NIH Collaboratory Ethics and Regulatory Core: Initial Consultation
Population Health Management Approaches to Increase Lung Cancer Screening in Community Health Centers (LungSMART)
March 19, 2025; 4:00-5:00 pm ET (via Zoom)

Attendees:

- Core, Coordinating Center, and NIH: Joe Ali (Johns Hopkins University), Luke Gelinas (Advarra), David Magnus (Stanford University), Kayla Mehl (Johns Hopkins University), Stephanie Morain (Johns Hopkins University), Pearl O'Rourke (retired), Tammy Reece (Duke University), Damon Seils (Duke University), Jeremy Sugarman (Johns Hopkins University)
- Study team: Guilherme Del Fiol (University of Utah)

AGENDA ITEMS	DISCUSSION	ACTION ITEMS	OWNER
Overview of the trial	Meeting attendees received the project's data management and resource sharing plan and data and safety monitoring plan with the agenda (see supplementary material attached). Jeremy Sugarman facilitated introductions and described the purpose of the consultation. Co–principal investigator Guilherme Del Fiol represented the LungSMART team. Co–principal investigators David Wetter and Kensaku Kawamoto did not join. **Project overview**: Guilherme gave an overview of the project, which is supported by the National Cancer Institute through a UG3/UH3 award mechanism. The goal of LungSMART is to increase the uptake of US Preventive Services Task Force–recommended lung cancer screening among patients in federally qualified health centers in Utah. **Research team**: University of Utah. **Healthcare system partners**: Community health centers in Utah and the Association for Utah Community Health. **NIH Institute Providing Support/Oversight**: National Cancer Institute.		

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	Study design: The study team plans to conduct a 2-phase trial with a sequential multiple assignment randomized trial (SMART) design. The study population will be identified through automated cohort selection algorithms in the electronic health record and will include all patients aged 50 to 80 years who are smokers or former smokers and who had a visit to a participating community health center in the previous 3 years. Identified patients will receive information about the trial by mail and email. The aim of phase 1 of the trial is to increase patients' completion of an eligibility assessment for lung cancer screening. The interventions to be compared in phase 1 include: 1A. Repeated text messages notifying the patient that they may be eligible for lung cancer screening, asking 2 validated eligibility screening questions, and offering a response option that allows the patient to opt out of the study. Depending on the responses to the eligibility screening questions, the patient will be notified that a registered nurse will call to talk about lung cancer screening. 1B. Intervention 1A plus a scripted, interactive chatbot that addresses commonly asked questions about lung cancer screening. 1C. Intervention 1A plus an educational video about lung cancer screening. 1D. Interventions 1A, 1B, and 1C combined. David Magnus asked why the study team chose not to use generative artificial intelligence for the chatbot. Guilherme replied that, although the study team has been testing an interactive feature based on a large language model, it is premature to release this feature without more development and better safeguards. The aim of phase 2 of the trial is to increase the completion of lung cancer screening by patients who completed the eligibility assessment in phase 1 and were referred for screening. Patients in phase 2 of the trial will receive repeated text messages plus an interactive chatbot that addresses general questions about lung cancer screening, and patient navigation by a community health worker that includes phone calls that address hesitancy and barriers and provide logistics for completing the screening appointment. All patients in phase 2 will be randomly assigned to 1 of 2 modes of engagement for patient navigation: (2A) reactive patient navigation provided upon request by the patient,		

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	or (2B) proactive patient navigation in which a community health worker calls every patient unless the patient requests not to be called. Every text message will include a reply option to opt out of the study. **Outcomes**: The primary outcome for phase 1 is completed eligibility assessments for lung cancer screening among randomized patients. The primary outcome for phase 2 is completed lung cancer screening among patients randomized into phase 2. **Discussion**: Pearl asked whether patients will be informed about potential costs associated with receiving text messages. Guilherme replied that any such costs will depend on the patient's telephone service provider and that the trial materials will inform patients about these potential costs. Jeremy asked about potential challenges with cell phone signals, especially in remote areas. Guilherme explained that the text messaging software being used in the study will give an error message when a text message cannot be delivered. To address instances of patients changing cell phones, the software platform will ping patients' phones to confirm they are still active. Joe asked about patients who share phones with other people. Guilherme described that the text messages will begin with the patient's name to indicate who the message is intended for. In addition, Guilherme explained the study team's procedure for identifying and either excluding patients with duplicate phone numbers or using alternative phone numbers. Guilherme offered to share a paper the study team is writing about their phone validation algorithm. In response to a question from Jeremy about the aggregate patient burden associated with receiving text messages from multiple screening initiatives, Guilherme noted that the community health centers share this concern and that the study team takes steps to minimize messages, spread out their timing, and in some cases exclude patients who are participating in other studies. The study team also only pursues projects the community health centers themselves have expressed interest in partnering in. Jeremy asked about cultural differences in hesitation around the word "cancer." Guilherme responded that a member of the study team is leading all message		

