TEXAS TECH UNIVERSITY
HEALTH SCIENCES CENTER™

Clinical Research Institute
Frequently Ask Questions

The Clinical Research Institute can be reached by phone (806) 743-4222, by email at clinical.research@ttuhsc.edu, by visiting our website http://www.ttuhsc.edu/clinicalresearch/,.

The link to the CRI work order system is as follows: https://app4.ttuhsc.edu/CRIWorkOrders/

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Table of Contents

General Questions ***3***

CRI Eligibility ***5***

CRI Support Activities ***7***

CRI Monitoring ***7***

Study Design & Grant Support ***10***

Protocol Development ***11***

IRB & Regulatory Policy ***12***

IRB Amendments ***15***

Industry-Sponsored Research ***15***

Study Implementation ***16***

Statistics ***17***

Publication ***21***

General Research Questions ***23***

General Questions

What is the Clinical Research Institute (CRI)?

- The CRI is in place to help facilitate research for all faculty, trainees, and students across all 6 schools of TTUHSC.
- The mission of the Clinical Research Institute (CRI) is to promote and facilitate the conduct of clinical research for while upholding the highest standards of excellence by assuring human subject investigation be performed ethically, responsibly, and professionally to contribute to the health sciences' body of knowledge.
- The Vision of the CRI is to improve the quality of healthcare in Texas and beyond through clinical research activities.
- The CRI is NOT the same as the institutional review board (IRB), but we work closely with the IRB.

What services does the CRI provide?

Facilitating Research:

- Discussion of study and developing protocol
- Study design
- Submissions to the Institutional Review Board
- Consenting and enrolling patients
- Conduct of the study
- Statistical analysis
- Preparation of reports and manuscripts

Provision of Research Education:

- Approved medical and graduate school electives
- Training programs with continuing medical education credit for new faculty and residents
- Training program for nurse coordinators
- Lecture series for students, residents, fellows and faculty
- Various presentations throughout the institution on clinical research

Why should I use the CRI?

- You should use the CRI because we offer years of clinical research expertise at no cost
- to you. We also have a close working relationship with the IRB, so we typically have little
- trouble getting studies approved.

What training do I have to complete in order to do research at TTUHSC?

- In order to take part in a research study at TTUHSC, Principal Investigators, Co-Investigators, and research staff are required to complete training regarding the protection of human research subjects prior to starting any human research-related activities.
- Research personnel must also complete training on Financial Conflicts of Interest, submit a Financial Disclosure, and request an iRIS account from the Institutional Review Board. Instructions for completing these tasks can be found here

How can I submit my study to the Institutional Review Board (IRB) for review?

- All submissions to a TTUHSC IRB must be submitted using the Cayuse software. In order to gain access to the system, all users must submit a Cayuse Access Request after completing other training requirements. The Clinical Research Institute can prepare or assist with IRB submissions.

Who can be the Principal Investigator of a study?

- TTUHSC IRB policy states that only TTUHSC/TTU faculty (full or part time) may serve as the Principal Investigator. Resident/student research projects required a TTUHSC/TTU faculty serve as a Principal Investigator. Residents and students may be listed on the study as Sub-Investigators or Study Personnel. There is also a process for Nursing research taking place at UMC Health System to be PI on nursing research studies.

When will the IRB review my study?

- Refer to the IRB website at www.ttuhsc.edu/research/RIO/irb/ for information on submission deadlines and meeting dates.

How do I know if my study is exempt?

- Only the IRB can make the determination of exempt status. The study investigator does not have the authority to make this determination. If you think your study qualifies as exempt, you must still submit an IRB application. The IRB will notify you in writing if your study qualifies as exempt.

How can I improve my study design?

- Complete a Study Design consult using the CRI work order system: https://app4.ttuhsc.edu/CRIWorkOrders/

How many study subjects will I need for my study?

- Complete a Power Analysis Request using the CRI work order system: https://app4.ttuhsc.edu/CRIWorkOrders/

Can the CRI help me get a statistical analysis for an upcoming abstract/article deadline?

- The CRI makes every effort to help with publication efforts, but we need at least 3 weeks' notice to complete a statistical analysis.

How can I register to be a volunteer in a research study?

- To register to be in a research study, anyone over the age of 18 can register through our secured website http://www.ttuhsc.edu/clinicalresearch/CRIVolunteer/. Parents with minor may register their children. Volunteers will be asked to answer a few health-related questions. Upon completing and submitting your health-related answers through the secured CRI Volunteer Website, you will receive an email notifying you receipt of the information has been received by our office.

Will I be compensated if I participate in a research study?

- Depending on the research study, there may be monetary compensation. The majority of research studies do not provide a monetary compensation.

Do I have to participate in a research study?

- The decision to participate in a research study is strictly a personal decision. Your medical care or services will not be affected by your decision to participate in a research study. If you have questions or concerns you may contact a Clinical Research Coordinator at (806) 743-4222. Clinical Research Coordinators can provide a basic description of the research study you are inquiring about.

What is investigator-initiated research?

- Investigator-initiated research begins with a faculty member's (investigator) idea of how to transform or improve healthcare. The investigator (and team) reviews the literature and prepares a research protocol then submits to the IRB for approval. Once approved, the study is implemented and the protocol followed precisely. After that comes data analysis and then dissemination of findings. Of course, the investigator is expected to be involved in all stages of the research process. The CRI can assist with all steps of the process and has expertise to guide novice investigators.

What are retrospective studies?

- Retrospective studies ask a question and look at medical/patient information from the historical point of view, i.e., chart reviews. A retrospective study does not require consent but does require IRB approval to ensure patient information is being protected and used appropriately.

What are prospective studies?

- Prospective studies look at medical/patient information wanting to know how a treatment or procedure will affect an individual or the process of healthcare delivery. Prospective studies follow the subjects moving forward. Prospective studies require formal written consent from the subject to participate.

What is an Industry-Sponsored Clinical Trial?

