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Randomized Control Trial Comparing Genetic Counseling Service Models for the Underserved

NCT06212310

10/15/2021

Form A

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Randomized Control Trial Comparing Genetic Counseling Service Models for the Underserved

PROTOCOL FORM / RESEARCH DESCRIPTION

If an item does not apply to your research project, indicate that the question is "**not applicable**" – do not leave sections blank

Click once on the highlighted entry in each box to provide your response. Click the item number/letter or word, if hyperlinked, for detailed instructions for that question. If your response requires inserting a table, picture, etc, you may need to first delete the box that surrounds the answer and then insert your table or other special document.

1. Purpose and objectives. *List the purpose and objectives:*

The overarching goal of this pilot prospective randomized controlled study is to compare patient-reported and clinical operations outcomes between in-person genetic counseling (IPGC – control) and telephone-based genetic counseling (TGC – intervention) in an indigent English or Spanish-speaking population seeking genetic counseling for hereditary cancer syndromes to create a framework for effective and efficient genetic service delivery in these populations nationally. General genetic education and principles will be conveyed through a standard genetic counseling session including a pre-test education video in both the TGC and IPGC arms. Our primary project objectives are to compare the following outcomes between the IPGC and TGC study arms. Aim 1: Patient reported outcomes – A. Patient satisfaction with genetic counseling visit; B. Knowledge of basic principles of cancer genetics and implications of genetic testing for personal healthcare and relatives. Secondary objectives for this aim are: 1. Patient ability to make informed choice; and 2. Genetic counseling-specific empowerment outcomes. Aim 2: Clinical outcomes – visit completion rate; Secondary objectives are: 1. Genetic testing completion rate; and 2. Genetic testing cancelation/failure rate. We hypothesize that patients in the TGC arm will not have significant differences in knowledge, satisfaction, informed choice or genetic counseling-specific empowerment compared to the IPGC arm. We also expect significantly increased visit completion rate and lower test completion rate in the TGC arm compared to the IPGC arm, but no significant difference in sample failure rate.

2. Background.

- Describe past experimental and/or clinical findings leading to the formulation of your study.
- For research involving investigational drugs, describe the previously conducted animal and human studies.
- For research that involves FDA approved drugs or devices, describe the FDA approved uses of this drug/device in relation to your protocol.
- Attach a copy of the approved labeling as a product package insert or from the Physician's Desk Reference.

You may reference sponsor's full protocol or grant application (section number and/or title) or if none, ensure background includes references.

Please respond to all components of this item, or clearly indicate which components are not applicable.

a. Background

Similar studies have been performed in primarily non-Hispanic white, above-average income, college-educated, English-speaking populations1-6 , but to our knowledge, a study comparing outcomes of TGC and IPGC service delivery models (SDMs) has not been reported in an entirely indigent population with a high volume of Latinx/Spanish-speaking patients. Indigent Populations. Less access to healthcare and hereditary risk assessment are well documented in indigent populations, often composed of ethnic/racial minorities, or geographically isolated and economically underserved groups. 7-9 Barriers include provider paucity, under-recognition of family history risk factors, financial hardship, and other factors. 10- 17 Internet use via mobile technologies has increased access to healthcare information in indigent populations .18, 19 National surveys revealed 91% of families living below the poverty level have some type of internet access, and of Americans earning <$30,000 annually, 701% owned a smart phone. Review of 2019 internal program data revealed 84-88% of safety-net hospital clinic uninsured/Medicaid patients provided an email address and reported internet connectivity. This access creates an avenue for genetic counselors to reach underserved populations. Genetic Counseling Service Delivery. Some randomized trials comparing outcomes of TGC v. IPGC cancer risk assessment sessions in resource-rich populations showed similar levels of patient satisfaction, knowledge, cancer worry, risk perception, decisional conflict, and motivation to change health-related behavior with similar data for telegenetics (video) studies. In one study, the majority of participants indicated they would not have pursued genetic counseling had TGV not been offered. Need for Project. A majority (89%) report already using a phone for medical discussions. Traditional healthcare infrastructures remain a barrier for indigent patients, and while the rise in telegenetics companies and platforms in a response to the increasing need for remote genetic counseling to

service under-resources and rural areas, outcomes of TGC in indigent populations have not been well-studied. Over 38 million people in the United States are considered low-income and are more likely to be patients in safety-net hospital systems, which necessitates optimization of genetic counseling SDMs in these cohorts. TGC, in particular, is critical to study in indigent populations given patient preference and accessibility to phone service. A UCSF study showed that indigent patients offered TGC versus video genetic counseling preferred the former and had an increased uptake of genetic counseling compared to other interventions.

