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Guidelines & Protocols Advisory Committee

# Genital Tract Cancers in Females: Ovarian, Fallopian Tube, and Primary Peritoneal Cancers

Effective Date: June 15, 2014

## Scope

This guideline provides recommendations for the screening, diagnosis, and follow-up care of ovarian, fallopian tube, and primary peritoneal cancers in females aged ≥ 19 years.

This guideline is part of the BCGuidelines.ca – *Genital Tract Cancers in Females* series. The series includes two other guidelines: *Human Papillomavirus Related Cancers (Cervical, Vaginal & Vulvar)* and *Endometrial Cancer*. Signs and symptoms for the different female genital tract cancers may overlap (e.g., abnormal uterine bleeding); and therefore these guidelines may need to be used in conjunction with each other when performing initial diagnostic investigations.

## Key Recommendations

- Maintain a high index of suspicion for ovarian cancer – symptoms are nonspecific and variable.
- Investigate immediately if abdominal mass or postmenopausal/abnormal bleeding is present, since these symptoms have the highest positive predictive value.[1]
- Refer patient immediately by telephone referral to gynecologic oncologist at the BC Cancer Agency's (BCCA) Division of Gynecologic Oncology if epithelial ovarian cancer or germ cell ovarian tumour is suspected.
- Refer patient with suspected hereditary cancer syndrome to the BCCA's Hereditary Cancer Program (HCP).
- Routine tumour markers or imaging is not needed during follow-up visits, unless indicated by symptoms or signs on examination.

## Risk Factors[2, 3, 4]

For Epithelial Ovarian Cancer (EOC):

- personal or family history* of cancer of breast, epithelial ovarian, fallopian tubes, primary peritoneal and/or Lynch syndrome (also known as hereditary non-polyposis colorectal cancer (HNPCC))
- personal or family history of confirmed breast cancer gene mutation (BRCA) 1 or 2
- nulliparity and/or infertility
- age

There may be other risk factors for ovarian cancer (e.g., use of fertility drugs, smoking); however, at present time they are not well enough understood.

* *Particularly in a patient's close relatives, including: children, brothers, sisters, parents, aunts, uncles, grandchildren and 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.*

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## Prevention & Risk Reduction Strategies

- Testing for hereditary cancer gene – refer those with suspected hereditary cancer syndrome to the BCCA's HCP for genetic counselling and carrier testing. For more information, refer to *Associated Document: Hereditary Cancer Program Referral Form*.
- Prophylactic bilateral salpingo-oophorectomy (BSO)[5] – refer those considered high-risk or with a confirmed genetic mutation of BRCA 1 or BRCA 2, to the BCCA's Division of Gynecologic Oncology. For these females, a prophylactic BSO may be considered as a risk-reduction strategy. This surgery provides an 85-95% risk reduction for ovarian and fallopian tube cancers. If performed premenopausally, it may decrease the patient's risk of breast cancer by 50% or more, even in females taking short-term hormone replacement therapy (HRT) for symptom control. It is recommended that the BSO surgery be performed once childbearing is complete.
- Removal of the fimbriated end of the fallopian tubes[6] - the emerging evidence is that EOC probably arises from the fimbriated end of the fallopian tubes. On the strength of this evidence, the BCCA Gynecology-Oncology Tumor Group recommends that gynecologists, when possible, remove the fimbriated portion of the tubes in all patients seeking tubal ligation for contraception or hysterectomy for benign disease.

## Screening[2, 5, 7, 8]

Routine screening of females, whether of high or average risk, is not recommended. Studies have consistently failed to identify any reduction in the morbidity or mortality from ovarian cancer in females screened with currently available technology such as transvaginal ultrasound or cancer antigen 125 (CA-125). The potential harms of screening are substantial and include false reassurance, high recall rates for false positive results, and surgery for benign conditions with the associated surgical risks.

