The WISDOM Study: Version 2.0

Fact Sheet for Healthcare Providers

www.thewisdomstudy.org

The WISDOM Study (Women Informed to Screen Depending on Measures of risk) began in 2016 as a preference-tolerant randomized clinical trial comparing annual breast cancer screening with a personalized, risk-based screening schedule. The WISDOM Study is conducted mostly online and there is no requirement to come to a study center to participate. Women can continue to receive their care with their regular physicians. In 2024 WISDOM implemented a new version of the study - WISDOM 2.0 - providing several important updates: removal of randomization so participants choose their study arm, expansion of the genetic test use, updates to the risk model used, and expanded eligibility criteria to women as young as age 30 (up to age 74).

Study Rationale The WISDOM Study is designed to test what we hope will be a transformative approach to breast cancer screening and prevention – identifying individual risk, optimizing breast cancer detection for higher-risk women, and reducing the unintended consequences of current screening practices for lower-risk women. We intend to show that personalized screening through comprehensive risk assessment makes better use of available resources, screens women at intervals appropriate to their risk, improves compliance and decreases patient anxiety; while providing an opportunity to offer precision-prevention to those identified at high risk before a cancer occurs.

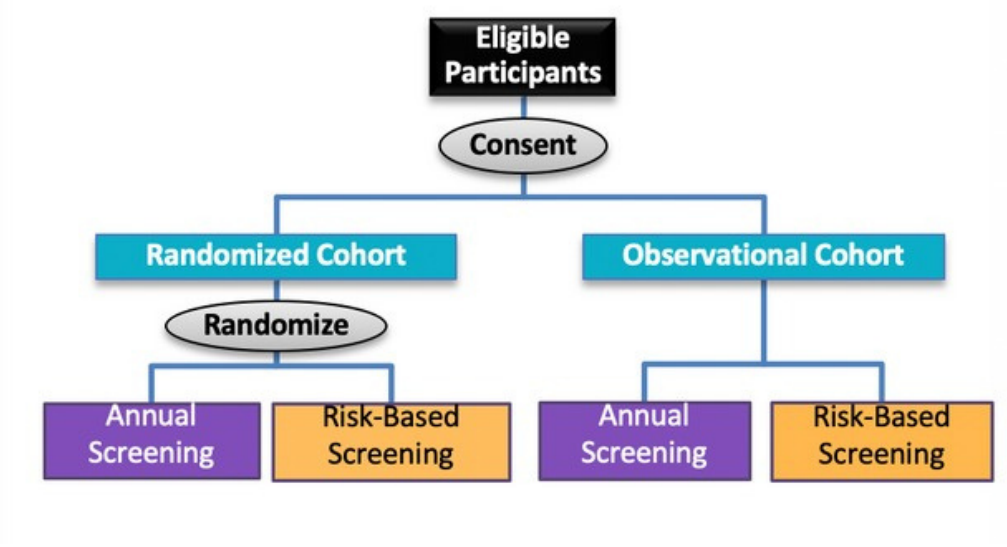
Athena Breast Health Network The WISDOM Study is run through the Athena Breast Health Network (a collaboration between the 5 University of California medical centers) and partnerships with Sanford Health in the Dakotas, plus recruitment centers at UChicago, Louisiana State University (LSU Health), University of Alabama Birmingham, Diagnostic Center for Women (Miami), and DHR Health (Texas). Women nationwide can join online, even if they don't receive care at these recruitment centers.

UCSF · UC Irvine · UC San Diego · UCDAVIS · UCLA Health

UAB The University of Alabama at Birmingham · UChicago Medicine · Sanford Health · TopLine MD Alliance · LSU Health New Orleans

Study Design

From 2016 - early 2023, WISDOM was a preference-tolerant randomized control trial. Participants were asked to select whether they felt comfortable being randomized to a study arm, or prefer to choose their study arm (see design below).



WISDOM 2.0 Design

Starting in 2023, WISDOM's design shifted to allow women to choose their study arm rather than be randomized. Women can choose whether they want to participate in the Personalized Arm, or the Annual Arm (see descriptions to right).

STUDY ARMS

Annual Arm

Participants will complete a breast health questionnaire and return for a screening mammogram in one year (unless at elevated risk and recommended for more frequent follow-up).

Personalized Arm

Participants will complete a breast health questionnaire and provide a saliva sample for genetic testing. They will receive a screening recommendation based on the results of the questionnaire and their genetic testing that is tailored to her individual risk level.

Support for High Risk Participants

In both groups, women at elevated risk have the opportunity to discuss their risk over the phone with an Athena Breast Health Specialist (licensed genetic counselor), who may then recommend risk-reducing interventions and provide counseling using our Breast Health Decisions interactive online tool.

Frequently Asked Questions

Q. How can women join the study?

A. Women can join the study on the study's website, http://www.thewisdomstudy.org. Participants register and check their eligibility, then complete study steps online. There is no requirement to come in for any study visits or to change their care provider. The study materials and participant experience (consent, questionnaires, communications) are available in Spanish and Spanish-speaking research coordinators are available.

