NHGRI IRB
Human Subjects Research Protocol

Project title: **Is it Feasible?: Self-Affirmation for Hereditary Breast and Ovarian Cancer Genetic Counseling**

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NHGRI Protocol Number: T-HG-0132

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Title/Section/Branch/Institute: Staff Scientist/Social & Behavioral Research Branch/NHGRI

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Collaborating Institutions: St. Luke's Health System, Kansas City, Missouri (FWA00024002), Medstar Washington Hospital Center, Washington, DC (FWA00000504)

List the name of the Site and FWA# for each institution; see http://ohrp.cit.nih.gov/search/asearch.asp#ASUR *for assurance #s*

Protocol Summary

Full Title:	*Is it Feasible?: Self-Affirmation for Hereditary Breast and Ovarian Cancer Genetic Counseling*
Principal Investigator:	*Dr. Lori Erby*
Sample Size:	*N= 74, patient control group =35, patient treatment group = 35, genetic counselors =4*
Accrual Ceiling:	*180 participants*
Study Population:	*Clients being seen for an initial visit in the hereditary breast and ovarian cancer (HBOC) clinic, both affected and unaffected with cancer, female, 18-90 years-old*
Accrual Period:	*July 2017 – February 2017*
Study Design:	*This study is a feasibility study to assess the acceptance and initial outcomes of a self-affirmation intervention in a novel HBOC genetic counseling context. The study relies on surveys of 4 genetic counselors and 70 clients after a small case control study. The purpose is to estimate effect sizes and preliminary outcomes of self-affirmation in a genetic counseling setting and to assess client and counselor interest in self-affirmation interventions.*
Study Duration:	Start Date: *June 2017* End Date: *March 2017*
Primary Objective:	*To identify outcomes that may be applicable for a larger SA intervention study in the genetic counseling context by randomly assigning clients to a control or intervention arm and then surveying them after the SA intervention and genetic counseling appointment.* *To assess clients' and counselors' opinions of an SA intervention by post study surveys.*
Secondary Objectives:	*To assess process outcomes of a SA intervention including the time required to complete the intervention, uptake, and attrition.*
Endpoints:	*Client's completion of follow-up survey; Counselor's completion of study review survey.*

Contents

List of Abbreviations

AE	Adverse Event/Adverse Experience
AI	Associate Investigator
DSMB	Data Safety and Monitoring Board
FWA	Federal Wide Assurance
ICF	Informed Consent Form
IRB	Institutional Review Board
GC	Genetic Counselor
HBOC	Hereditary Breast and Ovarian Cancer
N	Number (typically refers to number of subjects/sample size)
NCI	National Cancer Institute
NHGRI	National Human Genome Research Institute, NIH
NIH	National Institutes of Health
OHRP	Office for Human Research Protections
OHSRP	Office of Human Subjects Research Program
PI	Principal Investigator
SA	Self-Affirmation
SAE	Serious Adverse Event/Serious Adverse Experience
SI	Student investigator
SOP	Standard Operating Procedure
UP	Unanticipated Problem
UPnonAE	Unanticipated Problem that is not an Adverse Event

1.0 Precis

The proposed study is a feasibility study to assess the viability of implementing a Self-Affirmation (SA) intervention in a Hereditary Breast and Ovarian Cancer (HBOC) genetic counseling clinic to improve client communication and behavioral outcomes. Participants will be clients and genetic counselors at the St. Luke's Hospital System and Medstar Washington Hospital Center HBOC clinics. This study seeks to identify outcomes that would be most informative in a large-scale research protocol. As outcomes, we will assess clients' decision self-efficacy, intention to talk with family, genetic test uptake, empowerment, and HBOC knowledge. We will also assess counselors and clients perceived benefits, perceived harms, and acceptance of the affirmation intervention.

In this study clients will be invited to participate in an intervention before their genetic counseling appointment. The SA intervention is a short written exercise to reinforce clients' self-integrity (a global sense of personal adequacy), leading to more openness to threatening information within the genetic counseling session. Clients and counselors will be surveyed after the study to assess outcome measures and feasibility of the intervention.

Social science research has shown that when people are faced with threatening information they often seek to protect themselves and reject the threatening message. Message rejection can include minimizing the importance or discrediting the truth of the message. SA interventions aim to bolster self-integrity by focusing on aspects of subject's lives they value and thereby improving participants' self-perception and tolerance towards threatening messages. SA manipulations have been shown to increase patient communication within appointments and both intentions and actions toward behavior change.

Often in cancer genetic counseling appointments clients are confronted with the threat of having a significantly increased risk of cancers while being asked to make a decision about genetic testing. A self-affirmation intervention may facilitate greater client decision self-efficacy, empowerment, and positive behavior outcomes, such as communication with family regarding genetic risk and screening behaviors.

2.0 Objectives and specific aims

The objective of this study is to investigate if a self-affirmation intervention is feasible in the context of HBOC genetic counseling appointments.

Specific aims

1. To assess the preliminary impact of a SA intervention on outcomes that may be implemented in future studies, by assessing differences in the following between a SA intervention and unaffirmed standard SA control group of HBOC genetic counseling clients:
    a. Intentions to talk with family, test uptake
    b. Empowerment, decision self-efficacy
    c. HBOC knowledge
2. To describe genetic counselors' (GCs) and clients' response to a novel, client-based SA intervention, including perceived impact, barriers, and facilitators to implementing such an intervention on a wider scale

3. To assess the percentage of eligible clients that completed a pre-visit SA intervention and if the SA intervention is effective in affirming clients.

