CTR radon DaCCoTA

This title should include, where possible, information on the participants, condition being evaluated, and intervention(s) studied.

Unique Protocol Identification Number: CTR radon DaCCoTA

National Clinical Trial (NCT) Identified Number: NCT04980521

Principal Investigator: Soojung Kim

Sponsor: University of North Dakota

"Sponsor" indicates an institution, foundation, or individual who takes responsibility for and initiates a clinical investigation; often times this is the university with which the Principal Investigator is affiliated.

Grant Title: DaCCoTA Year 4 Request, Year 3 RPPR

Grant Number: U54GM128729

Funded by: NIGMS

Version Number: v.1.0

28 May 2024

All versions should have a version number and a date. Use an international date format (e.g.,YYYY-MM-DD [2017-12-21] or write out the month (e.g., 21 December 2017).

For the initial submission of a protocol to the IRB, indicate "Not applicable; this is the first version of the protocol." in the table below. For any subsequent amendment being submitted to the IRB, add details of the specific changes that are being implemented in the amendment. Please note that Section 10.4 is a high-level summary of <u>all</u> formal protocol versions/amendments.

CONFIDENTIALITY STATEMENT

This document is confidential communication. Acceptance of this document constitutes agreement by the recipient that no unpublished information contained herein will be published or disclosed without prior approval of the Principal Investigator or other participating study leadership and as consistent with the NIH terms of award.

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STATEMENT OF COMPLIANCE

The trial will be carried out in accordance with International Council on Harmonisation Good Clinical Practice (ICH GCP) and the following:

- United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 312, and/or 21 CFR Part 812).

National Institutes of Health (NIH)-funded investigators and clinical trial site staff who are responsible for the conduct, management, or oversight of NIH-funded clinical trials have completed Human Subjects Protection and ICH GCP Training.

INVESTIGATOR'S SIGNATURE

The signature below constitutes the approval of this protocol and provides the necessary assurances that this study will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable US federal regulations and ICH guidelines, as described in the *Statement of Compliance* above.

Principal Investigator or Clinical Site Investigator:

Signed:	**Soojung Kim**	**Date:**	**5/30/2024**

Name*: Soojung Kim

Title*: Associate Professor / Chair

Investigator Contact Information

Affiliation*: University of North Dakota

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1 PROTOCOL SUMMARY

No text is to be entered in this section; rather it should be included under the relevant subheadings below. It may be useful to complete this section after the relevant sections in the protocol have been completed.

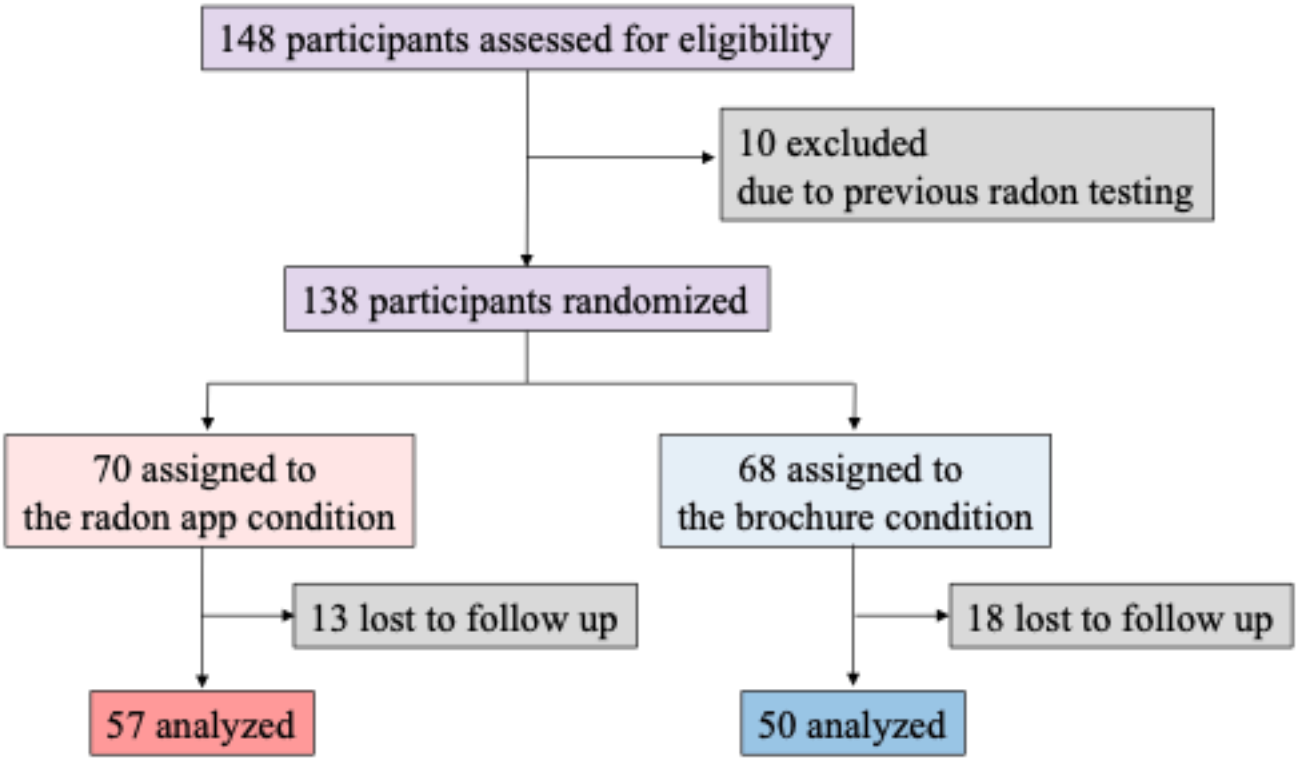
1.1 SYNOPSIS

Title:	CTR radon DaCCoTA
Grant Number:	U54GM128729
Study Description:	The overall goal of this research is to compare the effectiveness of radon information delivered via the radon app vs. a traditional approach (printed brochure). The two methods will be compared on outcomes pertinent to the stages of individuals' responses to radon interventions.
Objectives*:	Primary Objective: The primary objective of this research is to compare the effectiveness of radon information delivered via the radon app vs. a traditional approach (printed brochure) on behavioral outcomes, i.e., the rate at which individuals order free radon test kits and the rate at which they return them to the lab. Secondary Objectives: The secondary objective of this research is to conduct a clinical trial to compare the effects of the radon app vs. brochures on increasing radon knowledge.
Endpoints*:	Primary Endpoint: 1. Number of radon test kits requested by participants in the radon app and brochure conditions; and 2. Number of radon test kits used and returned to the laboratory by participants in the two conditions. Secondary Endpoints: Effectiveness of the radon app vs. brochure at 3 months re: changes in radon knowledge, as measured by the number of correct responses to a series of 20 true/false questions (e.g., "The EPA recommends that homes with 4 picocuries per liter (pCi/L) or more of radon should be fixed.").

