
Guidance and recommendations for referral to fertility services

September 2014



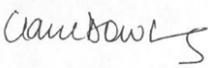
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1 Background

The LCA was established in 2011 in response to the *Model for Care* (2010) with the primary aims of improving cancer outcomes and cancer patient experience in south and west London. Tumour specific and cross-cutting pathway groups were set up to address identified areas for improvement, with smaller working groups used to complete specific areas of clinical practice when necessary.

The *Model for Care* (2010) tasked the LCA gynaecology pathway with ensuring fertility preservation was considered for its patient groups. However, the LCA recognised that fertility affects a much wider group of cancer diagnoses, namely haematology, breast, urology and teenage and young adult (TYA) and is a crosscutting survivorship issue for people diagnosed with these cancers. As a result, a working group was formed, comprising the Chairs (or nominated representatives with specific clinical knowledge/expertise) of those pathway groups. Clinical experts from the two identified onco-fertility services within the LCA (Imperial College Healthcare NHS Trust and Guy's and St Thomas' NHS Foundation Trust) joined the working party in addition.

In April 2014 the NHS England (London) Transforming Cancer Services Team (TCST) published its five-year commissioning strategy and two-year commissioning intentions, including those for cancer survivorship. Two of the requirements of these are the development of agreed pathways for those experiencing sexual dysfunction post cancer treatment and for those experiencing pelvic consequences post-radiotherapy. Fertility preservation and management fall within the scope of these and as such there is an additional drive through commissioning to address fertility in cancer.

This document is the result of the work of LCA fertility working group (see Appendix 2 for membership details) and lays out guidance and recommendations for fertility preservation for those with a cancer diagnosis treated within the LCA provider trusts.

2 Introduction

Male and female gonadal toxicity are common side effects of cancer treatments and of some cancers themselves. While cancer is most prevalent in older people, 4 % of all UK diagnoses, approximately 1100 per annum, are in those aged 15-40 years. *The effects of cancer treatment on reproductive functions: Guidance on management* (2007) made clear that all patients with reproductive potential who require anti-cancer treatment should be fully informed of the gonadotoxic side effects at the time of treatment and be offered specialist psychological support and counselling, with consideration for fertility preservation given and offered when possible.

This stance has progressed since 2007, and it is now mandatory for oncologists to advise and inform those undergoing treatments which carry a risk of gonadal failure, infertility and possible effects on sexual functioning of these consequences.

NICE published its first clinical guideline on fertility in 2004, with a second iteration published in February 2013. The 2013 document includes some important additions for provision of fertility preservation services for those with a cancer diagnosis.

- Early referral for specialist consultation should be made when there is a known clinical cause of infertility or a history of predisposing factors for infertility.
- Where treatment is planned that may result in infertility (such as treatment for cancer) early fertility specialist referral should be offered.
- When considering and using gamete cryopreservation for people before starting chemotherapy or radiotherapy that is likely to affect their fertility, follow the recommendations in 'The effects of cancer treatment on reproductive functions' (2007).
- For cancer-related fertility preservation, do not apply the eligibility criteria used for conventional infertility treatment.

- Do not use a lower age limit for gamete cryopreservation for fertility preservation in people diagnosed with cancer.
- When using gamete cryopreservation to preserve fertility in people with cancer, use sperm, embryos or oocytes.
- Offer sperm cryopreservation to men and adolescent boys who are preparing for medical treatment for cancer that is likely to make them infertile.
- Freeze in liquid nitrogen vapour as the preferred cryopreservation method technique for sperm.
- Offer oocyte or embryo cryopreservation as appropriate to women of reproductive age (including adolescent girls) who are preparing for medical treatment for cancer that is likely to make them infertile if:
 - They are well enough to undergo ovarian stimulation and egg collection and
 - This will not worsen their condition and
 - Enough time is available before the start of their cancer treatment
 - For cryopreservation of oocytes and embryos, use vitrification instead of controlled-rate freezing if the necessary equipment and expertise is available
- Store cryopreserved material for an initial period of 10 years
- Offer continued storage of cryopreserved sperm, beyond 10 years, to men who remain at risk of significant infertility

The draft NICE quality standard on fertility problems (May 2014) adds further weight, spelling out, amongst other things, the implications for providers and commissioners of implementing this guidance.

