National Survey to Understand Ethical, Legal and Social Issues in Communicating to the Public About Epigenetics

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CONFIDENTIALITY STATEMENT

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STATEMENT OF COMPLIANCE

The trial will be conducted in accordance with International Council on Harmonisation Good Clinical Practice (ICH GCP), applicable United States (US) Code of Federal Regulations (CFR), and the <specify NIH Institute or Center (IC) > Terms and Conditions of Award. The Principal Investigator will assure that no deviation from, or changes to the protocol will take place without prior agreement from the funding agency and documented approval from the Institutional Review Board (IRB), and the Investigational New Drug (IND) or Investigational Device Exemption (IDE) sponsor, if applicable, except where necessary to eliminate an immediate hazard(s) to the trial participants. All personnel involved in the conduct of this study have completed Human Subjects Protection and ICH GCP Training.

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the IRB for review and approval. Approval of both the protocol and the consent form(s) must be obtained before any participant is consented. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form(s) will be IRB approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

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: Signed by: Erika Waters 63E791D4F3F74D2... Date: 5/19/2026 | 2:37 PM CDT

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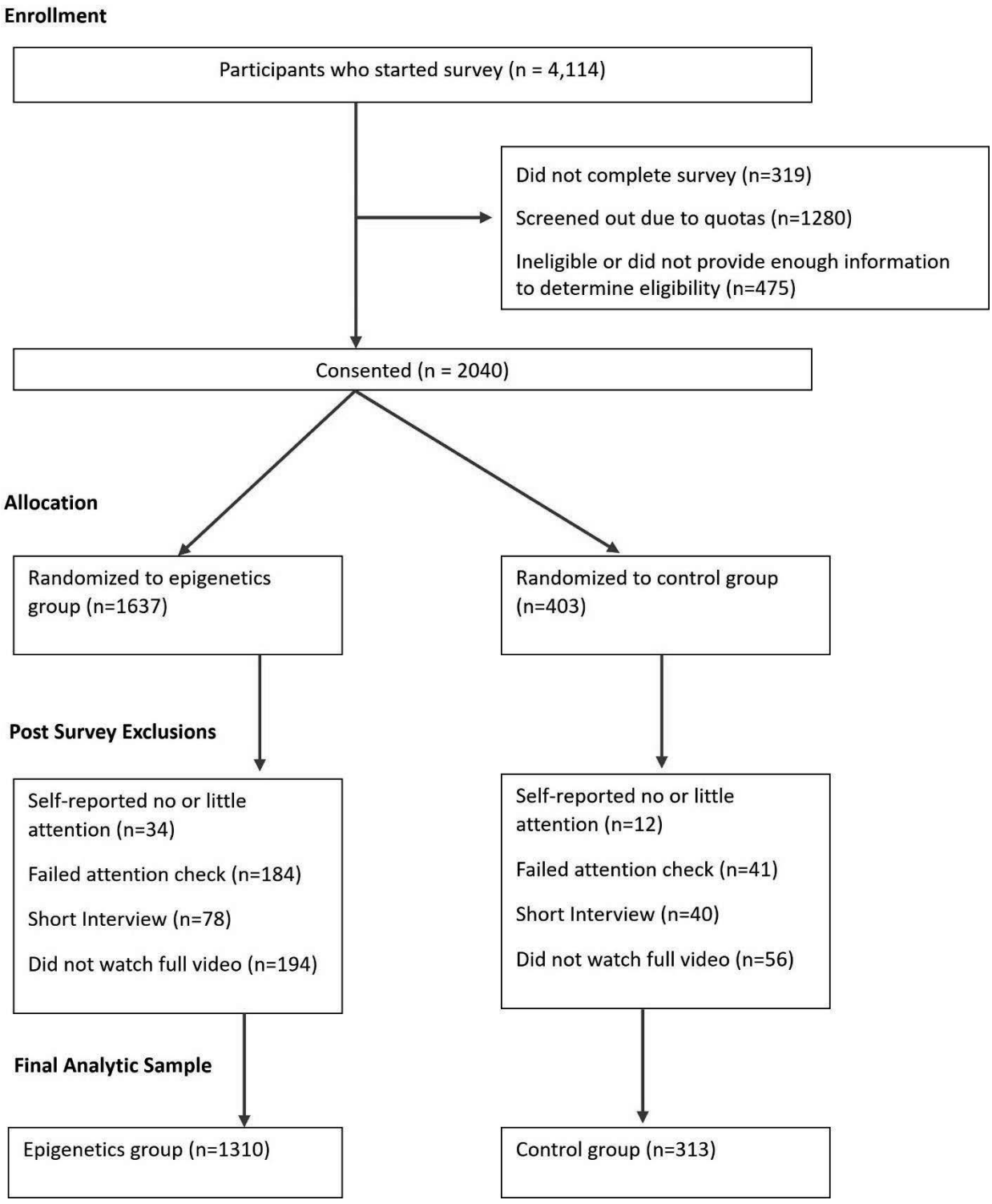
1 PROTOCOL SUMMARY

