Somatic Genetic Testing

FOUNDATIONONE

Patient Name | Report Date | Tumor Type: Lung adenocarcinoma

Genomic Findings Detected	FDA-Approved Therapies (in patient's tumor type)	FDA-Approved Therapies (in another tumor type)	Potential Clinical Trials
ERBB2 amplification - equivocal	Afatinib	Ado-trastuzumab emtansine Lapatinib Pertuzumab Trastuzumab	Yes, see clinical trials section
Tumor Mutation Burden TMB-High; 37.53 Muts/Mb	Nivolumab Pembrolizumab	Atezolizumab	Yes, see clinical trials section
NF2 E427*	None	Everolimus Temsirolimus	Yes, see clinical trials section
STK11 splice site 921-1G>C	None	Everolimus Temsirolimus	Yes, see clinical trials section
CDKN1B E105fs*14	None	None	None
FOXP1 E490*	None	None	None
KDM5C W983*	None	None	None
LRP1B loss exons 6-14	None	None	None
SPTA1 Q1346fs*3, splice site 3570-2A>T	None	None	None
TP53 I255S	None	None	None

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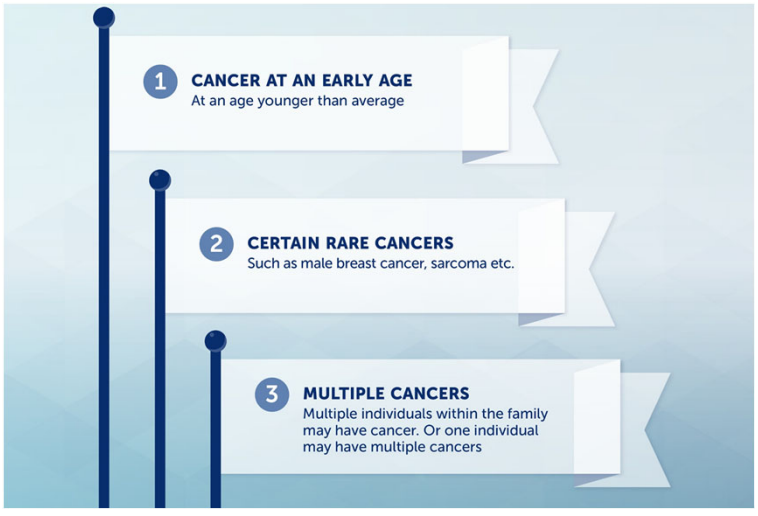
Hereditary Cancer Red Flags



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Genetic testing criteria

TESTING CRITERIA FOR HIGH-PENETRANCE BREAST CANCER SUSCEPTIBILITY GENES
(Specifically *BRCA1, BRCA2, CDH1, PALB2, PTEN, STK11,* and *TP53*. See GENE-A)[a,f,g,h,i]

Testing is clinically indicated in the following scenarios:

- See General Testing Criteria on CRIT-1.
- Personal history of breast cancer with specific features:
  - ≤50 y
  - Any age:
    - ◊ Treatment indications
      - – To aid in systemic treatment decisions using PARP inhibitors for breast cancer in the metastatic setting[j,k] (NCCN Guidelines for Breast Cancer)
      - – To aid in adjuvant treatment decisions with olaparib for high-risk,[l] HER2-negative breast cancer[j]
    - ◊ Pathology/histology
      - – Triple-negative breast cancer
      - – Multiple primary breast cancers (synchronous or metachronous)[m]
      - – Lobular breast cancer with personal or family history of diffuse gastric cancer NCCN Guidelines for Gastric Cancer
    - ◊ Male breast cancer
    - ◊ Ancestry: Ashkenazi Jewish ancestry
  - Any age (continued):
    - ◊ Family history[n]
      - – ≥1 close blood relative[o] with ANY:
        - breast cancer at age ≤50
        - male breast cancer
        - ovarian cancer
        - pancreatic cancer
        - prostate cancer with metastatic,[p] or high- or very-high-risk group (Initial Risk Stratification and Staging Workup in NCCN Guidelines for Prostate Cancer)
      - – ≥3 diagnoses of breast and/or prostate cancer (any grade) on the same side of the family including the patient with breast cancer

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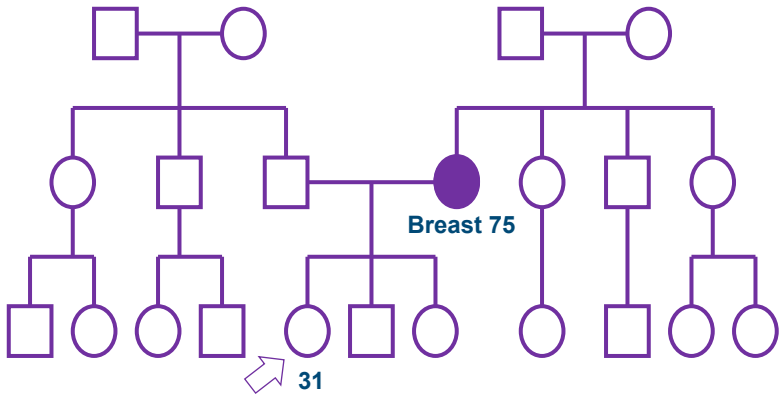
Family History Evaluation



