Prevention, Risk Reduction, & Screening for Hereditary Pancreatic Cancers

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Review of Disparities in Genetics

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Disclosures

- No disclosures

Objectives

1

Discuss ways to prevent or reduce risk for hereditary pancreatic cancer

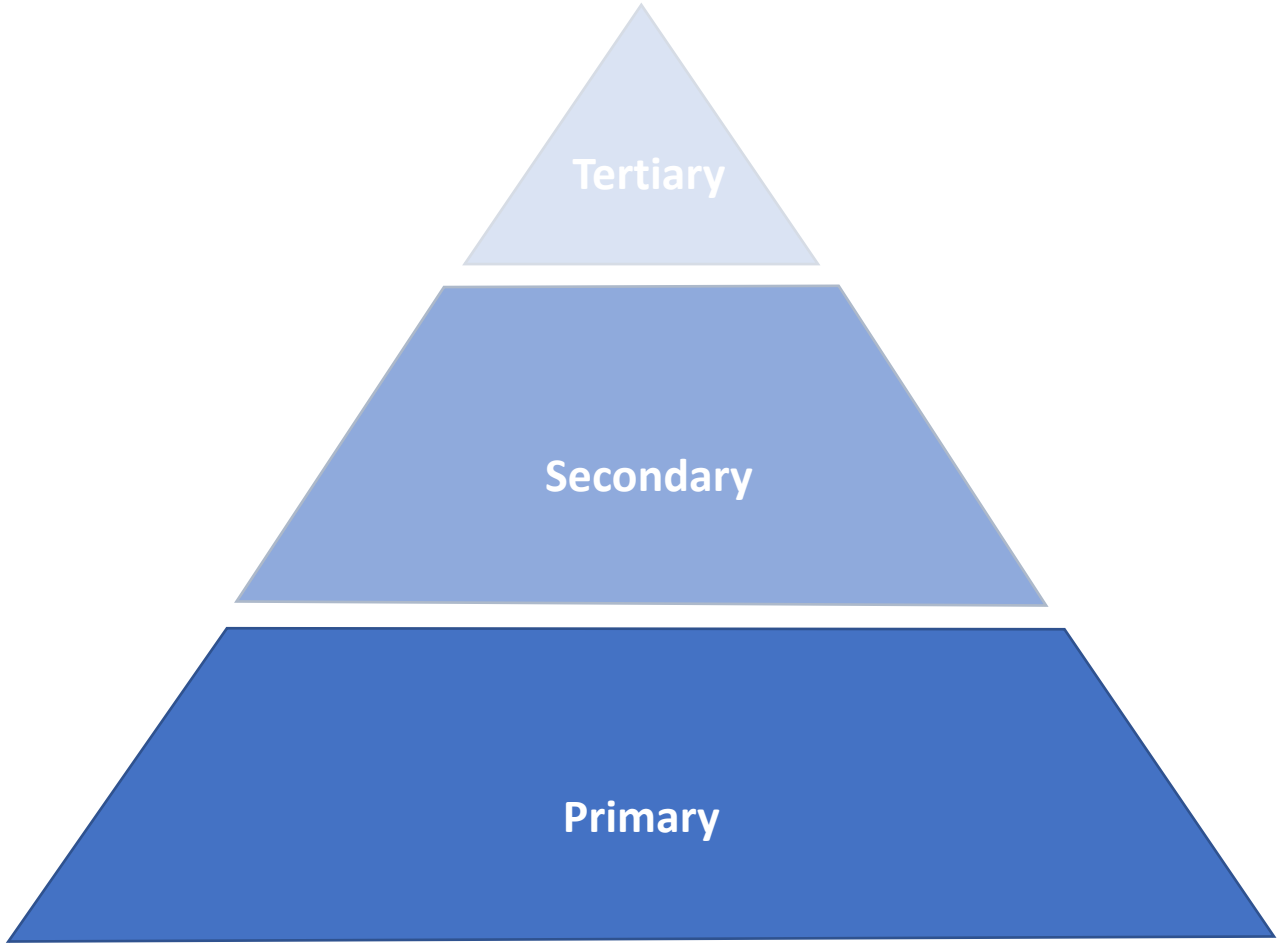
2

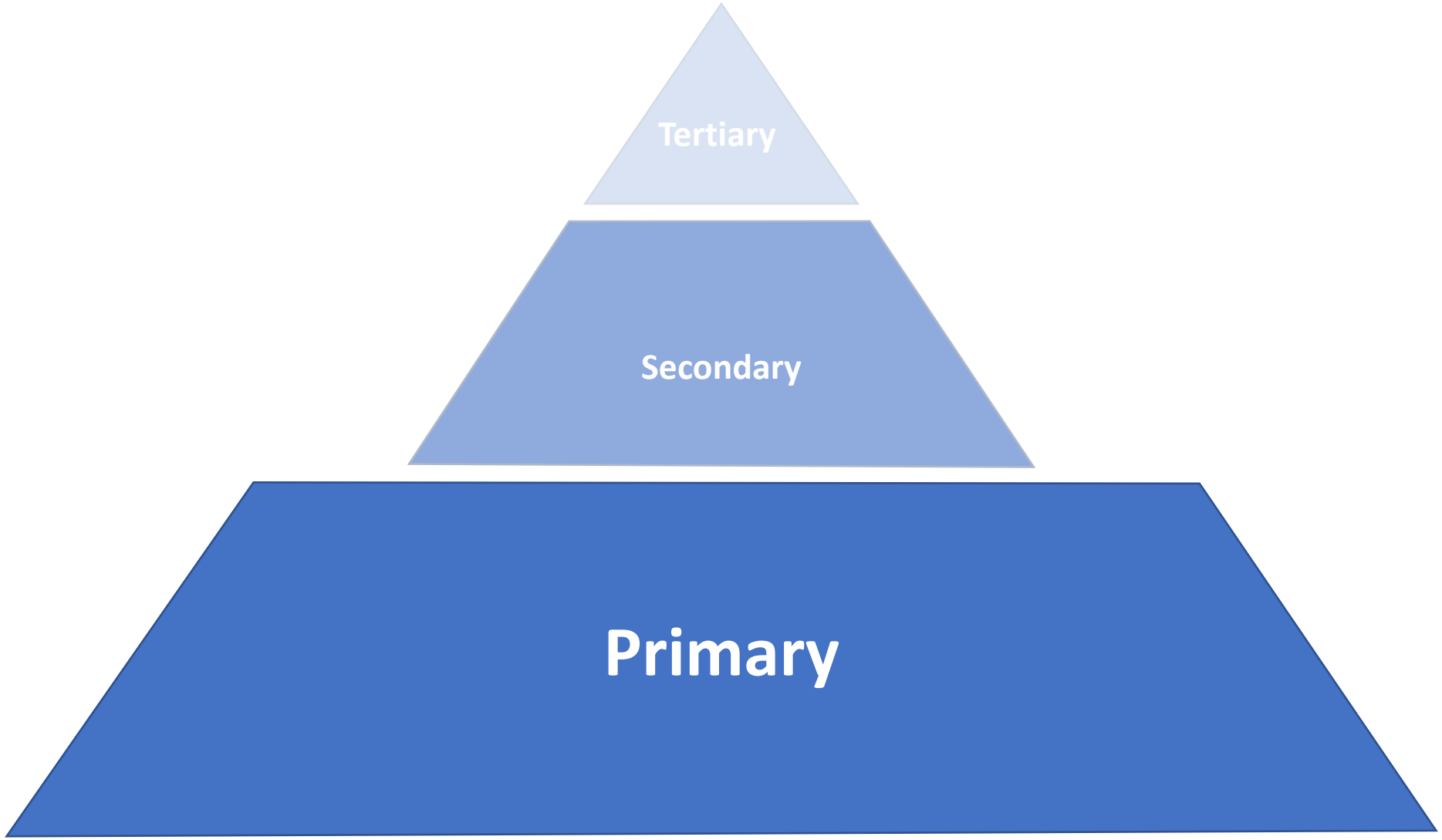
