Document Coversheet

Study Title: The PATH Home Trial: A Comparative Effectiveness Study of Peripartum Opioid Use Disorder in Rural Kentucky

Institution/Site:	University of Kentucky
Document (Approval/Update) Date:	8/22/2024
NCT Number:	NCT03725332
IRB Number	44929
Coversheet created:	3/3/2025

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

For guidance, see:

- Which IRB?
- Which Protocol Process Type?
- "Getting Started"

Please contact the Office of Research Integrity (ORI) at 859-257-9428, IRBsubmission@uky.edu, or request a consult to resolve any questions prior to saving your selections.

Which IRB

- (•) Medical ( ) NonMedical

Protocol Process Type

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

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.

PROJECT INFORMATION

0 unresolved comment(s)

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

PATH Home Trial: Comparative Effectiveness Study of Peripartum Opioid Use Disorder in Rural Kentucky

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

PATH Home Trial

Anticipated Ending Date of Research Project: 4/30/2026

Maximum number of human subjects (or records/specimens to be reviewed) 267

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

Are you requesting that the UK IRB serve as the lead IRB for a multi-site study, **OR** that the UK IRB defer review to another IRB? [Click here for "IRB Reliance" help]

(•) Yes ( ) No

If "Yes," before completing your IRB application, fill out the Reliance Request Form and submit it to irbreliance@uky.edu.

PI CONTACT INFORMATION

0 unresolved comment(s)

Principal Investigator (PI) role for E-IRB access
The PI is the individual holding primary responsibility on the research project with the following permissions on the E-IRB application:

1. Read;
2. write/edit;
3. receive communications; and
4. submit to the IRB (IR, CR, MR, Other Review*).

If research is being submitted to or supported by an extramural funding agency such as NIH, a private foundation or a pharmaceutical/manufacturing company, the PI listed on the grant application or the drug protocol must be listed as PI here.

Please fill in any blank fields with the appropriate contact information (gray shaded fields are not editable). Required fields left blank will be highlighted in pink after you click "Save".

To change home and work addresses, go to myUK and update using the Employee Self Service (ESS) portal. If name has changed, the individual with the name change will need to submit a 'Name Change Form' to the Human Resources Benefits Office for entering into SAP. The new name will need to be associated with the individual's Link Blue ID in SAP before the change is reflected in E-IRB. Contact the HR Benefits Office for additional information.

The Principal Investigator's (PI) contact information is filled in automatically based on who logged in to create the application.

If you are not the Principal Investigator, do NOT add yourself as study personnel.
To change the PI contact information on an application in Researcher edit status:

- click "Change Principal Investigator";
- search for the PI's name using the search feature;
- click "Select" by the name of the Principal Investigator, then "Save Contact Information".

You will automatically be added as study personnel with editing permissions to continue editing the application.

Change Principal Investigator:

First Name:	Wendy	Room# & Bldg:	800 Rose Street
Last Name:	Hansen	Speed Sort#:	405360293
Middle Name			
Department:	Obstetrics & Gynecology - 7H…	Dept Code:	7H500
PI's Employee/Student ID#:	00049420	Rank:	Professor
PI's Telephone #:	8593236434	Degree:	MD
PI's e-mail address:	wfhans2@uky.edu	PI's FAX Number:	8592571305
PI is R.N.	○ Yes ◉ No	HSP Trained:	Yes
		HSP Trained Date:	1/17/2023
		RCR Trained:	Yes

Do you, the PI, have a significant financial interest related to your responsibilities at the University of Kentucky (that requires disclosure per the UK administrative regulation 7:2)?

○ 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.

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

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

Age level of human subjects: (i.e., 6 mths.; 2yrs., etc..) 18 to 55

Study Population:

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

Provide the following information:

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

Please consider these resources:
NIH Diversity Policy
FDA Diversity Guidance

Pregnant women at 6 to 32 weeks' gestational age with a history of OUD (as defined by the DSM-5) who are receiving MAT (with either buprenorphine based products or methadone) and obtaining prenatal care at one of twelve study sites. Study sites are located throughout Central and Eastern Kentucky and have an established relationship with the University of Kentucky through an existing telemedicine network called the Kentucky Angels network.

Study sites include:

1. Ashland, KY - Karen's Place Maternity Center, ARC
2. Bowling Green, KY: Fairview Community Health Center
3. Corbin, KY: Grace Community Women's Health
4. Georgetown, KY: Brightview Health, LLC
5. Georgetown, KY: UK Women's Health Obstetrics and Gynecology – Georgetown
6. Louisville, KY: University of Louisville, HCOC/Prenatal Clinics
7. Middlesboro, KY: ARH Women's and Family Health Center-Middlesboro
8. Morehead, KY: UK Morehead Women's Healthcare
9. Prestonsburg, KY: Frontier Behavioral Health Center, PLLC
10. South Williamson, KY: ARH Women's and Family Health Center - Tug Valley
11. Vicco, KY: Primary Care Centers of Eastern Kentucky
12. Pikeville, KY - Pikeville Medical Center

Attachments

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

Participant Demographics

	Cisgender Man	Cisgender Woman	TGNB/TGE	Unknown/Not Reported
American Indian/Alaskan Native:	0	0		
Asian:	0	0		
Black/African American:	0	15		
Latinx:	0	15		
Native Hawaiian/Pacific Islander:	0	0		
White:	0	503		
American Arab/Middle Eastern/North African:				
Indigenous People Around the World:				
More than One Race:				
Unknown or Not Reported:	0	0		

If unknown, please explain why:

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

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

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

ADDITIONAL INFORMATION:

Please visit the IRB Survival Handbook for more information on:

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

Other Resources:

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

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

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

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

○ Yes ◉ No

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

Examples of such conditions include:

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

Attachments

SUBJECT CHILDREN

0 unresolved comment(s)

SECTION 1. Risk Level

Complete this section and include it with your IRB application submission. *In Kentucky, a child is an individual less than 18 years of age unless the individual is legally emancipated.*

Note: the explanation(s) you are being asked to provide in Section 1 correlate(s) to the risk level you selected in the Risk Level section.

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

FOR FDA REGULATED RESEARCH: Based on the 2013 FDA final rule Subpart D, a placebo control arm of a clinical trial must be approved under either Risk Category 1, Risk Category 3], or Risk Category 4]. FDA does not consider administration of a placebo to offer a prospect of direct benefit to an individual subject under Subpart D, Risk Category 2 [21 CFR 50.52].

Not involve greater than minimal risk.

In the Risk Level section of the IRB Application you indicated your research does not involve greater than minimal risk.

A. Explain why your research does not involve greater than minimal risk:

We are performing no direct medical intervention to the research participants - they will be given no study medications and their prenatal care and/or their substance abuse care will not be altered in any way. They will participate in a prenatal education curriculum which is not anticipated to increase their risk at all. We will collect infant developmental outcome data via maternal questionnaire at 3 and 6 months. There will be no study intervention performed on the neonates.

SECTION 2. Assessment and Evaluation of the Risks

For details, refer to the UK IRB's Policy on Children in Research.

A. Provide justification for the participation of children as research subjects in your study.

We will be following the outcomes of the neonates of our maternal study participants. We will be looking at delivery outcomes as well as developmental outcomes at 3 and 6 months.

B. Has this research been conducted in adults? ○ Yes ◉ No

If yes, is there any indication that the proposed research would benefit, or at least not be harmful to children?

C. Indicate how many children you propose to enroll in the study: 533

Note: Whenever possible, involve the fewest number of children necessary to obtain statistically significant data which will contribute to a meaningful analysis relative to the purpose of the study.

Justify this number: We will be including the same number of infants as maternal participants (these are the neonates that are delivered)

D. Check all that apply:

- [ ] My research involves children 6 years of age or older.
- [x] My research involves children under 6 years of age.

Indicate how assent will be solicited by selecting all that apply:

Assent will be solicited from: ○ All Children ○ Sub-group of children ○ None of the children

I am requesting waiver of the requirement for assent from: ○ All Children ○ Sub-group of children ○ N/A

Indicate justification for waiving assent for these children: (Check all that apply)

- [ ] 1. The intervention or prospect involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the child/children and is available only in the context of the research.
- [ ] 2. The children are not capable of providing assent based on the age, maturity, or psychological state.
- [ ] 3. The capability of the children is so limited that they cannot reasonably be consulted
- [ ] 4. Other (explain)

** If you checked question 3, please explain:

** If you checked question 4, please explain:

E. Unless you are requesting a waiver of the requirement for assent for ALL children, you must answer “yes” to at least one of the following two statements.

