Barriers to Screening Breast MRI Utilization Among Patients at Elevated Risk (B-SUPER)

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A. Specific Aims.

Breast cancer (BC) is the second leading cause of cancer death for women in the United States.[1] However, an estimated 6-15% of women are at high (≥20%[2]) lifetime risk based on personal health factors, family BC history, or pathogenic genetic mutations (e.g., *BRCA1/2*). Compared to the general population, these women are nearly twice as likely to develop BC. For them, screening guidelines include annual supplemental magnetic resonance imaging (MRI).[3-5] In high risk women, screening breast MRI significantly increases cancer detection compared to mammography alone[6] However, estimated uptake of MRI in high risk women is only 1-7%.[7-13] Thus, there is an urgent need to examine and address barriers to screening breast MRI among women with high BC risk.

Prior research on BC screening in the general population has identified patient, provider, and system-level barriers.[14-17] However, there are unique barriers/facilitators to screening breast MRI, above and beyond those for population-level BC screening.[18] Yet few studies have focused specifically on barriers to screening breast MRI in high risk women,[10,19] and those that have are largely based on retrospective secondary analysis of medical record and insurance claims data. To our knowledge, there has been limited study of patient-reported barriers to breast MRI. Without intervention, these missed screening opportunities may lead to later-stage diagnosis, more aggressive treatments with higher morbidity, and greater BC mortality for high risk women.[20]

This multisite study seeks to develop an explanatory framework for breast MRI utilization to inform future interventions. The Health Services Utilization Model (HSUM)[21] will guide the selection of specific patient-level factors for examination, including predisposing characteristics (knowledge, health/cultural beliefs), enabling resources (social support, cost/insurance coverage), and perceived need (perceived susceptibility, provider recommendation). Using a mixed methods approach, the aims of this study are to:

Aim 1: Assess HSUM factors influencing screening breast MRI utilization in a community-based sample (N=300). Approach: Women with high (≥20%) lifetime BC risk (N=300) will be recruited at Moffitt Cancer Center (MCC) and Georgetown Lombardi Comprehensive Cancer Center (LCCC). To identify specific factors impacting breast MRI utilization, we will sample women who are adherent to mammography screening (6-15% of whom have ≥20% risk). Patients will self-report predisposing characteristics, enabling resources, perceived need for, and receipt of MRI in the past 12 months. Hypothesis: Lack of MRI uptake will be associated with predisposing characteristics related to lower preventive service use (less knowledge, higher fatalism), fewer enabling resources (less social support, higher cost/less insurance coverage), and less perceived need for screening breast MRI (lower perceived susceptibility, lack of provider recommendation for screening).

Aim 2: Confirm, refine, or expand our conceptual model of screening breast MRI utilization through in-depth semi-structured qualitative interviews with a subset of Aim 1 patients (N=30). Approach: We will purposively select information-rich cases from Aim 1 (N=30) for semi-structured qualitative interviews exploring factors impacting utilization of screening breast MRI. Research Question: Are there additional barriers/facilitators of MRI uptake not specified in the HSUM?

Our long-term goal is to develop and test a community-based, multilevel intervention to increase screening breast MRI among high risk women. This study represents the first step in a new line of research, specifically focusing on developing interventions to facilitate personalized, risk-based cancer screening approaches. Successful completion of this study will provide an explanatory framework for screening breast MRI utilization. This explanatory framework will inform our program of research, ultimately leading to the development and testing of a community-based, multilevel intervention to increase screening breast MRI among high risk women. Given that early detection through screening MRI is a novel, important, and underutilized approach to prevention in high-risk populations, this research has potential for wide impact to improve guideline-concordant care and subsequent public health outcomes.

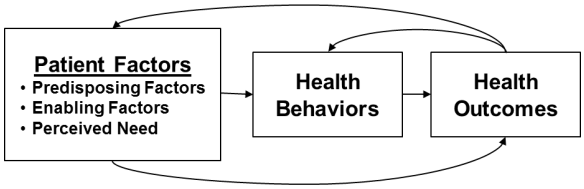
B. Background and Significance

Supplemental breast cancer (BC) screening modalities are recommended for women at elevated BC risk. In screening mammography populations, an estimated 6-15% of patients are at elevated BC risk (lifetime risk ≥20%[2]) based on personal health factors, family BC history, or pathogenic genetic mutations (e.g., *BRCA1/2*).[22-25] Statistical models incorporating these risk factors are used to estimate lifetime BC risk,[26-28] and national guidelines support their routine use to identify those with elevated BC risk.[5,29] Once identified, the National Comprehensive Cancer Network (NCCN), American Cancer Society (ACS), and American College of Radiology (ACR) recommend that high risk women receive annual mammography and supplemental breast magnetic resonance imaging (MRI).[4,5,30] In high risk women, MRI significantly increases BC detection (20-30 *additional* cancers per 1,000 women screened) compared to mammography alone.[6] MRI has high sensitivity (71-100% v. 16-40% for mammography) in high-risk populations, and detects small and node-negative invasive tumors and higher grade DCIS that are less likely to contribute to over-diagnosis.