Review pancreatic cancer screening guidelines for individuals with hereditary cancer syndromes

3

Identify groups of patients who are at risk to experience health disparities or inequities related to hereditary cancer assessment, testing, and follow up

Prevention


Tertiary
Secondary
Primary


Tertiary
Secondary
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Primary Prevention

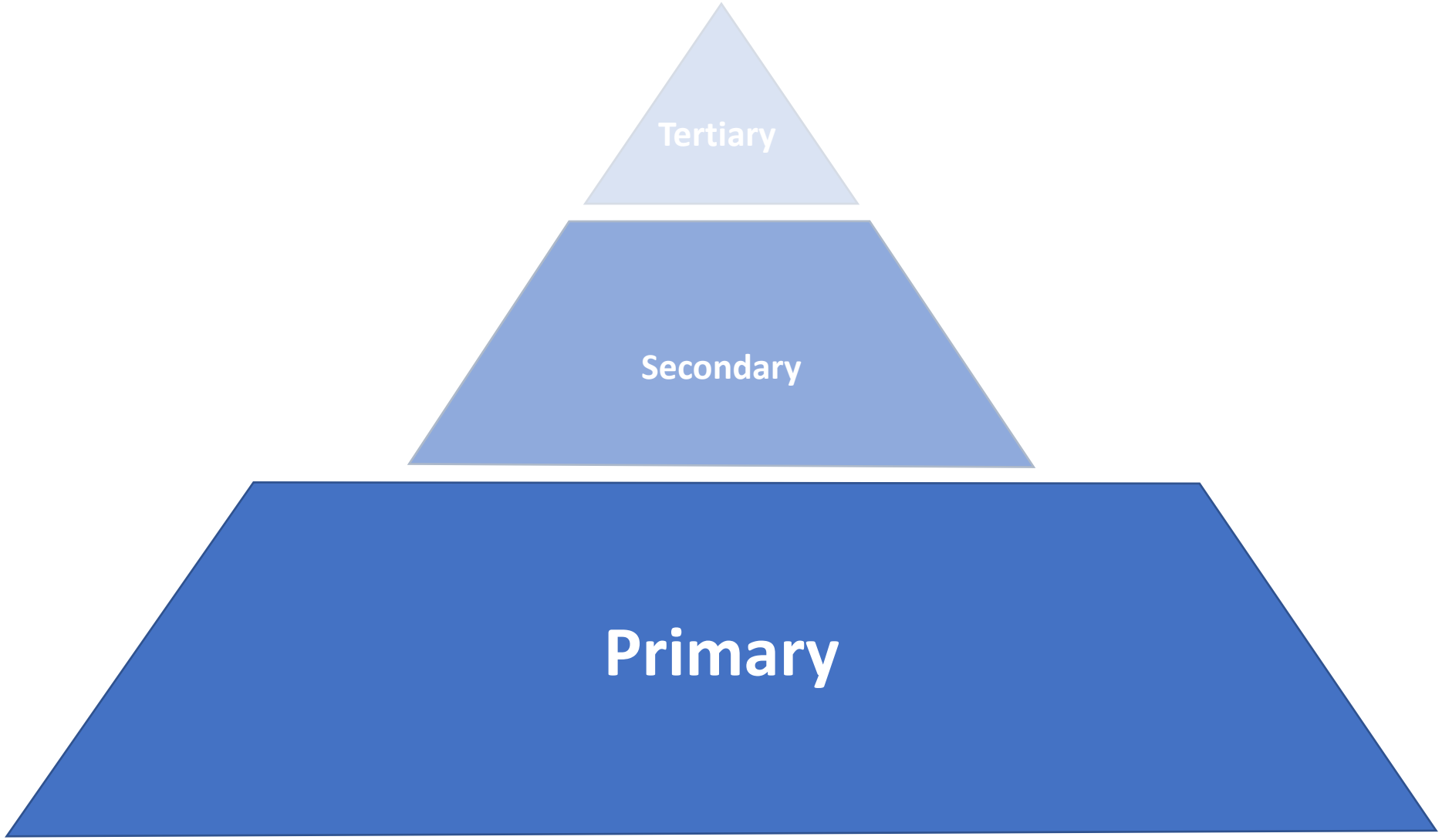
Correcting for modifiable risk factors may **reduce incidence of PC by 30%**