1.1 SYNOPSIS

Title:	**National Survey to Understand Ethical, Legal and Social Issues in Communicating to the Public About Epigenetics**
Grant Number:	**R01ES033743**
Study Description:	Few people realize that environmental pollution and some behaviors like physical activity and tobacco smoking can affect their health by "turning on" or "turning off" certain genes through a process called "epigenetic modification." This study will develop and test strategies for communicating about epigenetics that are understandable and that increase acceptance of using epigenetics in clinical settings.
Objectives*:	Primary Objective: Our primary objective is to develop communication strategies about epigenetic modification that are understandable to all audiences. Secondary Objectives: Our secondary objective is to evaluate the effects of communication strategies about epigenetic modification on perceptions of the information presented and to explore perceptions of the acceptability of using epigenetic technologies for clinical purposes.
Endpoints*:	Primary Endpoint: Knowledge & understanding of epigenetics Information Secondary Endpoints: Perceptions of epigenetics information and acceptability of using epigenetics in clinical settings.
Study Population:	2040 non-institutionalized adults (age 18 and older) residing in the United States who do not identify as a genetics expert. No one will be excluded based on race, ethnicity, or biological sex.
Phase* or Stage:	N/A
Description of Sites/Facilities Enrolling Participants:	All research activities will occur at Washington University School of Medicine.
Description of Study Intervention/Experimental Manipulation:	Experimental condition: Epigenetics Video - Participants will watch a brief (<5 minute) video about the concept of Epigenetics during an online survey. Active Comparator: Nanotechnology Video - Participants will watch a brief (<5 minute) video about nanotechnology during an online survey.
Study Duration*:	. 3 Months

Participant Duration: 30 Minutes

1.2 SCHEMA



1.3 SCHEDULE OF ACTIVITIES

	Pre-screening (Pre-consent)	Time 1
IPSOS invites participants	x	
Participants complete eligibility pre-screening questions	x	
Consent		x
Randomization		x
Survey Completion		x

2 INTRODUCTION

2.1 STUDY RATIONALE

Few people realize that environmental pollution and some behaviors like physical activity and tobacco smoking can affect their health by "turning on" or "turning off" certain genes through a process called "epigenetic modification." This study will develop and test strategies for communicating about epigenetics that are understandable and that increase acceptance of using epigenetics in clinical settings.

2.2 BACKGROUND

Environmental factors that influence disease may do so by chemically altering parts of the DNA that regulate gene expression.[1] Such “epigenetic modifications” can be propagated through multiple cell divisions, occur throughout the lifespan, and be transmitted to future generations.[2-4] Epigenetic changes can be acquired via exposure to environmental pollutants, severe and persistent social stress, or lifestyle behaviors (e.g., diet) and are associated with many chronic diseases (e.g., cancer, diabetes, cardiovascular disease).[5-7]

Unfortunately, there is a critical barrier to the translation of basic epigenetics research into clinical and public health practice: limited scientific knowledge about how to communicate information about the relationship between epigenetics and health in a way that is understandable and supports perceptions of acceptability of using epigenetic therapies in clinical settings to all audiences.

Overcoming this critical barrier is urgent. FDA-approved epigenetics-based therapeutics are currently in use in clinical settings.[7] Direct-to-consumer “epigenetic clock” test kits are sold on Amazon.[9] Nutritional supplements tailored to one’s epigenomic profile are being sold,[10] despite the absence of efficacy data. Incorrect information is also being disseminated through traditional media and the internet[11]. This rapidly-evolving clinical and information landscape indicates that now is the time to develop strategies for communicating epigenetics information to the public in a way that is understandable and acceptable.

