Personalized Cancer Genomic Medicine Resource Toolkit

Acknowledgements

This resource has been adapted with permission from the 2016 toolkit developed by CanImpact (The Canadian Team to Improve Community Based Cancer Care along the Continuum).
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Red Flags to Identify Individuals Who Are at Increased Risk of a Hereditary Cancer Syndrome

<table>
<thead>
<tr>
<th>Hereditary Cancer Red Flags</th>
</tr>
</thead>
<tbody>
<tr>
<td>In general, suspicion of a hereditary cancer syndrome should be raised if:</td>
</tr>
<tr>
<td>- There are multiple family members with cancer</td>
</tr>
<tr>
<td>- Cancers occur on the same side of family</td>
</tr>
<tr>
<td>- Cancer diagnoses occur at a younger than expected age</td>
</tr>
<tr>
<td>- Several generations are affected (demonstrating an autosomal dominant pattern – typical of most hereditary cancer syndromes)</td>
</tr>
<tr>
<td>- Clustering of certain types of cancers is present</td>
</tr>
<tr>
<td>- Multiple primary cancers are diagnosed in same individual</td>
</tr>
</tbody>
</table>
HEREDITARY BREAST AND OVARIAN CANCER SYNDROME

Bottom line: Breast cancer is relatively common in the general population (12% lifetime risk) and the majority of cases occur sporadically. About 5-10% of breast cancer is due to an inherited gene change. Mutations in the genes BRCA1 or BRCA2 are the most common cause of hereditary breast and ovarian cancer (HBOC) and BRCA1 and BRCA2 mutation carriers have a significant increased lifetime risk for breast and ovarian cancer in addition to other cancers. Risk-reducing surgeries and, for some women, chemoprevention, can reduce mortality from breast and ovarian cancers in both BRCA1 and BRCA2 carriers. Individuals with family histories of breast or ovarian cancer that are at high risk (generally >10%) to carry a BRCA1 or BRCA2 gene mutation can be offered referral to genetics services for a discussion of the benefits, harms and limitations of genetic testing, while women whose family histories suggest a low risk of carrying a BRCA1 or BRCA2 gene mutation can be reassured and offered screening following provincial guidelines.

WHAT IS HEREDITARY BREAST AND OVARIAN CANCER SYNDROME?

Approximately 80% of breast cancer occurs sporadically. About 10-15% of breast cancer is familial (when shared familial risk factors e.g. genes, environment, cause a higher incidence of cancer) and about 5-10% is hereditary (due to a single gene mutation). Harmful mutations in BRCA1 and BRCA2 appear to account for ~30% of high-risk breast cancer families. HBOC is an autosomal dominant cancer predisposition syndrome. Individuals with HBOC have a high risk for breast and ovarian cancers and a moderate risk for other cancers (Table 1). Not all individuals who inherit a mutation in BRCA1 or BRCA2 will develop cancer (reduced penetrance) and the signs and symptoms, type, and age of onset of cancer will vary within families (variable expressivity).

It is estimated that the general population prevalence of pathogenic mutations in the BRCA1 and BRCA2 genes is 1 in 300 to 1 in 500. Founder mutations are observed in individuals of Ashkenazi Jewish ethnicity occurring at an estimated frequency of about 1 in 50.

WHO SHOULD BE OFFERED GENETIC TESTING?

These are general guidelines to identify patients at high risk for HBOC. You should consider referring your patient to your local genetics centre or hereditary cancer program for further assessment if s/he has a family or personal history of:

- Breast cancer diagnosis at a young age (<35-45 years) [both invasive and ductal carcinoma in situ]
- Ovarian cancer at any age [epithelial]
- Male breast cancer
- Multiple primaries in the same individual e.g. bilateral breast cancer (particularly if the diagnosis was before age 50), breast and ovarian cancer
- Breast cancer diagnosis AND a family history of two or more additional HBOC-related cancers, including breast, ovarian, prostate (Gleason ≥7) and pancreatic cancer
- High risk ethnicity (Ashkenazi Jewish, Icelandic) and a personal and/or family history of breast, ovarian or pancreatic cancer
- Triple negative breast cancer diagnosed <age 60

OR if s/he has a personal

- Probability of 10% or higher to carry a BRCA mutation

Eligibility criteria for genetic testing vary among organizations. In general, criteria are based on clinical features that increase the likelihood of a hereditary cancer susceptibility syndrome.

If possible, testing is first offered to the affected individual in the family at highest risk to carry a mutation in order to maximize the likelihood of detecting a mutation. For example, this might be the youngest individual with breast cancer in a family with multiple cases of breast and ovarian cancer.

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Updated May 2018
HOW WILL GENETIC TESTING HELP YOU AND YOUR PATIENT?

