CANCER EDUCATION DAY

Hereditary Cancer Risk in GU Oncology

Sarah Muir, MS, CGC

November 13, 2026

Presenter Disclosure

- Relationships with financial sponsors:
  - Grants/Research Support: N/A
  - Speakers Bureau/Honoraria: N/A
  - Consulting Fees: N/A
  - Patents: N/A
  - Advisory Boards: N/A

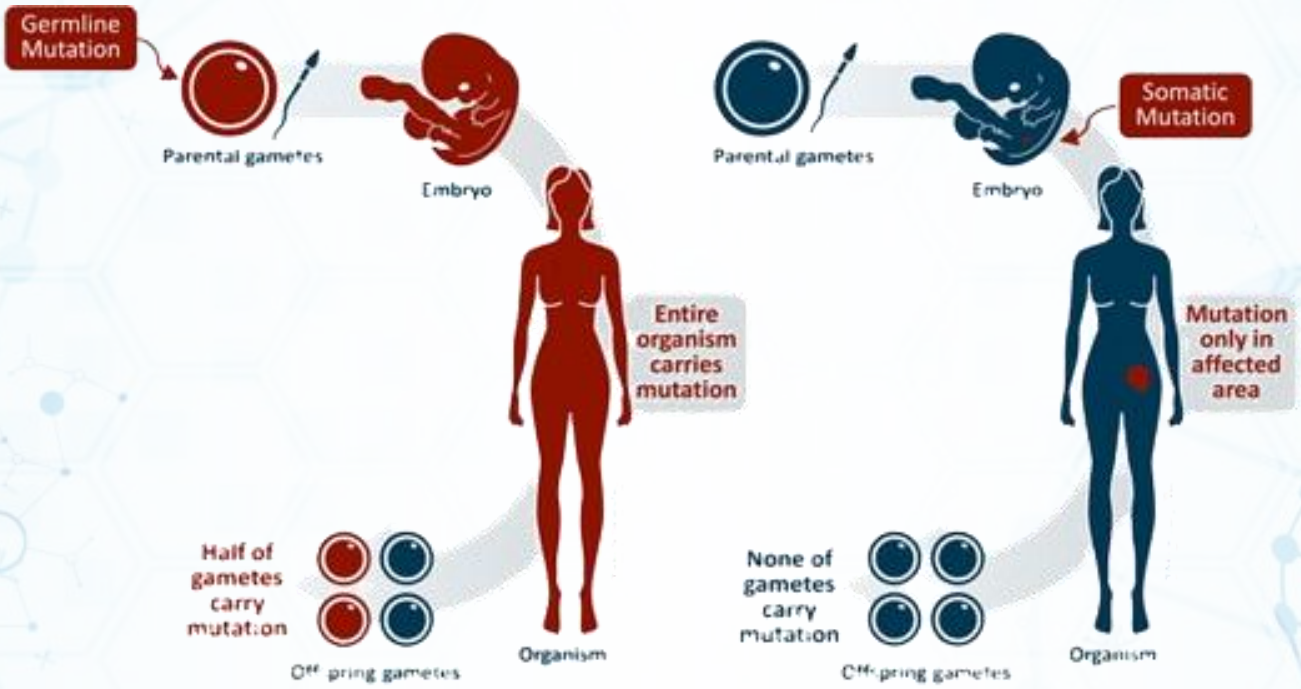
- Artificial Intelligence (AI) Disclosure:
  - AI was used to generate images (slide 11, 13)

