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Tackling Barriers to Genomic and Biomarker Testing in Precision Cancer Medicine: Integrating the Latest Evidence into Practice for Community Oncology Clinicians

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Part 2: Genetic Counseling: Accessibility and Availability

Supported by an educational grant from Merck Sharp & Dohme, LLC, a subsidiary of Merck & Co., Inc.

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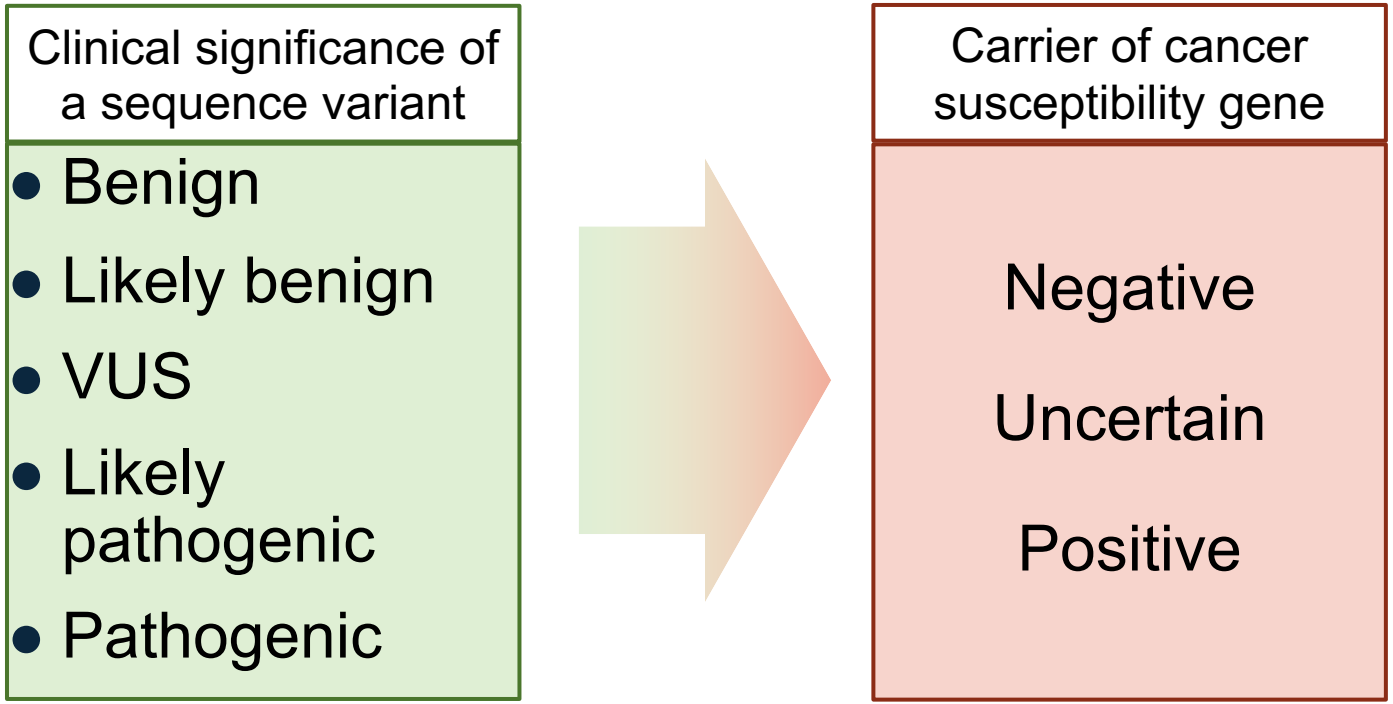
Learning Objective

