Study Title: **Promoting Informed Choice for Breast Cancer Screening: A Longitudinal Study**

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Principal Investigator: **Laura Scherer, PhD**

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1. Study Rationale

Breast cancer screening recommendations have changed considerably over recent years. Mammography guidelines have changed considerably as a result of accumulating evidence showing that screening has less benefit for some populations of women and can cause harm. We need to understand how to communicate more effectively when health messages reverse, to avoid potential negative reactions and promote evidence-based decisions. The problem, in our view, is that the evidence presents a balance of benefits and harms that is less favorable than what most women expect. The evidence may therefore arouse negative feelings in some women, and providers may be hesitant to discuss screening in a balanced way, wishing to avoid a discussion that could be emotionally strained and time-consuming. Altogether, the situation constitutes a health message reversal that requires special communication strategies to achieve guideline-recommended informed choice and shared decision-making. However, many questions remain unanswered: What proportion of women react to our best attempts at evidence communication with reactance, self-exemption, disbelief, or source derogation (REDS)? Who tends to react in a negative way, versus accepting the evidence with little issue or even receiving it positively (e.g., feeling empowered by being informed)? Given the reversal from previous health messages, does this evidence reduce trust in one's provider, or the healthcare system? Do these negative reactions influence screening decisions or conversations that women have with their doctor? Do attitudes toward the evidence become more positive (or negative) over time and with multiple exposures? The primary goals this longitudinal study are to identify how reactions to mammography evidence influence conversations with a doctor, change over time, and influence receipt of screening (as opposed to screening intentions). We also will explore through five surveys the influence of women's social environment, e.g., whether they choose to talk to family and friends about what they learned about mammography and how their friends' and family's attitudes toward screening influence how they choose to use the evidence and make decisions.

2. Background

Screening recommendations have changed considerably over recent years. Breast cancer is the second leading cause of cancer death among women in the U.S., and early detection can result in a cure before it spreads. For many years mammography was strongly promoted, with the aim of maximizing screening uptake.[iiiiii] However, mammography guidelines have changed considerably as a result of accumulating evidence showing that screening has less benefit for some populations of women, and can cause harm.[ivvvi]Harms include false positive results requiring follow-up tests and biopsies, and overdiagnosis—the diagnosis of asymptomatic cancer that will not cause symptoms or harm in a person's lifetime—and resultant overtreatment.[viviiiix]Although routine mammography is still strongly recommended for women in specific age ranges and with certain risk factors, many expert groups, including the United States Preventive Services Task Force (USPSTF) and the American Cancer Society (ACS), have de intensified screening recommendations and expanded the role of informed choice.[xxi] Most guidelines now emphasize that women in their 40s should receive balanced information about the benefits and harms of mammography so that they can engaged in shared decision making (SDM) and make an informed choice with their doctor about when to start, when to stop, and how frequently to screen.[xii]

A balanced presentation of both screening benefits and harms is very different from previous unequivocal recommendations to screen and can strongly contradict women's preexisting beliefs. Evidence-based information about breast cancer screening benefits and harms is very different from most people's expectations. Many

women overestimate their breast cancer risk and the benefits of screening, are unaware of the harms of screening, and are very enthusiastic about screening, so it should come as no surprise that mammography evidence and the recommendation for informed choice can elicit negative reactions. Qualitative research has shown that some women are suspicious and resistant to screening evidence, particularly the notion of overdiagnosis.[xiii] In a 2016 U.S. survey less than 1-in-4 women thought both overdiagnosis and overtreatment were "believable".[14] The notion of risk-based screening—that is, creating a screening plan tailored to a woman's objective cancer risk—is concerning for some women, and can raise suspicions of healthcare rationing.[13] We conducted 16 patient interviews in anticipation of this proposal in which we showed women a breast cancer screening decision support tool[xiv] and asked how they felt about the benefits and harms presented. Here is how one woman responded to the idea of harm from overdiagnosis: *"I think this might give people a false sense of security. Like it's giving them permission to not do screening. So, I don't think that this is reassuring, and I don't think it accurately represents the actual risk. This whole thing kinda makes me mad. I find it very frustrating because it, it feels like…it feels like propaganda."*

3. Objectives

1) Identify the prevalence and predictors of REDS (**R**eactance [i.e. perceived manipulation or influence, e.g. "this is trying to ration healthcare"], self-**E**xemption [e.g., "this doesn't apply to me"], **D**isbelief [e.g., "you can't believe all the research anyway"], and **S**ource derogation [e.g., "I don't trust this source"]), in reaction to evidence about mammography benefits and harms, and consequences for decision-making and trust.