Objectives

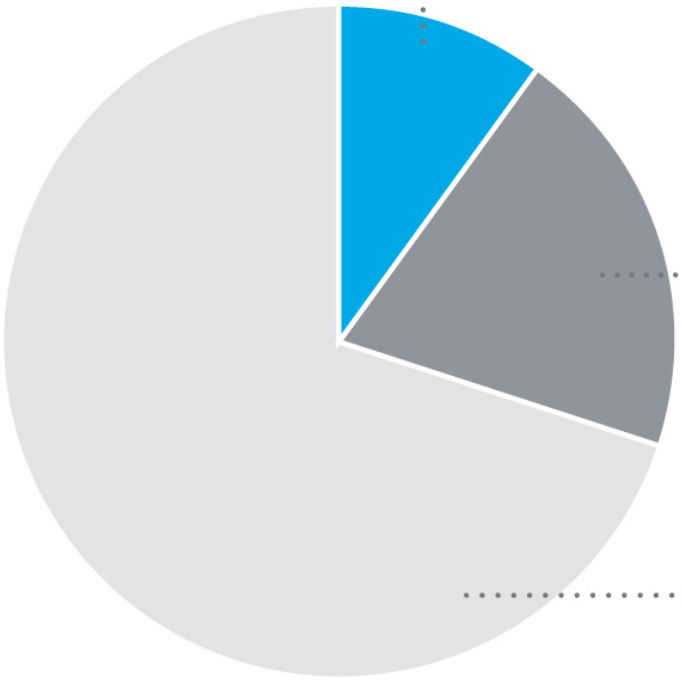
1. Review main concepts of hereditary cancer
2. Present hereditary syndromes/genes relating to genitourinary cancers
3. Share OH genetic testing criteria
4. Introduce the ESC Regional Cancer Genetics Program and how to refer

Concepts in Hereditary Cancer

- All cancer is *genetic*, not all cancer is *hereditary*
  - Accumulation of DNA damage in cells
  - Somatic vs. germline testing



Concepts in Hereditary Cancer



HEREDITARY CANCER

A clustering of cancer in a family due to inherited gene changes (mutations), which can be passed from parent to child

FAMILIAL CANCER

A clustering of cancer in a family that may be due to genes and/or other shared factors, such as environment and lifestyle

SPORADIC CANCER

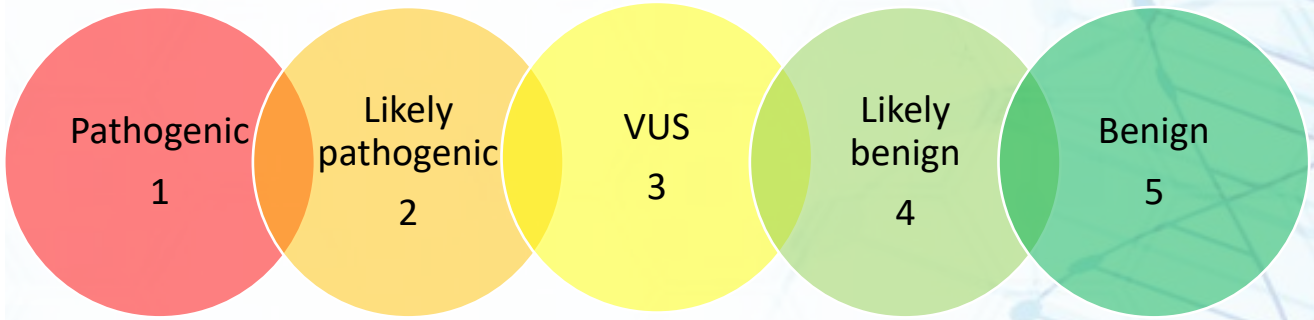
Happens by chance in one or two related family members, typically at older ages

