Updates in Cancer Screening

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TOWER HEALTH OSTEOPATHIC SYMPOSIUM

APRIL 6, 2024

Disclosures

I have no conflicts to disclose.

Objectives

Review the newest updates, evidence and controversies in screening for:

- Colorectal Cancer
- Breast Cancer
- Lung Cancer

Colorectal Cancer Screening

Recommendation Summary

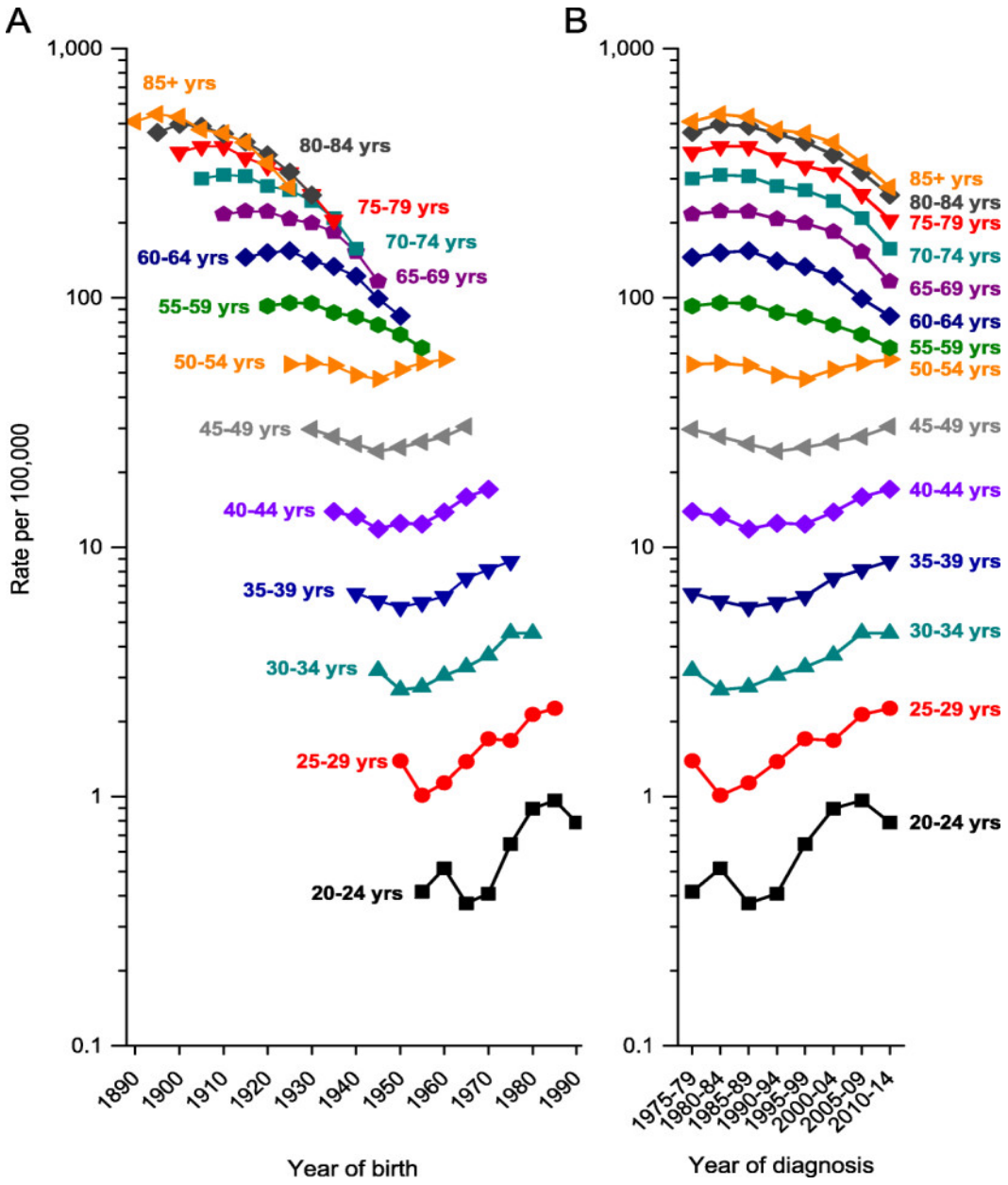
Population	Recommendation	Grade
Adults aged 50 to 75 years	The USPSTF recommends screening for colorectal cancer in all adults aged 50 to 75 years. See the "Practice Considerations" section and Table 1 for details about screening strategies.	A
Adults aged 45 to 49 years	The USPSTF recommends screening for colorectal cancer in adults aged 45 to 49 years. See the "Practice Considerations" section and Table 1 for details about screening strategies.	B
Adults aged 76 to 85 years	The USPSTF recommends that clinicians selectively offer screening for colorectal cancer in adults aged 76 to 85 years. Evidence indicates that the net benefit of screening all persons in this age group is small. In determining whether this service is appropriate in individual cases, patients and clinicians should consider the patient's overall health, prior screening history, and preferences.	C

USPSTF 2021

Who does this apply to?

