Post Approval Submissions

Modification Information

To modify an approved study, edit the individual answers that make up the application. The questions below are intended solely for the IRB to have a summary statement of your requested action. The modifications cannot be processed until the actual changes have been made throughout the application.

1. Provide a brief non-technical summary of any changes you will be making to the study (i.e., study application, project personnel, and/or study documents.) The text you enter here will be reproduced in the IRB approval document, and should contain the details that you and/or your sponsor find relevant (e.g., master protocol/amendment version number and date). Typical summaries are 50-100 words. PLEASE NOTE: THIS SECTION MAY BE EDITED BY THE IRB FOR CLARITY OR LENGTH.

   sdfsdfs

2. Is this study in Data Analysis only (i.e. enrollment, intervention and follow-up are complete)?

   No

Total number of subjects enrolled to date:

1500

Is this study currently open to the enrollment of new subjects?

Yes

Total number of subjects actively participating (i.e., Total number of subjects involved in the interventional part of this study. If the study is limited to data collection (e.g., surveys, questionnaires, collection of data from existing records), enter '0':

1500

3. Do you have plans to re-consent subjects as a result of this modification?

   No

4. Is this modification being submitted in response to New Safety Information?

   No

5. Have the risks as described in A.6., consent form, or any other study document changed? This may include new risks not previously listed, changes in frequency of known risks, or removal of previously listed risks.

   No

Continuing with Modifications

Click the "save and continue" button to access your existing application.
You may make any changes to the application that you are requesting at this time.

General Information

1. General Information

1. Project Title

   Evaluation of Critical limb Ischemia Patients presentation and outcomes

2. **Brief Summary**. Provide a **brief non-technical description** of the study, which will be used in IRB documentation as a description of the study. Typical summaries are 50-100 words. Please reply to each item below, retaining the subheading labels already in place, so that reviewers can readily identify the content. PLEASE NOTE: THIS SECTION MAY BE EDITED BY THE IRB FOR CLARITY OR LENGTH.

Purpose: Patients presenting with critical limb ischemia (CLI) and tissue loss are at high risk for limb loss. Standard treatment protocols include limb revascularization using percutaneous endovascular or open surgical methods, wound debridement, infection control, and offloading. Despite these efforts, a significant number of patients experience delayed wound healing, resulting in extended treatment time, recurrent infections, need for additional procedures for revascularization, and occasional limb loss. Limited data is available on the outcome of the wounds in this patient population and risk factors related to wound healing and limb preservation. We propose to retrospectively review patients with critical limb ischemia to create a registry of clinical and epidemiological data related to CLI for future unspecified research such as determining management methods and presenting criteria that lead to optimal outcomes.

Participants: Patients treated at UNC Hospitals from 2006-2016 meeting the hemodynamic criteria for critical limb ischemia. This includes patients with toe pressures <50, leg pressures <70, and Ankle Brachial Indeces (ABIs) <0.50.

Procedures (methods): Retrospective chart review.

2. Project Personnel

1. Will this project be led by a STUDENT (undergraduate, graduate) or TRAINEE (resident, fellow, postdoc), working in fulfillment of requirements for a University course, program or fellowship?

No

2. List all project personnel beginning with principal investigator, followed by faculty advisor, co-investigators, study coordinators, and anyone else who has contact with subjects or identifiable data from subjects.

- List ONLY those personnel for whom this IRB will be responsible; do NOT include collaborators who will remain under the oversight of another IRB **for this study**.
- If this is Community Based Participatory Research (CBPR) or you are otherwise working with community partners (who are not functioning as researchers), you may not be required to list them here as project personnel; consult with your IRB.
- If your extended research team includes multiple individuals with limited roles, you may not be required to list them here as project personnel; consult with your IRB.

The table below will access campus directory information; if you do not find your name, your directory listing may need to be updated.

Liaison	Last Name	First Name	Department Name	Role	
University of North Carolina at Chapel Hill (UNC-CH)					
	Kalbaugh	Corey	Epidemiology Operations	Principal Investigator	view
	Marston	William	Surgery	Co-investigator	view
	McGinigle	Katharine (Kate)	Surgery - Vascular	Co-investigator	view
	Browder	Barkley	Biology	Research Assistant	view
⭐	Browder	Sydney	Surgery - Vascular	Research Assistant	view
	Shenkute	Nathan	School of Medicine Office of Graduate Education	Research Assistant	view

	Young	Jessica	Student Recreation Center	Research Assistant	view

If your research includes personnel from a UNC Health Network Entity (NE), the UNC Health Office of Research Support and Compliance (ORSC) will review your IRB application and/or submitted UNC Health Collaboration Survey. You may be contacted by ORSC for additional information. IMPORTANT: In addition to obtaining IRB approval, you must also receive ORSC clearance for project personnel employed by the NE site(s). Project personnel MAY NOT proceed with research activities until you have obtained both approval from the IRB and clearance from the NE. Upon completed ORSC review, an ORSC NE Clearance Form will be provided and uploaded to the IRB application Study Documents section.

