NICE National Institute for Health and Care Excellence

Putting NICE guidance into practice

Resource impact report:
Testing strategies for Lynch syndrome in people with endometrial cancer (DG42)

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Summary

NICE has recommended testing strategies for Lynch syndrome in people with endometrial cancer.

We estimate that around:

- 7,600 people with endometrial cancer are eligible for testing for Lynch syndrome
- 7,200 people with endometrial cancer will have testing for Lynch syndrome from year 5 onwards once uptake has reached 95%.
- 320 people with endometrial cancer will be diagnosed with Lynch syndrome from year 5 onwards.
- 1,140 family members will have testing for Lynch syndrome from year 5 onwards
- 500 family members will be diagnosed with Lynch syndrome from year 5 onwards.

The estimated annual cost of implementing this guidance for the population of England based on the uptake in the resource impact assumptions is shown in table 1.

Table 1 Estimated annual cost of implementing the guidance for England

	2020/21	2021/22	2022/23	2023/24	2024/25
Population with endometrial cancer having testing for Lynch syndrome each year	1,734	3,107	4,480	5,852	7,225
People with endometrial cancer who have Lynch syndrome	77	138	199	260	321
Family members having testing for Lynch syndrome each year	275	492	710	927	1,144
Family members who have Lynch syndrome	121	217	312	408	504
Total number of people diagnosed with Lynch syndrome	**198**	**355**	**511**	**668**	**825**
Resource impact each year for people having testing for Lynch syndrome (£000s)	**875**	**1,749**	**2,624**	**3,499**	**4,374**

This report is supported by a resource impact template which may be used to calculate the resource impact of implementing the guidance by amending the variables.

Services for genetic testing for Lynch syndrome (MLH1 promoter hypermethylation testing of tumour DNA and genetic testing of germline DNA) are commissioned by NHS England and immunohistochemistry services are commissioned by clinical commissioning groups. Providers are NHS hospital trusts.

1 Testing strategies for Lynch syndrome in people with endometrial cancer

1.1 **Offer testing for Lynch syndrome to people who are diagnosed with endometrial cancer. Use immunohistochemistry (IHC) to identify tumours with mismatch repair (MMR) deficiency:**

- **If IHC is abnormal with loss of MLH1, or loss of both MLH1 and PMS2 protein expression, do MLH1 promoter hypermethylation testing of tumour DNA. If MLH1 promoter hypermethylation is not detected, offer germline genetic testing to confirm Lynch syndrome.**
- **If IHC is abnormal with loss of MSH2, MSH6 or isolated PMS2 protein expression, offer germline genetic testing to confirm Lynch syndrome.**

Healthcare professionals should inform people about the possible implications of test results for both themselves and their relatives and give support and information. Discussion of genetic testing and obtaining consent should be done by a healthcare professional with appropriate training.

Laboratories doing IHC for MMR proteins, MLH1 promoter hypermethylation testing or germline genetic testing should take part in a recognised external quality assurance programme.

1.2 Lynch syndrome is an inherited syndrome associated with a genetic increased risk to certain types of cancers, the most common are endometrial cancer and colorectal cancer. NICE has issued guidance recommending testing for Lynch syndrome in people with colorectal cancer (DG27 Molecular testing strategies for Lynch syndrome in people with colorectal cancer), but testing of people with endometrial cancer for Lynch syndrome is not routinely carried out.

1.3 After a diagnosis of Lynch syndrome, treatment and surveillance can be offered to reduce the risk of having another Lynch syndrome associated cancer.

1.4 Genetic testing for Lynch syndrome can also be offered to family members to allow risk reducing approaches for cancer to be offered with the aim of preventing cancer developing or detecting it at an early stage.

2 Resource impact of the guidance

2.1 We estimate that around:

- 7,600 people in England with endometrial cancer are eligible for testing for Lynch syndrome each year
- 7,200 people with endometrial cancer will have testing for Lynch syndrome from year 5 onwards once uptake has reached 95%.
- 320 people with endometrial cancer will be diagnosed with Lynch syndrome from year 5 onwards.
- 1,140 family members would have testing for Lynch syndrome from year 5
- 500 family members will be diagnosed with Lynch syndrome from year 5 onwards.

