

Cancer Risk Assessment: Does one size fit all?

Ann M. Maguire, MD, MPH, FACP

Associate Professor

Division of General Internal Medicine

Medical Director, Hereditary Cancer Risk Clinic

Objectives

- What is cancer risk assessment?
- How important is family history?
- Does lifestyle impact risk?
- What is the evidence for initiating cancer screening early or going beyond USPSTF? Are some people different?
- When is genetic testing indicated?
- What are MCED's and should we be using them?

Leading Sources of Evidence-Based Cancer Screening Guidance

USPSTF

Preventive
Care

ACS

Cancer
Prevention

NCCN

Oncology
Guidelines

ASCO

Clinical
Practice

WHO

Global Health

These organizations provide many of the cancer screening recommendations used by clinicians, health systems, researchers, and policymakers worldwide.

Where does USPSTF stand on Risk Assessment for Chronic Disease?

- USPSTF recommends universal screening for many common conditions.
- USPSTF explicitly recommends a formal risk assessment prior to screening for some conditions requiring the use of a validated tool.
- USPSTF also recognizes the role of certain patient characteristics to determine screening eligibility for specific conditions.
- Risk-based screening is different from universal screening – Not all individuals get the same service at the same time, but more patients get the service they need when they need it.
- Risk assessment takes time and expertise and we don't have tools for everything!

When Is Risk-Based Screening Recommended?

Answer: When patient characteristics can help identify individuals who may be at increased risk for a health condition.



Age



Family
History



Lifestyle



Medical
History



Other
Factors



**INCREASED
RISK**



Screening



Prevention



Monitoring

Screening Driven by Risk Factors

- Many USPSTF "screening" recommendations are essentially risk-based (screen only if risk factors present), including:
 - Abdominal aortic aneurysm (men who ever smoked, ages 65–75)
 - Lung cancer (smoking history + age)
 - Type 2 diabetes/prediabetes (overweight/obesity + age, or other risk factors)

Conditions Where USPSTF Specifically Recommends "Risk Assessment"

- **BRCA-Related Cancer (Breast, Ovarian, Tubal, Peritoneal) Grade B**
 - Recommends clinicians assess women with a personal or family history of these cancers, or with ancestry associated with BRCA1/2 mutations (e.g., Ashkenazi Jewish descent), using a brief validated familial risk-assessment tool (including Tyrer-Cuzick and BRCAPRO)
- **Cardiovascular Disease (CVD) Grade B**
 - Recommends using traditional risk factors (age, sex, blood pressure, cholesterol, smoking, diabetes) in a validated risk calculator (e.g., Pooled Cohort Equations, PREVENT calculator) to estimate 10-year CVD risk, primarily to guide statin therapy decisions.
- **Osteoporosis / Fracture Risk**
 - Recommends using a clinical risk-assessment tool (FRAX score) to identify younger postmenopausal women (under 65) who should get bone density screening.

USPSTF Cancer Screening Recommendations for Average Risk Adults



Breast

40-74 yrs

Mammography
Every 2 Years



Colorectal

45-75 yrs

Routine Screening
Approved Tests



Cervical

21-65 yrs

Pap and/or HPV
Based on Age



Lung

50-80 yrs

Annual Low-Dose CT
High Smoking Risk

Screening saves lives through early detection!

Cancers Without Universal USPSTF endorsed Screening



Prostate Cancer

Ages 55-69: individualized decision (Grade C); 70+: against (Grade D)



Ovarian Cancer

Against routine screening, average-risk women - Grade D



Pancreatic Cancer

Against screening in asymptomatic adults - Grade D



Testicular Cancer

Against screening in asymptomatic males - Grade D



Skin Cancer

Insufficient evidence for visual exams - I statement



Thyroid & Bladder Cancer

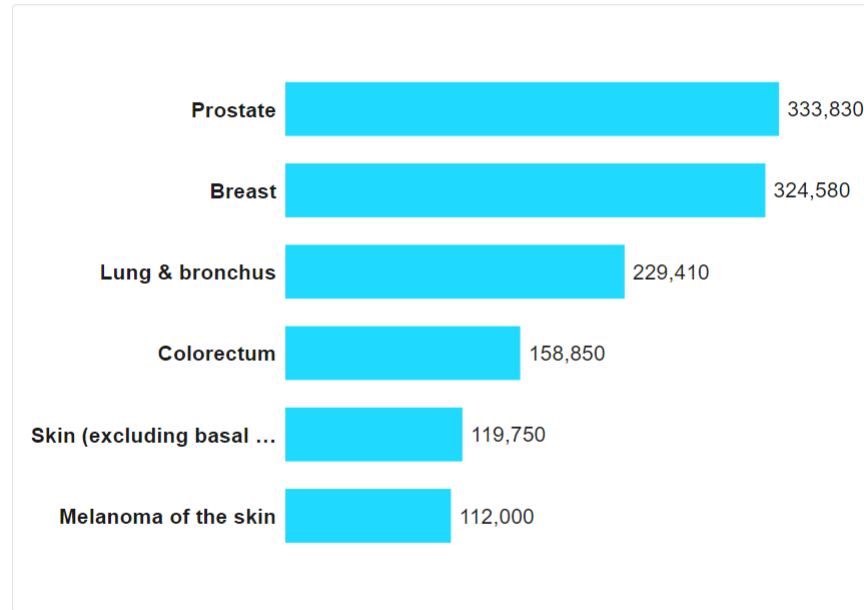
Against (thyroid, Grade D) / Insufficient evidence (bladder, I statement)

Cancer Incidence vs Cancer Death

2026 Estimated New Cancer Cases

Cases by Cancer Type

View by: Sex: Cancer Type:

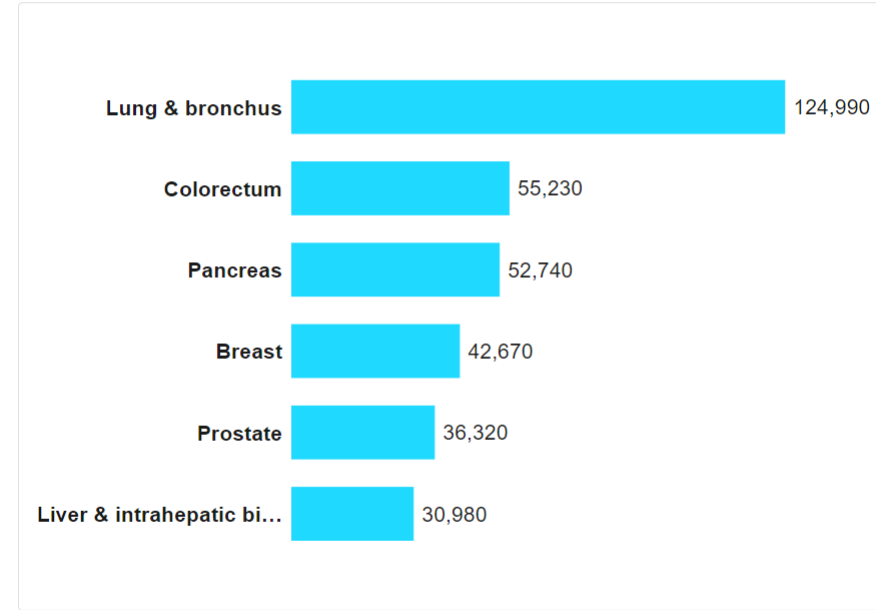


©American Cancer Society, 2026
Colon includes appendix.
Colorectum includes appendix.
Male & female breast cancers combined for whole U.S.
Urinary bladder includes in situ cases.

2026 Estimated Cancer Deaths

Deaths by Cancer Type

View by: Sex: Cancer Type:



©American Cancer Society, 2026
Colorectum includes appendix.
Male & female breast cancers combined for whole U.S.
Urinary bladder includes in situ cases.

Case #1

- 34 yo woman presents for annual exam and wants to discuss her risk for cancer
- BMI 31, Type 2 DM
- Nonsmoker
- Drinks 1-2 glasses of wine per day
- Family history: mom diagnosed with breast cancer age 42. Father has history of colon polyps. Paternal uncle and grandfather had colon cancer
- **What can you tell this patient about her cancer risk?**
- **When should she start screening?**
- **What recommendations can you offer for cancer prevention?**



Taking the family history

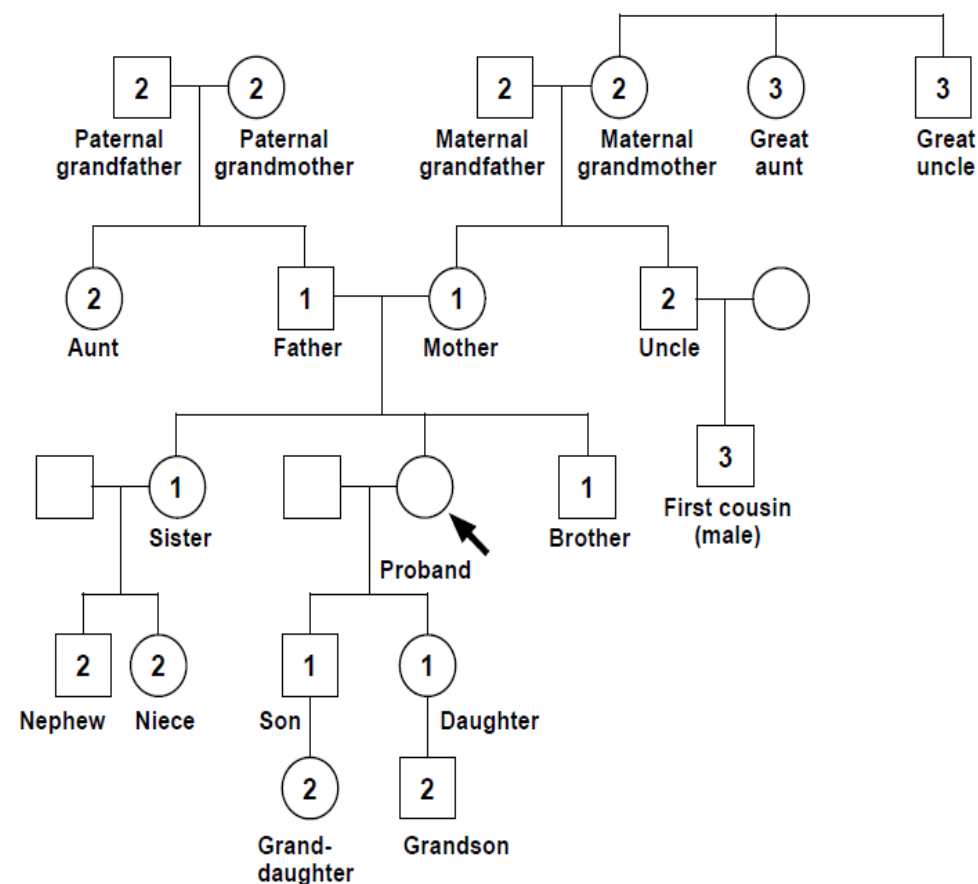
Recommended Key Elements for Minimum Adequate Cancer Family History

Family history should be taken at diagnosis and updated periodically.

