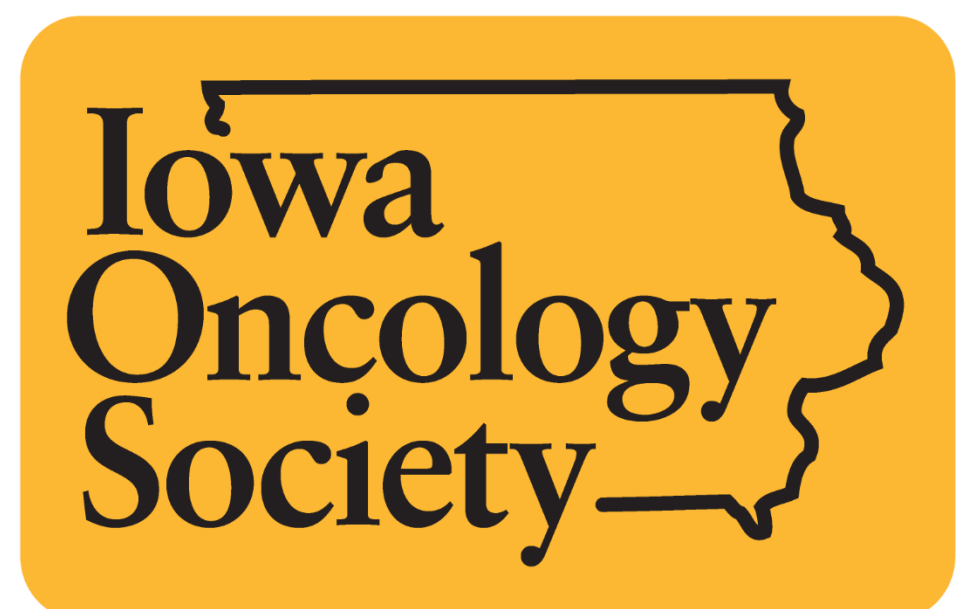


# **A Multidisciplinary Consortium to Advance Genetic Counseling in Oncology**

## **Lunch and Learn #3**

October 29, 2021



# Introductions: Staff

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*Association of Community Cancer Centers (ACCC)*

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# Background

The Iowa Oncology Society (IOS) and the Association of Community Cancer Centers (ACCC) are leading this initiative to explore gaps/barriers around hereditary genetic counseling and testing in patients with cancer and their family members.

# Consortium Members



# Genetic Counseling and Testing in Community Cancer Centers: Perspectives, Challenges, and Opportunities

Anne Frankl, MS, LGC

Licensed Genetic Counselor

*Mission Cancer + Blood*



# Projected Cancer Diagnoses in Iowa in 2021

20,000 projected new cancer diagnoses (ACS):

- Breast cancer (female): 2710
- Prostate: 2530
- Colorectum: 1570
- Melanoma (skin): 1290
- Kidney and renal pelvis: 800
- Uterine corpus: 700
- Pancreas: 620
- Ovary: 200
- Stomach: 200

Many patients will be seen in a community cancer setting.



# Commission on Cancer Accreditation

## *Policy and Procedure for Genetic Counseling and Risk Assessment Services*

Cancer programs must develop a policy and procedure for providing cancer risk assessment, genetic counseling, and genetic testing services on-site or by referral. Genetic services not provided on-site at the facility must be provided through a referral relationship to other facilities and/or local agencies. The policy and procedure must include information/processes for the following:

- Criteria for referral for a genetics evaluation
- Identification of the genetics professionals available on-site and/or by referral
- Identification of the genetics professionals qualified to perform post-test counseling either on-site and/or by referral

Cancer risk assessment and genetic counseling are performed by a genetics professional with an educational background in cancer genetics and hereditary cancer syndromes. Specialized training in cancer genetics is required. Educational seminars offered by commercial laboratories about how to perform genetic testing are not considered adequate training.

Genetics professionals require specialized training in cancer genetics, provide the service regularly, and obtain genetics-specific continuing education.

## PRINCIPLES OF CANCER RISK ASSESSMENT AND COUNSELING

- The decision to offer genetic testing involves three related stages: 1) pre-test counseling done prior to ordering testing; 2) consideration of the most appropriate tests to order; and 3) post-test counseling done when results are disclosed.<sup>1-5</sup> It is recommended that a genetic counselor, clinical geneticist, oncologist, surgeon, oncology nurse, or other health professional with expertise and experience in cancer genetics be involved at each stage whenever possible. Testing should be considered in appropriate high-risk individuals where it is likely to impact the risk management and/or treatment of the tested individuals and/or their at-risk family members.

