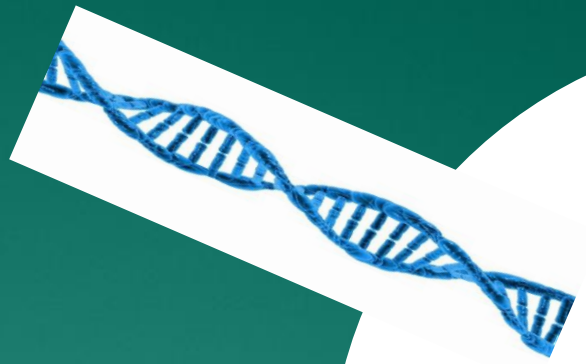
Inherited Cancer Predisposition



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Disclaimer

- No conflicts of interest
- Not a clinical geneticist

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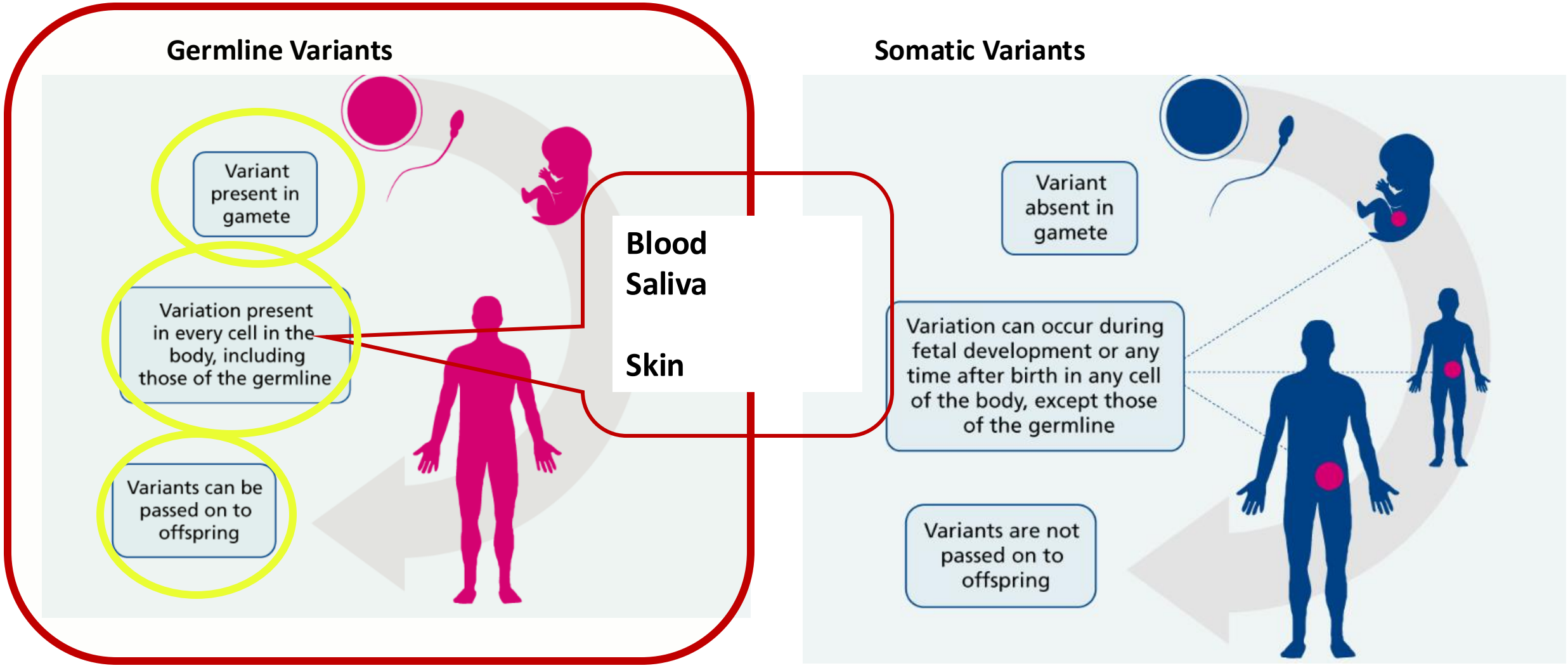
Inherited (Germline) v Acquired (Somatic) Variants



