
Ovarian Cancer: Genetic Counseling and Testing, Screening and Prevention

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Familial Risk for Ovarian

- Major risk and minor risk genes
- Hereditary cancer risk
- Sometimes source of cancer risk can be identified
- Targeted management plan to lower risk and maximize chances for early detection

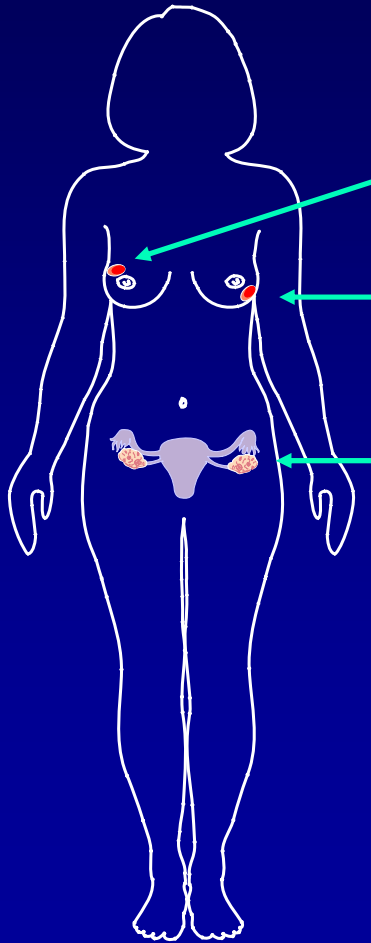
Family History of Ovarian Cancer

- Average woman risk of ovarian cancer is 1-2%
- One close relative with ovarian cancer
 - Mother, sister
 - Lifetime risk is 3-5%
- Two close relatives with ovarian cancer
 - Lifetime risk is about 20%

Hereditary Risk for Ovarian Cancer

- Single gene conferring significant risk
- *BRCA1* and *BRCA2*
- Lynch Syndrome (*MLH1*, *MSH2*, *MSH6*, *PMS2*)

BRCA1-Associated Cancers: Lifetime Risk



Breast cancer 60%–80% (often early age at onset)

Second primary breast cancer 40%–60%

Ovarian cancer 30-45% Slightly increased risk of
Uterine and Cervical cancer

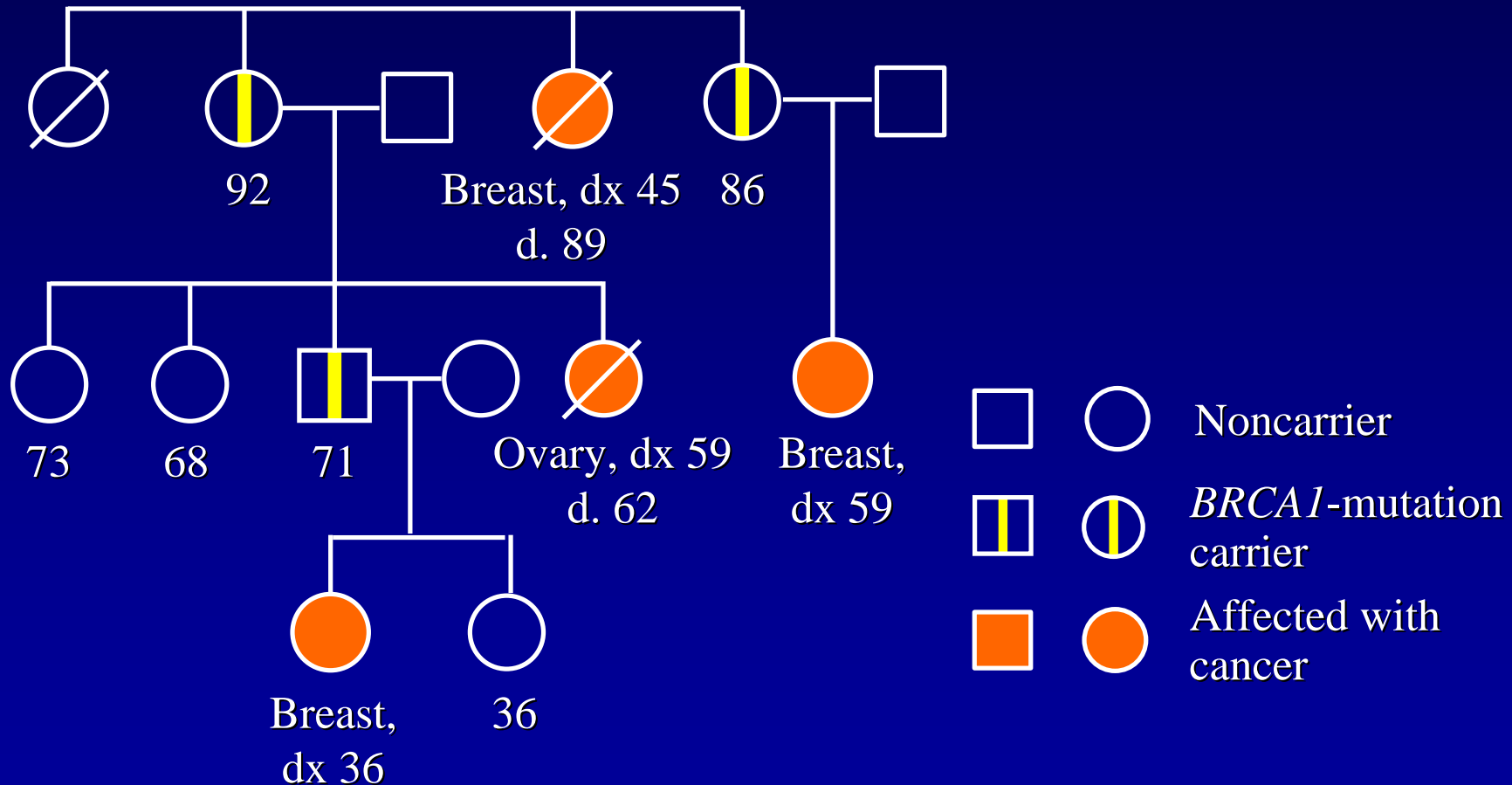
Increased risk of other cancers:

