Taking Control through Carrier and Cancer Screening

Disclosures

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Outline

Review of Genetics and Inheritance
Inheritance

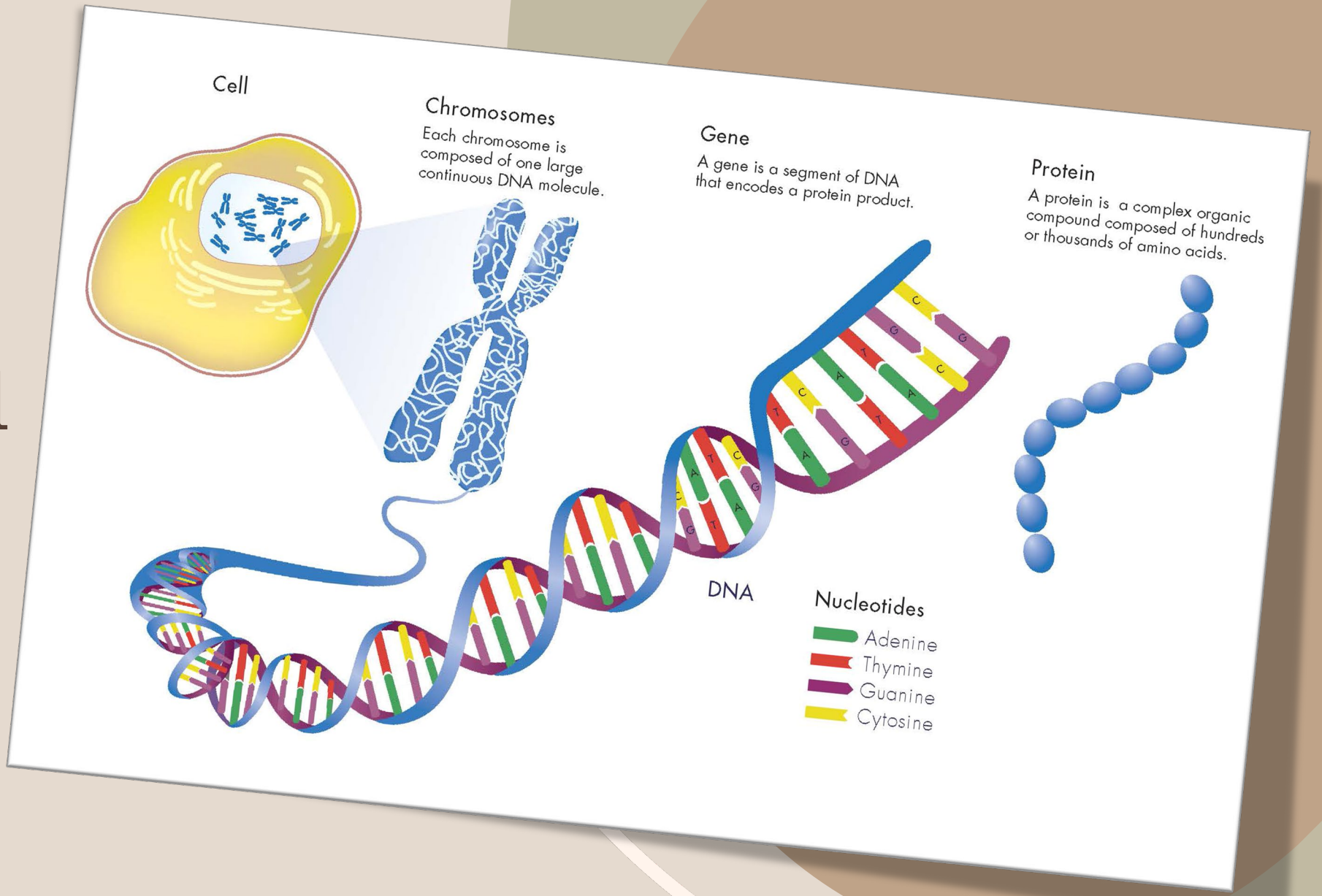
Importance of Family History

