PROTOCOL AND STATISTICAL ANALYSIS PLAN

Study Title: Consultation, Advice, and Tailored Support (CATS) for Cancer Survivors; MCC-17-1495-P3K

Institution/Site:	University of Kentucky
Document (Approval/Update) Date:	02/21/21
NCT Number:	NCT03316170
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Coversheet created:	03/22/21

PROTOCOL TYPE

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Which IRB

- (•) Medical ( ) NonMedical

Protocol Process Type

- ( ) Exemption
- (•) Expedited (Must be risk level 1)
- ( ) Full

IMPORTANT NOTE: Once you have saved your choices under "Which IRB" and "Protocol Process Type", you will not be able to change your selections. If you select the wrong IRB Type and/or your application is deemed eligible for a different Protocol Process Type, it may be necessary to create a new application.

Please see below for guidance on which selections to make, and/or go to ORI's "Getting Started" web page. If you still have questions about which IRB or Protocol Process Type to choose, please contact the Office of Research Integrity (ORI) at 859-257-9428 **prior** to saving your selections.

Which IRB

The **Medical IRB** reviews research emanating from the Colleges of Dentistry; Health Sciences; Medicine; Nursing; Pharmacy and Health Sciences; and Public Health.

The **Nonmedical IRB** reviews research originating from the Colleges of Agriculture; Arts & Sciences; Business & Economics; Communication & Information; Design; Education; Engineering; Fine Arts; Law; and Social Work. The Nonmedical IRB does not review studies that involve administration of drugs, testing safety or effectiveness of medical devices, or studies that involve invasive medical procedures, regardless of from what college the application originates.

Which Protocol Process Type

Under federal regulations, an investigator's application to conduct a research project involving human subjects can be processed by the IRBs in three ways:

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

The preliminary determination that a research project is eligible for exemption certification or expedited review is made by the investigator. For assistance in determining which review process type your IRB application is eligible for, please go to ORI's "Getting Started" web page.

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 (21 CFR Part 312) 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 (21 CFR Part 812) 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- 21 CFR 812.2(c)
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 [PDF] 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." 45 CFR 46.402(a) 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 collected or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). (Note: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)

☐ 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 45 CFR 46.101 (b)(2) and (b)(3). This listing refers only to research that is not exempt.)

PROJECT INFORMATION

0 unresolved comment(s)

Title of Project: (If applicable, use the exact title listed in the grant/contract application). *** Effective 4/16/2020: If your research involves investigating any aspect of COVID-19, please enter "COVID19" at the start of your Project and Short Titles ***

Consultation, Advice, and Tailored Support (CATS) for Cancer Survivors

Short Title Description

Note: "Short Title" should consist of a couple key words to easily identify your study - these key words (rather than the whole title) will be displayed on the Dashboard in the listing for your study.

CATS for Cancer Survivors

Anticipated Ending Date of Research Project: 7/31/2022

Number of human subjects (or records/specimens reviewed): 80

Study is/will be open to new subject enrollment or 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 [45 CFR 46.102(i)]

Download UK's guidance document on assessing the research risk for additional information on risk [PDF]

SUBJECT DEMOGRAPHICS

0 unresolved comment(s)

Age level of human subjects: (i.e., 6 mths.; 2yrs., etc..) 18 years to 75 years

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):

Enter Numbers Only!

Ethnic Origin	#Male	#Female
American Indian/Alaskan Native:	0	0
Asian:	0	1
Black/African American:	2	4
Hispanic/Latino:	1	1
Native Hawaiian/Pacific Islander:	0	0
White/Caucasian:	20	48
Other or Unknown:	1	2

If unknown, please explain why:

Indicate the categories of subjects and controls to be included in the study. Depending on the subject category applicable to your research you may be required to complete additional forms. [Note, if the study does not involve direct intervention or direct interaction with subjects, (e.g., record-review research, outcomes registries), do not check mark populations which the research does not specifically target. For instance, a large record review of a diverse population may incidentally include a prisoner or an international citizen, but, if the focus or intent of the study has nothing to do with that status, you do not need to check those category(ies).]

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

ADDITIONAL INFORMATION:

Please visit the IRB Survival Handbook under the named topic:

- Children/Emancipated Minors
- Students as Subjects
- Prisoners
- Impaired Consent Capacity Adults: Link to required Form

And/Or:

Adults
☐ Pregnant Women/Neonates/Fetal Material
☐ Prisoners
☐ Non-English Speaking
☐ International Citizens
☐ Normal Volunteers
☐ Military Personnel and/or DoD Civilian Employees
☑ Patients
☑ Appalachian Population

- UKMC Residents or House Officers [see requirement of GME]
- Non-English Speaking [see instructions for recruitment and E-IRB Research Description section on same topic]
- International Citizens [HTML] (DoD SOP may apply [PDF])
- Military Personnel and/or DoD Civilian Employees (DoD SOP may apply [PDF])

The next questions involve assessment of the study relative to 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). (you will not need to answer the impaired consent capacity questions)

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

○ Yes ◉ No

If Yes, go to the following link and complete and attach the indicated form unless you are filing for an exemption certification: https://ris.uky.edu/ori/oriforms/formt/Scale.asp

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

INFORMED CONSENT/ASSENT PROCESS/WAIVER

0 unresolved comment(s)

For 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 revise to be in accord with your research project.

Additional Resources:

- Sample Repository/Registry/Bank Consent (Word)
- Instructions for Proposed Informed Consent Document
- Instructions for Proposed Assent Form

Consent/Assent Tips:

- **If you have multiple consent documents, be sure to upload each individually (not all in a combined file).**
- **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**
  - **"Sponsor's Sample Consent Form".**

How to Get the Informed Consent Section Check Mark

1. **You must check the box for at least one of the consent items and/or check mark one of the waivers, then if applicable attach the corresponding document(s) as a PDF (if open to enrollment).**
2. **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 check mark the "Stamped Consent Doc(s) Not Needed".**
3. **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)
- ☐ Assent Form
- ☐ Cover Letter (for survey/questionnaire research)
- ☐ Phone Script
- ☐ Informed Consent/HIPAA Combined Form
- ☐ Debriefing and/or Permission to Use Data Form
- ☐ Sponsor's sample consent form for Dept. of Health and Human Services (DHHS)-approved protocol
- ☑ Stamped Consent Doc(s) Not Needed

Attachments

Attach Type	File Name
Informed ConsentHIPAA Combined Form	KLCR C Consent & HIPAA Authorization, clean.pdf

☐ Request for Waiver of Informed Consent Process

If you are requesting IRB approval for waiver of the requirement for the informed consent process, or alteration of some or all of the elements of informed consent (i.e. medical record review, deception research, or collection of biological specimens), 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 waiver of the requirement for the informed consent process.

☐ I am requesting 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.

The IRB may consider your request provided that **all** of the following conditions apply to your research and are appropriately justified. Explain in the space provided for each condition how it 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.

☐ Request for Waiver of Documentation of Informed Consent Process

If you are requesting IRB approval for waiver of the requirement for documentation of informed consent (i.e. telephone survey or mailed survey, internet research, or certain international research), **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 (i.e., 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 (i.e. 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, and 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, and explain in the space provided how your study meets the criteria for the selected regulatory option.

Note: The IRB cannot waive the requirement for documentation or alter the consent form for FDA-regulated research unless it meets Option #2 below. FDA does not accept Option #1.

Note: Even if a waiver of the requirement for documentation is approved by the IRB, participants must still be provided oral or written (e.g., cover letter) information including all required and appropriate elements of consent so they have the knowledge and opportunity to consider whether or not to participate. To help ensure required elements are included in your consent document, please use the **Cover Letter Template** as a guide: *English*- [WORD], Spanish- [WORD] The cover letter template was developed specifically for survey/questionnaire research; however, it may be useful as a guide for developing a consent document for other types of research as well.

○ **Option 1**

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**

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

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):

○ **Option 3**

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.

RESEARCH DESCRIPTION

0 unresolved comment(s)

****!!!PLEASE READ!!!** Known Issue: The below text boxes do not allow symbols, web addresses, or special characters (characters on a standard keyboard should be ok). If something is entered that the text boxes don't allow, user will lose unsaved information.**

Workaround(s):

- **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 the information with your application. During the document upload process, you will be able to provide a brief description of the attachment.**

Background: Provide an introduction and background information. Describe past experimental and/or clinical findings leading to the formulation of your study. For research involving investigational drugs, describe the previously conducted animal and human studies. You may reference grant application/sponsor's relevant protocol pages and attach as an appendix in the E-IRB "Additional Information" section, however, a summary paragraph must be provided in the text box below. For research that involves FDA approved drugs or devices, describe the FDA approved uses of this drug/device in relation to your protocol. Attach a copy of the approved labeling as a product package insert or from the Physician's Desk Reference in the applicable E-IRB "Study Drug" or "Study Device" section.

