CENTER FOR DATA INSIGHTS AND INNOVATION
CALIFORNIA HEALTH & HUMAN SERVICES AGENCY

View xForm - Project Application v6

This form is for new projects that have not been previously approved by CPHS.

Data entry
- Submitted 05/02/2024 1:49 PM ET by Jenny Nguyen, MPH

New Submission Study Personnel

NEW CONTACT INSTRUCTIONS

June 2024 cycle.

_____HSC_____

Requesting GBACR Data.
A LOS from CCR is attached.
A DSL from Stanford University.
List of variables is attached.

03/20/2024 • Sussan Atifeh • Internal

INTERNAL NOTE:
Researchers previously submitted this request as an amendment for project 13-03-1143 (titled as: California Cancer Registry Linkage with the Northern California Breast Cancer Family Registry Cohort)which was reviewed by Dr. Schaeuble. Dr. Schaeuble requested the researchers to resubmit the amendment as a New Project application (this application) since the requested changes proposed for the project 13-03-1143 exceeded what could be reviewed as an amendment.

Researchers submitted this application on 3/18/24 and clarified they had requested approval to:

1. Expand the BCFR Cohort through enrollment of additional young women with breast cancer diagnosed at age <45 years and their family members through case listings from the Greater Bay Area Cancer Registry.

2. Expand and update cohort characterization through efficient data linkages of existing and expanded BCFR Cohort members with treatment and outcomes databases and exposure databases; and collect new data elements (e.g., cardiotoxicity, healthy aging) through surveys for all cohort members.

3. Maintain the current extensive biospecimen resources and augment them through the collection of biospecimens from newly enrolled young women with breast cancer and their

families.

4. Continue to actively collaborate with the external research community and expand the use of the BCFR resources, including data and biospecimens collected.

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If personnel are not found by their email address while trying to complete the following questions, you can add them in the system with the link below. Click on the "New Contact Form" and complete it. Within a few minutes of completing the form, you will receive an email notifying you of the availability of the new contact. You should then be able to add them in the subsequent questions.

User had the option to start a different form here.

PRINCIPAL INVESTIGATOR (PI)

Enter the Principal Investigator's email address.

Esther John, PhD

Email: emjohn@stanford.edu **Business:** (650) 497-1221

Choose the institution with which the PI is affiliated (not the location at which the research is being conducted).

Stanford University

Enter the city in which the PI's institution is located.
Palo Alto

Enter the state in which the PI's institution is located.

Start typing in the state name to select the name from the list.

California

Attach a copy of the PI's Curriculum Vitae.

Attachment 1. CV Esther M John updated 1-23-2024 CPHS.doc	PI Curriculum Vitae

CO-PRINCIPAL INVESTIGATOR (CO-PI)

Enter the Co-PI's email address by clicking on the "Add Contact" button.

Dear Researchers: Please attach separate CVs for each Co-PI. thanks,

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Please the next time that the application is in your queue (data entry), attach the remaining CVs in any sections that provide you with an "Attachment" button.
Thanks,

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If there are multiple co-principal investigators, repeat this action for all Co-PIs. If there are no Co-PIs for this project, skip this question.

Allison Kurian, MD
Email: akurian@standford.edu **Business:** (650) 724-7375

Mary Beth Terry, Phd
Email: Mt146@columbia.edu **Business:** (212) 305-4915

Jeanine Genkinger, PhD
Email: jg3081@cumc.columbia.edu **Business:** (212) 342-0410

Mary Daly, MD
Email: mary.daly@fccc.edu **Business:** (888) 369-2427

Sarah Colonna, MD
Email: Sarah.Colonna@hsc.utah.edu **Business:** (801) 585-0262

Irene L Andrulis, PhD
Email: ANDRULIS@lunenfeld.ca **Business:** (416) 586-8256

John Hopper, PhD
Email: j.hopper@unimelb.edu.au **Business:** +6 (138) 344-0697

Melissa Southey, PhD
Email: melissa.southey@monash.edu **Business:** +6 (138) 559-7003

Attach a copy of each Co-PI's Curriculum Vitae.

Attachment 2. CVs of 8 Co-PIs.pdf	Co-PI Curriculum Vitae
Jeanine Genkinger CV	Co-PI Curriculum Vitae

Mary Beth Terry CV	Co-PI Curriculum Vitae
Sarah Colonna CV	Co-PI Curriculum Vitae
To Reviewer: We can only upload up to 5 attachments.	Co-PI Curriculum Vitae

ADMINISTRATIVE CONTACT

Enter the email address(es) for the administrative contact(s). If you are the administrative contact, enter your email address, and enter anyone else you want listed as an administrative contact.

Jenny Nguyen, MPH

Email: jennytnguyen@stanford.edu **Business:** (650) 498-0697

RESPONSIBLE OFFICIAL (RO)

Enter the RO's email address.

*The RO **cannot** be the same person as the PI or Co-PI. The RO must have supervisory authority, in the administrative structure of the institution, over the PI.*

Kathleen Thompson

Email: klt@stanford.edu **Business:** (650) 725-0661

OTHER RESEARCH STAFF

Enter the email address for any other research staff by clicking the "Add Contact" button.

Repeat this action for all other research staff not previously provided on this screen that should receive notifications about this project. If there are no additional research staff, skip this question.

No answer provided.

Check for PI same as RO (internal only question) *(Internal)*

False

Project Information

SUBMITTER

Application completed by:

Jenny Nguyen, MPH
Email: jennytnguyen@stanford.edu **Business:** (650) 498-0697

PREVIOUSLY APPROVED EXEMPTION

Is there a previously-approved exemption from CPHS for this project?

No

PROJECT TITLE

Enter the project title (please capitalize each word in your title).

Northern California Breast Cancer Family Registry

PROJECT SITE

Indicate the primary site at which the research will be conducted.

Stanford University

STUDY PROCEDURES

Indicate the study procedures involved in this research. Check all that apply.

Data Registry
Recruitment-Participant
Specimen Registry
Surveys

TYPE OF RESEARCH REQUEST

Indicate which of the following applies to this research. Check all that apply.

Please de-select "Common rule only" in this section.

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*Death Data Only refers to health-related studies requesting existing mortality data from **within** the California Human Health Services Agency (CHHSA)*

*SB-13 (Information Practices Act) refers to health-related studies requesting existing data from **outside** the CHHSA (e.g. California Department of Corrections and Rehabilitation [CDCR], California Department of Education [CDE], etc.) **OR** studies requesting data **within** the CHHSA that are not state funded or involving state staff.*

Common Rule/Human Subjects refers to health-related studies that involve direct or indirect interaction with human subjects (e.g. recruitment, interviews, etc.)

*Common Rule Only refers to health-related studies requesting existing data from **within** the CHHSA (e.g. Office of Statewide Health Planning and Development [OSHPD], California Department of Public Health [CDPH], etc)*

Common rule/Human subjects

PROJECT TYPE DETAILS

Indicate which, if any, apply to this research. Check all that apply.

If the research does not involve any of following, choose "None of the above."

Minimal Risk
Consent form

VULNERABLE POPULATIONS

Indicate which vulnerable populations, if any, will be involved with this research. Check all that apply.

If vulnerable populations are not part of the research, choose "Not applicable."
Note regarding minors: in the United States, a minor is under 18 years of age. If research is conducted outside the United States, a minor is under the age of majority in the countries where research is to be conducted.

Not applicable

FUNDING

Is this research funded?

Yes

Indicate the funding source for this project.
Federally funded

Enter name of federally-funded source.
National Cancer Institute (U01 CA164920)

EXPEDITED REVIEW CONSIDERATION

Please check the criteria below that you think your project meets to qualify for an expedited review. If none of these expedited criteria are appropriate for your project, choose 'not applicable'; your protocol will be reviewed by the full committee. Note that CPHS will make the final determination of whether the project meets the criteria for expedited review.

Your project involves human subjects contacts and is not qualified for an Expedited review and will be scheduled for the CPHS June 7th, 2024, full board meeting. Please select "Not Applicable."
Thanks,

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Protected Health Information/Personally Identifiable Data (PHI/PID) is defined as information in any format that identifies the individual, including demographic information collected from an individual that can reasonably be used to identify the individual. Additionally, PHI is information created or received by a healthcare provider, health plan, employer, or health care clearinghouse; and relates to the past, present, or future physical or mental health or condition of an individual, including any of the 18 HIPAA identifiers.

Note: Please be aware that individual participants may be identifiable by combining other items in the data even when none of the 18 HIPAA identifiers are present. Thus, a study may still contain PID even after removing or never acquiring the identifiers, and the investigator may still need to provide complete answers for the data security questions in the protocol.

***The Departments within the California Health and Human Services Agency (CHHSA) are: Aging, Alcohol and Drug Programs, Child Support Services, Community Services and Development, Developmental Services, Emergency Medical Services Authority, Health Care Services, Mental Health, Public Health, Rehabilitation, Social Services and Statewide Health Planning and Development.*

Not applicable

ANTICIPATED PROJECT START DATE

Projects cannot begin before they have been reviewed. The earliest possible start date is always the date of the next public meeting at which the project will be heard.

> Projects cannot begin before they have been reviewed. The earliest possible start date is always the date of the next public meeting at which the project will be heard. Please select "6/7/24" or a date after this date within a few weeks. Thanks,
>
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For a list of public meeting dates, see the CPHS website

06/07/2024

ANTICIPATED PROJECT END DATE

04/30/2028

Project Details

PURPOSE

Include a brief statement, less than 500 words, describing the research project. Be sure to address the background for the project, including relevant literature, the major research questions to be addressed, and the expected end product (e.g., article, report or other publications). Include the location(s) where the project will take place. The summary should be understandable to the general public.