2) Identify how women's evaluations of the evidence predict conversations with a primary care provider and how evaluations of the evidence change over time.

2b) Identify how women react to the new United States Preventive Services Task Force breast cancer screening guidelines, to determine what information about the harms and benefits of screening women now wish to receive in light of this change, and to evaluate how to more effectively communicate about the harms and benefits of screening to the public.

4. Study Design

Women who agree to participate will be sent five surveys via email and will have the option to participate in an optional follow-up focus group. The four surveys will be collected 1) immediately upon enrollment and prior to the primary care appointment; 2) immediately after the primary care appointment; 3) 3 months after enrollment; 4) 6 months after enrollment; 5) after the United states preventive services task force finalizes their new breast cancer screening guidelines. Follow-up focus groups will be conducted shortly after participants complete survey five. Survey three and four will offer an increased incentive to increase retention rates and we have powered the study to account for 20% attrition (see Statistical Design and Power attachment).

The **Time 1** survey will be a direct replication of Aim 1 and include the same measures (see Table 1). The **Time 2** survey will present a brief summary of mammography evidence as a reminder, and women will repeat from Time 1: 1. REDS responses, 2. Cognitive responses, 3. screening benefit and harm perceptions, 4. cancer risk perceptions, 5. trust in their doctor, 6. screening intentions.

The Time 2 survey will additionally assess the following: 1. Whether screening was discussed with their provider. 2. If screening was *not* discussed, why not (e.g. did not want to, no time, other pressing issues, etc.). 3. If screening *was* discussed, (a) what was discussed (i.e. benefits, false positives, overdiagnosis), (b) overall satisfaction with the discussion, (c) whether the provider offered a screening recommendation, (d) open-ended qualitative response eliciting how the discussion went. 4. Whether they discussed the BCS-DA with anyone else (e.g., friends or family); we will similarly probe the nature of those conversations. 5. Patient activation.[102] 6. Preferred role in decision-making.[103] 7. Perceived barriers to screening.[55] Finally, women's information environment will be assessed using questions from Pearlman et al. (1997)[64]: 8. information seeking (e.g. to what extent they valued opinions from their provider, friends, and family), 9. information sharing and communication (e.g. screening attitudes of friends and family), and 10. perception of self as disseminator of mammography-related information.

Of note, we made a purposeful decision to *not* audio record clinical encounters. Although audio recordings could provide an objective assessment of how mammography is discussed, it did not seem

prudent to extend the considerable time and effort required to do audio recordings if there was a possibility that many women would not discuss screening with their provider. Existing evidence and our team's clinical experience indicate that shared decision-making around mammography is uncommon,[29] and this study will help to elucidate why women may not discuss mammography with their provider, even after having just received a BCS-DA.

The **Time 3** and **Time 4** surveys (at 3 and 6 months, respectively) will repeat measures from Time 2, and will also provide summaries of the evidence for reminders. The main purpose of these repeated surveys is to assess how women's evaluation of the evidence and screening intentions change over time. We will assess whether screening was received up to one year after study enrollment using electronic medical records.

During our data collection process, the United States Preventive Services Task Force (USPSTF) announced new guideline recommendations for when women should begin mammography. Previously, the USPSTF recommended that women between the ages of 39-49 decide with their physicians when to start screening based on a weighting of personal risk and the balance of the harms and benefits of breast cancer screening. Now, the USPSTF recommends that women begin screening every other year starting at the age of 40. As such, survey 5 will randomize our previously recruited participants into one of two conditions. Condition one will provide the first cohort of women with the USPSTF recommendation and their rationale for the change. The second condition will provide women with the USPSTF recommendation, their rationale for the change, and information on how the data for the harms and benefits of screening have changed since the previous USPSTF recommendation. Both groups will then answer questions asking them to recall the information they received, provide information about their screening preferences/intentions, and to share what matters most to them in formulating their screening preferences. Both groups will also answer questions about their trust in medicine and medical provides, as well as their trust in the USPSTF. Follow-up focus groups will provide participants with additional space to discuss their reactions to the guideline change and its rationale, how the USPSTF guideline change has impacted their screening intentions, and to discuss ways we might better communicate about the harms and benefits of screening.

Hypotheses

1. REDS will become less extreme over time, with multiple exposures to the information.[63] This will be tested using linear mixed models (LMM) with a random intercept to account for correlations across subjects.

