NICE National Institute for Health and Care Excellence

Putting NICE guidance into practice

Resource impact report:

Molecular testing strategies for Lynch syndrome in people with colorectal cancer (DG27)

Published: February 2017

Summary

Molecular testing strategies for Lynch syndrome are detailed in the guidance see 1.2 for further detail.

Implementing the recommendations in the guidance will increase the number of people who have genetic testing for Lynch syndrome. People with Lynch syndrome have an increased risk of cancer. After a diagnosis of Lynch syndrome, risk-reducing strategies can be offered to prevent or allow early diagnosis of associated cancers. Screening tests are available for colorectal and endometrial cancer.

It is estimated that up to 2,500 people may have screening with colonoscopy for colorectal cancer and up to 2,190 people may have screening for endometrial cancer each year.

Table 1 People with Lynch syndrome having cancer screening

Population	2017/18	2018/19	2019/20	2020/21	2021/22
Colonoscopy screening	2,500	2,500	2,500	2,500	2,500
Endometrial Screening	2,190	2,190	2,190	2,190	2,190

The guidance may have resource implications at a local level because of variation in clinical practice across the country. Therefore, organisations are encouraged to evaluate their own practice against the recommendations in the NICE guidance and assess resource impact locally.

Services for testing for Lynch syndrome are commissioned by NHS England and Clinical Commissioning groups. Providers are NHS Hospital Trusts.

1 Introduction

1.1 This report looks at the resource impact of implementing the NICE guidance on molecular testing for Lynch syndrome in people with colorectal cancer in England.

1.2 The guidance states that:

- Offer testing to all people with colorectal cancer, when first diagnosed, using immunohistochemistry for mismatch repair proteins or microsatellite instability testing to identify tumours with deficient DNA mismatch repair, and to guide further sequential testing for Lynch syndrome (see 1.2 and 1.3). Do not wait for the results before starting treatment.
- If using immunohistochemistry, follow the steps in table 2.

Table 2 Steps in the immunohistochemistry testing strategy

Step 1	Do an immunohistochemistry 4-panel test for MLH1, MSH2, MSH6 and PMS2.	
Step 2	If the MLH1 immunohistochemistry result is abnormal, use sequential *BRAF* V600E and *MLH1* promoter hypermethylation testing to differentiate sporadic and Lynch syndrome-associated colorectal cancers. First do a *BRAF* V600E test.	If the MSH2, MSH6 or PMS2 immunohistochemistry results are abnormal, confirm Lynch syndrome by genetic testing of germline DNA.
Step 3	If the *BRAF* V600E test is negative, do an *MLH1* promoter hypermethylation test.	
Step 4	If the *MLH1* promoter hypermethylation test is negative, confirm Lynch syndrome by genetic testing of germline DNA.	

- If using microsatellite instability testing, follow the steps in table 3.

Table 3 Steps in the microsatellite instability testing strategy

Step 1	Do a microsatellite instability test.
Step 2	If the microsatellite instability test result is positive, use sequential *BRAF* V600E and *MLH1* promoter hypermethylation testing to differentiate sporadic and Lynch syndrome-associated colorectal cancers. First do a *BRAF* V600E test.
Step 3	If the *BRAF* V600E test is negative, do an *MLH1* promoter hypermethylation test.
Step 4	If the *MLH1* promoter hypermethylation test is negative, confirm Lynch syndrome by genetic testing of germline DNA.

- Healthcare professionals should ensure that people are informed of the possible implications of test results for both themselves and their relatives, and ensure that relevant support and information is available. Discussion of genetic testing should be done by a healthcare professional with appropriate training.
- Laboratories doing microsatellite instability testing or immunohistochemistry for mismatch repair proteins should take part in a recognised external quality assurance programme.

1.3 This report is supported by a resource impact template. The template aims to help organisations in England, Wales and Northern Ireland plan for the financial implications of implementing the NICE guidance by amending the variables.

1.4 Services for testing for Lynch syndrome are commissioned by NHS England and Clinical Commissioning Groups. Providers are NHS Hospital Trusts.

2 Background and epidemiology of Lynch syndrome

2.1 Lynch syndrome is an inherited genetic condition caused by mutations in DNA mismatch repair (MMR) genes and in another

non-MMR gene, known as EPCAM, which increase the risk of colorectal cancer, gynaecological cancers and other cancers. Risk-reducing interventions can be offered to people with mutations known to be due to Lynch syndrome.

2.2 Tumour-based tests, microsatellite instability (MSI) or MMR immunohistochemistry (IHC), may be used in people diagnosed with colorectal cancer (called 'probands') to identify those at high risk of Lynch syndrome and guide further testing. *MLH1* promoter hypermethylation and *BRAF* V600E testing can also be done on tumour material to identify sporadic colorectal cancers and rule out Lynch syndrome.

2.3 Although there are no national guidelines, the current guidelines for managing Lynch syndrome produced by the Mallorca Group (now known as the European Hereditary Tumour Group), a group of European experts recommend colonoscopy every 2 years starting from age 25 years.