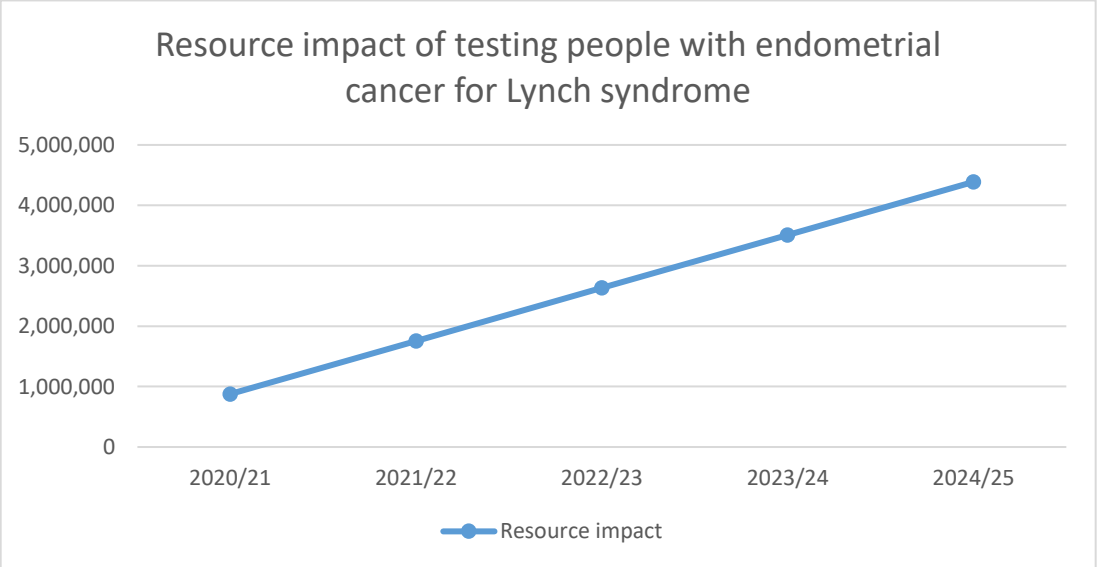
2.2 The current treatment and future uptake figure assumptions are based on the health economic model that supports this guidance and are shown in the resource impact template.

2.3 The estimated annual cost of implementing this guidance for the population of England, based on the uptake in the resource impact assumptions, is shown in table 2. The cost from year 5 once steady state is reached is equivalent to £7,800 per 100,000 population.

Table 2 Resource impact of implementing the guidance using NICE assumptions

	2020/21	2021/22	2022/23	2023/24	2024/25
Population with endometrial cancer having testing for Lynch syndrome each year	1,734	3,107	4,480	5,852	7,225
People with endometrial cancer who have Lynch syndrome	77	138	199	260	321
Family members having testing for Lynch syndrome each year	276	493	710	927	1,144
Family members who have Lynch syndrome	121	217	312	408	504
Total number of people diagnosed with Lynch syndrome	**198**	**355**	**511**	**668**	**825**
Resource impact each year for people having testing for Lynch syndrome (£000s)	**875**	**1,749**	**2,624**	**3,499**	**4,374**

Figure 1 Resource impact of testing people with endometrial cancer for Lynch syndrome (£)



2.4 This report is supported by a resource impact template which may be used to calculate the resource impact of implementing the guidance by amending the variables.

Savings and benefits

2.5 Genetic testing should reduce the incidence of endometrial and colorectal cancer. This should avoid costs relating to the treatment of these cancers in the future. Testing and identifying someone with Lynch syndrome results in greater surveillance for cancer, allowing earlier diagnosis, reducing the morbidity and mortality of advanced cancer, this will reduce the cost of treatment.

2.6 After a diagnosis of endometrial cancer and a subsequent diagnosis of Lynch syndrome, interventions and surveillance can be adopted to reduce the risk of other Lynch syndrome associated cancers or detect them earlier.

2.7 Testing family members identifies people as having Lynch syndrome before they have cancer. If a person knows they have Lynch syndrome they can make lifestyle changes to reduce their cancer risk and it may also help to inform decisions about family planning.

3 Implications for commissioners

3.1 Services for genetic testing for Lynch syndrome (MLH1 promoter hypermethylation testing of tumour DNA and genetic testing of germline DNA) are commissioned by NHS England and immunohistochemistry services are commissioned by clinical commissioning groups. Providers are NHS hospital trusts.

3.2 There will be an increase in the number of diagnostic colonoscopies, for people diagnosed with Lynch syndrome, to screen for colorectal cancer.

3.3 Genetic testing may increase after this guidance is implemented. This should reduce the incidence of Lynch syndrome associated cancers.

3.4 Endometrial cancer falls within the programme budgeting category 02G Cancer, Gynaecological.

4 How we estimated the resource impact

The population

4.1 The annual incidence of female adults with endometrial cancer is around 7,600 (Office for national statistics, 2017). It is expected that all these people will be eligible for testing for Lynch syndrome and that uptake of testing will be around 95% of people (around 7,200 people).

Table 3 Number of people eligible for treatment in England

Population	Proportion of previous row	Number of people
Total adult population		44,022,560
Female adult population		22,480,998
Incidence of endometrial cancer[1]	0.034%	7,605
Total number of people eligible for testing for Lynch syndrome	100%	7,605
People who accept tumour testing (IHC)[2]	95%	7,225
People having IHC testing who have positive results for PMS2, MSH2 and MSH6 who go on to be offered genetic counselling for Lynch syndrome **(a)**	5.87%	424
People having IHC testing who have a positive result for MLH1	16.7%	1,207
People with a positive result for MLH1 using IHC who gone on to have an MLH1 promoter hypermethylation test	100%	1,207
People with negative results for MLH1 promoter hypermethylation testing who go on to be offered genetic counselling for Lynch syndrome **(b)**	22.35%	270
People eligible for genetic testing **(a+b)**		694
People who accept genetic counselling	92.5%	642
People who have Lynch syndrome confirmed by genetic testing[3]	50%	321
Family members estimated to be offered testing for Lynch syndrome each year from 2024/25[3]	6	1,925
Family members who take up the offer of genetic counselling	77.5%	1,492
Family members who take up the offer of genetic testing for Lynch syndrome	76.7%	1,144
Family members who have Lynch syndrome confirmed by genetic testing[3]	44%	504