Breast MRI is underutilized among high risk women.[7,11] Among identified *BRCA1/2* carriers – a very select subpopulation of high risk women receiving personalized genetic risk information and screening recommendations – uptake of breast MRI is significantly lower than other breast screening options (e.g., 24-48% versus 43-82% for annual mammography).[11-13] Women at elevated risk for other reasons are even less likely to receive breast MRI: estimated uptake of MRI in the overall population of high risk women ranges from 1-7%.[7-11] Thus, efforts are needed to ensure risk-appropriate utilization of breast MRI.

The proposed research is theoretically driven. The **Health Services Utilization Model** (HSUM; Figure 1)[21] states that health-related service use is a function of an individual's predisposing factors, enabling factors, and perceived need. Our team has successfully used this model in prior studies[31,32] and we will adapt it to reflect constructs important to screening breast MRI.

Figure 1. Theoretical Model.



Prior research has demonstrated that patient-level barriers to BC screening in the general population exist at each of the HSUM levels. Predisposing factors associated with lower screening rates include less knowledge about BC and certain health/cultural beliefs (i.e., higher fatalism).[33-35] Data suggest a curvilinear relationship between screening and anxiety; adherence improves with increasing anxiety until the anxiety becomes too intense, resulting in avoidance.[36-38] Enabling factors such as more social support, lower cost/better insurance coverage, and greater access to care significantly predict higher screening rates.[34,39-42] Finally, BC screening may be influenced by perceived need, a social phenomenon that includes perceived susceptibility to BC, social norms (e.g., others' expectations for screening and one's willingness to adhere to these expectations), provider recommendation for screening, and attitudes towards screening; lower perceived need may deter utilization.[43,44]

However, few studies on BC screening have focused specifically on barriers/facilitators of breast MRI in high risk populations. Screening breast MRI is unique for three reasons. First, it is a supplemental procedure, to be done in addition to annual mammograms. Women who are adherent to mammography screening still have low rates of screening breast MRI.[45] Thus, the barriers to breast MRI are ones that do not prevent women from receiving mammograms. Second, screening breast MRI is only recommended for women with high BC risk. These women may differ significantly from the general population in terms of HSUM factors, including predisposing factors, enabling factors, and perceived need. Finally, the scant literature on screening breast MRI demonstrates unique features of the MRI procedure itself that may impact utilization, including medical contraindications, fewer MRI facilities, and significantly greater costs.[10,18,19] Furthermore, existing studies are limited; they are retrospective in nature and include homogeneous populations.

This project is based on rigorous prior research demonstrating (a) established risk factors for BC,[22-25] (b) a proven modality for screening this population (e.g., breast MRI),[6] and (c) under-utilization of screening breast MRI in women at high BC risk.[7,11] Thus, we propose a descriptive, cross-sectional, mixed-methods study of barriers to screening breast MRI utilization among high risk women. Guided by

the HSUM, we will conduct a comprehensive quantitative and qualitative assessment of barriers to MRI utilization. In Aim 1, community-based high risk women (N=300) will be surveyed regarding HSUM factors and breast MRI utilization. Results will identify patient-level HSUM factors significantly associated with screening outcomes. In Aim 2, a subset of Aim 1 patients (N=30), will complete semi-structured interviews to identify gaps in our theoretical conceptualization of breast MRI utilization. Successful completion of this study will provide an explanatory framework for screening breast MRI utilization. This explanatory framework will inform our program of research, ultimately leading to the development and testing of a community-based, multilevel intervention incorporating individual (e.g., education, motivational interviewing), provider (e.g., education, reminders/notifications), and/or systems-level (e.g., patient navigation, screening voucher) components.

The proposed research is a considerable shift from dominant current research on BC early detection. (1) This study extends the existing literature by **qualitatively examining personalized, risk-based cancer screening approaches**. Most of the extant work in this area has been quantitative. (2) Our **novel sampling plan** for Aim 2 will select information-rich cases that are both concordant and discordant with our conceptual model, enabling us to refine current theoretical models. (3) Previous studies of screening MRI utilization are retrospective and observational.[8-10] To our knowledge, **this study is among the first to assess patient-reported barriers and facilitators to screening MRI**. Thus, this study represents a substantive departure from the status quo.

C. Research Design and Methods.

C.1 Investigative Team. Our team has extensive, complementary experience and skills needed to complete the proposed study. Site PIs Dr. Vadaparampil (MCC) and Dr. Conley (LCCC) have experience working in cancer prevention research, including high risk populations. Support will be provided by a team of co-investigators with expertise in epidemiology and breast radiology (Dr. Niell) and biostatistics (Dr. Brownstein).

C.2 Community Advisory Board (CAB). Our CAB will be comprised of patients (n=3), primary care providers (n=3), and systems-level representatives (n=3, representatives from the American Cancer Society-Southeast Region [see LOS]). The CAB will work with the research team to: (1) develop study materials; (2) interpret results; and (3) disseminate findings. To achieve these goals, the CAB will have biannual, in-person meetings. CAB members will be compensated for their contributions ($35/meeting, for a total of $140).

