

ATHENA WISDOM INITIATIVE: RISK-BASED SCREENING FOR BREAST CANCER

UCLA | Center for SMART Health

A partnership between the UCLA Institute for Precision Health, Clinical & Translational Science Institute, and the Garrick Institute for the Risk Sciences

The Screening Debate in the US?

- ACS vs. USPSTF
 - When to start, when to stop, screening intervals, modality]
- Little guidance around operationalizing risk assessment
 - Some may be under-screened, some over-screened
- Preventive services are not reaching women who most need them
- Many women are confused and frustrated

Women Are Caught in the Middle

Rethink The Word 'Cancer'
Aim Is To Reduce Aggressive Treatment'

Long-term study questions benefits of mammogram screening

By **Jacque Wilson, CNN**
updated 2:02 PM EST
February 12, 2014
HEALTH

Vast Study Casts Doubts on Value of Mammograms

By **GINA KOLATA** FEB. 11, 2014

OPINION
Mammograms Save Lives
Criticism of breast-cancer screenings is more about rationing the

Scientists Seek to Rein In Diagnoses of Cancer

By **TARA PARKER-POPE** JULY 29, 2013 11:00 AM [Comment](#)

Breast Cancer Confusion Widespread, Survey Finds

Oct. 1, 2013

By **KATIE MOISSE** via **GOOD MORNING AMERICA**



Breast cancer screening guidelines confuse doctors

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OPINION

Mammograms Save Lives

Criticism of breast-cancer screenings is more about rationing the

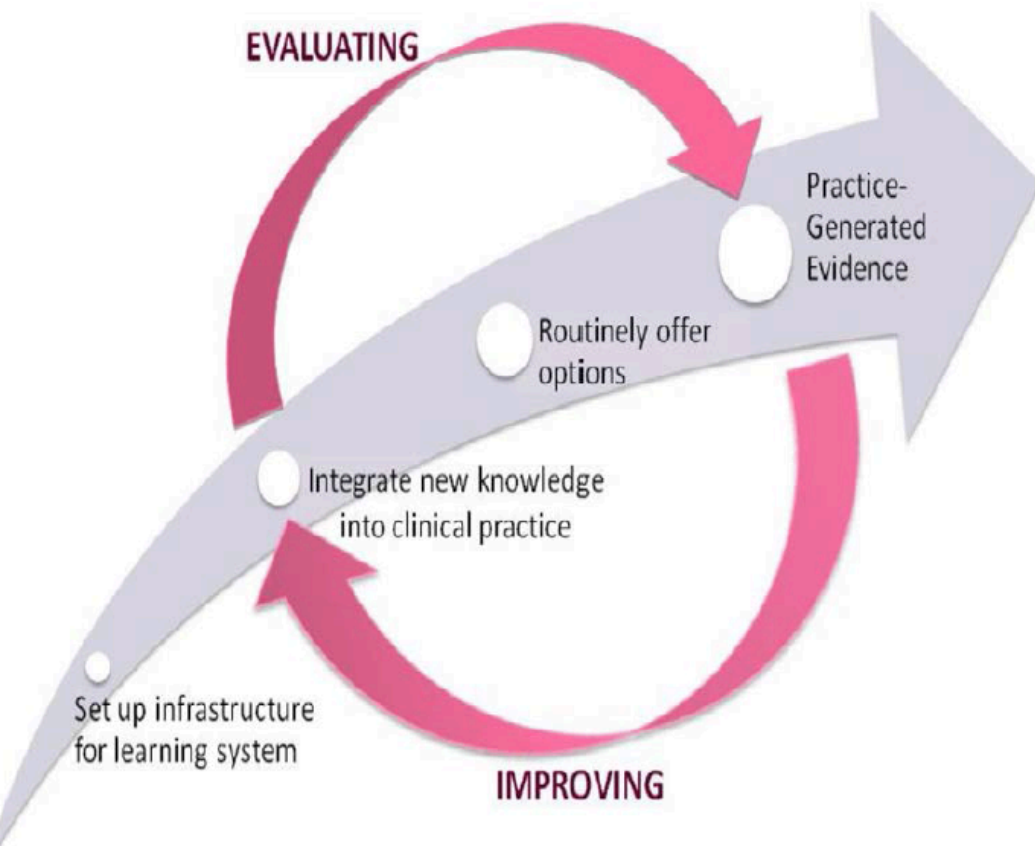
And many are choosing not to screen at all...

