Hereditary Cancer Risk Assessment: informing cancer screening, prevention and treatment

Mary McCullum, RN, MSN, CON(C)

Nurse Educator, Hereditary Cancer Program

BC Cancer

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Faculty/Presenter Disclosure

I have nothing to disclose

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Objectives

1. Review Hereditary Cancer Program (HCP) referral indications and process

2. Discuss some implications of current approaches to hereditary cancer genetic testing

3. Identify hereditary cancer resources for practice

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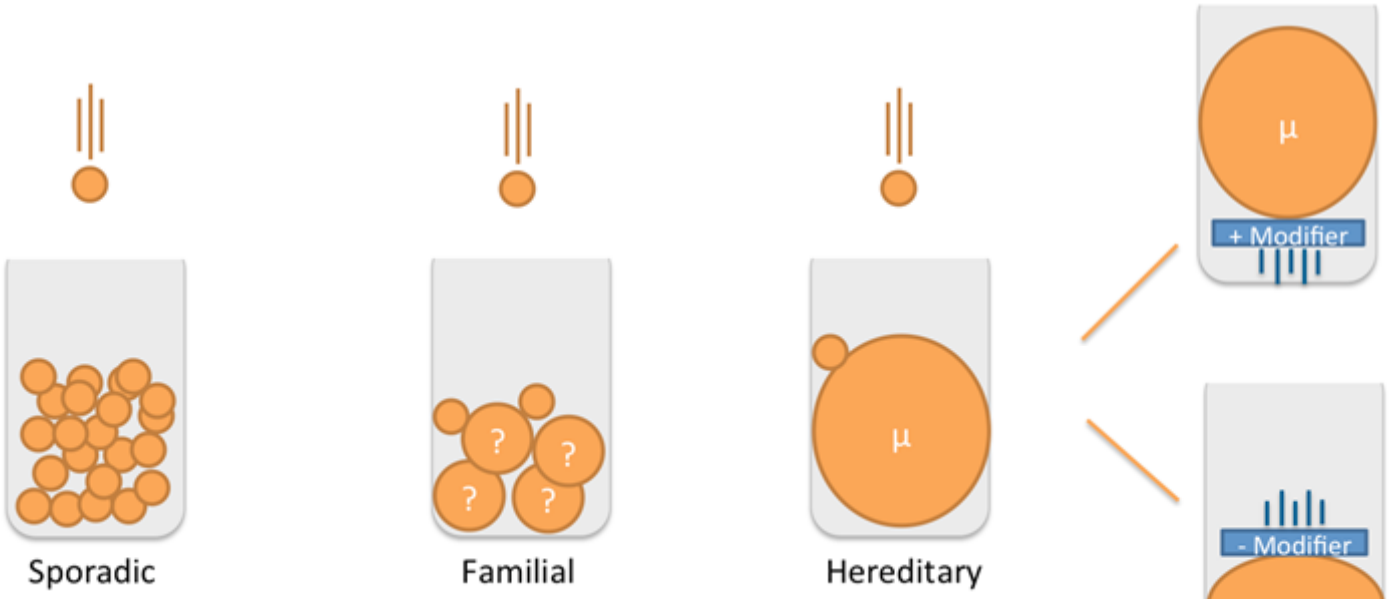

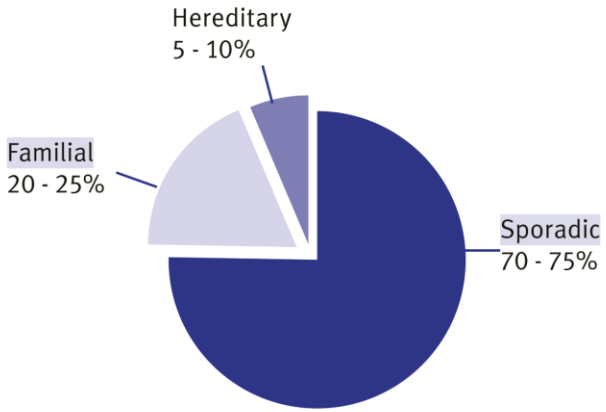

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When to consider hereditary cancer?