The Breast Cancer Family Registry (BCFR) is a Multi-Institution Study. It was established by the NCI in 1995 at 6 sites in the U.S., Canada, and Australia. The current 6 sites include Stanford University (Palo Alto, CA), Columbia University (New York City, NY), Fox Chase Cancer Center (Philadelphia, PA), the University of Utah (Salt Lake City, UT), Mount Sinai Hospital (Toronto, Canada), and the University of Melbourne (Australia). This new CPHS protocol is related to CPHS protocol 13-03-1143, titled "CCR linkage with the Northern California Breast Cancer Family Registry Cohort". Starting in 1996, the BCFR has enrolled and followed over 15,000 families affected with breast cancer, including individuals diagnosed with breast cancer, and relatives and population controls never diagnosed with breast cancer. Blood, saliva, and tumor tissue samples and data have been collected at enrollment and during follow-up for up to 26 years. The purpose of the BCFR is to identify genetic, hormonal, lifestyle, and environmental factors that are associated with the risk of developing breast cancer and outcomes (second cancers, survival) after breast cancer diagnosis in the context of familial breast cancer. With current funding (5/3/2023 to 4/30/2028), the BCFR will enroll an additional 950 families affected with breast cancer. The Stanford site will enroll 200 families identified through the Greater Bay Area Cancer Registry. The 6 sites will enroll women diagnosed with breast cancer under age 45 years and their first- or second-degree adult female relatives; collect questionnaire and other data and biospecimens; follow participants over time; maintain the data and biospecimens collected for the entire BCFR Cohort since 1996; perform linkages with cancer and death registries and other databases; conduct statistical analyses and laboratory analyses; and continue collaborative research.

MAJOR RESEARCH QUESTION

What is the major research question to be addressed in this project?

The establishment of the BCFR Cohort by the NCI in 1995 was a novel initiative at that time aimed at supporting multi-disciplinary research on breast cancer etiology, outcomes, and prevention across a wide spectrum of familial risk. The aims of the BCFR include gaining a better understanding of the genetic, hormonal, lifestyle, and environmental factors that affect a) a woman's risk of developing breast cancer, and b) the risk of adverse outcomes after diagnosis. A large number of families affected with breast cancer was recruited and followed at the 6 BCFR sites, and extensive data and biospecimens were collected to support etiology and outcomes research for breast cancer. Over the years, the BCFR Cohort was expanded several times and now comprises over 15,000 families, including over 4,000 families from the Northern California BCFR site. The BCFR Cohort is unique in that it is enriched with individuals who are at increased risk of breast cancer. The Northern California component of the BCFR is further enriched with a high proportion (67%) of families from racially and ethnically minoritized populations who are underrepresented in health-related research, including breast cancer.

The current funding cycle (5/3/2023 to 4/30/2028) is aimed at gaining a better understanding of genetic, hormonal, lifestyle, and environmental factors that impact women's risk of developing breast cancer at a young age. SEER analyses have shown that the incidence of distant-stage breast cancer has been increasing among young women under age 40 years. The reasons underlying this trend remain uncertain. Over the next 4 years, the 6 BCFR sites will recruit 950 women diagnosed with breast cancer under age 45 years from racially, ethnically, and socioeconomically diverse populations and 950 first- or second-degree relatives who have never been diagnosed with breast cancer; 200 families will be recruited in the San Francisco Bay Area by the Northern California BCFR site at Stanford University. Data from multiple sources will be collected for study participants: Clinical and vital status data from the California Cancer Registry (CCR) will complement other sources of data, such as questionnaires, medical records, pathology reports, National Death Index, U.S. census, and environmental databases. Questionnaire data will be collected on family history of breast and other cancers, medical history, menstrual and reproductive history, and lifestyle factors, as well as environmental exposures and other factors hypothesized to impact the risk of breast cancer among young women. We will collect data on treatment, stress, financial toxicity, quality of life, and other factors that may impact outcomes after diagnosis. We will also collect biospecimen samples in order to investigate the role of genetic factors and plasma-based biomarkers. We will use these data to perform a number of statistical analyses aimed at identifying risk factors for breast cancer in young women, as well as prognostic factors that impact adverse outcomes of young women diagnosed with breast cancer. Furthermore, we will compare risk factor profiles of young women recruited in the next 4 years to the risk factor profiles of young women diagnosed as far back as 1995, in order to

investigate to what extent risk factors have changed over time. As part of the current funding (2023-2028), the BCFR will continue to maintain the data and biospecimens collected for over 15,000 families since 1996, including 4,000 families from Northern California. The BCFR data and biospecimens are the foundation for continued research aimed at 1) identifying risk factors for first primary breast cancer and cancer at other sites using prospective or case-control designs; and 2) identifying prognostic factors associated with recurrences and second cancers, overall mortality, and cause-specific mortality.

STUDY PROCEDURES

Describe in detail all procedures for this research. Do not attach grant applications or similar documents. Information in this application must be sufficient to fully explain the procedures without such documents

> Would you please attach an updated copy of project 13-03-1143 in this section as well? Thanks,
>
> 03/25/2024 • Sussan Atifeh • *Not* Internal • Resolved

We seek CPHS IRB approval to 1) recruit an additional 200 families affected with breast cancer in the San Francisco Bay Area and collect data and biospecimens; 2) maintain the data and biospecimens that have been collected for over 4,000 families recruited in Northern California since 1996; 3) enhance the data through linkages with cancer and death registries and other databases; 4) continue to use the data and biospecimens for approved projects in collaboration with the Research Team that includes the Co-PIs of the other 5 BCFR sites, as well as other collaborating investigators.

The NCI renewal application (2023-2028) addresses the following specific aims:

1. Expand the BCFR Cohort through enrollment of additional young women with breast cancer diagnosed at age <45 years and their family members (at least one first-degree or second-degree adult female relative) while oversampling underrepresented populations to increase racial, ethnic, and socioeconomic diversity.

2. Expand and update cohort characterization through efficient data linkages of existing and expanded BCFR Cohort members with treatment and outcomes databases and exposure databases; and collect new data elements (e.g., cardiotoxicity, healthy aging) through surveys for all cohort members.

3. Maintain the current extensive biospecimen resources and augment them through the collection of biospecimens from newly enrolled young women with breast cancer and their families.

4. Continue to actively collaborate with the external research community and expand the use of the BCFR resources, including data and biospecimens collected.

Each BCFR site will have its own work scope and recruitment strategies. The work scope, recruitment goals, and research activities for the Northern California BCFR site are described below.

1) Recruitment of new probands and relatives

The Northern California BCFR will be expanded through the recruitment of 200 female probands with breast cancer and 200 first-degree and/or second-degree adult female relatives. We will identify young women newly diagnosed with breast cancer between 2024 and 2027 through case listings obtained from the Greater Bay Area Cancer Registry (GBACR). We will request case listings of young women newly diagnosed with a first primary invasive breast cancer before the age of 45 years in the following Bay Area counties: Alameda Country, Contra Costa County, Santa Clara, and San Mateo County. Cases who meet the eligibility criteria and are willing to participate in the study will be enrolled as probands. Our goal is to enroll 200 probands and 200 biological female first-degree and/or second-degree relatives (sisters, female first cousins, adult daughters, mothers, or aunts).

Young women with breast cancer will be sent an invitation letter that explains the study along with an eligibility screening questionnaire. Women will be asked to complete and return the screening questionnaire by mail or to complete the screening questionnaire online by using a URL link we provide in the invitation letter. Women who do not complete the screening questionnaire within a month will be called by trained staff to answer any questions and complete the screener by phone. If eligible and interested in the study, cases will be enrolled as probands and asked to complete the following study activities: sign the informed consent form; complete the baseline questionnaires; provide a blood sample and a first-morning urine sample; complete follow-up questionnaires; sign a release for the future collection of their digital mammograms, MRIs, and medical records; and sign a HIPAA authorization form for the future collection of their pathology report and a tumor tissue sample and use of their residential address for geocoding that will be linked to geospatial databases (e.g., census neighborhood characteristics, environmental exposures).

After the proband is enrolled and gives permission to contact her first-degree and/or second-degree adult female relatives, we will recruit the relatives. They will also be invited to sign the informed consent form; complete baseline questionnaires; provide a blood or saliva sample and a first-morning urine sample; complete follow-up questionnaires; sign a release for the future collection of their digital mammograms, MRIs, and medical records; and sign a HIPAA authorization form for the future collection of their pathology report and a tumor tissue sample, if they are diagnosed with breast cancer, and use of their residential address for geocoding that will be linked to geospatial databases.

Data Collection: Questionnaire data will be collected by mail, online, or telephone interviewer. Prospective participants who prefer to complete the documents on paper can request paper copies from the study staff. Eligible and consented participants who do not complete the questionnaires by mail or online will be contacted by a study interviewer, and if preferred, the questionnaires will be completed by telephone interview. The questionnaires and consent form are in development and will be submitted to the CPHS for review and approval when they are ready.

Document attached for review:

New Consent Form: After passing the eligibility screening, if an email address is provided, an invitation email to the prospective participant will include the link to their electronic consent form (e-Consent Form). They may use their personal mobile phone, electronic tablet, laptop, or desk computer to read the consent and to sign the e-Consent Form with an electronic signature. They can either use their finger or a mouse/stylus. The email to prospective participants will also include the contact information of Family Registry staff, who have been properly trained in obtaining informed consent and can be contacted if the participant has questions regarding the consent form or the study. For participants who request to complete the forms by mail, they will receive a package including 2 copies of the informed consent form (one to sign and return and one to keep for their personal records), 2 copies of the HIPAA authorization form (one to sign and return and one to keep for their personal records), and hard copies of the study questionnaires (baseline and family history questionnaire) with a prepaid return envelope. See attached the new consent form for review (see Attachment 3. NC-BCFR Consent Form - Case).

Documents to be approved:

Invitation Letter: Potential cases or young women identified by the GBACR to have a diagnosis of a first invasive breast cancer diagnosis before age 45 years will be sent an invitation packet by postal mail. Enclosed will be an invitation letter that explains the study along with information about where we received their name and contact information. The invitation letter will also provide the URL and QR code to scan if they prefer to complete the screening questionnaire online. A hard copy of the California Cancer Registry brochure, eligibility screening questionnaire, Relative Contact Form, and a prepaid envelope will also be enclosed in the invitation packet. Potential controls will be identified through the Relative Contact Form filled out by eligible cases. Depending on the contact information provided (mailing address, email, and/or phone number), the potential control may be contacted by mail and sent an invitation package. Like for cases, relatives will also receive an invitation letter that explains the study and tells them who referred to the study. We will include the referring case's first name in the letter. Their package will also include a brief eligibility screening questionnaire and a prepaid envelope. The relative may also choose to use the URL link or scan the QR code in the invitation letter to complete the screening questionnaire online. If only an email address is provided for the relative, we will send the same invitation letter in email format with the link to the eligibility screening form. If only a phone number is provided, a study staff will call the relative to obtain their mailing address or email address to mail/email them the invitation letter.

