Clearing up the Confusion: Breast Cancer Screening and Risk Evaluation

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May 16, 2025

Disclosures/Conflict of Interest

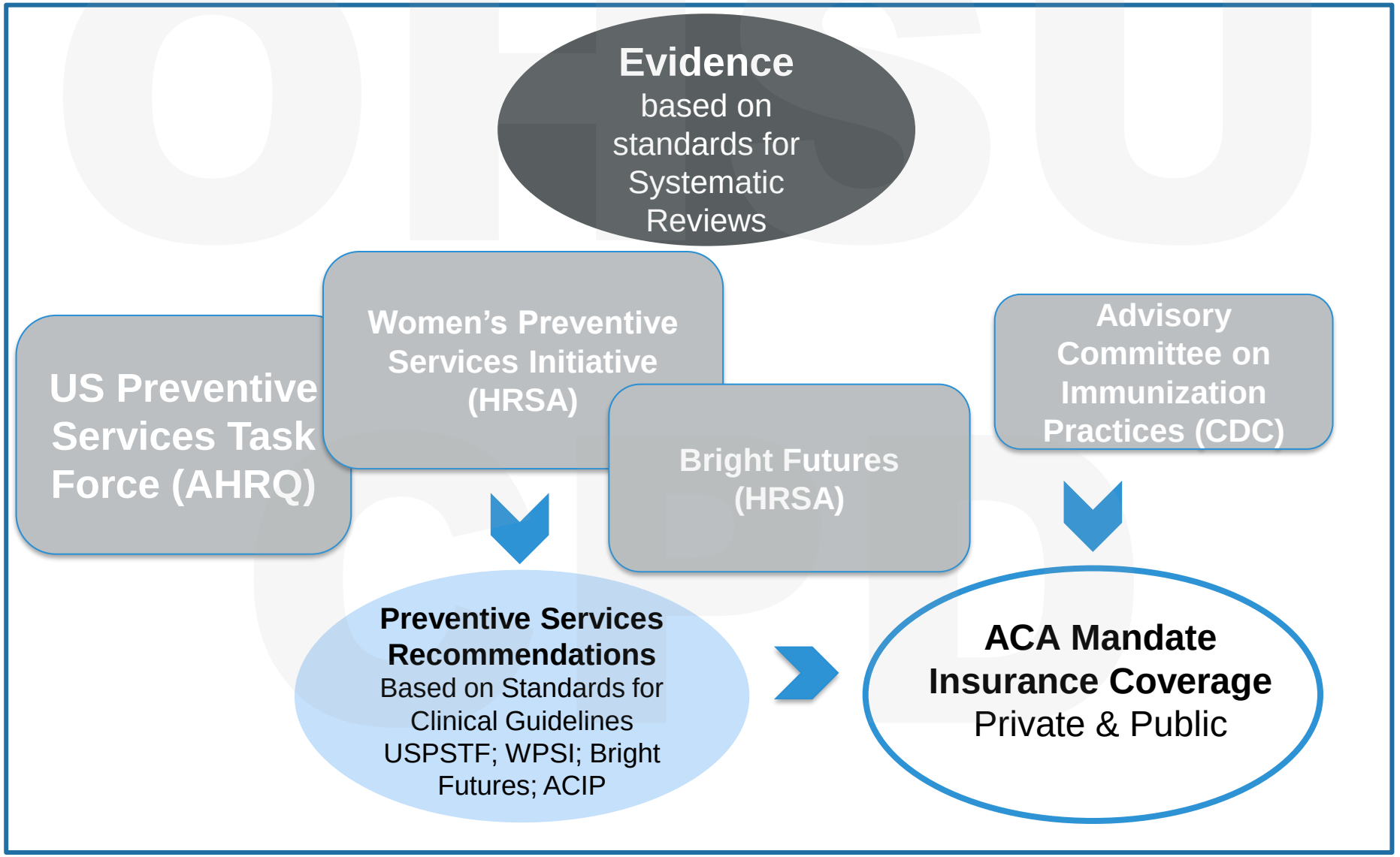
- No conflicts to disclose
- Research support from the Agency for Healthcare Research & Quality and Health Resources and Services Administration

Session Objectives

- Review current breast cancer screening recommendations.
- Understand strategies for risk stratification, referral or follow up.
- Interpret breast density and impact on screening.
- Identify high-risk patients for enhanced screening or genetics referral.

Breast Cancer Screening Clinical Guidelines

Federal Guideline Groups for Clinical Preventive Services



U.S. Preventive Services Task Force

- An *independent, non-governmental* panel of experts in primary care and prevention.
- Develops recommendations for clinical preventive services for primary care clinical practice.
- Based on standardized methodology and rigorous review of peer-reviewed evidence.
- Recommended preventive services include:
  - Screening tests
  - Counseling
  - Preventive medications

U.S. Preventive Services Task Force Recommendation Grades

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the clinical considerations section of USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

A and B recommendations are covered services under the ACA

Breast Cancer Screening Guidelines

U.S. Preventive Services Task Force, 2024

Age, *y*	Recommendation
40 to 74	Screen every 2 years (B)
75 and older	Insufficient (I)
Women with Dense Breasts	Insufficient (I)

Practice Considerations

- Digital breast tomosynthesis (DBT) or digital mammography as a primary screening method.
- Insufficient evidence for supplemental screening in women with dense breasts using breast ultrasonography, magnetic resonance imaging, DBT, or other methods.

US Preventive Services Task Force. Screening for Breast Cancer: US Preventive Services Task Force Recommendation Statement. *JAMA.* 2024;331(22):1918–1930. doi:10.1001/jama.2024.5534

WPSI
Women's Preventive Services Initiative

- National collaborative of women's health professional societies to develop, review, update, and disseminate recommendations for women's preventive health services.
- Launched in 2016 to continue the work of the IOM
- Supported by HRSA, led by ACOG, 2016 to 2025*
- http://www.womenspreventivehealth.org

MEMBERS OF THE ADVISORY PANEL SUPPORT THE WPSI

AMERICAN ACADEMY OF FAMILY PHYSICIANS
STRONG MEDICINE FOR AMERICA

The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

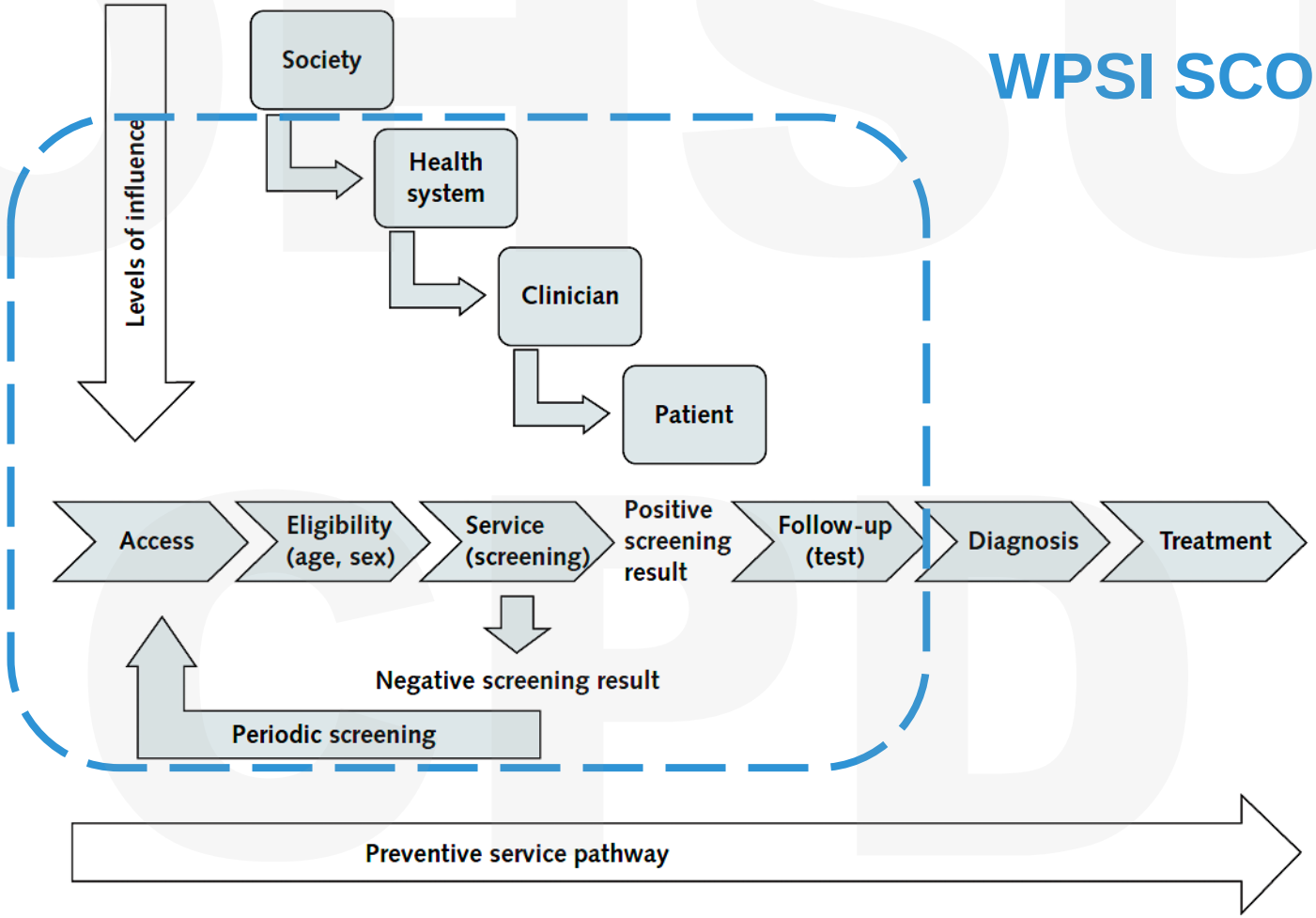
ACP
American College of Physicians
Leading Internal Medicine, Improving Lives

