient to be considered fertile). If a return to full spermatogenesis is confirmed, then funding of the patients stored material will cease 1 month following the outcome of the test results being communicated by recorded delivery to and acknowledged by the patient.
- 3.9 For all patients, if fertility returns as demonstrated by conception, funding for ongoing storage of remaining stored material will cease.
- 3.10 In the event the patient dies or lacks the capacity to make decisions during the funded storage period and has nominated next of kin for material to be passed to, the CCG will continue to fund storage of material for a further six months whilst the next of kin consider what to do with the stored material. Should the gamete provider's nominated next of kin wish to continue storing the material beyond this six-month period of grace, then they can make arrangements directly with the provider. Before the storage process begins, the clinic will ask the patient to sign consent forms which allow the patient to specify what should happen to the material if the gamete provider were to die or lack capacity to make decisions.
- 3.11 The CCGs will honour funding of a patients stored material for those already on a cryopreservation pathway and moving from outside of Suffolk into Ipswich and East Suffolk CCG practice boundaries, once registered with an Ipswich and East Suffolk GP. If there is a difference between the two CCG's policies on the length of time storage should be funded for, then the policy with the greater funded storage period will be honoured. Any funded storage time already accrued at this point will be considered.
- 3.12 If patients and their families wish to continue storage of their material beyond the specified CCG funded storage period and upper age thresholds for treatment they will need to explore privately funded options. Advice on the available storage options should be sought from the patient's secondary care specialist. The Human Fertilisation and Embryology Authority do not regulate the cost of treatment set by private UK fertility clinics. Before embarking on privately funded treatment, patients should be advised to ask for a personalised and costed treatment plan.

4. Rationale to the Decision

- 4.1 The policy has been informed and guided by relevant NICE guidance, other publications from national organisations, published literature and policies from other CCGs.
- 4.2 In particular, NICE Clinical Guidance (CG)156 '*Fertility: assessment and treatment for people with fertility problems*'⁶ provides guidance on fertility preservation in cancer patients only and outlines access criteria for this. The principles of this have been applied to this policy.

5. References

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