

**Cancer Risks and Screening/Risk Reduction Recommendations for Individuals with HNPCC/Lynch Syndrome (MLH1, MSH2, MSH6 mutations)**

▪ **Colorectal Cancer:**

- Lifetime risk ~65-80%
- Increased risk of second primary colon cancer
- Risk is higher for men than women
- Risk with MLH1 > MSH2 > MSH6

Screening:

- Colonoscopy every 1-2 years starting at age 20-25 or 10 years younger than the youngest colorectal cancer in the family, whichever is earlier.

Risk reduction:

- Consider total colectomy with ileorectal anastomosis upon a diagnosis of colon cancer.
- Prophylactic colectomy is usually not recommended as screening with regular colonoscopies and removal of polyps is generally effective.

▪ **Gynecologic Cancer:**

Endometrial Cancer:

- Lifetime risk ~20-60%
- Risk with MSH2 > MLH1 or MSH6

Ovarian Cancer:

- Lifetime risk ~9-12%
- Risk with MSH2 > MLH1

Screening:

- Educate patients about the symptoms of endometrial cancer (e.g. irregular vaginal bleeding, postmenopausal vaginal bleeding, pelvic pain, trouble urinating, pain during intercourse) and encourage them to seek prompt medical care for any symptoms.
- Consider annual transvaginal ultrasound, endometrial biopsy, and CA125 tumor marker blood test starting by age 30-35 (or 5-10 years younger than the youngest diagnosis in the family, whichever is earlier). In premenopausal women, this screening should preferably take place between day 1-10 of the menstrual cycle.
- *The efficacy of these screening options for women with HNPCC is unclear at this time.*

Risk Reduction:

- Consider oral contraceptives for risk reduction although the efficacy is not known specifically among women with HNPCC.
- Consider prophylactic total hysterectomy and bilateral salpingo-oophorectomy by age 35 or once childbearing is complete.

Data regarding the efficacy of screening for extracolonic cancers in individuals with HNPCC are very limited and thus there are few, if any, standard screening recommendations for these cancers. In addition, the lifetime risks for many of these extracolonic cancers are relatively low, making it difficult to justify costly and/or invasive screening. Therefore, the benefits, limitations, risks and costs of the screening options must be weighed carefully for each individual.

- **Upper Gastrointestinal Tract (including stomach and small bowel/duodenum):**
  - Lifetime risk of stomach cancer (intestinal type adenocarcinoma) is ~6-19%
  - Lifetime risk of small bowel cancer (mainly in duodenum and jejunum) is ~1-7%
  - Consider upper endoscopy every 1-2 years beginning by age 30-35.
  
- **Urinary Tract (transitional cell carcinomas of the ureter and renal pelvis):**
  - Lifetime risk is ~4-12%
  - Risk is greater in men vs. women
  - Risk with MSH2 > MLH1
  - Consider annual urinalysis with cytology beginning at age 30-35.
  
- **Hepatobiliary Tract (pancreatic, bile duct, and gall bladder):**
  - Lifetime risk is ~ 2-7%
  - No current screening recommendations at this time (if any of the available screening options are being considered, endoscopic ultrasound (EUS) would likely be preferred as it can be used to visualize the hepatobiliary tract in addition to the pancreas)
  
- **Brain/central nervous system:**
  - Lifetime risk is ~1-4%
  - No current screening recommendations at this time.
  
- **Sebaceous skin tumors and cancers:**
  - Increased risk for sebaceous skin tumors and cancers including sebaceous adenomas, sebaceous epitheliomas, sebaceous carcinomas, and keratoacanthomas.
  - The combination of sebaceous skin tumors and internal cancers is also called Muir-Torre syndrome.
  - Recent studies suggest that the rate of these tumors in individuals with Lynch syndrome is higher than previously recognized.
  - Annual dermatologic examination has been suggested for all individuals with Lynch syndrome.

References:

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