Colon: 10-15%

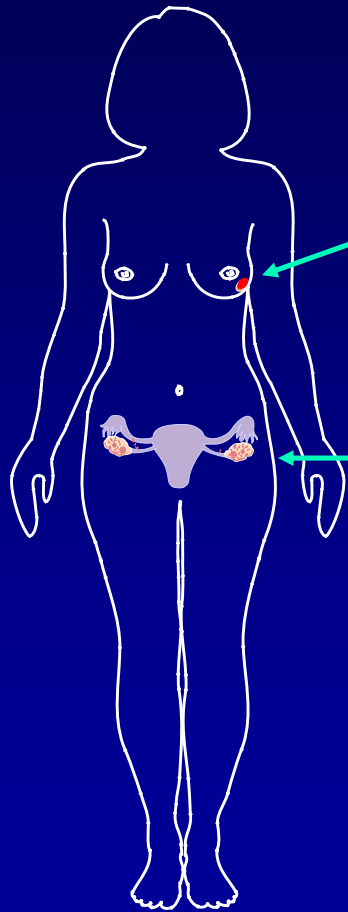
Male breast cancer: 1-5%

Pancreatic 2-3%

BRCA1-Linked Hereditary Breast and Ovarian Cancer



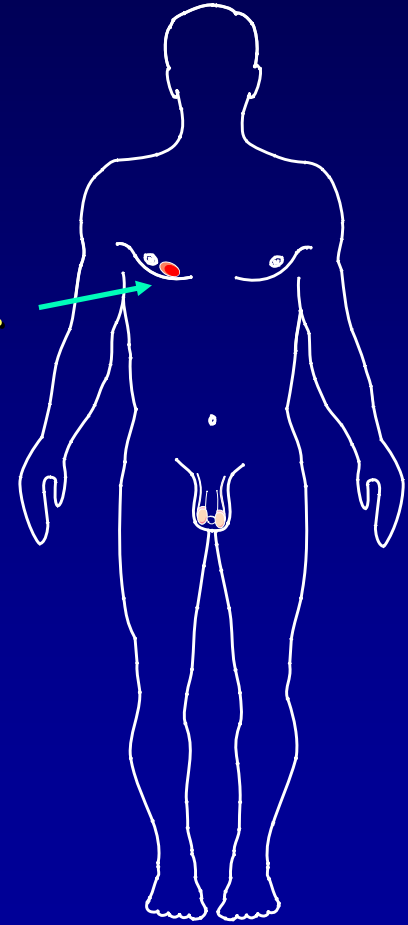
BRCA2-Associated Cancers: Lifetime Risk



breast cancer
(60%–80%)

ovarian cancer
(10%–20%)

male breast cancer
(5-10%)



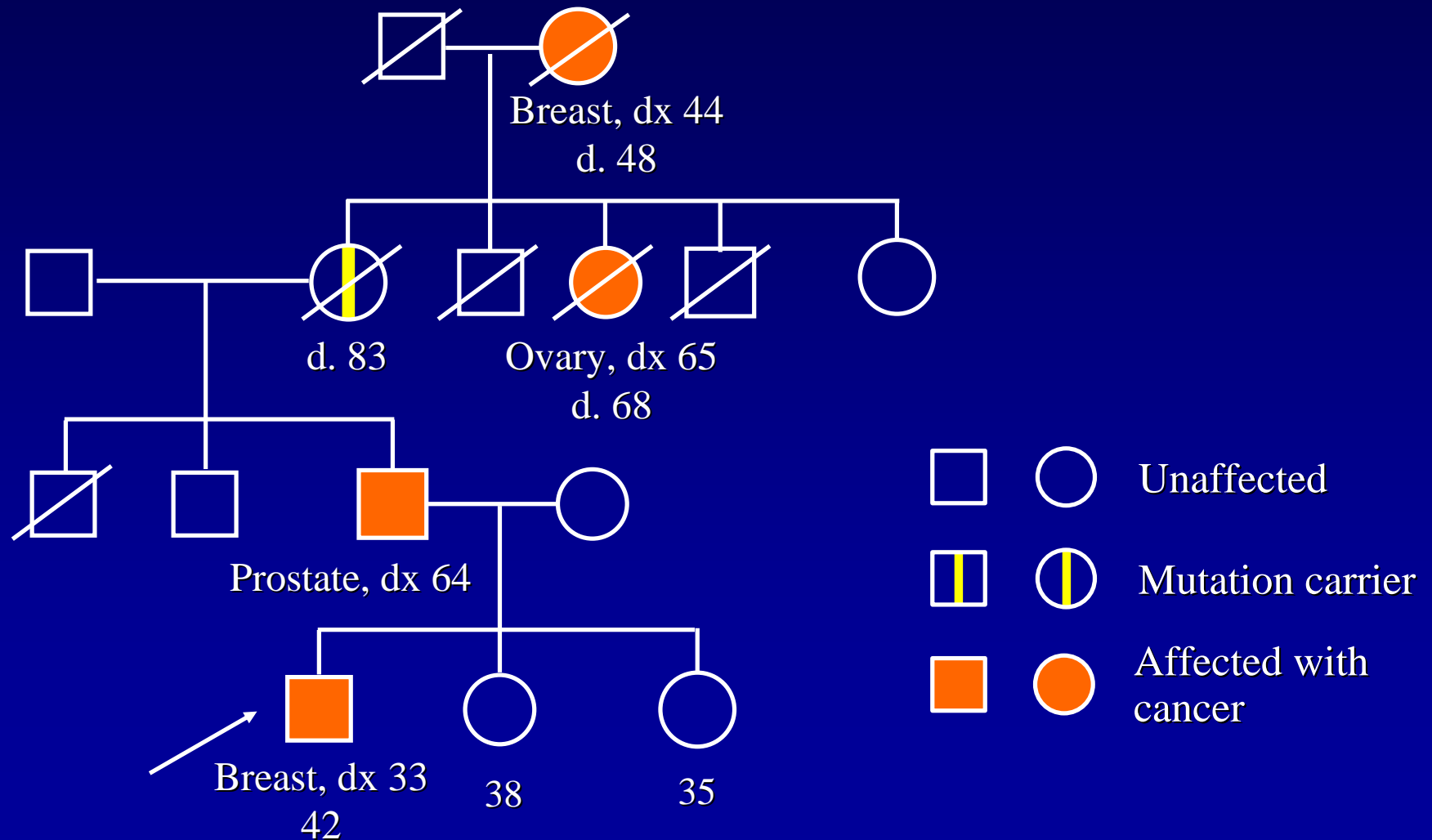
Other increased risks:

Prostate: 15-25%

Pancreatic: 3-5%

Melanoma: 3-5%

BRCA2-Linked Hereditary Breast Cancer



Clinical Management of BRCA Mutation-Positive Patient

Breast Screening starting at age 25

Mammography	Every 12 months
Clinical Breast Exams	Every 6 months
Breast Self Exam	Every month
MRI screening	Every 12 months (Alternate with mammos)