C.3 Preliminary Studies. As demonstrated by the studies detailed in Sections 3.a-3.c, our team has the ability to identify, accrue (46-54% consenting), and retain (69-93% completing follow-ups) diverse samples of women with high BC risk.

C.3.a Intentions for Risk Reducing Behaviors in Women with High BC Risk. Dr. Conley led a study to assess intentions for BC risk-reduction among high risk women.[46] Of 103 participants, only 25% reported intentions for future mastectomy, 11% for oophorectomy, and 23% for chemoprevention. Lifetime risk predicted intentions for oophorectomy only, such that *BRCA1/2* carriers had greater intentions for this behavior. Unfortunately, breast screening (mammography, screening MRI) was not assessed as a potential outcome.

C.3.b Screening Behaviors in High Risk BC Survivors Following Genetic Testing. Dr. Vadaparampil recently completed an ACS funded grant to examine the impact of genetic counseling/testing on BC recurrence risk management behaviors among Black women with invasive BC diagnosed age ≤50 years prospectively recruited via the Florida Cancer Data System. One year after genetic testing, 50% had not received a physician recommendation for breast MRI and only 33% received breast MRI in the past 12 months.[45] Further, *BRCA1/2* status was unrelated to MRI receipt (30% positive v. 33% negative/variant of uncertain significance; p=0.85).

C.3.c Screening Behaviors in Unaffected High Risk Women Following Risk Notification. In 2017, our team conducted a pilot study of risk-management behaviors among women presenting for routine mammography.[47] Of 66 high risk women, 80% had not received a physician recommendation for breast MRI 6-months post-mammography; only 8% had received screening breast MRI. Of those who obtained a breast MRI (n=6), 4 (67%) indicated that they did so because of a physician recommendation.

C.3.d Summary. Findings support the need for additional research to assess barriers/facilitators of screening breast MRI.

C.4 Study Design and Methods. We apply a sequential mixed methods design (Table 1);[48] the quantitative aim is implemented first, and the qualitative aim that follows is used to explain/extend the quantitative findings. The integration of qualitative and quantitative will occur at two time points: (1) Aim 1 quantitative data will be used to selectively sample participants and design interview guides for Aim 2; and (2) in final data interpretation.

Table 1. Study Design.

Strategy/Aim	Sample	Goals	Analysis
Phase I (QUAN): Survey Methodology **Aim 1.** To assess HSUM factors influencing screening breast MRI utilization.	Convenience sample of 150 women with high (≥20%) lifetime BC risk (n=50 non-Hispanic White, n=50 non-Hispanic Black, n=50 Latina).	Identify levels of influence and specific predictors of screening breast MRI.	Descriptive statistics Logistic regression
Phase II (qual): In-depth Individual Interviews **Aim 2.** To confirm, refine, or expand our conceptual model of screening breast MRI utilization.	Purposive sampling of 30 women from Aim 1, selected based on expected/actual MRI receipt.	Identify gaps in our theoretical conceptualization of breast MRI utilization	Content analysis

C.4.a Aim 1 Overview. The survey employed in this aim will be based on the HSUM and iteratively revised based on CAB feedback. Measures will be selected and adapted for relevance to MRI screening; potential measures are listed below (Section C.4.a.4). The Moffitt Cancer Center (MCC) Population Research, Interventions, and Measurement (PRISM) Core will assist with survey design and production. The PRISM Core has expertise in developing surveys that are acceptable and easy-to-understand, which subsequently enhances the quality of survey data.[49] The resulting survey will assess predisposing factors, enabling factors, perceived need, and health behaviors. The goal is to inform future intervention studies addressing patient barriers to screening breast MRI.

C.4.a.1 Aim 1 Inclusion/Exclusion Criteria. Biological females; able to speak/read English; within 2 years of last screening mammogram. Women will self-report *BRCA1/2* status; women with a pathogenic *BRCA1/2* mutation are eligible. Non-carriers, women with a variant of uncertain significance, and women with unknown carrier status will then be screened for lifetime BC risk using the National Cancer Institute (NCI) Breast Cancer Risk Assessment Tool (BCRAT).[26] For the proposed study, women with estimated lifetime risk ≥20% will be eligible. We will exclude women with a prior diagnosis of BC.

The inclusion criterion of age will vary based on *BRCA1/2* status. For women with a pathogenic *BRCA1/2* mutation, women ages 25-85 will be eligible, as breast MRI screening is recommended to be initiated at age 25 for this population. For women without a pathogenic *BRCA1/2* mutation, women ages 35-85 will be eligible.

C.4.a.2 Aim 1 Ascertainment and Enrollment. To enroll 300 participants, we will use five different recruitment strategies.

First, we will recruit via social media through Facebook targeted advertisement designed and promoted in collaboration with our Community Advisory Board (CAB). The language in the advertisements will indicate that the study is open to women with a family history of breast or ovarian cancer. In addition, we will target women age 25-85. This method has been used successfully in the area of health-related research.[50-53] Potential participants who click on the Facebook advertisement will be redirected to a secure website (Qualtrics) with eligibility screening questions based on the BCRAT. Women who screen eligible will be able to continue on to provide electronic informed consent and complete the web-based survey.