The role of the LCA is to respond to existing national guidance, including that outlined above, in addition to other evidence, tumour specific NICE guidance and expert opinion, to agree a streamlined fertility pathway for those from the point of cancer diagnosis and the offer of fertility preservation, through to post treatment referral for fertility assessment and intervention. In addition, the LCA is committed to sharing its work with the TCST to support their role in the commissioning of such services.

3 Fertility and onco-fertility services

Fertility services are able to provide:

- Assessment of fertility status
- Fertility preservation options
- Assistance with trying to conceive
- Exploration of alternative options for family building
- Referral to specialist fertility counselling services

Onco-fertility services have, in addition to the above:

- a comprehensive understanding of the cancer and cancer-treatment specific fertility consequences
- the ability to carry out a detailed assessment of gamete cryopreservation options in light of the cancer and its long term consequences relevant to fertility
- specialist knowledge in the field of onco-fertility, enabling counselling of the person, even if the likely outcome is that cryopreservation is not an option
- the ability to create a thorough plan for fertility preservation and future management taking the consequences of cancer and its treatment(s) into account
- an expert knowledge enabling them to be a reference point for Oncology specialists to discuss potential referrals
- ability to provide post-cancer treatment follow-up and to instigate fertility treatment when appropriate
- Onco-fertility services within the LCA are currently available at Guy's and St Thomas' NHS Foundation Trust and Imperial College Healthcare NHS Trust

4 Teenagers and Young Adults

Research shows that fertility is a major concern to teenage and young adult (TYA) cancer patients. Many TYA patients cannot recall fertility being discussed at the time of diagnosis, or are not satisfied with the discussion if one did happen. Those at the younger end of the population may not have considered their future fertility plans previously, making these discussions additionally complex.

TYAs with cancer should be provided with the opportunity to discuss fertility at the time of diagnosis, and should be referred to an appropriately skilled onco-fertility service to enable them to fully understand the potential fertility related consequences of cancer treatments and to make decisions regarding their preservation options.

5 Criteria for referral for fertility preservation

5.1 For men

- Boys who have entered puberty and show signs of sexual maturity
- Men below the age of 55 who wish to preserve their fertility
- Not have started chemotherapy/radiotherapy prior to sperm cryopreservation
- Be physically well enough to attend the ACU (Assisted Conception Unit) and be able to provide a sperm sample by masturbation unaided.
- If a man cannot travel to the fertility centre, but is able to produce a sample in the cancer unit, which can then be transported to the andrology unit, the fertility preservation service should be contacted directly for advice.
- Sperm retrieval directly from the testis can be arranged in the cancer unit if the man is undergoing another surgical procedure. This is uncommon and should be dealt with on an individual basis. Please contact the fertility preservation service directly for advice in these situations.
- Been screened and tested negative for hepatitis B surface antigen, hepatitis C core antibody, and HIV antigen antibody. The results must be available before acceptance of a referral for sperm cryopreservation by the fertility centre and is the responsibility of the referring oncology clinician to obtain.

5.2 For women

- Girls who have entered puberty and show signs of sexual maturity
- Women in a stable relationship below the age of 40 can have embryo cryopreservation
- Single women under 36 can cryopreserve oocytes in the presence of normal ovarian reserve
- Single women aged over 36 and under 40 with normal ovarian reserve are considered on an individual basis
- Be medically stable and physically well enough to defer cancer therapy for time stipulated to undergo fertility preservation
- Not have started chemotherapy. Those started on hydroxycarbamide will need to stop this during ovarian stimulation
- Should ideally have a BMI >19 and <30 to be eligible for NHS funding
- Ideally, have been screened for hepatitis B surface antigen, hepatitis B core antibody, hepatitis C antibody, HIV antigen/antibody. It is the responsibility of the referring clinician to provide the relevant results prior to cryopreservation.