Study Population:	Study participants are undergraduates in the Communication Department at the University of North Dakota. The principal eligibility criterion is that participants own a smartphone. The principal exclusion criterion is previous testing for radon within the past two years.
Phase* or Stage:	Phase II
Description of Sites/Facilities Enrolling Participants:	Enrolling participants was completed remotely via an online survey platform, Qualtrics.
Description of Study Intervention/Experimental Manipulation:	An online experiment with two experimental conditions using a pretest-posttest design: the radon app condition vs. brochure condition. Participants in both experimental conditions will complete an online pre-exposure survey during the baseline phase of the study. Upon completion of the pre-exposure survey, participants assigned to **the radon app condition** will be asked to install the radon app on their smartphones and use the app for three months. App installation will be verified electronically via text message sent to the investigators. To make the informational content of the radon app and EPA brochures equivalent, the informational content in the app condition will be repurposed from EPA brochures used in the brochure condition. Participants in the radon app condition will have the opportunity to order a free radon test kit through the app at any time during the three-month period. In contrast, individuals assigned to **the brochure condition** will receive three EPA brochures for the three-month period via postal mails. These brochures are (1) Basic radon facts (*https://bit.ly/2S6ryFw*); (2) A citizen's guide to radon (*https://bit.ly/3l3FhcJ*); and (3) Consumer's guide to radon reduction (*https://bit.ly/3ibt83n*). In each mailing, participants will receive a pre-addressed, pre-paid postcard to request a free radon test kit. The postcard will be addressed to a UND address so that we can track the number requested by participants in the brochure condition.
Study Duration*:	6 months.
Participant Duration:	3 months.

1.2 SCHEMA

Flow Diagram



1.3 SCHEDULE OF ACTIVITIES

The schedule of activities:

Category	**Pre-screening (Pre-consent)**	**Visit 1 Day 1**	**Visit 2 Day 14 ±7**	**Visit 3 Day 28 ±7**	**Visit 4 Day 42 ±7**	**Visit 5 Day 56 ±7**
EMR Review Eligibility	X					
Informed Consent		X				
Demographics and socioeconomic status		X				X
Baseline measures		X				
Outcome Evaluation: Radon knowledge		X				X
Outcome Evaluation: Ordering radon test kits						X
Outcome Evaluation: Utilizing radon test kits						X
Randomization		X				
Control & Experimental Interventions – The radon app vs. print brochures		X	X	X	X	
Adverse Events Reporting		X	X	X	X	X

2 INTRODUCTION

2.1 STUDY RATIONALE

Radon gas is a form of ionizing radiation that results from the natural decay of uranium present in rocks and soils. It is the largest cause of lung cancer after smoking and may contribute to death from other cancers, e.g., chronic lymphocytic leukemia[1,2] and malignant melanoma.[3] Radon causes more than 21,000 lung cancer deaths per year in the U.S.[4] This number of deaths greatly exceeds those of other, more-publicized causes, e.g., drunk driving (17,400) and the number of homicides involving hand guns.[5]

Radon-related deaths result from a failure to test homes for radon. In part, this failure has a cognitive cause: the public's limited knowledge about radon. Additionally, among radon-knowledgeable individuals, the deaths have a behavioral cause; the failure of individuals to carry out a series of behaviors, including obtaining a radon test kit, using it, returning the kit to the lab, interpreting the results, and (if warranted), remediating their homes.

Many educational interventions concerning radon have been attempted. However, most have performed poorly when measured against real world outcomes like increases in radon testing. Importantly, most previous interventions have employed traditional forms of communication, such as printed brochures.[6-9] Considerable evidence indicates that individuals may be more responsive to health information delivered via electronic media, e.g., the internet and smartphones.[10] We recently designed a radon-education mobile application for smartphones ("the radon app") and pilot-tested it in a clinical trial with 96 individuals.[11] Findings from our pilot trial suggest that the radon app is a promising tool for promoting radon testing.[11]

The overall goal of this research is to compare the effectiveness of radon information delivered via the radon app vs. a traditional approach (printed brochure). The two methods will be compared on outcomes pertinent to the stages of individuals' responses to radon interventions. These stages include radon knowledge, attitudes toward radon testing, ordering and using a test kit, and returning the kit to the lab for analysis.

2.2 BACKGROUND

In collaboration with a media services company (Triad Interactive Media, Greensboro, NC), we developed a radon app for smartphones.[11] Briefly, the app uses a framework in HTML5 and the open source Twitter API. Posts created by the app are cross-listed on Twitter. Once users log in via Twitter, they can view radon news and mobile-friendly informative content on radon repurposed from EPA brochures. Users also can access existing Tweets containing hashtags, e.g., #radon, #radonawareness, #radonmitigation, and #lungcancer. Individual users' activities on the radon app, along with their Twitter handle, are saved on Triad Interactive Media's server. Through the app, users could order a free radon test kit at any time.

We conducted a pilot clinical trial using this app. Ninety six (96) undergraduates at the University of North Dakota in Grand Forks, ND (UND) were assigned to use the radon app for one month and were tested on several aspects of radon knowledge and testing using a pretest-posttest design.[11] We have recently published our findings.[11] We found that the use of the radon app: (1) significantly improved individuals' radon knowledge and generated positive attitudes toward radon testing; (2) significantly increased self-efficacy (i.e., an individual's perceived capability to order a radon test kit and use it); (3) significantly increased response efficacy (i.e., an individual's evaluation of the effectiveness of radon testing in preventing radon exposure); and (4) resulted in 24% of study participants ordering a free radon test kit. However, only a small percentage of participants actually used the test kit they obtained (i.e., employed the test in their home and returned it to the lab; a total test completion rate of 9%).

In summary, our pilot trial demonstrated that the radon app improved radon knowledge, motivation to test, and stimulated requests for free test kits. However, our pilot trial had a key limitation: there was no control group (i.e., a group not exposed to the app). Our present research builds and improves upon these preliminary findings. To do so, we will include a control group that receives usual care (radon information communicated via EPA brochures).

