16-003707

# Latinas LEarning About Density (LLEAD Study)

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# IRB Minimal Risk Protocol Template

**Note: If this study establishes a human specimen repository (biobank) for research purposes, do not use this template. Use the Mayo Clinic Human Specimen Repository Protocol Template found on the IRB home page under Forms and Procedures at http://intranet.mayo.edu/charlie/irb/**

**First-time Use:** Use this template to describe your study for a new IRB submission.

1. Complete the questions that apply to your study.
2. Save an electronic copy of this protocol for future revisions.
3. When completing your IRBe application, you will be asked to upload this document to the protocol section.

**Modification:** To modify this document after your study has been approved:

1. Open your study in IRBe. Click on the study 'Documents' tab and select the most recent version of the protocol. Save it to your files.
2. Open the saved document and activate "Track Changes".
3. Revise the protocol template to reflect the modification points , save the template to your files
4. Create an IRBe Modification for the study and upload the revised protocol template.

## General Study Information

Principal Investigator: Celine Vachon, PhD

Study Title: Behavioral and Psychological Impact of Returning Breast Density Results to Latinas: Latinas LEarning About Density (LLEAD Study)

Protocol version number and date: V7 08/12/2022

## Research Question and Aims

Hypothesis:

This research addresses the following "big-picture" questions: "Is the density notification law recently adopted in AZ having the intended impact on patients receiving mammography at a Federally Qualified Health Center (FQHC)?" and "Are there positive or negative unintended consequences to this legislation?" We hypothesize that sending standard-language (as determined by legislators) notification about breast density along with a woman's mammogram results is a sub-optimal method of notification. Further, we hypothesize that the goals of educating women about their breast density, (including the impact that dense breast tissue can have on mammogram sensitivity and overall risk of breast cancer) and encouraging a discussion with their health care provider about breast cancer screening options, may not be achieved by sending written notification in the absence of additional efforts to educate women about breast density. We propose to answer these questions by conducting a 3-arm randomized trial. All arms will receive the standard density notification letter, but 2 arms will also receive educationally-enhanced notification about breast density. Thus, the 3 study arms are:

usual care (standard density notification only), enhanced (standard density notification + written educational materials on breast density), and interpersonal (standard density notification + written educational materials on breast density + verbal interaction with a *promotora*/health educator).

The impact of this research can only increase as additional states mandate that women attending mammography screening (many of whom have never heard of breast density before) receive written notification about their breast density and its role in breast cancer risk. Particularly in FQHC's and other community settings where breast imaging experts may not be on staff and patients may have limited English proficiency, lower health literacy, and fewer economic resources, it is critical that density notification occur in ways that optimize receptivity and comprehension, minimize anxiety and worry, and enhance self-efficacy and intention to continue screening and pursue supplemental breast screening, if appropriate.

## Aims, purpose, or objectives:

**Specific Aim 1:** Compare anxiety as well as knowledge gained between breast density notification approaches (usual care, enhanced, interpersonal). We hypothesize that Latinas randomized to the interpersonal group (receiving a density notification letter that is accompanied by written educational materials, plus interaction with a *promotora*) will have less anxiety and more knowledge gained relative to either the usual care or enhanced study groups.
**Specific Aim 2:** Compare adherence to next routine screening mammogram between breast density notification approaches (usual care, enhanced, interpersonal). We hypothesize that Latinas randomized to the interpersonal group (receiving a density notification letter that is accompanied by written educational materials, plus interaction with a *promotora*) will be more likely to adhere to next screening mammogram relative to either the usual care or enhanced study groups.
**Specific Aim 3:** Whether or not the interpersonal group is found to have more favorable outcomes, we will examine the experience of the *promotora* in order to understand their conversations with patients, identify patients' concerns about their notification, and understand contextual factors related to implementation of the intervention. If the interpersonal approach is found to be successful, this aim will inform refinement of the educational intervention for dissemination; if the interpersonal approach is not found to be successful, this aim will provide insight about potential shortcomings. This aim will involve qualitative inquiry.
**Exploratory Aim 1:** Estimate the financial impact of the *promotora* intervention by performing a cost analysis
**Exploratory Aim 2:** Examine the association between perceived BC risk and preferences for informed decision making. We hypothesize that Latina women with a higher perceived risk will report a greater desire for involvement in the decision to get a mammogram and more likely to report that they made the final decision to get mammography.
**Exploratory Aim 3.** Examine the association between risk communication and preferences for informed decision making. We hypothesize that Latina women interested in knowing their risk will report a greater desire for involvement in the decision to get a mammogram and more likely to report that they made the final decision.

