North West Thames Regional Genetics Service

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Principal Genetic Counsellor
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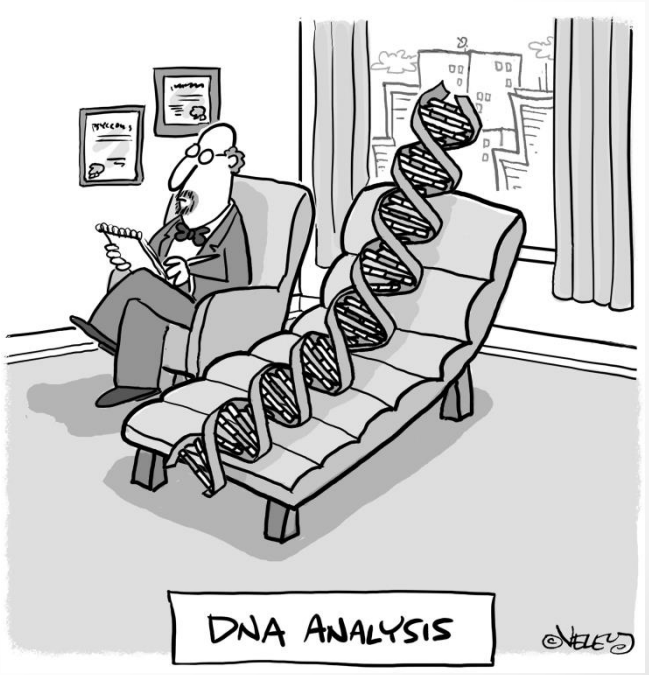
Objectives

- Introduction to our service
- Areas of speciality
- What happens at appointments
- Taking a family history
- Cancer genetics
- General genetics
- Referral guidelines



Who are we?

The role of Clinical Genetics department is:

- To identify genetic disorders and help people make informed decisions by:
  - Taking a detailed family history
  - Confirm/establish diagnosis
  - Determine risk to family members
  - Discuss options including prenatal diagnosis/risk management/ research
- Genetic services focus on the individual and their families.

A typical patient's journey…

- Referral received in genetics and assessed:
  - Can we offer a genetic test?
  - Is their risk increased?
- Taking a detailed medical history
- Taking a detailed family history
- Discussion of concerns
- Facilitate decision-making about genetic testing and/or screening
- Interpretation of test results

What is a genetic family history ?

A genetic family history consists of:

- Exactly how family members are related
- Any medical conditions they may have
- Ages they were diagnosed
- Ethnic background

This allows us to:

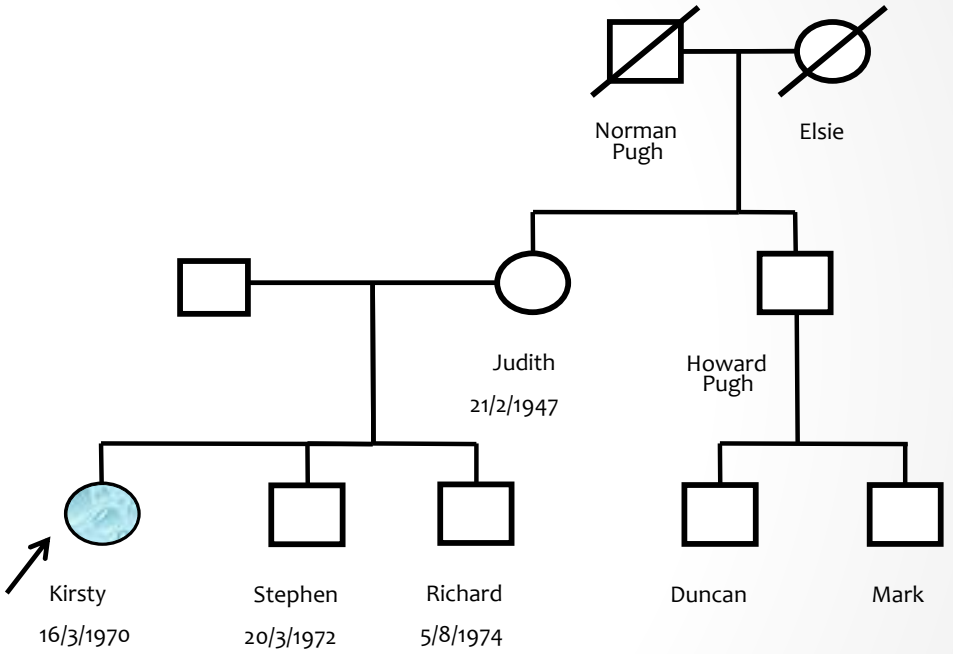
- Assess risk using patterns of disease/inheritance.
- Recommend management options for the patient
- Recommend management options for relatives
- Determine eligibility for genetic testing

What to include in a family history

- Both maternal and paternal family history
- Include 3 generations
  - The generation of the Proband, parents, and grandparents
- Ethnicity
- Ages of diagnoses
- Dead or alive
- Precise diagnoses
  - Include any confirmatory information eg. histology reports
- Unaffected family members
- Has anyone had genetic testing already?

