UNIVERSITY OF CALIFORNIA
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

WISDOM Study

Laura Esserman, MD, and her partners are conducting a clinical research study. This study will test whether a new approach to breast screening is better than standard yearly breast screening with a mammogram. The study Principal Investigators include:

University of California, San Francisco:	Laura van 't Veer, PhD
University of California, San Diego:	Andrea LaCroix, PhD
University of California, Irvine:	Hoda Anton-Culver, PhD
University of California, Davis:	Alexander Borowsky, MD
University of California, Los Angeles:	Arash Naeim, MD
University of Chicago	Olufunmilayo (Funmi) Olopade, MD
University of Chicago	Deepa Sheth, MD
University of Alabama at Birmingham	Rachael Lancaster, MD
Louisiana State University	Agustin Garcia, MD
Sanford Health (ND, SD, IA, MN):	Maria Bell, MD
Sanford Health (ND):	Andrea Kaster, MD
Diagnostic Center for Women (FL):	Michael Plaza, MD

Clinical studies include only volunteers who choose to take part. Please take your time to make a decision about whether to volunteer for this study. We have prepared information to help you decide. Discuss it with your friends and family and health care team. If you have any questions, you may call the study coordinator at (855) 729-2844.

WHY IS THIS STUDY BEING DONE?

This study is called the WISDOM Study (**W**omen **I**nformed to **S**creen **D**epending **O**n **M**easures of Risk). The purpose of this study is to test a new approach for breast cancer screening. The study will compare **routine annual screening** with **personalized screening:**

- **Routine annual screening** means getting a mammogram every year starting at age 40. **Routine annual screening** is the current guideline that most physicians follow and is recommended by various groups of medical professionals such as the American College of Obstetricians and Gynecologists, the American College of Radiology, and the American Medical Association.
- **Personalized screening** is a new screening schedule that we are testing in the Wisdom Study that is based on a woman's individual health circumstances, such as personal and family history. It is based on the mammography screening guidelines recommended by the United States Preventive Services Task Force (USPSTF).

Everyone participating in this study will receive screening on a schedule recommended by one of the major groups of medical professionals above.

Because experts disagree, there is a lot of confusion about when and how often a woman should get a mammogram. The Wisdom Study is hoping to see if more modern methods can be used to improve screening. We will test to see if **personalized screening** is as safe as and better than **routine annual screening**.

This study is funded by the Patient Centered Outcomes Research Institute, a branch of the U.S. Department of Health and Human Service, and the National Cancer Institute (NCI)/National Institutes of Health (NIH)

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Our goal is to include100,000 women in this study.

WHAT WILL HAPPEN IF I TAKE PART IN THIS RESEARCH STUDY?

Randomization

Once you decide to be part of the study, you will be asked whether you are willing to be randomized. Randomization is when you are assigned to one of two groups by chance, similar to the flip of a coin. You will be assigned to either the **Routine Annual Screening Group** or the **Personalized Screening Group**. Scientists agree that randomization is the best way to test two options to accurately determine which option delivers the best results. However, some women may be uncomfortable with the idea of randomization or have a strong preference for one of the study groups. Because we want to include as many women as possible in this important study, if you have a strong preference for which study group you would like to be a part of, you can choose either **Routine Annual Screening** or **Personalized Screening**. The data you provide by participating in this study will be used to answer our study questions, however the results from the randomized group are best for studies like this that will impact large numbers of women in the future.

If you are in the **Routine Annual Screening Group**:

1. You will complete a Breast Health Questionnaire to help determine your level of personal risk. Your breast density, measured by a recent mammogram, will also be used in the calculation of your risk.
2. You will continue to receive annual mammograms. However, if something changes, we may recommend more frequent screening.
3. If our team believes you are at higher than average risk for breast cancer at any point during the study, you will receive a copy of your detailed risk report. You will have the opportunity to discuss your risk over the phone with a Breast Health Specialist, an individual who has specialized training

in breast cancer risk assessment and genetics. They may recommend follow-up services and will answer questions about your breast cancer risk.

If you are in the **Personalized Screening Group**:

1. You will complete the Breast Health Questionnaire to help determine your level of personal risk. To further look for personal risk factors, you will also be asked to provide a saliva sample. This sample will be used to look for inherited (genetic) risk factors.
2. You will receive a screening recommendation that is based on a combination of: a) your questionnaire, b) whether you have dense breasts that are harder to screen, and c) the results of the genetic test. Based on this information, we will provide you with a recommendation for when you should return for your next mammogram or other screening test. You could be asked to return for your next breast screening in 6 months, 1 year, or 2 years after your last mammogram. We may recommend that you no longer need screening mammograms. For women in their 40's, we may recommend that you do not need a mammogram until you are 50 years old.
3. If it is determined that you are at higher than average risk based upon these factors, you will receive a phone call from a Breast Health Specialist. They may recommend follow-up services and will answer questions about your breast cancer risk.