Breast Cancer Screening: What It Can Be

- Based on advances in:
 - Risk-assessment
 - Biology
- More effective at finding “relevant” cancers
- Integrated with prevention
- More cost-effective (better health care value)
- Personalized

Merging research and innovation with care improvement

A New Approach to Screening



LEARN

who gets what kind of cancer

**CONTINUOUS
IMPROVEMENT**

ADAPT/TAILOR

Prevention

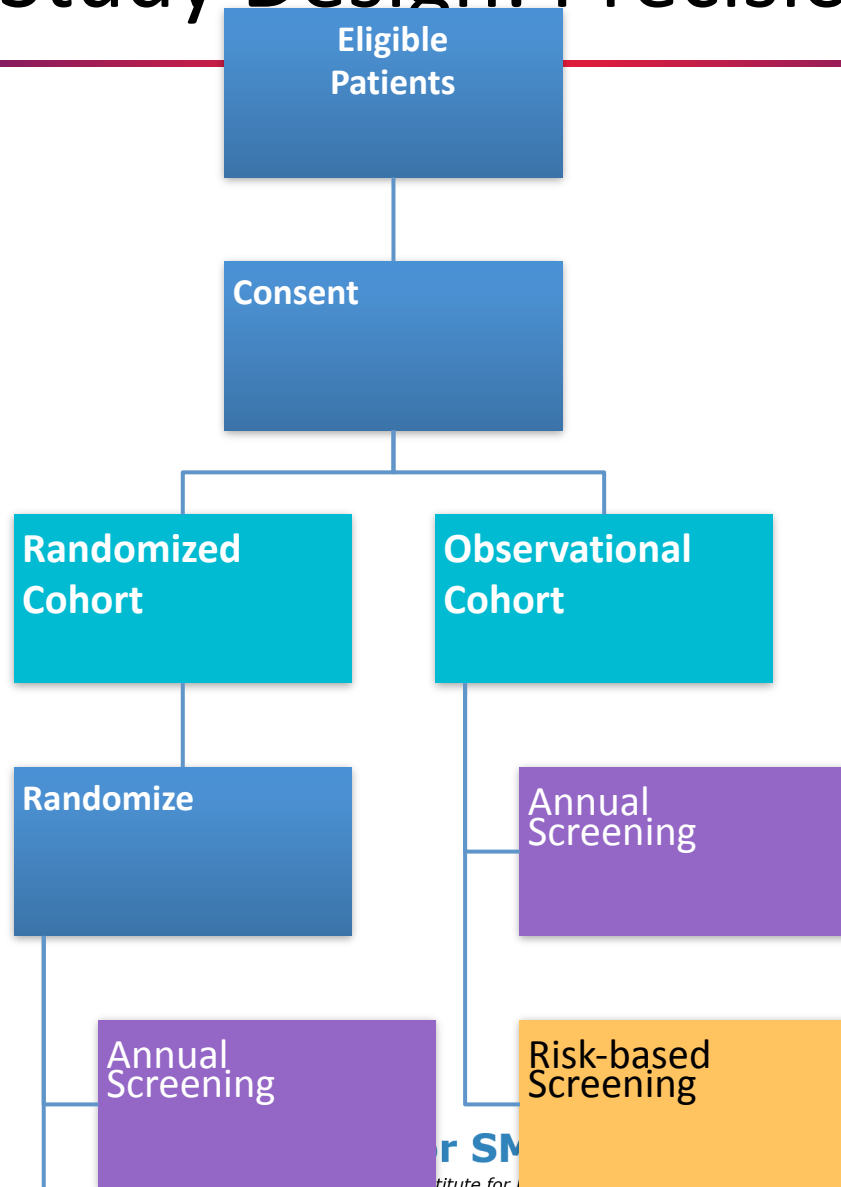
Biopsy

Treatment

Screening

WISDOM Study Design: Precision Medicine

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WISDOM Study

**Risk-based
Screening Arm**

**RBS Consumer
Engagement**

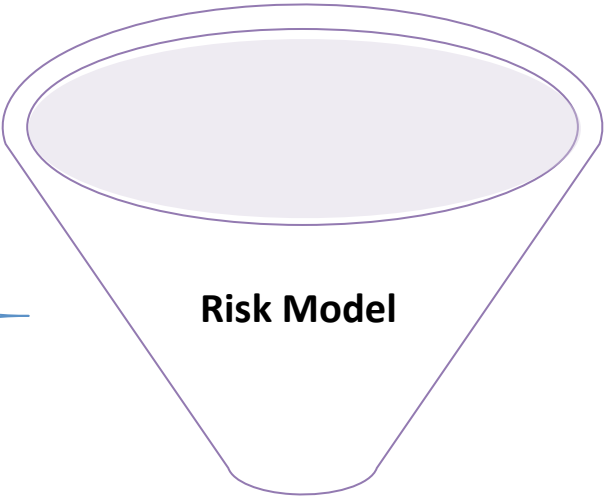


**Portal enrollment and
consent**

Mammogram
-breast density

**Athena Health
Questionnaire**
-family history,