Our study is not amenable to the following pieces of this question: *For research involving investigational drugs, describe the previously conducted animal and human studies. For research that involves FDA approved drugs or devices, describe the FDA approved uses of this drug/device in relation to your protocol. Attach a copy of the approved labeling as a product package insert or from the Physician's Desk Reference.*

b. Current practice

n/a

3. Study Design.
Describe the study design (e.g., single/double blind, parallel, crossover, etc.) Consider inserting a scheme to visually present the study design.

This is a two-arm parallel randomized controlled study of IPGC vs. TGC with two enrolling sites.

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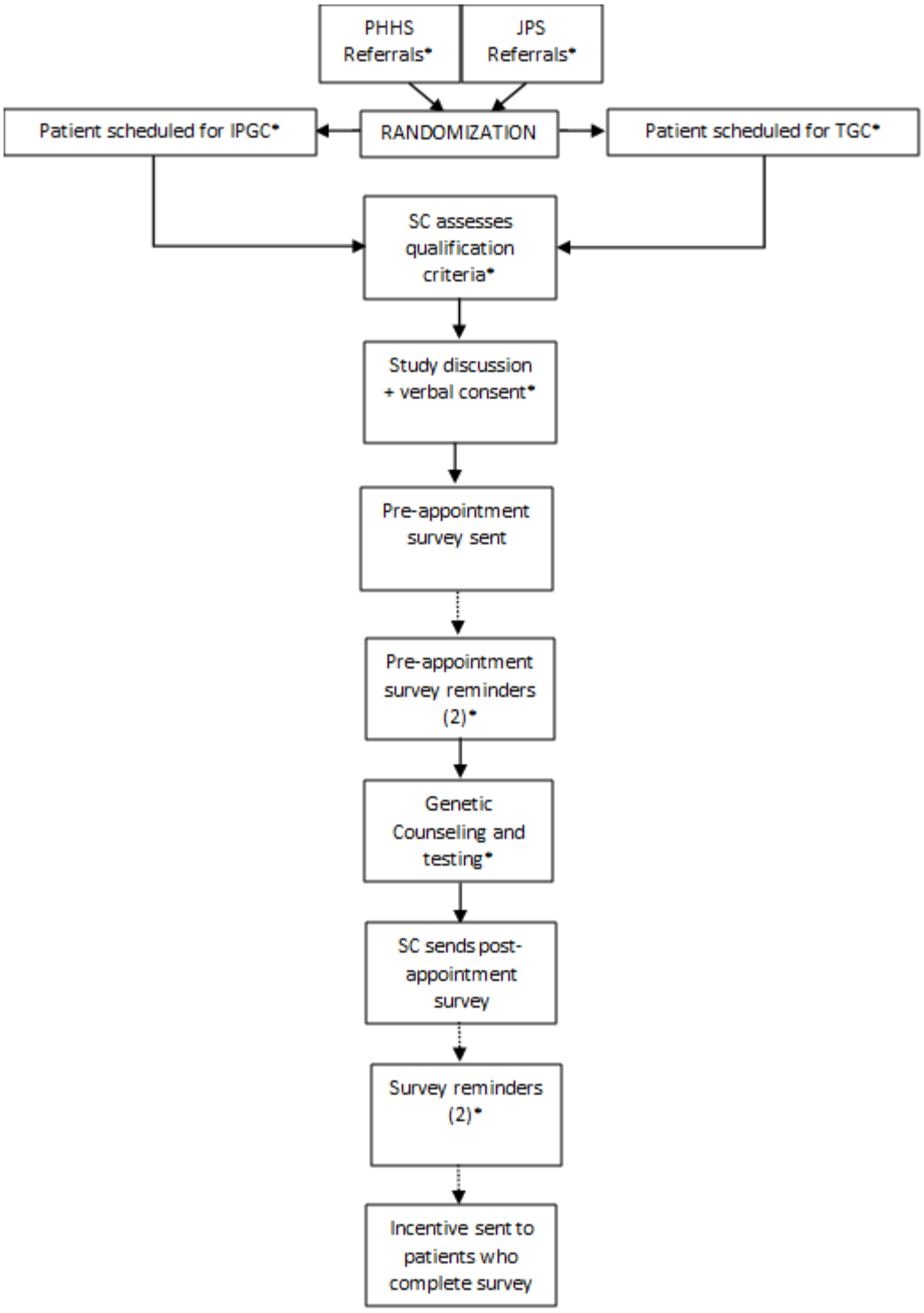