3.0 Brief rationale and background

Breast cancer is the most prevalent cancer in women, with 230,815 new diagnoses in women in 2013 alone (U.S. Cancer Statistics Working Group, 2016). It is estimated that 5-10% of women with breast cancer and 20% of women with ovarian cancer carry a gene variant that predisposes them to these cancers (Campeau et al., 2008; Walsh et al., 2011). Being at genetic risk for cancer means clients often face difficult decisions about testing, conversations with family members, prophylactic surgery, and preventative medications. As more people are faced with these decisions it is important to understand how to best aid them in the decision-making process. Self-affirmation has shown to increase patient engagement and problem solving. This proposed study is a feasibility, randomized control trial to assess the initial outcomes of self-affirmation and the openness of genetic counselors and clients to an intervention for improving clients' genetic counseling experiences and outcomes.

Self-affirmation.

Self-affirmation (SA) theory suggests that people work to maintain their perceptions of self-integrity, morality, and consistency (Sherman & Cohen, 2006; Steele, 1988). When they experience a threat to the self-concept they seek to neutralize it through defending themselves against the message. Self-integrity is an individual's perception of their efficacy across multiple domains, defined further as their cumulative moral and adaptive adequacy (Steele, 1988). Self-integrity can be best understood in context. For example, a woman may feel threatened by a negative health finding, but if she feels competent in her relationships, then her overall self-integrity is likely to be maintained and she can address the threat in a non-defensive manner. On the other hand, when self-integrity is compromised, and other areas of self-concept do not stabilize the threat, then individuals can become defensive against the threating message to protect their self-integrity (Sherman & Cohen, 2006; Steele, 1988). For example, they may try to discredit or ignore a concerning message.

SA theory further postulates that an affirmation intervention prior to facing a threat can reinforce an individual's self-integrity and increase openness to the threat (e.g., a threatening message or performance in a difficult task; Sherman & Cohen, 2006). SA has also been shown to increase openness to threatening health messages. In one study, 66 women were given an article stating that coffee consumption increases the risk for fibrocystic breast disease (Reed & Aspinwall, 1998). Half of the women were given a self-affirmation measure focusing on kindness before reading the article. Those who drank coffee and were self-affirmed oriented to and accepted risk confirming information significantly more quickly than did coffee drinkers who were un-affirmed. Other studies have shown similar results related to accepting threatening health messages (Harris & Epton, 2009).

Specific to genetic information, SA has been shown to improve openness. One survey of 594 participants in the ClinSeq cohort found that those who were higher in spontaneous self-affirmation were more likely to intend to seek out genetic risk information despite being high in anticipated affect, a correlate for worry (Ferrer et al., 2014). SA may affect people's desire for genetic test results. SA may increase clients' likelihood to talk with family members about genetic information. Not telling relatives could have negative outcomes for at-risk family members. Ferrer and colleagues' (2014) ClinSeq research found that those who were higher in spontaneous SA were significantly more likely to intend to share actionable genetic testing

results ($p = 0.05$) and non-actionable results ($p = 0.01$) with family members. Although spontaneous SA is distinct from prompted SA, this finding could suggest that an intervention would also increase discussions with family members. Additionally, SA interventions have been shown to significantly increase participants' feelings of love and connectedness to others compared to a control group, which may also be related to intentions to talk with family (Crocker, Niiya, & Mischkowski, 2008).

SA has also been shown to improve problem solving in stressful situations. A case-control study of 73 university students found that chronically stressed students who were self-affirmed before a remote associate problem-solving task (RAT) performed better than those who were chronically stressed and unaffirmed (Creswell et al., 2013). Both the main effect of SA ($p = 0.005$) and the interaction effect between chronic stress and SA (p=.041) were significant.

A meta-analysis of SA and responses to health messages assessing both intentions and behaviors in 16 studies found that aggregate effect sizes for health intentions and health behaviors were statistically significant but low at $d = 0.26$ and $d = 0.27$ respectively (Sweeney & Moyer, 2015). Behaviors and health intentions in this study were both negative (e.g. reducing caffeine intake or alcohol consumption) and positive (e.g. increasing sunscreen or condom use). It should be noted that 12 of the 16 studies reviewed used student samples where the threat was either far off (e.g. sunscreen use and skin cancer) or not personalized so the perceived threat of the message may have been low. In the proposed study the risk for HBOC cancer is personalized by family history or personal early onset cancer and the threat of cancer is either immediate or high. Since stress and heightened risk appraisals appear to moderate the effect of SA as an intervention, we would expect the effect of SA in this population to be higher than those in the meta-analysis.

Other studies have addressed SA and client engagement in a medical encounter. A randomized controlled trial of SA in African American clients with hypertension found that the SA treatment group requested and provided more information about their medical condition from their primary care provider in a medical encounter. Additionally, in the SA group, the patient-provider communication was characterized as being more interested, friendly, responsive, interactive, and respectful (Havranek et al., 2012). Since SA is postulated to increase message acceptance and to decrease motivation to avoid the threat, it is consistent that clients may attend to the threatening message more carefully and remember information about HBOC more accurately (Harris & Epton, 2009).