The foremost cancer professional organizations advocate for routine assessment and treatment of tobacco use among cancer survivors. Yet, smoking cessation treatment is not part of the standard of care in most cancer centers or community-based clinics and hospitals. Indeed, cancer survivors routinely describe inadequate implementation of evidence-based smoking cessation treatment by providers. Furthermore, of the small handful of adequately powered randomized clinical trials (RCTs) for smoking cessation treatments in cancer survivors, most yield non-significant treatment effects. Without question, there is need to develop smoking cessation treatments for cancer survivors that are both efficacious and scalable for real-world, population-level dissemination. For cancer survivors in rural or Appalachian areas in particular, new treatments need to engage them in the process of smoking cessation and help address unmet social support needs that might otherwise sustain smoking/undermine quitting (see grant for more info). While long-term abstinence is the key behavioral endpoint for smoking cessation, it is important to view quit attempts as a worthwhile behavioral target since so few smokers make a quit attempt in any given year and most quit attempts end in relapse. Therefore, smoking cessation induction strategies (that is, a gentle nudge or push toward a quit attempt) warrant consideration as a viable technique for how to address cancer survivors' smoking. Nicotine replacement therapy (NRT) is an efficacious smoking cessation treatment. NRT's major strengths include its accessibility (i.e., relatively low-cost, over-the-counter medication) and effectiveness that is largely independent of behavioral counseling or physician recommendation or prescription. Combination NRT (i.e., patch + acute/short-acting agent) is more effective than monotherapy, and it is a first-line treatment that doubles the odds of abstinence. The standard course of NRT is 12 weeks, but shorter durations of NRT use (inclusive of only 2-4 weeks of treatment) have demonstrated comparable effectiveness. NRT sampling involves provision of a free, brief (2-6 weeks) supply of NRT (i.e., "a NRT starter or sampling kit"), and it is a proven tactic of promoting NRT use, quit attempts, and abstinence among smokers who do and do not report current motivation to quit, and its simplicity makes it ideally suited for dissemination across diverse populations. See grant for references.

Objectives: List your research objectives. You may reference grant application/sponsor's relevant protocol pages and attach as an appendix in the E-IRB "Additional Information" section, however, a summary paragraph must be provided in the text box below.

Aim 1: Evaluate feasibility and acceptability of a new approach to smoking cessation treatment (specifically, provision of a free social support resource directory + NRT sampling toolkit) in cervical and head/neck cancer survivors with low social resources. Indicators of feasibility are recruitment and retention and indicators of acceptability are derived from a standardized measure plus knowledge and use of select social resources. Aim 2: Assess treatment efficacy for key events in the process of smoking cessation. Hypothesis 2ab: Relative to the control group, the treatment group will report greater motivation to quit and confidence in ability to quit/avoid smoking at each follow-up. Hypotheses 2c-2e: The treatment group will report a higher prevalence of any NRT use, 24-hr quit attempt, and 7-day point prevalence abstinence throughout follow-up.

Study Design: Describe the study design (e.g., single/double blind, parallel, crossover, etc.). Indicate whether or not the subjects will receive placebo medication at some point in the research procedures. Also, indicate whether or not the subjects will be randomized in this study. You may reference sponsor's protocol pages and attach as an appendix in the E-IRB "Additional Information" section, however, a summary paragraph must be provided in the text box below. (Including the study design table from a sponsor's protocol is helpful to IRB members.)

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.

Research Repositories: If the purpose of this submission is to establish a Research Repository (bank, registry) indicate whether the material you plan to collect would or would not be available from a commercial supplier, clinical lab, or established IRB approved research repository. Provide scientific justification for establishment of 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 [PDF] or the UK Research Registry Guidance [PDF]

This is a pilot (Phase II) randomized clinical trial with randomization in a 1:1 ratio. The control group will receive a brief consultation (10-15 minutes via phone) about free or low-cost resources that may help them address unmet social support needs. Additionally, a written directory of a range of social support resources will be delivered via mail. The treatment group will receive the aforesaid intervention plus brief advice to quit smoking (10-15 minutes via phone). Additionally, a written summary of the benefits of smoking cessation, evidence-based approaches to quit, and the basics of NRT in addition to a free, 2-week supply of nicotine patches and lozenges will be delivered via mail. As a pilot, this study focuses on the outcomes of feasibility (i.e., accrual and retention) and acceptability (e.g., participants' perceptions of appropriateness and effectiveness) as opposed to efficacy (though this is also important). Despite the use of an intervention, participants in this study are not "treatment seeking" smokers and the study will not be advertised as an "intervention" or "treatment" for smokers who want to quit. This is because the goal is to encourage the occurrence of quit attempts among smokers who may or may not be interested in smoking cessation in the near future as opposed to promotion of sustained abstinence among smokers who express readiness to quit. The emphasis on smoking cessation induction (that is, the inducement or promotion of a quit attempt) is an important aspect of the study design and is appropriate for smokers across the continuum of motivation to quit. Given the focus on "all comers" with respect to motivation to quit, the behavioral target of quit attempts instead of prolonged abstinence, and a minimal intervention (specifically, a 2-week supply of NRT), the period of follow-up is relatively brief (Day 0 to Day 60, or 2 months). All of the intervention components will be delivered remotely via mail or phone in order to test this intervention in the "real world" where it would be difficult for cancer survivors to travel far for smoking cessation treatment. Finally, it is important to note that biochemical verification of self-reported quit attempts will not occur (see "Alternative Methods" section of the grant for more the rationale). The anticipated start and end of enrollment is 10/01/17 and 07/31/19, respectively. The goal is to enroll 80 cervical and head/neck cancer survivors who at the time of enrollment are within 5 years from the date of cancer diagnosis. In the absence of any preliminary data, it is unknown how the final sample will be split in terms of cervical versus head/neck cancer survivors. The eligibility criteria (see Study Population) were selected to balance the needs of the study with the desire to increase generalizability of study findings to cancer survivors who are at high risk for persistent smoking (i.e., tobacco-related cancer survivors who were smokers at or near the time of cancer diagnosis; Burris et al., 2015). During the course of study participation, participants' health status may vary as a result of living with cancer and any other chronic disease. Nonetheless, this study is not expected to engender more than minimal risk to participants' physical health, as the anticipated adverse events (AE) are most likely to be mild or moderate in severity and short-term in duration (see "Potential Risks").

Attachments

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Study Population: Describe the characteristics of the subject population, such as anticipated number, age range, gender, ethnic background and health status. Identify the criteria for inclusion and exclusion. Explain the rationale for the use of special classes such as fetuses, pregnant women, children, institutionalized, adults with impaired consent capacity, prisoners, economically or educationally disadvantaged persons or others who are likely to be vulnerable.

If women or minorities are included, please address how the inclusion of women and members of minority groups and their subpopulations will help you meet your scientific objectives. Exclusion of women or minorities requires clear and compelling rationale that shows inclusion is inappropriate with respect to the health of the subjects or that inclusion is inappropriate for the purpose of the study. Cost is not an acceptable reason for exclusion except when the study would duplicate data from other sources. Women of childbearing potential should not be excluded routinely from participation in clinical research.

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;
- The proposed dates of enrollment (beginning and end);
- The proposed sample composition of subjects.

You may reference grant application/sponsor's relevant protocol pages and attach as an appendix using the below attachment button, however, a summary paragraph must be provided in the text box below.

The demographic composition of the sample should resemble the population of cervical and head/neck cancer survivors in Kentucky, within the confines of the eligibility criteria. Regarding the racial/ethnic breakdown of the sample, most participants are expected to describe themselves as White, non-Hispanic given that recent US census data indicates that 85% of all Kentucky residents are White, non-Hispanic (http://www.census.gov/). Regarding the gender breakdown of the sample, it is expected that 70% of the sample will be female. This is because cervical cancer survivors in the US population tend to report a high rate of current smoking (e.g., Coups & Ostroff, 2005), a phenomenon that should result in a relatively higher enrollment rate for (female) cervical cancer survivors as opposed to (the mixed gender group of) head/neck cancer survivors. More details about the expected demographic composition of the sample may be found in the Targeted/Planned Enrollment Table attached to this section. Finally, the operationalization of "current smoker" and both "rural" and "Appalachian" residence may be found in the "Participants" section of the grant.

