

Perfect protocol writing

Abdul Momin Kazi

A clearly written protocol is an essential component of a research study process.¹ It is a plan, intended to describe the study hypothesis, objectives, design, methodology and exact process of the research study. Development of a study manual or protocol is an intellectual and rigorous task that requires great attention. Protocol can be defined as an "operating manual" and is developed in order to ensure that the study procedure is followed in a scientific manner. It acts like a guide for all personnel involved in the study while ensuring all study related procedures are conducted as planned accordingly before the start of the study. During the preparation process one should keep in mind that a protocol will be viewed by people of different backgrounds. The content of the protocol should be easy to understand and not restricted to investigators only. The study protocol can also be viewed as an official document or agreement between investigators or organizations, as well as a guideline for study coordinators and staff.² With recent advancement in the research process, protocol has become a pivotal document that needs to be submitted when applying for a research grant or ethical approval. Budget should also be submitted with it. It is imperative to understand that deficiencies in the protocol which can result in protocol deviations, poor conduct and inadequate monitoring, reporting and publication of the research study.

Special emphasis is given to the clinical trial study protocol, for an experimental clinical trial SPIRIT 2013 checklist should be reviewed.³ However to cover a larger audience the aim of this paper is to cover essential elements required in a standard protocol before conducting any kind of research. See table 1 for outline of a protocol.

Title Page

This page includes title of the study, which should be informative but brief. It is good to identify the study design, population and intervention in a title, however sensationalizing should be avoided. Names, affiliation and contribution of the investigators and sponsor of the study should be clearly written below the main title.

.....
Department of Paediatrics and Child Health, Aga Khan University, Karachi, Pakistan.

Correspondence: Email: momin.kazi@aku.edu

Information on trial registration in case of clinical trial and latest date and protocol version should be included in the title page.⁴

Study Summary

It is advisable to have a study summary which should briefly describe the study and present an over all sketch of the protocol. The summary should include the study rational, objectives, design, population, methodology and duration.

Continuing with the protocol next main headings of the document are: Background/Introduction, Objective/s, Methodology, References. Budget should also be submitted with it. Appendices attached can have the data collection tools, description of the timeline involved and other informative materials needed to explain each step of the study process.

Background of the Study

The background of the study is a key component of a protocol and should describe study hypothesis to be tested. It should summarize the study question; justify the need of the research study and present available data regarding potential benefits or harm related to current study.⁵ Details on why this study is appropriate, its potential benefits and relevance to current policies should be included.

Study Objectives

The study objectives should be stated clearly and able to reflect the scientific questions to be answered and define its purpose and goals. They should clearly correspond with the study design and statistical plan. Primary and secondary objectives (if present) should be separately and distinctly defined. Clarity is crucial in this stage of protocol writing as the entire study and the document both are dependent on it.

Next is the methodology section including:

Study Design

It identifies the type of epidemiological study design proposed to answer the study specific question.⁶ The methodology section of the protocol starts with the description of the study design; there could be a single study design or combination. The type of study

design should be precisely described e.g. if experimental design than it should be elaborated as triple blinded, placebo controlled, rather than random clinical trial.

Study Setting and Population

This includes information regarding site of the study, e.g. hospital or community based, single or multiple site study etc. The target population of the study should be well defined and time and duration of the study should be clearly stated.

Eligibility Criteria

The eligibility criteria consist of the inclusion and exclusion criteria of the participants to be enrolled in the study. The eligibility criteria should be precisely documented as it can affect the recruitment process as well as the outcome rates of the study.⁷ Poorly defined criteria can result in ineligible participants being enrolled in the study and may undermine study scientific validity. Each component of inclusion and exclusion criteria are precisely considered. Simply keeping a point in the exclusion criteria because it does not fit the inclusion criteria is a wrong practice. Each criterion have indept scientific basis.

Sample Size Assumptions and Estimates

A formal sample size calculation should be documented, as it is key aspect for study design, budget and feasibility. The sample size should be sufficiently powered to detect a difference between the group if it exists, slight miscalculation in the sample size can have considerable effect on the study. The number of study subjects in the trial should be big enough to provide a reliable answer to the study question.⁸

Recruitment Process

Detailed recruitment process supported by flow diagram or chart should be described in the protocol. Where, when, and how will the participants be recruited and the process for administering the consent. Poorly described recruitment process can lead to low enrollment and delay in studies. Study withdrawal or elimination from the study should also be described in the protocol.

Intervention Allocation-Randomization

This is specific to experimental study design. Detail description on how the participants will be randomized and allocated to different interventions. Author should describe the process clearly in order to prevent issues like selection bias.

Data Collection and Management Process

The validity and reliability of the study depends on the tool or questionnaire as well as the data collection methods.⁹ Source of data collection tool should be described, whether it is a structured questionnaire, case report form, patient's notes, electronic data or any procedure. Mode of administration of the question e.g. self-administered or interview base should be explained.

