**Comparison of 3 Modes of Genetic Counseling in High-Risk Public Hospital Patients**

Rena J. Pasick, DrPH

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BACKGROUND: Hereditary breast and ovarian cancer is rare but serious. Practice guidelines call for counseling by a certified genetic counselor for those at risk to determine if a genetic test is appropriate and to assist in making an informed decision about testing. For more than two decades, genetic counseling (GC) has been widely available to those with the means to cover the high cost, but has only recently become financially accessible to low-income income patients through Medicaid and foundation grants. As a result, GC is concentrated in elite medical centers and is not offered in most safety net hospitals. Overall, there are too few Genetic Counselors to meet the growing demand. This inequity represents an early and ominous example of how advances in precision medicine *can exacerbate health disparities* – by leaving further behind those who already experience an excess burden of disease. GC may be extended to the underserved remotely by phone or video conference, but the benefits and harms of these delivery modes for safety net patients are not known. While recent research compared phone and in-person counseling in insured and rural populations, the dynamics are different in the safety net, and video conference and patient preference were not assessed. The complex and highly personal nature of this interaction, along with the importance of culture and health literacy, inform our research questions: i) what is the comparative effectiveness of GC delivered face to face, by phone, or via videoconference for public hospital patients with regard to knowledge, cancer distress, decisional conflict, perceived stress, risk perception, satisfaction, recall, and patient centeredness? ii) how do culture and health literacy influence these outcomes? iii) do safety net patients have a preference for mode of counseling and how does preference affect outcomes?

AIMS: 1. Compare 3 modes of genetic counseling with patients at high risk for HBOC in 3 public hospitals.
2. Explore inductively and qualitatively variation in patients' genetic counseling experiences and understandings; genetic counselors' satisfaction and perceptions; and counseling session similarities and differences.

METHODS: Using mixed methods, we will conduct a multicenter partially randomized preference noninferiority trial with high-risk English-, Spanish-, and Cantonese-speaking patients assigned by (1) patients´ preference or (2) randomization to three counseling modes: (a) in-person; (b) phone; or (c) video conference. A total of 600 patients will complete counseling and 540 will complete the final survey. Baseline and post-counseling surveys will use validated measures (adapted for literacy and language) of study outcomes. All counseling sessions will be audio-taped. A sample of 90 tapes will be analyzed for counseling content and to identify 30 participants for in-depth interviews and analysis triangulating all forms of data. Genetic counselors will be interviewed in depth to elicit their perceptions of the strengths and limitations of each counseling mode.

Collaborators:

Susan L. Stewart, PhD
Celia Kaplan, DrPH
Galen Joseph, PhD
Robin Lee, MS
Janice Tsoh, PhD
Niharika Dixit, MD
Lily Wang, MD
Richard Godfrey, MD

**Commented [PR1]:** The four prior sentences makes the case – this sentence drives it home….using a touch of drama. The italics signal that this is what it's all about.

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**Specific Aims**

Hereditary breast and ovarian cancer (HBOC) is rare but extremely serious. The lifetime risk of breast cancer for women with the BRCA1/2 gene mutations is as high as 85%, and up to 65% for ovarian cancer compared with 10% and 2% respectively for average risk women.[1] Approximately 5-10% of all breast cancer is associated with BRCA 1/2.[2,3] The medical technology exists to identify affected individuals and to substantially reduce their cancer risk.[4] However, throughout the more than 2 decades since HBOC risk services became available, they have been concentrated in academic medical centers[5] and nearly non-existent in safety net settings where diverse low-income patients receive care. This is despite the fact that there is no known difference in risk for HBOC by socioeconomic status.

For individuals whose personal and family history of cancer place them at risk for a BRCA1/2 or other breast cancer gene mutations, clinical practice guidelines call for a genetic risk assessment by a master's trained *licensed genetic counselor* to determine who can benefit from genetic testing, to assist high-risk individuals in decision-making, and to ensure patient understanding of results and their implications.[11] The unequal distribution of genetic counseling (GC) is largely due to financial constraints and a shortage of cancer-focused Genetic Counselors.[6] This inequity represents an early and ominous example of how advances in precision medicine *can exacerbate health disparities* – by leaving further behind those who already experience an excess burden of disease. We seek to bridge this gap by informing the extension of high quality HBOC genetic counseling to public hospitals via remote forms of communication (phone and video conference) that optimize available counseling resources. First, however, the strengths and limitations of these channels must be ascertained specifically as they relate to the diversity that characterizes safety net patient populations.

The proposed study is positioned at the intersection of key gaps in the genetic counseling literature and the strengths of our research team with its record of experience forging new channels of communication for underserved women on HBOC, and in-depth exploration of genetic counseling communication with ethnically and linguistically diverse patients of low-income and low health literacy. While two recent randomized noninferiority trials compared telephone and in-person GC in an academic hospital and in rural Utah community clinics with overall equivalent results,[7,8] it is unlikely that these findings translate directly to the safety net. As our current research is revealing, the meanings many public hospital patients take away from genetic counseling are inconsistent with counselors' intent due to cultural differences and health literacy. These dominant forces anchor this study in the real world as we blend research paradigms (deductive and inductive) and methods (quantitative and qualitative) to understand the benefits, limitations, and meanings of remote versus in-person genetic counseling in the context of the safety net.

An editorial accompanying the report from one of the above trials called for further study with more diverse patients and, noting the high rate of study refusals among patients who had a preference for mode of counseling, recommended additional research to explore the impact of GC preference on patient outcomes.[9]

All of these unknowns inform our research questions: i) what is the comparative effectiveness of GC delivered face to face, by phone, or via videoconference for public hospital patients with regard to *meaning to the patient* (operationalized quantitatively as knowledge, cancer distress, decisional conflict, perceived stress, risk perception, satisfaction, recall, and patient centeredness)? ii) how do culture and health literacy influence these outcomes? iii) do safety net patients have a preference for mode of counseling and does preference affect outcomes? The long-term goal of the proposed research is to extend high quality genetic counseling to safety net settings in order to increase ascertainment of breast cancer gene mutation carriers among low-income women, thereby dramatically improving outcomes in high-risk families. The specific aims of this mixed methods study are to:

1. Compare the effectiveness of 3 modes of genetic counseling in a diverse sample of patients at high risk for HBOC in 3 public hospitals.
   - Conduct a multicenter partially randomized preference noninferiority trial with high-risk patients assigned by (a) randomization to three counseling modes: in-person, phone, video conference; or (b) patients´ preference.
   - Utilize validated measures of study outcomes adapted as needed for literacy and language.
2. Explore inductively and qualitatively variation in patients' genetic counseling experiences and understandings, genetic counselor satisfaction and perceptions, and counseling session similarities and differences.

This application responds to the Health Disparities Funding Announcement (PA-13-292) by targeting a healthcare cause of a disparity and differences in quantity and quality of care, by moving beyond documentation of a disparity to research comparing solutions, and by our emphasis on social and cultural processes.