Concepts in Hereditary Cancer

Hereditary cancer = *pathogenic/likely pathogenic* germline DNA variants

- Not all variants are BAD





Abbreviations:
VUS – Variant of Uncertain Significance

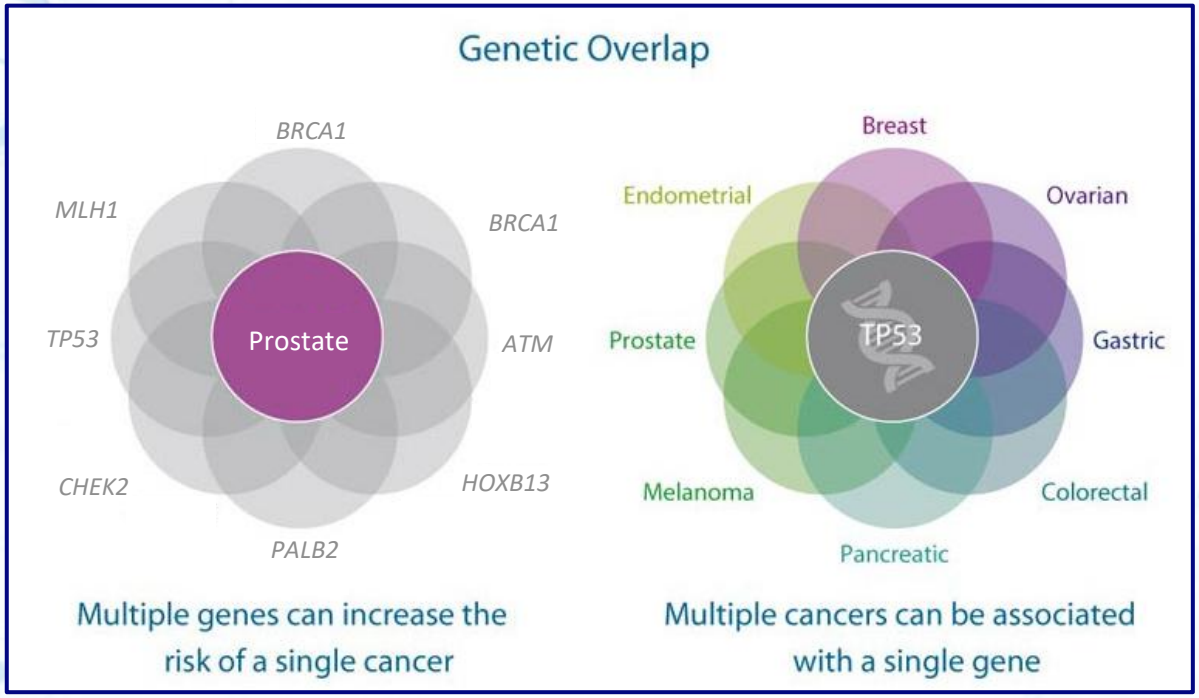
Common Hereditary GU Cancer Syndromes/Genes

When to think GENETICS!



- Genitourinary Cancers
  - Penile
  - Testicular
  - Prostate ✓
  - Renal Cell ✓
  - Urothelial ✓
    - Ureter/renal pelvis
    - Bladder