Tips when drawing a pedigree

- Use clear symbols: circles for females
  squares for males
- Start the tree with your patient and work out (arrowed)
- Siblings on the same line
- Children go on the line below
- Parents go on the line above
- Choose one parent - Ask about sibs and their children.
- Then grandparents go above parents
- Then go to other parent



It's all in the detail

Include a key:

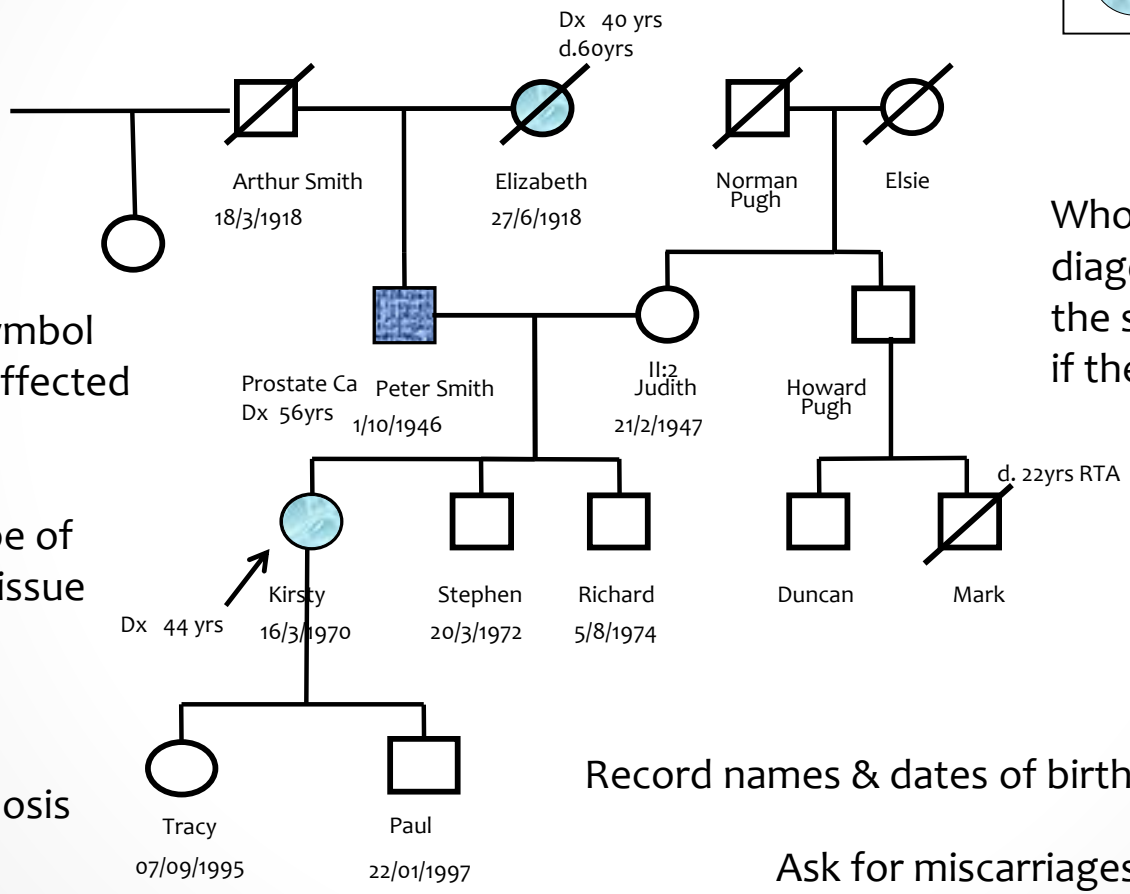
Key:

= prostate cancer

= breast cancer

Ethnic background

Ask about full and half siblings



Shade in the symbol if the person is affected

Who is alive? A diagonal line through the symbol shows if the person has died

Ask about type of cancer/health issue

Ask about consanguinity

Age at diagnosis

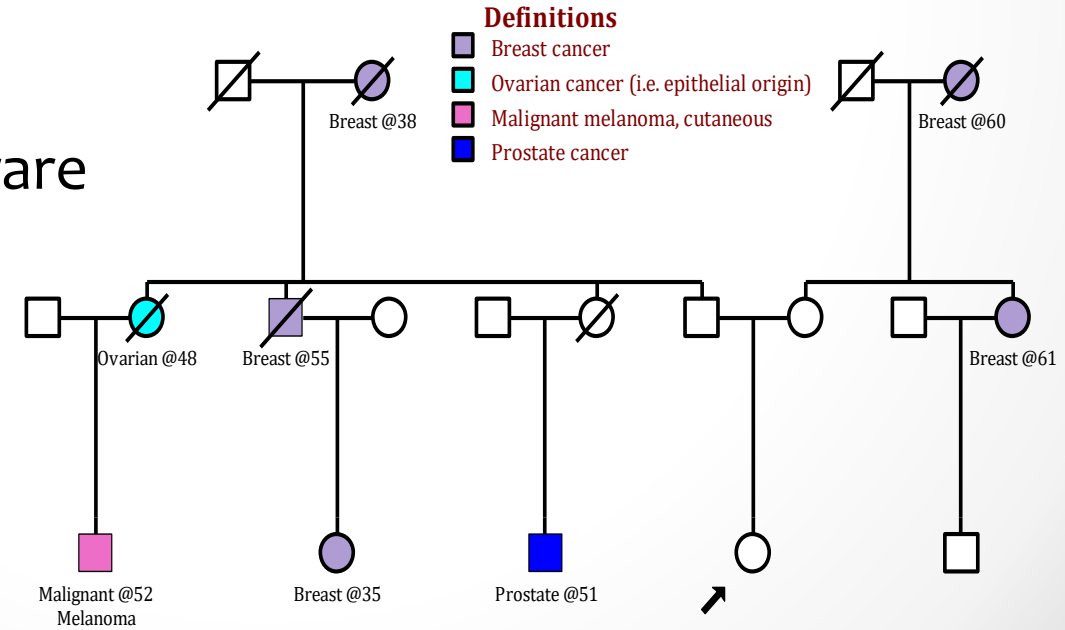
Record names & dates of birth

Ask for miscarriages, stillbirths or deaths in each partnership

What are we looking for?