Attachments

Attach Type	File Name
StudyPopulation	Inclusion Criteria Table.pdf

Subject Recruitment Methods & Privacy: Using active voice, describe plans for the identification and recruitment of subjects, including how the population will be identified, and how initial contact will be made with potential subjects by those having legitimate access to the subjects' identity and the subjects' information.

Describe the setting in which an individual will be interacting with an investigator or how and where members of the research team will meet potential participants. If applicable, describe proposed outreach programs for recruiting women, minorities, or disparate populations as participants in clinical research. Describe steps taken to minimize undue influence in recruiting potential participants.

Please note: Based upon both legal and ethical concerns, the UK IRB does not approve finder's fees or "cold call" procedures made by research staff unknown to the potential participant. The ORI/IRB does not control permission to any UK listserv, mass mailing list, etc. Investigators must secure prior approval for access and use from owners/managers.

For additional details, see topic "Recruitment of Subjects/Advertising" on ORI's IRB Survival Handbook web page and the PI Guide to Identification and Recruitment of Human Subjects for Research [PDF].

The PI will share responsibility for recruitment and enrollment (i.e., attainment of written informed consent) of eligible cancer survivors with the co-investigators and research assistants (RAs) who are authorized to obtain consent. Recruitment for this study involves three separate avenues: 1) a population-based approach, 2) a clinic-based approach, and 3) an individual approach. Advertising will not be performed. Population-Based: Kentucky Cancer Registry (KCR) will assist in recruitment to the extent that its staff will identify potential participants for this study. Potentially eligible cancer survivors from the perspective of the KCR will be defined as individuals who were: 1) diagnosed with cervical or head/neck cancer (e.g., larynx, oral cavity) in the past 5 years, 2) residents of a rural or Appalachian Kentucky county at the time of cancer diagnosis, 3) between 18 and 75 years old at time of cancer diagnosis, and 4) noted as having a history of tobacco use. All of these qualities are coded in KCR's database in a manner that easily allows for the identification of potential study participants for the purposes of recruitment. KCR will make initial contact with potentially eligible individuals using their established two-step procedure. Step one involves physician notification. Specifically, KCR will contact the physician of record, inform the physician of the study and the cancer survivor's potential for study participation, and then ask the physician to inform KCR if there is any reason why the cancer survivor should not be invited to participate in the study. If the physician of record indicates the cancer survivor should not be contacted, the cancer survivor will not be invited to participate in the study. All others will advance to the next step. Step two involves cancer survivor notification. Specifically, KCR will contact cancer survivors by mail to inform them of their potential for study participation. Cancer survivors will be provided a pre-addressed, postage-paid response card on which they may indicate if they do or do not want their name and contact information released to the PI. If a reply is not received within two weeks, then up to five phone calls will be made in an attempt to obtain verbal consent for the release of the cancer survivor's name and contact information. Only those caner survivors who "opt in" to the potential for study participation will have their names and contact information (i.e., phone number and mailing address) released to the PI. Once the PI has the names and contact information (i.e., phone number and address) of people who express interest in study participation, RAs will attempt to call these individuals and screen them for eligibility. Up to five calls will be made to each person. If someone cannot be reached by phone, then 1-2 introductory letters will be mailed to the address of record (see attachment in the "Research Procedures" section). These letters will contain office phone numbers that interested individuals can use to contact the PI or RAs. Over the phone (whether the call is initiated by the research team or the cancer survivor), cancer survivors will be given a brief overview of the study procedures, have their initial questions answered, and screened for eligibility (see attachment in the "Research Procedures" section). If interested and eligible, attempts will then be made to enroll them into the study (see "Informed Consent Process" below). A few notes about the KCR: First, its recruitment procedures are not subject to modification by an individual investigator and a standardized postcard is used for notification about potential study participation; this is outside the PI's control. Second, it is not part of a "covered entity" and therefore HIPAA authorization for release of Personal Health Information, including contact information, is not required. Finally, study personnel will not have access to any identifying information for any cancer survivor until the standardized recruitment procedures described below are complete. Clinic-Based: Clinic-based recruitment focuses on recently diagnosed cancer survivors because they are unlikely to be captured in KCR's database due to the lag time between cancer diagnosis and registry entry. Here participants will be recruited through Markey Cancer Center's 1) Multidisciplinary Clinic and 2) Gynecological Oncology Clinic. On a weekly basis, Dr. Joseph Valentino (Multidisciplinary Clinic – head/neck cancer care), Dr. Rachel Ware Miller (Gynecological Oncology Clinic – cervical cancer care), and/or RAs will access the UK HealthCare's electronic health record system in use in the Markey Cancer Center to review the relevant clinic schedules and identify patients presenting for an appointment related to a head/neck or cervical cancer diagnosis that occurred in the past year. If patients' healthcare provider agrees, then the PI or a RA will speak with the patient that day about the study (schedule permitting). As per the norm for the aforesaid clinics, an exam room or other private room will be used to give patients a brief overview of the study procedures and then screen them for eligibility. If interested and eligible, attempts will then be made to enroll patients into the study. If an in-person conversation is not possible the day of patients' appointment due to incompatible schedules or whatever else, then a RA will follow-up with that individual via phone within a couple of weeks. In this scenario, the same approach that is used to reach potential participants identified by KCR will be used (i.e., phone call(s) then letter(s)). Again, if individuals are found to be interested and eligible, attempts will then be made to enroll them into the study. In order to carryout this aspect of recruitment, we need to generate a list of individuals to be screened for eligibility (i.e., a list of individuals who are scheduled for an appointment related to a recent (i.e., past year) head/neck or cervical cancer diagnosis). This list will contain only this info: patients' first and last name, address, phone number, and appointment info (i.e., place, date, and time); no other PHI is needed for these individuals. This information is necessary in order to 1) have the RAs arrange their schedule so they can try to screen people in person and 2) have the RAs follow-up with someone missed in clinic. A HIPAA Waiver of Authorization is requested for this aspect of the study. Individuals: Cervical and head/neck cancer survivors in the PI's active studies (IRB #14-0599-P4S and 16-0517-P4S) who on their Consent Form answered "yes" to the question about being contacted for future studies will be contacted about this study. Once again, the same approach that is used to reach potential participants identified by KCR will be used (i.e., phone call(s) then letter(s)). And again, if individuals are found to be interested and eligible, attempts will then be made to enroll them into the study. Regardless of the avenue by which people are recruited, each individual identified as a potential participant will be assigned a unique identification number (e.g., 568, 254), and there will exist an electronic document that links each individual's name and contact info (address, and phone numbers) with their unique identification number.

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Advertising: Specify if any advertising will be performed. If yes, please see "IRB Application Instructions - Advertisements" for instructions on attaching copies of the information to be used in flyers or advertisements. Advertisements must be reviewed and approved by the IRB prior to use. For additional details, see topic "Recruitment of Subjects/Advertising" on ORI's IRB Survival Handbook web page for the *PI Guide to Identification and Recruitment of Human Subjects for Research* [D7.0000] document [PDF]. If you will be recruiting subjects via advertising at non-UK owned or operated sites, you should include a copy of written permission from that site to place the advertisement in their facilities.

Note: Print and media advertisements that will be presented to the public also require review by UK Public Relations (PR) to ensure compliance with UK graphic standards, and equal opportunity language. See Advertising Instructions for PR contacts.

Advertising will not be performed.

Attachments

Informed Consent Process: Using active voice, describe the consent/assent procedures to be followed, the circumstances under which consent will be sought and obtained, the timing of obtaining informed consent, whether there is any waiting period between informing the prospective subject and obtaining consent, who will seek consent., steps taken to minimize the possibility of coercion or undue influence, the method used for documenting consent, and if applicable who is authorized to provide permission or consent on behalf of the subject. Note: all individuals authorized to obtain informed consent should be designated as such in the E-IRB "Study Personnel" section of this application.

Describe provisions for obtaining consent/assent among any relevant special populations such as children (see Children in Research Policy [PDF] for guidance), prisoners (see Summary of Prisoner Regulations [PDF] for guidance), and persons with impaired decisional capacity (see Impaired Consent Capacity Policy [PDF] for guidance). Describe, if applicable, use of specific instruments or techniques to assess and confirm potential subjects' understanding of the nature of the elements of informed consent and/or a description of other written materials that will be provided to participants or legally authorized representatives. If you have a script, please prepare it using the informed consent template as a guide, and submit it on a separate page.