We will send the results of your risk assessment to your doctor. If you wish to have these results sent to additional health care providers, please notify the study coordinator.

Surveys (for both Screening Groups):

You will be asked to complete the following surveys:

1. Breast Health Questionnaire: This online survey will be given after you join the study, and every year thereafter. This is a survey given to all women coming in for mammography screening and is part of your usual health care. The purpose of this survey is to assess your health history, including family history of cancer. This questionnaire can take between 20- 30 minutes to complete the first time you take it. The next time you take the questionnaire, your past answers will be pre-filled so it should take 10-15 minutes to complete every year depending on how many changes you have since the previous completion. If you have completed a Breast Health Questionnaire as part of your mammogram visit in the past, we will pre-fill your survey to help make your completion easier.

2. Insurance and Provider survey: We will ask you to complete some questions about your insurance. This will allow us to confirm your eligibility for the study, work with your insurance company to cover the study services. We will also ask

for your doctor's information so we can provide your results to your doctor to inform your care.

3. Well-being Survey: This online survey will be given several times during the study (1) after you agree to participate, 2) once you have been given your screening recommendation, and 3) once every year after getting your screening recommendation). The purpose of this survey is to find out how you feel about the information that has been provided to you, and whether there are any changes to your anxiety, your worry about breast cancer, and your overall understanding of breast cancer risk. This survey should take no longer than 10-15 minutes to complete each time.

4. Health Status Survey: This online survey will be given to women aged 50 and above to learn more about your overall general health. It will be given when you join the study, and annually until the study ends. It should take no longer than 10 minutes to compete each time.

Optional Follow-up interviews: Whichever group you are in, you may be invited to participate in an interview or group discussion about your experience of participating in the trial. These interviews are optional.

Overview of Study Activities:
The following activities will be part of each Screening Group:

	Routine Annual Screening	**Personalized Screening**
Breast Health Intake Questionnaire	X	X
Insurance and Provider Survey	X	X
Well-being Surveys	X	X
Health Status Survey	X	X
Testing for inherited risk (genetic testing) – One time		X

	Routine Annual Screening	**Personalized Screening**
Breast Health Specialist consultation for women at higher than average risk	X	X

Screening recommendation and schedule based on personal risk	X

Mammogram:

If you have had a mammogram in the past, we will use the results of your mammogram to assess your level of breast density. If you have never had a mammogram, we may ask you to get one as part of the study. The mammogram you will receive is part of your usual health care, and should be scheduled with your medical facility.

You will have access to a tool called Mammosphere to obtain and send your breast health records electronically to the WISDOM Study team. This optional tool is available to you even if your mammogram is done at one of the recruiting centers (UCSF, UCD, UCI, UCLA, UCSD, Sanford Health, University of Chicago, Diagnostic Center for Women, University of Alabama at Birmingham, Louisiana State University). You will see the option to use Mammosphere in your Wisdom participant portal. If you choose to use this service, Wisdom will share your name, date of birth and email address with Mammosphere so we can ensure your outside records are matched back to your Wisdom Study account. Mammophere will not use your information for any other purposes.

Saliva Sample and Genetic Testing:

If you are in the **Personalized Screening Group**, you will need to provide a saliva sample that will be used to evaluate whether you have an inherited (genetic) risk for breast cancer. A lab company called Color Genomics will do this test. They will provide you with a saliva kit to collect your saliva sample along with a return box and shipping label to mail back to the lab. Color Genomics will return the results back to the Wisdom Study team to give to you. Any leftover samples will be returned to the Wisdom Study team for storage and future research.

Sometimes the variation in our genes can lead to an increased risk of cancer. As part of this study, a number of genes will be tested (such as BRCA1, BRCA2, ATM, CDH1, CHEK2, PALB2, PTEN, STK11 and TP53) to see if you have any variations in these genes that are known to increase cancer risk. Since there is rapid progress being made in the discovery of genes related to cancer, it is possible that we will continue to test new genes in your sample, even after you have been assigned to your screening group. If any new genetic changes are found that change your screening assignment, we will notify you. We will provide the results of your genetic testing to you as part of the study. A Breast Health Specialist will be available to talk with you about your results and what they mean to your health and to your family members' health.

Some gene variations are not fully understood at this time. These variations are called "variants of unknown significance" (or "VUS"), and they are not used in the WISDOM risk assessment. They will not be reported to you. However, if you have a VUS, and scientists determine during the course of the study that the VUS does increase cancer

risk, Color Genomics will issue an updated report reflecting that change and you will be notified by a Breast Health Specialist and receive the updated report.

In addition, Color Genomics will look for small variations in your genes that might increase or decrease breast cancer risk by a very small amount. Scientists call these minor differences “single nucleotide polymorphisms” (or “SNP”s). These results will be incorporated into a ‘polygenic risk score’ and included in your screening recommendation.