Second, we will approach potentially eligible patients in-person at mammography and primary care clinics in the catchment areas for MCC and LCCC. We have successfully recruited from clinics such as these in prior studies.[46,47] Working with clinical staff, we will screen clinic schedules for potentially eligible patients. A research assistant will approach these patients prior to their scheduled appointment, provide information about the study, and answer women's questions about the study. If interested, the research assistant will screen women for eligibility using the BCRAT. Eligible women will complete written informed consent, confirm their mailing address, and be given a survey packet (including a cover letter, paper survey, URL for the web-based survey, and postage paid return envelope). Follow-up mailings will occur as described below (see section C.4.a.3).

Third, we will recruit participants via CAB members at community-based outreach events (e.g., health fairs).[54-56] CAB members will promote the study as being open to women with a family history of breast or ovarian cancer. Potential participants will provide their contact information to CAB members, who will give this information to study staff. Potential participants will be contacted via telephone, provided information about the study, and assessed for eligibility. Eligible women will confirm their mailing address and be mailed the survey as described below (see section C.4.a.3). Informed consent will be documented on forms mailed and returned with the survey or via electronic signature on web-based forms, as preferred.

Fourth, we will partner with the group Facing Our Risk of Cancer Empowered (FORCE) to advertise the study on their e-mail list. FORCE is a non-profit organization with the mission of improving the lives of individuals and families affected by hereditary breast, ovarian, and related cancers. The FORCE e-mail list is comprised of men and women with an interest in issues related to hereditary breast and ovarian cancer. E-mail advertisements will describe the study and include contact information for study staff. Potential participants will contact study staff via phone or e-mail, be assessed for eligibility, confirm their mailing address or e-mail address, and be sent the survey as described below. Informed consent will be documented on forms mailed and returned with the survey or via electronic signature on web-based forms, as preferred.

Finally, we will advertise the study using flyers placed in mammography and primary care clinics and distributed by the Moffitt Program for Outreach Wellness Education and Resources (M-POWER) at community outreach events. Flyers will include a brief description of the study and contact information for study staff. Potential participants will contact study staff via phone or e-mail, be assessed for eligibility, confirm their mailing address or e-mail address, and be sent the survey as described below. Informed consent will be documented on forms mailed and returned with the survey or via electronic signature on web-based forms, as preferred.

We will monitor survey responses to ensure adequate representation (≥25%) of women reporting MRI receipt. If we are not on track for adequate accrual by 4 months, we will employ purposive sampling through the MCC high risk breast clinic, where screening MRI is standard.

C.4.a.3 Aim 1 Assessment Procedures. Assessment procedures will vary based on recruitment strategy.

Participants recruited via Facebook will complete the web-based survey. Several procedures will be put in place to deal with potential online scammers: (1) We will include several attention check items throughout the online survey. (2) Qualtrics can use cookies to prevent individuals from completing a survey more than once. A cookie is placed on the participants' browser when they submit a response. The next time the respondent clicks on the survey link, Qualtrics will see this cookie and not permit them to take the survey. (3) We will monitor the length of time that it takes participants to complete the survey; data from participants who complete the survey too quickly will be assumed to be invalid. (4) For online eligibility screening, ineligible participants will be excluded at the end of all screening items. This will prevent potential scammers from identifying how their responses disqualified them from study participation.

Participants recruited via mammography and primary care clinics will be given the option of completing the survey online or on paper. If they prefer to complete the survey online, they will be given a handout with instructions for accessing the online survey. If they prefer to complete a paper survey, they will be given a copy at the time of approach and informed consent. They will be asked to complete the survey, put it in the postage paid return envelope, and mail the survey back to MCC or LCCC (depending on site of recruitment). Follow-up mailings will be based on Dillman's Tailored Design Method (TDM). The TDM reduces errors related to survey coverage, sampling, measurement, and nonresponse.[57] Based on the TDM and our prior experience with survey studies,[58,59] we will use the following approach: (1) 1st thank you/reminder postcard; (2) replacement survey; (3) 2nd thank you/reminder postcard; and (4) a final survey with a letter stating a final date for survey submission. Materials will be mailed every 2 weeks.

Participants recruited via community-based outreach events, FORCE, or flyers will be given the option of completing the survey online or on paper. If they prefer to complete the survey online, they will be sent an e-mail with instructions for accessing the online survey. If they prefer to complete a paper survey, we will use the

TDM to distribute the survey. We will use the following approach: (1) mailed packet including a cover letter, two copies of the informed consent form, paper survey, URL for the web-based survey, and postage paid return envelope; (2) 1st thank you/reminder postcard; (3) replacement survey; (4) 2nd thank you/reminder postcard; and (5) a final survey with a letter stating a final date for survey submission. Materials will be mailed every 2 weeks.

