BC CANCER HEREDITARY CANCER
Provincial Health Services Authority

Lynch Syndrome – *MSH2* Cancer Risks and Management

Overview

Lynch syndrome is an inherited condition that increases the risk of certain cancers. It is caused by pathogenic variants in one of several genes involved in repairing DNA. One of these genes is *MSH2*.

People with a pathogenic variant in the *MSH2* gene have a higher chance of developing certain types of cancer, often at younger ages than the general population. These include colorectal, endometrial, and ovarian cancers, among others.

This page summarizes the cancer risks and management recommendations for individuals with a pathogenic variant in *MSH2*. These may be adjusted depending on a person's personal or family history of cancer.

Cancer Risks Associated with MSH2

Cancer Type	**Average Age** (years)	***MSH2*** (risk to age 75 years)	**General Population Risks**
Colorectal (male)	44	51%	6%
Colorectal (female)	44	47%	5.5%
Endometrial (uterine)	47	49%	2.6%
Ovarian	43	17%	1 to 2%
Prostate	59 to 63	Up to 24%	12.5%
Ureter/renal pelvis	55 to 61	18%	Less than 2%
Urinary bladder	59	8-13%	2%

Other cancers may include stomach, hepatobiliary tract, small intestine, pancreas and brain. The risk to age 75 for each of these is less than 10%.

Some families with Lynch syndrome have a higher risk (~ 9% lifetime) of developing sebaceous skin tumors such as sebaceous adenomas, sebaceous epitheliomas, sebaceous adenocarcinomas, keratoacanthomas, and squamous cell carcinomas. This group of skin conditions was once called Muir-Torre syndrome, but now it is recognized as part of the Lynch syndrome spectrum.

Cancer Screening and Risk Reduction

Colorectal Cancer

Screening:

Colonoscopy every 1–2 years from age 25, or 2–5 years earlier than the youngest colorectal cancer diagnosis in the family (if before age 25).

Risk Reduction:

- Daily low-dose aspirin (81 mg) is recommended, unless contraindicated, to reduce colorectal cancer risk in individuals with Lynch syndrome, with a double dose for those with a BMI of 30 or greater. Aspirin can be initiated five years prior to the start of colonoscopy screening and stop by age 70 (if the sole indication is colorectal cancer prevention). H. pylori testing and eradication as well as blood pressure control reduce the risk of aspirin-related adverse effects.
- Prophylactic colectomy is generally not recommended, except in specific situations outlined below. Surveillance of all remaining colonic mucosa should continue every 1–2 years.
    - Individuals not undergoing regular colonoscopic surveillance may benefit most
    - Segmental or extended colectomy may be considered in cases of adenomas not amenable to endoscopic removal or if high-grade dysplasia is present
    - Colectomy at the time of cancer diagnosis lowers the risk of a second primary colorectal cancer but has not been shown to improve overall survival.
    -

Endometrial and Ovarian Cancer

Screening:

- Transvaginal ultrasounds (TVUs), annual endometrial biopsies, pelvic exams, and/or CA-125 blood tests are not recommended in British Columbia, as they are either proven ineffective or lack sufficient evidence to support their use for screening purposes.
- Prompt evaluation by a physician is recommended for any unusual uterine bleeding (e.g., bleeding between menstrual periods or any postmenopausal bleeding), or for persistent symptoms such as pelvic or abdominal pain, bloating, increased abdominal girth, early satiety, difficulty eating, or urinary urgency/frequency that are a change from baseline.

Prevention:

- Recommend consultation with a gynecologic oncologist or gynecologist in community to discuss prevention strategies. Hysterectomy and bilateral salpingo-oophorectomy (BSO) recommended from age 40. Menopausal hormone therapy is

recommended at the time of risk-reducing BSO and should continue until the usual age of menopause.
- There may be a potential benefit to using the oral contraceptive pill (OCP) or Mirena IUD. In the general population, OCP use for at least 5 years reduces the risk of ovarian and endometrial cancer by 50% or more. This protective effect increases with longer duration of use and can persist for at least 20 years after discontinuation. However, it is unclear whether the same level of risk reduction applies to individuals with Lynch syndrome.