Hereditary Prostate Cancer



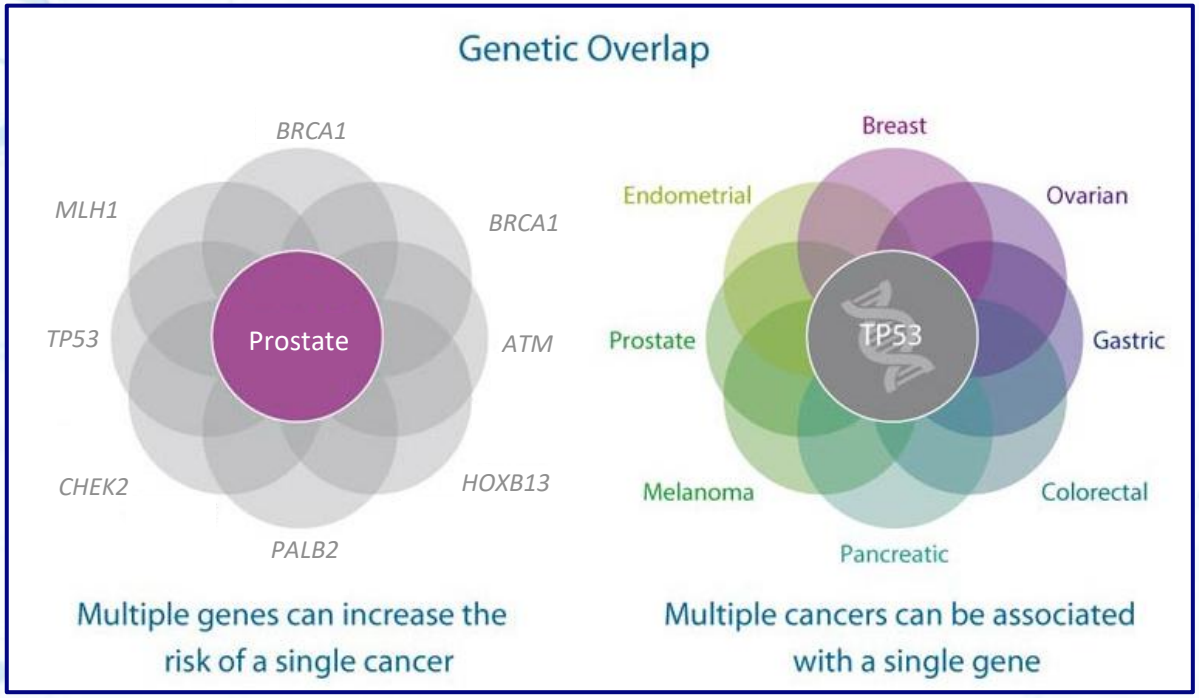
Genes

- *BRCA1*
- *BRCA2*
- *TP53*
- *HOXB13*
- *MSH2*
- *PALB2**
- *ATM**
- *CHEK2**

**emerging evidence*

NCCN Genetic/Familial High-Risk Assessment: Breast, Ovarian, Pancreatic, and Prostate V. 3.2026

