

COMMISSIONING POLICY FOR GAMETE AND EMBRYO CRYOPRESERVATION

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NHS FUNDING

CCGs buy healthcare on behalf of their local populations. They each have a fixed budget for this and are required by law to keep within this budget. Demand for healthcare is greater than can be funded from this fixed budget. Unfortunately, this means that some healthcare which patients might wish to receive and which professionals might wish to offer cannot be funded.

CCGs prioritise what they spend, so that their local populations get access to the healthcare that is most needed. This assessment of need is made across the whole population and wherever possible, on the basis of best evidence about what works. They aim to prioritise in a way that is fair, so that different people with equal need have equal opportunity to access services.

ASSISTANCE WITH THE APPLICATION OF THIS POLICY AND UPDATES

This policy has been prepared to reflect the situation at the time of its development, and will require periodic review to reflect subsequent changes in (law, guidelines, evidence etc.).

For advice and assistance in relation to the application of this policy, and to obtain updates, please contact your local CCG.

This policy has been prepared by East Midlands Affiliated Commissioning Committee (EMACC). EMACC has been established as a joint committee of nineteen participating CCGs in the East Midlands to enable CCGs to work collaboratively on the development and maintenance of Commissioning Policies.

1. NHS Southern Derbyshire CCG
2. NHS North Derbyshire CCG
3. NHS Erewash CCG
4. NHS Hardwick CCG
5. NHS Nottingham City CCG
6. NHS Nottingham West CCG
7. NHS Nottingham North & East CCG
8. NHS Rushcliffe CCG
9. NHS Newark & Sherwood CCG
10. NHS Mansfield & Ashfield CCG
11. NHS Corby CCG
12. NHS Nene CCG
13. NHS West Leicestershire CCG
14. NHS Leicester City CCG
15. NHS East Leicestershire & Rutland CCG
16. NHS Lincolnshire West CCG
17. NHS South West Lincolnshire CCG
18. NHS South Lincolnshire CCG
19. NHS Lincolnshire East CCG

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1. EQUALITY STATEMENT

EMACC and its participating CCGs aim to create policy documents that meet the diverse needs of the populations to be served and the NHS workforce has a duty to have regard to the need to reduce health inequalities in access to health services and health outcomes achieved as enshrined in the Health and Social Care Act 2012.

CCGs are committed to ensuring equality of access and non-discrimination, irrespective of age, disability (including learning disability), gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, sex (gender) or sexual orientation.

This policy takes into account current UK legislative requirements, including the Equality Act 2010 and the Human Rights Act 1998, and promotes equality of opportunity for all. This document has been designed to ensure that no-one receives less favourable treatment owing to their personal circumstances.

2. DUE REGARD

In carrying out their functions, CCGs must have due regard to the Public Sector Equality Duty (PSED). This applies to all the activities for which CCGs are responsible for, including policy development and review.

3. POLICY STATEMENT

EMACC's participating CCGs support the funding of gamete or embryo cryopreservation for individuals undergoing medical or surgical treatment (which would be funded by the NHS) who may be at risk of permanent infertility as a result of their treatment. Gamete or embryo cryopreservation will not be commissioned for social (non-clinical) reasons, or if gametes are being frozen for use by individuals other than the patient receiving treatment (with the exception of patients required to have their uterus removed, and female-to-male gender dysphoria patients).

Provision of gamete preservation under the terms of this policy is made without prejudice to the future determination of any subsequent fertility treatment. Approval of cryopreservation doesn't guarantee NHS funding for future fertility treatment, which will be determined by the relevant CCG policy at that time.

4. PURPOSE OF POLICY

The purpose of this policy is to confirm the commissioning arrangements regarding NHS-funded gamete or embryo cryopreservation services for patients who are the responsibility of CCGs in the East Midlands.

4.1 Aims and Objectives

The aim of the policy is to identify those individuals who will be eligible to receive NHS-funded cryopreservation of their gametes or embryos.

4.2 Scope of Policy

This policy does not address NHS funding for the future use of frozen gametes. Provision of gamete freezing and storage under the terms of this policy is made without prejudice to the future determination of funding of any subsequent fertility treatment. This policy will be reviewed to ensure that it remains in line with other local fertility policies.

This policy does not include cryopreservation of ovarian or testicular tissue which is considered to be an experimental procedure.

5. THE MEDICAL CONDITION

This policy does not apply to any single condition. It applies to people who are the responsibility of CCGs in the East Midlands undergoing NHS funded medical or surgical treatment with a risk of causing permanent infertility. Conditions where this policy may apply include, but are not limited to:

- malignancies or other autoimmune conditions requiring chemotherapy or total body irradiation or radiotherapy that may affect an individual's reproductive organs;
- conditions requiring urological or gynaecological surgery;
- conditions requiring specialist endocrinology services;
- rare mitochondrial disorders.