**RESEARCH STRATEGY**

**a) Significance**

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*i. Importance of the problem.* "Miraculously, the results of a single blood test can quantify an individual's future cancer risk with remarkable accuracy and simplicity."[10] While hereditary breast cancer is relatively rare (5-10% of breast cancers are due to an inherited mutation),[11] patients who learn that they are BRCA or other breast cancer mutation carriers can greatly reduce their very high risk for breast and ovarian cancer - not only for themselves but also for their families. Proven surgical and chemoprevention options as well as early detection via MRI have been shown to save the lives of high-risk patients.[4]

**The Disparity**

*Because of the severity of hereditary breast cancer, the efficacy of the test to determine risk, and the life-saving options available to mutation carriers, genetic counseling has become the standard of care…a standard that goes almost entirely unmet in public hospitals.*

While this early genetic discovery translated into practice among the most proactive consumers of health information with ready access to health care, estimates are that more than 90% of BRCA1/2 mutation carriers have not been identified[12] with the uninsured and people of color disproportionately represented in this undetected population (fewer than 13% of those tested are of non-European descent).[13-15] Importantly, a national study of young women newly diagnosed with breast cancer (for whom testing is not only indicated but can inform more aggressive treatment) found only 30% received genetic testing; this rate was even lower for Hispanic (18%) and African American (12%) women.[15]

Medical eligibility for genetic testing requires a complete pedigree (family history) including enumeration of family members who have and have not had cancer, types of cancer, and age at diagnosis. This is an essential component of genetic counseling (GC), "the process of helping people understand and adapt to the medical, psychological and familial implications of genetic contributions to disease [including] interpretation of family and medical histories to assess the chance of disease occurrence or recurrence, education about inheritance, testing, management, prevention, resources and research, and counseling to promote informed choices and adaptation to the risk or condition."[16] Because of the severity of hereditary breast cancer, the efficacy of the test to detect it, the importance and effectiveness of guiding patients to informed decisions regarding testing, GC has become the standard of care according to numerous national guidelines.[17-20] According to a recent systematic review to update the US Preventive Services Task Force on benefits and harms of GC, only benefits of genetic counseling were reported including improved accuracy of risk perception, decreased intention to test among unlikely mutation carriers, and decreased worry. No increases were reported in depression or anxiety; three studies found decreases in these outcomes.[4]

Yet the history of non-coverage by Medicare and Medicaid until very recently, coupled with a national shortage of credentialed genetic counselors (estimates of 1 genetics professional/300,000 population),[6] have resulted in GC services that are concentrated in urban academic medical centers and generally not available in safety net settings.[5] Additional barriers to use of GC among race/ethnically diverse communities include medical mistrust, lack of awareness of risk and services, and fear of discrimination[13,21,22] indicating at the very least the need to integrate risk assessment and GC into settings where low-income and minority patients already receive care.

**Potential of this Research**

- Demonstration of the effectiveness of remote counseling can increase access:
  - by extending GC resources to public hospitals and rural areas
  - by influencing insurance coverage of remote counseling
- Provision of remote counseling where previously there was none will profoundly improve cancer outcomes of mutation carriers and their family
- Findings from in-depth exploration of culture, health literacy, and GC can aid communication on other personalized medicine services in safety net settings.

*ii. Potential of proposed study to improve knowledge.* The reach of GC services can be extended to those who are underserved by provision of counseling remotely via phone or video conference ("telegenetics"). These delivery modes are becoming increasingly available, but lack of data on the *quality* of remote counseling impedes coverage for these services.[89] Until very recently, the evidence on remote counseling was mixed and there persisted a tacit understanding that in-person genetic counseling is optimal. However, two rigorous new trials suggest otherwise. Both consultant on this study Schwartz and colleagues[7] and Kinney *et al.*,[8] demonstrated the noninferiority of phone counseling compared with in-person for psycho-social outcomes in an academic medical center and a Utah statewide rural-urban population respectively. However, in both studies genetic testing rates were slightly lower for those receiving phone versus in-person counseling. The authors speculated that the added time delay or distance to ship test samples were impediments. Importantly, both study populations consisted of predominantly insured white women, video conferencing was not tested, and preference for counseling mode was not taken into account in the design. An editorial accompanying the Schwartz report noted both the importance of preference as a determinant of study non-participation and the likely impact on satisfaction with counseling, and the need for "further studies in settings with more diverse patient populations [that can] shed

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light on whether there are particular types of patients who benefit more when complex topics are discussed in person versus over the phone."[9]

**b) Innovation**

This is the first study to compare modes of HBOC genetic counseling: i) among low-income, ethnically diverse patients in public hospitals; ii) with a 3 arm comparison of video conference, phone, and in-person; and iii) including a preference group that allows patients with a strong preference to access the mode of their choice, protecting both internal and external validity (see Approach). Video conference is included because of the ease and increasing use of this technology, and the fact that it represents a blend of some qualities of in-person with the potential for greater access. The last point relates to another important and unique feature of this research, our experience with and attention to the cultural context of the genetic counseling interaction.

As our own research has shown, *relational culture* (the processes of interdependence and interconnectedness among individuals and groups and the prioritization of these connections above virtually all else) is a powerful influence on health communication.[87] It is likely to figure prominently in our exploration of GC. In-person counseling offers the greatest potential for a meaningful trusting connection between patient and counselor, and video conference could function similarly. This can be highly significant among the cultures represented in our study but, as we have learned, not necessarily at a conscious level, in a way that can be readily articulated by the patient. Our methods are designed to elucidate these processes for a deeper understanding of the three counseling modes. The inductive multi-qualitative methods used in our above-cited study, like those proposed here, are also consistent with new recommendations recently released by the NIH Office of Behavioral and Social Science Research calling for more dynamic, contextualized understandings of culture and noting that "operationalizing culture usually does not lend itself to the identification of a predetermined battery of scales so common to research in the health related sciences. Inductive methods are required and mixed methods are underscored."[23] (Dr. Pasick was on the panel that produced this document.) While our quantitative trial utilizes existing constructs and measures for comparability with other findings on remote GC, our qualitative inquiry will likely reveal new and different outcomes of importance while also explaining the quantitative findings. This inductive approach is patient-centered in allowing for new meanings and understandings rather than only measuring concepts known to apply to other patients in other settings.

**Innovation**
- First safety net comparison of GC mode
- 3 arms/inclusion of video conference
- Preference and randomized groups
- Contextualized inductive approach
- Centrality of culture and health literacy

**Relational Culture**

*I don't know you so I can't hear you.*

Unknown

*i. Preliminary Studies: Bringing diverse patients to genetic counseling*. This study is possible because of our experience in the practice of and research on genetic counseling for low income patients. San Francisco General Hospital (SFGH, an affiliate of UCSF) was the first US public hospital to offer free genetic counseling and testing with funding from the Avon Foundation beginning in 2002 and continuing today. The program has provided counseling to over 1500 patients, and genetic testing to over 400. With evolving standards of care, the public hospitals in nearby Alameda and Contra Costa counties sought assistance from SFGH. Currently, a nurse specialist in the Contra Costa Regional Medical Center (CC) endeavors to provide genetic counseling, and SFGH genetic counselors provide phone and SF-clinic based counseling to Alameda Health System (AHS) patients when possible. Both CC and AHS are enthusiastic participants in this research.

The proposed research team has extensive experience exploring genetic counseling in safety net settings. The current study evolved from a recently completed NCI-funded RO1 study, "Statewide Communication for High-Risk Low Income Women" (2007-12, Pasick PI, Kaplan, Joseph, Stewart, Lee, Luce Co-Investigators). This was a randomized delayed control trial to test the effectiveness of an intervention to identify uninsured women at risk for HBOC among callers to California's statewide free breast and cervical cancer screening phone service. Once identified using a brief family history screener, high-risk women were randomized to immediate appointment for free genetic counseling or receipt of a brochure on how to obtain counseling. Among 1212 eligible callers, 58.5% agreed to participate; of these, 102 (14%) were high risk (25% Hispanic, 46% White, 10% Black, 16% Asian, 3% other). Women who received counseling during the intervention period included 38.6% of those offered an immediate appointment vs. 4.5% receiving the brochure (p=0.0005).[24,25] Many women could not travel to UCSF for counseling, prompting implementation of phone counseling. Among all the women counseled through the study, 51% chose to be counseled by phone.