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	development and user-centered design, which includes cultural adaptation and testing. They also completed a large message testing study that compared multiple versions of questions with attention to understandability and preferences.		
Status of IRB approval	The study team received IRB approval for their work on user-centered design in the UG3 planning phase of the project. The trial planned for the UH3 implementation phase of the project is currently under IRB review. The University of Utah is the single IRB of record.		
Risk (Does the project meet regulatory criteria for being considered minimal risk?); and consent (planned processes for relevant subjects)	The study team anticipates that the trial will meet the criteria for being considered minimal risk with a waiver of informed consent. Potential participants will be informed about the trial and will have an up-front opportunity to opt out. **Discussion**: Given that the study team plans to use an opt-out strategy, Pearl asked how they will know whether patients have read the trial materials. Guilherme agreed they will not know. Jeremy asked about opt-out rates in other studies that have used this approach. Guilherme replied that the opt-out rate in an ongoing smoking cessation trial is very low, in single digits. Joe predicted that the up-front opt-out approach might reduce the rate of subsequent opting out in response to the text messages. Luke Gelinas observed that the study's screening procedure with its opt-out strategy arguably does not constitute a research procedure because it is the standard of care. Jeremy shared the following article reporting on the Core's collaboration with the study team for Nudge, another NIH Collaboratory Trial, to explore patients' reasons for opting out of that trial: • Sandy et al. Leave me out: Patients' characteristics and reasons for opting out of a pragmatic clinical trial involving medication adherence. *Medicine* (Baltimore). 2021 Dec 23;100(51):e28136. PMID: 34941059. https://pubmed.ncbi.nlm.nih.gov/34941059/		
Privacy (including HIPAA)	Concerns about the privacy of communications with patients will be addressed by hosting all digital health infrastructure at the University of Utah's Center for		

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	High Performance Computing, a HIPAA-compliant space designed for this kind of work. A data transfer agreement will govern data exchanges between the community health centers' central data warehouse and the University of Utah.		
Monitoring and oversight	The study will use a data and safety monitoring board. The data and safety monitoring plan is attached as supplementary material.		
Issues beyond this project (regulatory and ethics concerns raised by the project, if any)	None.		

DATA MANAGEMENT AND SHARING PLAN

1. **Data Type**
   a. **Types and amount of scientific** data **expected to be generated in the project**
   LungSMART Utah will enroll approximately 18,994 participants. Clinical data include demographic information (age, ethnicity, race, and sex/gender), data necessary to determine eligibility for, and expected net benefit from, lung cancer screening (LCS, smoking status, length of smoking, smoking intensity, years since quit for former smokers, co-morbidities, body mass index, family history of lung cancer, history of lung cancer, history of LCS and other chest computer tomography), conduct of shared decision making for LCS and resulting decision (referral for LCS or no referral for LCS), and LCS completion. These data will be captured by electronic health record (EHR) at participating community health centers (CHCs) and obtained from a Population Health Management (PHM) software. LCS eligibility will be determined by PHM software as well as by Decision Precision +, a Clinical Decision Support tool that facilitates Shared Decision Making that will be available at the Centralized Service Hub. Decision Precision + will also be used to capture the patient and provider's shared decision. Intervention data include the number of text messages received by a patient, the number of interactions a patient has with the conversational agent, whether or not a patient uses a link to connect to centralized assessment for LCS eligibility, number of call attempts made by a community health worker to a patient, and whether or not a patient answered the community health worker's proactive phone call. Data relating to text messages and conversational agent will be recorded in a detailed computerized log. Data relating to phone calls will be captured by REDCap.

   b. **Scientific data that will be preserved and shared, and the rationale for doing so**
   All clinical and intervention data will be preserved and shared.

   c. **Metadata, other relevant data, and associated documentation**
   The study protocol, participant flow table, data dictionary, outcome measure table will be made accessible in data repositories where data are shared.

