What does it mean to have a personal or family history of cancer?

Mary-Anne Young
June 2011

Overview

What is the difference between sporadic / familial cancer

How common is an inherited predisposition to cancer?

How is genetic risk assessed?

What is genetic testing?

Risk/protective factors for cancer

Age

Increasing

Environmental

smoking
sun exposure
chemical exposure

Hormonal

menarche
breast feeding
hormone usage

Lifestyle

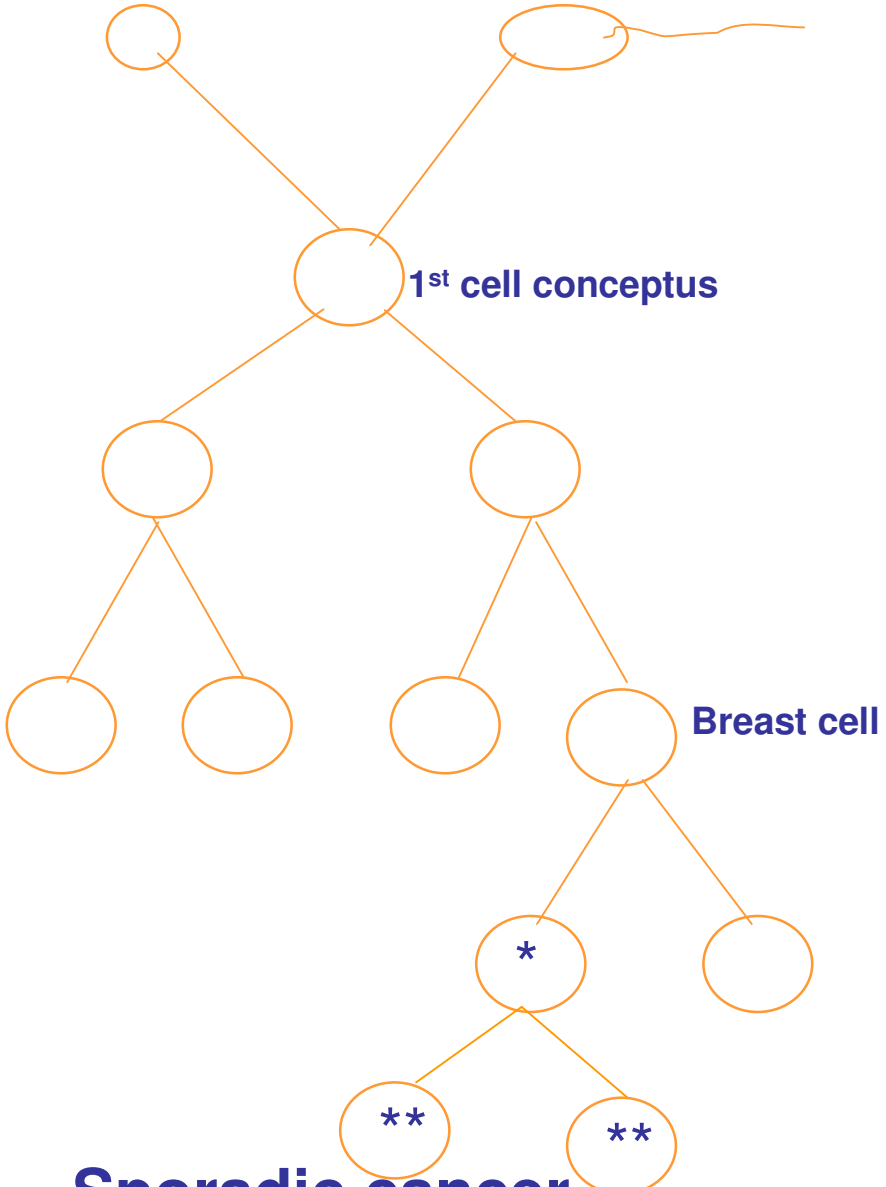
diet
alcohol
weight/activity

Genetic

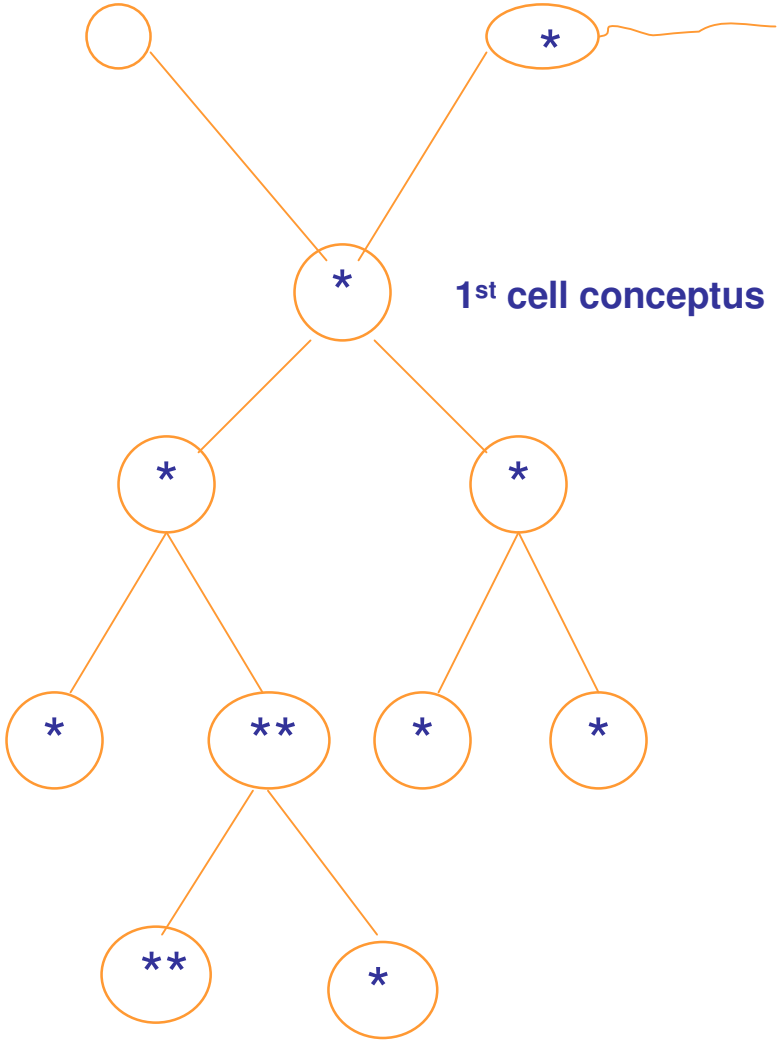
family history

All cancers are genetic
<u>BUT</u>

Only 5-10% of cancers are due to the inheritance of a single cancer susceptibility gene

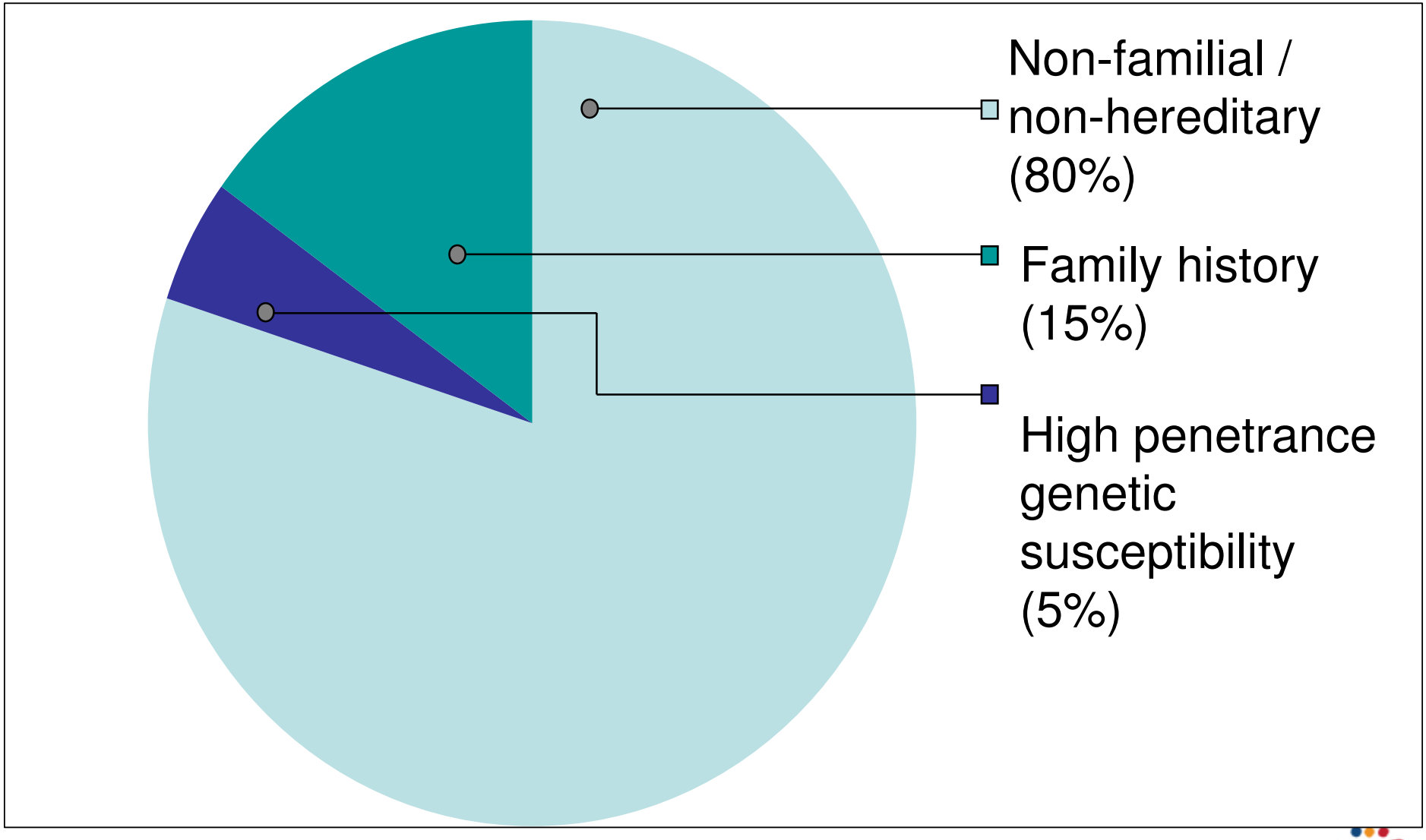


Sporadic cancer



Inherited predisposition

Incidence


Non-familial / non-hereditary (80%)
Family history (15%)
High penetrance genetic susceptibility (5%)

Estimated proportion of cancers due to genetic susceptibility

• Breast cancer	5-10%
• Ovarian cancer	10%
• Colon cancer	5-10%
• Prostate cancer	10%
• Melanoma	10%
• Medullary thyroid	25%
• Retinoblastoma	40%
• Wilms tumour	5%

Clues when assessing risk

Family history

- many cases of same type of cancer in a family

- cancer clusters:
  breast/ovarian,
  CRC/uterine in same person or in family

- age of onset of cancers (30's & 40's)

- individuals who had several cancers such as bilateral breast cancer, uterine and ovarian cancer

