Genetic Counseling as a part of multidisciplinary care in caring for young patients with cancer

Lauren Maynard, MS, CGC

Certified Genetic Counselor

High Risk Cancer Clinic

Banner Health University of Arizona Cancer Center

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Disclosures

- I have no disclosures or conflicts of interest to report.

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Today's Agenda

1. Review the basics of cancer genetics and medical recommendations for germline genetic testing
2. Review the role of a genetic counselor as a part of the multidisciplinary care team
3. Identify how genetic testing can impact young patients with cancer
4. Provide a list of resources for oncology centers

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Cancer Genetics Overview

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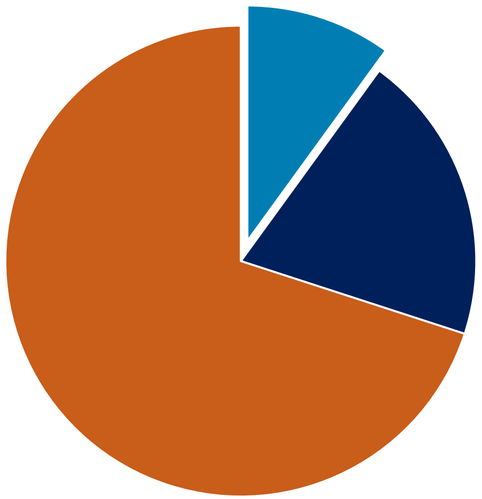
Hereditary Cancer

- All cancer is “genetic”, but MOST cancer is not “hereditary”



Hereditary
- Gene mutation is inherited in the family
- Significantly increased cancer risk and ***often younger age of diagnosis***

Familial
- Multiple genes and environmental factors may be involved
- Some increase in cancer risk

Sporadic
- Cancer occurs by chance or related to environmental factors
- General population cancer risk

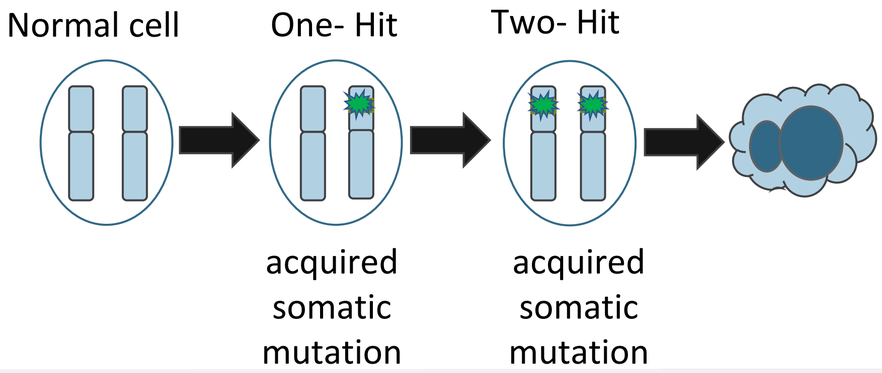
[1]Riley et al, 2012

Hereditary Cancer

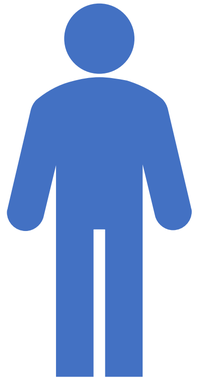
- All cancer is “genetic”, but MOST cancer is not “hereditary”

Somatic Mutations

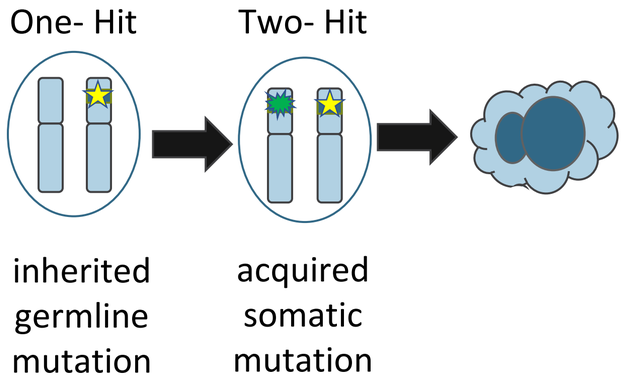
- Isolated to the tumor
- Almost all cancers have a somatic mutation
- Are not inherited