Employ strategies to provide genetic counseling for patients with cancer

ACMG/AMP Classification of Genetic Variants

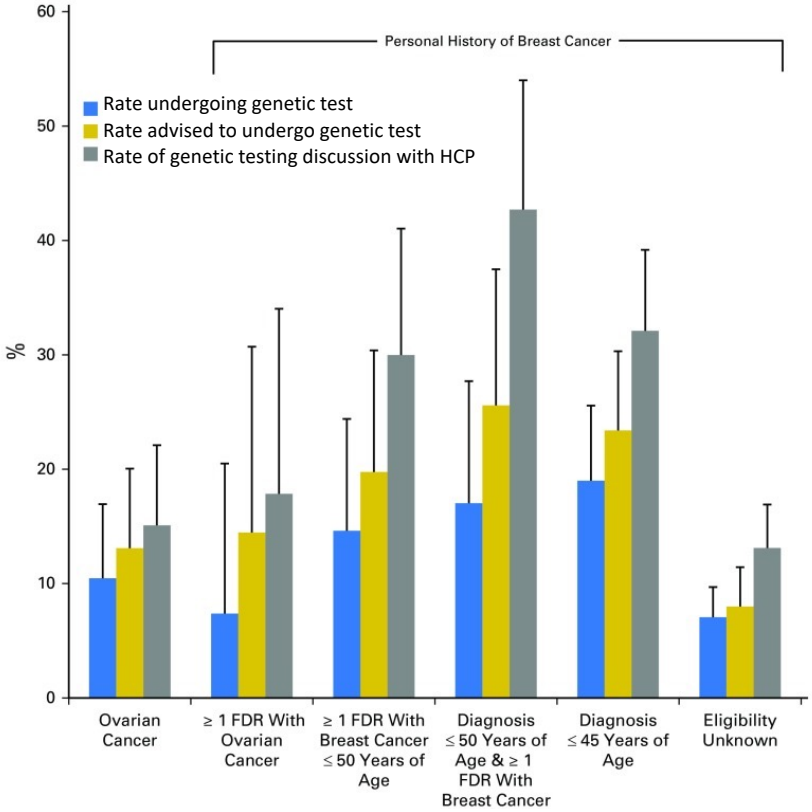


ACMG/AMP = American College of Medical Genetics and Genomics and Association for Molecular Pathology. VUS = variant of uncertain significance

Richards S, et al. *Genet Med*. 2015;17(5):405-424.

Suboptimal Genetic Testing for Patients with Cancer

- Indications for genetic testing in patients with cancer are expanding in academic and community settings
  - Incidence of pathogenic variants among individuals ranges:
    - 5% - 10% among unselected breast, colorectal, endometrial, pancreatic, and prostate cancer
    - Up to 18% among those with ovarian cancer
- Low testing and referral rates
  - Fewer than one in five individuals with a history of breast or ovarian cancer underwent genetic testing and most never discussed testing with a HCP

