

**The evolving role of germline genetic testing and management in prostate cancer: Report from the Princess Margaret Cancer Centre International Retreat**

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**Abstract**

**Introduction:** Prostate cancer is a significant cause of cancer mortality. It has been well-established that certain germline pathogenic variants confer both an increased risk of being diagnosed with prostate cancer and dying of prostate cancer.<sup>1</sup> There are exciting developments in both the availability of genetic testing and opportunities for improved treatment of patients. On August 19, 2020, the Princess Margaret Cancer Centre in Toronto, Ontario, hosted a virtual retreat, bringing together international experts in urology, medical oncology, radiation oncology, medical genetics, and translational research, as well as a patient representative. We are pleased to provide this manuscript as a review of those proceedings for Canadian clinicians.

**Recommendations:** We drafted several recommendations for future research and policy action based on this meeting:

- 1) Need for increased access to funding for germline testing for the common genetic disorders associated with increased risk of prostate cancer.
- 2) A need for increased research into identifying genetic factors influencing risk stratification, treatment response, and outcomes of prostate cancer within Canadian populations at increased genetic risk for prostate cancer.
- 3) Need for increased awareness about genetic risk factors among the Canadian public.
- 4) Need for research on patient perspectives and psychosocial outcomes in individuals identified to be at increased genetic risk of prostate cancer.
- 5) We support the creation of specialized multidisciplinary clinics that specialize in tailored care for patients at increased genetic risk of prostate cancer.

## Introduction

Certain germline pathogenic variants confer both an increased risk of being diagnosed with and dying of prostate cancer<sup>1</sup>. Mutations which disrupt the function of genes involved in repairing DNA damage (e.g. *BRCA2*) are associated with aggressive prostate cancers<sup>2,3</sup>. Research continues to identify associations between gene mutations and prostate cancer risk. Urologists can help identify at-risk individuals and ensure they receive appropriate treatment and access screening for additional at-risk disease sites.

Currently, access to province-reimbursed genetic testing for men with prostate cancer is limited<sup>4</sup>, despite growing patient and clinician interest in genetic testing. Recent Supreme Court decision upholding the Genetic Non-Discrimination Act in Canada<sup>5</sup> protects mutation carriers from genetic discrimination. Furthermore, due to the proliferation of private “lifestyle” low-cost genetic testing services (e.g. 23andMe ©), direct-to consumer, and, in some cases, clinical-grade germline testing, patients can receive germline genetic testing without the direction of a physician. Despite this, the patient will expect their medical professional (including their urologist) to provide counsel regarding the results. Increased public awareness of the risks of mutations in the *BRCA1/2* genes<sup>6</sup> to women and growing acceptance of prophylactic surgery for prevention of malignancies, in addition to the demand for personalized cancer treatments<sup>7</sup> have also contributed to the interest in germline genetic testing. Decreasing costs and shorter turnaround times associated with next generation gene sequencing have made genetic testing more affordable and feasible to integrate into routine oncology care<sup>8</sup>, with panel testing likely to become increasingly important in the future.

There are exciting developments in both the availability of genetic testing and opportunities for improving patient treatment. Currently, large high-quality randomized control

trials (e.g. IMPACT trial <sup>9</sup>) are re-evaluating prostate cancer screening for high-risk. Knowing that these opportunities are developing, we felt it was important to bring together international experts within this field to understand what has been done so far and where we need to go. On Aug 19<sup>th</sup>, 2020, the Princess Margaret Cancer Centre in Toronto, Ontario, hosted a virtual retreat bringing together international experts in urology, medical oncology, radiation oncology, medical genetics, and translational research, as well as a patient representative. The attendees developed Canadian recommendations for screening, treatment, and case identification for patients with/at risk of hereditary prostate cancer gene mutations. We are pleased to provide this manuscript as a review of those proceedings for Canadian clinicians.

## **Background**

### ***Somatic vs. germline mutations***

The two most common types of genetic analysis currently performed in Canada are either germline or tumor testing. Germline mutations are passed directly from a parent to a child. These genes will be present in every cell within the body and thus can be assayed from any tissue in the body, such as blood lymphocytes or saliva. Germline mutations commonly seen in urologic practice include many of the hereditary renal cell carcinoma syndromes (e.g. von Hippel-Lindau syndrome). Genetic testing for germline mutations identifies individuals who are at high risk for specific cancers. Tumor genetic testing identifies both somatic and germline mutations, but it can be difficult to distinguish between somatic and germline mutations unless matched germline source is also analyzed. Somatic mutations are those acquired within individuals' cells over the course of their lifespan. Identifying somatic mutations requires analysis of either tumor tissue or circulating cell-free fragments of tumor DNA from the affected tissue itself. Acquired (somatic) mutations are the most common cause of cancer. Somatic mutations commonly seen in urological practice include mutations in chromosome 12p in testicular cancer and mutations in FGFR3 in bladder cancer.