Carrier Screening

Cancer Screening

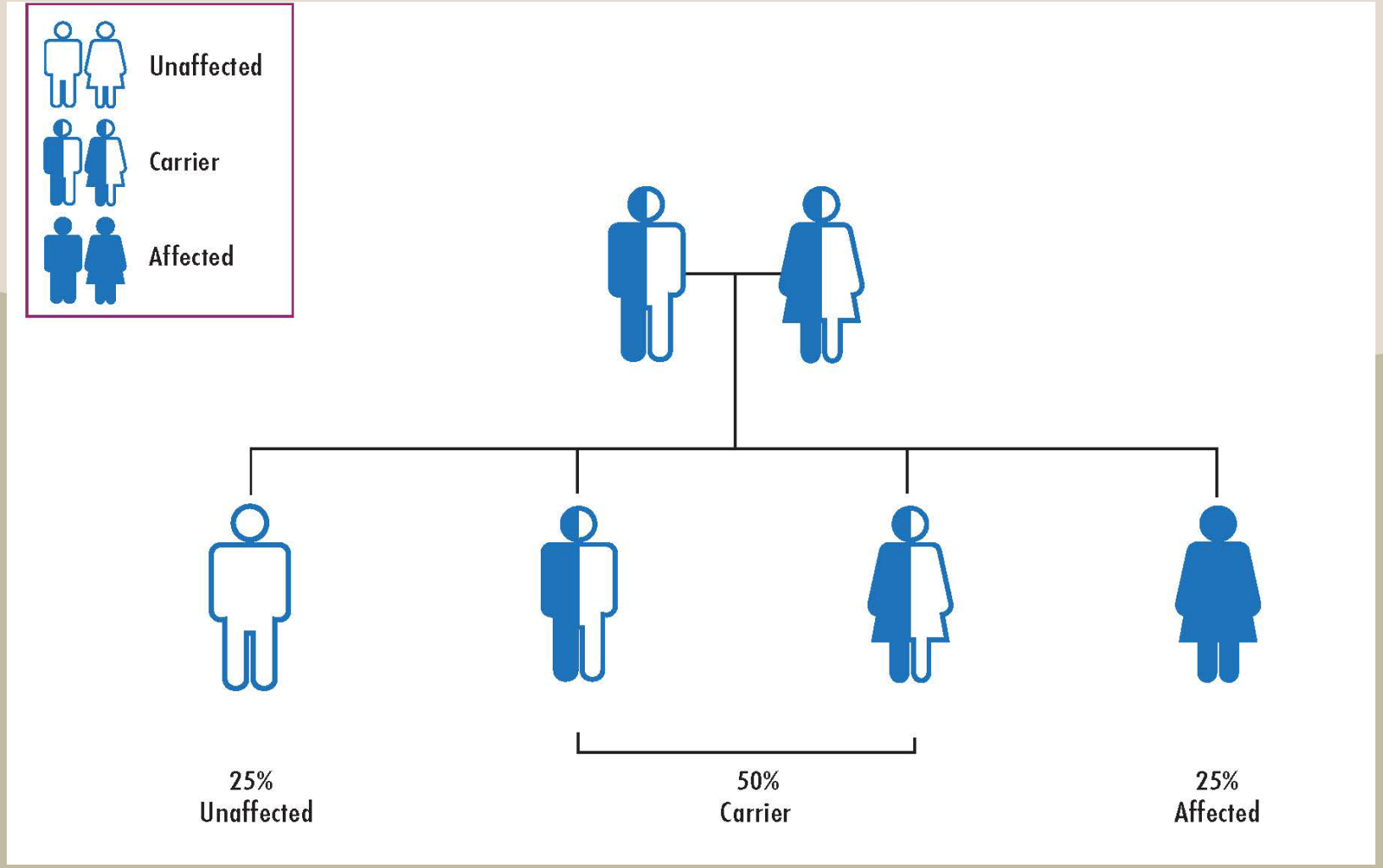
Final Takeaways

Genetics and Inheritance



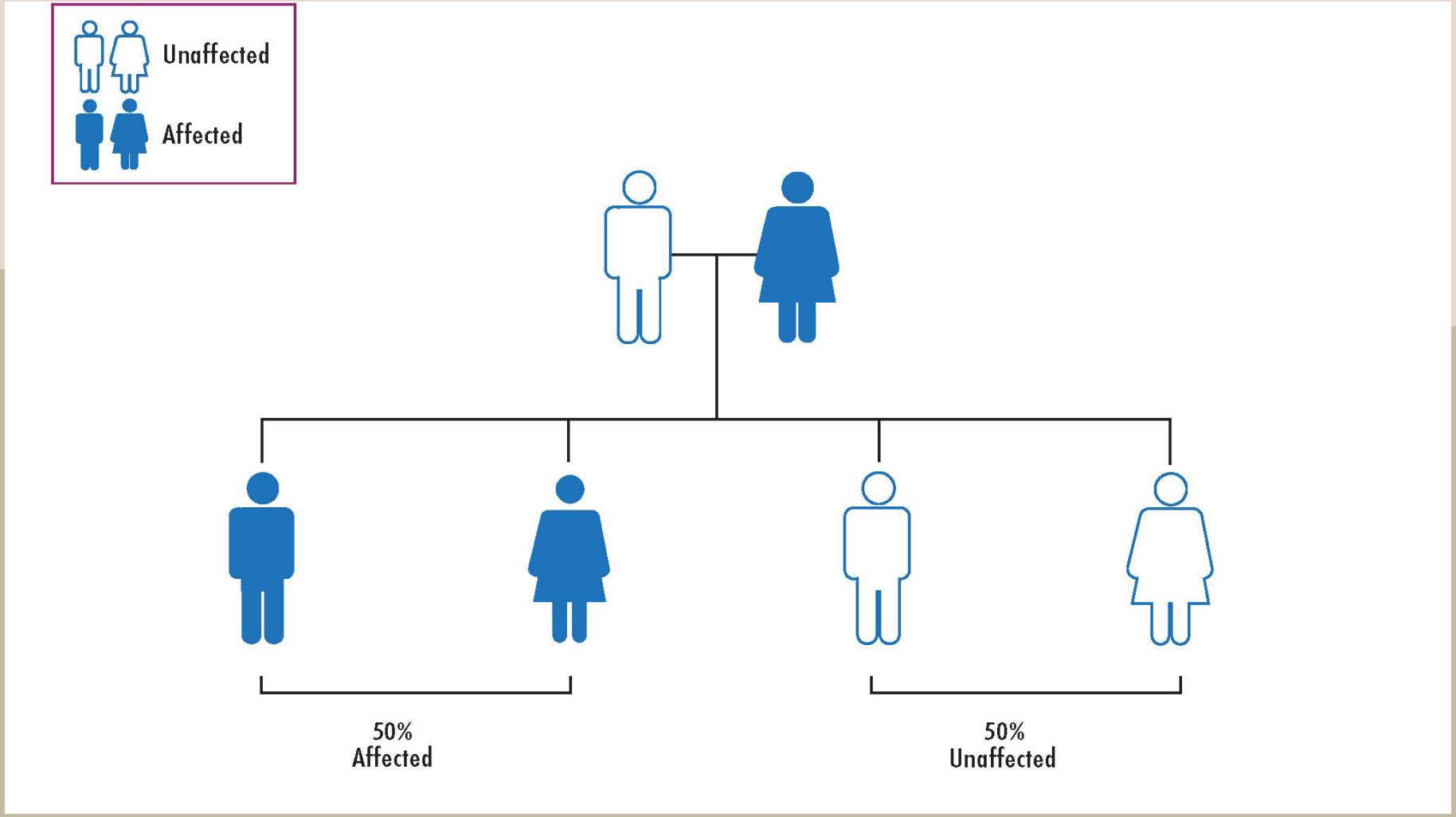
Source: Greenwood Genetics Center Genetic Counseling Aids, 2020 (7th edition)