Germline Mutations



- Found in every cell of our body
- Born with these mutations
- Are inherited



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Recommendations for germline genetic testing

- Clues for Hereditary cancer:
  - Abnormally **YOUNG** ages of diagnosis
  - **MULTIPLE** types of cancer
  - **RARE** forms of cancer
  - **FAMILY** history of cancer
  - Higher risk **ETHNICITY** based on known founder mutations

- Guidelines for genetic testing recommendations
  - National Comprehensive Cancer Network® (NCCN®)
    - Genetic/Familial High Risk Assessment: Breast, Ovarian, and Pancreatic[3]
    - Genetic/Familial High Risk Assessment: Colorectal, Endometrial, and Gastric[4]
    - Sections in 33 cancer specific treatment guidelines, 4 detection, prevention, and risk reduction guidelines, Survivorship supportive care guidelines, and ***Adolescent and Young Adult*** guidelines[15]
  - American Society for Clinical Oncology (ASCO), American Society for Breast Surgeons (ASBrS)[8], Society of Gynecologic Oncology, American College of Gastroenterology, Endocrine Society
  - American College of Medical Genetics (ACMG), National Society of Genetic Counselors (NSGC)

"As a part of an initial evaluation, a complete family history should be taken. If indicated, refer for subsequent evaluation by a genetic counselor for genetic and familial risk assessment/counseling"

[2]NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Version 2.2025: Adolescent and Young Adult Oncology

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Broad Summary of Recommendations for germline genetic testing *(not fully comprehensive)*

Referral based on cancer diagnosis regardless of age

- Breast[8]
- Male breast[3]
- Epithelial Ovarian[3]
- Exocrine pancreatic[3]
- Duodenal/Pancreatic NET[5]*
- Metastatic prostate cancer[3]
- Colorectal[4]*
- Endometrial[4]*
- Diffuse Gastric cancer[4]
- Paraganglioma or pheochromocytoma[5]
- Adrenocortical Carcinoma[5]
- Clinical suspicion for MEN2 due to the presence of Medullary thyroid carcinoma[5]

Referral based on cancer diagnosed AND young age

- Breast ≤50[3]
- Breast ≤65[3]*
- Colorectal <50[4]
- Endometrial <50[4]
- Renal Cell Carcinoma ≤46[6]
- AML <50[7]

Referral based on cancer and specific pathology features

- Prostate cancer: high or very high grade group[3]
- Renal Cell Carcinoma: multifocal papillary, histological features associated with HLRCC, FH or SDH deficiency, multiple chromophobe, oncocytoma, or oncocytic hybrid, angiomyolipomas of the kidney and one additional TSC criterion[6]
- Cribriform-morular variant of papillary thyroid cancer[4]
- Cancer with a somatic mutation that changes management if also germline[3]

But don’t forget about family history!

*denotes NCCN “may consider” or category 2B recommendation

[3]NCCN Guidelines® Version 1.2025 Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic
[4]NCCN Guidelines Version 2.2024 Genetic/Familial High-Risk Assessment: Colorectal, Endometrial, and Gastric
[5]NCCN Guidelines Version 2.2024 Neuroendocrine and Adrenal Tumors, [6]NCCN Guidelines Version 2.2025 Kidney Cancer, [7]NCCN Guidelines Version 3.2024 Myelodysplastic Syndromes, [8]ASBrS, Manahan et al 2019

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How often will I see a family history of cancer in my patients?