Pathology

Taking a family history of cancer

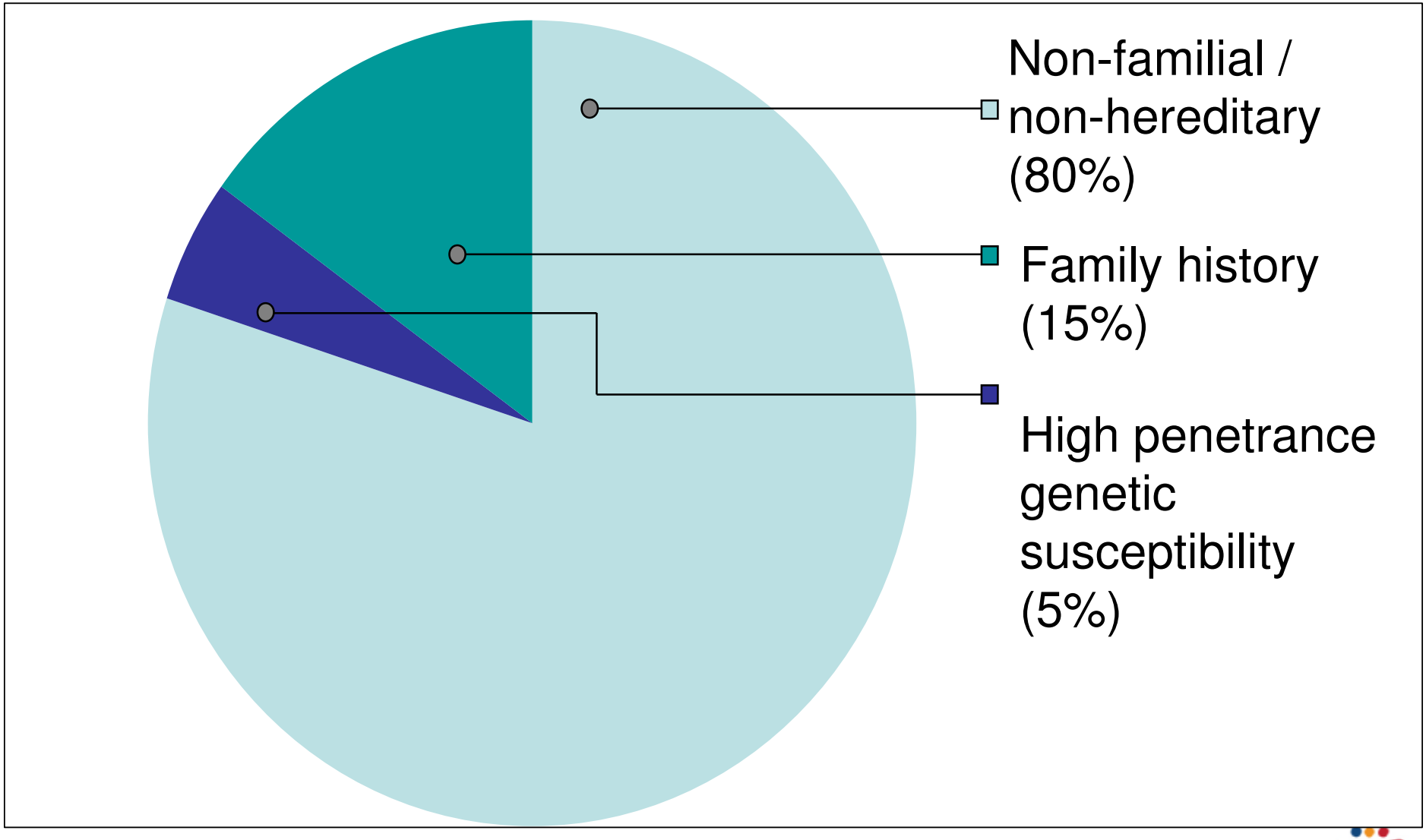
- Ask about three generations
- On each side of the family – male F/H relevant
- Include first and second degree relatives
- Note
  - Site of cancer
  - Age of onset

What health professionals should look for

- Number of people with cancer on each side of a family
- Age of onset and site of primary cancers
- Patterns of certain types of cancers e.g breast and ovary.
- Autosomal (both sexes) dominant inheritance
- Ethnicity – i.e Jewish ancestry (in the case of breast/ovarian cancer)

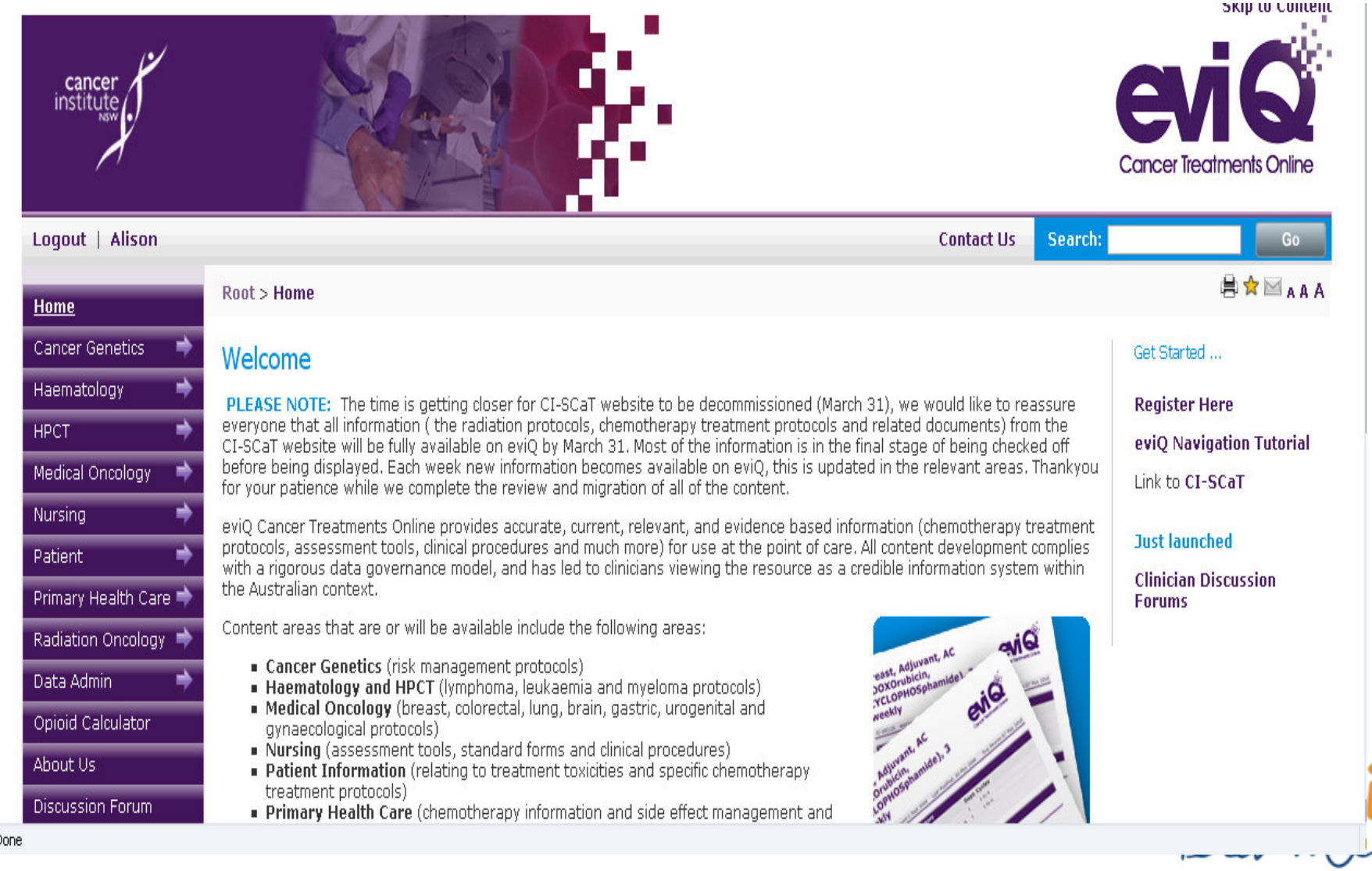
Remember:
Family history changes over time

Incidence


Non-familial / non-hereditary (80%)
Family history (15%)
High penetrance genetic susceptibility (5%)

RESOURCES

www.EviQ.org.au



NATIONAL BREAST CANCER CENTRE
incorporating the Ovarian Cancer Program

Advice about familial aspects of breast cancer and epithelial ovarian cancer

a guide for health professionals FEBRUARY 2006

These guidelines contain three parts:

1. Information for health professionals
2. Tables which describe risk based on family history and current suggested management
3. Information for consumers that may be photocopied for distribution.

The guidelines have been developed to cover familial aspects of both breast and epithelial ovarian cancer. In some families genetic testing can be used to assess risk. This testing is available through family cancer clinics.

The information on page two can be used to determine a woman's risk of developing breast cancer, based on her family history. The information on page three can similarly be used to determine her risk of developing ovarian cancer.

These guidelines are a general guide for appropriate practice to be followed subject to the health professional's judgement of each case. They are designed to provide information to assist decisions made by health professionals and their patients. They are based on the best available evidence or consensus opinion of experts where evidence does not exist at the date of publication.

ADVICE ABOUT FAMILIAL ASPECTS OF BREAST CANCER

The following categorisation applies to women without breast or ovarian cancer:

CATEGORIES OF RISK

1. At or slightly above average risk

Covers more than 95% of the female population

- No confirmed family history of breast cancer
- One 1° relative diagnosed with breast cancer at age 50 or older
- One 2° relative diagnosed with breast cancer at any age
- Two 2° relatives on the same side of the family diagnosed with breast cancer at age 50 or older
- Two 1° or 2° relatives diagnosed with breast cancer, at age 50 or older, but on different sides of the family (i.e. one on each side of the family)

As a group, lifetime risk of breast cancer is between 1 in 11 and 1 in 8. This risk is no more than 1.5 times the population average.

2. Moderately increased risk

Covers less than 4% of the female population

- One 1° relative diagnosed with breast cancer before the age of 50 (without the additional features of the potentially high-risk group – see section 3)
- Two 1° relatives, on the same side of the family, diagnosed with breast cancer (without the additional features of the potentially high-risk group - see section 3)
- Two 2° relatives, on the same side of the family, diagnosed with breast cancer, at least one before the age of 50, (without the additional features of the potentially high-risk group – see section 3)

As a group, lifetime risk of breast cancer is between 1 in 8 and 1 in 4. This risk is 1.5 to 3 times the population average.

3. Potentially high risk

Covers much less than 1% of the female population

- Women who are at potentially high risk of ovarian cancer (See Category 3 below)
- Two 1° or 2° relatives on one side of the family diagnosed with breast or ovarian cancer **plus** one or more of the following features on the same side of the family:
  - additional relative(s) with breast or ovarian cancer
  - breast cancer diagnosed before the age of 40
  - bilateral breast cancer
  - breast and ovarian cancer in the same woman
  - Ashkenazi Jewish ancestry
  - breast cancer in a male relative
- One 1° or 2° relative diagnosed with breast cancer at age 45 or younger **plus** another 1° or 2° relative on the same side of the family with sarcoma (bone/soft tissue) at age 45 or younger
- Member of a family in which the presence of a high risk breast cancer gene mutation has been established

As a group, lifetime risk of breast cancer is between 1 in 4 and 1 in 2. Risk may be more than 3 times the population average. Individual risk may be higher or lower if genetic test results are known.

Contact a specialist cancer genetic service[3] if concerned about a woman's family history of cancer

MANAGEMENT

1. Reassure the woman that her risk is the same as, or slightly above average for the general population and that **more than 90% of women in this group will not develop breast cancer**
2. It is recommended that women 50-69 years attend the BreastScreen Australia program for free screening mammograms every two years. Women aged 40-49 years are also eligible for this Program, but mammographic screening is not recommended for women younger than 40 years
3. A firm recommendation regarding clinical breast examination (CBE) is not possible as there is no evidence to either encourage or discourage the use of CBE as a screening method in women of any age.

1. Advise the woman that she has a moderately increased risk of developing breast cancer, but that **75% - 90% of women in this group will not develop breast cancer.** A more precise risk assessment and management plan may be available from a specialist cancer service or family cancer clinic.[3]
2. While evidence about optimal management strategies for this group does not exist, the following recommendations are based on expert consensus opinion:*
   - advise the woman to at the very least attend for screening mammograms as recommended for Category 1
   - additional surveillance, such as mammography from a younger age, or more frequently, should be considered on an individual basis.
3. A firm recommendation regarding clinical breast examination (CBE) is not possible as there is no evidence to either encourage or discourage the use of CBE as a screening method in women of any age.
4. Discuss possible participation in a relevant approved clinical trial for the prevention of breast cancer

1. Advise the woman that she has a potentially high risk of developing breast cancer and perhaps other cancers, but that **50% – 75% of women in this group will not develop breast cancer.**
2. Referral to a family cancer clinic for risk assessment and management plan should be discussed, especially if the woman wishes to clarify her genetic risk or that of her family, or wishes to consider risk-reducing surgery.
3. It is recommended than an individual surveillance program be developed in consultation with a cancer specialist. While evidence about optimal strategies for this group does not exist, an appropriate surveillance program may include:*
   - attending for regular clinical breast examination
   - annual mammography with or without other imaging techniques
   - surveillance for ovarian cancer
4. The age at which screening commences may be influenced by aspects of family history. Although this should be determined on an individual basis, it is generally accepted practice to begin screening at least five years prior to the age of diagnosis of the closest relative.
5. Discuss possible participation in a relevant approved clinical trial for the prevention of breast cancer.