- An industry-sponsored clinical trial occurs when a researcher, often a faculty member, collaborates with a sponsor—typically a pharmaceutical or medical device company—to conduct clinical research. In these trials, the sponsor provides funding to the research organization, and sometimes compensates participants, in exchange for the opportunity to test their product or device for treating a specific condition or diagnosis.
- Participation in sponsored trials requires informed consent, ensuring that patients are fully aware of the nature of the study. Patients are given the choice to participate, and their decision will have no impact on their relationship with their healthcare provider or clinical team. Clinical trials are often very cutting edge treatments for disease or medical problems.

<u>CRI Eligibility</u>

I am a full time faculty member; my study involves the collection of samples from study participants. I am not really able to assist with this collection during the academic semester when I have a full teaching schedule. Is the CRI able to collect the required samples during the semesters, and will I be able to resume collection between terms?

- Yes, the CRI will be happy to screen, consent and collect your samples during the teaching year. This is preferred by the CRI, especially if there are to be significant gaps in enrollment. However, you are still responsible for the study and its conduct and will need to meet with the coordinator assigned to your study regularly regarding progress. When you are able to resume your participation in the project, you can notify the CRI and we will work with you to make your project a success.

I am a medical student wanting to do clinical research, but have limited time for participation. Since the CRI is able to complete most of the study procedures and other study-related tasks, do I have to be actively involved, or can I just collect the data to write a paper after the study is complete?

- While the CRI is capable and willing to do what is needed to assist medical students with their research projects, we encourage participation from the entire study team. We understand that many students have limited time, but ethically speaking, it is important for students to be actively involved with research projects that are required as part of their degree.

I am a medical student and I want to be part of a research study involving a certain field or type of patient. Whom do I contact about this?

- The CRI can direct you to a project or PI who has a study that may interest you.

I'm a MD/PhD student working on a project for my PhD. Am I eligible to bring my project to the CRI for assistance?

- Absolutely, the CRI can assist you in several ways. Keep in mind that your research project is your responsibility for receiving the PhD. While CRI coordinators cannot take ownership for your project, they can assist you in your project. The more you are involved in your project, the better your learning experience with research will be.

I am working on my PhD and my research project is a part of my degree. I am aware that the CRI can assist with this research; however, I am a full time student and do not have a lot of extra time. While this is my research, I would like to know what is expected regarding my involvement with the actual study and data collection. I am aware the CRI can assist in enrollment and study procedures, but can the CRI also collect the data and complete the data sheet?

- The CRI is happy to assist you with your research; however, your involvement is critical for study success and in you obtaining your degree. Exactly how much the CRI can assist you is up to your Faculty Advisor. Keep in mind this is your project and your input is crucial.

I am a senior nursing student and am interested in research. Can I do my clinical hours in the CRI?

- Yes, the CRI has several research nurses who serve as coordinators; we can generally arrange for you to follow them to complete clinical hours. Come to the CRI and speak with the director.

CRI Support Activities

Why does the CRI review my protocol, rather than submit it to the IRB for me, as is?

- The CRI Directors, statistician, regulatory specialist, and monitor will use their extensive experience to review the draft documents you submit and help you finalize your protocol to give it the highest likelihood of success and seamless IRB approval with the best chance to publish the results. This review will ultimately save time and reduce the need for resubmission because the CRI staff is likely to be able to anticipate IRB needs and concerns. In addition, the CRI review ensures that TTUHSC resources will be used in the most appropriate, and efficient manner.

My project received IRB approval. The CRI asked to meet with me before they start enrolling subjects, but isn't the study ready to start once the IRB approves it?

- After a study is approved by the IRB, the study team will need to meet in order to confirm study logistics, such as who will perform certain tasks, to verify which study procedures are standard of care and which procedures will be billed to research funds, confirm contact information, etc. From time to time, the study team may also ask for the PI to meet in order to discuss questions/issues that arise with the study once it has started.

I am involved in a research project that requires many data points. I am not always able to collect all the data points for each subject. Will these subjects be excluded from the project? Is there a way to retain these subjects?

- Although it is preferred that all data points be captured, there are instances where data points are not available for different reasons. This missing data may be a result of procedures not being done, or lack of documentation, for example. As you begin to analyze and categorize your data, discuss these missing data points with your statistician. Together, you can determine if the data that have been captured for these subjects can be used for your project. It is best practice to anticipate the possibility of missing data and build this into your protocol from the beginning.

I've found or created a database that might be interesting to analyze. Can you help me clean and analyze the data?

- We typically do not have the resources to clean the study data. We can analyze the data, but with no pre-identified hypothesis to test, we would merely be fishing for significance. Please start by determining your research questions and hypotheses as well as the specific factors and outcome measures you want analyzed.

CRI Monitoring

What is a "study monitor" and why will my study be monitored by the CRI Monitor?

- The CRI wants your study to be the best it can be, and for you to have a good chance at publication. To meet that goal, the CRI uses a monitoring system to help navigate and manage projects, and we are pleased to offer this service to all of our investigators. A monitor is an individual trained to review research to support ongoing quality improvement, but is usually independent of study conduct activities. The monitor provides a second set of eyes to make sure that the data collected is accurate and that the protocol is being followed as designed in order to answer the scientific question(s) you posed.

What will the monitor look for? What should I do to prepare for the visit?

- The monitor will use the study protocol as a blue print for monitoring but will ensure that good clinical practices are being followed and that study subjects are safe. The usual procedure is for the monitor to contact the lead study coordinator working with you on the trial to schedule a monitoring date. The coordinator and PI will work together to make sure that all documentation has been signed, dated, de-identified and entered appropriately into whatever data collection form/system the study is using. The monitor will want to look at all the study documents, including correspondence and medical records associated with the study.

How often will my study be monitored?

- We will work with you to determine how often your study should be monitored. Typically, we suggest that monitoring occur after the first participant is enrolled. Such proactive assistance helps avoid problems related to data collection and communication that may occur with the recruitment process. After the first participant enrolled is monitored, we suggest that the trial be monitored every 2-3 months, more frequently if recruitment is happening at a rapid pace, less frequently if recruitment is predicted to be a challenge.

What are the typical mistakes a monitor finds when reviewing studies?