Key components should include information about the following:

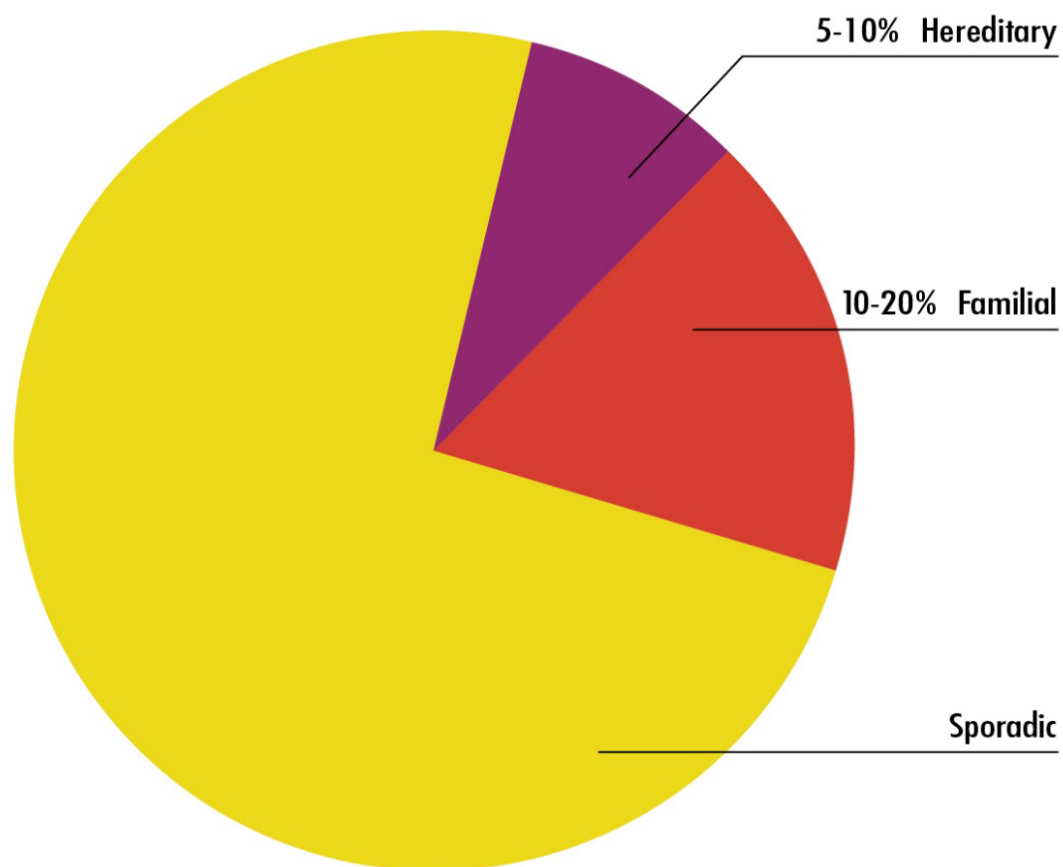
- First-degree relatives: siblings, parents, children
- Second-degree relatives: grandparents, aunts, uncles, grandchildren, nieces, nephews, half-siblings
- Maternal and paternal sides
- Ashkenazi ancestry
- For each cancer case in the family, establish
 - Age at cancer diagnosis
 - Type of primary cancer
- Prior genetic testing in family

PEDIGREE: FIRST-, SECOND-, AND THIRD-DEGREE RELATIVES OF PROBAND^a



^a First-degree relatives: parents, siblings, and children;
second-degree relatives: grandparents, aunts, uncles, nieces, nephews, grandchildren, and half-siblings;
third-degree relatives: great-grandparents, great-aunts, great-uncles, great-grandchildren, first cousins, and half aunts and uncles.

Causes of Cancer



Hereditary

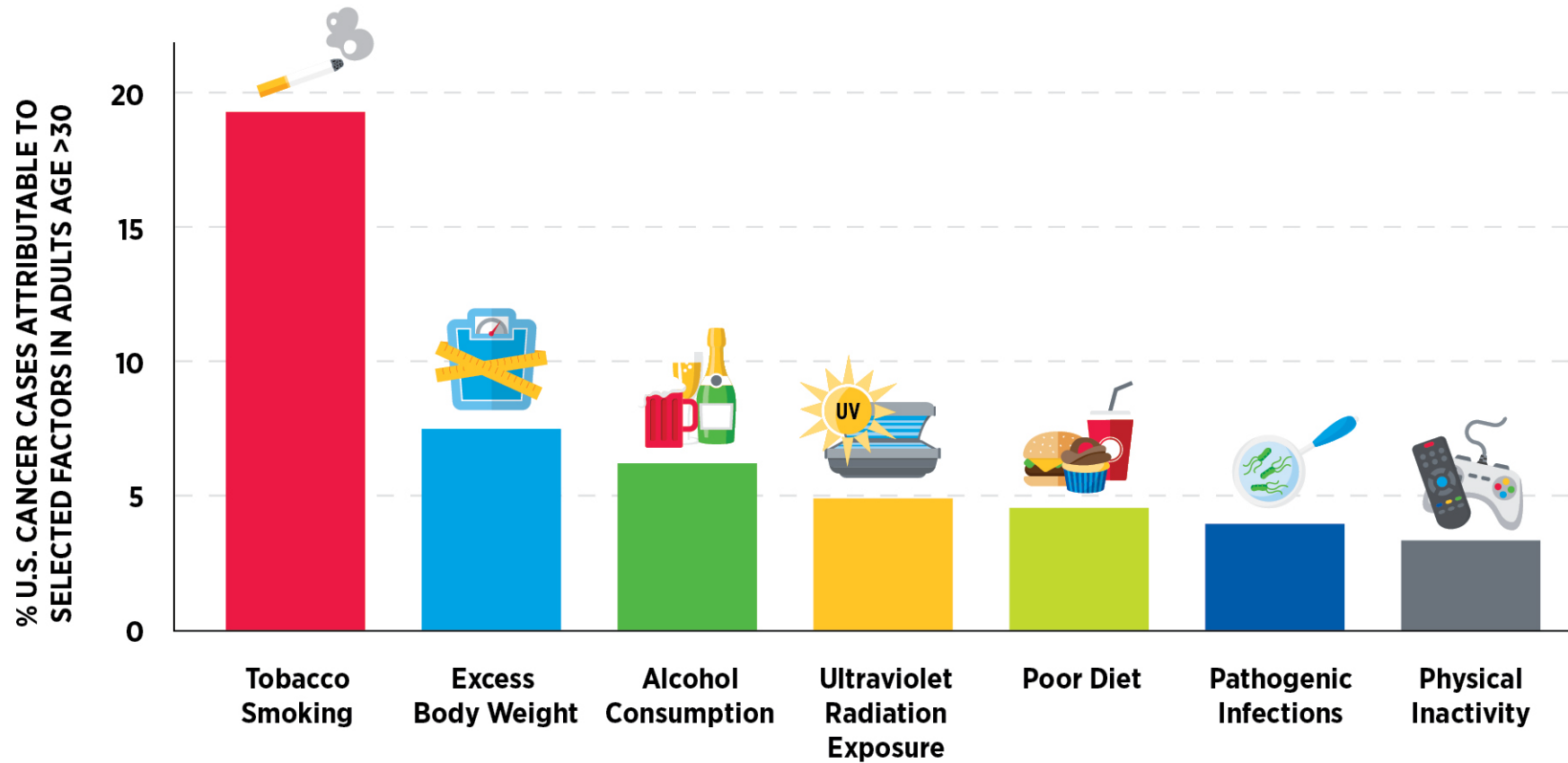
- Gene mutation is inherited in family
- Significantly increased cancer risk

Familial

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

Sporadic

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



Research has identified numerous factors that increase an individual's risk for developing cancer. By modifying behavior, individuals can eliminate or reduce many of these risks and thereby reduce their risk of developing

or dying from cancer. Developing and implementing additional public education and policy initiatives could help further reduce the burden of cancers related to preventable cancer risk factors.

Alcohol and Cancer: Key Evidence

Alcohol is a Group 1 carcinogen. Cancer risk increases with increasing alcohol consumption and may rise even at low levels of intake.

100,000
U.S. cancer
cases/year

20,000
cancer
deaths/year

Cancers associated with Alcohol Use

- Oral cavity
- Pharynx & larynx
- Esophagus
- Liver
- Colorectal
- Female breast

How Alcohol Causes Cancer

- Acetaldehyde-induced DNA damage
- Chronic inflammation
- Increased estrogen levels
- Enhanced tobacco carcinogen absorption

Take-Home Message: Less alcohol = lower cancer risk.

Key Sources: IARC; NCI Alcohol and Cancer Risk Fact Sheet; U.S. Surgeon General Advisory (2025).

Diet and Cancer: Key Evidence

↑ Increased Risk	↓ Reduced Risk
Processed meats → Colorectal cancer	Whole grains & fiber → Lower colorectal cancer risk
Red meat (high intake) → Colorectal cancer	Fruit- and vegetable-rich diets → Lower risk of several cancers
Excess calories/obesity → Increased risk of ≥13 cancers [	Healthy weight maintenance → Lower risk of obesity-related cancers
Alcohol consumption → Breast, colorectal, liver, and upper aerodigestive cancers	

Is sugar intake associated with Cancer Risk?

- High-sugar diets: May increase cancer risk indirectly through obesity.
- Excess sugar consumption from high sucrose or high fructose diets can activate glucose and lipid metabolic pathways that lead to cancer – independent of weight gain.
- Interest is growing in the potential future use of GLP1 agonists in cancer risk reduction.

Obesity and Cancer: What Is the Evidence?

13 CANCERS LINKED TO OBESITY

~40% of U.S. cancers occur
in cancer types associated
with overweight or obesity

Key Mechanisms

- Chronic inflammation
- Increased insulin & IGF-1
- Higher estrogen levels
- Altered immune function
- Changes in the tissue microenvironment

Cancers commonly associated with obesity:

Breast (postmenopausal), colorectal, endometrial, kidney, liver, pancreatic, ovarian, thyroid, esophageal adenocarcinoma and others.

Takeaway: Obesity is one of the leading modifiable cancer risk factors!