**Discussion should include information about the advantages and disadvantages of individual surveillance options*

It is recommended that all women, regardless of whether they attend for mammographic screening, are aware of how their breasts normally look and feel and promptly report any new or unusual changes to their general practitioner.

1 Family Health Tree Guide may assist you and your patients to complete a family history chart. Copies can be obtained from The Centre for Genetics Education. Tel 02 9904 7204 2 To make an appointment with BreastScreen Australia Tel 13 20 50 toll free. 3 For a list of the current specialist family cancer clinics please contact the National Breast Cancer Centre (NBCC), Locked Bag 14, Camperdown NSW 1450, Australia, Tel (02) 9034 2020 Fax 02 9034 2077, email:directorate@nbcc.org.au

ADVICE ABOUT FAMILIAL ASPECTS OF OVARIAN CANCER

The following categorisation applies to women without breast or ovarian cancer:

CATEGORIES OF RISK

1. At average risk or 2. At moderately increased risk

Covers more than 99% of the female population

- No confirmed family history of epithelial ovarian cancer.
- One 1° or 2° relative diagnosed with ovarian cancer at any age (provided the family is not of Ashkenazi Jewish ancestry* and does not have any additional cases of breast cancer).
- Two 1° or 2° relatives diagnosed with ovarian cancer, but on different sides of the family (i.e. one on each side of the family).

**High-risk ovarian and breast gene mutations are more common in people of Ashkenazi Jewish ancestry.*

As a group, lifetime risk of ovarian cancer is between 1 in 100 and 1 in 30. This risk is no more than 3 times than the population average.

3. Potentially high risk

Covers less than 1% of the female population

- Women who are at potentially high risk of breast cancer (see Category 3 above)
- One 1° relative diagnosed with epithelial ovarian cancer in a family of Ashkenazi Jewish ancestry*.
- One woman with ovarian cancer at any age, and another with breast cancer before the age of 50, where the women are 1° or 2° relatives of each other
- Two 1° or 2° relatives on the same side of the family diagnosed with epithelial ovarian cancer, especially if one or more of the following features occurs on the same side of the family:
  - additional relative(s) with breast or ovarian cancer.
  - breast cancer diagnosed before the age of 40.
  - bilateral breast cancer.
  - breast and ovarian cancer in the same woman.
  - breast cancer in a male relative.
- Three or more 1° or 2° degree relatives on the same side of the family diagnosed with any cancers associated with hereditary non-polyposis colorectal cancer (HNPCC): colorectal cancer (particularly if diagnosed before the age of 50), endometrial cancer, ovarian cancer, gastric cancer, and cancers involving the renal tract.
- A woman suspected to have HNPCC
- Member of a family in which the presence of a high-risk ovarian cancer gene mutation has been established.

As a group, lifetime risk of ovarian cancer is between 1 in 30 and 1 in 3. This risk is more than 3 times the population average. Individual risk may be higher or lower if genetic test results are known.

Contact a specialist cancer genetic service[1] if concerned about a woman's family history of cancer

MANAGEMENT

1. Reassure the woman that her risk is at or at most moderately above the average for the general population and that **more than 97% of women in this group will not develop ovarian cancer.**
2. Advise the woman about current best practice for the early detection of cancers for the population.
3. Advise the woman to visit her general practitioner promptly with any health changes.

Screening the general population for epithelial ovarian cancer cannot be justified on the basis of the low prevalence of ovarian cancer and the inadequate sensitivity of currently available tests.

1. Advise the woman that she has a potentially high risk of developing ovarian cancer and perhaps other cancers, such as breast cancer, but that **the majority of women in this group will not develop ovarian cancer.**
2. If the woman wishes to clarify her genetic risk or that of her family, or wishes to consider risk-reducing surgery, discuss referral to a specialist family cancer clinic for advice, appropriate counselling and management.
3. Because bilateral salpingo-oophorectomy has been shown to reduce the risk of ovarian and breast cancer in women with a mutation in BRCA1 or BRCA2, advise the woman to see a gynaecological oncologist to discuss her options.

   Should a woman choose not to have risk-reducing surgery, an appropriate individualised surveillance program may include:
   - visiting her general practitioner promptly with any health changes.
   - transvaginal ultrasonography.* (The age at which this commences may depend on the family cancer history and if a high-risk ovarian cancer gene mutation has been identified in the woman or her family).
   - CA125 measurement (after the menopause)*.
   - surveillance relevant to other cancers (e.g. attending for clinical breast examination, mammography for breast cancer; or other surveillance if the family cancer history is consistent with HNPCC).
4. Discuss possible participation in a relevant approved clinical trial.

** There is no evidence that these tests reduce mortality from ovarian cancer but they may be considered for women who have not undergone risk-reducing salpingo-oophorectomy).*

1 For a list of the current specialist family cancer clinics please contact the National Breast Cancer Centre (NBCC), Locked Bag 14, Camperdown NSW 1450, Australia, Tel (02) 9036 3000 Fax (02) 9036 3077, email:directorate@nbcc.org.au These guidelines for ovarian cancer are based on the *Clinical practice guidelines for the management of women with epithelial ovarian cancer*, The Australian Cancer Network and National Breast Cancer Centre, 2004. Levels of evidence: All statements about familial risk are based on Level III-2 evidence. The management recommendation for mammographic screening for Category 1 is based on Level I evidence. ▸ Levels of evidence are based on the rating detailed in the NHMRC Guidelines *for the development and implementation of clinical practice guidelines*. NHMRC. Canberra: Australian Government Publishing Service: 1999.

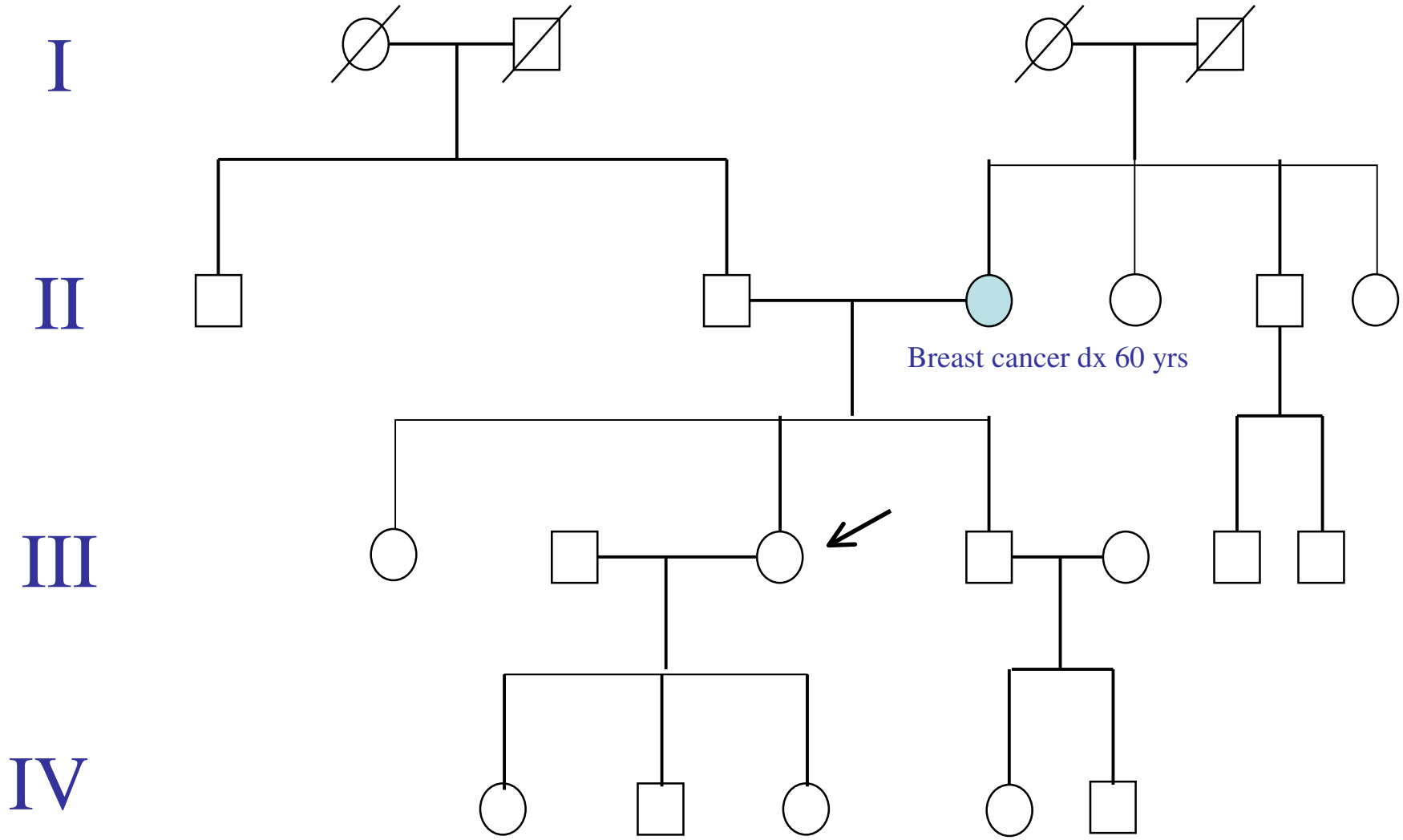
Risk assessment for unaffected individual