Hereditary Prostate Cancer



Genes

- *BRCA1*
- *BRCA2*
- *TP53*
- *HOXB13*
- *MSH2*
- *PALB2**
- *ATM**
- *CHEK2**

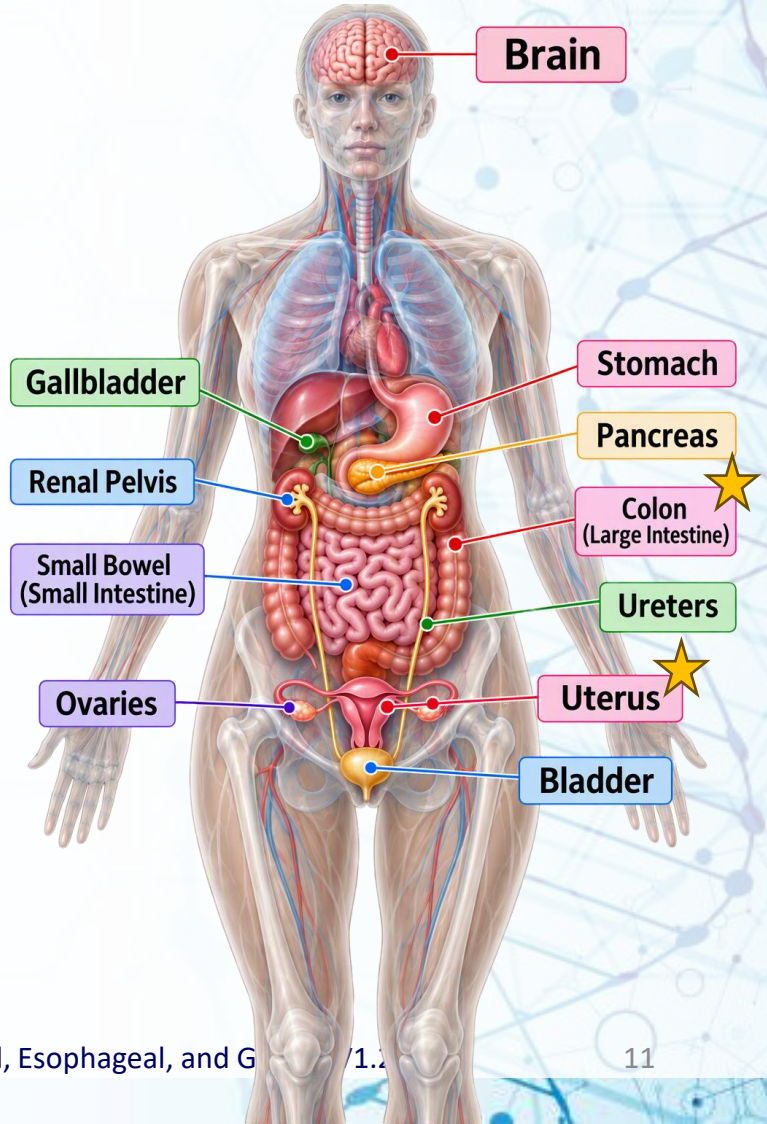
**emerging evidence*

NCCN Genetic/Familial High-Risk Assessment: Breast, Ovarian, Pancreatic, and Prostate V. 3.2026

Lynch Syndrome

formerly hereditary non-polyposis colorectal cancer (HNPCC) syndrome

- Affects >1 in 300
- Caused by pathogenic variants in genes involved with the DNA mismatch repair (MMR) pathway
  - ***MLH1, MSH2, MSH6, PMS2, EPCAM***
- Results in tumours that have high microsatellite instability (MSI)/loss of MMR protein expression via immunohistochemistry (IHC)
- GU Lynch syndrome-related cancers include:
  - Prostate
    - *MSH2* only, up to 24% risk
  - Ureter/renal pelvis
    - *MSH6, MSH2, MLH1* – up to 28% risk
  - Bladder
    - *MSH6, MSH2, MLH1* – up to 13% risk



Hereditary Renal Cell Cancer

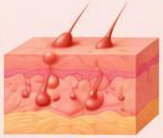


Hereditary Leiomyomatosis and Renal Cell Cancer (HLRCC) — FH



Renal features
- RCC (often aggressive)

Other key features
- Cutaneous leiomyomas
- Uterine leiomyomas



Skin (leiomyomas)



Uterus (leiomyomas)

von Hippel-Lindau disease (VHL) — VHL



Renal features
- Clear cell RCC

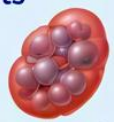
Other key features
- CNS hemangioblastomas
- Renal cysts
- Pancreatic cysts



CNS (hemangioblastomas)



Pancreas (cysts)



Renal cysts

Birt-Hogg-Dubé syndrome (BHD) — FLCN

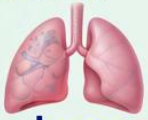


Renal features
- Several renal histologies

Other key features
- Cutaneous lesions
- Pulmonary cysts
- Pneumothorax



Skin (lesions)



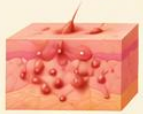
Lungs (cysts/pneumothorax)

Tuberous sclerosis complex (TSC) — TSC1 / TSC2



Renal features
- Renal angiomyolipoma and cysts
- Various renal tumour histologies

Other key features
- Cutaneous lesions
- Cortical dysplasia



Skin (lesions)



Brain (cortical dysplasia)



Heart (rhabdomyomas)



Lungs (lymphangioleiomyomatosis)