2.3 RISK/BENEFIT ASSESSMENT

2.3.1 KNOWN POTENTIAL RISKS

The research presents no more than minimal risk, as participants would use a smartphone as they would do normally or receive postal mails as part of experimental interventions, as indicated in a similar previous study.[11] In other words, there are neither immediate risks nor long-term risks.

2.3.2 KNOWN POTENTIAL BENEFITS

This research would provide a better understanding of how to increase the public's awareness of the radon issue. The immediate potential benefits would include increased awareness of the health threat posed by radon, as indicated in our similar previous study.[11] The long-term potential benefits would include the lower risks of developing lung cancer due to radon exposure.

2.3.3 ASSESSMENT OF POTENTIAL RISKS AND BENEFITS

There are no risks in participating in this research beyond those experienced in everyday life. Yet, just in case participants feel any psychological/emotional distress or discomfort, they will be instructed to withdraw from the study at any time without losing the course points assigned by their instructor. Also, they may meet the one-hour research requirement for their COMM 102 class or receive one extra credit for their COMM 110 class by completing an alternative task, which is to read an article related to this research and prepare a two-page reaction to it. Given the little to no risks and potential immediate and long-term benefits, the value of the information to be gained outweighs the risks of participation in the study.

3 OBJECTIVES AND ENDPOINTS

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS	PUTATIVE MECHANISMS OF ACTION
PRIMARY: *The primary objective of this research is to compare the effectiveness of radon information delivered via the radon app vs. a traditional approach (printed brochure) on behavioral outcomes, i.e., the rate at which individuals order free radon test kits and the rate at which they return them to the lab.*	1. Number of radon test kits requested by participants in the radon app and brochure conditions; and 2. Number of radon test kits used and returned to the laboratory by participants in the two conditions.	Each measure is the dependent variables to test the primary objective.	
SECONDARY: *The secondary objective of this research is to conduct a clinical trial to compare the effects of the radon app vs. brochures on increasing radon knowledge.*	Effectiveness of the radon app vs. brochure at 3 months re: changes in radon knowledge, as measured by the number of correct responses to a series of 20 true/false questions (e.g., "The EPA recommends that homes with 4 picocuries per liter (pCi/L) or more of radon should be fixed.").	The radon knowledge variable is a key dependent variable to test the secondary objective. The radon knowledge variable may potentially serve as the mediator of the effects of the interventions on two measures identified as primary endpoints.	

4 STUDY DESIGN

4.1 OVERALL DESIGN

The project begins by comparing the role of the radon app vs. brochures on the percentage of participants that request free test kits and use and return them to the laboratory for analysis and improving knowledge about radon (Phase II).

Experimental design. We designed an online experiment with two experimental conditions—the radon app condition vs. brochure condition—using a pretest-posttest design. Study participants are undergraduates in the Communication Department at UND, indicating that this is a single-site trial. The principal eligibility criterion is that participants own a smartphone. The principal exclusion criterion is previous testing for radon within the past two years.

We consider UND undergraduates to be an appropriate population to test the app for several reasons: (1) ND has the highest residential radon levels in the U.S.[2]; (2) Our recent review of radon knowledge indicated that most individuals less than 30 years old do not know what radon is[12]; and (3) The age of many undergraduate students is similar to that of first time home-buyers in the U.S.[13] We will assign recruited participants randomly to one of the two experimental conditions: app use and brochures.

Participants in both experimental conditions will complete an online pre-exposure survey during the baseline phase of the study. Upon completion of the pre-exposure survey, participants assigned to **the radon app condition** will be asked to install the radon app on their smartphones and use the app for three months. App installation will be verified electronically via text message sent to the investigators. To make the informational content of the radon app and EPA brochures equivalent, the informational content in the app condition will be repurposed from EPA brochures used in the brochure condition. Participants in the radon app condition will have the opportunity to order a free radon test kit through the app at any time during the three-month period.

In contrast, individuals assigned to **the brochure condition** receive three EPA brochures for the three-month period via postal mails. These brochures are (1) Basic radon facts (*https://bit.ly/2S6ryFw*); (2) A citizen's guide to radon (*https://bit.ly/3l3FhcJ*); and (3) Consumer's guide to radon reduction (*https://bit.ly/3ibt83n*). In each mailing, participants will receive a pre-addressed, pre-paid postcard to request a free radon test kit. The postcard will be addressed to a UND address so that we can track the number requested by participants in the brochure condition.

Outcome measures. Participants in both groups will complete the pre-exposure online survey at the beginning of the study and a post-exposure online survey at the three-month time point. This knowledge-based survey is similar to one we have used previously.[11] The primary endpoints used to compare the two approaches are:

1. Number of radon radon test kits requested by participants in the radon app and brochure conditions;
2. Number of radon test kits used and returned to the laboratory by participants in the two conditions.

3. Effectiveness of the radon app vs. brochure[11] at 3 months re: changes in: radon knowledge, as measured by the number of correct responses to a series of 20 true/false questions (e.g., "The EPA recommends that homes with 4 picocuries per liter (pCi/L) or more of radon should be fixed.").

4.2 SCIENTIFIC RATIONALE FOR STUDY DESIGN

The study design is a straight-forward clinical trial design with two arms. Participants will be randomized to each arm. There is no superior design than the one we have chosen. The control condition in this behavioral experiment is usual care, that is, the receipt of brochures containing radon information. As such, this is a straight-forward comparison of the new, or experimental approach, the use of a smartphone app, vs. usual care.

4.3 JUSTIFICATION FOR INTERVENTION

The mode of intervention delivery, the use of a smartphone, was defined in our previously published pilot study.[11] This was a college-aged population for which smartphone use is known to be highly prevalent (> 92% penetration into this demographic). Thus, this is a highly culturally and age-relevant intervention. The minimally acceptable participation rate was determined by our sample size calculations, presented in the published paper. These were exceeded.

4.4 END-OF-STUDY DEFINITION

A participant is considered to have completed the study if he/she has completed the baseline assessment and the 3-month follow-up assessment.

The end of the study is defined as completion of the 3-month follow-up assessment shown in the Schedule of Activities (SoA), **Section 1.3**.

5 STUDY POPULATION

5.1 INCLUSION CRITERIA

In order to be eligible to participate in this study, an individual must meet all of the following criteria:

1. Reading the informed consent form
2. Age >= 18
3. Own a smartphone

5.2 EXCLUSION CRITERIA

An individual who meets any of the following criteria will be excluded from participation in this study:

1. Previous testing for radon within the past two years

5.3 LIFESTYLE CONSIDERATIONS

N/A

5.4 SCREEN FAILURES

Screen failures are defined as participants who consent to participate in this study but are not subsequently assigned to the study intervention or entered in the study. Individuals who do not meet the criteria for participation in this trial (screen failures) are automatically directed to the end of the pre-exposure survey.