Autosomal Recessive Inheritance



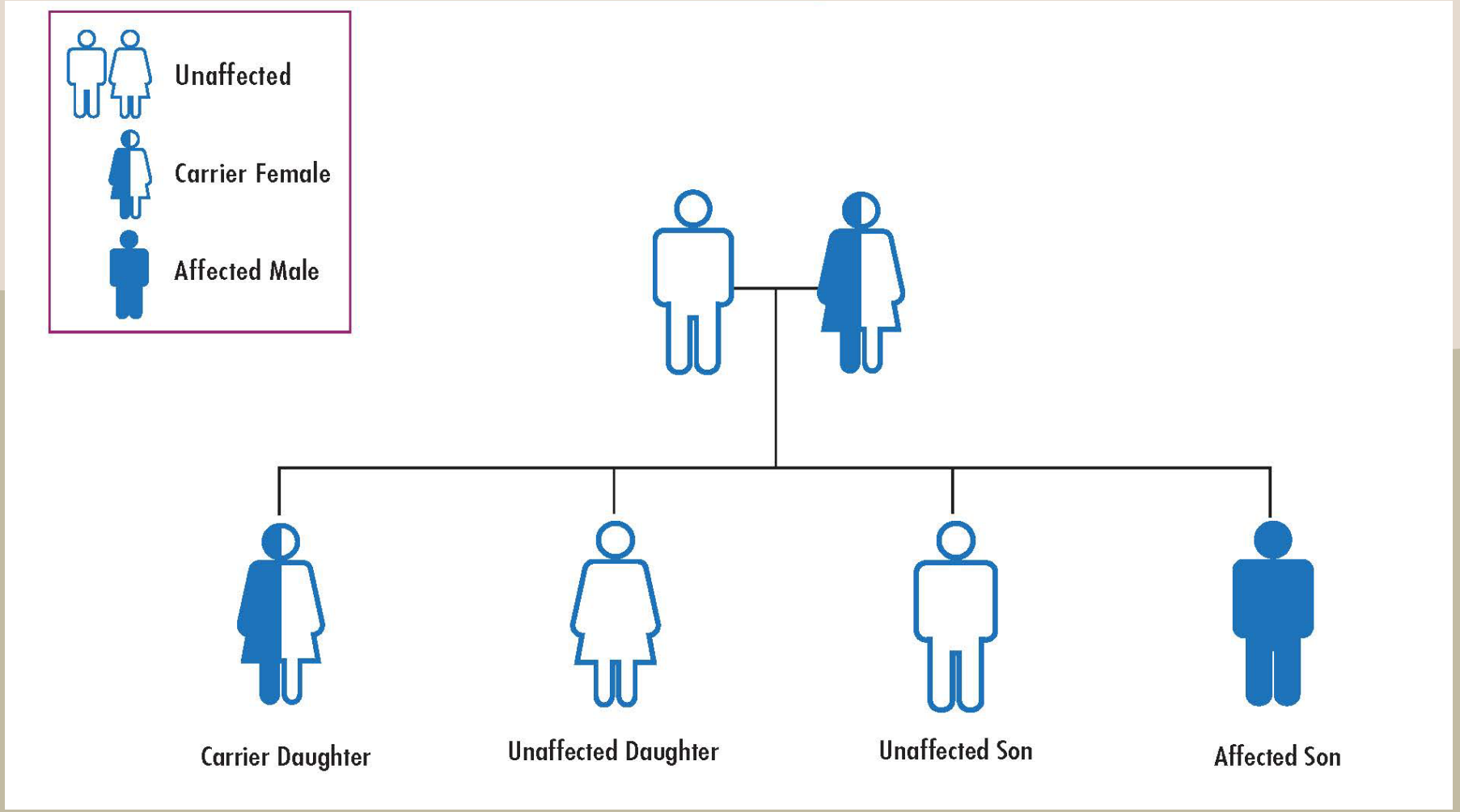
Source: Greenwood Genetics Center Genetic Counseling Aids, 2020 (7th edition)