2. We will test the effect of REDS on patients' reports of discussing screening with their provider with logistic regression (a binary yes/no outcome; we anticipate about ~50% of women will talk to their provider), and also test interactive effects involving provider trust, patient activation, and preferred role in decision making. For example, a woman who trusts her provider may be eager to discuss her negative feelings about the BCS-DA, whereas a woman who does not trust her provider might hesitate to start a discussion that could be tense and uncomfortable. We will also explore correlations between REDS and quality of discussions that occur.

In addition, we have a number of **secondary predictions**:

1. Among women who report discussing mammography with their provider, screening intentions at Time 2 will be highly correlated with the provider's recommendation. We will also explore the correlation between women's objective cancer risk and provider recommendation.

2. We will explore the influence of women's informational environment: Over time, women's screening intentions will become more strongly correlated with women's information environment, e.g. screening attitudes of friends and family, and less correlation with objective cancer risk. We will also explore correlations between REDS and talking with friends/family about screening.

3. We will also explore race disparities with regard to REDS responses, and expand these analyses to address potential disparities in reported discussion of mammography.

5. Study Population

Population:

Individuals who identify as female at birth age 39-49 without a prior breast cancer diagnosis (including DCIS or LCIS) or known BCRA1/2 gene mutations will be recruited from the patient population of Co-Investigator Carmen Lewis, MD (Internal Medicine UCHealth Metro clinics), Kelly Barnett, MD (Family Medicine UCHealth Metro clinics), and Co-Investigator Marilyn Schapira, MD (University of Pennsylvania Health System). 250 Individuals who meet inclusion criteria will be enrolled from the UCHealth Metro Clinics and 250 Individuals who meet inclusion criteria will be enrolled from the University of Pennsylvania Health System. Patients from the above clinics who have upcoming visits will be contacted by phone, email, or EMR and invited to participate in the study. Exclusion/inclusion criteria will be reviewed with possibly eligible participants from the UCHealth metro and UPenn medical systems, but no additional questions will be asked of the eligible participants until consent is complete. The University of Pennsylvania recruitment will enhance sample diversity relative to what can be obtained at UCHealth Metro clinics. We will aim for at least 25% of the sample identifying as non-White. Participants must have internet access as the BCS-DA was designed for online use only. At this time the BCS-DA is only available in English and therefore participants must be literate in English.

Inclusion Criteria:

Inclusion Criteria

- Individuals who identify as female at birth
- Ages 39-49 years old (inclusive) at the time of consent
- English literacy
- Internet access
- No prior diagnosis of breast cancer, ductal carcinoma in situ (DCIS, also known as "stage zero breast cancer"), or lobular carcinoma in situ
- No known BCRA1/2 gene mutation

Exclusion Criteria:

Exclusion Criteria

- Individuals who identify other than female at birth
- Individuals who are currently pregnant
- Individuals < 39 years old or 50 years old and > at the time of consent
- Lack English literacy
- Lack of internet access
- Prior diagnosis of breast cancer, ductal carcinoma in situ (DCIS, also known as "stage zero breast cancer"), or lobular carcinoma in situ
- Known BCRA1/2 gene mutation
- Decisionally Challenged Individuals
- Prisoners or those on alternative sentencing or probation

Strategies for Recruitment and Retention:

Women age 40-49 without breast cancer or BCRA1/2 gene mutations will be recruited from internal medicine and primary care clinics in the University of Colorado (N=300) and University of Pennsylvania (N=300) health care networks. Eligible patients will be prescreened through EMR by study personnel, Compass, and/or RECRUIT at University of Colorado for UCHealth Metro clinics and UPenn for University of Pennsylvania Health System clinics. RUCHealth RECRUIT will be providing the University of Colorado site with recruitment lists based on the inclusion/exclusion criteria approved by COMIRB. The My Health Connection (MHC) message initially sent to possible participants was previously approved by COMIRB in the initial submission and has since been approved by UCHealth RECRUIT on 3/3/23.Those who meet inclusion criteria will be contacted either by phone or email. At University of Colorado, study personnel may contact eligible patients through Myhealthconnection and inform them of the study and state they will contact them in 1-2 days about the study. Study personnel will leave a voicemail/email/ to contact patients no more than 3 times. Participants will receive a maximum of of $249 in gift cards if they complete all portions of the study. Visit 1: $25 gift card; Visit 2: $25 gift card; Visit 3: $49gift card; Visit 4: $50 gift card; Visit

5: $25; Visit 6 (optional focus-group): $75. Gift cards will be distributed after each survey is completed and will be dispersed via email or mail.