## Background (*Include relevant experience, gaps in current knowledge, preliminary data, etc*.):

Drs. Radecki Breitkopf (PI) and Vachon (PI) have been conducting research at Mountain Park Health Center (MPHC) since January 2012. The Mountain Park Mammography Screening Study (MPMSS) has demonstrated the feasibility of conducting research in the MPHC mammography suite and established a cohort of over 2,100 women, of whom 85% are Hispanic/Latina. The cohort was built over a 30 month period with one part-time CRC; the proposed study would support full-time recruitment efforts at MPHC, thus, recruitment of 2,000 Latinas in a 24-month enrollment period is highly feasible. The MPMSS attests to our ability to enroll English or Spanish-speaking patients into a prospective cohort, access mammogram reports, retrieve information from the MPHC electronic medical record (EMR) and collect data via an interviewer-facilitated questionnaire to examine risk profiles in this population.

Our experience has provided valuable data for planning the proposed study. For instance, MPHC patients are receptive to research participation; over 95% of women approached for the cohort study provided informed consent. While the time burden for the proposed study will be greater than for the cohort study, common features suggest patients will be similarly receptive; being minimal risk, related to breast cancer prevention, involving questionnaires, and requiring permission to share health information with Mayo Clinic researchers.
Ongoing analysis of our cohort data provides evidence that the proposed study is highly relevant to the MPHC patient population, as age- and BMI-adjusted percent density of the breast tissue was found to be similar between Latinas at MPHC and non-Hispanic whites in a long-standing Mayo Clinic patient cohort, thus Latinas and non-Hispanic whites appear to share a major independent risk factor for breast cancer. Furthermore, we conducted brief assessments of English language proficiency, health literacy, and awareness of breast density for some of the MPMSS participants and our data show that the MPHC screening mammography population reflects an important target group for educational interventions in the context of new density legislation. Specifically, our data reveal limited English proficiency: the percentage of women indicating "not too well" or "not at all" for understanding spoken English was 75%, for speaking English, 77%, and for reading English, was 72%. With regard to health literacy, 47% of women were "somewhat confident" or less that they could fill out medical forms by themselves. Importantly, only 8% of women indicated that they had heard of the term 'breast density.' Eighty-seven percent of women who enrolled in the cohort during the first 6 months of recruitment reported receiving their previous mammogram at MPHC. These preliminary data will guide our understanding of the needs of the population with regard to presenting educational information about breast density and provides evidence that the MPHC mammography screening population is a relatively stable one, and that longitudinal research is feasible.

Drs. Radecki Breitkopf (PI), Rhodes (Co-I), and Vachon (PI) led a national cross-sectional survey (in English and Spanish) of awareness and knowledge regarding breast density using a probability-based sample of U.S. women of mammography screening age (40-74 years). Overall, 58% of women had heard (were aware) of breast density; awareness was associated with age $\geq$ 50 years; white, non-Hispanic race/ethnicity; and higher income and educational attainment (all $P<0.001$). We included two knowledge items in the survey. The first item tested understanding of the masking effect of density: "*If a woman has dense breasts, what impact does this have on the ability of a mammogram to correctly detect cancer?"* with four response options: Dense breasts make it easier to see cancer on a mammogram; Dense breasts do not impact the ability to see cancer on a mammogram; Dense breasts make it more difficult to see cancer on a mammogram; and I don't know. A total of 49% of respondents correctly indicated that dense breasts make it more difficult to see cancer on a mammogram. After adjusting for awareness of breast density (Hispanic women had lower awareness), knowledge of the masking effect did not differ by race/ethnicity ($P=0.21$). The second item tested knowledge that density is an independent risk factor for breast cancer. Fifty-three percent of women correctly indicated that having dense breasts puts you at increased risk of breast cancer, with no differences by race/ethnicity after adjusting for awareness (P=0.61). In sum, this study identified disparities in breast density awareness by race/ethnicity, age, education, income and insurance status.

Analyses of the national data restricted to Hispanic women ($n=143$) demonstrated poor understanding of key risk factors for breast cancer, low awareness of breast density (24%), feeling anxiety about learning their own breast density (59% agree or strongly agree), and willingness to seek additional screening if the ability of their mammogram to detect cancer was compromised by high density (20-39%, depending on cost). When asked "What impact does breast density have on a mammogram?" 68% of Hispanic women selected the response "I don't know."

This study will utilize our prior research experience at MPHC and apply the knowledge that we learned conducting the national survey study. In short, we are well-prepared to conduct the proposed study. Mandatory notification imposed by legislation is gaining momentum in the absence of empirical data regarding its potential effect on women, which are assumed to be positive. Moreover, notification is gaining momentum in the absence of clear guidelines regarding appropriate supplemental screening for women with dense breast tissue and counseling regarding breast cancer risk. We

propose to conduct a randomized trial to compare behavioral and psychological outcomes among Latinas who receive notification per the mandate (usual care) relative to two enhanced approaches that are theory informed, culturally consistent, and novel in this context. Our findings will fill critical gaps in our knowledge and understanding of how this policy affects women who are already vulnerable to disparities. It will provide evidence on the feasibility and efficacy of a portable intervention to increase knowledge of breast density, and be able to determine approximate costs of intervention delivery in a FQHC setting.