- The most frequent problems found by monitors, as well as the FDA, are with consent forms/processes. Therefore, the monitor will review each informed consent to make sure that it was signed, dated, and timed by both the potential participant and the person who explained the clinical trial to the potential participant. The monitor will also look to see that the most current consent approved by the IRB was used, and that the consent process was completed before any protocol procedures were conducted. Another frequent problem identified by monitors and the FDA is enrollment of subjects who do not meet the study's defined inclusion/exclusion criteria. Therefore, the monitor will also review each inclusion/exclusion criteria that you have specified and make sure that there is documentation in the medical record to support enrolling each participant.

Will the monitor look at my data?

- Yes, the monitor will review the data for accuracy and completeness. The monitor will look at the medical record and compare it to the protocol and datasheet. If data are missing, the monitor will work with the study team to address it. For example, datasheets should not have blanks; this may lead someone to suspect a lapse in study methods or data collection. The monitor can facilitate best-practice use of datasheets to explain unreported data, such as

inserting a period "." and using appropriate abbreviations (UNK=unknown, ND=not done, NA= Not applicable).

Can the monitor help me with recruitment?

- If you wish, the monitor can provide you with an enrollment rate for your study as part of the monitoring report. Investigators often have a tendency to overestimate how quickly a trial can be completed. Typically, by the third month of a trial, key problems can be handled and a true enrollment rate can be estimated. Additionally, having scheduled meetings with the research team can keep enthusiasm up and recruitment moving forward.

Does the monitor have any role in evaluating the scientific validity of my trial?

- No, evaluating scientific validity is the IRB's responsibility. The CRI team can assist you with designing your study so that the scientific question you are posing is answered by your protocol. The IRB does appreciate receiving study applications that have been reviewed and managed by the CRI prior to IRB submission. Several years' experiences have assured the IRB that the CRI review helps ensure the T's are crossed and the I's are dotted.

The monitoring process sounds intrusive- very specific, and just another hoop that I have to go through to conduct research. I know what I am doing, so why should I agree to this?

- The CRI wants your study to be the best it can be, have a good chance at publication, and to help you avoid any compliance problems that could lead to trouble. The TTUHSC CRI has a wealth of knowledge and experience to help you with every aspect of your study. We are extremely familiar with what institutional and federal auditors will look for if they decide to review your study. The FDA has the right to visit TTUHSC at any time, and to look at any study. If FDA auditors find problems, they have the ability to suspend research activities for that investigator or for the entire institution, especially if the problems are thought to be institution- wide. The monitor is a resource to help ensure that problems are found and dealt with quickly so if the FDA comes to audit us, they will find that research is being conducted in compliance with institutional policies as well as federal regulations.

What power does the monitor have over me and my research?

- None. The monitor is here to help--to be a second set of eyes and make sure the protocol is being carried out as written. If discrepancies are found, the monitor reports them to the PI. It is up to the PI to do what they wish with the information the monitor provides.

Can the monitor stop a trial from continuing?

- No. That power rests with the PI, the IRB, and the FDA.

What purpose does the monitoring report serve?

- Monitoring reports should be reviewed by the PI and the coordinator for accuracy and agreement. The report can point out problems the PI might not have been aware of and generate discussion within the research team as how best to go about making changes. The FDA looks for PI involvement in the clinical trial. As the PI of a clinical trial, you are ultimately responsible for everything that happens as part of the trial. Signing and dating the

report serves as one of the tools the PI can use to demonstrate PI involvement and management.

Can the monitor help me if the FDA comes to review my study?

- The process of monitoring a clinical trial helps the PI manage and maintain accurate documentation, which is an essential aspect of FDA review; 85% of all official actions cited by the FDA are problems of documentation, which generates actionable violations. Research must be transparent to regulatory agencies that are tasked with protecting the rights and safety of subjects. Mistakes are inevitable; the appropriate response should be to recognize the mistake, take responsibility for it, and take corrective action. Documentation of what happened and what was done to correct the problem is the key to transparency in research. The act of monitoring helps everyone with documentation.

Does the CRI use Risk-Based Monitoring (RBM) when reviewing physician- initiated clinical trials?

- No. Although RBM is increasingly utilized in industry-sponsored trials, the CRI has found using more traditional monitoring methods to be more accurate and effective for maintaining participant safety and data quality.

Study Design & Grant Support

What are the different study designs that can be utilized in research studies?

- There are two major types of study designs: observational and experimental. Examples of observational studies include cross sectional surveys, cohort studies, and case-control studies. Experimental studies consist of randomized controlled trials and quasi-experiments. There are various advantages and disadvantages of each study design, and you should choose the design that is most appropriate for your research questions and data resources. Moreover, different statistical procedures are applicable for different study designs. For instance, the measure of association between variables in a cross sectional study may be prevalence odds ratios while a cohort study will allow you to calculate relative risks.

I'm wondering if my study design is appropriate. Can you review my study design?

- Yes, we can schedule a meeting to discuss your protocol. The CRI is here to help you with your project so it will be a success. Generally, the CRI advises you to be guided by your specific and testable hypothesis, which should be based upon your explanatory variable and primary clinical outcome. Take care to collect and account for potential confounding variables that may affect this outcome or be tied to the explanatory variable of interest. Specifically, if your study is a randomized control trial (RCT), you might use CONSORT as a guide to help refine your study: http://www.consort-statement.org/consort-2010. If your study is an observational study, try STROBE: https://strobe-statement.org/index.php?id=available-checklists.

I need help with developing a budget for my study. Can the CRI help?

- Yes, the CRI can help you develop your study budget. Come see us!

I want to use some of my grant money to buy a statistical analysis program. Can I do that?

- Yes, if you included such a cost in your project budget, you may be able to buy software that you will use for your project. However, you may wish to ascertain if the CRI has the statistical analysis program or knows of others in the institution that may be using the program. Before you use your grant money for something NOT listed in the grant application, you must notify the Office of Sponsored Programs and contact the granting agency to get approval.

Can you help me with sample size determination? In other words, will I have

- Yes, but we need to know your hypothesis, methods, and the intended statistical analysis. Also, it's critical to know the anticipated effect size of the factor of interest (from literature or from your clinical experience) upon the primary clinical outcome that you are using to evaluate efficacy in this study. Power analysis is only as reliable as the inputs for the calculations used.

My grant is about to expire, but I am not done with study recruitment and follow up. What do I do?