5.5 STRATEGIES FOR RECRUITMENT AND RETENTION

COMM 110 and 102 students were invited to participate in the study. In the communication department, students enrolled in COMM 102 are required to complete the 2-hour research participation requirement. The participation in both pre- and post-exposure surveys in each experiment would allow them to meet an hour of participation requirement. For COMM 110, students receive extra .5% in their final grade per an half-hour research participation, and they are allowed to earn up to extra 2% (i.e., 2-hour research participation), according to COMM 110's extra credit policy. The participation in both pre- and post-exposure surveys in each experiment would allow them to earn extra 1% for their final grade (i.e., one-hour research participation).

Approximately 200 students are enrolled in COMM 102 each semester, and about 600 students are enrolled in COMM 110 each semester. They are included in the Communication Department's SONA website, which is the research participation pool website run by the department. Once the study is available on SONA website, students receive an email from SONA, and if they agree to participate in the study, they will sign up for the study on SONA website. They will be able to sign up for a 30-minute time slot for the pre-exposure survey session. Those who complete the pre-exposure survey will receive the same recruitment email encouraging them to sign up for another 30-minute time slot for their post-exposure survey session. This method was deemed appropriate to reach this target study population because they were familiar with the SONA system overall and receiving study notification emails.

Participants who agree to be in the study will receive a pre-exposure online survey link. Once they click on the link, they will be asked to read the consent form first. Screening questions will appear on the next page. Those who met the eligibility criteria were then able to proceed with the questionnaire and randomized. Those who did not meet the eligibility criteria were directed to the end of the survey.

Half of the participants assigned to the radon app condition will be asked to provide their Twitter information. If participants don't have a Twitter ID, they will be asked to create a new one prior to

completing the pre-exposure survey. Once the app is installed in participants' own phones and they successfully log in through their Twitter credentials, they will be asked to keep the app on their phone for three months with the notification setting "on". After all these steps are completed, they will be asked to complete the pre-exposure survey. The radon app can be accessed via computer or smartphone: https://radon-production.herokuapp.com/

The other half of the participants assigned to the brochure condition will be asked to provide the mailing address prior to completing the pre-exposure survey so that they can receive EPA brochures in the next 3 months via postal mail. Once this step is completed, they will be asked to complete the pre-exposure survey. During the 3-month period, participants assigned to the radon app condition will receive the radon educational materials via the app. Materials include the informational content repurposed from EPA brochures and radon-education Tweets using hashtags, such as #radon, #lungcancer, #healthylungs, and #radonawareness. The app uses the Twitter's mechanism so that's why participants need to use their Twitter credentials to login, and those hashtags used in Tweets are automatically detected by the app, and will be populated in the app. While keeping the app for three months, if participants would like to test their homes for radon levels, as education materials they will be exposed to encourage to do so, they can request a free radon kit through the app. They will be asked to enter their mailing address, email, and phone number so that the kit will be delivered to their home address. Although the app would collect such personal information, this is only to provide them with the free radon kit, and such information won't be attached to their any survey responses. On the other hand, participants assigned to the brochure condition will receive a total of three EPA brochures, with each one being delivered once a month. In each mailing, participants will receive a pre-addressed, pre-paid postcard to request a free radon test kit. The postcard will be addressed to a UND address so that we can track the number requested by participants in the brochure condition.

Participants who completed the pre-exposure survey then received an email reminder including the link for the post-exposure survey three months after the completion of their pre-exposure survey. Participants who did not complete the post-exposure survey two weeks after the initial email received a reminder email.

A sample size of at least 100 students in each group was determined to have a power of .8 to .9 to detect differences in proportions of at least 20%, Chi-square values of five or more with one or two degrees of freedom, mean differences of at least 0.3, and odds ratios greater than three in logistic regression.

Participant incentives:

Students who were enrolled in COMM 110 class received 0.5 extra course credit point for the completion of pre-exposure survey, which was equivalent to the half-hour research participation. If they completed the second and final session (i.e., post-exposure survey), they received additional 0.5 extra credit point.

Students who were enrolled in COMM 102 class met the half-hour research participation requirement for completing the pre-exposure survey. If they completed the second and final session (i.e., post-exposure survey), they met additional half-hour research participation requirement.

In addition to extra credit or meeting the research requirement, students received a $10 gift card for the completion of pre-exposure survey. If they complete the second and final session (i.e., post-exposure survey), they received another $15 gift card.

All students included in the Comm department's SONA research pool are 110 and 102 students, and they are taught by GTAs (110) and a designated instructor (102). The PI has never taught 102 or 110 courses, and will not do so. But in case any of PI's students are invited to the study, they will be given an option to complete an alternative task as a way to avoid coercion or undue influence.

6 STUDY INTERVENTION(S) OR EXPERIMENTAL MANIPULATION(S)

6.1 STUDY INTERVENTION(S) OR EXPERIMENTAL MANIPULATION(S) ADMINISTRATION

6.1.1 STUDY INTERVENTION OR EXPERIMENTAL MANIPULATION DESCRIPTION

Participants in both experimental conditions will complete an online pre-exposure survey during the baseline phase of the study. Upon completion of the pre-exposure survey, participants assigned to **the radon app condition** will be asked to install the radon app on their smartphones and use the app for three months. App installation will be verified electronically via text message sent to the investigators. To make the informational content of the radon app and EPA brochures equivalent, the informational content in the app condition will be repurposed from EPA brochures used in the brochure condition. Participants in the radon app condition will have the opportunity to order a free radon test kit through the app at any time during the three-month period.

In contrast, individuals assigned to **the brochure condition** will receive three EPA brochures for the three-month period via postal mails. These brochures are (1) Basic radon facts (*https://bit.ly/2S6ryFw*); (2) A citizen's guide to radon (*https://bit.ly/3l3FhcJ*); and (3) Consumer's guide to radon reduction (*https://bit.ly/3ibt83n*). In each mailing, participants will receive a pre-addressed, pre-paid postcard to request a free radon test kit. The postcard will be addressed to a UND address so that we can track the number requested by participants in the brochure condition.