SA is postulated to decrease patient defensiveness. To our knowledge there are no direct measures of patient defensiveness but this construct has been assessed by measuring numerous downstream constructs in past research, including perceived threat, message acceptance, and defensive avoidance (Good & Abraham, 2007). In this study, we will be measuring the downstream effects of defensiveness by assessing patient empowerment and decision efficacy. SA intervention are theorized to decrease patient defensiveness, which will increase their openness to threatening information, which will increase decision self-efficacy. Furthermore, increased openness will increase the client's engagement in the genetic counseling session and result in greater patient empowerment. It is also possible that client self-integrity, their global sense of personal adequacy, is related to empowerment more directly than outlined above.

Feasibility study

To our knowledge studies have not examined the impact of SA interventions in genetic counseling (Etchegary & Perrier, 2007). The ClinSeq study, designed to identify health-related genetic changes through exome sequencing, examined SA related to genetic risk perception and

information seeking. Although the ClinSeq study did not include a SA intervention, surveys did include assessments of participants' tendencies to engage in spontaneous SA.

Given the lack of evidence in this context it is important to conduct a feasibility study prior to a full-scale intervention to assess genetic counselors' and clients' reactions to the SA intervention, and the logistics of and barriers to SA implementation. Feasibility research studies generally have smaller sample sizes and therefore statistically significant outcomes are not expected. These studies allow for exploration of many aspects of implementation and preliminary outcomes. The National Cancer Institute has recognized the need for more intervention-based feasibility studies prior to full-scale studies to determine "whether comprehensive and multilevel evaluations are justified (Bowen et al., 2009, p. 1)." A feasibility study of SA in genetic counseling would allow for preliminary examination of the impact of SA on genetic counseling session outcomes to provide estimates of effect size, confidence intervals and, consequently, necessary sample size for a future study.

4.0 Description of study design

This study is a randomized controlled feasibility study to assess the acceptance and initial outcomes of a self-affirmation intervention in a cancer genetic counseling context.

5.0 Description of procedures:

In this intervention-based randomized controlled feasibility study, Hereditary Breast and Ovarian Cancer (HBOC) genetic counseling clients will receive an intervention and short survey before their appointment and will complete a survey after their appointment. Genetic counselors who counsel participating clients will complete a post-appointment survey after each appointment with a participating client and a survey at the end of the study.

Thirty-five client participants will be randomly assigned to complete the self-affirmation intervention and 35 participants will complete the control condition. Client participants will be patients being seen for an initial appointment for genetic counseling at the HBOC genetic counseling clinic, regardless of current cancer status. All client participants will take a state anxiety measure before their appointment to control for some of the variability in indication. Client participants will also indicate if they have cancer, if they have received genetic testing, and if they were offered genetic testing at the current visit. Genetic counseling can be indicated for patients without cancer who have a family history of cancer, for patients with cancer, and for self-referred patients who are concerned about their cancer risk. Most often, the initial cancer genetic counseling appointment occurs before qualification for genetic testing is assessed and clients have a follow-up appointment to receive results. Sometimes oncologists or primary care physicians order genetic tests and the initial genetic counseling appointment includes results delivery and education. Any client with an initial genetic counseling appointment will be invited to participate in the study. Follow-up appointments will not be included because patients already have a relationship with the genetic counselor. The four genetic counselors, who have appointments with the participating clients, will be enrolled in the study as genetic counselor participants.

The SA intervention consists of participants ranking 11 items (artistic skills, athletics, business/money, creativity, independence, music, politics, relationships with friends and family, religious values, sense of humor, spontaneity) from most important to least important (See

Appendix C) (Creswell et al., 2013; Havranek et al., 2012). They will then be asked to write about the item that is most important to them and why it may be important to them. The control group will rank the same list and be asked to write about the 9th ranked item and why it might be important to someone else. The control condition is consistent with the control used in other SA intervention studies. The 9th ranked item is chosen to inhibit a reverse effect where participants feel affirmed because they do not value something that is averse to them. Both the intervention and control group will receive a 6-question survey of state anxiety along with the writing prompt, which will be used as a control measure.

Potential participants will be identified through the patient schedule and will be contacted by the student assistant investigator (AI), Anna Chassevent, about one week prior to their appointment to invite them to participate in the study and obtain verbal informed consent. Participants will be recommended to arrive 15 minutes prior to their scheduled appointment. When clients arrive at the HBOC clinic, the front desk staff will give client participants the SA or control intervention based on random assignment. The affirmation intervention or control condition will be completed directly before the regularly scheduled appointment.

Genetic counselors will be blinded to the study condition of their clients, although clients might choose to discuss the content of the intervention survey with the counselor. Counseling sessions will otherwise proceed according to protocol for the clinic. Clients will receive a paper survey as they leave the appointment regarding their demographic information (age, sex, education, race, ethnicity, cancer status) experience in the study, decision self-efficacy, empowerment, genetic knowledge, intentions to talk with family, information seeking, and intentions to pursue genetic testing if it was offered. They will be given the option to fill out the paper version or to access an electronic version online. Hard copy surveys will be returned to the front desk or by mail to the AI. Electronic versions will be sent to an email address provided by the client. A week after their appointment, all clients will receive an electronic reminder notification to complete the questionnaire. Upon completion of the online survey or paper questionnaire participants will be mailed a $15 gift card.

Genetic counselors at St. Luke's Health System volunteered to participate in this study and contacted the AI about their interest in participating and hosting the study. The counselors at Medstar Washington Hospital Center were contacted by the AI after initial IRB approval of this protocol in order to increase recruitment by adding an additional site.