Informed Consent for Research Involving Emancipated Individuals
If you plan to enroll some or all prospective subjects as emancipated, consult with UK legal counsel **when preparing the IRB application and prior to submitting the application to the IRB**. Include legal counsel's recommendations (legal counsel's recommendations may be attached in the E-IRB "Additional Information" section as a separate document, if necessary). For a complete definition of emancipated minors, see the section on *Emancipated Individuals* in the Informed Consent SOP [PDF].

Informed Consent for Research Involving Non-English Speaking Subjects
If you are recruiting non-English speaking subjects, the method by which consent is obtained should be in language in which the subject is proficient. Describe the process for obtaining informed consent from prospective subjects in their respective language (or the legally authorized representative's respective language). In order to ensure that individuals are appropriately informed about the study when English is their second-language, describe a plan for evaluating the level of English comprehension, and the threshold for providing a translation, or explain why an evaluation would not be necessary. For additional 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 [PDF]

Interested and eligible individuals will be asked to provide written informed consent and authorization. For individuals recruited via clinic, and for whom the PI, authorized co-investigators, or RAs are able to speak with them in person, the introductory letter and a blank consent form will be provided. They will be asked to read the documents, ask any study-related questions, and then sign the consent form. A copy of the consent form will then be made for them to take home for future reference. For individuals recruited via phone, the introductory letter and a blank consent form will be provided along with a pre-addressed, postage-paid envelope addressed to the PI. These individuals will be asked to read the documents, call and ask any study-related questions, and then sign and return the consent form. For their future reference, they will be provided with a copy of their signed consent form via mail. Since recruitment is linked to a cancer registry/clinical setting, care will be taken to minimize the possibility of coercion or undue influence. Specifically, when the study is first introduced to people it will be made clear that study participation or the lack thereof has no bearing on the healthcare they will/might receive in the future. Then, as part of the consent process, everyone will be reminded that study participation is entirely voluntary and will not impact his or her status as a patient at UK or elsewhere. Furthermore, as stated above, everyone will be given the opportunity to read the consent form, ask questions about any and all aspects of it before signing it, and provided with a signed copy for future reference.

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Research Procedures: Describe the research procedures that will be followed. Identify all procedures that will be carried out with each group of subjects. Differentiate between procedures that involve standard/routine clinical care and those that will be performed specifically for this research project.

Upon receipt of written informed consent, participants will be randomized to one of 2 groups (Social Support (SS) or Social Support + Nicotine Replacement Therapy (SS+NRT)) according to a protocol established by the study biostatistician. At this point, a graduate RA will make arrangements to conduct the Day 0 survey. Standard protocol will be for this and all other surveys (which will take 20-30 minutes to complete) to be administered by the RAs via phone. All surveys will be scheduled in advance, and up to four attempts will be made in order to complete each one. As a backup, participants will be able to complete the surveys via a paper and pencil questionnaire provided to them via mail along with a pre-addressed, postage-paid envelope for its return. After the Day 0 survey, whether it's done via phone or mail, participants in the SS group will receive a brief (10-15 minute) consultation about free or low-cost resources related to their two most pressing unmet social support needs as reported on the Day 0 survey (see the Social Support Screener on page 20 of the Data Collection attachment; the two unmet needs with the highest rating on the 0-10 scale will be the topic of discussion, and if there is a 3-way tie, the participant will be allowed to pick the 2 she or he would like to discuss). These resources might exist at the local, regional, state, or national level, and will be identified in concert with the Markey Cancer Center's Behavioral and Community-Based Research Shared Resource Facility (see the grant application for a draft list of the resources). This consultation will occur via phone, and will involve encouragement to use the resources discussed and to consider use of similar resources for all unmet social support needs. After the consultation, a written directory that contains a summary of various free and low-cost social support resources will be delivered to participants' preferred address via US Postal Service metered mail. This directory will also be developed in concert with the aforementioned Shared Resource Facility, with special attention to issues of literacy, visual appeal, and acceptability for the population among other things. (Examples of the sort of information that will be

provided can be found in the attachment to this section. The final product was already submitted to the IRB and should be on file.) Participants will be called on Day 14 to see if they received the shipment (if not a second shipment can be mailed), to answer any questions, and to encourage use of the informational resources provided as part of this study; this check-in should not last more than 3-5 minutes. After the Day 0 survey, whether it's done via phone or mail, participants in the SS+NRT group will receive the same consultation about free or low-cost resources related to their two most pressing unmet social support needs. In this same call, participants will receive brief advice related to smoking cessation (10-15 minutes). Consistent with the brief advice model described in the latest Clinical Practice Guideline for Treating Tobacco Use and Dependence (CPG-TTUD; Fiore et al., 2008), participants will be informed about the general health benefits of smoking cessation, given an overview of evidence-based approaches to smoking cessation (e.g., stimulus control, medication use, support seeking), and provided with a summary of the mechanism of action and potential benefits/risks of NRT specifically. They will be encouraged to try NRT in the context of a "practice" quit attempt, even if the abstinence they achieve only lasts a few hours. There will not be any pressure to achieve long-term success during the course of study participation, but participants will be told that multiple "practice" quit attempts could result in 1) learning which approaches and coping strategies do vs. do not work for them and 2) increasing their motivation/confidence in their ability to quit for good. It should also be noted that participants will be assured there is no requirement to quit, reduce smoking, or even try NRT as part of this study. The goal of this study is to encourage a "hassle-free" quit attempt. After the consultation, and in the same mailing as the social support resource directory, a free 2-week supply of nicotine patches (14mg; NicoDerm CQ - GlaxoSmithKline) and nicotine lozenge (2 or 4mg; Nicorette - GlaxoSmithKline) will be supplied; participants will be forewarned about the NRT shipment via the US Postal Service metered mail, and given the opportunity to opt out if they like. As for the amount of NRT, each participant who doesn't opt out of the shipment will be mailed one box of 14 nicotine patches (1 patch per day) and one box of 72 nicotine lozenges (2mg or 4mg supply based on time to first cigarette as per the package label, with 1 lozenge per 1-2 hours when awake) in their original packaging. A summary of the information discussed on the phone will be provided. Participants will be called on Day 14 to see if they received the shipment (if not a second shipment can be mailed), to answer any questions, and to encourage use of the informational and medication resources provided as part of this study; again, this check-in should not last more than 3-5 minutes. Participants in both groups will be asked to complete a Day 30 and 60 survey (see Data Collection attachment). Finally, on or shortly after Day 74, all participants will receive a final letter that briefly outlines the importance and benefits of smoking cessation for cancer survivors and provides up-to-date contact information and the latest flyer for the KY Quitline (see attachment in this section). It should be noted that women of childbearing potential will be asked to take a pregnancy exam before consenting to take part in this study because pregnancy is an exclusionary criterion; this is something they will need to do on their own. If participants of childbearing age are assigned to the SS+NRT group, they will be also asked to engage in an effective method of birth control (e.g., abstinence from sex, oral contraceptive, intrauterine contraceptive device) during study participation. Finally, if a woman becomes pregnant during this study, they will be asked to immediately inform the PI who will then have Dr. Miller, the Medical Supervisor for this study, contact them and advise them on stopping NRT, if appropriate. No information will be entered into participants' EHR as part of this study.

Attachments

Attach Type	File Name
ResearchProcedures	KLCR Appendix A Invitation Letter, clean.pdf
ResearchProcedures	KLCR Appendix B Phone Intro & Eligibility Screener, clean.pdf
ResearchProcedures	KLCR Appendix C Social Support Resource Info.pdf
ResearchProcedures	KLCR Appendix D Final Letter.pdf

Data Collection: List the data or attach a list of the data to be collected about or from each subject (e.g. interview script, survey tool, data collection form for existing data).

If the research includes survey or interview procedures, the questionnaire, interview questions or assessment scales should be included in the application (use attachment button below).

The data collection instrument(s) can be submitted with your application in draft form with the understanding that the final copy will be submitted to the IRB for approval prior to use (submit final version to the IRB for review as a modification request if initial IRB approval was issued while the data collection instrument was in draft form).

Note: The IRB approval process does not include a statistical review. Investigators are strongly encouraged to develop data management and analysis plans in consult with a statistician.