2.3 RISK/BENEFIT ASSESSMENT

2.3.1 KNOWN POTENTIAL RISKS

There is a small risk of discomfort when viewing information about health risks and exposures.

2.3.2 KNOWN POTENTIAL BENEFITS

This study has no known potential benefits.

2.3.3 ASSESSMENT OF POTENTIAL RISKS AND BENEFITS

N/A

3 OBJECTIVES AND ENDPOINTS

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS	PUTATIVE MECHANISMS OF ACTION
Primary			
Our primary objective is to develop communication strategies about epigenetic modification that are understandable to all audiences.	Knowledge & understanding of epigenetics Information	We hypothesized that compared to participants who viewed an attention control video, participants who viewed the epigenetics video would show higher knowledge and understanding of epigenetics information.	N/A
Secondary			
Our secondary objective is to evaluate the effects of communication strategies about epigenetic modification on perceptions of the information to explore perceptions of the acceptability of using epigenetic technologies for clinical purposes.	Acceptability of using epigenetics in clinical settings and Perceptions of epigenetic information		N/A
Tertiary/Exploratory			
N/A	*N/A*	N/A	

4 STUDY DESIGN

4.1 OVERALL DESIGN

This study is a single-site RCT. The experimental manipulation will include participants watching a brief (<5 minute) video about the concept of Epigenetics during an online survey. We will include an active

comparator where participants will watch a brief (<5 minute) video about nanotechnology during an online survey. Survey respondents will be randomized by IPSOS software. There is no blinding.

The intervention was developed based on standard science communication principles in which the goal is to increase knowledge about a topic (e.g., limit jargon, use visuals). There will only be one intervention contact and timepoint for this study for both the experimental condition and the active comparator group. Both groups will watch a video that is less than 5 minutes long and it will be administered online.

The study population includes non-institutionalized adults (age 18 and older) residing in the United States of any sex, race, or ethnicity. We worked with Ipsos Public Affairs to conduct the study using participants from their KnowledgePanel® (probability-based web panel that is designed to be representative of the non-institutionalized adults (age 18 and older) United States population) and through other online panels they have access to when recruitment quotas could not be met with the other sample.

Our hypotheses are as follows:

Primary Endpoint(s):

- We hypothesize that compared to participants who viewed an attention control video, participants who viewed the epigenetics video would show higher knowledge and understanding of epigenetics information. Our null hypothesis is that there will be no differences in knowledge and understanding of epigenetics information between the two groups.

Secondary Endpoint(s):

- We hypothesized that compared to participants who viewed an attention control video, participants who viewed the epigenetics video would show higher perceptions of epigenetic information. Our null hypothesis is that there will be no differences in perceptions of epigenetic information between the two groups.
- We explore perceptions of acceptability of epigenetics information. Acceptability of epigenetics information will be assessed only in the experimental group and is exploratory, thus there is no formal hypothesis tested and only descriptive statistics will be calculated.

4.2 SCIENTIFIC RATIONALE FOR STUDY DESIGN

The active comparator control group will watch a video on an unrelated topic in order account for attention effects of viewing a video while taking the survey. A video of similar length, style, and scientific complexity was chosen to minimize variation, and a non-health related topic was chosen to minimize any unintended effects on health-related survey items.

4.3 JUSTIFICATION FOR INTERVENTION

There will only be one intervention contact and timepoint for this study for both the experimental condition and the active comparator group. Both groups will watch a video that is less than 5 minutes long and it will be administered online, as this is an online survey. The experimental group will watch the full

video on basics of epigenetics, while the active comparator will watch a video on nanotechnology that is similar in style and length. Participants who did not watch the full video in either case will be excluded from analysis. This intervention duration and delivery is realistic for how people obtain health information in real life, making the findings relevant for future dissemination.

4.4 END-OF-STUDY DEFINITION

End of study is defined as completing the survey.