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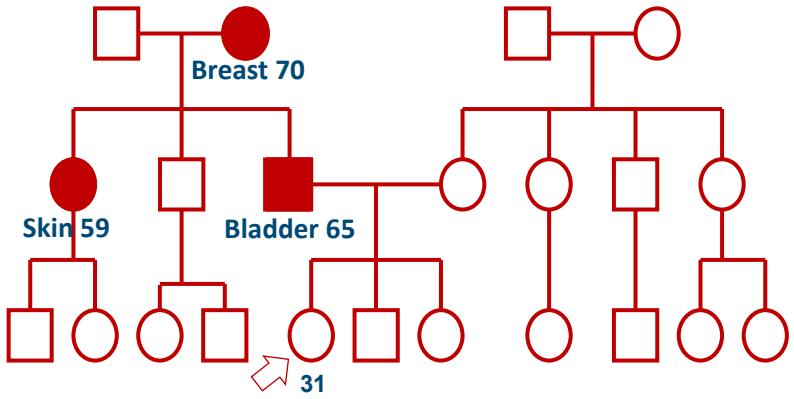
Family History Evaluation



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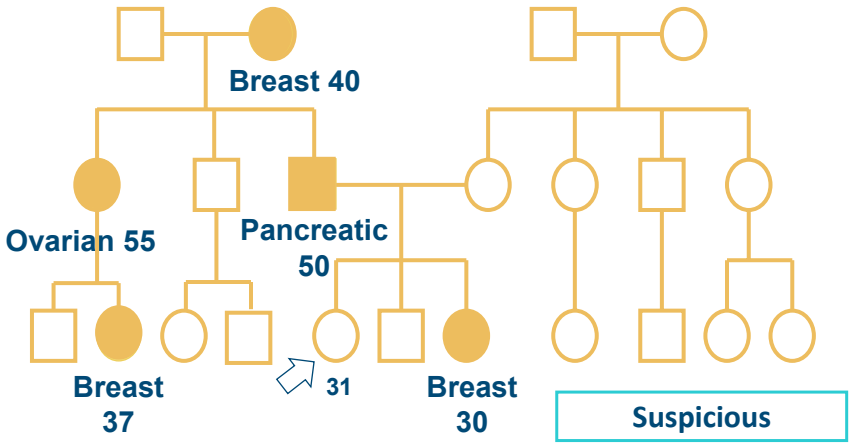
Family History Evaluation



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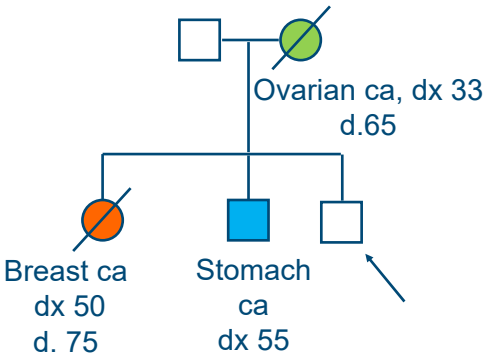
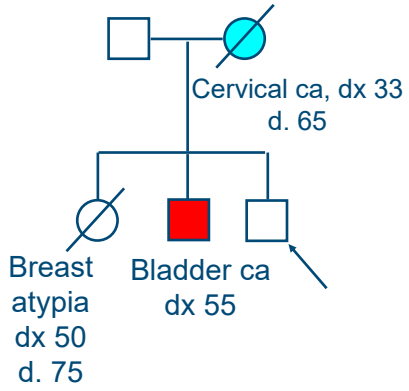
Family History Evaluation