Eligibility Screening Questionnaire: This questionnaire will take less than 5 minutes to complete and will determine whether a potential case meets the eligibility criteria to participate as a proband (i.e., diagnosed with a first primary invasive breast cancer before age 45, currently resides in the San Francisco Bay Area, willing to complete the baseline and follow-up questionnaires, willing to provide a blood sample, willing to provide contact information for at least one female adult relative, and if adopted, she must know of their biological relatives). Relatives are eligible if they are between

the ages of 18-79 years and are willing to complete the baseline and follow-up questionnaires. The hard copy of the eligibility screening questionnaire will be included in the mailing with the invitation letter along with a prepaid return envelope. As previously stated, a URL link will also be provided in the letter if the participant prefers to complete the questionnaire online. Cases and relatives who do not complete the screening questionnaire within a month will be called by trained staff to answer any questions and complete the screener by phone.

Relative Contact Form: The relative contact form will be included in the invitation package to all potential cases. If the potential case agrees to provide contact information for at least one female adult relatives in the eligibility screening questionnaire, she will be asked to complete this form on paper and return with her completed eligibility screening questionnaire. If completed online, this form is also programmed to appear after she selects that she give us permission to contact her relative to participate in the study.

HIPAA Authorization Form: After signing the e-Consent Form, all participants will be directed to their electronic HIPAA Authorization Form. By signing the form, the participant will allow us to request copies of current or past medical records and reports (pathology, radiology, treatment), and obtain a stored tissue sample from their diagnosis/treating hospital to confirm any new reports of breast cancer. It will also permit us to use of their past and current residential addresses for geocoding that will be linked to geospatial databases (e.g., census neighborhood characteristics, environmental exposures). A copy of their signed form will be offered to the participants. Participants may request to complete this form by mail; hard copies can be sent with a prepaid return envelope.

Baseline and Family History Questionnaires: Both the baseline questionnaire and family history questionnaire will be offered for mail or online completion. Participants will be asked to complete questions about their health history, family history of cancer, cancer screening, reproductive history, lifestyle, and other factors, as well as treatment for those who had a breast cancer diagnosis. Eligible and consented participants who do not complete the questionnaires will be contacted by a study interviewer, and if preferred, the questionnaires will be completed by telephone interview. Each questionnaire will be personalized with the participant's unique numeric study ID.

Authorization for Release of Mammograms and MRIs: To facilitate future planned research studies that will collect mammograms and MRIs for Northern California BCFR participants, we will ask female participants to complete and sign the Authorization form for the future release of their mammograms or MRIs.

Biospecimen Collection: Probands will be asked to provide a blood sample and a first-morning or spot urine sample. Relatives will be asked to provide a blood sample or saliva sample and a first-morning urine sample. A blood sample may be collected by a health care provider or a clinical laboratory. A urine sample may be collected using a mailed collection kit and then shipped back to the study lab or collected on-site if participants come to the Stanford

clinic for their blood draw. A saliva sample may be collected using a mailed collection kit. The biospecimens will be stored and used for future health-related research. The biospecimen collection procedures are described in more details below.

Blood Collection: Study staff will review the signed consent form to determine whether the participant has agreed to provide a blood and urine sample. To be eligible to be enrolled as a proband, the participant must be willing to provide a 30 mL non-fasting blood sample. Relatives must be willing to provide a blood or saliva sample. Participants willing to donate a blood sample will be called by phone by a study staff to schedule their blood draw appointment and offer three collection options (see below).

Urine Collection: Urine will be collected into a 4oz specimen container either in a study clinic or at home. First morning samples should be collected when possible; spot urine samples are also acceptable. The date and time that urine is collected should be recorded for all participants, as well as whether or not the sample is first morning avoid or spot urine collection. For participants who collect their specimen at home, a 4oz urine container, return shipping materials, and instructions will be sent to the participant by mail. Participants who collect their specimen at home will be instructed to collect a first-morning sample and to freeze the sample and a gel cold pack for at least 24 hours prior to shipping via overnight mail to the Stanford CTRU Laboratory. The time of day that urine was collected should be recorded for all participants (at-home or in-clinic collections). Participants who are scheduled to come to the CTRU clinic for their blood draw will be asked to provide a spot urine sample during their visit.

Participants will be offered three options for the collection of a blood and urine sample:

1. Schedule a blood draw appointment at the Stanford Clinical and Translational Research (CTRU) Clinic at 800 Welch Road in Palo Alto, CA. Participants who are scheduled to come to the CTRU clinic for their blood draw will be asked to provide a spot urine sample during their visit. They will provided with a pre-labeled urine cup to collect their sample. The nurse will fill out the biospecimen requisition form indicating that it is a spot urine sample and record the collection date and time.
2. Schedule a blood draw appointment at their local Quest Diagnostic laboratory. A blood collection kit along with mailing materials and FedEx prepaid airbill will be shipped to their home and participants can bring the kit to their Quest lab appointment. Collected samples will be shipped FedEx to the CTRU Laboratory for processing. Those who schedule a blood draw at their local Quest laboratory will also receive a urine collection kit that will be shipped to their home to collect and freeze their first-morning urine sample for 24 hours before either scheduling a FedEx pick-up at their residence or bringing their FedEx package to a drop-off location to ship overnight to the CTRU Laboratory for processing;
3. Schedule a home visit appointment with ExamOne. A trained ExamOne phlebotomist will perform the blood draw at the participants' home and pick up their urine sample. A urine collection kit along will be shipped to their home to collect and freeze their first-morning urine sample 24 hours before

the home visit. The phlebotomist will drop off both the blood and urine sample at a FedEx drop-off location to ship overnight to the CTRU Laboratory for processing.

Saliva Collection: Relatives who are not willing to provide a blood sample will be invited to provide a saliva sample (2mL) in addition to a first-morning urine sample. The saliva sample will be collected at home. Both saliva collection kit and urine collection kit will include pre-paid packaging materials for the return of the biospecimens to the study office and the CTRU Laboratory for processing.

Upon receipt of the biospecimen samples, the probands and relatives will receive a $25 gift card.

The recruitment and biospecimen collection flowchart for the Northern California BCFR is attached (see Attachment 4).

We will submit for CPHS review all of the new recruitment documents such as the eligibility screening questionnaire, study invitation letters, baseline questionnaires, medical release forms, and HIPAA forms when we are ready to begin recruitment. These documents are currently in development by the site PIs and staff. All study documents will be translated into Spanish. We will also hire bilingual Spanish-English staff who will communicate with participants who have questions about the study and who will administer the questionnaire by telephone if this is the participant's preference.

Our local BCFR Data Core at Stanford University will be responsible for tracking all recruitment and follow-up activities, data entry, quality control and data cleaning, regular submissions of de-identified data to the BCFR central database maintained at Columbia University, conducting queries to support new collaborative projects, updating progress reports, and preparing special reports. Throughout this protocol, "de-identified" is defined as a variable or analytic dataset that does not include any individual-level identifying information.

Personal identifying information (PII) (e.g., name, address, phone number, email address, diagnosis date, birth date, death date) will be maintained at Stanford University only and not shared with the BCFR central database or any collaborators.

2) Maintenance of Newly Recruited Families and Existing Cohort.

The new families enrolled in the Northern California BCFR will be followed and retained using similar approaches as those used for the existing Cohort, including follow-up questionnaires, newsletters, seasonal greeting cards, webinars, and website updates.

3) Data Linkages:

The Northern California BCFR cohort is comprised of over 10,000 participants from over 4,000 families. We will continue to follow existing Cohort members through linkages with cancer and death registries (e.g.,

California Cancer Registry, Virtual Pooled Registry (VPR), National Death Index) to identify new cancers or confirm previously self-reported cancers, to update vital status, and to the obtain cause of death for deceased probands and family members. We will include the newly recruited families in these linkages. In addition, linkages will be performed with databases on neighborhood characteristics or environmental exposures.

4) Data and biospecimen analyses and collaborations

The data and biospecimens collected for the 200 new families (2024-2027) and the 4,000 families enrolled from 1996-2011 will be used for statistical analyses and/or laboratory analyses led by the investigator team at Stanford University, investigators at the other BCFR sites, or collaborating investigators at external institutions. The continued use of the de-identified data and de-identified biospecimens through collaborative research is in accordance with the mission of the NCI when it funded the BCFR in 1995, namely to support multi-disciplinary research on breast cancer etiology, outcomes, and prevention.

5) Storage of CCR data

The raw data obtained from the CCR for women newly diagnosed with breast cancer (2024-2027) or for women previously diagnosed with breast cancer (1995-2009) and from CCR linkage will be stored at Stanford University only and can accessed only by select staff who work for the PI. The raw CCR data are never shared with anyone or stored anywhere else. We have obtained a Data Security Letter DSL from Stanford University (see Attachment 8).

As described below under section “LINKAGES - DATA SHARING”, select de-identified transformed CCR variables are maintained in the BCFR central database. Clinical and vital status variables on study participants come from multiple sources, including questionnaires, medical records, pathology reports, cancer or death registries, etc). If data on clinical and vital status variables are missing from these sources, they are complemented with CCR data. All CCR data are transformed, except for histology, which comes from the CCR only. Transformed variables include, for example, year of diagnosis or age at diagnosis (instead of a full date of diagnosis), age at death (instead of a full date of death), or person-years of follow-up (instead of full dates of start and end of follow-up), depending on the research questions being investigated. Only transformed variables from multiple sources related to clinical characteristics or vital status are used in statistical analyses.

Please upload here any tables or charts related to your study procedures and any materials (such as surveys or interview questions) that will be presented to participants.

Attachment 3. NC-BCFR Consent Form	Consent Form
Attachment 4. NC-BCFR - Recruitment & Biospecimen Flowchart.pptx	Other Documents
Amendment approved by Dr. Schaeuble on December 2022. (1).pdf	Protocol

Amendment approved by Dr. Schaeuble on September 2023. (1).pdf	Protocol

RECORDING

Will audio or video recording occur?

No

DECEPTION

Will deception be used in this study?

No

CALIFORNIA HEALTH AND HUMAN SERVICES AGENCY (CHHSA) DEPARTMENTS LIST

Indicate any of the following CHHSA department(s)' involvement in providing research staff, funding and/or patients from State mental hospitals for this project.

you selected CDPH in this section. Is CDPH providing research staff, funding and patients from State mental hospitals for this project? Please re-check your response and if it is correct, disregard this comment. Thanks,

03/25/2024 • Sussan Atifeh • *Not* Internal • Resolved

Not applicable

STATE DEPARTMENT DATA/SPECIMENS

Choose the department(s) from which you are requesting data and/or specimens and provide the formal name of the database or specimen registry. After you have selected the department from the drop down and entered the formal name of the database or specimen registry, click 'add' and repeat to add additional data and/or specimens if applicable.