NOTE: The IRB database will link automatically to UNC Human Research Ethics Training database and the UNC Conflict of Interest (COI) database. Once the study is certified by the PI, all personnel listed (for whom we have email addresses) will receive separate instructions about COI disclosures. The IRB will communicate with the personnel listed above or the PI if further documentation is required.

3. If this research is based in a center, institute, or department (Administering Department) other than the one listed above for the PI, select here. Be aware that if you do not enter anything here, the PI's home department will be AUTOMATICALLY inserted when you save this page.

Department	Surgery

3. Funding Sources

1. Is this project funded (or proposed to be funded) by a contract or grant from an organization EXTERNAL to UNC-Chapel Hill?

   No

2. Is this study funded by UNC-CH (e.g., department funds, internal pilot grants, trust accounts)?

   No

3. Is this research classified (e.g. requires governmental security clearance)?

   No

4. Is there a master protocol, grant application, or other proposal supporting this submission (check all that apply)?

- ✘ Grant Application
- ✘ Industry/Federal Sponsor Master Protocol
- ✘ Student Dissertation or Thesis Proposal
- ✘ Investigator Initiated Master Protocol
- ✘ Other Study Protocol

5. Is this a Clinical Study?
   Check YES if this study involves research using human volunteers that is intended to add to medical knowledge. There are two main types of clinical studies: clinical trials and observational studies. Do NOT check yes merely because you are conducting research in a clinical setting or using clinical data.
   Click here for additional definition of "Clinical Study"

   No

4. Screening Questions

The following questions will help you determine if your project will require IRB review and approval.

The first question is whether this is RESEARCH (click for details)

1. Does your project involve a systematic investigation, including research development, testing and evaluation, which is designed to develop or contribute to generalizable knowledge? PLEASE NOTE: You should only answer yes if your activity meets all the above.

   Yes

The next questions will determine if there are HUMAN SUBJECTS (click for details)

2. Will you be obtaining information or biospecimens through intervention or interaction with the individual, and use, study, or analysis of the information or biospecimens? This would include any communication or interpersonal contact between investigator and subject such as using in-person or online questionnaires/surveys, interviews, focus groups, observations, treatment interventions, etc. PLEASE NOTE: Merely obtaining information FROM an individual does not mean you should answer 'Yes,' unless the information is also ABOUT them.

   No

3. Will you be obtaining, using, studying, analyzing, or generating identifiable private information or identifiable biospecimens collected through means other than direct interaction? This would include data, records or biological specimens that are currently existing or will be collected in the future for purposes other than this proposed research (e.g., medical records, ongoing collection of specimens for a tissue repository).
   OR
   Will you be using human specimens that are not individually identifiable for FDA-regulated in vitro diagnostic (IVD) device investigations?

   Yes

The following questions will help build the remainder of your application.

4. Will subjects be studied in the Clinical and Translational Research Center (CTRC, previously known as the GCRC) or is the CTRC involved in any other way with the study? (If yes, this application will be reviewed by the CTRC and additional data will be collected.)

   No

5. Does this study directly recruit participants through the UNC Health Care clinical settings for cancer patients **or** does this study have a focus on cancer or a focus on a risk factor for cancer (e.g. increased physical activity to reduce colon cancer incidence) **or** does this study receive funding from a cancer agency, foundation, or other cancer related group? (If yes, this application may require additional review by the Oncology Protocol Review Committee.)

   No

6. Is the UNC Chapel Hill IRB taking or being asked to take responsibility for the oversight of research by individuals, groups or organizations outside of UNC Chapel Hill? Or you are asking the UNC Chapel Hill IRB to cede review to an External IRB. If so, a reliance agreement will need to be executed prior to conducting any research activities. See guidance.

   No

Location

1. Are UNC-affiliated researchers involved in research conducted at any locations outside of the United States?

   No

Part A. Questions Common to All Studies

A.1. Background and Rationale

A.1.1. Provide a summary of the background and rationale for this study (i.e., why is the study needed?). If a complete background and literature review are in an accompanying grant application or other type of proposal, only provide a brief summary here. If there is no proposal, provide a more extensive background and literature review, including references.

Critical limb ischemia (CLI) is the most severe form of peripheral arterial disease (PAD) and carries a worse prognosis than many forms of cancer. These patients have a life expectancy of less than 5 years on average and are at high risk for limb loss due to the severity of their arterial disease. Patients presenting with CLI may have pain in the limb at rest or tissue loss in the limb and have poor arterial supply to the foot as measured by an ankle pressure <70 mm Hg, a toe pressure of <50 mm Hg, or an Ankle Brachial Index (ABI) of <0.50. Standard treatment involves revascularization using percutaneous or surgical methods, but in some cases this is not possible due to anatomic factors or severe patient comorbidities. In a previous study from the UNC wound center, patients with CLI treated without revascularization had a one year risk of major amputation of 34%. Limb loss significantly accelerates the progression towards other complications leading to a high risk of death.