Q. Who is eligible for the study?

Inclusion criteria:
Females, ages 30-74, no prior breast cancer or DCIS diagnosis, no prior double mastectomy

Q. How will the study determine patient breast cancer risk?

WISDOM uses the Breast Cancer Surveillance Consortium (BSCS) risk model for all women in the study. The model includes:

- Age
- Race/ethnicity
- Family history of breast cancer
- History of prior breast biopsies and benign breast disease
- Breast density
- Body Mass Index (coming in 2023!)
- Menopausal status (coming in 2023!)

Those in the personalized arm will have risk determined by their BCSC score modified by a polygenic risk score (PRS) using single nucleotide polymorphisms (SNPs). In addition to the BCSC + PRS score, we are testing for 29 genes that increase cancer risk (including BRCA1, BRCA2, TP53, PTEN, STK11, CHD1, ATM, PALB2, CHEK2). The WISDOM risk thresholds then determine the recommended screening frequency for the personalized arm participants (see Shieh et al, JNCI 2017).

Phone: 1-855-729-2884
Email: info@wisdomstudy.org
San Francisco, CA
Website: www.thewisdomstudy.org

Frequently Asked Questions

Q. How will I know if my patients are participating in the WISDOM Study?

Your patient will be given a letter outlining her WISDOM Screening Plan, including the recommended breast screening schedule. For those in the Personalized Screening Arm, your patient will also be given her genetic test results. If the results are positive, this will first be disclosed during a telephone consult with our trained Breast Health Specialists/genetic counselors. We encourage participants to share their letters and results with their provider for review and discussion. If we discover a woman is at extremely high risk or has a positive genetic mutation, she will receive a Breast Health Specialist (BHS) consultation to discuss her risk. The BHS will request her provider name to deliver results and a consultation note to the participant's study portal to share directly to the woman's provider.

Q. How can I be involved in WISDOM Study?

You can discuss the WISDOM Study with your patients who might be interested in participating. You can refer them directly to the WISDOM Study website (www.thewisdomstudy.org), where they can join the study or email a study coordinator with questions. We also encourage you to record who indicates interest in joining so the coordinator can follow-up directly. For patients enrolled in the study, you can discuss the study's screening recommendation with them and promote adherence to their recommended screening interval.

Q. What are the possible screening recommendations for women in the Personalized Arm?

The table below outlines the possible screening recommendations for women in the Personalized Arm. Based on our results from WISDOM 1.0, we expect over 70% of participants to choose the Personalized arm. Please see Shieh et al (JNCI 2017) manuscript detailing our risk stratification approach.

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Frequently Asked Questions

Q. Who orders the mammograms and other imaging exams?

The participant's existing provider will order breast imaging as part of routine clinical care. We encourage providers and participants to follow the recommended screening frequency and modality recommended by the study. However, we cannot enforce this (and it is not considered a protocol deviation or violation) and will track adherence as one of our study outcomes in this pragmatic trial.

Q. What happens if I don't agree with the recommendations given for my patient or have questions about why she was assigned to a particular category?

We welcome questions from physicians and our staff can explain the rationale behind the screening assignment given. We do run additional risk models for reference as we understand you may be familiar with a different risk models in your practice. We encourage physicians to reach out to the study team with any questions.

Q. Do participants need to be seen at a study facility? Do they need to change doctors?

No. All study activities (enrollment, consent, surveys, genetic testing, risk assignments) will be completed in the online study portal. Participants will continue to see their regular doctors and there is no need to switch providers.

Q. Who can I contact with questions about the study?

Please contact a study coordinator at info@wisdomstudy.org or at 1-855-729-2884

We have an extensive FAQ section on our website. Please visit the study website for answers to more questions! ***www.thewisdomstudy.org/faqs/***

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Personalized Arm: Risk Thresholds

Breast Cancer risk	Screening recommendation Risk is calculated as BCSC 5-years risk plus SNP-PRS	Age 40-49 (i) Risk is calculated as BCSC 5-year risk plus SNP-PRS	Age 50 and older(ii) Risk is calculated as BCSC 5-year risk plus SNP-PRS
Low Risk	No Screening at this time	**5-year risk** < 1.3%*	**n/a**
	Stop Screening	**n/a**	**stop screening at age over 70**: **5-year risk** <1.3% OR **5-year risk** <2.2% AND 50% chance of mortality *(based on ePrognosis)*
	Every 2 years mammogram	**5-years risk** ≥ 1.3% AND **5-years risk** < 95th% by age	**5-year risk** < 95th% by age
	Every 2 years mammogram & Risk reduction consultation	**n/a**	**5-year risk** < 95-97.5th % by age
	Every 2 years mammogram + BHS review *("BHS Review-low risk participants" report)*	**Age 40-60 years** meets FH criteria for NCCN breast cancer risk reduction (see Δ)	
	Annual mammogram	extremely dense breasts based on prior mammogram (BIRADS = "D")	n/a
Moderate Risk	Annual mammogram +BHS active outreach & Risk reduction consultation	**5-years risk** ≥ 97.5th% by age OR ATM or CHEK2 mutation⌘ OR **5-years risk** ≥ 6% for women 65 and older (non-carriers)	
High Risk	Q6-Annual mammogram + annual MRI BHS active outreach & Risk reduction consultation	**5-years risk** ≥ 6%** for women 40-64 OR BRCA1/2, TP53, PTEN, STK11, CDH1, PALB2 mutation OR History of chest wall radiation received before age 35	

PLEASE NOTE: These thresholds are evaluated and updated throughout the trial.

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