comorbidities, previous
biopsies, age, race/ethnicity

Genomic profiling
-BRCA, BROCA, SNPs
-saliva collection



**Mammogram +
MRI**

**Annual
Mammogram**

**Biennial
Mammogram**

**No screening
until age 50**

Screening Recommendation Notification and Education

*Breast Health
Specialist counseling*

BREAST DENSITY

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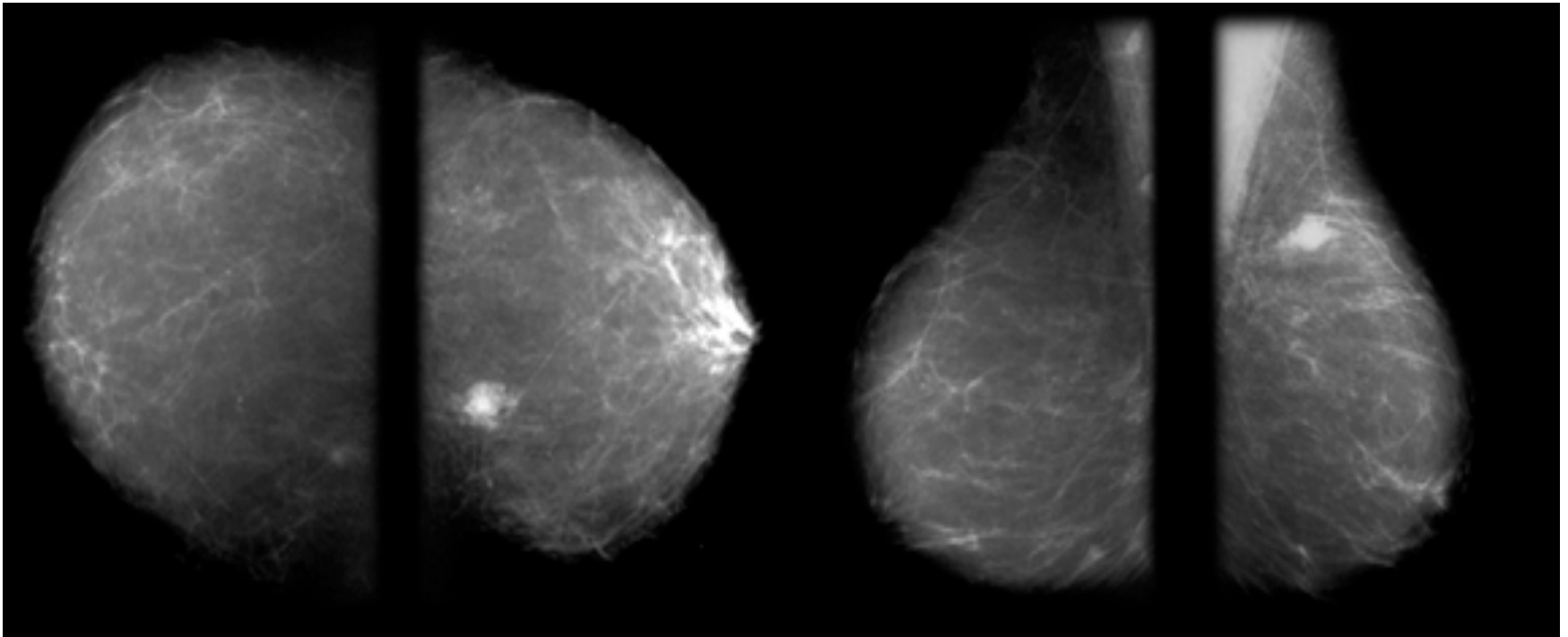
Breast Density

- ◎ The amount of fibroglandular parenchyma on a mammogram
- ◎ Mammogram reports describe density
 1. The breast is almost entirely fat
 2. There are scattered fibroglandular densities
 3. The breast tissue is heterogeneously dense. This may lower the sensitivity of mammography
 4. The breast tissue is extremely dense, which could obscure a lesion on mammography