- If your grant is about to expire, you should contact the TTUHSC Office of Sponsored Programs and work with them to submit a letter requesting a funding extension. You will include specifics about why the study is not completed and outline difficulties you may have had.

Protocol Development

I am a new faculty member at TTUHSC. I have a preliminary idea on a clinical research project. Who can help me develop my idea into a research protocol?

- The Clinical Research Institute would be pleased to help you with your project. We can also help direct you to a variety of personnel that can help your study come to fruition. Further information can be found on our website: http://www.ttuhsc.edu/clinicalresearch

I am writing my first protocol. I am not sure what should be in the introduction/background section.

- Your Introduction/background information does not necessarily have to be lengthy. It should include an objective review of the current literature identifying the magnitude of the problem. Include pertinent studies that have been done and information gained from such studies, as well as references to the most relevant studies. Identify some missing aspects in the literature and why these aspects are important. Finally, note how your proposed study addresses the missing information in the current medical literature and how your proposal will add significantly to the current knowledge on the topic. If you have performed studies in this field, it is reasonable to reference them because they may be a logical step to the current proposal.

Why can't I use my grant application as my study protocol?

- A grant application is not the same as a study protocol, but it does provide a starting place on which to build a good protocol document. A study protocol is a detailed plan of how you want your study done. A grant is a detailed proposal of why your topic is significant, contributes to generalizable knowledge, and deserves funding. While your grant application may include study conduct information, it also includes information that isn't necessary for a protocol.

I am currently writing the Methods section in my research proposal prior to IRB submission. What are some of the common areas of omission that occur in this section?

- The Methods section is critical to the success of your proposal and contributes significantly to the chances of successful publication. Many papers are rejected solely on the basis of insufficient or inappropriate methodology. The guiding principle should be to provide enough specific detail so that an interested party could duplicate your study exactly and confirm or refute its findings. For instance, if you are using assays to measure metabolites, specific details of these assays should be provided. Commonly used laboratory values do not generally need this kind of detail. If you use instruments, you should provide the name of the manufacturer and the details of the instruments. If you plan on using a questionnaire, it is helpful to indicate why it was chosen and note prior studies validating its use in a comparable setting. Statistical analysis is also commonly listed under the methods section. Statistical analysis should show that an appropriate analytic approach has been adopted and the appropriate statistical techniques are used for your study design. For instance, a cross sectional study design will allow you to conduct Chi Square techniques for categorical variables and t-test for continuous variables when you are to compare two groups (i.e., treatment vs. control at one point in time). This section should also address potential problems you might anticipate such as the study sample may not be normally distributed or there may be missing data points. Unless your proposal is a pilot study, a power analysis may also be required.

How can I improve a survey I've written?

- Please try to find a validated survey from the literature. A "home-made" survey may invalidate your study from the start, as we cannot be certain that it is accurately measuring the object of study. However, if you must write your own survey, here are some general rules to follow:
  - Keep it short and simple. (questions shouldn't require re-reading and the survey should take about 5 min)
  - Avoid double barreled questions (Ex: Rate the Safety AND Efficacy of this program)
  - Conduct a pilot study with your survey draft to evaluate what questions to refine.
  - Ultimately plan on validating your survey by comparing it to the study factor of interest

Why is it necessary to complete the "Inclusion/Exclusion" Form?

- The "Inclusion/Exclusion" form is required for all participants consented to research studies. This form is written documentation that the volunteer satisfied all requirements for the study and is eligible to participate.

<u>IRB & Regulatory Policy</u>

I have been informed that I will need to complete CITI training prior to beginning my research project. Where do I find this information?

- The on-line course is available at www.citiprogram.org. A handout entitled "Required Tasks for Research Personnel" can also be downloaded from the CRI website.

Do I need to complete all preliminary experiments prior to initial submission of the study to the IRB?

- Typically, the answer is "Yes." After the IRB approves a study and the study team has its study start-up meeting, the study should be ready to begin. If preliminary experiments are not complete prior to IRB approval, this delays the study team from being able to work on the study or to accept other studies that are ready to begin recruitment.

I've never written a consent form. How do I begin?

- The TTUHSC IRB has downloadable templates in iRIS that you can use to draft your consent form. Additionally, the CRI can complete the consent form for you or assist in reviewing your draft prior to study submission to ensure all the applicable elements are covered.

It is my understanding that the single case report does not have to be approved by the IRB. However, do I need IRB permission for a case series, such as 5 patients with similar findings, if I wish to publish these as a single case report?

- Yes, you should get IRB approval for a published case series, and do so before you begin collecting the data. IRB approval is important in this situation because there could be a case made for you doing a "systematic" look at the particular aspects of the cases that are being combined into the series. Your IRB application should be a review for exemption, provided that no identifying information is recorded on any of the data collection sheets. It should be noted that there may be considerable intra-institutional variations in IRB policies regarding such research.

I am interested in looking at existing databases. By using retrospective analysis, I can rapidly approach and address some clinically relevant issues. Do I have to have IRB approval for such projects?

- Some large databases have redacted and de-identified personal health information (PHI); use of these resources may not have to go before the IRB. Nevertheless, accessing large databases such as those involving Medicare and the CDC does require considerable expertise which takes time. Numeric as well as text data mining has become much more prevalent. We recommend that you approach databases with very specific research questions. In cases of doubt it is best to check with the IRB staff to determine whether approval is needed.

Does the CRI use electronic consent forms, electronic questionnaires and/or electronic source documents?

- We can put questionnaires on an electronic system so that participants can complete a questionnaire on an I-pad, tablet, laptop or desktop computer. This allows the statistician to

access the data easily. There is an electronic system called Medrio that can be used for data entry that has no cost associated with it if a study has fewer than 100,000 data points associated with it. Medrio offers cloud storage and, in some cases, allows data to be downloadable into statistical programs. Some other academic institutions use Red-cap. TTUHSC also uses Integrated Medical Research Informational System (iRIS) for paperless IRB submission and communication. At this time TTUHSC is not using electronic consent forms, but doing so is a matter for future consideration.

I just submitted a study to the IRB. When will it be approved?