The policy includes transgender patients receiving treatment for gender dysphoria which may cause permanent infertility (hormone therapy, reconstructive surgery etc.). Cryopreservation will be funded for patients on this pathway provided they meet the criteria within this policy.

This policy excludes the following patients:

- Patients wishing to store gametes for non-medical or non-surgical reasons, for example for social reasons;
- Patients undergoing experimental treatment as part of a research study where the treatment may cause infertility;

(see Section 12 for the full list of exclusions)

6. PROCEDURE / TREATMENT

Gamete or embryo cryopreservation are a set of techniques that freeze an individual's eggs, sperm or fertilised eggs for use in future fertility treatment. Cryopreservation of sperm is a well-established technique used to maintain an individual's fertility.

Cryopreservation of eggs is a newer technology, though has been widely used in relation to fertility treatment for a number of years.

7. REFERENCES / EXISTING CLINICAL GUIDANCE DOCUMENTS

'The Effects of Cancer Treatment on Reproductive Functions: Guidance on Management', published by the Royal College of Physicians, the Royal College of Radiologists and the Royal College of Obstetricians and Gynaecologists in 2007. The report recommends that

sperm banking should be universally available and funded for all males commencing treatment which has a risk of future infertility.

The National Institute for Health and Care Excellence (NICE) Guidance for fertility problems: assessment and treatment (CG156) recommends that people preparing to have treatment for cancer that is likely to result in fertility problems are given the option to preserve (freeze and store) their eggs, sperm or embryos for possible use in the future [5].

The Human Fertilisation and Embryology Authority has approved and regulates the storage of frozen sperm, oocytes and embryos. It sets out the mandatory requirements for legal storage of gametes and embryos. Storage can only be funded at appropriately licensed centres[1].

8. EPIDEMIOLOGY

There is a lack of data about the patient group at risk of infertility due to NHS funded treatments. It is therefore difficult to develop precise estimates of the numbers of individuals that may be referred for gamete or embryo cryopreservation.

Table 1 shows estimated rates of demand per 100,000 population based on historic referral levels to a local provider. When applied to the East Midlands population the data suggests a demand of 230 males and 42 females across the East Midlands per year, a full breakdown by CCG is shown in Appendix 2.

Table 1 Referral rates per 100,000 population for cryopreservation due to radiotherapy/chemotherapy for malignancy, other NHS funded medical/surgical treatment and privately funded patients on a transgender pathway, 2013/14-2016/17 (Source: provider data)

Sex	Reason for Referral/ca use of infertility	2013/14	2014/15	2015/16	2016/17	2013/14 - 2016/17
Male	All referrals	8.3	8.3	12.5	12.3	10.3
Female	All referrals	2.4	2.2	1.0	1.7	1.8

The data incorporates referrals due to radiotherapy/chemotherapy for malignancy, other NHS funded medical/surgical treatment and privately funded patients on a transgender pathway. They show that demand has increased in recent years for males, driven by an increase in cases referred for cancer treatment. The rate in women was much lower than males, possibly reflecting the increased time and complexity of egg extraction. Rates in females have fallen in recent years, however this may reflect variation due to small numbers of cases rather than a decreasing trend.

From 2013/14 to 2016/17 the vast majority of referrals were for patients undergoing cancer treatments (93% of males, 97% females), 1% of males and no females were referred for other medical/surgical treatments. Demand for privately funded cryopreservation from patients on a transgender pathway over the same period was relatively low (6% of males, 3% females), however there is likely to be residual unmet demand in the population.

9. CLINICAL EFFECTIVENESS EVIDENCE SUMMARY

Cryopreservation of sperm is a well-established technique which has been used for over 40 years [1]. Cryopreservation of eggs has been developed more recently with the first live birth in the 1980s [2].

The most established technique for fertility preservation is cryopreservation of embryos derived from the patient's eggs and partner sperm. Embryo cryopreservation is suitable for women in a relationship where both partners consent to creation and storage of embryos. Counselling should address the requirement for both partners to consent to the use of embryos in any future fertility treatment.

UK clinics providing licensed fertility treatment are obliged to consider all factors that may affect the welfare of any child conceived through treatment.