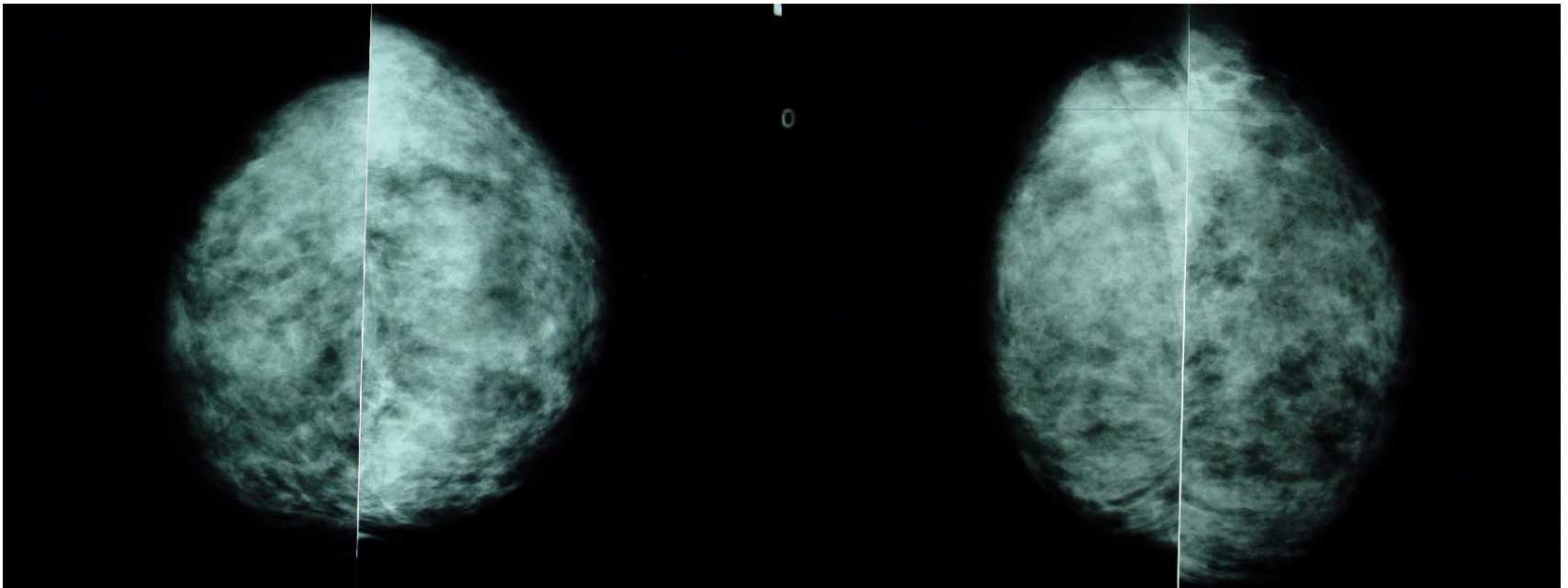
Breast Density

- Breast cancer and breast parenchyma are both white
- Fat is nearly black
- The greater amount of fat, the easier it is to recognize a cancer
- Heterogeneously dense and extremely dense breasts can obscure a cancer, even a large cancer

Cancer in Fatty Breasts



Cancer in Dense Breasts



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Breast Density

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- Sensitivity and specificity reduced

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 - Sensitivity 33 to 81%

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 - 4-5x relative risk

Breast Density

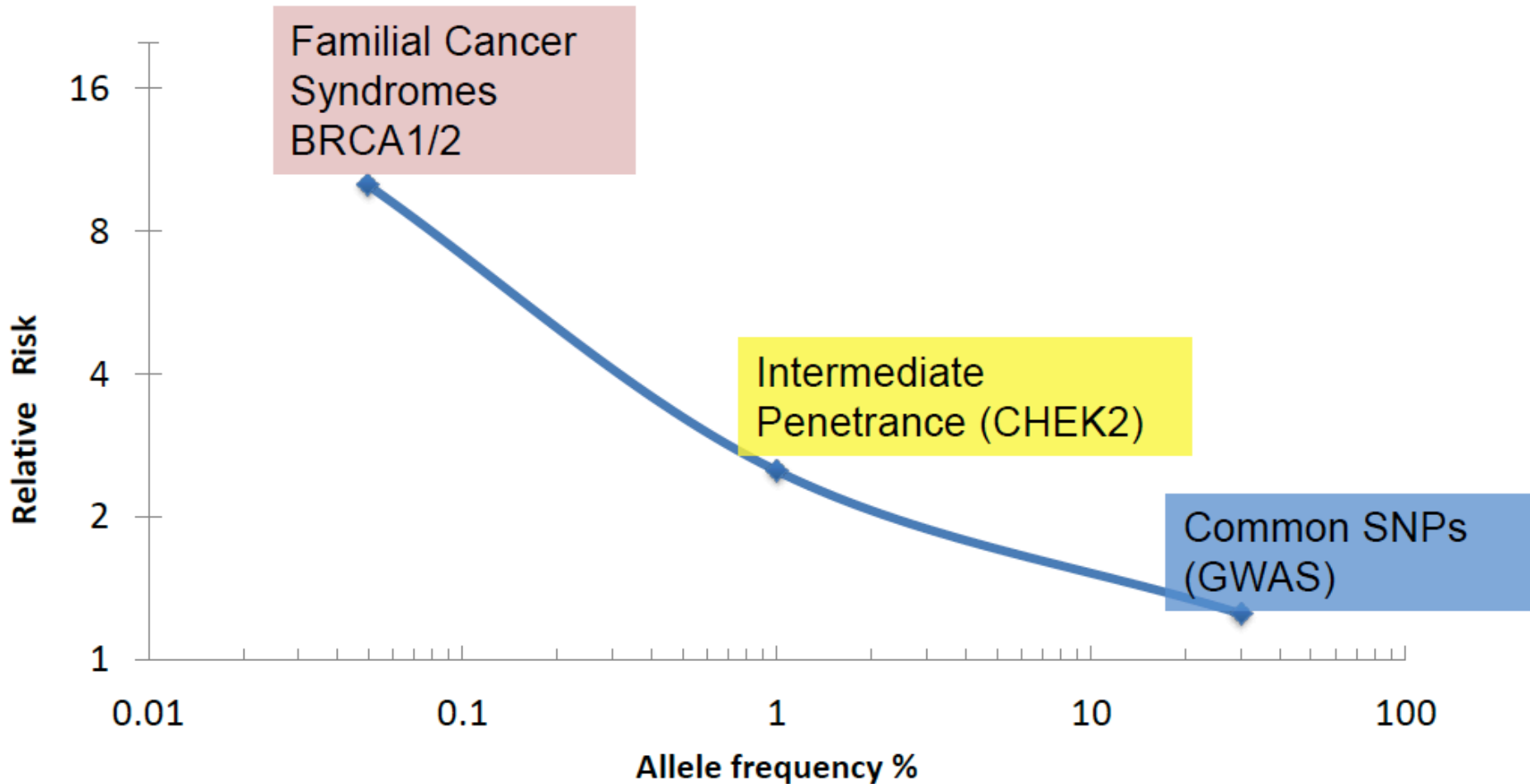
- Sensitivity and specificity reduced
 - Sensitivity 33 to 81%
 - False positives increased
- Breast density is a significant independent risk factor for breast cancer
 - 4-5x relative risk
- California law mandates patient notification