Currently, most physicians attempt to revascularize CLI patients to improve blood and oxygen supply relieving pain and supporting healing of ischemic wounds. Given the coexistent cardiac, renal and other high-risk conditions with which these patients present, the global trend has been to prefer less invasive strategies for revascularization whenever possible, using percutaneous approaches such as angioplasty and stenting. Typically, surgical bypass has better long-term results than percutaneous techniques but is associated with higher peri-procedural risks including a 1-3% risk of mortality. Percutanous procedures have limited patency and may supply additional blood to the limb for less than a year on average. A commonly stated justification for using these limited techniques is that the procedure will result in added blood supply long enough for the wound to heal and with good care the wound will not recur if the vessel re-occludes over time. Unfortunately, little information is available on the long-term outcome of patients treated in this category in terms of patient-centered outcomes. The actual incidence of wound closure, wound re-occurrence and quality of life are poorly documented. Additional information on the natural history of patients meeting the CLI hemodynamic and symptomatic criteria including their comorbidities, and future procedural outcomes from their incidental date if CLI would assist the decision making process of how to manage this high-risk population.

A.1.2. State the research question(s) (i.e., specific study aims and/or hypotheses).

The purpose of this study is to create a retrospective registry of clinical and epidemiological data related to CLI for future unspecified research that will receive IRB approval for research.

A.2. Subjects

A.2.1. Total number of subjects proposed across all sites by all investigators (provide exact number; if unlimited, enter 9999):

9999

A.2.2. Total number of subjects to be studied by investigators being provided oversight by the UNC IRB. (provide exact number; if unlimited, enter 9999):

9999

A.2.3. If the above numbers include multiple groups, cohorts, or ranges or are dependent on unknown factors, or need any explanation, describe here:

No Answer Provided

A.2.4. Do you plan to enroll subjects from these vulnerable or select populations:
If you will include children, prisoners or nonviable neonates or neonates of uncertain viability, please check the appropriate category below and complete the additional sections.

You should check "Pregnant women" if you specifically intend to recruit women who are pregnant or are not excluding pregnant women in biomedical research that is greater than minimal risk. Do not check if you are conducting a survey of the general public or conducting secondary data analysis or chart review not aimed at pregnant women.

Only check UNC-CH Student athletes, athletic teams, or coaches if you have specific plans to enroll these subjects. This is not applicable for intramural or club sports. For definitions and guidance see SOP 1201: Vulnerable subjects in research.

✗ Children (under the age of majority for their location)

Any minor subject who attains the age of majority during the course of the research study must provide consent as an adult, unless consent has been waived, which is requested in section D.3.1.

✗ Pregnant women

✗ Nonviable neonates or neonates of uncertain viability

✓ Prisoners, others involuntarily detained or incarcerated (this includes parolees held in treatment centers as a condition of their parole)

If an enrolled participant becomes incarcerated during the course of the research, they must be removed from the research project until such time as the IRB (and OHRP for NIH funded projects) approves the study to include prisoners, unless there is an immediate risk to the participant from ending treatments under the protocol.

✗ UNC-CH Student athletes, athletic teams, or coaches

A.2.5. Based on your recruitment plan and target sample population, are you likely to include any of the following as subjects? Select all that apply. This is not applicable to secondary data analysis or chart review.

Based on your responses, the consent form builder will insert the required text into your consent form template.

✗ Decisionally impaired individuals

(e.g., Mini mental state examination (MMSE), Montreal cognitive assessment (MOCA))

✗ Children who are wards of the State (Foster children)

✗ Non-English-speaking individuals

✗ UNC-CH Students

✗ UNC-CH Employees

✗ People, including children, who are likely to be involved in abusive relationships, either as perpetrator or victim.
This would include studies that might uncover or expose child, elder or domestic abuse/neglect. (See SOP Appendix A)

A.2.6. If any of the above populations are checked (excluding 'Decisionally impaired individuals' and 'Children who are wards of the State (Foster children)'), please describe your plans to provide additional protections for these subjects.

Patients will be de-identified and retrospectively searched. No direct patient contact will be made. Because of the nature of the disease population, some prisoners could be included in the data given

that the clinic provides these services to multiple patients in correctional facilities in NC.

A.2.7. Age range of subjects:

Minimum age of subject enrolled	21
	years
Maximum age of subject enrolled	99
» If no maximum age limit, indicate 99	
	years

A.2.D. Prisoners

Research involving prisoners and others involuntarily detained or incarcerated (45 CFR 46 Subpart C)

Prisoners may be involved in research if all of the seven (7) findings below are met:

A.2.D.1. The research under review represents one of the categories of research permissible under 45 CFR 46.306(a)(2) (Select the category that best describes your research.)

✗ (i) **Study of the possible causes, effects, and processes of incarceration, and of criminal behavior**, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;

✗ (ii) **Study of prisons as institutional structures or of prisoners as incarcerated persons**, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;

✗ (iii) **Research on conditions particularly affecting prisoners as a class** (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that the study may proceed only after the Secretary (through OHRP) has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of his intent to approve such research; OR

✗ (iv) **Research on practices, both innovative and accepted**, which have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the Secretary (through OHRP) has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of his intent to approve such research.