Family history may include:

- Same cancer, 2 or more close relatives (same side of family)
- Multiple generations affected
- Earlier than “usual” age at diagnosis
- Multiple primary tumours
- Rare cancers
- Tumours consistent with specific syndrome (e.g. colorectal and endometrial; breast and ovarian; polyposis)

Personal history:

- Pathology features (e.g. polyps)
- See specific syndromes

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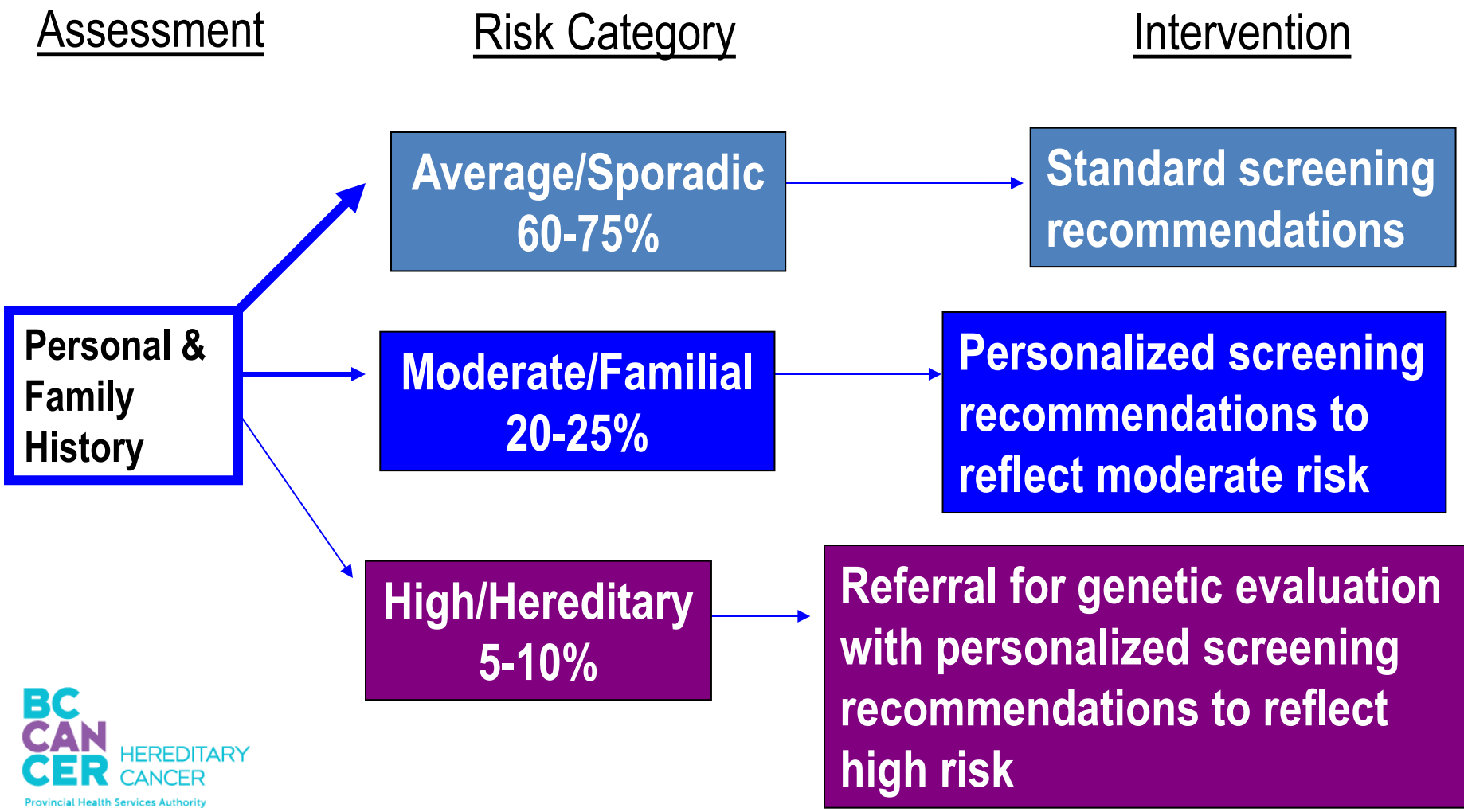
Risk stratification: Who needs what?