Dr. Kaplan's study "Breast Cancer Prevention: The Views of Women and Physicians" (California Breast Cancer Research Program, CBCRP,6PB-0053) recruited patients through the San Francisco Mammography Registry and assessed attitudes and practices of physicians and patients regarding breast cancer prevention and genetic testing.[26-29] Findings informed a recently completed study (funded by CBCRP150B-0158 and Komen - KG090504, Kaplan, PI, Pasick Co-Investigator) to develop and test a multilingual tablet-based intervention to

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inform patients and physicians of a woman's individual risk, and to encourage high-risk women to take preventive steps. This randomized controlled trial recruited over 1,600 Latina, African American, Asian American, and White women with no history of breast cancer. Compared to controls, women randomized to the tablet intervention had greater knowledge regarding chemoprevention and more discussion of breast cancer risk with their physician, particularly among the highest-risk women.[30]

With a current grant from Susan G. Komen for the Cure (2010-15, Pasick, PI, Joseph, Lee, Stewart, Co-Investigators) our team is conducting community-based participatory research with African American churches in three Bay Area counties evaluating a train-the-trainer model that enables health ministry leaders to conduct workshops on hereditary breast cancer. Pre-post- questionnaires and in-depth interviews show significant increases in comprehension of key concepts. In 2014, 418 family history forms were completed at ten churches - 86 indicated possible eligibility for counseling; 44 women have been counseled (testing is indicated for 7, not indicated for 21, 16 are in process); 9 women are scheduled for counseling; and 33 were referred to their church Health Ministry Leader to assist us in reaching these potentially high-risk women.

Dr. Joseph's current study, "Translating Cancer Genetics to the Safety Net Setting" (Susan G. Komen, 2012-2016, Co-Investigators Pasick and Luce) builds on pilot research with Latinas undergoing genetic counseling.[31] Based at two public hospitals this study will inductively describe current practices in hereditary breast cancer communication with low-income English-, Spanish- and Cantonese-speaking patients, identify key dimensions of genetic counseling communication across cultures and literacy levels, and pilot test an intervention to improve genetic counseling. Like the proposed research, genetic counseling sessions are observed and audiotaped, and patients are interviewed in-depth after counseling, including review of audiotaped segments of the conversation. Preliminary results indicate that patient information needs often do not match counseling content. For example, counselors spend a significant portion of the pre-test appointment explaining heredity, genetic testing, possible test results, etc. while patients report that they do not understand or remember much of what the counselor says, and their basic questions (e.g. Do I have cancer? Am I likely to get cancer? Are my family members likely to get cancer?) are not answered in a manner they can grasp. This mismatch in the amount and kind of information provided reflects the challenges of low health literacy. GCs and patients have also been found to differ in their assumptions regarding whether the GC or patient should decide if testing will be done. This is both a function of culture and the differences in biomedical practices in the US health care system and immigrant patients' healthcare experiences in their home countries. Some Chinese immigrant patients evidenced internal conflict about disclosing the test results to family members thinking that it was important for their family members to know so they could protect their own health, but they worried that this would cause psychological distress and were not sure if family members could cope.[31] All of these communication challenges are exacerbated when a medical interpreter is utilized, due to interpreters' variable skill level and degree of familiarity with genetics, and the counselors' variable ability to effectively utilize an interpreter. The use of interpreters via phone or video at the study sites has also raised issues about trust, e.g. some Chinese immigrant patients mentioned that not having the interpreter in the room makes it harder to trust him/her and makes them less likely to talk much or ask questions.

**c) Approach**

*i. Study Overview*. This study is designed to produce findings with policy and practice implications. Our mixed methods combine a multicenter partially randomized preference noninferiority trial with inductive methods that embed this research in the real world of public health system patients. This is practice-based research, designed to emphasize external validity, (relevance and generalizability that enhance translation into actual use),[32] as well as internal validity. Recognition of the multi-level nature of genetic counseling moves beyond the constraints of data obtained only at the level of individual cognition, including influences that occur outside of individual awareness.[33] The purpose of a non-inferiority trial is to compare an intervention to an active control or standard treatment when the intervention is not expected to have superior efficacy, but to have other benefits, e.g., greater convenience or fewer side effects.[34] In the case of genetic counseling, in-person counseling is the standard of care, with well-documented efficacy.[4] Since video and telephone counseling do not offer a more personalized approach or more pertinent content than in-person counseling, it seems unlikely that either mode would produce superior psychosocial outcomes or greater knowledge gains; similarly, we do not expect telephone counseling to be more efficacious than video counseling. Therefore, we selected a non-inferiority design to ascertain whether these less costly[7] and more convenient modes of delivery can produce results that are comparable to in-person counseling and to one another.

The gold standard for assessing the effectiveness of interventions is the randomized clinical trial; yet patients who have a strong preference for one of the intervention conditions may decline to participate, which is a threat to external validity, or (if randomized) participate half-heartedly or drop out, threatening internal validity.[7,9] We will address this issue with a partially randomized preference trial in which patients with a strong preference are

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Look for this throughout the grant – how did I do?

assigned to their preferred treatment (i.e., intervention condition) and those without a strong preference are randomized.[35] This study design enables comparison of treatment outcomes among patients who receive their preferred treatment (the desired real world situation) and ascertainment of the effects of preference—as well as the evaluation of treatment outcomes in a randomized trial. However, comparisons involving preference participants are subject to confounding, since patients who prefer a particular treatment may differ in ways that affect outcome. In analyses involving preference participants it is possible to reduce confounding substantially using covariate adjustment.[36] Nevertheless, because residual confounding may be present, preference participant outcomes should be considered observational data.[37]

We will blend qualitative and quantitative, deductive and inductive methods using varied forms of data from in-depth interviews, surveys, and audio taped observations. This will allow us to address our central question from different perspectives triangulated in the analysis for a rich understanding of patient-counselor-institution relationships,[38,39] most of which are too complex to describe using one dimension alone (e.g., cognitive understanding captured in surveys). While the randomized trial is the gold standard for comparative effectiveness, it cannot answer questions such as what it is about the counseling interaction that was reassuring or anxiety-provoking to a patient? what techniques enabled a patient to recall important points? or what about the conversation precluded such recall? It is only by embedding the survey data in open-ended inductive exploration and audio observations that we can determine if a counselor provided too much information to a low-literacy patient, or alternatively used plain language to emphasize key points, checking frequently for patient comprehension. Importantly, was the counselor able to do this as well by phone or video? Thus, mixed methods illuminates important dynamics that informants may not be consciously aware of.