Description of the process on how the data should be acquired and recorded, e.g. paper based and entered in a computer-based programme or directly in a computer or cell phone. Description of the operating software for data collection and management should be mentioned. It is good to describe the methods to be implemented for the validation of the data e.g. double data entry, cross validation etc. All data collection tools should be included as appendices.

Data Analysis

Data analysis plan is an integral part of a protocol as clear analysis leads to clear results. It is essential to write the analyses plan and rationale for conducting the specific tests, rather than just writing down the names of the test. It is good to document the software programme with version to be used. In some trials there is a separate document called statistical analysis plan (SAP) which fully describes the details of analysis plan.³

Ethical Regulations and Consideration

Information on ethical consideration should be well defined. Approvals from the concerned Institutional Review Boards/ Ethical Committees should be obtained and relevant documents including the certificates and consent form should be attached with the protocol.

Safety and Adverse Events

Information on definition of the study safety and adverse events should be documented distinctively, as well as the classification of the adverse events. The process and the time period of the reporting should be clearly stated. Also the process to record adverse events should be mentioned.

Study Timeline

It is highly recommended to note down the study timelines according to the different activities of the study for e.g. study planning and recruitment, data collection process, report writing etc. A Gantt chart is a type of bar chart and is extremely useful in describing the study timelines including the study start and finish dates (Figure).³

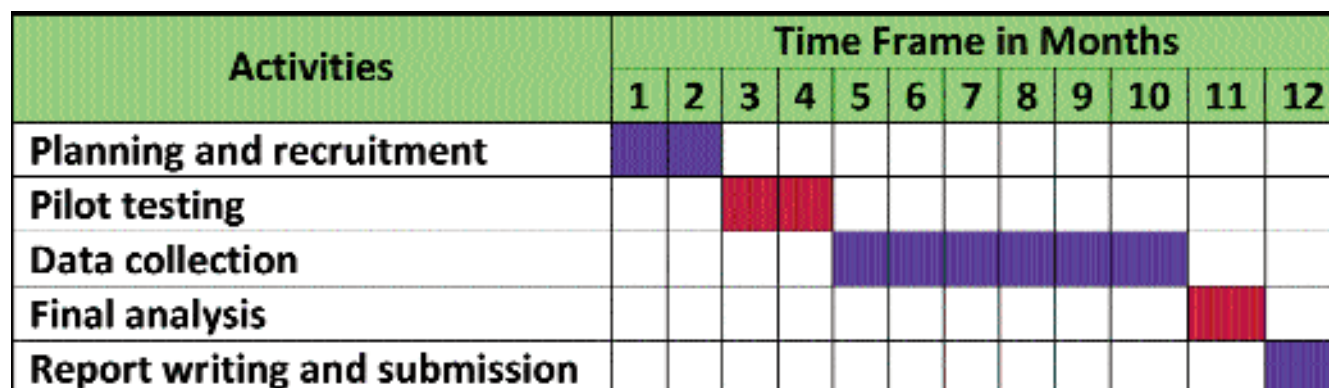


Figure: Example of Gantt Chart: Time Frame of Proposed Activities.

References

A numbered list of updated references quoting the literature review and any other procedures should be made. The most common style recommended for writing references is Vancouver style.⁵

In summary a protocol is a critical document. Dedicated time should be kept aside for protocol writing, as it requires high level of conceptualization and effort. A well described and clearly written protocol is essential for a successful research study.

References

1. O'Brien K, Wright J. How to write a protocol. *J Orthod* 2002; 29: 58-61.
2. Friedman L. *Fundamentals of Clinical Trials* Third ed:

Springer; 1998.

3. Chan AW, Tetzlaff JM, Gotzsche PC, et al. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. *BMJ*.346:e7586.
4. AM A. A Guide for Writing a Protocol for a Clinical Trial. *Sudanese J Pub Health* 2010; 5(2).
5. Betkerur J. Guidelines for writing a research project synopsis or protocol. *Indian J Dermatol Venereol Leprol* 2008; 74: 687-90.
6. Jehan F, Kazi AM. Basic study designs in health research. *J Pak Med Assoc* 2012; 62: 408-11.
7. Chan AW, Tetzlaff JM, Altman DG, et al. SPIRIT 2013 Statement: Defining Standard Protocol Items for Clinical Trials. *Ann Intern Med* 2013; 158: 200-7.
8. Christensen R, Langberg H. Statistical principles for prospective study protocols:: design, analysis, and reporting. *Int J Sports Phys Ther* 2012; 7: 504-11.
9. Kazi AM, Khalid W. Questionnaire designing and validation. *J Pak Med Assoc* 2012; 62: 514-6.