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Refer to HCP based on:

- Personal history
- Family history
  - Carrier testing (known hereditary cancer gene mutation)
- Re-assessment

Referrals from:

- Surgeons
- Gastroenterologists
- Oncologists
- Other Specialists
- Family physicians
- Nurse Practitioners
- Patients

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Personal Hx: Polyposis

Referral for polyposis assessment should be considered for any person with:

- 10 or more **adenomatous polyp**s, OR
- 2 or more **hamartomatous polyp**s, OR
- 5 or more **serrated polyps** (hyperplastic polyps, sessile serrated adenomas/polyps, traditional serrated adenomas) proximal to the sigmoid colon OR
- multiple polyps of different types (adenomatous, hamartomatous, serrated, hyperplastic)

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Case example – referral?

Colonoscopy #1 (age 55)

- Sessile serrated polyp x 1
- Tubulovillous adenoma x 1

Colonoscopy #2 (age 60)

- Tubular adenoma x 7
- Sessile serrated adenoma x 1

Colonoscopy #3 (age 61)

- Tubular adenoma x 2
- Sessile serrated adenoma x 1

Lynch Syndrome (formerly known as HNPCC)

Personal history:

- Colorectal cancer ≤ age 40
- Lynch syndrome cancer that is MMR-deficient (IHC/MSI-H report) - any age
- Colorectal cancer ≤ age 50 and adopted, with NO family hx available
- 2 Lynch syndrome cancers with at least 1 dx ≤ age 50

Family history:

- Confirmed *MLH1, MSH2, MSH6, PMS2, EPCAM* pathogenic variant
- Close relative with personal history as above
- 2 FDR with a Lynch syndrome cancer, both dx ≤ age 50
- 3 Lynch syndrome cancers, with at least 1 dx ≤ age 50

Lynch syndrome cancers: colorectal, endometrial, ovarian, gastric, small bowel, hepatobiliary, pancreatic, kidney, ureter, brain; also sebaceous adenomas or colorectal adenomas ≤ age 40

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Refer based on family history

1 or more close relatives with polyposis and /or

families with hereditary cancer are more likely to have:

- several people with the same type(s) of cancer
- more than 1 generation of relatives with cancer dx
- cancer at earlier ages than is common for that type of cancer (e.g. colon cancer ≤ age 50)
- people with more than 1 cancer diagnosis
- people with less common cancers

****each side of the family is assessed separately for hereditary cancer risk****

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Refer for carrier testing

information provided by a relative about a hereditary cancer gene mutation:

- "dear family" letter
- genetic testing report
- family member name/reference number

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Refer for re-assessment

Reasons may include:

- new cancer or polyps: patient or close relative
- new genetic test results in a family member
- request for updated information about:
    - new options for genetic testing
    - whether a VUS has been re-classified
    - cancer screening and risk-reduction
    - available support services