BAP1 tumour predisposition syndrome — BAP1



Renal features
- Clear cell RCC

Other key features
- Melanoma
- Mesothelioma



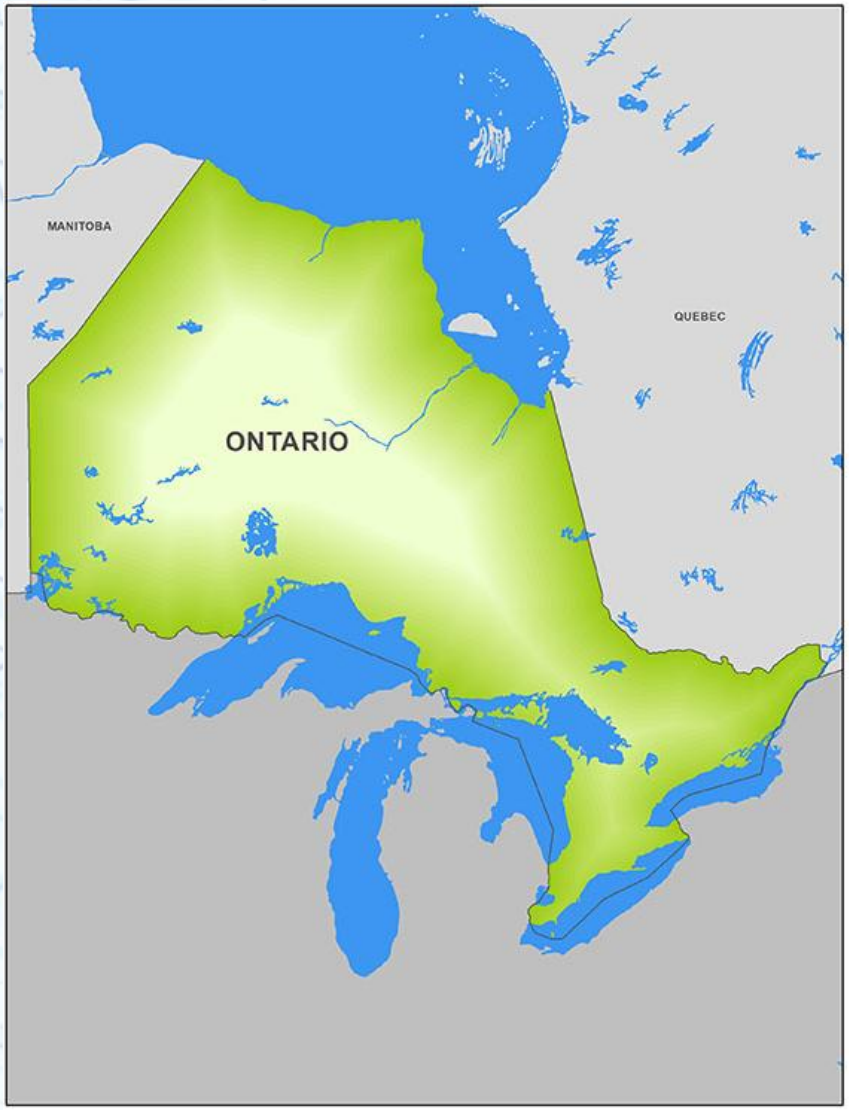
Skin (melanoma)



Pleura (mesothelioma)

NCCN Guidelines Kidney Cancer V1.2026; GeneReviews

Hereditary Cancer Testing (HCT) in Ontario



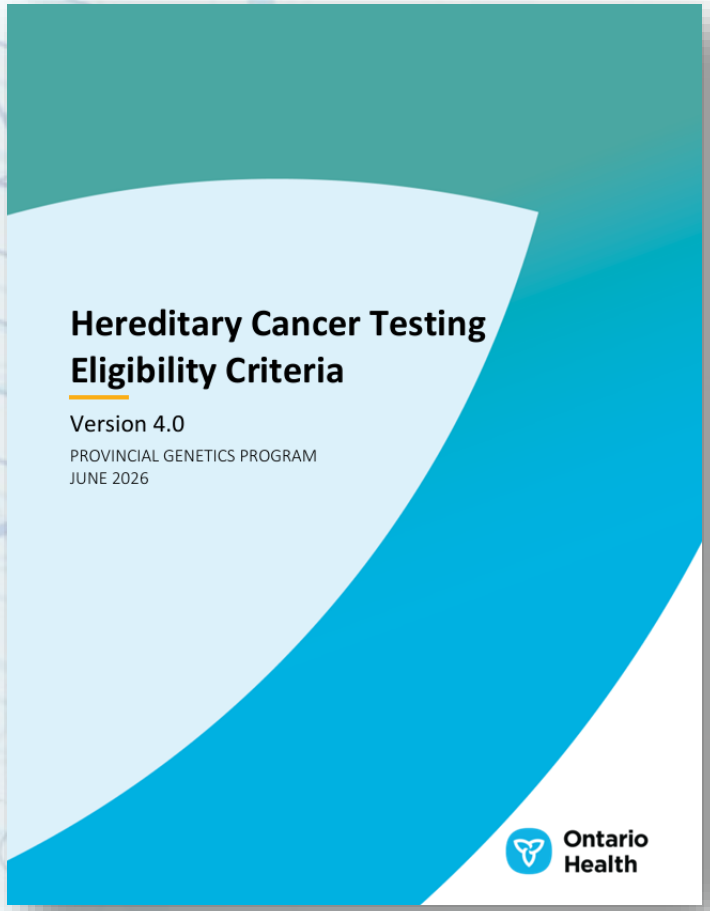
Versions 1-3 of the HCT criteria and gene lists were published in 2021/22. This work was led by the Pathology & Laboratory Medicine Program (PLMP) at Ontario Health.