✓ (v) **Research conducted under a waiver of epidemiology research** where the sole purposes of the research are 1) to describe the prevalence or incidence of a disease by identifying all cases, or, (2) to study the potential risk factor associations for a disease and the research involves no more than minimal risk and not more than inconvenience to the human subject participants and prisoners are not the a particular focus of the research.

Provide study-specific justification to support your selection above:

The nature of the research focuses on burden description and patient population outcomes as a whole not on the particular nature of prisoners experiencing CLI.

A.2.D.2. Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;

Provide study-specific justification to support this finding:

No advantages or changes in care should happen given there is NO contact with patients. This study is just a retrospective chart analysis of de-indentified data.

A.2.D.3. The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;

Provide study-specific justification to support this finding:

No more than minimal risks expected.

A.2.D.4. Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the IRB justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project;

Provide study-specific justification to support this finding:

All patients regardless of the presence of any conviction are recruited given that we are doing retrospective data analysis of de-identified medical data. Everyone that fits the diagnosis of CLI is a possibly included patient.

A.2.D.5. The information is presented in language which is understandable to the subject population;

Provide study-specific justification to support this finding:

No patient contact is required.

A.2.D.6. Adequate assurance exists that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole;

Provide study-specific justification to support this finding:

No patient contact will happen so this shouldn't be compromised.

A.2.D.7. Where the IRB finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing participants of this fact.

Provide study-specific justification to support this finding:

No follow up examination. Just data review.

A.3. Inclusion/exclusion criteria

A.3.1. List required characteristics of potential subjects (i.e., inclusion and exclusion criteria). If not covered, list also characteristics that would preclude their involvement.

Patients who are 21 years or older with critical limb ischemia and a patient in the UNC system.

A.3.2. Justify any exclusion based on race, gender or ethnicity

There will be no exclusion based on race, gender or ethnicity.

A.3.3. Will pregnant women or women who become pregnant be excluded?

No

A.4. Study design, methods and procedures

Your response to the next question will help determine what further questions you will be asked in the following sections.

A.4.1. Will you be using any **methods or procedures commonly used in biomedical or clinical research** (this would include but not be limited to drawing blood, performing lab tests or biological monitoring, conducting physical exams, administering drugs, or conducting a clinical trial)?

No

A.4.2. Describe the study design. List and describe study procedures, including a sequential description of what subjects will be asked to do, when relevant.

The study design is a completely retrospective chart review for followup post date of incidental finding of a subject meeting the hemodynamic criteria for CLI between the years 2006-06/08/17 seen at UNC. We will exclude those that met this criteria during a 2 year washout period from 1/06 to 12/07 in order to capture the first incidence of CLI. Data will be collected from the Carolina Data Warehouse.

Study Design: Retrospective chart review

- Viewing status of CLI patients post date of incidental finding per hemodynamic criteria
- Capturing the comorbidities of CLI patients (i.e. claudication, rest pain, ulceration, gangrene)
- Capturing subjects' demographics
- Capturing subject's procedural/outcome history following date of CLI incidence (i.e. endovascular procedure, bypass surgery, major or minor amputation, etc.)
- Capturing outcomes such as death, morbidities associated with treatment and amputation

A.4.3. If subjects are assigned or randomized to study "arms" or groups, describe how they are assigned.

- *Describe the methods of computing the randomization schedule (if any) and maintaining blinding (if any).*
- *Who will perform these computations?*
- *How will you verify each subject's eligibility prior to randomization?*

This study will integrate clinical and epidemiological data to provide a rich resource for research. There will be multiple research questions that can be answered over time utilizing this resource, although many of these questions are unknown at the moment. One example research question will be: What are the predictors of early mortality following CLI diagnosis?

A.4.4. Describe any follow up procedures.

Although the recruitment is retrospective, we will re-visit medical records for an undefined period of time to update registry given the prospective nature of any follow up for patients previously recruited. We will see if there are any changes in the fields we are collecting and we will document

new information in our RedCap registry.

A.4.5. Once this study has been approved by the IRB, for how many months or years will this study be active (you are collecting data or have access to identifiers)?

We will be rerunning the query for updated information for a number of undefined years given that is a retrospective analysis but there could be changes in the already recruited patients.

A.4.6. Will this study use any of the following methods?

- ✖ Audio Recording
- ✖ Video Recording
- ✖ Behavioral observation - (e.g., Participant, naturalistic, experimental, and other observational methods typically used in social science research)
- ✖ Pencil and paper questionnaires or surveys
- ✖ Electronic questionnaires or surveys
- ✖ Telephone questionnaires or surveys
- ✖ Interview questionnaires or surveys
- ✖ Other questionnaires or surveys
- ✖ Focus groups
- ✖ Diaries or journals
- ✖ Photovoice
- ✖ Still photography
- ✖ Unencrypted Messaging with Participants (e.g., text messages, unencrypted emails)

A.4.7. If there are procedures or methods that require specialized training, describe who (role/qualifications) will be involved and how they will be trained.