Note: All assent forms or scripts must be attached to the “Informed Consent" section of this application. Be sure to save your responses in this section first.

For Children 6-11:
Assent will be obtained verbally. I have attached an assent script for obtaining verbal assent for IRB review.

○ Yes ◉ No

For Children 12-17:
The children will document assent by signing an assent form, or provide assent verbally if approved by the IRB, depending on the circumstances outlined in the application. I have attached an assent form or script for IRB review.

○ Yes ◉ No

F. Explain how study personnel will evaluate dissent (e.g., behaviors that would indicate the child does not want to participate such as moving away, certain facial expressions, head movements, etc.). If your study involves only children under 6 years of age, enter “N/A” below.

N/A

G. Describe how parental permission will be obtained.

We will obtain maternal consent to obtain neonatal outcome data at the time of study enrollment.

I have attached a parental permission form for IRB review. ◉ Yes ○ No

Parental permission forms must be attached in the “Informed Consent" section of this application. Be sure to save your responses in this section first.

Note that for Risk Category 3 or Risk Category 4 where research involves more than minimal risk without the prospect of direct benefit to the individual child, the permissions of both parents is required unless one parent is deceased, unknown, incompetent, or not reasonably available OR or only one parent has legal responsibility for the care and custody of the child.)

I am requesting

☐ The permission of both parents unless one parent is deceased, unknown, incompetent, or not reasonably available or when only one parent has legal responsibility for the care and custody of the child. **(required for Risk Category 3 or Category 4 Research).**

☑ The permission of one parent even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child. **(permitted for Risk Category 1 or Category 2 Research).**

☐ Waiver of the requirement for signatures on parental permission forms. (Complete the “Request for Waiver of Signatures” questions in the in the Informed Consent/Assent Process/Waivers Section)

☐ Waiver of the requirement for parental permission.

Note: Parental/guardian permission cannot be waived for FDA regulated studies that are greater than minimal risk (Risk Categories 2-4).

Parental Permission Waiver Options

○ Complete the "Request for Waiver of Informed Consent Process” questions in the Informed Consent/Assent Process/Waivers Section.

○ Justify that the research study is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable request (e.g., abused children):

Justify:

H. Describe how study personnel will ensure that a parent is present when the child participates in any research activities.
Note: If the nature of the research is such that it is not appropriate to have a parent present (e.g., research into sensitive personal issues, physical examinations of teenagers, etc.), explain why.

The developmental outcome data is obtained through a questionnaire completed by the mother

I. Describe the study personnel expertise for dealing with children at the ages included and whether they are knowledgeable and sensitive to the physical and psychological needs of the children and their families. Explain how the facility in which the research will be conducted is appropriate in relation to environment and/or equipment accommodating to children.

Maternal questionnaire will be completed in the prenatal clinic environment where the Group Care or Telemedicine consults occur.

J. If applicable, provide additional information that may support your request to involve children in research.

n/a

SECTION 3. Wards of the State

If you need to activate this section:

- go to the Subject Demographics section;
- select “Wards of State (Children)” in the categories of subjects and controls to be included in your study;
- save that section.

A. 45 CFR 46.409(a)

Please indicate which category describes your research proposal:

- ○ Research is related to subjects’ status as ward of the state.
- ○ Research is conducted in schools, hospitals, or similar setting(s) in which the majority of children involved in the study are NOT wards.

B. 45 CFR 46.409(b)

Federal regulations state that an advocate must be appointed in circumstances where investigators enroll wards of the state for research studies which are greater than minimal risk **specifically risk category 3 or 4**. Please answer the following questions:

a) Will the advocate serve in addition to a guardian or in loco parents?

○ Yes ○ No

b) Check the applicable item:

- ○ Each child will have their own advocate.
- ○ One advocate will serve for all children enrolled in the study.
- ○ N/A

c) Explain why the advocate has the background and experience to serve as an advocate for the study.

d) Federal regulations state that an advocate cannot be associated with the study, investigator or organization. Please provide assurances that the advocate does not meet any of the criteria listed above.

SECTION 4. Children Located Outside the State of Kentucky

Does your study involve children outside the state of Kentucky? ○ Yes ◉ No

Provide information regarding the state definition of legally authorized representative, child, or guardian, as applicable to the research and to the federal definitions. [If the research is to be conducted in more than one state outside of Kentucky, provide this information for each state.]:

Guidance on Consent and/or Authorization by a Legally Authorized Representative
Consistent with Kentucky health care decision statutes for choosing a legally authorized representative for children, the following responsible parties in the order of priority listed shall be authorized to make research participation decisions on behalf of the child: (a) the judicially-appointed guardian of the person, if the guardian has been appointed and if the decisions to be made under the consent are within the scope of the guardianship; (b) the parent of the child.

Definitions
For definitions of “child/children”, emancipated individuals, “legally authorized representative”, “guardian”, “assent”, and “permission”, see the ORI/IRB Informed Consent Standard Operating Procedures (SOP).

PRISONERS

0 unresolved comment(s)

SECTION 1.

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

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

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

Prisoner Categories

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

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

All enrolled study patients will receive a standardized prenatal education curriculum for OUD in pregnancy. Sites have been randomized to receive group prenatal education (“group” arm) imparted through a nurse facilitator and peer support specialist, or through telemedicine sessions with experts in nursing and substance abuse counseling.

SECTION 2.

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

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

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

All trial participants receive multiple sessions of prenatal educational curriculum, and gift card incentives at 5 specific data collection points in the study. No other advantages are foreseen; these are not expected to have undue influence on decision to enroll.

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

We do not anticipate any risks for prisoner participants beyond those of non-prisoners. This is a minimal risk study of

prenatal education for women with
OUD, the primary risk for all participants is breach of confidentiality. All participants are already receiving treatment for OUD, so there is no additional risk
related to being identified with a substance use disorder.

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

a) Describe how prisoners will be selected for participation:

Participants are identified in the community-based clinic where they receive care by nursing staff; thus, we anticipate possible enrollment of women on
community supervision or home incarceration, not those in a prison setting where authorities would have influence. All women meeting eligibility, they are provided more information about participating by study staff in the clinic setting. We have no control group

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

All trial participation occurs at the woman's medical clinic or treatment facility. Women housed in a jail are easily identified by clothing worn by inmates and/or under escort or restrained by a guard or handcuffs and will not be screened by any staff.

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

We will add language to the study consent form stating that the parole board can not take into consideration the participation in the PATHHome Trial. Again, we will not be enrolling women from prison settings who would interface with a parole board.

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

The PATHHome Trial follows women through pregnancy and until their infant is 6 months old with their local healthcare provider facilitating engagement. The follow-up periods are detailed in the informed consent form so that women are aware. Follow-up appointments are made in conjunction with clinical visits for pregnancy and/or OUD care whenever possible.

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

The PATHHome consent forms and recruitment materials are written in plain language to improve comprehension. Materials and study curriculum were reviewed by peers who have experience working with pregnant and early parenting women who have Opioid Use Disorder.

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

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

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

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

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

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

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

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

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

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

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

The participants health care professional feels she could benefit from the education provided in the PATHHome Trial.

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

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

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

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

If the Department of Corrections is directly involved in your research as a sponsor or otherwise, contact Office of Legal Counsel at 859-257-2936 or email at UKOfficeofLegalCounsel@uky.edu and ask to be connected with a research attorney for additional information.

PREGNANT WOMEN/NEONATES/FETUSES

0 unresolved comment(s)

For studies involving pregnant women, human fetuses and/or neonates, check the option that best fits your research, then address the questions and requests for information.

Section 1: Research Involving Pregnant Women or Fetuses

Research Involving Pregnant Women or Fetuses

A. Explain why the proposed research is scientifically appropriate, including descriptions of any pre-clinical studies on pregnant animals and any clinical studies on non-pregnant women that have been conducted and have provided data for assessing potential risks to pregnant women and fetuses.

This study is scientifically appropriate due to the dire need for intervention in the ongoing opioid epidemic, particularly as it affects expectant mothers. The previous work of the PATHways program has shown great promise, and this study is an opportunity to build off that by implementing the processes into an often underserved population. Furthermore, this study has the opportunity to intervene in a population that is often unable to access adequate medical care for Opioid Use Disorder given their proximity in the state to opioid use disorder specialists. The risk to women and fetuses involved in this study is minimal, but the potential benefit is great.

B. Select the option that best describes the anticipated risk to the fetus:

- (●) Not greater than minimal; or
- ( ) Greater than minimal risk and the risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus.

C. Provide a rationale for anticipated risk:

There is no anticipated maternal or fetal risk. There is no anticipated direct risk to the expectant mothers involved in this study. The only risk present is a potential breach of confidentiality, of which the utmost precautions will be taken to prevent. See Research Description for additional information on precautionary measures.