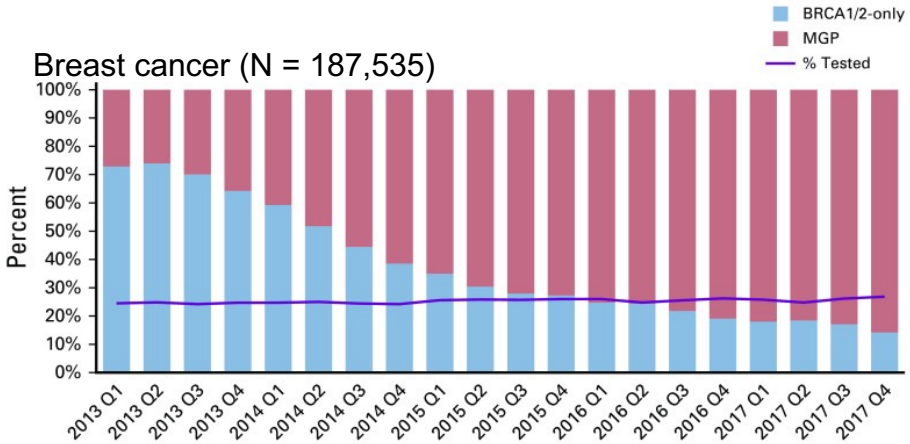


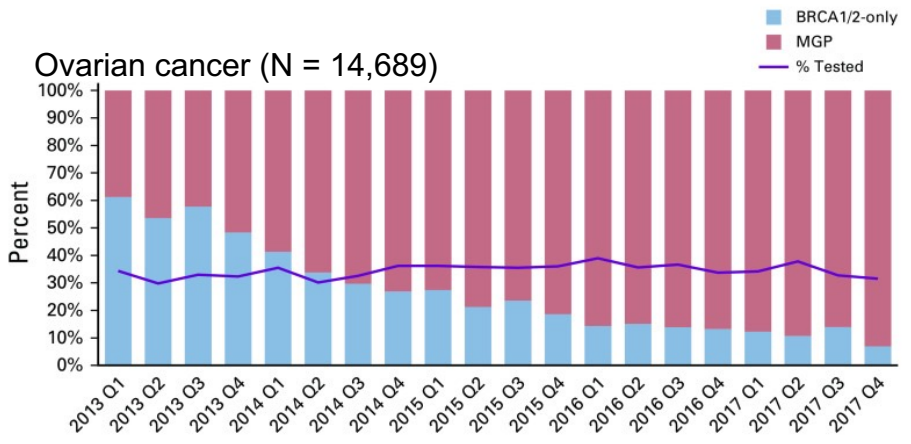
HCP = health care provider

Cohen SA, et al. American Society of Clinical Oncology Educational Book. 2019(39):e34-e44. Childers CP, et al. *J Clin Oncol*. 2017;35(34):3800-3806.

Trends in Genetic Test Rates and Test Type for Patients with Breast or Ovarian Cancer

- SEER records of women of age ≥ 20 years diagnosed with breast or ovarian cancer from 2013 to 2017 in California or Georgia were linked to the results of clinical germline testing through 2019
- One quarter (25%) of 187,535 patients with breast cancer and one third (34%) of 14,689 patients with ovarian cancer were tested; annually, testing increased by 2%, whereas the number of genes tested increased by 28%





MGP = multigene panel; SEER = Surveillance, Epidemiology, and End Results Program

Kurian AW, et al. *J Clin Oncol*. 2021;39(15):1631-1640.

Ovarian Cancer and Genetic Predispositions

- 20% of ovarian cancers are due to
  - Mutations in BRCA1, BRCA2, BRIP1, RAD51D, RAD51C, PALB2
  - Mismatch repair genes MLH1, MSH2, MSH6, and PMS2
- Universal genetic counseling and testing is recommended for all women with epithelial ovarian cancer
  - However, a meta-analysis of 35 studies with patients diagnosed with ovarian cancer found that only **39% of patients were referred to genetic counseling** and **80% went on to complete genetic testing** (~30% of the overall population)
    - Genetic **counseling** was completed by 43% of White patients, 24% of Black patients, and 23% of Asian patients
    - Genetic **testing** was completed by 40% of White patients, 26% of Black patients, and 14% of Asian patients
    - Uninsured patients were much less likely than those with private insurance to complete genetic testing (23% vs 47%)

Racial, ethnic, and socioeconomic barriers hinder uptake of genetic counseling

Norquist BM, et al. *JAMA Oncol*. 2016;2:482-490. Daly MB, et al. *JNCCN*. 2020;18(4):380-391. Society of Gynecologic Oncology. *Obstet Gynecol*. 2017;130(3):e110-e126. Randall LM, et al. *Gynecol Oncol*. 2017;146(2):217-224. Lin J, et al. *Gynecol Oncol*. 2021;162(2):506-516.