At the onset of data collection, counselors will complete a written consent. After each appointment with a study participant, genetic counselors will complete a short client empowerment survey. After the client study is complete, genetic counselors will be given a survey about their opinions about and experience with the self-affirmation intervention. Questions will include information on their experiences and opinions about the SA. Counselors at St. Luke's Health System will each be given a $1400 gift card at the completion of the latter questionnaire. The counselors at Medstar see fewer potential participants so their compensation will be $200. We expect to have approximately 16 patient participants from Medstar and 54 from St. Luke's Health System. In addition, the counselors at MedStar will be involved with recruitment over a shorter period of time and will not have to expend the effort expended by the St. Luke's counselors to work through logistics prior to the study's approval

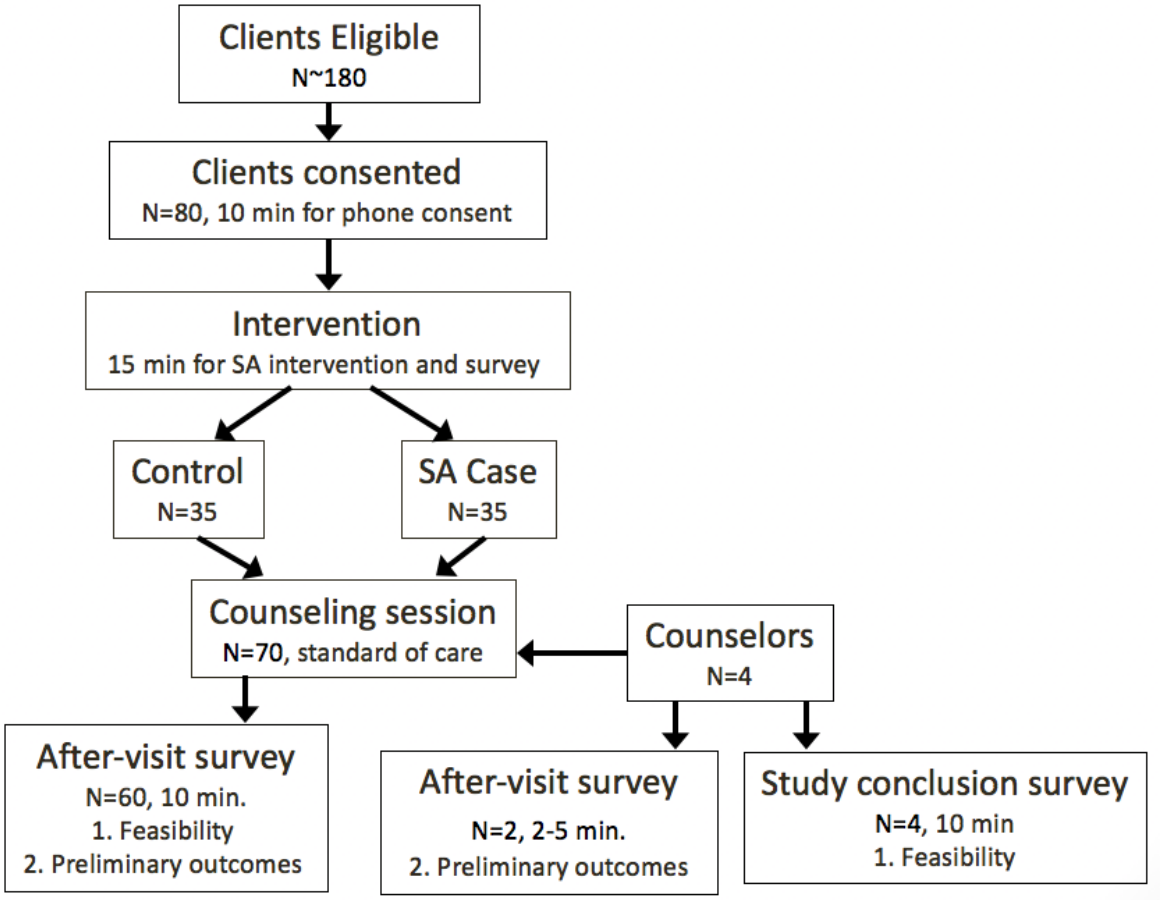

Figure 3: *Participants participation in protocol*

Responsibilities of NIH

This study was developed by the student associate investigator, Anna Chassevent, for her thesis project as a part of the Genetic Counseling Training Program at the NHGRI and her thesis advisor, Dr. Barbara Biesecker at the NIH. Clients will be consented for participation by phone by the SI. Counselors will be consented by email or fax by the AI. The AI will distribute the study materials (intervention and surveys) to the counselors at St. Luke's Health System and Medstar Washington Hospital Center. All data will be analyzed at the NIH by the PI and AI, who are researchers from the NIH.

Responsibilities of St. Luke's Health System and Medstar Washington Hospital Center

Whitney Ford and Kallie Woods are genetic counselors at St. Luke's Health System and non-NIH collaborators for this research study. The St. Luke's Health system HBOC scheduling coordinator will distribute and collect the intervention, client surveys, and contact cards on site at the St. Luke's health system HBOC clinic. The scheduling coordinator will also collect the genetic counselor after visit and end of study surveys. They will mail all deidentified materials to the NIH researchers for analysis.

Michael Setzer and Aime Agather are the genetic counselors at Medstar Washington Hospital Center and non-NIH collaborators for this research study. Similarly to St. Luke's Health System, the front desk personnel will distribute and collect the study intervention, client surveys,

and contact cards. Because this clinic does not have one assigned clinic coordinator, the counselors will confirm and oversee that study materials are appropriately returned to the AI.

The intervention and client survey will not include identifying information and contact information will be separated from the other study materials. All surveys and the intervention are self-administered.