6.1.2 ADMINISTRATION AND/OR DOSING

At the baseline, participants assigned to **the radon app condition** will be asked to install the radon app on their smartphones and use the app for three months. App installation will be verified electronically via text message sent to the investigators. In other words, the intervention is delivered virtually. Participants will not interact with other participants. To make the

informational content of the radon app and EPA brochures equivalent, the informational content in the app condition will be repurposed from EPA brochures used in the brochure condition. Participants in the radon app condition will have the opportunity to order a free radon test kit through the app at any time during the three-month period.

In contrast, individuals assigned to **the brochure condition** will receive three EPA brochures for the three-month period via postal mails. These brochures are (1) Basic radon facts (*https://bit.ly/2S6ryFw*); (2) A citizen's guide to radon (*https://bit.ly/3l3FhcJ*); and (3) Consumer's guide to radon reduction (*https://bit.ly/3ibt83n*). Participants will not interact with other participants. In each mailing, participants will receive a pre-addressed, pre-paid postcard to request a free radon test kit. The postcard will be addressed to a UND address so that we can track the number requested by participants in the brochure condition.

6.2 FIDELITY

6.2.1 INTERVENTIONIST TRAINING AND TRACKING

Ideally, the fidelity of delivery would be monitored by measuring the amount of time persons in the experimental group spent time on the smartphone app. However, this functionality was not developed for financial reasons (the app developer required more money that we had to spend), nor was there any parallel for the comparison group, since there was no way to guarantee that they had indeed read the brochures we sent. However, we did verify the downloading of the app to the experimental group.

With regard to adherence, this was measured indirectly, via the percentage correct of tests of radon knowledge.

6.3 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND BLINDING

Participants are assigned to either the radon app or brochure condition via the randomization function of Qualtrics. In other words, this trial will utilize the double-blind randomization.

There may be "contamination" of the exposures if participants assigned to the radon app share the app content with classmates assigned to the brochure condition. A consequence of this would be to dilute the effect of group exposure. Participants will be instructed not to share information with others about group assignment. Additionally, we will guard against this via a programming function that permits downloading of the radon app only by individuals assigned to the radon app condition.

6.4 STUDY INTERVENTION/EXPERIMENTAL MANIPULATION ADHERENCE

Participants' adherence with study procedures for the radon app condition will be tracked based on the back-end data provided by the app development company, Triad Interactive Media. A complete adherence is not expected, however, because participants were asked to use the app occasionally as they would do for other apps. Participants' adherence with study procedures for the brochure condition will be tracked based on the number of returned postal mails. A 100%

delivery of postal mails is not expected, however, because delivery failure reflects the real-life situations participants would face in other situations.

6.5 CONCOMITANT THERAPY

N/A

6.5.1 RESCUE THERAPY

N/A

7 STUDY INTERVENTION/EXPERIMENTAL MANIPULATION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1 DISCONTINUATION OF STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

When a subject discontinues from accessing the radon app or receiving printed brochures, but not from the study, remaining study procedures will be completed as indicated by the study protocol. If a clinically significant finding is identified (including, but not limited to changes from baseline) after enrollment, the investigator or qualified designee will determine if any change in participant management is needed. Any new clinically relevant finding will be reported as an adverse event (AE).

The data to be collected at the time of study intervention discontinuation will include the following:

- The reason(s) for discontinuing the participant from the intervention, and methods for determining the need to discontinue.
- If the participant is due to complete assessments within 2 weeks of being discontinued from the study intervention, those assessments will be administered at the time of discontinuation; if the next scheduled assessments are more than 2 weeks from the discontinuation date, the discontinued participant will wait for the next scheduled assessment. Thereafter, the participant will be included in all future scheduled assessments, even though not participating in the intervention.

7.2 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

Participants are free to withdraw from participation in the study at any time upon request.

An investigator may discontinue a participant from the study for the following reasons:

- Significant study intervention non-compliance, unless varying compliance is an aspect of the study objectives
- Lost-to-follow up; unable to contact subject (see **Section 7.3, Lost to Follow-Up**)

- Any event or medical condition or situation occurs such that continued collection of follow-up study data would not be in the best interest of the participant or might require an additional treatment that would confound the interpretation of the study
- The participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation

The reason for participant discontinuation or withdrawal from the study will be recorded by the PI. Subjects who read the informed consent form, and are randomized and receive the study intervention, and subsequently withdraw, or are discontinued from the study, will not be replaced.

7.3 LOST TO FOLLOW-UP

A participant will be considered lost to follow-up if he or she fails to complete the post-exposure survey and study staff are unable to contact the participant after at least 2 attempts.

The following actions must be taken if a participant fails to complete the post-exposure survey:

- The site will attempt to contact the participant, counsel the participant on the importance of maintaining the assigned visit schedule and ascertain if the participant wishes to and/or should continue in the study.
- Before a participant is deemed lost to follow-up, the investigator or designee will make every effort to regain contact with the participant via a reminder email. These contact attempts will be documented in the participant's medical record or study file.
- Should the participant continue to be unreachable, he or she will be considered to have withdrawn from the study with a primary reason of lost to follow-up.

8 STUDY ASSESSMENTS AND PROCEDURES

8.1 ENDPOINT AND OTHER NON-SAFETY ASSESSMENTS

Once a participant will be directed to the Qualtrics pre-exposure survey link, the consent form will appear on the first page of the survey. Participants will be asked to read it and proceed if they agree. All participants will be asked to answer pre-exposure survey questions measuring key variables, such as radon knowledge, and demographic information to be used in the analyses (e.g., age, gender, home-owner status, smoking status). They will then be randomly assigned to one of the two conditions (via Qualtrics survey's randomization function). Participants assigned to the radon app condition will receive instructions on how to install the app and be instructed to use the app for the next three months. On the other hand, participants assigned to the brochure condition will receive appropriate instructions and be asked to submit both their mailing and email addresses so that they can receive three brochures in the next three months and be contacted for the post-exposure survey. Next, Participants' email and mailing addresses will not be attached to their responses to the pre-exposure survey to protect participants' privacy and confidentiality. Once participants complete the pre-survey, we have the data telling us that: which email address was assigned to which condition, and the timing. After 3 months, we will send the post-exposure survey link to that email address individually. Participants' behaviors,

which are two primary endpoints (i.e., test kit ordering and utilizing behaviors) will be recorded as they become available during the 3-month period.

In summary, participants in both experimental conditions will complete an online pre-exposure survey during the baseline phase of the study and then are randomized to the app or the brochure group. *T*he experimental groups differ only in the means by which information is conveyed, not in the nature of the information. Participants in both conditions will have the opportunity to order a free radon test kit at any time during the three-month period.

