Module 2: Research Protocol

Introduction to Research Protocol

Welcome to the second module in the Social and Behavioral Research Best Practices for Clinical Research course. Here we'll cover the importance and overall structure of a well written research protocol. Let's get started by hearing from Connie, a principal investigator. She has been a clinician for a number of years and has begun working in the social and behavioral research field. During one of her first sleep intervention studies she encountered some challenges. Let's start by taking a look at some of them…

Connie's Vague Protocol

During a recent study my team and I were examining the efficacy of different sleep hygiene techniques for adolescents with chronic headaches. Specifically, we were looking at the differences between eight weeks of relaxation therapy versus the standard care that a participant might receive; this standard is usually an educational booklet on sleep hygiene. Our long-term goal was to develop a kit of headache pain management strategies.

Originally, I was really proud of the protocol document we submitted to the I.R.B. It outlined all the elements of our study, but I purposefully left some of the details kind of vague to allow for some leeway in decisions along the way. For example, we were not very specific in terms of how we defined who would be eligible for the study. This allowed us to cast a wide net when it came to recruiting.

Protocol Deviations

I feel like no matter what type of detail is put into the I.R.B. protocol, there is always going to be something that deviates from the plan. For example, we had one participant who refused to fall asleep without headphones on, which wasn't allowed under the intervention instructions…so that threw us a curve ball.

Study S.O.Ps

During our follow-up interviews, our study coordinator, Jeff, needed to go on an unexpected family leave. He had been handling all of the participant follow-up visits. The problem was that we weren't able to find any documentation of how Jeff actually conducted the interviews. We knew we had a Standard Operating Procedure for the follow-up visits, but weren't sure where Jeff had stored it. It certainly wasn't in our online database of S.O.Ps.

Course Study Manual

Take a minute to explore the Resources section of this course in the top right corner of your screen. Here you'll find your Social and Behavioral Research Course Study Manual for this course, Research Protocol. Be sure to print this before you continue.

Throughout this module you'll be able to pause the course and take notes specific to your institution. In the end, you'll have a roadmap to a successful social and behavioral research study.

What is a Protocol?

The initiation of a clinical trial often begins with the submission of a grant proposal which outlines, in detail, the science behind a study for the purposes of receiving funding. Once funding is received, much of the information in a grant proposal is re-purposed to create an I.R.B. protocol for I.R.B. review and approval. An additional document that is used to guide the actual conduct of the study is the Clinical Protocol. Because the term "protocol" is used to refer to both the document submitted to the I.R.B., and to a Clinical Protocol, the need for both documents can cause confusion. An I.R.B. protocol is required to receive I.R.B. approval to conduct the study, and tends to emphasize research ethics and participant safety. A Clinical Protocol is a description of study operations from start to finish, and is used by a study team to guide study conduct. Many sponsors require a Clinical Protocol in addition to the I.R.B. protocol.

A Clinical protocol serves as the team's guide for conducting the study. Every researcher has been there; we all work really hard on the scientific foundations of our study and let

that work inform our protocol. Unfortunately, we can often stumble during this step by underestimating the level of detail needed.

Thorough, well written protocols can prevent issues down the road and serve as a road map to success. Additionally, with the classification of some social and behavioral research studies as clinical trials, regulation has also increased. Social and behavioral researchers should always adhere to rigorous standards when developing protocols and processes for their studies.

Common Protocol Elements

There are common elements across I.R.B. protocols. Institutional Review Boards, or I.R.Bs, may require different sections of a protocol, and they may make special requests during the review process. We recommend that an I.R.B. protocol be broken into sections and sub sections to help any reader understand exactly what the topic of the study is, how research will be conducted and how data will be analyzed.

At a minimum, I.R.B. protocols should contain the Objectives, Methods, Quality Control and Assurance, Ethics/Protection of Human Subjects, and Data Handling and Record Keeping. A brief Background and Significance section is also typically included, since an I.R.B. evaluates whether there is a scientific basis to the study that would justify the effort of human participation. As all clinical trials involve some level of risk to the participants, the I.R.B. looks at the potential significance of the study to ensure this risk is reasonable, given the potential scientific impact.

Protocol Methods

The Methods section is generally the most detailed section of your I.R.B. protocol. Here, you must spell out the eligibility of your participants, the study procedures, and the way in which you'll analyze your data. During the review process, the I.R.B. will serve as your Sherlock Holmes to find clues indicating potential issues related to your participants' protection down the road.