- Patterns
- Numbers
- Age
- Consecutive generations

- Type of cancers
- Bilateral or multiple rare cancers

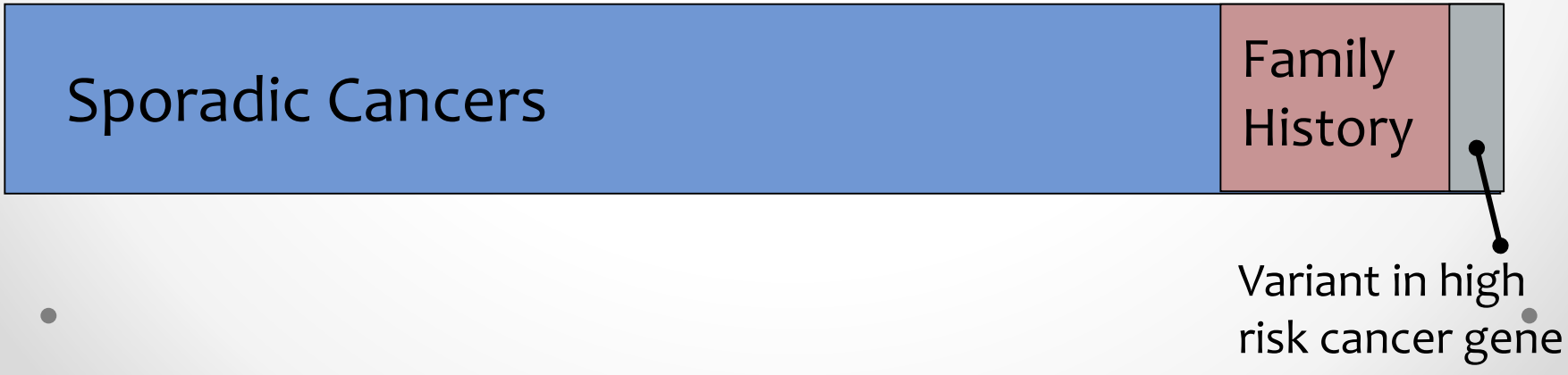


Cancer Genetic Referrals

- When in doubt contact us!
- We will reject referrals if:
  - Insufficient information is provided
  - Patients don't meet our referral criteria
  - We are not commissioned to see that condition
  - We cannot offer a genetic test
- If we need more information a family history questionnaire will be sent.
  - Once assessed, if eligible for testing we will send an appointment
  - If not eligible we will send a letter with screening advice

Cancer Genetic Counselling

- Assessing Risk
  - For our patient
  - For their relatives
- Organising screening/surveillance
- Facilitating decision-making
- Genetic Testing
- Interpreting results with family history
- Counselling regarding risk-management options



Why do we need to know the cause?

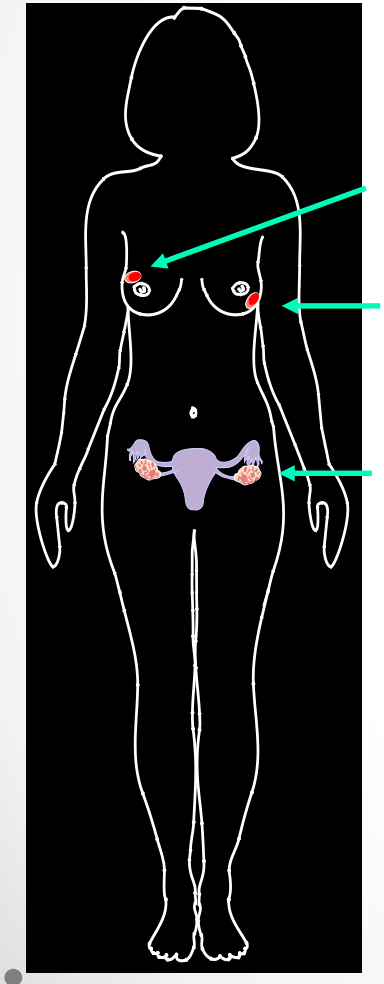
- Enables prediction of possible complications
  - Other cancers
  - Inheritance patterns
- Enables screening, risk reducing surgery and chemoprevention
- Enables informed decision-making about reproductive issues and prenatal testing
- Therefore know where to find referral guidelines
- Allows us to tell some relatives that they have no increased risk

Cancer predisposition syndromes

- *BRCA1/2*
- Lynch Syndrome

- Familial Adenomatous Polyposis (bowel polyposis)
- Li Fraumeni syndrome (sarcomas, breast cancer, childhood cancers)
- Multiple Endocrine Neoplasia (MEN) (endocrine cancers)
- Renal Cancer Syndromes (VHL, BHD, HRLCC)
- New cancer predisposition syndromes still being recognised

BRCA1 Lifetime Cancer Risk



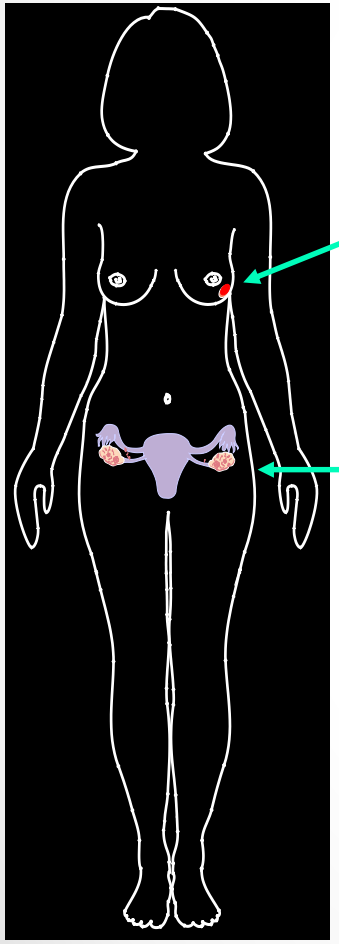
Breast cancer 60%–90%

Second primary breast cancer 50%

Ovarian cancer 40%-60%

Slight increased risk of male breast cancer and prostate cancer

BRCA2 Lifetime Cancer Risk

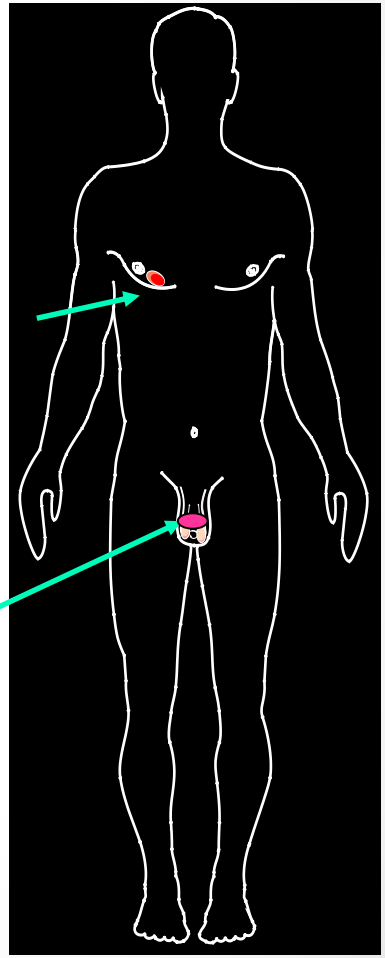


breast cancer
(35-60%)

ovarian cancer
(10-30%)