## Study Design and Methods

**Methods:** *Describe, in detail, the research activities that will be conducted under this protocol*:

The study will be conducted at MPHC in the mammography suite. The mammography suite is equipped to screen one patient at a time; there is ample space in the unit for research activities to take place. We will attempt to make pre-recruitment phone calls to women on the screening mammography patient logs, alerting them to a possible study opportunity on the day of their appointment, and to enable them to plan for a little extra time at the clinic if they think they may be interested in participating [Attachment 1]. Women entering the mammography suite will be given a study brochure [Attachment 2a] and if receptive, complete a brief screener to determine study eligibility [Attachment 2b]. The study will be introduced to the patient prior to undergoing mammography by a trained Spanish/English bilingual clinical research coordinator (CRC). If the patient is willing to participate, she will be asked to provide written informed consent [Attachment 3] and authorization to release medical records [Attachment 4] for this research study. She will then be randomized to one of the three notification approaches (study groups) – usual care, enhanced/written education [Attachment 5], interpersonal.

All consented patients will be asked to complete a baseline (T1) survey [Attachment 6] that includes: demographic characteristics; breast density risk factors (parity, age at menarche, menopausal status, hormonal contraceptive use, breastfeeding, and age at first birth); Family history of breast cancer; and mammography screening history (approximate lifetime number of mammograms, number of times recalled, number of breast biopsies). The primary outcome measure for Aim 1 is anxiety. Anxiety will be measured using the state anxiety subscale of the State-Trait Anxiety Inventory (STAI). This measure was selected because of its known psychometric properties, its use in the mammography literature, and our own experience with its use in an intervention study involving Latinas attending cancer screening. Additional psychosocial measures will include health literacy, cancer fatalism, self-efficacy to return for mammography at the next screening interval, breast cancer worry, perceived risk of breast cancer using numerical, verbal and comparative estimates, and the Patient-Reported Outcomes Measurement Information System (PROMIS) measure (short form) addressing depressive symptoms. Knowledge will be assessed using two previously developed items for the national survey regarding density as an independent risk factor and as having a masking effect as well as additional items derived from the written education materials. Our selection of short form assessments where available carefully balances capturing a comprehensive set of important psychosocial measures while reducing respondent burden. We have chosen published measures with favorable psychometric properties and use existing measures where available. Administering the depression measure from the PROMIS Initiative (www.nihpromis.org) will utilize an important resource for validated patient-reported outcomes (PROs) and position our study results within a larger, cross-institute NIH initiative. Based on our experience at MPHC, an interviewer-facilitated mode of survey completion is preferred by patients over self-administered surveys and results in higher quality data. We will provide paper surveys in English and Spanish; participants can mark their own answers or follow along and mark their answers as questions are read to them by the CRC. We anticipate the study assessments will take approximately 30 minutes to complete. The study coordinator will review the responses to the PROMIS items related to depression following completion of the T1 survey. Based on the responses, the study coordinator will follow the steps in the Plan for Depression Questions [Attachment 18]. If the plan

calls for the principal investigator to contact the patient, she will do so in accordance with the Plan for Depression Questions and using the Script for Depression Questions Follow-up [Attachment 19].

Additional data will be abstracted from the MPHC EMR [Attachment 7] including: body mass index, breast density category, screening mammogram results (normal or abnormal), and attendance and outcome of any additional/supplemental breast screening (breast ultrasound, MRI, etc.), or breast procedures (breast biopsy). These additional data will position our study to contribute to understanding risk profiles for breast cancer among Latinas and inform risk-based screening.

**Follow-up (T2) Assessment.** Participants will be contacted by study staff using Mayo Clinic or Mountain Park telephone that will display the Mountain Park phone number.[Attachment 8] approximately 2 weeks after patients have their mammogram to complete a follow-up survey [Attachment 9]. If the study staff is unsuccessful in reaching the participant by telephone, the T2 survey will be mailed to the participant with a cover letter [Attachment 10] and return postage-paid envelope. If the patient has not actively refused or withdrawn, or completed the T2 assessment, study staff will attempt to follow-up by telephone. Study staff may also send a certified letter asking the participant to call them and schedule a time to complete the survey (see Attached reminder letter). If telephone and mail contacts are not successful, participants will be coded in RAVE as a non-responder at T2. The CRC will collect the data over the telephone and mark the answers on a paper survey for double data entry by the Survey Research Center (SRC). The CRC will ask questions designed to measure acceptability of the method by which women received their breast density results and satisfaction with the content and clarity. Knowledge will be re-assessed using the same items described in the baseline assessment. Women will be queried about their own breast density as a check that the mailed notification was read and processed. Anxiety, depressive symptoms, perceived risk of breast cancer, self-efficacy, and breast cancer worry measures administered at baseline will be repeated. Behavioral intention to return for a screening mammogram at the recommended interval will also be assessed. All women will be asked if they discussed their breast density with their health care provider. Women with dense breasts will be asked if they discussed supplemental screening options with their health care provider (e.g., breast ultrasound, MRI). Questions will address whether each of these activities occurred, and if not, whether they are pending (requested by the patient). If not requested, intentions regarding these behaviors will be measured. The study coordinator will review the responses to the PROMIS items related to depression following completion of the T2 survey. Based on the responses, the study coordinator will follow the steps in the Plan for Depression Questions [Attachment 18]. If the plan calls for study personnel to contact the patient, she will do so in accordance with the Plan for Depression Questions and using the Script for Depression Questions Follow-up [Attachment 19].