Agency	Provide the formal name of the data base or specimen registry.
California Department of Public Health	Greater Bay Area Cancer Registry

Study Population

POPULATION DESCRIPTION

Provide a full description of how human subjects will be involved in the research. Address characteristics of subjects such as: age; sex; ethnicity; and number of participants. Include requested participant number.

The Northern California BCFR cohort is comprised of over 10,000 individuals from over 4,000 families affected with breast cancer that have been enrolled and followed since 1996. As of February 2024, 5,160 cohort members remain in the Northern California BCFR (i.e., not deceased, not lost, not permanently withdrawn from the study).

Recruitment of women diagnosed with breast cancer under age 45 years and their first-degree and/or second-degree adult female relatives:

Under aim 1 and aim 3 of the renewal funding (2023-2028), our goal is to enroll 200 women diagnosed with breast cancer under age 45 years and their family members (at least one first-degree or second-degree female relative). We estimate we need to contact and administer the screening questionnaire to about 1,600 women with breast cancer. We will collect questionnaire data and biospecimen samples (blood, saliva, and urine). After the proband is enrolled and gives permission to contact her first-degree or second-degree adult female relatives, we will recruit the relatives. See the Study Procedures section for all research procedures involved.

The newly recruited probands will be females aged <45 years when diagnosed with breast cancer. Enrolled relatives will be females of similar ages, but may be up to age 79 years (if mothers or aunts are enrolled). The newly recruited probands will be primarily from racially and ethnically minoritized populations. Our goal is to enroll 200 women with breast cancer, including 25% African American, 25% Asian American, 25% Hispanic, and 25% non-Hispanic White. Enrolled relatives will have a similar race and ethnicity distribution.

DATABASE DETAILS

DATABASE DETAILS

List the database(s) to be used and the time period(s) being requested. This may include requests for future data that is not available at this time.

List the variables being requested, including a brief description of each variable.
Justify the need for each variable and for the quantity of data being requested.
You may also attach a list of variables on the next question.

Also address if participants will be involved in any other studies.

The California Cancer Registry (CCR) dataset derived from our case listings request with the Greater Bay Area Cancer Registry (GBACR) will include administrative, patient demographics, tumor characteristics, treatment, and hospital and physician information for each case. Attached is the list of variables with the justification listed for each item (see Attachment 5).

Transformed variables will be used, to the extent possible, to carry out our proposed research activities. For example, date of diagnosis will not be used; instead, age at diagnosis or year of diagnosis will be used in statistical analyses.

We plan to submit our initial case listing request upon approval by the CPHS IRB and GBACR/CDPH, followed by requests every 3-4 months for up to 4 years (2024-2027), or until we reach our recruitment goals. We estimate we need to contact and administer the screening questionnaire to about 1,600 women with breast cancer in order to recruit and enroll 200 new probands. Participants will have the opportunity to participate in future studies conducted by the Northern California BCFR.

If you have a list of variables with the details requested in the above question, attach that here. If you provided all details on the database in the question above, skip this question.

Attachment 5. GBACR - Case-Listing - Requested_Variables.xlsx	List of Variables

RATIONALE

RATIONALE

What is the rationale for studying the requested group(s) of participants?

SEER analyses have shown that the incidence of distant-stage breast cancer has been increasing among young women under age 40 years. The reasons underlying this trend remain uncertain. To gain knowledge about breast cancer in young women, the BCFR will enroll an additional 950 women diagnosed with breast cancer under age 45 years, including 200 cases from the San Francisco Bay Area. The number of 950 families was determined by the budget available for new recruitment and the other research activities outlined above.

RECRUITMENT DETAILS

Describe how potential subjects will be identified for recruitment. Examples include: class rosters; group membership; individuals answering an advertisement; organization position titles (e.g., presidents, web designers, etc.). How will potential participants learn about the research and how will they be recruited (e.g., flyer, email, web posting, telephone, etc.)?

Important to remember: subjects cannot be contacted before IRB approval.

The Northern California BCFR site will recruit young breast cancer cases through the population-based Greater Bay Area Cancer Registry that is part of the California Cancer Registry (CCR) and the SEER Program. We will request case listings for young women diagnosed with breast cancer before age 45 years in four counties (Alameda, Contra Costa, Santa Clara, and San Mateo). We will oversample young African American, Asian American, and Hispanic women.

Initial contact will be by an invitation letter sent by postal mail. The letter will describe the study and also explain how we obtained their information from the Greater Bay Area Cancer Registry, as required by the Cancer Registry. They will also receive the screening questionnaire to assess study eligibility. Attached is the recruitment workflow for the Northern California BCFR (see Attachment 4).

Once the study materials and questionnaires are finalized, we will submit them to CPHS for review and approval. Until then, no subject contact or new recruitment will take place.

Attach copies of all recruitment materials.

Attachment 4. NC-BCFR - Recruitment & Biospecimen Flowchart.pptx	Recruitment Materials

SCREENING

Will subjects be screened prior to entry into the research?

No

COMPENSATION

Will subjects be compensated for participating in the study?

Yes

Compensation type
Gift card

Explain the amount and schedule of compensation that will be paid for participation in the study. Include provisions for prorating payment. The amount should not be coercive.
Newly recruited young women and their female relatives will receive $25 for the completion of the baseline questionnaires and $25 for the provision of a biospecimen sample. Similar monetary incentives were offered to the probands and relatives enrolled in the Northern California BCFR between 1996-2011.

STUDY DURATION

STUDY DURATION

Estimate the probable duration of the entire study. This estimate should include the total time each subject is to be involved and the duration of each data collection about the subject.

E.G., This is a two-year study. Participants will be interviewed three times per year; each interview will last approximately two hours. Total approximate time commitment for participants is 12 hours.

The study activities will take place over the next four years and will be completed by April 2028.

1) Probands will be recruited in years 2-5. Young women with breast cancer will first complete a screening questionnaire (5-10 minutes). If eligible, they will be invited to sign the informed consent form (5-10 minutes); complete online baseline questionnaires on epidemiologic risk factors and cancer family history 6-9 months after diagnosis (30-45 minutes); provide a blood sample and a urine sample (time varies); complete a questionnaire on treatment, stress, quality of life, and other epidemiologic risk factors 9-12 months after the first questionnaire (30-45 minutes), and one follow-up questionnaire towards the end of the study (15-20 minutes); sign a release for the future collection of their digital mammograms, MRIs, and medical records (5-10 minutes); and to sign a HIPAA authorization form for the future collection of their medical records, pathology report, and a tumor tissue sample and to use of their residential address for geocoding that will be linked to geospatial databases (e.g., census neighborhood characteristics, environmental exposures) (5 minutes).

2) After the proband is enrolled and permits us to contact her first-degree and/or second-degree relatives, we will recruit the relatives in years 2-5. Relatives will also be invited to sign the informed consent form (5-10 minutes); complete the online baseline questionnaire on epidemiologic risk factors and cancer family history (30-45 minutes); provide a blood or saliva sample and a urine sample (time varies); complete follow-up questionnaires about 12 months after baseline and one follow-up towards the end of the study (15-20 minutes each); sign a release for the future collection of their digital mammograms, MRIs, and medical records (5-10 minutes); and sign a HIPAA authorization form for the future collection of their medical records, pathology report, and a tumor tissue sample if they have been diagnosed with breast cancer and to use of their residential address for geocoding that will be linked to geospatial databases (e.g., census neighborhood characteristics, environmental exposures) (5 minutes).

3) Linkage with the California Cancer Registry will take place in year 5.

4) Additional linkages with databases on neighborhood characteristics and environmental exposures may take place throughout the study.

Risks and Benefits

RISK DESCRIPTION

RISK DESCRIPTION

Provide a description of possible risks to participants: physical, psychological, social, economic, loss of data security, and/or loss of confidentiality. Describe and justify whether the research is minimal risk or greater than minimal risk.

This study is no more than minimal risk. Participants will not be subjected to any medical interventions that pose known physical harm. It is unlikely that the completion of study questionnaires will result in physical harm for study participants. For the blood draw, there is a slight possibility of bruising or soreness at the puncture site. Trained and experienced phlebotomists will collect blood samples to reduce this risk. The amount of blood to be collected (three 10-ml tubes) is small and should not pose any physical harm. There are minimal risks to providing a saliva sample, such as dry mouth, and providing a urine sample, such as but not limited to contamination due to spillage during collection at the clinic or at home. Participants will be provided with proper materials and instructions on how to obtain samples to minimize any possible risks.

Sometimes study participants get nervous or uncomfortable when answering questions about themselves, and it is possible that Northern California BCFR participants feel that way. Any psychological or emotional discomforts are expected to be minimal, based on our experience following the cohort since 1996. Participants will be reminded that they can terminate the interview at any time, decline to answer certain questions, and participate in all parts or only certain parts of the study.

There are no costs to participating in the Northern California BCFR cohort as a new recruit (young women) or in continued follow-up (already enrolled individuals). Participant burden will be minimized by collecting questionnaire data by mail, online or telephone interview. Breach of confidentiality that may result in economic hardship is unlikely. Thus any risk to economic well-being is likely minimal.

All data collected from individuals are treated confidentially. We expect the risk of loss of confidentiality to be minimal. To minimize such risk, all study materials, including completed questionnaires and biospecimen containers will be labeled with a numeric Study ID number only. All study-related databases will be password-protected and individual records will be identified by Study ID number only. The key to link Study IDs and biospecimen IDs with names and other PHI will reside in a password-protected tracking system maintained by the local BCFR Data Core at Stanford University, with access restricted to select staff. The consent form specifies that results from the laboratory analyses of the biospecimen samples will not be shared with participants, and that publications in scientific journals will only present summary statistics and no individual results. All staff, including field and office staff, are trained to follow confidentiality guidelines and keep all study materials in locked file cabinets.

MEDICAL SERVICE RISKS

MEDICAL SERVICE RISKS

Describe how medical services will be provided if subjects suffer adverse mental or physical effects as result of research activity. If no services provided, state that clearly.

No service will be provided.

INTERNATIONAL RESEARCH

Will this research occur outside of the United States or U.S. territories?

Check with client to see if they consider territories to be outside the U.S. or not, as this can vary between institutions.

No

LESS RISKY METHODS

Describe any less risky methods and why they are not being used.

