



Study walk-through - What?

Elements

What is the Study Walk-through?

'The Study Walk-through' is a method to help translate your protocol into an accurate and successful study. This toolkit describes the study walkthrough approach, to allow you to implement it in your study.

The operational planning and delivery of a clinical study determines whether it can answer the question that it has set. Strong methodology is needed to ensure that the study endpoints are measured accurately, safely and ethically. The study walk-through is a method to ensure that every step in a study protocol is carefully considered in its operational context, and that those responsible for undertaking the step are tasked with overseeing it appropriately.



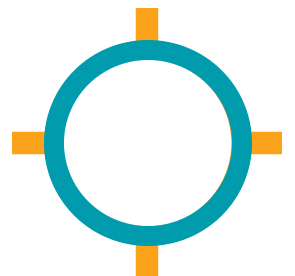
Background

The approach was developed and refined in Kenya. At the time of its development, there were many studies being run, ranging from complicated, regulatory standard vaccine trials in the Kenyan community through to paediatric trials in high dependency units. It was clear that an approach was needed to make sure that the studies ran well in the challenging clinical settings in which they were to be conducted.

Objective

The objective of the study walk-through is to identify and mitigate against errors that could jeopardise the accuracy, safety or ethical conduct of studies. It is designed to be a practical and achievable way to make sure that every step in a study protocol is carefully considered in its operational context, and that those responsible for undertaking the steps are tasked with overseeing it appropriately.

Taking the whole team through a study walk-through process allows everyone to foresee the whole study as it rolls out, from the participants' experience through to what happens to their samples and their data.



Approach overview

To implement the study walk-through method, the entire study team is gathered as early as possible in the planning of the study. An overview of the study protocol is presented, focusing on the primary endpoints and how these will be measured. One team member then leads the process of describing the study step-by-step, as it would be operated at the study centres. Each team member is encouraged to imagine each step from the participant's perspective.

The process covers steps from community engagement and recruitment, through each visit, until the end of the study. The processes and data collected are discussed in the context of actions that relate specifically to the participants, e.g. clinical assessments. The coordinator leads the discussion of each study step, which is recorded as the discussion flows.

This effective method ensures that each team member fully understands the protocol and research question, allowing them to identify elements of their role that are key to the study outcome. This process also uses the experience of each team member to inform the design and operational planning of the study, thereby raising standards and reducing errors.



Study walk-through - Why?

Why 'walk through'?

The process of turning a question into a protocol and a protocol into an operational study is an overlooked area, and undervalued in terms of being a fundamental methodology area in clinical research.

A study can utilise the most impressive, cutting-edge diagnostic technology or new statistical approach, but if the key endpoints have not been considered carefully, the study is difficult to implement in the clinical setting, or the study team are not conducting the processes in an accurate way, then errors can occur. Such errors may even go unnoticed.



Taking the whole team through a study walk-through process allows everyone to foresee the whole study as it rolls out, from the participants' experience through to what happens to their samples and their data. This process has always flagged potential issues that we had not considered when writing the protocol. Unless you consider every step from the perspective of the team member tasked with delivering that step, it is not possible to consider everything, because you cannot know the setting and the constraints as they do. SOPs written from afar fail precisely because of this.

Remote development of Standard Operating Procedures

Study protocols and standard operating procedures (SOPs) are commonly written away from the study site and without the involvement of the study team. As a result, generic SOPs can be produced that might set a standard and attempt to ensure that multiple centres run all their processes in the same way, but are impractical, inappropriate and do not reflect the real situation in the clinic or laboratory. The critical steps in a process, during which something could go wrong, may not be recognised or covered by a generic SOP and therefore, could be managed differently by different staff, incorrectly or not managed at all during the whole study period.

All study staff involved, including the study monitor, need to understand the relative importance of these critical steps to the final study findings. For this reason, it is important that the whole study team fully understands the protocol and the research question it is addressing. Mistakes and inaccuracies can go unnoticed in clinical studies, but informed team members who understand the science spot issues that others may not have thought of.