Ovarian Screening starting at age 30

CA-125	Every 6-12 months
Transvaginal ultrasound	Every 6-12 months

Preventative Surgery

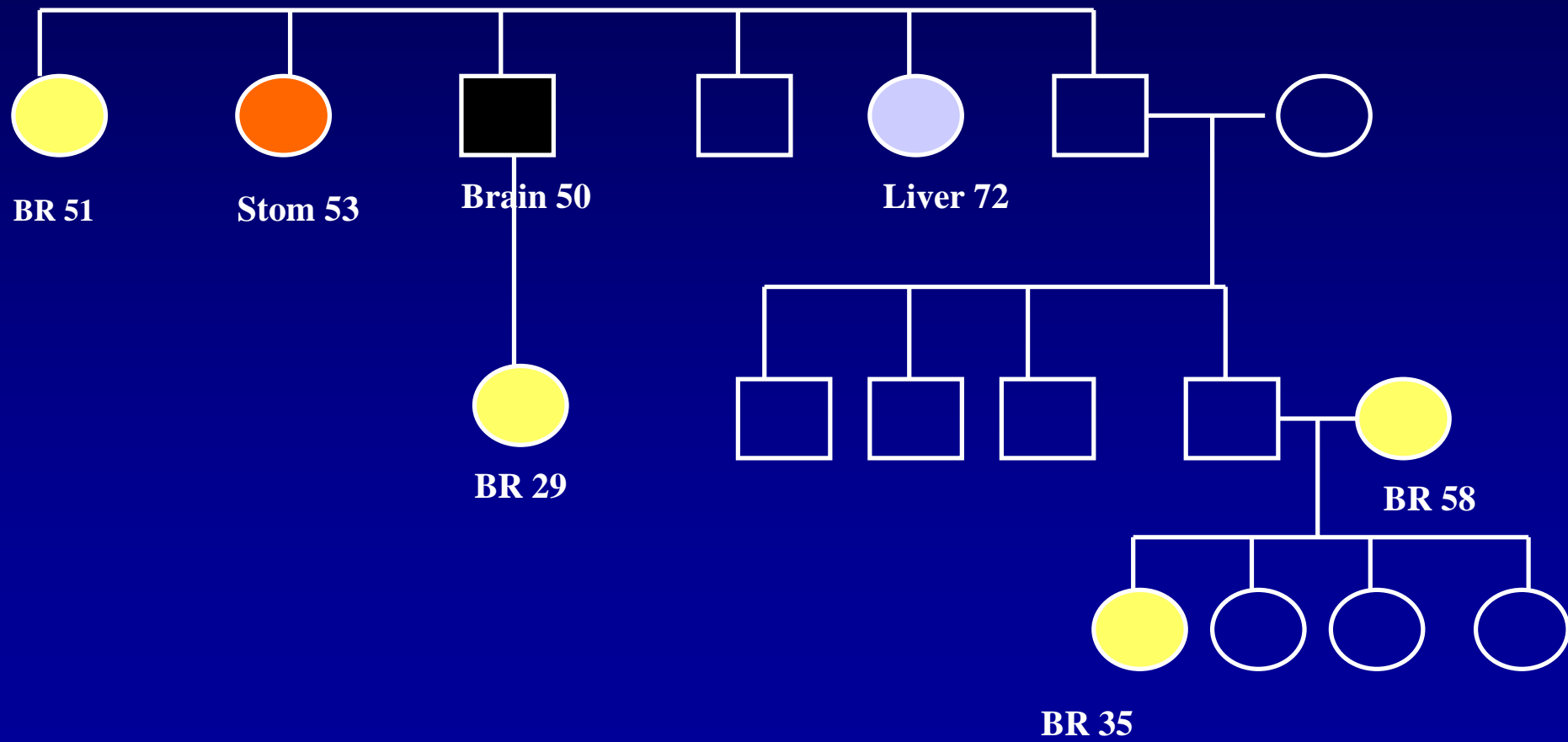
Prophylactic Mastectomy

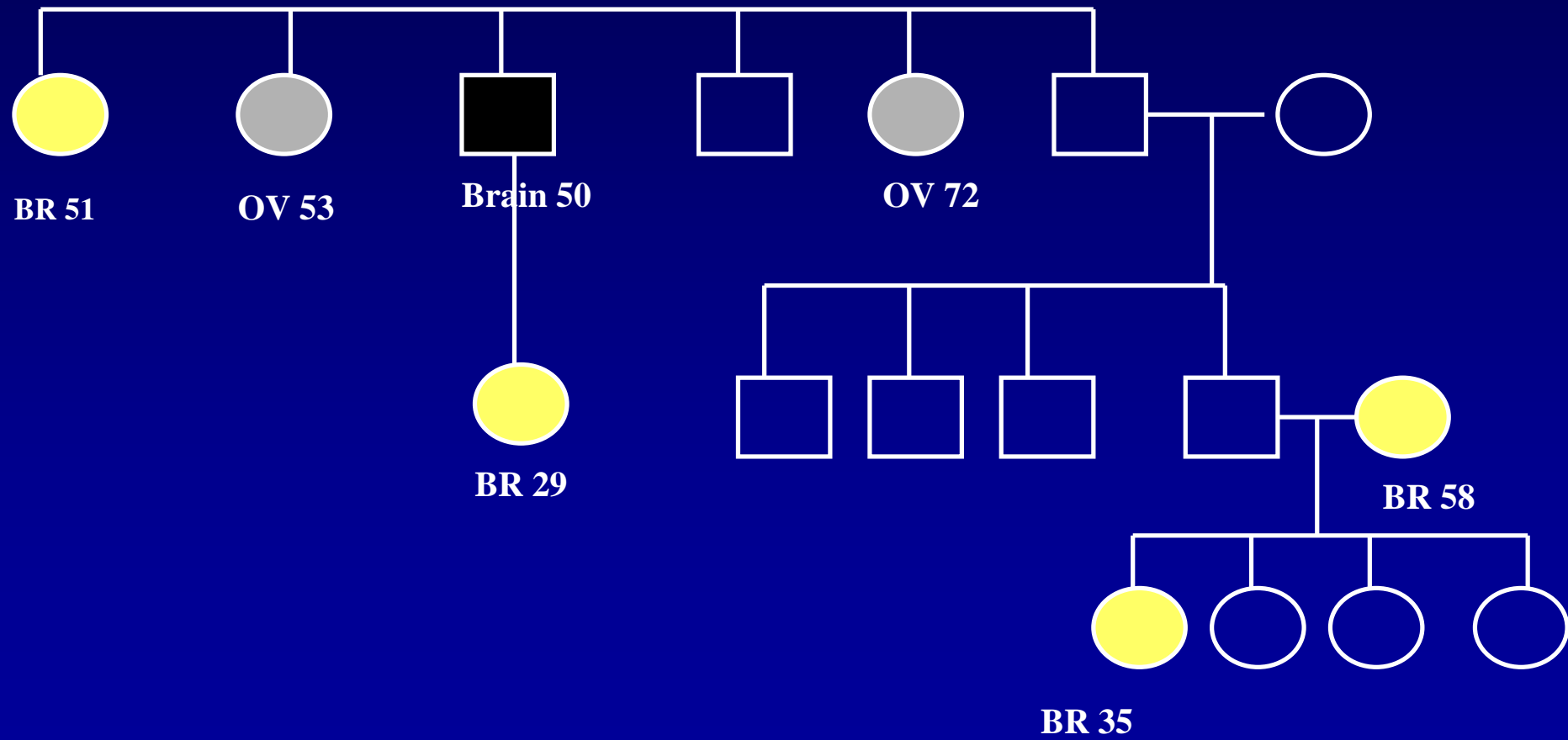
- At least 90% risk reduction
- Subcutaneous mastectomy not recommended