Association of Bariatric Surgery With Cancer Risk and Mortality in Adults With Obesity

Ali Aminian, MD¹; Rickesha Wilson, MD¹; Abbas Al-Kurd, MD¹; [et al](#)

[» Author Affiliations](#) | [Article Information](#)

JAMA

Published Online: June 3, 2022

2022;327;(24):2423-2433.

doi:10.1001/jama.2022.9009

JAMA 2022 (SPLENDID Study)

- Included **30,318 adults with obesity**
- Bariatric surgery was associated with:
 - **32% lower risk of obesity-associated cancers** (HR 0.68)
 - **48% lower risk of cancer-related death** (HR 0.52)
- Average long-term weight loss was approximately **19% greater** than in nonsurgical controls.

From: **Association of Bariatric Surgery With Cancer Risk and Mortality in Adults With Obesity**

JAMA. 2022;327(24):2423-2433. doi:10.1001/jama.2022.9009

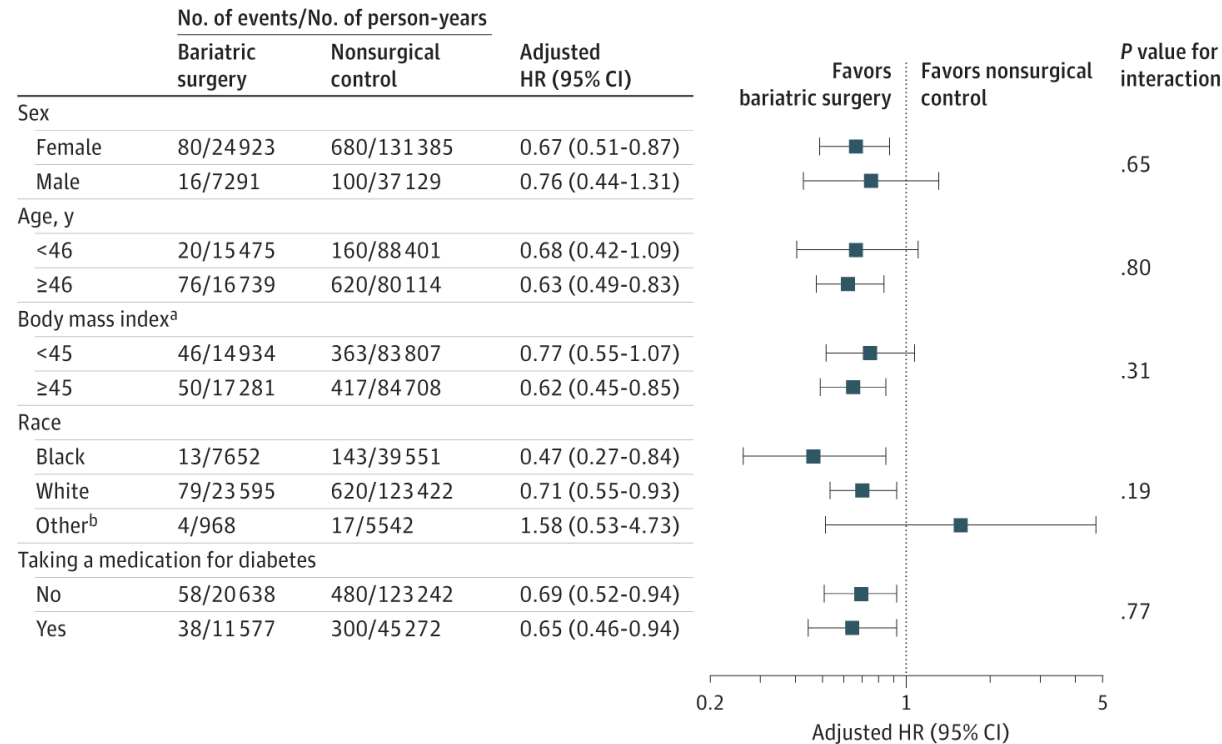


Figure Legend:

Association of Bariatric Surgery vs Nonsurgical Controls for the Primary End Point in Key Subgroups in the Fully Adjusted Cox Models Testing for interaction revealed no heterogeneity in the association of bariatric surgery with the primary end point in a wide range of patients including both men and women, young and old patients, Black and White patients, and patients with or without diabetes.

Women's Health Initiative

JNCI Cancer Spectrum (2019)

- Followed 58,667 postmenopausal women
- Women who intentionally lost $\geq 5\%$ of body weight had:
 - **12% lower risk of obesity-related cancers** overall (HR 0.88)
 - **39% lower risk of endometrial cancer** (HR 0.61)
- Reductions in waist circumference showed similar benefits

Cancers with the Strongest Evidence of Risk Reduction after Weight Loss

Cancer Type	Evidence of Reduced Risk After Weight Loss
Endometrial cancer	Strongest evidence; reductions up to ~39% in some studies oup
Postmenopausal breast cancer	Reduced incidence seen in weight-loss cohorts and bariatric studies cancer +1
Colorectal cancer	Lower risk associated with waist and weight reduction oup
Kidney cancer	Risk reductions seen in bariatric and observational studies diabetes +1
Obesity-related cancers overall	Consistent reductions across multiple studies jamanetwork +1

How can we assess our patient's Breast Cancer risk in the primary care setting?

Tyrer-Cuzick vs Gail Model for Breast Cancer Risk

Feature	Tyrer–Cuzick (IBIS)	Gail Model (BCRAT)
Risk Outputs	10-year & lifetime	5-year & lifetime
Family History	Includes first- & second-degree relatives , ovarian cancer	Only first-degree relatives
Genetic Factors	Includes BRCA1/2 and other mutations	Does not include genetic mutations
Breast Density	Included	Not included
Biopsy History	Includes benign disease categories	Includes biopsies & atypia
Calibration & Accuracy	More accurate; better discrimination (AUC 0.762)	Underestimates risk; lower discrimination (AUC 0.735)
Best For	Women with strong family history , genetic risk, dense breasts	Average-risk women without significant family history

Gail Model – Benefits and Limitations

Benefits

- Simple, fast, widely used
- **FDA-recognized threshold ($\geq 1.67\%$ 5-year risk) for chemoprevention decisions**

Limitations

- **Valid for women 35-85 years old**
- **Underestimates risk** in women with family history or genetic predisposition
- Lower accuracy and calibration compared with Tyrer–Cuzick (expected/observed ratio 0.48 vs. 0.81)
- Does not include second-degree relatives, ovarian cancer, or breast density

Tyrer-Cuzick – Benefits and Limitations

Benefits

- More comprehensive (family history, genetics, density)
- **Better calibrated for high-risk women**
- More accurate in women with familial cancer history
- **Valid for women age 25 and up – no age cutoff**

Limitations

- Can **overpredict** in higher-risk groups (overestimation noted in large cohorts)
- More complex data entry

Putting Risk Assessment into Practice

Risk Interpretation

- **Average Risk:** <15% lifetime
- **Intermediate Risk:** 15–19%
- **High Risk:** $\geq 20\%$
 - Eligible for **annual breast MRI**
 - Consider **chemoprevention** (tamoxifen, raloxifene, aromatase inhibitors)
 - Evaluate for **genetic counseling/testing**

Personal factors

Woman's age:
 Menarche:
 Height (m):
 Weight (kg):

Measurements
 Metric: ☒
 Imperial: ☐

Nulliparous: ☐
 No prior biopsy / no proliferative disease: ☒
 Premenopausal: ☒

Parous: ☐
 Prior biopsy, result unknown: ☐
 Perimenopausal: ☐
 Age at Menopause:

Unknown: ☒
 Hyperplasia (not atypia): ☐
 Postmenopausal: ☐

Age First Child:
 Atypical hyperplasia: ☐
 No information: ☐

Lobular Carcinoma in Situ (LCIS): ☐

Ovarian cancer: ☐

Patient id:
 Patient no.:
 Calculate Risk

Competing mortality ☒

Risk Options

HRT use
 Length of use (years):

Never: ☒
 5 or more years ago: ☐
 Less than 5 years ago: ☐
 Current user: ☐

Mammographic density (age 40+)

☒ % Volpara® Volumetric Density*
 ☐ % VAS Percentage Density*
 ☐ BI-RADS® ATLAS Density*

Ashkenazi inheritance: ☐

Show start up screen

Mother:

Ovarian: ☐
 Bilateral: ☐
 Breast cancer: ☒
 Age:

Sisters:

Number:
 Ovarian: ☐
 Bilateral: ☐
 Breast cancer: ☐
 Age:

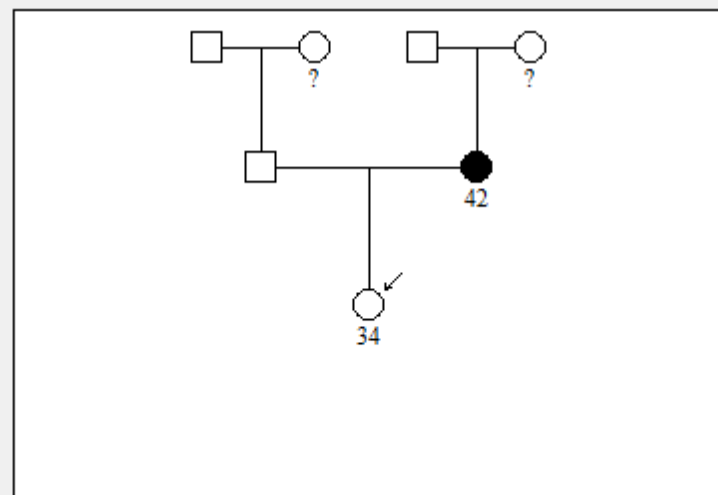
Genetic Testing

Male relatives

Half Sisters

Affected cousins

Affected Nieces



Paternal Gran:

Ovarian: ☐
 Breast cancer: ☐
 Age:

Maternal Gran:

Ovarian: ☐
 Breast cancer: ☐
 Age:

Paternal aunts:

Number:
 Ovarian: ☐
 Breast cancer: ☐
 Age:

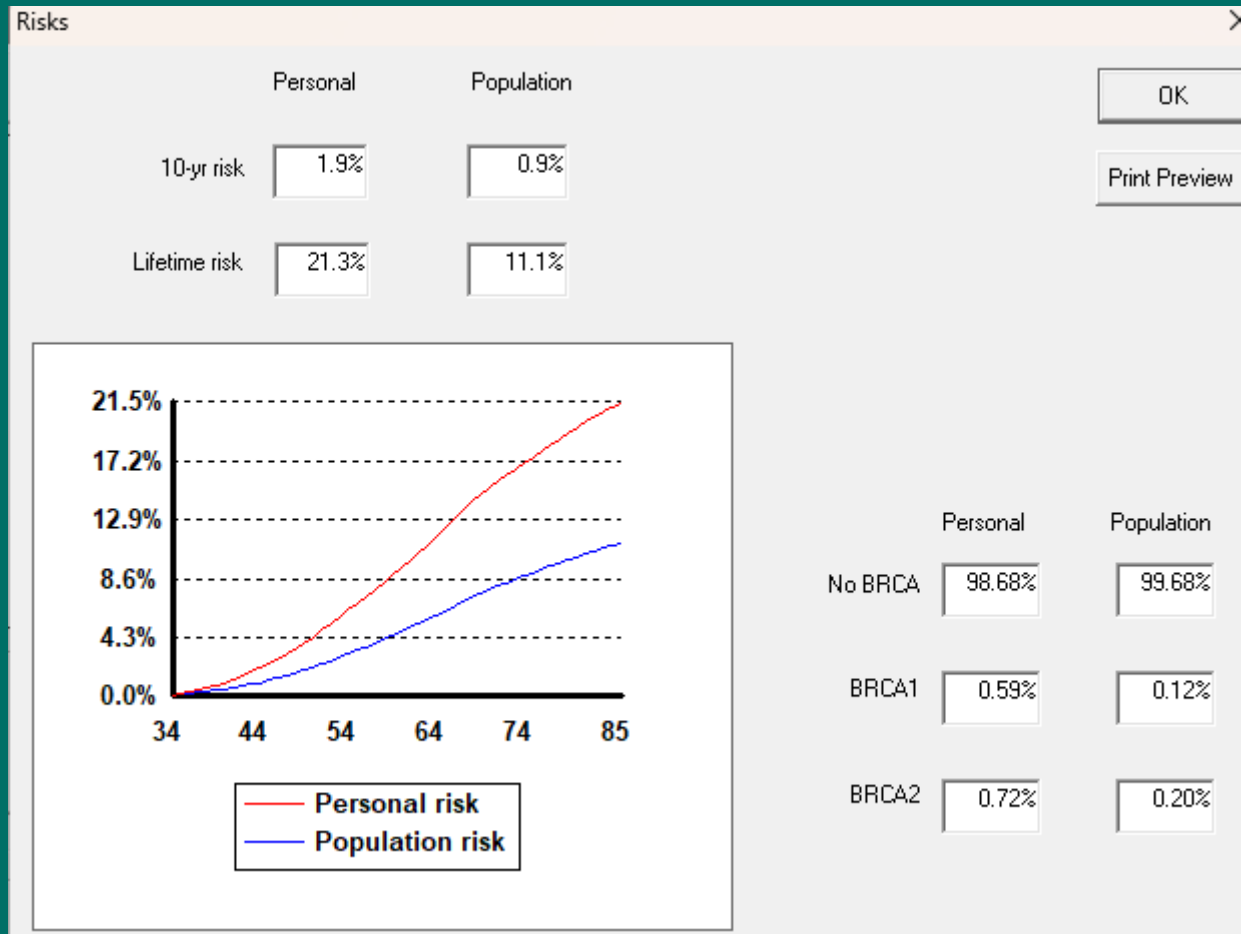
Maternal aunts:

Number:
 Ovarian: ☐
 Breast cancer: ☐
 Age:

Daughters:

Number:
 Ovarian: ☐
 Breast cancer: ☐
 Age:

View Family History



When should you start Breast Cancer Screening when Family History is Present?

When should you start Breast Cancer screening when Family History is Present?

- Lifetime Risk drives earlier screening.
- Family History is important in calculating lifetime risk.
- **High risk = Lifetime Risk $\geq$ 20%**
- NCCN recommends offering breast cancer screening to high-risk women starting 10 years prior to when the youngest family member was diagnosed, no later than age 40 – whichever comes earlier.
- High-risk screening includes annual contrast MRI in addition to Mammogram.

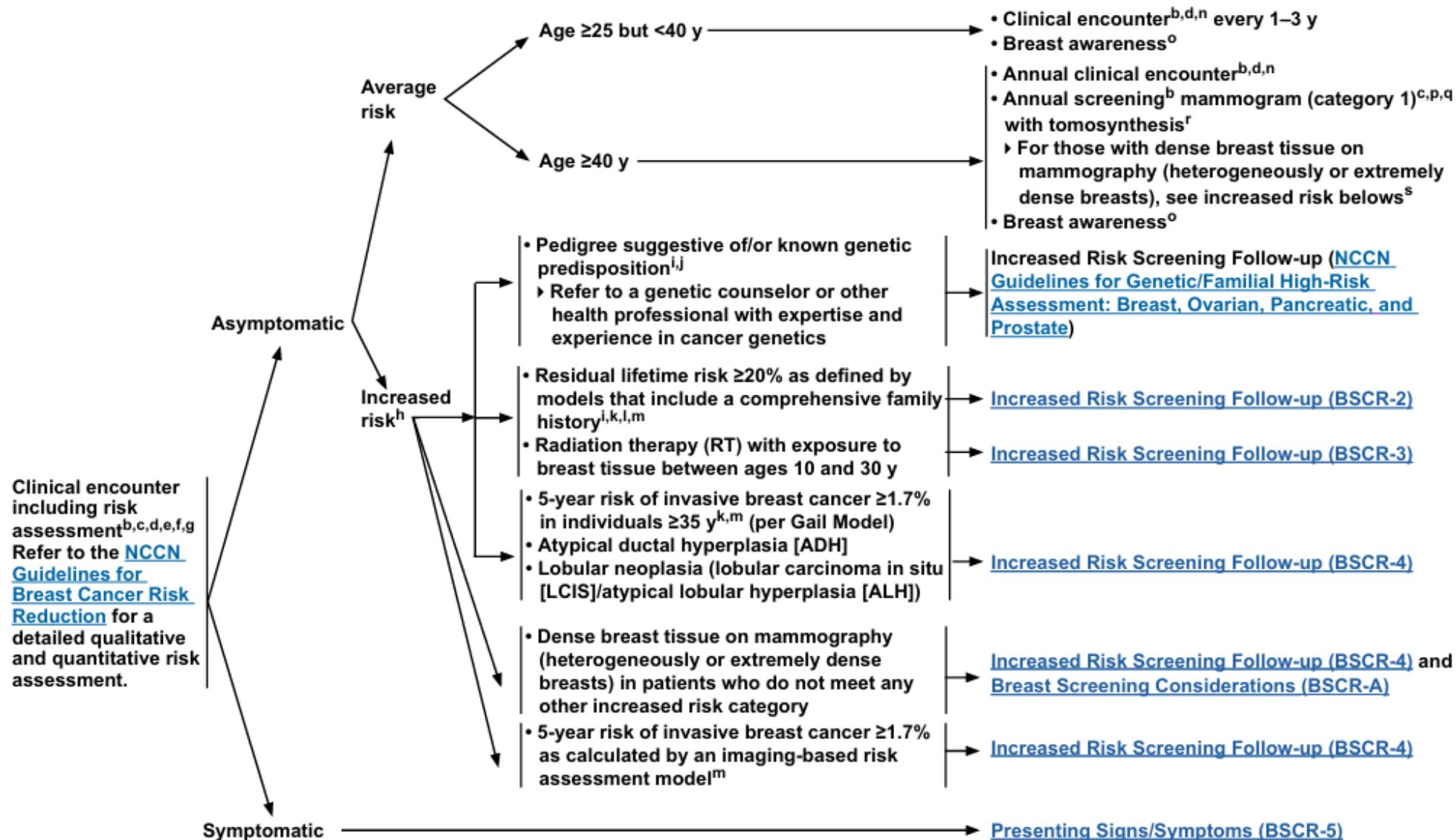


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Breast Cancer Screening and Diagnosis

SCREENING OR SYMPTOM CATEGORY^a

SCREENING/FOLLOW-UP^b





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NCCN Guidelines Version 1.2026

Breast Cancer Screening and Diagnosis

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SCREENING OR SYMPTOM CATEGORY^a

Increased Risk:

Residual lifetime risk
≥20% as defined by
models that include a
comprehensive family
history^{i,k,l,m}

SCREENING/FOLLOW-UP^b

- Clinical encounter^{b,d,n} every 6–12 mo
 - To begin when identified as being at increased risk
 - Consider referral to a genetic counselor or other health professional with expertise and experience in cancer genetics, if not already done
 - Consider referral to a breast specialist as appropriate
- Annual screening^b mammogram^{c,p} with tomosynthesis^r
 - To begin no later than age 40 y, or 10 y prior to when the youngest family member^t was diagnosed with breast cancer, not prior to age 30 y^u (whichever comes first)
- Annual breast MRI^{b,v,w} with and without contrast
 - To begin no later than age 40 y, or 10 years prior to when the youngest family member^t was diagnosed with breast cancer, not prior to age 25 y^{x,y} (whichever comes first)
 - Consider contrast-enhanced mammography (CEM)^b or molecular breast imaging (MBI)^b for those who qualify for but cannot undergo MRI. Whole breast ultrasound^b may be done if CEM or MBI is not available/accessible^z
- Consider risk reduction strategies (see [NCCN Guidelines for Breast Cancer Risk Reduction](#))
- Breast awareness^o

When should you start Colorectal Cancer Screening when Family History is Present?

