Familial Colorectal or Endometrial Cancer Syndromes

See also: Familial Cancer Syndromes pathway.

Disclaimer

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Background

About Familial Colorectal or Endometrial Cancer Syndromes

Around 10 to 15% of all patients with colorectal cancer have a significant family history. Only about 3 to 5% of all colorectal cancer is caused by an inherited predisposition gene mutation that can be identified. There are several familial colorectal cancer syndromes:

- **Lynch syndrome**
  - Formerly known as hereditary non-polyposis colorectal colon cancer (HNPCC). 1 in 280 Australians carries a gene mutation and 85,000 Australians are at risk of developing one or more cancers. □
  - Caused by mutations in one of 5 different genes (MLH1, MSH2, MSH6, PMS2, and EPCAM), each of which confers a different risk of associated cancers.
    - Mutation carriers have a 10 to 45% risk of colon cancer by age 70 years.
    - Female mutation carriers also have a 20 to 30% risk of endometrial cancer and a 10 to 15% risk of ovarian cancer by age 70 years.
  - Mutation carriers also have an increased risk of other cancers, e.g. urinary tract, small bowel, stomach, and brain.
  - Autosomal dominant, i.e. each child of a mutation carrier has a 1 in 2 chance of inheriting the mutation.

- **Familial adenomatous polyposis (FAP)**
  - Caused by mutations in the APC gene.
  - Without screening and treatment, mutation carriers have a 95% lifetime risk of colon cancer.
  - Hundreds of polyps develop from a young age and colon cancer usually develops from age 20 to 40 years.
  - Surgery and regular surveillance can help prevent bowel cancer.
  - Autosomal dominant i.e., each child of a mutation carrier has a 1 in 2 chance of inheriting the mutation.

- **MYH-associated polyposis (MAP)**
  - Caused by mutations in the MYH gene, also known as MutYH.
  - Associated with increased risk of colon cancer often with multiple polyps.
  - Autosomal recessive inheritance, there is usually no family history beyond the affected person.
  - The chance of developing bowel cancer is very high, in the absence of appropriate intervention.

- **Other rare conditions**
  - Peutz-Jegher syndrome (STK11 gene)
  - Juvenile polyposis (BMPR1A or SMAD4 gene)
  - Cowden syndrome (PTEN gene)

Assessment

**Practice Point**

Be alert to families with both bowel and endometrial cancers, as endometrial cancer is the first presenting cancer in 30% of women with Lynch syndrome.

- Clarify whether the patient has any current symptoms. If so, manage these symptoms appropriately before fully assessing the family history.
Ask about the family history on both sides of the family. Understand cultural considerations for Aboriginal and Torres Strait Islander patients. If there are relatives with cancer, consider constructing a 3-generation family tree and note in particular:

- the type of primary cancers present in the family.
- number of relatives affected.
- age of onset in the family members.
- multiple primary cancers.
- anyone in the family that has been found to carry a mutation in a predisposition gene, e.g. MLH1, MSH2, MSH6, PMS2, EPCAM, MYH, APC.
- personal or family history of colonic polyposis.

**Cultural Considerations**
- The concept of family is broader that being genetically related for many Aboriginal and Torres Strait Islander patients.
- Be sensitive when talking about cultural taboos such as Sorry Business (people who have died), Men’s Business, and Women’s Business, and references to members of the Stolen Generation.

**3-generation family**
- Genetic pedigrees are drawn using standardised symbols:

Reproduced with permission from Health Education England’s Genomics Education Programme – *Taking and Drawing a Family History*
• See the following example of a family tree:

- Start with the patient in the centre (note the arrow)
- Include first degree relatives (children, siblings, parents), and second-degree relatives (aunts, uncles, grandparents) on both sides of the family.
- Include age at diagnosis, other conditions as well as presenting condition, miscarriages, stillbirths, infertility and birth defects.