NPWH
NURSE PRACTITIONERS IN WOMEN'S HEALTH
Caring for Women

Project funding terminated 5/2025

- Target preventive health service *gaps*:
  - Not addressed by the U.S. Preventive Health Services Task Force (USPSTF) or Bright Futures
  - Research is limited or currently inconclusive
- Recommendations are based on evidence analyzed by the Evidence Review Team (ERT).
- Recommendations used to guide clinical practice and inform coverage of services for the ACA and other shareholders.

Preventive Health Services Framework



Nelson HD, Cantor, AG, et al. *Ann Intern Med* 2020;172:258-271.

WPSI/HRSA Recommendation, 2024

Breast Cancer Screening for Women at Average-risk

- Initiate mammography screening no earlier than age 40 and no later than age 50.
- Screening mammography should occur at least biennially and as frequently as annually.
- Screening should continue through at least age 74 and age alone should not be the basis to discontinue screening.
- Women at increased risk should also undergo periodic mammography screening, however, recommendations for additional services are beyond the scope of this recommendation.

Health Resources and Services Administration (HRSA). Update to the Health Resources and Services Administration-Supported Women's Preventive Services Guidelines. 2024;89(249):106522-106525.

WPSI
Women's Preventive Services Initiative

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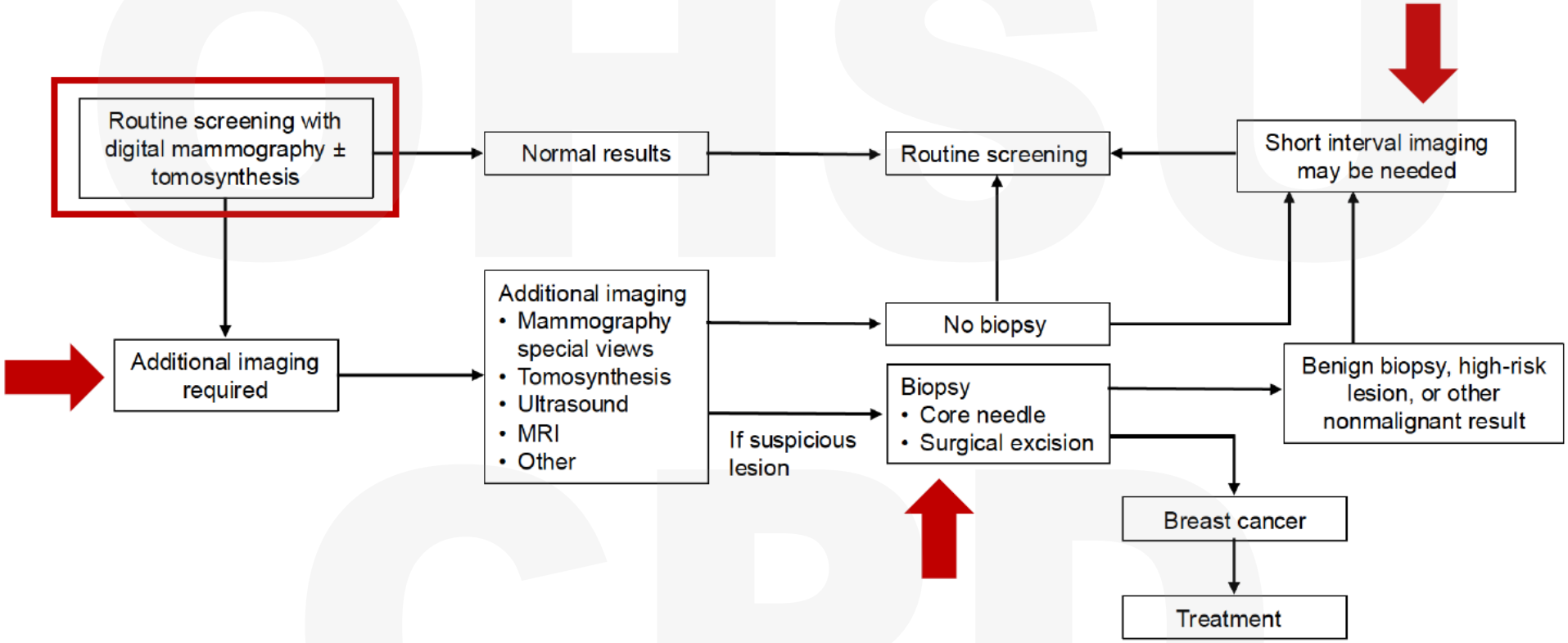
Breast Cancer Screening Clinical Pathway



Nelson HD, Cantor AG, et al. *WPSI Evidence Update*, 2024

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Breast Cancer Screening Follow-up

No follow-up after abnormal screening mammogram (rates)

- 7.2 -33% at 3 months
- 27.3-71.6% at 6 months

Due to multiple factors:

- Inadequate health system communication and support.
- Logistical barriers (e.g., transportation, distance, time).
- Lack of insurance coverage.
- Cost sharing for services beyond the initial screening mammogram.
- Lower rates for Black, Hispanic, Asian women; few studies on other population disparities.

Nelson HD, Cantor AG, et al. *WPSI Evidence Update*, 2024

WPSI/HRSA Recommendation, 2024

WPSI Conclusion: Data suggest that screening effectiveness could be improved with better delivery and coverage of prevention services that are already recommended by existing guidelines.

Breast Cancer Screening for Women at Average-risk

- Women may require additional imaging to complete the screening process or to address findings on the initial screening mammography. If additional imaging (e.g., MRI, ultrasound, mammography) and pathology exams are indicated, these services are also recommended to complete the screening process for malignancies.

Health Resources and Services Administration (HRSA). Update to the Health Resources and Services Administration-supported Women's Preventive Services Guidelines. 2024;89(249):106522-106525.