Autosomal Dominant Inheritance



Source: Greenwood Genetics Center Genetic Counseling Aids, 2020 (7th edition)

X-linked Inheritance



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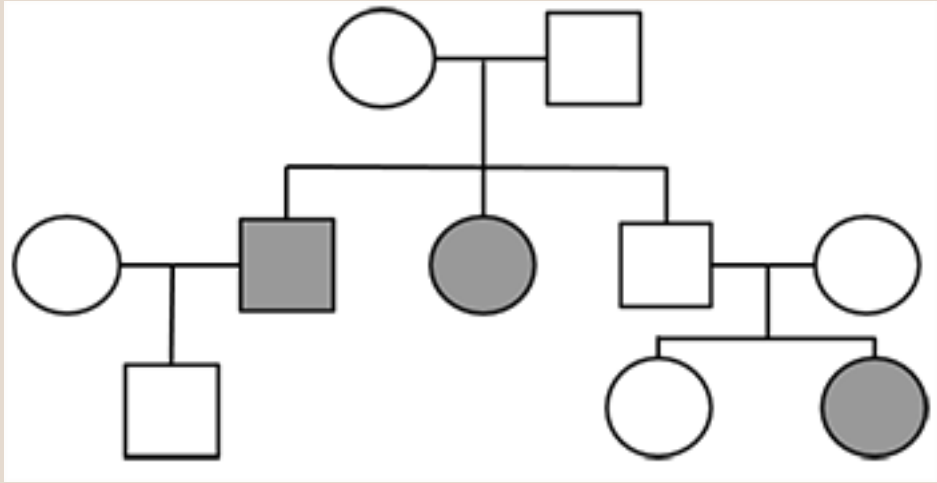
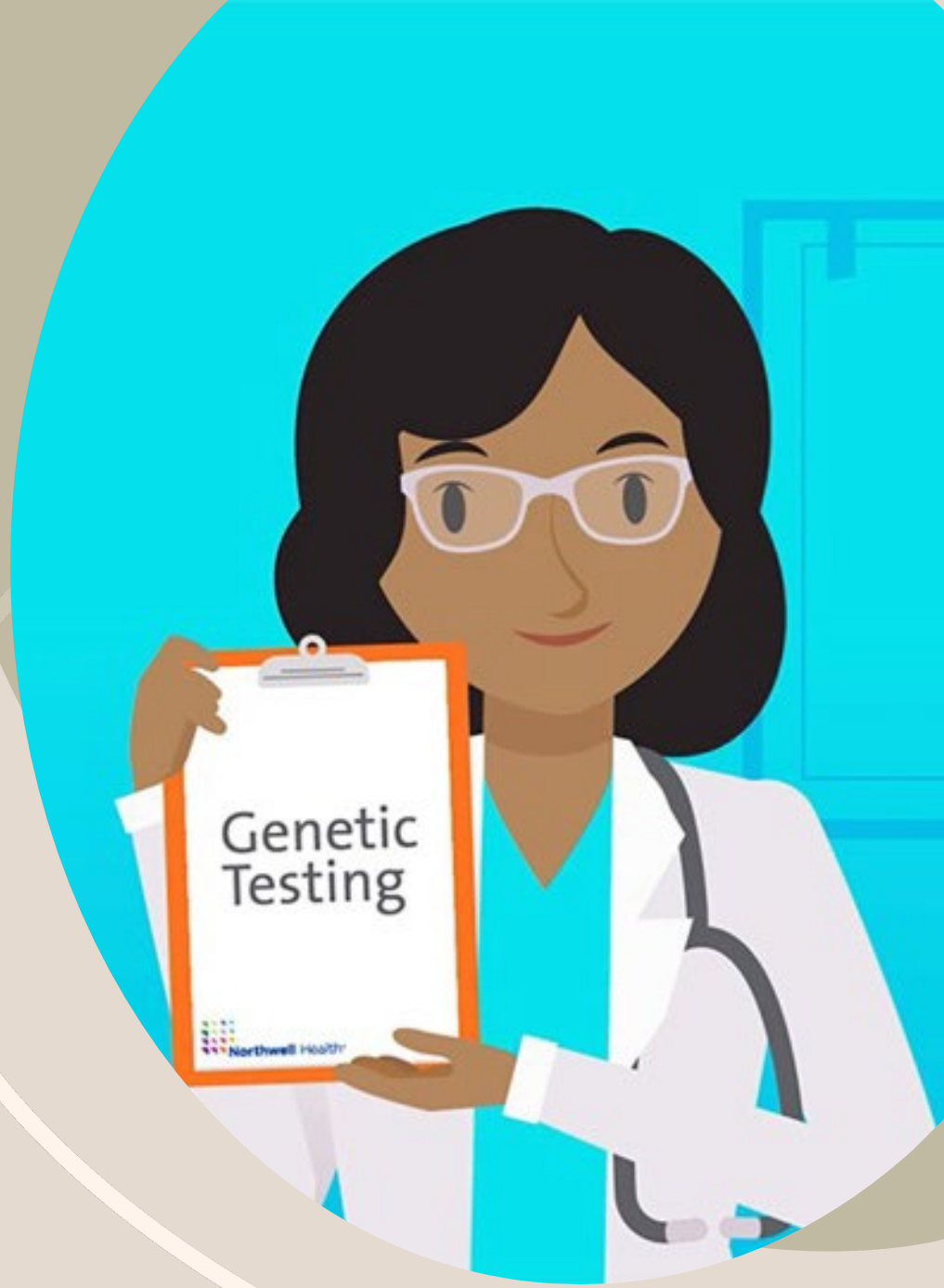
The importance of family history

