



BC Cancer Agency

CARE + RESEARCH

An agency of the Provincial Health Services Authority

Hereditary Cancer Program

Lynch Syndrome

(formerly known as HNPCC or hereditary nonpolyposis colon cancer)

Lynch syndrome (LS) is an autosomal dominant condition caused by a germline mutation in 1 of 4 DNA mismatch repair genes (*MLH1*, *MSH2*, *MSH6*, *PMS2*) or by deletions in the *EPCAM* gene. LS is characterized by an increased risk for cancers of the colon, endometrium, ovary, stomach, small intestine, hepatobiliary tract, urinary tract, brain, and skin. LS accounts for 2-4% of all colorectal cancers. While usually associated with colorectal cancer, it is important to understand that endometrial cancer is often the first cancer diagnosed in women with LS.

Muir-Torre syndrome is a subset of LS with an associated predisposition to sebaceous neoplasms and is primarily associated with *MSH2* gene mutations.

Confirmation of LS is important both for people with cancer, because of the associated risk for another LS cancer, and to inform appropriate cancer risk management for their adult family members.

Referral Criteria

Notes:

1. relevant **(LS) diagnoses** include: colorectal, endometrial, ovarian, gastric, small bowel, hepatobiliary, pancreatic, kidney, ureter, brain cancers; colorectal adenomas before age 40; sebaceous adenomas
2. **close relatives** include children, brothers, sisters, parents, aunts, uncles, grandchildren & grandparents on the same side of the family. History of cancer in cousins and more distant relatives from the same side of the family may also be relevant

Your patient's personal history (refer to notes above) – at least 1 of:

- any LS cancer with abnormal MSI/IHC screening test result (MMR deficient)
- colorectal cancer at age 40 or younger
- colorectal cancer at age 50 or younger AND no family history known due to adoption
- colorectal cancer and another LS cancer, at least 1 diagnosed at age 50 or younger

Your patient's family history (includes your patient; refer to notes above) – at least 1 of:

- family member with a confirmed *MLH1*, *MSH2*, *MSH6*, *PMS2*, or *EPCAM* gene mutation – refer for carrier testing
- a close relative with personal history as above
- 2 close relatives with a LS cancer, both diagnosed at age 50 or younger
- 3 or more close relatives with a LS cancer, at least 1 diagnosed at age 50 or younger

Estimated Lifetime Cancer Risks (to age 70) for Lynch Syndrome Mutation Carriers

Gene	* Colorectal cancer (men)	* Colorectal cancer (women)	Endometrial Cancer	Other cancers
MLH1	54-74%	30-52%	28-60%	1-15% (risks vary within and between families)
MSH2	54-74%	30-52%	28-60%	
MSH6	22-42%	20-42%	20-40%	Ovary, stomach, hepatobiliary tract, upper urinary tract, small intestine, pancreas, brain
PMS2	11-34%	8-26%	6-35%	

** risk of colorectal cancer without regular colonoscopy surveillance*

Cancer Risk Management Recommendations for Lynch syndrome mutation carriers

Note: Although the estimated lifetime cancer risks vary between genes, the following general recommendations apply to all Lynch syndrome families. Individualized recommendations based on personal and/or family medical histories may be provided through Hereditary Cancer Program assessment and/or by other specialists involved in a person's current care.

Colon Cancer:

- colonoscopy screening should begin at age 25, or 5-10 years younger than the youngest colorectal cancer diagnosis in the family, whichever is earlier
- colonoscopy should be performed every 1-2 years until age 40 and annually thereafter
- prophylactic colectomy may be considered in some individuals, taking into account their overall life expectancy and quality of life
- aspirin may reduce the risk of colorectal and other LS associated cancers although the optimal dose and duration has not yet been defined. It is reasonable for people with LS to consider using aspirin as a risk-reducing agent providing that they do not have any specific contraindications. In conjunction with a medical professional, they can decide whether to use 600mg daily or a lower dose (such as 75/100/150mg per day). A 600mg daily dosage was used in the CAPP2 (LS aspirin cancer prevention) trial while the lower doses have also been associated with a cancer prevention effect in population-based studies and are likely to have less side effects. An enteric coated form of aspirin should be used if possible

Endometrial and ovarian cancer:

- prompt investigation into any unusual bleeding between menstrual periods or after menopause
- no evidence to support endometrial cancer screening for women with LS. Some may consider annual endometrial biopsy with transvaginal ultrasound starting at age 35
- evidence does support risk-reducing hysterectomy and bilateral salpingo-oophorectomy for prevention of endometrial and ovarian cancers in women with LS. This is a reasonable option to consider after age 40, when childbearing is complete, or 5 years younger than the youngest endometrial cancer diagnosis in the family, whichever comes first

Gastric Cancer:

- consider gastroscopy every 2 years from age 30 if family history includes gastric cancer

Urothelial Cancer:

- prompt reporting and assessment of hematuria
- there is no evidence to support regular urine cytology as a screening modality

Pancreatic Cancer:

- if family history includes a first degree relative with early onset pancreatic cancer, refer to gastroenterology specific gastroenterologist to discuss pancreatic screening options, which may involve annual MRI and/or endoscopic ultrasound

Skin Cancer

- if personal or family history includes squamous cell carcinoma cancer or sebaceous neoplasm, annual dermatologic examination is a reasonable strategy for the detection of Muir-Torre syndrome associated skin lesions and to review risk modification such as minimizing sun exposure

Other cancers:

- no screening recommendations are currently available for other cancers associated with LS

Additional Information

The following websites offer support and information may be useful to people living with Lynch syndrome:

- Hereditary Colon Cancer Foundation: www.hcctakesguts.org
- Lynch Syndrome International: www.lynchcancers.com
- Familial Gastrointestinal Cancer Registry (Mount Sinai Hospital, Toronto): www.mountsinai.on.ca/care/fgicr

References available on request.

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