NCCN Testing Criteria for High-penetrance Breast Cancer Susceptibility Genes

Testing is clinically indicated in the following scenarios: Breast

- 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[h,i] (See NCCN Guidelines for Breast Cancer)
      - To aid in adjuvant treatment decisions with olaparib for high-risk,[j] HER2-negative breast cancer[h]
    - Pathology/histology
      - Triple-negative breast cancer
      - Multiple primary breast cancers (synchronous or metachronous)[k]
      - Lobular breast cancer with personal or family history of diffuse gastric cancer See NCCN Guidelines for Gastric Cancer
    - Male breast cancer
    - Ancestry: Ashkenazi Jewish ancestry
  - Any age (continued):
    - Family history[l]
      - ≥1 close blood relative[m] with ANY:
        - breast cancer at age ≤50
        - male breast cancer
        - ovarian cancer
        - pancreatic cancer
        - prostate cancer with metastatic,[n] or high- or very-high-risk group (Initial Risk Stratification and Staging Workup in NCCN Guidelines for Prostate Cancer)
      - ≥3 total diagnoses of breast cancer in patient and/or close blood relatives[m]
      - ≥2 close blood relatives[m] with either breast or prostate cancer (any grade)
- Family history of cancer only
  - An affected individual (not meeting testing criteria listed above) or unaffected individual with a first- or second-degree blood relative meeting any of the criteria listed above (except unaffected individuals whose relatives meet criteria only for systemic therapy decision-making).[o]
    - If the affected relative has pancreatic cancer or prostate cancer only first-degree relatives should be offered testing unless indicated based on additional family history.
  - An affected or unaffected individual who otherwise does not meet the criteria above but has a probability >5% of a *BRCA1/2* pathogenic variant based on prior probability models (eg, Tyrer-Cuzick, BRCAPro, CanRisk)[p]

Criteria met → See GENE-1

If testing criteria not met, consider testing criteria for other hereditary syndromes → If criteria for other hereditary syndromes not met, then cancer screening as per NCCN Screening Guidelines

National Comprehensive Cancer Network. https://www.nccn.org/professionals/physician_gls/pdf/genetics_bop.pdf. Accessed February 27, 2023

NCCN Testing Criteria for High-penetrance Breast Cancer Susceptibility Genes

Testing *may be* considered in the following scenarios (with appropriate pre-test education and access to post-test management): **Breast**
• Personal history of breast cancer <60 y not meeting any of the above criteria may approach a 2.5% probability of having a PV, based on recent data.[q] It is cautioned that the majority of those PVs will be in moderate penetrance genes, which are over-represented in older affected individuals, and for which data on appropriate management are often lacking. Access to an experienced genetic counseling team to discuss management options is particularly important in this setting. • Personal history of breast cancer diagnosed at any age with ≥1 close blood relative[m] with intermediate-risk prostate cancer with intraductal/cribriform histology (see Initial Risk Stratification and Staging Workup in NCCN Guidelines for Prostate Cancer) • An affected or unaffected individual who otherwise does not meet any of the above criteria but with a 2.5%–5% probability of *BRCA1/2* pathogenic variant based on prior probability models (eg, Tyrer-Cuzick, BRCAPro, CanRisk)[e]

There is a low probability (<2.5%) that testing will have findings of documented high-penetrance genes in the following scenarios: **Breast**
• Female diagnosed with breast cancer at age >60 y, with no close relative[m] with breast, ovarian, pancreatic, or prostate cancer. • Diagnosed with localized prostate cancer with Gleason Score <7 and no close relative[m] with breast, ovarian, pancreatic, or prostate cancer.

National Comprehensive Cancer Network. https://www.nccn.org/professionals/physician_gls/pdf/genetics_bop.pdf. Accessed February 27, 2023

NCCN Testing Criteria for Susceptibility Genes in Ovarian and Pancreatic Cancers

Testing is clinically indicated in the following scenarios: **Ovarian**
• See General Testing Criteria on CRIT-1.
• Personal history of epithelial ovarian cancer[r] (including fallopian tube cancer or peritoneal cancer) at any age
• Family history of cancer only ▸ An unaffected individual with a first- or second-degree blood relative with epithelial ovarian cancer[r] (including fallopian tube cancer or peritoneal cancer) at any age[o] ▸ An unaffected individual who otherwise does not meet the criteria above but has a probability >5% of a *BRCA1/2* pathogenic variant based on prior probability models (eg, Tyrer-Cuzick, BRCAPro, CanRisk)[p]