If a mutation is identified (a positive test result):

- Clinical intervention can improve outcomes. (See *GECKO Messenger for Screening and Management)
  - Risk-reducing mastectomy lessens the risk of breast cancer by at least 90%
  - Annual magnetic resonance imaging plus mammography increases detection rate for breast cancer
  - Risk-reducing salpingo-oophorectomy decreases the risk of ovarian cancer by at least 80% and, if performed prior to menopause, can reduce the risk of breast cancer by at least 50%
  - Chemoprevention, e.g. tamoxifen, may be considered for some women as a risk-reducing option.
- Other at-risk family members can be identified and given accurate risk assessments
- Positive health behaviours can be reinforced

If a mutation is not identified and testing was for a known familial mutation (true negative):

- Your patient is not considered to be at increased risk of developing hereditary cancer but may still be at increased risk of cancer depending on family history
- You can provide reassurance to your patient and their children

Table 1. Significant lifetime cancer risks for individuals who have inherited a mutation in the BRCA1 or BRCA2 gene as compared to the general population.

<table>
<thead>
<tr>
<th>Cancer type</th>
<th>Cancer risk in a mutation carriers of:</th>
<th>General Population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BRCA1</td>
<td>BRCA2</td>
</tr>
<tr>
<td>Cumulative lifetime invasive breast cancer risk in women (by age 70)</td>
<td>57%</td>
<td>49%</td>
</tr>
<tr>
<td>Cumulative lifetime ovarian cancer risk (by age 70)</td>
<td>40%</td>
<td>18%</td>
</tr>
<tr>
<td>Cumulative lifetime breast cancer risk in men (by age 70)</td>
<td>Increased (controversial)</td>
<td>6-7%</td>
</tr>
<tr>
<td>Lifetime prostate cancer risk (by age 70)</td>
<td>n/a</td>
<td>2-6x increased risk</td>
</tr>
</tbody>
</table>

NOTE: The literature suggests that there is also an increased lifetime risk for other cancers such as melanoma and pancreatic cancer in BRCA mutation carriers.


See www.geneticseducation.ca for the comprehensive *GECKO Messenger* with references and more on risks, benefits, limitations, screening and management, as well as for the made for practice*point of care tool.*

Authors: S Morrison MS CGC, C Cremin MS CGC, E Tomiak MD FRCPc, JE Allanson MD FRCPC and JC Carroll MD CCFP

GECKO on the run is for educational purposes only and should not be used as a substitute for clinical judgement. GECKO aims to aid the practicing clinician by providing informed opinions regarding genetic services that have been developed in a rigorous and evidence-based manner. Physicians must use their own clinical judgement in addition to published articles and the information presented herein. GECKO assumes no responsibility or liability resulting from the use of information contained herein.
Part 1: Hereditary Breast and Ovarian Cancer Patient-Completed Screening Tool to Identify Patients for Referral to Genetics

Part I of this tool is to be used with patients to predict who should be referred for genetic counselling due to increased risk for a hereditary breast cancer syndrome including but not limited to hereditary breast and ovarian cancer (HBOC) syndrome caused by mutations in BRCA1 and BRCA2 genes. Part II of this tool is used to identify individuals who are at high risk to carry a mutation in BRCA1 or BRCA2 genes.

| 1. Did any of your first degree relatives (parent, sibling, child) have breast or ovarian cancer? | Yes □ No □ |
| 2. Did any of your relatives have bilateral breast cancer? | Yes □ No □ |
| 3. Did any man in your family have breast cancer? | Yes □ No □ |
| 4. Did any woman in your family have breast and ovarian cancer? | Yes □ No □ |
| 5. Did any woman in your family have breast cancer before the age of 50 years? | Yes □ No □ |
| 6. Do you have 2 or more relatives with breast and/or ovarian cancer? | Yes □ No □ |
| 7. Do you have 2 or more relatives with breast and/or bowel cancer? | Yes □ No □ |

Management: With 1 or more positive responses, discuss referral to genetics

This POC tool is based on the Family History Screening-7 (FHS-7) (Ashton-Prolla et al 2009), which was designed for use in primary care settings and demonstrated an overall sensitivity of 97.0% and a specificity of 53.0% for HBOC syndrome. Overall, using as cut point one positive answer, the sensitivity and specificity of the instrument were 87.6% and 56.4%, respectively for hereditary breast cancer syndromes. (Reference: Ashton-Prolla P, Giacomazzi J, Schmidt AV, et al. Development and validation of a simple questionnaire for the identification of hereditary breast cancer in primary care. BMC Cancer 2009; 9:283 Licence: http://creativecommons.org/licenses/by/2.0/) 

On-line tool: Breast Cancer Genetics Referral Screening Tool (B-RST™)
This is an on-line screening tool for health care providers and the general public to enter family history information to determine who should be referred for cancer genetic counselling for Hereditary Breast and Ovarian Cancer. www.breastcancergenescreen.org
Part II: Red Flags for Providers to Identify Individuals Who Are at Increased Risk of Hereditary Breast and Ovarian Cancer Syndrome for Referral to Genetics

(TAKEN DIRECTLY from GECKO On the Run on Hereditary Breast/Ovarian Cancer)

These are general guidelines to identify patients at high risk for hereditary breast and ovarian cancer (HBOC) syndrome. You should consider referring your patient to your local genetics centre or hereditary cancer program for further assessment if s/he has a family or personal history of:

- Breast cancer diagnosis at a young age (<35-45 years) [both invasive and ductal carcinoma in situ]
- Ovarian cancer at any age [epithelial]
- Male breast cancer
- Multiple primaries in the same individual e.g. bilateral breast cancer (particularly if the diagnosis was before age 50), breast and ovarian cancer
- Breast cancer diagnosis AND a family history of two or more additional HBOC-related cancers, including breast, ovarian, prostate (Gleason ≥7) and pancreatic cancer
- High risk ethnicity (e.g., Ashkenazi Jewish, Icelandic) and a personal and/or family history of breast, ovarian or pancreatic cancer
- Triple negative breast cancer diagnosed <age 60

OR if s/he has a personal

- Probability of 10% or higher to carry a BRCA mutation

Eligibility criteria for genetic testing vary among organizations. In general, criteria are based on clinical features that increase the likelihood of a hereditary cancer susceptibility syndrome.

