Module 6: Participant Safety and Adverse Events

Detecting and Tracking Adverse Events

Welcome to the sixth module in the Social and Behavioral Research Best Practices for Clinical Research course. Here we'll cover what adverse events are and how to report them. Let's catch up with Marc, a seasoned principal investigator, and see how he handled adverse events within the context of an osteoarthritis study.

Dieting and Osteoarthritis

In our study, we were testing an exercise and diet intervention for participants who had painful osteoarthritis. We knew about the link between weight and strain on the body, but we wanted to better understand how motivated participants would be to lose weight and improve their osteoarthritis symptoms. During the study, participants were taught a series of exercises and given a diet plan. They were then asked to come in for weekly visits so we could measure their weight loss progress.

I've been in this game a long time and have a lot of confidence in my team and the way we do things. During this study, we knew what to watch for and had a top-notch communication plan in place.

Identifying Adverse Events

I've watched a few colleagues struggle with reporting events to the I.R.B. This usually happens because they don't really define what an adverse event means for them and how they would report it.

I always make sure that my entire team is familiar with our protocol, and that they know how to identify and report any possible adverse events to me, so we can report them to

the I.R.B.. Documentation is a big deal for us. We make note of all events, but only classify those that are unexpected, related to the research, and serious, as reportable.

When to Notify the I.R.B.

During this study, we did see a couple of potential adverse events. Because we were studying participants with osteoarthritis we knew there was a risk for a potential joint injury. Unfortunately, one month into the study one of our participants tripped on a curb coming out of the grocery store and broke her wrist.

At a follow up visit, our RA Lewis noticed the cast and asked her what had happened. Lewis documented the incident and brought it to my attention. We had a study-specific A.E. reporting plan in place with the I.R.B. This document required that we only report A.E.s that were unrelated to the study procedures annually to the I.R.B. Because of this, I decided to make note of the event in our study database, but *not* report it to the I.R.B. right away.

Course Study Manual

Take a minute to explore the Resources section in the top right corner of your screen. Here you'll find your Social and Behavioral Research Course Study Manual for this module, Participant Safety and Adverse Events. 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.

Overview of Participant Safety and A.E.

Throughout the course of a study, it's critical that all study team members understand the potential risks to participant safety and how to minimize them. All studies involve risks to participant safety, and can range from physical to psychological to even legal risks. However, social and behavioral trials typically pose lower physical risk to participants, when compared to those testing drugs or devices, and deal most frequently with the emotional and psychological side of this spectrum. These risks can include increased feelings of depression or anxiety while undergoing study procedures.

What is an Adverse Event?

An Adverse Event, or A.E., is any untoward medical occurrence that can occur during the course of a study, but that may or may not be caused by the treatment.

These events could be expected or unexpected. For example, when studying a population that includes participants with chronic dizziness, it is not unexpected that a participant falls during the course of the study. This event is untoward, but not unexpected, and might not necessarily qualify as a reportable adverse event, depending on how an I.R.B. protocol is written. We'll discuss the importance of creating a study specific definition of an adverse event in a moment.

Define an Adverse Event

Let's look at a systematic approach to defining adverse events and determining how they should be reported. There are three things to consider. Is the occurrence unexpected during the course of a study? Is the occurrence related or possibly related to the research in which the participant is taking part? Does the event put participants or others at greater risk of harm?

By answering these questions, you can typically determine if an event meets the definition of adverse, as well as how it should be reported to your Institutional Review Board. If the answer to any of these questions is “No,” then the event does not need to be reported. If the answers to these questions are “Yes,” then this event should be reported as an unanticipated problem.

Define an A.E. for Your Study

Within an I.R.B. protocol document, there should be a section that lists any potential risks a participant might experience. For example, a study requiring an exercise test in a younger population might result in a participant feeling out of breath; in an older population, in addition to feeling out of breath, there could be other side effects, such as dizziness, lightheadedness, angina or elevated blood pressure. A well-prepared P.I. defines what an adverse event is at the beginning of a study and uses that to help classify events during the study. This definition must be consistent with institutional guidelines, and also be approved by your I.R.B. Take a moment to pause this course to jot down how your institution defines an A.E.

Develop an Adverse Event Reporting Plan

All study team members should know how to identify and record incidents qualifying as adverse events, but the P.I. is responsible for classifying adverse events according to seriousness, relatedness, and expectedness. A serious event results in death, life threatening circumstances or long term hospitalization or disability. Within social and behavioral research, relatedness refers to the possibility that an event is related to a participant’s involvement in a study. Expectedness can be defined by whether or not the event has been observed before or was outlined as a potential event in the I.R.B. protocol.

Remember, the timeline for reporting an event will vary. Make sure that all members have access to an Adverse Event Reporting Plan to help guide them through the reporting process. This guide should include the type of event that has occurred and the corresponding timeframe for reporting the issue. This timeline should be based on an event's satisfaction of the three A.E. considerations: seriousness, relatedness, and expectedness. Finally, how an event will be reported must also be detailed. Consider whether a team member should just make note of the event in a study log, or whether the event merits an A.E. report and I.R.B. notification.