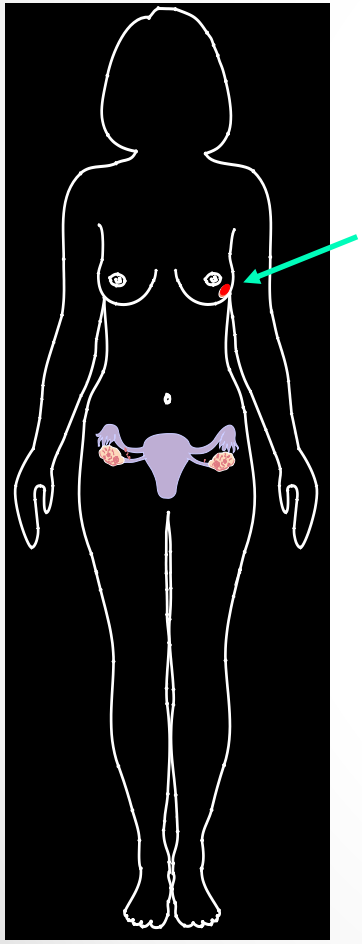
male breast cancer
(5-10%)

male prostate cancer
(25%)



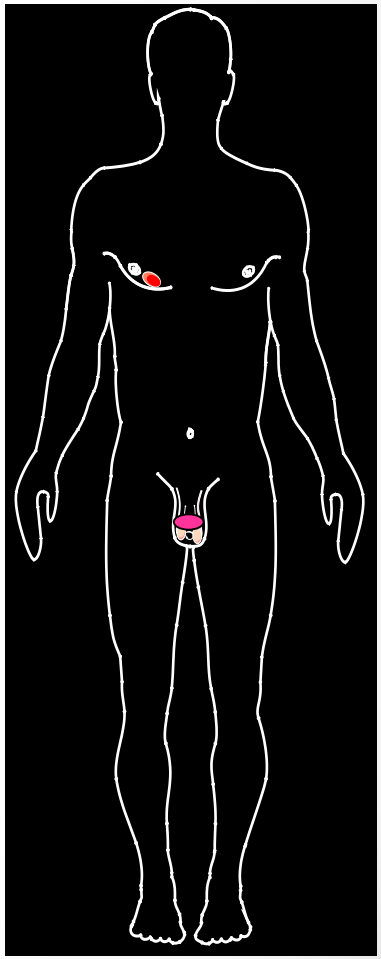
Slight increase risk of melanoma and pancreatic cancer

PALB2 Lifetime Cancer Risk



breast cancer
(45%-85%)

Pancreatic cancer (6%)



Referral criteria

Breast, Ovarian and Prostate

Breast / Ovarian cancer

- Breast cancer diagnosed before the age of 30
- Triple negative breast cancer diagnosed < 60
- Breast and ovarian cancer
- Bilateral breast cancer both diagnosed < 50
- Bilateral breast cancer and a relative diagnosed < 60
- Breast cancer and FDR or SDR with breast cancer both diagnosed < 45
- Non-mucinous ovarian cancer
- Male breast cancer and FDR or SDR relative with male breast cancer or ovarian cancer
- Breast cancer and Manchester Score* ≥15
- Ashkenazi Jewish – affected with breast or ovarian cancer
- Ashkenazi Jewish with a FDR or SDR (only if through the father) with breast cancer < 50 or ovarian cancer at any age. **Where affected relative is not available for testing.**
- Unaffected with Manchester score of ≥ 17 and no affected relative available for testing

Prostate cancer

- Prostate cancer and Manchester Score* of ≥15

Cancer, age at Diagnosis	Score
♀ Breast Cancer, <30	11
♀ Breast Cancer, 30-39	8
♀ Breast Cancer, 40-49	6
♀ Breast Cancer, 50-59	4
♀ Breast Cancer, >59	2
♂ Breast Cancer, <60	13
♂ Breast Cancer, >59	10
Ovarian cancer, <60	13
Ovarian cancer, >59	10
Pancreatic cancer	1
Prostate cancer, <60	2
Prostate cancer, >59	1

Manchester Scoring System

The ROYAL MARSDEN NHS Foundation Trust

ICR The Institute of Cancer Research

Protocol 2 (10% threshold)

BRCA1 and BRCA2 mutation testing guidelines

A
Woman with **breast cancer** who →
1) has bilateral BC and both cancers diagnosed < 50 yrs
2) has triple negative BC diagnosed < 50 yrs
3) has OC
4) has bilateral BC and a relative with BC < 60 yrs
5) has a relative with BC and both diagnosed < 45 yrs
6) has relatives with cancer and Manchester Score ≥15

B
Woman with **ovarian cancer** who →
1) has non-mucinous OC
2) has mucinous OC and another primary cancer
3) has a relative with OC or MBC
4) has relatives with cancer and Manchester Score ≥ 15

C
Male with **breast cancer** who →
1) has a relative with OC or MBC
2) has relatives with cancer and Manchester Score ≥ 15

D
Individual **unaffected** with cancer who →
1) has relatives with cancer and Manchester Score ≥ 17 (see FAQ for full eligibility)*