8.2 SAFETY ASSESSMENTS

N/A

8.3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

N/A

8.4 UNANTICIPATED PROBLEMS

8.4.1 DEFINITION OF UNANTICIPATED PROBLEMS

This protocol uses the definition of Unanticipated Problems as defined by the Office for Human Research Protections (OHRP). OHRP considers unanticipated problems involving risks to participants or others to include, in general, any incident, experience, or outcome that meets **all** of the following criteria:

- Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the Institutional Review Board (IRB)-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied;
- Related or possibly related to participation in the research ("possibly related" means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

8.4.2 UNANTICIPATED PROBLEMS REPORTING

The PI will report unanticipated problems (UPs) to the reviewing Institutional Review Board (IRB). The UP report will include the following information:

- Protocol identifying information: protocol title and number, PI's name, and the IRB project number
- A detailed description of the event, incident, experience, or outcome.

- An explanation of the basis for determining that the event, incident, experience, or outcome represents an UP.
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UP.

To satisfy the requirement for prompt reporting, UPs will be reported using the following timeline:

- UPs that are serious adverse events (SAEs) will be reported to the IRB within 14 working days of the investigator becoming aware of the event.
- Any other UP will be reported to the IRB within 14 working days of the investigator becoming aware of the problem.
- All UPs should be reported to appropriate institutional officials (as required by an institution's written reporting procedures), the supporting agency head (or designee), and the Office for Human Research Protections (OHRP) within 14 working days of the IRB's receipt of the report of the problem from the investigator.

8.4.3 REPORTING UNANTICIPATED PROBLEMS TO PARTICIPANTS

N/A

9 STATISTICAL CONSIDERATIONS

9.1 STATISTICAL HYPOTHESES

- Primary Endpoint(s): **Ho**: The incidence of: (a) participants' requests for free radon kits and (b) participants utilizing the test kits and returned to Alpha Energy Labs among those assigned to the radon app condition and those assigned to the brochure condition will not differ. **H1**: The incidence of: (a) participants' requests for free radon kits and (b) participants utilizing the test kits and returned to Alpha Energy Labs will be higher among those assigned to the radon app than the brochure condition.

  Ho: The difference in the incidence of request for and utilization of radon test kits between the radon app and brochure conditions will not be affected by participants' gender, age, race, smoking status, or geographic location (state/county of birth). **H1**: There is significant interaction between the radon app and brochure conditions and the variables above in terms of the proportion requesting and utilization of test kits.

- Secondary Endpoint(s): **Ho**: There will be no changes in radon knowledge among those assigned to the radon app condition and those assigned to the brochure condition. **H1**: There will be more positive changes in radon knowledge among participants assigned to the radon app condition.

9.2 SAMPLE SIZE DETERMINATION

Primary endpoints:

1. Number of radon test kits requested by participants in the radon app and brochure conditions; and

2. Number of radon test kits used and returned to the laboratory by participants in the two conditions.

Secondary endpoints:

Effectiveness of the radon app vs. brochure at 3 months re: changes in radon knowledge, as measured by the number of correct responses to a series of 20 true/false questions (e.g., "The EPA recommends that homes with 4 picocuries per liter (pCi/L) or more of radon should be fixed.").

Sample size determination:

A sample size of at least 100 people in each group will have a power of .8 to .9 to detect differences in proportions of at least 20%, Chi-square values of five or more with one or two degrees of freedom, mean differences of at least 0.3, and odds ratios greater than three in logistic regression.

Statistical analyses:

Ho: The incidence of: (a) participants' requests for free radon kits and (b) participants utilizing the test kits and returned to Alpha Energy Labs among those assigned to the radon app condition and those assigned to the brochure condition will not differ. **H1**: The incidence of: (a) participants' requests for free radon kits and (b) participants utilizing the test kits and returned to Alpha Energy Labs will be higher among those assigned to the radon app than the brochure condition. **Statistical test**: We will use a directional Z test for difference in proportions to determine whether the incidence of requested and returned kits is higher for those assigned to the radon app condition with SAS. Differences will be described using absolute and relative differences in proportions.

Ho: There will be no changes in radon knowledge among those assigned to the radon app condition and those assigned to the brochure condition. **H1**: There will be more positive changes in radon knowledge among participants assigned to the radon app condition. **Statistical test**: Differences in radon knowledge between the two groups will be tested with directional, independent t-tests, with SAS.

9.3 POPULATIONS FOR ANALYSES

All intent-to-treat (ITT) analysis population (i.e., all randomized participants) will be included in the data analyses.

9.4 STATISTICAL ANALYSES

9.4.1 GENERAL APPROACH

- For descriptive statistics, categorical and continuous data will be presented (e.g., percentages, means with standard deviations, median, range).
- Inferential tests will indicate the p-value and confidence intervals for statistical significance (Type I error) and whether one or two-tailed.
- Covariates will be pre-specified in the sections below.
- The checks of assumptions underlying statistical procedures will be performed and whether any corrective procedures will be applied (e.g., transformation or nonparametric tests) if needed.

9.4.2 ANALYSIS OF THE PRIMARY ENDPOINT(S)

Primary endpoints:

1. Number of radon test kits requested by participants in the radon app and brochure conditions; and

2. Number of radon test kits used and returned to the laboratory by participants in the two conditions.

Ho: The incidence of: (a) participants' requests for free radon kits and (b) participants utilizing the test kits and returned to Alpha Energy Labs among those assigned to the radon app condition and those assigned to the brochure condition will not differ. **H1**: The incidence of: (a) participants' requests for free radon kits and (b) participants utilizing the test kits and returned to Alpha Energy Labs will be higher among those assigned to the radon app than the brochure condition. **Statistical test**: We will use a directional Z test for difference in proportions to determine whether the incidence of requested and returned kits is higher for those assigned to the radon app condition with SAS. Differences will be described using absolute and relative differences in proportions.

9.4.3 ANALYSIS OF THE SECONDARY ENDPOINT(S)

Secondary endpoints:

Effectiveness of the radon app vs. brochure at 3 months re: changes in radon knowledge, as measured by the number of correct responses to a series of 20 true/false questions (e.g., "The EPA recommends that homes with 4 picocuries per liter (pCi/L) or more of radon should be fixed.").

Radon knowledge will be measured by the number of accurate responses to 20 True-False statements in T1 (baseline) and T2 (at 3 months).[11] The response options will be: "true," "false," and "I don't know." Participants' responses to each statement will then be re-coded to 1 ("correct") or 0 ("incorrect" or "I don't know"). After that, two radon knowledge index variables (continuous) will be created by summing participants' responses to each statement in T1 (baseline) and T2 (at 3 months). Lower numbers on index variables indicate a low level of knowledge, whereas higher numbers indicate greater knowledge.