5.1 *N/A*

5.2 *N/A*

5.3 *N/A*

5.4 *N/A*

5.5 *N/A*

5.6 Describe questionnaires or other psychological instruments and estimate how long they will take to complete, and whether they address sensitive topics (Appendix C-F)

Intervention (See appendix C)

For the SA intervention, participants will be asked to rank 11 items (artistic skills, athletics, business/money, creativity, independence, music, politics, relationships with friends and family, religious values, sense of humor, spontaneity) from most important to least important (Creswell et al., 2013; Havranek et al., 2012). They will then be asked to write about the item that is most important to them and why it may be important to them. The control group will rank the same list and be asked to will write about the 9th ranked item and why it might be important to someone else. The control condition is consistent with the control used in other SA intervention studies.
Immediately after the intervention or control condition, participants will complete a 2 minute survey that consists of the short version of the Stat-Trait Anxiety Inventory (STAI). This measurement entails 6 questions to assess the client's current anxiety. The purpose of the STAI is to control for anxiety, to identify if those who are more anxious are more effected by the SA intervention. The intervention and STAI should take about 10-15 minutes together. At the end of the intervention there will be a detachable page asking for the client's email address to send them with the post-intervention survey and a reminder to complete it. This document will be immediately separated from the study material by the scheduling coordinator.

Client post-intervention survey (Appendix D)

Client surveys will consist of questions on each category of outcome (information seeking, test uptake, empowerment, intention to talk with family, decision self-efficacy, and HBOC knowledge) as well as response to and acceptance of the SA measure. The survey will be offered online and in person. It should take less than 15 min for participants to complete. At the end the hard copy post-intervention there will be a page for clients to enter their mailing address to receive the gift card, this page will be immediately separated from the other study materials by the scheduling coordinator. The online survey will have a separate link for clients to enter their mailing address.

Decision self-efficacy. To measure decision self-efficacy in decisions regarding genetic testing for HBOC and we will use the Decision Self-Efficacy Scale (O'Connor, 1995). This scale focuses on the decision process and interactions with the medical professional so it gives insight into both decisional efficacy and clients' engagement with the clinician.

Test uptake. For this section we will ask two questions to test uptake; "Did your counselor offer you genetic testing in your counseling appointment?" (yes/no) and "If yes, do you plan to have genetic testing?" (yes/no).

Intention to talk with family. Intention to talk with family will be measured using two questions. The first is a question asking clients to select the categorical description of the family group they are most likely to share information with from a list of options, such as "I plan to talk to only a few people who are closest to me." The second question will state "How likely are you to share results with the relatives you selected?" will be rated on a 1-7 likert scale labeled "extremely likely to extremely unlikely."

Empowerment. Empowerment will be assessed using the valid and reliable Genetic Counseling Outcomes Survey (GCOS-24) (McAllister et al, 2011). The GCOS-24 is a 24 item instrument that was designed to measure positive outcomes of genetic counseling. Empowerment was conceptualized to include decisional control, cognitive control, behavioral control, emotional regulation, and hope. The scale has seven dimensions, which exist under a single higher order construct.

Client Knowledge. Client knowledge will be measured using modified questions based on the National Center for Human Genome Research Knowledge scale and genome sequencing knowledge items from Kaphingst and colleagues study of informed consent on genome sequencing knowledge (Kaphingst et al., 2012; Scherr, Christie, & Vadaparampil, 2015). These questions focus on the main knowledge concepts rather than specific details since counseling sessions may differ depending on patient's indication for genetic counseling.

Response to SA measure. This section will ask both open ended and yes/no questions regarding clients' acceptance of and response to the intervention or control. There is also a question asking if and how clients thought that the measure affected their counseling session to identify any overt interference of the measure with their session.

Counselor after visit survey (Appendix E)

The counselor after visit survey consists of a counselor version of the Genetic Counseling Outcome Scale (GCOS-24). This scale was modified from the original GCOS-24 for use by counselors and parallels the client version. This measure consists of 24 likert scale questions that assess counselor's perceptions of the client's empowerment. It should take 3-5 minutes for the counselors to complete after each session.

Counselor post-study survey (Appendix F)

The counselor post-intervention surveys will include four yes/no questions with related open-ended response questions regarding the intervention. It also includes one likert scaled question and a place for any other thoughts on the study. This survey should take about 10 minutes to complete.

6.0 Description of study population

6.1 Estimated number of participants, enrollment ceiling, and anticipated enrollment by year.

The client participants will be female patients being seen at the high-risk breast and ovarian cancer clinic at St. Luke's Health System and Medstar Washington Hospital Center, for their initial appointment for genetic counseling for HBOC. Participant selection will be indiscriminant of if they have cancer or if they have already had genetic testing through another provider. Participants must be at least 18 years of age. For a fully powered study of the effect of self-affirmation on genetic counseling outcomes, we estimate that we would need 296 participants to identify a small to medium effect (Cohen's $d = 0.35$) with beta being 0.85 and alpha being 0.05. This Cohen's d is based on other SA interventions in the education and emerging medical literature. For this feasibility study we seek to recruit 70 client participants and 4 genetic counselor participants. We chose this number for several reasons. The genetic counselors at St. Luke's Health System see about 40 new patients a month. Over the 4 months of data collection there will be 180 appointments. We believe that getting 70 of these clients to consent is an achievable estimation. Additionally, feasibility studies typically range from 30-50 participants to estimate attrition and confidence intervals. The enrolment ceiling is 180 participants. Genetic counselor participants two genetic counselors at the St. Luke's health system HBOC clinic. Participants will be enrolled by February of 2018. To this point, we have been recruiting about 8 patients a month instead of expected 17 through St. Luke's Health System. To our knowledge, this is because the counselors are seeing more colorectal and other cancer patients then expected instead of HBOC patients and we have been able to reach less patients for consent. About half decline to be contacted and 1/3 cannot be reached by the AI for consent. For this reason, we are adding the Medstar Washington Hospital Center site and extending the recruitment window.
Genetic counselor participants are two genetic counselors employed in the HBOC genetic counseling clinic at St. Luke's Hospital and two genetic counselors who see HBOC patients at Medstar Washington Hospital Center.