Colon Cancer Screening - USPSTF

- Recommended for average risk adults starting at age 45
- Screening for high-risk individuals including those with Family History of Colon Cancer starts earlier and is more frequent.
- Approved screening strategies include:
- **Stool-based tests:** High-sensitivity guaiac fecal occult blood test (HSgFOBT), Fecal immunochemical test (FIT) **every year** or **Stool DNA-FIT every 1 to 3 years**
- **Direct visualization tests:** Colonoscopy **every 10 years**, Computed tomography (CT) colonography (virtual colonoscopy) **every 5 years** and Flexible sigmoidoscopy **every 5 years**, or every 10 years combined with annual FIT.
- **Colonoscopy is the only acceptable method for screening high risk individuals.**



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Colorectal Cancer Screening

INCREASED RISK BASED ON POSITIVE FAMILY HISTORY

(Not meeting criteria for consideration of a hereditary cancer syndrome or appropriate testing negative for a hereditary cancer syndrome)^{fff}

FAMILY HISTORY CRITERIA

	SCREENING ^{ggg}	
≥1 first-degree relative with CRC at any age	Colonoscopy beginning at age 40 y or 10 y before earliest diagnosis of CRC, whichever is first	Repeat every 5 y ^{ggg,hhh,iii,jjj} or sooner depending on the size, number, and pathology of polyps removed on each exam
Second- and third-degree relatives with CRC at any age	Colonoscopy beginning at age 45 y ^{hhh}	Repeat every 10 y or if positive, repeat per colonoscopy findings
First-degree relative with confirmed advanced adenoma(s) (ie, high-grade dysplasia, ≥1 cm, villous or tubulovillous histology, TSA), or advanced SSP/SSL(s) (≥1 cm, any dysplasia) at any age ^{kkk,lll,mmm}	Colonoscopy beginning at age 40 y or at age of onset of advanced adenoma(s) or advanced SSP/SSL(s) or TSA(s) in relative, whichever is first	Repeat every 5–10 y ^{ggg,iii} or if positive, repeat per colonoscopy findings

Case #2

- 65 yo male who presents to establish care.
- BMI 26
- 30 pack year smoking history
- Family History: Sister has history of breast cancer and is recently diagnosed with pancreatic cancer, Father died of metastatic prostate cancer.
- **Patient states his wife insisted he make this appointment because she wants him to be tested for cancer.**
- **What screening do you recommend and what can you tell him about his risks?**
- **What about Genetic testing?**



Lung Cancer Screening

- The USPSTF recommends annual screening for lung cancer with low-dose CT scan in adults aged 50 to 80 years who:
 - have a 20 pack-year smoking history and
 - currently smoke or have quit within the past 15 years.
- Screening should be discontinued once a person has not smoked for 15 years or if they are too sick to allow surgery or treatment for a new cancer.

References:

Family History Gives us Clues

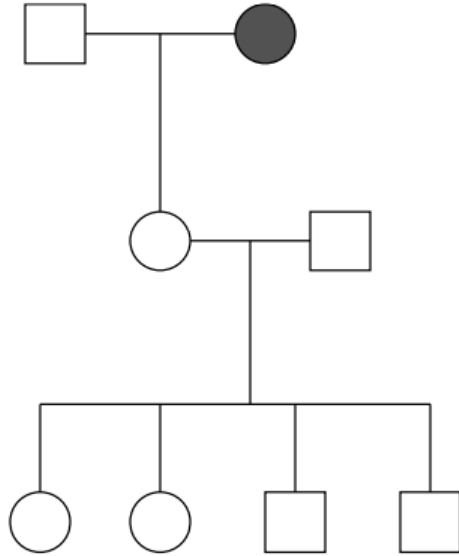
Families with Hereditary Cancer Syndromes often have the following “red flags”:

- *Younger than expected age of dx*
- Many affected family members
- More than one generation affected
- Pairing of cancers in the family
 - (Breast & ovarian cancer, colon & endometrial cancer)
- More than one cancer in same person
- Ashkenazi Jewish heritage

Red Flags for Hereditary Cancer: EMR

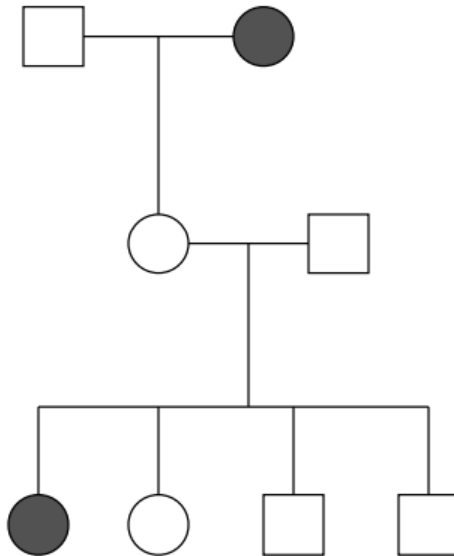
- **E**arly age at diagnosis
 - Ex. Breast cancer diagnosed ≤ 50 years of age regardless of family history
- **M**ultiple cancers, individuals or family members with the same type (or related types) of cancer
 - Ex. Three family members on the same side of the family with colon cancer regardless of age
 - Ex. One person with colon cancer, who also develops a separate primary endometrial cancer
- **R**are
 - Ex. A family member with ovarian cancer, pancreatic cancer, metastatic prostate cancer or male breast cancer

SPORADIC



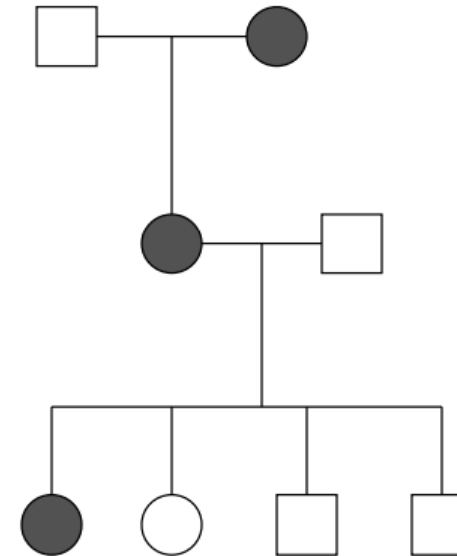
Features
Few affected family members
Caused by an accumulation of mutations throughout life
Not hereditary

FAMILIAL



Features
Clusters of cancer in a family
Genetic predisposition is not evident in the family history

HEREDITARY



Features
Cancer in more than 2 generations
Caused by mutations in genes
Bilateral breast cancer
Multiple related cancers

Should Men Screen for Prostate Cancer? Biden Diagnosis Reignites Debate

Guidelines have gone back and forth over years on whether men should be screened at all

By [Brianna Abbott](#) [Follow](#)

Updated May 22, 2025 11:22 am ET



370



Gift unlocked article

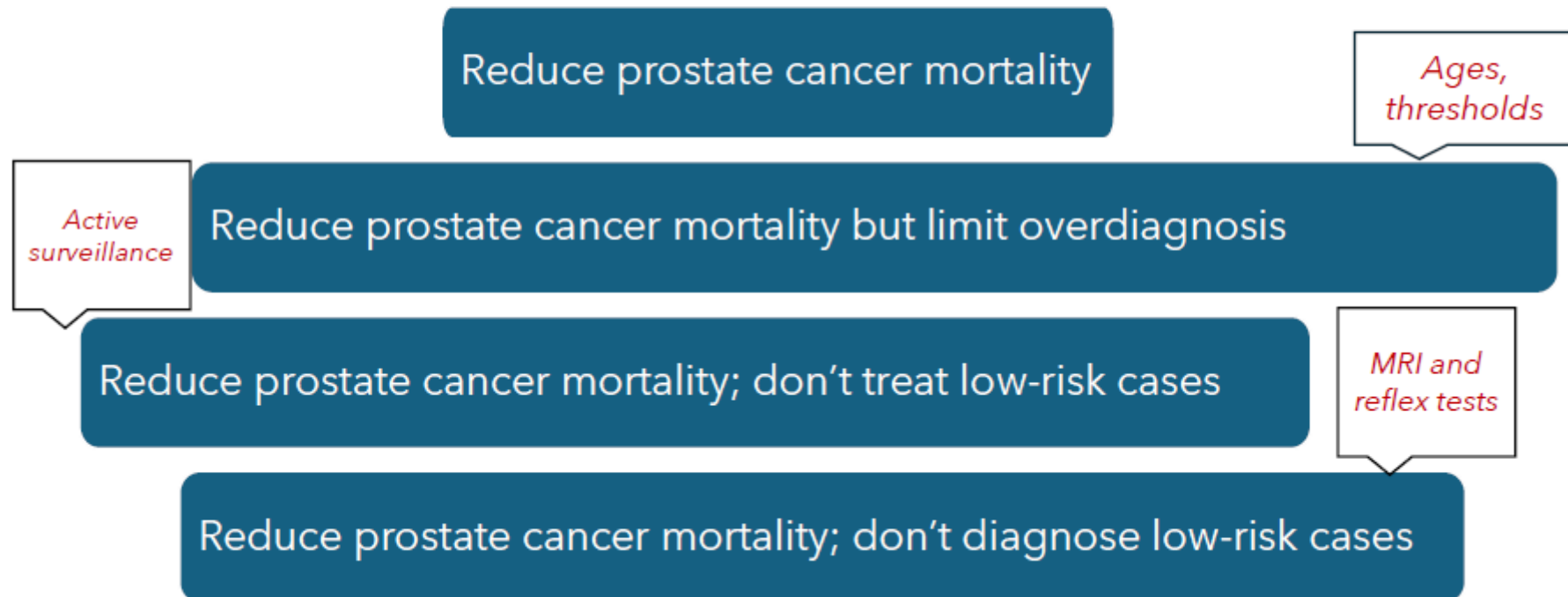


Listen (7 min)



At the heart of the issue is a simple test that looks for prostate-specific antigen, or PSA, in a man's blood. PHOTO: IMAGE SOURCE/GETTY IMAGES