Please see attachments

Attachments

Attach Type	File Name
DataCollection	List of Survey Measures.pdf
DataCollection	KLCR M Questionnaires, clean.pdf

Resources: Describe what resources/facilities are available to perform the research (i.e., staff, space, equipment). Such resources may include a) staffing and personnel, in terms of availability, number, expertise, and experience; b) psychological, social, or medical services, including counseling or social support services that may be required because of research participation; c) psychological, social, or medical monitoring, ancillary care, equipment needed to protect subjects; d) resources for subject communication, such as language translation services, and e) computer or other technological resources, mobile or otherwise, required or created during the conduct of the research. Please note: Some mobile apps may be considered mobile medical devices under FDA regulations (see FDA Guidance). Proximity or availability of other resources should also be taken into consideration, for example, the proximity of an emergency facility for care of subject injury, or availability of psychological support after participation.

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); supportive documentation can be attached in the E-IRB "Additional Information" section. Provide a written description of the role of the non-UK site(s) or non-UK personnel who will be participating in your research. The other site may need to complete its own IRB review, or a cooperative review arrangement may need to be established. Contact the Office of Research Integrity at (859) 257-9428 if you have questions about the participation of non-UK sites/personnel.

If the University of Kentucky is the lead site in a multi-site study, or the UK investigator is the lead investigator, describe the plan for managing the reporting of unanticipated problems, noncompliance and submission of protocol modifications and interim results from the non-UK sites.

The research team is multidisciplinary and includes scholars who specialize in clinical psychology, oncology, public health, and biostatistics. Collectively, the research team has the necessary content expertise and professional experience to carry out this study and insure the rights of participants are respected. Furthermore, with the inclusion of two licensed psychologists with expertise in smoking cessation treatment (Drs. Burris and Studts) and two physicians who regularly treat cancer survivors who smoke (Drs. Miller and Valentino), it will be possible to address all AEs in a responsible manner. It should also be noted that the PI has a Career Development Award from NCI, an award that involves the existence of a mentoring team. This is of particular relevance for this study because one of the PI's mentors (Dr. Matthew Carpenter) has published extensively on the topic of NRT sampling, and he is readily available for consult and guidance. It should be noted, however, that Dr. Carpenter is not listed as study personnel as he is not acting in that capacity (e.g., he will not interact with any patients/survivors/participants nor have access to study files or data). Personnel resources for the day-to-day management of the study are also sufficient, as both paid employees/research assistants and student volunteers are available to assist with this work. Furthermore, the UK Investigational Drug Service (IDS) has agreed to support this study as described below. The EHR in use within the Markey Cancer Center may also be considered as a resource as it will be used as one avenue to identify potentially eligible individuals. KCR is a resource because it will provide important cancer-specific health information. Financial support from this study comes from a grant from the Kentucky Lung Cancer Resource Foundation and resources given to the PI by her department. Additionally, the PI's has office and lab space in both the Department of Psychology (Kastle Hall) and Markey Cancer Center (Combs Research Building), and all the requisite computer/printer equipment, paper supplies, and data analytic tools are available through UK.

Potential Risks: Describe any potential risks or likely adverse effects of the drugs, biologics, devices or procedures subjects may encounter while in the study. Please describe any physical, psychological, social, legal or other risks and assess their likelihood and seriousness.

The overall risks to participants are low in terms of both their likelihood and seriousness. The physical risks associated with use of nicotine patch and/or nicotine lozenge in this study are expected to be rare and mild. In prior studies of NRT (many of which have much longer sampling periods), adverse events were documented to occur in the majority of participants (˜70%), but dropout due to AEs was low (˜7%) and the report of serious AEs was even lower (˜2%) (e.g., Carpenter et al., 2011; Jardin et al., 2014). The most common AEs for the NRT under study here are skin irritation (patch), headache (patch), insomnia (patch), mouth and throat soreness (lozenge), hiccups (lozenge), and nausea (patch and lozenge) (Hughes et al., 2004; Mills et al., 2010; Piper et al., 2011). It should be appreciated that concurrent use of cigarettes and NRT, which rarely occurs (Shiffman, Hughes, DiMarino, & Sweeney, 2003), is now considered to be safe (Fagerstrom & Hughes, 2002) despite the risk for nicotine "overdose" or "intoxication" as characterized by nausea, vomiting, dizziness, diarrhea, weakness, and rapid heartbeat. Therefore, the FDA now suggests that it is unnecessary to quit smoking before starting NRT and it is unnecessary to stop NRT if lapse or relapse to smoking occurs. The psychological risks are those associated with being asked questions about the following: 1) demographics, including access to health care, 2) cancer survivorship, 3) quality of life, 4) tobacco use and cessation, and 5) social environment/relationships. Although completion of the surveys might result in mild emotional discomfort, based on the PI's experience, the likelihood of psychological risk is low and the severity of this risk is mild. Furthermore, participants always have the option of not completing a survey or skipping an item. It should be noted that the extant data on NRT sampling (as opposed to provision or recommendation of a full, standard dose of NRT) does not suggest that it undermines smoking cessation, thus reductions in motivation, confidence, and behavior change are considered to be very low in likelihood and severity. There are confidentiality risks. The health-related and other private information obtained from KCR, EHR, and participants is considered sensitive in nature, and a breach of confidentiality for these data could pose a mild to moderate risk to participants. Since especially sensitive information regarding sexual orientation, criminal history, or a history of treatment for substance abuse/dependence (other than treatment for nicotine dependence) will not be collected for this study, the consequence of an individual's survey responses being revealed is thought to be mild. However, to minimize any adverse consequences of a breach of confidentiality for these data, solely participants' unique identification number will identify all survey data. The financial risks are the costs associated with regular use and maintenance of a landline or cellular phone. These risks are likely to be of little consequence, given that no one is required to modify their pre-existing phone access as part of study procedures. Finally, it should be noted that mailing NRT is a very well-accepted method to disseminate NRT (Carpenter et al., 2011 Archives of Internal Medicine; Cunningham et al., 2016 JAMA Internal Medicine; Kushner et al., 2017 Addictive Behaviors; Jardin et al., 2014 Nicotine and Tobacco Research; Solomon, Scharoun, Flynn, Secker-Walker, & Sepinwall, 2000 Preventive Medicine; Zawertailo et al., 2012 Tobacco Control). This is standard practice for state Quitlines, and like the Quitlines, NRT will be mailed to participants sans tracking or signature confirmation, both of which add unnecessary cost and burden to the procedures and participants alike. The approach proposed here is considered acceptable for several reasons, including largely NRT's over-the-counter status, relatively benign adverse event profile, and low abuse liability (West et al., 2000; Psychopharmacology) coupled with the fact that the treatment group in this study actually gains access to an evidence-based treatment for smoking cessation as part of study participation.

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Safety Precautions: Describe the procedures for protecting against or minimizing any potential risks, *including risks of breach of confidentiality or invasion of privacy*. Where appropriate, discuss provisions for ensuring necessary medical or professional intervention in the event of adverse events, or unanticipated problems involving subjects. Also, where appropriate, describe the provisions for monitoring the data collected to ensure the safety of subjects. If vulnerable populations other than adults with impaired consent capacity are to be recruited, describe additional safeguards for protecting the subjects' rights and welfare.