D. Explain why any risk is the least possible for achieving the objectives of the research:

The risk involved in this study is the minimal possible for achieving the desired goals.

E. Select the options that apply:

(●) Yes ( ) No 1) This research holds out the prospect of direct benefit to the pregnant woman.

(●) Yes ( ) No 2) This research holds out the prospect of a direct benefit both to the pregnant woman and the fetus; or

( ) Yes (●) No 3) This research does not hold out the prospect of direct benefit for the woman or the fetus, but the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means.

If "Yes" to any of these three questions, informed consent must be obtained from the pregnant woman or her legally authorized representative, but consent from the father is not required. The informed consent process should include a clear explanation regarding the reasonably foreseeable impact of the research on the fetus.

( ) Yes (●) No 4) This research holds out the prospect of a direct benefit solely to the fetus.

If "Yes", informed consent must be obtained from the pregnant woman AND the father. The informed consent process should include a clear explanation regarding the reasonably foreseeable impact of the research on the fetus. NOTE: The father's informed consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity, or the pregnancy resulted from rape or incest.

( ) Yes (●) No 5) This research will involve individuals under the age of 18 who are pregnant and are not considered emancipated minors.

If "Yes", assent from the pregnant child and permission from her parent or legal guardian must be obtained.

( ) Yes (●) No 6) Will there be any inducements, monetary or otherwise, offered to terminate a pregnancy?

( ) Yes (●) No 7) Will individuals performing research procedures have any part in any decisions as to the timing, method, or procedures used to terminate a pregnancy?

( ) Yes (●) No 8) Will individuals performing research procedures have any part in determining the viability of a fetus?

☑ **Section 2. Research Involving Neonates**

Research Involving Neonates

A. Viable Neonates - A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accordance with the requirement of 45 CFR 46 Subpart A and Subpart D.

◉ Yes ○ No Does your research involve viable neonates?

If yes, you will need to complete the Children subsection before submitting this application (if the Children subsection is not visible, go to the "Subject Demographics" section, checkmark "Children", and save).

B. Neonates of Uncertain Viability AND Nonviable Neonates - Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by 45 CFR 46 Subpart B unless the IRB determines that certain conditions are met. Your responses to the following will help the IRB determine whether the conditions are met.

Explain why the proposed research is scientifically appropriate and provide a description of any pre-clinical and clinical studies that have been conducted which provide data for assessing potential risks to neonates.
If not applicable, please enter "N/A".

We will be following up outcomes of neonates of mothers whom we follow through their pregnancies. We will be collecting delivery information, NAS information and collecting developmental outcome data on the infants at 3 and 6 months of life. Our primary outcome is Neonatal Abstinence Syndrome (NAS). We have seen a reduction in NAS at PATHways. NAS is our primary outcome for this study. As such, we will be collecting this data.

○ Yes ◉ No Will individuals engaged in the research have any part in determining the viability of a neonate?

C. Neonates of Uncertain Viability - Additional Requirements - Select the option that applies to your research.

☑ Not Applicable

○ The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, **AND** any risk is the least possible for achieving that objective.

○ The research has the main purpose of the development of important biomedical knowledge, which cannot be obtained by other means **AND** there will be no added risk to the neonate resulting from the research.

Explain the procedures that will be used to obtain legally effective informed consent of either parent of the neonate.

NOTE: If neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative will be obtained. **These procedures must ensure that each individual providing informed consent will be fully informed regarding the reasonably foreseeable impact of the research on the neonate. The father's informed consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.**

D. Nonviable Neonates – Additional Requirements - After delivery, a nonviable neonate may not be involved in research covered by 45 CFR 46 Subpart B unless the IRB determines that the following additional conditions are met.

☑ Not Applicable

○ Yes ○ No 1) Will the vital functions of the neonate be artificially maintained?

If "Yes", please explain:

Yes No 2) Does the research include procedures to terminate the heartbeat or respiration of the neonate?

Yes No 3) Will there be any added risk to the neonate resulting from this research?

If "Yes", please explain:

Yes No 4) Is the sole purpose of the research for the development of important biomedical knowledge that cannot be obtained by other means?

If "Yes", please explain:

5) Explain the procedures that will be used to obtain legally effective informed consent of both parents of the neonate.

Note: *If either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice. The consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice.* ***These procedures must ensure that each individual providing informed consent will be fully informed regarding the reasonably foreseeable impact of the research on the neonate.***

Section 3. Research Involving After Delivery, The Placenta, The Dead Fetus, Or Fetal Material

Research Involving After Delivery, The Placenta, The Dead Fetus, Or Fetal Material

A. This research proposes to use the following: (Check all that apply)

- Placenta
- The Dead Fetus
- Macerated Fetal Material
- Cells Excised from Dead Fetus
- Tissue Excised from Dead Fetus
- Organs Excised from Dead Fetus
- Other

If 'Other' Describe:

NOTE: The use of any of the above must be conducted in accordance with any applicable Federal, State, or local laws, regulations, and institutional policies regarding such activities.

B. Yes No Will any information associated with the material identified above be recorded for research purposes in such a manner that living individuals can be identified, directly or through identifiers linked to those individuals?

If "Yes", provide a rationale for the recording of identifiable information [Note: those individuals are considered to be research subjects and all pertinent human subject regulations are applicable to their participation.]:

Section 4. Research Not Otherwise Approvable Which Presents an Opportunity to Understand, Prevent, or Alleviate a Serious Problem

Affecting the Health or Welfare of Pregnant Women, Human Fetuses, or Neonates

If the study is Department of Health and Human Services (HHS) funded, or funding by HHS is sought, review by the Secretary of HHS and posting in the Federal Register for public comments and review is required. If this category is applicable, the Office of Research Integrity will prepare and submit a report of IRB review to the appropriate HHS institutional official.

Select all that apply:

- ☐ Neonates
- ☐ Pregnant Women
- ☐ Fetal Material

INFORMED CONSENT/ASSENT PROCESS/WAIVER

0 unresolved comment(s)

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

Additional Resources:

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

Consent/Assent Tips:

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

How to Get the Section Check Mark

1. You must:

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

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

Check All That Apply

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

Attachments

Informed Consent Process:

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

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

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

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

Special considerations may include:

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

Potential research subjects (those who are identified as being 6 - 32 weeks gestational age, with Opioid Use Disorder on Medication Assisted Therapy), will be approached for study enrollment by the trained study site research nurse. Study site research nurse (TBD) will consent patient for study enrollment. There is no required waiting period between informing prospective subject and obtaining consent. Only English speaking patients will be consented for study enrollment.
Patient participation or non-participation in the research protocol will not impact their routine clinical care in any way (prenatal or substance use care)

See HIPAA/Consent form (UK Sites) and Consent form (Non-UK Sites). We have updated the study consent forms to note that women under criminal justice supervision will not have information about participation disclosed to probation or parole and their decision to participate will not affect their status with any criminal justice agency, treatment, parole, or other agency.
Participant complaints may be fielded by either the primary PI or via the patient's primary obstetric care clinician. At the end of each session, participants will be asked if they have any questions or concerns, and contact information will be disseminated to participants. PI and attending clinicians will maintain and open line of contact in order to discuss any potential participant complaints or questions. Additionally, the informed consent forms provided to participants will contain all contact information necessary for lodging complaints or withdrawing from the study.

☐ Request for Waiver of Informed Consent Process

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

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

SECTION 1.

Check the appropriate item:

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

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

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

SECTION 2.

Explain how each condition applies to your research.

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

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

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

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

☐ Request for Waiver of Signatures

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

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

Select the option below that best fits your study.