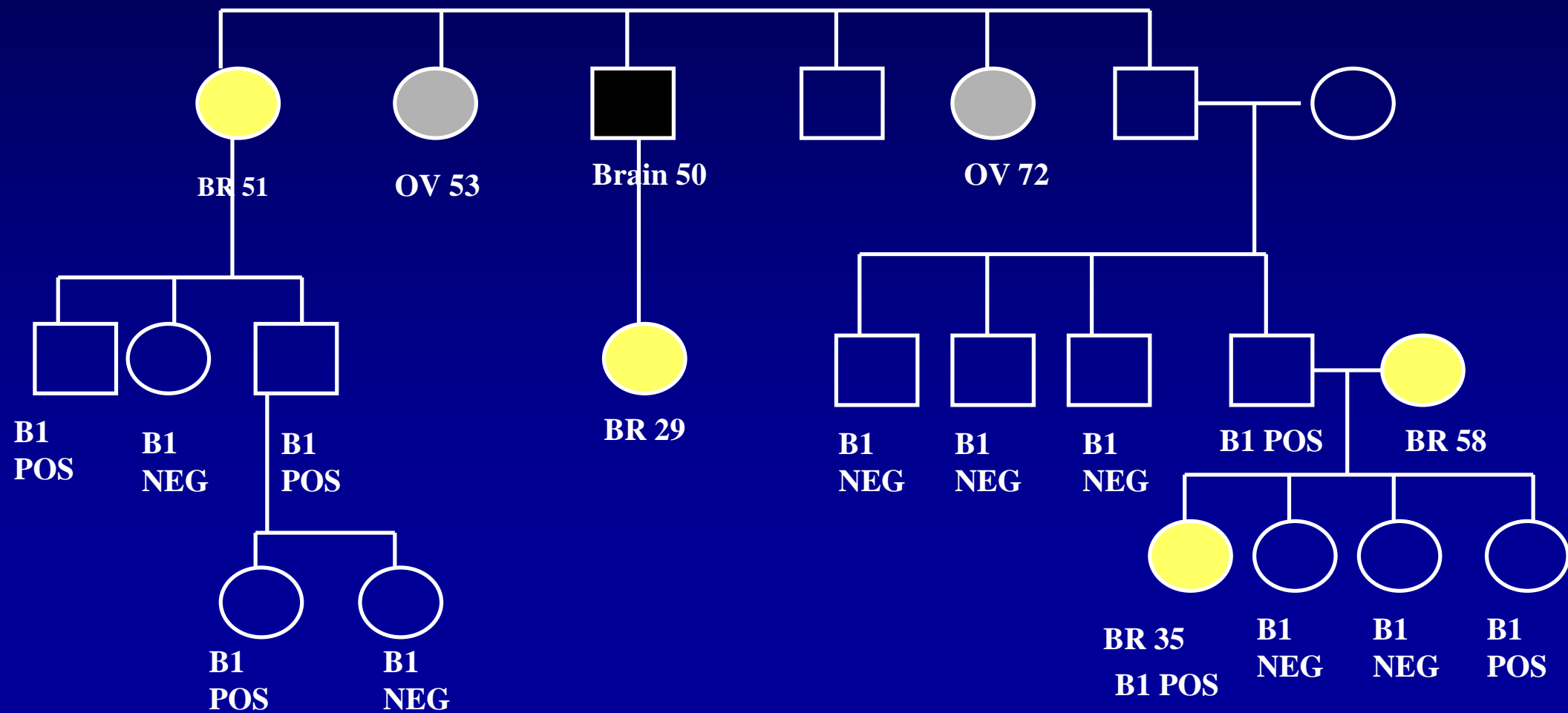
Prophylactic Oophorectomy

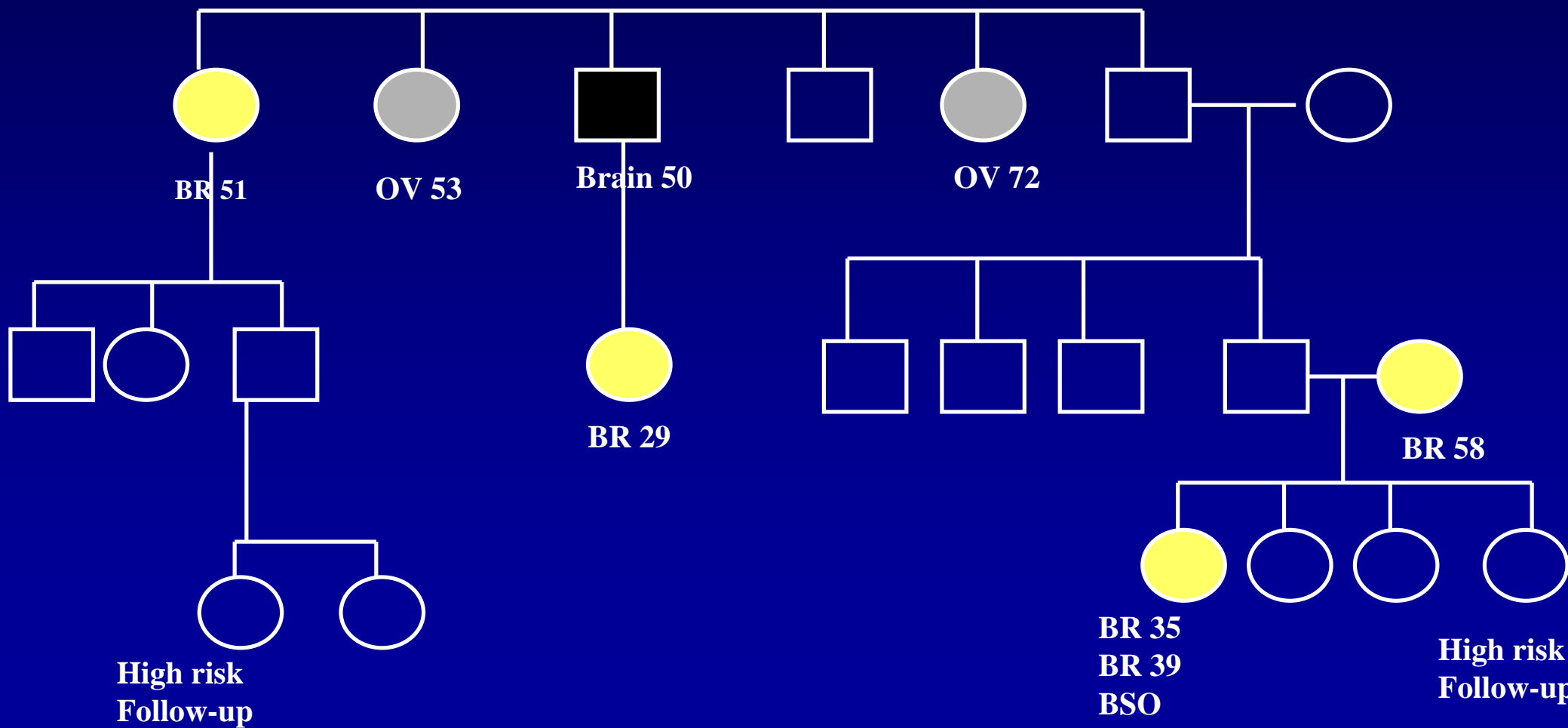
- Recommended after childbearing complete
- With or without hysterectomy
- HRT issues for young women