Example 1: a regulatory vaccine trial

An example taken from the point of view of one of the centres in the phase III RTS,S/AS01 malaria vaccine trial (NCT00866619) [1-3] who utilised the Study Walk-through method to plan how to set the study up in three distant community health clinics and then bring the samples collected back to the hospital.

Example 2: a pragmatic disease management trial

An example of the Study Walk-through method utilised prior to finalising the study protocol for a randomised controlled trial on delivering foot hygiene support and care to people living with podoconiosis in Ethiopia [4]. This challenging trial needed implementing by health workers in an area where there was no previous experience in research.

Example 3: a trial in a disease outbreak

When planning a phase 2 trial for the treatment of Ebola virus disease (PACTR201411000939962)[5], we undertook the study walk-through process at a very early point, before we knew which drug we would be evaluating. We used this process to set out the draft protocol, pinpoint where SOPs would be needed and identify the trial team's training needs.

Study walk-through examples

The study walk-through method has been applied and refined in highly varied clinical studies over 20 years. The practical application of this method is described in a soon to be published paper, using the three examples shown above. For each of the examples, results of using this approach can be seen in the published studies below.

Resources:

1. Clinical Trials Partnership. Efficacy and safety of RTS,S/AS01 malaria vaccine with or without a booster dose in infants and children in Africa: final results of a phase 3, individually randomised, controlled trial. Lancet. 2015;386:31-45.
2. Clinical Trials Partnership, Agnandji ST, Lell B, Fernandes JF, Abossolo BP, Methogo BG, et al. A phase 3 trial of RTS,S/AS01 malaria vaccine in African infants. N Engl J Med. 2012;367:2284-95.
3. Clinical Trials Partnership, Agnandji ST, Lell B, Soulanoudjingar SS, Fernandes JF, Abossolo BP, et al. First results of phase 3 trial of RTS,S/AS01 malaria vaccine in African children. N Engl J Med. 2011;365:1863-75.
4. Negussie H, Kassahun MM, Fegan G, Njuguna P, Enquselassie F, McKay A, et al. Podoconiosis treatment in northern Ethiopia (GoLBet): study protocol for a randomised controlled trial. Trials. 2015;16:307.
5. Dunning J, Kennedy SB, Antierens A, Whitehead J, Ciglenecki I, Carson G, et al. Experimental treatment of Ebola virus disease with brincidofovir. PLoS One. 2016;11:e0162199.



Study walk-through - How?

When to 'walk through'

The study walk-through method aims to identify every situation in which a consequential error could occur, and mitigate against this using a SOP, through training, or by changing a process.

To implement the method, the entire study team is gathered as early as possible in the development of the protocol. Ideally, this meeting would take place long before the protocol is finalised and submitted for regulatory approval, as this can reduce the need for protocol modifications and amendments later on.



At the beginning of the meeting, an overview of the study protocol is presented. This overview focuses on how the participants move through the study visits and interventions, and then on the primary endpoints and how these will be measured. If everyone on the team understands what needs to happen when and what matters in terms of capturing the key outcomes, then a successful study can be set up and a highly operational protocol can be generated.

How to 'walk through' your study

After the overview of the study protocol, the study is then 'walked through'. One team member, such as the study coordinator, leads the process of describing the study step-by-step, as it would be operated at the study centres.

Each team member is encouraged to imagine the experience of the participant, from when and where they first learn about the study, to them being enrolled, then receiving the intervention, and then attending the follow-up visits, the collection of the participant's samples and the information that this will provide. The coordinator leads the discussion of each study step, asking the team to consider who will be responsible for each step, where and when each step will happen, and how all steps could be carried out to ensure: the best experience for the participants and their families; the best experience for the study and healthcare staff involved; and adherence to the protocol.

The outcomes of the discussions are recorded as the discussion flows. Once the 'journey' of a participant through the study visits has been considered by the team in this way it becomes clear where SOPs will be needed. This study walk-through method provides a detailed view of the whole process and thereby highlights where things could go wrong.

We find that this works best when a large piece of paper, coloured pens and a big table are used at the meeting.