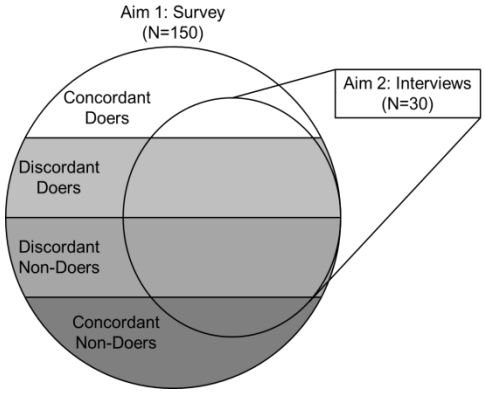
Upon completion, all survey respondents will receive a $10 gift card.

C.4.a.4 Aim 1 Measures. Predisposing factors: Sociodemographics, medical contraindications for MRI, BC Awareness Scale,[60] Multidimensional Health Locus of Control Scale[61]and Medical Outcomes Study 12-Item Short Form Health Survey (SF-12)[62]. Enabling factors: Medical Outcomes Study Social Support Survey,[63] cost/insurance factors (employment, income, insurance), site of care, access to on-site MRI, and travel time to site of care. Perceived need: Perceived susceptibility,[64] perceived norms,[65] provider recommendation for screening, and attitudes towards screening.[46] Health Behaviors: Patient-reported receipt of BC screening (mammogram, ultrasound, and MRI) and other BC risk management behaviors (chemoprevention, genetic counseling/testing) in the last 12 months.

C.4.a.5 Aim 1 Analytic Approach.

Data Management and Analysis: We will calculate descriptive statistics for predisposing factors, enabling factors, perceived need and health behaviors. We will use multivariable logistic regression to estimate odds ratios (ORs) for the relationships of the HSUM predictors with health behaviors. In the event that data is missing, we will use multiple imputation (with data assumed to be missing at random) to assess the robustness of results based on participants with complete data. We will account for site of recruitment (e.g., MCC or LCCC) in all analyses.

Figure 2. Sample Composition.



Sample Size*:* With N=300, we will have >80% power for multivariable logistic regression examining ORs at α=0.05 (two-tailed). We can detect OR=1.8 when the predictor (X) is continuous and normally distributed, the probability of screening at the mean of X is 0.2, and the coefficient of determination between X and a continuous covariate (Z) is 0.05. When X and Z are binary with 50% and 25% prevalence, respectively, we will have 75% power to detect OR=2.5, when the probability of screening is 0.25 when X=0 and Z=0.

Expected Outcomes: We expect to identify 2-4 most influential HSUM factors. We will also quantify the effect size, enabling appropriate powering of a future RCT. In line with our sequential mixed-methods design, Aim 1 data will inform Aim 2 interviews.

Table 2. Operational Definitions of HSUM Factors.

HSUM Factors	Definition	Operational Definition
Predisposing Factors	Socio-cultural characteristics of individuals	High: ≥3 of the following: (1) High BC awareness (median split); (2) Low fatalism (median split); (3) Low BC worry (median split); (4) Low depression (median split); (5) Low anxiety (median split).
Enabling Factors	Logistical aspects of obtaining care	High: ≥3 of the following: (1) High social support (median split); (2) Household income above poverty line (yes); (3) Insured (yes); (4) MRI at usual site of care (yes); (5) Travel time to closest MRI facility (≤30 minutes).
Perceived Need	How women view their need for breast MRI	High: ≥2 of the following: (1) High perceived BC susceptibility (median split); (2) High perceived norms for BC screening (median split); (3) Provider recommendation for screening (yes); (4) More positive attitudes towards screening (median split).

C.4.b Aim 2 Overview. We will conduct semi-structured qualitative interviews with a sub-sample of Aim 1 participants (N=30). We will select information-rich cases from Aim 1 for in-depth qualitative analysis in Aim 2 (Figure 3). To do so, we will categorize Aim 1 participants based on expected and actual MRI receipt (see C.4.b.1). From participants in each group, we will gather in-depth information about their breast MRI screening decisions. The goals of Aim 2 are to (a) obtain an in-depth understanding of barriers/facilitators to MRI from the patient perspective, and (b) identify gaps in our theoretical conceptualization of breast MRI utilization.

C.4.b.1 Aim 2 Sampling Plan. Data from Aim 1 will be used to develop individual participant profiles in order to purposively sample[66,67] participants for in-depth interviews about their screening choices. The goal of sampling for Aim 2 is to select information-rich cases to best enhance the post-hoc modification of the conceptual model. For each HSUM category (predisposing factors, enabling factors, perceived need), Aim 1 participants will be categorized as "high" or "low" based on a priori operational definitions (Table 2). If a woman is "high" in ≥2 HSUM categories, she will be categorized as "yes" for expected MRI receipt (and vice versa for "no"). From expected and self-reported MRI receipt, we will create 4 utilization categories (Table 3).

C.4.b.2 Aim 2 Ascertainment and Enrollment. Participants will be randomly selected from within each utilization group and invited to interview until we have achieved our desired N. As theory-discordant women are likely to be most informative for refining our theoretical model, we will over-sample women in these groups (n=10 per group) compared to the concordant groups (n=5 per group). If there are insufficient numbers in any group to allow for examination in Aim 2, we will continue Aim 1 surveys until we achieve our desired N.