Cryopreservation is recommended by NICE however there is a lack of evidence to support the effectiveness of gamete or embryo cryopreservation in the population of individuals at risk of infertility due to medical/surgical treatment. Four systematic reviews [6–9] were identified providing mixed evidence which was graded as low quality due to inconsistency, indirectness and impression. The studies concluded oocyte vitrification compared to slow freezing probably increases clinical pregnancy rates in women. Clinical pregnancy rates using vitrification freezing techniques ranged from 38-65% with no significant difference in ongoing or clinical pregnancy rates between vitrified and fresh oocytes.

One low quality systematic review of observational studies reported a crude aggregated parenthood rate of 49% following freezing of sperm in cancer patients, however this outcome was not well defined [10].

10. SAFETY

Gamete or embryo cryopreservation is routinely commissioned and provided within the NHS for patients receiving treatment for cancer. Collection of sperm is non-invasive, however collection of eggs requires sedation and is invasive. This may result in cramps or vaginal bleeding after the procedure. Both procedures are considered safe and are undertaken routinely.

One systematic review of low quality was identified which considered outcome data for 369 children born using frozen oocytes (both vitrification and slow freezing) between 1984 and 2008. This found birth weight was within normal ranges, following vitrification of oocytes 26% of singleton births were premature and 2.5% of children had congenital malformations, however the extent of these were not reported and this study was at high risk of bias. The authors also noted that long term follow up studies of these children was required [2].

11. COST EFFECTIVENESS EVIDENCE SUMMARY

No evidence reviewing the cost effectiveness of these interventions in this population has been identified. NICE state that no formal health economic investigation has been undertaken [4]. However it is likely that these procedures are cost effective.

The treatment costs for egg retrieval and freezing (eggs or embryos) are approximately £3,000 per patient. The treatment costs for sperm freezing are approximately £250 per patient per year. If surgical sperm retrieval is required then this would cost an additional £850 per patient. Storage costs are approximately £200 per year for males and females.

Using current estimates of demand the total cost for the East Midlands is estimated to be approximately £230,000 per year for gamete extraction and freezing and one year of storage. Cumulative storage costs will occur over time.

12. COMMISSIONING POLICY

Patients eligible for NHS-funded gamete or embryo cryopreservation should be about to commence treatment (which would be funded by the NHS) that may cause permanent infertility as a result of their treatment. Conditions considered appropriate for gamete or embryo cryopreservation include but are not limited to:

- malignancies or other autoimmune conditions requiring chemotherapy;
- malignancies requiring total body irradiation or radiotherapy that may affect an individual's reproductive organs;
- conditions requiring male urological or female gynaecological surgery (e.g. women with a BRCA 1 gene mutation not in a position to start a family and being prepared for bilateral salpingo-oophrectomy);
- conditions requiring specialist endocrinology services;
- rare mitochondrial disorders.

The policy includes retrieval and storage for transgender patients who are receiving treatment for gender dysphoria which may cause permanent infertility (hormone therapy, reconstructive surgery etc.). Cryopreservation will be funded for patients on a transgender pathway provided the criteria below are met.

Women who are preparing for medical treatment for cancer that is likely to make them permanently infertile, should only be offered oocyte or embryo cryopreservation if they meet all of the following criteria:

- they are well enough to undergo ovarian stimulation and egg collection; **and**
- there is sufficient time available to harvest eggs before the start of their cancer treatment.

Generally, women who are undergoing gynaecological surgery should only be offered oocyte cryopreservation if, following surgery, pregnancy would still be viable. In rare circumstances, such as women whose uterus will be removed completely (including patients on a transgender pathway), this should not limit their eligibility for gamete or embryo cryopreservation. However, the future use of frozen gametes will be in line with all relevant policies in place at the time, for example relating to surrogacy.

Individuals should also meet the following criteria:

- Females of reproductive age up to 42 years old (stimulation treatment to take place prior to individual's 43rd birthday). There is no minimum age limit;

- Males of reproductive age up to 55 years old (sperm retrieval to take place prior to individual's 56th birthday). There is no minimum age limit;
- Registered with a GP belonging to an East Midlands CCG (or unregistered but confirmed as the responsibility of the CCG);
- Written informed consent to treatment and gamete or embryo storage will be required.

Exclusion criteria

Individuals will not be eligible for NHS-funded gamete or embryo cryopreservation if:

- Gametes are being frozen for non-medical or non-surgical reasons, for example for social reasons;
- they are receiving experimental treatment as part of a research study where the treatment may cause infertility (this does not include treatment for cancer);
- they have previously been sterilised, even if sterilisation has been reversed;
- they have premature ovarian failure;
- they are not about to undergo specific treatment which may cause permanent infertility;
- gametes are being frozen for use by individuals other than the patient receiving treatment (with the rare exception of women whose uterus will be removed completely - including patients on a transgender pathway).