*Patient may be excluded from study at this step.

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4. Research Plan / Description of the Research Methods:

4.a. Provide a **comprehensive narrative** describing the **research methods**.

1) Provide the **order in which tests/procedures will be performed**,
2) Provide the **setting** for these events and a description of the **methods used to protect privacy** during the study.
3) Provide the **plan for data analysis** (include as applicable the **sample size calculation)**

Please respond to all components of this item, or clearly indicate which components are not applicable.

Data Tracking and Storage. All survey data will be captured, stored, tracked, and analyzed via Research Electronic Data Capture (REDCap), a secure, web-based application for research data.

Randomization and Scheduling:

Study coordinator (SC) will monitor referral queue daily

Randomization software (http://abtesting.ideas42.org/randomize/) will be used to randomize patients in the referral queue to each study arm (in-person genetic counseling or IPGC/ telephone genetic counseling or TGC). Patients who meet the following exclusion criteria will not be randomized to a study arm. Patients who are excluded from the study will be scheduled for an appointment as per normal clinic protocol by the clinic schedulers.

SC will monitor number of participants per study arm and adjust recruitment accordingly.

Patients who have been randomized to a study arm will be scheduled for IPGC or TGC by schedulers at John Peter Smith (JPS) and Parkland Hospital (PHHS). Schedulers will inform patients of their appointment as per normal clinic protocol. Spanish-speaking patients will be contacted with an interpreter.

Patients who elect alternative service delivery model for genetic counseling than what was assigned after randomization will be excluded from the study. The genetic counseling appointment type will be modified based on patient preference and patient will continue with scheduled visit, but not as part of the study.

SC will record the following data for all referred patients in Research Electronic Data Capture (RedCap), a secure, web-based application for research data: MRN; study arm assigned; genetic counseling appointment date; if patient was excluded from study, and reason for exclusion. The following demographic data will also be tracked: patient's age; patient's sex; patient's race and ethnicity; patient's preferred language; patient's contact information (phone number and e-mail address)

Study Eligibility Determination and Informed Consent. One week prior to scheduled genetic counseling appointment, SC will call patient to assess if patient meets study eligibility criteria. Spanish-speaking patients will be contacted with an interpreter.

If SC cannot reach the patient, SC will make second contact attempt the following business day.

Scheduled patients who cannot be reached or do not call back will be excluded from study.

SC will record the following data in RedCap: contact date and outcome; if eligibility criteria were met; if patient was excluded from study, and reason for exclusion.

If patient qualifies for study, SC will describe study protocol and get verbal consent for study participation using the consent script. All patients will be sent a hard copy of the consent document for their records (available in English and Spanish) electronically along with the study surveys via RedCap.

Patients who decline will be excluded from study. Study participation status will be recorded in RedCap (including reason for declining participation).

Patients who decline to be in the study will be sent an appointment letter and will continue with scheduled genetic counseling appointment as per normal clinic protocol, not as part of the study.