Ho: There will be no changes in radon knowledge among those assigned to the radon app condition and those assigned to the brochure condition. **H1**: There will be more positive changes in radon knowledge among participants assigned to the radon app condition. **Statistical test**: Differences in radon knowledge between the two groups will be tested with directional, independent t-tests, with SAS.

9.4.4 SAFETY ANALYSES

N/A

9.4.5 BASELINE DESCRIPTIVE STATISTICS

N/A

9.4.6 PLANNED INTERIM ANALYSES

N/A

9.4.7 SUB-GROUP ANALYSES

Primary endpoints will be analyzed based on gender, age, race, smoking status, or geographic location (state/county of birth):

Ho: The difference in the incidence of request for and utilization of radon test kits between the radon app and brochure conditions will not be affected by participants' gender, age, race, smoking status, or geographic location (state/county of birth). **H1**: There is significant interaction between the radon app and brochure conditions and the variables above in terms of the proportion requesting and utilization of test kits. **Statistical test:** We will use multivariate regression analyses predicting incidence of requesting and utilization of test, while controlling for gender, age, race, smoking status, location, and time spent using the app with SAS. Interactions will be tested in multivariate models and significant interactions will be described by levels of univariate Z or chi-square tests.

Secondary endpoints will not be analyzed based on gender, age, race, smoking status, or geographic location (state/county of birth).

9.4.8 TABULATION OF INDIVIDUAL PARTICIPANT DATA

Individual participant data will be listed by measure and time point.

9.4.9 EXPLORATORY ANALYSES

N/A

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

10.1.1 INFORMED CONSENT PROCESS

10.1.1.1 CONSENT/ASSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS

Consent forms describing in detail the study intervention, study procedures, and risks will appear in the first page of the online survey questionnaire. Participants will be asked to read and proceed if they consent. The following consent material is submitted with this protocol: IRB-approved consent forms for pre-exposure and post-exposure surveys.

10.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

The consent form for pre-exposure survey and post-exposure surveys will appear at the very beginning of each online survey. COMM110 and 102 students who are interested in participating in this study will be asked to read the consent form by themselves. Completion and return of the online survey form implies that they have read the information in this form and consent to participate in the research. Since the research presents no more than minimal risk and includes no procedures for which written consent is normally required outside the research context, the IRB granted the waiver of signature requirement for informed consent.

10.1.2 STUDY DISCONTINUATION AND CLOSURE

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to study participants, investigator, funding agency, and regulatory authorities. If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform study participants, the Institutional Review Board (IRB), and sponsor/funding agency and will provide the reason(s) for the termination or suspension. Study participants will be contacted, as applicable, and be informed of changes to study visit schedule.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Demonstration of efficacy that would warrant stopping
- Insufficient compliance of study staff to the protocol (i.e., significant protocol violations)
- Data that are not sufficiently complete and/or evaluable
- Determination that the primary endpoint has been met
- Determination of futility

The study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the funding agency, sponsor, IRB, Food and Drug Administration (FDA), or other relevant regulatory or oversight bodies (OHRP, DSMB).

10.1.3 CONFIDENTIALITY AND PRIVACY

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, the safety and oversight monitor(s), and the sponsor(s) and funding agency. This confidentiality is extended to the data being collected as part of this study. Data that could be used to identify a specific study participant will be held in strict confidence within the research team. No personally-identifiable information from the study will be released to any unauthorized third party without prior written approval of the sponsor/funding agency.

All research activities will be conducted in as private a setting as possible.

The study monitor, other authorized representatives of the sponsor or funding agency, representatives of the Institutional Review Board (IRB), regulatory agencies or representatives from companies or organizations supplying the product, may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the participants in this study. The clinical study site will permit access to such records.

The study participant's contact information will be securely stored at the clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by the reviewing IRB, Institutional policies, or sponsor/funding agency requirements.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored in the PI's password-protected computer. This will not include the participant's contact or identifying information. Rather, individual participants and their research data will be identified by a unique study identification number. The study data entry and study management systems used by the study team will be secured and password protected. At the end of the study, all study databases will be de-identified and archived in the PI's password-protected computer.

Measures Taken to Ensure Confidentiality of Data Shared per the NIH Data Sharing Policies

It is NIH policy that the results and accomplishments of the activities that it funds should be made available to the public (see *https://grants.nih.gov/policy/sharing.htm*). The PI will ensure all mechanisms used to share data will include proper plans and safeguards for the protection of privacy, confidentiality, and security for data dissemination and reuse (e.g., all data will be thoroughly de-identified and will not be traceable to a specific study participant). Plans for archiving and long-term preservation of the data will be implemented, as appropriate.

Certificate of Confidentiality

To further protect the privacy of study participants, the Secretary, Health and Human Services (HHS), has issued a Certificate of Confidentiality (CoC) to all researchers engaged in biomedical, behavioral, clinical or other human subjects research funded wholly or in part by the federal government. Recipients of NIH funding for human subjects research are required to protect identifiable research information from forced disclosure per the terms of the NIH Policy (see *https://humansubjects.nih.gov/coc/index*). As set forth in 45 CFR Part 75.303(a) and NIHGPS Chapter 8.3, recipients conducting NIH-supported research covered by this Policy are required to establish and maintain effective internal controls (e.g., policies and procedures) that provide reasonable assurance that the award is managed in compliance with Federal statutes, regulations, and the terms and conditions of award. It is the NIH policy that investigators and others who have access to research records will not disclose identifying information except when the participant consents or in certain instances when federal, state, or local law or regulation requires disclosure. NIH expects investigators to inform research participants of the protections and the limits to protections provided by a Certificate issued by this Policy.

10.1.4 FUTURE USE OF STORED SPECIMENS AND DATA

Data collected for this study will be analyzed and stored in the PI's password-protected computer. After the study is completed, the de-identified, archived data will continue to be stored in the PI's password-protected computer, for use by other researchers including those outside of the study.

10.1.5 KEY ROLES AND STUDY GOVERNANCE

Principal Investigator
Soojung Kim, PhD, MPH, Chair and Associate Professor
University of North Dakota
Address: 221 Centennial Dr. Stop 7169, Grand Forks, ND 58202-7169
Phone Number: 701.777.2473
Email *soojung.kim@UND.edu*

The research team included Drs. Gary Schwartz and Marilyn Klug both at the University of North Dakota School of Medicine and Health Sciences.