University of Pennsylvania recruitment will enhance sample diversity relative to what could be obtained at Colorado and we will aim for at least 25% of the sample identifying as non-White. Women must have internet access and read English. All participation will occur via online surveys because the BCS-DA was designed for online use. In earlier research validating the BCS-DA, the study achieved considerable diversity (e.g., 65% African American) despite being online.

6. Study Assessments and Procedures

Participants will be sent 5 surveys via email and will have the option to participate in follow-up focus groups. The five surveys will be collected 1) upon enrollment and prior to the primary care appointment; 2) following the primary care appointment; 3) 3 months after enrollment; 4) 1 year after enrollment; 5) after the USPSTF guideline is finalized. Survey three and four will offer an increased incentive to increase retention rates. **Time 1** will be an online survey (REDS survey) that addresses Aim 1. **Time 2** will present a brief summary of mammography evidence as a reminder for the participant. Participants will repeat the REDS survey. Time 2 will additionally assess the following: 1. Whether screening was discussed with their provider. 2. If screening was *not* discussed, why not (e.g. did not want to, no time, other pressing issues, etc.). 3. If screening *was* discussed, (a) what was discussed (i.e. benefits, false positives, overdiagnosis), (b) overall satisfaction with the discussion, (c) whether the provider offered a screening recommendation, (d) open-ended qualitative response eliciting how the discussion went. 4. Whether they discussed the BCS-DA with anyone else (e.g., friends or family). 5. Patient activation. 6. Preferred role in decision-making. 7. Perceived barriers to screening. Finally, participants' information environment will be assessed using questions from Pearlman et al. (1997), 8. information seeking (e.g. to what extent they valued opinions from their provider, friends, and family), 9. information sharing and communication (e.g. screening attitudes of friends and family), and 10. perception of self as disseminator of mammography-related information. **Time 3** and **Time 4** (at 3 and 1 year, respectively) will repeat the summary of mammography evidence and measures from Time 2. Additionally, we will assess whether screening was received up to one year after study enrollment using the participant's electronic medical record. **Survey 5** was added in light of the United States Preventive Services Task Force changing their guidelines for breast cancer screening midway through recruitment. In this survey we will randomize participants to either receive information about the new guideline change with, or without the statistical data, included to explain why the rationale for the guideline change. We will then ask participants to respond to questions about their current screening intentions, their reactions to the guideline change, their trust in the USPTSF and healthcare providers in general, and about what they think is most important to communicate to the public about screening moving forward. **Focus Groups** will also be conducted with a subset of participants who complete **Survey 5.** The purpose of these focus groups is to characterize participants general reactions to the new guideline change, to determine what women now believe is most important to convey to the general public about the harms and benefits of breast cancer screening, and to discuss more effective means of communicating about the harms and benefits of screening to the public.

Data Collected	Time 1	Time 2	Time 3	Time 4	Time 5	Follow-up Focus Group
	Enrollment (Prior to clinic visit)	Post clinic visit	3 months post enrollment	1 year post enrollment	Post USPSTF guideline change	Post USPSTF guideline change
Decision Aid and Risk model Questions	X					
Mammogram history	X					
Screening intentions	X	X	X		X	
Screening risk/benefit perceptions	X	X	X			
Breast cancer risk perceptions	X	X	X			
Screening knowledge	X	X	X			
Trust in providers Survey	X	X	X		X	
Decision Conflict Scale	X	X				
REDS questions	X	X	X			
DA Acceptability	X					
Discrete emotions	X					
Intentions to talk to provider about screening	X					
Preferred role in decision making	X					
Medical maximizing-minimizing	X					
Health literacy/numeracy	X					
Screening barriers	X					
Standard demographics	X					
Review of participant medical record for presence of				X		

mammography screening						
Nature of screening discussion with doctor and other people		X				
Shared decision making		X				
Receipt of mammogram & outcome of mammogram			X	X		
Breast cancer screening guideline change information					X	
Guideline Change Reactions					X	
Breast cancer screening guideline change Interview Guide						X
Participant Compensation	$25 Gift Card	$25 Gift Card	$49 Gift Card	$50 Gift Card	$25 Gift Card	$75 Gift Card

7. Risk/Benefit Assessment

Risks: Items presented to participants are brief surveys regarding their evaluation of medical information about mammography benefits and harms. There are no known risks associated with completing the survey questions.

Benefits: Benefit from participating in the research cannot be claimed. Women will learn about mammography benefit and harm, which may lead to more informed screening decisions. The decision aid about mammography included in the survey is designed to improve communication and decision quality and enhance overall decision making.