GENOMICS

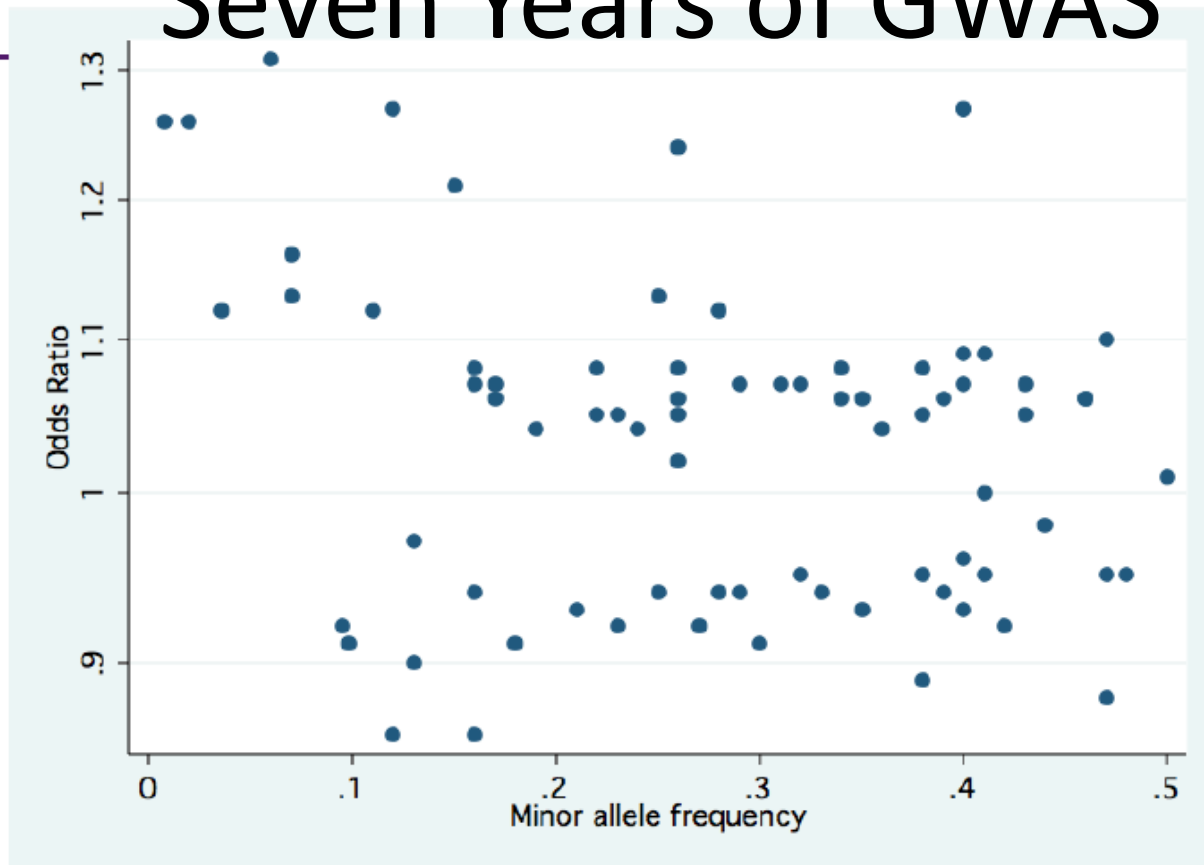
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Genetic “Architecture” of Breast Cancer



Seven Years of GWAS



76 SNPs genome wide significant, nearly all from European GWAS/replication

All have odds ratios <1.4 or >0.8

Loci include known candidates and novel genes/pathways



9 Key Genes

BRCA 1

- PALB2

BRCA 2

- CHEK 2

TP53

- CDH1

PTEN

- ATM

STK11

81 SNPs

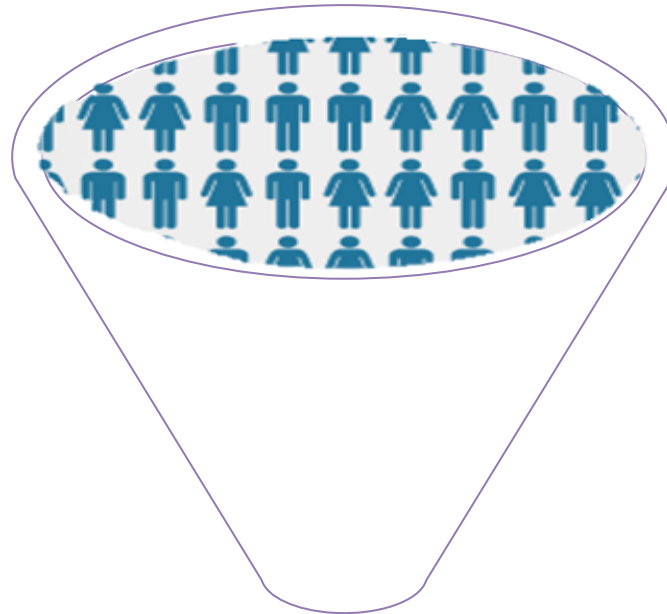
- **Known/Accepted Risk Variants**
 - Evidence from GWAS and COGS validation studies
- **Discovery Variants**
 - Coding variants in breast cancer pathways
 - Coding variants in 10-12 key cancer signaling pathways
- **Disease/Treatment Modifying Variants**
 - Key variants associated with ASME genes for pharmacogenetic studies