The Gynecologic Cancer Prevention and Survivorship Program provides menopause management, and surgical decision support for individuals considering risk-reducing surgery.

Urothelial Cancer (Renal Pelvis, Ureter, Bladder)
There is no clear data to recommend surveillance for urothelial cancers in Lynch syndrome. Patients are encouraged to report symptoms such as blood in the urine.

Urothelial cancer surveillance may be considered in those with a close relative with urothelial cancer (renal pelvis, ureter, bladder) or those with Lynch syndrome due to *MSH2* (especially males). Surveillance options may include annual urine cytology (urine analysis can also be performed; however, is less sensitive and does not replace urine cytology) and annual upper tract renal ultrasound starting at age 30-35 years.

Gastric and Small Bowel Cancer
There is currently limited scientific evidence to recommend gastric and small bowel cancer surveillance for people with Lynch syndrome. The surveillance below can be considered if there is a family history of gastric/small bowel cancer, additional risk factors, or at the discretion of the gastroenterologist.

High-quality esophagogastroduodenoscopy (EGD) every 2-4 years preferably at time of colonoscopy, beginning at age 30-40 years.

Screen for *Helicobacter pylori* and gastritis at the time of EGD, or as one-time noninvasive test if not undergoing endoscopy. Treat *H. pylori* if detected.

Pancreatic Cancer
- To lower the risk, avoid or quit cigarette smoking, exercise regularly, limit alcohol, maintain a weight that supports overall health and choose healthy foods and drinks.
- Begin screening for type 2 diabetes at age 40, repeat every 3 years.

- Investigate new onset of diabetes or unexplained changes in diabetic control carefully, with consideration of pancreatic imaging (CT pancreatic protocol or contrast-enhanced MRI/MRCP); refer to GI specialist if any abnormalities are found.

Surveillance may be recommended for patients with an *MSH2* pathogenic variant AND a close relative with pancreatic cancer, see this document for more information.

Skin Cancer
A dermatologic examination every 1–2 years is recommended to support early detection of associated skin lesions (e.g. sebaceous neoplasms) and to review risk factor modification strategies, including minimizing sun exposure.

Brain Cancer
Prompt evaluation by a physician is recommended for any new or persistent unexplained neurological symptoms.

Prostate Cancer
Some studies have suggested an increase in prostate cancer risk for people with Lynch syndrome, which may be specific to those with *MSH2*. The degree of risk remains unclear and there is a lack of consensus on the benefit of prostate cancer screening in the absence of a family history.

The two most common methods for prostate cancer screening are the digital rectal examination (DRE) and serum prostate specific antigen test (PSA). People may decide to pursue DRE and/or PSA testing as early as 40 years of age. Screening may be repeated annually or based on PSA levels in accordance with CUA 2022 and NCCN 2025 guidelines and continued until life expectancy is less than ten years.

The Canadian Urological Association recommends healthcare providers to engage in shared decision-making to guide individualized prostate cancer screening decisions after discussing the potential risks and benefits of PSA testing. In BC, PSA testing in people without symptoms is not an insured benefit.

Breast Cancer
General population breast cancer screening is sufficient for females with Lynch syndrome who do not have a close family history of breast cancer.

Family and Reproductive Considerations

Inheritance

Lynch syndrome follows an autosomal dominant inheritance pattern. Each child of someone with an *MSH2* pathogenic variant has a 50% chance of inheriting the variant.

Family members are encouraged to contact their local genetics clinic to learn more about genetic testing and cancer screening. Family members who live in British Columbia or the Yukon can contact our program directly at hereditarycancer@bccancer.bc.ca. In BC/Yukon, genetic testing is generally available starting at age 19.

CMMRD (Constitutional Mismatch Repair Deficiency)

CMMRD is a rare condition that happens when a child inherits two pathogenic variants (one from each parent) in the same Lynch gene (e.g. *MSH2*). It causes a high risk of childhood cancers, such as leukemia, brain, and intestinal cancers, usually diagnosed around age 10. If an individual with an *MSH2* pathogenic variant is planning a family, a review of their partner's family history of cancer may be helpful. Genetic counselling may be offered if there is a concern for the risk of CMMRD in children.

Note: In the information above, male/female refers to sex assigned at birth.