This study is no more than minimal risk. Participants will not be subjected to any medical interventions that pose known physical or psychological harm. It is unlikely that the completion of study questionnaires will result in psychological harm for study participants. The amount of blood to be collected (three 10-ml tubes) is small and should not pose any physical harm.

BENEFITS

BENEFITS

Describe the benefits, if any, to the subjects or to society that will be realized as a result of this project. Discuss the benefits that may accrue directly to the subjects as well as to society. If there is no direct benefit anticipated for the subjects, state that clearly.

Continued or new participation in the Northern California BCFR will not result in any direct benefits to study participants. Analyses of the data and biospecimens collected for women with breast cancer and their relatives without breast cancer will lead to a better understanding of genetic, hormonal, lifestyle, and environmental factors that impact the risk of developing breast cancer and outcomes after diagnosis. No individual study results are shared with cohort members, unless the participant has selected the option to be notified about genetic results resulting from future research studies. Information on risk factors and prognostic factors is critical for primary prevention and improving outcomes, including survival. Thus, the research utilizing the BCFR data and biospecimens will benefit society as a whole.

JUSTIFICATION OF RISKS

Explain why study risks are reasonable in relation to the potential benefits to subjects and to society.

We anticipate that study risks are low to participants who provide data and biospecimens. Analyses of the data and biospecimens collected will contribute to a better understanding of the etiology and outcomes of breast cancer, and therefore will benefit society as a whole. Anticipated benefits outweigh potential risks.

Adminstrative Safeguards

PERSONALLY IDENTIFIABLE DATA (PID) INSTRUCTIONS

Protected Health Information/Personally Identifiable Data (PHI/PID) is defined as information in any format that identifies the individual, including demographic information collected from an individual that can reasonably be used to identify the individual. Additionally, PHI is information created or received by a healthcare provider, health plan, employer, or health care clearinghouse; and relates to the past, present, or future physical or mental health or condition of an individual, including any of the 18 HIPAA identifiers.

Note: Please be aware that individual participants may be identifiable by combining other items in the data even when none of the 18 HIPAA identifiers are present. Thus, a study may still contain PID even after removing or never acquiring the identifiers, and the investigator may still need to provide complete answers for the data security questions in the protocol.

If the researcher demonstrates that he or she is unable to comply with any of the requirements below, he or she may request an exception from these requirements. The researcher should indicate any measures that will be taken to address this requirement. The exception request should be made in the text box of the corresponding requirement. An exception will only be granted if the researcher can demonstrate that adequate alternative measures have been taken to minimize risks so as to justify the exception.

HIPAA IDENTIFIERS

Please identify which HIPAA Identifiers you plan to request as part of your submission.

Name
Address (all geographic subdivisions smaller than state, including street address, city county, and zip code)
All elements (except years) of dates related to an individual (including birthdate, admission date, discharge date, date of death, and exact age if over 89)
Telephone numbers
Any other characteristic that could uniquely identify the individual

TRAINING PROCEDURES

TRAINING PROCEDURES

Describe the procedures for training all research staff who have access to PID on privacy and security. Indicate if staff are required to sign a confidentiality statement related to general use, security, and privacy.

Study staff has worked with the data and biospecimens from the Northern California BCFR for many years and are well trained to keep all data confidential, to never share any PHI data or any of the 18 HIPAA identifiers with anyone, except when requesting pathology reports and tumor tissue samples from hospitals, and to release only de-identified data without any of the 18 HIPAA identifiers and de-identified biospecimen vials identified by numeric Study ID numbers. Staff will be periodically reminded of this protocol. The password-protected ACCESS tracking system maintained by the local BCFR Data Core at Stanford University is the only file that contains the key that links Study IDs to names of study participants and other PHI data. Only select staff who work for the PI, Dr. Esther John, has access to the tracking system. All study staff are required to complete the HIPAA/Protect Patient Privacy or HIPAA Privacy for Research course on an annual basis and the CITI (Collaborative Institutional Training Initiative) Course in The Protection of Human Research Subjects every 3 years.

In order to share select de-identified CCR and vital status variables without any of the 18 HIPAA identifiers with the BCFR central database and investigators at the six BCFR sites, the Co-PIs are in the process of getting the CCR Appendix 3 and the Information Privacy and Security Requirements (IPSR) Agreement signed at the institutions involved in this Multi-Institution Study. The signed Appendix 3 and IPSR Agreements are being assembled at Stanford University by the Northern California BCFR Research Manager. Additionally, all individuals at the six BCFR sites (e.g., co-investigators, biostatisticians, data analysts) who will access select de-identified CCR and vital status variables in order to perform the statistical analyses for approved projects will be required to sign the CCR Appendix 2 and to submit the signed form to the BCFR Data Coordinating Center and the Northern California BCFR Research Manager at Stanford University before select de-identified CCR and vital status variables without any of the 18 HIPAA identifiers will be released. The signed Appendix 2 forms will be maintained at Stanford University by the Northern California BCFR Research Manager and an updated Assessee List will be submitted annually to the GBACR, as required. The Co-PI at each BCFR site will also submit updated copies of the Appendix 2 to the CCR annually, if there are any changes to the roles of individuals who analyze the de-identified data.

In order to share select de-identified CCR and vital status variables for approved projects with investigators external to the six BCFR sites, the CCR Appendix 3 and the IPSR Agreement will need to be signed by the recipient institutions, and CCR Appendix 2 will need to be signed by all individuals (e.g., co-investigators, biostatisticians, data analysts) who will access select de-identified CCR and vital status variables in order to perform the statistical

analyses for approved projects. The de-identified dataset with the select de-identified CCR and vital status variables without any of the 18 HIPAA identifiers will be shared with the external investigators by the local BCFR Data Core at Stanford University after receipt of the signed forms (CCR Appendix 3, Appendix 2, IPSR). The signed Appendix 2 forms will be maintained at Stanford University by the Northern California BCFR Research Manager and an updated Assessee List will be submitted annually to the GBACR, as required.

STAFF VETTING PROCEDURES

Describe procedures, either background check or thorough reference check, for vetting staff who will have access to PID.

Prior to hiring staff, all staff will undergo background checks and reference checks. The existing Northern California BCFR study staff are long-term employees who have worked on multiple research projects at Stanford. They participate in annual human subjects' protection and confidentiality training to ensure they are up-to-date and compliant with state and federal policies.

Access to electronic data is limited to designated study staff of the Northern California BCFR who are required to sign the Confidentiality Agreement (Appendix 2). The importance of keeping all data strictly confidential is emphasized during staff training and throughout the study.

SUPPORT LETTER

Obtain and submit a department support/data release letter.

Please note:

The Support Letter for release of cancer registry data must always come from CDPH/CCR. The reason for this is that CA law requires CCR to approve all data releases from the regional cancer registries for research purposes. CCR is responsible for reviewing the research, approving the data release, and ensuring that the data are released in compliance with all applicable state laws. Please attach a support letter from CCR. Thanks,

03/25/2024 • Sussan Atifeh • *Not* Internal • Resolved

This is a statement from the state agency or department you are receiving data from. It must be on that agency's/department's letterhead and should include both

1) *that the release of the desired data is legal and*

2) *that the entity is willing to release the desired data to you, the researcher. If you are not receiving data, this letter should indicate that you are supported.*

***For VSAC requests, if you do not have a Departmental Letter of Support (LOS)/Data Release, you may upload a copy of the Data Request Form (application) from the department to secure a review for the upcoming cycle. The protocol will not be approved until the LOS is uploaded to the protocol.*

Please also review the CPHS Statement for Birth and Death Data.

Attachment 6. CPHS_LOS_John, E - CCR.pdf	Department Letter of Support

PREVENTING RE-USE AND UNAUTHORIZED ACCESS

Explain how you will ensure that data will not be reused or provided to any unauthorized person or entity.

Unauthorized means that the person or entity does not have a need to access the data for purposes of the research project approved by CPHS.

In order to share select de-identified CCR and vital status variables for approved projects with investigators external to the six BCFR sites, the CCR Appendix 3 Confidentiality Agreement and the Information Privacy and Security Requirements (IPSR) Agreement will need to be signed by the recipient institutions, and CCR Appendix 2 will need to be signed by all individuals (e.g., co-investigators, biostatisticians, data analysts) who will access select de-identified CCR and vital status variables in order to perform the statistical analyses for the approved projects. The de-identified dataset with the select CCR and vital status variables without any of the 18 HIPAA identifiers will be shared with the external investigators by the local BCFR Data Core at Stanford University after receipt of the signed forms (CCR Appendix 3, Appendix 2, IPSR). The signed Appendix 2 forms will be maintained at Stanford University by the Northern California BCFR Research Manager and an updated Assessee List will be submitted annually to the GBACR, as required.

CONFIDENTIALITY OF PUBLISHED DATA

Indicate whether information will be published that could possibly be used to identify an individual subject.

No study results will be released or published with identifying information. Scientific publications will present statistical summaries only, no study participants will be identified by name or other PII. No information will be published that could be used to identify individual study participants.

DATA REQUEST JUSTIFICATION

Provide adequate justifications for the quantity of the data, the years and the variables being requested. Have you requested no more than the minimum necessary data to perform the research?

The California Cancer Registry (CCR) dataset derived from the case listings request with the Greater Bay Area Cancer Registry (GBACR) will allow our research team to recruit young women with breast cancer and enroll them in the Northern California BCFR. Specifically, we will enroll 200 new probands who were diagnosed with breast cancer before age 45 years in four counties in the San Francisco Bay Area. We plan to submit our initial case-listing request in mid-2024 and then every 3-4 months for up to 4 years (2024-2027), or until our recruitment goals are met. We estimate we need to contact and administer the screening questionnaire to about 1,600 women with breast cancer. Participants may have the opportunity to participate in future studies conducted by the Northern California BCFR.

All data items requested from the CCR will be used to carry out research activities. We will request administrative and patient demographic information such as full name, age, race, ethnicity, address, and age of diagnoses along with tumor characteristics and stage at diagnosis data to help our research team identify and recruit potentially eligible young women who were diagnosed with a first primary breast cancer before the age of 45 years in one of the four Bay Area countries. Tumor characteristics and stage at diagnosis date will also help us characterize the tumor and confirm the diagnosis reported by the participants. Treatment data will be used to confirm the treatment data collected from study participants and fill in any missing information. Treatment and clinical data will be used to address research questions such as associations with survival and other outcomes. Lastly, we will request hospital and physician information to request pathology reports and other medical records in the future. The requested CCR variables and justifications can be found in the attachments (see Attachment 5).