### Pre-test counseling includes the following elements:

- Evaluate patient's needs and concerns regarding:
  - ▶ Knowledge of genetic testing for cancer risk, including benefits, risks, and limitations
  - ▶ Goals for cancer family risk assessment
- Detailed family history including:
  - ▶ Collection of a comprehensive family history
    - ◊ Assessing family history; close blood relatives include first-, second-, and third-degree relatives on each side of the family, particularly around individuals with a diagnosis of cancer ([See EVAL-B](#))
    - ◊ Types of cancer, bilaterality, age at diagnosis, subtype, and pathology report confirmation
    - ◊ Ethnicity (specifically Ashkenazi Jewish ancestry)
- Detailed medical and surgical history including:
  - ▶ Documentation of prior genetic testing results for patients and their family members
  - ▶ Personal cancer history (eg, age, histology, laterality)
  - ▶ Pathology reports of primary cancers and/or benign lesions (eg, breast biopsies)
  - ▶ Carcinogen exposure (eg, history of radiation therapy)
  - ▶ Reproductive history
  - ▶ Hormone or oral contraceptive use
  - ▶ History of risk-reducing surgeries
- Focused physical exam (conducted by qualified clinician) when indicated:
  - ▶ CS/PHTS specific: dermatologic,<sup>a</sup> including oral mucosa, head circumference, and thyroid (enlarged or nodular on palpation)
  - ▶ Generate a differential diagnosis and educate the patient on inheritance patterns, penetrance, variable expressivity, and the possibility of genetic heterogeneity
  - ▶ Prepare for the possible outcomes of testing, including positive (pathogenic, likely pathogenic), true negative and uninformative negative, uncertain variants, and mosaic results
  - ▶ Obtain written informed consent, and document the informed consent in the patient's medical record
  - ▶ Discuss plan for results disclosure when appropriate, including the possibility of the patient consenting to Release of Information of test results to a close relative or spouse when results are released in case patient is deceased or incapacitated
  - ▶ Discuss possible management options if a mutation is identified (enhanced surveillance, risk-reducing agents, and risk-reducing surgery)
  - ▶ Advise about possible inherited cancer risk to relatives, options for risk assessment, testing, and management
  - ▶ Discuss cost of genetic testing
  - ▶ Provide overview of current legislation regarding genetic discrimination and the privacy of genetic information

[References on  
EVAL-A 7 of 7](#)