**Follow-up (T3) Assessment.** Participants will be contacted by study staff using Mayo Clinic or Mountain Park telephone that will display the Mountain Park phone number.[Attachment 11] approximately 1 year after patients have received their mammogram results to complete the third survey [Attachment 12]. Reminder calls and a T3 survey mailing with cover letter [Attachment 13] will follow the procedures outlined for the T2 assessment. Study staff may also send a certified letter asking the participant to call them and schedule a time to complete the survey (see Attached reminder letter). Study staff may also approach patients in clinic if they present to the mammography unit for screening.. If telephone, in-person and mail contacts are not successful, participants will be coded in RAVE as a non-responder at T3. The T3 assessment will include repeated measurement of anxiety, depressive symptoms, breast cancer worry, perceived risk, and discussion of their breast density with their health care provider. It will include questions regarding information seeking about the topic of breast density and re-assess breast density knowledge. Intentions regarding future utilization of mammography and supplemental breast screening will be measured. Attendance at mammography will be queried to capture self-reported screening behavior that may have occurred elsewhere and would not be documented in the MPHC EMR; however this is unlikely because many patients receive low-cost mammography through special programs at MPHC. All women will be queried at the T3 assessment about their attendance at mammography; these self-report data

will be corroborated with EMR data. Women who indicate they received a mammogram elsewhere will be asked where and when this occurred. The study coordinator will review the responses to the PROMIS items related to depression following completion of the T3 survey. Based on the responses, the study coordinator will follow the steps in the Plan for Depression Questions [Attachment 18]. If the plan calls for study personnel to contact the patient, she will do so in accordance with the Plan for Depression Questions and using the Script for Depression Questions Follow-up [Attachment 19].

**Follow-up (T4) Assessment.** We will identify women enrolled in LLEAD who have completed a mammography since January 1, 2020 to complete a follow-up survey for exploratory aims 2 and 3. The purpose of the T4 survey is to understand how women prefer to learn and receive information about breast cancer risk factors. The survey includes repeated items of perceived risk, demographic characteristics, breast cancer risk factors (i.e., family history, prior biopsy), and new items measuring risk communication, medical mistrust, provider trust, preferences for informed decision making, and social determinants of health (i.e., housing and food insecurity, transportation). Participants will have the option to complete the survey by phone, mail, email, or web-based platform (Zoom). All participants will receive an emailed and/or mailed letter notifying them about changes to the protocol, the purpose of the follow up survey with oral consent, and contact information for a bilingual research coordinator to complete the survey using another modality. The mailed letter will include a paper copy of the survey in English and Spanish with a pre-stamped envelope, and a QR code that participants can scan to complete the follow-up survey on their phone in English or Spanish. Approximately two weeks after the initial mailing/email, eligible participants will receive a reminder letter and email to complete the survey. Participants not responding to the email or mailed letters will receive a follow-up call from a bilingual research coordinator to elicit if the participant received the materials, if they would be interested in completing the survey, preferred mode of completion, and to obtain oral consent. Participants will be contacted up to 4 times (2X by mail/email, 2X by phone) before they will be considered non-responders.

Adherence to subsequent mammography screening or follow-up testing (diagnostic mammography, breast ultrasound), and delay in attending follow-up care will be ascertained from the EMR. We will record attendance (yes or no) at screening mammography 1 and 2 years following study enrollment. As recommended screening intervals differ by major consensus groups and may be annual or biennial, patient adherence to recommended screening interval will be determined based upon review of the clinic note. Presently, MPHC follows annual screening guidelines starting at age 40. Further, we will examine timeliness in returning for follow-up among women who are recalled for an abnormal mammogram, as delays in diagnosis may contribute to disparities in breast cancer outcomes. Specifically, we will record the number of weeks of delay in attending a follow-up appointment as a "time to adherence" variable; women who are adherent will be assigned a delay score of "0." It has been shown that delays in diagnosis of breast cancer as short as 3 months are associated with decreased survival, therefore we will also consider delay as a dichotomous variable: follow-up of an abnormal screening mammogram was received within 3 months of the scheduled appointment (not delayed) or sometime thereafter (delayed). Any uptake in supplemental breast screening among women with dense breasts will be captured in the EMR review.