Pre-Appointment Resources and Survey Completion. Patients who agree to participate in the study will be sent the pre-appointment survey (Appendix B). A Spanish version of the survey will be sent to Spanish-speaking patients. Surveys will include a hard copy of the consent document that can be downloaded as desired. Survey links will be sent to patients via email. All surveys will be available through REDCap.

The pre-appointment survey will consist of the Multi-dimensional Model of Informed Choice (MMIC) assessment and the Genomics Outcome Scale (GOS).

SC will check pre-appointment survey completion status two business days prior to appointment.

Patients with incomplete pre-appointment surveys will be contacted two business days prior to appointment and will be reminded to complete survey. Patients will be offered the option to complete survey via telephone with SC. Spanish-speaking patients will be contacted with an interpreter.

SC will attempt to contact patients who cannot be reached the following business day.

Patients who do not complete pre-appointment survey will be excluded from study but will continue with scheduled genetic counseling appointment as standard of care.

Pre-appointment survey completion status and survey completion method will be recorded in RedCap by SC.

Genetic Counseling and Genetic Testing. Patients who are unable to watch the educational video prior to, or during their genetic counseling visit will be excluded from the study. They will still continue with their appointment, but not through the study. Patients excluded for this reason will be recorded in RedCap by SC.

Sample failure and test completion status will be recorded in RedCap by SC. Failure to complete testing will not exclude patient from the study itself.

Post-Appointment Survey and Study Incentive. SC will send post-appointment survey within 24 hours of GC appointment. A Spanish version of the survey will be sent to Spanish-speaking patients.

The post-appointment survey will consist of the Multi-dimensional Model of Informed Choice (MMIC) assessment, the Genetics Outcome Scale (GOS) and the Genetic Counseling Satisfaction Scale (GCSS).

SC will monitor survey completion status. Those with incomplete post-appointment surveys will receive reminder two business days post-appointment and will be offered option to complete the survey via telephone with SC.

If patient is not reached, SC will attempt to contact patient the following day (three business days post-appointment).

Those with incomplete surveys one week after the genetic counseling appointment will be excluded from study. This data will be recorded in RedCap.

Those who complete study surveys will be sent a $15 gift card electronically.

Location/Setting. For IPGC, patients will be seen within PHHS/JPS clinics. Spanish translation services are provided through PHHS and JPS for patients in their institutions. TGC patients will not be required to be in a certain environment, but we anticipate they will be in their homes or workplace in a secure, private location. GCs will either be in a HIPPA compliant setting offsite or within a UTSW workspace for TGC visits.

Data Analysis. Our primary study outcomes are to compare change in knowledge pre and post visit (through MMIC knowledge questions), patient satisfaction with GC visit after completion (GCSS) and genetic counseling visit completion rate between IPGC and TGC. Secondary objectives include comparison of empowerment score (GCOS), informed choice (MMIC scale), genetic testing completion, and cancelation/failure rates between the arms.

To evaluate intervention effects, we will conduct univariable and multivariable analysis for comparisons of each outcome of interest between intervention (TGC) and control group (IPGC). For the survey data, we will examine the data from each survey as well as total score or overall index of multiple questionnaires and compare them between the two study arms. We will perform linear regression models for continuous outcomes (e.g., total score of questionnaires) and logistic regression models for binary outcomes that are based on binary response (e.g., visit completion rates, test cancelation/failure and test completion rates). To compare binary outcomes between arms (such as visit completion rate), we will test by comparing rates of each arm via Chi-squared analysis and control for potential confounders. Potential covariates under consideration (e.g., age, race, sex, language, etc.) will be assessed as necessary and adjusted in multivariable models accordingly. We will evaluate whether there is any evidence of multi-collinearity issues among these variables to be adjusted in the model. Possible effect modifiers of intervention effects will be also evaluated by testing interactions (e.g., sex) and addressed to develop the final multivariable models, as well as reporting the intervention effect stratified as an effect modifier. Underlying assumptions of aforementioned regression models including linearity of associations will be also evaluated. We will examine dropouts or missing data to be able to identify accurate missing data mechanisms and select the best statistical approach. All analyses will be performed using SAS 9.4 (SAS Institute Inc, Cary, NC) at a statistical significance level of p=.05.