5.3 Points to consider

- For some tumour groups, fertility may have been affected by the cancer itself, e.g. testicular. This may affect the success of subsequent fertility treatment attempts. However, cryopreservation should still be attempted as there are techniques available to achieve pregnancy with low numbers of sperm.
- The rationale for hepatitis B, C, and HIV screening pre-referral is to avoid delay in cryopreservation. Positive samples must be stored separately from negative samples to avoid cross contamination. Sperm samples are held in temporary storage and cryopreserved only when the screening status is confirmed. Storage for positive samples is currently available only in one LCA based fertility service (Chelsea & Westminster NHS Foundation Trust) and one onco-fertility service (Imperial College Healthcare NHS Trust).
- The presence of menstruation is not indicative of significant ovarian reserve. Therefore, return of a normal menstrual cycle post-gonadotoxic treatment should not prevent a referral for fertility assessment and possible intervention being made.
- Women currently taking oral contraception should continue to do so, unless contraindicated by the cancer diagnosis, until they are seen at the onco-fertility service
- To minimise delay between diagnosis and chemotherapy, the menstrual cycle can be manipulated and ovarian stimulation can be commenced at almost any stage in the cycle.

6 Follow-up

6.1 Short term

6.1.1 For women

Women who have undergone fertility treatment should be reviewed at one week post-egg retrieval to ensure the ovaries are reducing in size after ovarian stimulation and they are able to proceed with their oncological treatment. This is particularly relevant for women undergoing pelvic radiotherapy, as if the ovaries remain enlarged, radiation fields may be affected.

6.1.2 For men

Early post-oncology treatment review may be of benefit for men who have cryopreserved sperm at diagnosis but who have not had time to fully consider their future fertility plans.

6.2 Longer term

6.2.1 For women

Women who are at high risk of ovarian failure after cancer treatment should be re-referred to onco-fertility services to assess ovarian function, fertility status and/or management of premature ovarian failure where appropriate.

Women can be seen soon after completion of chemotherapy and within 6 weeks post-HSCT (haematopoietic stem cell transplant), (if they are well enough to do so). It is better not to wait for the onset of menopausal symptoms prior to making a referral. Women who wish to consider future fertility and have developed ovarian failure will benefit from early institution of appropriate hormone therapy, providing it is oncologically safe so to do.

Annual cervical smears are recommended post HSCT), due to the increased risk of cervical neoplasia.

6.2.2 For men

Assessment of sperm recovery in an onco-fertility clinic one to two years post cancer treatment is recommended. If function is normal, or on-going gamete storage is not needed, the samples may be discarded with written consent.

6.3 Consequences of treatment requiring referral

6.3.1 GVHD

Genital GVHD post-HSCT is under-diagnosed with late referrals being common. Appropriate questioning by the clinician will suggest genital involvement and early referral is encouraged to avoid possible irreversible complications. If there are concerns that genital GVHD has developed post HSCT, referral should be made to onco-fertility services, even if fertility preservation wasn't undertaken pre-cancer treatment.

6.3.2 Sexual dysfunction

Male and female sexual dysfunction is common post-cancer treatment and has been shown to negatively impact on quality of life, intimate relationships and self-confidence. These treatment consequences should be assessed during treatment follow-up and appropriate referrals to the patient's GP or an appropriate specialist sexual or erectile dysfunction (ED) service considered.

6.3.3 Contraception

Contraception should be discussed with those of reproductive age who have received cancer treatment, even in the absence of regular menstruation, or when sperm recovery is not known.

7 Funding and eligibility

There is currently no national policy for funding any of the techniques which aim to preserve fertility or treat the effects of gonadal damage associated with cancer treatment. All CCGs have separate funding criteria and as such, funding for any fertility preservation or treatment should not be assumed.