If requested by the individual participant, we will provide the SNP raw data back.

The Color test meets standards set by the government and professional associations for laboratory developed test, including being CLIA certified and CAP accredited. The Color test is not FDA approved.

A Breast Health Specialist will be available to talk to you about your results and what it means for your care.

Clinical follow-up

As part of the study, we are trying to learn as much as we can about changes in breast tissue. If you undergo a breast biopsy or breast surgery during the time that you are in the Wisdom Study, we ask that you contact your study team. We will request your permission to access any breast tissue and/or blood sample that may be collected that is not needed for your medical care.

STUDY LOCATION:

Most study procedures can be done online or over the phone, so travel to a study site is not required. Your risk assessment and recommendations will be delivered to you through our secure online study portal. If you are at greater than average risk for developing breast cancer, a Breast Health Specialist will contact you by phone to discuss your results. Clinical services that may be recommended to you, such as mammograms, MRIs, and other services that may be recommended, may be done at your local health care facility.

Although most of the study activities will be done online, we offer face to face study participation if you would like to meet with someone to better understand the procedures, consent, or to discuss your individual results. Call the study team at the number listed at the end of this form.

HOW LONG WILL I BE IN THE STUDY?

We expect the main study to last 5 years and ask participants to follow their recommended screening schedule until the study conclusion. Additionally, we plan to use your genetic information and other data for many years to come. It is important to understand the long term health of our study participants so researchers can understand the impact of the study results. This is particularly important for those who may be affected by breast cancer in the future.

We also request permission to stay in touch with you and review your medical records for an additional 10 years to follow your breast health. We will continue to follow up with you by sending you annual questionnaires. If you decide not to continue your participation, you will be offered the usual care at your institution.

CAN I STOP BEING IN THE STUDY?

Yes. Your participation in the study is entirely voluntary. You may withdraw from the study, at any time. Your medical care will not be affected by your decision to be in the study or to withdraw from the study. If you are thinking about stopping or decide to stop, please contact the study coordinator at the number listed at the end of this form.

When contacting the study coordinator, please specify in writing if you would like your data withdrawn from future research use. Your data will not be used for future research, however, any de-identified data that has already been distributed to study researchers cannot be retracted.

WHAT RISKS CAN I EXPECT FROM BEING IN THE STUDY?

Genetic Testing Risks: The Wisdom Study tests a personalized, risk-based approach to breast cancer screening. We will identify some women who have a higher than average risk of developing breast cancer and may need more screening and opportunities to reduce their cancer risk. Others may have lower risk and need less screening. It is important that we identify women who have truly elevated risk. There is a small chance we will find that you have inherited a variation in a gene (like the BRCA1 and BRCA2 genes) that is known to be related to breast cancer risk. Learning that you carry this type of variation (often called a “mutation”) in a gene can be uncomfortable, surprising, or cause some anxiety. The genes that will be tested may also affect your risk of ovarian and other cancers. Although this is a risk, there is also potential benefit to identifying these genes because it gives you the opportunity to take action to reduce cancer risks.

These mutations are rare. We estimate that only about 1% of WISDOM participants will be found to have one. If we discover that you carry one of these mutations, a Breast Health Specialist will contact you to discuss your result and what it means. Genetic test results may also have implications for blood relatives. If you have concerns, please discuss this with the study team.

In order to make progress in the science of understanding breast cancer risk, and for genetic tests to improve, we will share your inherited (genetic) risk data in a de-identified way to research databases. This means that none of the data can be traced back to you by anyone, including the study team. Your information may be stored in a limited access federally sponsored database. There will be no link between the records, therefore the study team will not be able to go back to link the data that was sent to the database with your identity. None of your genetic risk data is stored in these databases with your name, address, birth date, or Social Security number. If you have a genetic mutation that increases your risk of cancer, there are state and federal laws that protect your privacy. These include the Genetic Information Nondiscrimination Act, which makes it illegal for employers and health insurers to use certain kinds of information about your genes to discriminate against you.

Through this mechanism, the research community can learn from a larger collection of data and help inform us of the best way to interpret all genetic testing results. We will inform you if improvements are made to the interpretation of genetic data relevant to you.

Survey Risks: Some women may feel uncomfortable answering questions about wellbeing, anxiety and breast cancer worry.

Mammogram Risks: Mammograms are part of the standard of care and therefore pose no additional risk than what you would encounter if you were not in the study. As part of this study, you will receive recommendations for when to get your next mammogram. Both groups in the study will be receiving recommendations that align with national recommendations, and no one will get screened less frequently than the United States Preventative Services Task Force guidelines.