If possible, the affected individual in the family at highest risk to carry a mutation is offered testing first in order to maximize the likelihood of detecting a mutation.

Testing an unaffected individual should only be considered if an affected individual is not available for testing. There are significant limitations to interpretation of test results in an unaffected individual. Unaffected individuals can be referred for genetic counselling, risk assessment and information. It is important to note that any individual of Ashkenazi Jewish ethnicity or French Canadian ethnicities can be offered genetic testing for the mutations commonly found in these ethnic groups (e.g. three common mutations in those of Ashkenazi Jewish ethnicity). A negative result in this situation only rules out those ethnic-specific mutations.

For more information on Hereditary Breast and Ovarian Cancer such as screening recommendations and references see the complete *GEC-KO Messenger* at www.geneticseducation.ca.
LYNCH SYNDROME

Bottom line: Lynch syndrome (LS), also known as Hereditary Non-Polyposis Colorectal Cancer (HNPCC), is the most common hereditary colorectal (CRC) cancer predisposition syndrome. It is an autosomal dominant condition that causes a significant increased lifetime risk of CRC and endometrial (uterine) cancer in addition to other cancers. Individuals suspected of having LS should be referred for a genetic consultation for consideration of genetic testing. Screening, surveillance and management of CRC and other cancers should be guided by genetic test results and/or family/ personal history. Studies show that conversations between patients and their healthcare providers are the strongest driver of screening participation.

WHAT IS LYNCH SYNDROME?

Lynch syndrome (LS) is an autosomal dominant cancer predisposition syndrome caused by inherited mutations in genes responsible for correcting DNA replication errors, called mismatch repair (MMR) genes. **Individuals with LS have a high risk for colorectal and endometrial cancers** and a moderate risk for other cancers (Box 1 and Table 1). Not all individuals who inherit a mutation in a LS gene will develop cancer (reduced penetrance) and the signs and symptoms, type and age of onset of cancer will vary within families (variable expressivity).

**Box 1: Lynch Syndrome-related Cancers**

| ✓ Colorectal | ✓ Endometrial | ✓ Kidney | ✓ Gastric | ✓ Ovarian | ✓ Ureter |
| ✓ Small bowel | ✓ Hepatobiliary | ✓ Pancreatic | ✓ Brain | ✓ Sebaceous (adenoma or carcinoma) |

PREVALENCE

LS accounts for about 0.7-3.6% of cases of CRC. Research on LS-related endometrial cancer is still emerging; current data suggest that in North America between 1.8% and 4.5% of cases are attributed to LS.

PERSONAL HISTORY RED FLAGS TO CONSIDER GENETIC TESTING OR GENETIC CONSULTATION

These are general guidelines to identify patients at high risk for LS. You should check with your local genetics centre or hereditary cancer program for more specific details. Consider referring your patient if he/she has:

- An early age of CRC diagnosis (<50 years). Patients diagnosed <35 years are much more likely to have LS.
- An early age of endometrial cancer diagnosis (<50 years)
- Multiple primary LS-related cancer diagnoses, regardless of age
- A CRC diagnosis and one or more 1st degree relatives with a LS-related cancer, with one of the cancers being diagnosed <50 years
- A CRC diagnosis and two or more 1st or 2nd degree relatives with LS-related cancers regardless of age
- A CRC diagnosis <60 years with histological features suspicious for LS (excess infiltrating lymphocytes, mucinous/signet cell features, Crohn’s-like reaction), particularly when primary tumour is right-sided

FAMILY HISTORY RED FLAGS TO CONSIDER GENETIC CONSULTATION

You should consider referring your patient to your local genetics centre or hereditary cancer program for further assessment if he/she is at high risk for hereditary CRC syndrome.

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Updated May 2018
A patient is considered to be at **high risk** for LS syndrome if he/she

- Has a known LS causing mutation in the family

**Or if he/she meets the revised Amsterdam criteria, meaning he/she:**

- Has **at least three relatives** with a cancer associated with LS (Box 1); the following criteria should also be present:
  - One must be a first degree relative of the other two;
  - At least two successive generations must be affected (autosomal dominant inheritance);
  - At least one relative with LS-related cancer should be diagnosed before age 50;

  **Tumours should be verified when possible and other CRC syndromes should be ruled out**

If your patient does not have cancer, genetic testing of a relative with cancer may be recommended as a first step.