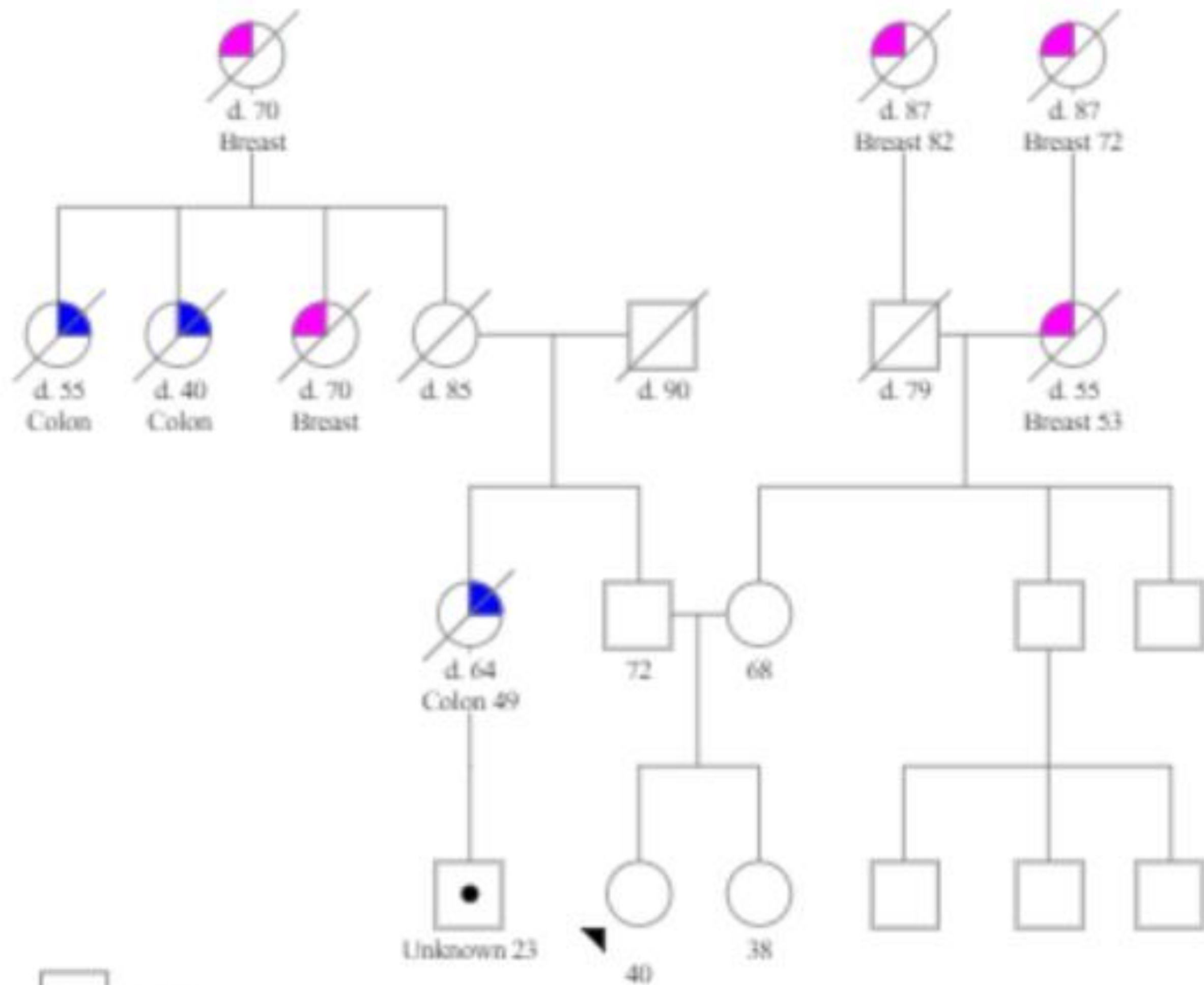


# Community Cancer Centers

- Community cancer centers face challenges in providing genetic counseling and testing services to patients. Genetics providers in these settings also face challenges in providing this care to patients.
- Models for providing care already discussed in previous talks
  - On-site genetics provider
  - Physician-led genetic testing
  - Telegenetics services
- Access to appropriate pre-test genetic counseling improves uptake of genetic testing and improves patient satisfaction and knowledge (McCuaig et al. 2018).

# Objectives

- Review difficulties in providing genetic counseling and testing and discuss opportunities to improve patient care.
- Highlight importance of appropriate genetic counseling and testing for patients.



40 y.o. woman with no personal hx of cancer

Mother reported to have BRCA mutation – report not available

Paternal family hx concerning for hereditary colorectal cancer

# Case Example

- Sent in sample for analysis of BRCA2, MLH1, MSH2, MSH6, PMS2, and EPCAM
- VUS in BRCA2: p.F1870Y
  - no pathogenic mutations identified in any gene on the panel
- Obtained mother's genetic counseling note – c.5609\_5610delTCinsAG



# Case Example

- The VUS in BRCA2 is c.5609T>A
- Contacted both laboratories – was the pathogenic mutation reported incorrectly, or was the VUS incorrect?
- Patient's lab issued a new report: pathogenic mutation identified, mislabeled due to human error

# Many Players, One Goal

- In the community setting, providers may work within different health systems from different organizations
- Surgery, radiology, pathology, medical oncology, radiation oncology, urology, gastroenterology, endocrinology, PCPs ...
- All have different systems and priorities, and there may not be consistency among providers about genetics workflows

# Identifying Appropriate Patients

- 2017 study (Childers et al.):
  - breast cancer patients: 35.6% met one or more select eligibility criteria; of those, 29.0% discussed, 20.2% were advised to undergo, and 15.3% underwent genetic testing.
  - ovarian cancer patients: 15.1% discussed, 13.1% were advised to undergo, and 10.5% underwent testing.
- Access, time, distance, and patient cost barriers likely contribute to disparities in both uptake and outcomes of genetic services (d'Agincourt-Canning 2004). However, genetic testing without genetic providers has been associated with inappropriate testing and overtesting, which could lead to increased healthcare costs. (Cohen et al. 2019)

# “Evaluation” of Patients

- “Genetics evaluation” - ???
  - Patients want testing, even if they don’t meet criteria, and think they will qualify for testing if their provider refers them.
  - Who determines appropriateness of referral (i.e. patient with DCIS at age 75)? What happens if a patient is not a good candidate?
  - Lack of consistency among providers describing genetic counseling process → improper patient expectations.

GCs can’t diagnose a syndrome based upon clinical features – can only suggest that features point to a diagnosis.



# “Evaluation” of Patients

- 51 y.o. male with a pheochromocytoma
- Reported diagnosis of Neurofibromatosis type 2 from PCP  
– has never been formally evaluated
- Clinically, describes features consistent with NF1, not NF2  
– or, could it be a different gene entirely?
- Declined medical genetics evaluation and genetic testing
- In the absence of a qualified clinician/genetic testing, this patient is undiagnosed, but his medical records show NF2 as a diagnosis

# “Evaluation” of Patients

- 55 y.o. woman with breast cancer diagnosed at age 42, then a second primary breast cancer (triple negative) at age 54
- Sister with breast cancer, sister with thyroid cancer, other relatives with breast cancer and kidney cancer
- Sister clinically diagnosed with Cowden syndrome
- Patient has lesion on her lip
- Negative genetic testing (BRCA1, BRCA2, CDH1, PALB2, PTEN, TP53)



(Molière & Mathelin 2020)

# “Evaluation” of Patients

- Meets clinical criteria for Cowden syndrome?
  - Evaluation with a clinical geneticist?
  - Declined by patient

- Document in chart that we have not ruled out Cowden syndrome with a negative test result

**A clinical diagnosis of CS** is established if an individual meets **any one** of the following criteria:

- Pathognomonic mucocutaneous lesions including one of the following:
  - Six or more facial papules, of which three or more must be trichilemmomas
  - Cutaneous facial papules and oral mucosal papillomatosis
  - Oral mucosal papillomatosis and acral keratoses
  - Six or more palmoplantar keratoses
- Two or more major criteria
- One major and three or more minor criteria
- Four or more minor criteria

# Management of Patients with Mutations

- For many patients with mutations, medical management is straightforward
- For others, medical management is complex and requires specific expertise
- Unexpected results from multi-gene panels
- Some patients require non-oncology care based upon gene
- High-risk clinics not often available