The lifetime risk cancer is 39.3% (SEER 2018-2021 data)[9]

Common Types of cancer	General population risk (lifetime)[9]	Prevalence reported in family history[10]
Breast cancer (female)	13.1%	26.4%
Lung and bronchus cancer	5.7%	22.9%
Prostate Cancer	12.8%	13.2%
Colorectal Cancer	4%	16.5%

[9]SEER database Cancer Statistics; [10]Mai et al., 2010

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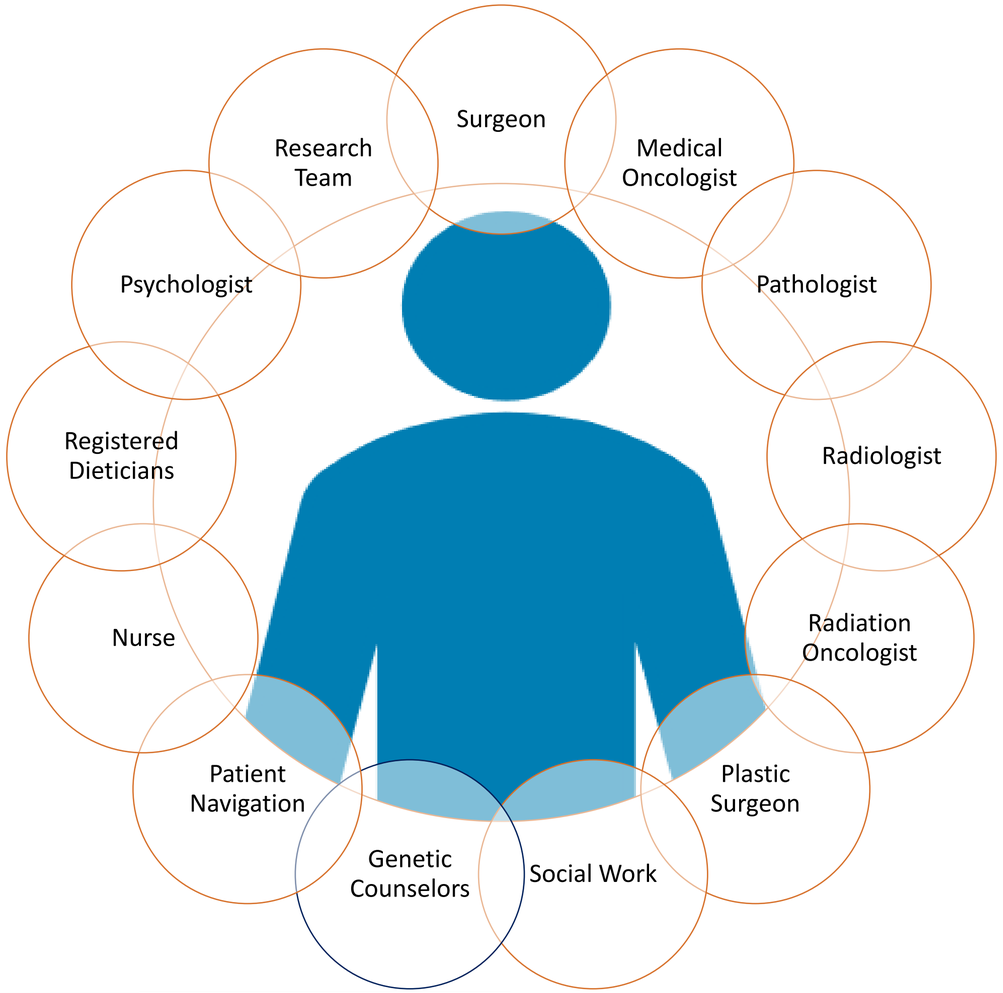
Genetic Counselors as a part of the multidisciplinary care team

What is the role of a genetic counselor in the multidisciplinary care team?

- Complete pre-test genetic counseling
  - Evaluate patient needs/goals/concerns
  - Personal and family history (3-4 generation pedigree)
  - Risk assessment
  - Patient education
  - Informed consent for genetic testing
  - Psychosocial assessment
  - Selection of appropriate genetic test and sample type
- Complete post-test genetic counseling
  - Disclose and interpret genetic test results
  - Discuss screening recommendations based on published guidelines
  - Family member follow up
- Multidisciplinary tumor boards
- Stay updated on genetic testing guidelines and management recommendations
- Accreditation Programs
- Support research, student education, patient outreach



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What is a genetic counselor?