If your patient does not meet any of the criteria above, but you are suspicious of a hereditary cancer syndrome, consult your local genetics centre or hereditary cancer program. In general, suspicion of a hereditary cancer syndrome should be raised if:

- There are multiple family members with cancer
- Cancers occur on the same side of family
- Cancer diagnoses occur at a younger than expected age
- Several generations are affected (demonstrating an autosomal dominant pattern – typical of most hereditary cancer syndromes)
- Clustering of certain types of cancers is present (for LS, see Box 1)
- Multiple primary cancers are diagnosed in same individual

**HOW IS GENETIC TESTING DONE?**

Ideally testing begins with immunohistochemical (IHC) analysis of a CRC tumour for the proteins associated with the LS genes (*MLH1, MSH2, MSH6, PMS2* and *EPCAM*). IHC analysis looks at the protein products of the LS genes.

If IHC analysis reveals a protein to be deficient, genetic testing can be offered to the affected individual and performed on a blood sample. If IHC analysis does not clearly show protein deficiency, the next step is often microsatellite instability (MSI) testing of the tumour sample. If MSI is stable or low, no further testing is indicated.

If MSI is high, genetic testing can be offered to the affected individual and performed on a blood sample. Some centres will arrange IHC or MSI alone; others will carry out both tests at the same time.

**WHAT DOES THE GENETIC TEST RESULT MEAN?**

If your patient has been found to carry a mutation in a LS gene, a **positive result**, he/she has an increased lifetime risk to develop certain cancers (Table 1 and Box 1). This also means that family members are at risk of carrying the same mutation and of having similar cancer risks.

If a mutation is **not** identified in someone from a family with a known mutation, this is a **true negative result**. You can provide reassurance to your patient. These individuals may still have modified screening recommendations based on their family history. Consult your local genetics centre or hereditary cancer program.

If a mutation is **not** identified in an affected patient who has no known familial mutation this result is **uninformative**. A variant of uncertain significance (VUS) could be identified, which is a gene change that has not yet been categorized as benign or as pathogenic. In both of these cases, the diagnosis of LS is not confirmed or ruled out, especially in families with a strong history of CRC.
Table 1. Significant lifetime cancer risks for individuals who have inherited a mutation in the LS genes, MLH1 and MSH2, as compared to the general population. Risks for other LS genes are lower.

<table>
<thead>
<tr>
<th>Cancer type</th>
<th>LS lifetime cancer risk in a carrier of a MLH1 or MSH2 gene mutation</th>
<th>General Population lifetime cancer risk &lt; 70 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Risk</td>
<td>Mean age of diagnosis</td>
</tr>
<tr>
<td>Colon</td>
<td>52-82%</td>
<td>44-61 years</td>
</tr>
<tr>
<td>Endometrium</td>
<td>25-60%</td>
<td>48-62 years</td>
</tr>
</tbody>
</table>

SCREENING AND SURVEILLANCE

In general, for high risk individuals (carriers of a mutation in a LS gene and their first degree relatives who have not yet had genetic testing) screening recommendations are as follows:

Colorectal Cancer: Colonoscopy every 1-2 years beginning between ages 20 and 25 or 2-5 years prior to the earliest diagnosis if that diagnosis was made before age 25 years, whichever is earlier.

Endometrial and Ovarian cancer: Screening for endometrial or ovarian cancer may include annual transvaginal ultrasound and endometrial biopsy, however, there is little evidence of the effectiveness of these tests. Most importantly, women should be educated about the symptoms of endometrial cancer. Prophylactic hysterectomy and bilateral salpingo-oophorectomy is a risk-reducing option that LS women who have completed childbearing can consider.

Individuals who have tested negative for a known familial LS gene should follow provincial guidelines for population risk CRC screening, i.e. Fecal Occult Blood Test every two years from age 50. For those individuals who have a family history of CRC unrelated to the mutation in their family (i.e. on the other side of the family), screening recommendations would be based on the family history. Consult your local genetics centre or hereditary cancer program.

For individuals where no mutation was identified and there was no known familial mutation (uninformative result) or when a variant of uncertain significance (VUS) was identified, screening recommendations will be based on a combination of factors, such as family history and in cases where a VUS was identified, information about the VUS.

CRC screening for intermediate risk individuals is dependent on family history. For a person with a:

- 1st degree relative with CRC diagnosis <50 years or two 1st degree relatives with CRC at any age → Colonoscopy at age 40 or 10 years younger than the youngest CRC diagnosis, repeat 3-5 yearly
- 1st degree relative with CRC diagnosis ≥50 years → Colonoscopy at age 50 or 10 years younger than the youngest CRC diagnosis, repeat 5 yearly
- 2nd degree relative with CRC diagnosis <50 years → Colonoscopy at age 50, repeat dictated by findings


Authors: S Morrison MS CGC, JE Allanson MD FRCPC, E Tomiak MD FRCPC, K Semotiuk MS (C)CGC and JC Carroll MD CCFP

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Updated May 2018
Part I: Colorectal Cancer Risk Assessment Tool to Identify Patients Most Likely to Benefit From Referral to Genetics

1) Do you have a first-degree relative (mother, father, brother, sister, or child) with any of the following conditions diagnosed before age 50?
   - Colon or rectal cancer
   - Cancer of the uterus, ovary, stomach, small intestine, urinary tract (kidney, ureter, bladder), bile ducts, pancreas, or brain

   YES  NO

2) Have you had any of the following conditions diagnosed before age 50?
   - Colon or rectal cancer
   - Colon or rectal polyps

   YES  NO

3) Do you have three or more relatives with a history of colon or rectal cancer?
   (this includes parents, brothers, sister, children, grandparents, aunts, uncles, and cousins)

   YES  NO

The cumulative sensitivity of these three questions to identify patients with characteristics suggestive of hereditary colorectal and who should undergo a more extensive risk assessment is 77%. When all 3 questions were answered “yes”, the tool correctly identified 95% of individuals with germline mutations causing Lynch syndrome. If a patient answers “yes” to all of these questions a referral to genetics should be offered. If a patient answers “yes” to any of these questions, consider further assessment using the criteria in Part II.