## Diagnosis

For ALL suspected cases (EOC or a germ cell ovarian tumour), urgent telephone referral to a gynecologic oncologist /BCCA's Division of Gynecological Oncology is recommended.† A tissue diagnosis or imaging is not required for a referral. Ovarian cancer progresses quickly and the stage strongly correlates with survival rates; urgent referrals could ensure timely treatment and better outcomes. Once a referral is made the assessment and management planning will be done by the BCCA multidisciplinary team.‡

### ▸ Symptoms

The symptoms of ovarian cancer are nonspecific and variable. They include persistent abdominal distention (i.e., bloating), abdominal discomfort or pain, abdominal mass, postmenopausal/ abnormal bleeding, early satiety, heartburn, change of bowel habits, pelvic pressure, urinary frequency, nocturia and/or unexplained thromboembolism. Assume a high index of suspicion and consider the possibility of ovarian cancer in females with symptoms lasting 2-3 weeks.

Abdominal mass and postmenopausal/abnormal bleeding are the symptoms with the highest positive predictive value. If either symptom is present, investigate immediately.[1]

† *The benchmark for an appointment at the BCCA is 2 weeks following referral; urgent cases may be seen sooner upon telephone consultation.*

‡ *This multidisciplinary team includes gynecologic oncologists (surgeons), radiation oncologists, medical oncologists, pathologists, radiologists, general practitioners in oncology, nurses, radiation therapists, counsellors and nutritionists.*

### Investigations

A physical examination of the abdomen and pelvis should precede all other investigations. A physical examination includes a pelvirectal examination as it increases the likelihood of identifying a pelvic mass.

Other investigations include:[§]

- CA-125 ($22.72);
- CA 19-9 ($20.88);
- CA 15-3 ($21.25); and
- carcinoembryonic antigen (CEA).

If the patient is aged < 40 years, testing should also include (to rule out germ cell tumour):

- alpha-fetoprotein (AFP) ($24.79);
- human chorionic gonadotropin (β-HCG) ($14.74); and
- lactate dehydrogenase (LDH) ($1.00 – 2.00).

Transvaginal or transabdominal ultrasound is recommended. Imaging is not essential for a referral to the BCCA.

Note that a normal tumour marker result or a normal imaging result does not rule out ovarian cancer.

## Treatment

Surgery and chemotherapy are the cornerstones of treatment. Surgical expertise improves survival.

***Epithelial Ovarian Cancer***

- Surgery - Debulking pelvi-abdominal surgery is the cornerstone of therapy. For those patients with intra-abdominal or systemic spread, chemotherapy is usually given up-front, followed by interval debulking surgery.
- Chemotherapy - If stage 1, certain histologic types often need no further therapy (e.g., mucinous, clear cell, endometrioid, low grade serous and borderline types). All the remainder will require adjuvant chemotherapy.
- Radiotherapy - Selected patients with non-serous histology may receive post-surgical (adjuvant) radiotherapy.

***Non-Epithelial Ovarian Cancer***

All non-EOC are rare, and treatment decisions are complex.

Stromal tumours are usually cured by surgery (full staging required). Germ cell tumours can be managed with conservative surgery, and usually require curative intent combination chemotherapy, except for stage 1 dysgerminoma. Note that germ cell cancers can occur in younger females.

## Follow-up

Once the patient has completed treatment, she will be discharged from the BCCA. Upon discharge, the family physician may be asked to manage the patient's follow-up care.

Follow-up care includes:

1) surveillance for recurrence or new cancer;
2) monitoring and treating complications and/or side effects from treatment; and
3) providing patient support.

§ *Prices as per the Medical Services Commission Payment Schedule (August 2013).*

**Specific recommendations will be provided in the patient's discharge letter**. Review any patients with symptoms immediately and re-refer to the BCCA. Arrange therapeutic thoracentesis / paracentesis in symptomatic women.

Below are general recommendations for a patient's follow-up visits with her family physician based on the type of cancer.

***Epithelial Ovarian Cancer*[9]**

The timing of the follow-up visits are:

- Years 1 & 2 = Every 4 months
- Years 3, 4 & 5 = Every 6 months
- Years 5+ = Annually

A follow-up visit consists of:

1) review of any symptoms (e.g., bloating, pain, dyspnea, bowel dysfunction, reflux) and of general health concerns; and
2) physical exam, including nodal areas (especially neck or groin), chest (for effusion) abdomen (for ascites and masses), and pelvic (for masses).