### ***Guidelines for germline genetic testing in prostate cancer***

There are no Canadian guidelines regarding indications for germline genetic testing among men with prostate cancer. Various international germline testing guidelines for prostate cancer patients have been recently published, notably from the 2019 Philadelphia Prostate Cancer Consensus (PPCC) Conference and two from the National Comprehensive Cancer Network (NCCN) <sup>10,11</sup>. These guidelines address several indications based on clinical and family-history with variable recommendations, summarized in Table 1.

### ***Current challenges with access to genetic testing in Canada***

Access to provincially funded genetic testing and counselling for Canadian prostate cancer patients is limited. Various provincial genetic testing guidelines exist, but do not account for

prostate cancer in a patient's personal or family history. Access to germline testing is typically assessed on a case-by-case basis and limited to patients with a strong family history of breast and ovarian cancer. Moreover, most institutions do not have enough genetic counsellors to facilitate timely genetic testing using traditional pre- and post-test genetic counselling appointments. Alternative models of genetics service delivery<sup>12,13</sup>, including testing ordered by clinicians (mainlining),<sup>14-16</sup> will be required to address this unmet need.

Recent consensus of Canadian urologists regarding which patients should undergo testing diverge from current international guidelines<sup>17,18</sup>. Long wait times for genetics assessment have contributed to low genetics referrals and testing rates. Additional barriers to urologist-ordered genetic testing for prostate cancer include: insufficient awareness and lack of educational materials for urologists and patients; lack of effective workflows; time and space constraints in busy clinics; and absence of insurance coverage<sup>19</sup>. Additionally, while increased awareness of *BRCA1/2* has dramatically increased genetics referrals for breast and ovarian cancer patients<sup>6</sup>, this trend has not been observed with prostate cancer patients.

#### ***Other methods of access to testing***

Patient-pay genetic testing options have emerged as an affordable and convenient option for many patients. Testing is typically conducted by a clinical grade laboratory at the cost ranges from \$250 to \$1,000 USD. Access varies depending on provider comfort with facilitating genetic testing, institutional policies, and patients' motivation to pursue testing. Limited data currently exist on the risks, benefits, and limitations of systematically incorporating patient-pay genetic testing options into publicly funded oncology clinics.

Sponsored genetic testing programs offer clinical-grade no-cost genetic testing to patients who meet specific medical eligibility criteria. Biopharma partners provide financial support for testing in exchange for patients' gene variant and clinical data. This approach may address the growing need for rapid access to testing. However, lack of information regarding privacy and data sharing concerns could act as a barrier for Canadian patients to participate.

#### **Natural history of prostate cancer in germline mutation carriers**

While it has been established that several germline mutations are associated with a higher risk of prostate cancer, there continues to be a paucity of prospective studies quantifying this risk. The following anomalies are considered relevant to prostate cancer.

#### ***Breast cancer type 1 and 2 susceptibility (BRCA1/2)***

The *BRCA 1* and *2* proteins are involved in the repair of chromosomal damage. Mutations in the *BRCA1/2* genes are associated with an increased risk of breast, ovarian, prostate and pancreatic cancers. Mutations in *BRCA2* are more common than those in *BRCA1* gene, but still only occurs in approximately 1/400 individuals<sup>20</sup>. PPCC conference concluded that there was grade A evidence of an association between *BRCA1/2* mutations and prostate cancer<sup>21</sup>. A recent meta-

analysis of retrospective studies established that individuals with mutations in *BRCA1/2* conferred 1.9-times greater odds of prostate cancer compared to the general population. Prospectively collected data have shown that mutations in the *BRCA2* gene are associated with an increased risk of high Gleason score prostate cancer (standardized Incidence ratio 5.07) and a higher risk of death from prostate cancer (standardized mortality ratio 3.85)<sup>23</sup>.