Asymptomatic adults 45 years or older at AVERAGE risk of colon cancer.

- No prior diagnosis of CRC, adenomatous polyps or IBD
- No personal diagnosis or family hx of genetic disorders w/ risk of CRC



When do we begin screening? Should we start at 45?

CA A Cancer J Clinicians, Volume: 68, Issue: 4, Pages: 250-281, First published: 30 May 2018, DOI: (10.3322/caac.21457)

CRC Screening at age 45

PRO

- USPSTF, ACS, MSTF
- “Qualified” recommendation
- Increase in CRC incidence in younger persons
- Favorable benefit to burden balance
- Expected reduction in CRC mortality and incidence
- High value on potential years of life saved
- Contribute to reducing disparities

CON

- ACP
- Very limited direct evidence
- Concerns about modeling data
- Net benefit of screening is less
- Absolute mortality benefit will be lower
- Limited resources and concern for exacerbating disparities

How do we screen?

2 options-

- Structural (visual) examination
- High sensitivity stool-based tests

Should be strongly dependent on patient preference and test availability

Trials consistently demonstrate a choice between stool test and structural exam leads to greater screening uptake

Direct Visualization

Test	Frequency	Considerations
Colonoscopy	Every 10 y	Screening and follow up during same exam Cancer prevention w/ polyp removal Less frequent Needs bowel prep, anesthesia, transportation Risks of bleeding and perforation
CT Colonography	Every 5 y	Requires bowel preparation but no anesthesia Can have incidental extracolonic findings Radiation exposure Would need colonoscopy for follow up ACP does not recommend
Flexible Sigmoidoscopy	Every 5 y	Risk of bleeding and perf but < colonoscopy Requires enema for prep Fewer life years gained alone Test availability Still could need Cscope for follow up
Flex Sig w/ FIT	FS every 10 y, FIT every 1 y	Benefits better than FS alone FIT requires good adherence

Stool Based Tests

Test	Frequency	Considerations
High Sensitivity gFOBT	Every 1 year	Vulnerable to false positive results Requires 3 stool samples May not be as sensitive for advanced adenomas and CRC as other stool tests Requires colonoscopy follow up Requires good adherence No prep, sedation
FIT	Every 1 year	No dietary restrictions Single stool sample Requires colonoscopy follow up Requires good adherence No prep, sedation
sDNA-FIT (Cologuard)	Every 1-3 years	Better sensitivity but worse specificity than FIT Modeling does not suggest favorably balance of benefits and harms w/ screening every 3 y Needs colonoscopy for follow up Longitudinal follow up is unclear Single stool sample, entire BM Requires good adherence No prep, sedation ACP does not recommend

"A Cell-free DNA Blood-Based Test for Colorectal Cancer Screening"

NEJM March 14, 2024

Table 2. Sensitivity and Specificity of the Cell-free DNA (cfDNA) Blood-Based Test for the Most Advanced Findings on Colonoscopy.*

Variable	Most Advanced Finding on Colonoscopy	cfDNA Blood-Based Test	
		Positive Test	Sensitivity (95% CI)
	no.	*no.*	%
Colorectal cancer			
Any	65	54	83.1 (72.2–90.3)
Stage I, II, or III*	48	42	87.5 (75.3–94.1)
Advanced precancerous lesions†	1116	147	13.2 (11.3–15.3)
			Specificity (95% CI)
Nonadvanced adenomas, nonneoplastic findings, and negative colonoscopy	6680	698	89.6 (88.8–90.3)
Nonneoplastic findings and negative colonoscopy	4514	457	89.9 (89.0–90.7)

* Excluded were 10 stage IV and 7 pathologically confirmed, incompletely staged colorectal cancers.
† Advanced precancerous lesions include advanced adenomas and sessile serrated lesions at least 10 mm in the largest dimension.

When do we stop?

