Document Coversheet

Study Title: Kentucky Communities and Researchers Engaging to Halt the Opioid Epidemic (CARE2HOPE) - UH3 PHASE

Institution/Site:	University of Kentucky
Document (Approval/Update) Date:	IRB 9/25/23
NCT Number:	NCT04134767
IRB Number	52439
Coversheet created:	10/26/23

PROTOCOL TYPE (VERSION 4)

0 u
co

IRB Approval
9/25/2023
IRB # 52439
IRB2

Which IRB

Medical NonMedical

Protocol Process Type

Exemption
Expedited (Must be risk level 1)
Full

IMPORTANT NOTE: You will not be able to change your selections for "Which IRB" and "Protocol Process Type" after saving this section. If you select the wrong IRB or Protocol Process Type, you may need to create a new application.

See below for guidance on these options, or refer to ORI's "Getting Started" page. Please contact the Office of Research Integrity (ORI) at 859-257-9428 with any questions prior to saving your selections.

Which IRB

The **Medical IRB** reviews research from the Colleges of:

- Dentistry
- Health Sciences
- Medicine
- Nursing
- Pharmacy and Health Sciences
- and Public Health.

The **Nonmedical IRB** reviews research from the Colleges of:

- Agriculture
- Arts and Sciences
- Business and Economics
- Communication and Information
- Design; Education
- Fine Arts
- Law
- and Social Work

Note: Studies that involve administration of drugs, testing safety or effectiveness of medical devices, or invasive medical procedures must be reviewed by the **Medical IRB** regardless of the college from which the application originates.

Which Protocol Process Type

Under federal regulations, the IRB can process an application to conduct research involving human subjects in one of three ways:

- by exemption certification
- by expedited review.
- by full review;

The investigator makes the preliminary determination of the type of review for which a study is eligible. Please refer to ORI's "Getting Started" page for more information about which activities are eligible for each type of review.

The revised Common Rule expanded exemption certification category 4 for certain secondary research with identifiable information or biospecimens. The regulations no longer require the information or biospecimens to be existing. For more information see the Exemption Categories Tool.

EXPEDITED CERTIFICATION

0 unresolved comment(s)

To Be Completed Only If Protocol is to Receive Expedited Review

Applicability

A. Research activities that (1) present no more than *minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories, may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.
B. The categories in this list apply regardless of the age of subjects, except as noted.
C. The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.
D. The expedited review procedure may not be used for classified research involving human subjects.
E. IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review—expedited or convened—utilized by the IRB.

**"Minimal risk" means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves from those ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests. 45 CFR 46.102(i)*

Check the appropriate categories that apply to your research project:

☑ Study was originally approved by the full IRB at a convened meeting.

☐ 1) Clinical studies of drugs and medical devices only when condition (a) or (b) is met.

A. Research on drugs for which an investigational new drug application is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)
B. Research on medical devices for which (i) an investigational device exemption application is not required*; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.**

* Study must meet one of the IDE Exempt categories listed on the Device Form Attachment.
** An approved Device used in research according to its approved labeling is considered Exempt from IDE requirements.
NOTE: Select Category 1 for compassionate use medical device applications or individual patient expanded access investigational drug applications for which FDA has waived the requirement for full review.

☐ 2) Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

A. From healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
B. From other adults and children* considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

NOTE: Intravenous (IV), Port, Central, or any other lines are NOT eligible under this category even if the research involves "minimal risk".

*In Kentucky, "child/children" refers to all individuals less than 18 years of age unless the individual(s) is/are legally emancipated. (See Informed Consent SOP for discussion of "Emancipated Individuals" under Kentucky state law.) Individuals less than 18 years of age who are not emancipated meet the federal definition for "child" (e.g., DHHS, FDA, and U.S. Department of Education). Children are defined in the HHS regulations as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted." If conducting research outside the state of Kentucky, you are responsible for complying with applicable state law.

☐ 3) Prospective collection of biological specimens for research purposes by noninvasive means. Examples:

A. Hair and nail clippings in a nondisfiguring manner;
B. Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction;
C. Permanent teeth if routine patient care indicates a need for extraction;
D. Excreta and external secretions (including sweat);
E. Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue;
F. placenta removed at delivery;
G. Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;
H. Supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques;
I. Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;
J. Sputum collected after saline mist nebulization.

☐ 4) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples:

A. Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy;
B. Weighing or testing sensory acuity;
C. Magnetic resonance imaging;
D. electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography;
E. moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

☐ 5) Research involving materials (data, documents, records, or specimens) that have been or will be collected solely for non-research purposes (such as medical treatment or diagnosis) as well as research involving existing information or specimens that were previously collected for research purposes, provided they were not collected for the currently proposed research. (Note: Some research in this category may qualify for Exempt review. This listing refers only to research that is not exempt.)
(Note: If submission includes materials previously collected for either non-research or research purposes in a protocol for which IRB approval expired, you may check Category 5. However, a separate category must also be selected for prospective collection of data/specimens obtained solely for research purposes)

☐ 6) Collection of data from voice, video, digital, or image recordings made for research purposes.

☐ 7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (Note: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. This listing refers only to research that is not exempt.)

52439

PROJECT INFORMATION

0 unresolved comment(s)

Title of Project: (Use the exact title listed in the grant/contract application, if applicable).
If your research investigates any aspect of COVID-19, please include "COVID19" at the beginning of your Project Title and Short Title

COVID19 Kentucky Communities and Researchers Engaging to Halt the Opioid Epidemic (CARE2HOPE) - UH3 PHASE

Short Title Description
Please use a few key words to easily identify your study - this text will be displayed in the Dashboard listing for your study.

COVID19 CARE2HOPE UH3

Anticipated Ending Date of Research Project: 7/31/2024

Maximum number of human subjects (or records/specimens to be reviewed) 1043

After approval, will the study be open to enrollment of new subjects or new data/specimen collection? (•) Yes ( ) No

RISK LEVEL

0 unresolved comment(s)

Indicate which of the categories listed below accurately describes this protocol

- (Risk Level 1) Not greater than minimal risk
- (Risk Level 2) Greater than minimal risk, but presenting the prospect of direct benefit to individual subjects
- (Risk Level 3) Greater than minimal risk, no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition.
- (Risk Level 4) Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of subjects.

*"Minimal risk" means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves from those ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests.

*****For Expedited and Exempt Applications, the research activities must be Risk Level 1 (no more than minimal risk to human subjects).*****

Refer to UK's guidance document on assessing the research risk for additional information.

SUBJECT DEMOGRAPHICS **0 unresolved comment(s)**

Age level of human subjects: (i.e., 6 mths.; 2yrs., etc..) 18 to 99

Study Population:

Describe the characteristics of the subject population, including age range, gender, ethnic background and health status. Identify the criteria for inclusion and exclusion.

Provide the following information:

- A description of the subject selection criteria and rationale for selection in terms of the scientific objectives and proposed study design;
- A compelling rationale for proposed exclusion of any sex/gender or racial/ethnic group;
- Justification for the inclusion of vulnerable groups such as children, prisoners, adults with impaired consent capacity, or others who may be vulnerable to coercion or undue influence.

Please consider these resources:
NIH Diversity Policy
FDA Diversity Guidance

CARE2HOPE covers the following counties: Rowan, Bath, Morgan, Menifee, Elliott, Lee, Owsley, Wolfe, Perry, Letcher, Leslie, Knott. We will recruit participants at all seven jails serving the 12 CARE2HOPE counties; these jails are either located in our CARE2HOPE counties (N=5; Rowan, Lee, Perry, Leslie, Letcher), or our counties have contracts with them to incarcerate their residents (N=2; Montgomery, Clark). To be eligible to take part in Project START-C2H, an individual must:

EITHER:
(1) be a participant in the CARE2HOPE longitudinal survey (IRB Protocol #43520) who consented to be contacted for future research; and
(2) be a resident of or anticipate being released to one of the 12 CARE2HOPE counties randomized to intervention or control data collection; and
(3) be incarcerated in a local jail and expected to be released in <21 days;
OR:
(1) Be a resident of or anticipate being released to one of the 12 CARE2HOPE counties randomized to intervention or control data collection
(2) Have used opioids to get high in the 30 days before they were incarcerated, or have injected any drug to get high during that period;
(3) Be aged 18 or older
(4) be incarcerated in a local jail and expected to be released in <21 days

We have the opportunity to offer the intervention to individuals enrolled in the comparison counties who have completed 3-month surveys, and feel that offering them this intervention is an ethical best practice. We are not proposing any additional quantitative data collection with them, but these individuals will be eligible for qualitative interviews as part of our continuous quality improvement component.

Exclusion criteria are: (1) not speaking English fluently; (2) residence in or move to a county not randomized to intervention or control data collection within 21 days of release; (3) transfer to prison; (4) having ever been convicted of or currently being charged with a violent crime (e.g., homicide, murder, rape and sexual assault, robbery, and/or felony assault); and (5) having been incarcerated for one year or more.

We anticipate that we will recruit 1200 individuals into the study (600 in the comparison group and 600 in the intervention group). The vast majority will be non-Hispanic White, aligned with the racial/ethnic composition of the area; slightly more than half will be men.

COVID-19 Policies
We are expanding the eligibility criteria to include individuals in community settings who report recent criminal justice involvement. To be eligible to take part in Project START-C2H, an individual must:
(1) Be aged 18 or older; and
(2) A resident of one of the 12 CARE2HOPE counties randomized to intervention or control data collection; and
(3) Have used opioids or have injected any drug to get high during the past 30 days (if incarcerated, on an ankle monitoring home incarceration program, out on bond, under warrant for arrest, arrested, court-involved, on pre-trial supervision, probation or parole, or enrolled in a substance use disorder treatment program, eligible if injected drugs or used opioids to get high in the 30 days before this particular involvement with the criminal justice system or substance use disorder treatment program),); and
(4) Have been recently involved in the criminal justice system defined as being incarcerated in jail or prison, out on bond, under warrant for arrest, arrested, under pre-trial supervision, on probation or parole, court-involved, or incarcerated at home under an electronic monitoring program (i.e., digital jail) in the past 30 days.

CQI
We will involve three groups of participants for CQI:
a) Pharmacists. Inclusion criteria: pharmacists from CARE2HOPE counties trained by the program on Vivitrol dispensing (one pharmacist per county, N=12). Exclusion criteria: none
b) Study staff – Rural Health Navigators (REHNs). Inclusion criteria: program staff delivering the intervention to the participants (N=6). Exclusion criteria: none.
c) Current START-C2H participants. Inclusion criteria: 1) being a START-C2H trial participant; and 2) participation in at least two START-C2H health linkage intervention sessions. Exclusion criteria: None.
(Note: REHNs are referred to as Re-Entry Health Navigators for our jail-based activities and Rural Health Navigators for our community-based activities.)

Attachments

Indicate the targeted/planned enrollment of the following members of minority groups and their subpopulations. Possible demographic sources: Census Regional Analyst Edition, Kentucky Race/Ethnic Table, Kentucky Population Data.
(Please note: The IRB will expect this information to be reported at Continuation Review time for Pre-2019 FDA-regulated Expedited review and Full review applications):

Participant Demographics

	Cisgender Man	Cisgender Woman	TGNB/TGE	Unknown/Not Reported
American Indian/Alaskan Native:	9	8		
Asian:	0	0		
Black/African American:	21	22		
Latinx:	6	6		
Native Hawaiian/Pacific Islander:	0	0		
White:	492	457		
American Arab/Middle Eastern/North African:				
Indigenous People Around the World:				
More than One Race:				
Unknown or Not Reported:	2	2		

If unknown, please explain why:

Indicate the categories of subjects and controls to be included in the study. You may be required to complete additional forms depending on the subject categories which apply to your research. If the study does not involve direct intervention or direct interaction with subjects, (e.g., record-review research, outcomes registries), do not check populations which the research does not specifically target. For example: a large record review of a diverse population may incidentally include a prisoner or an international citizen, but you should not check those categories if the focus of the study has nothing to do with that status.

Check All That Apply (at least one item must be selected)

- ☐ Children (individuals under age 18)
- ☐ Wards of the State (Children)
- ☐ Emancipated Minors
- ☐ Students
- ☐ College of Medicine Students
- ☐ UK Medical Center Residents or House Officers
- ☐ Impaired Consent Capacity Adults
- ☐ Pregnant Women/Neonates/Fetal Material
- ☑ Prisoners
- ☐ Non-English Speaking (translated long or short form)
- ☐ International Citizens
- ☑ Normal Volunteers
- ☐ Military Personnel and/or DoD Civilian Employees
- ☐ Patients
- ☑ Appalachian Population

ADDITIONAL INFORMATION:

Please visit the IRB Survival Handbook for more information on:

- Children/Emancipated Minors
- Students as Subjects
- Prisoners
- Impaired Consent Capacity Adults
- Economically or Educationally Disadvantaged Persons

Other Resources:

- UKMC Residents or House Officers [see requirement of GME]
- Non-English Speaking [see also the E-IRB Research Description section on this same topic]
- International Citizens [DoD SOP may apply]
- Military Personnel and/or DoD Civilian Employees

Assessment of the potential recruitment of subjects with impaired consent capacity (or likelihood):

☐ Check this box if your study does NOT involve direct intervention or direct interaction with subjects (e.g., record-review research, secondary data analysis). If there is no direct intervention/interaction you will not need to answer the impaired consent capacity questions.

Does this study focus on adult subjects with any conditions that present a high *likelihood* of impaired consent capacity or *fluctuations* in consent capacity? (see examples below)

○ Yes ◉ No

If Yes and you are not filing for exemption certification, go to "Form T", complete the form, and attach it using the button below.

Examples of such conditions include:

- Traumatic brain injury or acquired brain injury
- Severe depressive disorders or Bipolar disorders
- Schizophrenia or other mental disorders that involve serious cognitive disturbances
- Stroke
- Developmental disabilities
- Degenerative dementias
- CNS cancers and other cancers with possible CNS involvement
- Late stage Parkinson's Disease
- Late stage persistent substance dependence
- Ischemic heart disease
- HIV/AIDS
- COPD
- Renal insufficiency
- Diabetes
- Autoimmune or inflammatory disorders
- Chronic non-malignant pain disorders
- Drug effects
- Other acute medical crises

Attachments

PRISONERS

0 unresolved comment(s)

SECTION 1.

For studies involving **prisoners** or people at risk of becoming involuntarily detained during the research (e.g., subjects with substance abuse history), respond to the following items. For information on restrictions and regulatory requirements, see ORI's Research Involving Prisoners web page.

For research involving prisoners, the definition of minimal risk refers to the probability and magnitude of **physical** or **psychological** harm that is normally encountered in the daily lives, or in the routine medical, dental or psychological examination of healthy persons.

Select the category below that best represents your research and explain why your research meets the criteria.

Prisoner Categories

- ○ **Category 1: My research involves the study of possible causes, effects, processes of incarceration, and of criminal behavior.** (Processes of incarceration can be interpreted broadly to include substance abuse research, half-way houses, counseling techniques, criminal behavior, etc.)
- ○ **Category 2: My research involves the study of prisons as institutional structures, or of prisoners as incarcerated persons.** (This category is usually used fairly narrowly – i.e., looking at prisoner diet, conditions of prison, etc.)
- ○ **Category 3: My research involves the study of conditions particularly affecting prisoners as a class.** (This category is rarely used – e.g., vaccine trials, research on hepatitis, social and psychological problems such as alcoholism, drug addiction, sexual assaults. Minimal risk studies should not go under this category.)
- ◉ **Category 4: My research involves the study of practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject.** (Rare for research involving placebo or control groups to fall in this category because of the difficulty in justifying improvement of the health or well-being of the subject being given placebo or in a control group.) Note: Contact the Office of Research Integrity at (859) 257-9428 for more information.
- ○ **Epidemiologic Research Involving Prisoners [See also SECTION 3 below]**

Explain the research practices that will be used in this study and how they are intended to improve the health and well-being of the participants:

The purpose of this study is to test the effectiveness of an intervention to reduce substance use and related harms among people re-entering the community from rural jails and to provide better linkage to services upon re-entry. The study focuses on people re-entering from rural jails because this group is at higher risk for substance use and related harms (particularly overdose) compared to the general population, but often lacks linkage to needed services or encounters barriers to services because of their criminal justice involvement and/or stigma associated with their substance use, incarceration, or other factors. Participants in this study will be incarcerated at the time of enrollment and intervention activities will take place upon their release to the community. This study presents no more than minimal risk for the following reasons: (1) The procedures to be used by this study will involve conventional social science research methods that are routine in studies of this type. The potential risks will be discussed with participants during recruitment contacts and during the informed consent process to assist them in making a voluntary decision as to whether they wish to participate in the study protocol. (2) The core of the protocol has been developed specifically for and field tested among justice-involved populations. Specifically, the intervention is based on a CDC-recognized, evidence-based intervention called START which has been used to reduce risk behavior among people re-entering communities from prison. (3) If participants are interested in participating in the study, they will work with the study staff and jail staff to determine a time and date that is convenient for our staff person to meet them in a confidential room (i.e., the attorney-client room). Once with the participant, our staff will re-review the signed consent form to remind participants of what is involved and to make sure that they do indeed want to participate. If they do not want to participate, the research staff person will cancel the appointment without any consequences to the participant. Once people screen eligible for the study, all study activities will be done in the private attorney-client room at the jail for confidentiality and privacy. (4) Study activities within jails are limited to administering questionnaires and conducting motivational interviewing. We will NOT be conducting urine drug screening or any other form of biologic testing in jails. (5) Although this is an experimental study with an intervention and comparison group, there is no traditional “control” group in which nothing is received. The comparison group in this study will receive overdose education and response training prior to release from jail and a comprehensive printed guide to local community resources. (6) As with any participant in the study, incarcerated participants will have the option to skip any intervention component or question they are not comfortable answering and to stop their survey at any time and still receive their full participant incentive. Incarcerated participants’ incentives for participation will be deposited directly into their commissary. (7) Consent forms emphasize that study participation should be voluntary and that participation in the study will not affect your relationship with any criminal justice, treatment, parole, or other agency that you are or may become involved with. In fact, the consent form states that participants may be removed from the study if staff learn that they are participating because they were pressured to do so by peers or jail staff. Of note, participants in Department of Corrections custody will also be required to complete a Kentucky Department of Corrections Research Consent Form provided to the PI by the Department of Corrections (see

Informed Consent section of eIRB). (8) Staff undergo extensive training to work in corrections settings and with corrections populations in addition to their certification in human subjects research and training in intervention delivery (see Research Protocol for description).

SECTION 2.

When an IRB is reviewing a protocol in which a prisoner will be a subject, the IRB must find and document justification that six additional conditions are met. Describe in the space provided how each condition applies to your research.

NOTE: If your study **only** involves epidemiologic research, you may insert "N/A" in each of the text boxes in this section (Section 2). Your response to Section 3 will determine appropriateness for "N/A" answers here.

Condition 1. Advantages acquired through participation in the research, when compared to the prisoners' current situation, are not so great that they impair their ability to weigh risks.
Describe the possible advantages that can be expected for prisoner participants:

There are potential benefits of the proposed study, but they are not so great that they should impair a participant's ability to adequately weigh risks. All participants will receive screening for risk behavior, overdose education, and a resource guide describing local services available after release which could directly benefit participants. Participants in the intervention group will also receive help connecting with services after release, and HIV and hepatitis C testing and counseling, if they choose. The comprehensiveness of these services do exceed that typically offered to people re-entering communities from jail (hence, its status as an 'intervention'); however, they are not so far outside the scope of typical services to be coercive (i.e. people who leave jail on probation and parole often receive case management assistance from probation/parole officers and/or Community Social Service Clinicians). After release from jail, participants in the intervention group will also receive additional benefits, including overdose-reversing nasal spray naloxone (Narcan) to carry with them in case they encounter someone who overdoses or in case they overdose and a friend can use it to respond, harm reduction supplies like condoms, and HIV and hepatitis C testing and counseling. However, time elapses between when the decision is made to participate in jail and when these benefits occur (i.e., within the first few weeks of re-entry) and the fact that these benefits are not immediate should reduce coercion. Participants will receive $25 for completing the baseline survey (part 1) during the first in-jail session and $10 for completing the baseline survey (part 2) during the second in-jail session ; this is consistent with incentive amounts approved for incarcerated participants in a similar study (IRB protocol #43520) and not significant enough to cause undue coercion. Over the course of participants' 6 months of participation in the study after re-entry into the community, they could receive up to $120 for participation in all study activities. This amount is commensurate with burden and not coercive.

Condition 2. Risks are the same as those that would be accepted by non-prisoners.
Describe the possible risks that can be expected for prisoner participants and justify that they are the same as for non-prisoners:

The risks for participants in this study are not drastically different than those that would be experienced and accepted by people who are not incarcerated. Essentially, the risks involve potential for disclosure of information and psychological distress from answering survey questions about substance use and related harms and from receiving results on HIV and hepatitis C tests (which are done after release from jail). We have processes in place to minimize both risks, including allowing participants to skip questions or parts of the intervention that make them uncomfortable or stop participation in the intervention or the data collection at any time without impact on their incentives, and we have rigorous data security procedures in place in addition to a Federal Certificate of Confidentiality. In meeting with people while they are incarcerated, we will refuse to do the interview unless the facility can provide us with confidential space (i.e., the attorney-client room). If there is a camera in the room, we will turn the computer screen away from the camera so that facility staff cannot see the answers that respondents are entering. A full and detailed description of risks and strategies to minimize risks are presented on the consent form.

Condition 3. Procedures for selection are fair to all prisoners and are immune from intervention by prison authorities in prisons; control subjects must be randomly selected.

a) Describe how prisoners will be selected for participation:

Prisoners are not technically 'selected' for participation. Jail staff will be asked to invite ALL individuals incarcerated in a jail involved in the study who are within 10 days of their anticipated release will be invited to learn more about the study and be invited to be screened for eligibility. Specifically, we will recruit participants in the jail, conduct surveys, and complete the first START-C2H session post-release. Aligned with START protocols and similar to other team members' NIDA-funded studies in this area (IRB Protocol #43727), participant recruitment will occur in jail. Recruitment in the jail

will occur weekly, with one day dedicated to screening and assessment (with a follow-up visit to the jail for completion of assessments, if needed). Each week, a project staff person will visit the jail on a consistent day of the week chosen in collaboration with jail staff (i.e., to avoid court days and other standard events where inmate schedules may preclude participation). Before the staff person's arrival, the jail staff will have invited all inmates who are expected to be released in the next 10 days who are returning to one of the 12 CARE2HOPE counties currently randomized to the intervention or control conditions to attend a group session to learn more about the study. The jail staff's invitation to prospective participants will be in the form of a study handout (attached in Recruitment section of Research Description) that contains language emphasizing that attendance of the session is wholly voluntary and will not affect their probation, parole, or release terms. The handout will instruct the inmate to inform jail staff of their interest in attending the information session.