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

○ **Option 1**

Describe how your study meets these criteria:

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

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

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

○ **Option 2**

Describe how your study meets these criteria:

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

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**

Describe how your study meets these criteria:

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

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

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

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

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

(•) Yes ( ) No

Manage Study Personnel

Identify other study personnel assisting in research project:

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

To add an individual via the below feature:

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

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

Study personnel assisting in research project:

Last Name	First Name	Responsibility In Project	Role	AC	Contact	Degree	StatusFlag	(HSP)	(HSP)Date	(RCR)	Removed?	Last Updated	SFI	Active
Akers	Becky	Co-Investigator	SP	Y	N		P	Y	03/03/3000		N	04/11/2019	N	Y
Ashford	Kristin	Co-Investigator	SP	N	N		P	Y	07/13/2024	Y	N	05/08/2018	N	Y
Barnes	Rebecca	Project Assistance/Support	SP	N	N		P	Y	08/17/2023	Y	N	08/17/2023	N	Y
Bauer	John	Co-Investigator	SP	N	N		P	Y	07/30/2023	Y	N	05/08/2018	N	Y
Benton	Brooke	Co-Investigator	SP	N	N	DO	N	Y	03/03/3000		N	09/11/2023	N	Y
Boucher	Sandra	Data Collection	SP	Y	N	RN	N	Y	03/03/3000		N	01/03/2019	N	Y
Bowers-Pryor	Julie	Project Assistance/Support	SP	N	N		P	Y	08/03/2023	Y	N	03/04/2019	N	Y
Brown	Crystal	Data Collection	SP	Y	N		P	Y	12/02/2021	Y	N	01/03/2019	N	Y
Campbell	Deonna	Data Collection	SP	Y	N		N	Y	03/03/3000		N	03/26/2019	N	Y
Chamberlain	Anna	Data Collection	SP	N	N	RN	P	Y	12/10/2021	Y	N	01/29/2019	N	N
Cockerham-Morris	Cynthia	Project Assistance/Support	SP	N	N		P	Y	04/25/2022	Y	N	06/26/2019	N	Y
Davis	Olivia	Data Analysis/Processing	SP	N	N		S	Y	04/14/2024	Y	N	08/20/2024	N	Y
Esposito	Hope	Data Collection	SP	Y	N		P	Y	08/16/2022	Y	N	08/17/2022	N	Y
Fawcett	Karen	Study Coordinator	DP	Y	Y		P	Y	03/21/2023	Y	N	02/04/2020	N	Y
Flowers	Coy	Co-Investigator	SP	Y	N	MD	P	Y	02/23/2022	Y	N	02/28/2022	N	Y
Frankenburger	D	Medical Supervisor	SP	N	N	RN	P	Y	05/15/2022	Y	N	12/19/2018	N	Y
Hall	Hannah	Data Collection	SP	Y	N		N	Y	03/03/3000		N	02/22/2022	N	Y
Hausman	Elizabeth	Project Assistance/Support	SP	N	N		P	Y	01/18/2023	Y	N	05/15/2023	N	Y
Joy	Jason	Project Assistance/Support	SP	N	N		P	Y	07/26/2024	Y	N	05/08/2018	N	Y
Miller	Edward	Co-Investigator	SP	Y	N	MD	N	Y	03/03/3000		N	02/26/2021	N	Y
Miller	Melissa	Data Analysis/Processing	SP	N	N		P	Y	12/01/2021	Y	N	02/13/2019	N	Y
Nelson-Cooke	Elizabeth	Data Analysis/Processing	SP	N	N	PhD	P	Y	08/18/2022	Y	N	06/14/2024	N	Y
O'Brien	John	Co-Investigator	SP	N	N		P	Y	07/31/2023	N	N	05/08/2018	N	Y
Phelps	Beverly	Data Collection	SP	Y	N		N	Y	03/03/3000		N	05/30/2019	N	Y
Powell	Hayley	Project Assistance/Support	SP	Y	N		P	Y	01/29/2024	Y	N	05/19/2021	N	Y
Schadler	Aric	Data Collection	SP	N	N		P	Y	06/10/2024	Y	N	03/23/2020	N	Y
Schanbacher	Brandon	Data Collection	SP	N	N		P	Y	10/09/2023	Y	N	03/23/2020	N	Y
Shrestha	Asmita	Project Assistance/Support	SP	N	N	MPH	P	Y	10/10/2022	Y	N	07/10/2024	N	Y
Sizemore	Tammy	Data Collection	SP	Y	N	RN	N	Y	03/03/3000		N	12/19/2018	N	Y

Last Name	First Name	Responsibility In Project	Role	AC	Contact	Degree	StatusFlag	(HSP)	(HSP)Date	(RCR)	Removed?	Last Updated	SFI	Active
Slavov	Krassimir	Data Analysis/Processing	SP	N	N		P	Y	02/13/2024	Y	N	03/27/2024	N	Y
Sparkman	Wendolyn	Data Collection	SP	Y	N	RN	N	Y	03/03/3000		N	09/19/2022	N	Y
Stromberg	Arnold	Co-Investigator	SP	N	N		P	Y	09/07/2021	N	N	05/08/2018	N	N
Strong	Misty	Data Collection	SP	Y	N		P	Y	12/03/2021	Y	N	01/03/2019	N	Y
Surratt	Hilary	Co-Investigator	DP	Y	Y	PhD	P	Y	05/19/2022	Y	N	02/11/2020	N	Y
Thompson	Katherine	Co-Investigator	SP	N	N		P	Y	11/09/2021	Y	N	10/30/2023	N	Y
Thompson	Misty	Co-Investigator	SP	Y	N		N	Y	03/03/3000		N	02/13/2019	N	Y
Todd	Rebecca	Co-Investigator	SP	Y	N		P	Y	01/28/2023	Y	N	11/02/2021	N	Y
Unes Kunju	Shebna	Co-Investigator	SP	Y	N		N	Y	03/03/3000		N	12/10/2021	N	Y
Vice	Marie	Project Assistance/Support	SP	Y	N		P	Y	01/25/2022	Y	N	06/02/2020	N	Y
Whitley	Wendy	Data Collection	SP	Y	N		P	Y	11/06/2023	Y	N	09/20/2021	N	Y
Wilson	Bethany	Project Assistance/Support	SP	N	N		P	Y	01/28/2022	Y	N	01/29/2019	N	Y
Arriagada-Alvarado	Susana	Co-Investigator	SP	N	N		P	N	07/23/2018		Y	06/25/2020	N	N
Bassetti	Karen	Project Assistance/Support	SP	Y	N		P	N	09/14/2020		Y	02/22/2022	N	N
Benning	Grace	Project Assistance/Support	SP	Y	N	LPN	N	Y	03/03/3000		Y	07/16/2021	N	Y
Birch	Morgan	Co-Investigator	SP	Y	N		N	Y	03/03/3000		Y	02/22/2022	N	Y
Charles	Raeanna	Data Collection	SP	Y	N		N	Y	03/03/3000		Y	07/16/2021	N	Y
Chavan	Niraj	Co-Investigator	SP	N	N		S	N	03/03/2021		Y	02/22/2022	N	N
Collins	Paula	Data Collection	SP	Y	N		N	Y	03/03/3000		Y	05/09/2023	N	Y
Dicken	Christian	Data Collection	SP	Y	N	RN	N	Y	03/03/3000		Y	02/26/2021	N	Y
Dotson	Tony	Co-Investigator	SP	Y	N		N	Y	03/03/3000		Y	06/25/2020	N	Y
Elliott	Alyssa	Project Assistance/Support	SP	Y	N		P	N	10/01/2018		Y	02/26/2021	N	N
Gullett	Courtney	Project Assistance/Support	SP	Y	N		P	Y	10/18/2021		Y	05/09/2023	N	Y
Hafley	Amanda	Project Assistance/Support	SP	Y	N		P	N	03/16/2021	N	Y	05/09/2023	N	Y
Haynes	Joseph	Co-Investigator	SP	Y	N		P	N	02/08/2019		Y	06/25/2020	N	N
Holbrook	Haylee	Data Collection	SP	Y	N		N	Y	03/03/3000		Y	08/17/2023	N	Y
HOward	Douglas	Co-Investigator	SP	Y	N	MD	N	Y	03/03/3000		Y	05/12/2022	N	Y
Kelly	Kimberly	Project Assistance/Support	SP	N	N		P	Y	01/30/2024	Y	Y	02/26/2021	N	Y
Kindred	Michael	Co-Investigator	SP	N	N		P	N	11/12/2018		Y	07/09/2020	N	Y
Kuhl	Sara	Project Assistance/Support	SP	Y	N	BS	P	Y	08/10/2023	Y	Y	05/09/2023	N	Y
Mcknight	Alison	Data Collection	SP	Y	N	RN	N	Y	03/03/3000		Y	02/26/2021	N	Y
Milward	Brenda	Data Collection	SP	Y	N		S	N	04/10/2019		Y	12/10/2021	N	N
Milward	Nikki	Data Collection	SP	Y	N		N	Y	03/03/3000		Y	05/12/2022	N	Y
Nemec	Jeffery	Co-Investigator	SP	Y	N	MD	N	Y	03/03/3000		Y	12/16/2021	N	Y
Null	Angela	Co-Investigator	SP	Y	N	PSS/TCADC	N	Y	03/03/3000		Y	02/22/2022	N	Y
Partin	Martha	Data Collection	SP	Y	N	RN	N	Y	03/03/3000		Y	02/26/2021	N	Y
Perkins	Santana	Data Collection	SP	Y	N	RN	P	Y	12/16/2021	N	Y	08/17/2023	N	N
Playforth	Karen	Co-Investigator	SP	N	N		P	Y	06/28/2022	N	Y	07/29/2021	N	Y
Reaves	Angela	Data Collection	SP	Y	N		N	Y	03/03/3000		Y	02/26/2021	N	Y
Ruff	Kelly	Project Assistance/Support	SP	Y	N		P	N	10/09/2020	N	Y	05/09/2023	N	N
Ruth	Carla	Data Collection	SP	Y	N	RN	P	N	10/31/2018		Y	07/29/2021	N	Y
Slone	Alison	Co-Investigator	SP	N	N	MD	P	Y	11/08/2023	Y	Y	02/22/2022	N	Y
Smallwood	Pamela	Co-Investigator	SP	Y	N	MD	P	N	12/28/2020	Y	Y	05/12/2022	N	Y
Snowden	Linda	Data Collection	SP	Y	N	RN	N	Y	03/03/3000		Y	06/25/2020	N	Y
Sparks	Chasity	Data Collection	SP	Y	N		N	Y	03/03/3000		Y	06/25/2020	N	Y