Management Options: BRCA1/2 Carriers

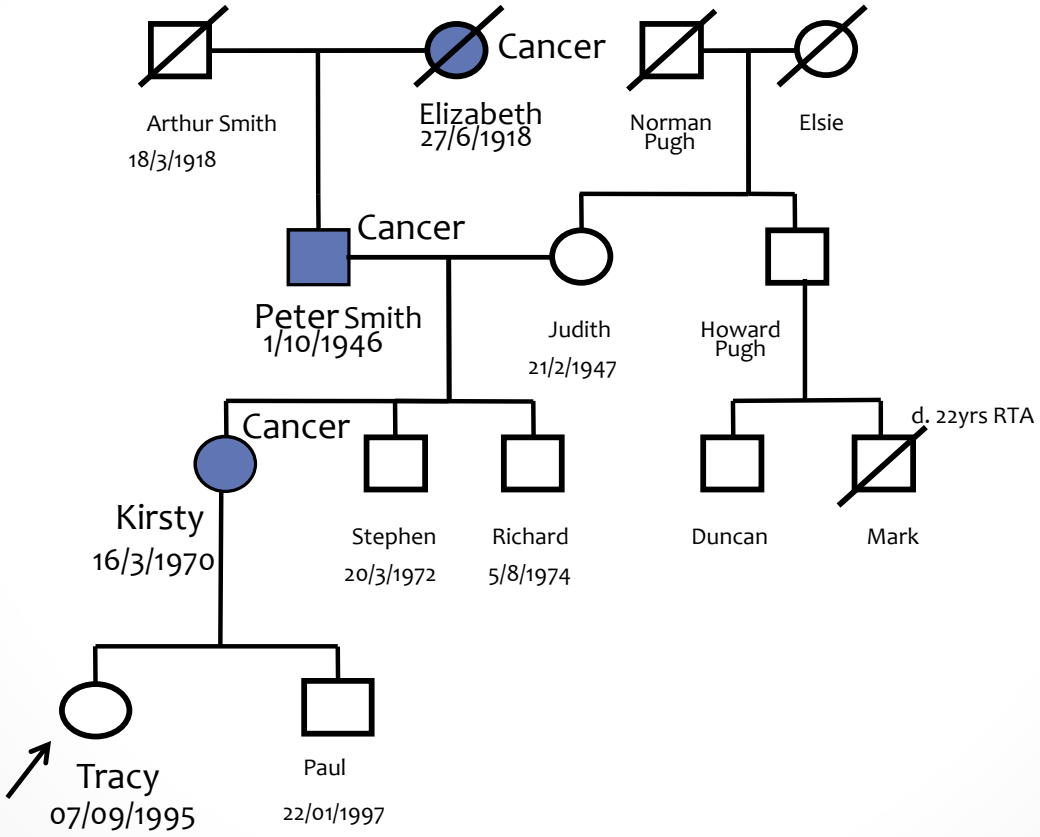
Management

- Annual MRI 30-50
- Annual mammograms 50 - 70
- Prophylactic bilateral mastectomy
  - ~90% reduction in breast CA risk
- Ovarian screening
  - Surveillance is not proven to save lives
  - Oral contraceptives for 5+ years lower the risk by 50%
- Prophylactic bilateral salpingo-oophorectomy
  - up to 96-98% reduction in ovarian CA risk
  - ~50% reduction in breast CA risk (if done pre-menopausal)
- Chemoprevention:
  - Tamoxifen in premenopausal women – BRCA2 only

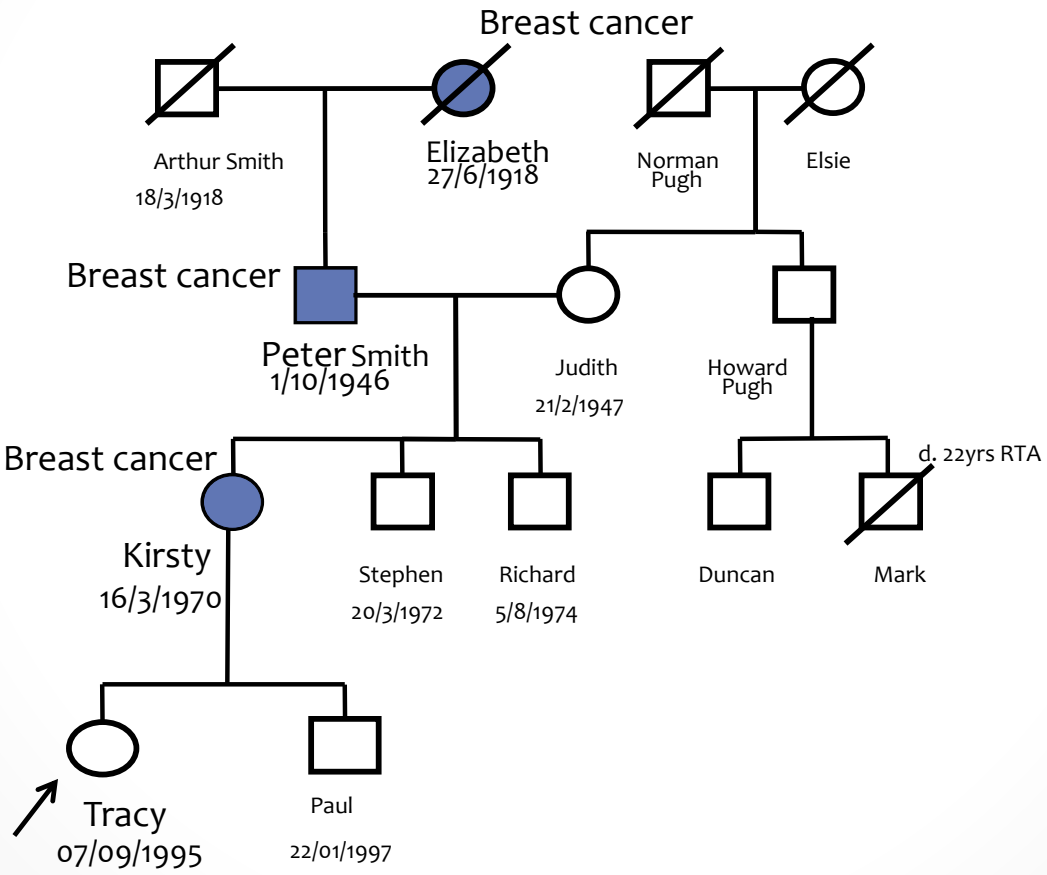
Treatment

- Use of carboplatin/PARP inhibitors chemotherapy
- More radical surgery

Does this patient need to be seen in Genetics?