- Help patients understand what their family history and/or genetic test results mean for their cancer risk and their family member's cancer risk
- Empower patients to make informed decisions about health

Image courtesy of Andrea Forman, MS, LCGC

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Impact of Genetic Testing

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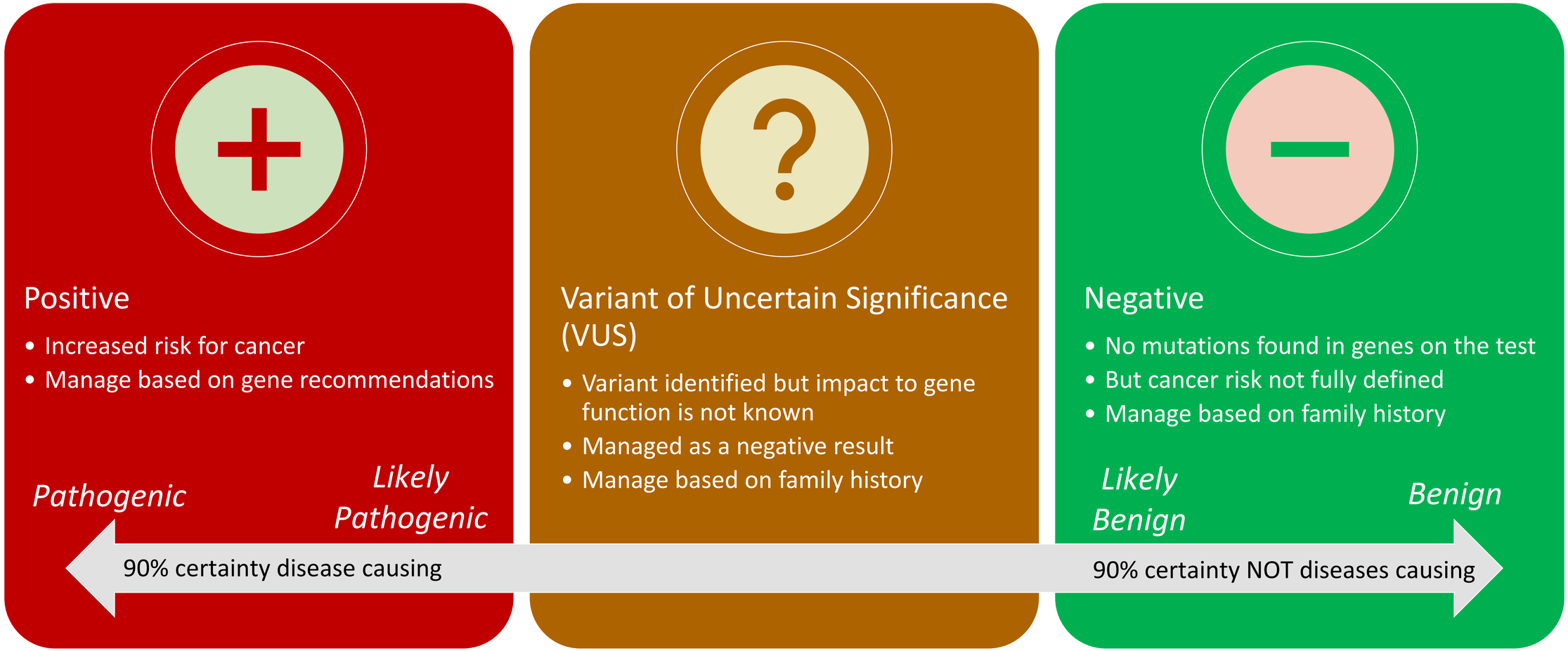
Types of Results