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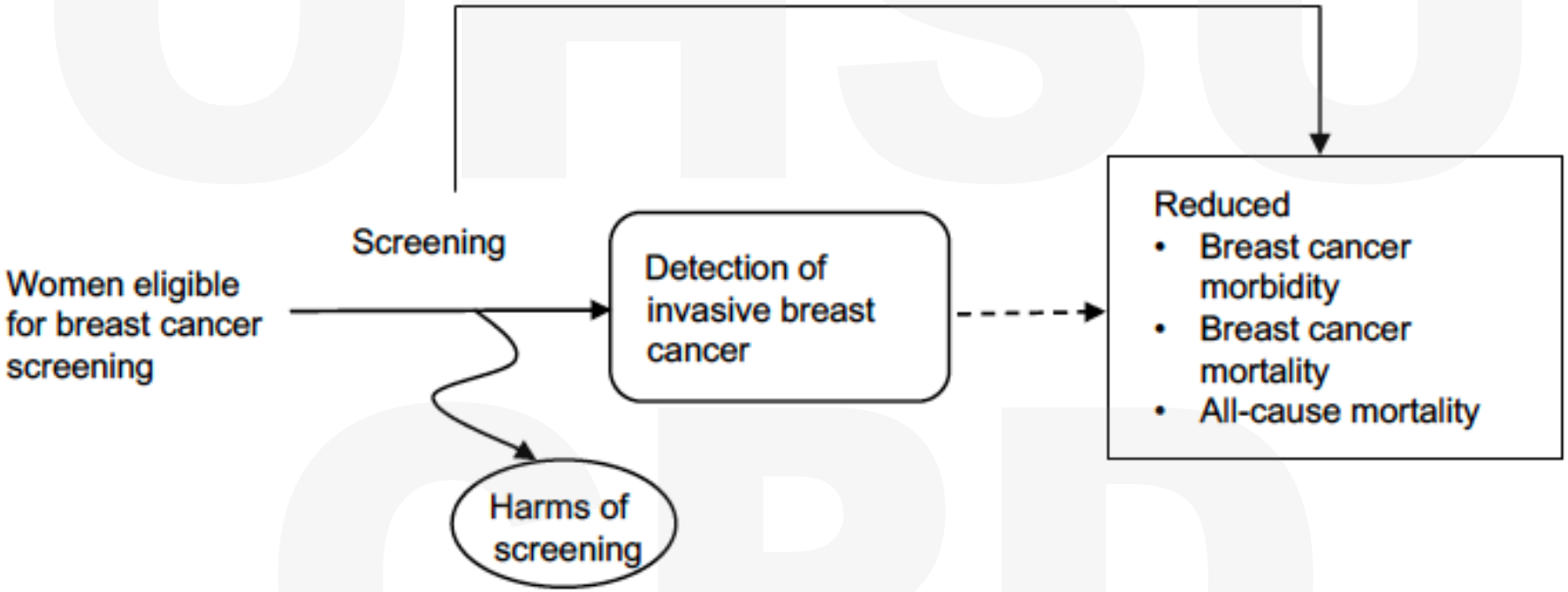
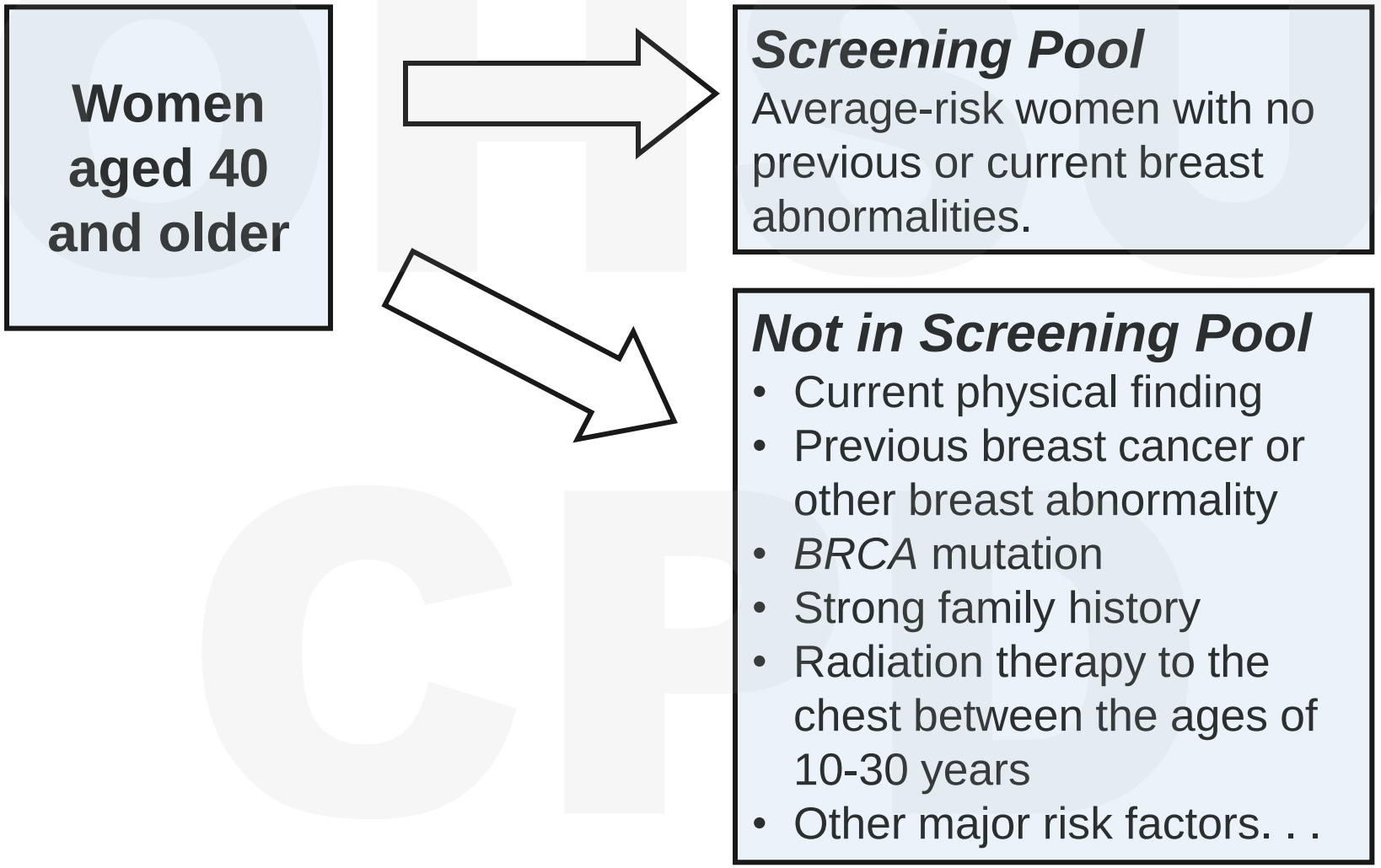
Understanding the Evidence

Analytic Framework



Risk Based Screening



Effectiveness of Screening
Strength of Evidence

Screening vs no screening	Outcome	
	Mortality	Advanced cancer
Age 40-49	Moderate/high	Moderate
Age 50-59	Moderate/high	Moderate
Age 60-69	Moderate	Moderate
Age >70	Insufficient	Insufficient
Age to start or stop screening	Insufficient	Insufficient
Screening interval	Insufficient	Insufficient
Digital vs tomosynthesis	Insufficient	Insufficient
Supplemental with ultrasound	Insufficient	Insufficient
Supplemental with MRI	Insufficient	Insufficient
Personalized screening	Insufficient	Insufficient
Differences by population characteristics and risk markers	Insufficient	Insufficient

Nelson HD, Fu R, Cantor, A, et al. *Ann Int Med. 2016;164(4):244-55.*
Henderson JT, Webber EM, et al. *JAMA*. 2024;331(22):1931-1946.
Nelson HD, Cantor AG, et al. *WPSI Evidence Update*, 2024

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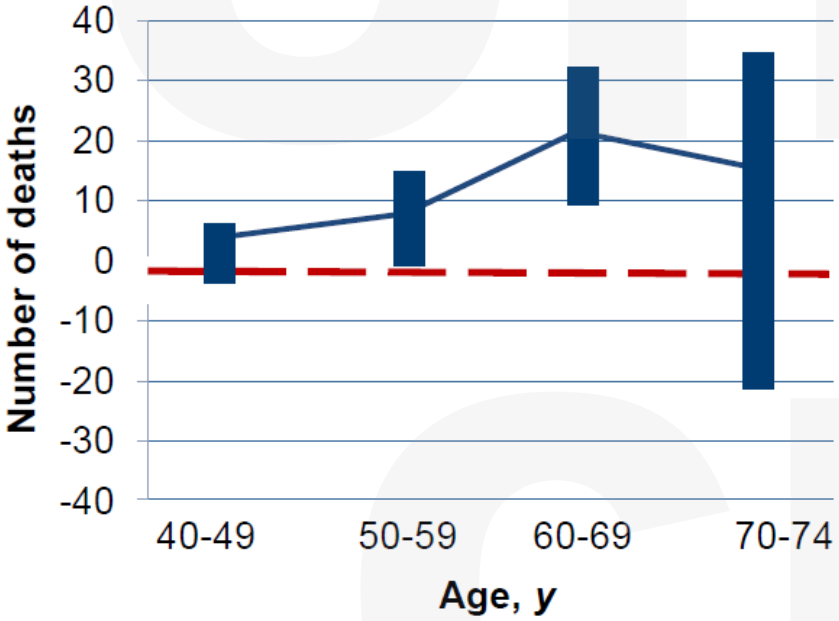
Breast Cancer Mortality

Deaths Prevented by Screening, meta-analysis of RCTS: 10,000 over 10 years



Age, *y*	No. deaths (95% CI)	Meta-analysis of RCTs: RR (95% CI)	Meta-analysis of RCTs: No. RCTs
40-49	3 (0 to 9)	0.92 (0.75 to 1.02)	9
50-59	8 (2 to 17)	0.86 (0.68 to 0.97)	7
60-69	21 (11 to 32)	0.67 (0.54 to 0.83)	5
70-74	13 (0 to 32)	0.80 (0.51 to 1.28)	3

Nelson HD, Fu R, Cantor, A, et al. *Ann Int Med. 2016;164(4):244-55.*

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Adverse Effects of Screening