Although the risk of developing prostate cancer per se appear to be marginally increased, the risk of metastatic disease is particularly striking among *BRCA2* carriers. Pritchard et al, examined the prevalence of germline genetic mutations among men exclusively with metastatic prostate cancer and found an approximate 26-fold increase in prevalence in patients with metastatic disease compared to the cancer genome atlas. Although lifelong risk of death from prostate cancer among carriers is unknown, it is estimated to be in the 20-40% from the work our group has performed (submitted, pending publication). Interestingly, *BRCA1* anomalies are thought to carry a much lower risk of metastases compared to *BRCA 2*. While no specific guidelines exist regarding screening in individuals with *BRCA1/2* mutations, an ongoing prospective screening study has shown the benefit of screening to identify tumors that are more likely to require treatment<sup>24</sup>.

#### ***Homeobox protein Hox-B13 gene (HOXB13)***

*HOXB13* is a gene involved in the regulation of the transcription of other genes and as a tumor suppressor gene. The PPCC conference found grade A level of evidence supporting an association between mutations in this gene and prostate cancer<sup>21</sup>. A large study in Swedish population found that mutations are associated with a 3.5-fold increase in prostate cancer risk and that 33% of men who have a specific mutation will develop prostate cancer<sup>25</sup>.

#### ***Ataxia-telangiectasia gene mutation (ATM)***

The *ATM* gene produces a protein which has a role in regulating cell growth and division, as well as the recognition of DNA strand breakage<sup>26</sup>. Mutations in *ATM* are associated with an increased risk of breast, pancreatic and prostate cancers. The PPCC conference found grade C-level evidence of an association between this gene and prostate cancer<sup>21</sup>. Early work evaluating the relationship between *ATM* mutations and prostate cancer found a high association between late complications of external beam radiotherapy and mutations in this gene<sup>27</sup>. Helgalson et al. found a 2-fold increased risk of being diagnosed with prostate cancer among *ATM* mutation carriers. Unfortunately, the possibility of false positives when performing chromatin immunoprecipitation is particularly high in individuals with *ATM* mutations, increasing the risk of a false-positive identification.

#### ***Checkpoint kinase 2 gene (CHEK2)***

*CHEK2* gene is involved in DNA repair, cell cycle arrest, and apoptosis in response to DNA damage<sup>13</sup>. Individuals with this mutation are at an increased risk for melanoma, breast, thyroid,

kidney and prostate cancers<sup>14</sup>. The PPCC conference found a grade D level of evidence of an association between this gene and prostate cancer<sup>21</sup>. A recent meta-analysis showed that only a subset of encountered mutations are associated with an increased risk of prostate cancer<sup>31</sup>. *CHEK2* mutations were the third most common mutations found in individuals with metastatic prostate cancer<sup>1</sup>. Further work is needed to define the relationship between this mutation and prostate cancer.

### **Management of germline carriers and their families**

#### ***Screening***

The Canadian Urological Association (CUA) guidelines on prostate cancer screening and early detection are not directed towards men with known germline mutations associated with prostate cancer development. Furthermore, these guidelines state that these men require individualized testing strategies after consulting with a clinical geneticist<sup>32</sup>. Similarly, the American Urological Association (AUA) guideline states that in the future there may be a method to identify individuals at higher risk of prostate cancer through genetic testing or biomarkers and that these individuals may benefit from more intense screening at a younger age<sup>33</sup>. As previously mentioned, there is one ongoing prospective screening study evaluating the benefits of prostate cancer screening but it is restricted to *BRCA1/2* carriers<sup>9</sup>. Interim results show that, after 3 years of screening, *BRCA2* carrier status is associated with a higher incidence of prostate cancer, younger age of diagnosis and the presence of clinically significant tumors. The authors recommend that systematic prostate specific antigen screening for men with *BRCA2* mutation. Currently, there are only retrospective studies looking at the possible benefit of screening and men with *HOXB13*, *ATM* and *CHEK2* mutations. We believe that screening should be individualized and risk stratification, based on genetic testing in consultation with a genetic counsellor, should be incorporated into a shared decision-making model for prostate cancer screening.

#### **The role of active surveillance in higher risk germline mutation carriers**

Unfortunately, there is little consensus on the role of active surveillance in the management of localized prostate cancer in individuals with high-risk germline mutations. The PPCC conference recommends that active surveillance strategies must be tailored to personalize risk profiles, while previous work has shown that mutation carriers are at higher risk of reclassification to more aggressive cancer over time<sup>34</sup>. There is an urgent need for randomized control trials assessing the safety of active surveillance protocols for individuals with high-risk germline mutations. These patients are likely to require a risk-adapted approach (e.g., yearly MRI surveillance) to account for their higher risk of disease progression and death.