Testing is clinically indicated in the following scenarios: **Pancreatic**
• See General Testing Criteria on CRIT-1.
• Exocrine pancreatic cancers[s] ▸ All individuals diagnosed with exocrine pancreatic cancer[t] ▸ First-degree relatives of individuals diagnosed with exocrine pancreatic cancer[u]
• Neuroendocrine pancreatic tumors - See NCCN Guidelines for Neuroendocrine and Adrenal Tumors

Criteria met → See GENE-1

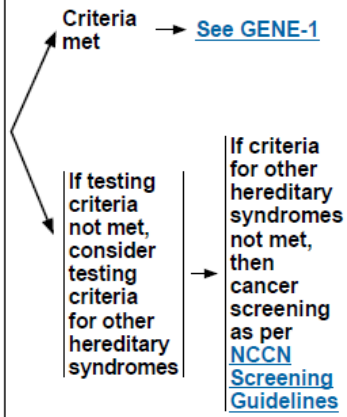
If testing criteria not met, consider testing criteria for other hereditary syndromes → If criteria for other hereditary syndromes not met, then cancer screening as per NCCN Screening Guidelines

National Comprehensive Cancer Network. https://www.nccn.org/professionals/physician_gls/pdf/genetics_bop.pdf. Accessed February 27, 2023

NCCN Testing Criteria for High-penetrance Prostate Cancer Susceptibility Genes

Testing is clinically indicated in the following scenarios: Prostate

- See General Tumor Criteria on CRIT-1.
- Personal history of prostate cancer with specific features:
  - By tumor characteristics (any age)
    - ◊ Metastatic[n]
    - ◊ Histology
      - – high- or very-high-risk group (see Initial Risk Stratification and Staging Workup in NCCN Guidelines for Prostate Cancer)
  - By family history and ancestry
    - ◊ ≥1 close blood relative[m] with:
      - – breast cancer at age ≤50 y
      - – triple-negative breast cancer at any age
      - – male breast cancer at any age
      - – ovarian cancer at any age
      - – pancreatic cancer at any age
      - – metastatic,[n] high- or very-high-risk group (see Initial Risk Stratification and Staging Workup in NCCN Guidelines for Prostate Cancer) at any age
    - ◊ ≥2 close blood relatives[m] with either breast or prostate cancer (any grade) at any age
    - ◊ Ashkenazi Jewish ancestry[c]
- Family history of cancer only
  - An affected (not meeting testing criteria listed above) or unaffected individual with a first-degree blood relative meeting any of the criteria listed above (except unaffected individuals whose relatives meet criteria only for systemic therapy decision-making)[o]



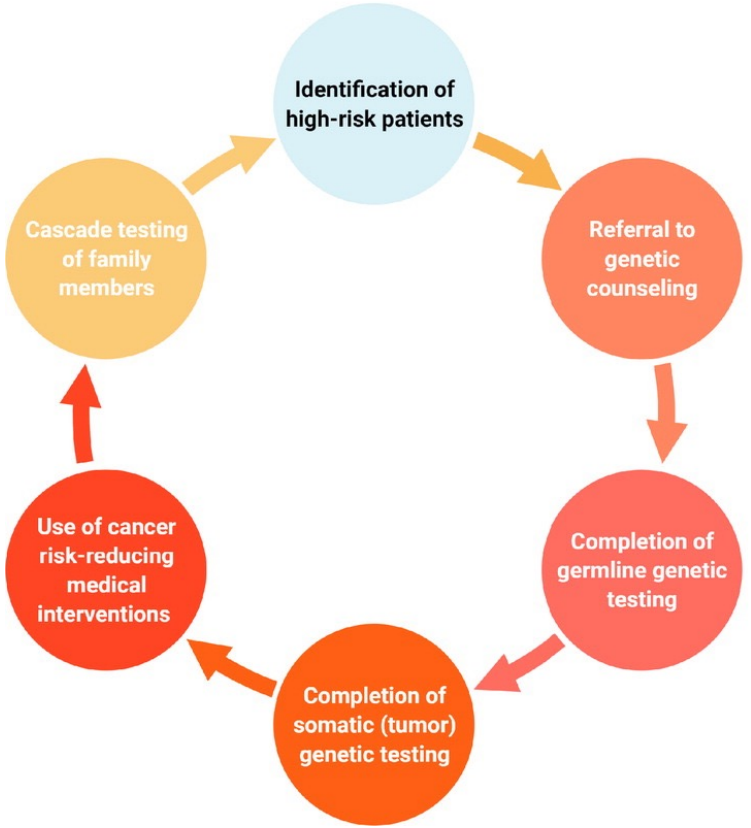
Testing *may be* considered in the following scenario:

- Personal history of prostate cancer with intermediate-risk prostate cancer with intraductal/cribriform histology (see Initial Risk Stratification and Staging Workup in NCCN Guidelines for Prostate Cancer) at any age

National Comprehensive Cancer Network. https://www.nccn.org/professionals/physician_gls/pdf/genetics_bop.pdf. Accessed February 27, 2023

Traditional Genetic Counseling

- Genetic counseling and testing traditionally has been provided in-person
  - Includes pre- and post-test counseling
  - Offered only to individuals who met very strict criteria
  - Primary care physicians, family medicine, and obstetrics and gynecology have the lowest rates of referral to genetic counselors



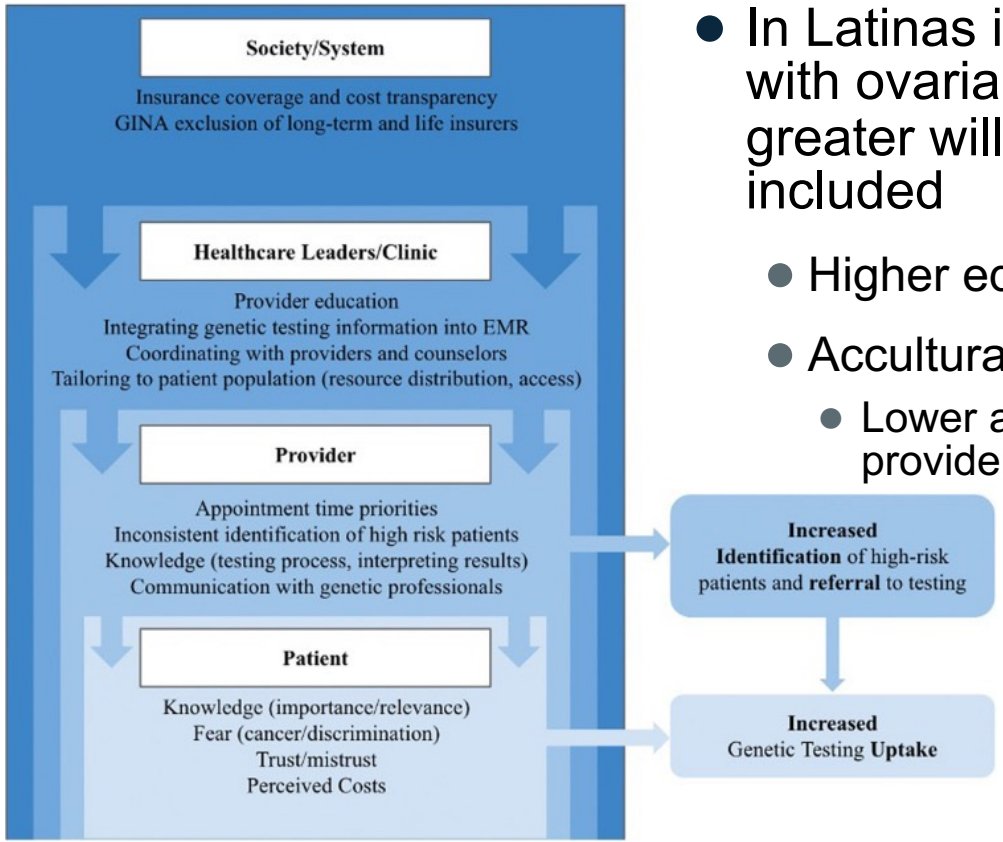
Frey MK, et al. American Society of Clinical Oncology Educational Book. 2022(42):471-482.