2. **Related Tools, Software and/or Code**
   Raw data will primarily be housed in a relational database (MariaDB). The analytical dataset(s) will be prepared by a combination of SQL and R. The data will be stored in a few metadata-enabled formats, such that the data and metadata are accessible via R, SAS, STATA, Python, Excel, etc. The data pipeline creating the analytical dataset will be stored in a publicly available git repository on GitHub and for R, the environment and package versions will be stored within there.

3. **Standards**
   To facilitate data sharing and interoperability, LungSMART Utah will use standard processing and documentation developed and adopted by the Inter-university Consortium for Political and Social Research (ICPSR) for data collection, format, archive, and exchange. Further, the Decision Precision+ software uses the Health Level Seven International (HL7) Fast Healthcare Interoperability Resources (FHIR) and Substitutable Medical Applications Reusable Technologies (SMART) interoperability standards.

4. **Data Preservation, Access, and Associated Timelines**
   a. **Repository where scientific data and metadata will be archived**
   ICPSR and Clinicaltrials.gov

   b. **How scientific data will be findable and identifiable**
   Datasets in ICPSR and Clinicaltrials.gov will be findable and identifiable through separate study digital object identifiers (DOI) created, respectively, by ICPSR and Clinicaltrials.gov.

   c. **When and how long the scientific data will be made available**
   Study data will be released approximately 12 months after the last participant has completed all study procedures. Data will be available to the public in perpetuity.

5. **Access, Distribution, or Reuse Considerations**

a. **Factors affecting subsequent access, distribution, or reuse of scientific data**
No additional limitations other than privacy protection described below.

b. **Whether access to scientific data will be controlled**
All study data will be made available for the research community. There will be no controlled or restricted access for study data.

c. **Protections for privacy, rights, and confidentiality of human research participants**
Privacy and confidentiality protections consistent with applicable federal, Tribal, state, and local laws, regulations, and policies will be followed. The privacy, rights, and confidentiality of study participants will be protected through the removal of all 18 HIPAA identifiers prior to sharing. Only deidentified data will be shared in data repositories.

6. **Oversight of Data Management and Sharing:**
Monitoring of and compliance with this Data Management and Sharing Plan will be the responsibility of the project's Multiple Principal Investigators (MPIs). The plan will be implemented and managed by professional staff working under the direction of the MPIs.

DATA AND SAFETY MONITORING PLAN

We have developed a data and safety monitoring plan for LungSMART Utah that is commensurate with the risks it poses to participants. Because LungSMART Utah meets criteria for being a Phase III clinical trial, a Data and Safety Monitoring Board (DSMB) will be established and will meet bi-annually during the study to permit close monitoring of all data and safety concerns.

The interventions used in LungSMART Utah (text messaging, conversational agent, and patient navigation) pose no or minimal risks to participants' safety. It is unlikely that these interventions will cause adverse events (AEs; an undesirable experience associated with the use of a medicine) or serious adverse events (SAEs; adverse events that cause disability, are life-threatening, result in hospitalization or death). As such, this data and safety monitoring plan will focus on procedures that protect the privacy of participants and safeguard data integrity. The plan includes procedures for:

a. Monitoring the progress of the study,
b. Assuring data accuracy and protocol compliance, and
c. Protecting the confidentiality of participant data.

Data privacy and integrity will be regularly (monthly) monitored by study staff, and be reviewed by the DSMB bi-annually. Because of the low risk involved with this study, we are not proposing any interim analyses or stopping rules. We do not expect that the interventions used in LungSMART Utah will cause AEs or SAEs. In rare circumstances when participants report AEs or SAEs that are deemed to be related to the trial, we will following the procedures set out by University of Utah's Institutional Review Board (IRB) to report and manage the events.