# Management of Patients with Mutations

- Lynch syndrome and HBOC (BRCA1/BRCA2 mutations) are two of the most common hereditary cancer syndromes
- Screening is intensive for affected individuals, and prophylactic options are available
- Lynch syndrome:
  - colonoscopies every 1-2 years
  - endometrial biopsies/TVUS
  - upper GI scopes
  - pancreatic cancer screening
  - regular physical exams, urinalysis
  - consideration of regular dermatologic evaluations

# Management of Patients with Mutations

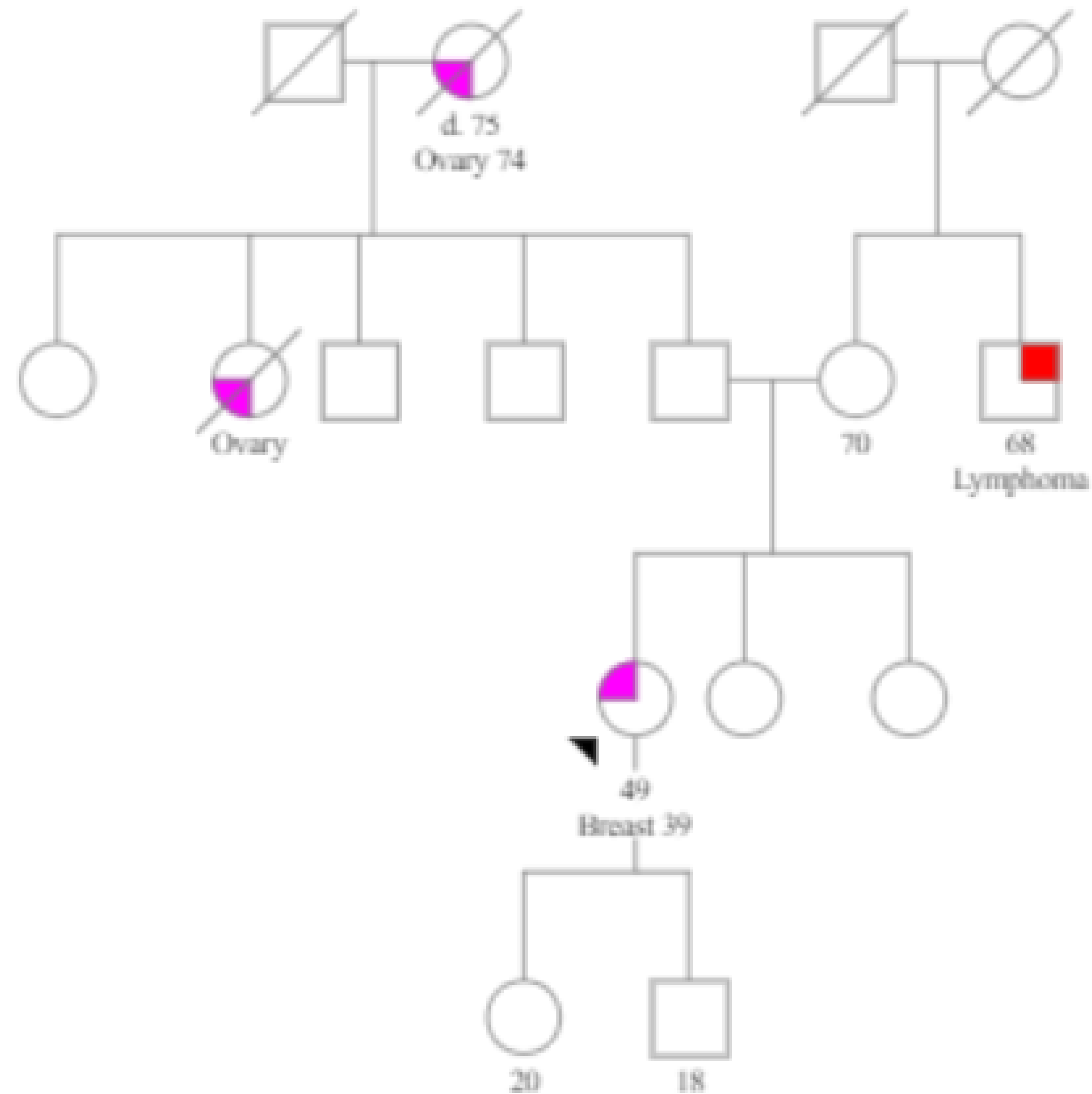
- Piecing care together among providers
  - gastroenterologist, gynecologist or gynecologic oncologist, PCP, dermatologist
- Guidelines for management change over time – how do these providers stay current?
- Find physician champions – providers with interest and expertise