Everyone agrees-

- Should continue routine screening up to age 75
- Should stop for almost everyone at age 85
- Screening benefit requires 10-year life expectancy

USPSTF & ACS recommend individual decisions from 76- 85

MSTF and ACP recommend stopping at age 75

- MSTF clarifies UTD w/ screening, particularly high-quality colonoscopy
- ACS agrees- little incremental benefit in individuals w/ regular screening
- **Focus should be on healthy individuals, few comorbidities, 10-year life expectancy and especially those NOT UTD w/ screening**

Breast Cancer Screening

Population	Recommendation	Grade
Women aged 50 to 74 years	The USPSTF recommends biennial screening mammography for women aged 50 to 74 years.	B
Women aged 40 to 49 years	The decision to start screening mammography in women prior to age 50 years should be an individual one. Women who place a higher value on the potential benefit than the potential harms may choose to begin biennial screening between the ages of 40 and 49 years. For women who are at average risk for breast cancer, most of the benefit of mammography results from biennial screening during ages 50 to 74 years. Of all of the age groups, women aged 60 to 69 years are most likely to avoid breast cancer death through mammography screening. While screening mammography in women aged 40 to 49 years may reduce the risk for breast cancer death, the number of deaths averted is smaller than that in older women and the number of false-positive results and unnecessary biopsies is larger. The balance of benefits and harms is likely to improve as women move from their early to late 40s. In addition to false-positive results and unnecessary biopsies, all women undergoing regular screening mammography are at risk for the diagnosis and treatment of noninvasive and invasive breast cancer that would otherwise not have become a threat to their health, or even apparent, during their lifetime (known as "overdiagnosis"). Beginning mammography screening at a younger age and screening more frequently may increase the risk for overdiagnosis and subsequent overtreatment. Women with a parent, sibling, or child with breast cancer are at higher risk for breast cancer and thus may benefit more than average-risk women from beginning screening in their 40s.	C
All women	The USPSTF concludes that the current evidence is insufficient to assess the benefits and harms of digital breast tomosynthesis (DBT) as a primary screening method for breast cancer.	I
Women with dense breasts	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of adjunctive screening for breast cancer using breast ultrasonography, magnetic resonance imaging, DBT, or other methods in women identified to have dense breasts on an otherwise negative screening mammogram.	I
Women aged 75 years or older	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening mammography in women aged 75 years or older.	I

USPSTF 2016

2023 Draft Update

Population	Recommendation	Grade
Women ages 40 to 74 years	The USPSTF recommends biennial screening mammography for women ages 40 to 74 years.	B
Women age 75 years or older	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening mammography in women age 75 years or older.	I
Women with dense breasts	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of supplemental screening for breast cancer using breast ultrasonography or magnetic resonance imaging (MRI) in women identified to have dense breasts on an otherwise negative screening mammogram. See the "Practice Considerations" section for more information on the patient population to whom this recommendation applies and on screening mammography modalities.	I

Who does this apply to?

USPSTF 2023

Cisgender women and other persons AFAB age 40 y or older at average risk of breast cancer.

Applies to persons with a family hx of breast cancer and to persons w/ other risk factors (such as dense breasts).

Does NOT apply to:

- women w/ genetic marker or syndrome associated w/ high risk
- women w/ hx of high dose radiation to the chest

When do we start?

Somewhere between 40 and 50

Everyone agrees women aged 50-74 should have screening

What about 40- 50?

- Should be a personal decision
- Consider individual risk
- Somewhat limited reduction in mortality and significant harms
- ACR- “Weighing…should be done by women not for women”

Table 4. Distribution of Female Population Size, 5-Year Absolute Breast Cancer Risk, and Age-Specific Breast Cancer Incidence Rates by Age

Age, y	2011 Population Size (in 1000s)[a]	5-Year Absolute Breast Cancer Risk, 2009-2011, %[b]	Breast Cancer Incidence Rate per 100 000 Population, 2007-2011[b]
30-34	10 232	0.1	26.8
35-39	9837	0.3	59.5
40-44	10 576	0.6	122.5
45-49	11 211	0.9	188.6
50-54	11 499	1.1	224.0
55-59	10 444	1.3	266.4
60-64	9271	1.6	346.7
65-69	6806	2.0	420.2
70-74	5204	2.1	433.8
75-79	4155	2.0	443.3
80-84	3444	1.9	420.6
≥85	3826	2.5	354.4

Distribution of Female Population Size, 5-Year Absolute Breast Cancer Risk, and Age-Specific Breast Cancer Incidence Rates by Age[a]Source: Populations: Total US [Katrina/Rita Adjustment], 1969-2011 Counties. National Cancer Institute, Division of Cancer Control and Population Sciences, Surveillance Research Program, Surveillance Systems Branch. Released October 2012.

