Cancer Genetics

Cancer in Families

1 in 2 people will develop cancer at some point in their lifetime

That means that most families will have a family history of cancer

Some families have a particular type of cancer that appears to have occurred more frequently than chance

- More common in the common cancers e.g. lung, breast, colorectal, prostate
- They occur around the typical ages for those particular cancers

This is due to multiple genes, each of small effect and shared environmental factors – polygenic / multifactorial

Why do some common cancers occur more often in some families than others?

We all carry variation in our genes that make us more or less likely to develop specific cancers, diabetes, hypertension, coronary artery disease, all common diseases

Each family unit, with shared genetic variants, is more or less susceptible to develop particular conditions

Compounded by a shared environment

Inherited Cancer

Breast / ovarian cancer

- Accounts for around 5% of breast cancer and 10-15% of ovarian cancer

Bowel cancer / Lynch Syndrome

- Accounts for around 2-4% of bowel cancer and 2.5% of endometrial cancer

A number of extremely rare “cancer syndromes” with more unusual tumour types

Important features in a family history of cancer

- Several family members affected with the same cancer, in several generations, on the same side of the family, who are closely related to the patient
- Young ages of diagnosis
- Incidence of associated cancers e.g. breast and ovarian cancer or bowel and uterine cancer
- Incidence of multiple primaries in a single family member

Inherited Breast / Ovarian cancer

About 5% of breast cancer and 10-15% of ovarian cancer
3 high risk genes – BRCA1, BRCA2 and PALB2
Autosomal dominant inheritance
More common in women diagnosed at young ages, under 40
More common with triple negative breast cancers
More common when there is a significant maternal or paternal family history of breast and ovarian cancer
50-70 % lifetime risk of breast cancer (population risk around 13%)
10–40% lifetime risk of ovarian cancer (population risk around 1-2%)

Inherited Breast and Ovarian cancer

Initial diagnostic testing done on blood from an affected individual that meets the current criteria based on age, tumour type and family history

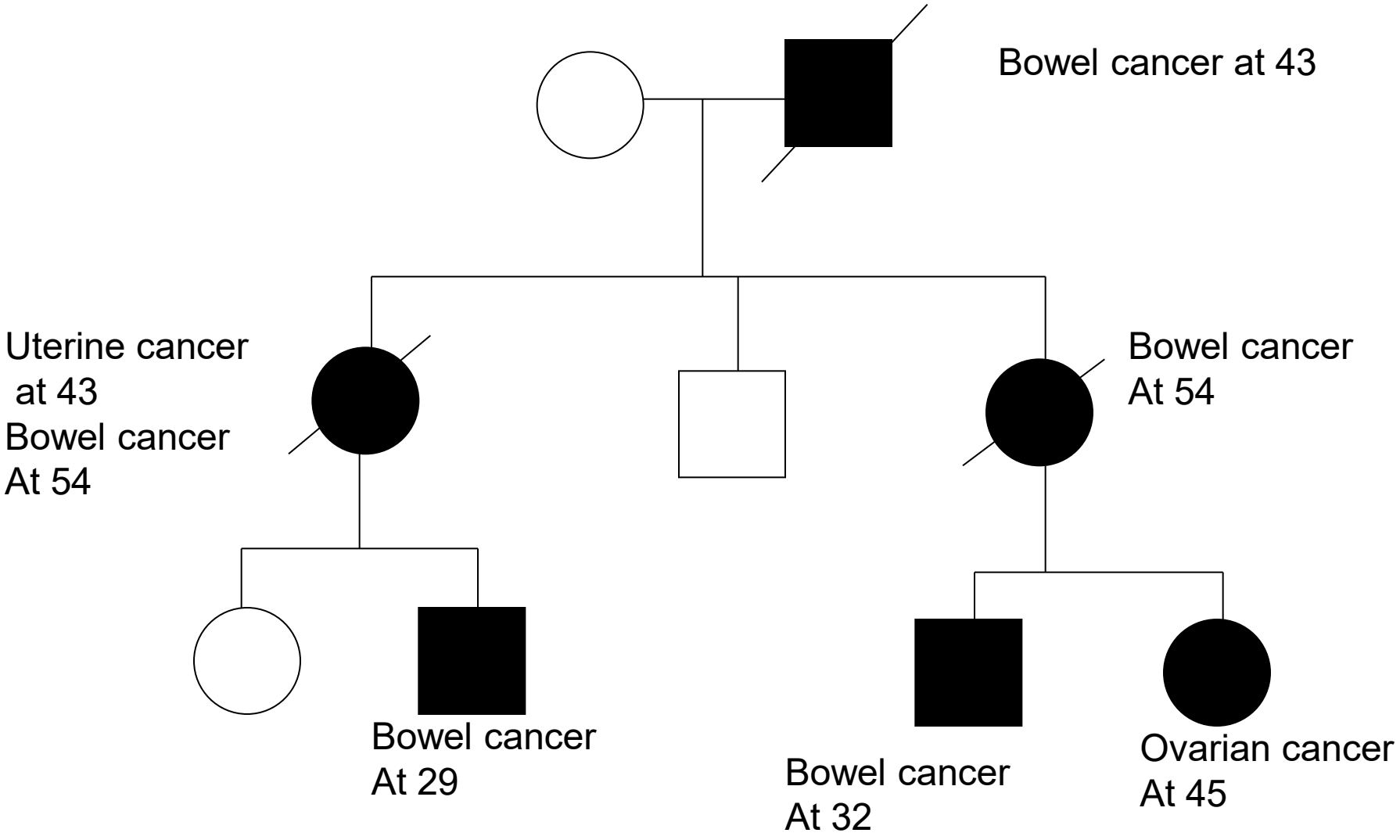
If a mutation is identified, cascade testing can be offered to family members