Images Courtesy of Genomics Education NHS

Terminology

- Inherited = Germline = Constitutional
- Mutation = Variant = Alteration
- Pathogenic Variant
- Likely Pathogenic Variant
- Variant of Uncertain Significance

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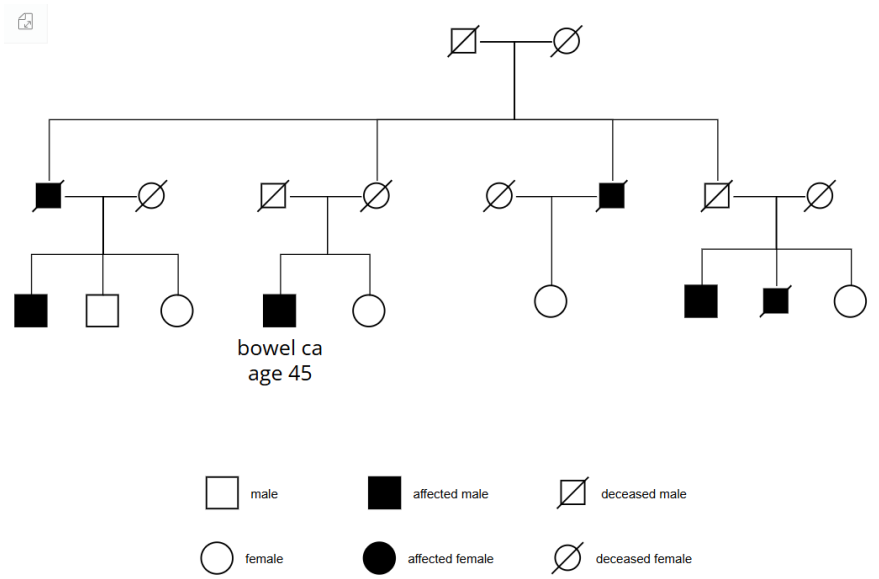
Features of ‘inherited’ cancer

- Multiple primary cancers in one individual
- Multiple cancers (same/related) in close family members
- Diagnosis of cancer at young age
- Bilateral or multiple rare cancers

- Histological features e.g.
  - High grade serous ovarian cancer
  - Endometrioid/ clear cell ovarian cancer



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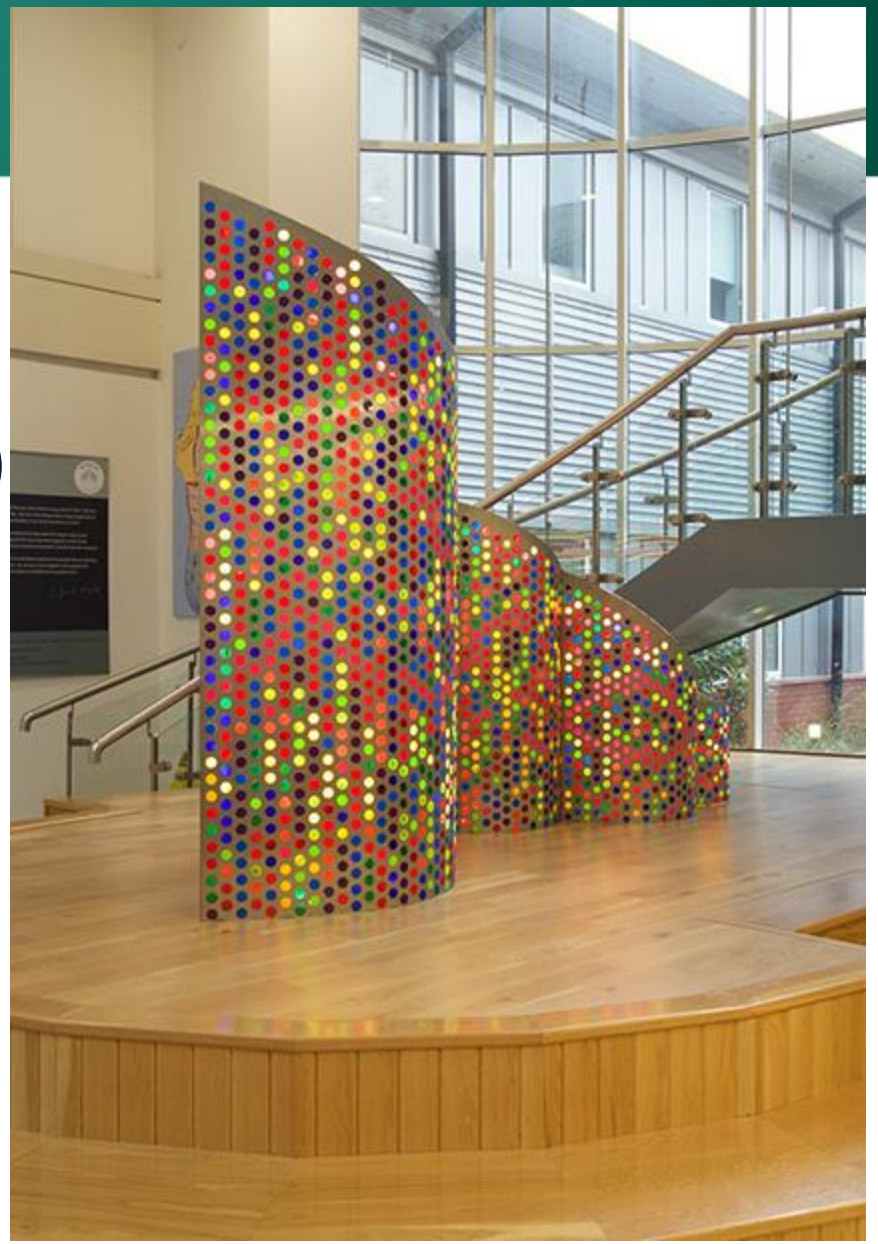
BRCA