*ii. Conceptual Framework*. Since the "noninferiority" of telephone counseling to in-person GC has been demonstrated among insured white patients,[7,8] our conceptual framework is designed to inform exploration of this question in a different context, and to elucidate differential outcomes by GC mode that reflect the low resource population and safety net setting, with a particular focus on culture and health literacy. We conceive 'setting' broadly, following Cultural Health Capital (CHC) which refers to a societally constructed set of "cultural skills, verbal and nonverbal competencies, and interactional styles" that can influence health care interactions" and that confer a health advantage to the educated and affluent in access to quality care and the ability to navigate complex health care systems and health communication. Importantly, CHC is relational: "a collective achievement of patient-provider interactions" that reflects not only the patient's skills but also the institution and provider's roles "as agents who can solicit, evaluate, shape and foster CHC."[40] We also draw on the Health Literacy Skills Framework[41] to elaborate our conceptualization of a key component of CHC, health literacy ("the degree to which individuals can obtain, process, understand, and communicate about health-related information needed to make informed health decisions"[86]). Health literacy is known to affect the outcomes of those with the greatest health needs, but has only recently been recognized as critical to public health genomics, a context where it is little studied and poorly understood.[85] The HLSF's socioecological perspective acknowledges culture, SES, and other contextual factors as influences on individual exposure to, cognitive processing of, and understanding of health information. The emphasis of the HLSF on the "health literacy demand" of a message (whereby the complexity and difficulty of a stimulus –messenger/message –interacts with a person's health literacy skills to influence comprehension) is expected to emerge as central in our analysis of communication in each of the three modes. The HLSF contends that this demand is determined by the communication channel, message content, and message source.[42]

**Medical Advances & Cultural Health Capital**

*When new diseases, risks, and knowledge emerge, those with access to broadly serviceable resources are better able to adapt to changing historical circumstances to avoid risks and cope with disease*.[40]

Within the frames of the CHC and the HLSF, we will quantitatively measure and qualitatively explore patient outcomes commonly associated with genetic counseling: knowledge, cancer-specific distress, attendance at counseling, appointment length, decisional conflict, satisfaction, recall, risk perception, and patient-centered communication as together constituting the *meaning* taken from the encounter by the patient. We will also utilize CHC to analyze the relational aspects of the counseling interactions, drawing on a variety of qualitative techniques (in-depth interviews with patients and counselors, and textual and rhetorical analysis of transcripts of genetic counseling) to examine how the GC-patient interactions are influenced by differential skills and social positioning, and power dynamics among patients and genetic counselors. We anticipate that in the context of the safety net, we will identify more problematic meanings of GC and more relational imbalance and disconnect between patients and counselors. Thus, our mixed methods will go beyond the question of which mode yields better outcomes by documenting detailed meanings and the processes through which they are enacted,[43-45] addressing such questions as: Does remote counseling minimize the influence of setting and thus potentially improve communication? Are relational connections degraded by the disembodied voice over the

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In this case, the framework is the conceptual glue that binds key concepts and methods. This one was very challenging though because the intervention is very practical and straightforward. To be honest, the framework was developed after the fact. But it was important to think this through to reflect the deeper meaning of this work.

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phone? How much of the benefits of in-person communication are maintained in a video conversation? Our methods follow the *interpretive approach* to health communication which examines how meaning is constituted through interaction and embedded in the narratives attributed to relevant concepts such as risk, hereditary, etc.[46,47] Through the CHC and HLSF frameworks, we will "unpack" meaning, explain the quantitative constructs and outcomes, and elucidate the relational aspects of the communication.

**Table 1. New Breast Cancer Cases - Demographics by Site**

| | ACMC (2013) n=73 | | CC (2014) n=129 | | SFGH (2013) n=90 | |
|---|---|---|---|---|---|---|
| **Race** | N | % | N | % | N | % |
| Black/African Amer | 23 | 31% | 16 | 12% | 5 | 6% |
| White/Caucasian | 29 | 40% | 52 | 40% | 34 | 38% |
| Asian/Pac Islander | 18 | 25% | 22 | 17% | 38 | 42% |
| Nat Amer/Nat Alas | 0 | 0 | 1 | 0 | 0 | 0 |
| Other/Unknown | 3 | 4% | 8 | 6% | 1 | 14% |
| **Ethnicity** | | | | | | |
| Hispanic or Latino | 17 | 23% | 30 | 23% | 21 | 24% |
| Not Hispanic | 56 | 77% | 99 | 76% | 56 | 62% |
| Unknown | 3 | 4 % | 0 | | 13 | 14% |

*iii. Settings and Sample.* This study will be conducted in public hospitals in three San Francisco Bay Area counties: San Francisco, Alameda, and Contra Costa. These very different institutions represent urban, suburban, and rural communities, and academic faculty clinicians (SFGH) or private contractual medical groups. Patients must travel substantial distances to reach the public hospitals in Contra Costa (population of 1,049,025 in 802 square miles) and Alameda counties (1,510,271 in 813 square miles). San Francisco, by contrast, has a population of 812,826 in 49 square miles. The race/ethnic distribution of patients by hospital is shown in Table 1. We will recruit patients from Oncology, Mammography and, where available, High Risk clinics in each hospital. (This is consistent with Kinney[8] whose study included women with personal or family history of breast or ovarian cancer, and distinct from Schwartz[7] who only studied women with cancer.) Mammography patients per week number about 115 (AHS and SFGH) to 150 (CC); High Risk clinics are provided at SFGH and CC, seeing approximately 15 patients each per week; and breast oncology patient visits number 40/week at CC and AHS, and 30-40 per week at SFGH. In all sites, the dominant languages spoken are English and Spanish, the latter is spoken by ~20% of patients in AHS and CC, and 33% at SFGH. Approximately 20% of SFGH mammography and breast cancer patients speak Cantonese. Limited English speakers in other languages will not be eligible.

**Aim 1.** *Compare the effectiveness of 3 modes of genetic counseling in a diverse sample of patients at high risk for HBOC in 3 public hospitals. Conduct a multicenter partially randomized preference noninferiority trial with high-risk patients assigned by (a) randomization to three counseling modes: in-person, phone, video conference; or (b) patients´ preference. Utilize validated measures of study outcomes adapted as needed for literacy and language.* Aim 1 poses the following research questions: Are the three modes of genetic counseling modes comparable to one another with respect to the primary outcomes (knowledge and cancer-specific distress) and secondary outcomes (attendance at counseling, appointment length, decisional conflict, satisfaction, recall, risk perception, and patient-centered communication). Recognizing that some potential participants may have a strong preference for one counseling mode, after explaining the study design and obtaining informed consent, participants will be asked if they have such a preference. Those who do will be offered that mode, and those who do not will be randomized. Randomization will be stratified according to hospital and personal history of breast cancer in order to ensure that there is no imbalance in important factors that may be associated with outcome. Blocked randomization will be performed to ensure that allocation to the study arms occurs evenly over time and that intervention effects will not be confounded with secular or seasonal trends. In addition, counseling will be conducted by three genetic counselors who will rotate through each of the modalities to ensure that individual counselor characteristics do not influence outcomes.

*iv. The intervention*. All genetic counseling will be provided by UCSF Genetic Counselors. Phone and in-person counseling is available at their base at SFGH. For the study, participating SFGH patients will be randomized/offered preference as in the other sites. At all sites, patients randomized to/preferring in-person counseling will meet with a UCSF counselor who will travel to AHS and CC. Patients in the phone arm will receive a scheduled call at their home. Because low income patients are not likely to have video conference capability at home, this service will be offered at all three hospitals, and patients will have scheduled appointments to come to the hospital to receive counseling delivered through a computer. Participating GCs will be master's level UCSF employees. These credentialed professionals are highly skilled. We will conduct an in-service training to ensure that participating counselors provide the essential elements of genetic counseling to every patient so that any differences in outcome will be due to the counseling mode. Dr. Pasick has experience developing and conducting training in use of plain language and active listening with oncology nurse telephone counselors and staff from the NCI's Cancer Information Service. Based on preliminary findings from Dr. Joseph's current study, we will focus on communication across culture, literacy and language/working with interpreters. We will emphasize the importance of psychosocial aspects of counseling in combination with education on risk. Two half-day trainings

**Commented [PR29]:** Critical to have the essential data on the population targeted to show that you will have an adequate sample.