Strength of Evidence

Type of Harm	Strength of evidence
Increased false-positive mammography results, biopsies, and follow-up: • Younger ages • More frequent screening • With supplemental screening	High
Overdiagnosis and treatment	Moderate
Anxiety and distress	Low
Pain from procedures	Low
Radiation exposure	Insufficient

Cumulative false-positive rates over 10 years of screening:

- 49% additional imaging
- 19% biopsy

Nelson HD, Fu R, Cantor, A, et al. *Ann Int Med. 2016;164(4):244-55.*
Henderson JT, Webber EM, et al. *JAMA*. 2024;331(22):1931-1946.
Nelson HD, Cantor AG, et al. *WPSI Evidence Update*, 2024

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Rates of Screening

Percentage of Women aged 50-74 years with a mammogram within the past 2 years (HEDIS)

Race and ethnicity	%
All groups	75.9
Hispanic (any race)	74.0
Non-Hispanic Black	82.1
Non-Hispanic White	76.3

Behavioral Risk Factor Surveillance System, 2020

Clinic population	%
Federally Qualified Health Center	45.4
General U.S.	78.2

Nelson HD, Cantor AG, et al. *WPSI Evidence Update*, 2024

Conclusions:
Comparison of Screening Strategies

- No evidence of lower breast cancer mortality or risk of progression to advanced cancer in eligible studies comparing different breast cancer screening strategies.
- Studies are either *inadequately* designed to determine effectiveness or have not been done. These include:
  - Age to start or discontinue screening
  - Screening interval
  - Type of modality (DBT vs DM)
  - Supplemental screening with ultrasound or MRI
  - Personalized screening based on risk factors
- Supplemental screening resulted in downstream consequences (e.g., more false-positive results and biopsy).

Summary of Benefits

- Breast cancer mortality reduction with screening:
  - Age 50 to 69 in RCTs and observational studies
  - No mortality differences for 40 to 49 in RCTs, limited observational data
  - Limited data for age 70 and older
- *All-cause* mortality was not reduced at any age with screening in RCTs.
- Advanced breast cancer outcomes were only reduced with screening for age 50 and older.

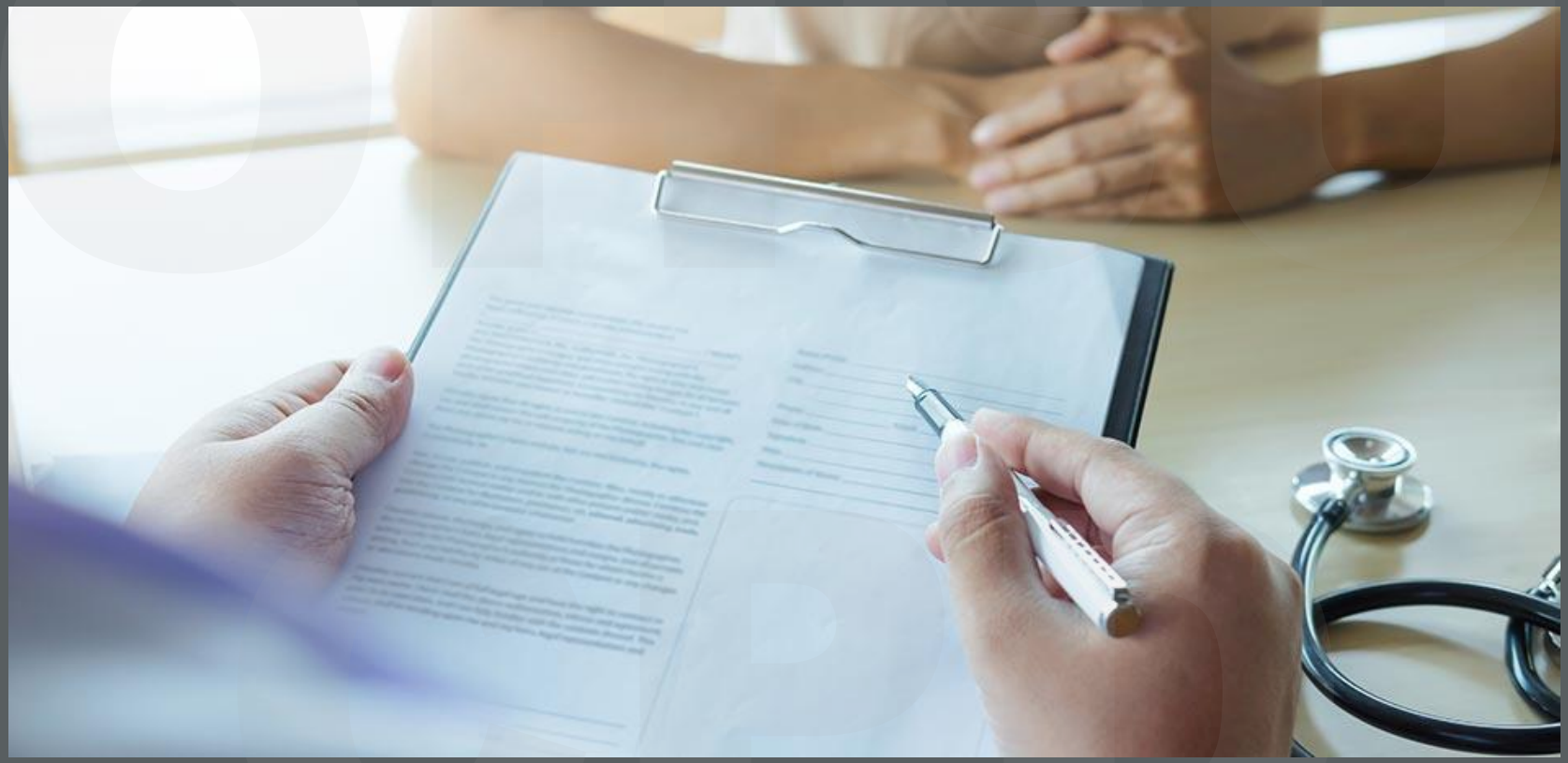
Summary of Harms

- False-positive results are common, especially among younger women.
- Cumulative false-positive rates are higher with annual screening.
- Women with false-positives have more anxiety and distress.
- Biopsy results may be inaccurate.
- Many women experience pain during mammography; some do not return for screening.

Screening Bottom Line

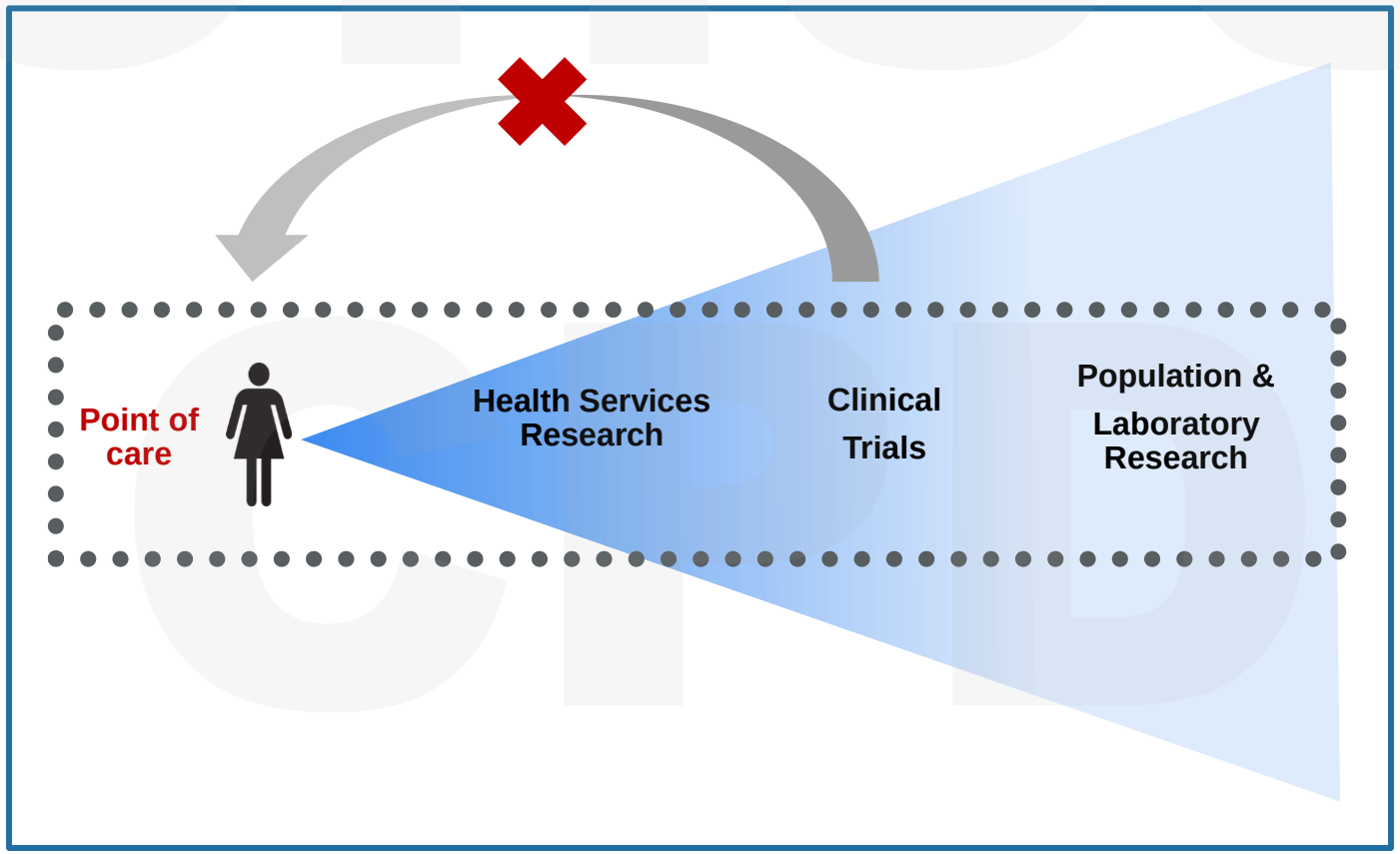
- Screening mammography reduces breast cancer deaths.
- Harms: false-positive results, overdiagnosis, anxiety.
- Screening Decisions: consider personal values and personal level of risk.
- Annual screening and digital breast tomosynthesis most appropriate for women with extremely dense breasts and those with 1-2 first degree family members with breast cancer.
- Reserve MRI for women at high/very high risk (>15-20% lifetime risk).