# Part II: Red Flags to Identify Patients at High Risk of Lynch Syndrome Most Likely to Benefit From Referral to Genetics

<table>
<thead>
<tr>
<th>Personal History LS Red Flags</th>
<th>Family History LS Red Flags</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consider referring your patient if he/she has:</td>
<td>Consider referring your patient if he/she:</td>
</tr>
<tr>
<td>- Colorectal cancer (CRC) diagnosis at an early age (&lt;50 years). Higher suspicion of LS if diagnosed &lt;35 years.</td>
<td>- Has a known LS causing mutation in the family</td>
</tr>
<tr>
<td>- Endometrial cancer diagnosis at an early age (&lt;50 years)</td>
<td>- Meets the revised Amsterdam criteria, meaning he/she has <strong>at least three relatives</strong> with a cancer associated with LS (Box 1). The following criteria should also be present:</td>
</tr>
<tr>
<td>- Multiple primary LS-related cancer diagnoses, regardless of age</td>
<td>- One must be a first degree relative of the other two;</td>
</tr>
<tr>
<td>- A CRC diagnosis <strong>and</strong> one or more 1st degree relatives with a LS-related cancer, with one of the cancers diagnosed &lt;50 years</td>
<td>- At least two successive generations must be affected (autosomal dominant inheritance);</td>
</tr>
<tr>
<td>- A CRC diagnosis <strong>and</strong> two or more 1st or 2nd degree relatives with LS-related cancers regardless of age</td>
<td>- At least one relative with LS-related cancer should be diagnosed before age 50;</td>
</tr>
<tr>
<td>- A CRC diagnosis &lt;60 years <strong>and</strong> histological features suspicious for LS* (excess infiltrating lymphocytes, mucinous/signet cell features, Crohn’s-like reaction), particularly when primary tumour is right sided</td>
<td>- Tumour pathology should be verified when possible and other CRC syndromes should be ruled out</td>
</tr>
</tbody>
</table>

*LS is the abbreviation for Lynch syndrome

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For more information on Lynch Syndrome such as screening recommendations see the complete [GEC-KO Messenger](https://www.geneticseducation.ca) at [www.geneticseducation.ca](http://www.geneticseducation.ca)

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**Updated May 2018**
**OBSP Requisition for High Risk Screening**

1. **Client Information** *(or affix label)*
   - First name
   - Date of birth (dd/mm/yyyy)
   - Telephone number
   - Last name
   - CHIP number
   - Secondary telephone number
   - Address (including postal code)

To receive high risk breast screening *(i.e.: annual MRI and mammogram)*, women must be between 30 and 69 and be at high risk for breast cancer as identified through Category A **or** Category B, after genetic assessment. Women with bilateral mastectomies are **not eligible**.

**Category A**: eligible for direct entry into the program. To fall under this category, **at least one** of the following criteria must be met:
- Known carrier of a gene mutation *(e.g. BRCA1, BRCA2 - fax results with form)*
- First degree relative of a carrier of a gene mutation *(e.g. BRCA1, BRCA2)*, has previously **had** genetic counselling, and has **declined** testing
- Previously assessed as having a ≥25% lifetime risk of breast cancer on basis of family history *(a genetic clinic must have used at least one of the tools below to complete this assessment – fax results with form)*
  - IBIS 10 Year Risk
  - IBIS Lifetime Risk
  - BOADICEA 5 Year Risk
  - BOADICEA Lifetime Risk
- Received chest radiation (not chest x-ray) before age 30 and at least 8 years previously *(e.g. as treatment for Hodgkin’s Lymphoma)*

**OR**

**Category B**: genetic assessment required *(i.e. counselling and/or testing)* to determine eligibility for the program. To fall under this category, **at least one** of the following criteria must be met:
- First degree relative of a carrier of a gene mutation *(e.g. BRCA1, BRCA2)* and has **not** had genetic counselling or testing
- A personal or family history of **at least one** of the following (please check all that apply):
  - Two or more cases of breast cancer and/or ovarian* cancer in closely related blood relatives
  - Bilateral breast cancers
  - Both breast and ovarian* cancer in the same woman
  - Breast cancer at ≤35 years of age
  - Invasive serous* ovarian cancer
  - Breast and/or ovarian* cancer in Ashkenazi Jewish families
  - An identified gene mutation *(e.g. BRCA1, BRCA2)* in any blood relatives
  - Male breast cancer