Women will be compensated a maximum of $100 upon completing this study. They will be given $25 upon completion of the T1 (baseline) assessment, $25 upon completion of the T2 assessment, $25 upon completion of the T3 assessment, and $25 upon completion of the T4 assessment.

**Aim 3 Data Collection.** Subsequent to completing the delivery of the interpersonal intervention with a patient [Attachment 14], the *promotora* will complete a form with open- and close-ended questions about the encounter [Attachment 15]. It will document standard information related to the conversation, such as what questions the patient asked and whether there were issues the *promotora* was unable to address, as well as serve as self-reported information on intervention delivery adherence. Once every 1-2 weeks, the *promotora* will respond to a set of longer, reflective questions

related to patient encounters, the intervention context, and other factors relevant to her role and the implementation of the intervention [Attachment 16]. A member of the research team will regularly review entries and provide feedback or ask for clarification from the *promotora* as needed. This iterative approach to concurrent data collection and initial data analysis will ensure the data collection is robust and can adapt and include new questions or issues as they emerge. This process will also act as a log for capturing any adaptations or variations to the intervention over time. Finally, calls audio-recorded for fidelity monitoring may also serve as qualitative data that capture information on patient perspectives.

If at any point a woman withdraws from the study, she will not receive future contacts and the study team will not collect additional data. Upon withdrawal, study staff will provide written confirmation that the participant has withdrawn from the study [Attachment 20].

**Resources:** *Describe the available resources to conduct the research (personnel, time, facilities, mentor commitment, etc.)*:

Financial resources for this study include a 5-year NIH/NIMHD grant, the PI's base budget funds, and supplemental funds from the Mayo Clinic Cancer Population Sciences program. The grant budget includes funding for study personnel time/effort, travel for training and site visits, building secure databases in RAVE, and data entry and analysis. MPHC has approved the use of their facility (mammography suite space) for the conduct of this research.

The study will employ a *promotora* who is also staff at MPHC and who is familiar with the patient population, clinic setting, language, and culture of the study population. She will undergo careful training in the delivery and documentation of each interaction in which breast density results are discussed with study patients. Training by Co-I Dr. Gosh will ensure that the *promotora* is knowledgeable about MBD, can respond factually to patient questions, and defer questions appropriately to the patient's health care provider. Training by Dr. Vachon and Ms. Ridgeway will ensure that the *promotora* fully appreciates the need for consistent delivery of the information as part of a research protocol, including documenting departures from protocol. When the *promotora* calls each patient, the following material will be available: the mammogram report, the density notification letter, and a written "interaction guide" that is based on factual information about MBD and tailored to the language and literacy appropriate for this setting. With patient permission, calls may be audio-recorded for monitoring by the PI to evaluate fidelity of the intervention and verify documentation by the *promotora* after the call. We will record at least 50% of the encounters during the first month of promotora intervention delivery or until 20 cases have been recorded. Two members of the study team will review the audio files and complete a checklist with adherence items (presence or absence of intervention components outlined in the interaction guide) as well as ratings of intervention delivery competence based on program theory [Attachment 17]. The expected performance level will be at least 95% on the adherence items. Retraining will take place if lower performance is found. The fidelity checklist will also be reviewed at the end of this case review and any necessary changes will be made before instituting long-term fidelity monitoring.

Long-term monitoring will begin when the 95% performance measure is met. From that point on we will randomly sample 20% of promotora interactions over the course of the study and the two observers will compare results monthly. If performance falls below 95%, we will address reasons and sample at 50% again until performance improves.

We will manage the study data using RAVE and REDCap databases designed specifically for the study. These systems are located behind the Mayo Clinic firewall. Users must have a Mayo Clinic provided ID/password to connect to the databases and their ID must be specifically authorized in order to access study data. Only the PI can grant such authorization. The tools are HIPAA-compliant, can be set up to use branching logic and field validation to help improve the accuracy of data entry, and the data can be easily exported for statistical analysis. Administration of survey assessments (T1, T2, and T3) will occur by telephone and be interviewer-facilitated by the bilingual CRC. Surveys will be

kept secure in a locked file cabinet until they are sent in batches to Rochester for data entry by the Survey Research Center.

☐ (1a) This is a multisite study involving Mayo Clinic and non Mayo Clinic sites. *When checked, describe in detail the research procedures or activities that will be conducted by Mayo Clinic study staff.*

☒ (1b) Mayo Clinic study staff will be engaged in research activity at a non Mayo Clinic site. *When checked, provide a detailed description of the activity that will be conducted by Mayo Clinic study staff.*

The study will be conducted at Mountain Park Health Center and Mayo Clinic Staff will be consenting and following the patient throughout the study through patient contact and through medical records.

## Subject Information

*Target accrual is the proposed total number of subjects to be included in this study at Mayo Clinic. A "Subject" may include medical records, images, or specimens generated at Mayo Clinic and/or received from external sources.*

Target accrual: 2,000

Subject population (children, adults, groups): Adult women presenting for a screening mammogram

Inclusion Criteria:
Speak English or Spanish
Women between the ages 40 and 74

Exclusion Criteria:
Age less than 40 or 75+

## Research Activity

Check all that apply and complete the appropriate sections as instructed.

