NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Guideline scope

Ovarian cancer: identifying and managing familial and genetic risk

May 2023: This scope has been amended.

We have updated section 3.1 to be clear that it includes all people who meet the characteristics in the bullets. Familial ovarian cancer affects people with female reproductive organs, but people with male reproductive organs are also at risk of having a pathogenic variant associated with ovarian cancer.

We have also clarified in the 'Areas that will not be covered' section that risk management and decision-making support for people with male reproductive organs who have, or are at risk of having, a pathogenic variant associated with ovarian cancer is outside the scope. This is because they are not at risk of developing ovarian cancer and the decisions that they would have to make (in relation to their children and their risk for other cancers) are different and outside the scope of this guideline.

The Department of Health and Social Care in England has asked NICE to develop a guideline on familial ovarian cancer. This guideline will focus on identifying and managing the risk of familial ovarian cancer using genetic testing and risk-reducing interventions.

The guideline will be developed using the methods and processes outlined in developing NICE guidelines: the manual.

This scope uses the term 'women' throughout, but this should be taken to include anyone born with some or all of the following organs: ovaries; fallopian tubes; and uterus.

1 Why the guideline is needed

About 340,000 to 440,000 women in the UK carry a pathogenic variant that increases their risk of ovarian cancer. This includes pathogenic variants in *BRCA1, BRCA2, RAD51C, RAD51D, BRIP1, PALB2, MLH1, MSH2* and *MSH6* genes. It is estimated that 15% to 20% of women with high-grade epithelial ovarian cancer also carry a pathogenic variant associated with increased risk of ovarian cancer.

The majority of women who carry a pathogenic variant for ovarian cancer do not have a family history suggestive of a genetic risk. This means many carriers have not sought testing for high risk ovarian cancer pathogenic variants. Current best estimates are that only 3% of pathogenic variant carriers know they are carriers. This proportion will increase with improved availability of genetic testing.

Most women who carry a pathogenic variant will not develop ovarian cancer. But guidance is needed on how to assess the risk of developing ovarian cancer, what risk-reducing interventions should or should not be offered, and what support should be given.

Current practice

- Germline genetic testing is defined in the NHS England National Genomic Test Directory. However not all eligible women are routinely offered this. In addition, women at increased risk could be missed because they do not fit the current criteria, for example on the basis of unaffected family history.
- Risk-reducing salpingo-oophorectomy is currently an option for preventing ovarian cancer in women at high risk of developing ovarian cancer. However, there is variation in practice. Some women could be having risk-reducing surgery when they do not need it and others who could benefit

from risk-reducing surgery may not be offered it. Also, use of hormone-replacement therapy after risk-reducing surgery varies.

- Some centres use a specific pathological protocol to assess histological samples removed during surgery to identify in situ or occult invasive lesions. But this is not uniformly done, so some in situ or occult invasive cancers may be missed.

Policy, legislation, regulation and commissioning

The Chief Medical Officer's 2016 report and the NHS independent Cancer Taskforce strategy (2015 to 2020) highlight the benefits of genetic testing in the NHS. The NHS Long Term Plan supports using genetic testing to provide more personalised care for people with cancer.

2 Who the guideline is for

This guideline is for:

- healthcare professionals working in primary, secondary and tertiary care
- cancer alliances
- commissioners of ovarian cancer services (including clinical commissioning groups and NHS England specialised commissioning)
- voluntary sector organisations working with women who have increased risk, or a diagnosis, of familial ovarian cancer
- women at increased risk of familial ovarian cancer
- women with suspected or diagnosed familial ovarian cancer, their families and carers
- women with ovarian cancer.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the Welsh Government, Scottish Government, and Northern Ireland Executive.

Equality considerations

NICE has carried out an equality impact assessment during scoping. The assessment:

- lists equality issues identified, and how they have been addressed
- explains why any groups are excluded from the scope.

The guideline will look at inequalities relating to:

- Accessing genetic testing, and fertility and menopause services, including socioeconomic and geographical factors, and factors relating to age, ethnicity and disabilities.
- Accessing and providing information that could inform decisions about genetic testing and risk-reducing options available following genetic testing for gene carriers. This includes people for whom English is not their first language or who have other communication needs.

The guideline will also consider potential inequalities for trans people (particularly trans men) and non-binary people in relation to accessing services, including genetic testing.

3 What the guideline will cover

3.1 Who is the focus?

Groups that will be covered

People who:

- carry a pathogenic variant that increases the risk of ovarian cancer, including in genes such as *BRCA1, BRCA2, RAD51C, RAD51D, BRIP1, PALB2, MLH1, MSH2* and *MSH6*
- have a relative who carries a pathogenic variant that increases the risk of ovarian cancer, including in genes such as *BRCA1, BRCA2, RAD51C, RAD51D, BRIP1, PALB2, MLH1, MSH2* and *MSH6*
- have a family history of ovarian cancer (with or without a family history of breast cancer)
- have a family history or a diagnosis of a syndrome associated with an increased risk of ovarian cancer, for example Lynch syndrome

- come from populations with an increased prevalence of pathogenic variants associated with ovarian cancer
- have suspected or diagnosed familial ovarian cancer
- have ovarian cancer (with or without breast cancer).

3.2 Settings

Settings that will be covered

All settings where NHS commissioned care is provided.

3.3 Activities, services or aspects of care

Key areas that will be covered

We will look at evidence in the areas below when developing the guideline, but it may not be possible to make recommendations in all the areas.