At the group session, staff will provide a brief overview of the study, including describing the certificate of confidentiality and eligibility screening process. After the overview, participants will have the ability to ask the REHN questions. Following questions, the REHN will distribute paper copies of the screening survey (attached in Research Description) with a cover letter appended describing risks, benefits, and procedures involved in completing the screener (see Informed Consent section). The REHN will read the cover letter, screener instructions, and questions aloud to the group to support low-literate individuals. Individuals who consent will complete the screener. The screening survey will include questions to collect full name and date of birth so that staff can (1) accurately provide compensation on their commissary for completing the screening survey, (2) identify instances in which people complete the screening more than once so that they are not compensated for participation more than once, and (3) so that staff can extend invitations (via jail staff) to those who are eligible to meet with them to learn more about the study, go through the consent process, and complete a study intake.

The REHN will collect the screeners and thank the prospective participants for screening. Those that are eligible will work with the facility staff to determine a time and date that is convenient, and our staff person will meet them in a confidential room (i.e., the attorney-client room). Once with the participant, our staff will re-review the signed consent form to remind participants of what is involved and to make sure that they do indeed want to do their survey. If they do not want to participate, the research staff person will cancel the appointment without any consequences to the participant. Of note, the consent form is followed by a consent quiz to make sure that participants understand the procedures; one of the questions on the consent quiz asks if study participation will affect probation, parole, or release (true/false). If the participant fails the consent quiz, they will not be able to participate.

b) Describe what measures will be taken to prevent intervention by prison authorities in the selection process:

Consistent with IRB protocol #12-0372 and #43520, jail staff may monitor participant entry and exit into the attorney-client or visitation room for the screening and interview process, but no jail staff will be present for the confidential interviews. These rooms have a video camera (but no audio recorder), and staff will be trained to ensure that the participant's back is to the camera.

Condition 4. Parole boards cannot take into consideration a prisoner's participation in research. Informed consent must state participation will not impact parole.
Describe what measures are in place to ensure parole boards are not influenced by prisoners' participation in research and how prisoners will be told their participation (or refusal or withdrawal from) will not impact parole:

Based on our current study, we anticipate that most of our participants will be on probation rather than parole. However, confidentiality issues will be stressed during informed consent and will include the description of a federal Certificate of Confidentiality. Parole boards will not be aware of the participants' participation unless the person discloses it to the board. The informed consent states that participation while incarcerated will not affect probation, parole, or relationships with other agencies. Participants will also be assured that their screening results, study participation, and study data will not be made available to any representative of the jail or criminal justice system. Consent form language reflects this emphasis on participant confidentiality.

Condition 5. For studies that require follow-up, provisions are made including consideration for the length of individual sentences; informed consent must reflect provisions for follow-up.
Describe what provisions have been made for follow-up and how this information will be relayed to the prisoner participants:

After the in-jail sessions, staff will meet with the participant within 10 days of release, check in by phone 1 month and 2 months after release, and meet with them in person again 3 months and 6 months after release. To facilitate follow up, during the one-on-one appointment with study staff in the attorney-client room, participants are asked to complete a detailed locator form and will choose a tentative time and date for the first post-release appointment based on the expected release date. The locator form shown in the Locator Form Appendix (attached to Research Protocol) is identical to the existing locator form approved under IRB protocol (#43520). The form is a strong retention tool tailored to this population. This form collects personal contact information (phone, email, address, etc), queries contact information for the participant and multiple key network members, and seeks consent to contact network members as needed. Our locator form asks participants to indicate whether they give permission for us to contact them via private messenger on social media (i.e., Facebook messenger) and language informing participants about privacy issues surrounding the use of social media. Research staff will monitor jail logs, JailTracker database, Courtnet, and Vinelink to identify when a participant gets released (as we know release dates can vary and change unexpectedly). Staff will contact the participant within the days following their release to schedule the first post-release appointment. At that appointment, staff will update the locator information as it is often the case that addresses, phone numbers, and other details may have changed. In addition to these strategies, staff will offer an appointment business card with the post-release appointment time, date, and location, and staff contact details with the person at the close of the one-on-one jail session. Because the person may be hesitant to take the card or lose the card, staff will also provide the card in a tamper-evident, tape-sealed envelope to jail staff so that they can place it with the individual's personal effects that they receive upon release. The envelope will also contain a printed local resource guide.

Condition 6. Information about the study is presented in a language understandable to prisoners.
Describe what efforts have been made to present information about the study in a language understandable to the prisoner population:

The entire sample for this study is comprised of people who use drugs, some of whom have limited education and low literacy. Therefore, all documents used in the study are written at a reading level accessible to someone with a 6th grade education. The same documents will be used for prisoners. Further, because all study procedures are interviewer-administered, the interviewer is able to read documents out loud, explain any concepts that are confusing, and answer questions that arise.

SECTION 3. Epidemiologic Research Involving Prisoners
Only complete if applicable:

Effective June 20, 2003, DHHS adopted policy that allows waiver of the requirement for documenting applicability of a category (as found in Section 1 of this form) for certain epidemiologic research involving prisoners. This waiver applies to epidemiologic research on prisoners that presents no more than minimal risk and no more than inconvenience to the prisoner-subjects.

☐ Check this box if your research meets all three criteria listed below, then provide justification in the space provided.

1. I request a waiver for meeting the category conditions under Section 1 of this form.
2. My research involves epidemiologic research intended to describe the prevalence/incidence of a disease by identifying all cases, or to study potential risk factor associations for a disease; **and**
3. Prisoners are not the sole focus of my research.

Justify how the research presents no more than minimal risk and no more than inconvenience to the subjects:

SECTION 4. Prisoners are not the targeted population
Only complete if applicable:

Although prisoners may not be the target population for your research, a subject could become a prisoner during the course of the study (particularly if studying a subject population at high-risk of incarceration).

Note: If you did not receive IRB approval for involvement of prisoners, and a subject becomes a prisoner during the study, **all research activities involving the now-incarcerated participant must cease** until IRB approval has been issued for their continuation in the research. If you need IRB approval for a prisoner subject to continue participation in your research, select and complete the applicable category from Section 1, complete section 2 and this section, then submit for IRB review.

In special circumstances where it is in the best interest of the subject to remain in the research study while incarcerated, the IRB Chairperson may determine that the subject may continue to participate in the research prior to satisfying the requirements of Subpart C. However, subsequent IRB review and approval of this completed form is required.

☐ Prisoners are not a target population for my research, but a subject became a prisoner during the study and I am seeking IRB approval so the subject can continue participation in the research.

Explain the importance of continuing to intervene, interact, or collect identifiable private information during the participant's incarceration:

SECTION 5. Kentucky (KY) Department of Corrections (DoC) Approval

Review the following conditions and determine whether any apply to your study:

- active recruitment of participants from a correctional facility (prison, jail, or community corrections institution);
- active recruitment of individuals under community supervision from a state probation and parole office.

If any of the above conditions apply to your research, refer to the Kentucky Department of Corrections Policy and Procedures, Management Information and Research (Chapter 5) for information about submitting a proposal for DoC approval of research including the DoC approved Research Consent and Research Agreement (5.1.G.1).

If your research involves a certificate of confidentiality or the Department of Corrections is directly involved in the study as a sponsor (or otherwise), contact David Kinsella, Legal Counsel, at David.Kinsella@uky.edu, or 859-323-1161, for additional information.

INFORMED CONSENT/ASSENT PROCESS/WAIVER

0 unresolved comment(s)

For creating your informed consent attachment(s), please download the most up-to-date version listed in "All Templates" under the APPLICATION LINKS menu on the left, and edit to match your research project.

Additional Resources:

- Informed Consent/Assent Website
- Waiver of Consent vs. Waiver of Signatures
- Sample Repository/Registry/Bank Consent Template

Consent/Assent Tips:

- If you have multiple consent documents, be sure to upload each individually (not all in a combined file).
- If another site is serving as the IRB for the project, attach the form as a "Reliance Consent Form" so the document will not receive a UK IRB approval stamp; the reviewing IRB will need to stamp the consent forms.
- Changes to consent documents (e.g., informed consent form, assent form, cover letter, etc...) should be reflected in a 'tracked changes' version and uploaded separately with the Document Type "Highlighted Changes".
- It is very important that only the documents you wish to have approved by the IRB are attached; DELETE OUTDATED FILES -- previously *approved* versions will still be available in Protocol History.
- Attachments that are assigned a Document Type to which an IRB approval stamp applies will be considered the version(s) to be used for enrolling subjects once IRB approval has been issued.
  Document Types that do NOT get an IRB approval stamp are:
  - "Highlighted Changes",
  - "Phone Script", and
  - "Reliance Consent Form",
  - "Sponsor's Sample Consent Form".

How to Get the Section Check Mark

1. You must:

   a) provide a response in the text box below describing how investigators will obtain consent/assent, and
   b) check the box for at least one of the consent items and/or check mark one of the waivers

2. If applicable attach each corresponding document(s) **as a read-only PDF**.
3. If you no longer need a consent document approved (e.g., closed to enrollment), or, the consent document submitted does not need a stamp for enrolling subjects (e.g., umbrella study, or sub-study), only select "Stamped Consent Doc(s) Not Needed".
4. After making your selection(s) be sure to scroll to the bottom of this section and SAVE your work!

Check All That Apply

- ☐ Informed Consent Form (and/or Parental Permission Form and/or translated short form)
- ☐ Assent Form
- ☐ Cover Letter (for survey/questionnaire research)
- ☐ Phone Script
- ☐ Informed Consent/HIPAA Combined Form
- ☐ Debriefing and/or Permission to Use Data Form
- ☐ Reliance Consent Form
- ☐ Sponsor's sample consent form for Dept. of Health and Human Services (DHHS)-approved protocol
- ☑ Stamped Consent Doc(s) Not Needed

Attachments

Informed Consent Process:

Using active voice, describe how investigators will obtain consent/assent. Include:

- the circumstances under which consent will be sought and obtained
- the timing of the consent process (including any waiting period between providing information and obtaining consent)

- who will seek consent
- how you will minimize the possibility of coercion or undue influence
- the method used for documenting consent
- if applicable, who is authorized to provide permission or consent on behalf of the subject
- if applicable, specific instruments or techniques to assess and confirm potential subjects' understanding of the information

Note: all individuals authorized to obtain informed consent should be designated as such in the E-IRB "Study Personnel" section of this application.

Special considerations may include:

- Obtaining consent/assent for special populations such as children, prisoners, or people with impaired decisional capacity
- *Research Involving Emancipated Individuals*
  If you plan to enroll some or all prospective subjects as emancipated, consult with UK legal counsel **prior to submitting this application to the IRB**. Include research legal counsel's recommendations in the "Additional Information" section as a separate document.
- *Research Involving Non-English Speaking Subjects*
  For information on inclusion of non-English speaking subjects, or subjects from a foreign culture, see IRB Application Instructions for Recruiting Non-English Speaking Participants or Participants from a Foreign Culture.
- *Research Repositories*
  If the purpose of this submission is to establish a research repository describe the informed consent process. For guidance regarding consent issues, process approaches, and sample language see the Sample Repository/Registry/Bank Consent Template.

The REHN will provide a brief overview of the study and of the certificate of confidentiality. After the overview, participants will have the ability to ask the REHN questions. Before providing the screening surveys to the group, the REHN will then read the Screening Survey Cover Letter (attached in Informed Consent section) aloud, and participants will be given a hard copy. The cover letter will describe the risks and benefits of taking part in the screening, and will note in particular that (1) a certificate of confidentiality protects their data; and (2) their decision about participating has no bearing on their legal status. It will review the contents of the screening form, and the screening's anticipated duration. There will be no screening items capturing information that might require mandated reporting. Individuals will have time to ask the REHN questions about the screening process. Individuals who are interested in being screened can complete the survey and keep a copy of the cover letter. Of note, the KY Department of Corrections does require that all incarcerated individuals complete a general DOC consent form (see DOC Consent Form attached in Informed Consent section) granting permission to participate in research and require that a copy of that consent form be deposited with the KY DOC headquarters. To protect participant confidentiality and avoid revealing to DOC staff who screened eligible and participated, we will administer the DOC consent form to all individuals attending the study overview session, rather than only to those who screen eligible. Therefore, jail officials and administrators who maintain a copy of those forms will not be able to decipher which participants screened eligible, participated, or refused to participate.

Individuals who screen eligible and are interested in learning more about the study will complete a second consent form in a one-on-one session. This session will be held in the Attorney/Client room. Jail staff are not allowed in these rooms during the sessions. Some rooms have video cameras (though none have audiorecorders). The REHN will ensure that the participant is facing away from the camera. The REHN will give a copy of the CARE2HOPE Phase 2 consent form (attached in Informed Consent section) to the participant and will review it aloud, the REHN will ask whether the person has any questions and answer them to the best of his/her ability. The REHN will then administer a brief quiz (see Consent Quiz attached in Additional Materials) about the contents of the consent forms to ensure that the individual is cognitively able to understand study risks at the time; individuals who fail the quiz will not be enrolled in the study.

Individuals who pass the quiz and are interested in taking part in CARE2HOPE will sign the IRB-approved consent form. Regardless of whether they consent, all individuals will be given a copy of the informed consent document. This document describes the study purpose, potential risks, and PIs' and IRBs' contact information for follow up questions. The consent document will also contain a statement informing participants that their name and contact information may be released without their consent to appropriate state authorities in instances that are required by state law (e.g., if they inform study staff that they are wanting to end their life or someone else's life, are abusing a child).

Participants can opt out of taking this full copy (which will discuss drug use, and thus might jeopardize confidentiality) and instead take a sheet that lists PI and IRB contact information. Signed consent forms will be kept in a locked cabinet in a locked office at the UK study field site in Morehead or the office rented in the local health department. Only IRB-approved study personnel will have access to the locked filing cabinets containing consent forms.

As explicitly stated in the consent form, participation is completely voluntary and there are no penalties or prejudice of any kind for not participating in the study. The informed consent will stress the voluntary nature of the study and the ability to withdraw from the study at any point. If the participant agrees to participate in the study, data collection will begin. Non-English speaking persons are not eligible for participation; therefore, the consent will only be in English. Of note, this study is automatically protected by a Federal Certificate of Confidentiality (see https://grants.nih.gov/grants/guide/notice-files/NOT-OD-17-109.html).

Individuals who do not consent will be allowed to leave without penalty.

Participants will not undergo another consent process post-release. However, participants will re-review the consent form with the REHN in the first post-release session, confirm with participants whether they still want to continue and REHNs will offer to provide

another copy of the consent form if the participant wants.

COVID-19 Policies
Jail
Individuals who are recruited in the jail via Zoom or by phone, screen eligible, and are interested in learning more about the study will complete the informed consent process. The REHN will review the consent form aloud with the individual and then answer any questions. The REHN will then administer a brief quiz about the contents of the consent forms to ensure that the individual is able to understand study risks at the time. Individuals who fails the quiz will not be enrolled in the study. Individuals who pass the quiz and are interested in taking part in CARE2HOPE will provide verbal consent, which the REHN will document on the IRB-approved consent form.

Community
The informed consent process for individuals recruited from the community (as well as all other research procedures) will take place in person as COVID restrictions allow. If the participant is not able to visit the study office (or another mutually agreed-upon location) or all research activities are reverted to remote only due to COVID-19 restrictions, informed consent will be completed online over UK Zoom, which is HIPAA compliant, or over the phone. We will check with the person if they are located in a private area where no one can overhear or see documents shared via Zoom or in hardcopies. If the person is not comfortable with the degree of privacy they have, the REHN will reschedule the meeting. The REHN will then administer a brief quiz about the contents of the consent forms to ensure that the individual is able to understand study risks at the time. Individuals who fails the quiz will not be enrolled in the study. A copy of the quiz is attached under research procedures.

CQi
The only research activity related to the CQI component is a one-time interview. We will use cover letters for each category of participants (CARE2HOPE participants, pharmacists and REHNs). These cover letters will include all applicable elements of informed consent, including information on data collection procedures, risks, participants rights and confidentiality measures. We will review these cover letters with the participants at the start of the interview.
Participants are encouraged to call the PI or research staff if any questions arise during the course of the research. Phone numbers for the PI and staff, as well as for the Office of Research Integrity (ORI) are included in the consent form. It is expected that providing contact information of the PIs will offer a safe, confidential, and reliable channel for participants to express problems, concerns or questions.

☐ Request for Waiver of Informed Consent Process

If you are requesting IRB approval to waive the requirement for the informed consent process, or to alter some or all of the elements of informed consent, complete, Section 1 and Section 2 below.

Note: The IRB does not approve waiver or alteration of the consent process for greater than minimal risk research, except for planned emergency/acute care research as provided under FDA regulations. Contact ORI for regulations that apply to single emergency use waiver or acute care research waiver (859-257-9428).

SECTION 1.

Check the appropriate item:

☐ I am requesting a waiver of the requirement for the informed consent process.

☐ I am requesting an alteration of the informed consent process.

If you checked the box for this item, describe which elements of consent will be altered and/or omitted, and justify the alteration.

SECTION 2.

Explain how each condition applies to your research.

a) The research involves no more than minimal risk to the subject.

b) The rights and welfare of subjects will not be adversely affected.

c) The research could not practicably be carried out without the requested waiver or alteration.

d) Whenever possible, the subjects or legally authorized representatives will be provided with additional pertinent information after they have participated in the study.

e) If the research involves using or accessing identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format.

- Private information/specimens are “identifiable” if the investigator may ascertain the identity of the subject or if identifiers are associated with the information (e.g., medical records). This could be any of the 18 HIPAA identifiers including dates of service.
- If not using identifiable private information or identifiable biospecimens, insert N/A below.

☑ Request for Waiver of Signatures

If you are requesting IRB approval to waive the requirement for signatures on informed consent forms, **your research activities must fit into one of three regulatory options**:

1. The only record linking the participant and the research would be the consent document, and the principal risk would be potential harm resulting from a breach of confidentiality (e.g., a study that involves participants who use illegal drugs).
2. The research presents no more than minimal risk to the participant and involves no procedures for which written consent is normally required outside of the research context (e.g., a cover letter on a survey, or a phone script).
3. The participant (or legally authorized representative) is a member of a distinct cultural group or community in which signing forms is not the norm, the research presents no more than minimal risk to the subject, and there is an appropriate alternative mechanism for documenting that informed consent was obtained.

Select the option below that best fits your study.

If the IRB approves a waiver of signatures, participants must still be provided oral or written information about the study. To ensure you include required elements in your consent document, use the ***Cover Letter Template*** *as a guide. There is an English and a Spanish version.*

○ **Option 1**

Describe how your study meets these criteria:

a) The only record linking the participant and the research would be the consent document:

b) The principal risk would be potential harm resulting from a breach of confidentiality (i.e., a study that involves subjects who use illegal drugs).

Under this option, each participant (or legally authorized representative) must be asked whether (s)he wants to sign a consent document; if the participant agrees to sign a consent document, only an IRB approved version should be used.

◉ **Option 2**

Describe how your study meets these criteria:

a) The research presents no more than minimal risk to the participant:

This is a minimal risk study involving an intervention to reduce substance use and related harms among people leaving jails. The intervention and control groups both received overdose education training prior to release and the intervention group meets with a Re-Entry Health Navigator post-release to develop a plan for reducing risks and accessing services.

The Continuous Quality Improvement is a minimal risk activity involving a one-time interview with participants including pharmacists, C2H participants, and REHNs (research study staff).

b) Involves no procedures for which written consent is normally required outside of the research context (i.e. a cover letter on a survey, or a phone script):

Re-Entry Health Navigators meet with potential participants during a group session or individually in the jail, providing an overview of the study and the certificate of confidentiality. Prior to providing the screening form to determine eligibility, the screening cover letter is read aloud and a hard copy is provided. The screening cover letter includes applicable elements of informed consent but does not include any signature lines as individuals who are eligible complete the informed consent process and consent form in a one-on-one session in a private room.

The Continuous Quality Improvement is a minimal risk activity involving a one-time interview with participants. We developed cover letters for each category of participants (CARE2HOPE participants, pharmacists and REHNs). These cover letters include all applicable elements of informed consent, including information on data collection procedures, risks, participants rights and confidentiality measures. We will review these cover letters with the participants at the start of the interview. Because the informed consent process for all participants will take place remotely, over UK Zoom or Facebook Messenger, we are requesting a waiver of documentation of informed consent

○ **Option 3**

Describe how your study meets these criteria:

a) The subject (or legally authorized representative) is a member of a distinct cultural group or community in which signing forms is not the norm.

b) The research presents no more than minimal risk to the subject.

c) There is an appropriate alternative mechanism for documenting that informed consent was obtained.

STUDY PERSONNEL **0 unresolved comment(s)**

Do you have study personnel who will be assisting with the research?
After selecting 'Yes' or 'No' you must click the 'Save Study Personnel Information' button.

Yes No

Manage Study Personnel

Identify other study personnel assisting in research project:

- The individual listed as PI in the 'PI Contact Information' section should NOT be added to this section.
- If the research is required for a University of Kentucky academic program, the faculty advisor is also considered study personnel and should be listed below. ***Residents and students who are PI's are encouraged to designate the faculty advisor or at least one other individual as a contact with an editor role (DP).***
- Role: DP = Editor (individual can view, navigate, and edit the application for any review phase (IR, CR/FR, MR) or 'Other Review", and submit Other Reviews on behalf of the PI.)
- Role: SP = Reader (individual can view and navigate through the currently approved application only.)

To add an individual via the below feature:

- Search for personnel;
- Click "select" by the listing for the person you want to add;
- For each person, specify responsibility in the project, whether authorized to obtain informed consent, AND denote who should receive E-IRB notifications (contact status).

NOTE: Study personnel must complete human subject protection (HSP) and Responsible Conduct of Research (RCR) training before implementing any research procedures. For information about training requirements for study personnel, visit UK's HSP FAQ page, the RCR Getting Started page, or contact ORI at 859-257-9428. If you have documentation of current HSP training other than that acquired through UK CITI, you may submit it to ORI (HSPTrainingSupport@uky.edu) for credit.