Family History



- The more details the better
- Looking for patterns
- Looking for what is there **and** what is not there
- Sometimes family history **will** give us clues about risk for a genetic condition **but** sometimes **will not**

Carrier Screening



Carrier Screening

- What is carrier screening?
  - Used to identify individuals or couples who are at risk to have a child with an autosomal recessive or X-linked genetic counseling

- Benefits of carrier screening
  - More information about genetic risks for your children
  - Allows for more informed reproductive planning

What conditions does carrier screening cover?

- What is included
  - Autosomal recessive conditions and X-linked conditions
  - Conditions that typically have symptoms starting in childhood
  - How many conditions
    - As few as 1 or 2 to as many as >600
- What is not included
  - Conditions with primarily adult-onset
  - Examples - cancer-predisposition conditions (*BRCA1/BRCA2)*, genes associated with Alzheimer's disease, Parkinson's disease

How do you choose the right panel for you?

- Guidelines
  - American College of Obstetricians and Gynecologists (ACOG)
    - Recommends at least cystic fibrosis, spinal muscular atrophy, hemoglobin conditions (like sickle cell anemia, alpha thalassemia beta thalassemia)
    - Known conditions in your family
    - Carrier screening for more conditions is an acceptable option
  - American College of Medical Genetics and Genomics (ACMG)
    - Recommends a testing for conditions with a carrier frequency of ≥ 1 in 200
    - 113 conditions
    - Larger panels also available and acceptable if desired

How do you choose the right panel for you: Things to think about

- How much do you want to know?
  - The more conditions tested for the more likely the results with be positive for something
- Timing?
  - Are you planning for a future pregnancy? Are you currently pregnant?
- Insurance coverage/cost
- What will you do with the information?
  - Nothing
  - Educate myself about the condition
  - Prenatal testing
  - IVF and embryo testing
  - Use a donor
  - Adopt
  - Not have biological children

When is the best time to have carrier screening? Should my partner also be tested?

Typical Approach	• Prenatally • Sequentially
Ideal Approach	• Preconceptionally • Concurrently

Should my partner also be tested?

- Ideally, yes if you are found to be a carrier

- What if my partner is not available to be tested and I am pregnant?
  - Prenatal Diagnostic Testing
  - Single Gene Non-invasive Prenatal Testing
    - Only available for certain conditions (CF, SMA, alpha thalassemia, beta thalassemia and sickle cell disease)

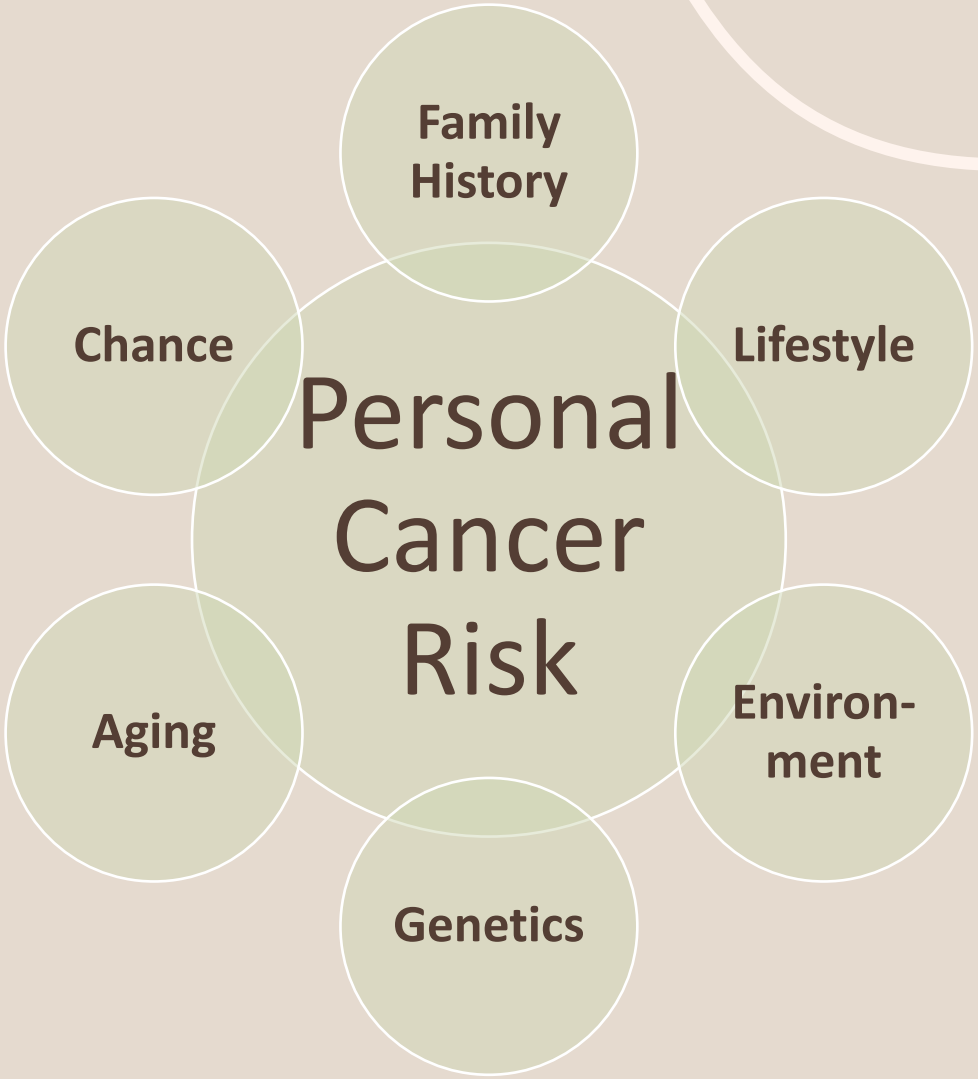
- What if I don't currently have a partner or will be using a donor?