1 Source: ONS UK Cancer registrations
2 Health economic model for NICE DG42 Testing strategies for Lynch syndrome in people with endometrial cancer
3 See resource impact template for pathway details

Assumptions

- Expert clinical opinion is that in current practice 5% of people (around 400 people) with endometrial cancer receive immunohistochemistry (IHC) testing for Lynch syndrome.

- Based on health economic model supporting this guidance, 95% of people will have IHC testing when offered (around 360 people).
- It is assumed in current practice that 16.7% of people (60) have a positive IHC test with loss of MLH1 and go on to have a MLH1 promoter hypermethylation test of tumour DNA.
- It is assumed in current practice that 22.35% of people (14) will be referred to a genetics service and will be offered genetic counselling.
- Based on the health economic model supporting this guidance, it is assumed that 92.5% will accept counselling, and have genetic testing. This is estimated to be around 20 people in current practice.
- Based on the health economic model supporting the guidance, 50% of people tested will test positive for Lynch syndrome. Everybody who tests positive for Lynch syndrome (around 10 people in current practice) will be offered screening for colorectal cancer.
- Based on the assumptions in the health economic model it is assumed that each person who tests positive for Lynch syndrome will have 6 family members who will be offered genetic counselling for Lynch syndrome.
- Based on Barrow PhD Thesis 2014, 77.5% of family members (around 50 people in current practice) accept the offer of genetic counselling. Of these people, 76.7% (around 40 people) will accept the offer of genetic testing.
- From these family members it is estimated that around 44% (around 20 people in current practice) will be diagnosed with Lynch syndrome and all these people will be offered screening for colorectal cancer. It is assumed that all these people will take up the colorectal cancer screening (based on the health economic model).

- Based on the health economics, around 50% of the family members (around 10 people) are estimated to be female and could be offered gynaecological cancer screening. In the template it is not assumed that people will have gynaecological cancer screening. If it is local practice to offer gynaecological screening then this can be adjusted in the template.
- In future practice it is assumed, based on the economic model, that 95% of people (around 7,200 people) with endometrial cancer will have IHC testing.
- According to the health economic model supporting this guidance 5.87% of people (around 420 people in future practice) who have IHC testing will test positive for PMS2, MSH2 and MSH6 and be offered genetic counselling. 16.7% of people (around 1,210 people) will test positive for MLH1.
- The health economic model also informs us that people who have a positive IHC test that shows loss of MLH1 will have a MLH1 promoter hypermethylation test of tumour DNA. It is expected that 22.35% (270 people) will be offered genetic testing for Lynch syndrome in future practice.
- It is assumed that 92.5% of these people (around 430 people) will accept genetic counselling and 50% (around 215) of them will test positive for Lynch syndrome.
- Based on the economic model, people who have a positive test result for Lynch syndrome will have an average of 6 family members (around 1,300 people) who will be eligible for testing for Lynch syndrome.
- As per current practice, it is assumed that 77.5% of the family members (around 990 people) will have genetic counselling and that 76.7% of people (around 760) will accept the offer of genetic counselling.
- It is assumed that 44% of family members (around 340 people) will test positive for Lynch syndrome and will be offered screening for colorectal cancer.

- Based on the health economic model, around 50% of the family members (170 people) are estimated to be female and could be offered screening for gynaecological cancer. In the template it is not assumed that people will have gynaecological cancer screening. If it is local practice to offer gynaecological screening, then this can be adjusted in the template.

Sensitivity analysis

4.2 There are some assumptions in the model for which no empirical evidence exists, so we cannot be as certain about them. Appropriate minimum and maximum values of variables were used in the sensitivity analysis to assess which variables have the biggest impact on the net cost or saving. This enables users to identify the significant cost drivers.

4.3 For people who test positive for Lynch syndrome, varying the number of family members in future practice who have cascade testing for Lynch syndrome between 4 and 8 people (baseline used in modelling is 6 people) leads to an estimated cost of between £3.8 million and £4.9 million for the population of England.

4.4 Varying the number of people who accept genetic counselling in future practice from 87.5% to 97.5% leads to an estimated cost of between £4.2 million and £4.5 million for the population of England.

4.5 Varying the number of people who accept IHC testing in future practice from 92.5% to 97.5% leads to an estimated cost of between £4.3 million and £4.5 million for the population of England.

About this resource impact report

This resource impact report accompanies the NICE guidance on testing strategies for Lynch syndrome in people with endometrial cancer and should be read with it.