
APPENDIX

Supplementary Figure 1. Germline and somatic variant classification.

<table>
<thead>
<tr>
<th>Classification</th>
<th>Impact on Gene Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathogenic</td>
<td>Disrupts gene function.</td>
</tr>
<tr>
<td>Likely Pathogenic</td>
<td>Likely disrupts gene function. Counseling of patient is the same as for a pathogenic variant.</td>
</tr>
<tr>
<td>Variant of Uncertain Significance (VUS)</td>
<td>Impact on gene function is not known. Most are eventually reclassified as benign.</td>
</tr>
<tr>
<td>Likely Benign</td>
<td>Likely doesn’t impact gene function. Generally not reported by labs.</td>
</tr>
<tr>
<td>Benign</td>
<td>Does not impact gene function. Generally not reported by labs.</td>
</tr>
</tbody>
</table>

Tumour/Somatic variants are generally classified into tiers based on clinical significance:

<table>
<thead>
<tr>
<th>Tier</th>
<th>Variants Significance</th>
<th>Clinical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tier I</td>
<td>Strong Clinical Significance</td>
<td>Impact gene function and have significant treatment/prognostic/predictive value.</td>
</tr>
<tr>
<td>Tier II</td>
<td>Potential Clinical Significance</td>
<td>Impact gene function and might have treatment/prognostic/predictive value.</td>
</tr>
<tr>
<td>Tier IIIA</td>
<td>Uncertain Clinical Significance</td>
<td>Impact gene function but may not have any treatment/prognostic/predictive value.</td>
</tr>
<tr>
<td>Tier IIIB</td>
<td>Uncertain Function</td>
<td>Uncertain impact on gene function and likely have no treatment/prognostic/predictive value.</td>
</tr>
<tr>
<td>Tier IV</td>
<td>Benign and Likely Benign</td>
<td>Likely have no impact on gene function. Generally not reported by labs.</td>
</tr>
</tbody>
</table>

Note – potential germline variants (pGVs) can show up in all five tiers. Offer or refer for germline confirmation testing for pGVs in Tiers I-III A.

1 Adapted from Richards et al. 41 2 Adapted from Li et al. 42
Supplementary Figure 2. Molecular genetic analysis for patients with PCa: Points to consider.

1. Pre-Test:
   1.1. Know what is covered/what your patient is eligible for in your province or territory, what you can order, and what has to be ordered by a genetics specialist:
      1.1.1. Tumour Testing
      1.1.2. ctDNA
      1.1.3. Germline Testing
   1.2. If you are ordering the testing:
      1.2.1. Know what genes are included in the test.
      1.2.2. Keep in mind that tissue/ctDNA testing is generally not equivalent to a germline test.
         1.2.2.1. Referral to genetics should be considered for patients who have a negative test, particularly in the context of a strong family history of cancer.
      1.2.3. Counsel patient on purpose and possible outcomes of genetic testing.
         1.2.3.1. The possible results (including VUS).
         1.2.3.2. The potential implications for themselves and their relatives.
         1.2.3.3. That tumour testing may identify a potential germline variant.
            1.2.3.3.1. Consider discussing implications of a positive result with patient prior to ordering the test.
         1.2.3.4. A referral to genetics/further genetic testing (e.g., germline confirmation) may be needed after you disclose the results.
      1.2.4. Consider providing an information sheet so the patient can review the main discussion points.
      1.2.5. Document your discussion and the patient’s consent in their chart.

2. Post-Test:
   2.1. Know when to refer to genetics and/or offer germline confirmation.
      2.1.1. All patients with a LP/P germline variant should be referred to discuss screening recommendations and testing for family members.
      2.1.2. Genetics may see some or all patients with a VUS.
      2.1.3. Are you able to order germline confirmation testing for variants detected on tumour tests, or do you need to refer to Genetics?
   2.2. Disclose the results to the patient.
   2.3. For patients with LP/P variants, discuss implications for family members and how they can access testing.
   **2.4. Do NOT alter cancer screening or management based on a VUS.**
   2.5. Let the patient know what the next steps are (e.g., appointment with Genetics) and where they can get more information.
   2.6. Consider providing an information sheet to the patient about their results.

2.7. Document your discussion with the patient in their chart.
3. When in doubt, contact Genetics!

ctDNA: circulating tumour DNA; LP/P: likely pathogenic/pathogenic variants; PCa: prostate cancer; VUS: variant of unknown significance.
What was the study about?
An estimated 24,600 Canadian men were diagnosed with prostate cancer in 2022. Certain therapies that treat prostate cancer work better when patients have been identified to have specific changes to their DNA through genetic testing. These changes can either be inherited (germline), which are passed down from parent to child, or acquired (somatic), which instead happen during a person’s lifetime.

What did we do?
We surveyed 38 Canadian academic specialist physicians, who treat prostate cancer, to understand: how they access genetic testing; what type of testing they offer; when they offer testing; and to which patients do they offer this testing.