1. Data Management Plan

The data collected during the study include participants' age, ethnicity, race, and sex/gender, smoking status, length of smoking, smoking intensity, years since quit for former smokers, co-morbidities, body mass index, family history of lung cancer, history of lung cancer, history of LCS and other chest computed tomography (CT), conduct of shared decision making for LCS and resulting decision (referral for LCS or no referral for LCS), LCS completion, the number of text messages received by a patient, the number of interactions a patient has with the conversational agent, whether or not a patient uses a link to connect to centralized assessment for LCS eligibility, number of call attempts made by a community health worker to a patient, and whether or not a patient answered the community health worker's proactive phone call. These data will be transferred to the study team, and will be stored at an encrypted, secure, and HIPAA-compliant server managed by University of Utah and be processed there.

Data sets will always move in and out of this server under control of an IRB trained data manager (who also acts as server system administrator), never among investigators directly. Data can be checked out by an investigator, and results, even intermediate ones, will be checked back in to the same server for use by other investigators. In this way, the data sets can be tracked, versioned, and managed to maintain control of the data and results obtained from data can always be linked to the original raw data.

Data set transfers among investigators/institutions will be done using either secure file transfer protocol or physical transport of encrypted media. Those granted access will receive user accounts with robust passwords that are valid only temporarily (no more than 1-week for any password) and then destroyed. The authorized user is notified via secured e-mail of the window during which they may upload or download data. The server is accessible over the network only during the agreed upon blocks of time, for accounts authorized for this block of time. The server is not accessible over the network, otherwise, to keep it secure.

The data manager will design a data-management protocol to ensure data is properly recorded, organized, archived offsite, and managed to ensure data security, integrity and availability. Data formats and exchange protocols for moving data between investigators/institutions will be established. Each investigator will be responsible for acquiring the software used for their data processing and analysis, whether it is custom written, open source, or commercial products. Best security and IRB practices will be followed throughout the study. At the end of the study, all data will be archived for 7 years according to NIH policies. Please see Data Management and Sharing Plan for public sharing of data.

2. Data Management Principles

The data management principles that will generally guide and inform the handling of all study data are:

a. "Data" refer to participants' age, ethnicity, race, and sex/gender, smoking status, length of smoking, smoking intensity, years since quit for former smokers, co-morbidities, body mass index, family history of lung cancer, history of lung cancer, history of LCS and other chest computed tomography (CT), conduct of shared decision making for LCS and resulting decision (referral for LCS or no referral for LCS), LCS completion, the number of text messages received by a patient, the number of interactions a patient has with the conversational agent, whether or not a patient uses a link to connect to centralized assessment for LCS eligibility, number of call attempts made by a community health worker to a patient, whether or not a patient answered the community health worker's proactive phone call, and all data sets derived from them.
b. These data need to be centrally stored, organized, and archived to ensure ongoing availability to the team, and to comply with sponsor requirements for archiving or sharing.
c. All team members have full access to the data in support of their research.
d. Team members may request remote access to the server, for high-performance processing.
e. Team members may request export of data copies, for local use.
f. All data usage is governed by appropriate, IRB-approved data safety protocols.
g. All data is de-identified.
h. Exported data must be encrypted during transport, and possibly anonymized.
i. All data-storing machines will limit access to team members only.
j. Physical media used for data transport will be securely erased after use.
k. Data transfers are managed by a data manager who supplies version numbers to track what version of the data is transferred and who receives it. The data manager also checks in and supplies version numbers for all new and derived data.
l. At study end all data will be archived according to NIH policies. Physical media used for data storage and not intended for long term archive will be erased.

3. Data Safety

Clinical data will be transferred to and stored at the University of Utah. We will use the University of Utah telecommunication services' HIPAA-compliant text messaging system to generate and send the messages. The system is secure, HIPAA-compliant, and used routinely by the University of Utah Health to send health appointment reminders to its patients.

Procedures to protect human subjects include: 1) study participation will be confidential, 2) participants will not be identified in any public reports or documents, and 3) data collected will be obtained and stored following HIPAA regulations and guidelines, and 4) data collected is stored in encrypted format on secure server. This server is in a protected facility monitored physically as well as virtually via secure alphanumeric login passwords. In total, we expect these procedures to be highly effective for protecting participant privacy.