Last Name	First Name	Responsibility In Project	Role	AC	Contact	Degree	StatusFlag	(HSP)	(HSP)Date	(RCR)	Removed?	Last Updated	SFI	Active
Sprang	Robert	Consultant/Advisor	SP	N	N		P	Y	07/02/2024	Y	Y	05/09/2023	N	Y
Stauble	Elaine	Co-Investigator	SP	Y	N	MD	N	Y	03/03/3000		Y	02/22/2022	N	Y
Tackett	Kayla	Project Assistance/Support	SP	Y	N		N	Y	03/03/3000		Y	08/17/2023	N	Y
Tate	Katelin	Project Assistance/Support	SP	Y	N	LPN	N	Y	03/03/3000		Y	05/09/2023	N	Y
Thompson	Melanie	Data Collection	SP	Y	N		N	Y	03/03/3000		Y	05/12/2022	N	Y
Thompson	Stephanie	Project Assistance/Support	SP	N	N		P	N	06/30/2021		Y	07/29/2021	N	Y
Tucker	Andrea	Co-Investigator	SP	Y	N		N	Y	03/03/3000		Y	02/26/2021	N	Y
Unes Kunju	Shebna	Co-Investigator	SP	Y	N		S	N	10/25/2017		Y	12/10/2021	N	Y
White	Kevin	Co-Investigator	SP	Y	N	MD	N	Y	03/03/3000		Y	09/11/2023	N	Y
Workman	Kara	Project Assistance/Support	SP	Y	N	RN	N	Y	03/03/3000		Y	05/12/2022	N	Y

RESEARCH DESCRIPTION

0 unresolved comment(s)

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

Pro Tips:

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

Background

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

Perinatal opioid use disorder (OUD) is a major health concern in the US with significant impact on mothers, infants, and communities. Our team at University of Kentucky/UK HealthCare (UK) has developed a comprehensive clinical care model for perinatal OUD (known as UK-PATHways) that has demonstrated success in maternal and neonatal outcomes. The overreaching goals of the proposed project are to 1) expand the reach of this successful clinical program, 2) to reduce the impact of perinatal OUD in underserved rural areas of our state, and 3) to compare the relative effectiveness methods of delivery active elements of the PATHways program for rural implementation (local group-support vs. telemedicine).
The UK-PATHways program preliminary successes during the first three years are clear: enrolled mothers (n>200) have reduced relapse, increased treatment compliance, and improved neonatal outcomes when compared to non-enrolled OUD mothers. 1However, at this time UK-PATHways is only available at our main healthcare campus in Lexington, KY. Many eligible patients reside great distances from our clinical home and some current patients travel hours to access this valuable resource. While Medication Assisted Therapy (MAT) has become increasingly available in our region, many of the components of the UK-PATHways program are not readily accessible in rural Central and Eastern Kentucky and the quality of programming with MAT treatment is not standardized in these locations. Furthermore, rural patients continue to face challenges related to stigma of their OUD and transportation difficulties if they desire more comprehensive services. The proposed study will evaluate the introduction of essential components of the UK-PATHways program into rural communities, and identify the optimal intervention strategies for expansion of services and to improve the treatment of OUD for rural patients.

Objectives

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

Aim 1.) Conduct a randomized cluster trial using a 'hub and spoke' study design, comparing two delivery modes (local GROUP care vs TELEMEDICINE) for the delivery of a PATHways based patient education curriculum at participating regional sites. Each regional site will be randomized to support one of two study arms: 1) Prenatal group care led by a Perinatal Nurse Facilitator and Peer Support Specialist (GROUP arm); or, 2) Telemedicine consultation provided by a Perinatal nurse educator, substance abuse counselor and/or Peer Support Specialists based at the 'hub' site (TELEMEDICINE arm).
Aim 2.) Evaluate the relative effectiveness of each study arm on primary and secondary maternal and neonatal outcomes as compared to the established PATHways program (UK-PATHways: Hub) at the University of Kentucky.

Study Design

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

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

We will perform a stratified cluster randomized controlled trial with randomization of participating clusters into a "GROUP CARE" or "TELEMEDICINE" arm. Sites will be stratified into "high volume" (>500 deliveries/year) and "low volume" (<500 deliveries/year). Randomization will be 1:1 within each strata. According to 2016 site specific delivery data, 6 sites are "low volume" and 6 sites are "high volume". All enrolled study patients will continue to receive regular prenatal care (PNC) through their community based obstetric

providers and medication assisted treatment (MAT) with buprenorphine or methadone for opioid use disorder (OUD) through their respective licensed prescribing providers. In addition to PNC and MAT, study patients will receive supplementary clinical care every two weeks either in the form of a structured group model (GROUP CARE) or in a telemedicine consult (TELEMEDICINE) for OUD in pregnancy through their allocation into the “group” or “telemedicine” arm of the trial. Half of the participating clusters will be randomized to receive group prenatal care (“group” arm) imparted through a perinatal nurse facilitator and community based peer support specialist. The remaining clusters will receive pregnancy specific education through telemedicine imparted by a Perinatal nurse educator, substance abuse counselor and/or Peer Support Specialists. The supplemental clinical care that patients will consist of a standardized rotating 8 topic patient education curriculum, including the following topics: 1. Treatment Options for Opioid Use Disorder 2. Smoking Cessation 3. Relapse Prevention Education 4. NAS Reduction Education 5. Breast Feeding Support/Education6. Domestic Violence Education 7. Postpartum Depression 8. Birth Control/Family Planning.
Meetings and consultations will occur every two weeks in each arm of the trial from enrollment until 8 weeks post-partum and will then continue monthly until 6 months post-partum.

Potential Perinatal Nurse Facilitators will be identified at each study site randomized to the “group” arm. These individuals will undergo a two-day training program with the UK-PATHways: Hub Perinatal Nurse Facilitator (Diana Frankenburger, see key personnel). The UK-PATHways: Hub Perinatal Nurse Facilitator will serve as a point person for study site Nurse Facilitators and lead monthly meetings via Skype or in person. Peer Support Specialists will be identified within the region (three total) and, if not previously certified/trained, training will be provided.
Telemedicine arm consultations will be provided by study personnel identified within this application including Jason Joy, LMFT, Diana Frankenburger and Anna Chamberlain.

Attachments

Subject Recruitment Methods & Advertising

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

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

For additional information on recruiting and advertising:

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

Participants will be recruited based on the following inclusion criteria: Pregnant women at 6-32 weeks gestational age; History of OUD; Who are receiving MAT and obtaining prenatal care at one of the 12 study sites. Patients will be identified by site research nurse (to be determined), viable pregnancy by ultrasound report will be confirmed and diagnosis of OUD and taking MAT will be confirmed. Patient will then be approached about possible recruitment in study. Each study site will have a contracted study nurse who will be identified, CITI trained and added to the IRB for patient recruitment. Although, not an inclusion or exclusion criteria, we have noted that a substantial proportion of potential study participants are under some type of criminal justice supervision at some point during their study participation. We have added a question to the study screener. Importantly, we will not screen or enroll women who are incarcerated in a detention center, easily identified by clothing worn by inmates and/or under escort or restrained by a guard or handcuffs.

