

***ATM* c.7271T>G (p.V2424G) Cancer Risks and Management**

Overview

People with a pathogenic variant in the *ATM* gene have a higher chance of developing certain types of cancer compared to the general population. Cancers often happen at a younger age for *ATM* carriers.

This document summarizes the cancer risks and management recommendations for individuals with a confirmed *ATM* pathogenic variant, specifically for variants (***ATM* c.7271T>G (p.V2424G)**) that confer higher risks than most *ATM* variants.

Cancer risks associated with *ATM*

Cancer Type	<i>ATM</i> (Risk to Age 80)	General Population
Breast cancer (female)	Most <i>ATM</i> variants: 20 - 30% <i>ATM</i> c.7271T>G (p.V2424G): 52%	12.5%
Ovarian cancer	2 - 3%	1 to 2%
Prostate cancer	Increased but not well quantified	12.5%
Pancreatic cancer	5 - 10%	1.3%

Females with the c.7570G>C (p.A2524P) variant in the *ATM* gene may have a similar risk of breast cancer as the c.7271T>G (p.V2424G) variant.

The risk for a second primary/contralateral breast cancer is not well known. There may be a small increase in risk for gastric cancer with *ATM*. Further studies are needed to confirm an association.

Cancer Screening and Risk Reduction

Female Breast Cancer

Female Breast Cancer Screening:

- Starting at age 18, females should become familiar with the normal look and feel of their breast tissue and to report any changes to their primary care provider promptly. Regular and consistent breast self-exams can support breast self-awareness and are often most effective when done at the end of menstruation.
- **Annual clinical exam** of the breast and regional nodes from age 30.
- **Annual breast MRI** beginning at age 30 until age 70.

- **Annual mammograms** beginning at age 30, or 5-10 years prior to the youngest diagnosis in the family, and continue as long as clinically indicated.

Female Breast Cancer Prevention:

- Discussion of **risk reducing medication** options and review of potential benefits and side effects is recommended. Medications such as tamoxifen, raloxifene, anastrozole and exemestane may reduce the risk of developing a hormone-receptor positive breast cancer.
- **Risk reducing bilateral mastectomy** (RRBM; removing both breasts) reduces the risk of breast cancer by over 90%. The decision to have RRBM is complex and requires discussion regarding benefits and risks of the surgery in the context of a person's general health, life expectancy and personal health beliefs. Routine breast imaging (mammogram and/or breast MRI) is not required after bilateral mastectomy.

Ovarian Cancer

Ovarian cancer screening (transvaginal ultrasound and/or pelvic exam and/or CA-125 blood test) is not recommended as it does not find cancer early.

There is insufficient evidence to recommend risk-reducing bilateral salpingo-oophorectomy (RRBSO; removing ovaries and tubes) for people who have a pathogenic *ATM* variant unless there is a close family history of ovarian cancer.

Prostate Cancer

Consider annual **digital rectal examination (DRE)** and/or serum **prostate specific antigen test (PSA)** testing as early as 40-45 years of age or 5-10 years before the youngest diagnosis of prostate cancer in the family (whichever is earlier)

The Canadian Urological Association recommends healthcare providers engage in shared decision-making with their patients to come to an individualized screening decision following a thorough discussion on the potential risks and benefits of the PSA test. In BC, PSA testing in asymptomatic men is not an insured benefit.

Pancreatic Cancer

- To lower the risk, avoid or quit cigarette smoking, exercise regularly, limit alcohol, maintain a weight that supports overall health and choose healthy foods and drinks.
- **Annual diabetes screen** at age 40 (fasting glucose or HbA1C).
- Investigate new onset of diabetes or unexplained changes in diabetic control carefully, with consideration of pancreatic imaging (CT pancreatic protocol or contrast-enhanced MRI/MRCP); refer to GI specialist if any abnormalities are found.
- **Imaging is not routinely recommended for those with *ATM* variants** who lack a close family history of pancreatic cancer. It may still be offered depending on individual circumstances, typically from age 50.

- **Consider referral to experienced, high-volume GI center** for baseline assessment and discussion of current surveillance methods:
 - o St. Paul's Hospital/Pacific Gastroenterology and Associates (tel: 604.688.6332; fax: 604.689.2004)
 - o Vancouver General Hospital (tel: 604.875.5474; fax: 604. 628.2419)
 - o Interior: KGA Gastroenterology (tel: 250.763.6433; fax 250.763.3818)
 - o Vancouver Island: Pacific Digestive Health (tel: 250.412.1864; fax: 1.888.398.7091).

Note: In the information above, male/female refers to sex assigned at birth.

High Risk Clinic

Individuals with breast tissue who carry a pathogenic variant in the *ATM* gene, or are at 50% risk of having inherited one, can be referred to the Hereditary Cancer Program's High Risk Screening Clinic for ongoing cancer risk management and decision support. Read more about the [High Risk Clinic](#).

Family and Reproductive Considerations

Inheritance

Each child of someone with an *ATM* pathogenic variant has a 50% chance of inheriting the variant.

Family members are encouraged to contact their local genetics clinic to learn more about whether genetic testing or cancer screening may be helpful for them. Family members who live in British Columbia or the Yukon can contact our program directly at hereditarycancer@bccancer.bc.ca. In BC/Yukon, genetic testing is generally available starting at age 19.

Ataxia Telangiectasia:

Children who inherit pathogenic *ATM* variants (PV) from both of their parents have ataxia telangiectasia (AT), a rare progressive disease characterized by movement/balance problems, immunodeficiency, and an increased risk for cancers such as leukemia and lymphoma. In order for a child to be at risk of AT, both of their parents would each have to have a single PV in *ATM*.

If an individual with an *ATM* pathogenic variant is planning a family, a review of their partner's family history of cancer may be helpful. Genetic counselling may be offered if there is a concern for the risk of AT in children.