6.2 Description and justification of clinical inclusion/exclusion criteria.

Participants must be female, at least 18 years old, and have an initial appointment for genetic counseling for HBOC risk at St. Luke's health system or Medstar Washington Hospital Center. Participants will not be discriminated against for race, ethnicity, or income. Participants must be able to read and write in English to participate. Non-English speakers and illiterate subjects will be excluded. The intervention and measures have not been validated in other languages and therefore we are limiting the language to English. We will assess feasibility before validating the measures and intervention in another language. Since this is a feasibility study we will not have sufficient power to validate the measures. Follow-up studies should include more diverse populations. Clients who are unable to provide consent will be excluded. Pregnant women will be included. This is appropriate under 45 CFR 46.204 because this is minimal risk research necessary to develop important knowledge that cannot be obtained by other means. It will be the case that: 1) no inducements, monetary or otherwise, will be offered to terminate a pregnancy; 2) individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and 3) individuals engaged in the research will have no part in determining the viability of a neonate.

The study will be limited to women because the majority of clients at a hereditary breast and ovarian cancer clinic are women and we do not estimate that there will be enough male clients to independently analyze their responses.
Genetic counselor participants must be certified genetic counselors and see clients with an indication for HBOC related genetic counseling.

6.3 Location of study.

This study will be conducted at the HBOC clinics at St. Luke's Health System in Kansas City, Missouri and Medstar Washington Hospital Center in Washington, DC.

6.4 Description of recruitment strategies.

Participants will be identified through the scheduling system at St. Luke's Health system HBOC clinic. The scheduling coordinator will identify participants on the schedule who may meet criteria for the study. During the routine reminder call to patients the coordinator will ask clients if they are willing to receive a phone call regarding a study. If clients agree the AI will contact clients to explain the study, identify clients interest, and complete the informed consent. Clients will also be sent an information leaflet (See appendix G) about the study in the pre-appointment packet that is sent to all clients to provide informed about the study before the AI contacts them.
Recruitment will occur in a similar fashion at Medstar Washington Hospital Center although the clinic does not have a single clinic coordinator. For this reason, the counselor will oversee the identification of participants who may qualify for the study. To minimize conflict of interest, clinic personnel other than the genetic counselors will then call the potential patient participants to seek permission for them to be contacted by the AI. If they agree, the AI will contact them in the same manner as at St. Luke's Health system.
Genetic counselor participants at St. Luke's Health System were contacted for interest in hosting the study through the National Society of Genetic Counselors cancer Special Interest Group (SIG). The two counselors at St. Luke's Health system voluntarily contacted the AI to both assist with this research at their site and to participate. The counselors at Medstar Washington Hospital Center were contacted by the AI after initial IRB approval in order to increase recruitment by adding an additional site.

6.5 Description of criteria for withdrawal from study.

Client participants may withdraw from the study at any time during or immediately following completion. While completing the survey, the participant may choose not to answer any particular question. Surveys will be anonymous, using a code word to coordinate documents (see Section 10) and never linked to contact information. If client participants request to withdraw from the study if they must provide their code word to identify and remove their documents.
Genetic counselor participants may with withdraw from the study at any time during the study. If genetic counselor participants withdraw any previous surveys will be included in the analysis but future patients will not be consented to participate. Surveys will not be linked to the individual counselor.

7.0 Description of study statistical considerations and/or analytic plan:

Aims have been copied here for ease of interpretation.

Aim 1: To assess the preliminary impact of a novel SA intervention on outcomes that may be targeted in future studies, by assessing differences in the following between a SA intervention and unaffirmed standard SA intervention control group of HBOC genetic counseling clients:

a. Intentions to talk with family, test uptake
b. Empowerment, decision self-efficacy
c. HBOC knowledge

The primary goal of analysis of aim 1 is to identify which outcomes would be most appropriate for follow up studies and the necessary sample size for adequate statistical power.

For decision efficacy, the scores on the Decision Self-Efficacy Scale (See section 2 of client survey, Appendix D) will be compared between groups using linear regression controlling for education, race, anxiety score, and effectiveness of intervention (based on last question on intervention Appendix C). Intention to talk with family, genetic testing uptake, and information seeking will be measured similarly using linear regression.

Client empowerment will be analyzed by using the GCOS-24 a 24-item likert scale completed by clients and parallel scale by genetic counselors (See section 3 of client survey of appendix D and appendix F). Both scales will be compared between groups using linear regression controlling for education, race, anxiety score, and effectiveness of intervention (based on last question on survey). Discrepancies between counselor and client surveys will be analyzed using dyadic analyses. For this analysis, we will assess the correlation between paired client and genetic counselor GCOS-24 for the compete survey and for the individual questions.