C.4.b.3 Aim 2 Procedures. Interviews will take place via phone. All interviews will be conducted by a research assistant (RA) with prior experience conducting qualitative interviews. The site PIs (Dr. Conley and Dr. Vadaparampil) will review 10% of interview recordings at random to ensure high quality/fidelity in the data collection. The interviews will be guided by the HSUM (Table 4). We will start with a broad overview of patients' experiences with screening breast MRI, followed by probing questions to address specific HSUM components. Patients will also be queried regarding Aim 1 survey responses. Upon completion, interview participants will receive a $20 gift card. Our team has extensive experience in conducting qualitative interviews[68,69] and will be supported by experts in qualitative research from MCC's PRISM Core.

Upon completion of both study aims, all participants will be sent (via mail or email) educational materials about breast MRI and screening recommendations, as well as a list of American College of Radiology (ACR) accredited breast MRI screening facilities in the greater Tampa Bay region or the Washington DC metro area, as appropriate.

C.4.b.4 Aim 2 Analytic Approach.

Data Management and Analysis: Interviews will be transcribed verbatim. The research team will analyze the transcript themes through open coding, axial coding, and selective coding.[70] The PI and RA will separately examine transcripts and inductively generate themes from the data, drawing on the conceptual model, to produce a codebook. We will present themes and codebook to our interdisciplinary team and the CAB, then iteratively revise our approach to enhance validity.[71] Once consensus is reached, this codebook will be uploaded into MAXQDA (a qualitative data analysis software program) and be systematically applied to the data. To ensure coding scheme reliability, the PI and RA will code 10% of transcripts independently, and Krippendorff's alpha will be calculated with the goal of achieving α≥0.70 (an acceptable level of agreement).[72] Following achievement of α≥0.70, the remainder of the data will be split between the two coders for analysis.

Table 4. Sample Questions for Aim 2 Qualitative Interviews.

HSUM Factor	Sample Questions
Predisposing Factors	Not all women at high risk for breast cancer receive breast MRIs. What are some characteristics of people that may affect whether or not they have a breast MRI?
Enabling Factors	Not all women at high risk for breast cancer have the ability to seek breast MRI if needed. What are some factors that may affect whether or not a woman *can* seek MRI screening?
Perceived Need	For a woman to get breast MRI screening, she first has to know that she needs one. What are some factors that may affect whether or not a woman thinks she needs a breast MRI?
Screening Concordance	In the survey you completed, your answers were most similar to those of women who do (not) get breast MRIs. This is (in)consistent with your screening history. Do you think that there are any other factors that we missed that affected whether or not you had a breast MRI?

Sample Size. We will follow the principle of theoretical saturation and continue interviews until no new information is obtained.[73] Based on our prior research[68,69] we anticipate 5-10 interviews will be required to reach saturation. Thus, we aim to interview 10 participants per discordant group and 5 participants per concordant group, for 30 interviews total.

Table 3. MRI Utilization

Group	Expected MRI Receipt Based on HSUM	Self-Reported MRI Receipt
Concordant Doers	Yes	Yes
Discordant Doers	No	Yes
Discordant Non-Doers	Yes	No
Concordant Non-Doers	No	No

Expected Outcomes: Upon completion of Aim 2, we expect to identify additional barriers/facilitators of MRI uptake that are not specified in the HSUM. This will allow us to refine the conceptual model in Aim 1.

C.4.c Integration of Findings. Qualitative and quantitative findings will be integrated during the post-hoc modification of the conceptual model. We will use the merging approach, which combines qualitative and quantitative data to compare and analyze.[74,75] Data display tables will be constructed so that corresponding qualitative and quantitative data can be juxtaposed, discussed, compared, and interpreted.[76] This will allow the team to use the qualitative and quantitative findings to inform modifications of the conceptual model.

D. Human Subjects.

D.1 Risks to Human Subjects

D.1.a Human Subjects Involvement, Characteristics, and Design

Aim 1 involves a one-time survey of women at high risk (n=300) for breast cancer (BC). The survey will assess predisposing characteristics, enabling resources, perceived need for, and receipt of MRI in the past 12 months. Breast MRI referral and uptake will be the primary outcome measures investigated in Aim 1. The survey will be completed on paper or via internet (as preferred). We will also utilize minimal intensity, low resource effective strategies including thank you/reminder post cards. Materials will be mailed every 2 weeks. Surveys are estimated to take 30-45 minutes. Upon completion, survey respondents will receive a $10 gift card.

To be eligible for Aim 1, participants must be: (a) biological females; (b) able to speak/read English or Spanish; (c) within 2 years of last screening mammogram; and (d) able to give informed consent. Women will self-report *BRCA1/2* carrier status; women with a pathogenic mutation in these genes are eligible. Non-carriers will then be screened for lifetime BC risk using the National Cancer Institute (NCI) Breast Cancer Risk Assessment Tool (BCRAT; https://bcrisktool.cancer.gov/calculator.html), an interactive web-based tool based on the Gail model[26]; women with estimated lifetime risk ≥20% are also eligible. We will exclude women with a personal history of BC.

