Lynch syndrome information for primary care

This letter is to provide information specific to your patient on a condition they have – **Lynch Syndrome (LS)**. LS was previously known as HNPCC (Hereditary Non-Polyposis Colorectal Cancer), and some patients may still have this terminology in their records.

Dr Aldred Warthin first recognised this condition in 1913 in “Family G”. Dr Henry Lynch and his team continued this work and in 1984 it was termed “Lynch” syndrome in honour of him. Advances in science have identified the cause of the condition and developed and researched how we can reduce future risk of developing cancers.

1. What is Lynch Syndrome?

L.S is an inherited cancer predisposition syndrome. It is caused by an alteration in one of the mis match repair genes. The protein product of these genes are involved in proof reading DNA (checking for spelling mistakes after DNA is copied). The genes involved are called mismatch repair genes (MMR). There are five genes that may be affected (MLH1, MSH2, MSH6, PMS2 and *EPCAM which switches off MSH2*).

The condition is inherited in an autosomal dominant way, meaning that there is a 50% chance of a parent passing the alteration on to a child. With an increase in age and the person’s lifestyle, the working copy may become affected and puts the individual at risk of developing cancers. It has been found that between 1:270 to 1:400 people in the UK have this genotype. However, it is estimated that only 5% of individuals with the condition know they have it. Both males and females are affected in all ethnicities.

Since 2017 NICE has supported testing of colorectal tumours to see if they were caused by a MMR gene problem, followed by testing of endometrial cancer in 2020 and specific ovarian cancers in 2024. All cancers have something that has gone wrong with the DNA in the cancer cells. If the tumour tests show one or more of the MMR proteins missing, then further tests will be actioned which may include a genetic test for Lynch syndrome.

An individual with LS, will be offered tailored information about risk reduction including screening, support to disseminate the information within the family, (first degree relatives in the first instance e.g. siblings, parents and children) and they are offered “cascade testing” through the local genetics team. Knowing that you have LS before you get cancer, means that you may be able to avoid it.

Since 2017, NICE has recommended routine testing of colorectal tumours for MMR deficiency, extended to endometrial cancers in 2020 and relevant ovarian cancers in 2024. When tumour testing indicates possible MMR dysfunction, further investigations determine whether the cause is a germline variant. **Identifying LS**

early can influence cancer management, as LS associated cancers may respond differently to standard treatments.

Your patient may have been diagnosed some time ago and may no longer be in regular contact with genetics services. Due to this they may not have received recent updates, which is why we are asking primary care to review and update their records accordingly.

Individuals with LS receive tailored advice on cancer risk reduction, including screening and discussions with first degree relatives (parents, siblings, and children). Genetic services offer cascade testing to family members. **Early identification of LS allows individuals to take preventive measures and potentially reduce their risk of developing cancer.**

2. Key actions for primary care:

1. **Check that Lynch Syndrome is coded** (SNOMED 716318002) and please put which gene is affected against this to help in any action that may be needed in the future (MLH1, MSH2, MSH6, PMS2 or EPCAM).

   The highest risk is colorectal and endometrial cancer. Other less commonly occurring cancers that are associated with L.S are; ovarian, stomach, small intestine, urinary tract, pancreatic, glioblastoma, sebaceous carcinomas, keratoacanthomas, prostate cancers, Gene & gender specific risks can be found at: https://www.ukcgg.org/information-education/ukcgg-leaflets-and-guidelines

2. **File this letter in the patient records** so that it is easily identifiable as a source of reference.

3. **Flag that this individual is at higher risk of developing cancer**. Consider flagging on the home page that this individual is at higher risk of developing cancer and to have a low threshold to investigate and refer. Many fast track referral forms either have LS listed as a risk factor or the option to free text as part of a referral.