No Answer Provided

A.4.8. Are there cultural issues, concerns or implications for the methods to be used with this study population?

No

A.5. Benefits to subjects and/or society

A.5.1. Describe how this study will contribute to generalizable knowledge that will benefit society.

There will not be any direct benefits to the participants of this study. Future benefits to society may include a better understanding of CLI-related treatment and outcomes.

A.5.2. Does this study have the potential for direct benefit to individual subjects in this study?

No

Consider the nature, magnitude, and likelihood of any direct benefit to subjects. If there is no direct benefit to the individual subject, say so here and in the consent form, if there is a consent form. Do not cite monetary payment or other compensation as a benefit.

Explain

We do not anticipate there will be any direct benefit to the participants of this study.

A.5.3. Are there plans to communicate the results of the research OR results of any clinical tests administered for the research back to the subjects?

No

A.6. Risks and measures to minimize risks

For each of the following categories of risk you will be asked to describe any items checked and what will be done to minimize the risks.

A.6.1. Psychological

- ✗ Emotional distress
- ✗ Embarrassment
- ✓ Consequences of breach of confidentiality (Check and describe only once on this page)
- ✗ Other

A.6.2. Describe any potential psychological risks checked above and what will be done to minimize these risks

Rare to none.

No subject identifiable data will be used. The subject's initals and a unique study number will be assigned to eahch subject. Only individuals with trained HIPPA, WEBcis and/or EPIC access, and IRB personnal will be working on this database using deidentified information. All information will be stored in a secure and password protected environment.

A.6.3. Social

- ✗ Loss of reputation or standing within the community
- ✗ Harms to a larger group or community beyond the subjects of the study (e.g., stigmatization)
- ✓ Consequences of breach of confidentiality (Check and describe only once on this page)
- ✗ Other

A.6.4. Describe any potential social risks checked above and what will be done to minimize these risks

There is a small (rare) risk of breach of confidentiality. However, all research staff will be instructed to keep data in strict confidence and information related to this research will be stored under conditions designed to protect the privacy of research participants. The link between any patient identifying and research information will be kept secure.

A.6.5. Economic

- ✗ Loss of income
- ✗ Loss of employment or insurability
- ✗ Loss of professional standing or reputation

- ✗ Loss of standing within the community
- ✓ Consequences of breach of confidentiality (Check and describe only once on this page)
- ✗ Other

A.6.6. Describe any potential economic risks checked above and what will be done to minimize these risks.

There is a small (rare) risk of breach of confidentiality. However, all research staff will be instructed to keep data in strict confidence and information related to this research will be stored under conditions designed to protect the privacy of research participants. The link between any patient identifying and research information will be kept secure.

A.6.7. Legal

- ✗ Disclosure of illegal activity
- ✗ Disclosure of negligence
- ✓ Consequences of breach of confidentiality (Check and describe only once on this page)
- ✗ Other

A.6.8. Describe any potential legal risks checked above and what will be done to minimize these risks

There is a small (rare) risk of breach of confidentiality. However, all research staff will be instructed to keep data in strict confidence and information related to this research will be stored under conditions designed to protect the privacy of research participants. The link between any patient identifying and research information will be kept secure.

A.6.9. Physical

- ✗ Medication side effects
- ✗ Pain
- ✗ Discomfort
- ✗ Injury
- ✗ To a nursing child or a fetus (either through mother or father)

A.6.10. Describe any potential physical risks checked above, including the category of likelihood and severity, and what will be done to minimize these risks. Where possible, describe the likelihood of the risks occurring, using the following terms:

- Very Common (approximate incidence > 50%)
- Common (approximate incidence > 25 - 50%)
- Likely (approximate incidence of > 10 - 25%)
- Infrequent (approximate incidence of > 1 - 10%)
- Rare (approximate incidence < 1%)

Describe severity of risks using the following grading scale:

- Mild- No disruption to the subject's ability to perform daily activities; may include non-prescription intervention only
- Moderate- Temporary interference with daily activities; may include prescription intervention
- Severe- Interference with daily activities; medically significant but not life threatening
- Life threatening

Examples:

Rare (< 1%) and Severe: blindness
Rare (< 1%) and Mild: dry skin, dry mouth, transient headache

If you are using these terms differently than described above, please provide your study-specific definitions.

Phase 1 trials: Due to limited experience, incidence may be better described as the number of events that have occurred in the total number of animals/humans studied.

There should be no physical risks.

A.6.11. Unless already addressed above, describe procedures for referring subjects who are found, during the course of this study, to be in need of medical follow-up or psychological counseling

Patients with CLI typically present for treatment or proceed to limb loss in a few months. We will not be identifying people in need for follow-up. Follow-ups will be recorded from 2006-2016.