The shifting objectives of prostate cancer screening



Prostate Cancer USPSTF History

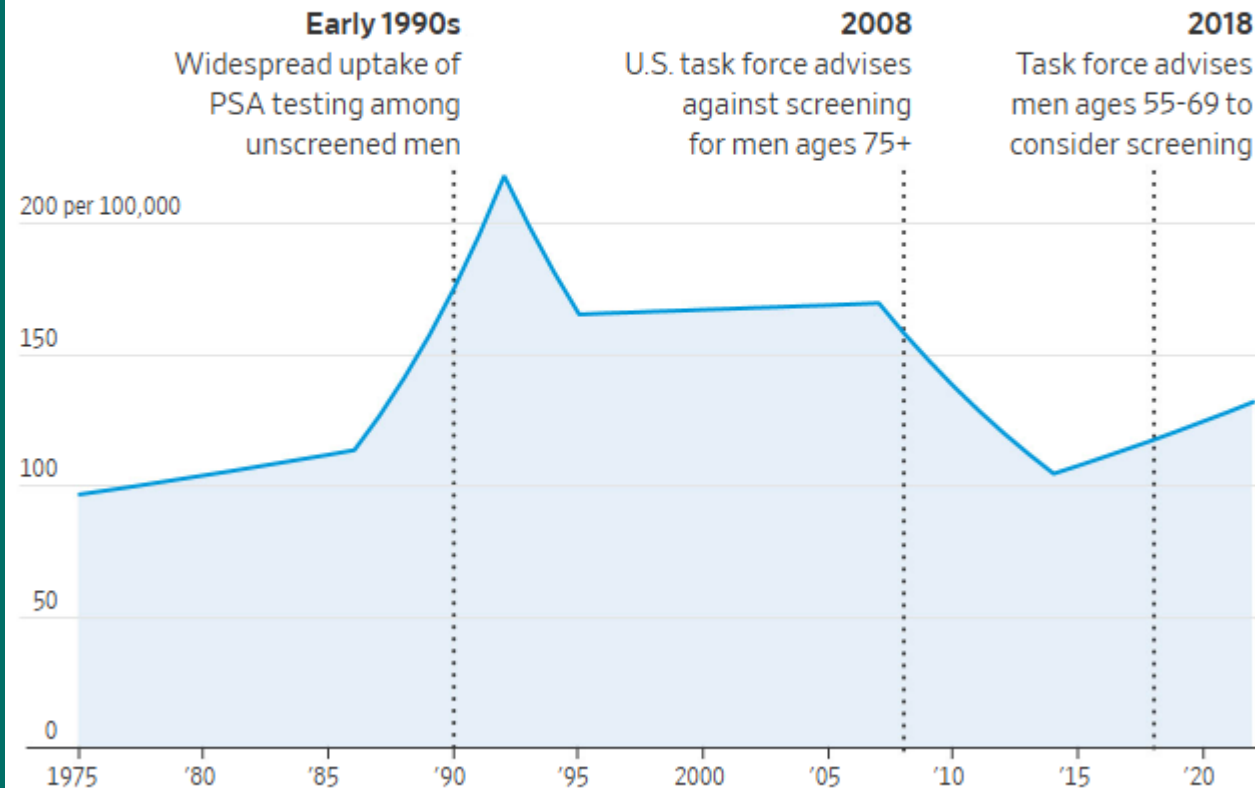
- **Evidence:** Two large trials looked at whether PSA testing provided a mortality benefit on a population level in men primarily in their 50s and 60s Results were mixed. Excluded older men above age 75.
- 2008 - USPSTF recommended against screening for men aged 75 and older. States there is “insufficient evidence” to make a recommendation for or against screening in men < 75.
- 2012 – USPSTF recommended against PSA based screening for all men – “potential benefit didn’t outweigh the harms”. Category D recommendation
- 2018 - USPSTF recommends “individualized decision making” for men ages 55 to 69 but advising against screening for men ages 70 and older.
- **Guidelines are currently under review.**

USPSTF Screening Guidelines may impact Diagnosis

Test Pattern

The number of newly diagnosed prostate cancer cases has waxed and waned depending on how aggressively doctors screen for the disease.

New U.S. prostate cancer diagnoses



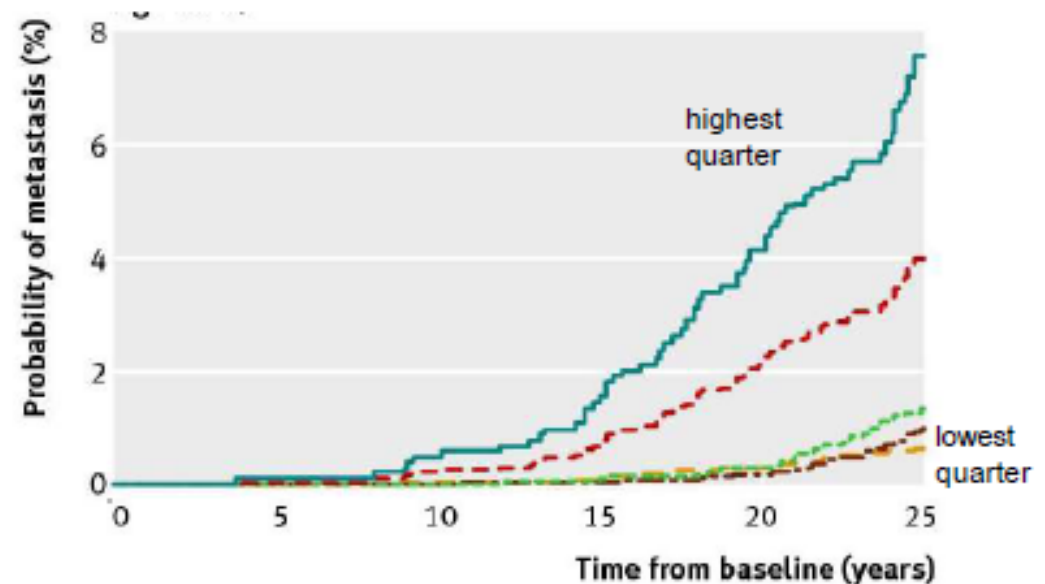
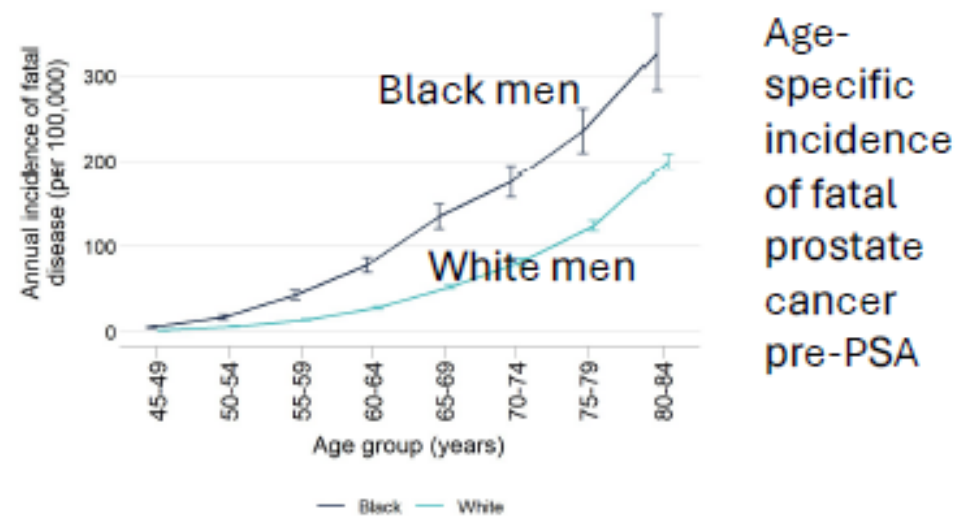
Source: National Cancer Institute (cases)

Prostate Cancer: The case for screening

- More men are being diagnosed with Prostate Cancer at a later stage.
- Since 2011, there is an approximately 5% increase each year in more-advanced diagnoses.
- Experts suspect the reduced screening may contribute to later stage at diagnosis.
- The death rate from Prostate Cancer declined by almost 50% from 1993 to 2022, but that decline has stalled in recent years (American Cancer Society data).

When to start?

- 50 or 55 has become default to start screening after trials
- Age to start depends on burden of potentially fatal disease
 - Starting younger than 50 risks high cost and low yield among screened men
 - Starting younger the 50 may be reasonable in high-risk groups
- Stored serum studies suggest baseline PSA in mid- 40's could help to inform whether to start earlier
 - Refer higher values to annual screening, lower values to standard screening starting at 50 or 55



PSA at age 45-49 strongly predicts 25-year risk of metastasis/death in Malmo preventive project



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Prostate Cancer Early Detection

BASELINE EVALUATION

- History and physical (H&P) including:
 - ▶ Family cancer history^{b,c,d}
 - ▶ Family or personal history of high-risk germline variant^{c,d}
 - ▶ History of prostate disease and cancer early detection, including prior prostate-specific antigen (PSA) and/or isoforms, exams, and biopsies
 - ▶ Black/African American identity^e
 - ▶ Medications^f
 - ▶ Environmental exposure^g

RISK ASSESSMENT

- Baseline PSA^h
- Consider baseline digital rectal examination (DRE)^h

- Age 40–75 y for:
- Black/African American individuals^e
 - Those with germline variants that increase the risk for prostate cancer^{b,c,d} (see [NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast, Ovarian, Pancreatic, and Prostate](#))
 - Those with concerning family or personal history^{b,d}

Age 45–75 y for all others

Age >75 y, in select patients (category 2B)ⁱ

EARLY DETECTION EVALUATION

PSA ≤ 3 ng/mL^{f,j} and DRE normal (if done)

PSA > 3 ng/mL^{f,j,k} and/or very suspicious DRE

PSA 1–3 ng/mL^{f,j} and DRE normal (if done)

PSA < 1 ng/mL^{f,j} and DRE normal (if done)

PSA ≥ 4 ng/mL^{f,j} or very suspicious DRE

PSA < 4 ng/mL^{f,j} and DRE normal (if done), and no other indications for biopsy

Not screenedⁱ

Repeat testing at 1- to 2-year intervals and For younger patients, consider further evaluation^k ([PROSD-3](#))

[Further Evaluation and Indications for Biopsy \(PROSD-3\)](#)

Repeat testing at 1- to 2-year intervals and For younger patients, consider further evaluation^k ([PROSD-3](#))

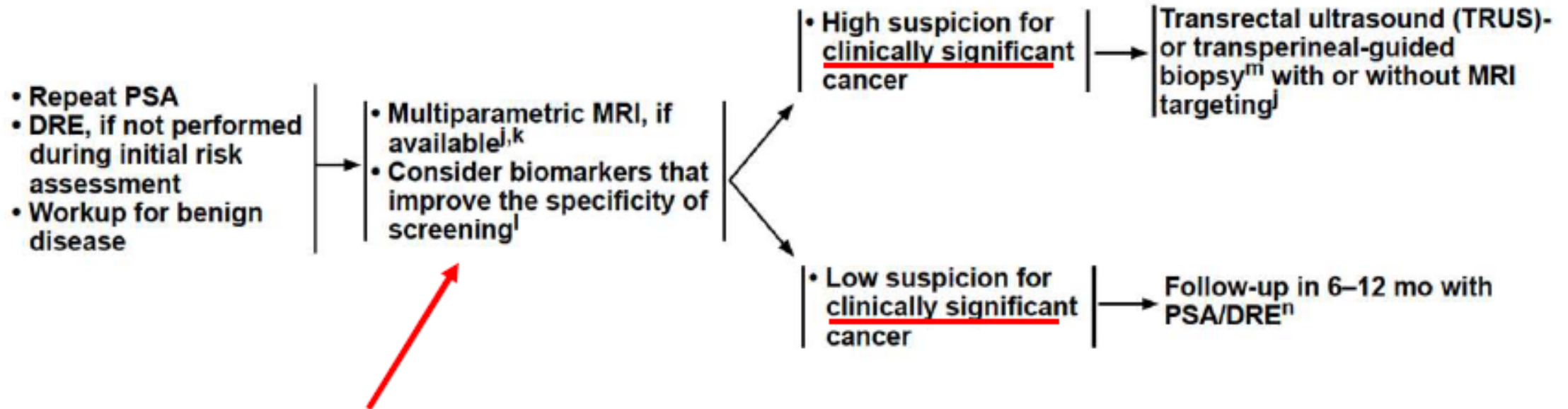
Repeat testing at 2- to 4-year intervals^l