Previous NHS funded assisted conception treatment will not be taken into consideration when determining eligibility for NHS-funded gamete or embryo cryopreservation.

Surgical sperm retrieval (if required) is not covered by this policy. NHS England hold the commissioning responsibility for this (see 'Clinical Commissioning Policy: Surgical Sperm Retrieval for Male Infertility').

Embryo storage using donor sperm is not routinely commissioned.

It should be explained that future use of frozen gametes will be in line with all relevant policies in place at the time, for example relating to surrogacy.

Cryopreservation of ovarian or testicular tissue is still considered to be an experimental procedure and therefore funding of this is not included under this policy.

13. EXCEPTIONAL CIRCUMSTANCES

CCGs will consider individual cases for funding outside this commissioning policy in accordance with their Individual Funding Request (IFR) Policy which sets out a decision making framework for determining these cases. For an IFR request to be considered, it must be demonstrated that the patient fulfils the strict criteria for exceptionality.

It should be noted that the criteria for exceptionality is very unlikely to be satisfied if an individual is part of an identifiable cohort of patients, who at the same disease stage would derive similar benefit from the intervention.

14. PATIENT PATHWAY

A single cycle of treatment only will be funded i.e. not multiple attempts. Treatment will only be funded at centres licensed by the Human Fertilisation and Embryology Authority.

Access into services for gamete or embryo cryopreservation should be by consultant referral. The consultant responsible for the care resulting in infertility will be required to provide the following information for all individuals referred for gamete or embryo cryopreservation:

- name
- date of birth
- address
- GP
- details of the underlying condition
- confirmation that the treatment carries with it a significant risk of permanent infertility
- for female cancers, confirmation that the use of stimulation drugs as part of the egg retrieval process will not be detrimental to the patient

The treatment provided will be the most appropriate for the patient's individual clinical circumstances and will include:

- confirmation that the individual meets the inclusion criteria for gamete or embryo cryopreservation as detailed in this policy, and does not meet any of the exclusion criteria;
- screening for patient and partner (if applicable) for HIV, hepatitis B and hepatitis C prior to treatment. This is because gametes or embryos will be processed by the laboratory and stored in a fridge where other samples are kept. People found to test positive for one or more of these should be offered specialist advice and counselling and appropriate clinical management;
- written consent for cryopreservation of individual's gametes or embryos and an individual patient agreement;
- provision of medication for stimulation of gamete production, as required;
- harvesting of gametes;
- gamete/embryo freezing.

Gamete or embryo storage will normally be funded for a maximum period of 10 years. Sperm will normally be stored for a maximum period of 10 years, or until a man reaches the age of 56 years old, whichever is sooner. Eggs and embryos will normally be stored for a maximum period of 10 years, or until a woman reaches the age of 43 years old, whichever is sooner.

Storage of sperm, eggs or embryos will not normally be funded for longer than 10 years, apart from in exceptional circumstances. If patients wish to continue to store their gametes beyond this or they no longer meet the eligibility criteria in this policy, they may choose to self-fund this.

CCGs will not fund any additional costs for the transportation of sperm, eggs or embryos if required.