Box 1 - Potential topics for discussion

- How will potential participants be identified and approached?
- Are the inclusion and exclusion criteria practical?
- What are the clinic room, bed, staffing or laboratory requirements for screening, recruitment and visits?
- Are the proposed recruitment targets feasible and how recruitment can be optimised?
- What are the timings and logistics around obtaining informed consent are they appropriate for the participant group?
- Are there any practical issues regarding the administration of any intervention?
- Consider the study visits plans and the expectation on participants. How follow-up can be optimised?
- What are the transportation logistics for samples or essential consumables?

Potential topics for discussion at the study

Potential topics for discussion at the study walk-through meeting are summarised in Box 1. The discussion would broadly follow [these steps](#), depending on the study design and complexity of the protocol.



Study walk-through - Questions?

Screening and enrolment

Approaching potential participants: The team would discuss how potential participants would be approached and what the requirements might be for community engagement. They may consider questions such as:

Is there a community advisory board in place? Is this a study of a chronic condition for which there are lists of patients who could be approached? Or is this a study of an infectious disease in which you will need to wait for patients to present with the condition? Where are these patients seen? If it is in the community, then what permissions will be needed? How can the community be consulted and involved? What clinic or health facility is this going to happen in? Will study staff or other staff be working for the health facility? Would it be important to brief the other staff members? Are there adverts being produced for this study? How can recruitment be optimised?

Additional questions that may be addressed as part of this walk-through procedure include the following: *how are the inclusion and exclusion criteria being applied, and are they going to work? Can reminder cards be made that outline these selection criteria, to be given to clinic staff to remind them about this study and to help identify potential patients? Does this study require laboratory or other diagnostics? Is this step part of standard care or a study procedure?*

Key factors to consider with respect to screening and enrolment are how long it will take and how many people it will need. If the study has a screening step, the team should discuss how long it will take and what it will involve. This will give an idea as to what staffing levels, facilities and training will be needed, and an idea of capacity. How many people could be recruited into the study in one day, for example? Might this depend on clinic rooms, beds, staffing or laboratory capacity? Discussing this with the people who will conduct the study, in their working environments, will answer such questions.

Taking consent to participate in the study

The team would also discuss issues around taking consent to participate in the study. They may consider questions such as:

At what point is consent needed? Consent is usually needed before the diagnostic step if it is not normally performed in that patient population. If patients are being considered for a study, who is going to explain this to them? Will the same person be seeking their consent to participate in the study? Where and when will this happen? How long will it take, and is the timing important? In an emergency setting or when a treatment needs to be administered, slowing down time to treatment would be unethical.

An additional point to consider is what is expected from the participant during the study relative to what would normally happen to a participant with this condition, in this setting. *What is being asked of the participant beyond expectations of them during standard care? Does the information sheet and consent form capture this properly? Other potential problems which* could arise with taking consent to participate in the study should also be included in discussion. *For example, are the participants vulnerable (children, unconscious, distressed, or unable to read or speak the relevant language)? What needs to be put in place to manage any of these situations? If a witness is needed, what if no-one is available? Is there a viable alternative approach, such as deferred consent?*

The study visits

The team would consider requirements for each of the study visits and any practical issues they may present. For example:

Will the participants progress into the first visit straightaway? This is common for studies of infectious diseases, but less so for studies of vaccinations or chronic conditions. Where would the first visit happen and what is needed? For example, how many participants could be managed at any one time? What would be the constraints? The time that the procedures take? Beds, staffing, laboratory capacity? How many other people may also be attending the study centres for follow-up visits or other clinics? Is this feasible?

The team would also discuss what should happen to the participant during the study visits and during follow-up. *For example, is the first visit when baseline samples and information will be taken and/or when the participants will be given an intervention? When will the participants need to return for subsequent visits? Is this beyond what would be normal in their usual care? What could be done to make sure that they do come back for subsequent visits? Or will they be visited at home? What could go wrong here? Would there be any concerns about privacy or stigma that might cause participants to change their minds? How well trained are the staff conducting these visits?*