4. **Aspirin** has been shown to reduce the future risk of bowel cancer in those with LS (**CAPP3 study**). Prior to prescribing Aspirin, test and treat for Helicobacter Pylori to reduce the risk of gastric cancer by 50% and reduce the risk of possible side effects from Aspirin. Prior to prescribing, please review the patient and discuss the risk/benefits (specific Aspirin summary on page 7).

5. **Confirm that the patient is linked into the National Bowel Screening Programme**. All those known to have LS are invited through the National NHS Bowel Screening for two yearly colonoscopies (some may remain under their local

6. hospital by choice). If you think your patient is not getting their screening, then please contact the local genetics team who can refer on if needed.

Starting age:

- 25y for those with MLH1, MSH2 or EPCAM
- 35y for those with MSH6 or PMS2

Colonoscopies are not risk free and they will routinely be ceased from recall at age 75 (patients referred via the portal who are currently 75 or over should contact the helpline on 0800 707 60 60 if they wish to access screening). If your patient presents with symptoms between the screening recalls or after the recall age, investigate as you would normally for suspected cancer and have a low threshold to refer. Do not rely on the last colonoscopy report *(individuals will also receive NHS BCSP FIT tests between 50 and 74y).*

3. Further risk reduction advice:

Lifestyle interventions and awareness
These patients may have been advised on health lifestyles and avoiding unnecessary risk factors (smoking, excess alcohol….) reminding them of this and how to seek help is important. Specific areas to be aware of:

- Maintain normal body weight
- Avoid smoking
- Minimise alcohol intake
- Resistant starch (fibre) intake of 30g daily to reduce the risk of non-colorectal cancer in LS
- Reduce red and processed meat
- Be skin cancer aware (not for PMS2 carriers)
- Be prostate aware and consider PSA from age 40 (MLH1 & MSH2)
- Be endometrial cancer aware (MLH1, MSH2 & MSH6)
- Be vigilant for symptoms (e.g. pain, lumps, weight loss, tired, losing blood, change in the bowel/urine pattern, erectile dysfunction) and seek a review.

Breast and Cervical Screening. Ensure that individuals are invited and reminded about the NHS cervical and breast invites (there is no current indication to have this done at an earlier age or more frequently.

What about other cancer screening?
There are no other national screening programs at present, but please be aware of:

- Endometrial cancer – surveillance should only be part of a clinical trial. One study is looking at urine samples looking for abnormal cells.
- Prostate cancer – men with MLH1, MSH2, MSH6 & EPCAM are higher risk of prostate cancer, and it may be appropriate to seek advice on screening with PSA from age 40.

Helicobacter Pylori testing prior to starting Aspirin will reduce the risk of stomach cancer by treating the infection if found and reduce the risk of irritation from Aspirin.

The ideal test is a stool antigen or breath test; blood antibody test will only confirm a past infection.

Risk reducing surgery
Some women may wish to discuss the option of reducing their risk of endometrial and ovarian cancer. It is important that women are offered an informed specialist review e.g. clinical genetics, to coordinate this – some may opt for surgery, but this is not risk free. There is no gold standard best practice, options may include offering an IUD LNG to reduce the endometrial thickness.

Horizon scanning
There are trials checking urine samples for possible changes in the endometrium, and trials to look at the role of vaccines to prevent LS associated cancers are in place, so watch this space.

4. How it effects my patient:

Thinking about a family?
Those with LS may wish to consider the option of pre-implantation diagnosis. The local genetics team will be able to support here, consider referring early. Further information: https://www.hfea.gov.uk/i-am/i-have-a-genetic-disease-in-my-family/

New patients with LS?
If you have identified a new patient with LS (e.g. moved in from another area/country) it would be good practice to ensure that they are linked into the local genetics team, who can add them to their database for any updates/ education events and ensure they on the national bowel screening recall.

New patient who has had a private test for LS?
It is important that anyone who may have such a result is referred to the local genetics team for follow up/discussion. There are accredited labs in the UK, and the test may not need to be repeated.