Average risk

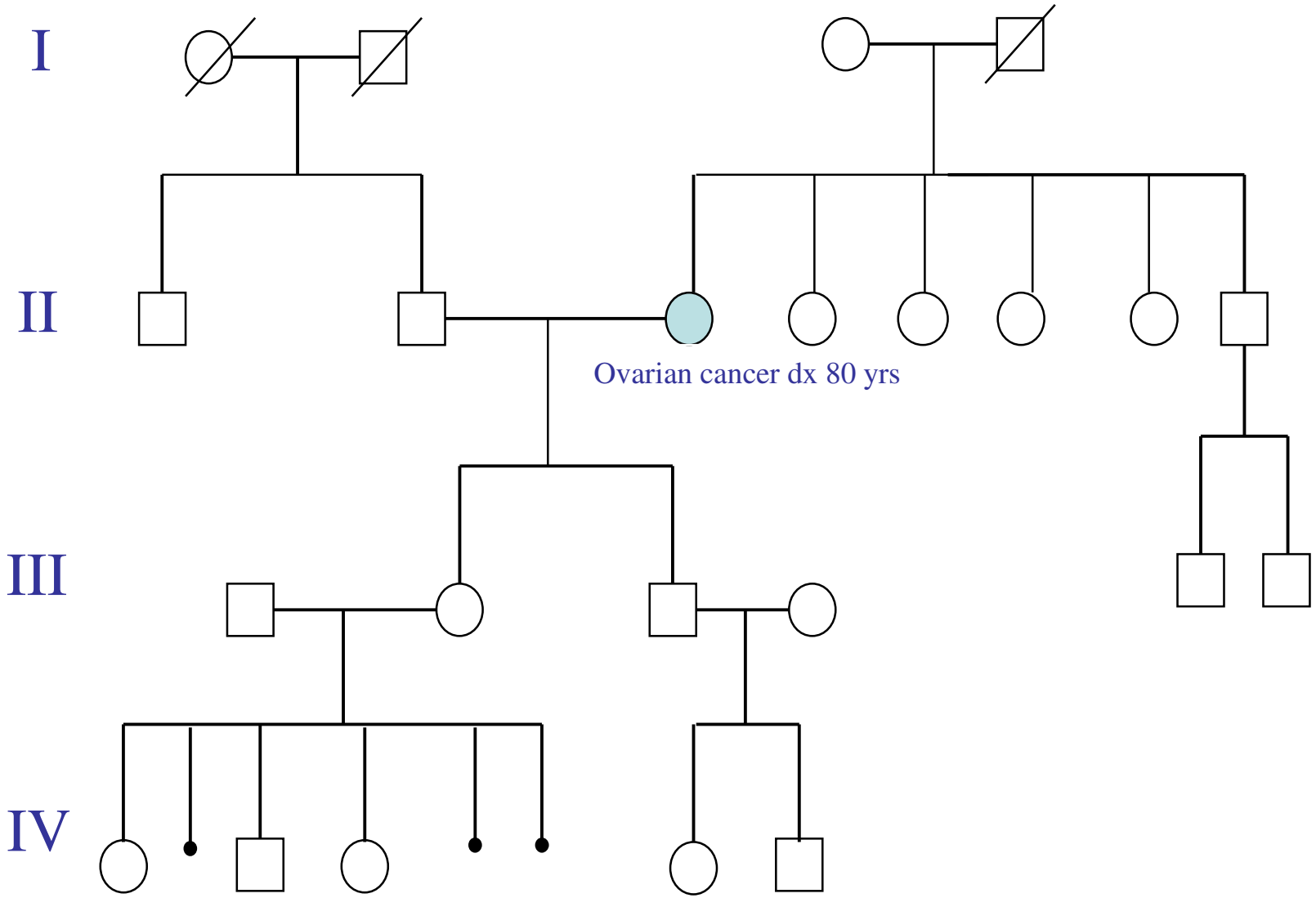
Moderately increased risk

High risk

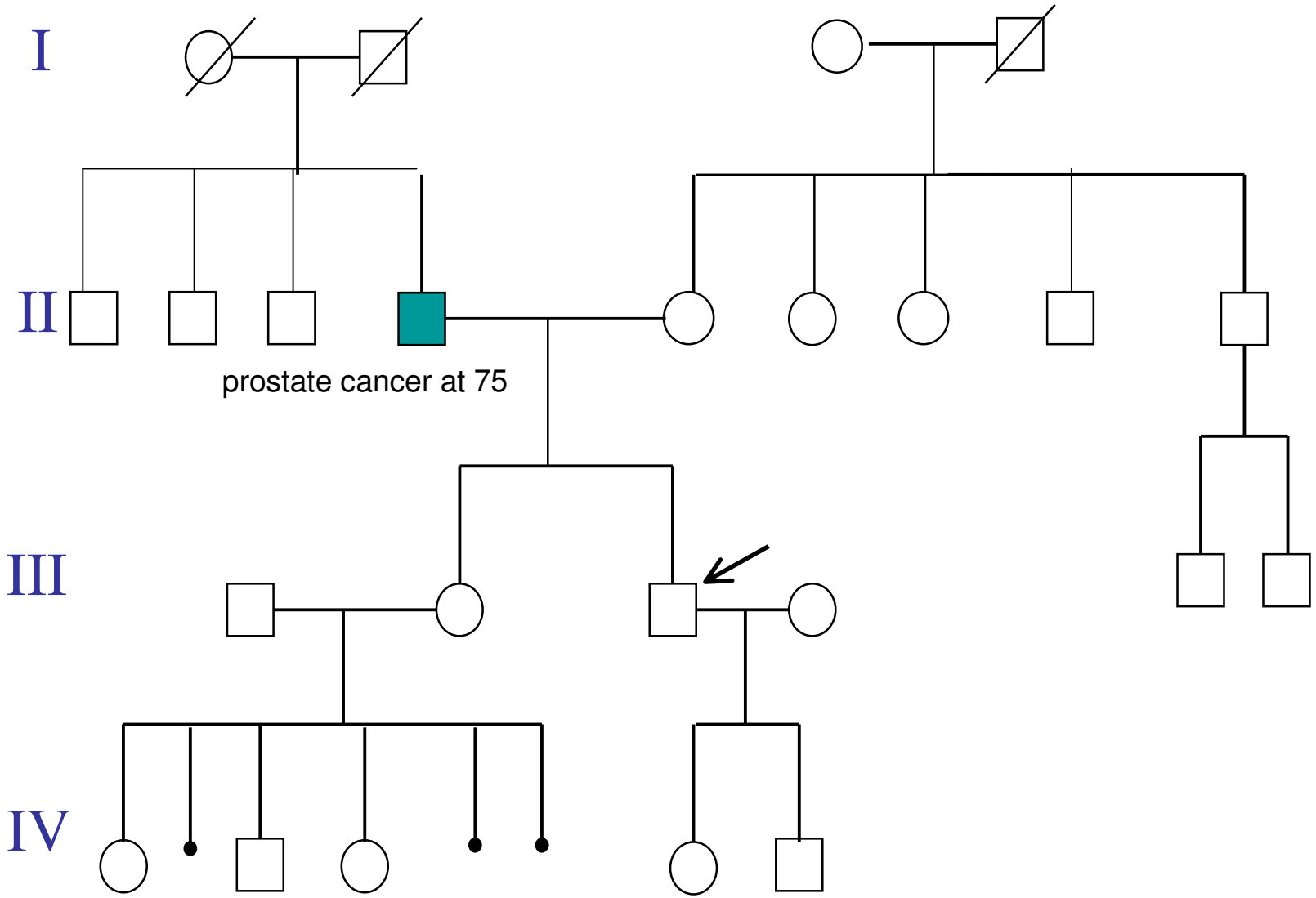
AVERAGE RISK



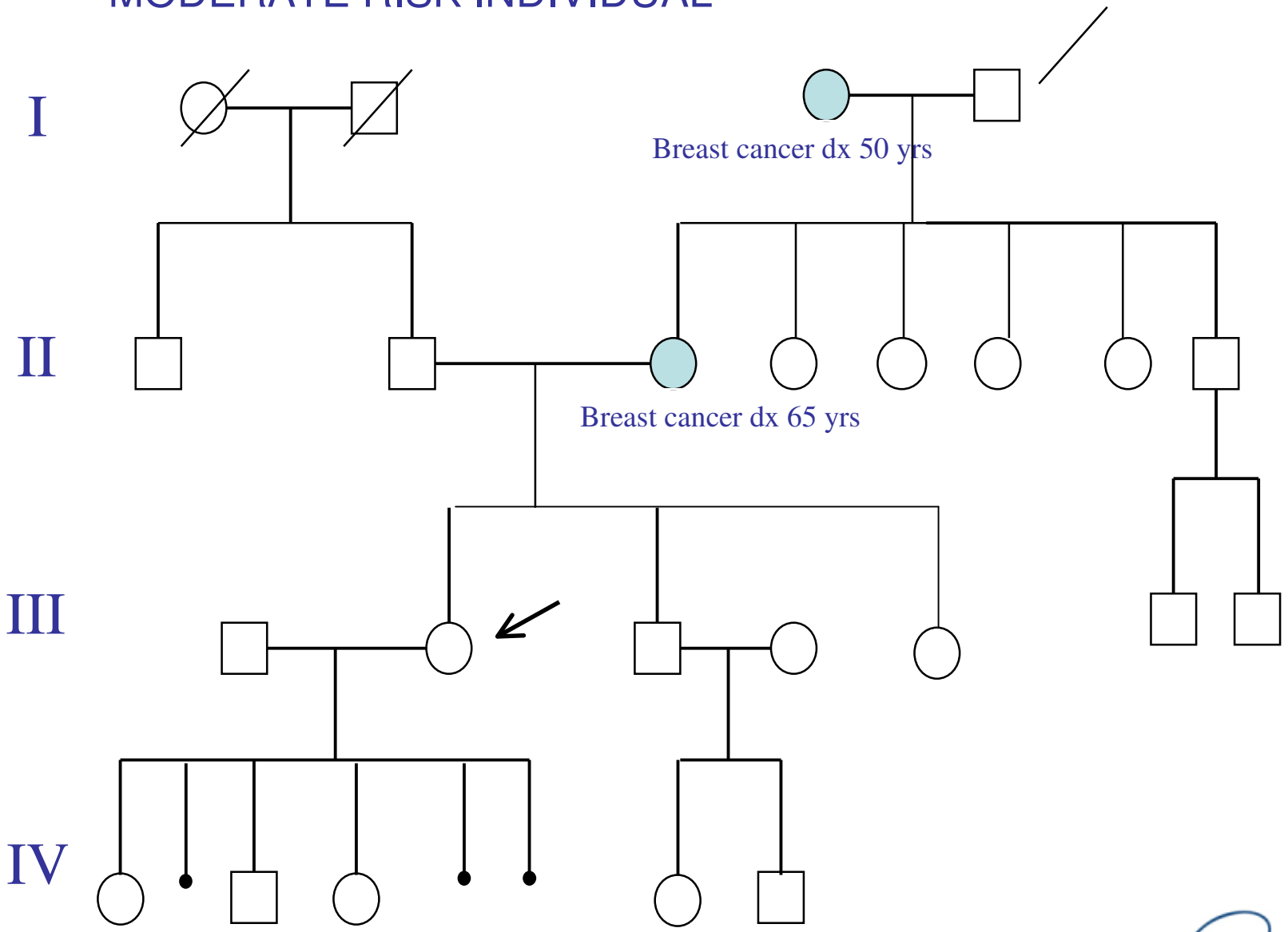
AVERAGE RISK FAMILY



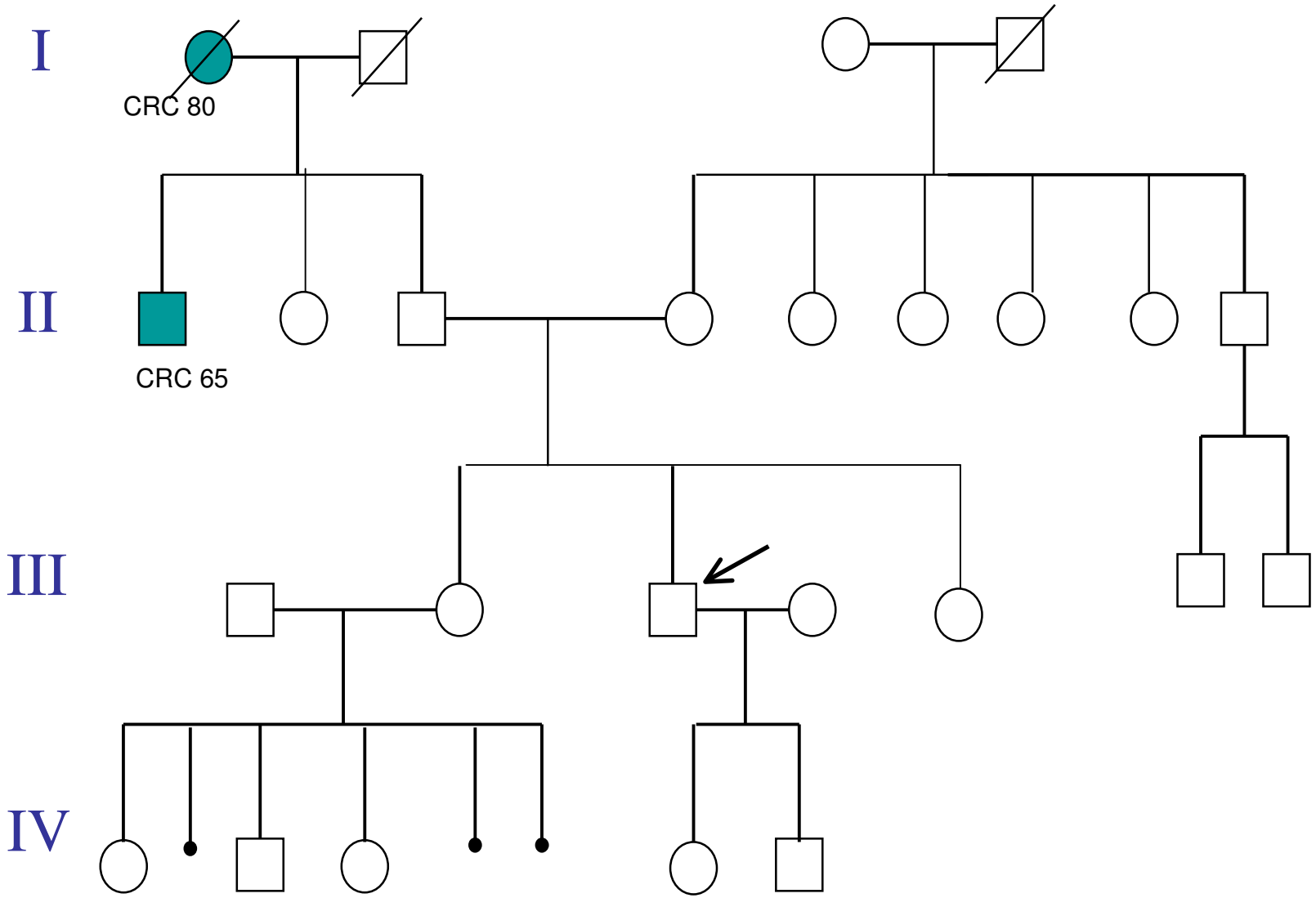
AVERAGE RISK FAMILY
AVERAGE RISK INDIVIDUAL