SMOKING

ALCOHOL ABUSE

OBESITY

DIABETES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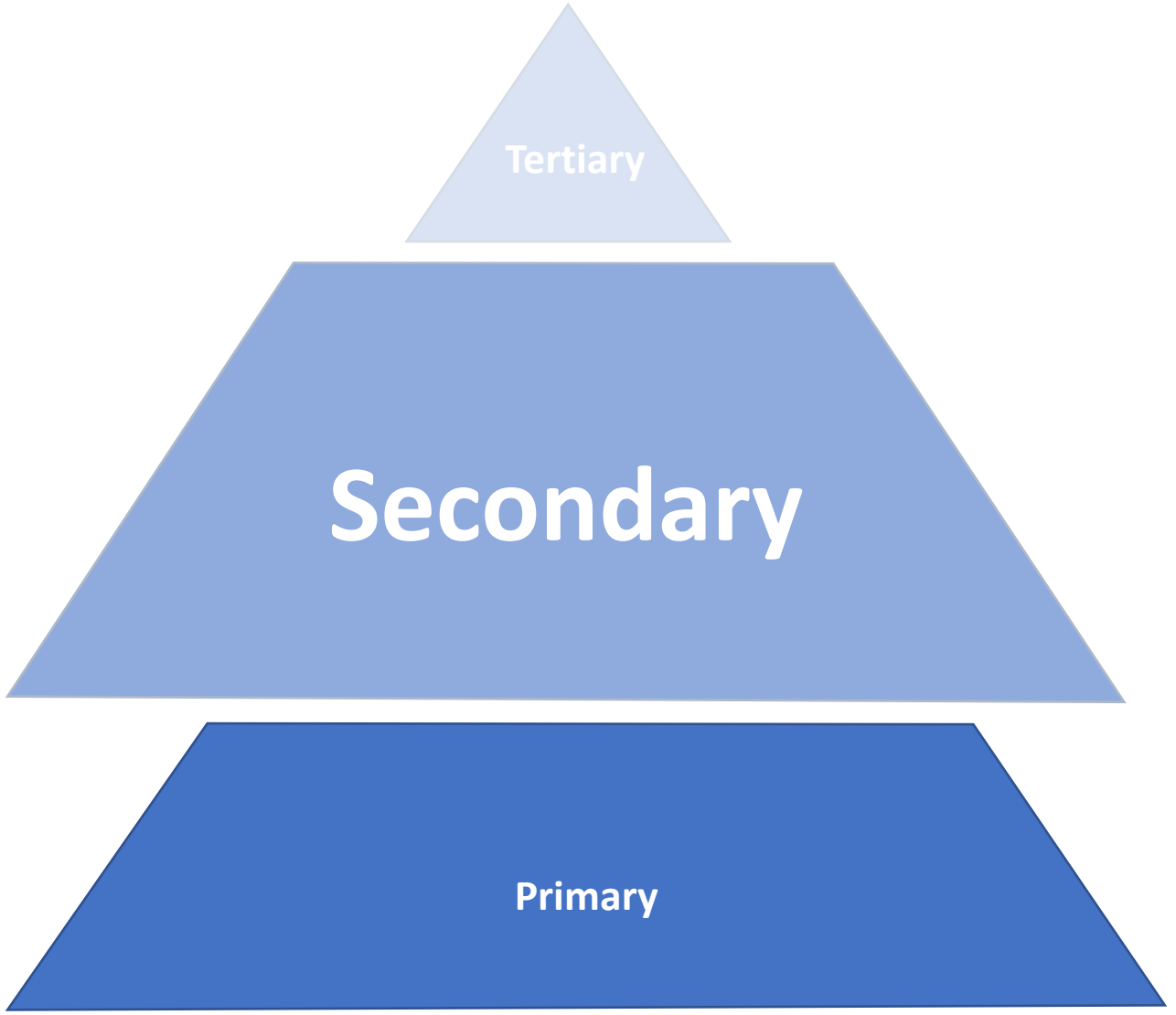

Tertiary
Secondary
Primary

Secondary Prevention

Not feasible to create population-based screening program due to low general population risk for PC (1.7%)