However, the eligibility criteria for conventional infertility treatment does not apply in the case of fertility cryopreservation provided by the NHS in the cancer setting, though will apply when using stored material for assisted conception in an NHS setting.

The NHS eligibility criteria, relevant for cancer, for fertility treatment are:

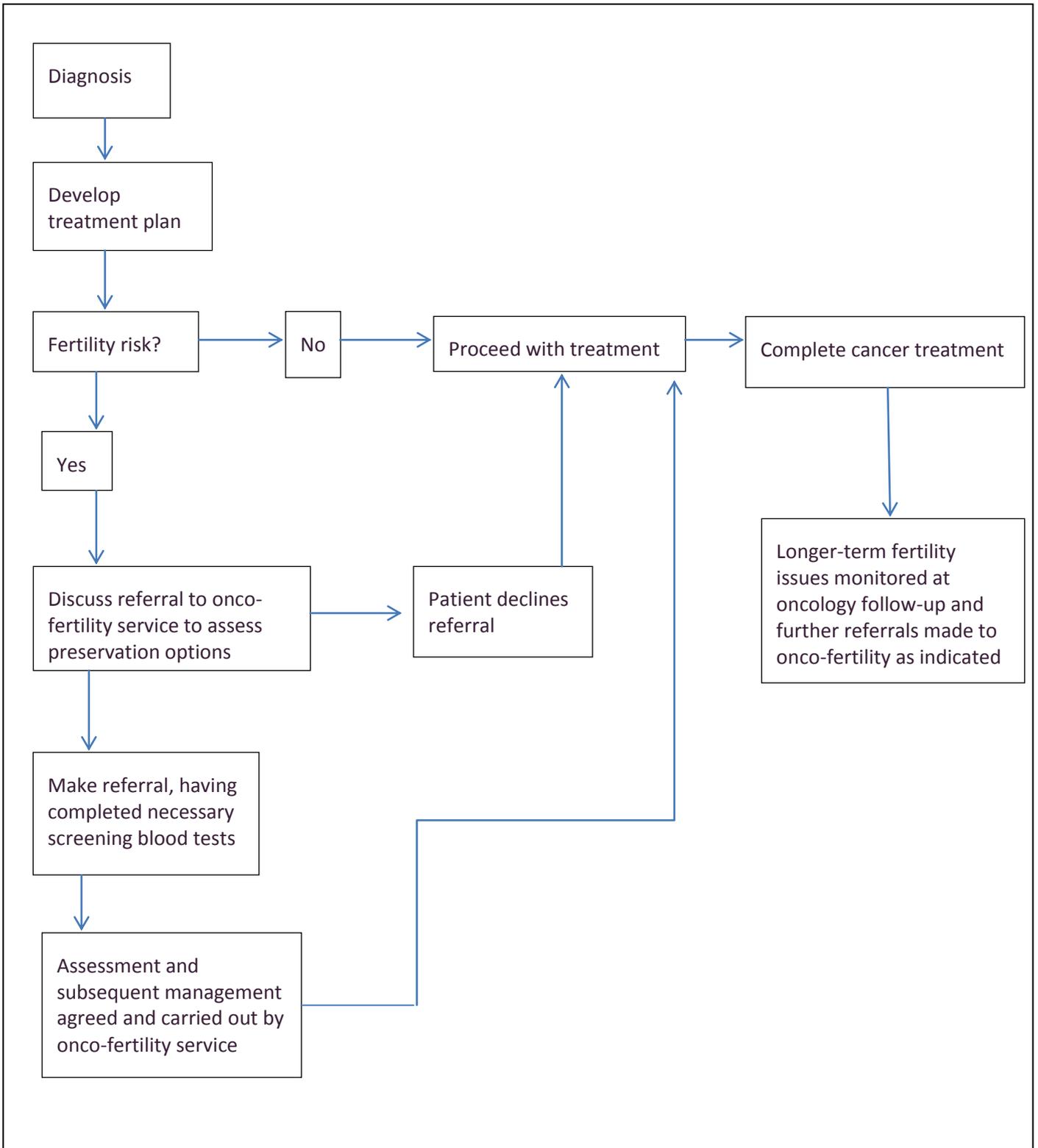
- Early referral for consultation to discuss options for attempting conception when there is a known clinical cause of infertility or a history of predisposing factors for infertility
- In women under 40, offer three full cycles of IVF. If the woman reaches 40 during treatment, complete the cycle but do not offer further cycles
- In women aged 40-42, offer one full cycle of IVF provided,
 - They have never previously had IVF
 - There is no evidence of low ovarian reserve
 - There has been a discussion of the additional implications of IVF and pregnancy at this age
- Women should ideally have a BMI of between 19 and 30
- Sperm can be stored for 55 years, at which time, it will be destroyed
- Sperm can be stored for boys. Parental consent is not required, and Gillick competence and Fraser guidelines will be used.