Should the practice look for possible LS patients?
There may be patients who have had several LS cancers but were not investigated at the time, due to guidelines that were in place. It is important to involve the patient if they wish to explore this further, if they do then refer to the local genetics team who can review. This may involve looking at stored tumour samples and/or a blood sample. There is no clear guidance to search for unknown LS patients.

High risk family background
An individual presents with family members with **confirmed** LS, such as a first degree relative (sibling, parent or child) who has a confirmed diagnosis then please refer to the local genetics team (the index case is normally provided with letters to share with family members).

An individual presents with family members that **may** have LS, think a bit further. A simple rule can be used "3:2:1 rule"; 3 individuals with LS cancers, across 2 generations including 1 diagnosed < 50y. If this individual has no red flags to justify an urgent referral for cancer, refer to the local genetics team who can explore further and help with a diagnosis.

An extended family member has LS like cancer, such as 2nd degree (uncle/cousin/grandparent) or 3rd degree (great aunt/2nd cousin) relative, it may be worth asking for more information and consider seeking advice from the local genetics service.

An individual has a first degree relative with LS and declines own genetic test. Individuals with a 1st degree relative may choose not to be tested for the pathogenic variant themselves. It is very important they are still offered discussion and colonoscopy screening through the local gastro/colorectal/genetics team these may be called the **"high-risk family clinics"** depending on where you practice (MLH1, MSH2 or EPCAM from age 25y and PMS2 or MSH6 from age 35y).

Does LS affect my patient's insurance?
No, there is clear guidance that LS will not impact on insurance please refer to the latest information at the link below.
https://www.gov.uk/government/collections/code-on-genetic-testing-and-insurance#full-publication-update-history

5. Aspirin Guidance for Lynch Syndrome:

Aspirin is a non-selective cyclooxygenase (COX) inhibitor, it blocks both COX-1 and COX-2 by irreversibly attaching to the acetyl group on the COX protein. COX enzymes create prostaglandins which cause pain, fever and inflammation. Aspirin strongly inhibits COX-1 (protects stomach lining and platelet function) and weakly inhibits COX-2 (inflammation).

The **CAPP3** study has shown that the risk of colorectal cancer in individual with LS, is reduced by 50% when Aspirin is taken for more than 2 years with protective effects lasting up to 10 years.

When to START prescribing:
Start five years prior to recommended colonoscopy screening (initiate from 20y for MHS2, MLH1 and EPCAM; 30y for MSH6 & PMS2)
Commence Aspirin prescription up until age 65y (if diagnosed later in life) but do not initiate after 65y.

Dose of Aspirin:
Based on BMI, recommended doses:
- BMI < 30, 75mg daily
- BMI ≥ 30, 150mg daily

***Prior to starting Aspirin please**:*

- **Review medical history** for GI ulceration/bleeding, renal/liver impairment/ sensitivity to Aspirin or NSAIDs.
- **Review other medication** to ensure that there are no interactions with Aspirin e.g. methotrexate toxicity can be enhanced by Aspirin.
- Ensure that **blood pressure is controlled** as this increases risk of bleeding associated with taking Aspirin, intracranial haemorrhage estimated RR is 1.4 (1.2-1.7), more common in older age group, polypharmacy, cerebral atrophy and high BP.
- Check for and treat **helicobacter pylori**.
- Ensure that **Aspirin prescription is recorded in the patient records**, including those who buy over the counter Aspirin.

Duration of prescribing?
Current guidance is for 5 years (this may change as more data comes through) and then consider a 5-year drug "holiday" before re-commencing on a rolling program. The benefits of Aspirin continue during the "holiday" period.

Which formulation?
Standard soluble Aspirin as first line, consider enteric coated aspirin or aspirin plus a PPI if any side effects (indigestion or abdominal pain).
(*The incidence of GI bleeding with low-dose aspirin is low, Meta analysis showing 0.48–3.64 cases per 1000 person-years, and the overall estimate of the Relative Risk of symptomatic GI bleeding with low-dose aspirin was 1.4, risks increase with age, polypharmacy and comorbidity)*.