Study personnel assisting in research project:

Last Name	First Name	Responsibility In Project	Role	AC	Contact	Degree	StatusFlag	(HSP)	(HSP)Date	(RCR)	Removed?	Last Updated	SFI
Alexander	Rhonda	Data Collection	SP	Y	N		P	Y	05/06/2022	Y	N	07/17/2019	N
Babalonis	Shanna	Co-Investigator	SP	Y	N	PhD	P	Y	02/21/2023	Y	N	07/17/2019	N
Burchett	Anne	Data Analysis/Processing	SP	N	N		P	Y	07/05/2022	Y	N	08/15/2022	N
Cooper	Hannah	Co-Investigator	SP	Y	N	ScD	N	Y	03/03/3000		N	07/17/2019	N
Dschaak	Zachary	Data Analysis/Processing	SP	N	N		P	N	08/10/2020	Y	N	09/03/2020	N
Duff	Madeline	Data Analysis/Processing	SP	N	N		S	Y	06/01/2022	Y	N	08/15/2022	N
Fadanelli	Monica	Project Assistance/Support	SP	N	N		N	Y	03/03/3000		N	08/27/2021	N
Falk	Dylan	Data Analysis/Processing	SP	N	N		N	Y	03/03/3000		N	06/23/2021	N
Feil	Dakotah	Data Analysis/Processing	SP	N	N		N	Y	03/03/3000		N	07/29/2021	N
Freeman	Edward	Project Assistance/Support	SP	N	N		P	Y	06/12/2023	Y	N	06/02/2020	N
Fuller	Grayson	Data Analysis/Processing	SP	N	N		P	Y	03/15/2023	Y	N	09/17/2021	N
Greenwood	Harris	Data Analysis/Processing	SP	N	N		N	Y	03/03/3000		N	06/23/2021	N
Grospitch	Ashley	Data Analysis/Processing	SP	N	N		P	Y	08/25/2023	Y	N	08/15/2022	N
Gugerty	Paige	Data Analysis/Processing	SP	N	N		N	Y	03/03/3000		N	07/29/2021	N
Havens	Jennifer	Co-Investigator	SP	N	N	PhD	P	Y	05/11/2022	Y	N	07/17/2019	N
Holt	Colton	Data Analysis/Processing	SP	N	N		S	Y	08/11/2022	Y	N	08/15/2022	N
Hurlburt	Sarah	Data Collection	SP	Y	N		P	Y	03/05/2021	Y	N	03/05/2021	N
Ibragimov	Umed	Project Assistance/Support	SP	N	N		N	Y	03/03/3000		N	02/21/2020	N
Jahangir	Tasfia	Data Analysis/Processing	SP	N	N		N	Y	03/03/3000		N	05/16/2023	N
Jones-Harrell	Carla	Project Assistance/Support	SP	N	N		N	Y	03/03/3000		N	08/19/2020	N
Kesich	Zora	Data Collection	SP	Y	N		N	Y	03/03/3000		N	02/04/2022	N

Last Name	First Name	Responsibility In Project	Role	AC	Contact	Degree	StatusFlag	(HSP)	(HSP)Date	(RCR)	Removed?	Last Updated	SFI
King	Annelise	Data Analysis/Processing	SP	N	N		S	Y	06/01/2022	Y	N	08/15/2022	N
Kollitz	Julia	Data Analysis/Processing	SP	N	N		S	Y	09/09/2023	Y	N	08/27/2021	N
Komro	Kelli	Co-Investigator	SP	N	N	PhD	N	Y	03/03/3000		N	07/18/2019	N
Lane	Kenneth	Data Collection	SP	Y	N		P	Y	11/04/2022	Y	N	10/24/2019	N
Lawson	Lauren	Data Analysis/Processing	SP	N	N		P	Y	08/19/2023	Y	N	09/17/2021	N
Littleton	Kelsey	Project Assistance/Support	SP	N	N		N	Y	03/03/3000		N	02/04/2021	N
Livingston	Melvin	Data Analysis/Processing	SP	N	N	PhD	N	Y	03/03/3000		N	07/18/2019	N
Lofwall	Michelle	Co-Investigator	SP	Y	N	MD	P	Y	06/29/2023	Y	N	07/17/2019	N
Love Pieczykolan	Lauren	Data Collection	SP	Y	N		N	Y	03/03/3000		N	02/04/2022	N
Maybrier	Lisa	Data Collection	SP	Y	N		P	Y	05/06/2022	Y	N	04/12/2021	N
Oliver	Cindy	Data Collection	SP	Y	N		P	Y	03/02/2022	Y	N	03/03/2022	N
Oser	Carrie	Co-Investigator	SP	Y	N	PhD	P	Y	12/08/2021	Y	N	07/03/2019	N
Peddireddy	Snigdha	Data Analysis/Processing	SP	N	N		N	Y	03/03/3000		N	09/17/2021	N
Plaisance	Karma	Data Analysis/Processing	SP	N	N		N	Y	03/03/3000		N	06/12/2023	N
Rippetoe Freeman	Patricia	Co-Investigator	SP	Y	N		P	Y	11/30/2020	Y	N	07/17/2019	N
Robbins	Sarah Jane	Project Assistance/Support	SP	Y	N		P	Y	11/07/2020	Y	N	10/24/2019	N
Rose	Lana	Data Collection	SP	Y	N		P	Y	12/14/2022	Y	N	10/24/2019	N
Staton	Christa	Co-Investigator	SP	Y	N	PhD	P	Y	05/26/2021	Y	N	07/03/2019	N
Tabor	Joy	Project Assistance/Support	SP	N	N		P	Y	07/12/2021	Y	N	09/25/2023	N
Vickers-Smith	Rachel	Project Assistance/Support	SP	Y	N		P	Y	05/31/2023	Y	N	09/03/2020	N
White	Carol	Study Coordinator	DP	Y	Y	MPH	P	Y	04/27/2023	Y	N	08/19/2019	N
Wilson	Jordan	Data Analysis/Processing	SP	N	N		P	Y	03/18/2021	N	N	09/08/2020	N
Xie	Kevin	Data Analysis/Processing	SP	N	N		P	Y	02/13/2023	Y	N	07/19/2021	N
Cooper	Daniel	Data Analysis/Processing	SP	N	N		P	N	01/09/2019	N	Y	05/26/2021	N
Green	Travis	Data Collection	SP	Y	N		P	N	03/05/2018	N	Y	05/26/2021	N
Hurst	Jennifer	Data Collection	SP	Y	N		P	Y	01/17/2022	Y	Y	04/25/2023	N
Jones	Veronica	Study Coordinator	SP	Y	N		P	Y	02/24/2022	Y	Y	04/25/2023	N
Knipp Conn	Kandi	Data Collection	SP	Y	N		P	Y	05/05/2021	Y	Y	04/25/2023	N
Littleton	Kia	Data Collection	SP	Y	N		P	Y	07/27/2023	Y	Y	04/25/2023	N
Lucas	Ripley	Project Assistance/Support	SP	Y	N		P	N	12/07/2018	N	Y	05/26/2021	N
Mackey	Judy	Data Collection	SP	Y	N		P	Y	01/12/2021	Y	Y	04/25/2023	N
Mansfield	Russell	Data Analysis/Processing	SP	N	N		N	Y	03/03/3000		Y	07/19/2021	N
Mullins	Amanda	Data Collection	SP	Y	N		P	N	02/13/2019		Y	05/26/2021	N
Powell	Phillip	Data Collection	SP	Y	N		P	Y	03/28/2022	Y	Y	04/25/2023	N
Stamper	Roscoe	Data Collection	SP	Y	N		P	N	10/03/2018		Y	05/26/2021	N
Tully	Damien	Data Analysis/Processing	SP	N	N		N	Y	03/03/3000		Y	03/18/2021	N
Vanlandingham	Emily	Data Collection	SP	Y	N		P	N	10/30/2019		Y	05/26/2021	N
VanMeter	Connor	Project Assistance/Support	DP	N	N		P	Y	10/10/2022	Y	Y	05/26/2021	N

Last Name	First Name	Responsibility In Project	Role	AC	Contact	Degree	StatusFlag	(HSP)	(HSP)Date	(RCR)	Removed?	Last Updated	SFI
Vermes	Ellen	Data Analysis/Processing	SP	N	N		N	Y	03/03/3000		Y	05/26/2021	N
Vickers Smith	Rachel	Data Analysis/Processing	SP	N	N		N	N	01/04/2018		Y	05/21/2020	N
Wright	Kasey	Data Collection	SP	Y	N		P	N	10/28/2019		Y	05/26/2021	N

RESEARCH DESCRIPTION

0 unresolved comment(s)

You may attach a sponsor's protocol pages in the "Additional Information" section and refer to them where necessary in the Research Description. However, each prompt that applies to your study should contain at least a summary paragraph.

Pro Tips:

- **Save your work often to avoid losing data.**
- **Use one of the attachment buttons in this section or under the Additional Information section to include supplemental information with your application. During the document upload process, you will be able to provide a brief description of the attachment.**

Background

Include a brief review of existing literature in the area of your research. You should identify gaps in knowledge that should be addressed and explain how your research will address those gaps or contribute to existing knowledge in this area. For interventional research, search PubMed and ClinicalTrials.gov for duplicative ongoing and completed trials with same condition and intervention(s).

The project described in this protocol is the 2nd phase of a 2-phase project, titled CARE2HOPE. The overarching aim of CARE2HOPE is to build evidence-based, community-rooted public health responses to the epidemics of non-medical prescription opioid (NMPO) and heroin injecting, overdoses (ODs), and HCV, and to imminent HIV outbreaks, in 12 rural Appalachian Kentucky counties at the epicenter of these intertwined national crises. The project is biphasic in design, as required by the UG3/UH3 funding structure, with a 2-year assessment phase (UG3) followed by a 3-year intervention phase (UH3) that is informed by results of the assessment. The UG3 phase began in August 2017 and is described in the approved IRB protocol # 43520. Briefly, in the UG3 we were guided by harm reduction principles, the Risk Environment Model, and Community/ Academic Partnerships (CAPs), with study aims to: (1) Assess and enhance each community's readiness to improve the local risk environment. (2) Examine the strengths, resources, needs, and gaps of each community's risk environment. (3) Select one EB-CRP that responds to local needs and strengths, using elements of Intervention Mapping. The UG3 protocol will remain active as some surveys and biologic testing will continue throughout the UH3 phase.

The current IRB protocol #52439 covers the 3-year UH3 phase which begins August 1, 2019. Although both phases are united under a common overarching study purpose, the two phases are submitted as separate IRB protocols because they differ in study design (UG3 phase involved coalition engagement, surveys, and interviews; the UH3 phase involves a community-level randomized trial of a health navigation intervention) and because the addition of the UH3 procedures to the UG3 would make the already complex protocol unwieldy. The decision to submit the phases as separate IRB protocols was made in consultation with IRB staff.

Background and Significance for Project

An "implementation chasm" – defined as gap between advances in scientific knowledge and the application of this knowledge in medical and public health programs -- exists for drug-related health services in most rural areas. A landmark 2015 Kentucky law, however, allowed this largely rural state to start closing this chasm: this law permitted syringe service programs (SSPs) to operate, expanded access to naloxone, and provided Good Samaritan protections. These policy changes have allowed 8 of the 12 counties to open SSPs. Harm reduction interventions, however, have yet to be adequately deployed in these 12 hard-hit counties. Previous and ongoing research by the scientific team reveal that in these counties access and linkage to medications for opioid use disorder (MOUD) are suboptimal; challenges to MOUD dispensing exist; naloxone access is poor, and partnerships among local justice, harm reduction, and SUD treatment programs are virtually nonexistent. High percentages of PWUD continue to overdose, and to engage in HIV and HCV risk behaviors.

This project continues to bridge the implementation chasm in these 12 counties. In the UH3, we will analyze the effectiveness of an evidence-based community response project, using an innovative stepped-wedge community randomized trial. Specifically, we will conduct an evidence-based, multilevel health navigation intervention that is designed to reduce SUD and increase engagement in the SUD care cascade; reduce vulnerability to HIV, STIs, and HCV and increase engagement in the HIV, STI, and HCV care cascades; and reduce vulnerability to overdose deaths among adults who use drugs and are leaving local jails. We will target individuals leaving jails, a high risk but almost entirely neglected population. The intervention is based on enhancements to START, a CDC-recognized, evidence-based, individual-level intervention designed to reduce HIV/STI/HCV risk.

COVID-19 Policies
Because of COVID-19 related pauses in the study and related barriers, we are changing the trial duration from three years to two years. To accommodate this shorter time period, we are modifying the study design from a stepped-wedge trial to a case crossover trial and we are expanding our eligibility criteria to include individuals in the community recently involved with the criminal justice system.

CQI
We are adding a continuous quality improvement (CQI) component to assess the implementation of CARE2HOPE health linkage (START-C2H) and pharmacy-based medication for opioid use disorder (MOUD-C2H) interventions. The CQI will be led by Hannah Cooper, Multiple Principal Investigator and Umed Ibragimov, Co-Investigator, both at Emory University.

Objectives

List your research objectives. Please include a summary of intended research objectives in the box below.

The overarching objective of this study is to determine the effectiveness of an evidence-based community response project using a stepped-wedge community randomized trial. Specifically, we will test the effect of an intervention to reduce substance use and related harms among people re-entering the community from rural jails.

COVID-19 Policies
We are modifying the study design from a stepped-wedge trial to a case crossover trial. We will test the effect of an intervention to reduce substance use and related harms among individuals re-entering the community from rural jails and among individuals in the community recently involved with the criminal justice system defined as being incarcerated in jail or prison, out on bond, under warrant for arrest, arrested, under pre-trial supervision, on probation or parole, court-involved, or individuals who are incarcerated at home under an electronic monitoring program (i.e., digital jail) in the past 30 days.

CQI
The objectives of the CQI are to:
a) Document the MOUD-C2H (pharmacy Vivitrol) program implementation outcomes, including client reach, effectiveness, fidelity and maintenance, and explore barriers and facilitators for ensuring optimal implementation outcomes.
b) Document START-C2H (health linkage) program implementation outcomes, including client reach, effectiveness, fidelity and maintenance, and explore barriers and facilitators for ensuring optimal implementation outcomes.
c) Explore CARE2HOPE participants' experience with START-C2H intervention and its perceived effectiveness in changing risky behaviors.

Study Design

Describe and explain the study design (e.g., observational, secondary analysis, single/double blind, parallel, crossover, deception, etc.).

- *Clinical Research*: Indicate whether subjects will be randomized and whether subjects will receive any placebo.
- *Community-Based Participatory Research*: If you are conducting community-based participatory research (CBPR), describe strategies for involvement of community members in the design and implementation of the study, and dissemination of results from the study.
- *Qualitative research*: Indicate ranges where flexibility is needed, if a fixed interview transcript is not available, describe interview topics including the most sensitive potential questions.
- *Research Repositories*: If the purpose of this submission is to establish a Research Repository (bank, registry) and the material you plan to collect is already available from a commercial supplier, clinical lab, or established IRB approved research repository, provide scientific justification for establishing an additional repository collecting duplicate material. Describe the repository design and operating procedures. For relevant information to include, see the UK Research Biospecimen Bank Guidance or the UK Research Registry Guidance.

This study will test the effects of an intervention to reduce substance use and related harms among people re-entering the community from rural jails. This study will compare people in a re-entry health navigation intervention with a comparison group of people who will get overdose education in jail. Everyone will take part in follow-up surveys after release. The intervention sessions and data collection will be delivered by project staff called "Re-entry Health Navigators" or "REHNs". Intervention and comparison conditions are described in more detail in the Research Procedures section.

Participants are assigned to one of the two groups by chance based on when they are released from jail and when their county is randomly chosen to start the project. In August 2019, we will randomize each of the 12 study counties to a start date. Four counties will be randomized to start the project each year, as shown in the Timeline and Study Design Figure. Four counties will be randomized to start the intervention each year. In each wave, four counties will be randomized to start 6 months of enrollment into a control condition, followed by 6 months of enrollment into the intervention condition, with follow-up data collection on both extending 6 months beyond enrollment. We anticipate an average enrollment of 25 participants per county per quarter, with a total final sample size for the trial of 1200 (n=600 intervention, n=600 control). After a county has met its target enrollment in both conditions, the intervention and comparison activities will no longer be offered in that county.

The stepped-wedge trial design is pragmatic and ethical. It is difficult to implement multicomponent interventions with fidelity in several communities simultaneously because of their scope. Stepped-wedge trials are thus pragmatic for tests of multicomponent interventions. They are also the most ethical trial design available for the proposed study. The intervention has proven effectiveness, though in other contexts. It is thus unethical to withhold an intervention entirely from one set of counties, as would happen in a traditional randomized trial with intervention and control groups.

COVID-19 Policies
We are changing the trial duration from three years to two years. To accommodate this shorter time period, we are modifying the study design from a stepped-wedge trial to a case crossover trial. We will randomize the 12 counties to two groups of six counties each versus three groups of four counties each. All counties will start at the same time. During months 1-6, counties randomized into Group 1 will receive the intervention, while counties randomized to Group 2 will serve as the comparison group. In Months 7-12, Group 1 counties will shift to the comparison group, and Group 2 counties will receive the intervention. In Months 13-18 we will conduct follow-up assessments in all counties. Months 19-24 will be devoted to data analysis and dissemination of the findings.

CQI
The CQI will involve one-time individual qualitative interviews to be conducted remotely (via videoconferencing). Each participant will take part in one interview only. Our target start date is February 2022. Data collection will occur in Months 1-5, data analysis will

commence at the same time and will continue until Month 8. Months 8-9 will be devoted to dissemination of the findings.

Attachments

Attach Type	File Name
StudyDesign	Timeline and Study Design Figure.pdf

Subject Recruitment Methods & Advertising

Describe how the study team will identify and recruit subjects. Please consider the following items and provide additional information as needed so that the IRB can follow each step of the recruitment process.

- How will the study team identify potential participants?
- Who will first contact the potential subjects, and how?
- Will you use advertisements? If so, how will you distribute those?
- How and where will the research team meet with potential participants?
- If applicable, describe proposed outreach programs for recruiting women, minorities, or disparate populations.
- How you will minimize undue influence in recruitment?
- Attach copies of all recruiting and advertising materials (emails, verbal scripts, flyers, posts, messages, etc.).

For additional information on recruiting and advertising:

- IRB Application Instructions - Advertisements
- PI Guide to Identification and Recruitment of Human Subjects for Research

START-C2H Recruitment: We will recruit participants and hold the first START-C2H session at the seven jails serving the 12 CARE2HOPE counties. Aligned with START protocols and similar to other team members' NIDA-funded studies in this area (IRB Protocol #43727), participant recruitment will occur in jail. Recruitment in the jail will occur weekly, with one or multiple sessions per week (depending on the needs of the jail) dedicated to screening and assessment (with a follow-up visit to the jail for completion of assessments, if needed). Each week, a project staff person will visit the jail on a consistent day(s) of the week chosen in collaboration with jail staff (i.e., to avoid court days and other standard events where inmate schedules may preclude participation). There will be three options for informing people about the study information sessions depending on whether jailers are able to provide lists of people nearing release to research staff in a timely fashion: (1) In jails where jailers are able to provide lists of people nearing release to research staff, staff will drop off envelopes for individuals who are within 21 days of release and ask jail staff to put them in the individuals' mailboxes (envelopes will be labeled with the individual's names). The envelope will include the recruitment letter (see attachments). The recruitment letter will be personalized for individuals who are participants in the CARE2HOPE longitudinal survey (IRB Protocol #43520) who consented to be contacted for future research (see attachments). Staff will obtain the names of these individuals from lists provided by the jail and/or jail databases. (2) In jails where jailers are not able to provide staff with up to date and timely information about people nearing release, the following will occur: Before the staff person's arrival, the jail staff will have invited all inmates who are expected to be released in the next 21 days who are returning to one of the 12 CARE2HOPE counties currently randomized to the intervention or control conditions to attend a group session to learn more about the study. The jail staff's invitation to prospective participants will be in the form of a study handout (see Jail Handout attached in Research Procedures secstion) that contains language emphasizing that attendance of the session is wholly voluntary and will not affect their probation, parole, or release terms. The handout will instruct the inmate to inform jail staff of their interest in attending the information session. (3) Staff will review jail databases weekly to identify individuals with addresses in our study counties. Research staff will work with the jail staff, asking them to provide the recruitment letter in the mailboxes of individuals who meet the county criterion.

At the group sessions, staff will provide a brief overview of the study, including describing the certificate of confidentiality and eligibility screening process. After the overview, participants will have the ability to ask the REHN questions. Following questions, the REHN will distribute paper copies of the screening survey (see Screener Appendix in Data Collection section) with a cover letter appended describing risks, benefits, and procedures involved in completing the screener (see Informed Consent section). The REHN will read the cover letter, screener instructions, and questions aloud to the group to support low-literate individuals. Individuals who consent will complete the screener. The screening survey will include questions to collect full name and date of birth so that staff can extend invitations (via jail staff) to those who are eligible to meet with them to learn more about the study, go through the consent process, and complete a study intake.

The REHN will collect the screeners, thank the prospective participants for screening, remind them that those who are eligible will be contacted later in the day to schedule a one-on-one appointment with the staff person to review the consent form, discuss the study, and if consent is granted, complete the intake process for the study (described below).

For individuals who participate in the screening session, who meet all eligibility criteria except "be incarcerated in a local jail and expected to be released in <21 days" but are interested in participating in the study, we will obtain their permission to contact them again closer to their release date to see if they are still interested in the study. If permission is provided, the REHN assigned to the local jail,will work closely with the jailer regarding the individual's release date and to arrange a time to meet with the potential participant again. The REHN will confirm the individual is still interested in the study; if so, the screening form will be completed again, ensuring the individual meets the eligibility criteria. If all criteria are met, the REHN will review the consent form, discuss the study, and if consent is granted, complete the intake process for the study.

COVID-19 Policies
Jails
Recruitment in jails make take place via Zoom or by phone depending on jail capacity if in-person meetings are not allowed per COVID-19 policies. We will work closely with each jail, providing them with a stack of recruitment packets and recruitment letters. The

packet will include the recruitment script, screener cover letter, UK consent form and the DOC consent form. Each REHN will work with jail staff to identify individuals who might be eligible, provide the recruitment letter in these individual's mailboxes, and schedule a recruitment session if an individual is interested in learning more about the study.
We will host the recruitment session using UK Zoom, which is HIPAA compliant or by phone. We will work closely with jail staff responsible for coordinating Zoom and phone sessions to schedule a recruitment session and to ensure the following:
• A confidential space will be available.
• For Zoom, a unique Zoom meeting ID will be provided to jail staff when the recruitment session is scheduled. The waiting room feature will be enabled prior before the individual joins the session. The individual will join with video. The REHN will read aloud all applicable documents and screen share these documents with the individual.
• For phone calls, the REHN will provide jail staff their dedicated phone number that the individual will use to call the REHN; the REHN will read aloud all applicable documents.
• At the start of the session, jail staff will provide the recruitment packet to the individual and the individual will confirm that that they are in a confidential space, free of foot traffic and feel comfortable completing the session. If these criteria are not met, study staff will end the session. Staff will reschedule the session if the individual is interested.
During the recruitment session, staff will provide a brief overview of the study (recruitment presentation text) including describing the certificate of confidentiality and eligibility screening process. The jail staff will remain in the room. After the overview, participants will have the ability to ask the REHN questions. If the individual is interested in screening for the project, the individual will sign the DOC consent and the jail staff will sign as well. The jail staff will then leave the room and the REHN will continue with the screening process including reading the screener cover letter, completing the screener form, and completing the applicable county quiz, ensuring the individual is from the study county. If the individual is eligible, the REHN will immediately conduct the informed consent process. If the individual is not eligible, the REHN will let them know that they are not eligible and the session will end.