5 STUDY POPULATION

The study population includes non-institutionalized adults (age 18 and older) residing in the United States of any sex, race, or ethnicity. We worked with Ipsos Public Affairs to conduct the study using participants from their KnowledgePanel® (probability-based web panel that is designed to be representative of the non-institutionalized adults (age 18 and older) United States population) and through other online panels they have access to when recruitment quotas could not be met with the other sample.

5.1 INCLUSION CRITERIA

- Age 18+,
- English-language speaker
- Identify as one of five Census-defined racial/ethnic groups:
  1. Non-Hispanic White
  2. Non-Hispanic Black,
  3. Non-Hispanic Asian
  4. Non-Hispanic Indigenous (i.e., Alaska Native/Native Hawaiian/American Indian/Other Pacific Islander)
  5. Hispanic (all races)

5.2 EXCLUSION CRITERIA

Self-identify as an expert in genetics

5.3 LIFESTYLE CONSIDERATIONS

N/A

5.4 SCREEN FAILURES

N/A

5.5 STRATEGIES FOR RECRUITMENT AND RETENTION

All recruitment activities and participant compensation will be conducted by IPSOS according to their standard practices. See Appendix A for a description of IPSOS methodologies.

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

The experimental manipulation will include participants watching a brief (<5 minute) video about the concept of Epigenetics during an online survey. We will include an active comparator where participants will watch a brief (<5 minute) video about nanotechnology during an online survey. The intervention was developed based on standard science communication principles in which the goal is to increase knowledge about a topic (e.g., limit jargon, use visuals).

6.1.2 ADMINISTRATION AND/OR DOSING

Participants will view the intervention or control video during survey administration.

6.2 FIDELITY

6.2.1 INTERVENTIONIST TRAINING AND TRACKING

N/A

6.3 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND BLINDING

Randomization will be done by IPSOS software. There is no blinding.

6.4 STUDY INTERVENTION/EXPERIMENTAL MANIPULATION ADHERENCE

N/A

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

N/A

7.2 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

Participants are free to withdraw from participation at any time. Any survey responses completed prior to discontinuing the survey will be retained. The statistical analysis plan discusses criteria for removal from the analytical sample.

7.3 LOST TO FOLLOW-UP

N/A

8 STUDY ASSESSMENTS AND PROCEDURES

8.1 ENDPOINT AND OTHER NON-SAFETY ASSESSMENTS

N/A

8.2 SAFETY ASSESSMENTS

N/A

8.3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

8.3.1 DEFINITION OF ADVERSE EVENTS

8.3.2 DEFINITION OF SERIOUS ADVERSE EVENTS

N/A

8.3.3 CLASSIFICATION OF AN ADVERSE EVENT

8.3.3.1 SEVERITY OF EVENT

N/A

8.3.3.2 RELATIONSHIP TO STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

N/A

8.3.3.3 EXPECTEDNESS

N/A

8.3.4 TIME PERIOD AND FREQUENCY FOR EVENT ASSESSMENT AND FOLLOW-UP

N/A

8.3.5 ADVERSE EVENT REPORTING

N/A

8.3.6 SERIOUS ADVERSE EVENT REPORTING

N/A

8.3.7 REPORTING EVENTS TO PARTICIPANTS

N/A

8.3.8 EVENTS OF SPECIAL INTEREST

N/A

8.3.9 REPORTING OF PREGNANCY

N/A

8.4 UNANTICIPATED PROBLEMS

8.4.1 DEFINITION OF UNANTICIPATED PROBLEMS

N/A

8.4.2 UNANTICIPATED PROBLEMS REPORTING

N/A

8.4.3 REPORTING UNANTICIPATED PROBLEMS TO PARTICIPANTS

N/A

9 STATISTICAL CONSIDERATIONS

9.1 STATISTICAL HYPOTHESES

- Primary Endpoint(s):
    - We hypothesize that compared to participants who viewed an attention control video, participants who viewed the epigenetics video would show higher knowledge and understanding of epigenetics information. Our null hypothesis is that there will be no differences in knowledge and understanding of epigenetics information between the two groups.

- Secondary Endpoint(s):
    - We hypothesized that compared to participants who viewed an attention control video, participants who viewed the epigenetics video would show higher perceptions of epigenetic information. Our null hypothesis is that there will be no differences in perceptions of epigenetic information between the two groups.
    - We explore perceptions of acceptability of epigenetics information. Acceptability of epigenetics information will be assessed only in the experimental group and is exploratory, thus there is no formal hypothesis tested and only descriptive statistics will be calculated.