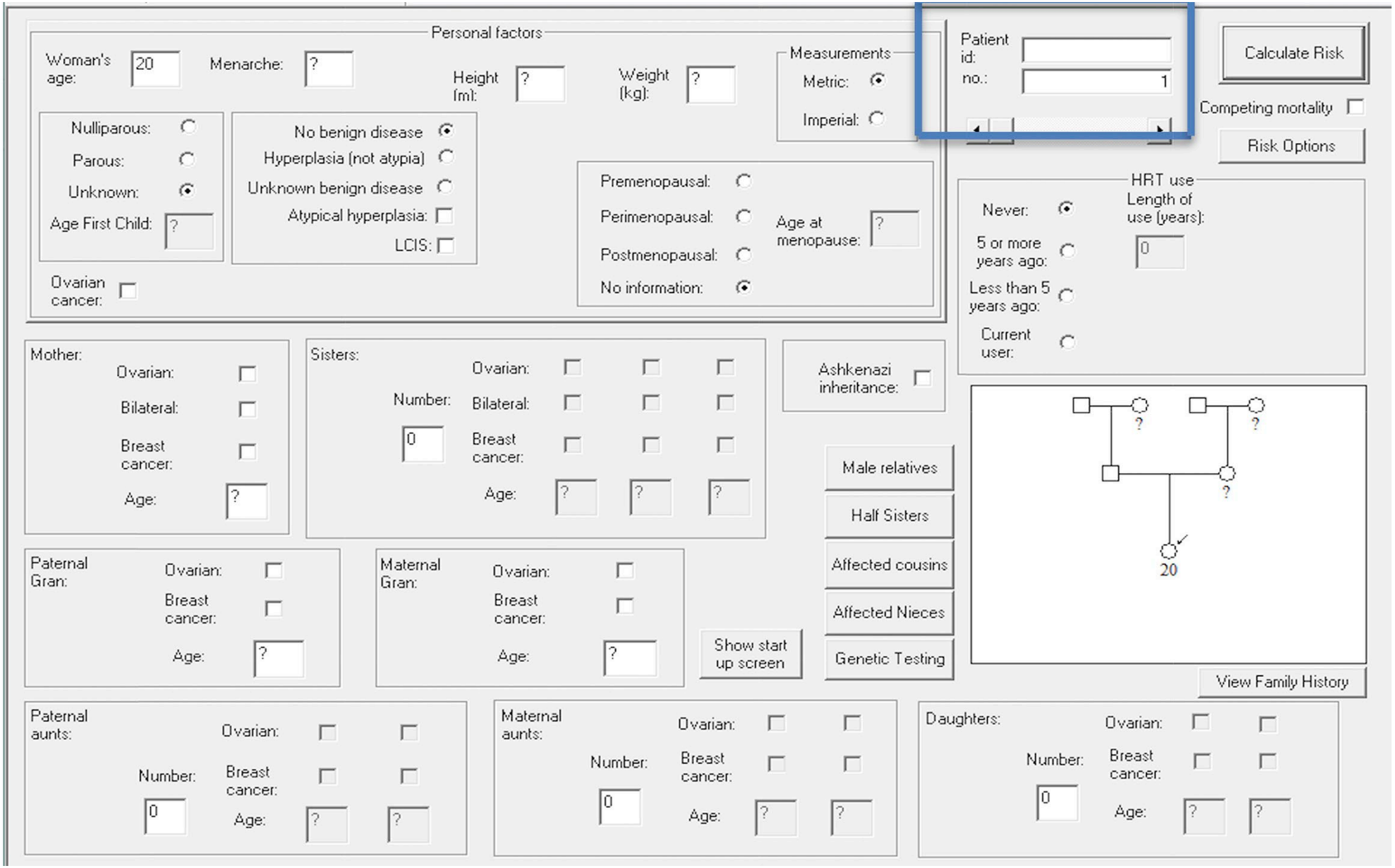
How do we calculate individual risk?

Gail Model

- Breast Cancer Risk Assessment Calculator – NCI

Tyrer Cuzick Model

- International Breast Cancer Intervention Studies (IBIS)



https://doi.org/10.1016/j.nurpra.2016.07.027.

How should we screen?