The cost of freezing and storage varies by provider and CCG. The fertility centres will usually make an application for funding on behalf of the person, providing they meet the eligibility criteria. In most cases, after a defined period of time, often five years, the person will have to self-fund on-going gamete storage

costs. Individual applications to the relevant CCG can be made and will be considered on an individual basis.

Appendix 1

Referral Process



Appendix 2

LCA Fertility Working Group Membership

Member	Designation	Organisation
Dr Nivedita Reddy	Lead Consultant, Assisted Conception Unit	Guy's and St Thomas' NHS Foundation Trust
Dr Stuart Lavery	Lead Consultant, IVF Hammersmith	Imperial College Hospital Healthcare NHS Trust
Dr William Teh	Breast Pathway Group Chair Consultant Radiologist	LCA North West London Hospitals NHS Trust
Dr Alexandra Taylor	Gynaecology Pathway Group Chair Consultant Clinical Oncologist	LCA The Royal Marsden NHS Foundation Trust
Ms Louise Soames	Teenage and Young Adult Pathway Group Chair Nurse Consultant	LCA The Royal Marsden NHS Foundation Trust
Dr Isabel White	Clinical Research Fellow in Psychosexual Practice	The Royal Marsden NHA Foundation Trust
Mr Nicholas Watkin	Urology Pathway Group Member Consultant Urological Surgeon	LCA St George's Healthcare NHS Trust
Ms Michelle Bull	Haematology and Gynaecology Pathways Project Manager	LCA
Ms Nicola Glover	Survivorship and Mental Health and Psychological Support Pathways Project Manager	LCA

Appendix 3

LCA Provider Trust Fertility Services

Chelsea and Westminster Hospital NHS Foundation Trust - <http://www.chelwest.nhs.uk/services/womens-health-services/assisted-conception-unit-acu>

Croydon Health Services NHS Trust - <http://www.croydonhealthservices.nhs.uk/services/Fertility/>

Epsom and St Helier University Hospitals NHS Trust - <http://www.epsom-sthelier.nhs.uk/our-services/a-to-z-of-services/women-and-children/gynaecology/assisted-conception-unit/>

Guy's and St Thomas' NHS Foundation Trust - <http://www.guysandstthomas.nhs.uk/our-services/acu/overview.aspx>

The Hillingdon Hospitals NHS Foundation Trust - http://www.thh.nhs.uk/services/women_babies/fertility/index.php

Imperial College Healthcare NHS Trust - <http://www.imperial.nhs.uk/services/gynaecology/fertilityandreproductivemedicine/index.htm>

King's College Hospital NHS Foundation Trust - <https://www.kch.nhs.uk/service/a-z/acu>

Kingston Hospital NHS Foundation Trust - <http://www.kingstonacu.org.uk/>

Mount Vernon Cancer Centre - <http://www.enherts-tr.nhs.uk/patients-visitors/our-services/gynaecology/>

St George's Healthcare NHS Trust - <https://www.stgeorges.nhs.uk/service/gynaecology/>

West Middlesex University Hospital NHS Trust - <http://www.west-middlesex-hospital.nhs.uk/patients-and-visitors/a-z-of-services/gynaecology/>