Clinical Referrals - clinical providers in the Division of Maternal Fetal Medicine, Department of OB-GYN, provide telemedicine consultations to women with high risk pregnancies through the Kentucky Angels program. At the end of a patient’s regular telemedicine consultation, the provider will briefly describe the PATH Home study to potentially eligible patients using a standard script. If a patient is interested in learning more about the study, the provider will ask the patient if it is okay for the research nurse at the PATH Home study site to contact them. If yes, the provider will ask the patient to provide a telephone number that can be shared with the research nurse. The provider will also explain to the patient that their contact information (name and telephone number) will be shared a member of the research team who will contact the research nurse at the study site The provider will add a note in “ViewPoint” (the ultrasound reporting system), documenting that the study was discussed with the patient, she was interested in learning more about the study, she gave permission for the research nurse at the study site to contact her, and provided a phone number.
Potential participants will be recruited for this study from among the patients presenting for prenatal care with OUD of pregnancy at any of the aforementioned study sites across the state of KY. Clinic providers and research staff may use a flyer as a recruitment tool with their patients. In addition, clinics may provide the flyer to other community-based providers and organizations and disseminate at community events to promote awareness about the study and referrals.

Attachments

Attach Type	File Name
Advertising	PATH Home Recruitment Flyer - PR Approval.pdf
Advertising	V5 clean 74853_Advertising_488609-111_24_2021.docx
Advertising	TC V4 74853_Advertising_488609-1.docx

Research Procedures

Describe how the research will be conducted.

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

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

Local staff at each of the 11 sites will be trained as Perinatal Nurse Facilitators, with local residents being trained as peer support specialists. All study participants will receive regular prenatal care through their community based obstetric providers and medication assisted treatment (MAT) with buprenorphine or methadone for opioid use disorder through their respective licensed prescribing providers. In addition to PNC and MAT, study patients will receive a rotating supplementary patient education curriculum (see below) based on the PATHways intervention for OUD in pregnancy. The method by which this will be delivered is based on their allocation into the "group" or "telemedicine" arm of the trial. Half of the participating clusters will be randomized to receive the patient education curriculum through a local group care model imparted through a perinatal nurse facilitator and community based peer support specialist. The remaining clusters will receive the augmented clinical care through telemedicine provided by a Perinatal nurse educator, substance abuse counselor and/or Peer Support Specialists. The research and intervention procedures are identical for participants regardless of their criminal justice status.

Potential perinatal nurse facilitators will be identified at each study site randomized to the "group" arm. These individuals will undergo a two day training program with the UK-PATHways: Hub Perinatal Nurse Facilitator (Diana Frankenburger - see key personnel). Ms. Frankenburger will serve as a point person for study site Nurse Facilitators and lead monthly meetings via skype or in person. Peer support specialists will be identified within the region (3 total), and, if not previously certified/trained, training will be provided.

Telemedicine arm consultations will be provided by study personnel identified within this application including Jason Joy, Diana Frankenburger and Anna Chamberlain.

GROUP CARE ARM: Study participants at the clusters randomized to the "group" arm will receive group care at 2 week intervals initiated from study enrollment. Group care sessions will be led by an on-site perinatal nurse facilitator and a local peer support specialist. The prenatal group sessions will be imparted in a structured fashion with each session lasting for 45-60 minutes. The content matter discussed will follow a rotating curriculum comprising 8 core sessions over a 16 week period, and will be repeated at each study site as long as there are enrolled active study patients. Once a patient is 8 weeks postpartum ,she will be seen monthly until 6 months postpartum. Data will be collected at each visit by trained study site personnel and entered in a secured online database (REDcap).

TELEMEDICINE ARM: Study participants at the clusters randomized to the telemedicine arm will receive the intervention through a telemedicine platform as part of the Kentucky Angels telemedicine program. The division of maternal fetal medicine has established a platform for obstetric outreach addressing perinatal issues pertaining to high risk pregnancies across Kentucky. As part of this cluster RCT, participants at study sites randomized to this arm will receive these telemedicine-based consultations with providers from perinatal nurse educators, peer support specialists, and substance abuse counselors at the University of Kentucky every two weeks until 8 weeks postpartum - and them monthly until 6 months post-partum. Should the patient have the need for additional sessions with a specialist, these will be provided . Data will be collected at each visit by trained study site personnel, and entered into a secured online database (REDcap). See data management plan for more information on the data storage.

The supplemental clinical care that patients will consist of a standardized rotating 8 topic patient education curriculum, including the following topics: 1. Treatment Options for Opioid Use Disorder 2. Smoking Cessation 3. Relapse Prevention Education 4. NAS Reduction Education 5. Breast Feeding Support/Education 6. Domestic Violence Education 7. Postpartum Depression 8. Birth Control/Family Planning.

Attachments

Data Collection & Research Materials

In this section, please provide the following:

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

We will be performing the following maternal patient surveys at the following study time-points:

SCHEDULE OF STUDY ASSESSMENTS
ENROLLMENT/INTAKE
1. DSM-5 Criteria for Opioid Use Disorder
2. Edinburgh Depression Scale
3. Fagerstrom Nicotine Dependence
4. GAD-7 (Anxiety)
5. Adverse Childhood Experience (ACE)
6. Abuse Assessment Screen

3rd Trimester
1) WHO QoL-BRF (Quality of Life measure)
2) Experience of Care and Health Outcomes (ECHO) - modified
3) Cornell Health Services Index (CHSI)
4) Fagerstrom Nicotine Dependence
5) Edinburgh Depression Scale
6) GAD-7

3 months Post-Partum
1) WHO QoL-BRF
2) Experience of Care and Health Outcomes (ECHO) - modified
3) Cornell Health Services Index (CHSI)
4) Fagerstrom Nicotine Dependence
5) Edinburgh Depression Scale
6) GAD-7
7) Ages and Stages

6 months Post-Partum
1) WHO QoL-BRF
2) Experience of Care and Health Outcomes (ECHO) - modified
3) Cornell Health Services Index (CHSI)
4) Fagerstrom nicotine Dependence
5) Edinburgh Depression Scale
6) GAD-7
7) Ages and Stages

Study participants will be asked to complete surveys in REDCap available on iPads dedicated specifically for this project; however, all participants will have the option to complete hard copies of the surveys if they prefer. Data from surveys completed on iPads will be uploaded directly into REDCap. Devices will be managed by UK Healthcare IT, which already deploys a large number of iPad devices and is very familiar with the security and management requirements of iOS based devices.UK Healthcare IT currently has a management app configured to ensure the security of the devices and to apply sufficient restrictions that the devices cannot be used for unintended purposes. All devices will be stored securely in locked cabinets.

We will be collecting the following maternal data:
1. Prenatal labs
2. Infectious complications
3. MAT program participation rate (by patient)
4. Study program participation rate (e.g. frequency of clinic attendance at telemedicine and/or group sessions);
5. Prenatal care attendance (medical record review).
6. Urine drug screen result on admission to labor and delivery, 3 and 6 months postpartum (obtained from medical records)
7. Smoking status: evaluated through patient interview and Fagerstrom Nicotine Dependence Scale at intake, 3rd trimester, 3 and 6 months postpartum.
8. Addiction severity: DSM-5 Criteria for Opioid Use Disorder at intake
9. Obstetric complications including but not limited to Preterm birth <37 GA, growth restriction (<10%ile), preterm rupture of membranes, preeclampsia, multiple gestation, gestational diabetes, chorioamnionitis, miscarriage, fetal demise, cesarean delivery (medical record review)
10. Overdose tracking (overdose reversal agent needed, admitted to hospital/ED for overdose): patient interview at every visit
11. Health services utilization: Cornell Health Service Index administered in 3rd trimester, 3 and 6 months post-partum
12. Patient experience of care: Experience of Care and Health Outcomes (modified) Survey administered in 3rd trimester, 3 and 6 months post-partum
13. Depression: Edinburgh Postpartum Depression Scale administered at intake, 3rd trimester, 3 and 6 months postpartum
14. Anxiety: GAD7 administered at intake, 3rd trimester, 3 and 6 months postpartum
15. Quality of life: WHO QoL-BRF administered in 3rd trimester, 3 and 6 months post-partum
16. Mother-Infant dyad status/Foster care requirement: retention of custody evaluated by patient interview at hospital discharge, 3 and 6 months postpartum
17. Maternal breastfeeding status: evaluated by patient interview at delivery, 3 and 6 months postpartum.

We will be collecting the following fetal data:
Fetal size per gestational age; Any genetic or structural anomalies; any other fetal complications.

We will be collecting the following neonatal data, including the following assessments:
Gestational age and weight at birth; 5 & 10min Apgar score; NICU/nursery hospital admission; NAS diagnosis & treatment requirement (primary outcome); NAS medication days; in-hospital growth (birth to discharge per day); other infant morbidities; total hospitalization length of stay, immunization compliance, ED visits, follow up with scheduled pediatric visits.