- Shown to reduce BREAST cancer risk by
at least 50% in pre-menopausal women
- Reduces Ovarian cancer risk dramatically
- Residual risk for primary peritoneal carcinoma









Risk Reduction from removing ovaries (oophorectomy) in women with *BRCA1/2* Mutations

Study	Ovarian Ca	Breast Ca
Kauff 2002	85%	68%
Rebbeck 2002	96%	53%
Rutter 2003	71%	*
Eisen 2005	*	56%
Domchek 2006	89%	64%
Finch 2006	80%	*
Rebbeck 2009	80%	51%

Breast Cancer Risk Post-BPO in pre-menopausal women who use short term Hormone Replacement Therapy (HRT)

<u>HRT after oophorectomy</u>	<u>Breast Ca Risk Reduction</u>
None	62%
Any	63%
Estrogen Alone	56%
Estrogen + Progesterone	57%

Rebbeck et al, *JCO* 2005

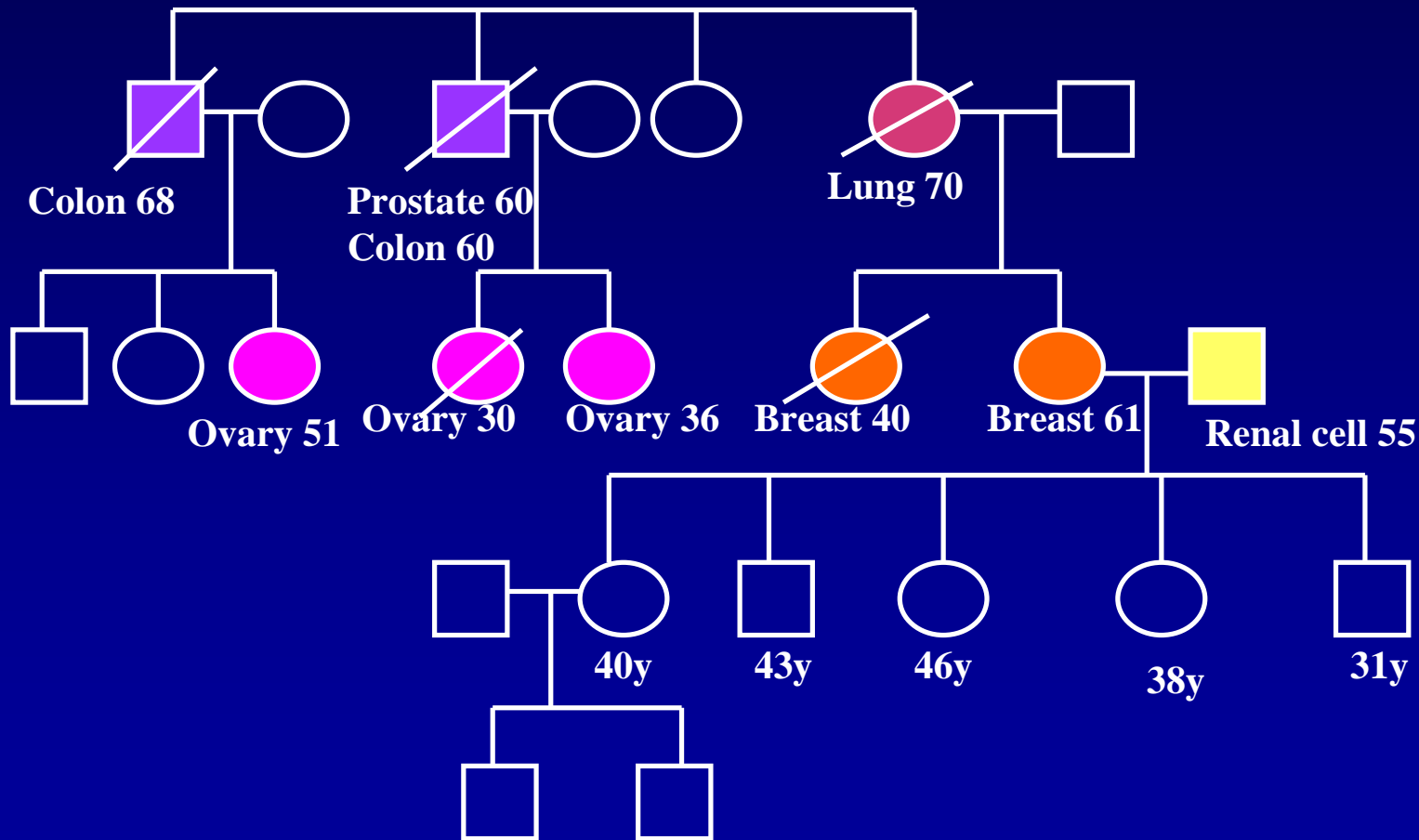
Other Benefits of Prophylactic Oophorectomy in BRCA1/2 Mutation Carriers