### *Surgical management*

#### *Prophylactic prostatectomy*

There are several anecdotal reports of men who have undergone prophylactic prostatectomy<sup>37</sup>, typically confined to men with *BRCA1/2* gene mutations. In our experience, young male *BRCA1/2* carriers are often identified incidentally after undergoing screening due to affected first/second degree relatives. Seeing a urologist after this incidental diagnosis is often surprising for patients but they should be counselled about the potential risk of prostate cancer. The benefits of prophylactic mastectomy and oophorectomy are well-established within the breast cancer research, with a 95% reduction in the risk of breast cancer<sup>38</sup> after mastectomy and a 50% reduction in breast cancer risk after oophorectomy if performed under the age of 40<sup>39</sup>. Translation of this paradigm to male *BRCA1/2* mutation carriers is tantalizing and clearly requires further investigation, not only in terms of cancer risk reduction, but also in terms of impact on the individual's quality of life.

#### *Testing family members (cascade testing)*

The identification of hereditary germline mutations in any prostate cancer gene can provide the opportunity for family members to pursue targeted genetic testing; if identified to be a carrier, family members can receive tailored cancer screening and consider risk-reducing options (e.g. prophylactic surgery). There are guidelines for ongoing surveillance of hereditary cancer syndrome patients, which may be coordinated through specialized clinics in multiple cancer centers across Canada.

### *Systemic treatments*

With the explosion of interest in personalized medicine and genetic testing has also come an interest in treatments specifically targeted towards individuals with DNA-repair defects. The two most widely accepted treatments for individuals with metastatic castrate resistant prostate cancer (CRPC) are platinum-based chemotherapy and poly (ADP-ribose) polymerase inhibitors (PARPi).

#### *Platinum-based chemotherapy*

Platinum based chemotherapy is generally not considered effective among unselected men with advanced prostate cancer<sup>40</sup>. Nonetheless, retrospective data from Pomerantz and others demonstrate that platinum responders in prostate cancer are almost exclusively those with *BRCA2* anomalies<sup>41</sup>. Gillissen et al. reported their multicenter pooled results utilizing platinum-based therapy among men with CRPC and DNA-repair defects<sup>42</sup>. They demonstrated that 47% of men had a PSA reduction greater than 50%. Although this has worked its way into clinical practice, debate still exists about whether to utilize taxane or platinum-based therapy first line for these men.

*Poly ADP ribose polymerase inhibitors (PARPi)*

PARP's are enzymes which catalyze the transfer of ADP-ribose to target proteins and have an important role in several cellular processes including DNA repair. This is of interest clinically given that certain tumors, defective in other methods of replication, may be reliant on PARP-mediated DNA repair pathways for continued survival<sup>43</sup>. Several PARPi agents have been approved as monotherapy for *BRCA*-mutated or platinum sensitive recurrent ovarian cancer or HER-2 negative breast cancer<sup>44</sup>. Within prostate cancer, olaparib is approved for the treatment of metastatic prostate cancer for tumors with *BRCA1/2* mutations, with several trials currently in progress<sup>45</sup>. An excellent review on the development and targets of PARPi is available by Dr. De Bono's group and these agents are likely to be increasingly integrated into the care of individuals with high risk genetic profiles and prostate cancer<sup>46</sup>. There are currently 15 phase 2 or phase 3 trials which have not yet reported their data, so there is expected to be significant evolution within this field over the coming years<sup>47</sup>.

**2020 Toronto Prostate Cancer Genetics Virtual Retreat**

The inaugural prostate cancer genetics virtual retreat was held on August 19<sup>th</sup> 2020 and included national and international researchers, clinicians, and patient representatives. The purpose of the retreat was to discuss transformative research, clinical implications, and applications of published findings, as well as to review front-line experiences of patients and genetic counsellors (Table 2).