A.6.12. Are there plans to withdraw or follow subjects (or partners of subjects) who become pregnant while enrolled in this study?

No

A.7. Data and safety monitoring

A.7.1. When appropriate, describe the plan for monitoring the data to ensure the safety of participants. These plans could range from the investigator monitoring subject data for any safety concerns to a sponsor-based data and safety monitoring board or committee (DSMB, DSMC, DMC), depending on the study. For studies that do not raise obvious safety concerns, you may still describe your plans for monitoring the study as it progresses.

The clinical research database will contain identifiers. However, this study has an 'honest -broker' model in which only those dealing with data entry, enrollment verification, and data QC will have access to the full data set. Only coded, limited data sets (only dates are included) are released for research projects. No other identifiers (other than dates) will ever be included in data sets for analysis.

All data collected in this study will be kept confidential as described above. Access to the participant files will not be permitted to anyone other than the study staff. Only the study staff involved in participant recruitment and data collection will know the identity of the participants. Study staff will be instructed to maintain complete confidentiality of all collected data. Datasets for analysis will be coded with a study ID. Dates will be the only identifiers included in data sets for statistical purposes.

No identifiers will ever be included in final research data for publication.

A.7.2. If not already addressed above, describe the plans for aggregate review of unanticipated problems (including but not limited to adverse events) across all sites, in order to monitor subject safety.

No Answer Provided

A.7.3. What are the criteria that will be used to withdraw an INDIVIDUAL SUBJECT from this study or halt the research intervention (e.g., abnormal lab tests, allergic reactions, failure or inability to comply with study procedures, etc.)?

NO criteria was developed for withdraw.

A.7.4. Are there criteria that will be used to stop the ENTIRE STUDY prematurely (e.g., safety, efficacy, unexpected adverse events, inability to recruit sufficient number of subjects, etc.)?

No

A.7.5. Will this study involve a data and safety monitoring board or committee?

No

A.8. Data analysis

A.8.1. Summarize the statistical analysis strategy for each specific aim.

No Answer Provided

A.8.2. If this is a pilot study, please describe the future study and say how its study design, aims, sample size, and methods differ from the pilot study you are proposing.

No Answer Provided

A.8.3. Provide a compelling justification for the proposed sample size in terms of the likelihood of achieving each aim.

No Answer Provided

A.8.4. Summarize the plans for data management.

No Answer Provided

A.9. Identifiers

A.9.1. Check which of the following identifiers you already have or will be receiving, or select "None of the above."

- ✔ Names (this would include names/signatures on consent forms)
- ✘ Telephone numbers
- ✔ Any elements of dates (other than year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death. For ages over 89: all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 and older
- ✔ Any geographic subdivisions smaller than a State, including street address, city, county, precinct, zip code and their equivalent geocodes (e.g. GPS coordinates), except for the initial three digits of a zip code
- ✘ Fax numbers
- ✘ Electronic mail addresses
- ✘ Social Security numbers

- ✔ Medical record numbers
- ✘ Health plan beneficiary numbers
- ✘ Account numbers
- ✘ Certificate/license numbers
- ✘ Vehicle identifiers and serial numbers (VIN), including license plate numbers
- ✘ Device identifiers and serial numbers (e.g., implanted medical device)
- ✘ Web universal resource locators (URLs)
- ✘ Internet protocol (IP) address numbers
- ✘ Biometric identifiers, including finger and voice prints
- ✘ Full face photographic images and any comparable images
- ✘ Any other unique identifying number, code, or characteristic, other than dummy identifiers that are not derived from actual identifiers and for which the re-identification key is maintained by the health care provider and not disclosed to the researcher
- ✘ None of the above

A.9.2. For any identifiers checked, how will these identifiers be stored in relationship to the research data?

- ✔ with the research data (i.e., in the same data set and/or physical location)
- ✔ separate from the research data (i.e., coded with a linkage file stored in a different physical location)

Provide details about the option you selected above:
The clinical research database will contain identifiers. However, this study has an 'honest -broker' model in which only those dealing with data entry, enrollment verification, and data QC will have access to the full data set. Only coded, limited data sets (only dates are included) are released for research projects. No other identifiers (other than dates) will ever be included in data sets for analysis.

A.9.3. Are you collecting Social Security Numbers to be used as a unique identifier for study tracking purposes for national registry or database? (Do not check yes if collecting SSN *only* for payment purposes; this will be addressed later.)

No

A.10. Confidentiality of the data

A.10.1. Describe procedures for maintaining confidentiality of the data you will collect or will receive (e.g., coding, anonymous responses, use of pseudonyms, etc.).

This is a retrospective chart review of preexisting data. Patient data will be coded with a unique study number that will not allow for a linkage back to the patient's MRN. The data abstracted will be truly de-identified with no way to make a link back to the patient for futher chart review or data collection. Data will be kept confidential and is only accessible to study personnel.

A.10.2. Describe how data will be transmitted among research team (i.e., personnel listed on this application).