The Fine Print: Details to know about carrier screening

- Not all carrier screening panels are the same
  - Different # of conditions included
  - Different conditions tested
- A negative test result reduces but does not eliminate your carrier risk
  - Never a 0% chance of being a carrier of a genetic condition
- Results have implications for members of your family

- Not all genetic variants are the same (severe versus mild)
- Not all positive results mean you are definitely a carrier or that you have a high risk of having a child with a genetic condition
- For some conditions, being a carrier is also associated with a personal health risk

Genetic Testing for Cancer

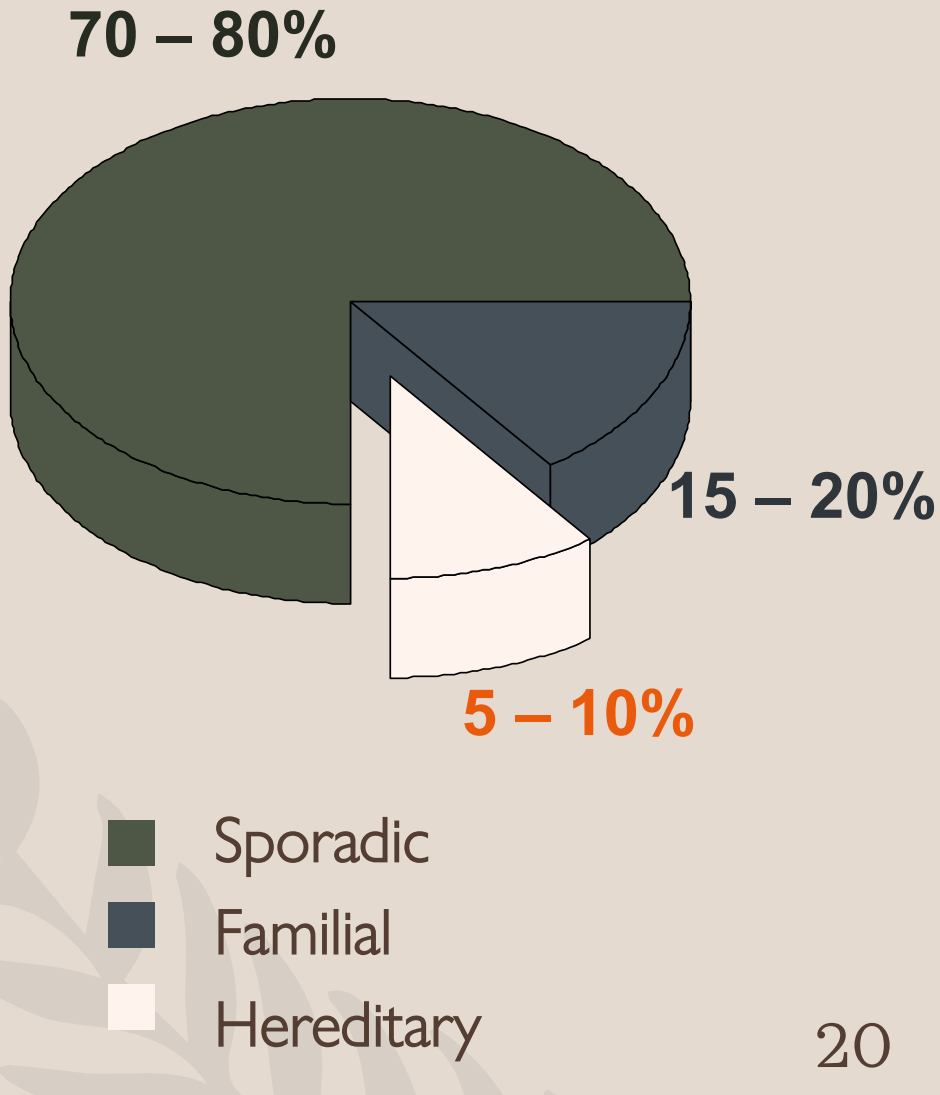

Family History
Chance
Lifestyle
Personal Cancer Risk
Aging
Environ-ment
Genetics

Hereditary Cancer

5-10% of all cancer is due to highly penetrant hereditary cancer predisposition syndromes