3. If the patient is unaffected, assess:
   - personal risk and appropriate screening, such as faecal occult blood testing, or colonoscopy.
   - need for genetic assessment.
   **Indications for referral include all of the following:**
     - Blood relative of a person with a known cancer-associated gene mutation, e.g. MLH1, MSH2, MSH6, PMS2, EPCAM, MYH, APC.
     - ≥ 2 first-degree or second-degree relatives with colorectal or endometrial cancer, one diagnosed aged < 50 years.
     - ≥ 3 first-degree or second-degree relatives with Lynch syndrome related cancer, regardless of age.
     - History of multiple polyps – especially if diagnosed with 10 or more polyps, juvenile or hamartomatous polyps with or without family history.

4. If the patient has had colorectal or endometrial cancer, indications for referral include:
   - **Personal history.**
     - Multiple Lynch syndrome related cancers in the same individual. These include colorectal, small bowel, endometrial, ovarian, gastric, and brain cancers, and urothelial transitional cell carcinoma.
     - Isolated colorectal cancer or endometrial cancer, aged < 50 years at diagnosis.
     - Rare tumours, e.g. Desmoid tumour, endometrial leiomyosarcoma, multiple gastric fundic polyps.
   - **Tumour pathology characteristics.**
     Consider individuals diagnosed with colorectal polyps at an early age (< 30 years), multiple polyps, or rare pathology according to eviQ polyposis referral guideline (see below).
- Hamartomatous polyps
- Juvenile polyps
- Peutz-Jeghers polyps

➢ **Significant family history.**
  - Blood relative of a person with a known cancer-associated gene mutation, e.g. MLH1, MSH2, MSH6, PMS2, EPCAM, MYH, APC.
  - Affected individual has:
    - 2 first-degree or second-degree relatives diagnosed with Lynch syndrome related cancer.
    - ≥ 1 first-degree or second-degree relatives with colorectal or endometrial cancer, aged < 50 years at diagnosis.

See also eviQ General Practitioner Referral Guidelines (below) for:
  - endometrial Cancer Risk Assessment and Consideration of Genetics Testing
  - colorectal Cancer or Polyposis Risk Assessment and Consideration of Genetic Testing

## Management

1. If potentially at high risk, arrange referral to a genetic health service.
2. For further assessment and advice, genetic testing for familial colorectal and endometrial cancer syndromes is currently not covered by Medicare.
3. If at average or moderate risk, or not meeting EviQ criteria for referral to a familial genetic counselling service, discuss bowel cancer screening as an alternative.
4. Discuss **general preventive strategies.**
   - Regular exercise
   - Diet – reduce dietary fat, increase poorly soluble cereal fibre, eat fruit and vegetables, avoid or limit alcohol
   - **Smoking cessation**
   - See also:
     - Bowel Cancer Australia – Bowel Cancer: Prevention and Causes
     - Cancer Australia – Lifestyle and Risk Reduction

## Referral

- If a patient meets referral criteria arrange referral to a genetic health service.
- Required referral information includes patient contact details, any known family history, and whether other family members have had genetic testing.

## Information

### For health professionals

- Cancer Council – [Optimal Care Pathways for Aboriginal and Torres Strait Islander People with Cancer](https://www.canercouncil.com.au/)
- eviQ:
  - General Practitioner Referral Guidelines for Cancer Genetics Assessment
  - Risk Management for Lynch Syndrome
  - Risk Management for MYH-associated polyposis (MAP)
  - Risk Management for Familial Adenomatous Polyposis (FAP)
Cancer Council Australia – Clinical Practice Guidelines for the Prevention, Early Detection and Management of Colorectal Cancer

**For patients**

- Cancer Australia
- Cancer Council – Checking for Cancer: What to Expect
- Cancer Council Victoria – Aboriginal Communities: Information
- Genetic Alliance – A Guide to Family Health History
- National Indigenous Cancer Network – About Cancer
- NSW Government Health Centre for Cancer Education:
  - Bowel Cancer and Inherited Predisposition
  - What if I Have a Family History of Cancer? (brochure)
- Lynch Syndrome Australia

**References**


2. eviQ. Eveleigh NSW: Cancer Insititute NSW; Cancer Genetics: Adult. [date unknown]. [cited 2019 Sep 16].

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