Only those involved in recruiting, verifying eligibility requirements, and data entry will have access to identifying information. In the rare case a clinician enrolls a subject, the clinician will

not know the subject code as it is assigned at a later time by the project manager or other staff trained to do so. The number of individuals with access to identifying information AND the study codes will be limited as much as possible.

The registry will be maintained on a secure server with password protection.

As noted above, this study uses the honest broker model, and data is distributed with only the unique research ID and possibly dates (for statistical puroposes only). Additional protections will be provided for in data sharing agreements.

Datasets will be emailed via UNC email system as per the data use agreement. If files are too large to email, a UNC approved secured sharing system will be utilized.

A.10.3. Are you collecting sensitive information such as sexual behavior, HIV status, recreational drug use, illegal behaviors, child/physical abuse, immigration status, etc?

No

A.10.4. Do you plan to obtain a federal Certificate of Confidentiality for this study? Please note that all ongoing or new research funded by NIH as of December 13, 2016 that is collecting or using identifiable information is automatically issued a Certificate of Confidentiality (CoC). You should also select "Yes" if your study is NIH funded and has been issued a CoC under this updated NIH policy.

NOTE: Investigators utilizing ANY federal funding to conduct this research should review the COC website to determine if their funding agency issues COCs automatically (as the NIH does) or if they might need to apply for the COC via the online COC system. Unfunded and non-federally funded investigators may also apply for a COC via the online COC system.

No

A.10.5. If this study is limited to data collection by survey or interview, discuss the potential for deductive disclosure (i.e., directly identifying subjects from a combination of indirect IDs).

no survey or interview will be done

A.10.6. Will any of the groupings or subgroupings used in analysis be small enough to allow individuals to be identified?

No

A.11. Data sharing and transmission

A.11.1. Check all of the following who will receive **identifiable data** (contains any of the 18 identifiers listed above) outside the immediate research team (i.e., not listed as personnel on this application)? *

- ✔ No one
- ✘ Coordinating Center
- ✘ Statisticians
- ✘ Consultants
- ✘ Other researchers
- ✘ Registries
- ✘ Sponsor and/or its designee(s)
- ✘ External labs for additional testing

✗ Journals

✗ Publicly available dataset

✗ Other

A.11.2. For any recipients checked above, explain the confidentiality measures to be taken

No Answer Provided

A.12. Post-study disposition of identifiable data or human biological materials

A.12.1. Describe your plans for disposition of data or human biological specimens that are identifiable in any way (directly or via indirect codes) once the study has ended. If you plan to destroy linkage codes or identifiers, describe how and when this will be done.

As noted above, data are labeled with the research ID and without identifiers; the 'honest broker' maintains the link between ID number and identifiers. After enrollment has ended, the specimens and data will remain in a repository with the same research ID. After enrollment has ended, the data will remain in a repository with the same research ID. The linkage file/table will be kept to allow follow-up clinical data to continue being collected.

Part C. Existing Data, Records, Specimens

C.1. Data Sources

C.1.1. What existing records, data or human biological specimens will you be using? (Indicate all that apply or select 'None of the above'):

✓ Medical records in any format.

ALERT: You must check both boxes: 1) Medical records in any format and 2) Electronic medical record using Epic, or you/your study team will not be granted access to Epic for research purposes.

✓ Electronic medical records using Epic, WebCIS or other electronic system

✓ Carolina Data Warehouse for Health (CDW-H) (for UNC and its affiliates only)

✗ Carolinas Collaborative Data Request and Review Committee (DRRC)

✗ Paper medical records

If you access the medical records of fewer than 50 patients under a full or limited waiver of HIPAA, submit a copy of your IRB approval letter and a completed Research Disclosure Form to Health Information Management (HIM). Do not submit this information to the IRB. For additional information about this process, you should contact HIM directly at : 919-595-5591 or 919-966-1225 or 919-595-5580.

✗ Data already collected from another research study

Were the investigators for the current application involved in the original collection? --

✗ Patient specimens (tissues, blood, serum, surgical discards, etc.)

Has the clinical purpose for which they were collected been met before removal of any excess? --

✓ Data already collected for administrative purposes

✗ Student records (You will need to satisfy FERPA requirements: see SOP 3101, section 3.1 for guidance)

✗ UNC Dental Records

✗ Data coming directly from a health plan, health care clearinghouse, or health care provider?

✗ Publicly available data

✗ Other

✗ None of the above

For EACH data source checked above, provide a description of the data, proposed use, how data were collected (including consent procedures), and where data currently reside.

The data for the study is all pre-existing and will be collected from WebCIS or EPIC. Our plan is to identify information on comorbidities, hospitalizations, etc from an internal administrative data source such as Business Objects. All study team members are employed within the division of vascular surgery and have received the proper training and already have access to the EMRs mentioned above.

C.1.2. Describe your plans for obtaining permission from the custodians of the data, records or specimens (e.g., pathology dept, tissue bank, original researcher):

N/A

C.1.3. Do the custodians of the data, records or specimens require a data use agreement?

