



Hereditary Breast and Ovarian Cancer Syndrome

Hereditary breast and/or ovarian cancer (HBOC) is an autosomal dominant cancer susceptibility syndrome, most commonly associated with an inherited *BRCA1* or *BRCA2* gene mutation. Approximately 1 in 300 to 1 in 400 people in the general population are born with an inherited mutation in either the *BRCA1* or *BRCA2* genes. The frequency of *BRCA1* or *BRCA2* gene mutations is approximately 1 in 40 for people with Ashkenazi Jewish heritage.

Other high-risk genes associated with hereditary breast and/or ovarian cancers include: *PALB2*, *TP53*, *PTEN*, *STK11*, *CDH1*. Additional genes may also be discussed in the context of Hereditary Cancer Program assessment.

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

Note to oncologists/GPOs: if your regular practice includes women who are eligible for *BRCA1/BRCA2* testing, we offer training to prepare you to initiate genetic testing for patients whose personal history meets specific criteria. Please contact the Hereditary Cancer Program's Clinical Coordinator (604-877-6000 local 672198) if you are interested in this **oncology clinic based genetic testing** (GENONC) process.

Referral Criteria

Notes:

1. **breast cancer** includes DCIS (ductal carcinoma in situ) and excludes LCIS (lobular carcinoma in situ)
2. **ovarian cancer** refers to invasive non-mucinous epithelial ovarian cancer; includes cancer of the fallopian tubes, primary peritoneal cancer and STIC (serous tubal intraepithelial carcinoma); excludes borderline/LMP ovarian tumours
3. **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:

- breast cancer diagnosed at age 35 or younger
- "triple negative" (ER, PR, HER2 receptors) breast cancer diagnosed at age 60 or younger
- breast cancer diagnosed at age 50 or younger AND no family history known due to adoption
- male breast cancer
- 2 primary breast cancers with at least 1 diagnosed at age 50 or younger
- ovarian cancer at any age
- breast or ovarian cancer and Ashkenazi Jewish heritage

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

- family member with confirmed *BRCA1*, *BRCA2*, or other gene mutation – refer for carrier testing
- a close relative with personal history as above
- 1 breast cancer and 1 ovarian cancer in close relatives
- 2 close relatives with breast cancer diagnosed at age 50 or younger
- 2 close relatives with ovarian cancer
- 3 breast cancers in close relatives, with 1 diagnosed at age 50 or younger
- breast or ovarian cancer and Ashkenazi Jewish heritage

Cancer Risks to age 70 for *BRCA1* or *BRCA2* mutation carriers

Type of cancer	Risk in general population	<i>BRCA1</i> carrier	<i>BRCA2</i> carrier
Breast cancer – women*	11% (lifetime)	47-66%	40-57%
Ovarian cancer	1-2% (lifetime)	35-46%	13-23%
Breast cancer – men	0.1%	~1%	7%
Prostate cancer	5.9%	8.6%	15%
Pancreatic cancer	1%	slight increase	
Other cancers	varies		slight increase

* risk of a new 2nd breast cancer depends on the age of diagnosis for the 1st breast cancer

PALB2 Lifetime Cancer Risks and Management Recommendations

Women who are born with an inherited mutation in *PALB2* (Partner and Localizer of *BRCA2*) have an increased lifetime risk of developing breast cancer that is understood to be similar to the risk for a *BRCA2* mutation carrier. Inherited *PALB2* mutations are also associated with increased pancreatic cancer risk. Risks for other cancers in male and female *PALB2* mutations carriers are reported but not well established.

At this time, women with *PALB2* mutations are generally advised to follow the breast cancer risk management guidelines outlined below for women with *BRCA1/BRCA2* gene mutations.

Cancer Risk Management Recommendations for *BRCA1/BRCA2* mutation carriers

Breast Cancer (women) – may also apply to *PALB2* mutation carriers:

- women should be breast aware
- **annual breast MRI** from age 25 - 65
- **annual mammograms** beginning at age 30 (continue as long as clinically indicated)
- **clinical examination** of the breast and regional nodes by an experienced health professional every 12 months, in conjunction with appropriate breast imaging
- **risk-reducing bilateral mastectomy** reduces breast cancer risk by over 90%. The decision to have this surgery is complex and requires discussion regarding benefits and risks in the context of a woman's general health, life expectancy and personal health beliefs.
- **risk-reducing medication** (e.g. tamoxifen, raloxifene, anastrozole, exemestane) can almost halve the risk of developing a hormone-receptor positive breast cancer. A decision to use such medication requires discussion about the relative benefits and the potential risk of side effects in the setting of a woman's general health, menopausal status and childbearing plans.

Breast Cancer (men):

- men should be aware of any changes in the chest wall and axillae
- consider an annual physical exam including a clinical exam of the chest/breast by an experienced health professional every 12 months

Ovarian Cancer:

- there is no evidence to support the effectiveness of any screening tests for the early detection of ovarian cancer
- **bilateral salpingo-oophorectomy** (BSO, removing ovaries and fallopian tubes) is recommended for confirmed *BRCA1* and *BRCA2* carriers, by age 35-40 and when childbearing is complete. It may be reasonable to delay BSO until age 45 for women with *BRCA2* gene mutations (average age of ovarian cancer diagnosis is older with *BRCA2*). If performed before the age of natural menopause, BSO may also reduce breast cancer risk with the level of risk reduction varying with the age at BSO. Pathology review of the ovaries and fallopian tubes should follow SEE-FIM protocol for detection of precursor lesions or early microscopic carcinoma.
- **bilateral salpingectomy (removing fallopian tubes) with delayed oophorectomy** has been proposed as a temporary means of reducing ovarian cancer risk in pre-menopausal women wishing to delay oophorectomy until closer to natural menopause. Evidence is not yet available to support the effectiveness of this approach for ovarian cancer risk reduction.
- **oral contraceptive (birth control) pill** significantly reduces the risk of ovarian cancer by 50% or more, if used for at least 5 years. This benefit increases with duration of use, persists for at least 20 years after the pill is stopped, and is observed in *BRCA1* and *BRCA2* carriers as well as the general population. Most studies have shown a small increase in breast cancer risk from oral contraceptive use, similar to that of hormone replacement therapy. A decision about using this medication for cancer prevention requires careful discussion about cancer risks, benefits and side effects within a woman's particular situation and contraceptive needs.

Prostate Cancer:

- discussion with family doctor about prostate cancer screening beginning at age 40

Pancreatic Cancer:

- options for pancreatic cancer screening will be discussed if the family history includes close relatives with pancreatic cancer

Special Consideration

Inheriting *BRCA2* or *PALB2* mutations from BOTH parents causes specific types of Fanconi anemia. This rare condition is characterized by progressive bone marrow dysfunction, growth delays, variable congenital malformations and a high risk for leukemia and early onset solid tumours. A woman or man with a confirmed *BRCA2* or *PALB2* mutation may, therefore, consider pre-conception genetic counselling to clarify their partner's chance of also carrying a mutation in the same gene.

Additional Information

The following websites offer support and information which may be helpful to people living with HBOC:

- Canadian Cancer Society: <http://support.cbcf.org/get-information/hereditary-breast-ovarian-cancer-hboc/>
- Facing Our Risk of Cancer Empowered (FORCE): www.facingourrisk.org
- Hereditary Breast and Ovarian Cancer Society of Alberta: www.hbocsociety.org
- Bright Pink: www.bebrightpink.org

References available on request.

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