HBOC knowledge will be analyzed between groups using linear regression testing the knowledge scale (See section 4 of client survey, Appendix D) and controlling for education, race, anxiety score, and effectiveness of intervention.

Effect sizes and standard deviations for each outcome will be identified, and an estimated sample size for a fully powered study will be estimated based on power calculations.

Aim 2: To describe genetic counselors' (GCs) and clients' response to a novel, client-based SA intervention, including perceived impact, barriers, and facilitators to implementing such an intervention on a wider scale

This aim will be analyzed as percent of yes/no response to intervention survey questions for both clients and counselors. There will also be open ended questions for specific impacts, barriers, and facilitators to be mentioned, which will be analyzed using thematic analysis of answers. The AI will create a codebook based on initial read through and subsequently code all answers. A separate coder will validate ten percent of answers for consistency.

Aim 3: To assess the percentage of clients that completed a pre-visit SA intervention among client participants and if the SA intervention is affective in affirming clients.

Intervention uptake will be reported as a percentage of participants who were eligible based on counselor referral and who were contacted by AI that completed the SA intervention and client survey. Effectiveness of affirmation is an internal control and will be assessed by screening the last question on the intervention for those in the intervention group who report higher than a 2 and those in the control group who report lower than a 5. Additionally, transcripts of intervention essays will be analyzed for affirmation themes.

8.0 Description of potential benefits of study:

8.1 Direct benefits to participants

There are minimal direct benefits to participants. Client participants in the intervention group may benefit from a richer counseling experience through greater openness and exploration of values if the intervention is successful.

8.2 Collateral benefit to participants

A collateral benefit that could result from this study is that those in the self-affirmation group may be more likely to spontaneously self-affirm in future situations after engaging in the SA measure (Brady et al, 2016).

8.3 Benefits to society

This study could benefit society by building on our knowledge about which outcomes are subject to SA. It could also enlighten counselors on ways to engage clients in a genetic counseling session. Furthermore, the feasibility study can give information about possible barriers to other similar interventions delivered prior to a genetic counseling visit.

9.0 Description of likelihood and seriousness of harms and how safety will be maximized:

This study is unlikely to cause serious harms. There is small chance that there could be low level psychological harm caused by this study because SA has been shown to increase openness to a threatening message and therefore increase feelings of vulnerability and possibly anxiety (Klein et al., 2011). While this may occur among participants in the intervention arm, the magnitude of the risk is likely small and will be mitigated by the fact that they will be seen by genetic counselors who have training to manage clients' anxiety. There also could be benefit to increasing anxiety in a situation where action needs to be taken to avoid a threat, such as continuing recommended screening for early detection of breast cancer. There is no increased risk to pregnant women or fetus related to this study protocol.

9.1 Therapeutic interventions *N/A*

9.2 Diagnostic interventions *N/A*

9.3 Radiation *N/A*

9.4 Sedation *N/A*

9.5 Risks to family relationships and other psychosocial or economic harms *N/A*

10.0 Description of how privacy and confidentiality of medical information/biological specimens will be maximized

Code words will be used to coordinate assembly of study documents and identifiable client information will not be connected with study documents. For initial surveys to be matched with post-session surveys for later analysis, clients will choose a code word compiled by asking: What is the first street that you lived on? What was your first pet's name? (e.g. OakMondo). This code word will be put on all documents relating to a given participant. The client will tell the counselor the code word during the appointment in order to label the counselors' post-visit survey, but no record of the code word in association with the client's name will be created. Cancer is a common condition and we do not expect clients to be identifiable through their diagnosis. Code words will be destroyed at completion of the study.

Genetic counselor surveys will not include identifying information for the counselor or which after-visit survey was conducted by each counselor. After-visit genetic counselor surveys will include the client code-word that will aid in confirming that surveys are being completed by counselors.

10.1 Description of any clinical/demographic information that will be included.

For clients, demographic information will be collected including: education, age, sex, race, and clinic site. No demographic information will be collected for counselors.

10.2 How might this information make specific individuals or families identifiable?

Since an indication for HBOC genetic counseling is common it is unlikely that individuals will be identifiable from this information.

10.3 If research data will be coded, how will access to the "key" for the code be limited? Include description of security measures (e.g., password-protected database, other). List names or positions of persons with access to the "key" for the code.

The client will generate the code word based off the prompt "first street you grew up on + first pets name." There will not be a key to link the code word with the clients. The code word is designed to be easy for clients to remember. If the study materials do not have consistent code words than the AI will attempt to match surveys based on one of the two prompted words. If this cannot be accomplished with reasonable certainty that documents are from the same client, then the data will not be included in analysis. Counselors will know the code word to attach it to the counselor post-visit survey but will not keep a record of the code word associated with identifying client information.

10.4 N/A

10.5 Will personally identifiable information be released to third parties?

The genetic counselors working with the project will know the code word label to record on their after-visit survey but will not keep a record of the code word associated with the patient name. No other third parties will have access to identifiable information.

10.6 Data sharing.

No data will be deposited in any repositories or databases. De-identified data could potentially be shared with other researchers in the future under an IRB approved amendment to this protocol or separate IRB-approved research protocol. Data shared would only include de-identified surveys, de-identified intervention, and demographic information.

10.7 Describe any additional features to protect confidentiality.

Gift cards will be sent to client participants who fill out the survey in person by having clients fill out an address card that is included in the survey information and returned separately. Online survey participants will enter gift card information through a separate link within the survey site.

Genetic counselors will be sent gift cards at the conclusion of the study by mail. Counselors will provide their addresses to the AI via email.