* includes cancer of the fallopian tubes and primary peritoneal cancer
† Closely related blood relative: 1st degree = parent, sibling, or child; 2nd degree = grandparent, aunt, uncle, niece, or nephew

2. **Clinical History**
   - Date and location of most recent mammogram
   - Previous breast cancer? ☐ Yes ☐ No
   - Date and location of most recent MRI *(if done)*
   - Breast implants? ☐ Yes ☐ No
   - Previous genetic assessment for inherited breast cancer risk? ☐ Yes (attach results) ☐ No
   - Specify genetic assessment centre

3. **Referring Physician**
   - First and last name
   - Address (including postal code)
   - Signature
   - Date (dd/mm/yyyy)
   - CPSO Number
   - Telephone Number
   - Fax number

By signing this form, you authorize your client to receive screening mammography and MRI *(or, if appropriate, screening ultrasound)*. You also authorize the OBSP to book these screens, additional screens, as well as any follow-up appointments, including imaging tests and biopsies for evaluation of abnormal results. Fax completed form to the OBSP High Risk Screening Referral Contact in your area *(cancercare.on.ca/obsphighrisk)*.

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Updated May 2018
Breast Cancer Screening
Summary of the Clinical Practice Guideline | September 2013

AVERAGE RISK POPULATION: RECOMMENDATIONS
Use Mammography for Screening

39 years & under
Screening is not recommended

40 to 49 years
The balance of benefits and risks is not great enough to recommend routine screening
Consider woman’s preference
If screened, the optimal interval is annual

50 to 74 years
Screening recommended

75+ years
Consider individual health factors and woman’s preference
Screen every 2 years

Breast augmentation, breast reduction, sex-reassignment: As above
Note presence of implants in history section of mammography requisition form

Clinical Breast Exam (CBE): Do not use for screening. Consider as part of physical exam

Not recommended for routine screening: MRI, ultrasound, tomosynthesis, thermography, breast self-examination

HIGH RISK POPULATION: RECOMMENDATIONS

Women Requiring More Intensive Screening
One or two first degree relatives with invasive breast cancer, but do not meet the criteria for referral to Medical Genetics

Annual mammography starting 5 to 10 years younger than the youngest case in the family, but no earlier than age 25 and no later than age 40
Annual CBE starting age 25

Breast biopsy showing atypical hyperplasia or lobular carcinoma in situ and following surgical management to rule out invasive carcinoma

Annual mammography
Annual CBE

History of chest wall radiation at age 30 or younger

Annual mammography and screening breast MRI starting 5 to 10 years after radiation given, but no earlier than age 25 and no later than age 40
Annual CBE

Women Requiring Referral to Medical Genetics
Maternal or paternal family history of:
- Multiple individuals with breast and/or ovarian* cancer (e.g., 3 or more cases in 2 or more generations, at least one case onset before age 50), related to each other
- Bilateral primary breast cancer, first onset age 50 or younger
- Breast cancer at age 35 or younger
- Breast cancer that is hormone receptor negative and HER2 negative (a.k.a. triple negative), age 60 or younger
- Primary breast and primary ovarian cancer in the same individual
- Male breast cancer, age 65 or younger, or at any age with close family history of breast cancer
- Breast or ovarian cancer in a family with Ashkenazi Jewish heritage
- BRCA1 or BRCA2 mutation in the family
*Serous epithelial cancer of the ovaries, fallopian tube cancer or primary peritoneal cancer

- Refer to Medical Genetics in Edmonton or Calgary for potential counseling +/- genetic testing
- Follow recommendations from Medical Genetics regarding screening and risk reduction
- For eligible women who decline or are unable to attend counseling, follow the recommendations for women with one or two first degree relatives with invasive breast cancer (see above)

Note: Telehealth services are available for women living in remote areas

These recommendations are systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances. They should be used as an adjunct to sound clinical decision making.

www.geneticseducation.ca | @GECKOgenetics

Updated May 2018
KEY DISCUSSION POINTS FOR HEALTH CARE PROVIDERS AND WOMEN

1. Initiate discussion about screening mammography with women of the appropriate age, including potential benefits and risks of mammography

Health care providers should remind women of the possibility of additional tests in order to reduce anxiety. For age-specific benefits and risks, refer to Information on Mammography for Women Aged 40 and Older: A Decision Aid for Breast Cancer Screening in Canada, Public Health Agency of Canada, 2009. Available at: www.phac-aspc.gc.ca/cd-mc/mammography-mammographie-eng.php.

2. Encourage breast awareness

Women should report changes in their breasts, in particular, nipple discharge, rash on nipples, inversion, dimpling or new mass in the breast or axilla.

3. Discuss modifiable risk factor(s)

While some risk factors for breast cancer are not modifiable (e.g., gene mutation, breast density), the ones more amenable to modification include: alcohol consumption, physical activity, weight management, and smoking. These should be addressed in the context of overall disease prevention, as should appropriate use of hormone replacement therapy.

IMPLEMENTATION STRATEGIES

Use outreach, opportunistic screening and checklists to increase the likelihood of engaging women to make informed decisions about screening.