Community
Community participants will be recruited through: a) Probation, Parole and Pre-Trial Services Offices; b) digital jails; c) peer referral; d) existing CARE2HOPEand PROUD-R2 (Peer-Based Retention of People Who Use Drugs in Rural Research) participants who have consented to be contacted to learn about future studies; e) harm reduction and social service programs serving people who use drugs; and f) community-based organizations.
a) Recruitment via Probation, Parole and Pre-Trial Services Offices.
Probation, parole, and pre-trial supervision officers will share the recruitment flyer specific to probation, parole, and pre-trial services with their clients.
We continue to collaborate with the Department of Corrections (DOC) for recruitment strategies. The DOC uses an online and mobile phone app to communicate with people who are on community supervision (probation and parole, etc.). We recently received approval from DOC to provide text messaging scripts to the vendor who disseminates content to enrollees through their text messaging platform (scripts attached). The vendor will send our text message to all app service enrollees in our target counties at a no more than monthly frequency. As described in the script, individuals who receive the message will be instructed to contact our team if they are interested in the study. We will not have access to enrollees' personal information; all text messaging will be managed by DOC's approved vendor. This strategy is analogous to the IRB-approved forms of DOC outreach via email, phone, and flyers in that information is provided to individuals who then have the ability to decide whether to contact the team about the study.
b) Digital jails.
We will share our recruitment flyer with programs who supervise individuals incarcerated at home under an electronic monitoring program (i.e., digital jail). The administration of these programs varies by county. These programs are administered either through the jail or through the Court. We will identify the point of contact for each county and work directly with these individuals to share flyers.
c) Peer referral.
We will encourage enrolled participants to refer their potentially eligible peers to study staff. Each participant will be compensated $10 per eligible referral. We will cap the number of eligible referrals that a single participant can make to three persons, which will also limit the compensation amount the referring participant may receive. This policy will be implemented by REHNs who will ask the referred individuals the name of the person who referred them and check this information against the participant database.
d) Recruitment via existing study cohorts.
Study staff will contact participants enrolled in Kentucky CARE2HOPE (IRB # 43520), this protocol (CARE2HOPE UH3 Phase), and PROUD-R2, who gave their consent to be contacted about future studies. Note that PROUD-R2 is a collaborative project with Oregon Health and Science University (main site) and the Ohio State University and under the purview of the University of Utah IRB (IRB 00117831). We implemented IRB # 52430 in November 2019 randomizing the first four counties in the stepped-wedge design to the control group including Leslie, Letcher, Menifee, and Perry counties. These counties are randomized to the intervention group with the new study design. All participants currently enrolled will now be eligible for the intervention.
e) Recruitment via programs working with people who use drugs.
We will ask staff at local syringe service programs, substance use disorder treatment facilities and other health and social service providers to distribute recruitment flyers with the study information to their participants.
f) Social service and public health organizations: We will actively engage with social service and public health organizations to reach potential participants. This engagement will include: 1) With agency permission, we will have a REHN staff member on site at the agency or just outside the agency describing the study to agency clients and inviting them to be screened to learn if they are eligible. 2) With agency permission, we will have a REHN staff member provide a presentation about the study to agency clients as applicable.
g) We will also host picnics with boxed meals periodically to recruit potential participants. These events will be held outside in parks, parking lots (with permission of store attendant/owner), and other public locations where community members can meet project staff and learn about the study through conversations with staff and through study flyers disseminated by staff. Interested individuals will be invited to join staff at seats that are spaced 6 feet apart. Staff will tell individuals about the study. When individuals wish to be screened, REHN staff will either connect them to another REHN via phone to be screened, or screen them personally. If other community members are present, screenings will happen at least 20 feet from the picnic area to preserve confidentiality. Eligible and interested individuals will then schedule an appointment for an enrollment and baseline visit.

Paper copies of the pre-screening survey will be available for staff to complete with interested individuals should they not have their

laptop and access to the electronic screener during any recruitment event. Staff will then follow-up with the individuals to let them know if they are potentially eligible/not eligible; if eligible, staff will ask if the individual would like to complete the screener. Interested individuals may also complete the pre-screening survey themselves if preferred due to limited time, share with staff, who will then follow-up with them to let them know if they are potentially eligible/not eligible; if eligible, staff will ask if the individual would like to to complete the screener. Staff will store completed paper screeners in a lock box and then in a locked filing cabinet in their field office upon return.

Once we enroll 15 individuals in a county, we will place a hold on additional recruitment efforts for that county; however, we will resume recruitment again when all intervention counties are switched to control and all control counties are switched to intervention per our study design (cross-over trial).

6/28/22 Modification - Study staff will contact participants currently enrolled in comparison counties and offer them enrollment in the intervention group.

CQI
Pharmacists: Using the contact information from the program records, Graduate Research Assistants, Emory University, will invite the pharmacists trained by CARE2HOPE study on Vivitrol dispensing via e-mails and follow-up phone calls.
REHNs (research study staff): Graduate Research Assistants, Emory University, will invite the REHNs to take part via e-mail and follow-up phone calls. To avoid undue pressure, REHNs' decisions to enroll or refuse to participate will be kept confidential from the study leadership and management team (MPIs Young and Cooper, Project Director, White and Project Manager, Lane).
START-C2H participants: We will stratify the study roster from the REDCap database by county (n=12), then by gender (women and men), then by pharmacy-based Vivitrol participation status (Yes or No), resulting in 48 strata). Next, we will randomly select one participant from each stratum and will contact them using contact information from the study database. We will invite these individuals via phone; if a participant from a particular stratum refuses to participate, we will randomly select a replacement from the same stratum. Prior to the phone calls by the research assistants, our Re-entry Health Navigators (REHNs) will notify all eligible participants (i.e., those who participated in at least two START-C2H health linkage intervention sessions) about the forthcoming CQI interviews. This notification will be sent via text message to participants' phones using contact information from the study database or through Facebook Messenger (private CARE2HOPE account). This short notification will inform the participants that CARE2HOPE research assistants will call them to invite the for the interview and clarify that participation is voluntary. The notification text is proved as an attachment. Each REHN, will provide their own phone numbers as part of the text.
COVID-19 Policies
We will use UK PR-approved flyers to recruit individuals from the community. We will post flyers in places where potentially eligible people may gather, including, but not limited to homeless shelters, grocery stores, Walmart stores, etc. We will also continue to work with jails, asking them to distribute flyers in the personal effects of individuals incarcerated. Individuals who are interested in learning more about the study can scan the QR code on the flyer to access an online eligibility survey through REDCap. If a potential participant is eligible, they will be asked to submit their contact information and the study team member will contact them. A copy of the survey is attached. UK-PR approved flyers including one for the community in general and one specifically for probation, parole, and pre-trial services are attached. We will provided business cards to Syringe Service Programs and other agencies as requested to enclose with packets provided to their clients. Given the volume of potential clients, it's more cost effective to print business cards than flyers for the packets. The content is the same as the UK PR and IRB-approved flyer with the exception of an additional number for screening. We are collaborating with the Department of Corrections to increase awareness about our study. DOC staff will provide a brief description about our study when they meet with a client in-person, via text or email messages, and through letters. CARE2HOPE study staff will provide the letters (printed on UK letterhead) and flyers in sealed envelopes to DOC staff who will then address the envelopes and send to potentially eligible clients. Scripts are provided for each of these strategies.

We will advertise the study on our CARE2HOPE facebook page using our approved community flyer. Additionally, we will promote the study through paid advertisement through Facebook Ads. Our approved flyer will be used for the ad and we will target our 12 study counties. We will advertise the study through radio ads in our study counties. We will also promote the study through newspaper ads, use a flyer that highlights key information about the intervention, use a flyer focusing on rural health issues, and use yard signs in varied locations. To enhance our retention efforts, we will use a flyer for reminding participants about follow-up appointments.

We will encourage participants to make referrals to the study. Participants will receive $10 per eligible referral, up to three, for a total of $30. We will ask study participants to give a coupon to each referral, allowing us to track the number of individuals who are eligible and ineligible. The coupon number is a unique alpha numeric code that study staff will assign and track through an excel file. The referral coupon is attached.

Attachments

Attach Type	File Name
Advertising	Pre-Screening Survey 110421 - Clean.pdf
Advertising	Scripts for Radio - PR Clean 091621.pdf
Advertising	Scripts for Radio Ads - PR Approval 091621.pdf
Advertising	Business Cards Version 2 100821 - Clean.pdf
Advertising	Business Cards Version 2 100821 - PR Approval.pdf
Advertising	Classified Ads for Newspapers 100821 - Clean.pdf
Advertising	Classified Ads for Newspapers 100821- PR Approval.pdf
Advertising	Follow Up Appointment Flyer Template 100821 - Clean.pdf
Advertising	Follow Up Appointment Flyer Template 100821 - PR Approval.pdf
Advertising	Intervention Flyer 100821 - Clean.pdf
Advertising	Intervention Flyer 100821 - PR Approval.pdf

Advertising	Radio Ads Version 2 100821 - Clean.pdf
Advertising	Community Flyer Version 2 100821- Clean.pdf
Advertising	Community Flyer Version 2 100821- PR Approval.pdf
Advertising	Rural Health Study Flyer 101521.pdf
Advertising	Yard Sign 101521.pdf
Advertising	Flyer Cookout 072721 - Clean.pdf
Advertising	Flyer Cookout 072721 - PR Approval.pdf
Advertising	Facebook Ad 081621 - PR Approval.pdf
Advertising	Facebook Ad 081621 - Clean.pdf
Advertising	DOC Scripts 031921 - Clean.pdf
Advertising	DOC Letter 031821.pdf
Advertising	Flyer Community 021121 - Clean.pdf
Advertising	Flyer Probation, Parole, Pre-Trial Flyer 021121 - Clean.pdf
Advertising	Business Cards 021121 - Clean.pdf
Advertising	Referral Coupon.pdf
Advertising	Flyer - Community 120220 - PR Approval.pdf
Advertising	Flyer - Probation, Parole, Pre-Trial 120220 - PR Approval.pdf
Advertising	DOH and Social Service Agencies Scripts 042621.pdf

Research Procedures

Describe how the research will be conducted.

- What experience will study participants have?
- What will study participants be expected to do?
- How long will the study last?
- Outline the schedule and timing of study procedures.
- Provide visit-by-visit listing of all procedures that will take place.
- Identify all procedures that will be carried out with each group of participants.
- Describe deception and debrief procedures if deception is involved.

Differentiate between procedures that involve standard/routine clinical care and those that will be performed specifically for this research project. List medications that are explicitly forbidden or permitted during study participation.

This study will test the effects of an intervention to reduce substance use and related harms among people re-entering the community from rural jails or in the community. This study will compare people in a re-entry health navigation intervention with a comparison group of people who will get overdose education in jail or in the community. Everyone will take part in follow-up surveys for up to 6 months after release. The intervention is a health navigation intervention designed to reduce SUD and increase engagement in the SUD care cascade; reduce vulnerability to HIV, STIs, and HCV and increase engagement in the HIV, STI, and HCV care cascades; and reduce vulnerability to overdose deaths among adults who use drugs and are leaving local jails. The intervention is based on enhancements to START, a CDC-recognized, evidence-based, individual-level intervention designed to reduce HIV/STI/HCV risk. Individuals enrolled in the intervention arm will also be referred by the REHN to pharmacy-based Vivitrol administration services supported by the Kentucky Opioid Response Effort (a SAMHSA-funded, state level program); this is described in more detail below.

Overview of START

START, in its original format, is a manualized, six-session individual-level intervention that evidence indicates reduces vulnerability to HIV and STIs among people who are returning to the community from correctional settings. START has been adapted over the last several months for use with individuals who have been released into the community after being involved with the criminal justice system (i.e. spending time in a correctional institution or on probation or parole). START originally was designed to have 6 sessions: two with inmates before release from jail and 4 in the community after release. The modified version of START consists of 4 intervention visits that all take place in the community.

START core components: (1) Hold pre- and post-release program sessions with clients transitioning back to the community from a correctional setting; this component has been modified to included individuals who have been criminal justice involved in the last thirty days who are living in communities covered by our project; (2) Use a client-focused incremental risk reduction approach; (3) Use assessment & documentation tools to provide structure; (4) Hire program staff that are familiar with HIV/STIs/HCV prevention and with the specific needs of people being released; (5) Staff /client relationships must be maintained post-release; in the case of those individuals recruited from the community the relationship must be built and maintained in the community setting; (6) Conduct enrollment and schedule four intervention visits in the community over the span of 3 months that: a. give HIV/STI/HCV information; b. review client's HIV/STI/HCV risk; c. identify transitional needs; d. develop a personalized risk reduction and transitional plan; e. make facilitated referrals; (7) Schedule four post-release sessions, or for those enrolled in the community, post-enrollment sessions, to review and update the risk reduction/transitional plan(s) and provide facilitated referrals; (8) Provide fentanyl education, asking participants to watch a 4-minute educational video for FTS cited in previous research and available on YouTube at https://www.youtube.com/watch?v=gIovAAV-Amg, assess fentanyl knowledge through a quiz (attached), and provide fentanyl test strips at the first post-release session or for those enrolled in the community, the first post-enrollment session; and, provide fentanyl test strips and condoms at each subsequent post-release session or for those enrolled in the community, post enrollment sessions; (9) Actively maintain contact with clients.

START supports incremental risk reduction and transitions through motivational interviewing (MI) and facilitated referral. Aligned with harm reduction principles, MI is a non-confrontational approach that encourage thoughtful reflection on personal drug use, sexual relationships, and their consequences in the context of personal values and goals; it is an evidence-based approach to engage clients in their own ongoing process of change. In a facilitated referral, intervention staff are far more involved in connecting participants to services than is typical. Rather than simply handing a participant a pamphlet, in facilitated referral staff have already identified a specific contact at the referring agency, and may actively set up appointments for participants with this individual; in addition, they may organize transportation to and from the appointment, as needed.

CARE2HOPE's enhancements to START
We will modify START a priori as follows:
1) Though originally designed for young men, START has been successfully applied to women leaving correctional settings. We will implement START with all genders.
2) START's post-release sessions primarily occurred in homes and community venues, such as restaurants. Staff who will deliver START will be stationed at UK-leased space within or near the local department of health (DOH) and/or virtually.
3) To enhance START's impact on drug use and HIV/HCV-related harms (e.g., IDU frequency), we will integrate the NIDA Standard HIV intervention into START, including rapid HIV and HCV antibody testing and counseling. The NIDA Standard has been demonstrated to reduce drug use frequency, high-risk injection practices, and sexual risk.
4) START was not designed to reduce overdoses. We will provide an education video, How to Use Narcan (Naloxone), developed by the University of Kentucky HEALing Communities Study Team. Participants will receive naloxone, at their baseline visit or their first

intervention visit for those recruited in the jail.. Interventionists will encompass OD in risk reduction MI. Additional naloxone will be given to give participants in the event that they use/lose their Narcan, enter treatment, then leave treatment and have no Narcan.

The project will start with the first intervention visit once someone is released or, for those recruited in the community, after their baseline surveys and biological testing for HIV, HCV and drug screen have been completed, followed by 3 more intervention visits, at 1 month*, 2, and 3-months* (*in person, others by phone, unless in-person is needed). These sessions are described in detail below.

Pre-release Enrollment and Assessment (Session 1)

After recruitment (described above, see Jail Handout attached) and screening (described in sections above, Screening Survey attached in Data Collection section), we will conduct a one-on-one session to go through the consent process (described above) and conduct participant intake. To strengthen participant confidentiality, this session will take place in the Attorney/Client room in each jail and at the local REHN office for those recruited from the community. The Attorney/Client rooms provide privacy, and no correctional officers are allowed inside. CARE2HOPE staff use these rooms to conduct interviews with incarcerated survey participants in the current IRB-approved protocol (#43520). These rooms have a video camera (but no audio recorder), and staff have been trained to ensure that the participant's back is to the camera. In rare circumstances, this first meeting may be held in the community for those who were incarcerated at screening, if the individual leaves shortly after the recruitment session. The goals of this session are:
(1) To complete the consent process and enroll the individual in the study; complete the locator form to assist with follow-up; and set up the post-release appointment or baseline 2 appointment for those recruited in the community. The consent is described in sections above. The locator form is described in the data collection section. At the close of the session, the second session will be scheduled and the participant will be given an appointment card (see attachments, post-release appointment card) with the appointment date, location, time, and staff contact information. The card will also be provided in a sealed envelope to jail staff so that they can place it with the individual's personal effects that they receive upon release.

(2) To conduct risk-reduction planning: The participant will complete START's risk reduction assessment (see Risk Assessment appendix), which assesses knowledge of and engagement in drug and sexual risk behaviors. Based on this assessment, the REHN will work with the participant to develop a risk-reduction plan. The REHN will use diverse counseling microskills (reflective listening, affirmations, summaries) to build rapport and highlight possible directions for change. Participants will be administered the NIDA-modified ASSIST (NIDA, 2009) to measure high risk opioid use, including injection and OUD, prior to entering jail; we have used this measure in our team's other NIDA-supported studies in jails (R01DA033866, R34DA045856, PI: Staton); see NIDA ASSIST appendix. The participant and the REHN will then set risk-reduction goals that are attainable, and create a plan for attaining those goals and strategies to overcome related barriers.

(3) To deliver OD prevention intervention: Given the high risk of OD post-release, participants will watch an educational video. When allowed by jail leadership, naloxone will be provided to jail staff to include with the participants' CARE2HOPE appointment reminder and personal effects upon release (i.e., so that it is immediately available rather than the participant having to wait until the first in-person visit to receive it). Naloxone will be provided to participants recruited in the community at their baseline visit. All participants will receive a handout describing Good Samaritan & Naloxone Laws in Kentucky.

(4) Next, the participant will complete a transitional needs assessment to identify immediate release challenges. The REHN will work with the participant to create a transitional plan to address critical life needs at re-entry, such as housing and food; and, for those recruited in the community, challenges they have faced since release. A risk and needs assessment will be completed to create a transitional plan identifying needs and resources the participant deems most important. After the session, the REHN will initiate the process of linking the participant to needed services. Efforts will include contacting known individuals at relevant agencies to learn if slots are available, re-confirm eligibility criteria, and reserve a slot if possible; the REHN may need to develop new relationships at new agencies.

Pre-release Assessment (Session 2)
During this session, the REHN will meet with the participant in the Attorney/Client room to complete the baseline survey (Part 2). Depending on the participant's release date, this visit might take place post-release. For those recruited in the community, the baseline sessions will take place in the REHNs office.

Post-release, DOH-centered Session

REHN staff will monitor public jail logs to determine when a participant is released from jail. After the participant is released from jail, per START protocols and following locator procedures approved by the UK IRB in Protocol #43520, the REHN will remind participants of each upcoming meeting, via text message, Facebook messenger, or phone (depending on the participant's preference, per the locator form). The purposes of this first, in-community session are to:

(1) Conduct the HIV and hepatitis C education following the NIDA Standard Intervention protocol, with HIV and HCV testing and counseling. The NIDA Standard is a single-session structured, evidence-based intervention designed to educate high-risk PWUD about HIV/HCV and encourage adoption of safer practices. It includes rapid HIV and HCV testing, and includes education on HIV/HCV transmission, identifying risk behaviors and risk reduction; and the importance of referrals to treatment, and has evolved to suit incarcerated populations. Following currently approved CARE2HOPE protocol (#43520) for survey participants, participants can opt into or out of HIV and HCV testing. Testing and counseling protocols will be identical to those currently approved in the CARE2HOPE protocol (#43520) and are described in the Data Collection section below. People recruited in the community will receive testing as part of the baseline visit.

(2) Provide harm reduction materials: The REHN will distribute naloxone (unless provided in jail to be distributed with personal effects upon release; see above), fentanyl test strips, and condoms.

(3) Connect with DOH services: A great strength of the proposed intervention is that, as noted, many services – often including SSP – are available on site at each DOH. The REHN will review the wide range of services offered by the DOH that might be relevant to the participant or their family. For each needed DOH service, including SSP, the REHN will walk the participant down the hall to meet relevant DOH staff to learn about the service. Participants will also be linked to DOH staff who can provide confidential, on-site testing for chlamydia, gonorrhea, and syphilis. Study staff will not have access to the results of DOH testing and services.

(4) Create the risk-reduction plan and the transitional plan. Goal sheets and risk reduction plans (for SUD, HIV, HCV, and ODs) will be created to assess risk behaviors and needs and identify current concerns which will be assessed and ranked. Plans and Goal Sheets will be revised as needed. If the participant is on probation or parole, the REHN will review the supervision document with the participant to learn its stipulations (e.g., no buprenorphine, no positive tests for any illegal drug). As proposed by the START manual, this document will become a part of the participant's weighing of advantages and disadvantages of particular post-release risk reduction and transition strategies. Consistent with START's harm reduction philosophy, the REHN will work with the participant to determine the level of support needed to connect successfully to health and social services. Some may be comfortable contacting programs independently; others may need the REHN to make the appointment on their behalf and/or to organize or provide transportation.

(5) Connect with medication for opioid use disorder: Individuals who express interest in medication for opioid use disorder (i.e., buprenorphine, methadone, and/or extended release naltrexone) will be referred to local providers for services, including pharmacies. In intervention counties, CARE2HOPE has partnered with the Kentucky Opioid Response Effort (KORE) to support pharmacy-based extended-release naltrexone (i.e., Vivitrol) administration under the leadership of College of Pharmacy faculty member, Dr. Patricia Freeman. Pharmacy-based Vivitrol administration is currently within the authorized scope of practice for pharmacists in Kentucky. However, few pharmacies in the state offer it. Dr. Freeman and her colleagues are currently funded by the KORE to offer technical assistance and support to pharmacists interested in initiating Vivitrol administration in their pharmacies. Dr. Freeman and KORE have agreed to include CARE2HOPE counties as a target area for training and technical assistance and to do so in a sequence/timing that aligns with the timing that counties are randomly assigned to the intervention group. This effort will improve the capacity of pharmacists to provide Vivitrol to everyone in the community, including to those involved in CARE2HOPE.

At the end of this session, the next visit will be scheduled, and the locator form reviewed and updated.

Post-release Month 1, Month 2, and Month 3 Sessions

The 1 month and 2 month sessions will take place in-person. The REHN will review the participants risk reduction plan, troubleshoot issues the participant has been having with completing their goals and the risk reduction plan will be revised as needed. The Month 3 session will be in person, as well, to facilitate troubleshooting, data collection, and urine testing. Reminders will be sent as described above for the first intervention session. The Month 3 session will be in person, as well, to facilitate troubleshooting, data collection, and urine testing. Reminders will be sent as described above for the first post-release session. These sessions will be used to monitor and enhance the implementation of the risk reduction plans. The REHN will partner with the participant to consider progress and alter plans, as needed. Specifically, the REHN and the participant will: (1) Review and revise the risk reduction and transitional plan together; and (2) Discuss and address facilitators and barriers to implementing the risk reduction and transitional plans, and connect to services as needed. The REHN will provide fentanyl test strips and condoms during in-person sessions.