The inclusion criterion of age will vary based on *BRCA1/2* status. For women with a pathogenic *BRCA1/2* mutation, women ages 25-85 will be eligible, as breast MRI screening is recommended to be initiated at age 25 for this population. For women without a pathogenic *BRCA1/2* mutation, women ages 35-85 will be eligible.

Aim 2 involves qualitative interviews with a sub-sample of participants from Aim 1 (N=30). The interviews will be completed via telephone. Guided by Andersen's Health Services Utilization Model, interviews will assess multilevel factors promoting or limiting breast MRI utilization. Each interview is expected to last 45-60 minutes and will be audio-recorded. Upon completion, interview participants will receive a $20 gift card.

Aim 2 participants will all be selected from the Aim 1 sample. Participants will be asked to provide their contact information for potential future follow-up at the end of the Aim 1 survey. Aim 1 participants who provide contact information for future follow-up will be randomly selected and invited to interview until we have achieved our desired N. Thus, Aim 2 participants will have the same inclusion criteria as in Aim 1.

D.1.b Study Procedures, Materials, and Potential Risks

All study procedures will be reviewed by the Advarra Institutional Review Board (IRB) and the MedStar/Georgetown University Joint Oncology IRB. All recommendations made by those committees will be honored.

For Aim 1, we will use Dillman's Tailored Design Method (TDM) to distribute the survey to the full sample (N=300). The TDM reduces errors related to survey coverage, sampling, measurement, and nonresponse. Based on the TDM and our prior experience with survey studies, we will use the following approach: (1) mailed packet, addressed to the patient, including a cover letter, two copies of the informed consent form, paper survey, URL for the web-based survey, and postage paid return envelope; (2) 1st thank you/reminder postcard; (3) replacement survey; (4) 2nd thank you/reminder postcard; and (5) a final survey with a letter stating a final

date for survey submission. Materials will be mailed every 2 weeks. Upon completion, survey respondents will receive a $10 gift card. Participants will be asked to provide their contact information for potential future follow-up at the end of the Aim 1 survey.

For Aim 2, participants who provide contact information at the end of the Aim 1 survey will be randomly selected and invited to interview until we have achieved our desired sample size (N=30). Participants will be contacted using their preferred method. Upon confirmation of interest, participants will be sent two copies of the informed consent, one of which will be signed and returned to MCC or LCCC (depending on site of recruitment). Consenting participants will be scheduled for an individual interview via telephone.

Sources of research material (to be used for research purposes only) include the following:

a) Self-report inventories assessing: sociodemographic, clinical, and cultural characteristics; BC awareness, psychological well-being, perceived social support, perceived BC susceptibility, perceived norms, provider recommendation for BC screening, attitudes towards BC screening, receipt of BC screening in the last 12 months, and other BC risk management behaviors in the last 12 months.

b) Audio-tapes and transcripts of interviews.

There are no physical risks to the participant posed by this study, and no adverse events are anticipated. Participation in this project will require the investment of time in responding to interviews and survey questionnaires. This is a minimal risk study. We are using standard interview and survey techniques. Study participants will not encounter risk greater than those ordinarily encountered in daily life, including clinical encounters in the primary care and BC screening settings. These minimal risks are described in detail below.

a) Confidentiality and loss of privacy. Subjects may provide personal information about themselves during the in-depth interviews, as well as on screening or demographic questionnaires. Disclosure of personal or health-related information may affect a participant's employability or reputation.

b) Psychological distress and cancer risk data, which is sensitive and personal information, will be collected in this study. Participants may feel embarrassed or uncomfortable with disclosing such information.

D.2 Adequacy of Protection Against Risks

D.2.a Informed Consent

These studies do not involve any deception. Informed consent and consenting procedures will adhere to the Advarra IRB and the MedStar/Georgetown University Joint Oncology IRB guidelines. All subjects will sign consent forms prior to their participation. They will be asked to review the consent form prior to signing and will be provided the opportunity to ask any questions. Participant consent is ongoing, and all will be informed that they do not have to participate. If a person is not eligible or if she decides that she is no longer interested, the informed consent (or the remainder of the assessment) will end. Consent in minors is not applicable, as participants less than 25 years old are not eligible for the present study.

In Aim 1, participants will be self-identified. We will use five different recruitment strategies to enroll 300 participants, as described in Section 2.5 ("Recruitment and Retention Plan"). Once identified, potential participants will be assessed for eligibility using the NCI BCRAT; this method has been successfully used to identify high risk women in our prior studies and by our consultant, Dr. Onega, in her large, population-based studies of women at high risk for BC.[46,47] Eligible women will provide informed consent via forms mailed and returned with the survey materials or via electronic signature on web-based forms, as preferred.

In Aim 2, participants will be selectively sampled from Aim 1. Women will be randomly sampled and invited to participate in Aim 2 interviews until we achieve n=30 participating women.

Participants will be asked to provide their contact information for potential future follow-up at the end of the Aim 1 survey. Participants will be contacted using their preferred method. Upon confirmation of interest, participants will be sent two copies of the informed consent, one of which will be signed and returned to MCC or LCCC (depending on site of recruitment). Thus, informed consent will be documented by signature on forms approved by the Advarra IRB and the MedStar/Georgetown University Joint Oncology IRB.