Giving too little information within the I.R.B. protocol can lead to confusion among your team members - as you've given them an incomplete map to guide them through the study. A lightweight I.R.B. protocol can also be met with resistance by the I.R.B. However, keep in mind that a protocol can also be too restrictive. If indicating when a clinic visit will occur, it is best to include a range within the I.R.B. protocol, rather than a single figure. For example, rather than saying a follow-up visit is one month after the baseline visit, you could suggest that the visit will occur 30 days after the baseline visit, plus or minus seven days. Too much specificity in an I.R.B. protocol can pigeon hole a researcher and result in many protocol deviations or amendments.

Remember, all amendments must be submitted to and approved by the I.R.B.

Check with Your I.R.B.

Now that the Goldilocks of I.R.B. protocols, with the perfect amount of detail, has been created, it's time to submit for I.R.B. approval. This process can vary from institution to institution and you should explore yours.

Remember that I.R.Bs include members with varied backgrounds. Some may have a scientific background while others are professionals from other areas. It's a good idea to keep this in mind while writing an I.R.B. protocol. While participant recruitment cannot begin until I.R.B. approval is received, that doesn't mean that everyone should take a vacation. Take this time to plan, gather supplies, write Standard Operating Procedures, and train team members on processes.

Take a moment to pause this course and find your submission portal. What requirements does your I.R.B. have when it comes to the content of a protocol? Make notes in your Course Study Manual.

Supporting Documents for a Study

There are many documents used by research teams to help support their study efforts.

While not part of an I.R.B. protocol, Standard Operating Procedures, or S.O.Ps, are often part of the clinical protocol. S.O.Ps help ensure that every team member understands what they are doing and how, when, and why it should be done. This relates directly to ensuring fidelity of your treatment and avoiding protocol deviations, two topics which we'll discuss in a moment.

Remember the difficulty Connie's team had when Jeff had to leave unexpectedly? If an S.O.P. had been created to detail the questions asked at each interview, the rest of the team would have been able to pick up where Jeff left off without any issues.

A team's procedures manual is essentially a collection of S.O.Ps, compiled into a how-to manual for any activities in a lab. Topics in this manual can range from a standard method of taking a participant's weight, to instructions for conducting an intervention or participant interview. A good rule of thumb is to make these documents as detailed as possible. A team member should be able to pick it up and execute any activity.

A data safety monitoring plan outlines the steps that will be taken by a study team to ensure the safety of participants and the integrity of a trial's data. All clinical trials require this document.

Finally, there are a few additional resources that can help study teams to demonstrate quality research practices and transparency during a clinical trial. The use of the Consolidated Standard of Reporting Trials or CONSORT checklist and Flow Diagram is a process that is increasingly being adopted in medical publications as a way to evaluate the scientific quality of a study. Specifically, the CONSORT Flow Diagram demonstrates how participants move through the study, when and why dropout is occurring, and whose data remained in the final data set. CONSORT can be particularly helpful in the planning of how to collect data in a study. Check your resources section for these documents.

Developing S.O.Ps

Now that we have reviewed a few supporting documents used by study teams, let's explore how S.O.Ps are developed and written in more detail.

The task of writing S.O.Ps often falls to the coordinator, if your team has one. He or she is responsible for taking the approved I.R.B. protocol and fleshing out step by step instructions for any and all applicable study activity. This helps to guarantee tasks are completed in a standard way, and ensures that all participants receive the same treatment. After an S.O.P. is written, we recommend a little practice. Running a mock participant through the steps of a study is a great idea. These practice rounds will give insight into an activity's feasibility, and allow for team members to become more efficient.

Also, remember that you don't have to recreate the wheel with every new study. If there are some repeated actions across several studies, it's OK to reuse information. Fellow colleagues are also great resources for S.O.Ps. Adjust as necessary, and move ahead!

Standards for S.O.Ps

There is no clear consensus about what format an S.O.P. should follow. However, in general, you should include a purpose, the methods and procedures to be followed, clarification of any non-standard terminology, required equipment and supplies, the types of credentials and training required to complete the study activity, and a clear plan for quality control. A reader must be able to understand the document, and then do his or her job correctly without needing much clarification. You should also remember that journals commonly require research teams to address how a staff was trained to carry out a treatment. Well-written S.O.Ps make this process much easier!

Reasons for S.O.Ps

Now, let's see what you know! On the left, you'll see several real world scenarios requiring an S.O.P. On the right are key differentiators describing a reason why an S.O.P. would be critical to that procedure. Match the column on the left to the column on the right.

What is Treatment Fidelity?