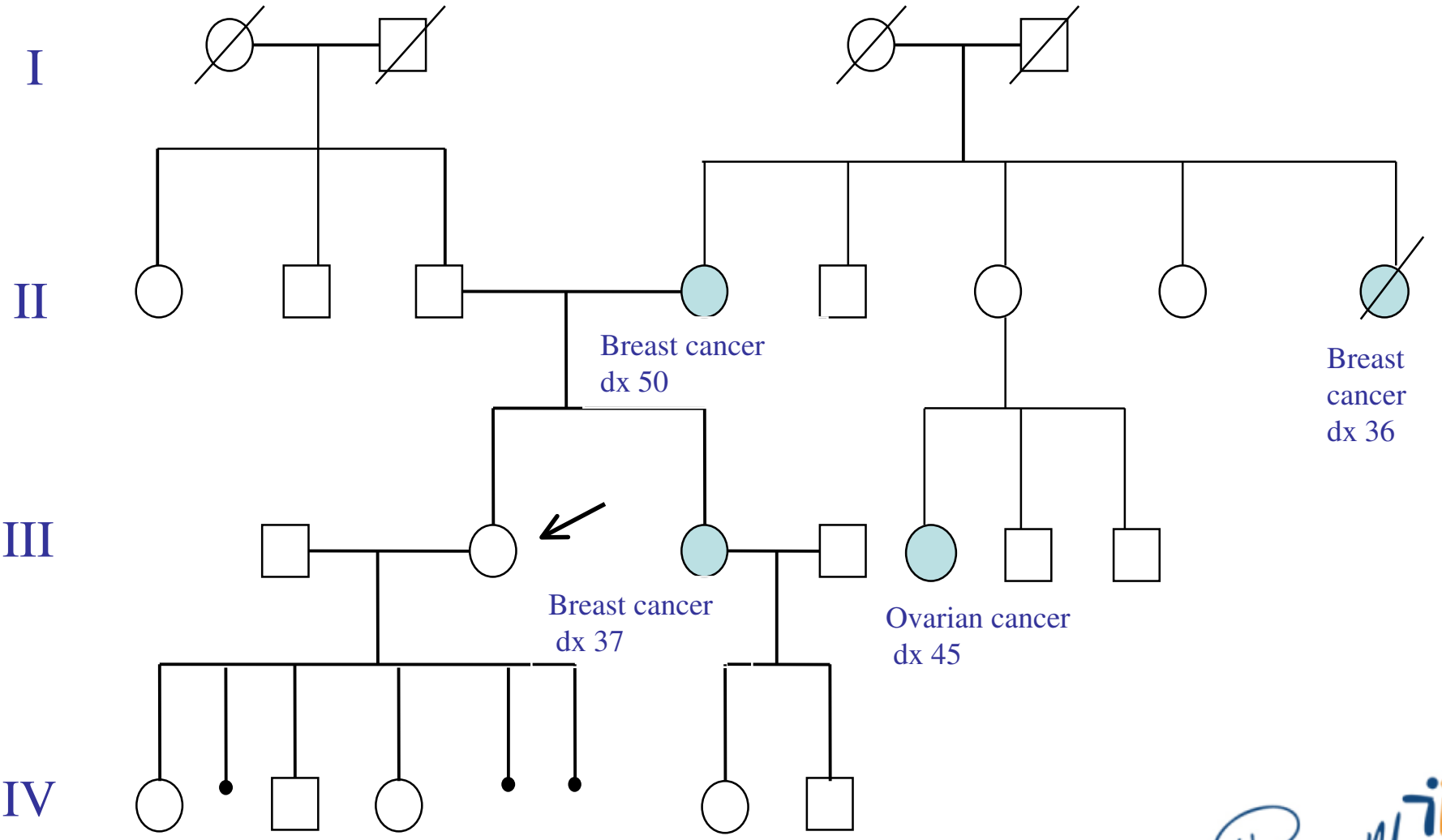
MODERATE RISK FAMILY
MODERATE RISK INDIVIDUAL



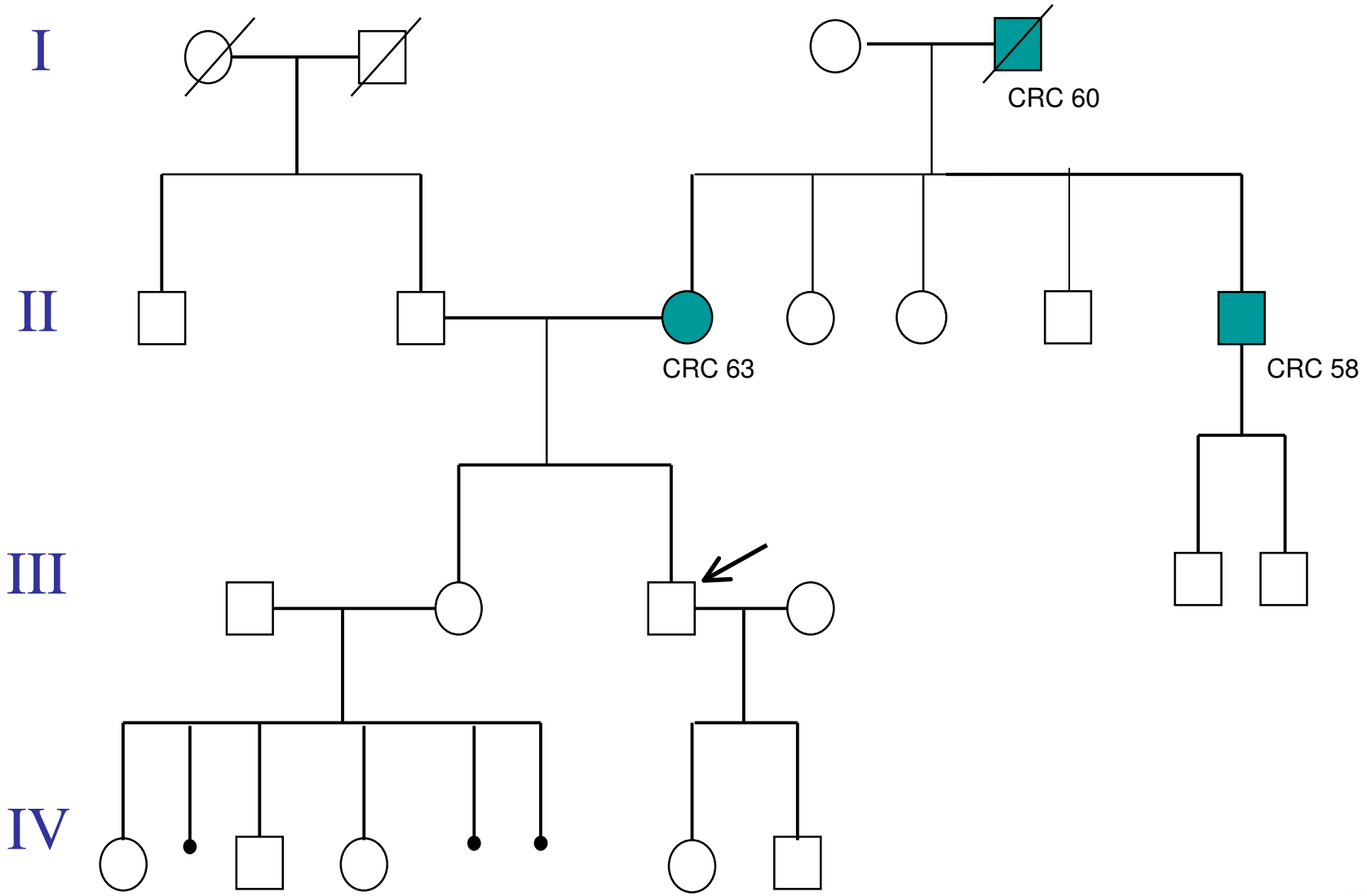
MODERATE RISK FAMILY
AVERAGE RISK INDIVIDUAL



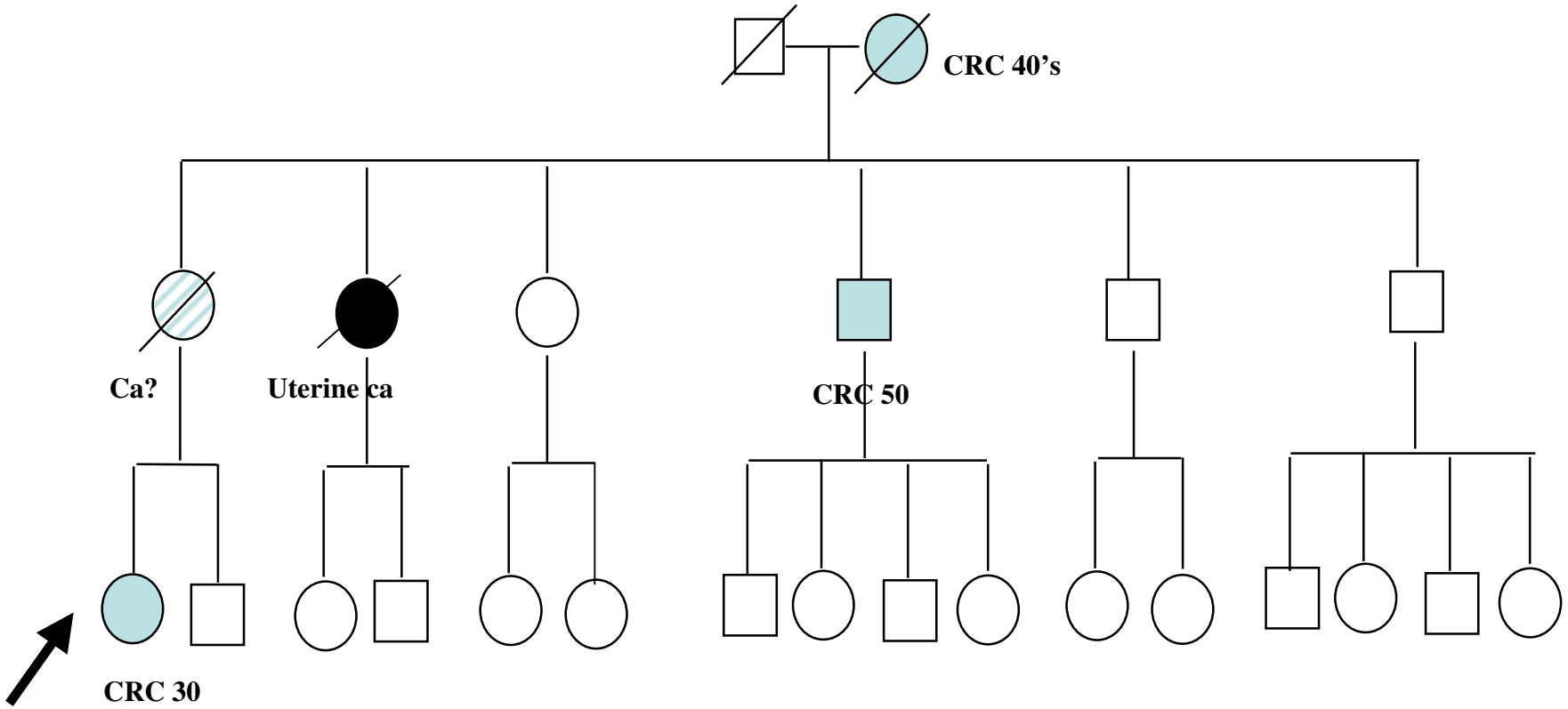
HIGH RISK FAMILY
POTENTIALLY HIGH RISK INDIVIDUAL