Breast Cancer Mortality	90% reduction
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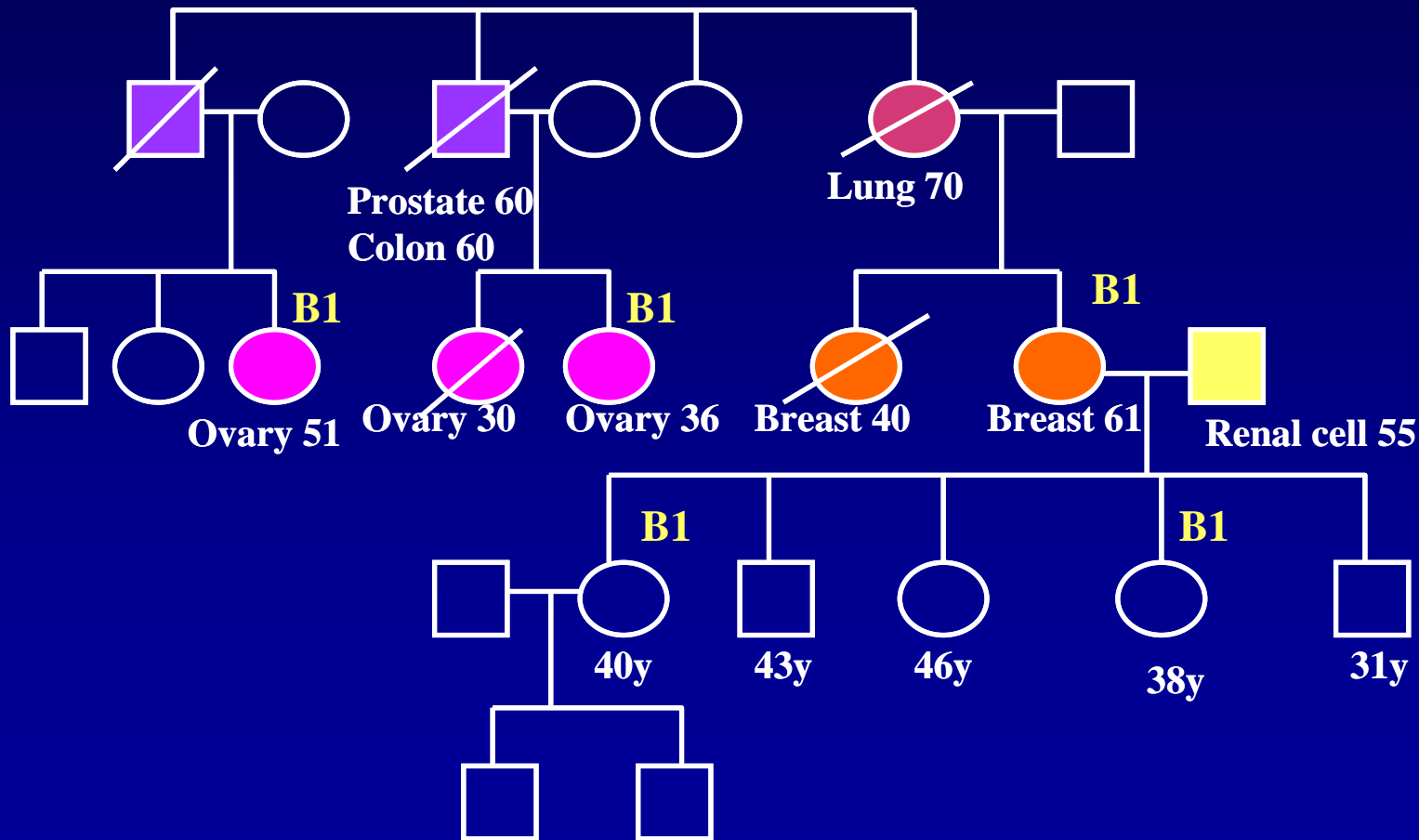
Ovarian Cancer Mortality	95% reduction
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Overall Mortality	76% reduction
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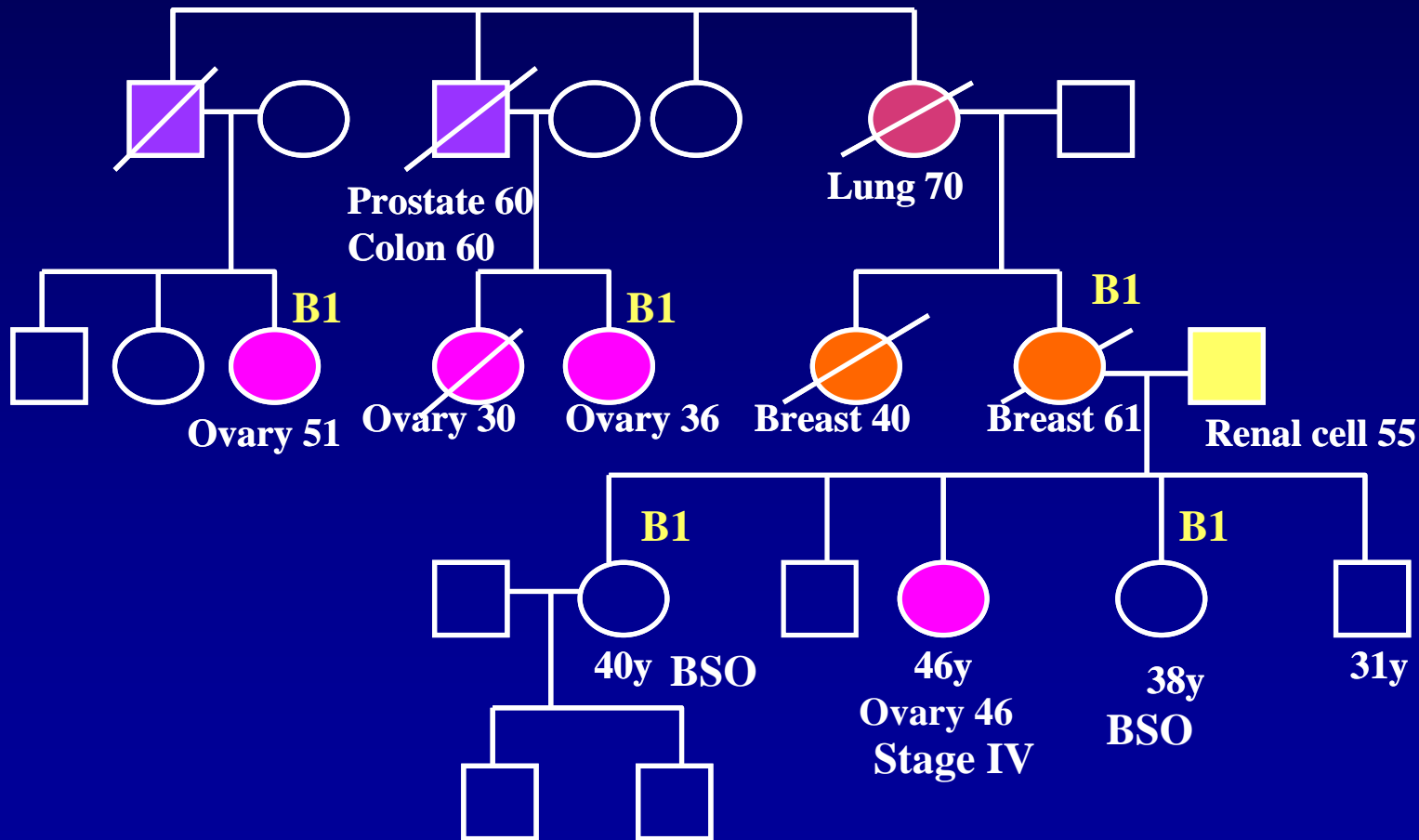
Ignorance is not bliss