Loss of Confidentiality: Loss of confidentiality is also a potential risk of research participation. All precautions will be taken to make sure your name and medical record number will not be associated with your study data, but a risk to your confidentiality will always be present. Your genetic test results and health information may be placed into a scientific database. Study data will be physically and electronically secured. As with any use of electronic means to store data, there is a risk of breach of data security. Even though this will not be labeled with your name or any other identifying information there is a small risk it could be traced back to you. The risk of these things happening is small.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

By participating in this study, you will help our efforts to answer two important questions. One is what the best schedule is for mammograms for all women. The other is how to identify the most important risk factors that determine a woman's risk for breast cancer. You may also have access to genetic testing that is not part of routine health care. Advances in the prevention, diagnosis and treatment of breast cancer are due to participation of women like you in studies like this. By participating you can gain more understanding of

your health history as it relates to breast cancer, and help the study team find a solution in the breast screening debate.

WHAT OTHER CHOICES DO I HAVE IF I DO NOT TAKE PART IN THIS STUDY?

You may choose to have routine breast cancer screening without being in the study. Your participation is voluntary.

WILL MY MEDICAL INFORMATION BE KEPT PRIVATE?

We will do our best to make sure that the personal information in your medical record is kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. When information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- Patient Centered Outcomes Research Institute, and the National Cancer Institute (NCI)/National Institutes of Health (NIH) which provides funding for the WISDOM trial
- The University of California, Sanford Health, University of Chicago, University of Alabama at Birmingham, Louisiana State University, Diagnostic Center for Women (the study team)
- Color Genomics, the lab providing the genetic test (if applicable)
- Mammosphere, the breast health records request portal (if you choose to use it)
- Service provider for data management & IT The Data Safety and Monitoring Board, a selected group of scientists who oversee the quality of the study and evaluate the risks to study participants

Participation in research may involve a loss of privacy, but information about you will be handled as confidentially as possible. Your consent form and some of your research test results will be included in your medical record as appropriate to guide your care. Therefore, your doctors may become aware of your research participation. Hospital regulations require that all health care providers treat information in medical records confidentially.

ELECTRONIC MEDICAL RECORDS AND RESEARCH RESULT

An Electronic Medical Record (EMR) is an electronic version of the record of your care within a health system. An EMR is simply a computerized version of a paper medical record. If you are receiving care or have received care at the University of California, Sanford Health, University of Alabama at Birmingham, Louisiana State University, Diagnostic Center for Women or University of Chicago (outpatient or inpatient) and are participating in this research study, results of research related procedures (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR.

WHAT ARE THE COSTS OF TAKING PART IN THE STUDY?

The WISDOM Study has an agreement with certain insurance companies to cover the procedures that are part of this study, therefore participating insurers will be billed. No copays will be charged to you for research related tests. You may see charges related to the WISDOM Study on your Explanation of Benefits (EOB) from your health plan. This includes your risk assessment, Breast Health Specialist consultation about your results, your genetic testing, and your annual risk evaluations.

In addition, federal regulation allows for providers to charge reasonable fees for copies of medical records. If you reach out to your provider to request a copy of your breast health records, please ask them in advance if a fee will be charged. If so, the WISDOM Study will be happy to request your breast health records for you, in order to avoid this fee.

For those who are not covered by a participating insurer, funding sources may also be available through your study institution for the research related procedures. You will not be charged for any research related procedures. Insurance coverage and co-pays for mammograms will not change because of study participation.

Over the course of the study, some women will discover they are at higher than average risk and some may develop breast cancer. If that happens, any services that you require will be billed to your insurance, and may be subject to your standard co-pays. This includes additional genetic counseling, breast biopsy, more frequent examinations of your breasts, blood tests, or any treatment required if a diagnosis of breast cancer is made.

WILL I BE PAID FOR TAKING PART IN THIS STUDY?

You will not be paid for taking part in this study.

WHAT ARE MY RIGHTS IF I TAKE PART IN THIS STUDY?

You are free to choose whether or not to participate in this study without penalty. We will inform you of any new information or changes to the study that may affect your health or willingness to continue in the study.

WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?

Questions for the Wisdom Study Team: 1-855-729-2844 or info@wisdomstudy.org

CONSENT

CONSENT TO RANDOMIZATION:

1) I choose to be randomized, which means that I will be assigned by chance to either be in the Routine Annual Screening Group or in the Personalized Screening

Group. Choosing this option helps researchers to answer questions faster and more completely:

☐ Yes

☐ No

OR

2) I wish to participate, but I choose not to be randomized and wish to be assigned to (please check one):

☐ Routine Annual Screening Group

☐ Personalized Screening Group

A copy of this consent form will be available to you through your secure login on the study portal, and is available by request from the study team at any time.

You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you. This is called HIPAA authorization.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

If you wish to participate in this study, please enter your electronic signature below.

_____ _____

Participant Date

_____

Participant name (print)