HIGH RISK



HIGH RISK



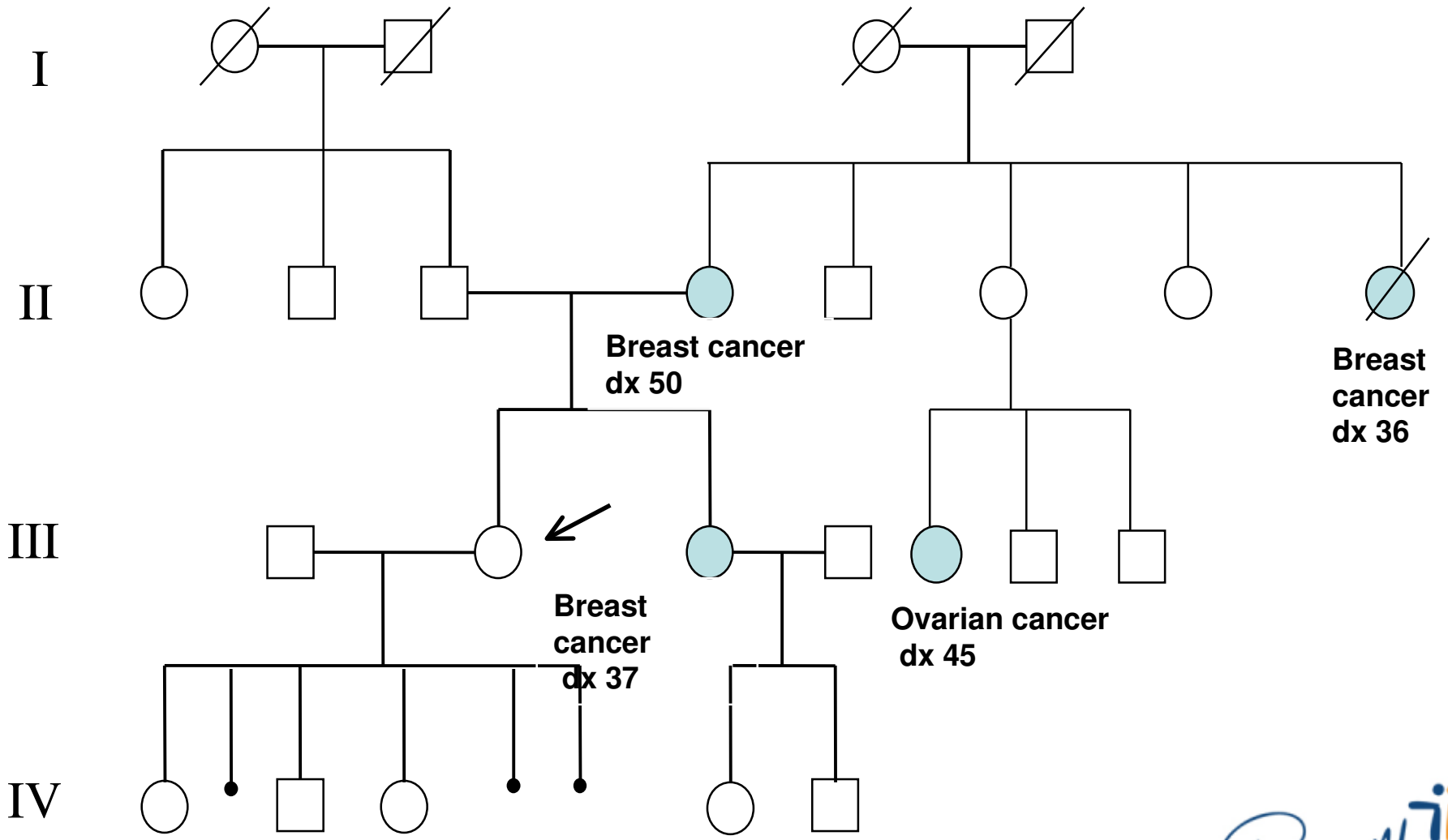
Familial Cancer Syndromes

(inherited susceptibility to develop cancer)

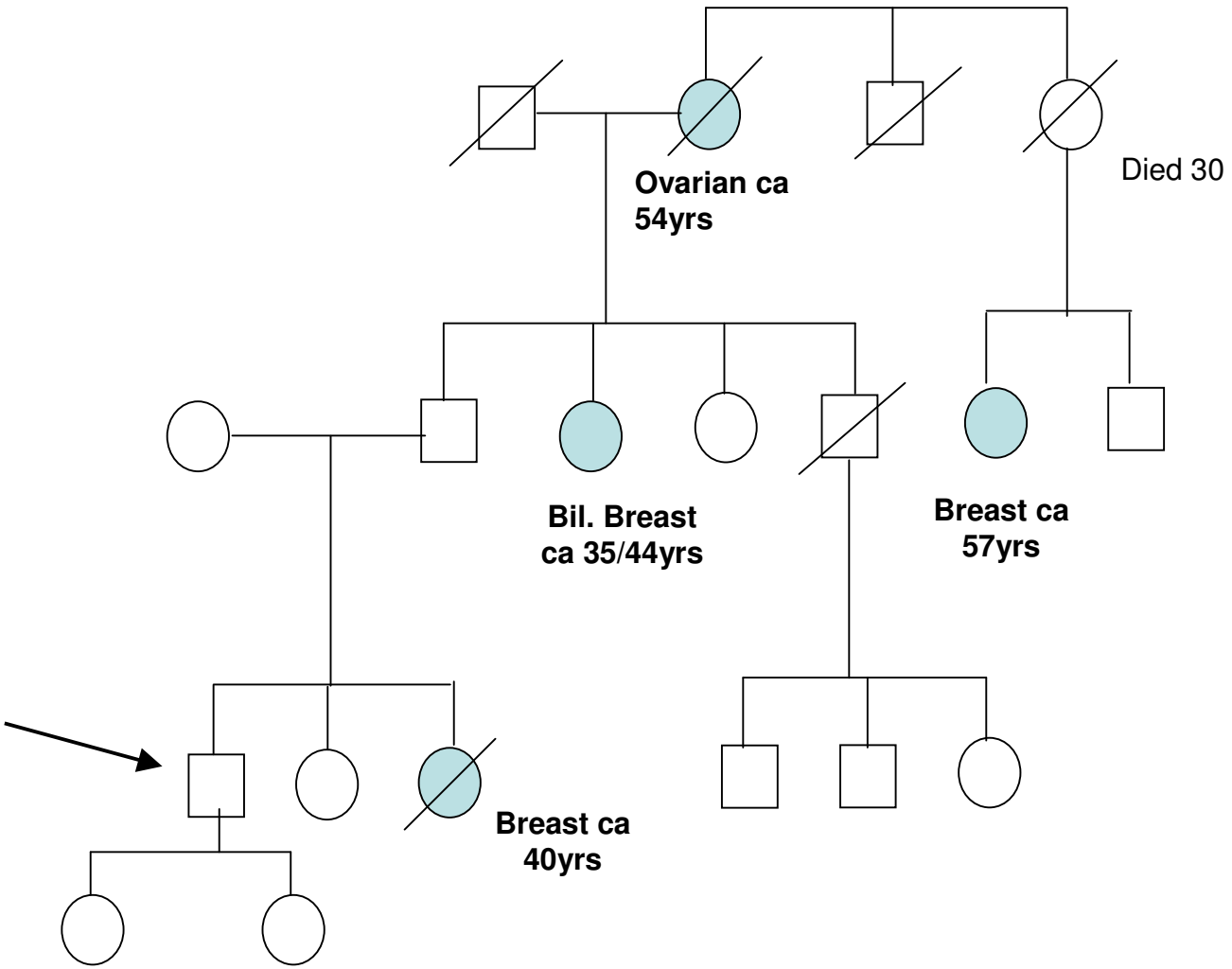
Familial Cancer Syndromes

- **Bowel cancer: HNPCC, FAP**
- **Breast cancer: BRCA1/2**
- Melanoma
- Li-Fraumeni, MEN1/2, von Hippel-Lindau

High risk of FCS



High risk FCS



Lifetime risk associated with BRCA1 and BRCA2

BRCA1

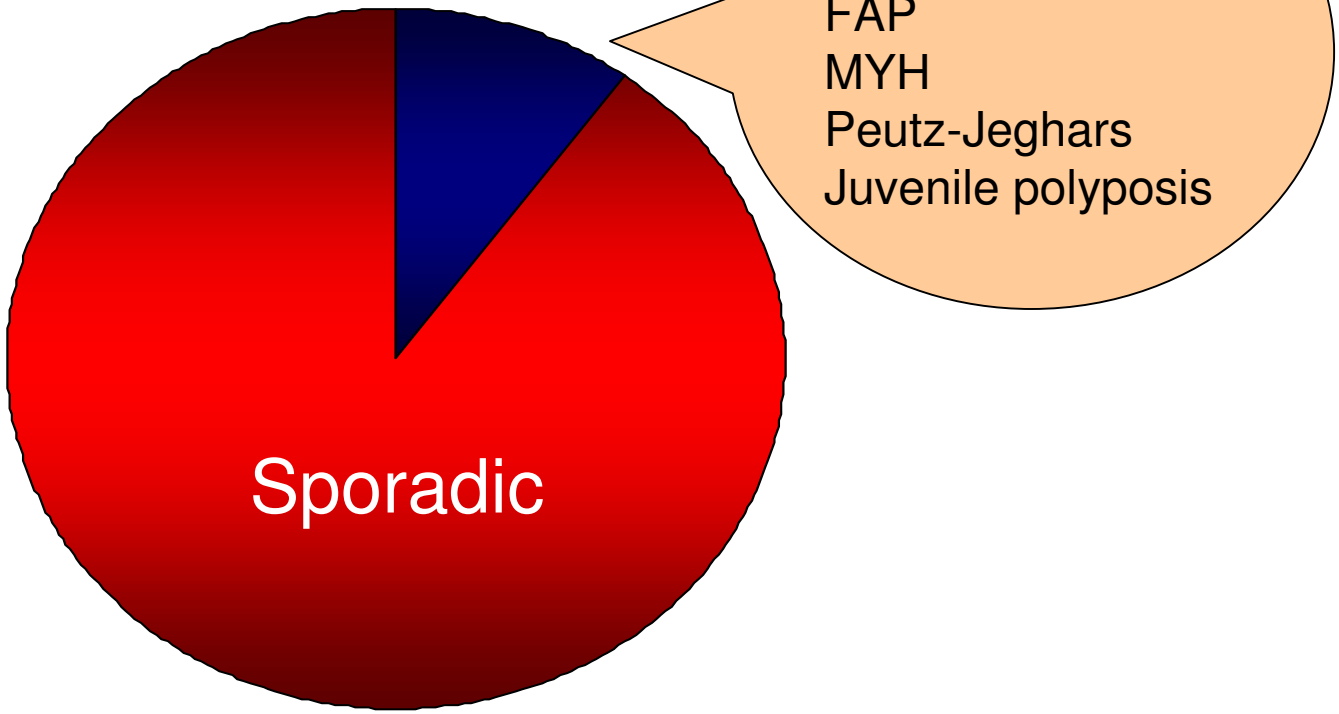
• Breast cancer risk	50-80%
• Ovarian cancer risk	10-60%

BRCA2

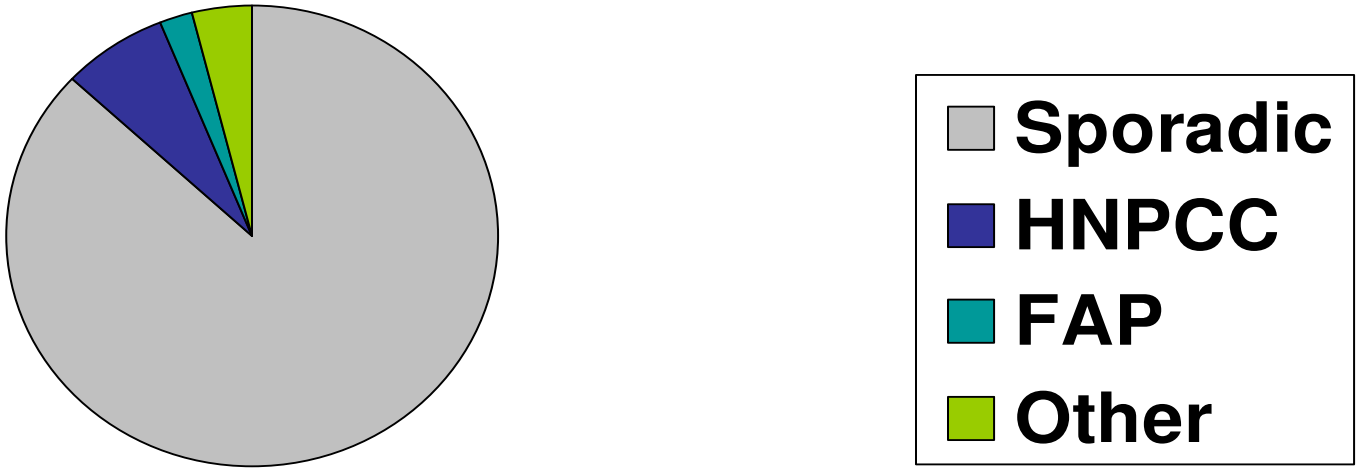
• Breast cancer risk	50-80%
• Ovarian cancer risk	10-40%
• Prostate cancer risk for males	15%
• Male breast cancer risk	6%
• Pancreatic cancer	slightly increased
• Melanoma	slightly increased