Instead, screening programs are targeted to at-risk groups

Screening for At-Risk Groups

Emerging data has largely focused on:

P/LP variant in PC susceptibility gene AND family hx PC

Family history of PC:

≥2 FDR from the same side of the family	≥3 FDR and/or SDR from the same side of the family

General Guidance for PC Screening

- Performed in experienced high-volume centers
- After an in-depth discussion of potential limitations of screening
  - Cost
  - High incidence of benign or indeterminate pancreatic abnormalities
  - Uncertainties about potential benefits of screening
- Consider annual contrast-enhanced MRI/MRCP and/or EUS
  - Consider shorter screening intervals based on clinical judgement
- Most small cystic lesions will NOT warrant biopsy, surgical resection, or any other intervention

Screening for At-Risk Groups: Benefits

Suggestion of downstaging

- 75-90% of screening-detected PC is surgically resectable
- Higher than historical rates of PC detected by symptoms

Suggestion of improved mortality. Studies demonstrate:

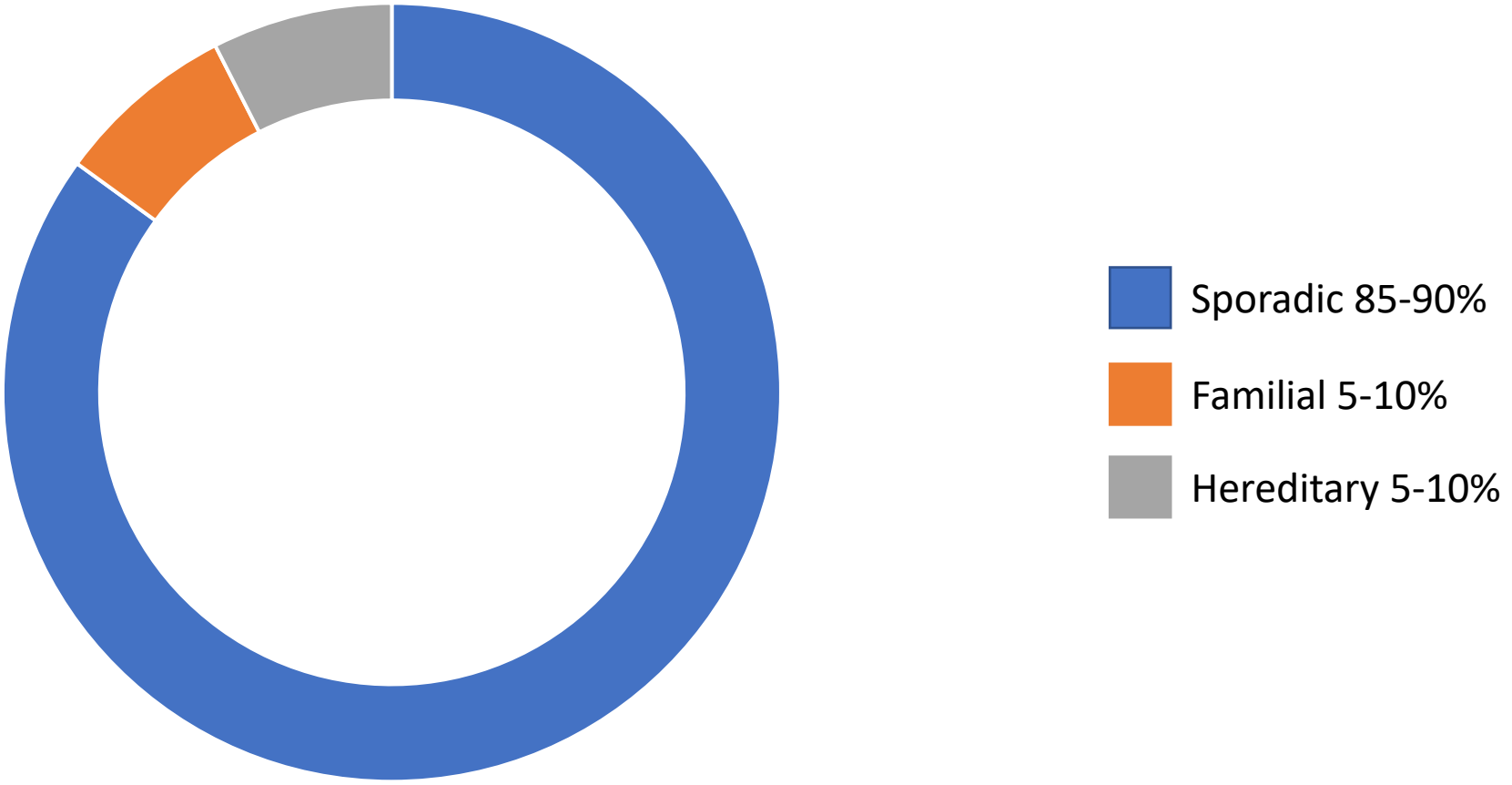
- 85% 3-year survival rate for screen-detected PC
- 24% 5-year survival rate for screen-detected PC in those with germline *CDKN2A* (c.67G>C) variants
- 100% overall survival for 10 individuals with screen-detected precursor lesions treated with surgical resection