What did we find?
Access to genetic testing is not equal across regions in Canada. Many physicians must refer patients to a genetic specialist to gain access to genetic testing, which can delay treatment. Most physicians offer genetic testing for both germline and somatic changes to patients with:
- High-risk prostate cancer,
- Prostate cancer that has spread to other parts of the body, or
- Family history of cancer,

Many physicians find it more difficult to access somatic testing than germline testing. Physicians believe testing for germline and somatic changes should occur at the same time. Knowing the results of both types of testing help physicians determine the best available treatment for patients. Germline testing also helps identify family relatives who should be offered testing, who may have higher risk of developing cancer given their risk of inheriting a change to their own genetics.

**PLAIN LANGUAGE SUMMARY: INFOGRAPHIC**

**Genetic testing practices among Canadian physicians who treat prostate cancer**

This study asked doctors who treat prostate cancer in Canada to describe what type of genetic changes they test for when selecting a treatment for patients with prostate cancer, approximately how many of their patients are tested, when they offer testing to patients over the disease course, and which patients should be offered testing.

**Background**

*Genes*, found in DNA, carry information, which determine physical and other traits. Many genes contain instructions for making proteins, which carry out various functions in the body.

When treating prostate cancer doctors sometimes use clinical tests to look for genetic changes, or mutations, to better understand a patient's prostate cancer. Some mutations are harmless while others can increase cancer risk.

The two different types of mutations, *inherited* also known as *germline* and *acquired*, also known as *somatic*.

Inherited mutations are present from birth and are usually passed down from the parents and can be further passed down to children.

Acquired mutations are not passed down and can be caused by the environment, diet, aging, or by unknown reasons.

Mutations affecting certain genes can increase the risk of developing certain cancers. Information obtained from these tests can help doctors determine optimal treatment plans.

The inherited genetic changes in BRCA 1 or 2 and PARP genes increase the odds that a man will develop hereditary prostate cancer.

PARP inhibitors (e.g., olaparib, niraparib) are oral targeted medication that improve patient outcomes and prolong the survival of patients with BRCA 1/2 gene changes and advanced prostate cancer.

**What was the study about?**

- This main goal of this study was to better understand genetic testing practices among physicians who treat prostate cancer in Canada.

- Access to genetic testing is known to vary across Canadian both in genes screened and how these tests are made available to patients.

- Certain therapies that treat prostate cancer work better when patients have specific genetic changes. Information from genetic testing can help physicians develop optimal treatment plans for patients with prostate cancer.

**What did we do?**

The Canadian Genitourinary Research Consortium (GURC) conducted a one-time survey of physicians treating in prostate cancer across 22 study sites in Canada between January to June 2022.

The purpose of the survey was to understand what type of genetic testing physicians offer to patients with prostate cancer, including when in the disease course they offer testing and which patients are most likely to benefit from genetic testing.

**38 Physicians**

21 principal investigators and 17 sub-investigators were surveyed across 22 GURC sites.

**87%**

Practice in an academic setting

Note: BRCA is short for Breast Cancer gene and PARP stands for poly ADP ribose polymerase.

**What did we find?**

**Current Situation**
- Most physicians offer genetic testing to prostate cancer patients and recognize the need for both germline and somatic testing.
- A large proportion require referral to a genetic specialist to start germline genetic testing.

**Referral Process**
- Most physicians refer to a genetic specialist when high-risk mutations are found (e.g., BRCA or ATM mutations).

**Access**
- Most physicians have access to germline testing, with fewer having access to somatic testing.
- An access gap and uncertainty around how to order genetic tests were the most common reasons for not testing.

**Risk Stratification**
- Generally, physicians indicated that germline and somatic testing should be offered to prostate cancer patients with high-risk disease or disease that has spread to other parts of the body, especially when there is a family history of cancer.

**Provincial Differences**
- There are differences across regions in Canada regarding the availability of genetic testing.
- Patients are encouraged to discuss testing practices in their region with their health care provider.

**Who orders the test?**
- 45% Genetic specialist
- 34% Main treating physician
- 21% Other

**Which genetic changes are tested?**
- 94% are referred to a genetic specialist when BRCA1, BRCA2 or ATM genetic changes are identified.
- Compared to 27% when any other genetic changes are identified.

**The type of testing currently available to physicians**
- Somatic: 58%
- Germline: 91%

**Physicians who did not offer genetic testing, did not because of...**
- Access gap: 50%
- Uncertainty about how to order or interpret results: 33%
- No impact on patient management: 17%

**Recommendation**

**Genomic Testing in Prostate Cancer**
- For patients with prostate cancer that has spread to other parts of the body, both germline and somatic testing are recommended to identify targets for treatment and to inform future cancer risk in patients and their family relatives.
- Patients with specific genetic changes (e.g., BRCA1 or BRCA2) and advanced prostate cancer may be offered treatment with targeted therapies (i.e., PARP inhibitor) or platinum-based chemotherapy at some point in their course of treatment.

Note: BRCA is short for Breast Cancer gene, ATM stands for ataxia-telangiectasia mutated, and PARP stands for poly-ADP ribose polymerase.