- The length of time for IRB approval depends on the type of study you are submitting. If you submitted a retrospective chart review or a survey study, typically these studies are reviewed within a week or two depending on the IRB's workload and whether or not the study qualifies for expedited review. If you are randomizing patients to an experimental procedure or if the study poses greater than minimal risk to subjects, then this study will need to be reviewed by the full board. This meeting occurs once a month and the study must be submitted and the appropriate signatures obtained prior to the deadline for that month. Any questions the IRB has will need to be addressed to their satisfaction prior to granting approval.

I have submitted a protocol to the IRB. The IRB has requested that I provide additional information and consider changing the protocol. Am I obligated to comply?

- The institutional review board (IRB) serves a vital role in ensuring patient as well as institutional safety in conducting clinical research. The IRB's other function is to determine if proposed projects have enough scientific merit to be approved. You should seriously consider the suggestions made by the IRB; however, if you feel that the suggestions are not appropriate, you are free to rebut these suggestions in writing and you can request to make a personal presentation to the IRB panel. If you do choose to rebut IRB requests, you will need to provide a solid scientific rationale for each concern you wish to address.

I am having subjects complete an anonymous survey. Do they need to sign an informed consent?

- Usually no. It is best practice to have a discussion with the regulatory specialist at the CRI to see if there are concerns that indicate a consent form may be needed. You can submit an information sheet which covers the main points that would be outlined in the consent form such as: why you are doing the study, what is involved in participation, any risks or benefits, etc. If your survey is posted online, then this sheet can be the first page at your study link. Subjects will proceed to the survey and submit it if they agree to participate.

Why does the IRB want to see my data collection form?

- The IRB wants to see your data collection form to make sure you are collecting all the data you need, and that you are collecting ONLY the data you say you will collect. This review helps ensure patient privacy and protection of PHI.

I am finished collecting data for my study and am analyzing the data. Do I need to keep my study open with the IRB?

- No. If you have completed data collection and you have de-identified the data, then

you may close the study with the IRB. Additionally, if you have any posters, publications or manuscripts that result from the research you should submit them to the IRB in your closure report.

What is required from the PI when a participant experiences an Adverse Event?

- The PI must determine whether or not the Adverse Event is study related, its severity, and whether the event was expected. The PI can document this by placing his/her initials and the date on the study specific adverse event log or make a specific note in the participant's records. In some cases, the AE will need to be reported to the IRB.

IRB Amendments

One of my colleagues wants to work with me on a study. Do I need to do anything?

- Yes, your colleague will need to open an iRIS account and be added to the study via an amendment. The CRI can send you a list of the steps your colleague needs to complete to open their iRIS account and we can submit the amendment to add new personnel to the study to the IRB. Please note that new study personnel must complete any required training and be added to the study prior to starting study activities.

My protocol was previously approved by the IRB. The age range of the study group is 25-89 years of age. A collaborator has suggested that we would be able to recruit more expeditiously if we expanded the age range to 18-89 years of age. Since this is a minor modification and essentially does not change the protocol, can I simply implement this change?

- No. It is very important that any modification of the protocol be reviewed by the IRB and approval obtained. . Implementing the proposed change without IRB approval would constitute a regulatory and protocol violation and place you and the institute at risk. Once IRB approval is received you can then expand the recruitment age range for your sample.

I am doing a research project in my clinic, but my study has faced a number of screen failures--promising candidates who did not meet inclusion criteria. What can I do about this?

- Meet with your CRI coordinator and discuss submitting an IRB amendment to your subject inclusion/exclusion criteria that does not compromise the study question.

Industry-Sponsored Research

I have limited experience in clinical research but have been offered a pharmaceutical company protocol to study a new drug for use in a clinical condition. The company will provide the protocol and funds to complete the study. Will the CRI be able to help me implement this study?

- The CRI currently is focused on investigator initiated research. However, we suggest you talk to your Chairman or supervisor, since you may be able to recruit a coordinator and conduct the study within your department if appropriate approval is received. There are currently faculty at TTUHSC conducting such studies within their respective departments.

I am considering adding a separate personal protocol onto a pharmaceutical sponsored study. This protocol will be initiated by me as an investigator and be related, but separate from the industry-designed research protocol. Can the CRI help me with implementation of my study?

- The CRI supports investigator-initiated research. We are pleased to discuss your role with regard to your personal protocol.

Do I have to submit data collection forms or case report form to the IRB if the study is industry-sponsored?

- No, if the study is sponsored by Industry, the IRB does not require the data collection forms to be submitted to them. They know the documents are often too big for submission and TTUHSC has a contract in place to help protect TTUHSC and study participants' privacy and confidentiality.

Study Implementation

The IRB has approved my protocol and I have requested research funds. Can I start the study even though the funds are not yet in the designated account?

- Unless you wish to pay for the study out of your own pocket, the best practice would be to wait to start the study until funding has been secured. Procedures specific to the research are required to be paid for by the research team and cannot be billed to the patient or the patient's insurance. Thus, funds must be secured for study procedures to last the duration of the study prior to enrolling the first subject.

I would like to consent subjects myself, and I have consented subjects for studies at other institutions. Why do I have to be in-serviced before I'm allowed to consent subjects at TTUHSC and/or UMC?

- TTUHSC and UMC often work together on studies in order to recruit subjects. Our contract with UMC requires that study team members are properly in-serviced prior to beginning work on studies as policies can differ between institutions.

I have devised a data sheet for my data collection. Can you help me determine whether my data sheet will work when we start collecting data?

- Yes, but you may need to experiment with your data sheet by sending it back to the CRI after you've gathered 10-20 observations. This will help the statistician spot any red flags when it comes to how your data is actually being coded. Here are some general rules to follow for data sheets:
  - Avoid putting more than 1 item in each cell (example: listing multiple medications)
  - Use short letter codes for categorical variables (example: White=W, Black=B, Asian=A)
  - Code Y/N variables with 1/0 (example: mortality = 1, non-mortality = 0)
  - Code ordinal variables from 0 to 5 (e.g.: no degree=0, HS = 1, BS =2, Grad = 3, PG= 4)
  - Categorical variables with more than 5 factors might need to have some items collapsed/combined (example: combine no insurance, self-pay, minimal insurance)

What is a data collection sheet/form?