LIMITATIONS TO DATA ACCESS

LIMITATIONS TO DATA ACCESS

Indicate if access to data is limited only to those with a need to know for purposes of implementing or evaluating the research.

Access to CCR data at Stanford University will be limited to the project staff minimally necessary to successfully complete the objectives of the approved protocol. Access privileges will be documented and updated regularly reflecting any change of change of staff.

In order to share select de-identified CCR and vital status variables for approved projects with investigators external to the six BCFR sites, the CCR Appendix 3 and the IPSR Agreement will need to be signed by the recipient institutions, and CCR Appendix 2 will need to be signed by all individuals (i.e., co-investigators, biostatisticians, data analysts) who will access the de-identified analytic dataset in order to perform the statistical analyses for the approved projects. The de-identified dataset with the select de-identified CCR and vital status variables without any of the 18 HIPAA identifiers will be shared with the external investigators by the local BCFR Data Core at Stanford University after receipt of the signed forms (CCR Appendix 3, Appendix 2, IPSR). The signed Appendix 2 forms will be maintained at Stanford University by the Northern California BCFR Research Manager and an updated Assessee List will be submitted annually to the GBACR, as required.

PROTECTION AGAINST SMALL CELL SIZES AND ASSOCIATED PROBLEMS

Describe appropriate and sufficient methods to protect the identity of individual subjects when small cells or small numbers and/or data linkage to another data set are involved in the research project.

No results will be released or published with identifying information on cancer patients or participating their relatives and all data will be presented as statistical summaries such that individuals cannot be identified.

LINKAGES

LINKAGES

Will the data set be linked with any other data sets?

Yes

Identify all data sets and each of the variables to be linked, with a brief description of each variable and justification for each linkage. If there is an extensive list, you may attach that list in the next question and indicate such here.

The Northern California BCFR Cohort is currently comprised of over 10,000 individuals from over 4,000 families that have been enrolled in the study and followed since 1996 through follow-up questionnaires and several linkages with the California Cancer Registry (CCR) (CPHS protocol 13-03-1143). Unlike in previous years, there will no longer be active follow-up of the existing Cohort except for ancillary studies with subsets of Cohort members. Instead, we will continue to follow existing Cohort members through data linkages with the CCR, the Virtual Tumor Registry, and the National Death Index to identify new cancers (cancer site, date of diagnosis, tumor characteristics, first-course treatment) or confirm previously self-reported cancers, update vital status and date of last follow-up, and obtain data on vital status and death outcomes (date of death, underlying cause of death) for deceased probands and family members. We will include the newly recruited families in these data linkages. In addition, linkages may be performed in the future with geospatial databases on neighborhood characteristics and environmental exposures. We will seek IRB approval before any specific linkages are carried out. For the existing BCFR Cohort, we plan to ask for waivers of consent. It would not be feasible to re-consent over 10,000 cohort members. For the newly recruited families, the new consent form will include participant consent to be included in data linkages.

DATA SHARING

Data Sharing with the BCFR Central Database required by NCI

The BCFR Cohort is a Multi-Institution Study and was established in 1995 to support multi-disciplinary research on breast cancer etiology, outcomes, and prevention. With continuous funding since 1995, NCI provided financial support to recruit and follow families affected with breast cancer at six international BCFR sites in the U.S., Canada, and Australia. Additionally, NCI provided funding for and contingent upon assembling and maintaining all collected data in a central database. Each renewal funding cycle included funding for the BCFR Data Coordinating Center (DCC) to maintain the BCFR central database. The BCFR central database is key to efficient statistical analyses of the extensive de-identified data collected for BCFR Cohort members, thereby maximizing the impact of the data collection efforts for nearly three decades. De-identified baseline and follow-up data collected for the families at the six BCFR sites, identified by numeric Study ID only, are submitted to the BCFR central database on a regular basis. The BCFR central database also contains de-identified data generated by collaborative studies

led by external investigators (e.g., genetic variants, blood biomarkers, tumor characteristics from tumor tissue analyses). All data are de-identified with a unique numeric study identification number assigned to each study participant at study enrollment. Personal identifiable information (i.e., name, address, phone number, email address) are never submitted to the BCFR central database, such data remain at the recruitment sites only. Only de-identified data are submitted to the BCFR central database.

The current BCFR DCC is located at the Columbia University, the home of the New York BCFR site. The DCC has implemented a comprehensive system for processing, quality controlling, storing, and distributing de-identified core data for approved projects as well as to ensure the quality, accuracy, and completeness of any BCFR data elements collected; implemented data dictionaries and standards for all data collection instruments; and established quality control procedures ensuring transmission of high-quality data from each data collection site to the BCFR central database. The DCC developed a secure web upload tool for study sites to encrypt and upload their de-identified data files quarterly to ensure that data exchanges occur without risk of data security breaches and to receive secure and direct feeds of all newly collected online data. The DCC established quality control protocols for the incorporation of all app-based data. The DCC runs extensive computer edits on transmitted data and posts the resulting edit discrepancies at each site on a secure website. The DCC team implements quality control via a data framework that validates the submitted de-identified data against very strict business logic requirements. Deviations identified from tiers of validation checks (e.g., Quality Control Tool (QCT)) are reported as errors, which trigger follow-up actions at each BCFR site. The DCC also derives analytic variables, including risk scores, and has integrated genomic data.

One of the functions of the BCFR DCC is to prepare and share de-identified analytic datasets with investigators who have BCFR approval to perform specific statistical analyses addressing research questions regarding etiology, outcomes, and prevention of breast cancer, as well as research methodology. The BCFR has a process in place for internal (based at the six BCFR sites) and external researchers to apply for statistical analysis of de-identified BCFR data and/or use of de-identified biospecimens for collaborative research. Instructions for requesting data and/or biospecimens using a streamlined online application system are available on the public BCFR website https://www.bcfamilyregistry.org/ The Executive Committee, comprised of the Co-PI at each BCFR site and the leader of the DCC, reviews applications on a rolling basis. For approved projects, the DCC prepares the de-identified analytic datasets which are securely transferred to collaborating investigators upon IRB approvals and signing of Data Use Agreements (DUA). All BCFR sites, including Stanford University, have signed a multi-way DUA with Columbia University which allows the sharing of de-identified data for approved analyses.

Sharing of select de-identified CCR and vital status variables

Select clinical variables on cancer diagnoses and outcomes (e.g., date of breast cancer diagnosis, stage, grade, laterality, histology, behavior, tumor size, ER/PR/HER2 status, first-course treatment, subsequent primary

cancers, vital status, date and underlying cause of death if deceased) are essential data items depending on the research questions being investigated (for example, investigations of risk factors for breast cancer subtype defined by ER/PR/HER2 status; investigation of prognostic factors associated with worse survival after breast cancer diagnosis). At the Northern California BCFR site, the above clinical data are obtained from the CCR and may be combined with other data sources (e.g., self-report on questionnaires, medical records, pathology reports, National Death Index, etc.). Select de-identified CCR and vital status variables are submitted to the BCFR central database. Attachment 7 shows the clinical and vital status variables that are maintained in the BCFR central database. They come from multiple sources across the 6 BCFR sites (i.e., questionnaires, medical records, pathology reports, cancer or death registries, etc). In the Northern California BCFR, missing data from these sources are complemented with CCR data. All variables are transformed, except for histology, which comes from the CCR only. Full dates (i.e., date of cancer diagnosis, date of death) are never shared with approved investigators. Only transformed variables are shared, such as year of diagnosis, age at diagnosis, age at death, or person-years of follow-up, depending on the research questions being investigated.

Sharing of select de-identified CCR and vital status variables with investigators within the BCFR:

In order to share select de-identified CCR and vital status variables with investigators at the six BCFR sites collaborating in this Multi-Institution Study since 1995, the Co-PIs are in the process of getting the CCR Appendix 3 and the Information Privacy and Security Requirements (IPSR) Agreement signed at their institutions. The signed Appendix 3 and IPSR Agreements are being assembled at Stanford University by the Northern California BCFR Research Manager. Additionally, all individuals at the six BCFR sites (e.g., co-investigators, biostatisticians, data analysts) who will access select de-identified CCR and vital status variables in order to perform the statistical analyses for approved projects will be required to sign the CCR Appendix 2 and submit the signed form to the BCFR Data Coordinating Center before select de-identified CCR and vital status variables will be released. The Co-PI at each BCFR site will be required to submit updated copies of the Appendix 2 to the CCR annually, if there are any changes to the roles of individuals who analyze the de-identified data. The Research Manager of the Northern California BCFR will also keep track of signed Appendices 2 and submit an updated Assessee List annually to the GBACR, as required.

Sharing of select de-identified CCR and vital status variables with investigators external to the six BCFR sites:

In order to share select de-identified CCR and vital status variables for approved projects with investigators external to the 6 BCFR sites, the CCR Appendix 3 and the IPSR Agreement will need to be signed by the recipient institution, and the signed forms need to be submitted to the PI of the Northern California BCFR site. Additionally, individuals (e.g., co-investigators, biostatisticians, data analysts) who will access select de-identified CCR and vital status variables in order to perform the statistical analyses for approved projects will be required to sign the CCR Appendix 2. The de-identified

dataset with the select de-identified CCR and vital status variables without any of the 18 HIPAA identifiers will be shared with the external investigators by the local BCFR Data Core at Stanford University after receipt of the signed forms (CCR Appendix 3, Appendix 2, IPSR). The Research Manager of the Northern California BCFR will keep track of signed Appendices 2 and submit an updated Assessee List annually to the GBACR, as required.

Data Sharing mandated by NIH

In compliance with NIH funding requirements, the BCFR adheres to a data-sharing policy that aligns with the NIH Data Sharing Policy (NOT-OD-03-032) and the Common Rule (45 CFR Part 46). The BCFR's data-sharing policy is also consistent with CDPH CCR's Health and Safety Code §103885. As part of renewal funding conditions, the BCFR is required to submit select de-identified data variables to a data repository. The BCFR selected the Database of Genotypes and Phenotypes (dbGaP) for required data deposition. The de-identified data submitted to dbGaP include primarily baseline questionnaire data on epidemiologic risk factors and dietary intake, and select variables related to a cancer diagnosis, including tumor site (ICD-O-3 code), laterality, histology, behavior, age at diagnosis, person-time or survival-time (in years) for breast cancer and ovarian cancer.