Screening for At-Risk Groups: More Data Needed

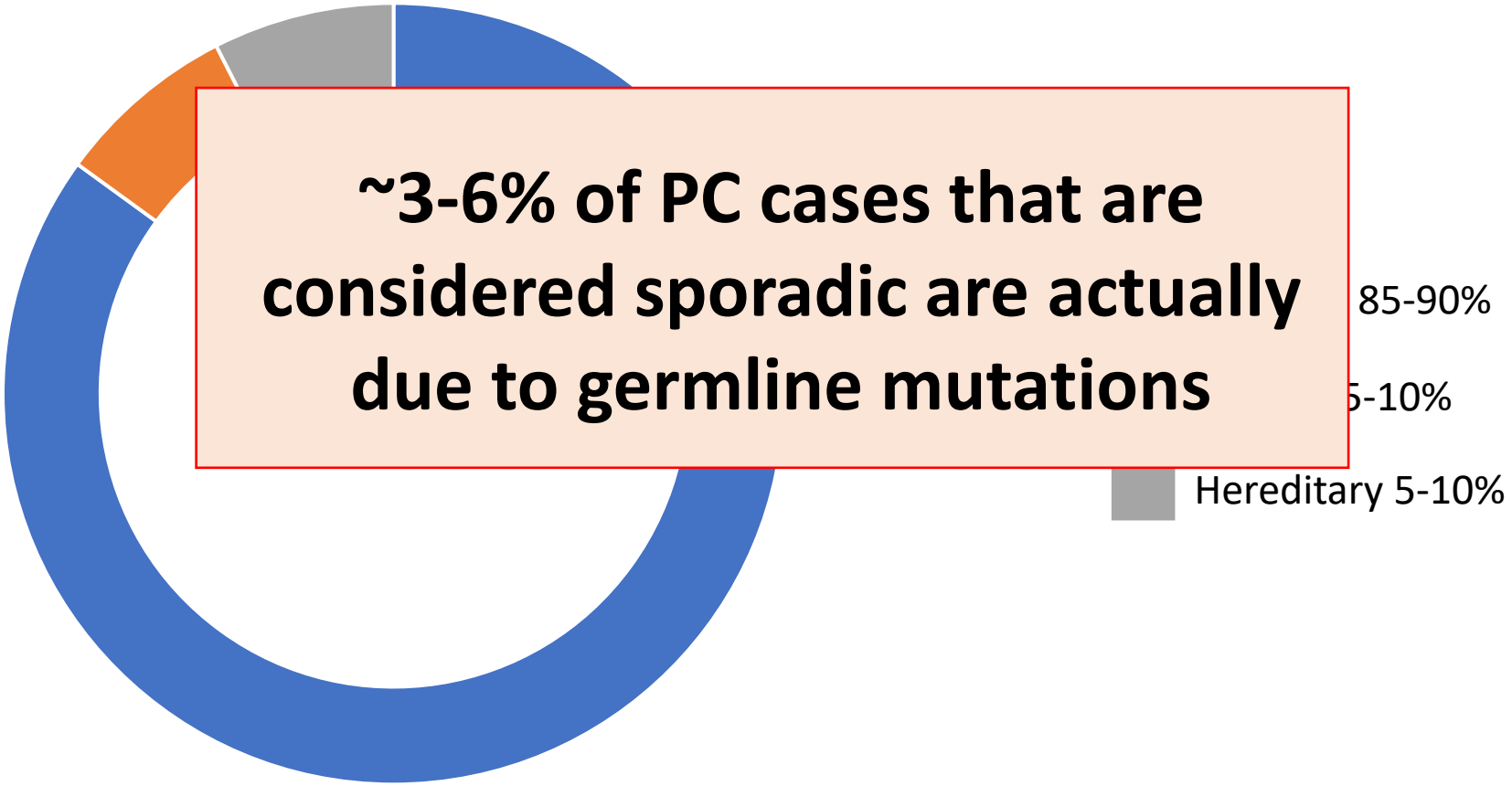
- Longer-term studies needed to determine if suggested downstaging translates to improved survival
- Potential for unnecessary intervention
- Determining overall risks/benefits requires more study
- Data is beginning to identify which screen-detected lesions should be treated as high risk for neoplastic progression
- Ultimately, more data is needed to define the threshold for surgical intervention in high-risk individuals

Hereditary Pancreatic Cancer Susceptibility

Pancreatic Cancers



Pancreatic Cancers



~3-6% of PC cases that are considered sporadic are actually due to germline mutations

Hereditary Pancreatic Cancer

Gene	Risk of Pancreatic Cancer	Other Associated Cancers/Findings
ATM	5-10%	Breast, prostate, ovarian, colon
BRCA1	≤5%	Breast, ovarian, prostate, melanoma, male breast
BRCA2	5-10%	Breast, ovarian, prostate, melanoma, male breast
CDKN2A	>15%	Melanoma
MLH1, MSH2, MSH6, EPCAM*	<5-10%	Colon, uterine, ovarian, gastric, urothelial, brain, biliary tract, small intestine
PALB2	5-10%	Breast, ovarian, male breast
STK11	>15%	Colon, breast, stomach, small intestine, lung, testicular, gynecological
TP53	5-10%	Adrenocortical carcinoma, breast, CNS tumors, osteosarcomas, soft tissue sarcomas
Familial Pancreatitis (PRSS1, SPINK1, CFTR)	Increased	Chronic pancreatitis

PC Screening Recommendations:
STK11

Consider screening beginning at **age 30-35**

Or 10 years before the youngest exocrine PC diagnosis in the family, whichever is earlier

PC Screening Recommendations:
CDKN2A

Consider screening beginning at **age 40**

Or 10 years before the youngest exocrine PC diagnosis in the family, whichever is earlier