The primary protection against the physical risks associated with both nicotine patch and nicotine lozenge (both over-the-counter medications) is that it will only be provided for a short duration and smokers with FDA contraindications will not be enrolled in this study. Second, the Data and Safety Monitoring Plan (DSMP) includes AE monitoring, and the PI, RAs, and Medical Supervisor (Dr. Rachel Miller) will work closely together to make sure that participants' AEs are handled in a timely and responsible manner. Third, females of childbearing potential will be asked to use effective contraception to guard against pregnancy during the course of the study (this is on top of exclusion criteria related to pregnancy/breastfeeding). Fourth, participants will be encouraged to contact the PI and stop the use of the nicotine patch and consult with their physician or advanced practice registered nurse as instructed on the package insert. Finally, participants who report a serious AE will be withdrawn from the study. Several steps will be taken to minimize psychological risks. First, participants will be alerted to the possibility of mild emotional discomfort prior to their enrollment in the study, as the consent form will provide information about the nature of the surveys. Second, participants will be assured via the consent form and verbal assurances from the PI and RAs that their data are confidential. Third, participants will be allowed to skip any question or withdraw from the study at any time. Finally, participants who experience emotional discomfort as a result of this study will be: 1) allowed to withdraw from the study without penalty and 2) provided with contact information for mental health professionals near their place of residence. Note that as a licensed clinical psychologist in Kentucky, the PI has access to a list of licensed psychologists and related mental health professionals who practice throughout the state, and can provide said information to anyone who requests it. To address confidentiality risks, well-established guidelines for security best practices will be followed, with particular attention to guidelines for data collected electronically. Although not specific to this study, both KCR and UK HealthCare have established safety precautions: 1) KCR has an established means of encrypted electronic file transfer that involves unique username and password authentication, and will only release participant data through that avenue and 2) UK HealthCare Enterprise has an established means of training everyone prior to granting them access to one or more of their EHR systems, and once access is given, an audit trail is created via the requirement of unique username and password authentication prior to each log-in. The safety precautions specific to this study are as follows: First, the responses of any one participant will never be reported apart from those of other participants. Second, all participants will be assigned a unique identification number. Only participants' unique identification number will identify their survey data. Within a month of receiving participants' health information from KCR, these data will be coded such that only participants' unique identification number is associated with their health information (e.g., if names are used to identify cases in the file given to me by the registry, then the names will be removed and replaced with participants' unique identification number). In this way, only participants' unique identification number will identify their sensitive health information and survey data. Third, the electronic document that links participants' unique identification number with their private individually identifiable information (i.e., name, address, phone number) will be strictly protected (only the PI and RAs will have access), password protected, and stored on a secure server maintained by the UK College of Arts & Sciences. Fourth, the electronic document that contains a list of patients to be screened will be strictly protected (only the PI and RAs will have access), password protected, and stored on a secure server maintained by the UK College of Arts & Sciences. Fifth, this study will use UK computers that will: 1) be protected from access by outside parties through the use of a firewall, 2) be password protected, 3) have regular backups performed, and 4) have operating system patches and antivirus
software kept up-to-date. These computers will be physically housed on the 2nd and 3rd floor of the UK Combs Cancer Research Building and the basement and 2nd floor of UK Kastle Hall, as the PI's office and lab space is spread across these two buildings. Sixth, access to electronic study files will be restricted to the PI and select RAs, and all individuals who are granted access will need to pass through username and password authentication as these files will be stored on the College of Arts & Sciences secure server. Similarly, access to paper study files will be restricted to key study personnel, as these files will be kept in lockable filing cabinets that are stored on the basement floor of the Kastle Hall behind locked doors. Seventh, the surveys will be administered with the use of Research Electronic Data Capture (REDCap) whenever they are done by phone, and whenever they are done by paper, participants' responses will then be entered into REDCap. REDCap is designed to provide a secure, reliable, and valid means of electronic data capture as it will: 1) operate behind a firewall on a secure UK server, 2) minimize data entry errors via automatic data validation, 3) provide a "real time" searchable log of input and output, and 4) allow the creation of audit trails. Seventh, any transfer of electronic files between the PI and KCR will be completed using their established means of encrypted file transfer that involves unique username and password authentication. Finally, all study personnel will maintain up-to-date human subjects protection training. It should also be noted that we will not retain beyond the anticipated end of the study (07/31/20) the name or contact information (i.e., phone number and mailing address) for cancer survivors who "opt in" to KCR's releasing this info to the PI, but ultimately do not enroll in the study. Additionally, we will not retain beyond the aforesaid date the list of patients to be screened as part of the clinic-based recruitment. That is, unless someone provides written informed consent to study participation, we will not keep a record of his or her personal information. This personal information will be destroyed according to UK Policy A13-050. Financial Risks: These risks will be explained to potential participants as part of the informed consent process and will be offset by the financial compensation participants will receive.

Benefit vs. Risk: Describe potential benefits to the subject(s); include potential benefits to society and/or general knowledge to be gained. Describe why the risks to subjects are reasonable in relation to the anticipated benefit(s) to subjects and in relation to the importance of the knowledge that may reasonably be expected to result. If you are using vulnerable subjects (e.g., impaired consent capacity, pregnant women, etc…), justify their inclusion by describing the potential benefits of the research in comparison to the subjects' vulnerability and the risks to them. For information about inclusion of certain vulnerable populations, see the IRB/ORI Standard Operating Procedure for Protection of Vulnerable Subjects [C3.0100] [PDF].

This is a low risk study and the potential benefits are plentiful. It is possible that participants' reflection upon their cancer survivorship, quality of life, tobacco use, and social environment/relationships – in combination with their receipt of information about social support resources – may lead to the initiation of positive change in their life. In addition, it is possible the receipt of brief advice to quit and

referral to the KY Quitline (and in some cases free NRT samples) could benefit participants directly via an increase in the level of motivation/confidence to quit and the likelihood of making a quit attempt. Another real strength of this study is not in its ability to benefit participants directly, however, but to provide meaningful and clinically relevant information that will benefit the lives of future cancer survivors who smoke. Overall, then, the benefit to risk ratio is considered to favor the potential benefits.

Available Alternative Treatment(s): Describe alternative treatments and procedures that might be advantageous to the subjects, should they choose not to participate in the study. This should include a discussion of the current standard of care treatment(s).

If individuals do not want to take part in the study, there are other choices such as calling the United Way of Kentucky (2-1-1) to learn about various social support and other resources available to them or calling the Kentucky Quitline (1-800-QUIT-NOW) to receive information, counseling, and other support related to smoking cessation. Most smokers have the intention to quit at some point in the future, but very few make a quit attempt in any given year and even fewer seek treatment in the form of medication and/or counseling. Thus, most smokers in the general population are not "treatment seeking." Given the population-based emphasis on recruitment via KCR, the PI does not expect to encounter many "treatment seeking" smokers during the recruitment process (that is, most individuals recruited for this study are not expected to be actively engaged in the process of quitting or to have plans to quit in the near future). That said, the aforesaid alternatives are free and available to all Kentucky residents. It should also be noted that if a smoker were to consult with a healthcare provider about his or her intent to quit, the standard of care as per the Clinical Practice Guideline for Treating Tobacco Use and Dependence (Fiore et al., 2008) is implementation of AAR: Advise smoking cessation, Assist with the formulation of a plan that involves first-line medication (e.g., combination NRT), and Refer to the Quitline or other tobacco treatment specialist for counseling and other support, all of which is accomplished by the end of the study for every participant.

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Research Materials, Records and Privacy: Identify the sources of research material obtained from living human subjects. Indicate what information (specimens, records, data, genetic information, etc.) will be recorded and whether use will be made of existing specimens, records or data. Explain why this information is needed to conduct the study.

Return of Research Results or Incidental Findings (if applicable):
If research has the potential to identify individual results or discover incidental findings that could affect the health of a subject, describe plans to assess, manage, and if applicable disclose findings with individual subjects or provide justification for not disclosing. For IRB expectations, refer to the UK IRB "Frequently Asked Questions (FAQs) on the Return of Research Results or Incidental Research Findings" [PDF].

Data for this study comes from one of two sources: 1) KCR and 2) surveys. All data collected for this study are required in order to meet the specific aims (see "Objectives"), or describe the study sample whenever the findings are disseminated. Once the PI obtains approval from KCR regarding the conduct of this study, KCR will provide this information about each participant: date of cancer diagnosis, age at cancer diagnosis, site of cancer at diagnosis, stage of cancer at diagnosis, type of cancer treatment, date of initiation and completion of cancer treatment, and insurance coverage at cancer diagnosis. For the surveys, standardized measures and individual questions commonly used in cancer survivorship, quality of life, and/or tobacco use research will be asked. Permission is not needed to use any of the measures listed below as they are all either developed by the PI or in the public domain. The baseline (Day 0) and follow-up (Day 30 and 60) surveys contain similar measures, but the baseline is longer than the follow-up and some modifications to individual items were made as appropriate; see Data Collection attachment for more information. No information will be entered into participants' EHR as part of this study.

Confidentiality: Specify where the data and/or specimens will be stored and how the researcher will ensure the privacy and confidentiality of both. Please address the following items or indicate if the following has been addressed in a HIPAA or Limited Review form:

- physical security measures (e.g., locked facility, limited access);
- data security (e.g., password-protection, data encryption);
- who will have access to the data/specimens and identifiers;
- safeguards to protect identifiable research information (e.g., coding, links, certificate of confidentiality);
- procedures employed when sharing material or data, (e.g., honest broker if applicable, written agreement with recipient not to re-identify, measures to ensure that subject identifiers are not shared with recipients).
- management after the study

Describe whether data/specimens will be maintained indefinitely or destroyed. If maintained, specify whether identifiers will be removed from the maintained information/material. If identifiers will not be removed, provide justification for retaining them. If the data/specimens will be destroyed, describe how and when the data/specimens will be destroyed. For multi-site studies, the PI consults the study sponsor regarding retention requirements, but must maintain records for a minimum of six years after study closure. Also, specify who will access the identified data/specimens, and why they need access. If applicable, 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 entities not affiliated with UK.