Colorectal Cancer (CRC) in Australia

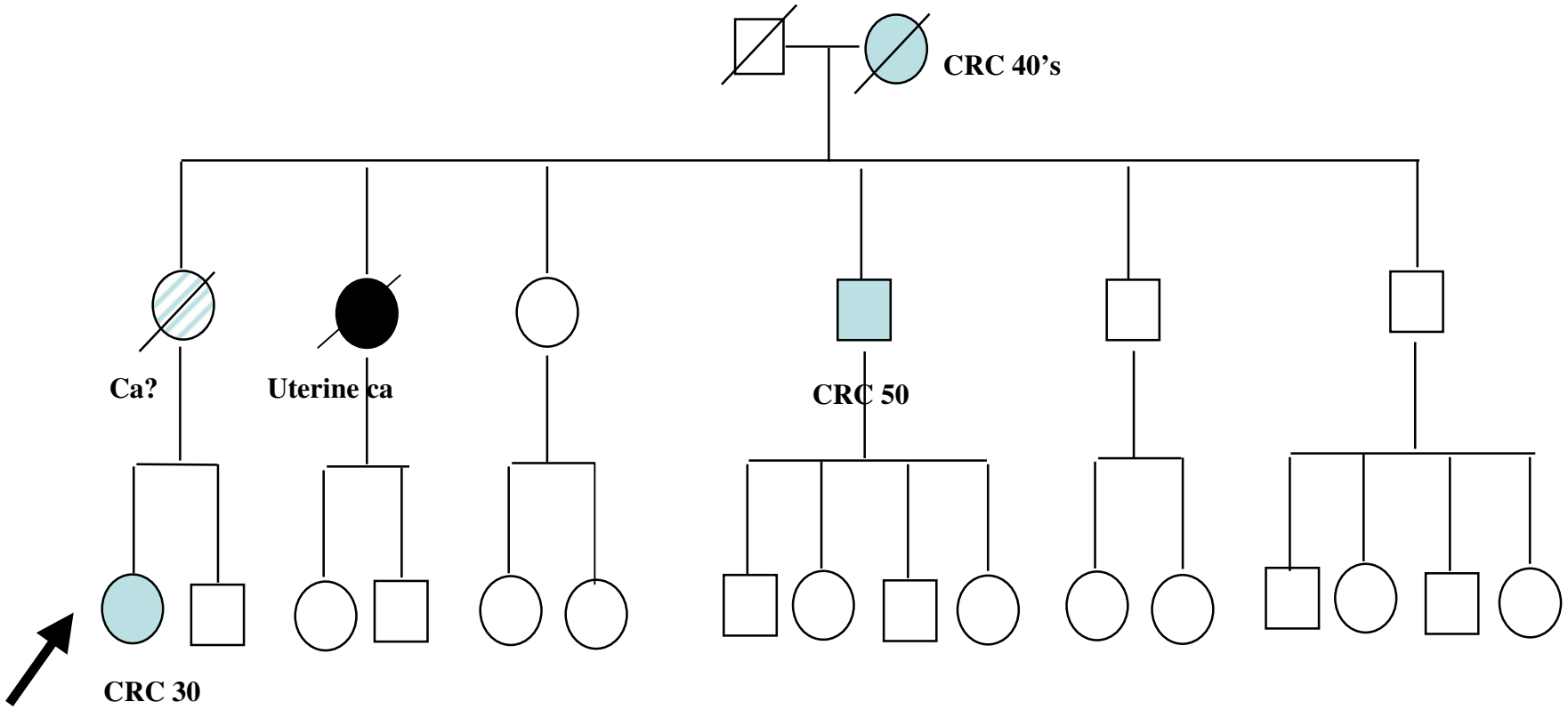
In 2003; 12,536 new cases of CRC diagnosed
>4000 people died from CRC
Loss of >30,000 years of life.



Colorectal Cancer (CRC)



HIGH RISK
LYNCH SYNDROME



LYNCH SYNDROME

	Life-time risk
Bowel cancer	80%
Endometrial	50%
Ovarian	
Transitional cell	
Small bowel	<10%
Stomach	
Biliary tract	

skin, brain, bladder, cervix

Genetic testing

- Technically complex
- Expensive
- Not available to everyone in public sector

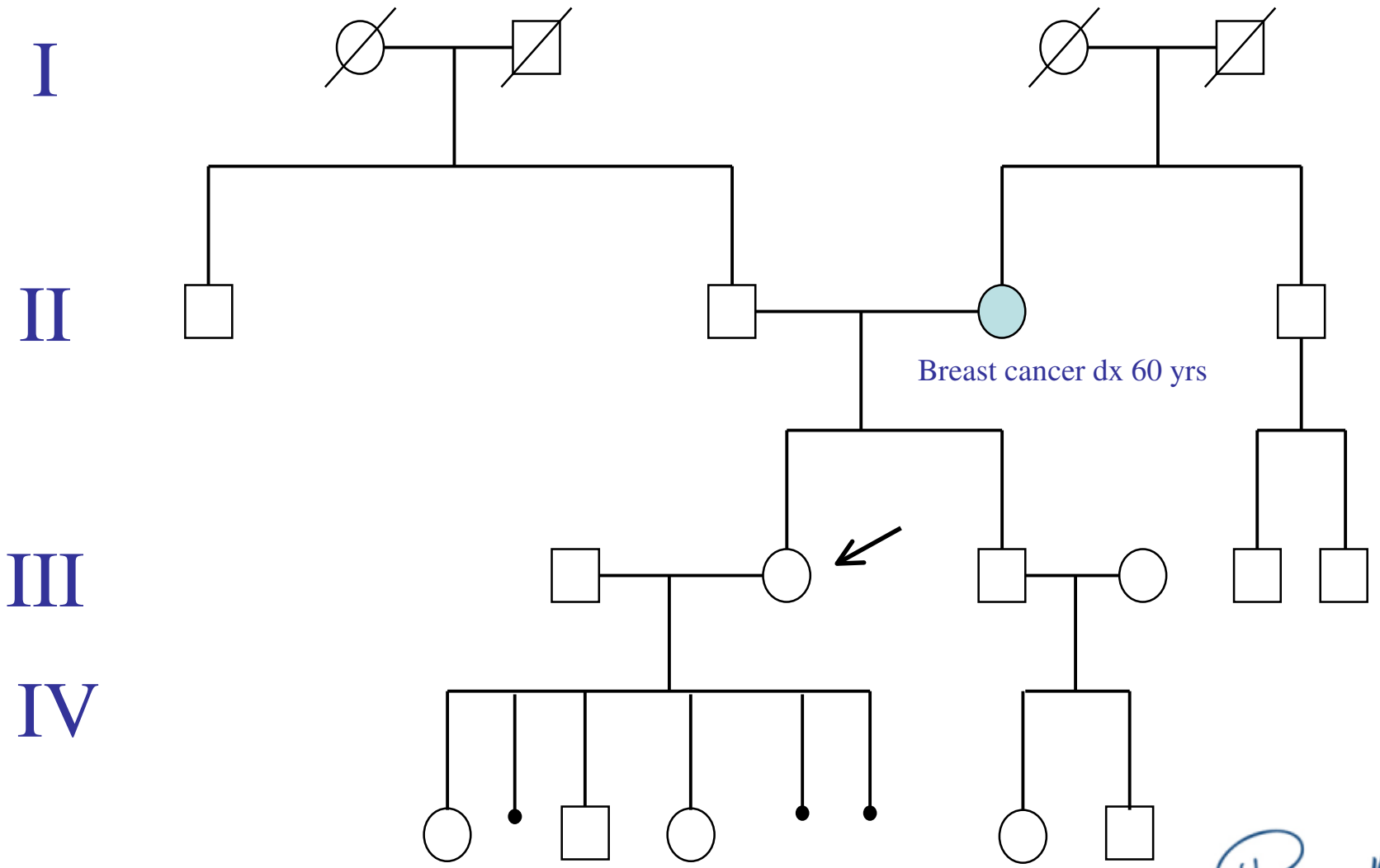
Genetic testing

- Genetic testing is a type of medical test that identifies changes in chromosomes, genes, or proteins.

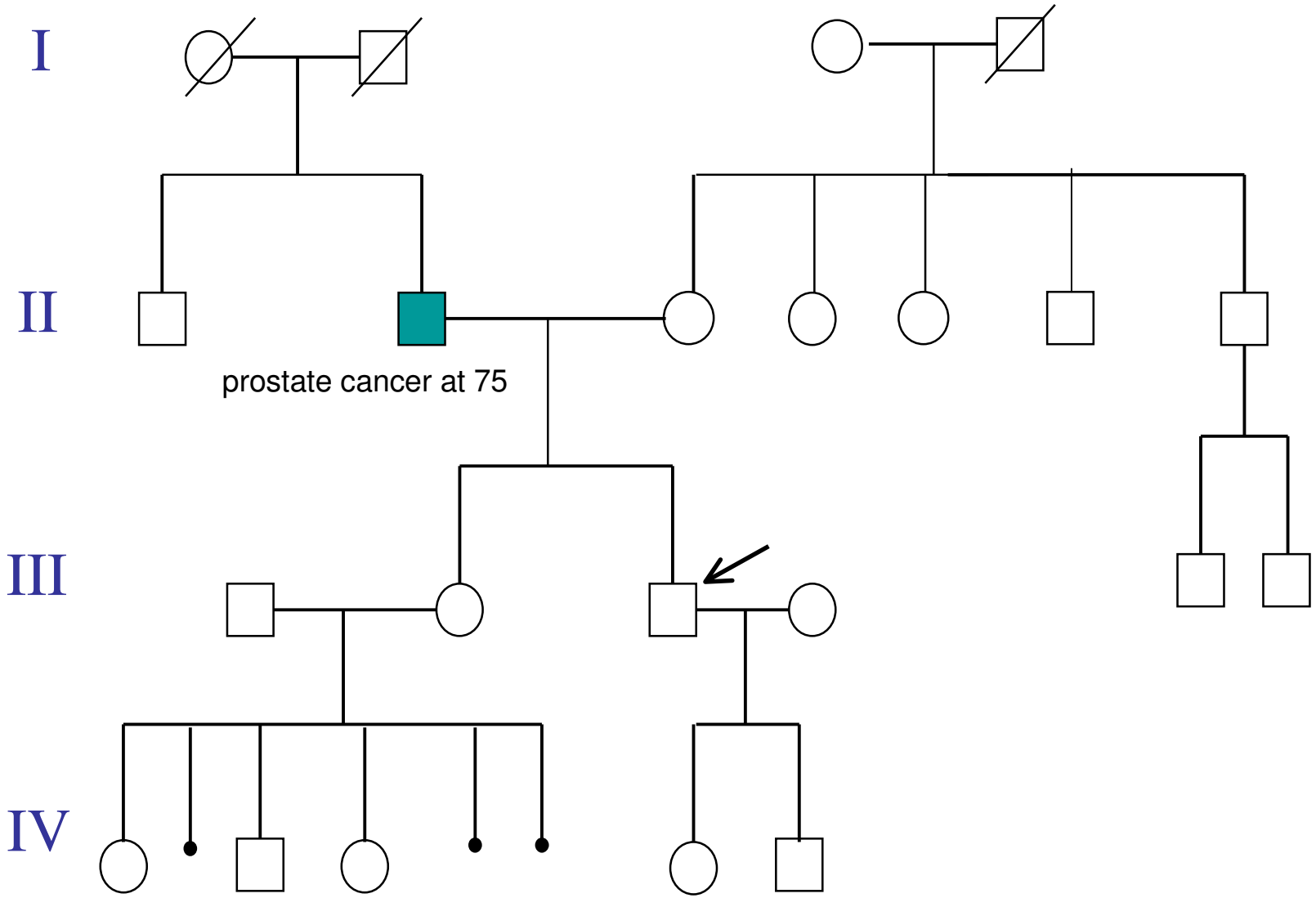
Genetic testing for familial cancer in public sector