Both mammography and DBT are effective primary screening

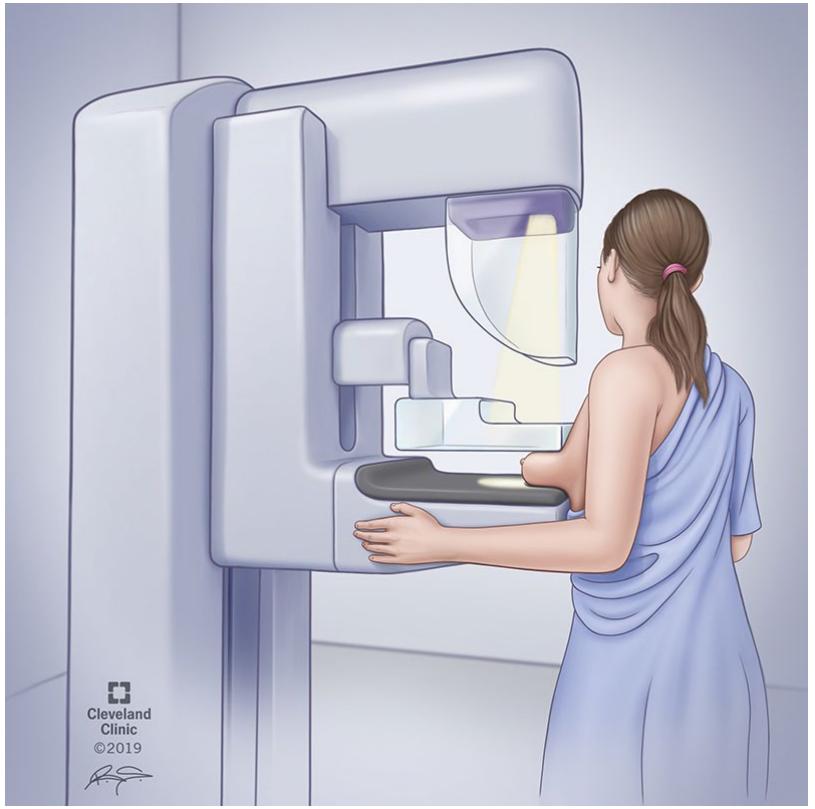
DBT has slightly better cancer detection and smaller recall rates

- May be more beneficial for dense breasts

ACOG recommends “breast self awareness”

Clinical breast exam?

Breast MRI and US are not recommended for primary screening



https://my.clevelandclinic.org/health/diagnostics/4877-mammogram

Breast MRI

Breast MRI has higher sensitivity but variable specificity.

False positives are common

Recommended for high-risk women in addition to mammography

- genetic mutation
- radiation to the chest
- >20% lifetime risk
- diagnosed with breast cancer prior to age 50 or with personal history of breast cancer and dense breasts (ACR)

How often?

Debate between annual vs biennial screening

Shorter screening intervals associated w/ improved outcomes but increased call backs and biopsies

Annual Screening-

- 2 more lives saved
- 82 additional biopsies
- 6 over diagnosed breast tumors
- (per 1000 women aged 50-74)

ACS suggests annual to 55 y/o, biennial offered after

When do we stop?

Continue until age 74 unless significant comorbidities, life expectancy less than 10 years

What happens after 75?

USPSTF says insufficient evidence to make a recommendation	ACS says continue if overall health is good and life expectancy of >10 yrs	ACOG says shared decision making based on health status and longevity	ACR says no upper age limit

“Breast tissue can be either dense or not dense. Dense tissue makes it harder to find breast cancer on a mammogram and also raises the risk of developing breast cancer. Your breast tissue is dense. In some people with dense tissue, other imaging tests in addition to a mammogram may help find cancers. Talk to your healthcare provider about breast density, risks for breast cancer, and your individual situation.”

FDA 2023

What about breast density?