# Management of Patients with Mutations

49 y.o. woman with hx of breast cancer at 39

Prior negative BRCA1/BRCA2 analysis

Presents for updated testing



# Management of Patients with Mutations

## *BRCA1/2 Analyses with CancerNext-Expanded® +RNAinsight®*

### RESULTS

*NF1*

Variant, Likely Pathogenic: c.1261-1G>A

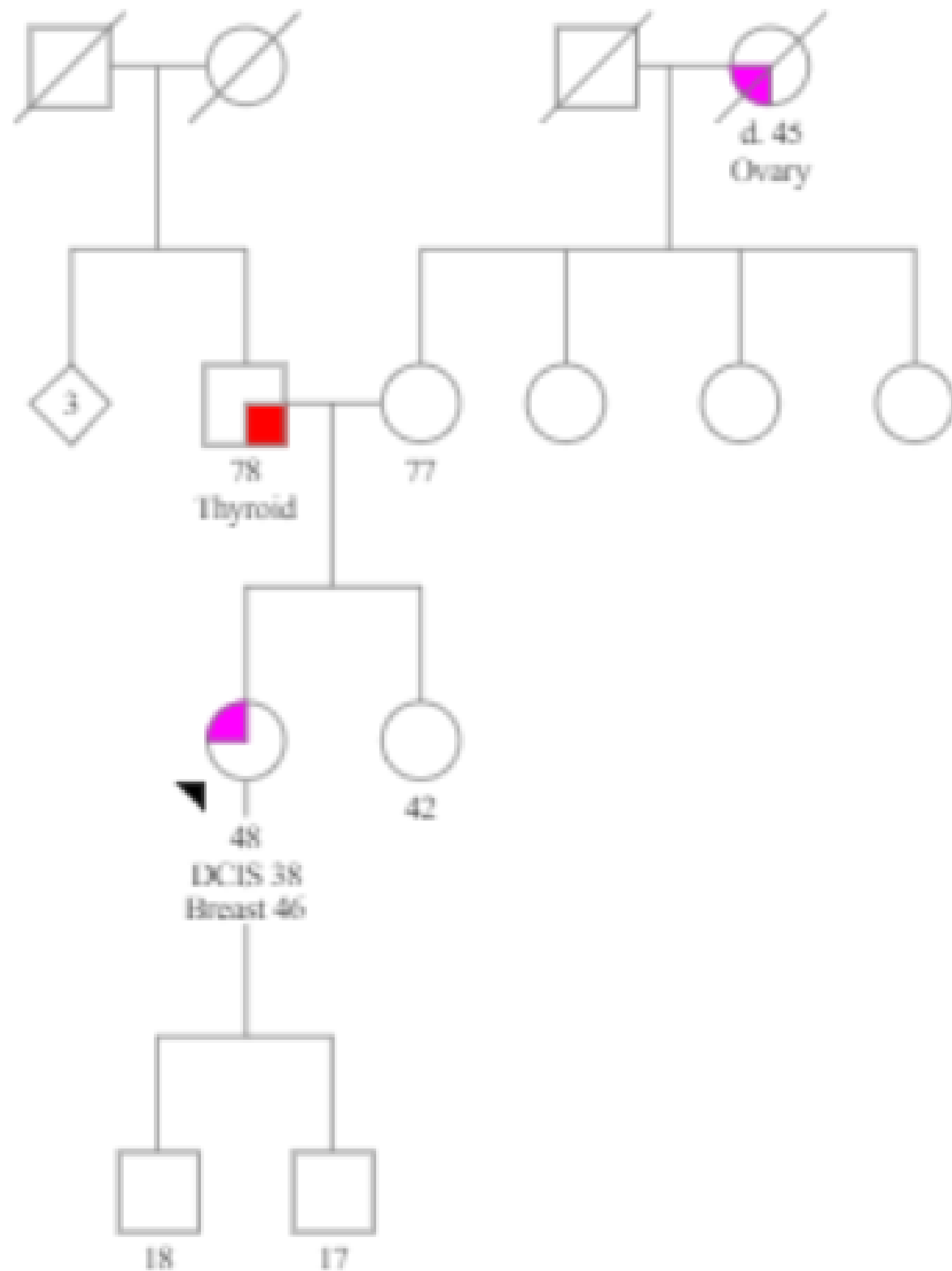
### SUMMARY

**POSITIVE: Likely Pathogenic Variant Detected**

- Does she clinically have NF1? How can we find out?
  - What about her children?
- What management does she need?



# Management of Patients with Mutations



48 y.o. woman with DCIS @ 38 and an invasive ductal carcinoma at 46

Prior negative BRCA1/2 testing

Presented for updated testing given her second primary cancer



## RESULTS

*TP53*

Variant, Likely Pathogenic: c.1101-2A>G

## SUMMARY

### POSITIVE: Likely Pathogenic Variant Detected

## INTERPRETATION

- The **c.1101-2A>G** risk likely pathogenic variant in the *TP53* gene was detected in this individual's sample.
- **Risk estimate:** This result may be consistent with Li Fraumeni syndrome.
- The expression and severity of disease for this individual cannot be predicted.
- Genetic testing for likely pathogenic variants (VLPs) in family members can be helpful in identifying at-risk individuals.
- Genetic counseling is a recommended option for all individuals undergoing genetic testing.
- It is expected that the DNA isolated from peripheral blood lymphocytes or saliva would be representative of an individual's germline DNA; however, the current methodology cannot definitively determine whether the results reported herein represent an alteration of germline versus somatic origin. Somatic *TP53* mutation(s) may also be detected in blood or saliva for a variety of reasons, including but not limited to: clonal hematopoiesis, secondary to chemotherapy, hematologic malignancy/pre-malignancy, or circulating tumor cells. As such, there exists the possibility that this finding is not diagnostic of Li-Fraumeni syndrome (LFS) or Li-Fraumeni-like syndrome. However, if clinical phenotype is consistent with LFS, it is most likely that the identified alteration is germline in origin. Clinical correlation is advised.