Comparison Condition

We will initiate the comparison group in each county six months before the intervention begins. The current "treatment as usual" condition for most individuals, especially individuals not entering parole/probation supervision, is to provide no post-release services. Given the high risk of overdose post-release, we will conduct a pre-release overdose intervention with the comparison cohort. Individuals recruited in the community will receive overdose education during their baseline visit as well. Overdoses are not a primary study outcome, and it would be unethical to withhold overdose education from this cohort. Six months before the intervention starts in a county, REHNs will use the same pre-release recruitment, consent, and enrollment protocols (including eligibility criteria, except individuals must live in counties that are currently randomized to the comparison group) as proposed for the intervention condition. As with START's original evaluation, we will administer a single session, pre-release intervention for the comparison group; if someone is recruited in the community, they will receive this visit as well. . Specifically, the comparison group participants will complete the a training with people demonstrating how to respond to an overdose and narration on preventing, recognizing, and responding effectively to an opioid OD, accompanied by information about Kentucky's Good Samaritan Law and Naloxone Access Law. REHNs will answer questions after the video. Individuals will receive a Community Resource Guide at this visit.

As in the intervention group, comparison group participants will complete assessments at pre-release (two sessions), for those recruited in the community this will happen at the REHNs office, and at 3 months and 6 months weeks post-release (post-enrollment for those recruited in the community). Surveys will be identical to those delivered to the intervention cohort, as will incentives. No interventions will be delivered at these follow up appointments. Retention efforts for comparison participants will be identical to those for intervention participants (described previously).

COVID-19 Policies

Pre-Release Assessment (Session 1). We will work closely with each jail, providing them with a stack of Pre-Release Assessment packets. If an individual is eligible, agrees to participate in the project, and provides verbal consent, the REHN will move immediately to the Pre-Release Assessment (Session 1). If time does not permit, then the REHN will work with the jail staff to reschedule this session. During this assessment, the REHN will:

1) Read the script designed to build rapport with the participant given the session will be less personable than an in-person session.
2) Complete the Baseline Part 1 survey.
3) Share the How to Use Narcan (Naloxone) Educational Video. For phone interviews, the REHN will read aloud the Care2Hope Narcan

Patient Brochure and answer any questions the participant might have. This pamphlet is new and provided in all attachments. The REHN will explain to the participant that, at their first in-person meeting, the REHN will play the How to Use Narcan (Naloxone) Educational Video
4) Read the Good Samaritan Law document and answer any questions the participant might have.
5) Complete the Locator Form with the participant.
6) Schedule the second Pre-Release Assessment within 7 days of the first assessment.
Following the session, The REHN will work with jail staff to let them know which individuals need the Pre-Release Assessment packet. Jail staff will add the packet to the participant's personal belongings. The packet will include the following:
• A business card with the contact information for the REHN on it with a note letting the participant know that they should contact the REHN to set-up their post-release visit and to get their incentive card mailed to them if they elected to not get their incentive placed on their commissary.
• How to use Narcan (Naloxone) Patient Brochure
• Good Samaritan Law Handout
• Resource guide
• How to Use your Incentive Card Handout
• Certificate of Confidentiality One-Pager

Pre-Release Assessment (Session 2). During this session, the REHN will complete the Baseline Part 2 survey with the participant via Zoom or by phone.

All post-release sessions including completion of surveys may be held via phone due to polices related to the COVID-19 pandemic. Phone calls may be conducted through Facebook Messenger if the participant provided permission to be contacted by Facebook Messenger on the locator form. We will message individuals to set-up their follow-up appointment and in the message, ask their permission to conduct the follow-up interview via Messenger. We will only conduct phone (or video) interviews via Messenger if permission is provided and we will update their locator form. The locator form is routinely updated either in-person or by phone. The REHN may conduct these phone sessions remotely in the privacy of their home or in their office depending on current COVID-19 policies at the time of the session. If the session is conducted remotely, the REHN will conduct all activities in a private space, using their UK cell phone, laptop, and earbugs (or some other type of headset) and the study participant will also be in a private setting of their choice. The REHN will ask the study participants to answer a short security assessment at the time he/she schedules the session to ensure the individual is a study participant (see attachment in data collection section). If the individual does not answer all questions correctly, the REHN will not continue. If the individual answers all questions correctly, additional questions will be asked. These same questions will be repeated at the time of the phone session, confirming the identity of the study participant based on the initial responses provided.

Follow-up sessions including completion of surveys may take place in the jail via Zoom. We will host the interview using UK Zoom, which is HIPAA compliant. We will work closely with jail staff responsible for coordinating Zoom sessions to schedule the interview and to ensure the following:
• A confidential space will be available.
• A unique Zoom meeting ID will be provided to jail staff when the interview is scheduled.
• The waiting room feature will be enabled prior before the participant joins the session.
• The participant will join with video so study staff can confirm the individual's identity; once confirmed, the video will be disabled.
• At the start of the session, the participant will confirm that they are in a confidential space, free of foot traffic and feel comfortable completing the interview. If these criteria are not met, study staff will end the session. The participant will be encouraged to follow-up with study staff once released from jail. If all criteria are met, prior to starting the interview, study staff will inform the participant how confidentiality will be protected via Zoom, for example, using UK Zoom, which is HIPPA compliant and that the waiting room will be enabled during the interview. There is a chance that jail staff could be close to the confidential space and potentially overhear so we cannot guarantee confidentiality completely.

Retention efforts are described in the data collection section. In addition to the locator form, we will also send reminder letters to study participants, reminding them about follow-up appointments or to contacts provided by study participants. Letters for phone calls due to COVID-19 and for normal operations are attached. We will distribute flyers in varied locations in the community as reminder that study participants are eligible for follow-up surveys as an additional strategy to ensure retention.

6/28/22 Modification: As noted in the data collection section, we will drop the 6-month follow-up surveys for newly recruited participants once approved by the IRB.

CQI
We will collect data via 1:1 interviews using semi-structured interview guides. All interviews will be conducted over Zoom or Facebook Messenger with participants located in a private area of their choosing. The participants who cannot secure a private area for the interview will have an option to attend the online interview from one of the study offices following COVID-19 safety protocols. We will not record participants' names or other personal identifiers (except for voice recording). All interviews will be audio-recorded and transcribed verbatim. To ensure confidentiality of REHN data, the interviews with REHN staff will be conducted by Graduate Research Assistants, Emory; the study leadership and management team (Cooper, Young, White and Lane) will not have access to REHN interview transcripts. Interviews with the pharmacists and intervention participants will also be conducted by Graduate Research Assistants, Emory. The interviews will take about 60 to 90 minutes. There will be no follow-up with the participants. The audio-recordings will be stored at encrypted and password-protected computer network until the end of CAER2HOPE study and then will be deleted.
Participant interview guide: we are expanding the interview domains covered to include the perceived effectiveness of the intervention. These qualitative data will complement quantitative data on intervention effectiveness, by illuminating perceived pathways through which the intervention might (or might not) have worked, and also allow us to explore participant perceptions of effectiveness. The

revised guide is attached (data collection section).

Attachments

Attach Type	File Name
ResearchProcedures	Participant Notification Text 033022.pdf
ResearchProcedures	Recruitment Email Text and Phone Scripts 020422.pdf
ResearchProcedures	Screener 081721 - Clean.pdf
ResearchProcedures	Fentanyl Quiz 061521.pdf
ResearchProcedures	Naloxone Brochure 120420.pdf
ResearchProcedures	Intervention Individual Risk and Needs Assessment 111820.pdf
ResearchProcedures	Rapport Script.pdf
ResearchProcedures	C2H Retention Flyer 061020 - Clean.pdf
ResearchProcedures	C2H Retention Flyer 061020 - PR Approval.pdf
ResearchProcedures	Pre-Appointment (Normal Operations).pdf
ResearchProcedures	Pre-Appointment (phone).pdf
ResearchProcedures	Missed Appointment (Normal Operations).pdf
ResearchProcedures	Missed Appointment (phone).pdf
ResearchProcedures	Letter to Contact (Normal Operations).pdf
ResearchProcedures	Letter to Contact (phone).pdf
ResearchProcedures	Recruitment Presentation Text 031820 - Clean.pdf
ResearchProcedures	Recruitment Letter - Personalized for G2H.pdf
ResearchProcedures	Jail Handout Good Samaritan and Naloxone Laws - Clean.pdf
ResearchProcedures	recruitment letter.pdf
ResearchProcedures	Jail Handout - PR Approval 101719.pdf
ResearchProcedures	Jail Handout - PR Clean 101719.pdf
ResearchProcedures	NIDA Modified ASSIST.pdf
ResearchProcedures	Pre-release Appointment Card.pdf
ResearchProcedures	Post-release Appointment Card.pdf

Data Collection & Research Materials

In this section, please provide the following:

- Describe all sources or methods for obtaining research materials about or from living individuals (such as specimens, records, surveys, interviews, participant observation, etc.), and explain why this information is needed to conduct the study.
- For each source or method described, please list or attach all data to be collected (such as genetic information, interview scripts, survey tools, data collection forms for existing data, etc.).
- If you will conduct a record or chart review, list the beginning and end dates of the records you will view.

Process data tracked by staff: Fidelity will be assessed through the Project Manager who will review case notes for 10% of randomly selected sessions. Reach will be assessed calculating the percent of eligible individuals who enroll (e.g., the # enrolled divided by the number of individuals who screen eligible for START-C2H). Dose will be assessed by calculating the percent of START-C2H sessions attended. START-C2H's immediate impact will be assessed via the START-C2H participants' survey data (described below) to assess immediate impacts on linkage to services.

Survey administration: START-C2H comparison condition and intervention participants will complete longitudinal data collection at pre-release session 1 (baseline part 1), at pre-release session 2 (baseline part 2) within 7 days of session 1, three months post-release, and 6 months post-release. Longitudinal data collection will be completed in the community for those recruited in the community. Baseline survey data will be collected in the jail or community (session 1) after enrollment and consent, in jail or community (session 2) within 7 days of session 1. Sections of the baseline survey will be repeated at START-C2H's in-person session, post-release or post-enrollment for those recruited in the community, including at 3-month session and in-person 6-month session, to assess change over time. Participants will complete surveys using computer assisted personal interviewing (CAPI); CAPI has been used previously in jails (and outside of jail) to assess START and is effective with low-literacy populations. In CAPI, the survey is displayed to study staff on a computer screen and the computer program lists the questions and responses and the study staff reads them aloud to the participant in person or by phone. We will use timeline follow-back methodology to improve participant recall (see attachment, Timeline Follow Back, for example of how this method is applied). To avoid social desirability and other forms of reporting bias, portions of the survey will be administered by an off-site staff person (i.e., rather than by the participant's re-entry health navigator) via UK's HIPAA-compliant instance of the web-conferencing platform called Zoom. Zoom is a cloud-based platform for video and audio conferencing, collaboration, chat, and webinars across mobile devices, desktops, telephones, and room systems (similar to Skype). UK supports two instances of Zoom -- one that is HIPAA compliant and one that is not HIPAA. UK has a signed Business Associate Agreement, providing a separate instance of Zoom that is HIPAA compliant. Data collection is possible as Zoom users can share their screens. Study staff will open a copy of the survey via Zoom, allowing a participant to view and answer questions orally while the staff member records the answer. Administration of the survey will take place in a private room to ensure privacy and confidentiality of data.

Survey content: Prospective participants will complete a screening survey (described above, see Screening Survey attached) to determine eligibility. Surveys (see START-C2H Survey appendix) will capture the following domains: (1) sociodemographic characteristics; (2) all possible behavioral targets; and (3) health and social service engagement. The survey will closely resemble that

used in the currently approved CARE2HOPE study under IRB protocol #43520. Of note, the survey instructions will clearly indicate that time periods at baseline refer to time before incarceration and, when repeated for follow-up visits, recall periods will be adjusted accordingly (i.e., language referring to lifetime or past 6 month behavior will be changed to past 3 months). Surveys will take 45-60 minutes to complete (survey administration methods are described above).

Drug screening: We will conduct Urine or saliva drug Screens at the 1-week, 3-month, and 6-month appointments. We will not conduct drug screening in the jail. As in CARE2HOPE UG3 phase (Protocol #43520), we will use HomeHealth's iCup Drug Test that tests for 13 drugs including opiates (heroin and morphine), buprenorphine, methadone, oxycodone, as well as various stimulants, sedatives, and other drugs. For saliva test, we will use SalivaConfirm (TestCountry, San Diego, CA) drug screening kit that detects 10 types of illicit drugs in the sample in 10 minutes.

HIV Testing: The REHN will conduct HIV testing using the rapid-rapid protocol approved for HIV surveillance and confirmatory testing by the state health department and CDC. Participants will be tested using rapid INSTI HIV 1/HIV 2 Rapid AntibodyTest (bioLytical Laboratories, USA), which is a 60-second immunoassay for the detection of HIV-1 and HIV-2 antibodies in blood obtained from finger stick (sensitivity: 99.6, specificity: 99.3) followed by confirmatory re-testing with the Sure Check® HIV-1/2 Antibody Test (ChemBio Diagnostic Laboratories, Medford NY) on blood obtained from finger stick (sensitivity: 99.8, specificity: 99.9). When a participant tests HIV positive on BOTH of the rapid tests, they are considered to be confirmed as HIV positive and therefore require reporting to the state health department. Participants are informed of this reporting requirement and procedures involved in a case investigation in their informed consent form. Upon a positive test, we will complete the KY DPH's HIV Case Report form found here: http://chfs.ky.gov/NR/rdonlyres/36B936F0-AD69-4B95-83A7-FE4E37201364/0/AdultCaseReportForm2016.pdf. We will fill in the participant's name and contact information, information about our facility, participant demographic data, residential data, risk behavior data, treatment history, and testing history. We will not complete the section describing children of the participant. The REHN will complete a facilitated referral to their district Ryan White Part B HIV care coordinator for participants who test positive on both tests. More detail about safety precautions and referrals are described in sections below.

HCV testing. REHNs will use the OraQuick® HCV Rapid Antibody Test (OraSure, Bethlehem, PA), a 20-minute indirect immunoassay test to detect HCV antibodies in blood from fingerstick. Participants who test positive for HCV will be referred to UK Kentucky Clinic Digestive Diseases and Nutrition (859-323-0079) or St. Claire Regional Medical Center in Morehead, KY or encouraged to visit their primary care doctor for confirmatory (HCV RNA) testing.

Locator form. The locator form shown in the Locator Form Appendix (attached) is identical to the existing CARE2HOPE locator form approved under IRB protocol (#43520). The form is a strong retention tool tailored to this population. This form queries contact information for the participant and multiple key network members, and seeks consent to contact network members as needed. Participants can opt into using Facebook messenger for retention contacts. Our locator form asks participants to indicate whether they give permission for us to contact them via private messenger on social media (i.e., Facebook messenger) and IRB-approved language informing participants about privacy issues surrounding the use of social media. Additionally, we will use the locator form to obtain limited contact information from individuals from the community who screen eligible and are interested in participating in the study. We will only obtain their phone number, an alternate phone number, and social media information to ensure we can reschedule individuals who do not show up for their first appointment. The locator form will be completed in REDCap. We will attempt to reach an individual once a week for four weeks; if we cannot reach them after four attempts, we will delete the record in REDCap.

COVID-19 Policies.
We will offer all participants in the intervention arm HIV and HCV testing. Research staff will perform testing as described above in the office. However, if a participant prefers, we will help them perform the test using a self-test kit, or we we will make a referral to a local health department.

Testing is offered in the local health departments through UK's Kentucky Income Reinvestment Program (KIRP) with UK staff based at the health departments. The Kentucky Cabinet for Health and Family Services' Department for Public Health and UK established KIRP to improve health care delivery via disease education, prevention, treatment and professional services for persons living with HIV through collaborations with existing Ryan White HIV/AIDS funded programs and harm reduction programs at local health departments. Testing is offered through collaboration with the harm reduction programs.

For participants who prefer to test themselves, we will offer home-based (self-test) HIV and HCV testing and drug screening to be completed in-person at the study office. If the participant does not feel comfortable coming to the office or all research activities are remote only due to COVID-19 restrictions, we will offer to meet the participant at a mutually agreed-upon location or their home to complete home-based (self-test) HIV and HCV testing.

For home-based (self-test) HIV testing we will use FDA-approved OraQuick In-Home HIV Test (OraSure Technologies, Inc., Bethlehem, PA) that tests for HIV antibodies in human saliva (gum swab) with 91.67% sensitivity and 99.9% specificity, with results ready in 20 minutes. For home-based (self-test) HCV testing we will use EverlyWell HCV human antibody test (Everlywell, Inc., Austin, TX), which requires finger stick to obtain blood for a dry spot sample that will be mailed to a laboratory for processing. Both sensitivity and specificity for this test are above 99%. We will conduct saliva drug test using SalivaConfirm (TestCountry, San Diego, CA) drug screening kit that detects 10 types of illicit drugs in the sample in 10 minutes.

After the baseline survey, if the participant does not feel comfortable coming to the office or all research activities are remote only due to COVID-19 restrictions, the REHN will meet the participant at a mutually agreed-upon location or at their home. The REHN will bring a biological test kit (HIV, HCV and drug tests) and harm reduction kit (nasal Naloxone spray, Naloxone brochure, Good Samaritan and Naloxone Laws, resource guide, information on incentive card and Certificate of Confidentiality). The REHN will drop the package off at the participants' home (placing the kit on a porch or car hood to permit social distancing) or will meet at a mutually agreed-upon location that is safe, following social distancing rules to avoid COVID-19 exposure for participants and staff. If the REHN is conducting

HIV/HCV testing, the REHN will conduct pre-test HIV/HCV counselling over the phone. The participant will be asked to collect biospecimens (oral swabs for HIV and drug testing, finger stick for HIV testing) in their home or at a in a mutually agreed-upon location that is safe (e.g. a gas station restroom or in their car). The participant will provide the completed test kits to the REHN following social distancing rules (e.g., placing the completed kits on their porch or the REHN's car hood). The drug test and HIV test will be read by the REHN, while HCV test will be sent to a lab for processing. If HIV or HCV tests are positive, the participant will be referred to the Department of Health for confirmatory testing.

During 3-month and 6-month data collection waves we will conduct drug screening only, so the REHN will bring drug screening kit only.

CQI
Interview guides for the qualitative interviews are attached.

6/28/22 Modification: We will drop the 6-month survey for newly recruited participants once approved by the IRB.

Attachments

Attach Type	File Name
DataCollection	Qualitative Interview Guide 040222 - Pharmacist.pdf
DataCollection	Qualitative Interview Guide 040222 - REHN.pdf
DataCollection	Baseline Survey Part 1 081721 - Clean.pdf
DataCollection	Baseline Survey Part 2 081721 - Clean.pdf
DataCollection	3 Month Survey 051021 - Clean.pdf
DataCollection	6 Month Survey 061121.pdf
DataCollection	Locator 031821 - Clean.pdf
DataCollection	Security Assessment 111820 - Clean.pdf
DataCollection	Timeline Follow-Back.pdf
DataCollection	Script for Rehab and Others Facilities 013120.pdf
DataCollection	Qualitative Interview Guide 062822 Participants - Clean.pdf

Resources

Describe the availability of the resources and adequacy of the facilities that you will use to perform the research. Such resources may include:

- Staffing and personnel, in terms of availability, number, expertise, and experience;
- Computer or other technological resources, mobile or otherwise, required or created during the conduct of the research;
- Psychological, social, or medical services, including equipment needed to protect subjects, medical monitoring, ancillary care, or counseling or social support services that may be required because of research participation;
- Resources for communication with subjects, such as language translation/interpretation services.

This study will involve the PIs, co-investigators, a project director, project coordinator, community-based research assistants, a research assistant from the College of Public Health, and community-based Re-entry Health Navigators (REHNs). The PIs and research staff will be responsible for scheduling surveys, submitting IRB modifications, conducting all surveys, filing consent forms, and managing incoming data, uploading data to a secure server, and assuring data quality and protection of human subjects. The study will have a UK leased field offices in Morehead and Hazard that houses a project coordinator and community researchers and a retention coordinator, and UK-leased offices in local departments of health staffed by REHNs.

Potential Risks & Benefits

Risks

- Describe any potential risks – including physical, psychological, social, legal, ability to re-identify subjects, or other risks. Assess the seriousness and likelihood of each risk.
- Which risks may affect a subject's willingness to participate in the study?
- Describe likely adverse effects of drugs, biologics, devices or procedures participants may encounter while in the study.
- *Qualitative research* - describe ethical issues that could arise while conducting research in the field and strategies you may use to handle those situations.
- Describe any steps to mitigate these risks.

Benefits

- Describe potential direct benefits to study participants – including diagnostic or therapeutic, physical, psychological or emotional, learning benefits. This cannot include incentives or payments.
- State if there are no direct benefits.
- Describe potential benefits to society and/or general knowledge to be gained.

Describe why potential benefits are reasonable in relation to potential risks. If applicable, justify why risks to vulnerable subjects are reasonable to potential benefits.

The procedures to be used by this study will involve conventional social science research methods that are routine in studies of this type. The potential psychological risks will be discussed with participants to assist them in making an informed decision as to whether they wish to participate in the survey. These potential psychological risks are primarily related to being asked questions in the surveys about illegal behaviors that they do not feel comfortable answering. There is also a risk that there may be a breach of confidentiality of their survey. Every effort will be taken to ensure that this does not happen. No files – hard copy or electronic – will be stored in the jail. REHN records for client sessions will be completed and stored in the research field office. Confidentiality issues will be stressed during informed consent, which will include the description of a federal Certificate of Confidentiality, which provides an additional layer of human subject protection. Participants will also be assured that their survey answers will not be made available to any representative of the jail or criminal justice system.

Of note, the KY Department of Corrections does require that all incarcerated individuals complete a general DOC consent form granting permission to participate in research and require that a copy of that consent form be deposited with the KY DOC headquarters. To protect participant confidentiality and avoid revealing to DOC staff who screened eligible and participated, we will administer the DOC consent form to all individuals attending the study overview session, rather than only to those who screen eligible. Therefore, jail officials and administrators will not be able to decipher which participants screened eligible, participated, or refused to participate. It is possible, that a study participant may experience anxiety, emotional distress, or other negative reactions due to the content of the screening questions. Based on our experiences working with this population, such occurrences are rare. However, with the participant's permission, they will be referred to the medical staff at the jail for additional help and support related to psychological distress. The Community Resource guide also contains information on mental health and substance abuse services in the community.

Potential psychological risks will be communicated during the informed consent process to help people make an informed decision as to whether they wish to participate. Some participants may be uncomfortable about discussing drug-related health concerns, social service needs, and related goals with REHNs; connecting with services at unfamiliar agencies may also be challenging, particularly if staff at those agencies stigmatize them for their substance use disorder. They may also be uncomfortable answering personal questions about stigmatizing and in some cases illegal behaviors (drug use, condomless sex), health outcomes (ODs, HIV, HCV), and PWUD-related healthcare service use. If these data, or data on the results of the urine test administered at baseline, were accessed by people outside of the study, the participant could experience legal actions, social stigma, or other social sanctions (e.g., job loss). The START intervention may also cause distress, as participants seek to reconcile goals with realities, and discuss personal sexual and drug-related behaviors. In addition, individuals who test positive for HIV or HCV may experience considerable distress. If confidentiality were breached, participants may experience stigma, lose their job or housing, or be ostracized.