Evaluating Risk



Population vs Individual Risk

Average risk: 12.8% lifetime risk of breast cancer (1:8 women)
Moderate risk: 15-20% lifetime risk
High risk: >20% lifetime risk



Defining Risk – Minor Risk (RR<2.0)

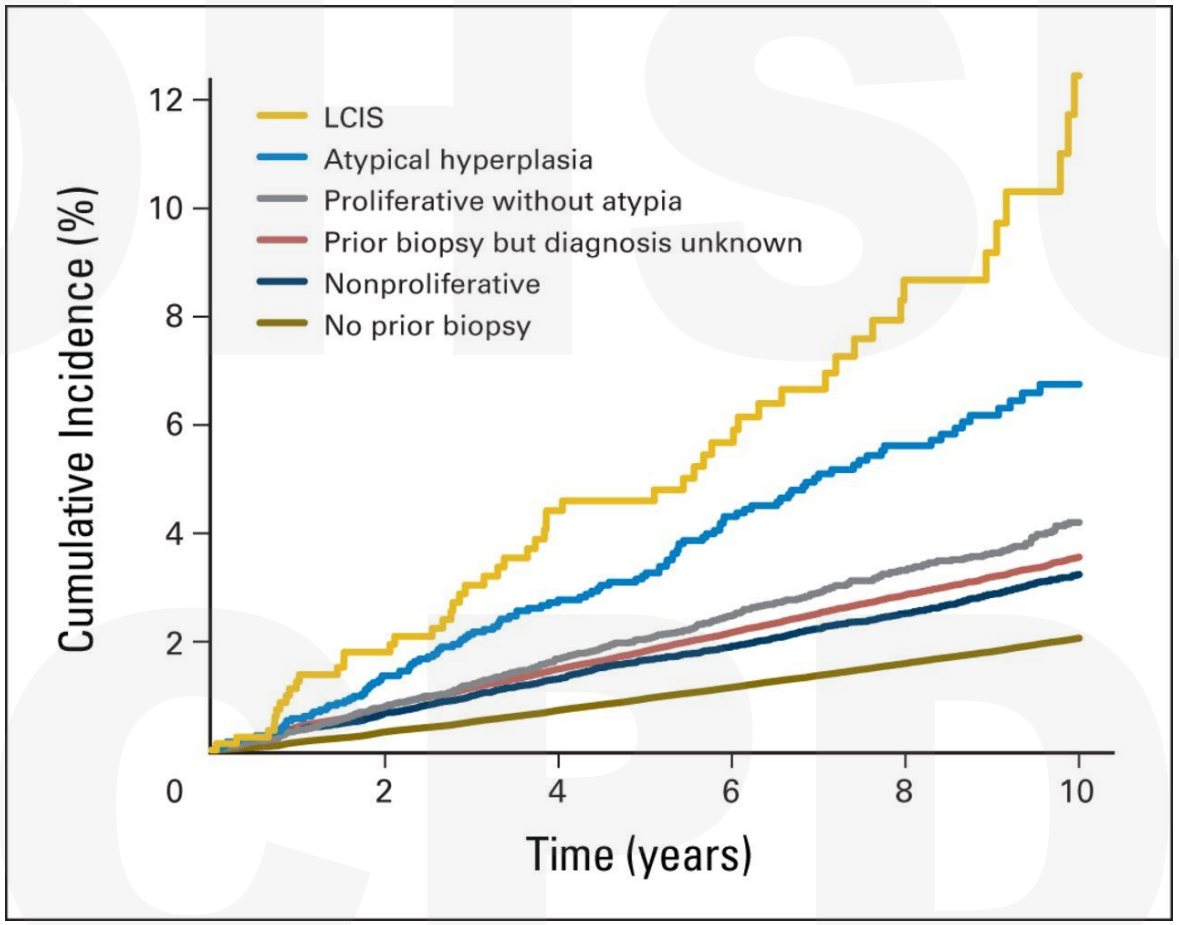
Modifiable and Non-modifiable	Risk estimate (Relative risk)
Lifestyle	
○ Alcohol use (>2 drinks/day)	RR 1.2
○ Smoking	RR 1.1 (NS)
○ Physical activity	RR 0.62-0.82
○ Dietary patterns – high fat diet	RR 1.2
BMI	
○ Decreased risk: overweight/obese *before* menopause	RR 0.9
○ Increased risk: obese/overweight *after* menopause	RR 1.5
Reproductive Factors	RR 1.0-1.5
○ Menarche age <12	
○ Menopause age >55	
○ Nulliparity; birth of first child age >30	
○ Breastfeeding	RR 0.8
Menopausal Hormone Therapy	
○ E+P	RR 1.2
○ E only	RR 0.8

- Nelson HD, Zakher B, Cantor A, et al. Risk factors for breast cancer for women aged 40 to 49 years: a systematic review and meta-analysis. Ann Intern Med. 2012 May 1;156(9):635-48. doi: 10.7326/0003-4819-156-9-201205010-00006.
- Collaborative Group on Hormonal Factors in Breast Cancer. Menarche, menopause, and breast cancer risk: individual participant meta-analysis. Lancet Oncol. 2012 Nov;13(11):1141-51. doi: 10.1016/S1470-2045(12)70425-4.

Defining Risk – Moderate and High Risk

Non-Modifiable	Risk estimate (Relative risk)
Genetic risk: 25% cases, 60,000 cases/year (>20% lifetime risk)	
• BRCA1/2: 5-10% of cancers (55-72% lifetime risk)	RR 10
• Other genetic variants: 10-15% of cancers	
Family History	
• 1st, 2nd degree relatives	RR 1.4-1.5
• 1-2 1st degree relatives with breast cancer	RR 2.0-3.5
• ≥3 1st degree relatives with breast cancer	RR 12
High risk breast lesions (15-20% lifetime risk):	
• ADH, ALH (35% lifetime risk)*	RR 4.0
• LCIS*	RR 5-8
• DCIS	
Benign dx:	RR 1.5-2.0
• Prior breast biopsy	RR 1.4-1.8
Breast Density	
• Heterogeneously dense	RR 1.2-1.6
• Extremely dense	RR 2.1

High Risk Breast Lesions



Tice, J et al. Breast Density and Benign Breast Disease: Risk Assessment to Identify Women at High Risk of Breast Cancer. *JCO* **33**, 3137-3143(2015).DOI:10.1200/JCO.2015.60.8869

Primary Care Approaches for Risk Based Evaluation

The New York Times

What a Breast Cancer Risk Calculator Can and Can't Tell You

- **Gail model** – 5 questions; 1st degree relatives only; missing key risk factors (eg, density, other relatives); AUC 0.58-0.64
- **BCSC calculator** – includes density; 1st deg relatives only; AUC 0.63-0.68
- **Tyrer-Cuzick** (IBIS tool), V8 – includes FH and breast density, biopsy history; AUC 0.76

https://bcrisktool.cancer.gov/
https://tools.bcsc-scc.ucdavis.edu/BC5yearRisk/#/
https://magview.com/ibis-risk-calculator/