8. Unanticipated Problems

The study team will monitor participants for unanticipated problems (UPs). A UP is any untoward medical event associated with the study procedures, if the nature, severity, or frequency of the event is not consistent with the risk information previously described or provided for the study procedures. UPs will be reported to the IRB as soon as possible, but in no event later than 5 working days after the PI first learns of the event.

9. Data Analysis

1. REDS will become less extreme over time, with multiple exposures to the information. This will be tested using linear mixed models (LMM) with a random intercept to account for correlations across subjects. **2.** We will test the effect of REDS on patients' reports of discussing screening with their provider with logistic regression (a binary yes/no outcome; we anticipate about ~50% of participants will talk to their provider), and also test interactive effects involving provider trust, patient activation, and preferred role in decision making. For example, a woman who trusts her provider may be eager to discuss her negative feelings about the BCS-DA, whereas a woman who

does not trust her provider might hesitate to start a discussion that could be tense and uncomfortable. We will also explore correlations between REDS and quality of discussions that occur. In addition, we have a number of **secondary predictions**: **1.** Among women who report discussing mammography with their provider, screening intentions at Time 2 will be highly correlated with the provider's recommendation. We will also explore the correlation between objective cancer risk and provider recommendation. **2.** We will explore the influence of an individual's informational environment: Over time, participant's screening intentions will become more strongly correlated with the participant's information environment, e.g. screening attitudes of friends and family, and less correlation with objective cancer risk. We will also explore correlations between REDS and talking with friends/family about screening. **3.** We will explore race disparities with regard to REDS responses and expand these analyses to address potential disparities in reported discussion of mammography.

11. Informed Consent Process

Study personnel will contact the participants via phone while the participants receive an electronic informed consent. Participants will read and complete the ICF in their own private setting. Participants will be given time to read the consent, ask questions, and have time to consider whether or not to be involved in this study. Participants will be asked to verbally describe the purpose and process of the study to ensure comprehension. Participants will be allowed to ask questions during and after explanation of the study. Comprehension and autonomy will be assessed by asking questions about the study and assessing their response. The subject will then provide consent to participate in the study. Participants then provide an electronic signature to enroll in the study.

12. Confidentiality and Privacy

Qualtrics will be used to collect data and REDCap will store data. All data will be stored in Redcap. REDCap is a HIPAA-compliant research data management system developed at Vanderbilt University and deployed at over 1500 institutions. At UCD-Anschutz, REDCap is supported by the Office of Information Technology's Development and Informatics Service Center (DISC) and the CCTSI Informatics Core. The UCD REDCap installation has passed a rigorous 6-week security threat analysis performed by the UCD-Anschutz HIPAA Security Officer. All study data are stored on a secure database server which is separate from the web-facing server -- a best-practices for internet-based security. All user access requires unique user accounts and passwords. All user actions are recorded in a secure audit log. The database server is routinely backed-up. All security patches and application updates are applied immediately upon release by DISC. All data will be stored on secure servers with restricted access to only study personnel. Study personnel at University of Colorado will have access to UCHealth metro site data and UPenn study personnel will have access to UPenn site data. This study is covered by a certificate of confidentiality. The study team will nto disclose identifying information except when the participant consents or in instances prescribed the certificate of confidentiality (i.e., when federal, state, or local law or regulation requires disclosure).

13. References

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The primary goal of this study is to identify how reactions to mammography evidence influence womens' conversations with a doctor/health care provider, change over time, and influence receipt of screening (as opposed to screening intentions). We look to identify the prevalence and predictors of REDS: Reactance (perceived manipulation or influence) self-Exemption (e.g., "this doesn't apply to me"), Disbelief (e.g., "you can't believe all the research"), and Source derogation (e.g., "I don't trust the source") in reaction to evidence about mammography benefits and harms, and consequences for decision-making and trust. We also look to identify how women's evaluations of the evidence predict conversations with a medical provider and change over time. Women who have upcoming well visit appointments at UCHealth Internal medicine and Family medicine clinics and University of Pennsylvania Health Care System clinics will be invited to participate. Participants will complete 5 surveys over the course of a year from the time of their enrollment: 1. upon enrollment and prior to their targeted medical appointment, 2. immediately following the targeted medical appointment, 3. 3 months after enrollment, 4. 1 year after enrollment, and 5. after the United States Preventive Services Task Force finalizes their new breast cancer screening guidelines. Participants wil also have the option to participate in an optional follow-up focus group