1 Individual and family support
2 Configuration of referral, risk assessment and risk management services
3 Risk prediction or assessment methods for familial ovarian cancer
4 Risk thresholds for genetic testing for familial ovarian cancer
5 Genetic testing for familial ovarian cancer
6 Familial ovarian cancer surveillance
7 Primary preventive medicines for familial ovarian cancer
8 Risk-reducing surgery for familial ovarian cancer

Note that guideline recommendations for medicines will normally fall within licensed indications; exceptionally, and only if clearly supported by evidence, use outside a licensed indication may be recommended. The guideline will assume that prescribers will use a medicine's summary of product characteristics to inform decisions made with individual patients.

Areas that will not be covered

1 Recognition and initial management of ovarian cancer
2 Risk management and decision-making support for men, trans women and non-binary people (who have male reproductive organs) who have,

or are at risk of having, a pathogenic variant associated with ovarian cancer

Related NICE guidance

Published

- Colorectal cancer (2020, updated 2021) NICE guideline NG151
- Early and locally advanced breast cancer: diagnosis and management (2018) NICE guideline NG101
- Pancreatic cancer in adults: diagnosis and management (2018) NICE guideline NG85
- Menopause: diagnosis and management (currently being updated, publication expected August 2023) NICE guideline NG23
- Suspected cancer: recognition and referral (2015, updated 2021) NICE guideline NG12
- Familial breast cancer: classification, care and managing breast cancer and related risks in people with a family history of breast cancer (2013, updated 2019) NICE guideline CG164
- Fertility problems: assessment and management (2013, currently being updated, publication tbc) NICE guideline CG156
- Ovarian cancer: recognition and initial management (2011) NICE guideline CG122
- Metastatic malignant disease of unknown primary origin in adults: diagnosis and management (2010) NICE guideline CG104
- Testing strategies for Lynch syndrome in people with endometrial cancer (2020) NICE diagnostics guidance DG42
- Tests in secondary care to identify people at high risk of ovarian cancer (2017) NICE diagnostic guidance DG31
- Molecular testing strategies for Lynch syndrome in people with colorectal cancer (2017) NICE diagnostics guidance DG27

NICE guidance about the experience of people using NHS services

NICE has produced the following guidance on the experience of people using the NHS. This guideline will not include additional recommendations on these topics unless there are specific issues related to familial ovarian cancer:

- Medicines optimisation (2015) NICE guideline NG5
- Patient experience in adult NHS services (2012) NICE guideline CG138
- Medicines adherence (2009) NICE guideline CG76

3.4 Economic aspects

We will take economic aspects into account when making recommendations. We will develop an economic plan that states for each review question (or key area in the scope) whether economic considerations are relevant, and if so whether this is an area that should be prioritised for economic modelling and analysis. We will review the economic evidence and carry out economic analyses, using an NHS and personal social services perspective, as appropriate.

3.5 Key issues and draft questions

While writing this scope, we have identified the following key issues and draft questions related to them:

1 Individual and family support

1.1 What information and support is needed by women with familial ovarian cancer or who are at increased risk of ovarian cancer (with or without breast cancer), and their families and carers?

1.2 Which interventions are effective for supporting women at increased risk of ovarian cancer to make decisions about management options?

2 Configuration of referral, risk assessment and risk management services

2.1 What is the most effective configuration of services for referral, risk assessment and risk management for women at increased risk

of ovarian cancer (including fertility, menopause and psychological support services)?

3 Risk prediction or assessment methods for familial ovarian cancer

3.1 What are the optimal methods of assessing the probability of having a pathogenic variant associated with familial ovarian cancer?

3.2 What are the optimal methods of assessing the absolute risk of ovarian cancer in women at increased risk of ovarian cancer?

4 Risk thresholds for genetic testing for familial ovarian cancer

4.1 At what carrier probability should a person with a family history of ovarian cancer (with or without breast cancer) be offered genetic testing?

4.2 On the basis of what carrier probability or criteria should a person with a family history of a syndrome associated with an increased risk of ovarian cancer, (for example Lynch syndrome) be offered genetic testing?

4.3 Which populations with a high prevalence of pathogenic variants would meet the risk threshold for genetic testing?

4.4 At what carrier probability should women with ovarian cancer (with or without breast cancer) be offered genetic testing?

5 Genetic testing for familial ovarian cancer

5.1 Which genes should be included in a gene panel when testing for pathogenic variants that increase the risk of familial ovarian cancer?

6 Familial ovarian cancer surveillance

6.1 What are the benefits and risks of surveillance for women at increased risk of familial ovarian cancer?

6.2 How effective are different methods of surveillance for women at increased risk of familial ovarian cancer?

7 Primary preventive medicines for familial ovarian cancer

7.1 How effective are preventive medicines for reducing the incidence of ovarian cancer for women at increased risk of familial ovarian cancer?

8 Risk-reducing surgery for familial ovarian cancer

8.1 How effective is risk-reducing surgery for women at increased risk of familial ovarian cancer (also considering risk threshold, age and extent and types of surgery)?

8.2 What pathological protocol for handling specimens from risk reducing surgery should be followed for risk-reducing surgery for women at increased risk of familial ovarian cancer?

8.3 What are the benefits and risks of hormone replacement therapy after risk-reducing surgery for women at increased risk of familial ovarian cancer?

3.6 Main outcomes

The main outcomes that may be considered when searching for and assessing the evidence are:

- disease-related morbidity
- disease-specific survival
- fertility
- health-related quality of life
- ovarian cancer
- overall survival
- prognostic accuracy
- psychological wellbeing
- resource use
- symptoms related to the menopause

- test accuracy
- treatment-related morbidity.

4 NICE quality standards

NICE quality standards that will use this guideline as an evidence source when they are being developed

- It has not been confirmed whether the guideline will be used to develop a quality standard.

Further information

This is the final scope, which takes into account comments from registered stakeholders during consultation.

The guideline is expected to be published in March 2024.

You can follow progress of the guideline.

Our website has information about how NICE guidelines are developed.