Treatment fidelity is your commitment that, as a research team member, you have a plan and you're sticking to it. This is a process ensuring every team member is delivering a treatment intervention in the way the I.R.B. protocol specifies, and that treatment is being received by participants as it should.

One method of ensuring fidelity is to record participant interactions and observe whether or not these are consistent day to day and participant to participant. While it may be tempting to offer one participant a little extra encouragement because they're nice, show up on time and make your job easier, don't. Other methods include asking questions to ensure universal understanding and keeping track of notes in logs.

Additionally, it is important to track data back to its source and fully understand the circumstances surrounding its collection. Who collected the data and when? Understanding these facts helps to ensure rigorous, quality data.

In 2004, the Treatment Fidelity Workgroup of the National Institutes of Health Behavior Change Consortium gathered to define best practices around treatment fidelity.

Remember, it's not enough to just gather the treatment fidelity data - it must be analyzed if it's going to be of any use at all. The word "audit" can strike fear into the hearts and minds of many, but in this case, it's good practice and can really help you down the road.

Importance of Treatment Fidelity?

Over time, the importance of treatment fidelity has grown. Increasingly, journals and research sponsors have begun to require that any study manuscripts report how fidelity is tracked. It's not uncommon for study teams to have an entire S.O.P. dedicated to how fidelity is measured and maintained. Because this is so important, the impetus to track these things falls to every team member.

The bottom line? Ignoring the importance of treatment fidelity can cost time, money, and the credibility of the study findings.

What are Protocol Deviations?

One of the biggest truths in social and behavioral research is that deviations will likely occur during your study. If your team has made it through without a single one, it is likely that something has been missed.

Deviations from an I.R.B. protocol occur when methods outlined are not followed or when events do not go as planned. If the safety of a participant is put at risk, deviations can have associated adverse events, but most of the time they do not. We will cover adverse events in a later module.

Deviations can range from missing pages of a survey to missed study visits. A well written I.R.B. protocol will address any potential deviations when possible. For example, a protocol might require that a young child remain still during a visit. If, at the moment of a visit the child can't sit still resulting in incomplete data collection, the protocol might say that the lack of data is not a deviation. It is always important to know your protocol! Deviations can also include an error made by a team member, such as using the wrong questionnaire or consent form.

Not all deviations are bad! Keeping a log of deviations can be helpful in identifying a pattern. If the same deviations are continuing to occur in a study this likely indicates that an S.O.P. needs to be updated to prevent further issues. If there is ever any question about how a deviation should be recorded or reported, remember to contact your I.R.B. for guidance.

Recognizing Protocol Deviations

Sometimes protocol deviations are avoidable and sometimes they're not. Regardless, you still have to report them. Take a look at the list of events on the screen. Classify the ones you feel are deviations by dragging them in to the deviations box.

Reporting Protocol Deviations

Speaking of reporting, what's the best way to let your study team know when a deviation has occurred? Again, it varies. Your study team may use an old-school method of tracking, using pen and paper. Or they may use a spreadsheet. Whatever the method, make sure you stick to it.

A well tracked series of deviations can help explain odd data down the road. Take the example of a participant who was unable to adhere to a prescribed sleep intervention. Even with the best of intentions, the participant's participation did not follow the I.R.B. protocol and must be tracked as a deviation. When data are finally analyzed at the end of the study, we can now look at this participant more clearly and draw accurate conclusions because we know how his experience was different from the rest.

Minimizing Protocol Deviations

How can we minimize deviations? The best thing you can do is inspire a culture of open communication among team members. Everyone should be on the same page about how to recognize and report a protocol deviation. Keep in mind that they aren't something to be feared… in fact, you should be encouraged when you recognize a deviation. It means you're doing your job and that you are really paying attention to the I.R.B. protocol and S.O.Ps.

Deviations will show you I.R.B. protocol holes that you may have missed. Make appropriate amendments with the I.R.B. throughout the study to minimize future deviations.

Course Study Manual Check-In

By now you should have filled in the Research Protocol section of your Course Study Manual. If you haven't, take some time to complete this job aid. And don't forget to check out the Resources section for additional information and links, as well. When you're ready, click Next to move to the final assessment for this module.

Lessons Learned

There's a lot to consider when writing an I.R.B. protocol document. But, as long as my study team and I plan ahead, we're able to minimize errors, while maintaining the personal element common in social and behavioral trials.

I learned a lot of lessons during that study…most of all, the importance of including detail in my I.R.B. protocol. I was definitely wrong to think that a general protocol was the way to go. As a team, we also learned the importance of developing good S.O.Ps that can help maintain treatment fidelity. I'm excited to tackle my next study as a much wiser P.I.