Prescribed a similar medication.
There is currently no alternative drug for Aspirin. Other COX inhibitors may show some benefit, but their mode of action is reversible COX inhibition (Aspirin is irreversible). NSAIDS e.g. Ibuprofen do target both COX-1 and COX-2, whereas some are COX-2 selective e.g. Celecoxib. If a patient is prescribed regular use of a COX inhibitor there may be some benefit in reduced colorectal cancer risk, but there are no studies to back this up. This will need to be a case-by-case discussion to consider the risks/benefits of taking any medication. This is especially important if your patient takes Aspirin with another COX inhibitor (as many are OTC) with the possible risk of GI bleeds and renal impairment – ensure to discuss as required.

Allergic or intolerant to Aspirin
If your patient cannot take Aspirin please ensure that they are engaged with bowel cancer screening, informed on lifestyle modifications and aware to seek early review if any red flags.

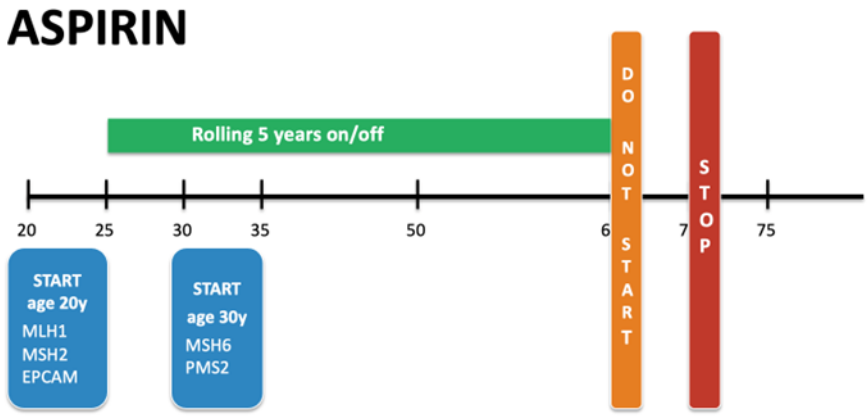
When to STOP prescribing:
At age **70y** the risks of Aspirin are greater than the benefit. Please note, the benefit continues for 10 years after discontinuation.

Patient specific:

Under 16y	do not start Aspirin as risk of Reyes Syndrome.
Over 65y	do not start Aspirin for LS as risk outweighs the benefits.
Already on Aspirin	optimise dose, i.e. *75 mg if BMI < 30 or 150mg if BMI ≥ 30.*
Pregnancy	no evidence that Aspirin causes harm when taken at lower doses early in pregnancy, or higher doses in the short term (before 20 weeks). Current guidance is to stop by 36 weeks' gestation due to the bleeding risk. Please ensure that the local obstetric team are aware a woman is taking Aspirin for LS, as they may only be aware of women prescribed in high-risk pregnancy e.g. risk of pre-eclampsia.
Breast feeding	not recommended.
Previous bowel surgery	recommended if hemicolectomy or partial removal of the bowel, some evidence of benefit on reduction on other cancers so please consider prescribing for those who have had a total colectomy.
Due a colonoscopy	not essential to stop prior to the procedure, advise to discuss with the endoscopy unit when called.
Prescribed an anti-platelet or anti-coagulation	(e.g. Clopidogrel, Dipyridamole, Warfarin or DOAC etc) please seek advice from a specialist before starting Aspirin.
Due surgery	discuss with the surgeon, it is normally fine to stop temporarily prior to an operation.
Inflammatory bowel disease	discuss with the clinician responsible for the IBD care, helpful website for information https://bnf.nice.org.uk/drugs/aspirin/#cautions
Diverticulosis	safe to take Aspirin, but if there is inflammation (diverticulitis) may wish to hold the Aspirin (individual case discussion).
Receiving chemotherapy	this should be discussed with the oncologist/surgeon as risk of possible interactions and side effects.
Comorbidities e.g. CVD	Aspirin may be indicated for another reason, and treatment duration and/or age of stopping may be past the age of 70y, use clinical acumen to ensure optimal and best practice care.