- Verbally reported family history



- Revised family history based on pathology reports



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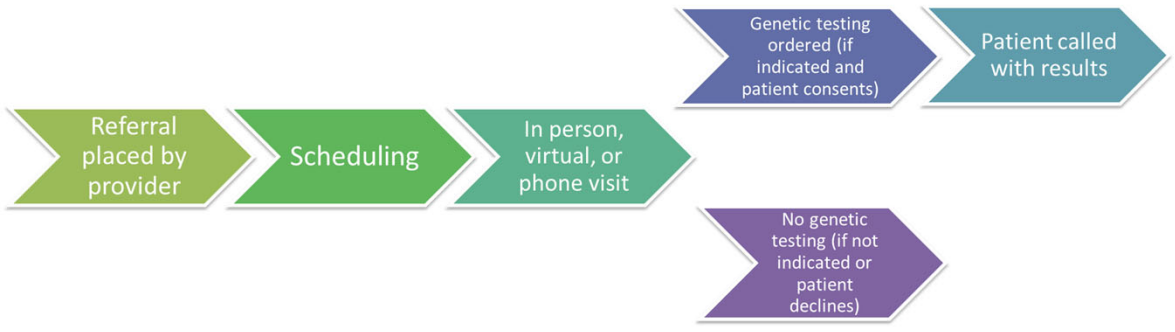
Genetic Counseling Process



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Genetic testing

- Limitations and Risks
  - Unable to screen/prevent all cancers
  - Anxiety/distress
  - Possibility of unclear/unexpected results
  - Positive results with limited information
  - Insurance discrimination

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Genetic testing

- Genetic Information Nondiscrimination Act of 2008 (GINA)

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Genetic Testing

- Where?
  - National clinical genetic testing labs such as Invitae, Ambry, Myriad, GeneDx, etc

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Genetic Testing

- What?
  - DNA sequencing and deletion/duplication analysis of genes related to inherited cancer syndromes
  - Multi-gene panels are commonly used to test for multiple genes at once

	GENES	BREAST & GYN	ENDOCRINE	GASTROINTESTINAL	GENITOURINARY	HEMATOLOGIC	NERVOUS SYSTEM/BRAIN	PROSTATE	SARCOMA	SKIN
INVITAE BREAST CANCER GUIDELINES-BASED PANEL	ATM	■		■		■		■		
	BRCA1	■		■	■			■		
	BRCA2	■		■	■			■		■
INVITAE BREAST CANCER STAT PANEL	CDH1	■		■						
	CHEK2	■	■	■	■			■		
	PALB2	■		■				■		
	PTEN	■	■	■	■		■			■
	STK11	■		■						
	TP53	■	■	■	■	■	■	■	■	■
	NBN	■			■	■		■	■	
	NF1	■	■	■		■	■		■	

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Genetic Testing

- Why?
  - Guide screening and risk management recommendations for the patient and their relatives

PALB2 gene		
Cancer risk	Associated cancer management	Age to begin management
Breast cancer	Annual mammogram and breast MRI	Age 30
Ovarian cancer	Consider surgery to remove ovaries and fallopian tubes	Age 45-50
Pancreatic cancer	Annual screening only recommended with fhx of pancreatic cancer	Age 50

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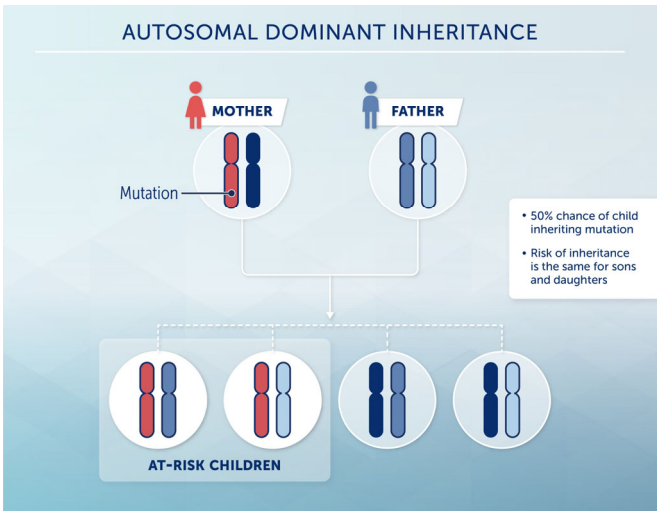
Genetic Testing



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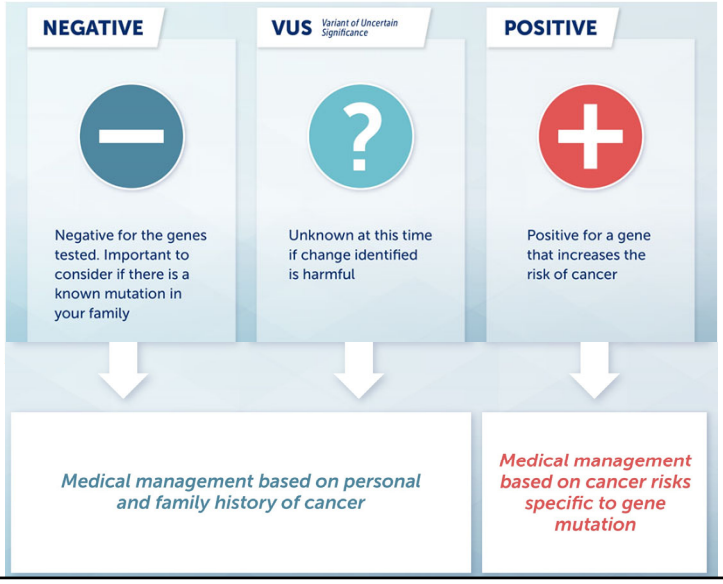
Genetic Testing