- A data collection sheet/form is also known as a case report form (CRF). This document or file is where all of your study data is collected. It can be in an Excel spreadsheet or an online electronic database.

If specimens that must be processed soon after collection are acquired on a weekend, will there be lab personnel available or on call to accept and process the specimens?

- This depends on whether or not the lab in which the specimens will be processed is typically staffed on weekends. If a PI wishes to collect specimens on a day that TTUHSC is typically closed, then the PI needs to ensure that the lab will be properly staffed during the time specimens are to be delivered and processed.

What happens if my study is not completed, but I am leaving TTUHSC?

- Sometimes circumstances change during research, but that does not mean that all of the hard work you have done was for nothing. Depending on the type of study and your role on the study team, you may still be able to collaborate with TTUHSC to bring the study to completion and work on a publication.

Statistics

What statistical software is used by the CRI biostatisticians?

- Typically, we use the latest version of SAS, STATA, SPSS, or R, depending on the preference of the biostatistician assigned to your study. Regardless of the statistical package used, you can collect your data using a simple spreadsheet, since all packages can import different formats.

If I want to run a very specific statistical test on my data, can the CRI run that for me?

- Yes, but we will need to know as much as possible about your hypothesis and study design. Our statisticians will work with you to make sure test is the most appropriate procedure for your needs.

I have a presentation later this week. Can the CRI help me run some numbers?

- The CRI will do everything possible to respond to your needs, but due to the high frequency of short-notice requests in peak months, our policy is to submit your request a minimum of 10 business days before results are needed. In most cases we expect to be able to get you this analysis in approximately two weeks' time.

I have some data. Would you help me test my 7 hypotheses of interest?

- Yes. But perhaps we should narrow the focus of this study from 7 to a more manageable number. Let's start by specifying which outcomes are of primary/secondary importance to this study. Based on what we find in the primary analysis, we can always do a sub-analysis or follow-up study, which may result in multiple publications from this effort.

What are type I and type II statistical errors?

- A type I error is rejecting the null hypothesis when the null hypothesis is true; this is commonly compared to "sending an innocent man to prison" (in the US system), where innocence is presumed. A type I error is generally viewed as a more egregious error, which is why we typically control the alpha-level significance. A type II error is failing to reject the null hypothesis when the null hypothesis is false; this might be compared to "letting a guilty man go free," which is associated with the beta-level significance. These errors can be minimized by performing a power analysis in order to determine the appropriate sample size that balances type I and II errors according to the expected effect size.

Could you give me an example of results that are statistically highly significant but clinically irrelevant?

- A new drug for hypertension drops the systolic BP by 1 mm HG from 141 to 140 (0.2 to 2 mm HG) ($p < 0.01$), in a sample of 105,000 patients. While this drop in BP is statistically significant, it is clearly not clinically relevant. This type of discordance may emerge with larger sample sizes due to an excessive power and should be interpreted with caution.

What does a p-value of 0.05 actually tell me?

- Every p-value is tied to the null hypothesis; for instance, "(The Intervention) is no different than (standard-of-care) with respect to (some clinical outcome)." In technical terms, the p-value quantifies the probability of obtaining an effect at least as extreme as the one in your sample data assuming that the null hypothesis (of no difference) holds. The idea is that a small p-value is strong evidence to the contrary (a true difference) between the intervention and standard of care as stated in your null hypothesis, while a large p-value is insufficient evidence to reject the assumption of no effect. Note that the null hypothesis CANNOT be proved, but only disproved using traditional statistical methods (though equivalence/non-inferiority tests can be used to show the 95% confidence interval of the difference between treatments lies between some pre-specified threshold for clinical significance, like ±10%. However, these typically require massive sample sizes and are often infeasible in a single center
study).

Could you give me an example of a clinically relevant result that is statistically insignificant?

- Drug X drops systolic BP by 10 mm from 145 to 135 mmHG (4 to 15 mm HG) in 10 patients. Given the small number in this study, statistical significance may not be achieved because this study is underpowered. A large sample size may confirm clinical efficacy if the effect size was not overestimated.

Which is best for graphically depicting data -- standard error of the mean or standard deviation and why?

- The answer to this question may depend on the preferences of the publisher, since using the standard error is still common practice in some areas. The SAMPL guidelines state that one should report standard deviation in tables, using the form: mean (SD), not mean + SD. The standard error of the mean (SE) is not recommended to indicate the precision of an

estimate because it is essentially a 68% confidence interval. The 95% confidence interval should be used instead; this consists of two numerical values defining a range of values within which the parameter falls with a specific degree of confidence, in this case 95%.

I would like to use a one-tailed statistical test since I achieve statistical significance using this approach, whereas using the more common two-tailed statistical test produces only marginal significance for my findings. When am I allowed to use one- tailed statistical tests?

- A reason for using a particular statistical test should never be acquiring statistical significance in one over the other. One-sided tests are appropriate when your initial hypothesis was one-sided in nature (X is greater/less than in A vs. B). However, if your hypothesis assumes no direction of difference between the outcomes in question, you must conduct a two-sided statistical test. When reporting your methods, you will have to state whether tests were one- or two-tailed and justify the use of one-tailed tests.

I have compared oral glucose tolerance tests in patients with neurologic dysfunction using timed glucose samples drawn every 30 minutes between 0 and 120 minutes. Can I use a T-test to compare the glucose values at various time points?

- Since you are studying a series of measurements events, comparing T-tests at individual points of the curve is not best practice. The reason this may be problematic is that your observations within each individual subject are auto-correlated (correlated in time). As such, it is necessary to model the correlation between times. We recommend a repeated measures analysis of variance (ANOVA) to evaluate differences or perhaps a mixed modeling method if some values are missing.

I see that several articles use a variety of p-values, denoting statistical significance ranging from $p< 0.05$ to $p< 0.0001$. Can I use the commonly accepted standard $p< 0.05$ as the statistical standard for significance in my paper? What advantage do I get with using more stringent criteria?