COGS= Collaborative ovarian, prostate, and breast gene-environment study

GWAS= Genome Wide Association Studies

Population Medicine → Precision Medicine

100,000



*Tailored screening recommendation
for individual woman*



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RBS Consumer Engagement



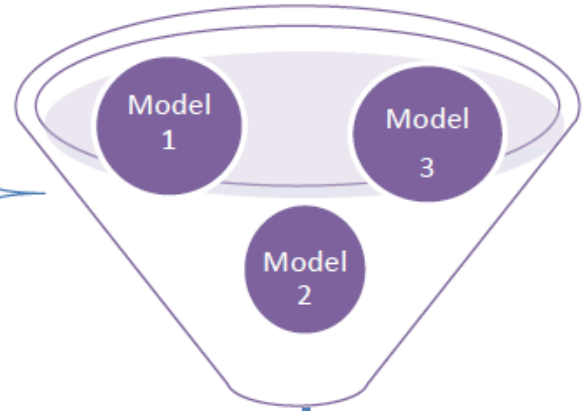
RBS trial consent

Mammogram
-breast density

Athena Health Questionnaire
-family history, comorbidities, previous biopsies, age, race/ethnicity

Genomic profiling
-BRCA, BROCA, SNPs
-saliva collection

Risk Calculator



Personalized Risk Profile

Highest risk

Elevated risk

Average risk

Lowest risk

Risk Assignment Notification and Education
Assigned screening frequency and modality (if applicable)

Follow-Up

Cancer detected: Molecular profiling

Screening Frequency

- Trial Inclusion:
- Receiving care within UC/Athena
 - No prior breast cancer diagnosis