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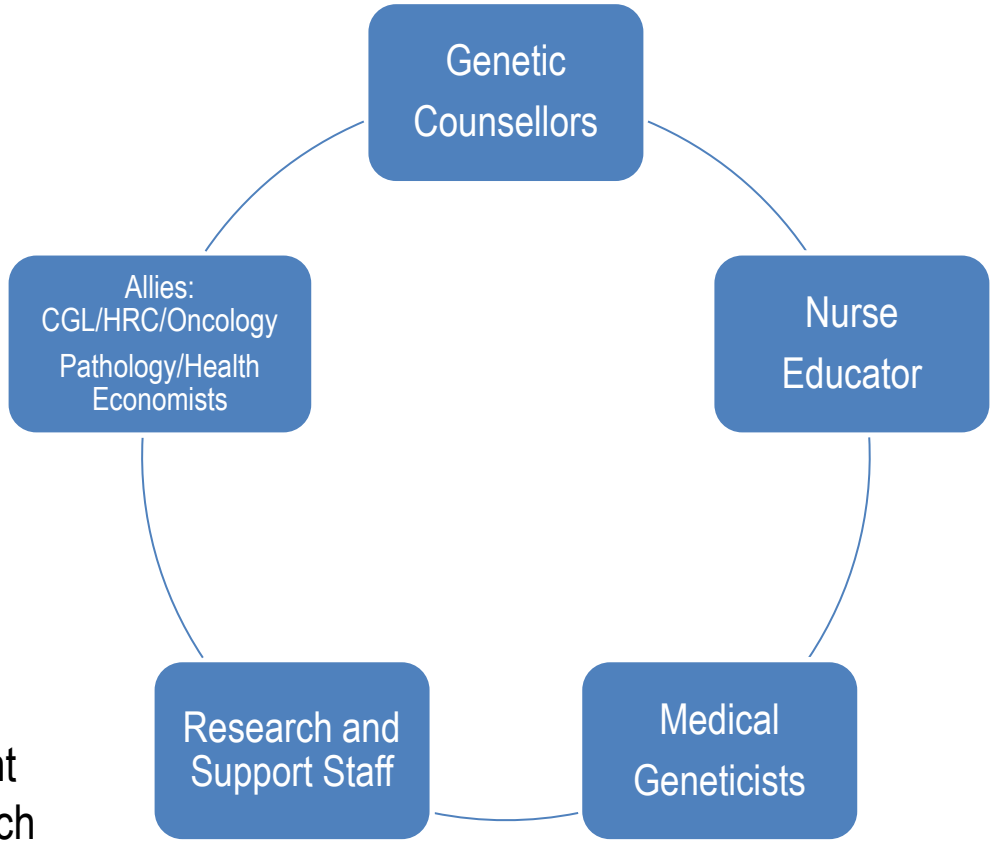
Hereditary Cancer Program

Co-Medical Directors: Dr. Intan Schrader & Dr. Sophie Sun



Provide:

- Genetic counselling
- Genetic testing
- Clinical management
- Evaluation & research
- Education

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Reduce the morbidity and mortality from hereditary cancer syndromes

Find people with hereditary cancer syndromes

Provide risk management advice

Help with cancer treatment decisions

Identify resources and supports

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Provincial Clinical Service

Permanent Clinics
- Vancouver
- Abbotsford
- Victoria (Feb 2018)

Outreach Clinics
- Surrey

Videoconference/Telehealth
- most BC/Yukon communities

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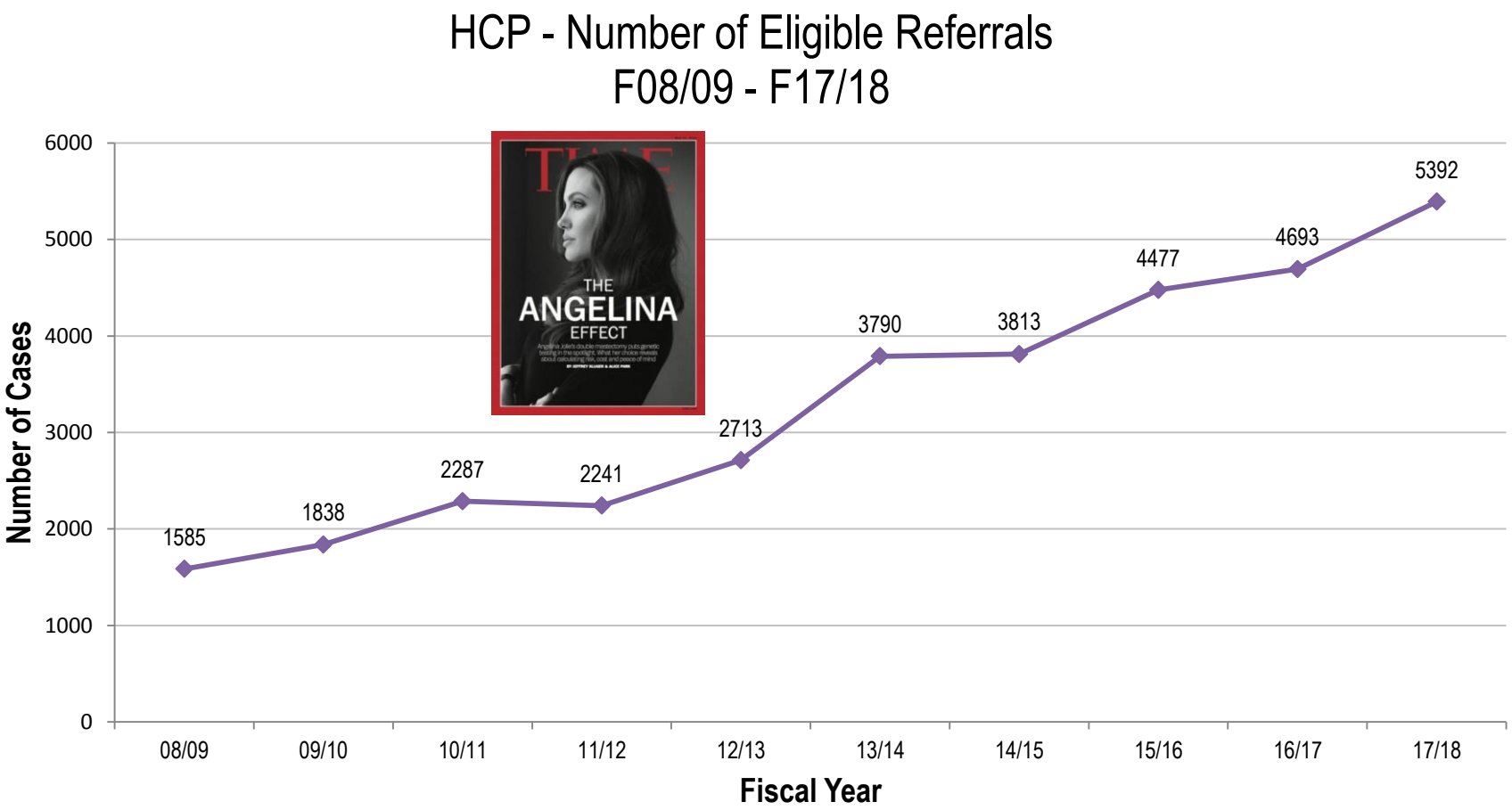
Referrals