BRCA1 family



BRCA1 family



Features That Indicate Increased Likelihood of Having BRCA Mutations

- Multiple cases of early onset breast cancer
- Ovarian cancer (with family history of breast or ovarian cancer)
- Breast and ovarian cancer in the same woman
- Bilateral breast cancer
- Ashkenazi Jewish heritage
- Male breast cancer

Lynch Syndrome – also called Hereditary Non-Polyposis Colorectal Cancer (HNPCC)

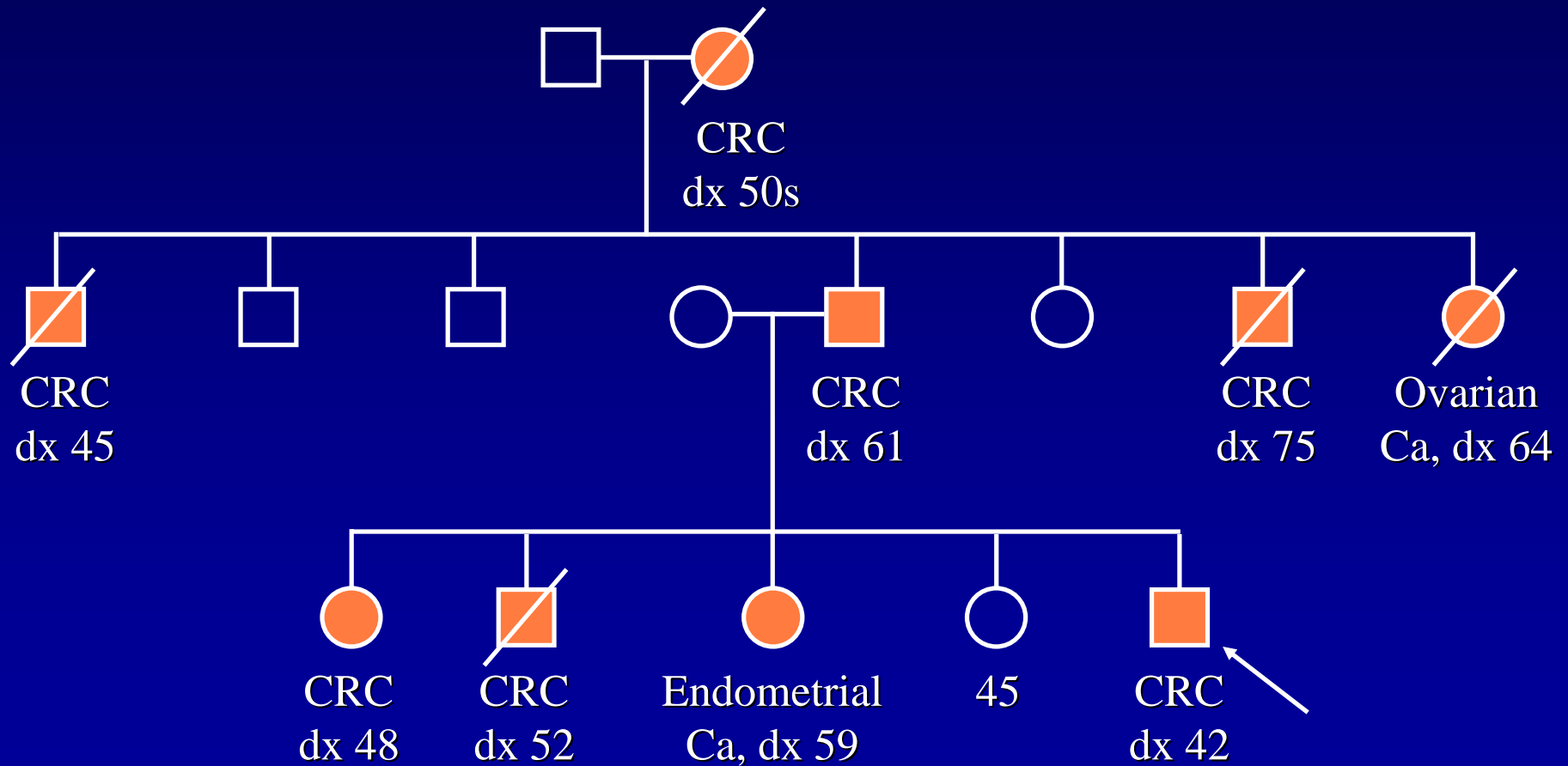
- **Colon cancer risk – 80% risk**
- **Extracolonic cancers:**
 - **Endometrium: 40-60% risk**
 - **Ovary: 10% risk**
 - **Less than 10% risk:** stomach, urinary tract, small bowel, bile ducts, pancreas, sebaceous skin tumors