10.1.6 SAFETY OVERSIGHT

Safety oversight will be under the direction of the study team based on its self-assessments guided by sub-components of a Quality Management Plan (see Section 10.1.8).

10.1.7 CLINICAL MONITORING

N/A

10.1.8 QUALITY ASSURANCE AND QUALITY CONTROL

The clinical site will perform internal quality management of study conduct, data collection, documentation and completion.

Quality control (QC) procedures will be implemented as follows:

Informed consent --- Study staff will review both the documentation of the consenting process as well as a percentage of the completed consent documents. This review will evaluate compliance with GCP, accuracy, and completeness. Feedback will be provided to the study team to ensure proper consenting procedures are followed**.**

Source documents and the electronic data --- Data will be initially captured on source documents (see **Section 10.1.9, Data Handling and Record Keeping**) and will ultimately be entered into the study database. To ensure accuracy site staff will compare a representative sample of source data against the database, targeting key data points in that review.

Intervention Fidelity — Consistent delivery of the study interventions will be monitored throughout the intervention phase of the study. Procedures for ensuring fidelity of intervention delivery are described in **Section 6.2.1, Interventionist Training and Tracking**.

Protocol Deviations – The study team will review protocol deviations on an ongoing basis and will implement corrective actions when the quantity or nature of deviations are deemed to be at a level of concern.

Should independent monitoring become necessary, the PI will provide direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor/funding agency, and inspection by local and regulatory authorities.

10.1.9 DATA HANDLING AND RECORD KEEPING

10.1.9.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

Data collection will be the responsibility of the clinical trial staff at the site under the supervision of the site investigator. The investigator will be responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

All source documents will be completed in a neat, legible manner to ensure accurate interpretation of data. Electronic data will be saved in excel spreadsheets and Qualtrics where the pre-exposure and post-exposure surveys were hosted. They will be saved on the PI's password-protected computer.

10.1.9.2 STUDY RECORDS RETENTION

Study documents will be retained for a minimum of 2 years after the last approval of a marketing application in an International Council on Harmonisation (ICH) region and until there are no pending or contemplated marketing applications in an ICH region or until at least 2 years have elapsed since the formal discontinuation of clinical development of the study intervention. These documents should be retained for a longer period, however, if required by local regulations. No records will be destroyed without the written consent of the sponsor/funding agency, if applicable. It is the responsibility of the sponsor/funding agency to inform the investigator when these documents no longer need to be retained.

10.1.10 PROTOCOL DEVIATIONS

This protocol defines a protocol deviation as any noncompliance with the clinical trial protocol, International Council on Harmonisation Good Clinical Practice (ICH GCP), or Manual of Procedures (MOP) requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions will be developed by the site and implemented promptly.

These practices are consistent with ICH GCP:

- Section 4.5 Compliance with Protocol, subsections 4.5.1, 4.5.2, and 4.5.3
- Section 5.1 Quality Assurance and Quality Control, subsection 5.1.1
- Section 5.20 Noncompliance, subsections 5.20.1, and 5.20.2.

It will be the responsibility of the site investigator to use continuous vigilance to identify and report deviations within 14 working days of identification of the protocol deviation, or within 14 working days of the scheduled protocol-required activity. All deviations will be addressed in study source documents, reported to National Institute of General Medical Sciences Program Official and the University of North Dakota. Protocol deviations will be sent to the reviewing Institutional Review Board (IRB) per their policies. The site investigator will be responsible for knowing and adhering to the reviewing IRB requirements.

10.1.11 PUBLICATION AND DATA SHARING POLICY

This study will be conducted in accordance with the following publication and data sharing policies and regulations:

National Institutes of Health (NIH) Public Access Policy, which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central upon acceptance for publication.

This study will comply with the NIH Data Sharing Policy and Policy on the Dissemination of NIH-Funded Clinical Trial Information and the Clinical Trials Registration and Results Information Submission rule. As such, this trial will be registered at ClinicalTrials.gov, and results information from this trial will be submitted to ClinicalTrials.gov. In addition, every attempt will be made to publish results in peer-reviewed journals. Data from this study may be requested from other researchers 3 years after the completion of the primary endpoint by contacting Soojung Kim at *soojung.kim@und.edu*. Considerations for ensuring confidentiality of these shared data are described in Section 10.1.3.

10.1.12 CONFLICT OF INTEREST POLICY

The independence of this study from any actual or perceived influence, such as by the pharmaceutical industry, is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the design and conduct of this trial. The study leadership in conjunction with the National Institute of General Medical Sciences has established policies and procedures for all study group members to disclose all conflicts of interest and will establish a mechanism for the management of all reported dualities of interest.

10.2 ADDITIONAL CONSIDERATIONS

N/A

10.3 ABBREVIATIONS AND SPECIAL TERMS

AE	Adverse Event
CFR	Code of Federal Regulations
CLIA	Clinical Laboratory Improvement Amendments
CMP	Clinical Monitoring Plan
COC	Certificate of Confidentiality
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Form
DCC	Data Coordinating Center
DHHS	Department of Health and Human Services
DSMB	Data Safety Monitoring Board
DRE	Disease-Related Event
EC	Ethics Committee
eCRF	Electronic Case Report Forms
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Amendments Act of 2007
FFR	Federal Financial Report
GCP	Good Clinical Practice
GLP	Good Laboratory Practices
GMP	Good Manufacturing Practices
GWAS	Genome-Wide Association Studies
HIPAA	Health Insurance Portability and Accountability Act
IB	Investigator's Brochure

ICH	International Council on Harmonisation
ICMJE	International Committee of Medical Journal Editors
IDE	Investigational Device Exemption
IND	Investigational New Drug Application
IRB	Institutional Review Board
ISM	Independent Safety Monitor
ITT	Intention-To-Treat
LSMEANS	Least-squares Means
MedDRA	Medical Dictionary for Regulatory Activities
MOP	Manual of Procedures
NCT	National Clinical Trial
NIH	National Institutes of Health
NIH IC	NIH Institute or Center
OHRP	Office for Human Research Protections
PI	Principal Investigator
QA	Quality Assurance
QC	Quality Control
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SMC	Safety Monitoring Committee
SOA	Schedule of Activities
SOP	Standard Operating Procedure
UND	University of North Dakota
UP	Unanticipated Problem
US	United States

10.4 PROTOCOL AMENDMENT HISTORY

Version	Date	Description of Change	Brief Rationale

11 REFERENCES

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