- Alpha = 0.05 is merely a 1 in 20 chance of making a type I error. Having a 1 in 20 chance of being wrong in an assertion is not a great deal of confidence. For example, if lives are on the line, you might want to be more certain than 1 in 20. Furthermore, if you publish 20 manuscripts in your career with $p<0.05$, there's a good chance that one of your conclusions was wrong. It's probably wise to go with the standard p-value for your field/area of expertise. Still, this is the reason that we should all strive for publishing reproducible studies, as we are in the business of seeking the truth about an intervention. However, in the case of having multiple comparisons in a single study, you may want to utilize a more stringent p-value for statistical significance since comparing multiple associations is more likely to give you a higher chance of finding significant results.

Why should I use confidence intervals in my paper?

- Confidence intervals are generally more informative than p-values because they summarize both the central tendency and potential variation of this estimate due to chance. They also help the reader better apply/utilize your findings by tying the result to a meaningful clinical measure. For example, reporting the difference in mortality rates between two

treatments in terms of a 99% confidence interval may allow the reader to easily estimate the potential variation in the number needed to treat to save a life using the experimental treatment.

I have just received review feedback on my submitted manuscript. One major critique appears to be that I have used parametric statistical methodology as opposed to non-parametric statistical methodology. Could you please explain the important differences?

- Parametric statistics assume that the sample distribution comes from a population that is typically bell-curve distributed (normally distributed) and deals with the estimation of population parameters (i.e., the mean). Non-parametric statistics are distribution-free methods; they rely on ordering or ranking of observations. Skewed distributions, such as length of stay, may result in the need to use non-parametric statistics, or data transformation (see question 17). Also, in the event that your scale does not use equal intervals (example: Likert scale), non-parametric methods may be more appropriate. However, consulting with an expert will help you make the best decision for your research, since each case may require a different solution.

I had projected a sample size of 100 patients for my study based on power analysis. I now have obtained data on 80 patients. Should I wait for the complete number of subjects to be recruited and the study finishes or should I run statistical analysis on currently available data?

- If the sample size was projected based on a rigorous power analysis, the number is expected to reflect an appropriate balance between the effect size and the required power. Therefore, you should wait until you collect all the data. However, if your study is facing other issues related to low recruitment of study participants, you may not have other options. In such a case, a preliminary analysis using what data you have may be sufficient but should be noted in any publication.

In a graphical representation of my data, I noticed some extreme outliers. These outlying data appear to significantly affect the analysis. What are my options?

- Sometimes outliers are due to measurement errors or simple typos. You should investigate these cases carefully to determine if they are systematically different from the other observations in your sample. If this is the case, you may need to post-exclude these subjects and report your findings based on your effective sample (i.e. individuals with CF but not Turner or Noonan syndrome). However, if there is no identifiable difference in these individuals and you suspect the outliers, it's possible to perform the analysis with and without outliers to see if conclusions differ.

I noticed my data are not normally distributed. Can I convert my data into normal distribution prior to analysis?

- Some statisticians use inverse, root, or log transformation for skewed data. More generally, the Box-Cox transformation may be applied, but be aware that all confidence intervals on the transformed outcome will need to be back-transformed to allow for meaningful reporting of the outcome of interest. If your sample size is large enough, the assumption of normally distributed data/error terms in model estimates can generally be overlooked, as it is

encapsulated in the Central Limit Theorem. If your sample size is small and transformations are insufficient in achieving a normal distribution, you may need to employ some non-parametric methods.

I have recently reviewed data obtained from a research project and noticed that there are some missing data values in 3 out of the 56 objects. What are my analytic options?

- You could state in your methods section that you have included only complete data sets. Ideally, a missing data plan was written into your protocol, but with approximately 5% missing data, this complete-case analysis is probably safe. Most journals will accept an analysis with as much as 15% missing data. Ideally, it will be good to find out and report if there are socio-demographic differences between the samples which are being excluded from the analysis due to missing values and being included in the analysis. Otherwise, missing data methods such as EM (expectation maximization) or MI (Multiple Imputation) methods may help. Generally speaking, methods that replace missing data with a single number (mean substitution or last observation carried forward) should be avoided as they artificially reduce variation and can bias results. When designing your study, be aware that some designs, such as involving multiple assessments, also increase the probability of having missing data and appropriate steps to prevent this issue should be taken in advance.

Publication

What are the guidelines for co-authorship on a publication, as compared to a list for an article's acknowledgements?

- Acknowledging support and helpful resources is an important part of a publication. Whether an individual is included as a co-author or listed in the acknowledgements should reflect the workload of the entity and relationships that were negotiated or determined in advance. All clinical researchers have been assisted by a variety of people, resources and institutions and it is important to acknowledge the help you received. However, if an individual or individuals have contributed substantially and meaningfully to the publication, it is appropriate to list them as co-authors. In biomedical publications, the initial author is often the "mentee" within a collaborating group who assumed a major role in the study conduct; the final author is often the "mentor" or the scientists within whose laboratory or clinic the study occurred. However, this is not an absolute distinction. Academic institutions are more likely to give the first, second, and last authors more credit for meaningful participation than someone listed further down the paper's author list.

How do I write a good abstract when submitting my paper for publication?

- It is important to follow specific journal recommendations about the abstract. Most abstracts are about 250 words or less and many are highly structured, with headings that mirror the article's organization. You will note that some longer abstracts are truncated in PubMed. Writing a good abstract is quite difficult since you have to condense your project, its findings, and its conclusions in a limited number of words. One way to look at this is to consider the essential findings about your project and what information a reader needs to determine subsequent use of the article or what information would serve as a project overview.

For structured abstracts, consider writing or identifying in the text 1 or 2 sentences for each major section of the manuscript, then edit for length and to ensure that the article's findings receive the most emphasis.

How important is the letter to the editor that accompanies manuscript submission?

- We believe that the letter to the editor is very important and is worth spending time to craft. The letter should outline the potential importance of the study and the appropriateness of the manuscript to the journal in question. You could point out unique features of your study, and you may be asked to recommend potential reviewers. You are also allowed to request that the editor not send it to specific individuals for review if you can justify the reasons for such a request.

I am reading a lot about the importance of citation indices. I know that I can use Google Scholar to track my citations. Should I focus my efforts on articles that are highly cited?