When There Are Not Enough Genetic Counselors

- Few board-certified genetic counselors, particularly in the community setting
  - Reduces equity of access that may result in worse cancer outcomes and preventable cancer deaths
  - Hispanic and Black patients are consistently less likely to be referred for genetic counseling across all specialties
    - Referral most often after a cancer diagnosis and not based on family history
  - Disparities in genetic medicine are not limited to germline testing and extend to somatic tumor profiling

Cohen SA, et al. American Society of Clinical Oncology Educational Book. 2019(39):e34-e44. Frey MK, et al. American Society of Clinical Oncology Educational Book. 2022(42):471-482.

Factors Affecting the Intention to Test



- In Latinas in southern California diagnosed with ovarian cancer, factors associated with a greater willingness to receive genetic testing included
  - Higher educational levels
  - Acculturation
    - Lower acculturation increased dependency on provider characteristics (female, Spanish-speaking)
  - Presence of social support
  - Insurance coverage
  - Higher medical literacy

Ioffe YJ, et al. *Gynecol Oncol*. 2023;169:125-130. Dusic EJ, et al. *Front Digit Health*. 2022;4:961128.

Leveraging Health Technologies to Improve Access to Genetic Counseling

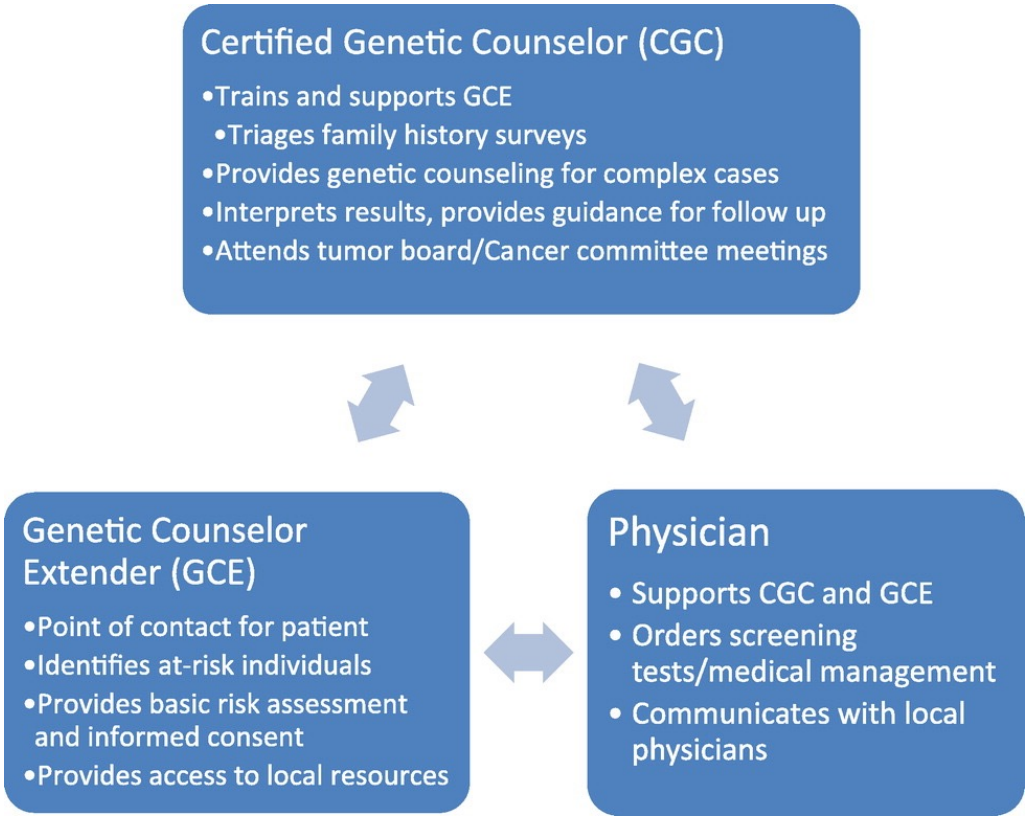
- Eligibility criteria for genetic testing based on family history miss > 50% of carriers
  - Approximately 20% of eligible US women undergo genetic testing for breast and ovarian susceptibility
  - However, population-based screen is challenging (high VUS and false negative rate; low infrastructure and personnel)