- BRCA 1, BRCA 2
  (Hereditary Breast & Ovarian Cancer Syndrome)

- Breast cancer risk (60-80%)
- Ovarian cancer risk (10-50%)

- Also: prostate, pancreatic cancer risk
  with BRCA 2



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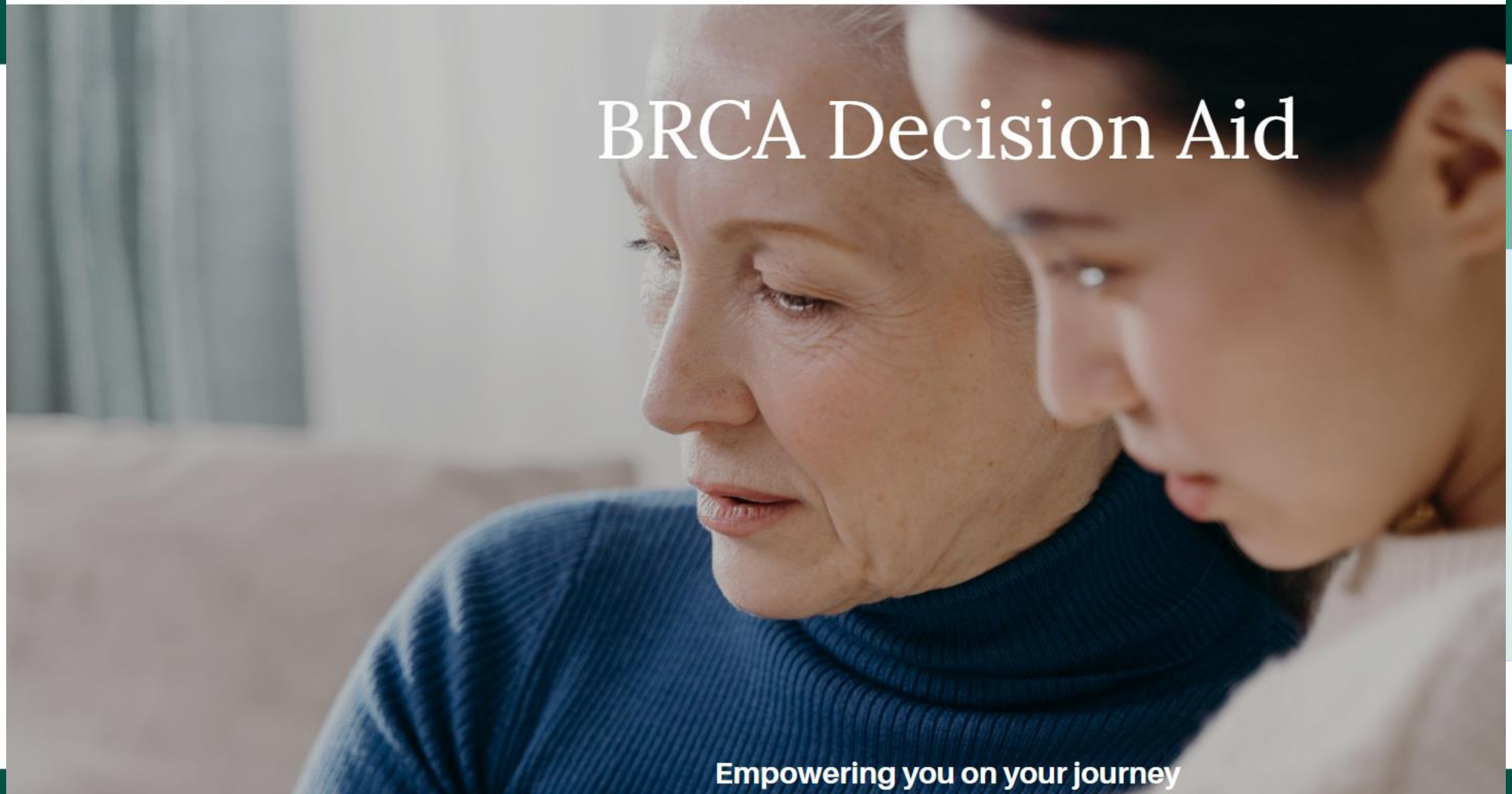
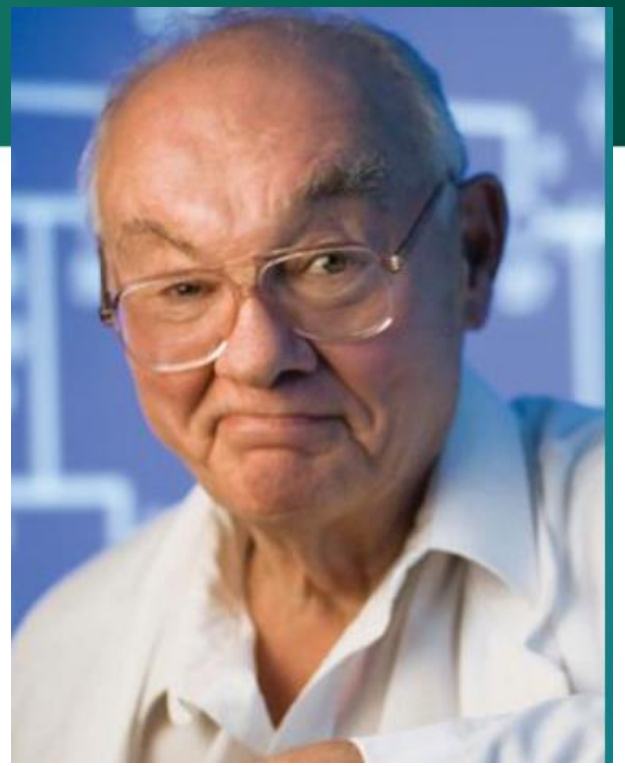

BRCA Decision Aid
Empowering you on your journey

Lynch Syndrome



- ‘Hereditary NonPolyposis Colorectal Cancer HNPCC’
- Mismatch repair genes: MLH1, MSH2, MSH6 or PMS2 (or EPCAM affecting MSH2)

40-80% risk of cancers such as

- bowel cancer (2-3% are lynch related)
- endometrial cancer
- ovarian cancer
- Also – upper GI, pancreatic, urinary tract, depending on gene affected

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Prospective Lynch syndrome database (PLSD) – www.plsd.eu

Calculation of cumulative risk for cancer in selected organ(s)
irrespective of cancer(s) in any other organ

Select organ, variant, current age, and sex below.