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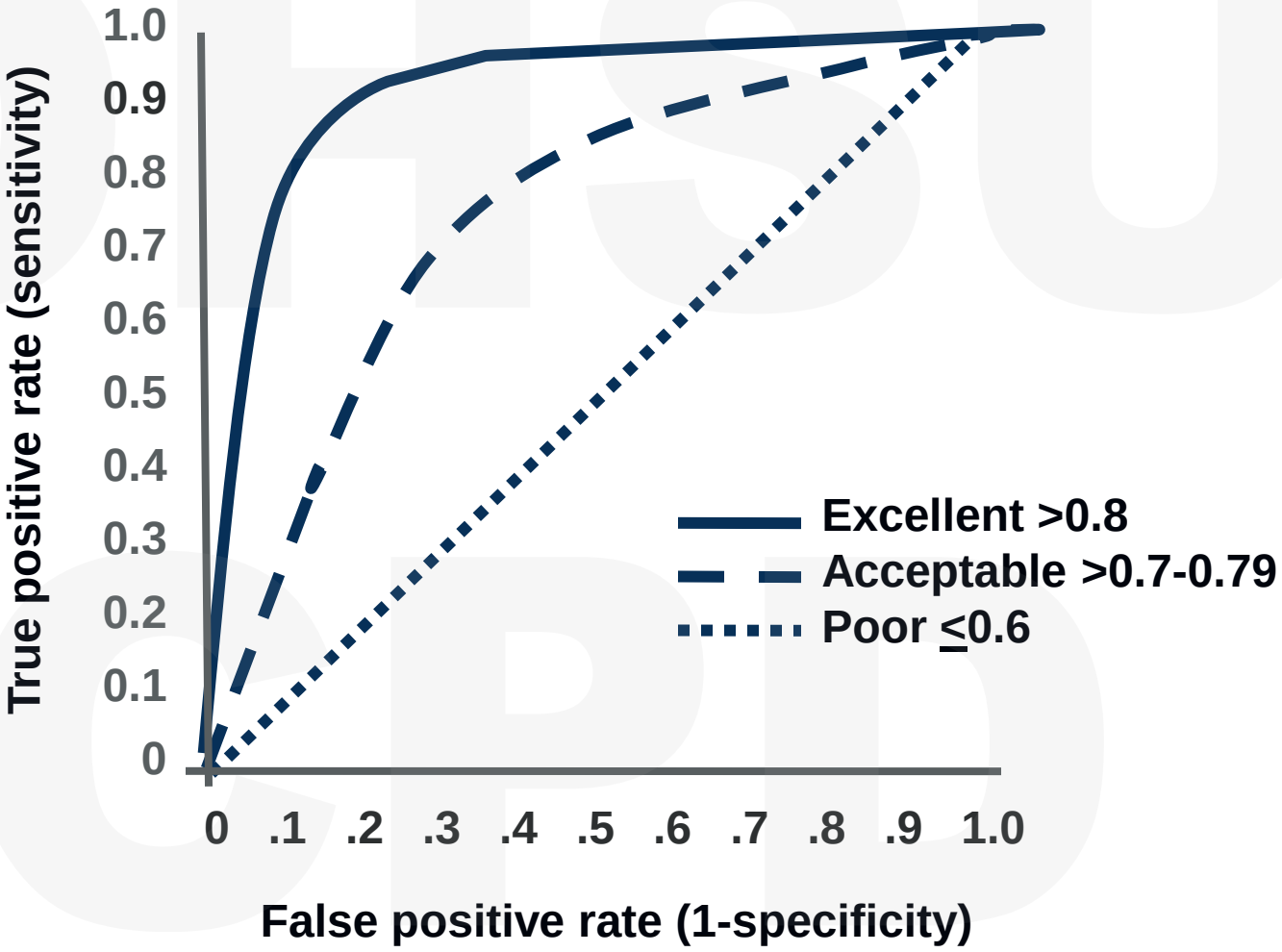
Summary of Risk Models

Discriminatory Accuracy



Identifying Risk in a Short Visit

Key Indicators:

- Strong family history (multiple relatives, young diagnoses)
- Personal history of atypical hyperplasia, LCIS
- History of chest radiation therapy
- Pathogenic genetic variant carriers (BRCA1/2, PALB2, etc.)

Bottom line: Start with family and personal history and consider risk calculators

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Management Guidelines for Women with Increased Risk

High and Moderate Risk

- Genetic counseling and testing if appropriate
- Enhanced screening: earlier and more frequent mammography
- Monitoring: use of additional technologies, such as MRI and ultrasound
- Consider risk reducing medications (chemoprevention) for breast cancer such as tamoxifen, raloxifine or aromatase inhibitors
- Careful physical examinations

https://www.nccn.org/professionals/physician_gls/pdf/breast_risk.pdf

Managing Risk in a Short Visit

Everyone

- Educate about individual risk
- Discuss preventive strategies for modifiable risks (nutrition, physical activity, ETOH, smoking, etc)

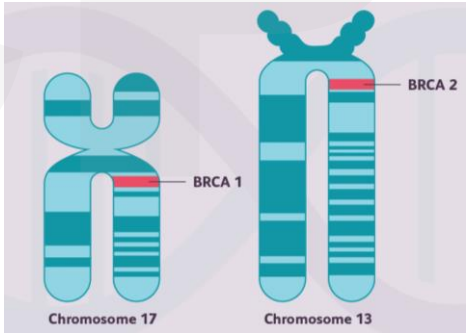
Based on Calculated Risk:

- Consider Genetic counseling and testing
- Consider enhanced screening
- Consider chemoprevention

Risk Assessment, Genetic Counseling, and Genetic Testing

Background

- Pathogenic variants in *BRCA1* and *BRCA2* genes are associated with increased risks for breast, ovarian, fallopian tube, peritoneal, and pancreatic cancer.
  - Increase breast cancer risk 55-72% (*BRCA1); 45-69% (BRCA2)*
  - Increase ovarian cancer risk 39-44% (*BRCA1)*; 11-17% (*BRCA2)*
- *BRCA1/2* Mutations account for 5-10% of breast cancers; 15% ovarian cancers.
- Identification of BRCA mutations could potentially benefit carriers who choose interventions to reduce risks for cancer.



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Background

- Pathogenic *BRCA1/2* variants occur in 1 in 300-500 in the general population.
- Higher prevalence in specific high-risk groups:
  - Populations with *founder mutations*: specific variant observed with high frequency in a group due to common ancestry.
    - Ashkenazi Jewish (most studied); Icelandic, Norwegian, Dutch, Swedish, West African, Sephardi Jewish, Bahamian
    - Specific U.S. Black, Hispanic, Asian, non-Hispanic White groups
- Family history can indicate heritable patterns and susceptibility.

Risk Assessment

- Determining risk for clinically significant *BRCA1/2* pathogenic variants starts with family history then genetic counseling to determine appropriateness of mutation testing for individuals identified at increased risk
- Risk assessment determines the likelihood of pathogenic variant based on:
  - Personal breast history (density, biopsies, cancer, prior testing)
  - Reproductive/hormone history (menarche, childbirth history; menopausal status, HT)
  - 1st/2nd degree relatives, female/male relatives with breast, ovarian, prostate, pancreatic cancers; age at diagnosis
  - Ancestry (AJ); other high-risk groups

Genetic Counseling

- Process of identifying and counseling individuals at risk for familial or inherited cancer.
- Recommended prior to genetic testing to support complex clinical decision making.
- Genetic counseling:
  - Identifies appropriate candidates for testing.
  - Determines likelihood of pathogenic variant based on family history of cancer.
  - Helps interpret results and guides patients through clinical decisions.
- Direct-to-consumer advertising and testing and reduced cost has led to increased testing, often without counseling.