**Commented [PR30]:** Reviewers wanted us to include Chinese speakers. We did. It's been a challenge.

will be conducted prior to the pilot study in year one. Monthly team meetings will assess progress and troubleshoot challenges throughout the trial.

*v. Study procedures.* Identical protocols for patient identification, recruitment, and delivery of the three modes of genetic counseling will be implemented in each location. Recruitment procedures will begin in month 13, following one year of materials and protocol development, personnel training, and pilot-testing. Trial implementation will rotate through the sites in 4-month blocks where the first two months consist of active recruitment in a site followed by two months of patient follow-up. That is four months in Hospital A, followed by B, then C. The cycle will repeat over a thirty-six month period. In this way genetic counselors and study staff will be able to focus on one location at a time for maximum efficiency; overlap will occur as final counseling sessions are provided at one hospital after recruitment begins in the next. Randomizing within each site will avoid the introduction of bias. Our goal is to obtain a sufficient number of initial family history screeners to yield a final sample of 540 high-risk patients who complete the baseline and final surveys and genetic counseling.

**Table 2.**
**Participant *Recruitment* Strategy Annual Accrual by Clinic Source & Total Patients Available**

| | | | **Bases for Assumptions** | |
|---|---|---|---|---|
| | | | **Pasick Statewide R01** | **Kaplan BreastCARE** |
| | Mammog-raphy | High Risk/Onc | | |
| Patients available per year | 24000 | 1450 | 1212 eligible | 3473 eligible |
| 50% complete screener | 12000 | 725 | 709 (58%) | N/A |
| Eligible according to RST<br>10% Mammography<br>20% High Risk/Oncology | 1200 | 145 | 102 (14%) eligible for Genetic Counseling | N/A |
| 30% enroll, complete baseline survey, & assigned to mode | 360 | 44 | 88 (86%) | 1635 (47%)* |
| 50% complete gen counseling | 180 | 22 | 51 (58%) | 1278 (78%)** |
| 90% complete final survey | 162 | 20 | 49 (96%) | 1235 (97%)*** |

**182 patients complete survey/yr x 3 years = 546 (Target: 540)**
* Completed baseline and were randomized
** RA met patient at clinic to complete tablet-based assessment
*** Completed follow-up survey

*vi. Sample recruitment assumptions*. Our assumptions vary by recruitment clinic since our experience shows that high-risk and cancer patients are more likely to participate in research on this topic (Table2). Regarding mammography clinic recruitment, approximately 24,000 mammograms are performed annually in the three sites combined. We estimate that half these patients will complete the family history screener (12,000 forms per year) of whom 10% will have a score (based on the *Referral Screening Tool*, RST[48,49]) indicating eligibility for genetic counseling (1200/year); 30% of eligible patients will be invited and consent to participate in the study (360/year); 50% will attend a genetic counseling session (180/year); and, as found in our two prior studies, 90% will complete the follow-up survey (162/year). Regarding breast cancer and high-risk clinics, we expect 100 monthly high-risk patients (reduced to allow for overlap with breast oncology), for a total of 1200 per year. Hospital data show at least 250 breast cancer cases are identified annually at our target sites, for a total of 1450 high risk/oncology clinic attendees per year, plus patients diagnosed with breast cancer in previous years who are still in follow-up. Assuming that 20% of these patients will be eligible to participate and (conservatively) that participation rates are similar to those recruited through the mammography clinic, we expect to enroll 20 high risk/oncology patients/year, for a total of 182 high-risk patients completing genetic counseling. Should these rates fall below expectations, we will increase the rate at which we invite into the study patients who are eligible for counseling. In addition, we can lengthen the recruitment period and extend recruitment to each of the participating hospital's primary care clinics.

*vii. Identification of eligible participants*. Patients (both women and men) attending selected clinics will be given a short form at intake that uses the RST criteria to identify those eligible for genetic counseling in mammography clinics. These criteria include first and second degree family members with breast or ovarian cancer, Jewish heritage, and male breast cancer in the family. The information is presented in an easy to complete grid that includes all the necessary information. During year 1 of the study we will assess different presentations of the form. Questions will use simple language appropriate for patients with low literacy and will be translated into Spanish and Chinese following strict translation procedures (details below). The form will end with a question regarding the patient's willingness to be contacted for participation in a research study including telephone number and best time to be reached. Once per week, the Project Coordinator will visit the site, scan the forms and send them in a HIPAA compliant manner to our offices for further evaluation. Genetic Counselor, Ms. Lee will review all the forms for accuracy and identify those who are eligible to be contacted by the GCA for further evaluation of family pedigree to establish final eligibility. Eligible patients will be entered in a database and a participant log will be created for tracking. To save time in the recruitment call, a study information brochure will be mailed in the patient's language, briefly describing the study purpose and participant components including a brief introduction to randomization.

**Commented [PR31]:** All of this required months and months of wrangling, all of which had to be distilled down into clear straightforward text.

**Commented [PR32]:** It took that long, and more.

**Commented [PR33]:** We didn't end up doing it this way. The hospital staff found it too confusing. They needed to just adopt the new practices and keep them.

**Commented [PR34]:** Must state and justify all assumptions related to sample size. It's important to get other peoples' eyes on this because it must be convincing and accurate!

*viii. Consent, baseline survey and randomization.* Following procedures we used in our Statewide study, a bilingual Spanish/English and a Cantonese/English Genetic Counseling Assistant (GCA) will call eligible patients. A minimum of 6 call attempts, on different days of the week and at different times of the day will be made to each patient. GCAs will review each family history form prior to the call to identify responses that require verification (e.g., often people will indicate ovarian cancer in the family when the reality was cervical cancer), and they will then confirm positive scores. Patients who meet the study eligibility criteria will be read a standard verbal consent script, and they will be invited to participate. Those who agree will be asked to complete a 20 minute baseline survey in their choice of Spanish, Chinese, or English. The randomization process and three study arms will be described, and participants will be asked if they have a strong preference. Those who do not will be randomized 1:1:1 to the three study arms in blocks, stratified by hospital and personal history of breast cancer (yes or no) using randomization tables provided by the study statistician. Those with a preference will be assigned to that modality up to 100 patients per counseling modality. GCAs will provide instructions on how to participate in the counseling session which will be scheduled within two weeks of the call. Through pilot-testing and GCA training, we will refine this process so that it takes a maximum of 30 minutes. Prospective respondents will be offered a $15 incentive to encourage participation in the baseline survey. A reminder call will be made 1-2 days prior to the counseling session.

*ix. Description of the intervention***.** The three counseling modalities are in person, telephone, and hospital-based videoconferencing using the Vsee system (a secure video chat, screen share, and medical device streaming telemedicine software created at Stanford with funding from Salesforce and the National Science Foundation).[51] The software is HIPAA compliant, can accommodate several users at the same time, and allows for document sharing. No installation is required and it can easily be used with any computer that has video and voice capabilities. Three UCSF genetic counselors will deliver counseling with each participating equally in all three modes. Genetic testing when needed will be covered by MediCal, Medicare, Laboratory Hardship programs, or philanthropic sources. Counselors will rotate through each of the different modalities to assure that individual provider characteristics are not associated with outcomes. At each location, a private room will be available for in-person and VSee appointments. Patients receiving counseling by video conference will be directed to check in at a clinic where a site team member will set up the connection with the genetic counselor at UCSF. Patients to be counseled by phone will be given an appointment time when a genetic counselor will call and, following Schwartz and Kinney,[7,8] will receive visual aids in advance by mail. To replicate usual care, hospital interpreters will be used for Spanish and Chinese speakers for all modalities. Patients who miss a scheduled appointment will be called three times by the GCA to reschedule.