Organ

Colon/sigmoid/rectum

Genetic variant

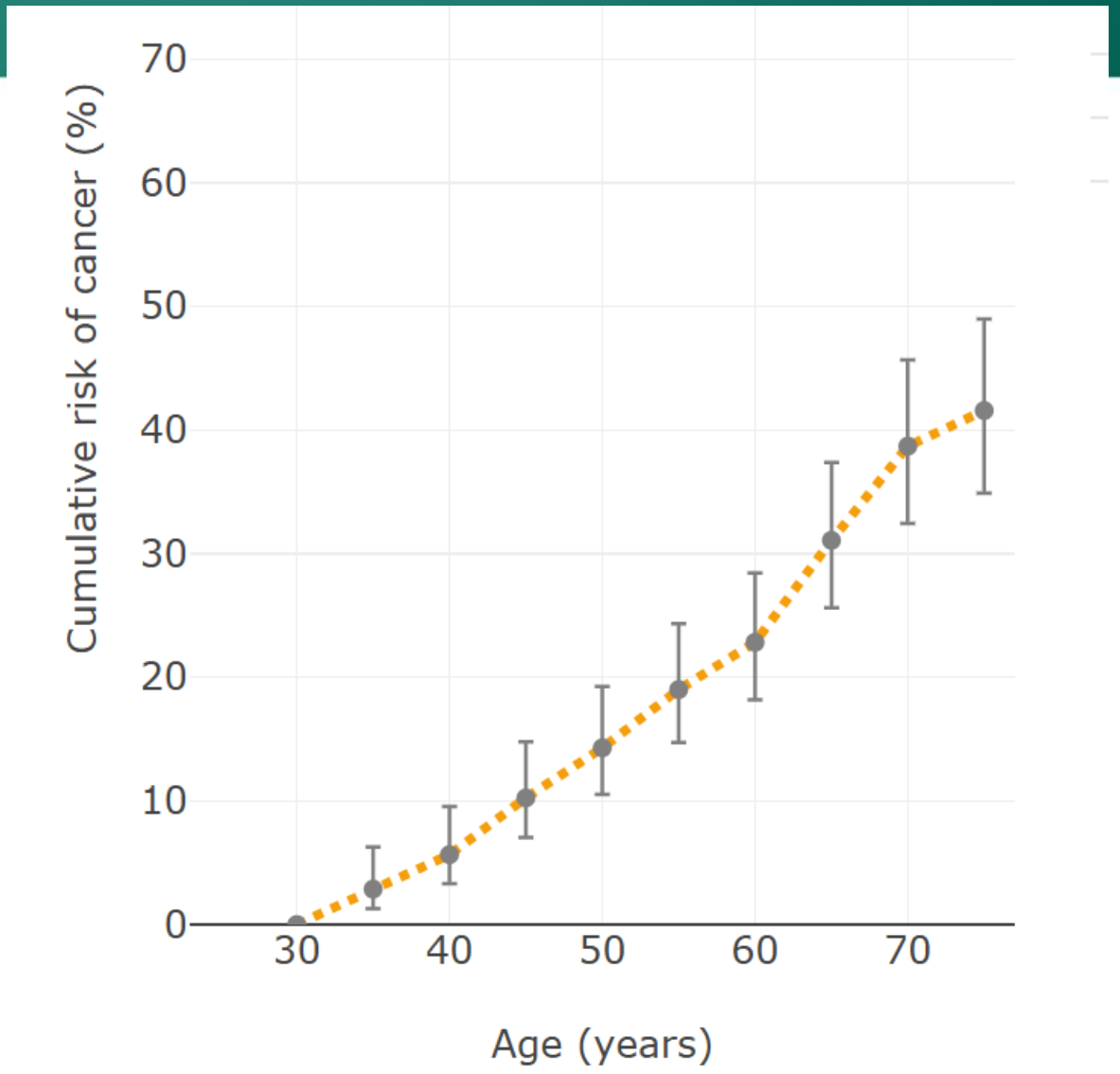
path_MLH1	*path_MSH2*
path_MSH6	*path_PMS2*