**Future directions and research**

Although much has been learned over the past decade regarding germline defects and prostate cancer natural history/treatment, this body of knowledge remains in its infancy. Current recommendations regarding men with this condition are largely based on pragmatic considerations and more research is needed to set priorities and define future directions. Our panel has made the following recommendations for practicing urologists:

***1) Increased access to funding for germline testing for common genetic disorders associated with increased risk of prostate cancer.***

No Canadian or provincial guidelines currently exist for genetic testing in prostate cancer patients. Multi-gene panel testing is available to metastatic prostate cancer patients through selected Canadian genetic clinics, although this is typically offered on a case by case basis. We support broad access to genetic testing for Canadian individuals, including prostate cancer patients, through public, private or mixed funding models. The Genetic Non-Discrimination Act protects patients' rights to control their genetic information and not face discrimination based on their results (e.g. no increase in insurance premiums based on profile). Consideration should be given to for-pay services, which offer robust clinical testing and counselling for under \$300.



**2) *A need for increased research into identifying genetic risk factors, risk stratification, treatment modalities and outcomes of prostate cancer within Canadian populations at increased genetic risk for prostate cancer***

Given increasing diversity within the Canadian population, it is essential that we continue to conduct research into genetics and prostate cancer within our population. Research will allow us to both improve patient treatment and inform international efforts to improve patient outcomes.

**3) *General awareness about genetic abnormalities and risk needs to increase among the Canadian Public***

There continues to be a lack of awareness of the increased risk of prostate cancer among clinicians and patients. Personal experience indicates that many of the men who present to the urology clinic with *BRCA1/2* germline mutations have undergone testing for the benefit of their daughters and often are surprised to hear about the association with prostate cancer. Increased awareness in the public and among primary care physicians is essential to ensure patients are triaged and treated appropriately.

**4) *There is a current need to develop patient specific and reported outcomes research in tailored care for patients at increased genetic risk of prostate cancer***

During our virtual retreat we heard from a patient, a genetic counsellor, an expert in patient reported outcomes research and numerous clinicians that patients who are at increased genetic risk of prostate cancer may have important differences in their disease experience compared to the usual patient population. It is essential that patients and their loved ones help set the research priorities and new directions.

**5) *We support the creation of specialized multidisciplinary clinics which specialize in catering to patients at increased genetic risk of prostate cancer***

Multidisciplinary clinics are proliferating throughout the medical field and allow patients to get high quality health information from multiple practitioners in a convenient format. They are also beneficial to practitioners as they improve interdisciplinary communication and can expand our understanding of other practice patterns. Multidisciplinary clinics providing genetic testing, risk assessment, and counselling to men at increased risk for prostate cancer would present a streamlined and cost-efficient approach to implementing more widespread genetic testing and counselling for these men<sup>48</sup>.

## **Conclusions**

The virtual retreat on genetics in prostate cancer highlighted the significant amount of interest and diversity in the field of prostate cancer genetics. There are opportunities for ongoing research and clinical implementation to advance this field. We have made the presentations from the virtual retreat available for viewing (link attached). Based on the seminars and discussions

during the virtual retreat, we have outlined several recommendations for research and practice within this field. We would be happy to discuss the approach to implementing these recommendations and look forward to the second prostate cancer genetics meeting.

DRAFT

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## Figures and Tables

<b>Category</b>	<b>NCCN HBOPC Version 1.2021</b>	<b>NCCN Prostate Version 2.2020</b>	<b>Philadelphia (Giri et al 2020)</b>
Metastatic disease	Metastatic PCa	Metastatic PCa	Metastatic PCa (castrate resistant or sensitive; <i>Recommend</i> )
Histology	Intraductal/cribriform histology	Intraductal/cribriform histology	Intraductal/ductal pathology ( <i>Consider</i> )
Grade, stage, PSA	<ul style="list-style-type: none"> <li>• High-risk, very high-risk group</li> <li>• <math>\geq</math>stage T3a</li> <li>• <math>\geq</math>grade group 4</li> <li>• PSA <math>&gt;20</math> ng/mL</li> </ul>	High-risk, very high-risk, or regional	<p>Advanced disease (T3a or higher; <i>Consider</i>)</p> <p>Grade Group 4 (Gleason sum 8) or above (<i>Consider</i>)</p>
Ancestry	Ashkenazi Jewish ancestry	Ashkenazi Jewish ancestry	Ashkenazi Jewish ancestry ( <i>Consider</i> )
Family history	<p><b>Personal Hx PCa with:</b></p> <p>a) <math>\geq 1</math> close relative with breast <math>&lt;50</math> y and/or ovarian and/or pancreatic and/or metastatic/intraductal/cribriform PCa at any age</p> <p>b) <math>\geq 2</math> close relatives with breast or PCa (any grade) at any age</p>	<p><b>Positive family history of cancer:</b></p> <p>a) Brother or father or multiple family members diagnosed with PCa (not clinically localized grade group 1) at <math>&lt;60</math> y of age or who died from PCa <i>OR</i></p> <p>b) <math>\geq 3</math> cancers on the same side of the family, especially diagnosed <math>\leq 50</math> y: <i>bile duct, breast, CRC, endometrial, gastric, kidney,</i></p>	<p><b>One brother/father or <math>\geq 2</math> male relatives:</b></p> <p>a) Diagnosed with PCa at age <math>&lt;60</math> y (<i>Recommend</i>)</p> <p>b) Any of whom died of PCa (<i>Recommend</i>)</p> <p>c) Any of whom had metastatic PCa (<i>Recommend</i>)</p> <p><b>FH of other cancers:</b></p> <p><math>\geq 2</math> cancers in HBOC or Lynch spectrum in</p>