Amsterdam Criteria

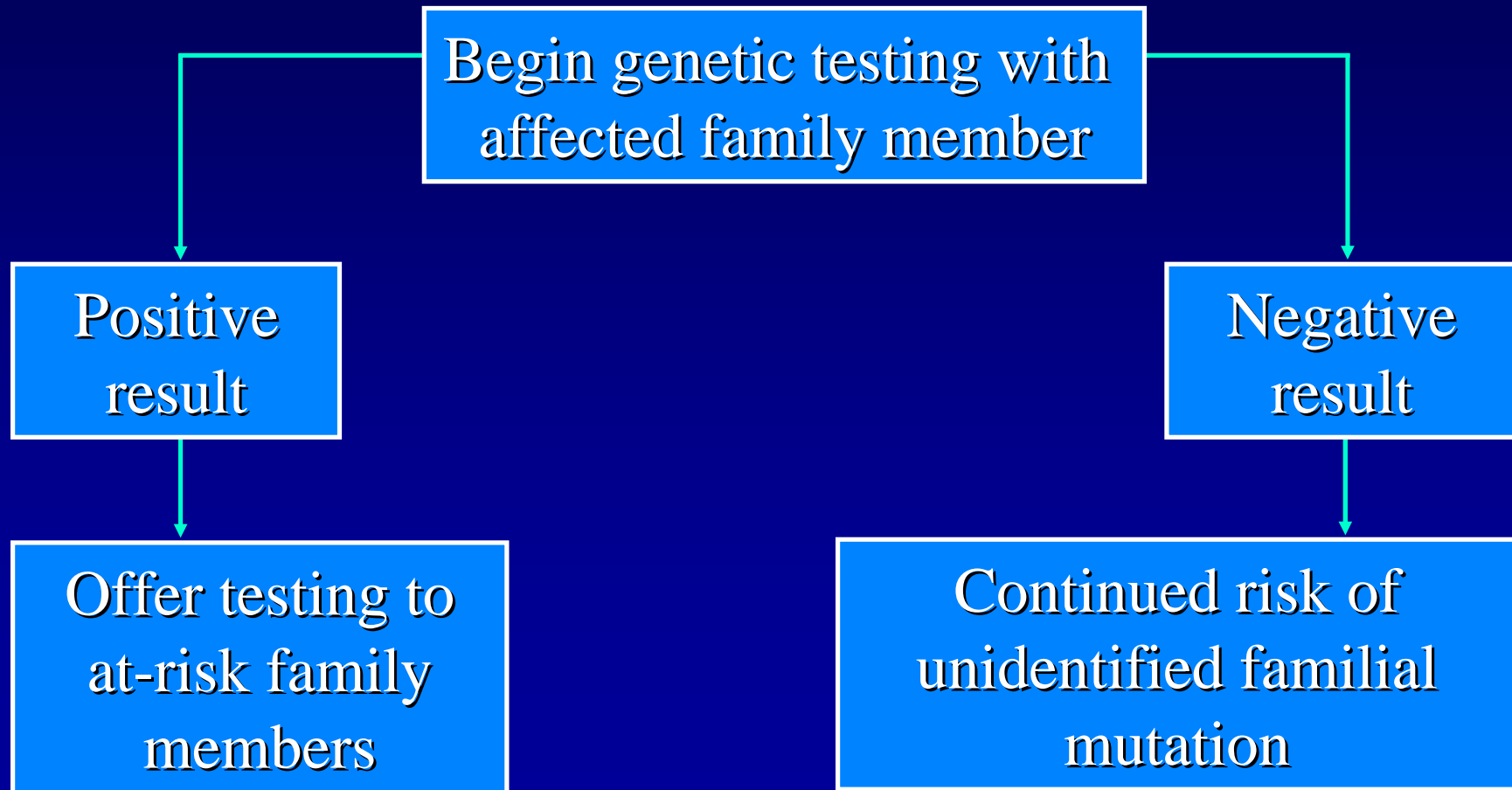
- 3 or more relatives with verified CRC in family
- One case a first-degree relative of the other two
- Two or more generations
- One CRC by age 50
- FAP excluded

Failure to meet these criteria
does *not* exclude HNPCC

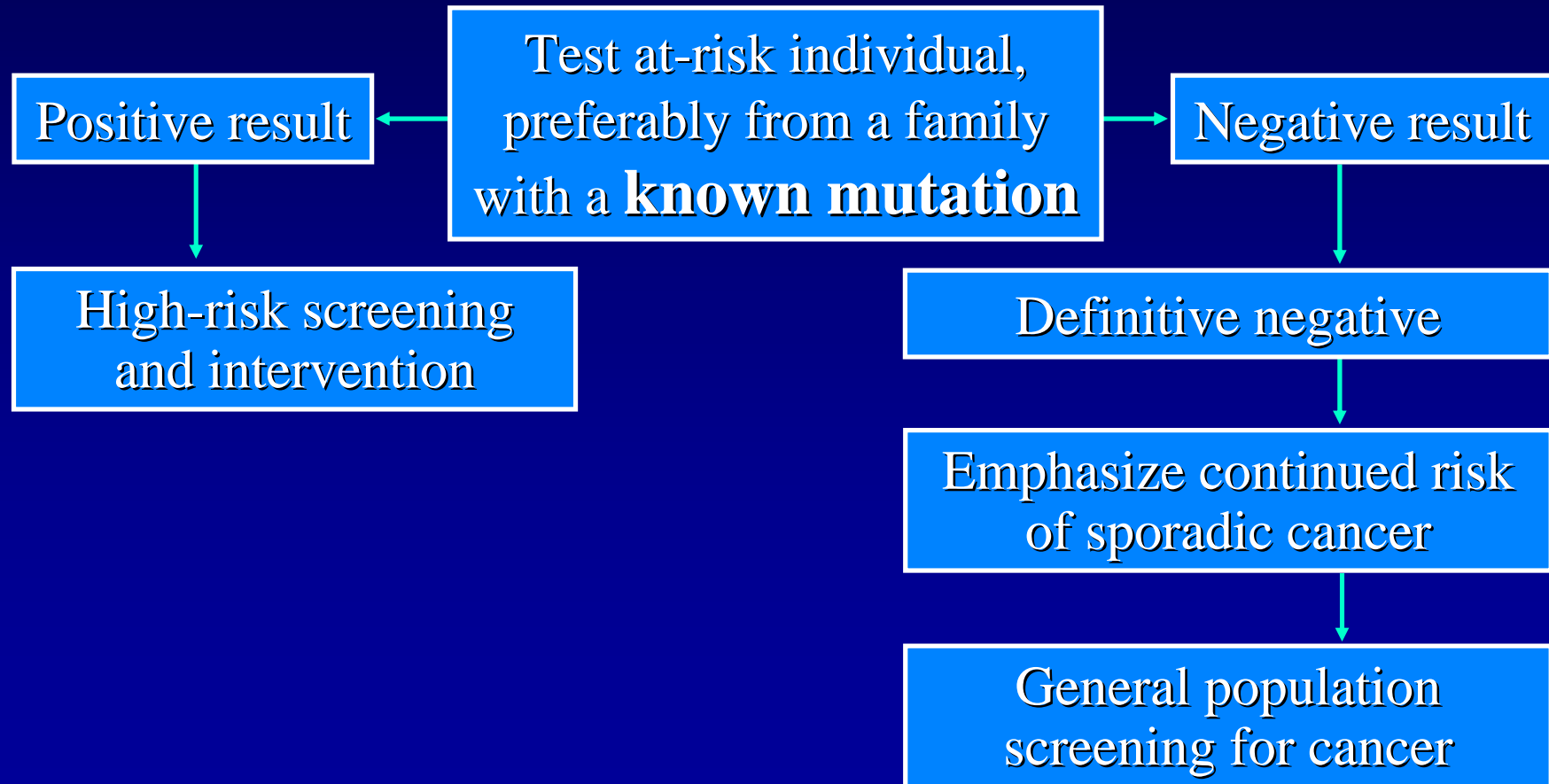
The Family History Is Key to Diagnosing HNPCC



Genetic Testing for Cancer Susceptibility



Genetic Testing for Cancer Risk in Cancer-free Patients



Genetic Testing for Cancer Risk

- Can establish what the source is for cancer risk in the family
- Can help individuals know more about risks for additional cancer, and targeted screening
- Can help family members by identifying those who are NOT at increased risk despite family history

Psychological issues in Genetic Testing

- Fear of the future, anxiety
- Relief from uncertainty
- Concern and worry for family members
- Comfort in being able to provide helpful health information to other family members

- The issue of when to test, is as important as whether to have testing

Concerns regarding discrimination

- GINA – Genetic Information Non-Discrimination Act of 2008
- HIPAA protections of 1996