Current Age

25 30 35 40 45 50 55 60 65 70

Sex

Female Male



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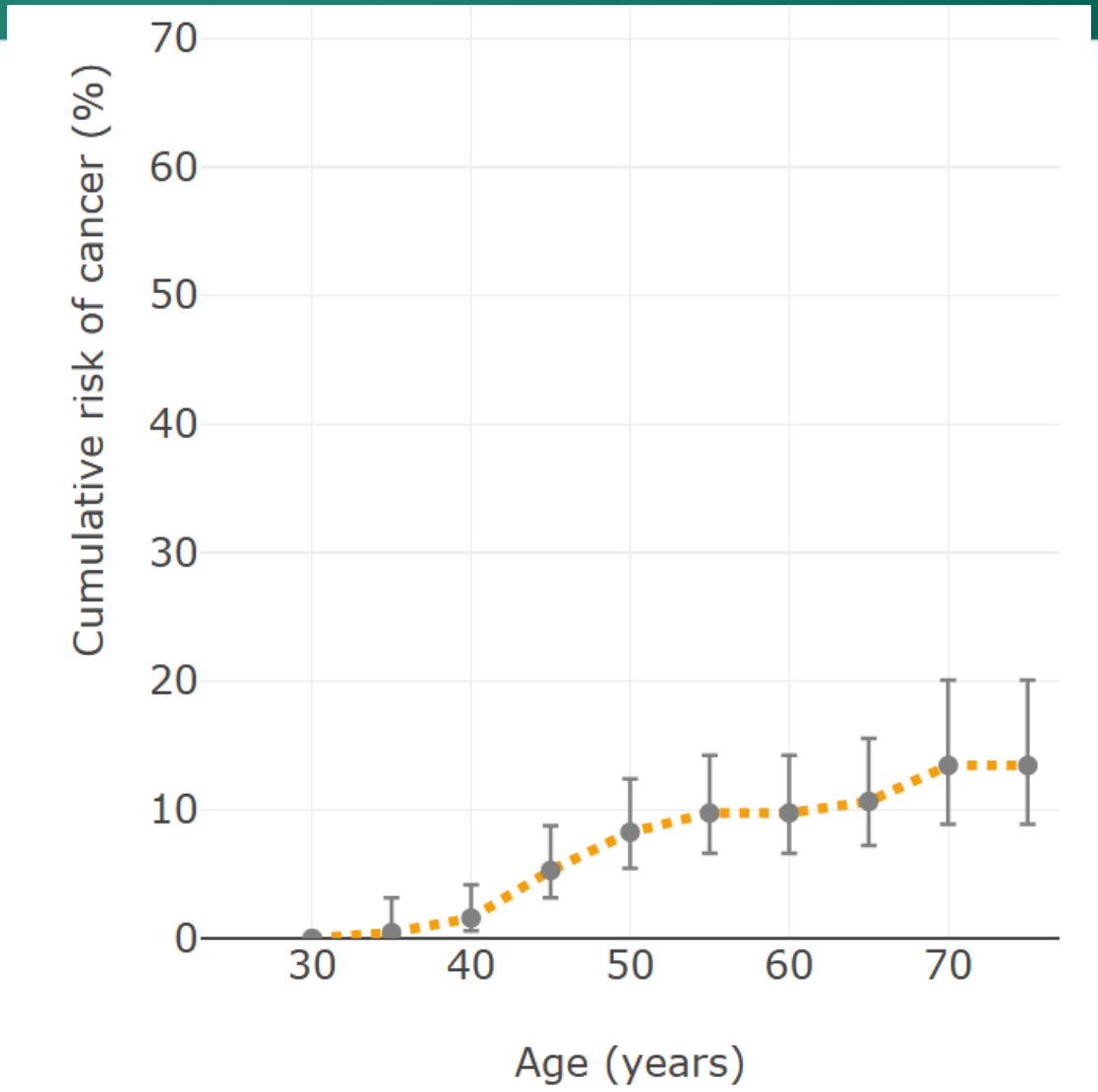
Female Male



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Management of Lynch Syndrome

Surveillance	Chemoprevention	Surgery
• Colonoscopy every 2 yrs • From age 25/35	• Aspirin 2+years • H Pylori eradication • Research: LynchVax	• Bilateral salpingo oophorectomy and total hysterectomy

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Informed by specific gene affected

If a cancer diagnosed

Choice of surgery – prophylactic surgery also?