4. Data Access and Data Transfer

Secure network transfer methods will be used to move data. All data access will be approved by the Multiple Principal Investigators (MPIs) and managed by the data manager. Data set releases will be versioned and tracked by a data manager, who checks in new data sets and documents which data sets have been released to which groups.

5. Data Archiving and Backup

All data versioning, data security, data storage, site security, and data transfer is managed by the data manager. The main server storage array will be the central data repository and all remote workstations will periodically transfer (physically or via secure network connection) working data sets and final processed data to the main server. In this way when the main server is backed up all the supporting data is also backed up.

6. Data and Safety Monitoring Board (DSMB)

We will establish a data and safety monitoring board (DSMB) for this study commensurate with the level of risk, size, and complexity of the project to ensure the safety of participants as well as the validity and

integrity of the data collected in the project.

Composition of the DSMB

The role of DSMB for this proposed project will be assumed by the established Huntsman Cancer Institute Data Safety and Monitoring Committee (DSMC). Members of the DSMC have appropriate expertise in disciplines relevant to the conduct of this study, are not involved in the study, and have no conflict of interest or economic interest in the results of the study. The DSCM currently serves as a DSMB for a similar, pragmatic clinical trial (QuitSMART Utah).

Frequency and Character of DSMB Meetings

We propose to hold DSMB meetings on a bi-annual basis during the UH3 phase the project. Meetings will be conducted by face-to-face meeting or conference call. Each meeting will begin with an open session that may be attended by research team members, and stakeholder/participant representatives as non-voting members. The open session will review study procedures, plans for data and safety monitoring, recruitment and retention, gender and minority inclusion, protocol adherence, data management, the occurrence of any adverse events. The open session will be followed by a closed session that will be attended by only the DSMB members unless the members deem it appropriate to invite research team staff to the closed session. The closed session will be used to discuss data to which the investigators must remain masked.

Principles for Conduct of DSMB

The following principles are proposed as essential elements for all DSMB meetings. These principles will be reviewed and approved by the DSMB at the first meeting:

a. DSMB members are independent of influence from any interested party including research team members and project sponsor staff.
b DSMB's role is to protect the interests of research participants and ensure they are not exposed to undue risk.
c. DSMB will have access to unmasked data if necessary to protect the interests of research participants
d. DSMB members will be the only individuals who may access unmasked data except other individuals identified by the DSMB at the outset of the project.
e. The Research Team will provide the DSMB with any external evidence requested including publications and study protocols.
f. Minutes of all DSMB meetings will be taken. Minutes will include a summary of the discussion, any recommendations and reporting requirements for the investigators related to recommendations made.
g. DSMB members will provide annual conflict of interest disclosures.

Content of DSMB Meeting Reports

The DSMB report from each meeting will review the topics discussed at the meeting with respect to study procedures, accrual and retention, data management, etc. The DSMB report will include a recommendation concerning continuation of the study.

It is unlikely that the interventions used in the proposed project will cause AEs or SAEs. Nevertheless, should any adverse events occur, they will be detailed in the DSMB report using the following definitions from the University of Utah:

a. SAEs: any adverse experience occurring during the course of the study that results in death, is life threatening, requires or prolongs hospitalization, results in persistent/significant disability or incapacity, or results in congenital anomaly or birth defect.
b. Unanticipated Problem: any incident, experience or outcome that meets all of the following criteria:
    i. Unforeseen (not expected by the researcher or the research participant) given the research procedures and the subject population being studied;
    ii. Related or probably related to participation in the research or if the event or problem probably or definitely affects the safety, rights and welfare of current participants; and
    iii. Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic or social harm) than was previously known or recognized
c. Expected AEs: any adverse experience, the specificity and severity of which is consistent with the current standard of care.

Each DSMB report will provide a tally of all AEs in each of the categories listed above in treatment groups. Masking of AE results will be maintained and will be broken only if the DSMB indicates a need to unblind groups for serious safety reasons. DSMB reports will be submitted to the MPIs and the University of Utah IRB. Any serious unanticipated problems or serious adverse events will be reported to the MPIs and the University of Utah IRB promptly after identification, no later than 10 days.