APPENDICIES

Appendix 1 Evidence Summary

Source	Evidence	Comments
<p>Glujovsky, D., Riestra, B., Sueldo, C., Fiszbajn, G., Repping, S., Nodar, F., ... Ciapponi, A. (2014). Vitrification versus slow freezing for women undergoing oocyte cryopreservation. <i>The Cochrane Database of Systematic Reviews</i>, 9, CD010047. https://doi.org/10.1002/14651858.CD010047.pub2</p>	<p>Clinical pregnancy rate following Vitrification of oocytes: 44.9% of cycles</p> <p>Clinical pregnancy rate following Slow freezing of oocytes: 11.6% of cycles</p> <p>Relative risk of clinical pregnancy = 3.86 (95%CI 1.63 to 9.11, P = 0.002), verification vs slow freezing.</p>	<p>These data do not relate directly to the population considered here but may be indicative.</p> <p>Moderate risk of bias. Systematic review included 106 women from two RCTs.</p>
<p>Cil, A. P., Bang, H., & Oktay, K. (2013). Age-specific probability of live birth with oocyte cryopreservation: An individual patient data meta-analysis. <i>Fertility and Sterility</i>, 100(2), 492–499.e3. https://doi.org/10.1016/j.fertnstert.2013.04.023</p>	<p>Clinical pregnancy rate following vitrification or slow freezing of oocytes ranged from 10.8-43.3%</p> <p>Live birth success rates declined with age regardless of the freezing technique</p> <p>Estimated probabilities of live birth for vitrified oocytes were higher than those for slowly frozen</p>	<p>Low quality evidence at high risk of bias for this outcome</p> <p>Original data from 10 studies including 2,265 cycles from 1,805 patients were obtained</p>
<p>Cobo, A., & Diaz, C. (2011). Clinical application of oocyte vitrification: A systematic review and meta-analysis of randomized controlled trials. <i>Fertility and Sterility</i>, 96(2), 277–285. https://doi.org/10.1016/j.fertnstert.2011.06.030</p>	<p>Clinical pregnancy rates using vitrification freezing techniques ranged from 38-65%.</p> <p>The meta-analysis reported no significant difference in ongoing or clinical pregnancy rates between vitrified and fresh oocytes and significantly higher oocyte survival and fertilisation rates using vitrified oocytes compared to slow-frozen oocytes.</p>	<p>Systematic review of five randomised controlled trials of oocyte preservation, undertaken between 2005 and 2009</p>
<p>Oktay, K., Cil, A. P., & Bang, H. (2006). Efficiency of oocyte cryopreservation: a meta-analysis. <i>Fertility and Sterility</i>, 86(1), 70–80. https://doi.org/10.1016/j.fertnstert.2006.03.017</p>	<p>Live-birth rate used as a proxy for clinical pregnancy rate.</p> <p>Live-birth rates per cycle following slow freezing before June 2005 = 21.6%</p> <p>Higher rates achieved with vitrification after June 2005.</p> <p>Author conclusion: oocyte cryopreservation appears to be justified for preserving fertility when a medical indication exists.</p>	<p>Systematic review of observational studies and case reports. Low quality evidence at high risk of bias for this outcome</p>

<p>Ferrari, S., Paffoni, A., Filippi, F., Busnelli, A., Vegetti, W., & Somigliana, E. (2016). Sperm cryopreservation and reproductive outcome in male cancer patients: a systematic review. <i>Reproductive BioMedicine Online</i>, 33(1), 29–38. https://doi.org/10.1016/j.rbmo.2016.04.002</p>	<p>Effectiveness of sperm banking programmes for cancer patients</p> <p>Of patients who used their frozen semen and achieved parenthood was reported in 19 studies. The crude aggregated rate across studies was 49% (95% CI 44 to 53%), however this outcome was not well defined.</p>	<p>Low quality systematic review of observational studies</p> <p>Moderate to high risk of bias</p>
<p>Wennerholm, U.-B., Soderstrom-Anttila, V., Bergh, C., Aittomaki, K., Hazekamp, J., Nygren, K.-G., ... Loft, A. (2009). Children born after cryopreservation of embryos or oocytes: a systematic review of outcome data. <i>Human Reproduction</i>, 24(9), 2158–2172. https://doi.org/10.1093/humrep/dep125</p>	<p>Safety profile</p> <p>This found birth weight was within normal ranges, following vitrification of oocytes 26% of singleton births were premature 2.5% of children had congenital malformations, however the extent of these were not reported</p>	<p>Systematic review of low quality which considered outcome data for 369 children born between 1984 and 2008.</p> <p>Authors noted long term follow up studies of these children are required</p>

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Appendix 2

Table 1: Estimates of demand for cryopreservation based on historic referral data 2013/14-2016/17 mid-2015 CCG population estimates (Source: ONS population estimates)

CCG Area	Population	Estimated demand	Population	Estimated demand
NHS Corby	32,779	3	34,075	1
NHS East Leicestershire and Rutland	160,593	17	165,306	3
NHS Leicester City	170,336	18	172,291	3
NHS Lincolnshire East	113,708	12	118,322	2
NHS Lincolnshire West	114,841	12	119,497	2
NHS Nene	315,959	33	324,076	6
NHS South Lincolnshire	70,822	7	75,158	1
NHS South West Lincolnshire	60,759	6	63,558	1
NHS West Leicestershire	193,141	20	194,315	3
NHS Erewash	47,254	5	49,063	1
NHS Hardwick	54,342	6	56,129	1
NHS Mansfield and Ashfield	96,574	10	99,804	2
NHS Newark & Sherwood	58,021	6	60,712	1
NHS North Derbyshire	133,814	14	139,084	2
NHS Nottingham City	161,093	17	157,808	3
NHS Nottingham North and East	73,256	8	76,221	1
NHS Nottingham West	55,600	6	56,653	1
NHS Rushcliffe	56,386	6	58,088	1
NHS Southern Derbyshire	258,905	27	264,848	5
East Midlands	2,228,183	233	2,285,008	40

GLOSSARY

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