In 2024, the Provincial Genetics Program (PGP) formed the Hereditary Cancer Expert Group which now advises on hereditary cancer genetic testing and clinical genetics services for all ages.

The HCT Expert Group includes 24 individuals from:

- Medical Genetics
- Laboratory Genetics and Pathology
- Genetic Counselling
- Oncology

Hereditary Cancer Testing (HCT) in Ontario



- Reviewed entire document for **clarity and standardization**
- Comprehensive **gene evidence review** resulted in both additions and removals of genes for various indications
- Move towards using **standard larger multigene panels** for associated and/or common cancers
- Move towards **more inclusive age thresholds** in line with other leading organizations (ASCO, NCCN, ESMO, NHS)
- Included pediatric perspectives in our criteria plus **pediatric specific indications**

Hereditary Cancer Testing (HCT) in Ontario



Criteria for Hereditary Prostate Cancer

Personal history of:

- Prostate cancer diagnosed ≤50 years of age
- Metastatic prostate cancer
- High risk, locally advanced, prostate cancer, confirmed with evidence of ≥1 of the following features:
  - T3(or higher) staging
  - Grade Group 4 or 5 (Gleason Score 8 to 10)
  - Lymph node involvement
  - PSA ≥20

→ option of Mainstreaming with **Hereditary Cancer Core Panel** OR referring to Genetics Program

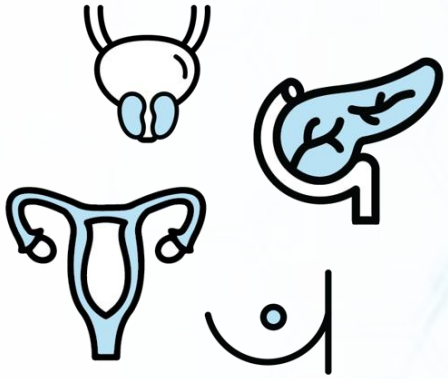
Hereditary Cancer Testing (HCT) in Ontario



Criteria for Hereditary Prostate Cancer

Additional eligibility for personal history prostate cancer + family history, including:

- Breast cancer
- Ovarian cancer
- Prostate cancer
- Biliary tract cancer
- Pancreatic cancer



→ refer to Genetics Program for assessment

Hereditary Cancer Testing (HCT) in Ontario

A standard 40-gene **Hereditary Cancer Core Panel** will now be recommended for the disease sites listed rather than specific sub-panels.

Breast	Gastrointestinal	Gastric
Ovary	Endometrial	Polyposis
Prostate	Biliary Tract	Pancreas

- Standardize testing across sites
- Recognize overlapping family and personal histories for GI and HBOP indications
- Optimize mainstreaming with simplified panel selection
- Balance clinic workload and variant curation workload in laboratories
- Align with guidance from other sources/jurisdictions (e.g., ASCO, NCCN, BC, etc.)