Table 4 Annual number of probands with colorectal cancer tested for Lynch in England

Population	Percentage/ number	Number of people
Total adult population of England		42,724,917
Incidence of colorectal cancer	0.08%	34,000
People with colorectal cancer who have tumour testing with either MSI or IHC[1]	100%	34,000
People with Lynch syndrome[2]	4.59%	1,600
1 Clinical expert opinion 2 NICE Resource Impact template Molecular testing strategies for Lynch syndrome in people with colorectal cancer (DG27)		

Table 5 Annual number of relatives tested for Lynch syndrome and eligible for screening with colonoscopy

Population	Percentage/ number	Number of People
Probands with Lynch syndrome identified annually from testing people with colorectal cancer[1]		1,600
Number of relatives, per proband identified with Lynch syndrome, who would be offered testing for Lynch syndrome[2]	6	7,800
Number of relatives who would have testing for Lynch syndrome[2]	60.06%	5,600
Percentage of relatives testing positive for Lynch syndrome[2]	44%	2,500
Total number of relatives eligible for screening with colonoscopy[2]	100%	2,500
Total number of relatives estimated to have screening with colonoscopy every second year from year 1	100%	2,500

1 NICE Resource Impact template Molecular testing strategies for Lynch syndrome in people with colorectal cancer (DG27)
2 Diagnostics Assessment Report for Molecular testing for Lynch syndrome in people with colorectal cancer

Table 6 Annual number of people diagnosed with Lynch syndrome who are eligible for endometrial screening

Population	Percentage/ number	Number of People
People with Lynch syndrome identified annually from testing people with colorectal cancer[1]		1,600
Percentage of people with colorectal cancer and Lynch syndrome who are women and eligible for endometrial screening[2]	44%	690
Number of relatives, per proband identified with Lynch syndrome, who would be offered testing for Lynch syndrome[3]	6	9,400
Number of relatives who would have testing for Lynch syndrome[3]	60.06%	5,600
Relatives who would have Lynch syndrome[3]	44%	2,500
Relatives who are women and eligible for endometrial screening[4]	62%	1,500
Total number of people eligible for endometrial screening		2,190
Total number of people estimated to have endometrial screening each year from year 1	100%	2,190

1 NICE Resource Impact template Molecular testing strategies for Lynch syndrome in people with colorectal cancer (DG27)
2 Cancer registration statistics, England: 2014
3 Diagnostics Assessment Report for Molecular testing for Lynch syndrome in people with colorectal cancer
4 Diagnostics Assessment Report for Molecular testing for Lynch syndrome in people with colorectal cancer. Pooling of Wales and Wessex data for proportion of relatives of the person with Lynch syndrome who are women.

2.4 From year 1 it is estimated that 2,500 people will have screening with colonoscopy for colorectal cancer and 2,190 people will have screening for endometrial cancer each year because uptake is estimated to be 100% from implementation.

3 Assumptions made

3.1 The resource impact template makes the following assumptions:

- It is assumed that when a person with colorectal cancer is found to have Lynch syndrome, 6 relatives will be offered cascade testing for Lynch syndrome. This is the identification of relatives who are then tested to find out if they also have the condition. Of these people, it is assumed that 60.06% will have genetic testing for Lynch syndrome.
- It is assumed that 44% of relatives who are tested will have Lynch syndrome based on Diagnostic Assessment Report analysis of Jenkins 2006 and Hampel 2008.
- It is assumed that people with Lynch syndrome will have a screening colonoscopy and polypectomy every 2 years based on clinical expert opinion and current Mallorca group guidelines
- It is assumed that 44% of probands with Lynch syndrome and 62% of relatives diagnosed with Lynch syndrome would be women.
- It is assumed that women with Lynch syndrome will have endometrial screening every year based on clinical expert opinion.
- It is assumed that the endometrial screening would be a blood test to establish CA125 levels and a gynaecology follow up outpatient appointment. This would be followed by an ultrasound and endometrial aspiration.

4 Resource impact

4.1 This guidance is anticipated to have an impact, which should be assessed at a local level. Therefore, we encourage organisations to evaluate their own practice against the recommendations in the NICE guidance and assess costs using the local resource impact template.

4.2 Implementing the recommendations in the guidance will increase the number of people who have genetic testing for Lynch syndrome. This may increase use of pathology and genetic testing services.

4.3 People with Lynch syndrome have an increased risk of cancer. Screening tests are available for colorectal and endometrial cancer. It is anticipated that implementing this guidance will increase the numbers of screening tests for colorectal and endometrial cancers, see table 7.

Table 7 People with Lynch syndrome having cancer screening

Population	2017/18	2018/19	2019/20	2020/21	2021/22
Colonoscopy screening	2,500	2,500	2,500	2,500	2,500
Endometrial Screening	2,190	2,190	2,190	2,190	2,190

4.4 Cascade testing of relatives of people identified as having Lynch syndrome will increase the numbers of colonoscopies and gynaecological examinations being carried out.

4.5 It has been assumed that the 60% of relatives of people with Lynch syndrome would have genetic testing. It is estimated, that if only people under 50 are currently tested, the resource impact for England would be £13,554,000. The effect of varying the proportion of relatives who have genetic testing is shown in table 8.

Table 8 Estimated resource impact of implementing the guidance on Molecular testing strategies for Lynch syndrome in people with colorectal cancer for England

Proportion of relatives who have genetic testing for Lynch syndrome	Estimated resource impact for England (£)
40%	12,487,000
60%	13,554,000
80%	14,614,000

5 Savings and benefits

5.1 Increased screening of people with Lynch syndrome is shown to reduce the number of people who develop colorectal cancer. This reduces the amount of costly chemotherapy or radiotherapy used to treat people with colorectal cancer.

5.2 Outcomes improve if colorectal cancer and endometrial cancer is diagnosed at an early stage. The person may need less invasive, lower cost treatment.

6 Implications for commissioners

6.1 Genetic testing may increase after this guidance is implemented. This should reduce the incidence of colorectal cancer and endometrial cancer.

About this resource impact report

This resource impact report accompanies the NICE guidance on molecular testing for Lynch syndrome in people with colorectal cancer and should be read in conjunction with it. See terms and conditions on the NICE website.