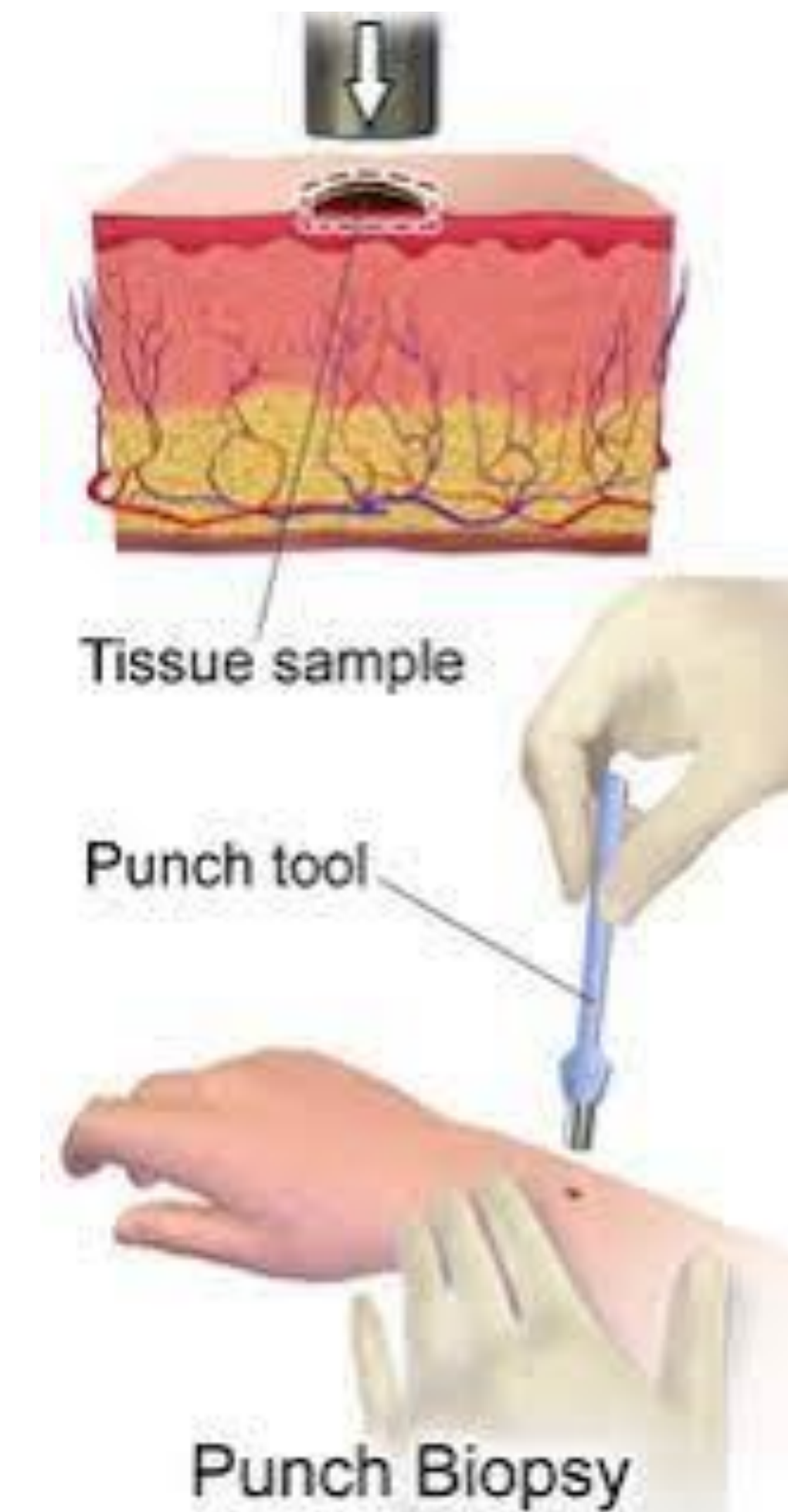


# Management of Patients with Mutations

- TP53 mutations now routinely included in hereditary cancer panels
- “Incidental” mutations – patient doesn’t meet TP53 criteria but has a mutation identified. How is this patient going to be managed?
- VAF  $\neq$  30-70%: how to interpret results?
  - mosaicism
  - CHIP
  - hematologic malignancy or circulating tumor cells
- What about children?

# Obtaining Alternate Specimens

- Some patients require a skin biopsy for testing: patients with hematologic malignancies, individuals with results that could indicate a mutation is not germline
- Difficult to obtain:
  - Who will perform it?
  - How will it be billed?
  - Cost to patient?
  - Where to send sample?
- Answer: find a provider to whom you can refer these patients and help them set up a process.