Genetic Testing

- In 2024, the FDA published guidance on oversight of laboratory-developed tests, including genetic tests:
  - 193 multi-gene panels that include *BRCA1 or BRCA2* in CLIA certified U.S. laboratories
- Results of genetic testing (ACMG) provided in five categories:
  - Pathogenic (P): known to cause disease
  - Likely pathogenic (LP): likely to cause disease
  - Variant of Uncertain significance (VUS): clinical significance unknown
  - Likely benign: likely not to cause disease
  - Benign: not known to cause disease

USPSTF 2019 recommendation*

Population	Recommendation	Grade
Women with a personal or family history of breast, ovarian, tubal, or peritoneal cancer or who have an ancestry associated with *BRCA1/2* gene mutations	Primary care clinicians assess women with a personal or family history of breast, ovarian, tubal, or peritoneal cancer or who have an ancestry associated with breast cancer susceptibility 1 and 2 (BRCA1/2) gene mutations with an appropriate brief familial risk assessment tool. Women with a positive result on the risk assessment tool should receive genetic counseling and, if indicated after counseling, genetic testing.	**B**
Women whose personal or family history or ancestry is not associated with potential harmful BRCA1/2 gene mutations	The USPSTF recommends against routine risk assessment, genetic counseling, or genetic testing for women whose personal or family history or ancestry is not associated with potentially harmful BRCA1/2 gene mutations.	**D**

***CURRENTLY BEING UPDATED**

Risk Assessment Methods to Determine *Genetic Risk*

Methods include variations of key factors:

- *BRCA 1/2* detected in relative
- Ashkenazi Jewish
- Numbers and types of relatives affected
- Types of cancer
- Ages diagnosed
- Presentations
  - Male breast cancer
  - Bilateral breast cancer
  - Breast and ovarian cancer in same person
  - <50 years old

Risk Assessment Methods

Table 1. Ontario Family History Assessment Tool[a]

Risk Factor	Points
Breast and ovarian cancer	
Mother	10
Sibling	7
Second-/third-degree relative	5
Breast cancer relatives	
Parent	4
Sibling	3
Second-/third-degree relative	2
Male relative (add to above)	2
Breast cancer characteristics	
Onset age, y	
20-29	
30-39	
40-49	
Premenopausal/perimenopau	

Table 2. Manchester Scoring System[a,b]

Risk Factor (Age at Onset for Relative in Direct Lineage)	*BRCA1* Score	*BRCA2* Score
Female breast cancer, y		
<30	6	5
30-39	4	4
40-49	3	
50-59	2	
≥60	1	
Male breast cancer, y		
<60	5[c]	
≥60	5[c]	
	8	
	5	5

Table 6. International Breast Cancer Intervention Study Model[a,b]

No.	Risk Factor
1	Personal history: current age, age at menopause, age at me childbirth history, menopausal status, use of menopausal hormone therapy
2	Personal breast history, breast density (optional), prior brea biopsy, history of cancer (breast or ovarian), genetic testing
3	Ashkenazi Jewish inheritance
4	Family history (genetic risk)—relatives with breast or ovarian cancer, age at diagnosis, genetic testing

Table 4. Pedigree Assessment Tool[a,b]

Risk Factor	Score for Every Family Member With Breast or Ovarian Cancer Diagnosis, Including Second-/Third-Degree Relatives
Breast cancer at age ≥50 y	3
Breast cancer at age <50 y	4

Table 3. Referral Screening Tool[a,b]

History of Breast or Ovarian Cancer in the Family? If Yes, Complete Checklist		
Risk Factor	Breast Cancer at Age ≤50 y	Ovarian Cancer at any Age
Yourself		
Mother		
Sister		
Daughter		
Mother's side		
Grandmother		
Aunt		
Father's side		
Grandmother		
Aunt		
≥2 cases of breast cancer after age 50		

Table 5. Seven-Question Family History Screening[a,b]

No.	Questions
1	Did any of your first-degree relatives have breast *or* ovarian cancer?
2	Did any of your relatives have bilateral breast cancer?
3	Did any man in your family have breast cancer?
4	Did any woman in your family have breast *and* ovarian cancer?
5	Did any woman in your family have breast cancer before age 50 y?
6	Do you have 2 or more relatives with breast *and/or* ovarian cancer?
7	Do you have 2 or more relatives with breast *and/or* bowel cancer?

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Risk Assessment Methods Discriminatory Accuracy

Compared Against Results of Mutation Testing or Other Models

Method	# Studies	Reference	AUC
Family History Screening-7	1	Models	0.96
IBIS	1	Testing	0.75
Manchester Scoring System	7	Testing	0.75-0.80
Family History Assess Tool	4	Testing	0.68-0.83
Pedigree Assessment Tool	2	Testing	0.71
Referral Screening Tool	1	Models	0.87

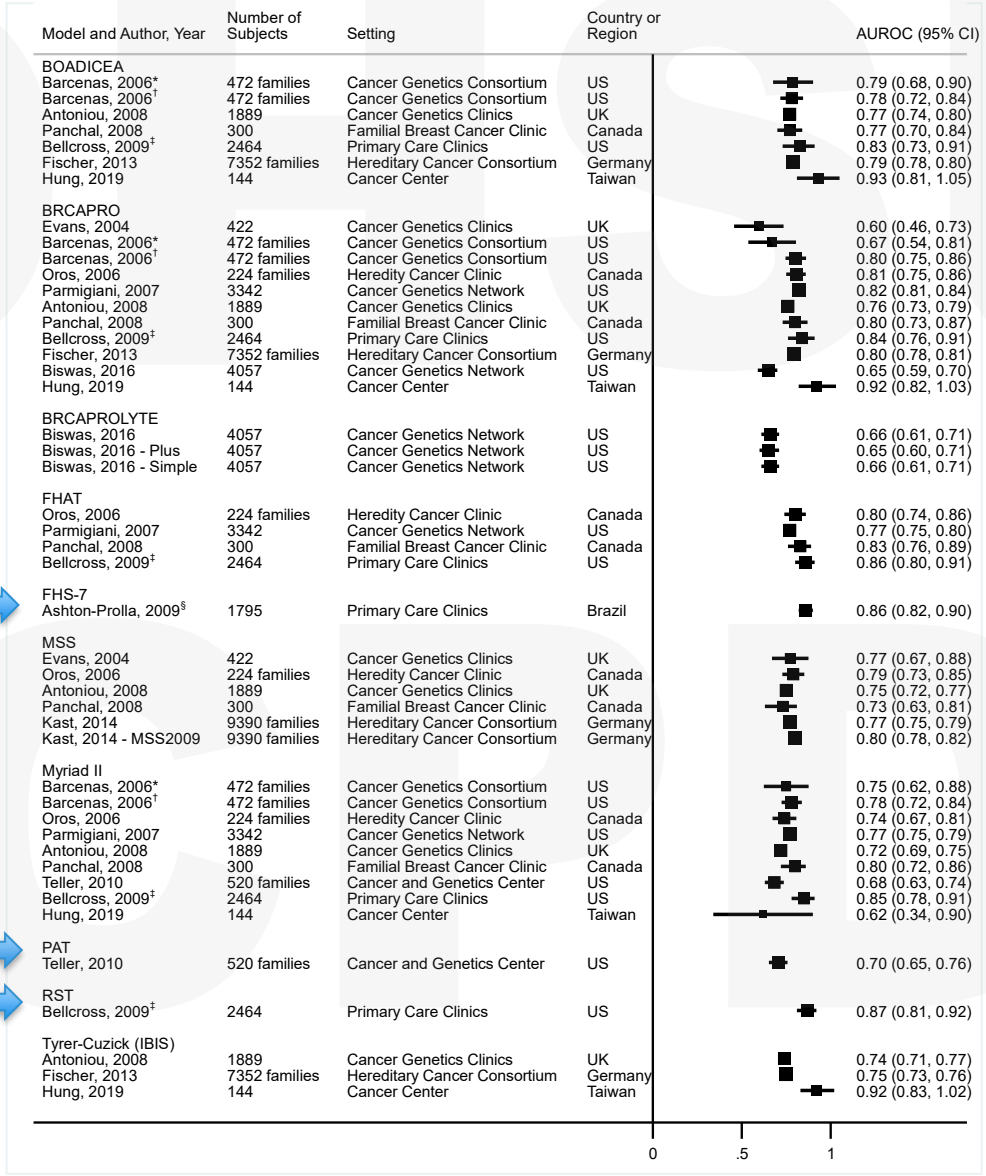
Summary of Risk Model Results

Discriminatory Accuracy for Predicting Mutations

Figure 2:

- AUC 0.60 to 0.93 for all tools
- 7 predictive tools with *fair to excellent* discriminative ability (>0.7)