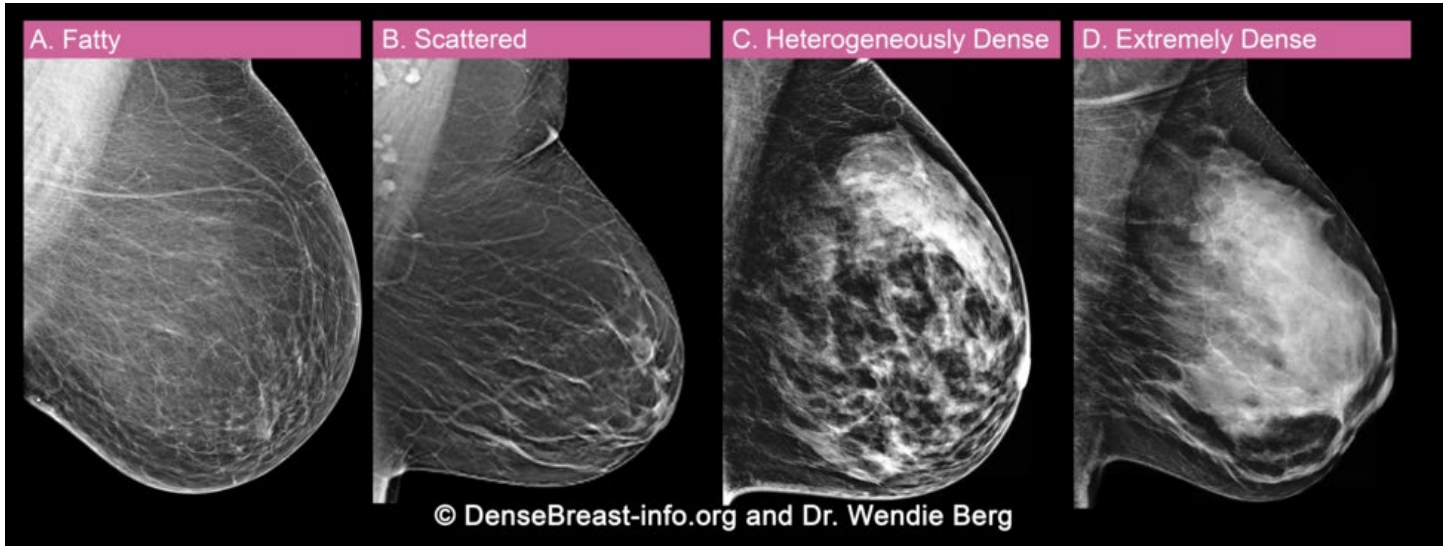
Increased breast density results in decreased sensitivity and specificity of mammography

Slightly higher risk of breast cancer

FDA 2023 requires reporting of breast density

Current recommendation do not recommend additional testing

Ongoing research needed



Lung Cancer Screening

Recommendation Summary

Population	Recommendation	Grade
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	The USPSTF recommends annual screening for lung cancer with low-dose computed tomography (LDCT) 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 develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.	B

USPSTF 2021

NLST & NELSON

	NLST	NELSON
Country	USA	BE/NL
Enrollment	53,454	15,792
Screening Interval	3 Annual CTs	4 CTs- Initial, 1 yr, 3 yrs, 5.5 yrs
Comparison	CXR	No Imaging
Population	55- 74 YO, >30 PYs, < 15 YSQ	50-74 YO, >15 PYs*, <10 YSQ
Reduction in LC Mortality	20%	26%, 33% in women

	2013 Guidelines	2021 Guidelines
Eligibility	Adults **aged 55** to 80 years who have a **30 pack-year** smoking history and currently smoke or have quit within the past 15 years	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
Estimated population	8.1 million people in the US	14.5 million people in the US

USPSTF Changes from 2013- 2021

https://www.advisory.com/sponsored/lung-cancer

Years since quitting?

Screening scenario[a]	Eligible, %	LDCT screens, No.	Screen-detected LC, No.	LC mortality reduction, %	Deaths averted, No.	LYG, No.	NNS to save one life
With YSQ 50-80-20-15[b]	22.6	419,030	1401	13.0	503	6918	45
With YSQ 50-80-20-15[c]	23	425,373	1727	10.8	506	8471	45
NoYSQExit 50-80-20-15[d]	23.0	556,275	2070	12.8	599	9920	38
NoYSQExit 50-80-20-30	24.0	584,013	2099	13.0	609	10,084	39
NoYSQ 50-80-20[e]	24.0	584,062	2097	13.0	611	10,090	39

Screening scenario[a]	LDCT screens, No.	Mean LDCTs per person screened, No.	Mean false positives per person screened, No.	Biopsies, No.	Overdiagnosis versus overdiagnosis if ≥5 years' life expectancy, No.	Overdiagnosis as a % of all cases/as a % of all screen-detected cases	Radiation-induced lung cancer deaths, No.
With YSQ 50-80-20-15[b]	419,030	18.5	2.2	518	84	1.7/6.0	38.6
With YSQ 50-80-20-15[c]	425,373	18.5	1.06	754	72/37	1.2/4.1	12.8
NoYSQExit 50-80-20-15[d]	556,275	24.2	1.35	945	98/45	1.7/4.7	16.0
NoYSQExit 50-80-20-30	584,013	24.3	1.36	966	100/45	1.7/4.7	16.7
NoYSQ 50-80-20[e]	584,062	24.3	1.35	966	100/45	1.7/4.8	16.7

https://acsjournals.onlinelibrary.wiley.com/doi/10.3322/caac.21811

Shared Decision Making

- Screening test
- Eligibility criteria
- Benefits of screening
- Health status that may preclude screening benefits
- Harms and limitations
- How often to get screened
- Importance of smoking cessation