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Referral Process

- Referral form/Criteria
- Medical records to provide
  - Pathology reports
  - Operative reports
  - Consult letters
- Waiting lists
- What to expect
  - patient
  - provider

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www.bccancer.bc.ca/health-professionals/clinical-resources/hereditary-cancer

Hereditary Cancer

The Hereditary Cancer Program (HCP) provides genetic counselling and genetic testing for BC/Yukon residents who may have inherited an increased risk for specific types of cancer. Similar services are available across Canada and in other countries.

This section provides direction about HCP referrals, information and resources for health professionals to use when discussing hereditary cancer assessment with your patients/families.

Referral | Syndromes | Resources

People are encouraged to review their personal and/or family history with a health care provider to clarify whether HCP referral is indicated.

How to refer

To refer a patient, print the current HCP Referral form, complete all sections and fax it to the appropriate HCP office.

HCP referrals are accepted for BC/Yukon residents with:

Download the Hereditary Cancer Program Referral form >

Download the Urgent DNA Storage Requisition >

Contact the Hereditary Cancer Program

Vancouver
Phone: 604-877-6000 local 672198
Fax: 604-707-5931

Abbotsford
Phone: 604-851-4710 local 645236
Fax: 604-851-4720

Send an email to HCP.

Cancer Genetic Counselling Session

- Personal medical history
- Review of family history
- Education
  - ✓ Review of genes & inheritance
  - ✓ Discussion of sporadic, familial, hereditary cancer
- Empiric risk and likelihood of specific cancer syndrome
  - ✓ Associated cancer probabilities
  - ✓ Strategies for cancer screening & risk reduction
- Genetic testing
  - ✓ Eligibility, potential harms & benefits, limitations
  - ✓ Results
- Psychosocial issues, resources
- Communication with family members
- Documentation to referring provider and patient

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Genetic Non-Discrimination Act

- Canadian federal legislation passed May 2017
- Illegal to require disclosure of genetic test results or uptake of genetic testing as condition of a contract
- Protections added to:
  - Canadian Human Rights Act
  - Canada Federal Labour Code