[11]Richards et al., 2015

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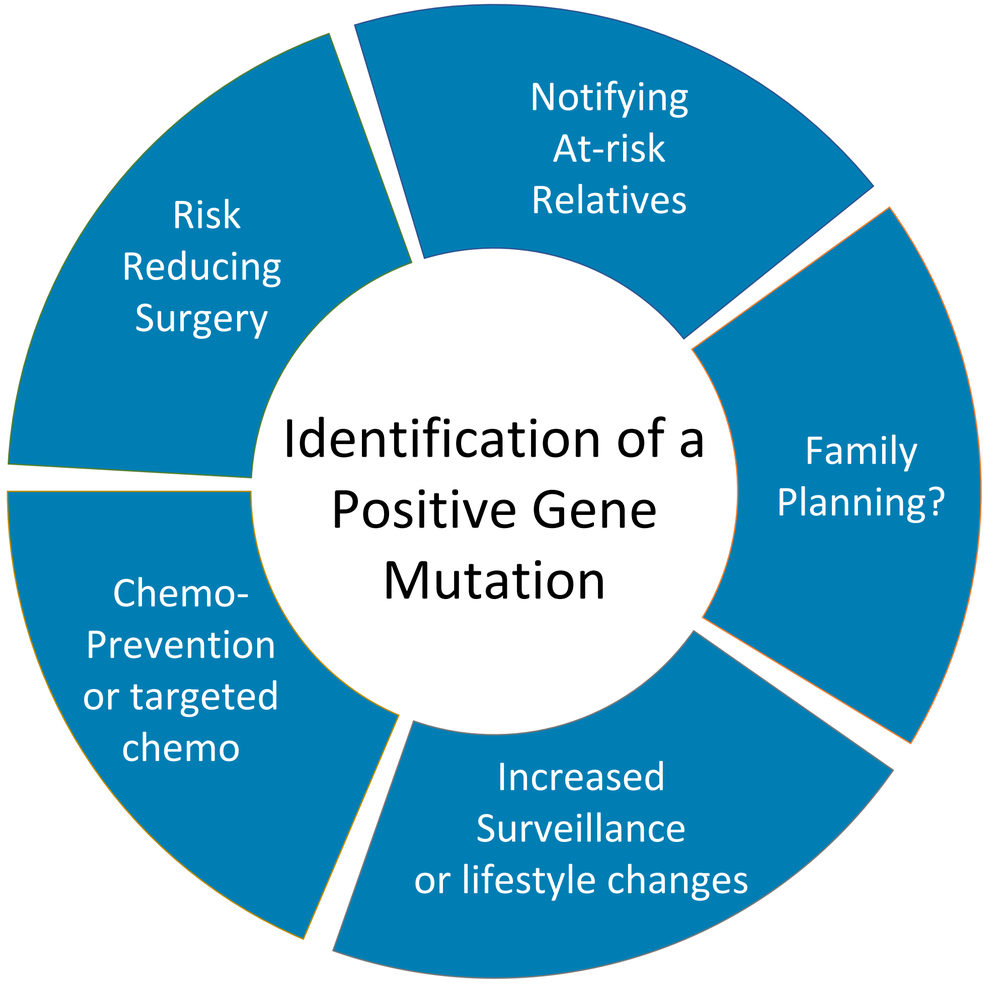
Managing a Positive Result

- Cancer detection and risk reducing options are available for patients with hereditary cancer syndromes
- These are depending upon specific management guidelines for that gene
  - NCCN Guidelines[15]
  - ASCO
  - Published Literature
  - GeneReviews
- However, not every gene has published management guidelines
- Management guidelines may change over time with additional research



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Complications in Positive Results

Limited penetrance mutations

- These mutations have a documented lower risk for cancer than other mutations in that gene
- May have different management guidelines than other mutations, or there may not be a difference yet and it's "up to family history"
- Common or founder mutations

Genotype/Phenotype correlations

- Potential to a positive test result for a patient with cancer, but that cancer type is not known to be linked with that gene

Mosaic results

- The mutation may be found in a lower percentage of cells than we typically expect
- Need to consider sample type and cancer diagnosis, may need additional confirmation by a fibroblast culture

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Psychosocial Concerns

- Guilt over passing this mutation on to family members
- Anxiety over future cancer diagnosis
- Overwhelmed at the screening options and doctor appointments
- Uncertain about surgical decision options
- Anxiety about lack of data abut cancer risks?
- Concerns about affects on future life insurance?