GENERAL RESOURCES


RESOURCES FOR HIGH RISK POPULATION

- Calgary Cancer Genetics Clinic: Dr. R.B. Lowry Genetics Clinic, Alberta Children’s Hospital, 2888 Shaganappi Trail NW, Calgary, AB T3B 6A8. Phone: (403) 955-7137. Fax (403) 955-2701.
- Calgary High Risk Breast Cancer Clinic: The High Risk Breast Cancer Clinic, Calgary Zone Alberta Health Services accepts referrals using the Central Access and Triage system. Phone (403) 944-2240.
- Edmonton Cancer Genetics Clinic Referral Criteria: www.medicalgenetics.med.ualberta.ca, Edmonton Medical Genetics Clinic, 8-53 Medical Sciences Building, University of Alberta, Edmonton, Alberta T6G 2H7, Phone (780) 407-7333, Fax (780) 407-6845.
- Allard Hereditary Breast and Ovarian Clinic, Royal Alexandra Hospital, Robbins Pavilion, Ground Level, 10240 Kingsway Avenue, Edmonton, Alberta, T5H 3V9. Phone (780) 735-4718, Fax (780) 735-4020.

For the complete guideline refer to the TOP website: www.topalbertadoctors.org

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TARGET POPULATION
Asymptomatic men and women of all ages

EXCLUSIONS
Men and women with signs or symptoms suggesting colorectal cancer screening (CRC)

RECOMMENDATIONS

RISK ASSESSMENT
✓ Assess risk for colorectal cancer (CRC) for all men and women to determine when to start screening, the appropriate screening test and frequency
✓ DO NOT wait for patient to turn 50 years of age to assess risk for CRC
✓ Assess for indicators of increased risk including family and/or personal history of colorectal cancer, colonic adenomas or inflammatory bowel disease, and high risk CRC conditions, i.e., Lynch syndrome, familial adenoma polyposis

AVERAGE RISK POPULATION

Fecal Immunochemical Test (FIT)

50 to 74 Years of Age
✓ Screening is recommended with the Fecal Immunochemical Test (FIT)
✓ Screen with FIT every one to two years
✓ If the FIT result is positive, promptly refer for a colonoscopy. Use local CRC screening program (see Appendix A) or endoscopist, depending on available resources
✓ Wait 10 years after a normal colonoscopy to start or re-start screening with FIT. If the quality of the colonoscopy was uncertain, start or re-start screening with FIT five years after the colonoscopy

PRACTICE POINT
FIT is the recommended screening test for average risk men and women between 50 and 74 years of age
Screen with FIT every one to two years

These recommendations are systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances. They should be used as an adjunct to sound clinical decision making.
75 YEARS OF AGE AND OLDER

- As a general practice, DO NOT screen asymptomatic patients with a life expectancy of less than 10 years and no family or personal history of colorectal neoplasia
- Discuss the risks and benefits of screening with the patient. The decision to screen should be individualized, based on informed patient preference, and between the patient and his/her physician

**WHEN NOT TO USE FIT**

- DO NOT use as a diagnostic test for CRC in SYMPTOMATIC patients (e.g., reported bloody stools or recent change in bowel habit)
- DO NOT use to determine or exclude a cause for anemia
- DO NOT use when an average risk patient has had a high quality colonoscopy within the past 10 years
- DO NOT use as a CRC screening test when the patient has an acute gastrointestinal (GI) condition and/or where bleeding is occurring or highly likely:
  - Inflammatory bowel disease
  - Acute gastroenteritis or C. difficile colitis
  - Actively bleeding hemorrhoids or anal fissure

**OTHER SCREENING TESTS**

The FIT is the recommended method of screening for the average risk population. Appendix B summarizes the evidence for other CRC screening tests, e.g., colonoscopy, flexible sigmoidoscopy, CT colonography, and others. Expertise and availability varies across the province.

**INCREASED RISK POPULATIONS**

**Family history** of colorectal cancer and/or high risk colonic adenomas are warning signs of increased risk (see Risk Assessment section for definition of high risk adenomas). Use clinical judgment.

One first degree relative > 60 years at diagnosis of colorectal cancer and/or high risk adenomas

- Screen with FIT every one to two years starting at age 40
- If the FIT result is positive, promptly refer for a colonoscopy. Use local CRC screening program (see Appendix A) or endoscopist, depending on available resources

One first degree relative ≤ 60 years at diagnosis of colorectal cancer and/or high risk adenomas or two or more affected relatives

- Refer for consideration of colonoscopy at age 40, or 10 years prior to the index case, whichever is earliest. Use local CRC screening program (see Appendix A) or endoscopist
Alberta

Alberta Prevents Cancer web site – [www.albertapreventscancer.ca](http://www.albertapreventscancer.ca)

- Alberta Prevents is a joint Alberta Health Services (AHS) Population Public and Aboriginal Health and Strategic Clinic Network initiative that will create an online platform for AHS to efficiently integrate the most effective messages, tools and resources for cancer and chronic disease prevention in one easily accessible source.