VUS = variant of uncertain significance

Cohen SA, et al. American Society of Clinical Oncology Educational Book. 2019(39):e34-e44. Frey MK, et al. American Society of Clinical Oncology Educational Book. 2022(42):471-482.

Expanding Reach of Genetic Counselors

- Telehealth/telegenetic counseling
  - Reduced cost of genetic services
  - Similar patient-reported knowledge, perceived stress, and satisfaction
  - Reduced completion of genetic counseling compared to in-person
  - Still relies on genetic counselor
- Collaboration with genetics HCPs



Cohen SA, et al. American Society of Clinical Oncology Educational Book. 2019(39):e34-e44. Frey MK, et al. American Society of Clinical Oncology Educational Book. 2022(42):471-482.

Innovative Service Delivery Models

- Education of nongenetist HCPs
  - Improve medical history and risk screening at sites of primary care, (eg: gynecology clinics, breast imaging centers)
- Electronic aids
  - Can assist with personal and family history collection, calculate the probability of carrying a pathogenic variant, assess concordance with guidelines, offer interactive patient counseling, and facilitate genetic testing process, and alert providers that a patient would benefit from a genetic assessment
  - Examples:
    - EHR reviews can be automated
    - Interactive AI and chatbots

AI = artificial intelligence; EHR = electronic health records

Cohen SA, et al. American Society of Clinical Oncology Educational Book. 2019(39):e34-e44. Frey MK, et al. American Society of Clinical Oncology Educational Book. 2022(42):471-482. Arun B et.al *Cancer*. 2022 Jan 1;128(1):94-102

Summary

- There is suboptimal genetic testing in patients with cancer, with < 20% of individuals with a history of breast or ovarian cancer undergoing genetic testing
  - Leads to disparities in care
- Universal genetic counseling and testing is recommended for all women with epithelial ovarian cancer, but only 39% of patients were referred to genetic counseling and 30% completed genetic testing
- There are guideline definitions for patients with a high-risk of harboring cancer susceptibility genes
- There are insufficient numbers of board-certified genetic counselors, particularly in the community setting
- Innovative strategies to provide genetic counseling for all patients includes, telehealth/telegenetics, improved education of non-genetic counselors and greater collaboration with genetics counselors, electronic aids, and clinical decision support tools

SMART Goals

Specific, Measurable, Attainable, Relevant, Timely

- Use guideline definitions for patients with a high-risk of harboring cancer susceptibility genes
  - Refer these patients to genetic counseling
- Follow up with your patients who are recommended to have genetic counseling and address any barriers that reduce adherence to guideline recommendations
- Encourage your clinic administration to investigate the breadth of innovative strategies to provide genetic counseling for all patients

To Receive Credit

To receive CME/CE credit for this activity, participants must complete the post-test and evaluation online.

Participants will be able to download and print their certificate immediately upon completion.

CME OUTFITTERS

Oncology Hub

Free resources and education to educate health care providers and patients on oncology **https://www.cmeoutfitters.com/oncology-education-hub/**

Diversity and Inclusion Hub

Free resources and education to educate health care providers and patients on health-related inequities
https://www.cmeoutfitters.com/diversity-and-inclusion-hub/