- There is no doubt that highly cited articles reflect well on your efforts. It is quite difficult to predict which articles may end up being highly cited whereas others may just receive a casual mention. Consequently, we would recommend that you focus on getting your publications into journals that are PubMed linked. You may find that you are unnecessarily restricting your publication options if you submit your paper only to the most highly cited journals. A good research question should mitigate some of these concerns. Moreover, you may come across a fabulous research project while you are working on a more mundane project.

I am writing an invited review of a topic. The journal requests that references appear in alphabetical order. What is the best way of doing this?

- Bibliographic database software is very useful for downloading references from PubMed and other online databases. These programs can also catalog your references and provide a searchable database of the downloaded data. Many of these software programs also provide customization of the format for references. We encourage you to explore specific bibliographic databases to ensure that they accomplish what you are trying to do. Some programs that you may look into are Refworks and Endnote.

I have just received feedback regarding my manuscript. The editor offered me the option of resubmission once the reviewer's comments are addressed. However, I strongly disagree with many of the reviewer's comments. Should I submit my manuscript to a different journal or should I go to the trouble of responding to the reviewers' comments and resubmitting?

- This is an individual decision. In general, authors should strongly consider resubmitting a manuscript with an attempt to address the reviewers' comments. You are certainly within your rights to explain your thinking and provide the reasons why you feel that some or all of the reviewers' comments are inapplicable or inaccurate. It is important that your responses are polite and professional with acknowledgment of the reviewers' time and effort and rely on facts and literature references rather than opinion. The option of submitting elsewhere may also be worth considering but doing so is likely to be lengthy and you may also get back a similar critique as the one you have now obtained. The CRI may be able to help you craft a

good response.

I have just completed my study and I am excited about being asked to present a poster at a national scientific meeting. I realize there are variations in the size, content, and design of the posters allowed at various meetings. Could you help me avoid some of the common pitfalls of poster presentations?

- Congratulations on your acceptance! Poster presentations are a great way of learning and interacting at scientific and medical meetings. In many ways, poster presentations are better than verbal presentations at a podium since they enable a much closer interaction with interested parties. There are many steps that you can take to ensure a great experience and these include consulting your collaborators and faculty mentors for timely input on the crafting of your poster; also read carefully any guidelines provided to you by the meeting organizers regarding the maximum size and any formatting details. You need to ensure that visitors to your poster as well as the judges can read the poster font from a distance of 6 feet, such as with a title of at least 1" (72 points) and text of at least .5" (36 points) or more. A common error is to make the poster too busy or text-heavy, which is also distracting since visitors may be reading your poster while listening to you present your findings. Therefore, include only essential content with adequate visuals, and practice your verbal presentation. Extensive references are usually not needed but do include contact information such as your name and e-mail address. At the presentation site, mount your poster at the appropriate time, since the judges may be looking at the posters at unscheduled times. Be sure to dress appropriately and be on time for your presentation. Be cognizant of the venue and the theme of the presentation. It is also a good idea to have a few hard copies of your poster printed in case you connect with someone who may be interested and/or an expert in your area for future collaboration. TTUHSC's Educational Media Services has a number of poster templates and can provide assistance with design and printing: http://www.ttuhsc.edu/som/medicaleducation/mededmedia.aspx

I have recently read about predatory journals. It is my understanding that predatory journals require payment and thus any journal that requires payment may be suspect. An article has recently been accepted in the journal PLOS ONE; should I be concerned?

- Investigators should be careful about predatory journals that require high page costs but have low status. However, you cannot use only the amount of payment or the fact that payment is required as the sole criterion for determining if the journal is predatory. Your best guideline is to publish in journals that are listed in PubMed. While this FAQ cannot comment on the merits of specific journals, PLOS ONE is listed in PubMed and as such has passed rigorous criteria for inclusion.

General Research Questions

I am a busy clinician on primarily a clinical track. Why should I bother to do research at TTUHSC?

- As health providers, we have chosen occupations that involve perpetual learning. Doing clinical research that can be sculpted to your interests will likely develop your

critical thinking skills further and as such has the potential to make you a better health care provider. Participation in research has the potential to establish you as a local (and potentially national) expert in an area of your research and clinical interests, which may further generate clinical consults to you and reflect well on TTUHSC. Selected publications in approved medical journals may help with promotion and membership into learned medical societies. There is generally an expectation that academic faculty participate in research and scholarship. You have the option to collaborate with other researchers, and this may allow meaningful participation given your time constraints.

How do I come up with an idea that I can translate into a clinical research question?

- Ideas for medical research can come from a variety of sources. These sources include friends, colleagues, medical journals, patient encounters, medical conferences, etc. The key is to define an important question to be addressed and then have a time sensitive and plausible method for addressing it. Ideas that provide a new or improved technique for measurement, reduce health care costs or improve health outcomes, or address a current deficiency in research, such as racial or gender disparities in health care, are worth considering. You should also consider regional and local variations in health practice. Perusing highly acclaimed medical journals may also provide research areas that need further attention.

As a busy clinician, I have a limited amount of time for research but am interested in seeking promotion and tenure. How can I best use my time to be productive in research?

- There are a number of potential options that require less dedicated time to conduct clinical research than full-blown prospective double-blind clinical trials. These options include collaborating with an established investigator, working with trainees, and writing medical case reports, as well as data mining through the use of existing data either locally, regionally, or nationally.

I know what I want to research, and generally how I want to go about conducting the project. However, my understanding of the official research process and the requirements is limited, so I've put it off. At what point am I ready to start?

- It sounds like you're ready to contact us, and to fill out a CRI Work Order. It is our goal to smoothly facilitate your research in whatever ways that you need. This may mean guiding you in the early stages, or helping with protocol development, or data collection and entry, or all of the above. Our aim is to promote research. We are on your side and want to help you succeed!

I have identified a database of interest to me and would like to do some data mining. However, the database operators require not only an institutional agreement but a personal liability agreement from me. The reason given is that some of the data is identifiable. Given the personal liability risk, should I undertake access to this database?

- An increasing number of databases are requesting an assurance that the database confidentiality will be maintained by the individual investigator as well as by the affiliated institution. Since there is personal liability involved, the decision to use these databases for research should be taken after a great deal of thought and reflection. You should discuss this

with your family and colleagues as well as the institution. There are still some databases which can be accessed without onerous restrictions, for example, those from the National Center for Health Statistics.