We anticipate a post-enrollment dropout (failure to complete the surveys) rate of 30% given our work with the underserved population.55 We plan to enroll 280 patients at a 1:1 ratio per arm (100 individuals enrolled per arm), expecting 200 to complete measured responses. We will monitor the dropout rate after the initial 50 individual responses are completed and adjust accrual for study-specific dropout until we have 200 participants' complete measured responses. With 200 patients we will enroll, we can detect mean differences of 0.398 standard deviation (SD) between two study arms with 80% power at a significance level of 0.05 (Table 1). For example, assuming SD of 2 for the GCSS, we will be able to detect a minimum difference of 0.8 (=0.398*2) between two study arms with 100 participants enrolled per arm. For GCOS, assuming SD of 46.58, we will be able to detect a minimum difference of 18.54 between pre- and post-visit scores. For visit completion as the primary binary outcome variable, we will be able to detect a minimum difference of 18.6% assuming 63% in the control group, e.g., 81.6% (intervention) vs. 63% (control) with 80% power at significance level of 0.05. Of note, previously published outcomes and unpublished internal data will serve as a baseline for the study population.56

Table 1. Summary of instrumentation with objectives, measures and distribution plan. Summary of data analysis plan per primary and secondary objectives. Minimum detectable difference between two study arms with 80% power at 2-sided significant level of 0.05 (n=100 per arm)

Aims	Objective Type	Instrumentation	Outcome Measure	Distribution	Minimum Detectable Effect Size at 80% power
Aim 1: Patient Satisfaction	Primary	GCSS	Whole scale score	Post	+/-0.8 points, assuming SD = 2[1]
Aim 1: Knowledge	Primary	MMIC (8 knowledge questions)	Measure score difference from pre/post	Pre and Post	+/-2 points, assuming SD = 5.03
Aim 1: Informed Decision Making	Second	MMIC (entire measure)	Measure score difference from pre/post	Pre and Post	n/a
Aim 1: GC-specific empowerment	Second	GOS	Measure score difference pre/post	Pre and Post	+/-18.54 points, assuming SD = 46.58[50]
Aim 2: GC visit completion	Primary	Database query	Proportion of visits scheduled and completed	n/a	18.6%, assuming 63% in control group[57]
Aim 2: Genetic test completion	Second	Database query	Proportion of genetic tests completed w/n 60d of visit	n/a	19.4%, assuming 77.4% in control group[57]
Aim 2: Genetic test cancelation/failure	Second	Database query	Proportion of genetic tests initiated compared to tests canceled/failure	n/a	15%, assuming 9% in control group[57]

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4.b. List of the study intervention(s) being tested or evaluated under this protocol

☑ **N/A -** this study does not test or evaluate an intervention. Skip to item 4.d.

#	Study intervention(s) being tested or evaluated under the protocol *Add or delete rows as needed*	Affiliate Place a check next to institution(s) where the intervention will be performed	Local Standard Practice? Indicate whether the intervention is considered acceptable practice locally for applicable institutions
1	Insert study intervention 1 here	☐ UTSW	☐ Yes
		☐ PHHS	☐ Yes
		☐CMC	☐ Yes
		☐THR	☐ Yes
		☐TSRH	☐ Yes
		☐ Other:	☐ Yes
2	Insert study intervention 2 here	☐ UTSW	☐ Yes
		☐ PHHS	☐ Yes
		☐CMC	☐ Yes
		☐THR	☐ Yes
		☐TSRH	☐ Yes
		☐ Other:	☐ Yes

4.c. Risk:Benefit Analysis of study interventions being tested or evaluated under this protocol

For each study intervention identified in section 6b above, complete a risk:benefit analysis table.

(Two tables are provided, copy & paste additional tables as needed or delete both tables if this study does not test an intervention)

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4.c.
Study Intervention #1
Insert name used in 4.b.

List each group exposed to this intervention on a separate line. (e.g., experimental, control, Arm A, Arm B, etc) **Or** state All Groups/Subjects	For each group, list the **benefits** of this intervention. (Benefits can be directly from the intervention or from a monitoring procedure likely to contribute to the subject's well being). If there are no benefits, state "none".