Routine tumour markers and imaging are not needed during follow-up visits, unless indicated by symptoms or signs on examination.

***Non-Epithelial Ovarian Cancer*[10]**

The timing of the follow-up visits are:

- Year 1 = Every 3 months
- Years 2 & 3 = Every 4 months
- Years 4 & 5 = Every 6 months
- Years 5+ = Annually

Follow-up visits are individualized, with patient-specific recommendations provided upon completion of therapy. In general, any initially elevated tumour markers will be followed routinely and some may require investigation through imaging.

## Resources

### References


1. National Collaborating Centre for Cancer. The recognition and initial management of ovarian cancer: Evidence review. 2011.
2. BC Cancer Agency. Cancer Management Guidelines - Gynecology – Ovary – Epithelial Carcinoma – 1.1 Predisposing Factors & Screening [cited 2014 April].
3. Rooth C. Ovarian cancer: Risk factors, treatment and management. Br J Nurs. 2013; 22(17):S23-S30
4. Kelsey JL, Whittemore AS. Epidemiology and primary prevention of cancers of the breast, endometrium and ovary: a brief overview. Ann Epidemiol.1994;4:89-95.
5. Horsman D, Wilson BJ, Avard D, et al. Clinical management recommendations for surveillance and risk-reduction strategies for hereditary breast and ovarian cancer among individuals carrying a deleterious BRCA1 or BRCA2 mutation. J Obstet Gynaecol Can. 2007;29(1):45-60.
6. Tone AA, Salvador S, Finlayson SJ, et al. The role of the fallopian tube in ovarian cancer. Clin Adv Hematol Oncol. 2012;10(5):296-306.
7. Barton MB, Lin K. Screening for ovarian cancer: Evidence update for the U.S. Preventive Services Task Force reaffirmation Recommendation Statement. AHRQ Publication No. 12-05165-EF3. Rockville, MD: Agency for Healthcare Research and Quality; April 2012.
8. Buys SS, Partridge E, Black A, et al. Effect of screening on ovarian cancer mortality: the Prostate, Lung, Colorectal and Ovarian (PLCO) cancer screening randomized controlled trial. JAMA 2011;305(22):2295-303.
9. BC Cancer Agency. Cancer Management Guidelines - Gynecology – Ovary – Non Epithelial Carcinoma – 2.3 Follow-up [cited 2014 April].
10. BC Cancer Agency. Cancer Management Guidelines - Gynecology – Ovary – Epithelial Carcinoma – 1.5 Follow-up [cited 2014 April].


### Resources

- BC Cancer Agency, www.bccancer.bc.ca, which includes many patient resources.
    - Division of Gynecologic Oncology, telephone 1-800-663-3333 (extensions 2353, 2365, or 2367)
    - Hereditary Cancer Program, www.screeningbc.ca/Hereditary/ForHealthProfessionals/Default.htm
- HealthlinkBC, www.healthlinkbc.ca or by telephone (toll free in BC) 8-1-1 or 7-1-1 (for the hearing impaired) for health information, translation services and dieticians.

## Associated Documents

The following documents accompany this guideline:

- BCGuidelines.ca - *Genital Tract Cancers in Females: Human Papillomavirus Related Cancers (Cervical, Vaginal & Vulvar)*
- BCGuidelines.ca - Genital Tract Cancers in Females: *Endometrial Cancer*
- Hereditary Cancer Program Referral Form

This guideline is based on scientific evidence current as of the Effective Date.

The guideline was developed by the Family Practice Oncology Network and the Guidelines and Protocols Advisory Committee. The guideline was approved by the British Columbia Medical Association and adopted by the Medical Services Commission.

**THE GUIDELINES AND PROTOCOLS ADVISORY COMMITTEE**

**The principles of the Guidelines and Protocols Advisory Committee are to:**

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- recommend actions that are sufficient and efficient, neither excessive nor deficient
- permit exceptions when justified by clinical circumstances

**Contact Information:**

Guidelines and Protocols Advisory Committee
PO Box 9642 STN PROV GOVT
Victoria BC V8W 9P1

Email:hlth.guidelines@gov.bc.ca
Website: www.BCGuidelines.ca

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