PC Screening Recommendations:
ATM, BRCA1/2, MLH1, MSH2, MSH6, EPCAM, PALB2, TP53

Consider screening beginning at age 50 **IF** there is a family hx of ≥1 FDR or SDR from the same side of the family

Or 10 years before the youngest exocrine PC diagnosis in the family, whichever is earlier

PC Screening Recommendations:
Hereditary pancreatitis

For individuals with a P/LP variant in a hereditary pancreatitis gene AND a clinical phenotype consistent with hereditary pancreatitis

Consider screening 20 years after onset of pancreatitis or at age 40, whichever is earlier

Genetic Testing Guidelines for Hereditary Pancreatic Cancers

NCCN Guidelines for Exocrine Pancreatic Cancer

All individuals diagnosed with exocrine pancreatic cancer

FDR of individuals diagnosed with exocrine pancreatic cancer

Disparities in Genetics

Terms and Conditions

Health equity

- Attainment of the highest level of health for all people

Healthcare disparity

- **Preventable differences** in burden of disease or opportunities to achieve optimal health
  - Differences in incidence, prevalence, mortality, morbidity, survivorship, screening, staging at diagnosis, and financial burden

Health inequity

- Disparities in health that are **systematic**, unfair, and **avoidable injustices**

Social determinants of health

Non-medical factors influencing health outcomes

Education	Health care	Environment	Community	Economic
• Literacy • Language • Higher education • Early childhood education	• Insurance coverage • Provider availability • Provider cultural competency • Quality of care • Interpretive services	• Housing • Transportation • Walkability • Urban vs rural	• Food security • Social integration • Support system • Community engagement • Discrimination • Stress	• Income • Expenses • Debt • Medical bills • Support • Employment

Race

- A social construct
- Dividing people based on physical differences

Ethnicity

- A social construct
- Encompassing shared cultural background, language, norms, and values

Ancestry

- Ancestors originating from the same geographic origin
  - Genomic ancestry is the difference in variant frequencies between ancestral populations

- Race and ethnicity can correlate with ancestry, but are not the same thing

Health Disparities in Cancer

Breast cancer	Black and Hispanic women have higher prevalence of triple negative
	Black women have higher mortality rates
	Hispanic women are younger ages at diagnosis
Colon cancer	Black men have higher mortality rates
	Hispanic and Indigenous Americans are the least likely to have colonoscopy in past 10 years
Prostate cancer	Black men have higher incidence rate and earlier age at diagnosis
Trans and non-binary	Higher rates of mortality from cancer than cis individuals
	19% have been refused care, higher among people of color
	28% subjected to harassment in medical settings

Health Disparities in Hereditary Cancer

General Risk Assessment

- Risk prediction models are based on data from white populations
- No risk models for trans or non-binary

- **Gail model** used for determining chemoprevention

The tool has been validated for white women, black/African American women, Hispanic women and for Asian and Pacific Islander women in the United States. The tool may underestimate risk in black women with previous biopsies and Hispanic women born outside the United States. Because data on American Indian/Alaska Native women are limited, their risk estimates are partly based on data for white women and may be inaccurate. Further studies are needed to refine and validate these models.

bcrisktool.cancer.gov

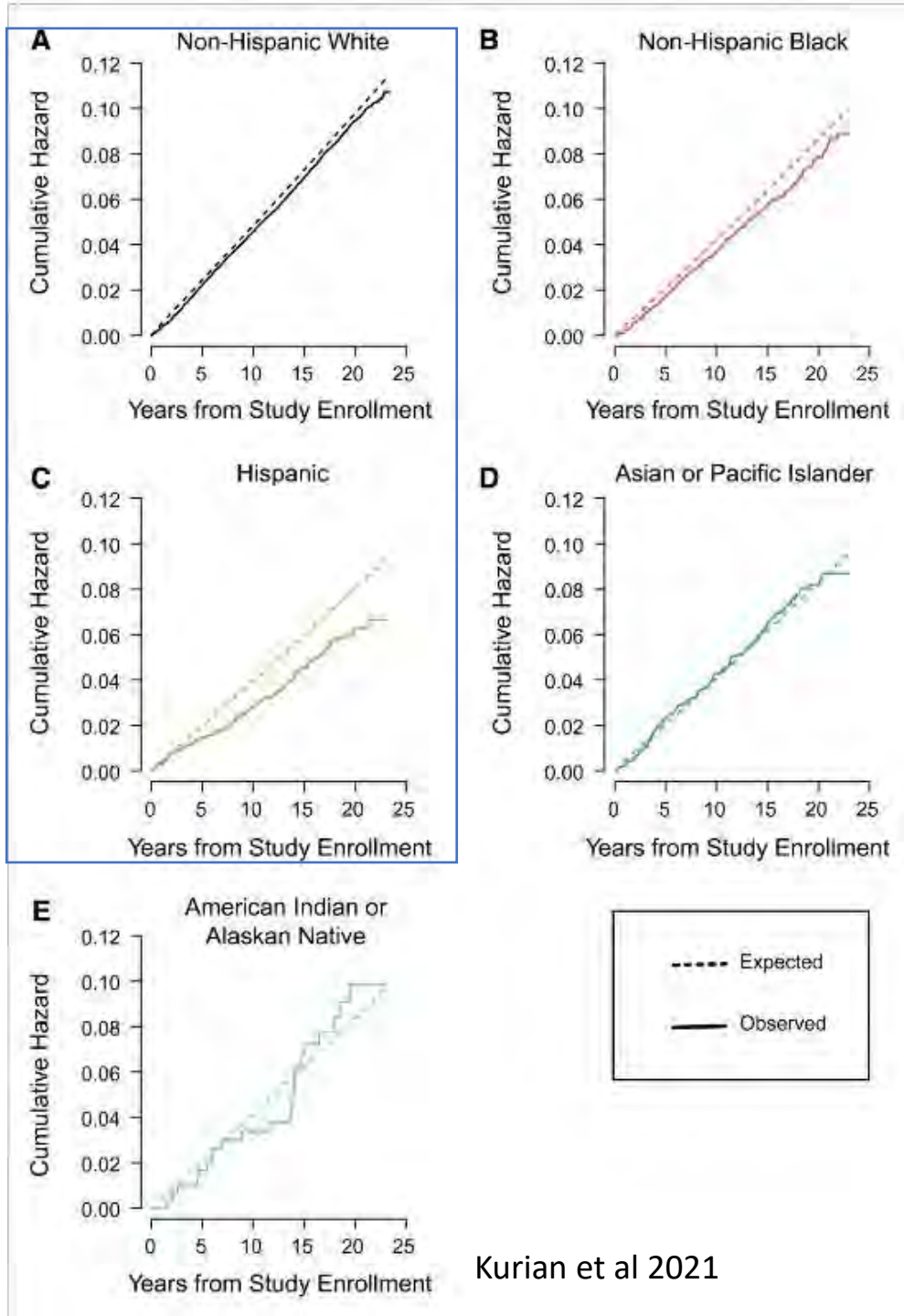
- **Tyrer Cuzick** used for determining MRI screening