1. ☐ **Drug & Device**: Drugs for which an investigational new drug application is not required. Device for which (i) an investigational device exemption application is not required; or the medical device is cleared/approved for marketing and being used in accordance with its cleared/approved labeling. (Specify in the Methods section)

2. ☐ **Blood**: Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture.

3. ☐ **Biological specimens other than blood**: Prospective collection of human biological specimens by noninvasive means that may include: urine, sweat, saliva, buccal scraping, oral/anal/vaginal swab, sputum, hair and nail clippings, etc.

4. ☐ **Tests & Procedures:** Collection of data through noninvasive tests and procedures routinely employed in clinical practice that may include: MRI, surface EEG, echo, ultrasound, moderate exercise, muscular strength & flexibility testing, biometrics, cognition testing, eye exam, etc. (Specify in the Methods section)

5. ☒ **Data** (medical record, images, or specimens): Research involving use of existing and/or prospectively collected data.

6. ☒ **Digital Record**: Collection of electronic data from voice, video, digital, or image recording. (Specify in the Methods section)

7. ☒ **Survey, Interview, Focus Group**: Research on individual or group characteristics or behavior, survey, interview, oral history, focus group, program evaluation, etc. (Specify in the Methods section)

☐ NIH has issued a *Certificate of Confidentiality* (COC). *When checked, provide the institution and investigator named on the COC and explain why one was requested*. _____

**Biospecimens** – Categories 2 and 3

(2) Collection of blood samples. When multiple groups are involved copy and paste the appropriate section below for example repeat section b when drawing blood from children and adults with cancer.

a. **From healthy, non-pregnant, adult subjects who weigh at least 110 pounds**. For a minimal risk application, the amount of blood drawn from these subjects may not exceed 550ml in an 8 week period and collection may not occur more frequently than 2 times per week.
   Volume per blood draw: _____ml
   Frequency of blood draw (e.g. single draw, time(s) per week, per year, etc.) _____

b. **From other adults and children considering age, weight, and health of subject.** For a minimal risk application, the amount of blood drawn from these subjects may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period, and collection may not occur more frequently than 2 times per week.
   Volume per blood draw: _____ml
   Frequency of blood draw (e.g. single draw, time(s) per week, per year, etc.) _____

(3) Prospective collection of biological specimens other than blood: _____

**Review of medical records, images, specimens** – Category 5

**For review of existing data**: provide a date range or an end date for when the data was generated. The end date can be the date this application was submitted to the IRB. Example: *01/01/1999 to 12/31/2015* or all records through *mm/dd/yyyy*.

**Date Range: 07/01/2016 to 12/01/2022**

Check all that apply (data includes medical records, images, specimens).

☐ (5a) No data will be collected beyond the IRB submission date.

☐ (5b) The study involves data that exist at the time of IRB submission **and** data that will be collected after IRB submission. Include this activity in the Methods section.
Examples

- The study plans to conduct a retrospective chart review and ask subjects to complete a questionnaire.
- The study plans to include subjects previously diagnosed with a specific disease and add newly diagnosed subjects in the future.

☐ (5c) The study will use data that have been collected under another IRB protocol. Include in the Methods section and enter the IRB number from which the research material will be obtained. *When appropriate, note when subjects have provided consent for future use of their data and/or specimens as described in this protocol*.

Enter one IRB number per line, add more lines as needed

☐ Data ☐ Specimens ☐ Data & Specimens _____

☐ Data ☐ Specimens ☐ Data & Specimens _____

☐ Data ☐ Specimens ☐ Data & Specimens _____

☒ (5d) This study will obtain data generated from other sources. Examples may include receiving data from participating sites or an external collaborator, accessing an external database or registry, etc. Explain the source and how the data will be used in the Methods section.

☒ (6) Video audio recording: *Describe the plan to maintain subject privacy and data confidentiality, transcription, store or destroy, etc.*

With patient permission, calls will be audio-recorded for monitoring by the PI to evaluate fidelity of the intervention and verify documentation by the promotora after the call. Audio recordings will be obtained on a portable audio-recording device and uploaded at the end of each day. The device will kept in a locked cabinet at all times when not in use. Audio files will be labeled only by Study ID number and will be stored in a secure study server which is located behind the Mayo Clinic firewall with limited access by approved Mayo Clinic study personnel. After a 24-hour period (enough time for the server to be backed up to guard against data loss), the audio files will be permanently deleted from the portable device. Transcription of files will be performed internally at Mayo Clinic, utilizing secure file transfer processes and Spanish language translators (as needed).

## HIPAA Identifiers and Protected Health Information (PHI)

Protected health information is medical data that can be linked to the subject directly or through a combination of indirect identifiers.