Data will be obtained via medical record review, patient interview, physician/staff report, review of state Medicaid data, and hospital discharge data by the study site research staff with the oversight of the UK-study team.

We will perform fidelity monitoring of intervention delivery. Research nurses/facilitators (group arm), providers (telemedicine arm), and all study participants will be asked to complete a fidelity form, similar to an evaluation form, at the end of each educational session. We will evaluate intervention fidelity by comparing provider and participant responses. If any discordance is identified between provider and participant responses for a given topic, additional training related to intervention delivery may be required.

In each arm, patients will be randomly selected to participant in a qualitative interview process at each participating site at the time of the 6 month postpartum follow-up. The interviews will be facilitated by Co-I Hilary Surratt, who has extensive experience using qualitative techniques with substance-involved patients in community based and treatment settings, with the assistance of research coordinators trained in qualitative interviewing techniques. Patients will be offered a fifty dollar stipend for their time to participate in the interview. 3 patients will be randomly selected from each participating site for a total of 33 interviews.

In addition, we will perform in-depth qualitative interviews (also by Co-I Surratt) of both physician and research nurses from each site at study conclusion in order to evaluate the acceptability of the study intervention in the practice setting.

Attachments

Attach Type	File Name
DataCollection	Ages and Stages 6 month instrument.pdf
DataCollection	ASQ-3-4-M.pdf
DataCollection	Adverse Childhood Experience (ACE).pdf
DataCollection	Abuse Assessment Screen.pdf
DataCollection	ECHO (Modified).docx
DataCollection	dsm-5-dx-oud-8-28-2017.pdf
DataCollection	WHO QoL-BRF.pdf
DataCollection	Fagerstrom_test.pdf
DataCollection	GAD_with_Info_Sheet.pdf
DataCollection	Edinburgh.pdf
DataCollection	CSI Primary Care version.ACedit.doc
DataCollection	Fidelity Monitoring - Participant Forms.pdf
DataCollection	Fidelity Monitoring - Provider Forms.pdf

Resources

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

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

This study takes place at 11 individual sites throughout Eastern Kentucky. As such, the resources at each may vary slightly. A general list of available resources includes the following:

University of Kentucky College of Medicine will be the primary hub of this study, and as such will be responsible for the storage and processing of data. Computer access, office space, and locked file storage are available for use in the Department of Obstetrics and Gynecology, located on the third floor of Chandler Hospital. Kentucky children's hospital will volunteer resources such as RedCap creation, additional office space, and staff support. Administrative support, accessibility to fax, high-speed copiers, and printers will be provided by the department of Obstetrics and GYnecology. Research coordinators have access to offices that are well-equipped with PC's and laptops for data entry and internet access for transmission of information. All computers are password protected to ensure confidentiality.

All computer related data will be stored securely under the governance of the PI team. All research labs and common equipment areas are fully equipped with standard items for modern molecular biological research.

A dedicated Research Information Services group provides a high-speed, secure network of microcomputers with access to high-quality printing services, and a variety of sophisticated software packages to the research community. Services include data management and storage, information backup, publication and presentation graphic support services, high-definition audio-visual systems, and VPN connectivity to networks outside the organization for collaborative research including Kentucky Children's Hospital Mainframe Information System.

The 11 sites throughout the state will provide office space for those overseeing the work done at the site, in addition to providing staffing to collect data, computer and internet access, and secure file storage methods which, if paper, will include a locked office. Each research nurse will have a password protected computer on which to enter data. Tablets will be used by research participants (UK-issued) for survey completion.

Finally, the University of Kentucky department of Ob/GYN will provide telemedicine access to sites randomized to the telemedicine arm of this study. This will be done through contract, relying on much of the same information set forth in the Kentucky Angels telemedicine project.

Fidelity Monitoring will also be utilized.

Potential Risks & Benefits

Risks

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

Benefits

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

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

Study participants will not be required to undergo any invasive procedures as part of this study. Given that we are collecting PHI, risks of study participation pertain to breach of patient confidentiality in the event that PHI may be accessed/misused by non study personnel. We are unable to collect anonymized data since an evaluation of the primary study outcomes relies heavily on relevant clinical information that cannot be collected in an anonymized fashion. We have updated the study consent forms to note that women under criminal justice supervision will not have information about participation disclosed to probation or parole and their decision to participate will not affect their status with any criminal justice agency, treatment, parole, or other agency.
The findings of this study will have considerable societal and public health benefits at large. The benefits from the study will also accrue to the study participants in subsequent pregnancies if results from the data analysis were to predict different practice patterns from the current management protocols for prenatal care with a strong emphasis on the inclusion of patient counseling while undergoing MAT for OUD in pregnancy. These potential benefits strongly outweigh the risk of a breach in patient confidentiality, which is mitigated by the precautions above. Participants criminal justice status does not alter risk/benefit ratio.

Available Alternative Opportunities/Treatments

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

N/A

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Records, Privacy, and Confidentiality

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

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

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

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

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

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

There will be no biologic material collected from pregnant women, as there are no invasive procedures being performed as part of the study. Women will continue to receive prenatal care throughout the course of pregnancy, just as they would have otherwise received regardless of study participation. While we will be using some of the clinical data that is relevant to the prenatal care of pregnant women, study participants will be undergoing these investigations as part of their prenatal care and not separately for the purposes of the study alone.

Some of the research materials to be collected includes gestational outcomes data, including but not limited to: details of maternal prenatal care, labor and delivery outcomes, details pertaining to the course of their OUD in pregnancy and details pertaining to individual patient MAT course, as well as neonatal data including hospital course, Finnegan scoring, incident NAS, neonatal treatment and follow up. These will be abstracted from a review of the standardized and template based electronic medical record system. These will be collected and stored in a HIPAA compliant safe and secure environment by personnel specifically trained in the handling of PHI.
Healthcare related data that will be collected will be stored in a secure, password protected electronic file on a single computer workstation with limited access. Similarly, all paper based documentation bearing identifying information will be stored in a secure locked filing cabinet under the PI's supervision. All data will be De-identified by stripping it of all identifiable PHI at the time of collection. Hence the data that will be used for analyses and review will be entirely De-identified, with study participants being referenced only through randomly generated numbers assigned to each study participant. This is being done to ensure the maintenance of confidentiality for the study participants and safety with regard to the use of healthcare data.
Healthcare related data will be collected from study participants and stored in a secured, password protected electronic file on a single computer workstation with limited access - solely to authorized study personnel as decided by the study PI. Similarly, all paper based documentation bearing patient identifying information (e.g. consent forms) will be stored in a secure locked filing cabinet under the PI's supervision with access granted solely to authorixed study personnel as decided by the PI. All data will be de-identified by stripping it of all identifiable PHI at the time of collection. Hence, the data used for analyses and review will be entirely de-identified, with study participants being referenced only through randomly generated numbers assigned to each study participant. This is being done to ensure the maintenance of confidentiality doe the study participants and safety with regard to the use of healthcare data. We do not anticipate any risks for prisoner participants beyond those of non-prisoners. This is a minimal risk study of prenatal education for women with OUD, the primary risk for all participants is breach of confidentiality. All participants are already receiving treatment for OUD, so there is no additional risk related to being identified with a substance use disorder.

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

◉ Yes ○ No

Payment

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

Participants will be provided with gift cards based on participation at five prescribed time points that are tied to data collection and essential monitoring. The timepoints are: 1. initial enrollment and consent to participate within the project ($50 gift card), 2. 28-32 week prenatal data collection ($50 gift card), 3. report and receipt of infant measures upon delivery ($50 gift card), 4. post-delivery data collection and receipt of measures on participant and baby at three (3) months ($50 gift card), and 5. a final post-delivery data collection and receipt of measures on participant and baby at six (6) months ($50 gift card). In addition, those patients who participate in the in- depth qualitative interview process (n=33) will be offered an addition participation incentive ($50 gift card).
Following enrollment, participants will be informed about the opportunity to recruit other potential participants to the PATHHome Trial. Participants will be asked to share contact information for study staff and the partner clinic with potentially interested participants in their networks. Should a participant referral result in a confirmed study enrollment, the referring participant will receive a $50 gift card.

Costs to Subjects

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

There are no reported costs to participants.