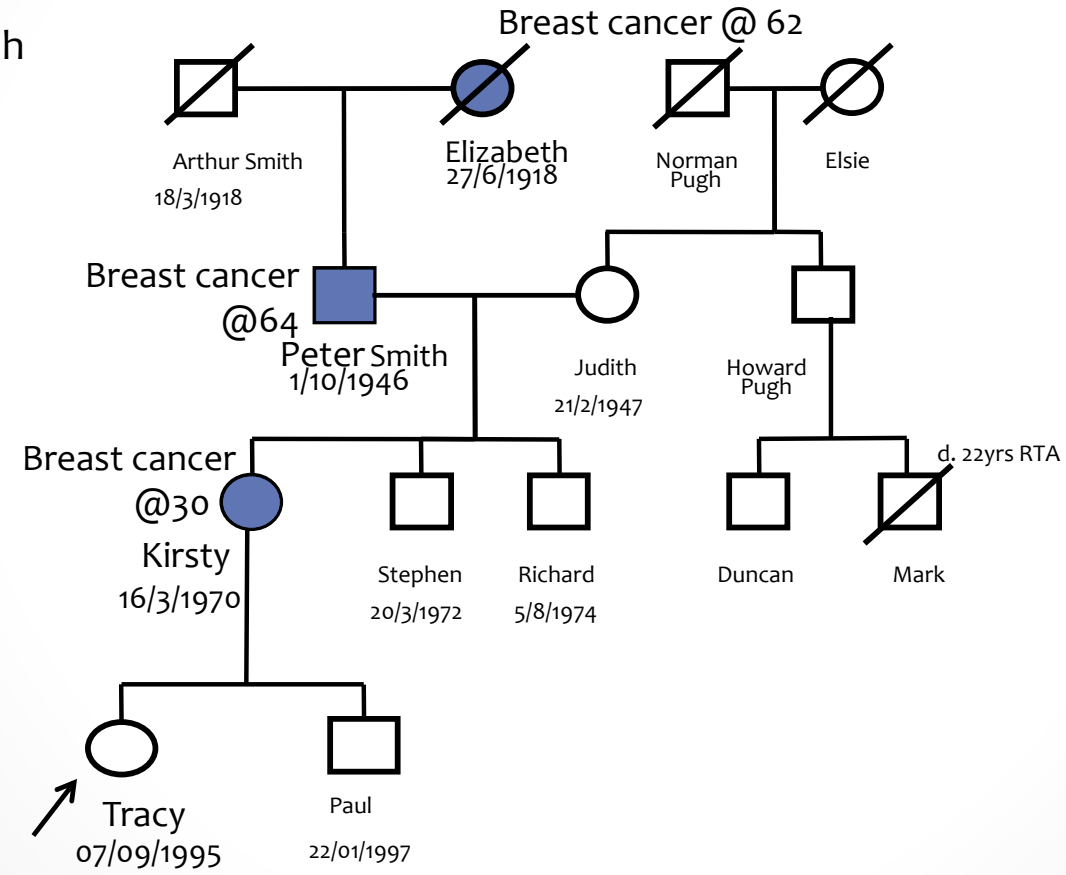


Does this patient need to be seen in Genetics?



Does this patient need to be seen in Genetics?

Ashkenazi Jewish ancestry



ICR

The Royal Marsden NHS

Protocol 1

Mammographic screening guidelines for women With a family history of breast and/or ovarian cancer

Key
FDR = First degree relative
SDR = Second degree relative
TDR = Third degree relative
BC = Breast Cancer
OC = Ovarian Cancer

Category B1 screening
Annual mammography 40-50 years
Three-yearly mammography 50-70 years

Category B2 screening
Annual mammography 40-50 years
18-monthly mammography 50-60 years
Three-yearly mammography 60-70 years

1 relative with breast cancer[1]	One female FDR with BC < 40 yrs	
	One male FDR with BC at any age	
	One FDR with bilateral BC at any age	Both cancers < 50 yrs
1 relative with breast and ovarian cancer[2]	One FDR with BC and OC at any age	BC < 50 yrs
2 relatives with breast cancer[1]	Two female FDR with BC at any age	Both < 50 yrs or One < 35 yrs
	One female FDR and one female SDR with BC at any age	Both < 40 yrs or FDR < 35 yrs
	Bilateral BC any age and another relative < 60 yrs (at least one must be FDR)	At least two cancers < 55 yrs
	One male BC and one female BC at any age (at least one must be FDR)	Female BC < 50 yrs
2 relatives: one with breast and one with ovarian cancer[2]	One OC and one BC at any age (at least one must be FDR)	BC < 50 yrs
2 or more relatives with ovarian cancer[2]		Two OC any age (at least one must be FDR)
3 relatives with breast cancer[1]	Three female FDR or SDR with BC at any age	Two are FDR or Two < 55 yrs and one is FDR or FDR < 35 yrs
	Three FDR or SDR with BC at any age at least one must be male BC	Two are MBC or Two are female BC < 60 yrs (at least one must be FDR)
	Three FDR or SDR with BC at any age at least one must be bilateral BC	One relative is a FDR
3 relatives with breast or ovarian cancer[2]	Three FDR or SDR with BC or OC at any age	All BC < 60 yrs or At least two are OC (at least one must be FDR
4 or more relatives with breast or ovarian cancer[2]	FDR/SDR/TDR with BC or OC at any age (at least one must be SDR)	One relative is a FDR

Notes*
- If the consultee is affected with breast cancer and has residual breast tissue, count as a FDR.
- An affected female SDR through a male FDR is equivalent to a FDR
- One relative must be a FDR of the consultee, unless otherwise specified.