- Overestimates risk in Hispanic women

	Black or African American	White
Breast cancer incidence rate per 100,000 [5]	126.7	130.8
Breast cancer mortality rate per 100,000 [5]	28.4	20.3
% High-risk TC8 scores	10.7%	17.5%

Porterhouse et al 2022

New version (v8) may underestimate risk in black women



Kurian et al 2021

Referrals to Genetic Services

- We are not close to testing all patients who meet NCCN criteria for testing
  - ~50% of patients with high-risk breast cancer are tested (Hafertepen et al 2017)
  - ~39% of patients with ovarian cancer are tested (Lin et al 2021)

- The most common reason high-risk patients reported not testing was "my doctor didn't recommend it" (Kaurin et al 2017)

  - Largest barrier to genetic testing from patients is lack of physician referral

Lowest referral rates from:

- Primary care
- Family medicine
- Obstetrics/gynecology

Lowest referral rates for:

- Patients with public insurance or no insurance
- Patients of color

- **Non-white patients are less likely to discuss testing with a provider**
  - Black patients were **16 times** less likely
  - Spanish speaking Hispanic women **2 times** less likely

Racial disparities in *BRCA* testing and cancer risk management across a population-based sample of young breast cancer survivors

Deborah Cragun, PhD[1,2], **Anne Weidner, MPH**[1], **Courtney Lewis, MPH**[1], **Devon Bonner, BA**[1], **Jongphil Kim, PhD**[1], **Susan T. Vadaparampil, PhD**[1], and **Tuya Pal, MD**[1]

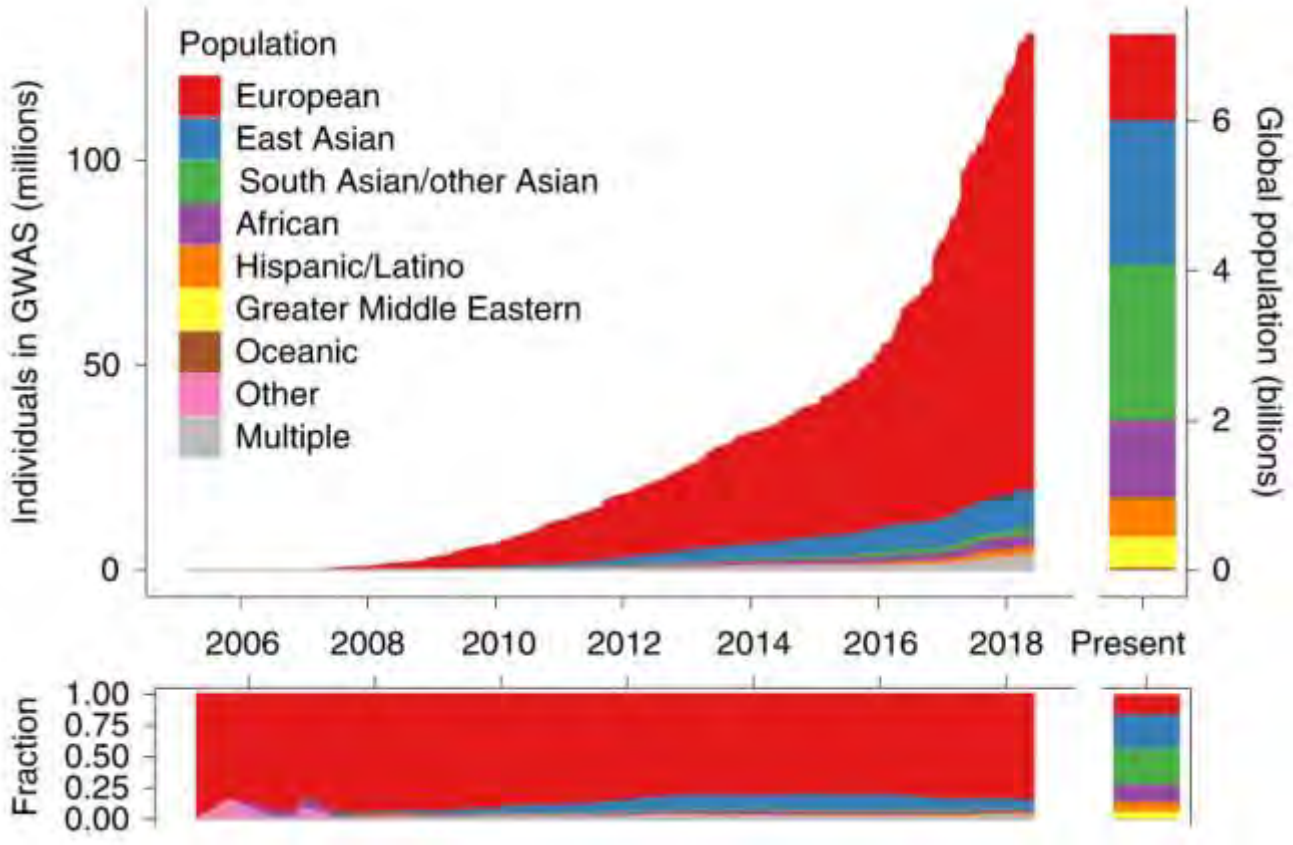
[1]Population Sciences, Moffitt Cancer Center, 12902 Magnolia Drive, Tampa, FL, USA