Data and Safety Monitoring

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

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

Due to the vulnerable nature of the study population, the PI, will with input from Co-Investigators, be responsible for all data and safety. The principal investigator, with input from Co-Investigators, will be responsible for monitoring the data quality, and participant safety throughout this study, executing the DSMP and complying with the reporting requirements. The PI will also be responsible for providing a summary of the Data and Safety monitoring report on a semi-annual basis as a part of the progress report. The Data and Safety monitoring report will include the participants' socio-demographic characteristics, expected versus actual recruitment and retention rates, any relevant quality assurance or regulatory issues, summary of adverse events (AEs) and serious adverse events (SAEs), if any and any changes to the protocol as necessary.

Perinatal (maternal and neonatal / infant) data will be collected from the review of the electronic medical record system. Standardized data collection templates (REDCap) will be employed for data abstraction and management. Data will be de-identified and stripped of all identifying information prior to analysis. All data will be coded in a manner so that identifying data is not present on study materials. Each subject will have a unique identifier that will be linked to their name and medical record number in a file kept securely, and separately from other study data. All data will be kept in a secure place, with access restricted solely to study personnel authorized by the study PI. No patient will be identified individually in a manner that might reasonably subject the patient to identification in any publication or other presentation.

Monitoring for AEs will be based upon spontaneous self-report by the study participants and verification by medical and research staff. All AEs occurring during the study period will be documented and reported to the PI. The PI and Co-Investigators will follow all AEs to the point of satisfactory resolution, as outlined above. We do not anticipate any Serious Adverse Events (SAEs) (as defined by the FDA) with the interventions being proposed in the study. There are no invasive procedures being performed on pregnant women in the study.

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

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

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

n/a

Are you recruiting or expect to enroll **Non-English Speaking Subjects or Subjects from a Foreign Culture**? (does not include short form use for incidentally encountered non-English subjects)

○ Yes ◉ No

Non-English Speaking Subjects or Subjects from a Foreign Culture

Recruitment and Consent:

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

Cultural and Language Consultants:

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

- This person should be familiar with the culture of the subject population and/or be able to verify that translated documents are the equivalent of the English version of documents submitted.

- The consultant should not be involved with the study or have any interest in its IRB approval.
- Please include the name, address, telephone number, and email of the person who agrees to be the cultural consultant for your study.
- ORI staff will facilitate the review process with your consultant. Please do not ask them to review your protocol separately.

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

Local Requirements:

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

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

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

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

○ Yes ◉ No

HIV/AIDS Research

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

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

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

PI-Sponsored FDA-Regulated Research

Is this an investigator-initiated study that:

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

○ Yes ◉ No

PI-Sponsored FDA-Regulated Research

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

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

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

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

○ Yes ○ No

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

Attachments

HIPAA

0 unresolved comment(s)

Is HIPAA applicable? ◉ Yes ○ No

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

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

☐ HIPAA De-identification Certification Form

☐ HIPAA Waiver of Authorization

Attachments

STUDY DRUG INFORMATION

0 unresolved comment(s)

The term drug may include:

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

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

○ Yes ◉ No

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

LIST EACH DRUG INVOLVED IN STUDY IN THE SPACE BELOW

Drug Name:

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

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

☐ Investigational Drug Service (IDS) UK Hospital

Other Location:

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

○ Yes ○ No

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

IND Submitted/Held by:

Sponsor: ☐	Held By:	
Investigator: ☐	Held By:	
Other: ☐	Held By:	

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

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

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

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

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

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

Attachments

STUDY DEVICE INFORMATION

0 unresolved comment(s)

A DEVICE may be a:

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

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

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

○ Yes ◉ No

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

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

LIST EACH DEVICE BEING TESTED IN STUDY IN THE SPACE BELOW

Device Name:

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

○ Yes ○ No

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

IDE/HDE Submitted/Held by:

Sponsor: ☐ Held By:

Investigator: ☐ Held By:

Other: ☐ Held By:

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

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

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

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

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

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

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

Attachments

RESEARCH SITES

0 unresolved comment(s)

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

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

UK Sites

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

Schools/Education Institutions

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

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

Other Medical Facilities

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

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

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

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

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

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

Study sites include:

1. Ashland, KY - Karen's Place Maternity Center, ARC
2. Bowling Green, KY: Fairview Community Health Center
3. Corbin, KY: Grace Community Women's Health
4. Georgetown, KY: Brightview Health, LLC
5. Georgetown, KY: UK Women's Health Obstetrics and Gynecology – Georgetown
6. Louisville, KY: University of Louisville, HCOC/Prenatal Clinics
7. Middlesboro, KY: ARH Women's and Family Health Center-Middlesboro
8. Morehead, KY: UK Morehead Women's Healthcare
9. Prestonsburg, KY: Frontier Behavioral Health Center, PLLC
10. South Williamson, KY: ARH Women's and Family Health Center - Tug Valley
11. Vicco, KY: Primary Care Centers of Eastern Kentucky
12. Pikeville, KY - Pikeville Medical Center

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

Attachments

Attach Type	File Name
-IRB Authorization Agreement	IAA - Corbin (Grace Community Women's Health).pdf
-IRB Authorization Agreement	IAA - Hazard (Primary Care Centers of Eastern Kentucky).pdf
-IRB Authorization Agreement	IAA - Middlesboro (Appalachian Regional Healthcare Women's Health Center).pdf
-IRB Authorization Agreement	IAA - Tug Valley (Appalachian Regional Healthcare Women's Health Center).pdf
-IRB Authorization Agreement	Medical Center at Bowling Green IAA 4.29.19.pdf
-IRB Authorization Agreement	Hansen path home FULLY executed IAA 1.6.20.pdf
-IRB Authorization Agreement	IRB reliance for Karen's Place 9_14_2020.pdf
-IRB Authorization Agreement	fully executed IAA Frontier 5_2021.pdf
-IRB Authorization Agreement	Brightview IAA 11_2021.pdf
-IRB Authorization Agreement	Pikeville Med Center IAA - UK-PMC (UKY 44929).pdf

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

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

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

RESEARCH ATTRIBUTES

0 unresolved comment(s)

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

☐ Not applicable

Check All That Apply

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

FUNDING/SUPPORT

0 unresolved comment(s)

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

☐ Not applicable

Check All That Apply

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

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

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

Other:

Patient Centered Outcomes Research Institute (PCORI)

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.):

Patient Centered Outcomes Research Institute (PCORI)

Add Related Grants

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

Add Related Grants

Grant/Contract Attachments

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

○ Yes ◉ No

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

DOD SOP Attachments

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

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

Assurance/Certification Attachments

OTHER REVIEW COMMITTEES

0 unresolved comment(s)

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

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

○ Yes ◉ No

Additional Information

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

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

Attachments

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

ADDITIONAL INFORMATION/MATERIALS

0 unresolved comment(s)

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

Approval Letter Details:

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

Additional Materials:

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

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

Protocol/Other Attachments

Attach Type	File Name
Other	CR Comp AE_SAE listing.pdf

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

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

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

SIGNATURES (ASSURANCES)

0 unresolved comment(s)

Introduction

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

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

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

Required Signatures:

First Name	Last Name	Role	Department	Date Signed	
Frederick	Ueland	Department Authorization	Obstetrics & Gynecology	08/29/2019 03:39 PM	View/Sign
Wendy	Hansen	Principal Investigator	Obstetrics & Gynecology	08/30/2019 12:41 PM	View/Sign

Department Authorization

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

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

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

Principal Investigator's Assurance Statement

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

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

education (e.g., CITI);
8. Each individual listed as study personnel in this application possesses the necessary experience for conducting research activities in the role described for this research study.
9. To recognize and accept additional regulatory responsibilities if serving as both a sponsor and investigator for FDA regulated research.

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

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

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

SUBMISSION INFORMATION

0 unresolved comment(s)

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

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

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

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

Your protocol has been submitted.

Statistical Analysis Plan NCT03725332

To begin, continuous variables (gestational age at birth, neonatal weight, infant hospitalization length of stay, etc.) will be summarized with descriptive statistics (n, mean, standard error, first and third quartiles, and minimum and maximum); categorical variables (NAS treatment required, mother-infant dyad status, preterm birth, maternal smoking status, etc.) will be summarized with counts and percentages. To investigate differences in outcomes between treatment arms, a generalized linear mixed model will be performed. Mixed models allow for additional flexibility to control clustering while controlling for covariates such as socioeconomic status, race, age, addiction severity, if needed. Results will be presented with means (standard error) by treatment arm. Note that the primary outcome requires a noninferiority analysis; the secondary outcomes require superiority analysis to identify between-group differences. Mixed model assumptions will be assessed using plots of each outcome, diagnostics, and/or residual plots. If deviations from distributional assumptions are identified, remedial measures will be deployed as needed. In the case that methods assumptions are not satisfied, remedial measures (eg, variable transformations, nonparametric methods) will be employed.