Other Cancer Screenings

Prostate Cancer Screening

Recommendation Summary

Population	Recommendation	Grade
Men aged 55 to 69 years	For men aged 55 to 69 years, the decision to undergo periodic prostate-specific antigen (PSA)-based screening for prostate cancer should be an individual one. Before deciding whether to be screened, men should have an opportunity to discuss the potential benefits and harms of screening with their clinician and to incorporate their values and preferences in the decision. Screening offers a small potential benefit of reducing the chance of death from prostate cancer in some men. However, many men will experience potential harms of screening, including false-positive results that require additional testing and possible prostate biopsy; overdiagnosis and overtreatment; and treatment complications, such as incontinence and erectile dysfunction. In determining whether this service is appropriate in individual cases, patients and clinicians should consider the balance of benefits and harms on the basis of family history, race/ethnicity, comorbid medical conditions, patient values about the benefits and harms of screening and treatment-specific outcomes, and other health needs. Clinicians should not screen men who do not express a preference for screening.	C
Men 70 years and older	The USPSTF recommends against PSA-based screening for prostate cancer in men 70 years and older.	D

USPSTF 2018

Cervical Cancer Screening

Recommendation Summary

Population	Recommendation	Grade
Women aged 21 to 65 years	The USPSTF recommends screening for cervical cancer every 3 years with cervical cytology alone in women aged 21 to 29 years. For women aged 30 to 65 years, the USPSTF recommends screening every 3 years with cervical cytology alone, every 5 years with high-risk human papillomavirus (hrHPV) testing alone, or every 5 years with hrHPV testing in combination with cytology (cotesting). See the Clinical Considerations section for the relative benefits and harms of alternative screening strategies for women 21 years or older.	A
Women younger than 21 years	The USPSTF recommends against screening for cervical cancer in women younger than 21 years.	D
Women who have had a hysterectomy	The USPSTF recommends against screening for cervical cancer in women who have had a hysterectomy with removal of the cervix and do not have a history of a high-grade precancerous lesion (ie, cervical intraepithelial neoplasia [CIN] grade 2 or 3) or cervical cancer.	D
Women older than 65 years	The USPSTF recommends against screening for cervical cancer in women older than 65 years who have had adequate prior screening and are not otherwise at high risk for cervical cancer. See the Clinical Considerations section for discussion of adequate prior screening and risk factors that support screening after age 65 years.	D

USPSTF 2018

References

Wolf, A.M.D., Fontham, E.T.H., Church, T.R., Flowers, C.R., Guerra, C.E., LaMonte, S.J., Etzioni, R., McKenna, M.T., Oeffinger, K.C., Shih, Y.-C.T., Walter, L.C., Andrews, K.S., Brawley, O.W., Brooks, D., Fedewa, S.A., Manassaram-Baptiste, D., Siegel, R.L., Wender, R.C. and Smith, R.A. (2018), Colorectal cancer screening for average-risk adults: 2018 guideline update from the American Cancer Society. CA: A Cancer Journal for Clinicians, 68: 250-281. https://doi.org/10.3322/caac.21457

US Preventive Services Task Force. Screening for Colorectal Cancer: US Preventive Services Task Force Recommendation Statement. *JAMA.* 2021;325(19):1965–1977. doi:10.1001/jama.2021.6238

Amir Qaseem, Curtis S. Harrod, Carolyn J. Crandall, et al; Clinical Guidelines Committee of the American College of Physicians. Screening for Colorectal Cancer in Asymptomatic Average-Risk Adults: A Guidance Statement From the American College of Physicians (Version 2). Ann Intern Med.2023;176:1092-1100. [Epub 1 August 2023]. doi:10.7326/M23-0779