[2]Department of Global Health, College of Public Health, University of South Florida

- **Reasons for referral differ based on race/ethnicity**
- White patients are referred due to family history
- Non-white (Black, Hispanic, Asian) due to personal history
  - **25-40%** would have met criteria prior to their personal diagnosis

Genetic testing

- **Reference and base of genetic testing is European**
- GWAS studies for cancer risk were 84% European
  - Homogeneity increased statistical power→ prioritized European ancestry
- Omaha is 66% White non-Hispanic
- Only 16% of the global population is European descent



- **Because of this, VUS rates are higher in non-white individuals**
- 25% in White, 38% in non-White (Caswell-Jin et al 2017)
- White 9%, Hispanic 17.2% (Soewito et al 2022)

Kurian et al 2023: Testing Results by Race/Ethnicity

Uncertain results increased at a greater rate in races/ethnicities other than White

Race/Ethnicity	% VUS in 2013	% VUS in 2019	Increase
Non-Hispanic White	6.3	24.9	18.6
Asian	12.2	40.0	27.8
Black	7.5	39.0	31.5
Hispanic	8.6	29.3	20.7
Other	3.8	34.6	30.8

Kurian et al 2023: Testing Uptake by Race/Ethnicity

- **Patients pursuing testing with a history of male breast, female breast, or ovarian cancer:**

Race/Ethnicity	% of patients who underwent testing
Non-Hispanic White	31
Asian	22
Black	25
Hispanic	23

Kurian et al 2023: Testing Uptake by Race/Ethnicity

Racial/ethnic differences in genetic testing uptake showed no improvement over time

Odds of testing by year decreased for Hispanic patients compared to White patients

Addressing disparities

Self education

College of Public Health Series

Becoming an Antiracist Public Health System

NSGC Cancer SIG

Antiracism Cancer Curriculum Toolkit

UCSF

Gender Affirming Care Guidelines

Nebraska Medicine

Gender Care Clinic

Decrease barriers to genetics

- Remote and telehealth options
  - Available through Nebraska Med/UNMC
- Involvement with community healthcare
- Population based genetic testing
  - Already recommended for **ovarian** and **pancreatic**
  - Already "considered" for **colon**
- Talk to patients about genetics **before** referring
- Refer <u>regardless</u> of presumed insurance barriers

For high-risk patients

- Follow risk-reducing and screening recommendations
- Help with patient care coordination
  - PCP
  - Cancer Risk and Prevention Clinic
  - Survivorship Clinic
- Assist in recommending cascade testing for family members
- Support groups and resources
  - Emotional and financial support

- **Referrals in Epic**
- **Fax: 402-559-6688**
- **Phone: 402-559-3602**

Yes / No	Known genetic cancer risk in the family (sometimes called a gene mutation)
Yes / No	Cancer diagnosed younger than age 50
Yes / No	3 or more relatives with the same type of cancer
Yes / No	Ovarian cancer, triple negative breast cancer, or pancreatic cancer
Yes / No	Prostate cancer that has spread (metastasized)
Yes / No	Male with breast cancer
Yes / No	3 or more relatives on the same side of the family with breast, prostate, and/or ovarian cancer
Yes / No	3 or more relatives on the same side of the family with colon and/or uterine cancer
Yes / No	Female with breast cancer under the age of 45
Yes / No	10 or more colon polyps (in a lifetime)
Yes / No	Kidney cancer under the age 46
Yes / No	Stomach cancer under the age of 40
Yes / No	Adrenal cortical carcinoma (cancer of the adrenal gland)
Yes / No	Neuroendocrine type of pancreatic tumor
Yes / No	Paraganglioma or pheochromocytoma (type of neuroendocrine tumor)
Yes / No	Medullary thyroid cancer at any age
Yes / No	Ashkenazi Jewish ancestry (heritage)
Yes / No	3 or more diagnoses of invasive melanoma (in a lifetime)

If you circled YES to any of the questions, genetic counseling and testing may be helpful for you. Please talk to your doctor or contact us to make an appointment to discuss your family history further.

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