Medication Review

Annual medication reviews should identify any concerns with Aspirin.
Routine checks renal/liver or FBC are not indicated for Aspirin alone (unless there is a reason or for another medication monitoring).



6. Contacts:

UHS genetics team: GeneticsTeam@uhs.nhs.uk

Bowel Screening Programme: **0800 707 60 60**

Wessex Cancer Alliance: wessexcanceralliance@wca.uhs.nhs.uk

7. Further information and education resources:

Patient decision aid on Aspirin
https://www.nice.org.uk/guidance/ng151/resources/lynch-syndrome-should-i-take-aspirin-to-reduce-my-chance-of-getting-bowel-cancer-pdf-8834927869

"Lynch Syndrome UK" patient leaflet on Aspirin
https://www.lynch-syndrome-uk.org/post/aspirin-and-lynch-syndrome-your-questions-answered

Lynch Syndrome Charity
https://www.lynch-syndrome-uk.org

Wessex Cancer Alliance (presentations from national speakers on Lynch Syndrome)
https://wessexcanceralliance.nhs.uk/lynch-syndrome/

RM Partners
https://rmpartners.nhs.uk/our-work/improving-diagnostic-treatment-pathways/lynch-syndrome-quality-improvement-project/lynch-syndrome-information/

E-LfH
https://learninghub.nhs.uk/catalogue/national-lynch-syndrome-project

GeNOTES education page
https://www.genomicseducation.hee.nhs.uk/genotes/knowledge-hub/lynch-syndrome/

Patient Apps
https://canchoose.org.uk

Information on consumer testing
https://bsgm.org.uk/media/12844/direct-to-consumer-genomic-testing-joint-position-statement-2025.pdf

NICE information on Lynch and Colorectal Cancer
https://www.nice.org.uk/guidance/ng151/resources

Aspirin further information:
BNF guidance
https://cks.nice.org.uk/topics/antiplatelet-treatment/prescribing-information/low-dose-aspirin/

Practical prescribing on Aspirin
https://www.bmj.com/content/390/bmj-2024-081606

Helicobacter testing benefits in the HEAT study
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)01843-8/fulltext

Cancer Prevention Fact Sheet by Sir John Burn August 2014
cancer_prevention_with_aspirin_fact_sheet.pdf (capp3.org)

García Rodríguez LA, Martín-Pérez M, Hennekens CH, Rothwell PM, Lanas A. Bleeding Risk with Long-Term Low-Dose Aspirin: A Systematic Review of Observational Studies. PLoS One. 2016 Aug 4;11(8): e0160046. doi: 10.1371/journal.pone.0160046. PMID: 27490468; PMCID: PMC4973997.

Burn J, Gerdes AM, Macrae F, et al. Long-term effect of Aspirin on cancer risk in carriers of hereditary colorectal cancer: an analysis from the CAPP2 randomised controlled trial. *The Lancet*. 2011; **378**: 2081-87.

García Rodríguez LA, Martín-Pérez M, Hennekens CH, Rothwell PM, Lanas A. Bleeding Risk with Long-Term Low-Dose Aspirin: A Systematic Review of Observational Studies. PLoS One. 2016 Aug 4;11(8): e0160046. doi: 10.1371/journal.pone.0160046. PMID: 27490468; PMCID: PMC4973997.

Ishikawa H, Nakamura T, Kawano A, et al. Chemoprevention of colorectal cancer in Japan: a brief introduction to current trials. *Journal of Gastroenterology*. 2009; **44**: 77-81.