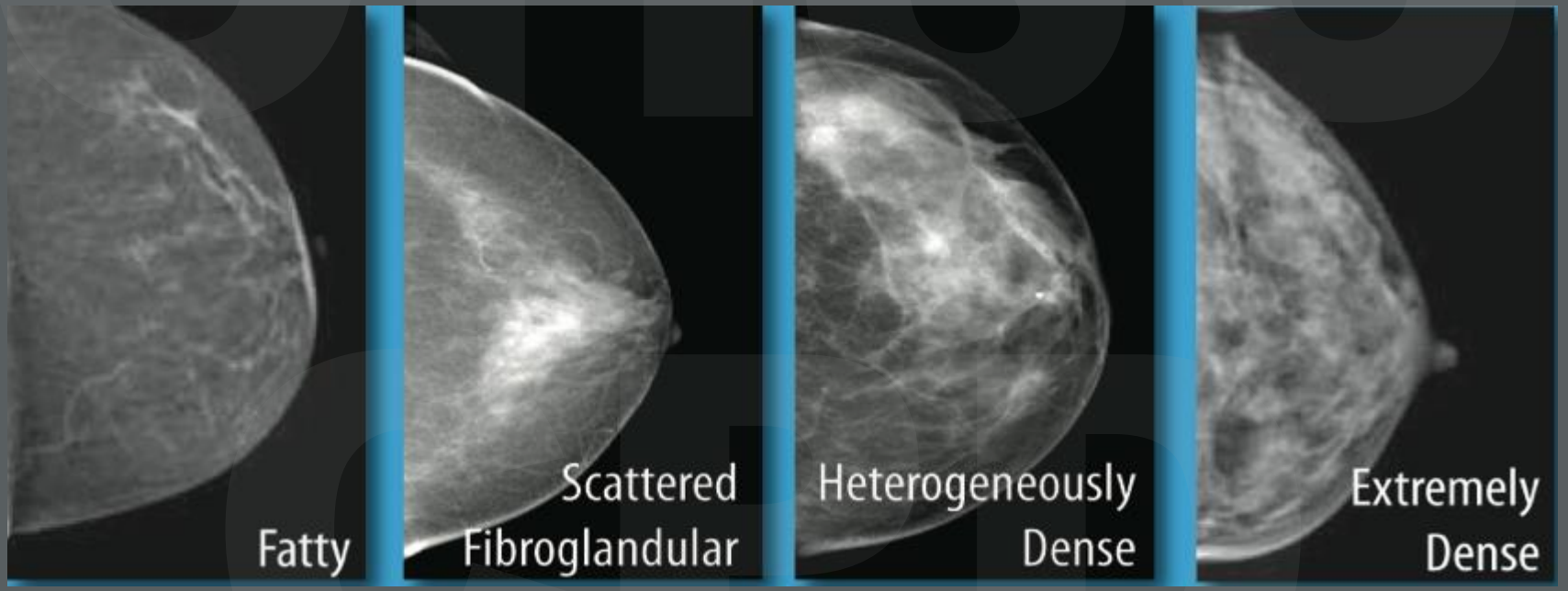
Model and Author, Year	Number of Subjects	Setting	Country or Region	AUROC (95% CI)
BOADICEA				
Barcenas, 2006*	472 families	Cancer Genetics Consortium	US	0.79 (0.68, 0.90)
Barcenas, 2006†	472 families	Cancer Genetics Consortium	US	0.78 (0.72, 0.84)
Antoniou, 2008	1889	Cancer Genetics Clinics	UK	0.77 (0.74, 0.80)
Panchal, 2008	300	Familial Breast Cancer Clinic	Canada	0.77 (0.70, 0.84)
Bellcross, 2009‡	2464	Primary Care Clinics	US	0.83 (0.73, 0.91)
Fischer, 2013	7352 families	Hereditary Cancer Consortium	Germany	0.79 (0.78, 0.80)
Hung, 2019	144	Cancer Center	Taiwan	0.93 (0.81, 1.05)
BRCAPRO				
Evans, 2004	422	Cancer Genetics Clinics	UK	0.60 (0.46, 0.73)
Barcenas, 2006*	472 families	Cancer Genetics Consortium	US	0.67 (0.54, 0.81)
Barcenas, 2006†	472 families	Cancer Genetics Consortium	US	0.80 (0.75, 0.86)
Oros, 2006	224 families	Heredity Cancer Clinic	Canada	0.81 (0.75, 0.86)
Parmigiani, 2007	3342	Cancer Genetics Network	US	0.82 (0.81, 0.84)
Antoniou, 2008	1889	Cancer Genetics Clinics	UK	0.76 (0.73, 0.79)
Panchal, 2008	300	Familial Breast Cancer Clinic	Canada	0.80 (0.73, 0.87)
Bellcross, 2009‡	2464	Primary Care Clinics	US	0.84 (0.76, 0.91)
Fischer, 2013	7352 families	Hereditary Cancer Consortium	Germany	0.80 (0.78, 0.81)
Biswas, 2016	4057	Cancer Genetics Network	US	0.65 (0.59, 0.70)
Hung, 2019	144	Cancer Center	Taiwan	0.92 (0.82, 1.03)
BRCAPROLYTE				
Biswas, 2016	4057	Cancer Genetics Network	US	0.66 (0.61, 0.71)
Biswas, 2016 - Plus	4057	Cancer Genetics Network	US	0.65 (0.60, 0.71)
Biswas, 2016 - Simple	4057	Cancer Genetics Network	US	0.66 (0.61, 0.71)
FHAT				
Oros, 2006	224 families	Heredity Cancer Clinic	Canada	0.80 (0.74, 0.86)
Parmigiani, 2007	3342	Cancer Genetics Network	US	0.77 (0.75, 0.80)
Panchal, 2008	300	Familial Breast Cancer Clinic	Canada	0.83 (0.76, 0.89)
Bellcross, 2009‡	2464	Primary Care Clinics	US	0.86 (0.80, 0.91)
FHS-7				
Ashton-Prolla, 2009§	1795	Primary Care Clinics	Brazil	0.86 (0.82, 0.90)
MSS				
Evans, 2004	422	Cancer Genetics Clinics	UK	0.77 (0.67, 0.88)
Oros, 2006	224 families	Heredity Cancer Clinic	Canada	0.79 (0.73, 0.85)
Antoniou, 2008	1889	Cancer Genetics Clinics	UK	0.75 (0.72, 0.77)
Panchal, 2008	300	Familial Breast Cancer Clinic	Canada	0.73 (0.63, 0.81)
Kast, 2014	9390 families	Hereditary Cancer Consortium	Germany	0.77 (0.75, 0.79)
Kast, 2014 - MSS2009	9390 families	Hereditary Cancer Consortium	Germany	0.80 (0.78, 0.82)
Myriad II				
Barcenas, 2006*	472 families	Cancer Genetics Consortium	US	0.75 (0.62, 0.88)
Barcenas, 2006†	472 families	Cancer Genetics Consortium	US	0.78 (0.72, 0.84)
Oros, 2006	224 families	Heredity Cancer Clinic	Canada	0.74 (0.67, 0.81)
Parmigiani, 2007	3342	Cancer Genetics Network	US	0.77 (0.75, 0.79)
Antoniou, 2008	1889	Cancer Genetics Clinics	UK	0.72 (0.69, 0.75)
Panchal, 2008	300	Familial Breast Cancer Clinic	Canada	0.80 (0.72, 0.86)
Teller, 2010	520 families	Cancer and Genetics Center	US	0.68 (0.63, 0.74)
Bellcross, 2009‡	2464	Primary Care Clinics	US	0.85 (0.78, 0.91)
Hung, 2019	144	Cancer Center	Taiwan	0.62 (0.34, 0.90)
PAT				
Teller, 2010	520 families	Cancer and Genetics Center	US	0.70 (0.65, 0.76)
RST				
Bellcross, 2009‡	2464	Primary Care Clinics	US	0.87 (0.81, 0.92)
Tyrer-Cuzick (IBIS)				
Antoniou, 2008	1889	Cancer Genetics Clinics	UK	0.74 (0.71, 0.77)
Fischer, 2013	7352 families	Hereditary Cancer Consortium	Germany	0.75 (0.73, 0.76)
Hung, 2019	144	Cancer Center	Taiwan	0.92 (0.83, 1.02)



Conclusions

- Risk assessment for BRCA mutations using familial risk models to guide referrals is accurate.
- Periodic risk assessment can mitigate high risk and develop individualized screening plan.
- Genetic counseling reduces anxiety, depression, and intention for mutation testing and increases accuracy of risk perception.
- Risk perception improves after mutation testing.
- The effectiveness of intensive screening is not known, but it increases false positive results and procedures.

What About Breast Density?



Defining Density

A: Almost entirely fat

B: Scattered fibroglandular densities

C: Heterogeneously dense

D: Extremely dense

- Half of all women have “dense” breasts
- Impact on reporting and coverage
- Insufficient evidence for supplemental screening

Which Screening Method to Choose?

- Mammography: for women at average-risk
- Tomosynthesis: when breast cancer risk is increased (i.e. density)
- MRI: lack of evidence for effectiveness in average-risk women, because of excessive false-positives, high cost; insufficient evidence for dense breasts
- Ultrasonography: no evidence it improves results over mammography screening for average-risk women; insufficient for dense breasts
- Breast self-exam: instructing average-risk women does not improve mortality, causes excess benign biopsies

Screening Summary

- Routine screening mammography for average risk women:
  - No earlier than age 40 and no later than age 50
  - At least biennially and as frequently as annually
  - Should continue through at least age 74; age alone should not be the basis to discontinue screening.
- Women may require additional imaging to complete the screening process or to address findings on the initial screening mammography.
- Risk factors: increased breast density, presence of proliferative breast disease, family history of breast cancer, personal history.
- Prevention strategies for modifiable risks.
- Pathogenic variants in *BRCA1/2* substantially increase risk of breast cancer; consider referral to genetics after reviewing family history.

Questions?

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