- Reassured by having an answer for their diagnosis
- Hopeful about the option for targeted therapies
- Relieved they have information to tell family members

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Managing a Negative Result

- Even if a patient has negative genetic testing, their family history may warrant additional screening or prevention strategies
  - Empiric risk assessment can also change management recommendations (Examples: Tyrer-Cuzick, Gail)[12, 16]
- Other individuals in the family may be a more informative person for genetic testing
- Must consider technical limitations of genetic testing and possible clinical diagnoses

[12]NCCN Guidelines Version 2.2024 Breast Cancer Screening and Diagnosis
[16]NCCN Guidelines Version 1.2025 Breast Cancer Risk Reduction

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Psychosocial Concerns

- Frustrated they still don’t have an answer
- Irritated they can’t have the preventative surgery they wanted
- Disappointed they don’t have access to a targeted therapy
- Relieved their family members aren’t at risk
- Relieved they aren’t at as high of a risk as they previously thought

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Managing a VUS Result

- Manage the same as a negative result
  - Usually inappropriate to change clinical management[17]
  - We DO NOT manage these as a positive even if the gene looks suspicious because we cannot confirm it is the “cause”
- Important to check how other labs classify this VUS (ClinVar)
- Important to consider a possible clinical diagnosis of certain rare hereditary cancer syndromes
- Labs will continue to investigate a VUS and will update the ordering provider if there’s a new classification
  - Expected to share these reclassifications with the patient, especially if the variant is upgraded to a “pathogenic”[3, 13]
    - Important to know your genetic testing laboratory’s policy and facility’s policy on recontact for reclassifications

A VUS is inconclusive and should NOT be factored into medical management

[3]NCCN Guidelines Version 1.2025 Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic, [13]Tung et al., 2024, [17]Robson et al., 2015

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Psychosocial Concerns

- Frustrated they still don’t have an answer
- Irritated they can’t have the preventative surgery they wanted
- Disappointed they don’t have access to a targeted therapy
- Confused on what the result means
- Annoyed they don’t have more information about the classification or can’t take action

- Relieved their family members aren’t at risk
- Relieved they aren’t at as high of a risk as they previously thought
- Hopeful they may receive an update from the lab later

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When to refer to a genetics provider[3]

When the testing provider/facility does not include pre-test counseling or have resources for facilitating follow up testing, management, or family testing referral to genetics provider is recommended. Especially for the following test results:

1. Positive genetic test results
2. Negative genetic test results, but suspicion remains for an inherited condition (personal or family history or tumor profiling)
3. VUS results that warrants further evaluation
4. Mosaic/possibly mosaic test results which may not be a true germline finding
5. Genetic variants with discrepant interpretations across labs
6. Interpretation of polygenic risk scores (clinical value considered unestablished by NCCN)
7. Interpretation and follow up genetic testing for patients with a positive genetic test result through a direct-to-consumer genetic test

[3]NCCN Guidelines Version 1.2025 Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic

Resources

- Local Organizations:
  - Arizona Genetics Alliance https://www.azgeneticsalliance.com/
    - Contact list to find a local genetic counselor for referral
    - Job creation if you want to hire a genetic counselor (Expansion Committee)
  - National Society of Genetic Counselors https://www.nsgc.org/
    - Find a genetic counselor (https://findageneticcounselor.nsgc.org/)
- Published guidelines/literature:
  - NCCN Guidelines® - NCCN.org
  - Selection of Germline Genetic Testing Panels in Patients With Cancer: ASCO Guideline[13]
  - Guideline Development Group, American College of Medical Genetics and Genomics Professional Practice and Guidelines Committee and National Society of Genetic Counselors Practice Guidelines Committee. A practice guideline from the American College of Medical Genetics and Genomics and the National Society of Genetic Counselors: referral indications for cancer predisposition assessment[14]

[13]Tung et al., 2024, [14]Hampel et al., 2015

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Thank you.

Lauren Maynard, MS, CGC
Lauren.Maynard@bannerhealth.com