Key elements of the informed consent procedure that are explained to participants for both study aims include: (1) the research status of the study; (2) the confidentiality of the participant's responses; (3) the voluntary nature of the study; and (4) the freedom to withdraw from the study or refuse to answer specific questions at any time. All participants who consent will be provided with a copy of the informed consent form and may contact with the research staff as needed with any questions/concerns.

D.2.b Protections Against Risk

Planned strategies for minimizing potential risks are described in detail below.

a) **Risk:** Confidentiality and loss of privacy.

Minimization: The risk of inappropriate disclosure of the participant's identity or sensitive data is appropriately minimized. We will make every effort to inform participants about the steps we are taking to ensure the confidentiality and privacy of their responses. In order to protect confidentiality, data will be securely stored and protected as described below.

For Aim 1, participants will have the option of completing the inventories via a secure website (Qualtrics.com) using a unique login ID or password hosted by our Survey Methods Core. Qualtrics, an online data collection website, has SAS 70 Certification and meets rigorous privacy standards. All Qualtrics accounts are hidden behind passwords and all data is protected with real-time data replication (see https://www.qualtrics.com/security-statement/ for additional information).

For Aim 2, participants will be audio recorded. Once the interviews are recorded, they will be transcribed verbatim by a study team member. Each transcript will be reviewed for accuracy by a second, independent study team member, after which the audio recordings will be destroyed. Audio recordings of interviews will not be used for educational or training purposes.

Data collected at MCC will be maintained at MCC, and data collected at LCCC will be maintained at LCCC. Data sharing will take place as described in section D.3 below. For all aims, physical study data will be kept in locked storage with access restricted to approved study personnel. All electronic data will be uploaded to a secure Access database on a password-protected terminal and server. Only key research personnel will have password access to electronic study data. Participants will be assigned a subject number (001, 002, etc.) that is unique to the study in question, and all data will be stored under that subject number. Participants are only identified by their subject numbers in data analyses/publications. One master list of subject names and corresponding subject numbers will be kept electronically. Only the study coordinator and key research personnel will have access to this list. The list will be password protected and stored on a password protected server that is firewall protected. All research data will remain separate from the master list and identifiers. De-identified data will be kept on file for at least 5 years from the time the IRB accepts the final review and closes the study. At the end of the 5th year of study closure, the de-identified data will be deleted.

b) **Risk:** Psychological distress, embarrassment, or discomfort.

Minimization: In conducting self-report assessments and interviews, we make every effort to obtain data in a humane, effective, and professional manner. The questions to be employed are standardized and have been used extensively and successfully in prior research. Participants will be informed that they can omit answers to any questions that make them feel uncomfortable without consequence. Participants will be told that they may discontinue a single assessment or participation in the study at any time. Contact information for the site principal investigators (PIs) is provided should participants

have any questions or concerns. Of note, the PIs have extensive experience in collaborative clinical research with human subjects related to cancer and cancer risk. Thus, the PIs have experience managing participant discomfort in the rare situations it arises.

Finally, we note that all members of the research team and personnel involved in recruitment will complete and maintain the necessary Human Subjects and HIPAA Training (e.g. CITI Courses), and copies of these certifications will be kept on file with the site PI.

D.3 Data Sharing

Data elements outlined in this protocol will be exchanged between MCC and LCCC. The following collaborators at Georgetown University Lombardi Cancer Center will have access to MCC data:

Claire Conley, PhD
Assistant Professor of Oncology
Member, Cancer Prevention and Control Program

Only de-identified data will be shared via secure file sharing service (ShareFile). Elements of dates will be shared; however, outside collaborators will not have access to our EMR system that would allow for direct identification of patients/participants. A data sharing agreement between Moffitt Cancer Center and Georgetown University Lombardi Cancer Center will be established through Moffitt's legal office.

D.4 Potential Benefits of the Proposed Research to Research Participants and Others

Participants will not directly benefit as a result of taking part in this study, and no guarantee of personal benefit based on study participation will be made to participants. The benefits to society could include a better understanding of the predictors of breast MRI utilization in the high risk population.

The potential risks of this study are not estimated to be over or above stresses encountered in everyday life. The main benefit to participants is involvement in research that may lead to the development of interventions to increase screening breast MRI among future high risk women. In sum, the risks to participants in this study are reasonable in relation to anticipated benefits.

D.5 Importance of the Knowledge to be Gained

Ultimately, we expect this research to lead to the design and development of interventions to increase screening breast MRI among high risk women. Such approaches have the potential to improve guideline concordant care, BC early detection, and BC treatment outcomes. The development and dissemination of efficacious education and intervention materials will offer a significant benefit to at-risk populations as well as the practitioners who treat them.

E. Future Research.

This is the first project in a program of research specifically focusing on developing interventions facilitating personalized, risk-based cancer screening. Data will be used to inform the next critical steps: (1) examine provider- and systems-level factors impacting utilization of breast MRI; (2) development and pilot testing of a community-based, multilevel intervention aimed at increasing breast MRI among high risk women; and (3) a fully powered RCT testing this intervention against practice as usual.

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