9.2 SAMPLE SIZE DETERMINATION

Based on our primary outcome, knowledge and understanding of epigenetics information, and having 2 experimental groups, we conduct sample size calculations for a t-test. Setting alpha at 0.05, power at 0.80, and an estimated effect size of Cohen's D at 0.20, we need a required N of 788, thus our sample size meets this requirement. This will also provide sufficient power for addressing secondary and exploratory analysis.

9.3 POPULATIONS FOR ANALYSES

We will analyze the per-protocol dataset which will include all eligible participants who completed the survey and watched the full video for their condition. We will also exclude participants who were considered inattentive responders (defined as answering incorrectly to an attention check question [to show you read carefully, leave this question blank] OR participants who self-reported paying no or a little bit of attention to the survey questions) and those participants who complete the survey in less than half of the median response time from the analytic dataset.

9.4 STATISTICAL ANALYSES

9.4.1 GENERAL APPROACH

We will calculate mean, standard deviation, median, and ranges for all continuous variables, including all variables with Likert scale response options, as these will be treated as continuous variables. We will calculate frequencies and percentages for all categorical variables.

We will use two-tailed tests and specify our alpha as 0.05. We will report 95% confidence intervals with all point estimates and effect sizes in addition to p-values.

For averaged scales, we will use the average of all non-missing items. Missing data will be handled using list-wise deletion.

9.4.2 ANALYSIS OF THE PRIMARY ENDPOINT(S)

We will measure knowledge & understanding of epigenetics Information using a sum score of correct answers for 8 individual items. This variable will be treated as a continuous variable and it is measured only at one time-point. We will use a t-test to test for statistically significant differences in mean score between experimental and control group. We will present means and 95% confidence intervals both overall and by experimental group. Missing data will be handled using list-wise deletion.

9.4.3 ANALYSIS OF THE SECONDARY ENDPOINT(S)

We will measure perceptions of epigenetic information using an averaged score of 6 individual items. This variable will be treated as a continuous variable and it is measured only at one time-point. We will use a t-test to test for statistically significant differences in mean score between experimental and control group. We will present means and 95% confidence intervals both overall and by experimental group. Missing data will be handled using list-wise deletion.

We will measure acceptability of epigenetics information as single items using 3 different constructs including perceived benefits of epigenetic research (7 items), perceived drawbacks of epigenetic research (3 items), and acceptance of using epigenetic research in medical support (3 items). Because we only ask these questions of those in the experimental group, we do not formally test for statistical differences and present descriptive statistics for all items.

9.4.4 SAFETY ANALYSES

N/A

9.4.5 BASELINE DESCRIPTIVE STATISTICS

We will present baseline descriptive statistics on race/ethnicity, age, and sex both for the overall sample and by experimental group.

9.4.6 PLANNED INTERIM ANALYSES

N/A

9.4.7 SUB-GROUP ANALYSES

We will explore differences in the effect of the experimental condition on the primary and secondary endpoints by age (continuous), race/ethnicity, and gender. We will use linear regression models with the endpoints as the outcome, experimental condition as the main exposure, and then the respective demographic characteristic as a moderator, adding an interaction term between the demographic factor and main exposure to the model. We will consider the experimental condition to have a differential effect on the endpoints (by demographic factor) if the interaction term is statistically significant (p-value <0.05).

9.4.8 TABULATION OF INDIVIDUAL PARTICIPANT DATA

We will not provide individual participant data.

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

Participants will be shown a consent information sheet prior to enrolling. The consent information sheet is submitted with this protocol.

10.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

Participants will be shown a consent information sheet prior to enrolling. Continuing on to complete the survey will be considered consent to complete the survey. This study is exempt, so more detailed consent procedures are not required.

10.1.2 STUDY DISCONTINUATION AND CLOSURE

N/A

10.1.3 CONFIDENTIALITY AND PRIVACY

The study team will not obtain any private identifiable information about participants from IPSOS. IPSOS will follow their standard procedures for protecting the privacy and confidentiality of its panel participants.