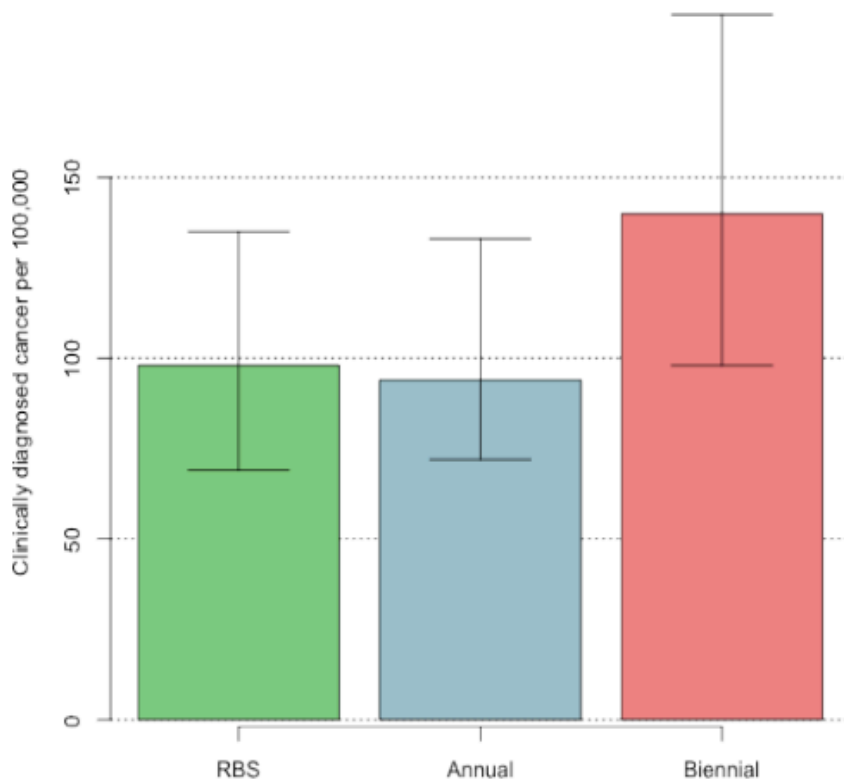


Risk-based Approach

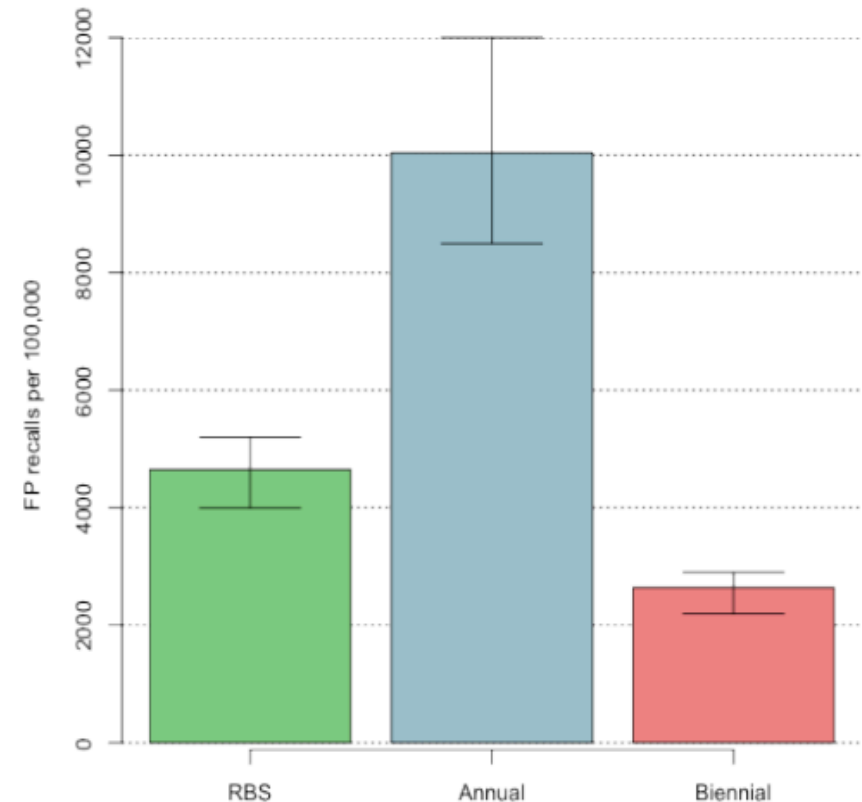
Screening interval	6 months: <i>Highest Risk</i>	Annual: <i>Elevated Risk</i>	Biennial: <i>Average Risk</i>	Not screened: <i>Lowest Risk</i>
Age 40-50	≥ 2% overall risk	≥ 1% risk of ER- or BIRADS 4	≥ 1% risk of ER+	< 2% overall risk < 1% risk of ER- < 1% risk of ER+ <i>Not screened again until 50</i>
Age 50-65	≥ 7% overall risk	≥ 1.5% ER-risk	< 7% overall risk < 1.5% risk of ER- < 2.5% risk of ER+	NA
Age >65	≥ 7% overall risk and low comorbidity	≥ 1.5% ER-risk and low comorbidity	< 7% overall risk < 1.5% risk of ER- < 2.5% risk of ER+	High comorbidity

How does risk-based screening compare ?