HIPAA/FERPA Minimal Access Standards: The IRB expects researchers to access the minimal amount of identifiers to conduct the study and comply with applicable HIPAA and Family Educational Rights and Privacy Act (FERPA) requirements. If data are going to be collected, transmitted, and/or stored electronically, for appropriate procedures please refer to the guidance document "Confidentiality and Data Security Guidelines for Electronic Data" [PDF].

Cloud storage: For storage of data on cloud services other than UK OneDrive, please verify security settings are sufficient and in accordance with respective departmental, UK Corporate Compliance, and/or UK Information Technology requirements.

Creation of digital data application/program: If a research protocol involves the creation and/or use of a computer program or application, mobile or otherwise, please specify whether the program/application is being developed by a commercial software developer or the research team and provide any relevant information regarding the security and encryption standards used, how data is stored and/or transmitted to the research team, what information about the subjects the program/application will collect, etc. For relevant information to include, see Considerations for Protocol Design Concerning Digital Data [PDF]. The IRB may require software programs created or used for research purposes be examined by a consultant with appropriate Internet technology expertise to ensure subject privacy and data are appropriately protected.

NIH-funded genomic research: The National Institutes of Health (NIH) Genomic Data Sharing (GDS) Policy sets forth expectations that ensure the broad and responsible sharing of genomic research data consistent with the informed consent of study participants from which the data was obtained. If you are submitting genomic data to an NIH data repository, describe your NIH data sharing plan.

Management after study: Describe how the collected data/specimens will be managed after the end of the study. Specify whether identifiers will be removed from the maintained information/material. If identifiers will not be removed, provide justification for retaining them and specify what steps will be taken to secure the data/specimens (e.g., maintaining a coded list of identifiers separate from the data/specimens).

If the data/specimens will be destroyed, describe how, when, and why this will be done. Note that destruction of primary data may violate NIH and NSF retention and sharing requirements, journal publication guidance, and University Data-Retention policies. Additionally, primary data may be necessary for other purposes (to validate reproducibility, for data sharing, or for evidence in various investigations). PIs should carefully consider whether the destruction of data is justified.

The investigator is responsible for retaining signed consent and assent documents and IRB research records for at least six years after study closure, as outlined in the Study Closure SOP [PDF]. If the research falls under the authority of the FDA or other regulatory agencies, or a study sponsor is involved, additional requirements may apply.

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Details about how participants' confidentiality will be maintained can be found above in "Safety Precautions". Data and electronic records will be kept for at least six years post study closure then destroyed according to UK Policy A13-050.

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Payment: Describe the incentives (e.g., inducements) being offered to subjects for their time during participation in the research study. If monetary compensation is offered, indicate how much the subjects will be paid and describe the terms and schedule of payment. (It is IRB policy that provision should be made for providing partial payment to subjects who withdraw before the completion of the research. Monetary payments should be prorated or paid in full.)

Participants will receive $25 for each survey, which means they can earn up to $75 total. Payment for the baseline and follow-up surveys are the same despite differences in the length of the surveys in order to incentivize participants against dropout. This is a common approach for survey research, especially in the case of clinical trials, and is not considered problematic in any way. Participants will be paid for whatever survey(s) they complete, even if they formally withdraw from the study or do not complete the study in its entirety. Payment will be initiated within three weeks of completing the assessment in the form of a check that is disbursed by the UK Department of Psychology's Integrated Business Unit.

Costs to Subjects: Describe any costs for care associated with research (including a breakdown of standard of care procedures versus research procedures), costs of test drugs or devices, and research procedure costs that are the subject's responsibility as a consequence of participating in the research. Describe any offer for reimbursement of costs by the sponsor for research related injury care.

The directory of social support resources, and if applicable, the 2-week supply of NRT, will be provided to participants at no cost. The only known cost for participants is the time they spend completing the surveys and speaking to the study coordinator. However, if participants seek medical or other care for any research-related AEs, they will be responsible for these costs.

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

If you are conducting greater than minimal risk research, clinical research, or your clinical investigation is NIH-funded/FDA-regulated, 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, clinical research, or your clinical investigation is FDA-regulated, *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.

If relying on an independent agent or committee for DSMB services, it is the PI's responsibility to establish the services with the agent or committee. Please be reminded that the PI must submit DSMB reports to the IRB via modification or continuing review.

Overview. This DSMP is tailored to the potential risks, complexity, and nature of this pilot randomized clinical trial. Administrative aspects of this study will be jointly managed by the UK Department of Psychology and Markey Cancer Center, including its Data Safety Monitoring Committee. The PI and her research assistants will coordinate enrollment of participants, who will primarily be recruited through KCR and the Markey Cancer Center's Multidisciplinary Clinic and Gynecological Oncology Clinic. Recruitment will involve a mix of phone, in person, and mail interactions. Treatment delivery and data collection will be remote involving both phone and mail. A total of 80 participants should be enrolled over the course of the study. NRT Management. The UK Investigational Drug Service has verbally agreed to purchase, store, label, and maintain inventory of all of the NRT to be used in this study. The IDS will prepare and dispense the medication in accordance with the IRB-approved protocol and will complete and maintain drug accountability logs as appropriate. The IDS will only dispense the medication upon a pharmacist's receipt of a request by the PI (which will include verbal or written confirmation of the completed informed consent process), at which time the medication will be picked up by a research assistant and then packaged for delivery to participants via the US Postal Service. The PI will keep an electronic record of all shipments of NRT to participants including the type (patch, lozenge), quantity, dose, and date. Data Management. KCR and survey data will be entered into/stored in a REDCap database that only the PI and RAs can access. KCRprovided
health information and participant-provided survey data will be identified only by participants' unique identification number,
and the document that links participants' unique identification number with their individually identifiable contact information (i.e., name, address, and phone number) will be strictly protected via entry that requires a 2-step username and password authentication. Other guidelines for security best practices will be followed and are described above (see "Confidentiality"). Quality Assurance. As a recipient of a Career Development Award, the PI has regular meetings with a more senior faculty person who serves as a mentor: Dr. Jamie Studts, Co-Investigator for this study. Additionally, the PI maintains weekly meetings with all RAs to discuss problems with or concerns about data gathered in all studies. As it pertains to data collection, REDCap will assist in quality assurance (see "14. Confidentiality"). Once all data are collected, preliminary data analysis done by the study biostatistician (Dr. Brent Shelton) will provide a check for quality, the results of which will guide all subsequent data analysis. DSMP Administration and Other Regulatory Issues. This study will be registered on ClinicalTrials.gov prior to the start of enrollment and will be updated as required. Filing for an Investigational New Drug (IND) application with the FDA is not appropriate for this study, as the FDA has stated so several times in the past for studies that very closely align with this one (as per Dr. Carpenter, one of the PI's mentors). The PI will be responsible for monitoring all the human subjects aspects of this study. She will be responsible for reporting all adverse events (including whether or not they are related to study participation) to the IRB and funding agency at the appropriate times; a report will be submitted at least once a year, but this could occur more frequently if the circumstances call for immediate disclosure (e.g., in the case of a serious AE). If any significant action is taken by the IRB in response to an AE, procedural changes will be relayed to granting agency. In addition, the PI will report any change to the study's risk/benefit ratio to the IRB as soon as she becomes aware of it and will modify the informed consent procedures to reflect such change. The PI will also ensure that any conflicts of interest will be reported for all presentations and manuscripts that result from this study. Finally, the UK IRB and Markey Cancer Center's Protocol Review Monitoring Committee will provide oversight for this study, and the PI will seek their approval and enforce their regulations at all times.

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Subject Complaints: Describe procedures (other than information provided in consent document) for handling subject complaints or requests for information about the research. The procedures should offer a safe, confidential, and reliable channel for current, prospective, or past research subjects (or their designated representative) permitting them to discuss problems, concerns and questions, or obtain information.