10.1.4 FUTURE USE OF STORED SPECIMENS AND DATA

Data collected for this study will be analyzed and stored at Washington University School of Medicine. After the study is completed, the de-identified, archived data will be transmitted to and stored at Open Science Framework (*www.osf.io*) for use by other researchers including those outside of the study. When the study is completed, access to study data and/or samples will be provided through Open Science Framework.

10.1.5 KEY ROLES AND STUDY GOVERNANCE

Principal Investigator	**Medical Monitor or Independent Safety Monitor**
Erika Waters, PhD, MPH, Professor of Surgery	*N/A*
Washington University School of Medicine	
660 S Euclid Ave, St Louis MO 63110	
314-747-5707	
waterse@wustl.edu	

10.1.6 SAFETY OVERSIGHT

This study is exempt and requires no safety oversight or monitoring.

10.1.7 CLINICAL MONITORING

This study is exempt and requires no clinical monitoring.

10.1.8 QUALITY ASSURANCE AND QUALITY CONTROL

The study team will perform internal quality management of study data for analysis. No additional monitoring is required.

10.1.9 DATA HANDLING AND RECORD KEEPING

10.1.9.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

All survey data will be stored on encrypted and password-protected servers. If data need to be physically transported between locations, we will use an encrypted flash drive. If data need to be electronically transferred, we will do so using WUSM's network, which protects data in transit and at rest. No personally identifying information will be included in dissemination materials (e.g., conference presentations, publications, toolkit).

Ipsos prohibits clients, including academic researchers, from having any access to any personally identifiable information (PII) about any of the KnowledgePanel panelists without explicit informed consent and a non-disclosure agreement. The proposed research does not require PII, and so no members of the research team will have any access to personally identifiable information from any survey participant.

Ipsos has several measures in place to protect data, including via encryption, password-protection, firewalls, and controlled access to data only by individuals with a specific need to prevent unauthorized access. Each panel member is given a unique numerical identifier, and this identifier is kept separate from their PII on Ipsos' servers. Any communication about the member, including to clients, is conducted with this numerical identifier, not their name. Ipsos has implemented Good Practice Guidelines to assure compliance with FDA requirements for systems documentation and privacy of stored survey data, and to assure panelists' confidentiality and privacy. They are HIPAA-compliant and adhere to the European Union's General Data Protection Regulation policy, which includes the appointment of a Chief Privacy Officer, anonymized data and access security, employee training, encryption, and privacy requirements for suppliers and data transfers. Ipsos also publishes a privacy and confidentiality document for panelists, which describes what data Ipsos collects and why, how it is used, and the panelists' legal rights regarding their data.

10.1.9.2 STUDY RECORDS RETENTION

Study documents will be retained until all study related activities and analyses are completed and the study is closed with the local IRB. After the study is completed, the de-identified, archived data will be transmitted to and stored at Open Science Framework (*www.osf.io*) for use by other researchers including those outside of the study.

10.1.10 PROTOCOL DEVIATIONS

N/A

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 1 years after the completion of the primary endpoint. The de-identified data will be made available to researchers who enter into a data sharing agreement. Data will be transmitted from the PI to external researchers via WUSTLBox, which is Washington University's dedicated HIPAA-compliant large file sharing program.

10.1.12 CONFLICT OF INTEREST POLICY

The study leadership has established policies and procedures for all study group members to disclose any conflicts of interest and will establish a mechanism for the management of all reported dualities of interest if any arise.

10.2 ADDITIONAL CONSIDERATIONS

N/A

10.3 ABBREVIATIONS AND SPECIAL TERMS

AE	Adverse Event
CFR	Code of Federal Regulations
CONSORT	Consolidated Standards of Reporting Trials
DSMB	Data Safety Monitoring Board
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
ICH	International Council on Harmonisation
IRB	Institutional Review Board
NIH	National Institutes of Health
NIH IC	NIH Institute or Center
OHRP	Office for Human Research Protections
PI	Principal Investigator
SAP	Statistical Analysis Plan
US	United States

10.4 PROTOCOL AMENDMENT HISTORY

*The table below is intended to capture changes of IRB-approved versions of the protocol, including a description of the change and rationale. A **Summary of Changes** table for the current amendment is located in the **Protocol Title Page**.*

Version	Date	Description of Change	Brief Rationale

11 REFERENCES

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