For each modality, there will be a primary encounter (Visit 1) which will include an initial discussion regarding the reason and goals for the visit and counselor elicitation of patient questions and concerns. The counselor will obtain a detailed pedigree (family history), provide education about hereditary cancer, and discuss risk assessment and appropriateness of genetic testing. The counselor usually obtains enough information at the first visit to do this or may need something more, such as medical record data, or information from relatives. If additional information is needed, the counselor will make a plan to obtain what is needed and discuss risk assessment at a future appointment. If testing is not indicated, the counselor will provide the patient with screening guidelines and a number to call for additional questions, concerns, or if their family or personal history of cancer changes. If the counselor determines that another family member is a better person to test, she will discuss and make a plan to test the family member. If testing for the participant is indicated, the counselor will discuss the benefits and limitations of testing. If the patient is interested in testing and is seen in person, the counselor will test at the first visit and schedule the result appointment. If the patient is not seen in person, a sample collection kit and consent will be sent to the patient or clinic. For remote patients, if the logistics of obtaining a sample and consent are too difficult, the counselor will travel to the patient's clinic to obtain sample and consent. The counselor will conclude Visit 1 by asking whether the patient has any additional questions and understands the details of the follow-up plan. Because it might be necessary to change mode of delivery after the first visit, and also because considerable time can elapse between visits, *the research component of the intervention includes only Visit 1.* Disclosure of all positive results, or any result appointment, will occur in person at the patient's home facility if desired by the patient. Medical follow-up will be provided for mutation positive patients. Patients in all three counties have access to high risk breast cancer care and screening including chemoprevention medications, and breast MRI. Breast surgery and breast reconstruction are also available in all three counties for patients with cancer and those opting for surgical risk reduction. Risk reduction for ovarian cancer by oophorectomy is also available to high risk patients. For patients unable to access these services, philanthropic resources will be tapped to meet their needs.

*x. Follow-up interviews.* Within one week after the first/only genetic counseling session, all participants will be contacted for a 20 minute follow-up telephone survey to assess their level of satisfaction with and recall of

the counseling session and to measure changes from baseline in other key outcomes. We will follow the procedures described in the prior section including the number of attempts and calls at different times of day. Our interviewers will be bilingual research associates who will be trained similarly to the GSAs. We propose a $35 incentive to encourage completion of the follow-up interview.

*xi. Translation of materials.* Our team has extensive experience in translation and back-translation of educational and data collection materials.[52,53] There will be Spanish and Chinese versions of all patient materials (including the initial family history assessment, baseline and follow-up interviews, reminder letter, and visual aids for counseling). We will follow a rigorous translation method that ensures comparable levels of cultural meaning across languages. Initially, the English version will be translated into Spanish and Chinese, and reviewed by bilingual staff. The materials will then be independently back-translated into English, a method suggested by Brislin.[54] Drs. Kaplan and Tsoh, native Spanish and Cantonese speakers respectively, will monitor all translations. Discrepancies will be discussed and resolved, including adapting the original English.

*xii. Measurement:* A wide range of outcome measures has been used in research assessing genetic counseling outcomes with little consensus. We prioritize outcomes that i) will best ascertain the non-inferiority of remote counseling (do patients receive the same benefits – or no more harm – from remote counseling?); ii) are most readily answerable by low literacy respondents over the phone; and iii) allow us to limit respondent burden. Since genetic counseling is defined as "the process of helping people understand and adapt to the medical, psychological, and familial implications of genetic contributions to disease,"[16] knowledge/ comprehension and psychosocial factors are paramount and must be compared across counseling modes.

**Table 3**.
Statewide R01 Baseline Knowledge n=88

| | Yes | No |
|---|---|---|
| Have you ever heard about genes that are passed down from parents to children that increase the chance of getting breast cancer? | 74% | 26% |
| Sometimes a patient has a special appointment to talk with a health professional about her family's cancer history. This appointment is called genetic counseling. Before today, had you ever heard of genetic counseling for cancer? | 40% | 60% |
| Have you ever heard about the test to see if you have the breast cancer gene? The test can be done with either blood or saliva. | 51% | 49% |

Where most knowledge scales assume prior exposure to the concept of genes,[e.g.,61] as Table 3 shows, our items have been basic, starting with "Have you ever heard about genes that are passed down from parents to children that increase the chance of getting breast cancer?" With a maximum of ten items pre- and post-counseling, we will measure knowledge of mutations that increase risk, the implications for the patient and offspring, the relative rarity but seriousness of carrying a mutation, the risk to male and female family members, what can be learned from a blood test and what determines if it is appropriate, and risk-reducing options available to those who test positive. Our second primary outcome will be cancer-specific distress as measured by the Impacts of Event Scale (15-items, where the event, i.e., the stressor, is having a higher risk for breast cancer). [56,57] Based on the amount of time needed for respondents to complete the knowledge and EIS in pretesting, we will add secondary outcomes to the baseline survey in this order of priority: Decisional Conflict (10 items),[58,62] Perceived Stress[63] (4 items), and risk perception (1-3 items). At post-test only, we will measure satisfaction with genetic counseling[68] (6 items) and recall of key counseling components[64] (7 items), delivery mode preference (which mode of delivery respondents would prefer in the future if all three were available to them – 1 item),[67] and patient-centered communication (13 items).[66] We will also measure the duration of and attendance at counseling (yes or no), per counselor's records. While the scales we have identified have been validated, many have not been tested with low literacy patients. Based on our experience in this regard,[52,53,55] we will modify questions to simplify structure and language, and for comparability in Spanish, Chinese, and English. For example, knowledge questions will be true/false. All items will be pretested with up to ten each Spanish- Cantonese-, and English-speaking public hospital patients.

*xiii. Pilot test.* By month ten we will complete the training of the genetic counselors, GCAs, and follow-up interviewers. The training will consist of a review of study objectives, methods to recruit patients, methods of providing counseling, randomization and interview content, interviewing techniques to facilitate responses, probing techniques, role-playing, and record-keeping requirements. At that point we will conduct a pilot test at each clinical site (18 participants representing diverse race/ethnicity and languages; 6 at each site; 2 in each mode) assessing all elements of the intervention including recruitment, implementation, and evaluation. Evaluation of the pilot test will consist of direct observation and interviews with participants and participating staff who will be asked to rate their satisfaction with all components of the intervention. Based on the results, we will make final changes to the recruitment procedures and intervention protocol.

*xiv. Data Management and Quality Control.* Under Dr. Kaplan's direction, a dedicated data manager will oversee data collection, and creation, data entry and maintenance of all analysis files. Data will come from three

sources: participant surveys, genetic counselors' records, and tracking information. All survey responses will be keyed directly into the secure RedCap web-based program at the time of interview; family history screeners will be entered there as well. Genetic counselors will record pertinent information in an Excel file, including attendance at genetic counseling (yes or no), dates and modes of counseling, missed appointments, and participation in genetic testing (yes, no, not applicable). The study coordinator will record tracking information in an Excel file, including randomization assignment, attempts to contact, and dates of survey completion. An individual patient log form will be used to record all processes as participants move through the project. All information required for CONSORT reporting will be gathered. Data files will be imported, merged by study ID, and analyzed with SAS, version 9.3. All data will be password protected and stored on secure devices. The interactive program will be displayed to the interviewer on his/her computer screen during the interview and will contain all of the survey specifications including skip patterns and valid response ranges. Data quality is influenced by the accuracy of data collection procedures and data entry. Both of these will be maximized through periodic monitoring procedures. Data entered into the system will be automatically checked for legitimate values and logical errors. Data cleaning and analysis will be ongoing to assist in identifying interviewer, data entry and coding problems. Regular staff meetings will keep all study personnel informed of procedural refinements and issues concerning subject contact and protocol implementation.