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Germline Genetic Testing

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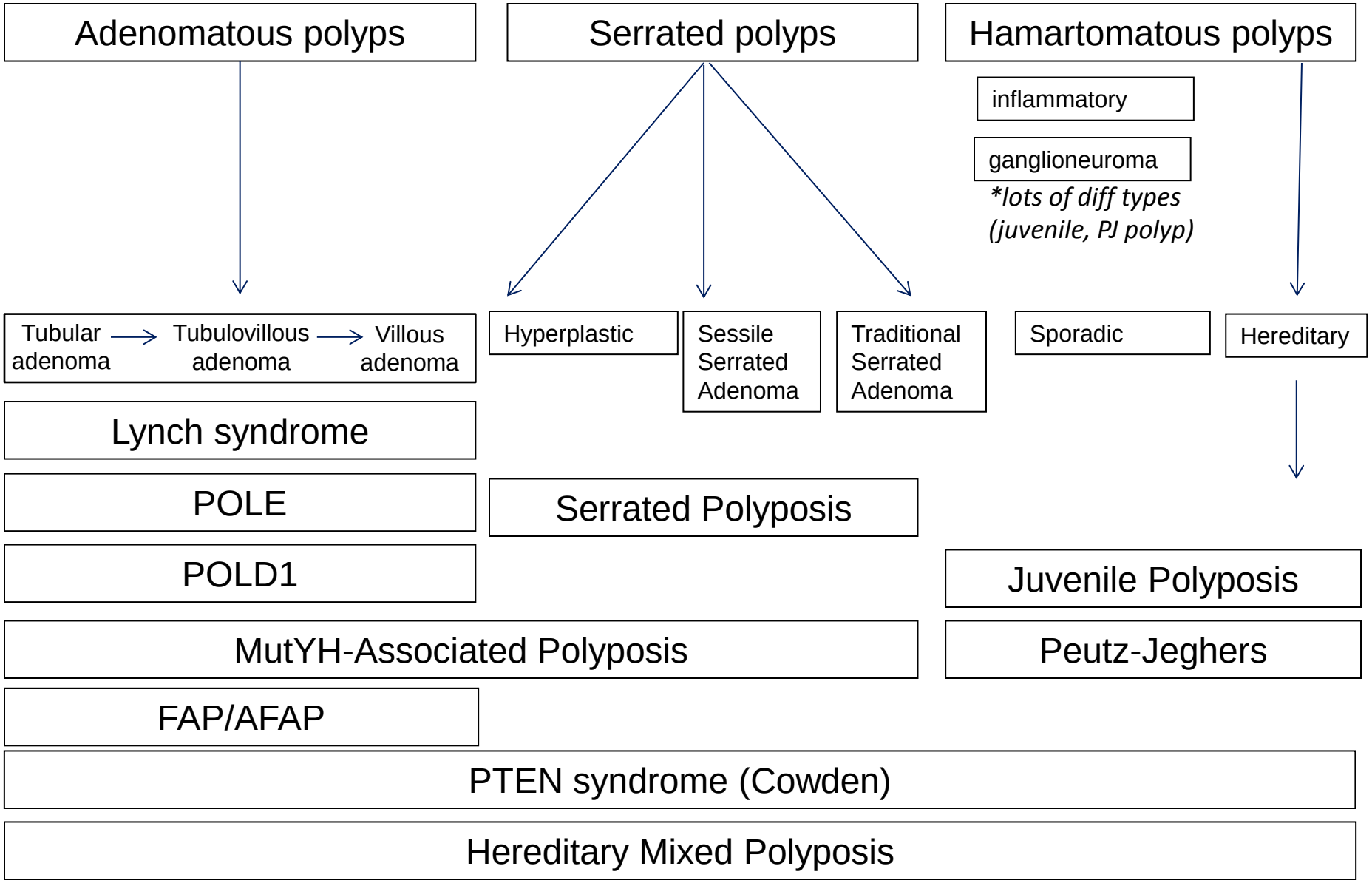
Index test:

- 1st genetic test in family
- trying to identify a mutation in a specific gene
- usually affected individual (relevant diagnosis)
  - storing a blood sample prior to death may be important
- usually blood test; sometimes begin with tumour tissue