High risk individuals are offered screening and risk reducing surgery

Referral Pathways from Primary Care

- Affected individuals, that meet the testing criteria (all ovarian cancers, breast cancer <40, triple negative breast cancer <60, bilateral breast cancer <60, male breast cancer) are tested either in secondary care or Clinical Genetics
- Unaffected individuals with a family history that meets the NICE guidelines should be referred to the breast cancer family history units in secondary care. Most will not be offered genetic testing but will be offered enhanced breast screening
- Individuals with a known familial pathogenic variant in one of the breast/ovarian cancer genes should be referred to Clinical Genetics for predictive testing

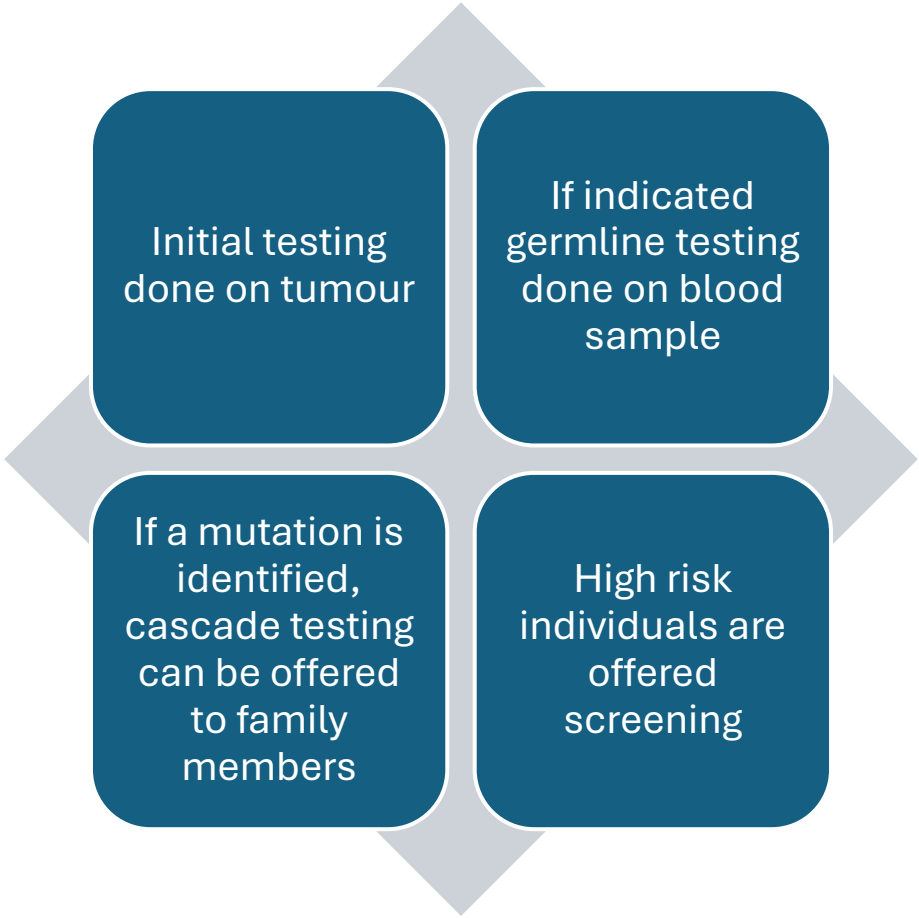
Hereditary Bowel Cancer



Lynch Syndrome

- About 2-4% of bowel cancer and 2.5% of endometrial cancer
- 3 high risk genes – MLH1, MSH2 and MSH6
- 1 moderate risk gene PMS2
- Autosomal dominant inheritance
- More common if diagnosed at young age
- More common when significant family history of bowel and endometrial cancer
- High risk genes 40-70% lifetime risk of bowel cancer (population risk about 5%), 40% risk of endometrial cancer (population risk about 3%)

Lynch syndrome



Referral pathways from Primary Care

- All patients affected with colorectal or endometrial cancer now have Lynch genetic testing on the tumour and are referred to Clinical Genetics if positive
- There are no bowel cancer family history clinics so we will accept referrals for a family history of bowel cancer where there are multiple affecteds particularly diagnosed at young ages
- Individuals with a known familial pathogenic variant in one of the Lynch cancer genes should be referred to Clinical Genetics for predictive testing