Hereditary Cancer Testing (HCT) in Ontario



Criteria for Hereditary Renal Tumour Syndromes

Personal history of a renal tumour with of ≥1 of the following features:

- Bilateral/multifocal disease
- Diagnosis ≤45 years of age
- Non-clear cell pathology (papillary, chromophobe, oncocytic, hybrid tumours)
- Evidence of syndromic presentation (e.g., seizures, pneumothorax)
- Associated tumours (e.g., hemangioblastoma, leiomyomas, angiomyolipomas)

→ option of Mainstreaming with **Hereditary Renal Tumour Syndromes Panel**
OR referring to Genetics Program

Hereditary Cancer Testing (HCT) in Ontario



Criteria for Hereditary Renal Tumour Syndromes

Additional eligibility for:

- Personal history renal tumour + family history of renal tumour(s) or associated tumours (e.g., hemangioblastoma, leiomyomas, angiomyolipomas)
- Personal history nephroblastoma (Wilms tumour)

→ refer to Genetics Program for assessment

Erie St. Clair Regional Cancer Genetics Program



Erie St. Clair Regional Cancer Genetics Program

- Referrals from community providers, primary care, oncology, specialists
- Cancer genetic risk assessments, assessments for the High Risk OBSP, germline genetic testing, management recommendations based on gene/family history, cascade testing
- Primarily offer phone appointments

NEW Appointment Wait Times

- Routine (unaffected): ≤ 180 calendar days
- Semi-Urgent: ≤ 90 calendar days → e.g. recent cancer diagnosis, known variant in the family
- Urgent: ≤ 30 calendar days → e.g. mainstreaming, concern for longevity, upcoming treatment



Dr. Victoria Mok Siu
Medical Geneticist



Sarah Muir
Genetic Counsellor



Shelby Wright
Genetic Counsellor



Elana Wishnefsky
Genetic Counsellor



Shannon MacKinnon
Genetics Program Assistant

How to Refer

- E-referrals placed through Cerner via “Referral to Cancer Genetics”
- Fax a referral form

WINDSOR REGIONAL HOSPITAL
OUTSTANDING CARE – NO EXCEPTIONS!

Cancer Genetics Program
2220 Kildare Road
Windsor, ON N8W 2X3
Phone: 519-254-5577 ext. 58620

Erie St. Clair Regional Cancer Program
Ontario Health (Cancer Care Ontario)

Cancer Genetics Referral Form

FAX: 519-255-8688

Referral date (DD/MM/YYYY): _____ □ Female □ Male □ Other: _____

Patient name: _____

DOB (DD/MM/YYYY): _____ Health Card #: _____

Address: _____ City: _____ Postal Code: _____

Tel (preferred): _____ Email: _____

Tel (alt): _____ Ashkenazi Jewish ancestry? □ Yes □ No

Interpreter req'd: □ No □ Yes, specify language: _____

Does your patient have a PERSONAL history of cancer? ****If YES, please send all relevant cancer pathology reports with referral****

□ NO □ YES, type(s): _____ age(s) diagnosed: _____

Does your patient need to be seen URGENTLY? (i.e. for upcoming surgical decision-making or treatment options)**?**

□ NO □ YES, reason for urgency & date of medical intervention: _____

Has your patient HAD GENETIC TESTING (incl. germline & tumour testing)**?** ****If YES, please send copies of all results with referral****

□ NO □ YES, result: _____

Please check reason(s) for referral:

□ Personal history suggestive of hereditary cancer syndrome (*see OH's Referral Guidance for Hereditary Cancer Genetic Assessment*)

Please specify: _____

_____

_____

□ Family history suggestive of hereditary cancer syndrome (*see page 2 for outline of current genetic testing criteria*)

Please specify family history including types of cancer, ages of diagnosis, and relationships to patient: _____

_____

_____

_____

_____

_____

□ Family member with a known hereditary cancer gene mutation (i.e. *BRCA1, BRCA2, MLH1, MSH2, MSH6, PMS2, TP53*)

Gene: _____

Relative's full name & DOB: _____

Relative's biological relationship to patient (e.g. maternal aunt): _____

Genetics clinic where relative seen: _____

Referring physician: _____ Billing number: _____

Address: _____

Tel: _____ Fax: _____

July 2026

Questions?

Erie St. Clair Regional Cancer Genetics Program

genetics.program@wrh.on.ca

519-254-5577 x58620