Patel, Swati G. MD, MS[1,2]; May, Folasade P. MD, PhD, MPhil[3,4]; Anderson, Joseph C. MD[5,6]; Burke, Carol A. MD[7]; Dominitz, Jason A. MD, MHS[8]; Gross, Seth A. MD[9]; Jacobson, Brian C. MD, MPH[10]; Shaukat, Aasma MD, MPH[11]; Robertson, Douglas J. MD, MPH[5]. Updates on Age to Start and Stop Colorectal Cancer Screening: Recommendations From the U.S. Multi-Society Task Force on Colorectal Cancer. The American Journal of Gastroenterology 117(1):p 57-69, January 2022. | DOI: 10.14309/ajg.0000000000001548

Oeffinger KC, Fontham ETH, Etzioni R, et al. Breast Cancer Screening for Women at Average Risk: 2015 Guideline Update From the American Cancer Society. *JAMA.* 2015;314(15):1599–1614. doi:10.1001/jama.2015.12783

Consensus Guideline on Diagnostic and Screening Magnetic Resonance Imaging of the Breast (breastsurgeons.org) https://www.breastsurgeons.org/docs/statements/Consensus-Guideline-on-Diagnostic-and-Screening-Magnetic-Resonance-Imaging-of-the-Breast.pdf

Saslow, D., Boetes, C., Burke, W., Harms, S., Leach, M.O., Lehman, C.D., Morris, E., Pisano, E., Schnall, M., Sener, S., Smith, R.A., Warner, E., Yaffe, M., Andrews, K.S., Russell, C.A. and (2007), American Cancer Society Guidelines for Breast Screening with MRI as an Adjunct to Mammography[†]. CA: A Cancer Journal for Clinicians, 57: 75-89. https://doi.org/10.3322/canjclin.57.2.75

Amir Qaseem, Jennifer S. Lin, Reem A. Mustafa, et al; for the Clinical Guidelines Committee of the American College of Physicians . Screening for Breast Cancer in Average-Risk Women: A Guidance Statement From the American College of Physicians. Ann Intern Med.2019;170:547-560. [Epub 9 April 2019]. doi:10.7326/M18-2147

References Continued

Reduced Lung-Cancer Mortality with Volume CT Screening in a Randomized Trial. Authors: Harry J. de Koning, M.D., Ph.D., Carlijn M. van der Aalst, Ph.D., Pim A. de Jong, M.D., Ph.D., Ernst T. Scholten, M.D., Ph.D., Kristiaan Nackaerts, M.D., Ph.D., Marjolein A. Heuvelmans, M.D., Ph.D., Jan-Willem J. Lammers, M.D., Ph.D., +16, and Matthijs Oudkerk, M.D., Ph.D. Published January 29, 2020. N Engl J Med 2020;382:503-513. DOI: 10.1056/NEJMoa1911793

Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening. Author: The National Lung Screening Trial Research Team. Published August 4, 2011. N Engl J Med 2011;365:395-409. DOI: 10.1056/NEJMoa1102873

Breast Cancer Risk Assessment and Screening in Average-Risk Women. ACOG. https://www.acog.org/clinical/clinical-guidance/practice-bulletin/articles/2017/07/breast-cancer-risk-assessment-and-screening-in-average-risk-women

Breast Cancer Screening for Women at Higher-Than-Average Risk: Updated Recommendations From the ACR. Monticciolo, Debra L. et al. Journal of the American College of Radiology, Volume 20, Issue 9, 902 - 914

Siu AL; U.S. Preventive Services Task Force. Screening for Breast Cancer: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med. 2016 Feb 16;164(4):279-96. doi: 10.7326/M15-2886. Epub 2016 Jan 12. Erratum in: Ann Intern Med. 2016 Mar 15;164(6):448. PMID: 26757170.

Draft Recommendation Statement. Breast Cancer: Screening. May 09, 2023. USPSTF. https://www.uspreventiveservicestaskforce.org/uspstf/draft-recommendation/breast-cancer-screening-adults#fullrecommendationstart.

Wolf AMD, Oeffinger KC, Shih TY-C, et al. Screening for lung cancer: 2023 guideline update from the American Cancer Society. *CA Cancer J Clin*. 2024; 74(1): 50-81. doi:10.3322/caac.21811

US Preventive Services Task Force. Screening for Lung Cancer: US Preventive Services Task Force Recommendation Statement. *JAMA.* 2021;325(10):962–970. doi:10.1001/jama.2021.1117

Screening for Lung Cancer. Mazzone, Peter J. et al.. CHEST, Volume 160, Issue 5, e427 - e494

A Cell-free DNA Blood-Based Test for Colorectal Cancer Screening. Chung et al. March 14, 2024 N Engl J Med 2024; 390:973-983 DOI: 10.1056/NEJMoa2304714

Questions?