Participants in the intervention group will receive the nasal spray naloxone (Narcan) to carry with them in case they encounter someone who has an opioid overdose or in case they have an opioid overdose and a friend can use the naloxone to respond. Additional naloxone will be given to participants in the event that they use/lose their Narcan, enter treatment, then leave treatment and have no Narcan. Research staff will show a short video that shows how to use the naloxone kit and perform rescue breathing. Research staff will answer questions and will provide a handout explaining how to use it and possible side effects (see attached Naloxone handout; note: this is the same handout approved by Kentucky Pharmacists Association for use by pharmacists when distributing naloxone). In the consent form, participants are informed that naloxone temporarily reverses the effects of opioid overdose and is not a substitute for emergency medical care and that they should call 911 if they witness an overdose. They are also informed that naloxone can cause side effects, including but not limited to sudden opioid withdrawal symptoms and that the signs and symptoms of an opioid emergency can return after the nasal spray is given. They are also informed that naloxone only works on opioid-related overdoses and has no effect on people who are not using opioids. Witnessing an overdose can cause physical, psychological, or emotional problems such as anxiety or depression. If a participant administers naloxone, they may experience additional physical, psychological, or emotional problems because the naloxone effects may wear off and overdose symptoms could return, the person may experience side effects, and/or the person may become irritable or violent. These risks are explained in the consent form. In addition, the consent form explains that Kentucky's Good Samaritan law is supposed to protect them from being charged or prosecuted for drug or paraphernalia possession if they call 911 because they witness an overdose and stay with that person. But in rare cases, law enforcement may arrest them if you have warrants for another crime or if they have a search warrant or if they are unfamiliar with the law. Participants are also informed that if people find out that they have naloxone, it might cause embarrassment and could hurt their standing with people in the community who have a negative attitude toward people who use drugs and/or toward naloxone.

Comparison group: Protocols will be identical to those described for the intervention group, but the comparison group members will not take part in any intervention aside from the naloxone training, including HIV or HCV testing. Risks and benefits will be limited to those pertaining to data collection, as described above.

Collection of Biological Specimens: The biological procedures to be used by this study will involve conventional medical research methods that are routine in studies of this type. The potential psychological risks will be discussed with participants during the consent process to assist them in making an informed decision as to whether they wish to participate in this part of the study. First, there is the potential for receiving a "false positive" on HIV/HCV testing. This potential is statistically remote because every positive HIV/HCV test result will be confirmed through a confirmatory test. Second, depression is likely when a subject receives a positive result. Similarly, there are emotional liabilities in some cases associated with receiving a negative test result (relief versus survivor's guilt). In either case, post test counseling will be provided and referral to the appropriate human service resources will be offered. The potential risks for a subject revealing her positive serostatus, or experiencing a breach of confidentiality, will also be discussed during post test counseling. These risks involve loss of employment or insurance, rejection by family or friends, and others. The immediate risks associated with the finger pricks and blood draw are slight pain and local bleeding at the site, and are comparable to those incurred during routine medical care.
Intervention group participants: The proposed study has potential benefits. First, individuals will have opportunity to be screened for risk behavior including injection drug use and risky sexual activity and receive feedback on results. Second, the study REHN will share important prevention intervention information with high-risk PWUD during the transition from jail to the community with the overall goal of reducing risk behavior and increasing community service utilization. Third, participants will receive an interactive training with animated

scenarios and narration on preventing, recognizing, and responding effectively to an opioid OD, accompanied by information about Kentucky's Good Samaritan Law and Naloxone Access Law, and HIV and HCV rapid testing. Fourth, there will be significant potential benefits to science because the study will provide important information about intervention delivery with high-risk PWUD in rural areas who otherwise face enormous challenges to service utilization. The study will also provide information, which can be used to improve the reach and scope of evidence-based interventions during the transition from jail to community re-entry. Finally, the project will generate important information related to the feasibility of interventions for rural PWUD.

Comparison group participants: Although comparison group participants will receive fewer benefits from study participation compared to intervention participants, they will receive greater benefits than their counterparts in the general public who do not participate. The current "treatment as usual" condition for most individuals re-entering the community from jail, especially individuals not entering parole/probation supervision, is that they receive no or very limited overdose education. Given the high risk of overdose post-release, we will conduct a pre-release overdose intervention with the comparison cohort. Overdoses are not a primary study outcome, and it would be unethical to withhold overdose education from this cohort. Specifically, comparison group participants will complete an interactive training with animated scenarios and narration on preventing, recognizing, and responding effectively to an opioid OD, accompanied by information about Kentucky's Good Samaritan Law and Naloxone Access Law. The training covers how to recognize and respond to an overdose and how to administer naloxone. Individuals will also receive a Community Resource Guide to be left with their personal effects that they receive upon release.

This important study will advance knowledge on the delivery of an evidence-based intervention for high-risk, hard-to-reach, vulnerable rural PWUD who have traditionally been less likely to engage in formal treatment services. Innovation is heightened by the use of rural jails for recruiting and screening high-risk rural PWUD. The overall aim of this study is to decrease substance use, HIV/HCV risk behaviors, and improve access to treatment and harm reduction services through the use of a REHN. The long-term goal of this study is to improve the quality of health of high-risk, underserved populations.

Available Alternative Opportunities/Treatments

Describe alternative treatments or opportunities that might be available to those who choose not to participate in the study, and which offer the subject equal or greater advantages. If applicable, this should include a discussion of the current standard of care treatment(s).

Not applicable

Back to Top

Records, Privacy, and Confidentiality

Specify where the data and/or specimens will be stored and how the researcher will ensure the privacy and confidentiality of both. Specify who will have access to the data/specimens and why they need access.

Describe how data will be managed after the study is complete:

- If data/specimens will be maintained, specify whether identifiers will be removed from the maintained information/material.
- If identifiers will not be removed, provide justification for retaining them and describe how you will protect confidentiality.
- If the data/specimens will be destroyed, verify that this will not violate retention policies and will adhere to applicable facility requirements.

If this study will use de-identified data from another source, describe what measures will be taken to ensure that subject identifiers are not given to the investigator.

If applicable, describe procedures for sharing data/specimens with collaborators not affiliated with UK.

For additional considerations:
Return of Research Results or Incidental Research Findings
HIPAA policies
FERPA policies
Procedures for Transfer agreements
Information regarding multi-site studies
NIH Genomic Data Sharing (GDS) Policy
Digital Data

For all CARE2HOPE components, we will conduct the interventions and gather data in private spaces that reduce the risk that others will overhear study activities.
Interviewer-administered surveys will be conducted using Questionnaire Development Software's CAPI program, respectively. This platform allow surveys to be programmed and data to be entered by interviewers using a touchscreen laptop. Data are automatically password protected and are uploaded to a Data Warehouse on the HIPAA-compliant server at the UK Center on Drug and Alcohol Research (storefront staff and Emory-based team members can VPN into this server). We will enter locator data and biological test results in a password protected database and store audio files and transcriptions of audio recordings on a secure, HIPAA-compliant server managed by the UK College of Public Health and Rollins Schools of Public Health at Emory University. Specifically, quantitative survey databases, biological testing databases, audio files, and transcriptions will be stored on both UK College of Public Health and Rollins School of Public Health servers. Each participant will receive a unique identifying number and all research data collection instruments will be identified by this number only. The master list matching identifiers to specific participants will be maintained in a

separate, double-password protected database on the secure HIPAA-compliant server at the UK College of Public Health and Rollins School of Public Health at Emory University. We will store handwritten notes recorded during the survey and signed consent forms in a locked filing cabinet in a locked office in the UK College of Public Health. Audio recorders will be wiped of audiofiles after data have been uploaded to the server; if participants mention specific people by name, we will delete this part of the recording prior to uploading it (unless it is a public figure); notetakers will not record names in their notes (except those of public officials). Participants will not be identified by name in analytic data files. Research data will be reported in aggregate form only. The study is protected by a federal Certificate of Confidentiality, which will protect the investigators from being forced to release any identifying data, even under a court order or a subpoena

All staff will sign a confidentiality agreement, stating that they will not disclose information about participants to others outside the study team.

Data sharing with the University of Washington Data Harmonization Coordinating Center (DCC) and within the Rural Opioid Initiative (ROI) consortium: Data from Kentucky CARE2HOPE are required to be submitted to the University of Washington as part of the NIH-funded Rural Opioid Initiative (ROI) data harmonization project. The University of Washington Data Harmonization Coordinating Center will be harmonizing data across 8 ROI studies in order to create new, harmonized datasets to be used for analyses across the consortium. The University of Washington and other ROI grantees will perform data analyses on these data for peer-reviewed publication. University of Kentucky and Emory investigators for this grant may be included as authors on manuscripts using these data. The harmonized datasets will be provided to other ROI grantees as required for analysis and will be considered under the umbrella of mandated DCC activities.

Once data are at the DCC it will be harmonized with data from the other 7 NIH-funded ROI sites to create new, harmonized datasets to be used for analyses across the consortium. Both the University of Washington and other ROI grantees will perform analyses on harmonized data sets, but no third parties outside of the ROI will be given access to this harmonized data. Harmonized datasets will be built to specific project concept proposals (i.e. will contain only necessary and pertinent data elements), and all project proposals must be reviewed and approved by the ROI consortium's Publications Working Group before distribution of the customized dataset.

All data submitted to the DCC will be de-identified with the exception of zip code, city name, and county of residence. The consent form specifes that identifying data will not be shared with other researchers with the exception of zip code, city name, and county residence (What Else Do I Need To Know Section). The consent also specifies that data will be shared with the University of Washington Data Coordinating Center. Data will be uploaded to the ROI Upload Server through a web interface. Access to the interface is controlled by usernames and passwords. Access is assigned to individual, designated ROI study staff by the University of Washington DCC. Staff are associated with their own studies only, and each ROI study may upload and manage its own data but is not able to view data from other studies. The web page uses the HTTPS protocol to transfer ROI data files securely to the Upload Server. HTTPS transfers are encrypted using Transport Layer Security (TLS, the successor to SSL), protecting the data enroute to the server. The Upload Server is managed in accordance with the DCC's information security policies (https://uwcirg.github.io/hipaa-policies), and authorization for specific DCC staff is based on their project-related needs and responsibilities.

We will also submit transcriptions for audio-recorded interviews to the DCC using the same protocol for transferring files securely.
A Certificate of Confidentiality has been obtained from the National Institute of Health which, under federal law, prohibits all data collected during the course of a study protocol from being used in any legal or criminal proceedings. Participants will receive a copy of the consent showing the Certificate provisions and safeguards.

All research data will be kept in locked file cabinets at the University of Kentucky College of Public Health in Office 211c at 111 Washington Avenue. Each participant will receive a unique identifying number. All research data collection instruments will be identified by this number only. The master list matching identifiers to specific participants will be maintained in a double-password protected database on a server at the Center on Drug and Alcohol Research at the University of Kentucky. Research data will be reported in aggregate form only without names or identifying information.
During interview and survey administration, should any participant feel uncomfortable answering any question, he or she will be free to abstain from answering that question or any other question. Likewise, participants can end their participation in intervention activities (e.g., START-C2H goal setting, or HIV testing and counseling) at any time, or choose not to engage in any component of the intervention they wish.

All study staff will be trained in Human Subjects protocols and will have passed the appropriate Collaborative Institutional Training Initiative (CITI) exams on human subjects research. Research staff will not press participants to answer questions that seem to be distressing to them. During interview administration, should any participant feel uncomfortable answering any question, he or she will be free to abstain from answering that question or any other question. In addition, research staff will respond to participants who show or express psychological distress and/or suicidal or homicidal thoughts by following the procedure Distressed and Suicidal/Homicidal Participants that has been a standard operating procedure in previous NIDA-funded trials (e.g., R01 DA027068). To offset the risk of distress associated with the data collection, all participants who express an interest will be provided with an information sheet on local resources. The list of referral agencies will include mental health centers, substance abuse facilities and support groups, and counseling facilities. Participants will receive the name of the referral agency, location, telephone number, fee, if applicable, statement describing the agency and the work that they do. If participants wish, we will assist them to make contact with services; however, we will not disclose any information about participants to referral agencies. The consent document will also contain a statement informing participants that their name and contact information may be released without their consent to appropriate state authorities in instances that are required by state law (e.g., if they inform study staff that they are wanting to end their life or someone else's life, or are abusing a child). Furthermore, a Certificate of Confidentiality has been granted to this study automatically (see https://grants.nih.gov/grants/guide/notice-files/NOT-OD-17-109.html). Under the Certificate of Confidentiality, section 301(d) of the Public Health Service Act (42 U.S.C. 241(d)) prohibits all data collected during the course of a study protocol from being used in any legal or criminal proceedings. Participants will receive a copy of the NIH Notice NOT-OD-17-109 granting the Certificate of

Confidentiality if so requested.

All research staff on this project will attend an intensive training that covers topics including human subjects protection and issues that could arise during jail-based data collection. Prior to any member of the research staff initiating contact with research participants, they will also be trained in the following areas: 1) Understanding the project grant (background, application, and aims); 2) Demonstrated understanding of all interview data collection forms; 3) Understanding how all forms are filed, both electronic and material (i.e. exact location, computer drive, folders, and which electronic files need to be password protected); 4) Understanding which type of events need to be reported and the process of reporting (e.g., emotional reports related to incidence of victimization or violence, adverse events reporting, exclusions after consent was obtained, cases of child abuse, active suicidal/homicidal ideation, releasing information, etc.); 5) Jail security training and familiarity with the environment (scheduling interview rooms, general etiquette); and 6) Interview and follow-up retention techniques (building participant rapport, tracking via weekly letters and phone calls, flexibility of interview times, dates, and locations, etc.). Training tasks will be organized by a checklist which will be completed during orientation. Staff will also complete training by the Kentucky Department of Corrections that covers codes of conduct for people visiting/working in correctional facilities and provides training on personal safety and on the importance of ensuring that all materials brought into the jail are also taken out of the jail by the interviewers (e.g., pens, study materials, etc.). Consistent with other studies led by Co-Is Oser and Staton involving justice-based populations, a two-day training session for REHNs (study interventionists) is proposed, in addition to on-going supervision for quality control to assure consistent delivery of services. The training approach will follow the procedures outlined by Carroll & Nuro (2002) which incorporates the following session content: 1) Overview; 2) Discussion of issues, including re-entry service coordination approaches; 3) Intervention goals and targeted behavior; 4) Discussion of similar approaches; 5) Specifications for intervention session content; and 6) Format for delivery and structure. Weekly clinical supervision will be provided by Dr. Staton and will focus on general clinical issues as well as intervention adherence issues. Individual sessions will be reviewed for adherence to the approach and will highlight fidelity.

REHNs will attend Project START trainings, offered through the CDC, to ensure that they understand how to ethically implement the intervention with fidelity to the original design.

REHNs will attend an HIV certification program offered by the Kentucky Cabinet for Health and Family Services to become certified HIV counselors. In addition, all staff will attend an in-house training sessions at the UK Center on Drug and Alcohol Research hosted by the PI (Young) on how to use the INSTI and SureCheck HIV 1/2 Test specimen collection kits, and OraQuick® HCV Rapid Antibody Test. Staff will undergo training on how to respond to participants who show or express psychological distress and/or suicidal or homicidal thoughts. In addition, all study staff will undergo training on how to respond to participants who show or express psychological distress and/or suicidal or homicidal thoughts (e.g., facilitated by board certified psychiatrist, Co-I Michelle Lofwall). The procedure will follow the protocol for Distressed and Suicidal/Homicidal Participants that has been a standard operating procedure in previous NIDA-funded trials (e.g., R01 DA027068).

People who test negative will be provided with an information sheet on local resources. The list of referral agencies will include mental health centers, substance abuse facilities and support groups, and counseling facilities. Participants will receive the name of the referral agency, location, telephone number, fee, if applicable, statement describing the agency and the work that they do. If participants wish, we will assist them to make contact with services; however, we will not disclose any information about participants to referral agencies. The consent document will also contain a statement informing participants that their name and contact information may be released without their consent to appropriate state authorities in instances that are required by state law (e.g., if they inform study staff that they are wanting to end their life or someone else's life, are abusing a child).

Participants who test positive for HIV will be referred to their district Ryan White Part B HIV care coordinator. To maximize linkage to care, research staff performing testing will offer to call a Patient Services Coordinator at the UK Bluegrass Care Clinic (BCC; the HIV clinic serving Appalachian Kentucky) to set up an intake appointment on the participant's behalf while the participant is present. The BCC accepts all forms of private and public insurance and has grant funding to support services for uninsured patients. Participants who test positive for HCV will be referred to UK Kentucky Clinic Digestive Diseases and Nutrition (859-323-0079) or St. Claire Regional Medical Center in Morehead, KY or encouraged to visit their primary care doctor for confirmatory (HCV RNA) testing.

Each individual will receive a unique identifying number and the screener form will be identified by this number only. The master list matching identifiers to specific participants will be maintained in a double-password protected database on the secure HIPAA-compliant server at the UK Center on Drug and Alcohol Research. Screener data will be reported in aggregate form only. Participants will not be identified by name in analytic data files. All electronic research data will be kept on the HIPAA-compliant server at the UK Center on Drug and Alcohol Research.

A Data Safety Monitoring Board will oversee the study.

UK IRB policies state that IRB-related research records must be retained for a minimum of 6 years after study closure. Do you confirm that you will retain all IRB-related records for a minimum of 6 years after study closure?

◉ Yes ○ No

Payment

Describe the incentives (monetary or other) being offered to subjects for their participation. If monetary compensation is offered, indicate the amount and describe the terms and schedule of payment. Please review this guidance for more information on payments to subjects, including restrictions and expectations.

Project START-C2H In-Jail Eligibility Screening, Consent, and Assessment: All participants who consent to participate and complete

the two in-jail assessments will receive $25 for their time to complete the first assessment and $10 to complete the second assessment.. This amount has been used previously by CARE2HOPE staff for a similar time commitment and is commensurate with the burden and not coercive in this context. As is currently approved by the UK IRB and Kentucky Department of Corrections for CARE2HOPE UG3 phase (Protocol #43520), participants can receive their incentive by staff depositing the money into their commissary account upon departure from the facility. Staff obtain a receipt for the deposit for record keeping. If the jail's policy is to withdraw jail fees from the commissary account (thereby creating a situation where participants may not directly receive their research incentives), the staff will deposit the funds in their in-jail phone account (if shielded from fees) or provided the incentive in the form of cash or gift card with their personal belongings upon release.

Post-release Intervention and Data Collection: Participants will be compensated $25 for completion of 3-month and $25 for completion of 6-month follow-up surveys. Participants who update or verify their locator information between the baseline and 3-month and between the 3-month and 6-month follow-up will receive $10 each time (total of $20). Additionally, participants who refer individuals to the study and who screen eligible, will be offered $10 for each referral, up to 3 individuals (total of $30)This incentive structure and amounts are consistent with the IRB-approved CARE2HOPE UG3 (Protocol #43520). These amounts are commensurate with other studies, and not coercive. Payments will be made in cash for surveys completed in-person. Payments will be made by mailed cash card (e.g., electronic Visa card) for surveys completed by phone. Payments for follow-up surveys completed in jail (i.e., if a person is re-incarcerated) will be made on their commissary account, in-jail phone account, or provided in form of cash or gift card with personal belongings upon release (depending on policy of jail, as described above).

COVIID-19 Policies
Pre-Release. If surveys are completed in the jail via Zoom or by phone, the incentive cash card cannot be provided to the participant directly until in-person meetings resume. However, the individual will be offered two options to receive payment: the REHN will place the incentive amount on their commissary account using an online app available through the jail or the REHN will mail the card with the incentive amount after their release.

Participants recruited from the community will be compensated $25 for Baseline Part 1, $10 for Baseline Part 2, $25 for the 3-month follow-up, and $25 for the 6-month survey. Participants who update or verify their locator information between baseline and 3-month and between 3-month and 6-month follow-up will receive $10 each time (total of $20). Additionally, participants who refer individuals to the study and who screen eligible, will be offered $10 for each referral, up to 3 individuals (total of $30). Participants in the intervention arm only will be compensated $15 for HIV and HCV home-based (self-test) testing (optional). The total amount a participant will be compensated will be $120-$150.

CQI
We will offer all categories of participants (pharmacists, REHNs and CARE2HOPE participants a $30 Western Union card as a compensation for their time and effort.

Costs to Subjects

Include a list of services and/or tests that will not be paid for by the sponsor and/or the study (e.g., MRI, HIV). Keep in mind that a subject will not know what is “standard” – and thus not covered by the sponsor/study – unless you tell them.

Not applicable

Data and Safety Monitoring

The IRB requires review and approval of data and safety monitoring plans for greater than minimal risk research or NIH-funded/FDA-regulated clinical investigations.

- If you are conducting greater than minimal risk research, or your clinical investigation is NIH-funded, describe your Data and Safety Monitoring Plan (DSMP). Click here for additional guidance on developing a Data and Safety Monitoring Plan.
- If this is a non-sponsored investigator-initiated protocol considered greater than minimal risk research, and if you are planning on using a Data and Safety Monitoring Board (DSMB) as part of your DSMP, click here for additional guidance for information to include with your IRB application.

This research project involves non-exempt human subjects as defined by DHHS regulations. It is an NIH-Defined Phase IV Clinical Trial as defined by DHHS regulations outlined in 45 CFR Part 46 - that is, the intervention’s effectiveness has already been established in a large group of people, and we are now testing its effectiveness in other populations (for details, see https://www.nlm.nih.gov/services/ctphases.html). Therefore, the PIs will be responsible for developing and executing the Data and Safety Monitoring Plan (DSMP), including establishment of an independent DSMB for the study.

For all CARE2HOPE components, we will gather data in private spaces that reduce the risk that others will overhear data collection activities. Interviewer-administered surveys will be conducted using Questionnaire Development Software’s CAPI program. This platforms allow surveys to be programmed and data to be entered by interviewers using a touchscreen laptop. Data are automatically password protected and are uploaded to a Data Warehouse on the HIPAA-compliant server at the UK Center on Drug and Alcohol Research (storefront staff and Emory-based team members can VPN into this server).

Similarly, electronic versions of the biologic test results and audio files from qualitative interviews will be stored in password-protected databases on the HIPAA-compliant server at the UK Center on Drug and Alcohol Research. Audio recorders will be wiped of audiofiles

after data have been uploaded to the server. Qualitative interviews will be recorded on recorders that can be password protected.

Each participant will receive a unique identifying number and all research data collection instruments will be identified by this number only. The master list matching identifiers to specific participants will be maintained in a double-password protected database on the secure HIPAA-compliant server at the UK Center on Drug and Alcohol Research. Research data will be reported in aggregate form only. Participants will not be identified by name in analytic data files.