*xv. Quantitative Data analyses.* In order to obtain an unbiased estimate of the prevalence of preference for counseling mode in this population, we will assess preference among all potential participants, even if the target number of preference or randomized participants has been enrolled (i.e. if one part of the study is closed to enrollment); we will compute the proportion of participants who express a strong preference, along with its 95% confidence interval. Among enrolled participants we will determine characteristics associated with being a preference participant using chi-square tests for categorical variables and t-tests for numeric variables. We will make three sets of comparisons with respect to each counseling outcome: 1) randomized trial participants will be compared by study arm, 2) preference participants will be compared by study arm, and 3) participants assigned to each mode of counseling will be compared by assignment type (randomized vs. preference). Among randomized trial participants who attend at least one counseling appointment and complete the post-test survey, we will compare the study arms with respect to patient-reported outcomes, such as satisfaction with counseling and pre-post change in cancer-specific distress, by constructing a 1-sided 97.5% Bonferroni-adjusted confidence interval for each pairwise difference and observing whether or not the confidence interval crosses the non-inferiority limit of 0.5 standard deviations (SD). If video or telephone turns out to be superior to in-person counseling for a particular outcome, this will be demonstrated by the confidence interval for the difference in means between video or telephone and in-person being entirely above zero (or below zero, if lower values are better), and similarly for telephone vs. video. A sample size of 90/arm at post-test (assuming 90% retention, per our previous study) will provide at least 80% power to detect non-inferiority within a 0.5 SD margin between any two arms at the 0.025 level, 1-sided, with a Bonferroni adjustment for 3 comparisons; this effect size is considered a minimally important difference in health-related quality of life outcomes.[69]

To determine which patients appear to achieve greater benefit from counseling we will construct a multiple regression model of pre-post change in each outcome as a function of study arm, hospital, personal history of breast cancer, and other participant characteristics, including language, race/ethnicity, age, education, marital/partner status, and distance of residence from the hospital, controlling for pre-counseling level of the outcome variable; in addition, we will construct models with a study arm-language interaction to determine whether there is evidence that the effect of counseling mode differs for Spanish or Chinese speakers. We will also construct models of satisfaction with counseling, first including study arm, hospital, and patient characteristics, and then adding other outcomes, such as change in cancer-specific distress level, as independent variables, and testing a study arm-language interaction. Similar analyses will be conducted among preference participants. We will also compare randomized and preference participants with respect to counseling outcomes (again using a Bonferroni adjustment for 3 comparisons). All analyses of preference participant outcomes will be adjusted for potential confounders, including participant characteristics found to be associated with preference in bivariate analyses. To analyze attendance at counseling, our secondary outcomes, among randomized trial participants the study arms will be compared with respect to the proportion of participants who attend at least one genetic counseling appointment using a chi-square test. We will also investigate factors associated with attending counseling by developing logistic regression models of attendance (yes or no) as a function of study arm, hospital, personal history of breast cancer, and participants' demographic characteristics; additional models will be constructed that include baseline levels of outcome variables (e.g., cancer-specific distress); similar analyses will be conducted among preference participants. We will also compare randomized and preference participants with respect to attendance at counseling. We do not anticipate missing data. Attendance at counseling will be ascertained from counselors' records. Based on our previous study, we expect

minimal attrition. Our primary analysis of outcomes will use complete cases; then, we will redo the analyses using multiple imputation to assess the robustness of our findings.

**Aim 2.** *Explore inductively and qualitatively variation in patients' genetic counseling experiences and understandings, genetic counselor satisfaction and perceptions, counseling session similarities and differences, and implications of organizational context across three modes of genetic counseling.*

Aim 2 employs inductive, qualitative methods to explore in depth the cases of 30 patients using their pre- and post-counseling survey responses, audio tapes of their counseling session, and in-depth interviews to explore questions common to all respondents and those specific to what was learned about the individual from the other data sources. In-depth interviews will also be conducted with genetic counselors. These varied forms of qualitative data will be triangulated to create a multidimensional understanding of the GC process and experiences of both patient and provider participants. Dr. Joseph will lead qualitative data collection in close collaboration with Dr. Pasick and the bilingual research associates/project coordinator.

*xvi. Audio Recordings of genetic counseling sessions.* We will audio record all 600 genetic counseling sessions (for phone sessions via in-line recording) for quality control and to allow for multiple analyses. First, we will conduct a *basic content analysis* with a selection of 90 recordings (30 for each counselor, 10 from each mode – 5 each from preference and RCT groups). An RA will listen to each recording and code the content using a checklist which includes key components of genetic counseling that should be covered in each session, and the use of techniques identified in the initial GC interviews and taught in the GC training. We will also measure "oral literacy demand" following Roter's analysis of prenatal genetic counseling.[88] Second, the selection of 90 will also be used to *identify patients for the 30 case studies* and to inform questions for individual patient interviews. The selection of cases will be decided jointly by Drs. Pasick, Joseph, Tsoh, and Kaplan with input from the RAs. The goal will be to select 10 from each counseling mode, including at least 3 Spanish and 3 Chinese speakers in each mode, and representing all GCs and hospitals. In particular, we will look for sessions where cultural/literacy dynamics and variations stand out. These 30 recordings will be translated as needed and transcribed. Analyses will identify objective measures of counseling content and seek to explain why and how counseling components happen or do not happen in each mode or vary with patient circumstances (e.g. affected by cancer/unaffected). These analyses will enable us to identify substantive differences and similarities in the content of GC associated with each of the three modes. For example, if telephone counseling is shorter than in person or video, as some studies have found[72] what specifically is left out, and why? The recordings will also be a rich resource for subsequent research. Based on Dr. Joseph's experience audio recording at two public hospitals we expect most participants to consent.

*xvii. Patient Interviews.* The purpose of these interviews is to understand patients' experiences with each counseling mode and the meaning they took from the exchange. The interviews will enable us to explore how the dynamics of Cultural Health Capital (CHC) play out from the patient's perspective, (e.g. how the different modes impact key relational components of counseling, and how health literacy and culture may influence various aspects of the counseling experience). We will conduct in-person qualitative interviews with 30 patients identified from the audio tapes as described above as soon as possible after their follow-up survey. We will use an in-depth interview protocol that allows participants to introduce substantive topics not anticipated by the interviewer and to address topics in their own words and manner.[70] Prior to each interview, the interviewer will review the recording of the GC session and survey results to generate specific questions for each patient and to identify any discrepancies between the two sets of data. Interview topics will include: (1) subjective experience with genetic counseling and testing; (2) communication with counselors including each of the four key components of GC communication (elicitation of family history; education about genetics, cancer risk and risk reduction strategies; counseling/psychosocial support; and informed consent for genetic testing (GT);[71] (3) values and perceptions regarding the mode of counseling (e.g. for remote modes, to explore what the patient may lose/ what may be lost by not meeting in person) and how this varies by randomization and preference; (4) values and perceptions regarding the receipt of information vs psychosocial support during the session; (5) aspects of each mode that affected patient's comfort with the GC and counseling process, interest and ability to engage etc.; and (6) for monolingual Spanish and Chinese speakers, the experience and effectiveness of the medical interpretation in each counseling mode. The interviews will further explore outcomes patients care about, such as clarity of information, usefulness for decision-making, psycho-social support, ability to help family, alleviation of cancer worry, travel, wait time, loss of work, child care, and *how and why* these outcomes are successfully achieved or not in each mode.