[Further Evaluation and Indications for Biopsy \(PROSD-3\)](#)

Consider discontinuing screening if clinically appropriate or Repeat testing at 1- to 3-year intervals^{i,l}

NCCN guideline

Further evaluation: biomarkers or MRI



Guidelines now suggest clinicians use MRI or biomarkers prior to biopsy to define the probability of **clinically-significant cancer (GG $\geq$ 2, GS $\geq$ 7)**

Pancreatic Cancer remains deadly

Common Types of Cancer	Estimated New Cases 2025	Estimated Deaths 2025
1. Breast Cancer (Female)	316,950	42,170
2. Prostate Cancer	313,780	35,770
3. Lung and Bronchus Cancer	226,650	124,730
4. Colorectal Cancer	154,270	52,900
5. Melanoma of the Skin	104,960	8,430
6. Bladder Cancer	84,870	17,420
7. Kidney and Renal Pelvis Cancer	80,980	14,510
8. Non-Hodgkin Lymphoma	80,350	19,390
9. Uterine Cancer	69,120	13,860
10. Pancreatic Cancer	67,440	51,980

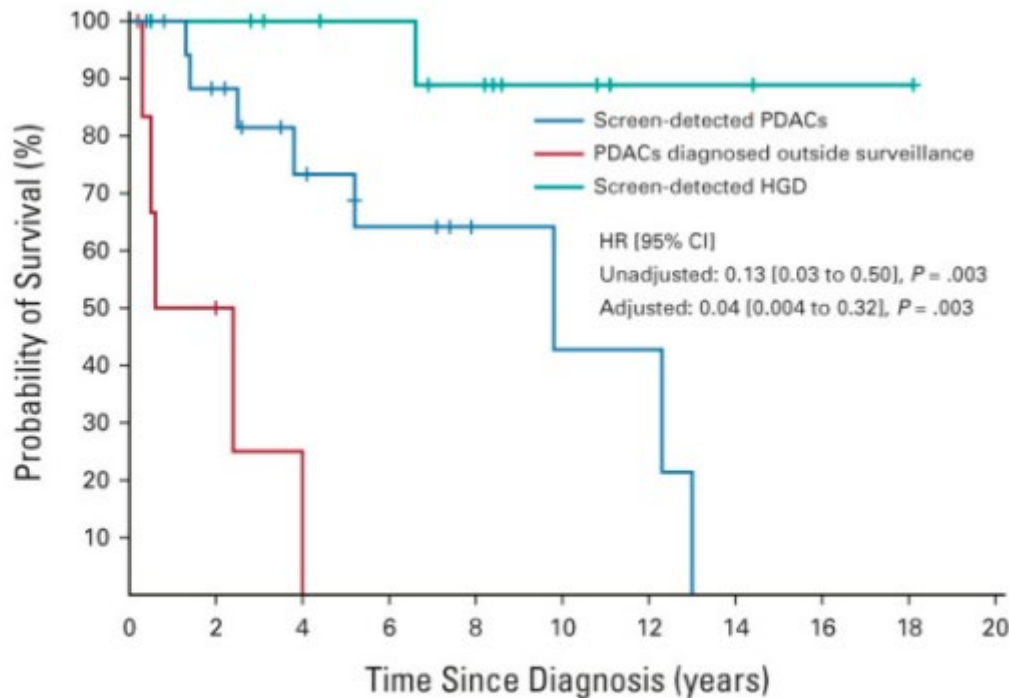
Pancreatic cancer represents 3.3% of all new cancer cases in the U.S.



Making a case for Pancreatic Cancer Screening

- Rates of Pancreatic Adenocarcinoma have gradually increased, particularly among younger women in part because of rising obesity rates.
- Some experts estimate that by 2030 Pancreatic cancer will overtake Colorectal cancer deaths as other cancers have become more treatable and are diagnosed earlier.
- Drugs targeting KRAS, gene which helps control cell growth, show promise. 90% of Pancreatic cancers have KRAS mutations.

Screening and “Stage Shift” means improved Survival



No. at risk:											
Screen-detected HGD	13	12	10	9	7	4	2	2	1	1	0
PDACs outside surveillance	7	3	1	0	0	0	0	0	0	0	0
Screen-detected PDACs	19	14	9	6	3	2	2	0	0	0	0

- 57.9% of screen detected pancreatic cancers were Stage 1
- 85.7% of pancreatic cancer detected outside surveillance is Stage 4

Incidence of Pancreatic Cancer by Number of Affected First Degree Relatives

10-15% of patients with pancreatic cancer have a familial aggregation or an inherited predisposition

Number of FDRs	Standardized Incidence Ratio (95% CI)	Incidence (per 100,000 in U.S. population)
General U.S. Population	-	9
1	4.5 (0.54 - 16.3)	41
2	6.4 (1.8 – 16.4)	58
3 or more	32 (10.4 – 74.7)	288

Pancreatic Cancer by Smoking Status in Patients with ≥ 1 FDR

	Standardized Incidence Ratio (95% Confidence Intervals)
Smokers	19.2 (7.7 – 39.5)
Non Smokers	6.25 (1.70 – 16.0)

Who should we screen for Pancreatic Cancer?

Screen patients at high risk.

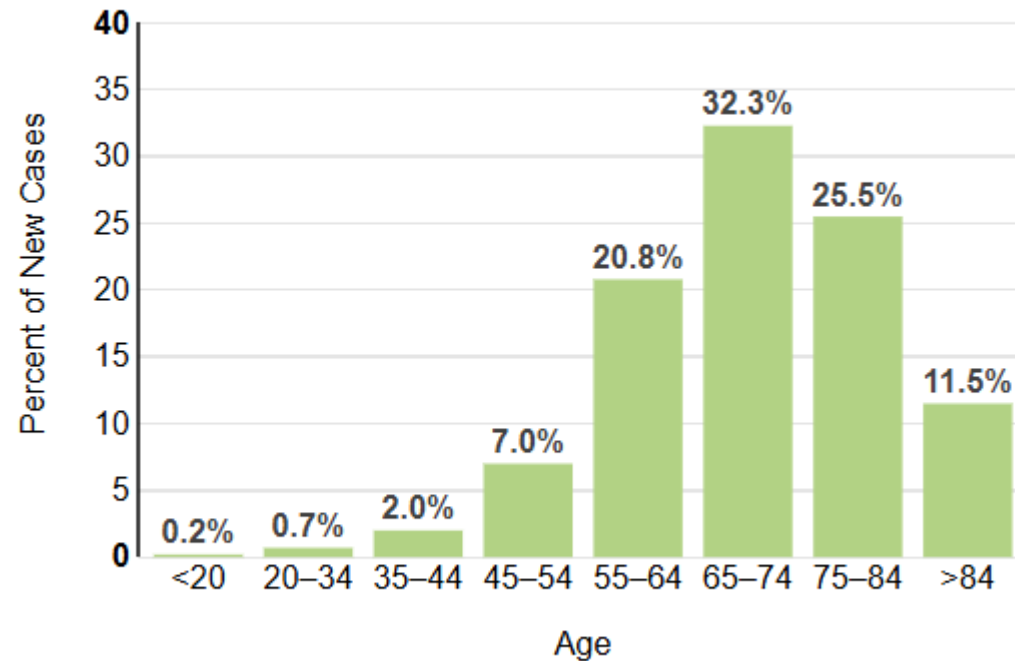
1. Familial Pancreatic Cancer – Families with > 2 First Degree Relatives (FDRs) diagnosed with Pancreatic Cancer
2. Any patient with a likely pathogenic mutation in any of the known Pancreatic Cancer susceptibility genes.

Pancreatic Cancer Surveillance Options

	Endoscopic Ultrasound	MRI
Invasive	Yes	No
Ability to sample	Yes	No
Patient Tolerance	Sedation required	Patient tolerance varies
Availability/Exp ertise	Requires Advanced Endoscopy Training	Requires experienced Radiologists

- **Abdominal CT Scan is NOT an acceptable substitute for MRI!**
- Some guidelines recommend alternating EUS and MRI
- Some experts advise serial MRI to allow precise comparisons
- NCCN advises annual screening in experienced, high-volume centers

When to start screening



Pancreatic cancer is most frequently diagnosed among people aged 65–74.

Median Age
At Diagnosis

71

Guidelines recommend initiating screening for high risk individuals at age 50 or 10 years earlier than youngest affected family member, whichever is earliest.



NCCN Guidelines Version 1.2026

Hereditary Cancer Testing Criteria

TESTING CRITERIA FOR PROSTATE CANCER SUSCEPTIBILITY GENES

(Genes such as *ATM*, *BRCA1*, *BRCA2*, *CHEK2*, *HOXB13*,^{ff} *PALB2*, and *TP53*) ([GENE-A](#))^{a,gg,hh}

Testing is clinically indicated in the following scenarios:

- See General Tumor Criteria on [CRIT-1](#).

- Personal history of prostate cancer at any age with:

- ▶ Metastatic^q (Stage IVB) or node-positive (Stage IVA) prostate cancer
- ▶ Very high-risk or high-risk disease (See Initial Risk Stratification and Staging Workup [PROS-2] - [NCCN Guidelines for Prostate Cancer](#))
- ▶ Ancestry: Ashkenazi Jewish
- ▶ Family history^c

- ◊ ≥1 close blood relative^p with ANY:

- breast cancer at age ≤50 y
- male breast cancer
- ovarian cancer
- pancreatic cancer
- metastatic,^q node positive, or very high-risk or high-risk prostate cancer

- ◊ ≥3 close blood relatives^p with prostate cancer (any grade) and/or breast cancer on the same side of the family including the patient with prostate cancer

- ◊ For additional family history considerations, see [NCCN Guidelines for Genetic/Familial High-Risk Assessment: Colorectal, Endometrial, and Gastric](#)

- Family history criteria: unaffected; or affected but does not meet criteria above

- ◊ Individual with a first-degree 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)^r

Criteria
met

[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](#)