If you are requesting a Waiver of Informed Consent, complete the table below.

If you have a consent form, **list the reasonably foreseeable risks in the consent form (and do not complete this section).**

List the risks according to the probability (likely, less likely or rare) and magnitude (serious or not serious).
(include: 1) expected adverse events; 2) rare and serious adverse events; 3) all other psychological, social, legal harms)
Do not delete frequency. Frequency must be estimated because it will assist you with determining which adverse events will require prompt reporting.

	Not serious	**Serious**
Likely These risks are expected to occur in more than **20** out of **100** subjects.	•	•
	Not serious	**Serious**
Less likely These risks are expected to occur in **5-20** subjects or less out of **100** subjects.	•	•
		Serious
Rare These risks are expected to occur in less than **5** subjects out of **100**		•

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4.c.
Study Intervention #1
Insert name used in 4.b.

List each group exposed to this intervention on a separate line. (e.g., experimental, control, Arm A, Arm B, etc) **Or** state All Groups/Subjects	For each group, list the **benefits** of this intervention. (Benefits can be directly from the intervention or from a monitoring procedure likely to contribute to the subject's well being). If there are no benefits, state "none".

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List the risks according to the probability (likely, less likely or rare) and magnitude (serious or not serious).
(include: 1) expected adverse events; 2) rare and serious adverse events; 3) all other psychological, social, legal harms)
Do not delete frequency. Frequency must be estimated because it will assist you with determining which adverse events will require prompt reporting.

	Not serious	**Serious**
Likely These risks are expected to occur in more than **20** out of **100** subjects.	•	•
	Not serious	**Serious**
Less likely These risks are expected to occur in **5-20** subjects or less out of **100** subjects.	•	•
		Serious
Rare These risks are expected to occur in less than **5** subjects out of **100**		•

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	4.d. List ALL other research procedures or components not listed in table 4.b. ***The combination of Tables 4b and 4d should account for all of the research procedures that will take place during this study.*** Consider grouping similar procedures under a single component (e.g., blood work, CT = safety assessments)			
#	**Research component** • **individual procedures** *example:* **Eligibility Assessments** • History and physical • Questionnaire • Laboratory tests *Add or delete rows as needed*	**Column A** **Local Standard Practice** Indicate the number of times each procedure will be performed as stipulated in the research plan **that would be performed if the participant were not participating in the study.**	**Column B** **Research Only** Indicate the number of times each procedure will be performed solely for research purposes *(meaning that the participant would not undergo the same number of procedures or would not undergo the procedure(s) at the same frequency if they were not participating in the study)*	**Column D** **Risks** **If you are requesting a Waiver of Informed Consent, complete the table below.** List the reasonably expected risks for each procedure or group of procedures under the following categories as appropriate: • Serious and likely; • Serious and less likely; • Serious and rare; • Not serious and likely; • Not serious and less likely
1	**Eligibility Assessments**			
	Review inclusion/exclusion criteria		1	Not serious and less likely
2	**Questionnaires**			
	Pre-visit: MMIC/GOS		1	Not serious and less likely
	Post-visit: MMIC/GOS/GCSS		1	Not serious and less likely
3	**Video education viewing**			
	Educational video sent to telephone GC patients for viewing prior/during visit	1		Not serious and less likely
	Educational video for in-person GC patients viewed in session	1		Not serious and less likely
4				

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5. Safety Precautions. *(Describe safeguards to address the serious risks listed above.)*

a. Describe the procedures for protecting against or minimizing any potential risks for each of the more than minimal risk research procedures listed above.

n/a

b. Where appropriate, discuss provisions for ensuring necessary medical or professional intervention in the event of adverse events, or unanticipated problems involving subjects.

In the event of a research-related injury or if you experience an adverse reaction, we advise in the consent for to immediately contact the study coordinator. We advise the participant to see the section “Contact Information” for phone numbers and additional information in the consent form. Risks related to this study are not above standard clinical care.

c. Will the safeguards be different between/among groups?

☐ Yes ☑ No

n/a