- must have high probability of AD cancer predisposition gene - BRCA1, BRCA2, CRC genes
- must test affected family member 1st (*mutation detection*)
- if mutation found - predictive testing for unaffected family members
- no mutation - no test

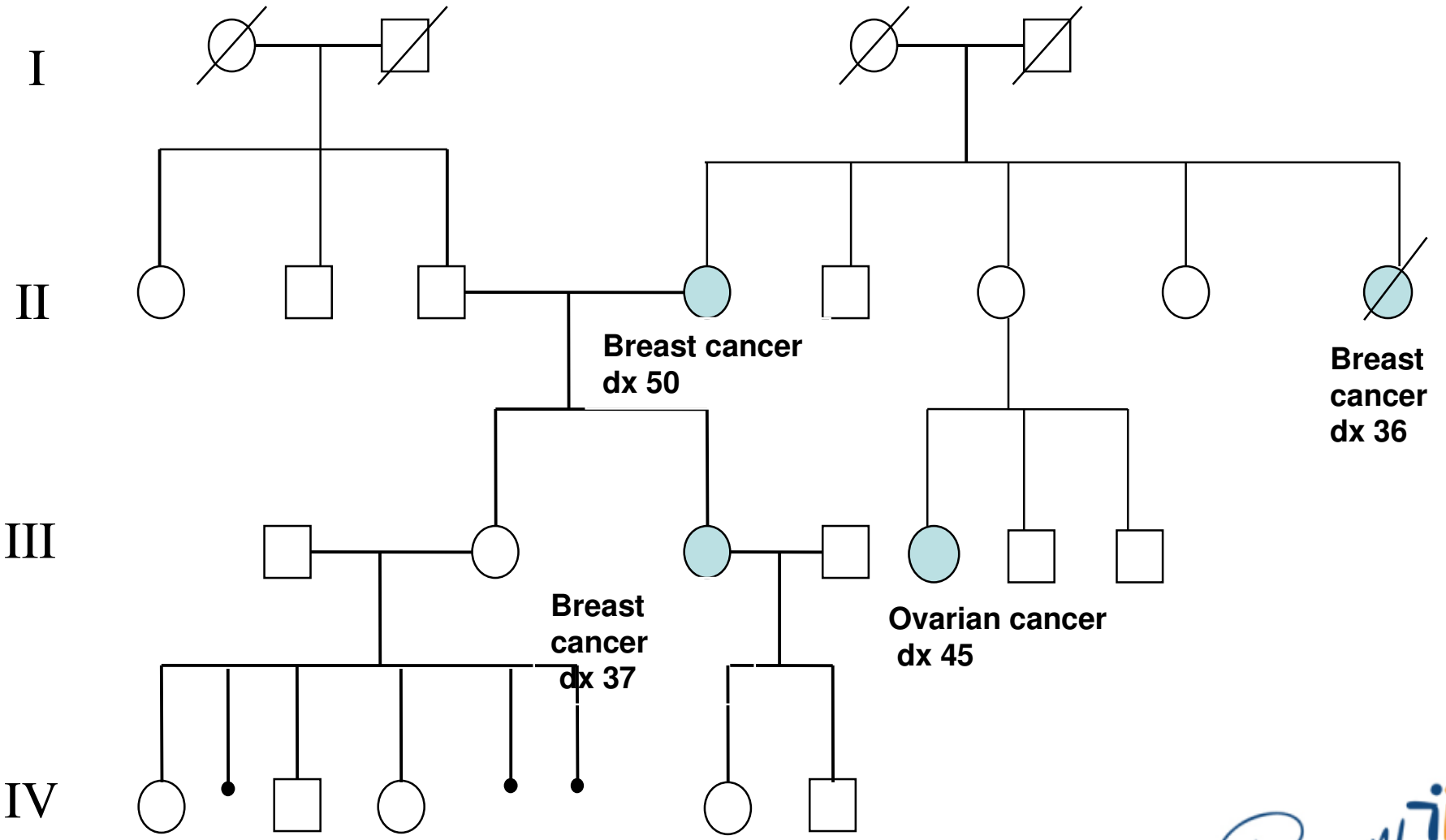
GENETIC TESTING FOR AVERAGE RISK INDIVIDUAL FOR BREAST CANCER



GENETIC TESTING FOR AVERAGE RISK FOR PROSTATE CANCER



GENETIC TESTING
HIGH RISK BRCA1/2 MUTATION



Benefits of testing for genes predisposing to cancer

Gene testing can identify individuals who carry cancer susceptibility genes

- who may benefit from regular follow up enabling early detection of cancer

- who may undergo surgery to reduce the risk of a cancer ever developing

Benefits of testing for cancer predisposing genes

Gene testing can identify individuals who do not carry cancer susceptibility genes

- may relieve anxiety
- avoiding unnecessary follow up
- enabling the resources to be used for the benefit of gene carriers at high risk of cancer

Problems in testing for cancer predisposing genes

- Not everyone who carries a cancer susceptibility gene will develop cancer

- a person who does not carry a gene will still have the population risk of developing cancer
  - breast cancer 10% life-time risk
  - ovarian cancer 2% life-time risk
  - bowel cancer 5% life-time risk

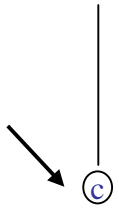
- Psychosocial / ethical issues

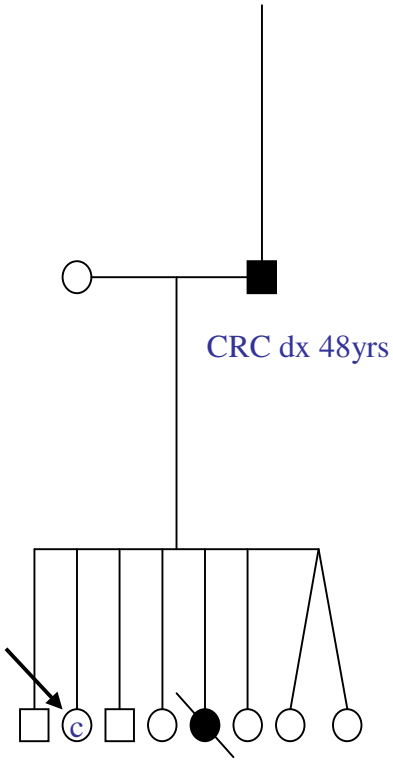
Importance of genetic testing from a public health perspective

Each hereditary cancer comes from a family that would benefit from

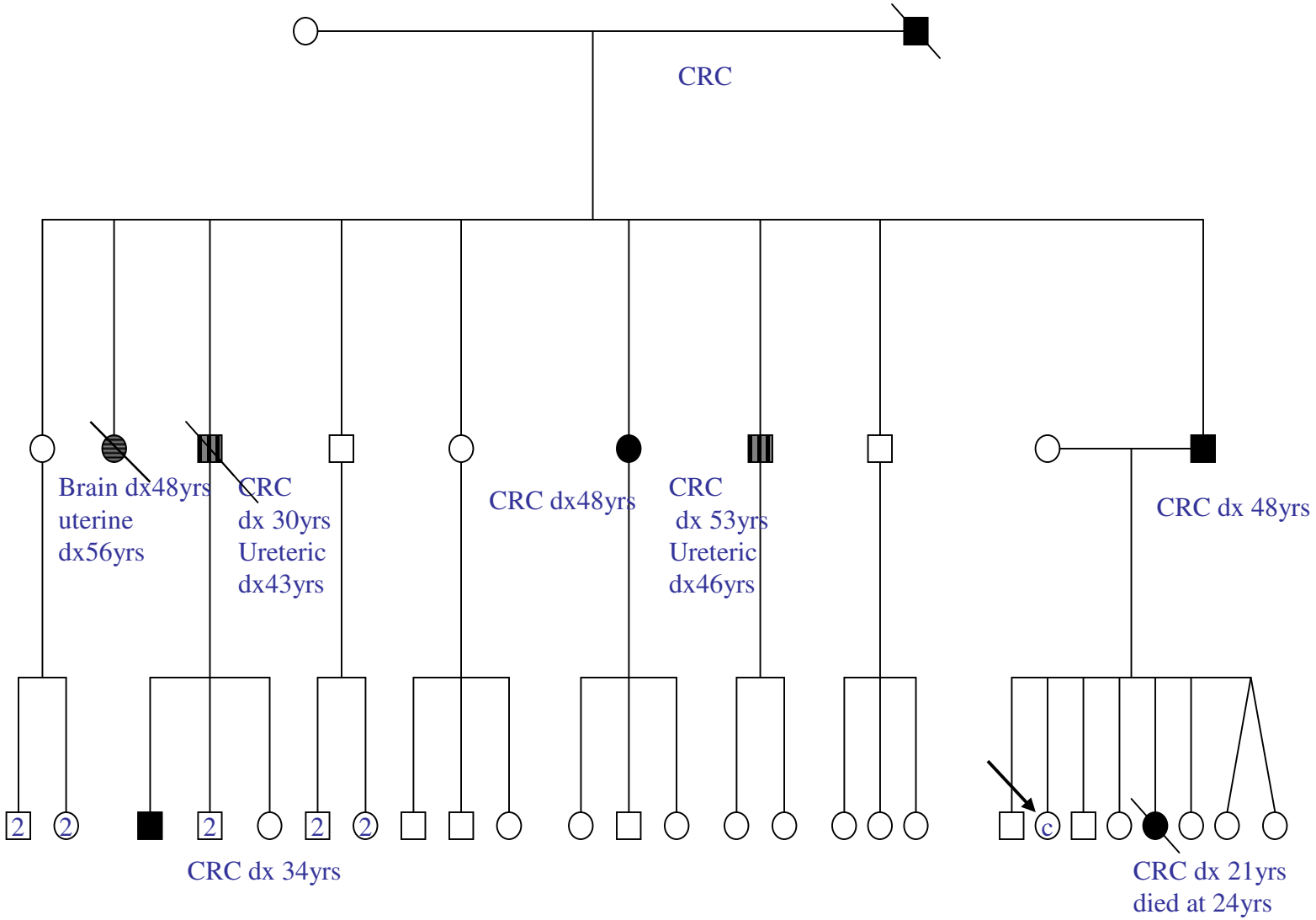
- genetic counselling
- DNA testing
- surveillance
- highly targeted management

SIGNIFICANCE OF FAMILY OFTEN MISSED/UNDERESTIMATED




CRC dx 48yrs
c
CRC dx 21yrs
died at 24yrs

SIGNIFICANCE OF FAMILY



When to refer – GP's role

- GPs should manage low/population risk patients
- For moderate to high risk patients – *refer to a Family Cancer Centre*
- When unsure about familial risk – *contact a Family Cancer Centre*
- Phone, fax or write a letter of referral
- Patients can also self refer to a FCC

FCC's

Peter Mac,
Royal Melbourne,
Monash Medical Centre and
Austin Hospital

FCC encourages individuals to call with any questions re F/H

FCC at Peter Mac call **9656 1199**

FCC in Bendigo **5454 8822**
(Morgan Murphy)

Clinic at Bendigo monthly,

Mildura 3 monthly

Process at an FCC

- Construction/verification of accurate, extended pedigree
- Risk assessment
- Communication of risk
- Offer genetic testing (if appropriate)
- Discuss strategies for early detection / risk reduction
- Ongoing risk management

Summary

- For most people, having a family history of cancer will not alter their personal risk of developing the disease

- To have an inherited a single gene which gives a predisposition to develop cancer is uncommon

- If any questions, please call an FCC

FCC's

Peter Mac,
Royal Melbourne,
Monash Medical Centre and
Austin Hospital

FCC encourages individuals to call with any questions re F/H

FCC at Peter Mac call **9656 1199**

FCC in Bendigo **5454 8822**
(Morgan Murphy)

Clinic at Bendigo monthly,

Mildura 3 monthly