NCCN Guidelines Version 3.2026

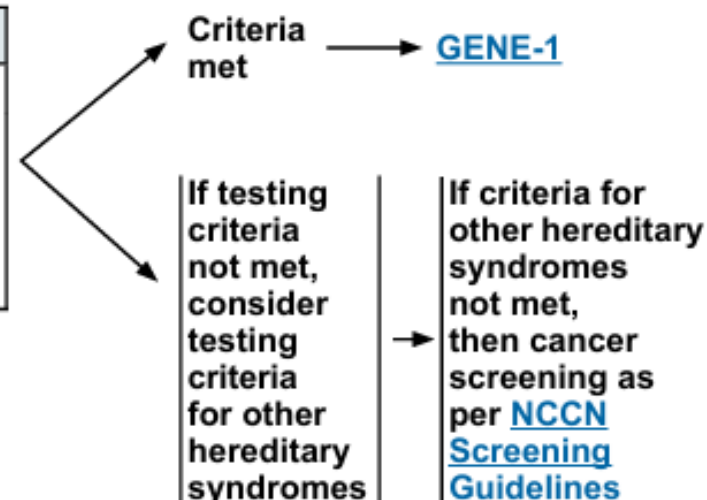
Hereditary Cancer Testing Criteria

TESTING CRITERIA FOR PANCREATIC CANCER SUSCEPTIBILITY GENES

(Genes such as *ATM*, *BRCA1*, *BRCA2*, *CDKN2A*, LS genes [*MLH1*, *MSH2*, *MSH6*, *EPCAM*], *PALB2*, *STK11*, and *TP53*) ([GENE-A](#))^{a,bb}

Testing is clinically indicated in the following scenarios:

- See General Testing Criteria on [CRIT-1](#).
- Exocrine pancreatic cancers
 - ▶ All individuals diagnosed with exocrine pancreatic cancer including acinar cell carcinoma^{cc,dd}
 - ▶ First-degree relatives of individuals diagnosed with exocrine pancreatic cancer^{ee}
- Neuroendocrine pancreatic tumors - [NCCN Guidelines for Neuroendocrine and Adrenal Tumors](#)

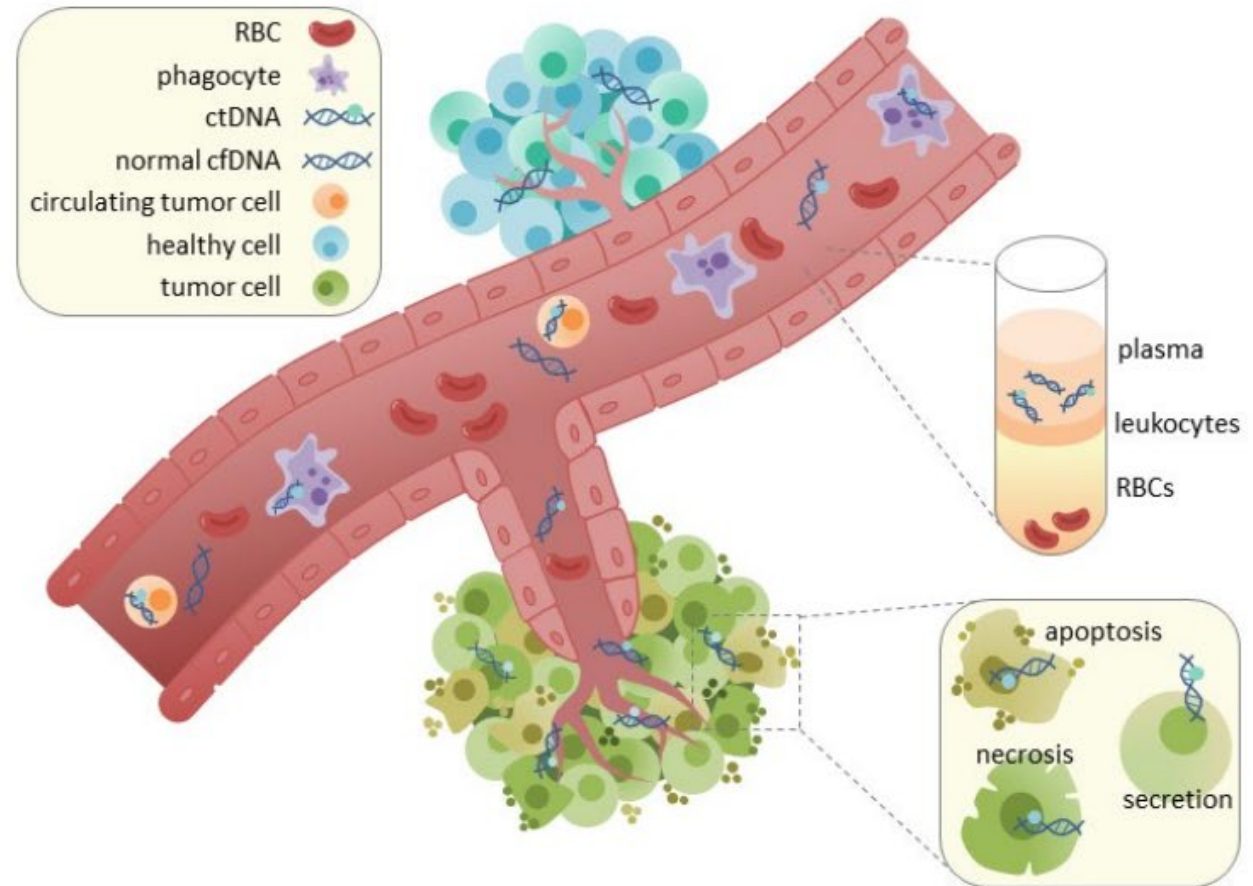


What is Multi-Cancer Early Detection (MCED)?

- This is a new field.
- Goal is to screen for multiple cancers with a single blood test that looks at multiple biomarkers:
 - Aneuploidy – cells with extra or missing chromosomes
 - Proteins – expressed by cancer genes
 - DNA methylation – alterations to cancer genes
 - Mutations – changes to DNA that may cause cancer
- Sensitivity can vary based on disease stage from 30% in Stage 1 to almost 90% in Stage 4

Sources of circulating DNA

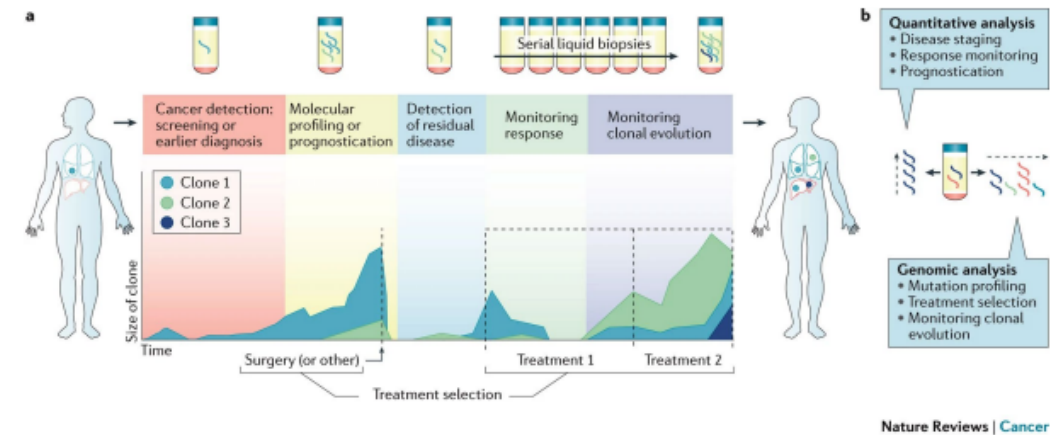
Clonal hematopoiesis and ctDNA/metastatic disease



[https://upload.wikimedia.org/wikipedia/commons/0/0f/CtDNA in circulation.png](https://upload.wikimedia.org/wikipedia/commons/0/0f/CtDNA_in_circulation.png)

Circulating Tumor DNA: Definition

- **Circulating tumor DNA (ctDNA):**
Fragmented cell-free DNA *derived from tumor cells* in the bloodstream
 - Released material from apoptosis/necrosis of tumor cells
- Incidental capture depends on availability of tumor genome DNA
 - Most likely with large burden of metastatic disease
 - Higher sensitivity from germline testing platform



Wan et al. *Nature Reviews Cancer* 2017

Grail's Multi-Cancer Blood Test Gets FDA Committee Vote for Premarket Approval

The FDA is expected to make its final ruling on Galleri's premarket approval in the coming months

By **Katherine Hamilton**

Sept. 23, 2026 6:55 pm ET



Aa



Gift unlocked article



Listen (2 min)



The FDA designated Galleri as a breakthrough device in 2018. BUSINESS WIRE

Galleri

- Sept 22: FDA panel voted for premarket approval based on Galleri's safety, effectiveness and overall benefit-risk profile for screening and early detection of multiple types of cancer in adults aged 50 and older.
- Galleri looks for DNA shed by cancer cells. The DNA is tagged by molecules specific to a cancer's origin—say, the colon or pancreas. Grail uses genetic sequencing and machine learning to recognize links between these DNA signatures and particular cancers.
- The test is intended to be used in addition to recommended screenings, rather than as a replacement.

Galleri NHS Trial

- A randomized controlled trial conducted with the U.K.'s National Health Service tracked about 142,000 asymptomatic patients ages 50 to 77. Half received the Galleri test every year. Galleri caught four times as many cancers in total than the U.K.'s four recommended screenings for colon, breast, lung and cervical cancer.
- The test also increased diagnoses of the 12 most deadly cancers at stages one and two by 16%.
- Galleri didn't reduce the total number of stage three and four cancers that were diagnosed compared to the control group.
- **Galleri didn't significantly reduce the combined number of stage III and IV cancers but reduced stage IV diagnoses by 14% overall, with reductions of 22% and 26% during the second and third yearly screening rounds.**
- Diagnoses of stage three cancers increased by 25% compared to the control group, while diagnoses for stage four declined 14%. Reductions in stage four cancer diagnoses grew the longer the trial went on, which strongly suggests that the tests were detecting cancers at earlier stages.

Take Home Points

- Use Family History as part of your risk assessment when talking to patients about cancer
- Apply the USPSTF Guidelines but consider earlier screening when family history or other risk factors support it.
- Screening is one important way to reduce Cancer related mortality but NOT the only way.
- Don't forget about Lifestyle measures!!!
- Recommend vaccines that reduce cancer risk – HPV, Hepatitis B

FMLH/MCW Hereditary Cancer Risk Clinic

- Patients eligible:
 - Known positive germline testing
 - Blood relative with a known pathogenic or likely pathogenic germline mutation
 - Pedigree suggestive of inherited mutation
- Located in the Froedtert Cancer Center Life/Quality of Life Clinic
- Call 414-805-0505

Our Team



Ann Maguire, MD, MPH
Internal Medicine, Primary
Care



Anna C Purdy ,NP,
MSN
Surgical Oncology Nurse
Practitioner



Muhammad Faizan Ali, MD
Hospitalist, Internal Medicine,
Primary Care



Joanne Mattingly, NP,
MS
Surgical Oncology Nurse
Practitioner



Samantha M. Stachowiak,
MS, CGC
Genetic Counselor, Genetics



Morgan Armstrong, MS,
CGC
Genetic Counselor, Genetics



Thank
you!