Predicted response to Systemic Anti Cancer Therapy – guide choice

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Broader Implications

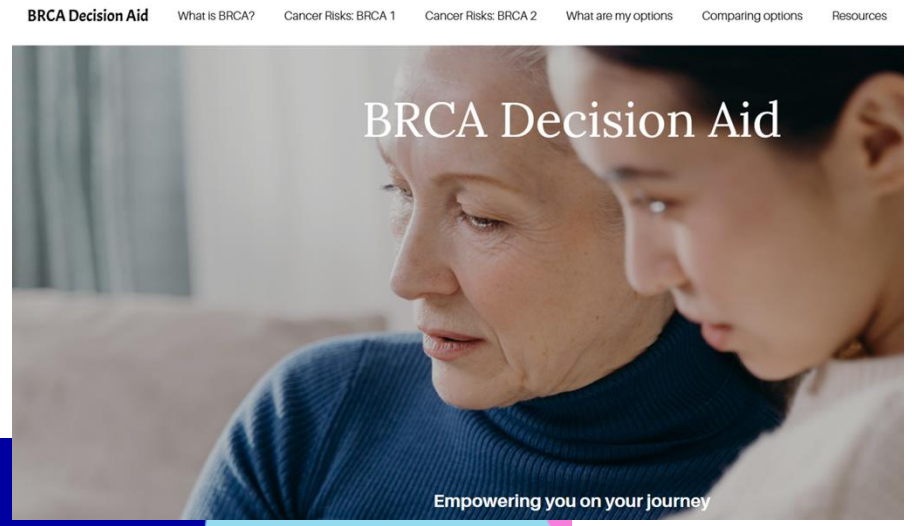
- Implications for family
  - Cascade testing
  - Planning a family
- Psychological impact
- Adverse effects of management
  - Prophylactic surgery – reconstruction, early menopause
  - Chemoprevention

- NB: role of healthcare professionals – genetic counsellors, Advanced Nurse Practitioners, psychologists – beyond diagnosis

Patient information and support

Marie Keating FOUNDATION

BRCA Peer to Peer Support Network



Lynch Syndrome Ireland

Cancer and genes

Irish Cancer Society

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Identification of Cancer Predisposition

- Cascade testing – i.e. a relative diagnosed first
- Diagnosis of cancer and family history raises suspicion
- Diagnosis of cancer and age/ features raise suspicion
- Diagnosis of cancer and somatic/ germline test carried out

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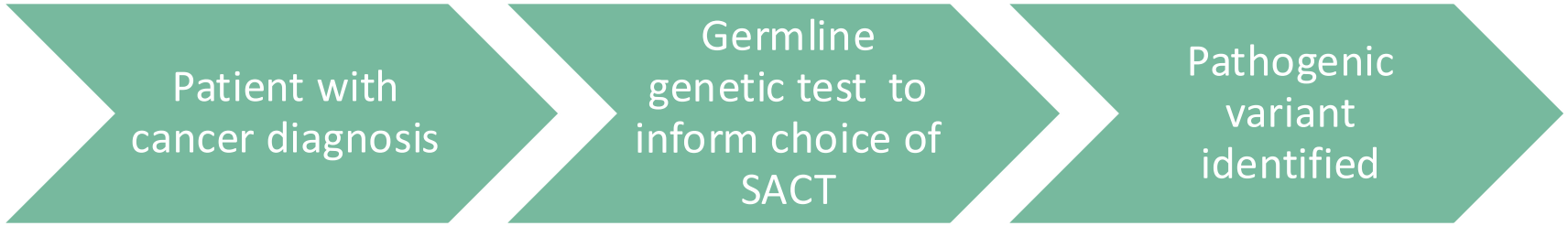
Identification of Cancer Predisposition



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Mainstreamed testing

- Patient with a cancer diagnosis but no known cancer predisposition gene
- Germline genetic testing offered by patient's oncology team

- Team member trained to provide pre-test counselling, consent, testing and deliver result to patient
- Patient still sees specialist services with result as required, e.g. if pathogenic variant or unclear result (variant of uncertain significance)

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Go raibh maith agaibh
Thank you

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