Maintaining identifiers (including a code) during the conduct of the study allows you to return to the medical record or data source to delete duplicate subjects, check a missing or questionable entry, add new data points, etc. De-identified data is medical information that has been stripped of all HIPAA identifiers so that it cannot be linked back to the subject. De-identified data is **rarely** used in the conduct of a research study involving a chart review.

Review the list of subject identifiers below and, if applicable, check the box next to each HIPAA identifier being recorded at the time of data collection or abstraction. Identifiers apply to any subject enrolled in the study including Mayo Clinic staff, patients and their relatives and household members.

**Internal** refers to the subject's identifier that will be maintained at Mayo Clinic by the study staff.
**External** refers to the subject's identifier that will be shared outside of Mayo Clinic.

| **Check all that apply:** | INTERNAL | EXTERNAL |
|---|---|---|
| Name | X | X |
| Mayo Clinic medical record or patient registration number, lab accession, specimen or radiologic image number | | X |
| Subject ID, subject code or any other person-specific unique identifying number, characteristic or code that can link the subject to their medical data | X | X |
| Dates: All elements of dates [month, day, and year] directly related to an individual, their birth date, date of death, date of diagnosis, etc.<br>**Note:** Recording a year only is not a unique identifier. | X | X |
| Social Security number | | |
| Medical device identifiers and serial numbers | | |
| Biometric identifiers, including finger and voice prints, full face photographic images and any comparable images | X | X |
| Web Universal Resource Locators (URLs), Internet Protocol (IP) address numbers, email address | | |

| | | |
|---|---|---|
| Street address, city, county, precinct, zip code, and their equivalent geocodes | X | X |
| Phone or fax numbers | X | X |
| Account, member, certificate or professional license numbers, health beneficiary numbers | | |
| Vehicle identifiers and serial numbers, including license plate numbers | | |
| **Check 'None' when none of the identifiers listed above will be recorded, maintained, or shared during the conduct of this study.** (exempt category 4) | ☐ None | ☐ None |

In all cases, "External" refers to our trained study team members at MPHC. Information will not be shared with any other External entities.

## Data Analysis

*Power analyses and study endpoints are not required for minimal risk research, pilot or feasibility studies*.

☐ No statistical information. *If checked, please explain*:

Power Statement:

A total of 2,000 Latinas will complete baseline assessments and be randomized to one of three groups of breast density notification: usual care, enhanced, or interpersonal approaches (approximately 667 women per group) (see Figure 1). Applying a 10% attrition rate between enrollment and the first follow-up time point and an additional 20% after one year, we have planned for a sample size of 1,800 (2,000*0.90, 600 per group) for T2 measures and a sample size of 1,400 (2,000*0.70, 466 per group) for T3 measures.

**Aim 1** will compare the percent change in anxiety (STAI) from baseline between the three study groups at one month (T1) and 1 year (T3) following notification. Assuming the percent change may likely range from -100% to +100% (range of 200 percentage points), we conservatively assume a standard deviation of 50 percentage points (range/4) in the percent change measure. We will have 80% power (along with 1.7% type-I error rate) to detect a difference of 9.3 in average percent change between any two of the groups with a two-sample t-test at T2 with 600 per group. At T3, we will have 80% power to detect a difference of 10.6 (466 per group).

The second outcome will be knowledge regarding breast density, measured ordinally as the number correct of 3 key items (range 0-3 correct). This will be tested with pairwise Wilcoxon rank-sum tests, for which the null hypothesis is that the probability of someone answering more items correctly in one group versus another is 0.5 (i.e. equal chance). At T2, with 600 women per group, we will have 80% power (along with 1.7% type-I error rate) to detect a probability of 0.554 or more between any two of the groups. At T3, we will have 80% power to detect a probability of 0.561 (466 per group).

**Aim 2** will compare adherence to next routine screening mammogram between the three notification groups. This outcome "adherence to next annual screening" is pertinent to all 2,000 women and will be obtained via EMR. A sample size of 666 in each group will yield 80% power to detect a difference of 9 percentage points between the any two of the groups (type-I error rate 1.7%) based on a chi-square test.

**Aim 3** will qualitatively analyze documentation provided by the *promotora* after each patient interaction in the interpersonal study group. Based on the recommendation of Morse,[119] we will have ample data from over 600 patient-*promotora* interactions to capture a range of responses. Furthermore, this large sample size will offer the opportunity to qualitatively examine the type of information exchanged for particular subgroups of patients, such as Spanish-speaking only, those receiving notification that they have dense breasts, and those receiving notification that they do NOT have dense breasts. The analysis of Aim 3 qualitative data will provide a rich resource for informing the design of targeted educational materials for specific populations and developing generalizable tools to enhance communication about appropriate risk-based screening for breast cancer.