First, the PI will be available to field any questions or complaints about this study. Participants will receive a copy of their signed consent/authorization form. Second, individuals will be told they have the option to contact the ORI about this study, thereby providing a confidential means of communication. To facilitate contacting the ORI, the consent form will contain the ORI's contact information and a copy will be mailed to any individual who requests it. Third, individuals will be informed they may contact the Markey Cancer Center's Protocol Review Monitoring Committee (PRMC) to discuss this study, and the consent form contains the PRMC's contact information. Finally, information about this study will be available on ClinicalTrials.gov and Markey Cancer Center's online database of clinical trials (http://ukhealthcare.uky.edu/markey/Researchers/Clinical-Trials/Find-a-Clinical-Trial/). Thus, prospective, current, and past research participants will have safe, confidential, and reliable channels to discuss problems, concerns, and questions about this study.

Does your research involve **Non-English Speaking Subjects or Subjects from a Foreign Culture**?

○ Yes ◉ No

Non-English Speaking Subjects or Subjects from a Foreign Culture

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.

Include contact information for someone who can act as a cultural consultant for your study. The 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 have any direct involvement with the study. If you do not know someone who would be willing to act as your cultural consultant, the Office of Research Integrity will try to find

someone to fill this role (this may delay the approval process for your protocol). Please include the name, address, telephone number, and email of the person who will act as the cultural consultant for your study. For more details, see the IRB Application Instructions on Research Involving Non-English Speaking Subjects or Subjects from a Foreign Culture.

For recruitment of Non-English speaking subjects, the consent document needs to be in the subject's native language. Download the informed consent template available in the E-IRB "Informed Consent/Assent Process" section and use it as a guide for developing the consent document. (Note: Your translated consent document can be attached to your application in the "Informed Consent" section; **be sure to save your responses in this section first.**)

If research is to be conducted at an international location, identify local regulations, laws, or ethics review requirements for human subject protection. If the project has been or will be reviewed by a local Ethics Committee, attach a copy of the review to the UK IRB using the attachment button below. 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.

PI-Sponsored FDA-Regulated Research

Is this an investigator-initiated study that:

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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 PI 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 your (the PI's) experience/knowledge/training (if any) in serving as a sponsor (e.g., previously held an IND/IDE); and
- Indicate if you have transferred any sponsor obligations 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 PI completed the mandatory PI-sponsor training prior to this submission?

○ Yes ○ No

If you (the PI) have completed equivalent sponsor-investigator training, you may 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

Attach Type	File Name
Authorization	KLCR K HIPAA Waiver, clean.pdf

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:

Nicorette lozenge - GlaxoSmithKline &
NicoDerm
CQ - GlaxoSmithKline

Note: Inpatient studies are required by Hospital Policy to utilize the Investigational Drug Service (IDS). 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" [PDF].

Please also complete and attach the Study Drug Form (PDF) (required):

Attachments

Attach Type	File Name
StudyDrug	KLCR O Study Drug Attachment, EIRB revision (patch).pdf
StudyDrug	KLCR O Study Drug Attachment, EIRB revision (lozenge).pdf
StudyDrug	KLCR S FDA Package Insert (2013) - Nicotine Lozenge, original flavor.pdf
StudyDrug	KLCR S FDA Package Insert (2015) - Nicotine Patch, 14mg.pdf

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) or Humanitarian Device Exemption (HDE) application? See UK HUD SOP (PDF) for guidance.

○ Yes ○ No

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

IDE/HDE Submitted/Held by:

Sponsor: ☐ Held By:

Investigator: ☐ Held By:

Other: ☐ Held By:

☐ Check if this is a Treatment or Compassionate Use IDE under the Food and Drug Administration (FDA) Early 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 Clinical Investigations, Compassionate Use, and Treatment IDE SOP" [PDF]

Does the intended use of any device used in this study meet the regulatory definition of Significant Risk (SR) device?

- Yes. Device(s) as used 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, as used in this study do not present a potential for serious risk to the health, safety, or welfare of subjects/participants.

Please also complete and attach the Study Device Form (PDF) (required):

Attachments

RESEARCH SITES

0 unresolved comment(s)

In order for this section to be considered complete, you must click "SAVE" after ensuring all responses are accurate.

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

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

*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.

Attachments

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

If **YES**, you must describe the plan for the management of reporting unanticipated problems, noncompliance, and submission of protocol modifications and interim results from the non-UK sites in the E-IRB "Research Description" section under *Resources*.

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, such as the establishment of a cooperative IRB review agreement with the non-UK site. Questions about the participation of non-UK sites/personnel should be discussed with the ORI staff at (859) 257-9428.

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

☐ Academic Degree/Required Research
☐ Aging Research
☐ Alcohol Abuse Research
☑ Cancer Research
☐ Certificate of Confidentiality
☐ CCTS-Center for Clinical & Translational Science
☑ Clinical Research
☑ Clinical Trial
☐ Clinical Trial Multicenter(excluding NIH Cooperative Groups)
☐ Clinical Trial NIH cooperative groups (i.e., SWOG, RTOG)
☐ Clinical Trial Placebo Controlled Trial
☑ Clinical Trial UK Only
☐ Collection of Biological Specimens
☐ Collection of Biological Specimens for Banking
☐ Community-Based Participatory Research
☐ Data & Safety Monitoring Board
☑ Data & Safety Monitoring Plan
☐ Deception
☑ Drug/Substance Abuse Research
☐ Educational/Student Records (e.g., GPA, test scores)
☐ Emergency Use (Single Patient)
☐ Genetic Research
☐ Gene Transfer
☐ GWAS (Genome-Wide Association Study) or NIH-funded study generating large scale genomic data
☐ International Research
☐ Internet Research
☐ Planned Emergency Research Involving Waiver of Informed Consent
☐ Pluripotent Stem Cell Research
☐ Recombinant DNA
☑ Survey Research
☐ Transplants
☐ Use of radioactive material, ionizing radiation, or x-rays [Radiation Safety Committee review required]
☐ Vaccine Trials

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

- Cancer Research (MCC PRMC)
- Certificate of Confidentiality (look up "Confidentiality/Privacy...")
- CCTS (Center for Clinical and Translational Science)
- Clinical Research (look up "What is the definition of....)
- Clinical Trial (look up "What is the definition of....)

  Determine if research meets NIH definition of clinical trial;
  *Reminder: Ensure compliance with applicable requirements including:
  - Clinicaltrials.gov registration;
  - Good Clinical Practice (GCP) training; and
  - Consent Posting Requirement [PDF] for federal funded trials.

- Collection of Biological Specimens for Banking (look up "Specimen/Tissue Collection...")
- Collection of Biological Specimens (look up "Specimen/Tissue Collection...")
- Community-Based Participatory Research (look up "Community-Engaged...")
- Data & Safety Monitoring Board (DSMB)

  *For Medical IRB: Service Request Form for CCTS DSMB

- Data & Safety Monitoring Plan
- Deception*

  *For deception research, also go to the E-IRB Application Informed Consent section, checkmark and complete "Request for Waiver of Informed Consent Process"

- Emergency Use (Single Patient) [attach Emergency Use Checklist] (PDF)
- Genetic Research (look up "Specimen/Tissue Collection...")
- Gene Transfer
- HIV/AIDS Research (look up "Reportable Diseases/Conditions")
- Screening for Reportable Diseases [E2.0000] (PDF)
- International Research (look up "International & Non-English Speaking")
- NIH Genomic Data Sharing (GDS) Policy (PDF)
- 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"

- Use of radioactive material, ionizing radiation or x-rays for research

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:

Kentucky Lung Cancer Research Foundation

Click applicable listing(s) for additional requirements and/or 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 [PDF]
- DoJ) Department of Justice or Bureau of Prisons ([PDF]
- (DoE) Department of Energy Summary [PDF] and Department of Energy Identifiable Information Compliance Checklist [PDF]
- (EPA) Environmental Protection Agency [PDF]

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.):

Kentucky Lung Cancer Research Foundation

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

Attach Type	File Name
GrantContract	KLCR AA Grant Application.pdf

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

Statistical Analysis Plan

Outcome Measures

1. Accrual will be calculated as the number of participants enrolled divided by the number of individuals contacted about study participation. It will be reported as a percentage. No inferential statistical test will be conducted for this outcome. Only descriptive analyses apply.
2. Retention will be calculated as the number of assessments at the end of study divided by the number of participants enrolled. It will be reported as a percentage. No inferential statistical test will be conducted for this outcome. Only descriptive analyses apply.
3. Acceptability will be determined by the total score on the Treatment Acceptability and Preferences measure. It will be reported as a mean. An Independent samples t-test (2 sided) will be used to examine if the treatment group reports a better outcome than the control group.