BRCA1/2* negative families
[1] For breast only families, a negative *BRCA1/2* test does not alter the mammographic screening category.
[2] For breast-ovarian families, a negative *BRCA1/2* test, may alter mammographic screening category. The screening category should be recalculated on the basis of the breast cancers in the family alone.

* *See FAQ document. http://www.icr.ac.uk/protocols*

01/01/2013

Referral Criteria

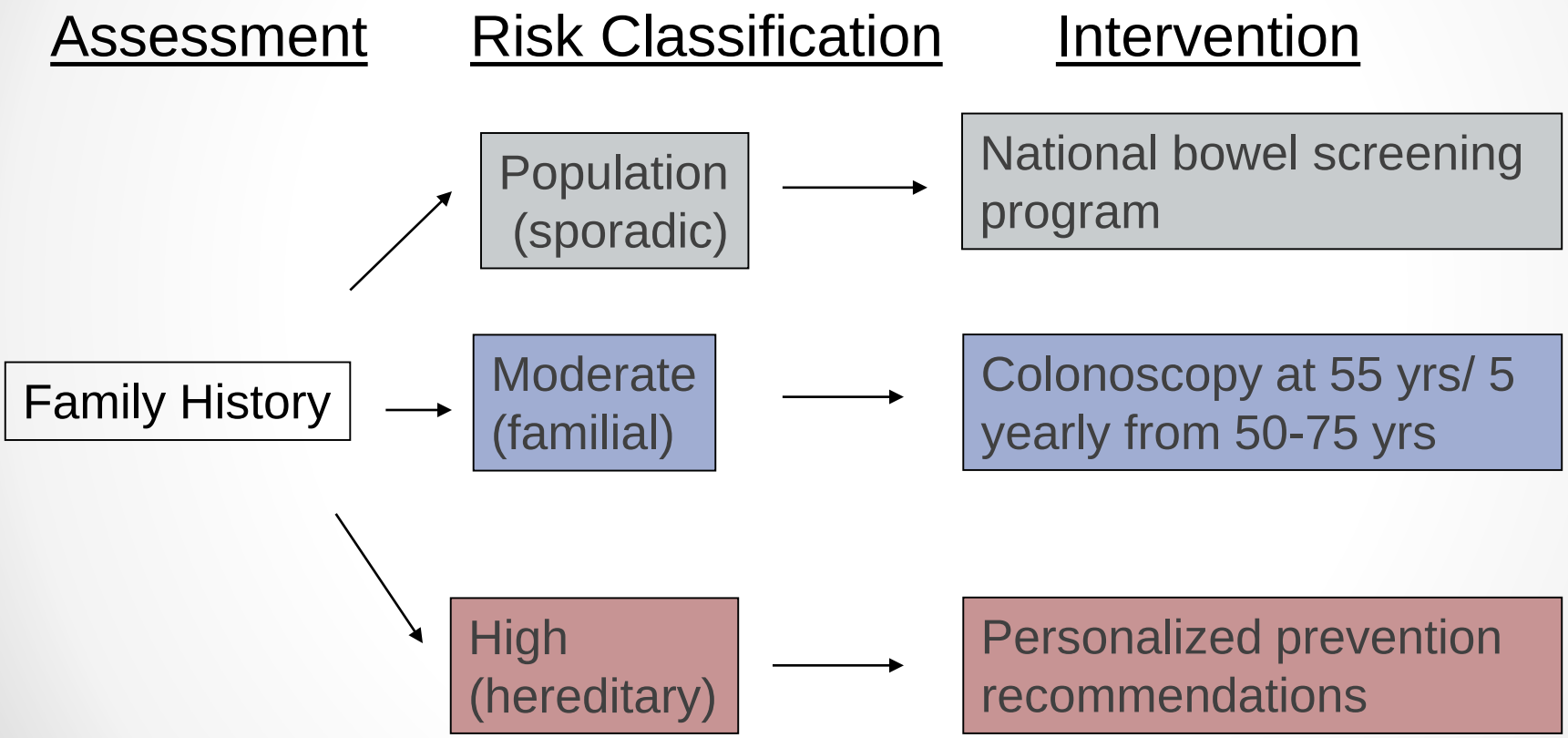
Bowel / Gynaecological Cancer

Colorectal / Gynaecological cancer

Immunohistochemistry (IHC) testing for mismatch repair genes testing should be done in all new diagnosis of Colorectal (CRC) - NICE 2017 and endometrial cancer (EC) diagnosed under the age of 50 years.

- Loss or MSH2, MSH6 or isolated loss of PMS2
- Isolated loss of MLH1 or loss of MLH1/PMS2 and normal methylation or absence BRAF mutation
- Abnormal microsatellite instability (MSI) in patient or FDR (who is unavailable for testing).
- Colorectal cancer diagnosed <50
- Colorectal cancer and FDR with Colorectal cancer any age
- Colon cancer and uterine or ovarian / urinary tract / gastrointestinal tumours at any age.
- More than 10 bowel polyps
- More than 5 adenomatous bowel polyps, at any age, with family history of bowel polyps/cancer
- Unusual bowel polyps such as harmatomatous polyps
- Synchronous endometrial and ovarian cancer
- Endometrial cancer and FDR with endometrial cancer both < 60