# Genetic Testing for Cancer Treatment

- When patients require genetic testing to access targeted therapies, is the process for referral and genetic testing the same?

## ◇ Any Age

- To aid in systemic treatment decisions using PARP inhibitors for breast cancer in the metastatic setting<sup>l,k</sup>
- To aid in adjuvant treatment decisions with olaparib for high-risk,<sup>l</sup> HER-2 negative breast cancer<sup>l</sup>
- Triple-negative breast cancer

<sup>k</sup> As indicated in the criteria, testing is recommended for all triple negative breast cancers, and these indications are specifically for PARP inhibitor eligibility.

<sup>l</sup> The definition of high-risk disease is that used in the Phase III OlympiA trial which compared adjuvant Olaparib to placebo among BRCA1/BRCA2 carriers with high-risk disease (Tutt ANJ, et al. NEJM 2021;384:2394-2405). The definition includes:

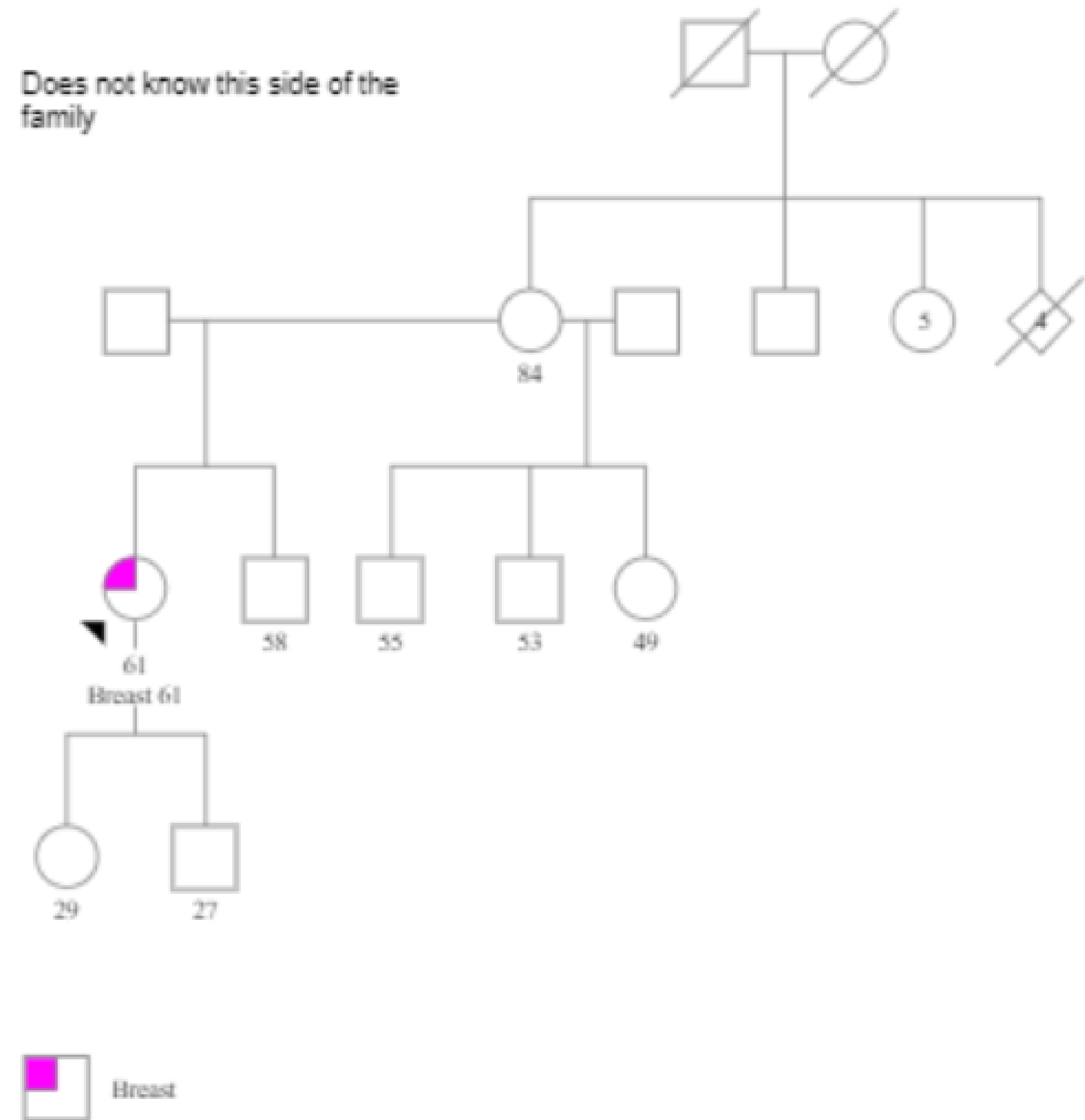
- Triple negative breast cancer treated with either:
  - adjuvant chemotherapy with axillary node-positive disease or an invasive primary tumor  $\geq 2$  cm on pathology analysis
  - neoadjuvant chemotherapy with residual invasive breast cancer in the breast or resected lymph nodes.
- Hormone receptor positive disease treated with either:
  - adjuvant chemotherapy with  $\geq 4$  positive pathologically confirmed lymph nodes
  - neoadjuvant chemotherapy which did not have a complete pathologic response, with a CPS+EG score of 3 or higher.
- The CPS+EG scoring system is based on a combination of clinical and pathologic stage, estrogen receptor status and histologic grade. [See Neoadjuvant Therapy Outcomes Calculator](#) (Jeruss JS, et al. J Clin Oncol 2008;26:246-252; Mittendorf EA, et al. J Clin Oncol 2011;29:1956-1962). See [NCCN Guidelines for Breast Cancer](#) for further details.