No

C.2. Coding and Data Use Agreements

C.2.1. When you receive these data, records or human biological specimens will they be coded? Coded means identifying information that would enable the research team to readily ascertain the individual's identity has been replaced with a number, letter, symbol, or combination thereof (i.e., a code). If you will not be using existing materials, check "No."

No

Part D. The Consent Process

D.3. Full or partial waiver of consent

The default is for subjects to give informed consent. A waiver might be requested for research involving only existing data or human biological specimens. More rarely, it might be requested when the research design requires withholding some study details at the outset (e.g., behavioral research involving deception). In limited circumstances, parental permission may be waived. This section should also be completed for a waiver of HIPAA authorization if research involves Protected Health Information (PHI) subject to HIPAA regulation, such as patient records.

D.3.1. Are you requesting any of the following:

✓ a waiver of informed consent in its entirety

✗ a waiver or alteration of some of the elements of informed consent

✓ a waiver of HIPAA authorization (If you are accessing patient records for this research, you must also request a waiver of HIPAA authorization)

Will you access the records of 50 or more patients under this waiver?

Yes

If you access the records of fewer than 50 patients under this waiver, submit a copy of your IRB approval letter and a completed Research Disclosure Form to Health Information Management (HIM). Do not submit this information to the IRB. For additional information about this process, you should contact HIM directly at : 984-974-3226.

To justify a waiver of the requirement for informed consent, you must affirm, by checking each of the following items that apply to this study. Provide an explanation.

Explain how the research involves no greater than minimal risk to subjects or to their privacy
The data will be gathered through massive record extraction of the CDW therefore and cumulative analysis will be done, patient identifiers will be used solely for medical record data extraction because data reporting will be done as a whole without identifiers.

Explain how the waiver will not adversely affect the rights and welfare of subjects (Consider the right of privacy and possible risk of breach of confidentiality in light of the information you wish to gather.)
Individual patient medical record review will be done only by researchers for data extraction purposes into a registry that does not have direct identifiers and which has a specific de-intentified code for each patient. Patients will not be contacted

Please explain why it would not be possible to conduct the study with only de-identified data (i.e. without any identifiers listed in A.9.)
This study requires examination of patient medical records.

Explain how the requirement to obtain consent would make the research impracticable, e.g., most of the subjects are lost to follow-up or are deceased.
Given the amount of patients and the range of dates involved contacting patients (some which might be no longer alive), is impractical. This type of data is not available otherwise so we feel it is a justified waiver.

Explain (or indicate if not applicable) how, when appropriate, there are plans to provide subjects with pertinent information after their participation is over. (e.g., Will you provide details withheld during consent, or tell subjects if you found information with direct clinical relevance? This may be an uncommon scenario.)
This is not relevant to this retrospective study.

Explain how the risk to privacy is reasonable in relation to the importance of the knowledge to be gained
This is a registry study that collects data that already exists. Hence, the risk to privacy is minimal. We will take necessary precautions (described elsewhere) to protect patient information.

In addition, please check the following and provide a brief explanation to justify a waiver of HIPAA Authorization (see SOP 1801, 2.3).

Explain how not recording or using Protected Health Information (PHI) would make the research impracticable.
We need direct data extraction of the medical record to populate some parts of the fields in out registry given that the data information systems are not bridged to redcap.

D.3.2. If your request for a waiver applies to some but not all of your subject groups and/or consent forms, please describe and justify

No Answer Provided

D.3.3. Does this request for waiver support a study design that involves deception or withholding of information?

No

Attachments

This submission requires the following attachments

Document Type

This submission includes the following attachments

File Name	Document Type
PI Change Form_Kalbaugh.pdf	Other
Young_citiCompletionReport4286913.pdf	Research Ethics Training

view attachments

Addenda

Data Security Requirements

view addenda

If Principal Investigator of this study is a Student or Trainee Investigator, the Faculty Advisor certifies the following:

I accept ultimate responsibility for ensuring that this study complies with all the obligations listed above for the PI.

By certifying below, the Principal Investigator affirms the following:

I will personally conduct or supervise this research study. I will ensure that this study is performed in compliance with all applicable laws, regulations and University policies regarding human subjects research. I will obtain IRB approval before making any changes or additions to the project. I will notify the IRB of any other changes in the information provided in this application. I will provide progress reports to the IRB at least annually, or as requested. I will report promptly to the IRB all unanticipated problems or serious adverse events involving risk to human subjects. I will follow the IRB approved consent process for all subjects. I will ensure that all collaborators, students and employees assisting in this research study are informed about these obligations. All information given in this form is accurate and complete.

This study proposes research that has been determined to include Security Level 3 data security requirements. I agree to accept responsibility for managing these risks appropriately in consultation with departmental and/or campus security personnel. The Data Security Requirements addendum can be reviewed here.

Certifying Signatures:

Signature: Electronic Signature Received **Date:** 2/05/2021 09:37:45 AM

Corey Kalbaugh