Individual-level data in dbGaP are considered controlled access, and researchers can apply to access de-identified BCFR data via the dbGaP website. Access is granted following review and approval by the NCI Data Access Committee, and researchers must comply with the BCFR's Data Use Certification Agreement (https://dbgap.ncbi.nlm.nih.gov/aa/wga.cgi?view_pdf&stacc=phs002835.v1.p1) for analyzing these de-identified BCFR data.

Attach a copy of the document detailing all data sets and each of the variables to be linked. If you provided this information in the answer to the above question, skip this question.

Attachment 7. Clinical Variables in BCFR Central Database 3-7-2024.docx	Other Documents

Will a third party be used for data linkage?
No

DESTRUCTION OF PID VERIFICATION

Indicate that you will provide CPHS with a letter certifying that PID has been destroyed and/or returned to the data source once research is concluded.

Yes

DATA SECURITY LETTER

DATA SECURITY LETTER

You have attached one Data Security Letter (DSL) from the Stanford University. Please confirm in the "Purpose" or "Procedures" sections of this application that Stanford University is the only site of servers, data storage, analysis and linkage for this study. Thanks,

03/25/2024 • Sussan Atifeh • *Not* Internal • Resolved

Upload a certification/statement from the Chief Information Officer, Privacy Officer, Security Officer or equivalent position of the researcher's institution that CPHS Data Security Standards are met.

- *Data security letters cannot be signed by the Principal Investigator or Responsible Official.*
- *The data security letter must be on your institution's letterhead.*
- *Example of data security letter*

Attachment 8. Data Security Letter CPHS EJohn, 2024-0312.pdf	Data Security Letter

Physical Safeguards

DATA PROTECTION

Indicate that research records and physical samples will be protected through the use of locked cabinets and locked rooms; PID in paper form will not be left unattended unless locked in a file cabinet, file room, desk, or office.

Yes

DATA DESTRUCTION

Will data/samples will be destroyed or returned as soon as it is no longer needed for the research project.

Yes

RETAINED DATA

Will the retained data/samples have personal identifiers or be de-identified?

data will be de-identified

Explain what identifiers will be removed and how.
Data and biospecimens are labeled by unique numeric Study IDs assigned to study participants when they were enrolled in the Northern California BCFR between 1995-2011. New recruits (2024-2027) will be assigned Study IDs and biospecimen IDs, as we have done in the past, and tracked in the ACCESS tracking system maintained by the local BCFR Data Core at Stanford University. These Study IDs are numeric and do not contain any names or other information that could be linked to study participants.

DESTRUCTION METHODS

Describe how you will ensure the PID in paper form is disposed of through confidential means, such as cross cut shredding or pulverizing.

When no longer required, papers containing confidential information will be placed in the confidential shredder bins at Stanford University that provide for secure document destruction.

FAXING

Describe how you will ensure that faxes with PID are not left unattended and fax machines are in secure areas.

Faxing will be sent electronically through Cardinal Fax, which is approved by the Stanford Information Security office to send and receive high risk PHI data. No physical/paper copies of PID will be sent or received by fax. Study staff are trained to enter "SECURE:" in the subject line for any faxes that can may contain PHI or highly sensitive information. Outgoing faxes need to contain the minimum necessary amount of confidential data required for the intended communication, reducing risks of identification and unintended disclosure.

Receiving faxes will be delivered to a designated study fax number that is connected to a study email address. Only designated study staff will have access to the email inbox to receive and open faxes. Care will be taken not to leave faxes with PHI information open on the computer monitor. If printed, the faxes will be picked up and placed in a locked cabinet or placed in a shredder bin for secure document destruction when no longer in use.

MAILING

Indicate whether mailings of PID are sealed and secured from inappropriate viewing; and whether mailings of 500 or more individually identifiable records of PID in a single package, and all mailings of PID to vendors/contractors/co-researchers, are sent using a tracked mailing method, which includes verification of delivery and receipt, such as UPS, U.S. Express Mail, or Federal Express, or by bonded courier.

When mailing confidential information, staff will place the confidential data inside an envelope, seal the envelope, stamp it "confidential," and place it in a mailing envelope. A stamp "confidential" is also used on the enclosed business reply envelope and on the mailing envelope. Stanford has an account with Federal Express which enables tracking information and verification of delivery and receipt. Outgoing mail needs to contain the minimum necessary amount of confidential data required for the intended communication, reducing risks of identification and unintended disclosure.

ELECTRONIC STORAGE

State whether PID in paper or electronic form, e.g., stored on laptop computers and portable electronic storage media (e.g., USB drives and CDs), will ever be left unattended in cars or other unsecured locations.

Personally Identifiable Data (PID) in paper or electronic form, e.g., stored on laptop computers and portable electronic storage media (e.g., USB drives and CDs) will never be left unattended in cars or other unsecured locations. All computers or mobile devices used for the study are encrypted and monitored by Stanford University IT. If lost or stolen, the University's IT team can lock the devices and remotely wipe all data from the devices.

PHYSICAL STORAGE

Describe whether facilities, which store PID in paper or electronic form, have controlled access procedures, and 24 hour guard or monitored alarm service.

All paper containing PID will be stored in a locked cabinet in a badge access-only facility on Stanford's campus. This facility remains locked at all hours. Campus security services are provided 24 hours a day and 7 days a week. Study lab access is restricted to specific, authorized persons. Access to the lab where specific samples are stored is restricted to approved staff with authorized badge access. All biospecimen samples are labeled with a study ID and do not contain any PID.

SERVER SECURITY

SERVER SECURITY

Provide a description of whether all servers containing unencrypted PID are housed in a secure room with controlled access procedures.

Study staff will store databases and files that may contain unencrypted PID in Stanford Medicine Box. Medicine Box is a file sync and share service for the Stanford Health community. It includes special technologies to secure Protected Health Information. It is approved by the Stanford Information Security Department to store PHI (Protected Health Information) or PII (Personally Identifiable Information). Computers accessing PHI must meet HIPAA safe harbor requirements. Desktops and laptops must be protected by full disk encryption (BitLocker Drive Encryption).

Our Northern California BCFR ACCESS database at Stanford University that contains PII for the over 10,000 study participants is hosted on Microsoft Azure and managed by the Stanford's Technology Consulting Group (TCG). Access to the database is granted to specific research team members only. There is no public access to the data. Access is regulated by an Azure access group policy open to Stanford's VPN pool of IPs. Log-in requires two-factor authentication. Azure SQL service encrypts all data at rest: https://docs.microsoft.com/en-us/sql/relational-databases/security/encryption/transparent-data-encryption-azure-sql?view=azuresqldb-current though we are choosing to have Microsoft manage the keys automatically. Account access to the SQL instance and administration is managed by Active Directory and our Office 365 Group tcg-azure-estherjohn@office365stanford.onmicrosoft.com which TCG manages: See: https://docs.microsoft.com/en-us/azure/sql-database/sql-database-aad-authentication.
The TCG team enabled Azure’s Advance Threat Protection: https://azure.microsoft.com/en-us/features/azure-advanced-threat-protection/ and server Auditing Service: https://docs.microsoft.com/en-us/azure/sql-data-warehouse/sql-data-warehouse-auditing-overview. TCG separately integrates the Azure account with the CloudCheckr application in order to audit configuration changes and to ensure security parameters are met.

STORING IDENTIFIERS

STORING IDENTIFIERS

Indicate whether identifiers will be stored separately from analysis data.

Personal Identifying information such as names, addresses and phone numbers and the link to numeric study IDs are stored in the Northern California BCFR study ACCESS tracking database maintained by the local BCFR Data Core at Stanford University. This tracking database is password-protected and accessible only to designated study staff. This is the only file that contains the link between Study IDs and study participants' personal identifying information.

DISK STORAGE

State whether all disks with PID will be destroyed.

NA

Electronic Safeguard

COMPUTER ACCESS OVERVIEW

State whether all computer access will be protected through the use of encryption, passwords, and other protections.

All computer access will be protected through the use of encryption, passwords, and other protections.

FIPS 140-2 COMPLIANCE: WORKSTATIONS

Indicate whether all workstations that contain PID have full disc encryption that uses FIPS 140-2 compliant software. If not, explain why not and what encryption will be used.

All workstations are protected using the Stanford Whole Disk Encryption (SWDE). The SWDE service is for both Windows and Macintosh desktop and laptop computers that support native encryption. The purpose of the Stanford Whole Disk Encryption (SWDE) service is to protect Moderate and High-Risk Data that must be stored on faculty and staff computers. Once installed, all files are automatically encrypted. The data are protected while the computer is in standby or hibernation mode as long as the hard disk is password-protected.

FIPS 140-2 COMPLIANCE: LAPTOPS

FIPS 140-2 COMPLIANCE: LAPTOPS

Indicate if all laptops that contain PID have full disc encryption that uses FIPS 140-2 compliant software. If not, explain why not and what encryption will be used.

All laptop and desktop computers that are being used for the study are protected using the Stanford Whole Disk Encryption (SWDE). The SWDE service is for both Windows and Macintosh desktop and laptop computers that support native encryption. The purpose of the Stanford Whole Disk Encryption (SWDE) service is to protect Moderate and High-Risk Data that must be stored on faculty and staff computers. Once installed, all files are automatically encrypted. The data are protected while the computer is in standby or hibernation mode as long as the hard disk is password-protected.

FIPS 140-2 COMPLIANCE: REMOVABLE MEDIA DEVICES

Indicate if PID on removable media devices (e.g. USB thumb drives, CD/DVD, smartphones, backup recordings) are encrypted with software that is FIPS 140-2 compliant.

Our study complies with University Policy that states that ALL electronic devices, including computers (laptops and desktops, OFFICE or HOME), smartphones, tablets, external hard disks, USB drives, etc. that may hold identifiable participant data, will be password protected, backed up, and encrypted. See http://med.stanford.edu/datasecurity/ for more information on the Data Security Policy.

SECURITY PATCHES

Indicate if all workstations, laptops and other systems that process and/or store PID have security patches applied in a reasonable time frame.

Stanford University uses IBM BigFix to deploy patches and updates to Windows and Macintosh computers. BigFix is administered by the Information Security Office in collaboration with IT organizations across the University. BigFix will apply security patches within seven days of publish. Back up user data at least daily. Backup data are encrypted in transit and at rest.

PASSWORD CONTROLS

Indicate if sufficiently strong password controls are in place to protect PID stored on workstations, laptops, servers, and removable media.