61 y.o. woman with locally advanced HER2 negative breast cancer

Neoadjuvant chemotherapy, bilateral mastectomies, adjuvant XRT

Considering maintenance therapy with PARP inhibitor





## GENETIC RESULT: POSITIVE - CLINICALLY SIGNIFICANT MUTATION IDENTIFIED

Note: "CLINICALLY SIGNIFICANT," as defined in this report, is a genetic change that is associated with the potential to alter medical intervention.

GENE	MUTATION	INTERPRETATION
<i>BRCA2</i>	c.7288G>T (p.Glu2430*) Heterozygous	DELETERIOUS

- What if this patient hadn't already had bilateral mastectomies?
- Where does the genetics referral "fit in" to this patient's care? Is there a different workflow needed for patients like her? What should be ordered?
- A process needs to be decided upon with the oncology team.

# Somatic Testing – GC Workflows

- Somatic test results with germline implications
- What if I know a patient needs somatic testing AND germline testing?
- Paired testing? What does that process look like? When is genetics provider involved?
- Answer: genetics provider embedded in oncology practice or reviewing somatic results?

# Picking up the Pieces

- Genetics providers are sometimes involved only after testing has been completed.
  - Or, genetic counseling was provided, but by a GC employed by a laboratory
- What if testing was inappropriate? (test selection, lab selection)
  - May need further testing that won't be covered by insurance
- Completing post-test counseling for patients that didn't have pre-test counseling
  - Un-ringing the bell

# Access to Genetic Counselors

**Summary: H.R.2144 — 117th Congress (2021-2022)**

[All Information](#) (Except Text)

 Listen to this page



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There is one summary for H.R.2144. Bill summaries are authored by [CRS](#).

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## Shown Here:

**Introduced in House (03/23/2021)**

**Access to Genetic Counselor Services Act of 2021**

This bill provides for coverage under Medicare of genetic counseling services that are furnished by genetic counselors. Covered services include those services, as well as incidental services and supplies, that would otherwise be covered under Medicare if provided by a physician.



# Conclusions

In the community cancer setting, there are challenges throughout the genetic counseling and testing process.

An on-site genetics provider is ideal, but other solutions can be employed to provide access to this important service, including use of GC-extenders.

Genetics providers are going to have to build relationships within their community in order to best serve their patients.

**Questions?**

**Thank You!**

Commission on Cancer: Optimal Resources for Cancer Care 2020 Standards | Effective January 2020 Updated February 2021

Cohen SA, Bradbury A, Henderson V, Hoskins K, Bednar E, Arun BK. Genetic Counseling and Testing in a Community Setting: Quality, Access, and Efficiency. *Am Soc Clin Oncol Educ Book*. 2019 Jan;39:e34-e44. doi: 10.1200/EDBK\_238937. Epub 2019 May 17. PMID: 31099680.

Cragun D, Lewis C, Camperlengo L, Pal T. Hereditary Cancer: Example of a Public Health Approach to Ensure Population Health Benefits of Genetic Medicine. *Healthcare (Basel)*. 2016;4(1):6. Published 2016 Jan 8. doi:10.3390/healthcare4010006

Childers CP, Childers KK, Maggard-Gibbons M, et al. National estimates of genetic testing in women with a history of breast or ovarian cancer. *J Clin Oncol*. 2017;35:3800-3806.

d'Agincourt-Canning L . Genetic testing for hereditary cancer: challenges to ethical care in rural and remote communities. *HEC Forum* 2004; **16**: 222–233.

McCuaig JM, Armel SR, Care M, Volenik A, Kim RH, Metcalfe KA. Next-Generation Service Delivery: A Scoping Review of Patient Outcomes Associated with Alternative Models of Genetic Counseling and Genetic Testing for Hereditary Cancer. *Cancers (Basel)*. 2018;10(11):435. Published 2018 Nov 13. doi:10.3390/cancers10110435

Molière S, Mathelin C. The Cowden Syndrome. *N Engl J Med*. 2020 Apr 9;382(15):e29. doi: 10.1056/NEJMicm1910478. PMID: 32268030

National Comprehensive Cancer Network. Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic (Version 1.2022). [https://www.nccn.org/professionals/physician\\_gls/pdf/genetics\\_bop.pdf](https://www.nccn.org/professionals/physician_gls/pdf/genetics_bop.pdf). Accessed October 14, 2021.