Some of these events will need to be reported to the I.R.B. Refer to the sample A.E. reporting plan in the Resources section of this module and your I.R.B.'s A.E. guidance to determine what events to report and when.

Importance of Systematic Strategies

In general, study teams often fall short in identifying adverse events during a study. Not because they mischaracterize an event when it occurs, but because they are unaware something even happened. To prevent this, develop systematic strategies that can be used by the entire study team.

Remember, never miss an opportunity to ask probing questions. These questions should be phrased so that the participant is encouraged to provide more than just simple yes or no responses. If a participant responds with a one-word answer, have a follow up question ready. Good questions to ask can include: Can you tell me about any illnesses or incidents that have occurred since we saw you last? If you've been put on any new medications, what are they? Have you had any medical procedures or accidents? Have you noticed anything out of the ordinary? If so, what happened?

To ensure a consistent experience, ask all participants the same set of questions and make note of their responses so that they can be reviewed if needed.

In addition to asking questions at regular intervals, consider having participants keep a study diary in which they note anything out of the ordinary. Things are much easier to remember in the moment, rather than two months later at a study visit.

Think back to the example of the participant who broke her wrist. Because Marc's team had a good adverse event reporting plan in place, Lewis knew to ask the right questions.

Report to the Right People

Coordinators and research assistants are often on the front lines of a study and must be aware of what an adverse event is and how to report it. As we've just discussed, knowing a clinical protocol inside and out is critical in understanding what constitutes an adverse event according to your study. Make sure that you are uncovering details and getting the full picture of a participant's experiences over time.

If a suspected adverse event is encountered, that information needs to get to the right people. It is up to the P.I. to make the final call on an adverse event and report it to the I.R.B. and study sponsor.

Open communication is also vital to the reporting process. A dialogue between participants and coordinators alerts the team to a possible issue. Communication among coordinators, research assistants and P.I.s ensures that suspected A.E.s are given the attention they deserve.

Check Institution Guidelines

The way in which adverse events are reported to an I.R.B. can vary based on an institution's requirements. In general, be sure to note the date of an incident, whether or not it was expected, the relation to the study, a description of what occurred, and what was done to address it. Remember, participants should be identified in these reports by their ID number rather than by their full name to protect their privacy. Finally, be sure to note how the issue was resolved. A resolution can range from referring a participant for further medical care, to acquiring the participant's medical records, to simply getting more information. Occasionally, adverse events, such as strained muscles, can resolve on their own over time. Finally, if a pattern of adverse events is occurring within a study, an I.R.B. protocol amendment or updated consent form may need to be submitted to the I.R.B.

In addition to what is reported, there may be institution-specific guidelines on when something is reported. For example, an adverse event that is classified as serious may need to be reported more quickly than one that is not considered serious. Additionally, an I.R.B. may prefer that study teams compile their milder adverse events and report them to the I.R.B. at the time of a continuing review. Be sure to know the requirements of your own I.R.B.!

Your Turn

Now it's your turn. Let's take another example from Marc's osteoarthritis study. During a routine study visit, one of the participants told Lewis that he felt nauseous since he started the study's diet plan. According to the team's I.R.B. protocol and informed consent documents, this event has been outlined as a potential risk for participants.

In the next few screens, you'll answer questions to help you classify the adverse event, which is nausea, by seriousness, relatedness, and expectedness. This information, along with your A.E. Reporting Plan, will help you determine if this adverse event needs to be reported to your I.R.B., and if so, when it must be reported.

Scenario Summary

In summary, this occurrence of participant nausea is a related, expected and non-serious adverse event. It may not need to be reported directly to the I.R.B., but the study team should continue to monitor the participants to see if others begin to feel nausea at an unexpected frequency.

About Data Safety Monitoring Boards

All studies have a data safety and monitoring plan detailing how participant safety and data integrity are observed. Some complex or high risk studies may also have a Data Safety Monitoring Board or D.S.M.B. This is a collection of people who monitor the data on a regular basis for any signs that a study should be stopped. Members of this board are experts with knowledge of the study biostatistics and an understanding of the science behind it. They are recruited to the task by the P.I. or the study sponsor and are independent from the study.

D.S.M.Bs monitor studies by looking for trends, violations, and study milestones. Consider a study that has been unable to recruit the required number of participants. It is the D.S.M.B.'s job to determine if the study should continue. Additionally, if a study has shown a trend of adverse events or deviations, the D.S.M.B. may advocate for clinical protocol changes to protect participant safety. On the other hand, the D.S.M.B. may approve the early completion of a study that has been overwhelmingly successful and has sufficiently answered its objectives.

Course Study Manual Check-In

By now you should have filled in the Safety and Adverse Event Reporting 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

At the end of my studies, I always like to review what went well and what needed a little work. All in all, I'd say that our study ran really smoothly. Because we laid the ground work to understand the potential risks to our participant population, and fully defined what an adverse event was and how we would report it, we were able to handle some curve balls along the way.

I really can't stress enough the importance of setting yourself up for success with a well written protocol and then sticking to it.