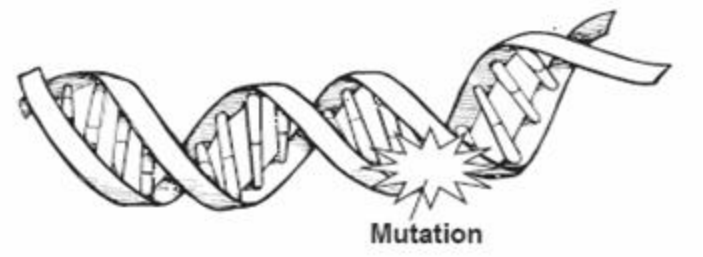
Carrier (cascade) test:

- for specific mutation confirmed in the family
- true positive/negative result to inform cancer risk management

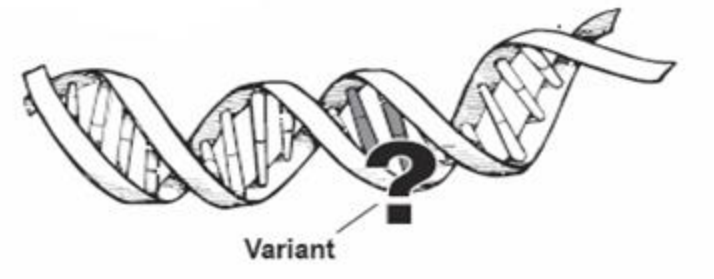
Hereditary Polyposis/Colorectal Cancer Syndromes



- Sporadic
- Familial
- Missed a mutation



- Confirms hereditary cancer syndrome
- Cascade carrier testing in family
- Recommendations for cancer risk management
- Treatment



- Sporadic
- Familial
- Missed a mutation
- VUS is a mutation

- Sporadic
- Familial
- Missed a mutation

APC

- BMPR1A
- CDH1
- CHEK2
- EPCAM
- MLH1
- MSH2
- MSH6
- MUTYH
- PMS2
- POLD1
- POLE
- PTEN
- SMAD4
- STK11

- ATM
- AXIN1
- BARD1
- BRCA1
- BRCA2
- BRIP1
- CDK4
- CDKN2A
- FANCC
- NBN
- PALB2
- RAD51C
- RAD51D
- SCG5/GREM1
- TP53
- VHL
- XRCC2

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Multi Gene Panels

Benefits

- Increased mutation detection rate (comprehensive test)
- Cost-effective
- Less testing fatigue
- Incidental findings

Drawbacks

- Information overload
- Uncertainty if poorly understood genes are analyzed
- VUS rate
- Incidental findings

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Traditional approach to hereditary cancer risk assessment

- Referral to cancer genetics clinic
  - Eligibility criteria, review of medical records
- Genetic counselling (GC) appointment #1
- Blood (saliva) test with appropriate consent
- GC appointment #2 for results disclosure
  - Implications for cancer risk management
  - Implications for family members
- Consult letter(s) to referring physician/patient

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Alternate models of service delivery

- Abbreviated pre/post test genetic counselling
- Only post test genetic counselling
- Group genetic counselling
- Collaborative approach between GC and other health care providers
- Public health approach

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Take Home Messages

- Referral may be indicated for: personal history, family history, carrier testing, re-assessment
- Genetic Non-Discrimination Act (2017)
- New options for genetic testing bring additional complexity
- New models of service delivery
- Resources available for patients and providers

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Selected Resources

www.bccancer.bc.ca/health-professionals/clinical-resources/hereditary-cancer#Syndromes

- HCP fact sheets on Lynch syndrome, polyposis, and other hereditary cancer syndromes

www.bccancer.bc.ca/health-professionals/networks/family-practice-oncology-network/journal-of-family-practice-oncology

- see Spring 2018 issue, page 12 for “Lynch syndrome – improving cancer prevention for the next generation”

www.nccn.org/professionals/physician_gls/f_guidelines.asp#detection

- National Comprehensive Cancer Network (USA) - guidelines

www.ncbi.nlm.nih.gov/books/NBK1116/

- Gene Reviews – comprehensive overview of specific syndromes

Mary McCullum, Nurse Educator, Hereditary Cancer Program
604-877-6000, local 672325
mmccullum@bccancer.bc.ca

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