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Risk Modeling

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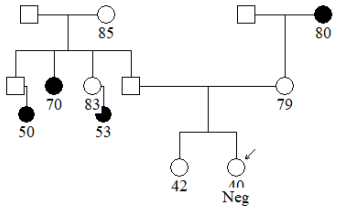
Risk Modeling

- IBIS risk model
  - Personal history (menarche, menopause, breast density, HRT, age at first child, etc)
  - Family history
  - Genetic test results

ID:
Age is 40-yrs.
Age at menarche 13-yrs.
Nulliparous.
Premenopausal.
Height is 1.778 m.
Weighs 63.5 kg.
Never used HRT.
BI-RADS® density c (heterogeneous)

Competing mortality projection
Risk after 10 years is 3.2%.
10 year population risk is 1.6%.
Lifetime risk is 20.4%.
Lifetime population risk is 10.8%.
Probability of a BRCA1 gene is 0%.
Probability of a BRCA2 gene is 0%.



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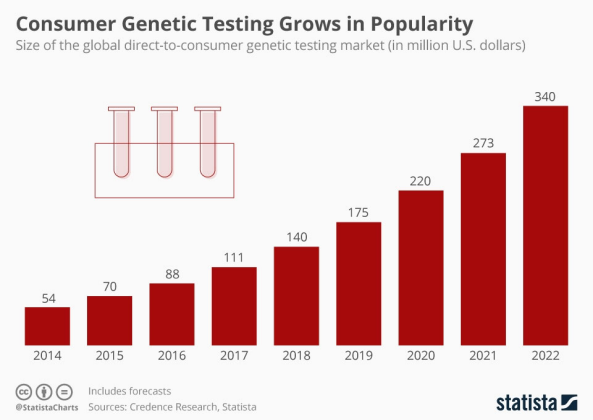
Direct to Consumer Tests

- **Who?**
  - 23andMe, AncestryDNA, FamilyTreeDNA, etc.
- **What?**
  - Tests for a selection of SNPs, including those related to inherited conditions, health risks, drug responses, and inherited traits
- **Why?**
  - Can provide information in disease risk
  - Patient curiosity
- **Limitations**
  - Most risks are multifactorial
  - Clinician involvement not required
  - Unexpected results (APOE-4, 3-site Jewish *BRCA1/2*)
  - Overly reassured by results (3-site Jewish *BRCA1/2*)



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Genetics in Oncology Nursing

Oncology Essentials

Cancer Genetics and Genomics: Essentials for Oncology Nurses

Jean Boucher Karleen Habin Meghan Underhill Biotherapy Targeted Therapies Genetics and Genomics

CJON 2014, 18(3), 355-359 DOI: 10.1188/14.CJON.355-359

Review > Nurs Clin North Am. 2017 Mar;52(1):1-25. doi: 10.1016/j.cnur.2016.11.001.

Genetics and Genomics in Oncology Nursing: What Does Every Nurse Need to Know?

Julie Eggert [1]

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Summary

- Genetic testing for hereditary cancer is a complex, ever evolving field
- Be careful to clarify when asking a patient “have you had genetic testing?”
- Identifying a hereditary cause for cancer in a family can aid prevention/screening for the patient and family members
- Genetic counselors are here to help! ☺

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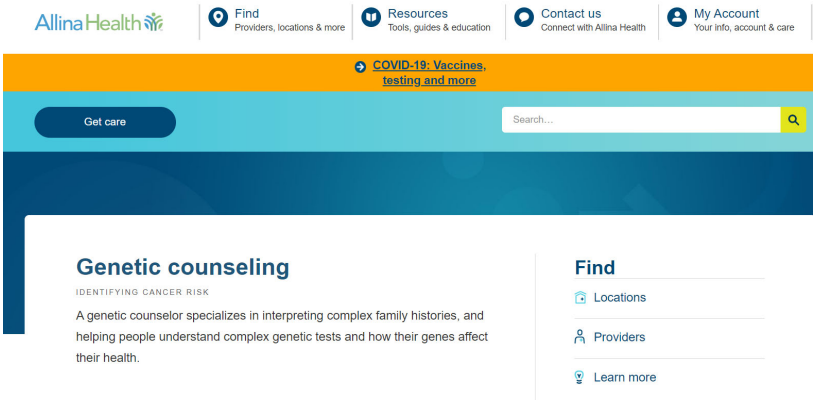

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