Over 150 cancer-related genes have been identified to date

- Not all of these are well associated with hereditary cancer
- Not all available for clinical testing



Red Flags for Hereditary Cancer

3 OR MORE FAMILY MEMBERS WITH THE SAME OR SIMILAR TYPES OF CANCER

2 OR MORE GENERATIONS AFFECTED

1 OR MORE CANCERS DIAGNOSED BEFORE THE AGE OF 50

Personal/Family History

CANCER DIAGNOSED YOUNG (I.E. BREAST CANCER DIAGNOSED ≤50)

RARE TUMOR (I.E. PHEOCHROMOCYTOMA)

MALE BREAST CANCER

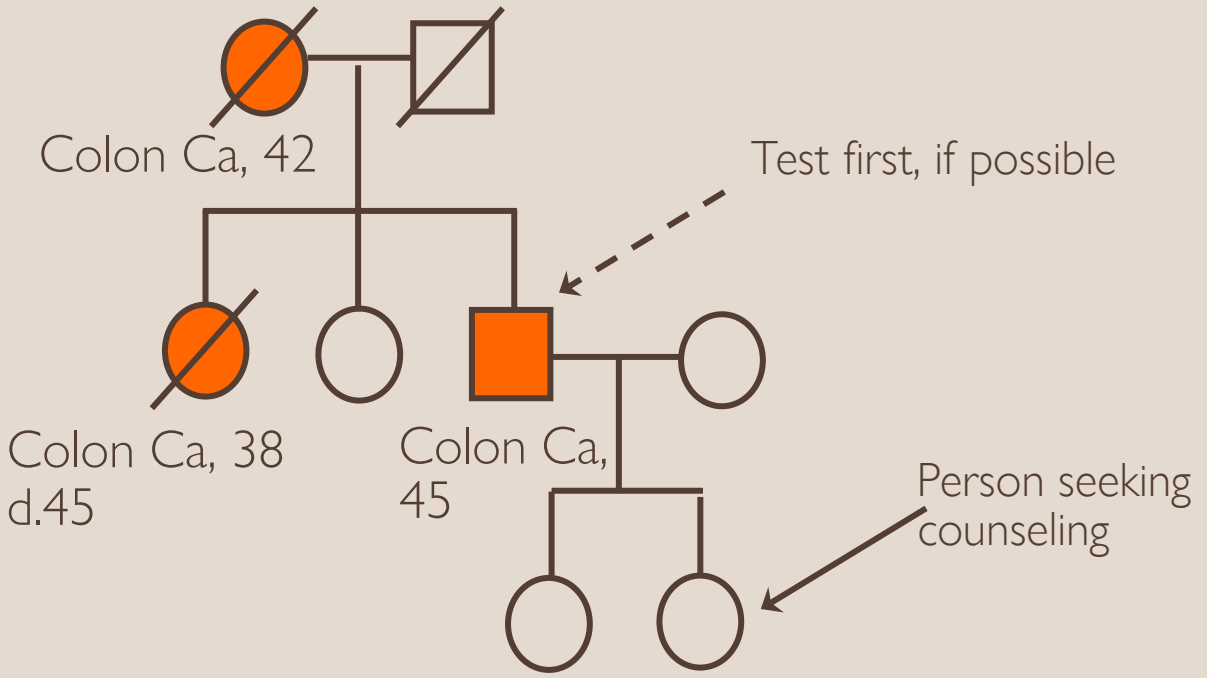
MULTIPLE PRIMARY CANCERS IN THE SAME INDIVIDUAL

POLYPOSIS

PATHOLOGY CONCERNING FOR HEREDITARY CANCER (I.E. TRIPLE NEGATIVE BREAST CANCER, POLYPS WITH LOSS OF MMR STAINING ON IHC)

ASHKENAZI JEWISH ANCESTRY WITH FAMILY HISTORY OF CANCER

Testing the most appropriate family member



If a pathogenic variant is found in an affected person, testing will be more informative for other family members

Common autosomal dominant hereditary cancer syndromes

Condition	Gene(s)	Primary cancer/tumor
Hereditary Breast and Ovarian Cancer syndrome	BRCA1, BRCA2	Breast, ovarian, prostate, pancreatic, melanoma
Lynch syndrome	MLH1, MSH2, MSH6, PMS2, EPCAM	Colon, uterine, ovarian, GI
Cowden syndrome	PTEN	Breast, thyroid, uterine, colon
Familial Adenomatous Polyposis	APC	Polyps, colon
Li Fraumeni	TP53	Breast, sarcoma, leukemia

Hereditary Breast and Ovarian Cancer syndrome (HBOC)

- Pathogenic variants in *BRCA1* and *BRCA2* genes
- 1 in 400 in the general population
    - Ashkenazi Jewish:1 in 40
- Risk associations:
    - 60-87% risk of invasive breast carcinoma for females
        - 7% risk for males
    - 13-58% risk of serous ovarian carcinoma
    - 20-60% risk of prostate cancer
    - Up to 10% risk of pancreatic cancer
    - Increased risk for melanoma

Lynch syndrome

- Pathogenic variants in *MLH1, MSH2, MSH6, PMS2*, and *EPCAM* genes
- 1 in 440 in the general population
- Risk associations:
  - Up to 60% lifetime risk of colorectal cancer
  - Up to 60% of endometrial cancer
  - Up to 38% risk of ovarian cancer
  - Increased risk for kidney, bladder, gastric, small bowel, pancreatic, prostate, and brain cancers