10.8 Loss or destruction of samples.

Any loss of data, either paper based surveys or breach of electronic data, will be reported promptly to the IRB.

11.0 Assessment of risk/benefit ratio

Adults: Research does not involve greater than minimal risk and involves the prospect of direct benefit to the individual subjects as well as yielding generalizable knowledge about improving genetic counseling practice. Efforts to reduce risk include those aimed at maintaining confidentiality and obtaining informed consent prior to survey completion.

Pregnant women: Research does not involve greater than minimal risk and involves the prospect of direct benefit to the individual subjects as well as yielding generalizable knowledge about improving genetic counseling practice. The research meets the criteria contained under 45 CFR 46.204 for research activities involving pregnant women.

12.0 Unanticipated Problems: Collection, monitoring, analysis and reporting of adverse events and protocol deviations

12.1 N/A

12.1.1 N/A

12.1.2 N/A

12.2 Describe plan to monitor and report adverse events and protocol deviations.

Protocol deviations, unanticipated problems, or non-compliance are defined as described in NIH HRPP SOP 16 ("Reporting Requirements for Unanticipated Problems, Adverse Events and Protocol Deviations"). All protocol deviations, unanticipated problems, or non-compliance occurring during the study, including those observed by or reported to the research team, will be recorded. Serious protocol deviations, unanticipated problems, or non-compliance will be reported to the IRB and CD (Clinical Director) as soon as possible but not more than 7 days after the PI first learns of the event. Not serious

protocol deviations, unanticipated problems, or non-compliance will be reported to the IRB and CD as soon as possible but not more than 14 days after the PI first learns of the event.

No adverse events, serious adverse events, or unanticipated adverse device effects are anticipated in this study since there are no medical devices or pharmaceutical interventions.

12.3 *N/A*

13.0 Description of alternatives to participation

Participation in this study is completely voluntary for both clients and genetic counselors. There will be no negative consequences or changes in standard care for not participating or for withdrawing from the study.

14.0 Description of consent process

14.1 Who will obtain consent *(PI, AIs)?*

A written informed consent review will be sent to all potential client participants along with the standard clinic information packet. The AI will call all potential participants a week prior to their appointment to consent clients, after they have received the information packet, and assess clients' interest in participating in the study.

Genetic counselors' consent will be obtained at the beginning of the study through a written consent document. Counselors will have an opportunity to ask the AI or PI questions regarding the consent through email or phone. Both the counselor and AI or PI will sign the informed consent and both parties will receive a copy by email.

14.2 Setting where consent will be obtained *(location of in-person discussion, phone, mail).*

Verbal consent will be obtained from clients by phone. An information leaflet describing the consent information will be include in the pre-appointment packet sent to all patients.

Written consent will be obtained from counselors in the medical office.

14.3 What information will be provided to participants? *(See attached consent appendix B.).*

On the initial phone call with potential client participants, the AI will explain the purpose of the study, the risks and benefits, the process of participation, the voluntary nature of the study, and withdraw information. The AI will explain that this is a study about using an intervention to improve the genetic counseling session.

The written consent document for counselors will explain the purpose of the study, the risks and benefits, the process of participation, the voluntary nature of the study, and withdrawal from the study.

14.4 Protections for participants who may be vulnerable to coercion or undue influences *(pregnant women, fetuses, children, people with impaired decision-making ability).*

Since this is a feasibility study to assess initial application of SA to a HBOC genetics clinic those with intellectual disabilities noted in their medical chart will not be referred by genetic counselors for study participation. Pregnant women will be included in the study population and we foresee no additional harms caused by study participation. Participants must be 18 years of age to participate.
This research involves no more than minimal risk.

14.5 Are there special circumstances regarding obtaining *consent?*

We are requesting a waiver of the requirement to obtained signed consent from client participants under the grounds of no more than minimal risk 45 CFR 46.110 (c). We believe this study meets the criteria for minimal risk and this waiver can be granted because "the research presents no more than minimal risk of harm to participants and involves no procedures for which written consent is normally required outside of the research context." Counselor participants will complete a signed consent.

14.6 If this study involves collaborating sites, indicate if there is a single IRB review or if each site's IRB will review their site's participation in the study. Describe plans for ensuring appropriate IRB review and approval of consent forms at each site.

All client and genetic counselor participants will be from St. Luke's Health System or Medstar Washington Hospital Center. The NIH will be the IRB of Record for St. Luke's Health System. The reliance agreement forms have been submitted to the OHSRP. Concurrently to this amendment we are seeking exempt review through the Medstar Washington Hospital Center IRB.

15.0 Description of any financial compensation

15.1 Describe the rationale for and amount of any proposed compensation, consistent with SOP 13.

This protocol includes the intervention, which requires early attendance at the medical appointment by the participants, and the post intervention survey. To compensate clients for the study participation they will receive a $15 gift card when they complete the study.

Genetic counselors at St. Luke's will receive a $1400 gift card for their participation in this research. Counselors at Medstar Washington Hospital Center will receive $200 each based on lower planned recruitment at this site, shorter time involved in the study, and less upfront logistics planning. This will be mailed to the genetic counselor at the conclusion of the study. Counselors will be asked to complete a survey after every appointment and at the end of the study.

15.2 Describe whether compensation will be modified if participant withdraws early.

If clients withdraw early or do not complete all surveys they will forfeit their compensation. If counselors withdraw before the conclusion of the study they will receive $100 per week they counseled clients involved in the study.

16.0 References

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