		<i>melanoma, ovarian, pancreatic, PCa (not clinically localized grade group 1), small bowel, or urothelial cancer</i>	any relatives on the same side of the family (especially if diagnosed at <50 y; Consider)
Prior probability	>5% risk of carrying a pathogenic variant based on prior probability models (e.g., Tyrer-Cuzick, PennII).	N/A	N/A
Treatment decisions	To aid in systemic therapy decision-making.	N/A	<i>...an unremarkable FH does not necessarily negate consideration of GT, particularly for treatment decisions in the metastatic setting.</i>
Tumor genetic testing	A mutation identified on tumor genomic testing with clinical implications if identified in the germline.	<i>If mutations in BRCA1/2, ATM, CHEK2, or PALB2, are found, refer to genetics for germline testing.</i>	N/A
Germline tumor testing	Multi-gene panel testing using next-generation sequencing technology to include <i>MLH1, MSH2, MSH6</i> and <i>PMS2</i> , as well as homologous recombination genes <i>BRCA1/2, ATM, PALB2</i> and <i>CHEK2</i> . Additional genes, such as <i>HOXB13</i> , may be considered depending on clinical and family history.		Panel-based testing for patients with metastatic prostate cancer that includes priority genes <i>BRCA1/2</i> , DNA MMR genes (recommend), <i>ATM</i> (consider) and additional genes based on cancer family history (recommend)



<b>Table 2. 2020 Prostate Cancer Virtual Retreat</b>		
<b>Introduction</b>		
15:00–15:10	Introduction and overview	Dr. Neil Fleshner, Princess Margaret
<b>Session 1: Genetics (Moderator Raymond Kim)</b>		
15:10–15:20	Overview of genetics testing for prostate cancer patients in Toronto	Dr. Raymond Kim, Princess Margaret
15:20–15:30	Utility of germline genetic testing in the clinical context for prostate cancer	Dr. Colin Pritchard, University of Washington
15:30–15:40	Novel models of delivering genetic testing	Dr. Robert Nussbaum, CMO, Invitae Laboratories
15:40–15:50	Cell-free DNA assays, and their role in prostate cancer management	Dr. Alex Wyatt, University of British Columbia
15:50–16:30	Discussion	Dr. Raymond Kim
<b>Session 2: Management of Carriers (Moderator Neil Fleshner)</b>		
16:30–16:50	Systemic treatment options for germline carriers with prostate cancer	Dr. Johann De Bono, Royal Marsden
16:50–17:00	Surveillance for germline carriers in the Canadian Context	Dr. Danny Vesprini, Sunnybrook, Toronto
17:00–17:10	Surgical perspective for germline carriers	Dr. Neil Fleshner
17:10–17:50	Discussion	Dr. Neil Fleshner
17:50–18:10	Break	
<b>Session 3: Patient Perspectives (Moderator Emily Thain, Genetic Counsellor, Princess Margaret)</b>		
18:10–18:20	My journey as a carrier	Dr. Barry Rubin
18:20–18:30	Measuring patient decisions	Dr. Yvonne Bombard, St Michael's Hospital Toronto,
18:30–18:40	Genetic counselling for men's health	Justin Lorentz, Genetic Counsellor, Sunnybrook
18:40–19:10	Discussion	Emily Thain
19:10–19:30	Wrapup and next steps	Drs. Fleshner and Kim