Goals of Genetic Testing

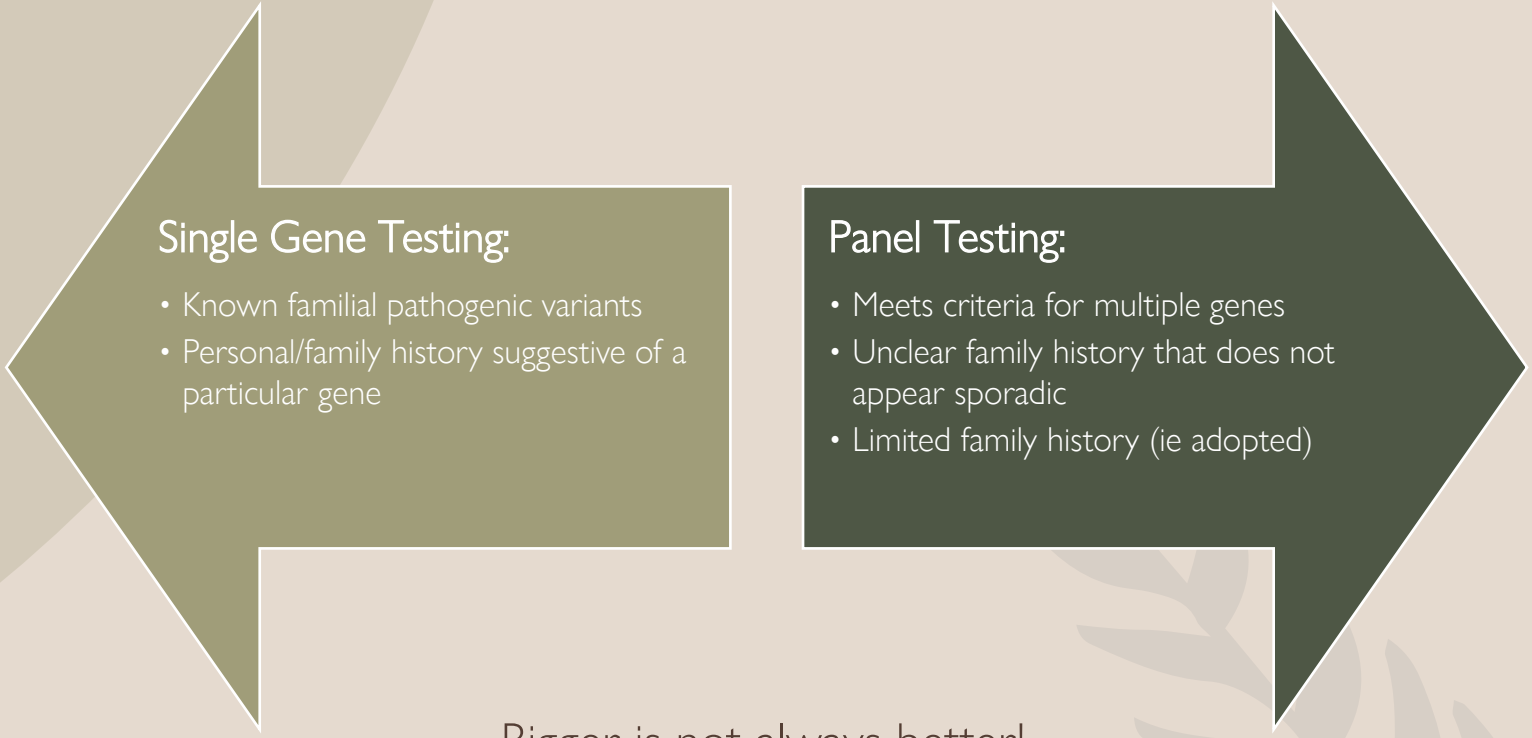
Identify the cause of cancer in a family

Recommend surveillance and risk-reduction options to prevent other cancers

Allow unaffected family members to test

- Surveillance
- Prevention options
- Family planning

Single Gene vs. Panel



Bigger is not always better!

Types of Results and Management

Positive Results

- Variant is identified that disrupts gene function
- Management: based on NCCN guideline recommendations

Negative Results

- **True negative:** there is a known pathogenic variant in the family and the patient has tested negative
- **Uninformative negative**: there is not an identified cancer mutation in the family
- Management: General population screening with consideration of increased surveillance based on family history

Variants of Uncertain Significance

- Variant is identified but its function is not clear
- Management: No change. Treat as a negative result. Follow-up with healthcare provider annually for variant reclassification status.

Summary

- Genetic testing is optional
- Preconception testing is ideal
- Carrier screening is risk reducing, not risk eliminating
- Negative cancer screening does not eliminate the risk to develop cancer
- Not all positive results are the same → talk to a genetic counselor
- If I have a positive result, I have options
- Screening results might tell me about my own health risks
- Risks should be shared with family members – genetic information is family information

If you want to learn more about your genetic testing options:

Baylor Consultagene Clinic:

- 713-798-5054

Texas Children's Reproductive Genetics:

- 832-826-4636

Baylor Adult Genetics Clinic:

- 713-798-7820

Questions?

thank you

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