All staff will sign a confidentiality agreement, stating that they will not disclose information about participants to others outside the study team.

Procedures for preventing and addressing breaches of confidentiality: If a breach is identified, the PIs will immediately inform the UK IRB; NIH will be informed as decided by the UK IRB. Next steps will depend on the nature of the breach. Examples of possible steps include: retraining staff in confidentiality protocols; firing a staff member for a serious violation or repeated minor violations, despite training; or informing UK IT of a threat to HIPPA protections.

Potential Adverse Events Reporting Procedure and Database: Adverse events (AEs) that may occur during data collection may include violation of confidentiality, discomfort due to assessment procedures, embarrassment in disclosing sensitive personal information, disclosure of information about current and/or intended physical harm to persons; current and/or intended abuse of children that would be reported to a child welfare agency; and/or an investigation of such allegations(s) that could ensue, dissatisfaction with the assessment procedures, and dissatisfaction with the intervention activities. Serious adverse events (SAE) may also occur in our study population of people who use drugs and could include infections, hospitalizations, overdose, and death. AEs and SAEs events following randomization will be recorded on an Adverse Events Log. All potential adverse events will be reviewed as to the assigned treatment group and further classified by severity (life-threatening, serious, non-serious) and expected vs. unexpected. Expected adverse events, determined by consensus with the DSMB, will be monitored at each enrolling site, reported to overseeing agencies as required by federal regulations and local requirements, and reviewed periodically by the independent DSMB.

Adverse events will be reported to the NIDA Project Officer in the annual progress report. This report will describe the event, when it occurred, the study arm of the participant, and the outcome/resolution. If there were no AEs, we will so state in the progress report.

SAEs will be reported to the NIDA Project Officer within 24 hours of the event by email. This notification will include a brief explanation of the SAE and when it occurred. Within 72 hours of the event, we will send a follow up email that describes the date of the event, what occurred, actions taken by project staff, planned follow up (if any), the intervention group/study arm of the affected participant, whether the event appears to be related to the intervention, and whether participant will continue in the study. We will create a standard form to use for these communications.

Interim Analyses of Efficacy Data. We have proposed interim analyses of Project START-C2H data after approximately 50% the Project START-C2H participants have been recruited. During the first DSMB meeting, convened in the pre-implementation phase for Wave 1, the DSMB will work with the study statistician to establish stopping rules for this study. If there are large differences in serious adverse events or outcomes in blinded group comparisons, the DSMB may request that the statistician present an unblinded analysis of interim results to the DSMB who will determine if these rules and met and if the study can continue.

Trial stopping rules. The DSMB will determine if we should stop the trial. The DSMB will meet during the pre-implementation phase for Wave 1 to determine stopping rules.

All AEs will be reported to NIDA at least once per year as a part of the annual progress report. This report will describe the event, when it occurred, the study arm of the participant, and the outcome/resolution. If there were no AEs, a statement that no AEs occurred will be included in the progress report or communicated to NIDA in writing.

SAEs will be reported to NIDA within 24 hours of the event by email. The notification will include a brief explanation of the SAE and when it occurred. A written follow up will be sent within 72 hours of the event. The written follow up will include information on the date of the event, what occurred, actions taken by project staff, planned follow up (if any), the intervention group/study arm of the affected participant, whether the event appears to be related to the intervention, and whether participant will continue in the study).

Reporting of IRB actions to NIDA: All IRB actions will be reported to NIDA. The IRB director will provide guidance as to whether the action is reported in the progress report, or more rapidly, following SAE protocols described above.

Data Safety Monitoring Board (DSMB): The DSMB will be convened prior to initiation of the trial and will decide stopping rules, review the final protocol and consent process prior to trial implementation, and will provide input and approval. DSMB activities will include reviewing emerging trial data, and making recommendations about the trial's conduct, including possibly stopping the trial. At the close of each meeting, the DSMB will make one of four recommendations: continue as is, continue but with specific modifications; stop temporarily until specific conditions are met; or terminate. The PIs will report DSMB activity as part of their annual project progress report to NIDA.

The DSMB will meet via teleconference to review protocol changes, data collection procedures, evaluate the benefit and risk ratio to participants, and review and approve the statistical analysis plan for the study. The DSMB will advise the PIs if a change in the protocol is warranted and at each visit, will formally vote to allow the study to continue. The DSMB may vote to discontinue the study due to safety concerns.

A report on DSMB meetings and activities will be sent to NIDA within a month after each DSMB meeting. The update will include the following: meeting dates (past and upcoming if known), meeting minutes or summary, current board membership, changes in

membership (if applicable), information about any new member(s) (if applicable) including statement that new members have no conflict of interest, and specific board recommendations regarding the research project (if any).
We will submit reports from the DSMB to the UK IRB at continuation review summarizing the annual meetings; the DSMB will elect a chair who will write those reports. The first meeting will be scheduled at the beginning of Year 1 of the UH3, before the trial begins. Annual meetings will be held thereafter, with a final report due in Year 3 of the UH3. The DSMB's responsibilities will be to create stopping rules, and monitor the trial's safety, efficacy, and statistical assumptions and analyses.

The DSMB members shall have no conflicts of interest and no DSMB member will have ties to any study center or study team member to ensure independence. Should a conflict arise, the DSMB will step down and be replaced. Our DSMB will meet in during the pre-implementation phase for the first Wave of counties, and will establish the frequency of subsequent meetings, with a frequency of no less than once per year.

Back to Top

Future Use and Sharing of Material (e.g., Data/Specimens/Information)

If the material collected for this study will be used by members of the research team or shared with other researchers for future studies, please address the following:

- list the biological specimens and/or information that will be kept
- briefly describe the types, categories and/or purposes of the future research
- describe any risks of the additional use
- describe privacy/confidentiality protections that will be put into place
- describe the period of time specimens/information may be used
- describe procedures for sharing specimens/information with secondary researchers
- describe the process for, and limitations to, withdrawal of specimens/data

The following information is provided in the consent form: Identifiable information (e.g., your name or date of birth) with the exception of ZIP code, city name, and county name will be removed from the information or samples collected in this study. By consenting to this study, you agree to allow researchers on this study to share information, including ZIP code, city name, and county name, with other researchers, including the University of Washington who serves as the Data Coordinating Center for this project, without your additional informed consent. We may also share these data in aggregate with members of the community coalition who will be trained in research privacy and confidentiality and who will be deciding what services to add to your community to address local drug-related harms. If we share other data with researchers or the community coalitions in the future, it will not have information that can identify you unless you give your consent/authorization or the UK Institutional Review Board (IRB) approves the research. The IRB is a committee that reviews ethical issues, according to federal, state and local regulations on research with human subjects, to make sure the study complies with these before approval of a research study is issued.

Are you recruiting or expect to enroll **Non-English Speaking Subjects or Subjects from a Foreign Culture**? (does not include short form use for incidentally encountered non-English subjects)
○ Yes ◉ No

Non-English Speaking Subjects or Subjects from a Foreign Culture

Recruitment and Consent:

Describe how information about the study will be communicated to potential subjects appropriate for their culture, and if necessary, how new information about the research may be relayed to subjects during the study.
When recruiting Non-English-speaking subjects, provide a consent document in the subject's primary language. After saving this section, attach both the English and translated consent documents in the "Informed Consent" section.

Cultural and Language Consultants:

The PI is required to identify someone who is willing to serve as the cultural consultant to the IRB.

- This person should be familiar with the culture of the subject population and/or be able to verify that translated documents are the equivalent of the English version of documents submitted.
- The consultant should not be involved with the study or have any interest in its IRB approval.
- Please include the name, address, telephone number, and email of the person who agrees to be the cultural consultant for your study.
- ORI staff will facilitate the review process with your consultant. Please do not ask them to review your protocol separately.

For more details, see the IRB Application Instructions on Research Involving Non-English Speaking Subjects or Subjects from a Foreign Culture.

Local Requirements:

If you will conduct research at an international location, identify and describe:

- relevant local regulations
- data privacy regulations
- applicable laws
- ethics review requirements for human subject protection

Please provide links or sources where possible. If the project has been or will be reviewed by a local ethics review board, attach a copy in the “Additional Information/Materials” section. You may also consult the current edition of the International Compilation of Human Research Standards

Does your study involve **HIV/AIDS research and/or screening for other reportable diseases (e.g., Hepatitis C, etc…)**?

(•) Yes ( ) No

HIV/AIDS Research

If you have questions about what constitutes a reportable disease and/or condition in the state of Kentucky, see ORI's summary sheet: "Reporting Requirements for Diseases and Conditions in Kentucky" [PDF].

HIV/AIDS Research: There are additional IRB requirements for designing and implementing the research and for obtaining informed consent. Describe additional safeguards to minimize risk to subjects in the space provided below.

For additional information, visit the online IRB Survival Handbook to download a copy of the "Medical IRB's requirements for Protection of Human Subjects in Research Involving HIV Testing" [D65.0000] [PDF], and visit the Office for Human Research Protections web site for statements on AIDS research, or contact the Office of Research Integrity at 859-257-9428.

HIV testing will be carried out using the rapid-rapid protocol recently approved for HIV surveillance and confirmatory testing by the Kentucky Department for Public Health and CDC. KY DPH guidelines on this were released in April 2016 (see http://chfs.ky.gov/dph/epi/HIVAIDS/prevention.htm). First, participants will be tested using rapid INSTI HIV 1/HIV 2 Rapid AntibodyTest (bioLytical Laboratories, USA), which is a manually performed, visually read, 60-second immunoassay for the detection of HIV-1 and HIV-2 antibodies in blood obtained from finger stick (sensitivity: 99.6, specificity: 99.3). This test will be followed by Sure Check® HIV-1/2 Antibody Test (ChemBio Diagnostic Laboratories, Medford, NY) on blood obtained from finger stick (sensitivity: 99.8, specificity: 99.9). These tests are approved for use in rapid testing in non-clinical settings by CDC (https://www.cdc.gov/hiv/pdf/testing/rapid-hiv-tests-non-clinical.pdf). Post test HIV counseling will be used, per CDC protocols. All interviewers will attend an HIV certification program offered by the Kentucky Cabinet for Health and Family Services to become certified HIV counselors. In addition, all interviewers will attend in-house training sessions at the Kentucky Department for Public Health on how to use the INSTI and SureCheck HIV 1/2 Test specimen collection kits, and OraQuick® HCV Rapid Antibody Test.

All research participants will be consented with the IRB approved interviewing consent form to ensure that they are informed of limitations to confidentiality about the self-reported data they provide. Under the terms of Kentucky statute, the legal duty falls on medical personnel responsible for diagnosing and treating HIV, not non-medical staff who are involved as epidemiological researchers (see 902 KAR 2:020). However, we will report infections to the state health department and participants will be informed of this in the informed consent document.

When a participant tests HIV positive on BOTH of the rapid tests, they are considered to be confirmed as HIV positive and therefore require reporting to the state health department. Participants are informed of this reporting requirement and procedures involved in a case investigation in their informed consent form. Upon a positive test, we will complete the KY DPH's HIV Case Report form found here: http://chfs.ky.gov/NR/rdonlyres/36B936F0-AD69-4B95-83A7-FE4E37201364/0/AdultCaseReportForm2016.pdf. We will fill in the participant's name and contact information, information about our facility, participant demographic data, residential data, risk behavior data, treatment history, and testing history. We will not complete the section describing children of the participant. Following protocols given to us by the state health department, we will mail the form to the state health department. Upon receipt of the form, the state health department will provide the information to the state's Disease Intervention Specialist (DIS) team and a DIS officer make contact with the participant (usually occurs within a few days). The DIS officer will meet with the participant to review the information and to initiate the process of contact tracing.

To maximize linkage to care for participants, research staff will offer to call a Patient Services Coordinator at the UK Bluegrass Care Clinic (BCC) to set up an intake appointment on the participant's behalf while the he/she is present. BCC accepts all forms of private and public insurance and has grant funding to support services for uninsured patients. The REHN will conduct facilitated referrals to a range of other needed medical and social services, with discussions during follow-up visits about additional needs and barriers to linkage to care.

People who test negative will be provided with an information sheet on local resources. The list of referral agencies will include mental health centers, substance abuse facilities and support groups, and counseling facilities. Participants will receive the name of the referral agency, location, telephone number, fee, if applicable, statement describing the agency and the work that they do. If participants wish, we will assist them to make contact with services; however, we will not disclose any information about participants to referral agencies. The consent document will also contain a statement informing participants that their name and contact information may be released without their consent to appropriate state authorities in instances that are required by state law (e.g., if they inform study staff that they are wanting to end their life or someone else's life, are abusing a child).

Biosample collection staff will undergo training on how to respond to participants who show or express psychological distress and/or suicidal or homicidal thoughts. In addition, all study staff will undergo training on how to respond to participants who show or express psychological distress and/or suicidal or homicidal thoughts (e.g., facilitated by board certified psychiatrist, Co-I Michelle Lofwall). The procedure will follow the protocol for Distressed and Suicidal/Homicidal Participants that has been a standard operating procedure in previous NIDA-funded trials (e.g., R01 DA027068).

COVID-19 Policies.
We will offer all participants in the intervention arm HIV and HCV testing. Research staff will perform testing as described above in the office. However, if a participant prefers, we will help them perform the test using a self-test kit, or we we will make a referral to a local health department.

HIV and HCV testing are only offered to participants in the intervention arm. Testing is offered in the local health departments through UK's Kentucky Income Reinvestment Program (KIRP) with UK staff based at the health departments. The Kentucky

Cabinet for Health and Family Services' Department for Public Health and UK established KIRP to improve health care delivery via disease education, prevention, treatment and professional services for persons living with HIV through collaborations with existing Ryan White HIV/AIDS funded programs and harm reduction programs at local health departments. Testing is offered through collaboration with the harm reduction programs.

For participants who prefer to test themselves, we will offer home-based (self-test)HIV and HCV testing and drug screening to be completed in-person at the study office. If the participant does not feel comfortable coming to the office or all research activities are remote only due to COVID-19 restrictions, we will offer to meet the participant at a mutually agreed-upon location or their home to complete home-based (self-test) HIV and HCV testing.

For home-based (self-test) HIV testing we will use FDA-approved OraQuick In-Home HIV Test (OraSure Technologies, Inc., Bethlehem, PA) that tests for HIV antibodies in human saliva (gum swab) with 91.67% sensitivity and 99.9% specificity, with results ready in 20 minutes. For home-based(self-test) HCV testing we will use EverlyWell HCV human antibody test (Everlywell, Inc., Austin, TX), which requires finger stick to obtain blood for a dry spot sample that will be mailed to a laboratory for processing. Both sensitivity and specificity for this test are above 99%. We will conduct saliva drug test using SalivaConfirm (TestCountry, San Diego, CA) drug screening kit that detects 10 types of illicit drugs in the sample in 10 minutes.

PI-Sponsored FDA-Regulated Research

Is this an investigator-initiated study that:

1) involves testing a Nonsignificant Risk (NSR) Device, or
2) is being conducted under an investigator-held Investigational New Drug (IND) or Investigational Device Exemption (IDE)?

○ Yes ◉ No

PI-Sponsored FDA-Regulated Research

If the answer above is yes, then the investigator assumes the regulatory responsibilities of both the investigator and sponsor. The Office of Research Integrity provides a summary list of sponsor IND regulatory requirements for drug trials [PDF], IDE regulatory requirements for SR device trials [PDF], and abbreviated regulatory requirements for NSR device trials [PDF]. For detailed descriptions see FDA Responsibilities for Device Study Sponsors or FDA Responsibilities for IND Drug Study Sponsor-Investigators.

- Describe the experience/knowledge/training (if any) of the investigator serving as a sponsor (e.g., previously held an IND/IDE); and
- Indicate if any sponsor obligations have been transferred to a commercial sponsor, contract research organization (CRO), contract monitor, or other entity (provide details or attach FDA 1571).

IRB policy requires mandatory training for all investigators who are also FDA-regulated sponsors (see Sponsor-Investigator FAQs). A sponsor-investigator must complete the applicable Office of Research Integrity web based training, (drug or device) before final IRB approval is granted.

Has the sponsor-investigator completed the mandatory PI-sponsor training prior to this submission?

○ Yes ○ No

If the sponsor-investigator has completed equivalent sponsor-investigator training, submit documentation of the content for the IRB's consideration.

Attachments

HIPAA

0 unresolved comment(s)

Is HIPAA applicable? ○ Yes ◉ No

(Visit ORI's Health Insurance Portability and Accountability Act (HIPAA) web page to determine if your research falls under the HIPAA Privacy Regulation.)

If yes, check below all that apply and attach the applicable document(s):

- ☐ HIPAA De-identification Certification Form
- ☐ HIPAA Waiver of Authorization

Attachments

STUDY DRUG INFORMATION

0 unresolved comment(s)

The term drug may include:

- FDA approved drugs,
- unapproved use of approved drugs,
- investigational drugs or biologics,
- other compounds or products intended to affect structure or function of the body, and/or
- complementary and alternative medicine products such as dietary supplements, substances generally recognized as safe (GRAS) when used to diagnose, cure mitigate, treat or prevent disease, or clinical studies of e-cigarettes examining a potential therapeutic purpose.

Does this protocol involve a drug including an FDA approved drug; unapproved use of an FDA approved drug; and/or an investigational drug?

○ Yes ◉ No

If yes, complete the questions below. Additional study drug guidance.

LIST EACH DRUG INVOLVED IN STUDY IN THE SPACE BELOW

Drug Name:

Note: Inpatient studies are required by Hospital Policy to utilize Investigational Drug Service (IDS) pharmacies (Oncology or Non-Oncology). Use of IDS is highly recommended, but optional for outpatient studies. Outpatient studies not using IDS services are subject to periodic inspection by the IDS for compliance with drug accountability good clinical practices.

Indicate where study drug(s) will be housed and managed:

☐ Investigational Drug Service (IDS) UK Hospital

Other Location:

Is the study being conducted under a valid Investigational New Drug (IND) application?

○ Yes ○ No

If Yes, list IND #(s) and complete the following:

IND Submitted/Held by:

Sponsor: ☐ Held By:

Investigator: ☐ Held By:

Other: ☐ Held By:

☐ Checkmark if the study is being conducted under FDA's Expanded Access Program (e.g., Treatment IND) or if this is an Individual Patient Expanded Access IND (FDA Form 3926).

FDA's Expanded Access Program Information for Individual Patient Expanded Access INDs, and attach the following:

- FDA Form 3926;
- FDA expanded access approval or correspondence;
- Confirmation of agreement from manufacturer or entity authorized to provide access to the product.

For guidance and reporting requirements at the conclusion of treatment see the Expanded Access SOP.

Complete and attach the required Study Drug Form picking "Study Drug Form" for the document type. Any

applicable drug documentation (e.g., Investigator Brochure; approved labeling; publication; FDA correspondence, etc.) should be attached using "Other Drug Documentation" for the document type.

Attachments

STUDY DEVICE INFORMATION

0 unresolved comment(s)

A DEVICE may be a:

- component, part, accessory;
- assay, reagent, or in-vitro diagnostic device;
- software, digital health, or mobile medical app;
- other instrument if intended to affect the structure or function of the body, diagnose, cure, mitigate, treat or prevent disease; or
- a homemade device developed by an investigator or other non-commercial entity and not approved for marketing by FDA.

For additional information, helpful resources, and definitions, see ORI's Use of Any Device Being Tested in Research web page.

Does this protocol involve testing (collecting safety or efficacy data) of a medical device including an FDA approved device, unapproved use of an approved device, humanitarian use device, and/or an investigational device?

○ Yes ◉ No

[Note: If a marketed device(s) is only being used to elicit or measure a physiologic response or clinical outcome, AND, NO data will be collected on or about the device itself, you may answer "no" above, save and exit this section, (Examples: a chemo drug study uses an MRI to measure tumor growth but does NOT assess how effective the MRI is at making the measurement; an exercise study uses a heart monitor to measure athletic performance but no safety or efficacy information will be collected about the device itself, nor will the data collected be used for comparative purposes against any other similar device).]

If you answered yes above, please complete the following questions.

LIST EACH DEVICE BEING TESTED IN STUDY IN THE SPACE BELOW

Device Name:

Is the study being conducted under a valid Investigational Device Exemption (IDE), Humanitarian Device Exemption (HDE) or Compassionate Use?

○ Yes ○ No

If Yes, complete the following:
IDE or HDE #(s)

IDE/HDE Submitted/Held by:

Sponsor: ☐ Held By:

Investigator: ☐ Held By:

Other: ☐ Held By:

☐ Check if this is a Treatment IDE or Compassionate Use under the Food and Drug Administration (FDA) Expanded Access program.

For Individual or Small Group Expanded Access, see FDA's Early Expanded Access Program Information, and attach the following:

- FDA expanded access approval or sponsor's authorization;
- An independent assessment from an uninvolved physician, if available;
- Confirmation of agreement from manufacturer or entity authorized to provide access to the product.

For guidance and reporting requirements at the conclusion of treatment see the Medical Device SOP.

Does the intended use of any research device being tested (not clinically observed) in this study meet the regulatory definition of Significant Risk (SR) device?

- Yes. Device(s) being tested in this study presents a potential for serious risk to the health, safety, or welfare of a subject and (1) is intended as an implant; or (2) is used in supporting or sustaining human life; or (3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.
- No. All devices being tested in this study do not present a potential for serious risk to the health, safety, or welfare of subjects/participants.

Complete and attach the required Study Device Form, picking the "Study Device Form" for the document type. Any applicable device documentation (e.g., Manufacturer information; patient information packet; approved labeling; FDA correspondence, etc.) should be attached using "Other Device Documentation" for the document type.

Attachments

RESEARCH SITES

0 unresolved comment(s)

To complete this section, ensure the responses are accurate then click "SAVE".

A) Check all the applicable sites listed below at which the research will be conducted. If none apply, you do not need to check any boxes.

UK Sites

- ☐ UK Classroom(s)/Lab(s)
- ☐ UK Clinics in Lexington
- ☐ UK Clinics outside of Lexington
- ☐ UK Healthcare Good Samaritan Hospital
- ☐ UK Hospital

Schools/Education Institutions

- ☐ Fayette Co. School Systems *
- ☐ Other State/Regional School Systems
- ☐ Institutions of Higher Education (other than UK)

***Fayette Co. School systems, as well as other non-UK sites, have additional requirements that must be addressed. See ORI's IRB Application Instructions - Off-site Research web page for details.**

Other Medical Facilities

- ☐ Bluegrass Regional Mental Health Retardation Board
- ☐ Cardinal Hill Hospital
- ☐ Eastern State Hospital
- ☐ Norton Healthcare
- ☐ Nursing Homes
- ☐ Shriner's Children's Hospital
- ☐ Veterans Affairs Medical Center
- ☐ Other Hospitals and Med. Centers

- ☑ Correctional Facilities
- ☐ Home Health Agencies
- ☐ International Sites

Research activities conducted at performance sites that are not owned or operated by the University of Kentucky, at sites that are geographically separate from UK, or at sites that do not fall under the UK IRB's authority, are subject to special procedures for coordination of research review. Additional information is required (see IRB Application Instructions - Off-Site Research web page), including:

- A letter of support and local context is required from non-UK sites. See *Letters of Support and Local Context* on the IRB Application Instructions - Off-Site Research web page for more information.
- Supportive documentation, including letters of support, can be attached below.
- NOTE: If the non-UK sites or non-UK personnel are engaged in the research, there are additional federal and university requirements which need to be completed for their participation. For instance, the other site(s) may need to complete their own IRB review, or a cooperative review arrangement may need to be established with non-UK

sites.
- Questions about the participation of non-UK sites/personnel should be discussed with the ORI staff at (859) 257-9428.