Data Analysis Plan:

**Analytic Approach for Specific Aim 1**
This Aim will compare anxiety as well as knowledge gained between breast density notification approaches (usual care, enhanced, interpersonal). Anxiety will be measured using the state anxiety scale within the State Trait Anxiety Inventory (STAI). Items within this scale are rated on a 0 to 3 Likert-type scale and scores are calculated as the sum of the items. The possible scores can range from 0-60, with higher scores indicative of greater anxiety. To adjust for baseline anxiety levels, we will calculate the percent change in anxiety from baseline at each follow-up: 100*(follow-up anxiety – baseline anxiety) / baseline anxiety. We hypothesize that there will be less increase in anxiety for the interpersonal group as compared to the enhanced or usual care groups. The percent change will be compared between the three notification study groups with pairwise t-tests at one month as well as at one year following notification. To account for three pairwise comparisons within each time point, P-values less than 0.017 will be considered statistically significant, to preserve an overall type-I error rate of 0.05 within each time point.
Knowledge regarding breast density will be measured as the number of statements answered correctly as previously described. The number of items answered correctly (range of 0-3) will be compared between the three notification groups with pairwise Wilcoxon-rank-sum tests at one month as well as at 1 year following notification. We assume that baseline knowledge will be similar between the groups due to randomization, and we hypothesize that knowledge will be greater in the interpersonal group as compared to the enhanced or usual care groups. To account for three pairwise comparisons within each time point, P-values less than 0.017 will be considered statistically significant, to preserve an overall type-I error rate of 0.05 within each time point.

**Analytic Approach for Specific Aim 2**
This Aim will compare adherence to next routine screening mammogram between breast density notification approaches (usual care, enhanced, interpersonal). This information will be obtained from the EMR. The percentage of women who adhere to their next routine screening mammogram will be compared between the three notification groups with pairwise chi-square tests. We hypothesize that women randomized to the interpersonal group will be more likely to adhere to next screening mammogram relative to either the usual care or enhanced study groups. To account for three pairwise comparisons P-values less than 0.017 will be considered statistically significant to preserve an overall type-I error rate of 0.05

**Analytic Approach for Specific Aim 3**
Framework analysis will be used to understand and analyze the qualitative data provided by the *promotora*. This approach is based in content analysis and allows for *a priori* themes to be identified and categorized as well as *de novo* themes that emerge through inductive analysis. The process begins with familiarization in which the content and range of responses is examined. Next, a thematic framework is generated by identifying key issues, concepts, and themes which will be used to reference the data. We anticipate that issues regarding understanding MBD, supplemental breast screening, and breast cancer risk will arise in the data, but emerging issues will also be captured. Finally, the analytic framework will be applied

to the narrative data, which will be indexed using NVivo (Nvivo 10, QSR International Pty Ltd.). All Nvivo datafiles are housed behind the Mayo Clinic firewall. Subsequently, the research team will review the audio-recorded *promotora*-patient interactions and apply the analytic framework to them using Nvivo in order to triangulate the perspective of the *promotora* and observation of the intervention's delivery by the study team.

**Analytic Approach for Exploratory Aim 1**
There are no standard approaches to performing a financial evaluation of *promotora* interventions; a systematic review identified only 6 studies that provided economic analyses of community health worker interventions, with insufficient evidence to conclude a cost benefit. The time spent by the *promotora* contacting and educating each patient randomized to the interpersonal study group about her breast density results will be recorded, and the mean *promotora* time per patient will be estimated. The prevailing hourly salary plus benefits will be used to estimate the mean cost of *promotora* time per patient.

**Analytic Approach For Exploratory Aims 2 and 3**
We will test each hypothesis using multivariate regression analyses, adjusting for relevant confounders. We will also explore differences in perceived risk, risk communication, and preferences for informed decision-making using chi-square tests.

**List of Attachments** (Documents to be found in IRBe)
Attachment 1: Pre-Recruitment Study Notification Telephone Script (English)
Attachment 2a: Study Brochure
Attachment 2b: Eligibility Screener (English)
Attachment 3: LLEAD Study Informed Consent (English)
Attachment 4: MPHC Authorization to Release Medical Information
Attachment 5: Breast Density Written Education (English)
Attachment 6: Baseline/Time 1 (T1) Survey Items (English, unformatted)
Attachment 7: EMR Data Collection Sheet
Attachment 8: T2 Telephone Script (English)
Attachment 9: T2 Survey Items (English, unformatted)
Attachment 10: T2 Cover Letter (English)
Attachment 11: T3 Telephone Script (English)
Attachment 12: T3 Survey Items (English, unformatted)
Attachment 13: T3 Cover Letter (English)
Attachment 14: Interpersonal Intervention Guide
Attachment 15: *Promotora* Documentation
Attachment 16: *Promotora* Diary
Attachment 17: Observer Checklist
Attachment 18: Plan for Depression Questions
Attachment 19: Script for Depression Questions Follow-up
Attachment 20: Withdrawal Confirmation Letter
Attachment Reminder Letter: Reminder Letter