Together we can reduce the risk of cancer in Alberta by up to 50%

Find proven ways to reduce your risk. [Learn More ›](#)

8 WAYS TO REDUCE YOUR RISK

THINGS TO LIMIT AND AVOID

- Tobacco
- UV Radiation
- Alcohol

THINGS TO DO

- Eat Healthy
- Be Active
- Get Screened
- Healthy Weight
- Get Vaccinated

[View all available tools and resources ›](#)
British Columbia

BC Cancer Web Site - [www.bccancer.bc.ca/](http://www.bccancer.bc.ca/)

- **BC Cancer provides a comprehensive cancer control program for the people of BC in partnership with regional health authorities. BC Cancer covers the entire spectrum of cancer care, from prevention and screening to diagnosis, treatment and rehabilitation.**

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**Hereditary Cancer**

Hereditary cancer happens when a gene mutation that increases cancer risk is passed down from a parent to a child.

Being born with that gene mutation means that a person has a higher chance to develop specific types of cancer, and those cancers may happen at younger than average ages.

**Hereditary Cancer Program**

The Hereditary Cancer Program provides genetic counselling and genetic testing for BC/Yukon residents who may have inherited an increased risk for specific types of cancer. Similar services are available across Canada and in other countries.

Use the tabs below to find information about hereditary cancer, genetic testing and genetic counselling.

- **Common Questions**
- **Eligibility**
- **What to Expect**

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**Contact the Hereditary Cancer Program (HCP)**

**Vancouver**

Phone: 604-877-6000 local 672198
Fax: 604-767-5931

**Abbotsford**

Phone: 604-851-4710 local 645236
Fax: 604-851-4720

Send an email to HCP.

**HCP Clinic Locations**

**Vancouver**

Crimson Medical Building, 360 West
Manitoba

CancerCare Manitoba Web Site - www.cancercare.mb.ca

- **CancerCare Manitoba (CCMB) is the provincially mandated cancer agency and is responsible for setting strategic priorities and long-term planning for cancer and blood disorders. CCMB provides clinical services to both children and adults. The cancer services the organization provides to Manitobans include prevention, early detection, multidisciplinary cancer treatment, supportive and end-of-life care.**
New Brunswick

Government of New Brunswick Web Site –
www2.gnb.ca/content/gnb/en/departments/health/NewBrunswickCancerNetwork/content/NewBrunswickBreastCancerScreeningProgram.html

New Brunswick Breast Cancer Screening Program

Breast cancer is the most commonly diagnosed cancer among New Brunswick women and is a leading cause of cancer-related death. Regular breast cancer screening can detect tumors at an earlier stage and reduce breast cancer mortality.

Screening

The New Brunswick Breast Cancer Screening Program was established in 1995 with the purpose of finding cancers of the breast as early as possible. The program encourages women between the ages of 50-74 to be screened every two years at one of the 14 screening mammography sites across the province.
Newfoundland and Labrador

Eastern Health Web Site –
www.easternhealth.ca/WebInWeb.aspx?d=3&id=1091&p=1078

- Eastern Health is the largest integrated health organization in Newfoundland and Labrador. We provide the full continuum of health services to a regional population of more than 300,000 and are responsible for a number of unique provincial programs.
Nova Scotia

Nova Scotia Cancer Care Program – [www.nshealth.ca/cancer-care](http://www.nshealth.ca/cancer-care)

The Nova Scotia Cancer Care Program is responsible for cancer programs and services across the province including: cancer prevention and early detection, treatment, follow-up, supportive care, palliative care and end-of-life care.
Ontario

My Cancer IQ Web Site – www.mycanceriq.ca

For a cancer risk assessment and personalized action plan
Health PEI - www.princeedwardisland.ca/en/topic/cancer-screening

Health PEI provides information on cancer screening and how to access screening services.

Cancer Screening and Early Detection

Screening is an important part of your health routine. Cancer screening is available for some types of cancers. Screening tests help identify and detect cancer early before there are symptoms, so that abnormal cells can be removed before they become cancer.

It is important to understand your risk of developing cancer and what type of screening is right for you. Talk to your family doctor and nurse practitioner about ways you can screen for cancer, and remember to discuss any history of cancer you may have in your family as this may increase your risk.

The following cancer screening programs and services are available in PEI:
- Breast Cancer Screening Program
- Colorectal Cancer Screening Program
- Pap Test Clinics for Cervical Cancer Prevention

For more information on cancer screening guidelines and recommendations in Canada, including on prostate and lung cancer screening, visit the Canadian Task Force on Preventive Health Care.

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Quebec

Ministère de la Santé et des Services sociaux
- www.quebec.ca/sante/conseils-et-prevention/depistage-et-offre-de-tests-de-porteur/programme-quebecois-de-depistage-du-cancer-du-sein/

- The Ministère de la Santé et des Services sociaux launched the Québec Breast Cancer Screening Program (PQDCS) in May 1998. The PQDCS invites women aged 50 to 69 to have a mammogram every 2 years. A mammogram is the only screening exam that can reduce the number of deaths from breast cancer. The PQDCS’s objective is to reduce breast cancer deaths in women between the ages of 50 and 69 by 25%.
Saskatchewan

Saskatchewan Cancer Agency – [www.saskcancer.ca](http://www.saskcancer.ca)

- The Saskatchewan Cancer Agency operates prevention and early detection programs, conducts innovative research and provides safe, patient and family-centred care at our two cancer centres. Their mission is to provide leadership in health promotion, early detection, treatment and research for cancer.