At the end of the follow-up survey, all participants will be asked if they are willing to participate in an in-person interview sometime in the next 2 weeks should they be chosen for that component. For those who agree and whose counseling audio recording was selected for case study, Dr. Joseph will work with RAs to review all data sources to devise individual interview questions addressing patient level of engagement in the conversation, how

responsive the counselor was to patient cues, to be familiar with the content of the conversation so that points that come up in the interview can be explored in relation to the counseling interaction and particularly with regard to patient's report of satisfaction, recall, etc. from the survey. A bilingual RA will conduct in-person interviews at a time and location that is convenient for patients. Written consent will be obtained immediately prior to the interview, and a $35 gift card will be provided upon completion of the interview. With participant permission, interviews will be audio-recorded.

*xviii. Genetic Counselor Interviews.* The purpose of these interviews is to understand the genetic counselors' perspectives on counseling in the safety net setting and their expectations and experiences with each of the three modes of counseling. At three points during the study, Dr. Joseph or an RA will conduct in-depth interviews with the study's 3 genetic counselors, first during the developmental period to assess counselors' perspectives and expectations regarding the three counseling modes, anticipated strategies for each, and any concerns about logistical or other implementation issues. These data will inform the training GCs receive prior to the trial to ensure a unified approach to counseling in each mode. The second interview will occur halfway through the accrual of study participants, and the third after the trial is complete. Interview topics for the second and third interviews will include: (1) specific cases, using examples from audio recordings of counseling sessions; (2) strategies employed in each mode, e.g. if and how communication is tailored; (3) the challenges faced by and satisfaction with each mode; (4) experiences working with interpreters in each mode; (5) perceived differences in effectiveness of counseling modes with patients of different characteristics, e.g. ethnicity, language, affected v. unaffected, other characteristics the counselors identify as relevant. Interviews will be conducted in-person at a private location of the participant's choosing (e.g. the GC's office) and will last approximately 60 minutes. Written informed consent will be obtained immediately prior to the interviews, and participants will be provided with a $50 gift card in appreciation for their time.

*xix. Qualitative Data Analyses.* Analyses will integrate data from all sources to produce a well-contextualized understanding of the major themes and issues that will inform understanding of the relevant factors to consider when using each of the three counseling modes. To analyze the qualitative data, we will use standard techniques based in grounded theory.[73-76] This iterative process of inductive analysis involves examining and re-examining the facts and meanings contained in the data to develop successively more refined ideas about domains of interest. Specifically, this process involves: 1) the parsing of descriptive data according to themes; 2) the development of a set of taxonomic principles (a coding manual for significant concepts) and subsequent classification (coding) of themes and concepts; and 3) the identification of associations among themes. We will initially code the data according to the conceptual framework for this study and as data accumulate, the coding scheme will evolve to reflect new insights.[73] Through this iterative process, we will identify salient dimensions of culture, health literacy and language in GC-patient communication. All transcribed interview text will be entered into a qualitative data analysis software that enables searching and retrieval of coded text and audio (Atlas-ti).[76] Two study staff will independently code and analyze the data and will meet regularly with Drs. Joseph and Pasick to discuss coding and come to consensus on any discrepancies, create and discuss coding memos to summarize interim findings, and as the basis for discussion with the rest of the research team.

Analyses will proceed along three main tracks. First, patient interviews will be examined and coded to identify benefits and harms of the three delivery modes as perceived and experienced by the patients. We will code both the patients' experiences with the logistics of each mode, as well as their perceptions of the informational and psychosocial content. Thus the qualitative data will expand upon the findings from the survey data with regard to the patients' satisfaction and subjective experience of each mode. These qualitative data will also be ideal for examining if and how cultural differences may impact the benefits and harms of each mode. For example, recent studies of genetic counseling have indicated that the standard practice of non-directive GC communication (where the provider emphasizes individual autonomy in decision-making) may not always be culturally appropriate.[78,79] One study showed that for some Asian Americans, the non-directive approach can cause confusion about roles and disrupt the authority usually granted to the medical provider,[77] and a study of Mexican Americans in prenatal genetic counseling found that the non-directive approach could be a source of miscommunication.[80] We will examine how patients interpret non-directive communication in each of the three modes, and whether counselors are more directive when counseling remotely than in-person.

Second, we will analyze GC interview data to elucidate the thinking behind counselors' strategies, describe the key challenges they face in each mode, identify their preferences and reasoning for preferences with regard to each mode, and to interpret audio recordings that we discuss with counselors in relation to survey outcomes with regard to satisfaction and understanding. We will compare GC perspectives across each of the three time points and across the three counselors. Third, following research on provider-patient communication,[81] we will code the 30 counseling session transcripts for: (1) GC use of standardized language in delivering information vs. tailoring; (2) GC use of jargon or technical terms;[82] (3) patient participation and question asking;[83] (4) interpretation

for Spanish and Chinese speakers (accuracy, and interpreter as cultural broker or advocate);[84] and (5) duration of each of the key components of GC communication and the overall session. From the in-depth analysis of the 30 transcripts of counseling recordings, as well as the coding the basic content of the 90 recordings in accord with the checklist described above, we will empirically identify substantive differences in the content of GC that is provided via each mode, and assess why and how key components happen or don't happen. For example, although counselors will be trained to ensure a uniform approach in each mode, we expect there will be differences in implementation and style. Through comparisons across recordings, we will identify particularly effective strategies in each mode. The iterative analytic process will allow us to integrate these data by tacking between the three tracks, using insights gleaned on one track to elucidate data in another. The ***expected outcome*** will be a multifaceted understanding that explains the strengths and limitations of each mode from both the patient and counselor perspectives examining how CHC, in particular culture and health literacy, shape the dynamics of counseling in each mode and in each of three hospitals.

*xx. Dissemination.* Our dissemination plan will target practitioners and academics in safety net hospitals, genetics/genetic counseling, breast oncology, and public health genomics. Nationally, we will present our findings to the American Public Health Association Genomics Forum, the CDC meetings on Public Health Genomics, the San Antonio Breast Cancer Symposium, the American Society for Clinical Genetics, the American Society of Preventive Oncology, and the National Society for Genetic Counselors (see Hoskovec letter). The NSGC has numerous communication channels available to us. We will also publish in the journals of the last two societies. Our UCSF colleagues are part of a network of California's 21 safety net hospitals. Dr. Urmimala Sarkar is Principal Investigator of the AHRQ-funded Public Healthcare systems Evidence Network and iNnovation eXchange (PHoENIX -see letter), a dissemination partnership between the UCSF Center for Vulnerable Populations and the California Association of Public Hospital's Safety Net Institute. During Y5, we will develop and disseminate a toolkit based on our findings including training materials, protocols, and peer-to-peer learning opportunities as part of PHoENIX's core activities.

xxi. *Limitations.* This study has some limitations. It is possible that the size of the preference group will be smaller than that for randomization, and the number of limited English patients may be too small to determine if use of interpreters affects outcomes. It would be ideal to include all counseling sessions in our analyses. However, we believe that the first session (which will be all, for a great many patients) will yield sufficient data to comprehensively assess the three counseling modes. Lastly, long-term follow-up, while desirable, will not be possible within the scope of this study. We will, nonetheless, produce rich and actionable findings.

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