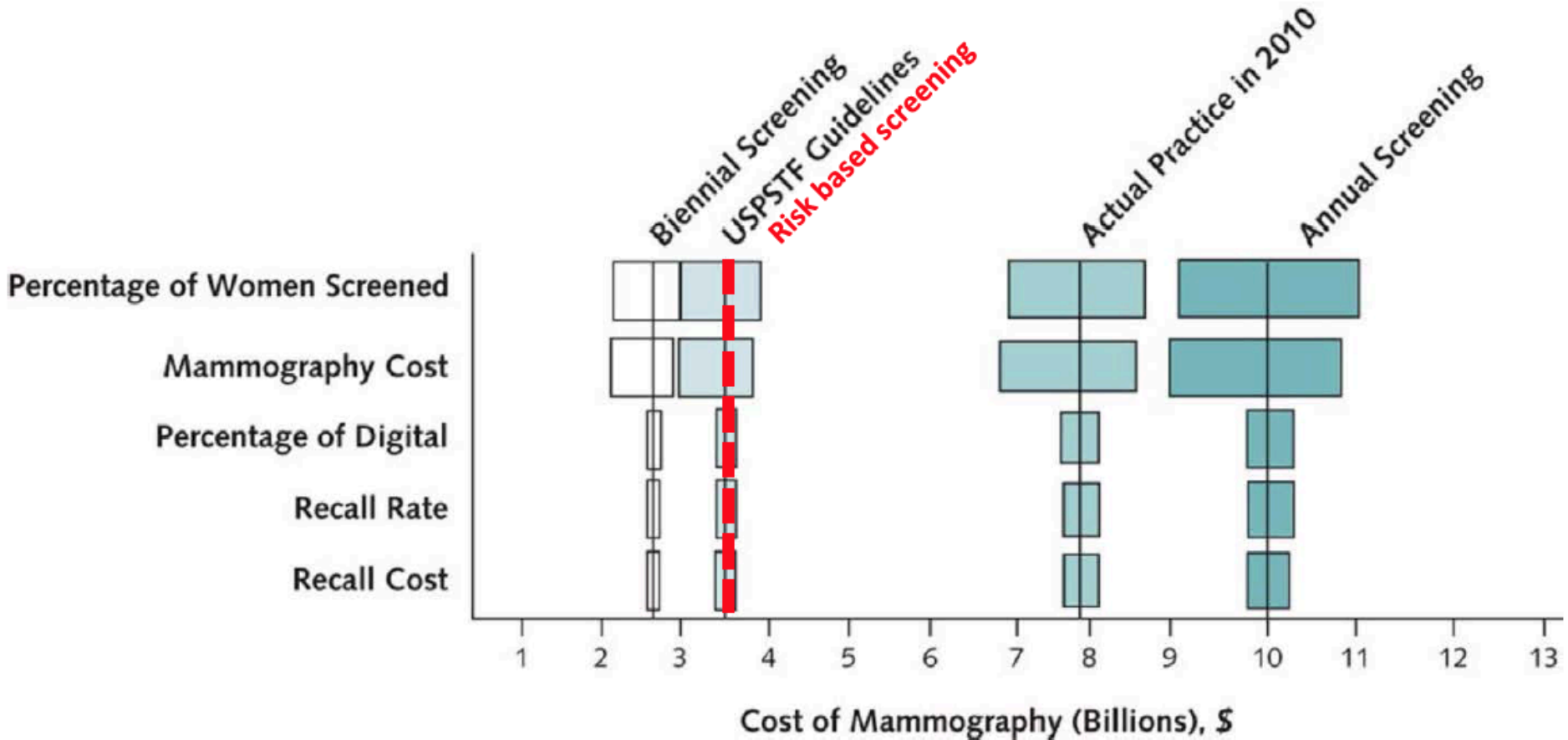
Safety: Clinically detected cancer



Efficacy: False positive recalls



Risk Based Screening: Higher Value/



O'Donoghue, Eklund, Ozanne, Esserman. Aggregate Cost of Mammography Screening in the United States: Comparison of Current Practice and Advocated Guidelines. Ann Intern Med. 2014, 160(3):145-153

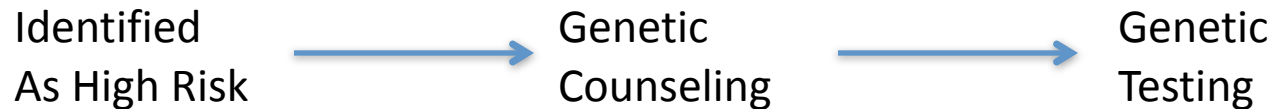
TRANSFORMATIVE AND INNOVATIVE POSSIBILITIES

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High Risk Patient and Genetic Testing

Current Paradigm

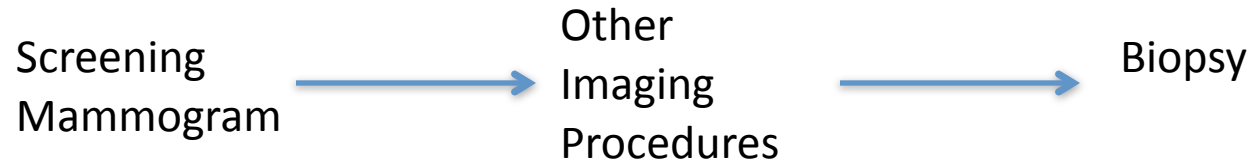


Possible Future Paradigm

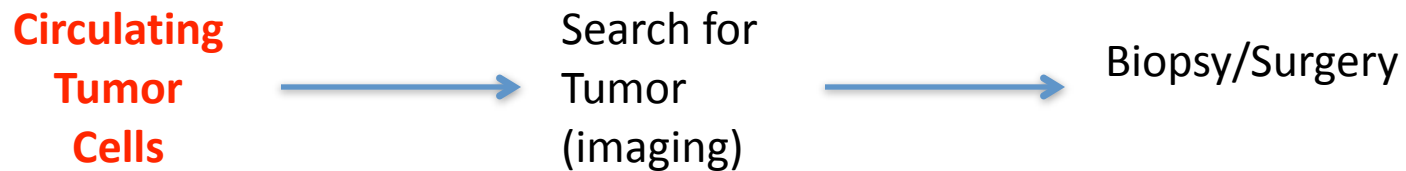


Screening and Imaging

Current Paradigm



Possible Future Paradigm

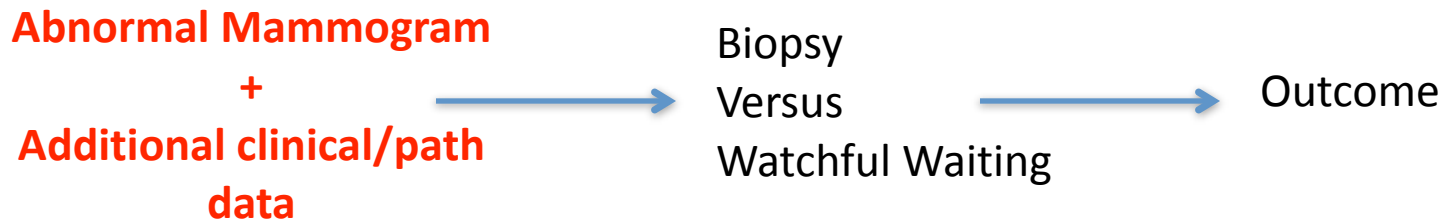


Improving utilization of invasive

Current Paradigm



Possible Future Paradigm



Smart Imaging

- Quantitative Breast Density
- Automated image interpretation and computer assisted diagnostics