List all other non-UK owned/operated locations where the research will be conducted:

Local health departments, government offices, substance use treatment facilities, social service agencies, jails, and prisons that serve the following counties: Perry, Leslie, Knott, Letcher, Morgan, Elliott, Rowan, Owsley, Lee, Wolfe, Menifee, and Bath); UK-leased field offices in Morehead and Hazard.

The sites are where we will meet participants to conduct interviews; sites are not "engaged" in the researcher.

Describe the role of any non-UK site(s) or non-UK personnel who will be participating in your research.

Karma Plaisance is an MPH student who will be analyzing data for her thesis.

Attachments

Attach Type	File Name
-IRB Authorization Agreement	Young IAA Emory.pdf
-Letter of Support & Local Context	LOS - Appalachian Wellness Center.pdf

B) Is this a multi-site study for which **you are the lead investigator or UK is the lead site**? ○ Yes ◉ No

If YES, describe the plan for the management of reporting unanticipated problems, noncompliance, and submission of protocol modifications and interim results from the non-UK sites:

C) If your research involves collaboration with any sites and/or personnel outside the University of Kentucky, then it is considered multisite research and IRB reliance issues will need to be addressed. This may include national multi-center trials as well local studies involving sites/personnel external to UK. If you would like to request that the University of Kentucky IRB (UK IRB) serve as the lead IRB for your study, or if you would like the UK IRB to defer review to another IRB, please contact the IRBReliance@uky.edu.

RESEARCH ATTRIBUTES

0 unresolved comment(s)

Indicate the items below that apply to your research. Depending on the items applicable to your research, you may be required to complete additional forms or meet additional requirements. Contact the ORI (859-257-9428) if you have questions about additional requirements.

☐ Not applicable

Check All That Apply

	For additional requirements and information:
☐ Academic Degree/Required Research	• Cancer Research (MCC PRMC) • Certificate of Confidentiality (look up "Confidentiality/Privacy...") • CCTS (Center for Clinical and Translational Science)
☑ Alcohol/Drug/Substance Abuse Research	• Clinical Research (look up "What is the definition of....)
☐ Biological Specimen Bank Creation (for sharing)	• Clinical Trial
☐ Cancer Research	• Collection of Biological Specimens for Banking (look up "Specimen/Tissue Collection. ")
☐ CCTS-Center for Clinical & Translational Science	• Collection of Biological Specimens (look up "Specimen/Tissue Collection. ")
☑ Certificate of Confidentiality	• Community-Based Participatory Research (look up "Community-Engaged. ")
☐ Clinical Research	• Data & Safety Monitoring Board (DSMB) *For Medical IRB: Service Request Form for CCTS DSMB
☐ Clinical Trial - Phase 1	
☑ Clinical Trial	
☐ Collection of Biological Specimens for internal banking and use (not sharing)	• Data & Safety Monitoring Plan
☐ Community-Based Participatory Research	• Deception* *For deception research, also go to the E-IRB Application Informed Consent section, checkmark and complete "Request for Waiver of Informed Consent Process"
☐ Deception	
☐ Educational/Student Records (e.g., GPA, test scores)	
☐ Emergency Use (Single Patient)	• Emergency Use (Single Patient) [attach Emergency Use Checklist] (PDF)
☐ Gene Transfer	• Genetic Research (look up "Specimen/Tissue Collection. ")
☐ Genetic Research	• Gene Transfer
☐ GWAS (Genome-Wide Association Study) or NIH Genomic Data Sharing (GDS)	• HIV/AIDS Research (look up "Reportable Diseases/Conditions") • Screening for Reportable Diseases [E2.0000] (PDF)
☐ Human Cells, Tissues, and Cellular and Tissue Based Products	• International Research (look up "International & Non-English Speaking")
☐ Individual Expanded Access or Compassionate Use	• NIH Genomic Data Sharing (GDS) Policy (PDF)
☐ International Research	• Planned Emergency Research Involving Waiver of Informed Consent* *For Planned Emergency Research Involving Waiver of Informed Consent, also go to the E-IRB Application Informed Consent section, checkmark and complete "Request for Waiver of Informed Consent Process"
☐ Planned Emergency Research Involving Exception from Informed Consent	
☐ Recombinant DNA	
☐ Registry or data repository creation	
☐ Stem Cell Research	
☐ Suicide Ideation or Behavior Research	• Use, storage and disposal of radioactive material and radiation producing devices
☑ Survey Research	
☐ Transplants	
☐ Use, storage and disposal of radioactive material and radiation producing devices	
☐ Vaccine Trials	

FUNDING/SUPPORT

0 unresolved comment(s)

If the research is being submitted to, supported by, or conducted in cooperation with an external or internal agency or funding program, indicate below all the categories that apply.

☐ Not applicable

Check All That Apply

- ☑ Grant application pending
- ☑ (HHS) Dept. of Health & Human Services
  - ☑ (NIH) National Institutes of Health
  - ☑ (CDC) Centers for Disease Control & Prevention
  - ☐ (HRSA) Health Resources and Services Administration
  - ☑ (SAMHSA) Substance Abuse and Mental Health Services Administration
- ☐ (DoJ) Department of Justice or Bureau of Prisons
- ☐ (DoE) Department of Energy
- ☐ (EPA) Environmental Protection Agency
- ☑ Federal Agencies Other Than Those Listed Here
- ☐ Industry (Other than Pharmaceutical Companies)
- ☐ Internal Grant Program w/ proposal
- ☐ Internal Grant Program w/o proposal
- ☐ National Science Foundation
- ☐ Other Institutions of Higher Education
- ☐ Pharmaceutical Company
- ☐ Private Foundation/Association
- ☐ U.S. Department of Education
- ☐ State

Other:

Appalachian Regional Commission

Click applicable listing(s) for additional requirements and information:

- (HHS) Dept. of Health & Human Services
- (NIH) National Institutes of Health
- (CDC) Centers for Disease Control & Prevention
- (HRSA) Health Resources & Services Administration
- (SAMHSA) Substance Abuse & Mental Health Services Administration
- Industry (Other than Pharmaceutical Companies) [IRB Fee Info]
- National Science Foundation
- (DoEd) U.S. Department of Education
- (DoJ) Department of Justice or Bureau of Prisons
- (DoE) Department of Energy Summary and Department of Energy Identifiable Information Compliance Checklist
- (EPA) Environmental Protection Agency

Specify the funding source and/or cooperating organization(s) (e.g., National Cancer Institute, Ford Foundation, Eli Lilly & Company, South Western Oncology Group, Bureau of Prisons, etc.):

The project is biphasic in design, as required by the NIH UG3/UH3 funding structure, with a 2-year assessment phase (UG3) followed by a 3-year intervention phase (UH3) that is informed by results of the assessment. The UG3 phase began in August 2017 and is described in the approved IRB protocol # 43520. The current IRB protocol covers the 3-year UH3 phase which begins August 1, 2019. UH3 funding is with the National Institute on Drug Abuse. The initiative is co-funded by NIH, CDC, SAMHSA, and the Appalachian Regional Commission.

Add Related Grants

If applicable, please search for and select the OSPA Account number or Electronic Internal Approval Form (eIAF) # (notif #) associated with this IRB application using the "Add Related Grants" button.
If required by your funding agency, upload your grant using the "Grant/Contract Attachments" button.

Add Related Grants

Grant/Contract Attachments

The research involves use of Department of Defense (DoD) funding, military personnel, DoD facilities, or other DoD resources. (See DoD SOP and DoD Summary for details)

○ Yes ◉ No

Using the “attachments” button (below), attach applicable materials addressing the specific processes described in the DoD SOP.

DOD SOP Attachments

Additional Certification: (If your project is federally funded, your funding agency may request an Assurance/ Certification/Declaration of Exemption form.) Check the following if needed:

☐ Protection of Human Subjects Assurance/Certification/Declaration of Exemption (Formerly Optional Form – 310)

Assurance/Certification Attachments

OTHER REVIEW COMMITTEES

0 unresolved comment(s)

If you check any of the below committees, additional materials may be required with your application submission.

Does your research fall under the purview of any of the other review committees listed below? [*If yes, check all that apply and attach applicable materials using the attachment button at the bottom of your screen.*]

○ Yes ◉ No

Additional Information

- ☐ Institutional Biosafety Committee
- ☐ Radiation Safety Committee
- ☐ Radioactive Drug Research Committee
- ☐ Markey Cancer Center (MCC) Protocol Review and Monitoring Committee (PRMC)
- ☐ Graduate Medical Education Committee (GME)
- ☐ Office of Medical Education (OME)

- Institutional Biosafety Committee (IBC) - Attach required IBC materials
- Radiation Safety Committee (RSC) - For applicability, see instructions and attach form
- Radioactive Drug Research Committee (RDRC)
- Markey Cancer Center (MCC) Protocol Review and Monitoring Committee (PRMC)** - Attach MCC PRMC materials, if any, per instructions.
- Office of Medical Education (OME)
- Graduate Medical Education Committee (GME)

Attachments

**** If your study involves cancer research, be sure to select "Cancer Research" in the "Research Attributes" section.** ORI will send your research protocol to the Markey Cancer Center (MCC) Protocol Review and Monitoring Committee (PRMC). The MCC PRMC is responsible for determining whether the study meets the National Cancer Institute (NCI) definition of a clinical trial and for issuing documentation to you (the investigator) which confirms either that PRMC approval has been obtained or that PRMC review is not required. Your IRB application will be processed and reviewed independently from the PRMC review.

ADDITIONAL INFORMATION/MATERIALS

0 unresolved comment(s)

Do you want specific information inserted into your approval letter? ○ Yes ◉ No

Approval Letter Details:

If you wish to have specific language included in your approval letter (e.g., serial #, internal tracking identifier, etc…), type that language in the box below exactly as it should appear in the letter. The text you enter will automatically appear at the top of all approval letters, identical to how you typed it, until you update it. Don't include instructions or questions to ORI staff as those will appear in your approval letter. **If these details need to be changed for any reason, you are responsible for updating the content of this field.**

Additional Materials:

If you have other materials you would like to include for the IRB's consideration, check all that apply and attach the corresponding documents using the Attachments button below.

- ☐ Detailed protocol
- ☐ Dept. of Health & Human Services (DHHS) approved protocol (such as NIH sponsored Cooperative Group Clinical Trial)
- ☐ Other Documents

Protocol/Other Attachments

Attach Type	File Name
Other	Summary of Adverse and Serious Adverse Events.pdf
Other	Modification Request Memo 092123.pdf

NOTE: [Instructions for Dept. of Health & Human Services (DHHS)-approved protocol]

If you have password protected documents, that feature should be disabled prior to uploading to ensure access for IRB review.

To view the materials currently attached to your application, click “All Attachments” on the left menu bar.

SIGNATURES (ASSURANCES)

0 unresolved comment(s)

Introduction

All IRB applications require additional assurances by a Department Chairperson or equivalent (DA), and when applicable, a Faculty Advisor or equivalent (FA). This signifies the acceptance of certain responsibilities and that the science is meritorious and deserving of conduct in humans. The person assigned as DA *should not* also be listed in the Study Personnel section, and the individual assigned as FA *should* be listed in the Study Personnel section.

For a list of responsibilities reflected by signing the Assurance Statement, refer to "What does the Department Chairperson's Assurance Statement on the IRB application mean?"

For a detailed illustration of how to complete this section, please review the short online video tutorial "Signatures (Assurance) Section - How to Complete." Otherwise, follow the steps below.

Required Signatures:

First Name	Last Name	Role	Department	Date Signed	
April	Young	Principal Investigator	Dept Of Epidemiology	07/03/2019 12:17 PM	View/Sign
Erin	Haynes	Department Authorization	Dept Of Epidemiology	07/03/2019 01:34 PM	View/Sign

Principal Investigator's Assurance Statement

I understand the University of Kentucky's policies concerning research involving human subjects and I agree:

1. To comply with all IRB policies, decisions, conditions, and requirements;
2. To accept responsibility for the scientific and ethical conduct of this research study;
3. To obtain prior approval from the Institutional Review Board before amending or altering the research protocol or implementing changes in the approved consent/assent form;
4. To report to the IRB in accord with IRB/IBC policy, any adverse event(s) and/or unanticipated problem(s) involving risks to subjects;
5. To complete, on request by the IRB for Full and Expedited studies, the Continuation/Final Review Forms;
6. To notify the Office of Sponsored Projects Administration (OSPA) and/or the IRB (when applicable) of the development of any financial interest not already disclosed;
7. Each individual listed as study personnel in this application has received the mandatory human research protections education (e.g., CITI);
8. Each individual listed as study personnel in this application possesses the necessary experience for conducting research activities in the role described for this research study.
9. To recognize and accept additional regulatory responsibilities if serving as both a sponsor and investigator for FDA regulated research.

☑ Furthermore, by checking this box, I also attest that:

- I have appropriate facilities and resources for conducting the study;
- I am aware of and take full responsibility for the accuracy of all materials submitted to the IRB for review;
- If applying for an exemption, I also certify that the only involvement of human subjects in this research study will be in the categories specified in the Protocol Type: Exemption Categories section.
- If applying for an Abbreviated Application (AA) to rely on an external IRB, I understand that certain items above (1, 3, 4, 7-8) may not apply, or may be altered due to external institutional/IRB policies. I document my agreement with the Principal Investigator Reliance Assurance Statement by digitally signing this application.

*You will be able to "sign" your assurance after you have sent your application for signatures (use Submission section). Please notify the personnel required for signing your IRB application after sending for signatures. Once all signatures have been recorded, you will need to return to this section to submit your application to ORI.

Department Authorization

☑ This is to certify that I have reviewed this research protocol and that I attest to the scientific validity and importance of this study; to the qualifications of the investigator(s) to conduct the project and their time available for the project; that facilities, equipment, and personnel are adequate to conduct the research; and that continued guidance will be provided as appropriate. When the principal investigator assumes a sponsor function, the investigator has been notified of the additional regulatory requirements of the sponsor and by signing the principal investigator Assurance Statement, confirms he/she can comply with them.

*If the Principal Investigator is also the Chairperson of the department, the Vice Chairperson or equivalent should complete the "Department Authorization".

**IF APPLICABLE FOR RELIANCE: I attest that the principal investigator has been notified of the regulatory requirements of both the Reviewing and Relying IRBs, according to the information provided in the E-IRB application. The attached Reliance Assurance Statement, signed by the principal investigator, confirms that he/she can comply with both sets of IRB requirements.

SUBMISSION INFORMATION

0 unresolved comment(s)

Each Section/Subsection in the menu on the left must have a checkmark beside it (except this Submission section) indicating the Section/Subsection has been completed. Otherwise your submission for IRB review and approval cannot be sent to the Office of Research Integrity/IRB.

If applicable, remember to update the Approval Letter Details text box under the Additional Information section

If your materials require review at a convened IRB meeting which you will be asked to attend, it will be scheduled on the next available agenda and you will receive a message to notify you of the date.

If you are making a change to an attachment, you need to delete the attachment, upload a highlighted version that contains the changes (use Document Type of "Highlighted Changes"), and a version that contains the changes without any highlights (use the appropriate Document Type for the item(s)). Do **not** delete approved attachments that are still in use.

Your protocol has been submitted.

Statistical Design and Power

We will explore intervention effects on PWUD using: (1) longitudinal quantitative data from START-C2H participants; and (2) qualitative data with PWUD START-C2H participants about the intervention's perceived effectiveness, and the perceived pathways through which it operates.

Exploratory Quantitative Analysis of START-C2H survey data:

Our community randomized trial consists of clustered data with participants nested within counties. To account for this "doubly-repeated" measures design, we will analyze all results using generalized linear mixed models. The covariance matrix for all observations within a county may be written as the Kronecker product of the compound symmetric covariance matrix for participants nested within county and a 2 by 2 residual covariance matrix for repeated measures nested within participants. Implementing the covariance model can be done in both PROC MIXED (for continuous measures) and PROC GLIMMIX (for categorical measures) in SAS by specifying a random intercept for county, and a compound symmetric residual matrix across time (repeated measures within participant). To estimate change in our primary outcomes due to the intervention we will begin by analyzing models of the following form: $g(y)=\beta 0 + \beta 1 Time + \beta 2 Int + \beta 3 Time*Int$ where g() represents the appropriate link function for outcome y, Time is a pre-post indicator variable , and Int is an indicator for the intervention group. The parameter of primary interest is β3, the difference in slope between the intervention and control group. While our primary outcomes can be approximated as normally distributed, the link function g() will be modified as necessary to properly model the distribution for each outcome.

Missing Data. We will use multiple imputation to account for non-response over time and potential attrition. Additional augmentation variables found to be predictive of missingness will also be included in the imputation model. Ten imputations will be implemented. Additionally, we will use multiple imputation by chained equations to allow for imputation of non-normally distributed variables. All imputation analyses will be done using PROC MI and PROC MIANALYZE in SAS.

Power. We estimated the statistical power to preliminarily detect a change in our outcomes using PROC GLMPOWER in SAS v9.4., accounting for autocorrelation within participants and nesting within counties. We estimate power for a multivariate model equivalent to our planned repeated measures models previously described. Because these analyses are exploratory (due to the smaller-than-anticipated sample size), we set the alpha to 0.10. Based on existing data, we assume a within-county ICC of 0.05 and a within-person autocorrelation of 0.35. We estimate power for all outcomes as approximately Gaussian. We further assume a type-1 error rate of 0.10, 12 counties, and 20 participants per county. At these sample sizes and with an exploratory p-value=0.10, we achieve statistical power of 0.80 for standardized mean of 0.55, or moderate sized effects with an alpha=0.10.

Qualitative data analysis with START-C2H intervention cohort:

Qualitative Analysis Plan: We will use constructivist grounded theory (CGT) methods to develop grounded theories about the perceived relationships and pathways linking (or failing to link) the intervention and changes in primary and secondary outcomes (or lack thereof). CGT provides rigorous methods that will (1) foster *discovery*; (2) elicit *rich descriptions* of participants' experiences of primary and secondary outcomes and of each intervention component; (3) support the creation of *grounded theories* about *perceived pathways* through which these phenomena influence one another; and (4) support comparisons of #1-#3 by participant age gender etc. We will use 3 CGT stages: open coding, axial coding, and theoretical coding.

Open coding: The open coding stage is designed to develop a rich understanding of salient phenomena by systematically and comprehensively labelling and defining concepts of interest in the transcripts. In the open coding process, Cooper and the GRA will iterate between developing code labels, code definitions, and codebooks independently (to enhance feasibility), and meeting to develop consensus (to enhance validity); they will double code every 3rd transcript. Line-by-line analyses, conducted in NVIVO, will both explore intervention components and primary and secondary outcomes, and also be open to discovering new phenomena that are salient to the aims.

Axial Coding: The purpose of Axial Coding is to develop high-level categories that are more abstract than the "open coded" phenomena, and are both internally coherent and distinct from one another. During Axial Coding, categories are defined, and their properties and dimensions identified (i.e., their characteristics and the ways in which they vary, respectively). The GRA and Cooper will iterate between independent analyses of open-coded transcripts, and consensus building about emerging learnings. They will independently develop a Category Memo for each emerging category that (1) defines it; (2) identifies and defines its properties and dimensions and possible subcategories; (3) inventories associated codes; and (4) describes how the category differs from other similar categories under development. Cooper and the GRA will meet weekly to review one another's emerging findings and memos, and develop a suite of consensus categories,

definitions, properties, and dimensions. Categories will be expanded as additional transcripts undergo open coding, and offer new evidence.

Theoretical coding: Theoretical coding is designed to develop grounded theories that describe how categories relate to one another along properties and dimensions. Here, grounded theories will explore the perceived pathways through which each intervention component is affecting each outcome, and also explore ruptures in anticipated pathways (e.g., perhaps FTS distribution does not seem to protect against overdose). We expect to have a separate grounded theory for each intervention component →outcome dyad. We will start with foundational analytic questions, drawn from CGT: *What are the perceived pathways through which specific intervention components "**C**ause" change in specific outcomes? What **C**ontingencies must be present for these pathways to operate? What **C**onditions rupture the pathways linking an intervention component to an outcome?* Cooper and the GRA will start by examining 3 axially coded transcripts for participants' perspectives on answers to these questions, developing "relational statements" that provisionally answer them. *Relational Statements* succinctly describe relationships between or among two or more categories along their properties and dimensions. We will test each relational statement using a chart, in which each axis is a property that ranges along a particular dimension. In some cases, participants will have "off diagonal" experiences. These "off diagonal" participants are opportunities to deepen the analysis by exploring whether categories or their posited relationships need to be amended. Learnings will be recorded in Relational Memos.

We will use the constant comparison method to systematically compare findings across participant subgroups (e.g., defined by gender, houselessness status). To support these comparisons, we will color-code each relational chart by these subgroup characteristics. When we find variation across subgroups, we will return to the data to identify conditions and contingencies that may explain these variations, and expand relational statements accordingly, or the categories they link. As needed, we will present different sets of relational statements for specific subgroups. These relational statements will form the foundations of grounded theories exploring perceptions of each intervention component's effect on each outcome, and the pathways through which it does (or does not) operate to change primary and secondary outcomes, for particular subgroups.

Triangulating across qualitative and quantitative findings: We will use joint displays to systematically compare and contrast qualitative and quantitative findings for each intervention component/outcome relationship (e.g., preliminary [i.e., $p<0.10$] hypothesis test results about the relationship of receiving FTS to subsequent overdose vs. qualitative grounded theory about this same relationship). When qualitative and quantitative findings both suggest an ameliorative relationship, we will conclude that the available evidence supports a beneficial effect. When both find an adverse relationship, we will conclude that the evidence indicates a harmful effect. When neither suggests a relationship, we will conclude that the evidence indicates no effect. When quantitative and qualitative results diverge, we will return to the qualitative and quantitative data to learn if we can resolve this discrepancy. Qualitative data may illuminate an unexpected confounder for the quantitative hypothesis test. Alternatively, qualitative data may suggest that the intervention only has an effect in one subgroup (e.g., individuals residing in counties with more services) and the quantitative findings reach a null conclusion because the quantitative sample is small, and includes both people who do and do not live in such counties. We will seek to systematically explore all divergences using these tables, and seek to refine relational statements and grounded theories accordingly. We will rely solely on qualitative data to learn whether the intervention effect is attenuated in a subgroup (e.g., women), given that the quantitative sample is underpowered to detect effect moderation.