At Stanford, all systems that rely solely on user and password for authentication must confirm to Stanford's Password Policy Requirements:
- 8-11: mixed case letters, numbers, & symbols
- 12-15: mixed case letters & numbers
- 16-19: mixed case letters
- 20+: no restrictions

It must not be equal to your current password, previous passwords, SUNet ID, or password reset answer. It must not be a single word that appears in the dictionary (English or non-English). It must be composed only of characters in the Roman alphabet, numbers, or symbols on the US keyboard. Examples include characters such as # $ % ! @.

ELECTRONIC SECURITY CONTROLS

Indicate if sufficient system security controls are in place for automatic screen timeout, automated audit trails, intrusion detection, anti-virus, and periodic system security/log reviews.

The operating system will initiate a session lock after a 15-minute period of inactivity. A screensaver must be enabled and set to require a password to unlock. Cardinal Protect provides an all-in-one managed secure desktop that includes modern endpoint management, enhanced threat detection, and automatic backups for optimal data protection. Cardinal Protect systems is highly secured and monitor endpoints designed to defend both the device and user against advanced cyber threats. It uploads a transcript of system events like program launches and network connections to a cloud-based detection infrastructure, and those logs are used to detect threats. The CrowdStrike agent continues to protect systems even while they are offline. The system is centrally managed by the Stanford University IT. For more information: https://uit.stanford.edu/service/cardinalprotect.

FIPS 140-2 COMPLIANCE: ELECTRONIC TRANSMISSION

Explain whether all transmissions of electronic PID outside the secure internal network (e.g., emails, website access, and file transfer) are encrypted using software which is compliant with FIPS 140-2.

Data transfer of identifiable information between Stanford and the GBACR will be done only via secured FTP, which is FIPS 140-2 compliant. Data are encrypted at rest and in transit.

INTERNET ACCESSIBILITY

INTERNET ACCESSIBILITY

Note if PID in an electronic form will be accessible to the internet.

Data will not be accessible to the internet.

DISPOSING OF PID

When disposing of electronic PID, indicate whether sufficiently secure wiping, degaussing, or physical destruction will be used.

Upon close-out of the study, all electronic PIDs will be sanitized per the University policy: https://uit.stanford.edu/security/data-sanitization. The guidance is derived from the government's National Institute of Standard and Technology guideline on media sanitization (https://ws680.nist.gov/publication/get_pdf.cfm?pub_id=917935).

Conflict of Interest Information

CONFLICT OF INTEREST (COI) INSTRUCTIONS

A COI is defined as any financial or other relationships of the researcher(s) or the institution that could be perceived as affecting the objective conduct of the research, including the interpretation and publication of the findings. Researchers must disclose any COI, including perceived COI.

Financial relationships to be disclosed include but are not limited to the following:

- **Present or anticipated ownership of stock, stock options, or other financial obligations of the source of funding.**
- **Receipt or expectation of payment of any sort in connection with papers, symposia, consulting, editing, etc. from the source of funding.**
- **The sale or licensing or anticipated sale or licensing of medical or other products or intellectual property, such as patents, copyrights, or trade secrets to the source of funding or other entities.**
- **Any past, present or anticipated receipt of money or other valuable consideration from the source of research funding by the researcher(s), the family of the researcher(s), the research institution, or by an institution in which the researcher(s) or the family of the researcher(s) has an interest as owner, creditor, or officer.**

DISCLOSURES

Does any member of the study team, members' spouses, or members' dependent children have any significant financial interests related to the work to be conducted as part of the above-referenced project?

No

Informed Consent Procedures

INFORMED CONSENT PROCEDURES

Provide a description of procedures to be used in obtaining and documenting informed consent from participants.

See instructions and examples on CPHS website.

Young women with breast cancer will be sent an invitation letter to join the Breast Cancer Family Registry, along with an eligibility screening questionnaire. Women will be asked to complete and return the screening questionnaire or to complete the screening questionnaire online by using the URL link we provide in the letter. If eligible and interested in the study, they will be invited to sign the informed consent form and HIPAA Authorization form in REDCap. They may use their personal mobile phone, electronic tablet, laptop or desk computer to read the consent form and to sign these forms with an Electronic Signature. They can either use their finger or mouse/stylus to sign.

The email to prospective participants includes the contact information of Family Registry staff, who have been properly trained in obtaining informed consent, and can be contacted if the participant has questions regarding the consent form or about the study.

The email invitation to participate in the Family Registry will include an attachment that contains a copy of the consent form. That way the young women can read the consent form before they enter the e-consent procedure. If they have questions about the study procedures or any other aspect of the study, they will be able to contact a staff member. It is possible that women who do not understand the consent form because they are not competent will not further pursue enrollment in the study.

Please find attached the informed consent form for the Northern California Breast Cancer Family Registry (NC-BCFR) (see Attachment 3).

All other recruitment materials are currently in development by the site Co-PIs and staff. Before we begin recruitment, we will submit for IRB review (at Stanford and CPHS) all documents that will be used for the new family recruitment for review and approval.

CONSENT FORMS

CONSENT FORMS

Attach copies of consent forms and any other documents or oral scripts used to inform potential research subjects about the study. See examples of consent and assent forms on the CPHS website.

For projects with Human Subjects' Contacts, all recruitment materials should be attached before assigning the application to the CPHS reviewers. Please attach a copy of the consent form(s) before resubmitting the application. Thanks,

03/25/2024 • Sussan Atifeh • *Not* Internal • Resolved

Be sure to include a concise explanation of key information for participants at the beginning of your consent form, as shown in the examples on the website. Also attach the Participant's Bill of Rights (download the revised version from the same CPHS website). CPHS may approve the use of a consent procedure which does not include, or which alters, some or all of the elements of informed consent. If a waiver or alteration of informed consent is being requested, attach a document that explains how all of the criteria below will be satisfied.

Attachment 3. NC-BCFR Consent Form - Case 3-26-2024.docx	Consent Form

HIPAA Determination

HIPAA INSTRUCTIONS

To determine if this project is covered by HIPAA, answer the following questions.

COVERED ENTITY

Will health information be obtained from a covered entity, known as a clearinghouse, such as Blue Cross, that processes or facilitates processing health data from another entity, including but not limited to state databases?

No

HEALTHCARE PROVISIONS

Will the study involve the provision of healthcare by a covered entity, such as the UCD Medical Center?

No

OTHER HIPAA CRITERIA

Will the study involve other HIPAA criteria not listed above?

No

Cover Letter and PI Signature for PI Submission

BUDGET

Does this project have a budget?

Yes

Attach a copy of your project budget here

Attachment 9. Subcontract Agreement-RENEWAL-137092.pdf — Project Budget

COVER LETTER

Attach a copy of your project cover letter.

Cover letter must have the requesting institution's letterhead.

Attachment 10. Cover letter to CPHS 5-2-2024.docx — Cover Letter

In order for the PI to review and sign this form, you will need to click "Next" and on the next page, click "Submit." At that point the PI will receive notification that will need to review the application and if they request changes, they will return the form to you and you will receive an email notification.

Calculated Field for agency plus data set *(Internal)*

California Department of Public Health: Greater Bay Area Cancer Registry

PI Signature for Coordinator Submission (Initial) - Submitted 05/02/2024 2:01 PM ET by Esther John, PhD

PI Review

Please click "Next" and "Submit" in order to submit this application, regardless of whether or not it is ready for review. If you indicated it is ready for review, it will go to the Responsible Official for review and signature, and if not, it will be returned to the individual who completed the form for changes.

Is this application ready to be reviewed by the IRB? If not, choose no to have the application sent back to the coordinator for revisions.

Yes

To sign this form, enter your IRBManager password. By signing this form, you are indicating that the information within this application is accurate and reflects the proposed research and that you attest to the conflict of interest disclosures for all study team members.

Signed Thursday, May 2, 2024 2:01:29 PM ET by Esther John, PhD

Responsible Official Signature
- Submitted 03/18/2024 5:10 PM ET by Kathleen Thompson

Responsible Official Signature

After reviewing this application, is it ready for submission to the CPHS IRB?

Yes, ready for submission to IRB.

Enter your password to sign this protocol. By signing this protocol, you are attesting that the information within is accurate and reflects the details of the proposed research project.

Signed Monday, March 18, 2024 5:09:56 PM ET by Kathleen Thompson

After choosing whether or not the submission is ready for CPHS IRB review, please click "next" and "submit" (on the next screen) to move the form forward to the CPHS IRB or back to the Researcher.

Notify IRB for Pre-Screening
- Submitted 05/02/2024 4:31 PM ET by Sussan Atifeh

Internal IRB Screening

CPHS Office: The questions on this page will appear every time the project is resubmitted to the CPHS IRB (even after review). Once the project has been reviewed by a committee member, unless researcher has changed questions on the form that impact the level of review, you do not need to update the questions here. If the changes made are not clear and require additional clarification change the 'ready for review' to 'no' and require changes. When you change the answer back to yes, it will remember your previous answers.

Is this study ready to be reviewed by the CPHS panel?

Yes

Choose the IRB committee to review this study (this defaults to CPHS)

CPHS

Level of Review Determination (once the level of review is assigned for this project, do not change this answer unless the reviewer/committee has decided that the study requires a different level of review)

Full Board Minimal Risk

Please provide a rationale for your level of review preliminary determination

Researchers from the Stanford University submitted this application to request approval to:
1. Expand the BCFR Cohort through enrollment of additional 200 young women with breast cancer diagnosed between 2024 and 2027 through case listings obtained from GBACR.
2. Expand and update cohort characterization through efficient data linkages of existing and expanded BCFR Cohort members with treatment and outcomes databases and exposure databases; and collect new data elements (e.g., cardiotoxicity, healthy aging) through surveys for all cohort members.
3. Maintain the current extensive biospecimen resources and augment them through the collection of biospecimens from newly enrolled young women with breast cancer and their families.
4. Continue to actively collaborate with the external research community (the investigator team at Stanford University, investigators at the other BCFR sites, or collaborating investigators at external institutions) and expand the use of the BCFR resources, including data and biospecimens collected.

Choose the CPHS Chair
Darci Delgado, PsyD

Select the vice chair of the committee
Larry Dickey, MD, MPH, MSW

Assign to Cycle

June

Assign to cycle year
2024

Load into IRBManager (Initial Submission)
- Submitted 05/02/2024 4:31 PM ET by The System

Chair Review and Full Board Set-Up

Full Board Set Up

Project number

2024-095

The office will complete the questions on this page and submit the form after the teleconference with the chairs regarding this project is completed.

Confirmation of level of review

No answer provided.

Provide the rationale for the level of review determination
No answer provided.