CRC Risk assessment



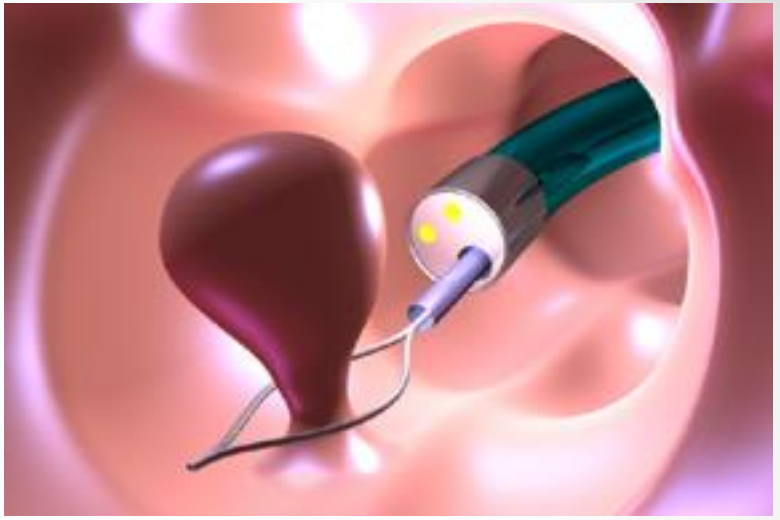
Lynch Syndrome

- 2-3% of all colorectal cancer cases
- Autosomal dominant; high penetrance
- Typical age of CA onset is 40-50 yrs
- Multiple affected generations
- Several genes – genotype- phenotype correlation

- NICE has recommended all bowel cancers have IHC testing to determine likelihood of Lynch syndrome –
  - -currently being rolled out
- If IHC is abnormal genetic testing is offered

Management options

Lynch syndrome



Management

- Two yearly colonoscopy
- Chemoprevention – Aspirin
- RR TAH and ?BSO
- H. pylori testing
- Skin checks for Muir-Torre Syndrome families

Treatment

- Colectomy or extended hemicolectomy for treatment of cancers

Endocrine Cancer

Endocrine Cancer

- Medullary thyroid carcinoma
- Two or more endocrine tumours
- Paragangliomas at any age
- Pheochromocytomas at any age
- Parathyroid carcinoma or familial hyperparathyroidism or hyperparathyroidism < 35
- Symptomatic pituitary tumours in children (<18) or pituitary macroadenoma < 30

Other

Other:
We also run specialist renal cancer genetics clinic and will accept referrals for patients with renal cancer < 40 years.
You can contact the department for more information about the specialist renal and endocrine clinics.

Any family with multiple malignant melanoma a FDR Kinship (affected relatives who are FDR of each other and one is FDR of the proband)

Any family with an unusual pattern of cancer in the family, such as: three or more primary cancers in a single individual, more than one close relative diagnosed with a rare cancer at an unusually young age for that type of cancer.

General Genetics Referrals

- Please include as much information as possible about condition.
- Please include any familial genetic reports
- Please include any other relevant test reports
- The exact biological relationship between the affected individual and the person being referred e.g. maternal half-sister (shared mother).

Who should you refer?

- There is a vast range of conditions seen :
  - Neurogenetics
  - Dysmorphology
  - Cardiac genetics
  - Endocrine genetics
  - Eye genetics
  - Renal genetics
  - Prenatal genetics

- **Ehlers-Danlos Syndrome Service**
- **JNETICS service**

Who shouldn't you refer?

- People at population risk
- People at risk of conditions for non-genetic reasons
- People who cannot be offered a genetic test
- People best served by other specialist services:
  - **Haemophilia**
  - **Haemoglobinopathies**
  - **Thrombophilia**
  - **MTHFR**
  - **Familial Hypercholesterolaemia**
  - **Alpha 1 Antitrypsin Deficiency**
  - **Haemochromatosis**

General Genetic genetic counselling

- Assessing Risk
  - For our patient
  - For their relatives
- Organising screening/surveillance
- Facilitating decision-making
- Genetic Testing
- Interpreting results with family history
- Counselling regarding risk-management options
- **Reproductive counselling**
  - **PND**
  - **PGD**

Prenatal Genetics Types of GP referrals

- Types of referral:
  - Previous baby with a trisomy or chromosome anomaly
  - Patient/partner/fhx of chromosomal translocation/deletion
  - Family history of any genetic condition e.g. CF, CAH, SMA, metabolic disorder, DMD
  - Couple are consanguineous and have had previous child who has died or has a genetic diagnosis
  - Ethnicity-related condition in the family e.g. Tay Sachs, thalassemia, sickle cell anaemia

What we need to know

- Is there a family history of any genetic condition?
- If yes, and patient wishes to discuss please email referral ASAP
- **TIMEFRAME IS KEY**
  - If the lady presents to GP at 6/40 pregnant and needs a CVS at 12 weeks, we have time to:
    - Confirm the diagnosis of genetic condition in family
    - Instigate urgent genetic testing of affected relative, if appropriate
    - Arrange carrier testing of parents, if appropriate
    - Arrange an early dating scan if CVS planned
    - Arrange non-invasive testing at 9/40 to sex the pregnancy if X-linked

    - The earlier results are received the better

Prenatal Genetics

Use our urgent referral form including:

- Patient's full details
- LMP
- Mobile number - essential
- Where is she booking?
- Name of condition in the family
- Brief description of family history
- Has anyone had genetic testing?
- What does the patient want to do about it?

- Inform patient they will need to provide full details about the affected relative in their family

Predictive genetic testing

- Offered to asymptomatic relatives of an individual shown to carry a gene mutation (cancer and general)
- This is a huge life-changing decision
- Many different implications for a well person
  - Perception of self and personal risks
  - Family dynamics
  - Insurance/Mortgages
  - Life-planning
  - Family-planning

Take home messages

Please tell your patient:

- We must confirm the family history to provide an accurate risk assessment.
  - This can take time. (Especially if we don't have enough information at the beginning of the process)
- If your patient is eligible for genetic testing for a mutation in their family, we will need a copy of the genetic test report from the family member who has been tested.
- We usually only offer an appointment to patients who are eligible for genetic testing

Contact details

- Website: www.lnwh.nhs.uk/service-finder/service/genetics-34/
- Email: lnwh-tr.nwtrgsclinicalgenetics@nhs.net
- Tel: 020 8869 2795.
  - We have an call genetic counsellor or consultant every day