How to Write a Research Protocol: Tips and Tricks

The first drafting of the protocol for a new research project should start from a solid idea with one or more of these goals:

1. Overcoming the limits of the current knowledge in a determinate field with the aim of bridging a "knowledge gap"
2. Bringing something new in a scarcely explored field
3. Validating or nullifying previous results obtained in limited records by studies on a wider population.

A research proposal born with the intent to convince the others that your project is worthy and you are able to manage it with a complete and specific work plan. With a strong idea in mind, it is time to write a document where all the aspects of the future research project must be explained in a precise, understandable manner. This will successively help the researcher to present it and process and elaborate the obtained results.[1] The protocol manuscript should also underline both the pros and the potentialities of the idea to put it under a new light.[2]

Our paper will give the authors suggestions and advices regarding how to organize a research protocol, step by step [Table 1].

Table 1: Main sections and subsections in a complete research protocol

Main investigator
Name
Address
Phone/fax
E-mail
Number of involved centers (for multi-centric studies)
Indicate the reference center
Title of the study
Protocol ID (acronym)
Keywords (up to 7 specific keywords)
Rationale of the study (describe current scientific evidence in support of the research with a possible sub-section for the references)
Study design
Monocentric/multicentric
Perspective/retrospective
Controlled/uncontrolled
Open-label/single-blinded or double-blinded
Randomized/nonrandomized
n parallel branches/*n* overlapped branches
Experimental/observational
Others
Primary objective
Endpoints (main primary and secondary endpoints to be listed)
Expected results
Analyzed criteria
Main variables/endpoints of the primary analysis
Main variables/endpoints of the secondary analysis
Safety variables
Quality of life (if applicable)
Health economy (if applicable)
Visits and examinations
Therapeutic plan and goals
Visits/controls schedule (also with graphics)
Comparison to treatment products (if applicable)
Dose and dosage for the whole time period
Formulation and power of the studied drugs
Method of administration of the studied drugs
Informed consent
Study population
Short description of the main inclusion and exclusion criteria
Sample size
Estimate of the duration of the study
Best supposed perspective
Safety advisory
Classification needed
Requested funds
Additional features
On the main concept of the study

First section: Description of the core center, contacts of the investigator/s, quantification of the involved centers

A research protocol must start from the definition of the coordinator of the whole study: all the details of the main investigator must be reported in the first paragraph. This will allow each participant to know who ask for in case of doubts or criticalities during the research. If the study will be multicentric, in the first section must be written also the number of the involved centers, each one possibly matched with the corresponding reference investigator.

Second section: Specific features of the research study

After completing the administrative details, the next step is to provide and extend title of the study: This is made for identifying the field of research and the aim of the study itself in a sort of brief summary of the research; the title must be followed by a unique acronym, like an ID of the protocol. If the protocol has been already exposed and approved by the Ethical Committee, it is appropriate to include also protocol number.

A list of 3–7 keywords must be listed to simplify the collocation of the protocol in its field of research, including, for example, disease, research tools, and analyzed parameters (e.g. three-dimensional echocardiography, right ventricle, end-stage heart failure, and prognosis).

The protocol must continue stating the research background that is the rational cause on the base on which the study is pursued. This section is written to answer some of these questions: what is the project about? What is already available in this field in the current knowledge? Why we need to overcome that data? and How will the community will from the present study?

As for an original research manuscript, the introduction to the project must include a brief review of the literature (with corresponding references). It is also fundamental to support the premises of the study, to underline the importance of the project in that particular time period and above all, of the materials and methods that will be employed. The rationale should accurately put in evidence the current lack in that field of scientific knowledge, following a precise, logical thread with concrete solutions regarding how to overcome the gaps and to conclude with the hypothesis of the project. A distinct paragraph can be dedicated to references, paying attention to select only the previous papers that can help the reader to focus the attention on the topic and to not excessively extend the list. In the references paragraph, the main studies regarding the object of the research but also state-of-art reviews updating the most recent discoveries in the field should be inserted.

The section should successively expose the study design: monocentric or multicentric, retrospective or prospective, controlled or uncontrolled, open-label or blinded, randomized or nonrandomized, and observational or experimental. It should also be explained why that particular design has been chosen.

At this point, the author must include the primary objective of the research, that is, the main goal of the study. This is a crucial part of the proposal and more than 4–5 aims should be avoided to do not reduce the accuracy of the project. Using verbs as "to demonstrate," "to assess," "to verify," "to improve," "to reduce," and "to compare" help to give relevance to this section. Add also a description of the general characteristics of the population that will be enrolled in the study (if different subgroups are planned, the criteria on the base of which they will be divided should be specified); primary and secondary end-points, including all the variables that represent the measure of the objective (e.g., all-cause death, cardiovascular death, hospitalization, and side effects of a drug) follow in this section.

All the single parameters and variables that will be assessed during the study must be accurately and precisely listed along with the tools, the methods, the process schedule timing, and the technical details by which they will be acquired; Here, the author should explain how the Investigators who work in the other involved centers have to sent their results and acquired data to the Core Laboratory (e.g. by filled databases or by sending images).

A special attention must then be paid to clarify the planning of each examination the study patients will undergo: basal evaluation, potential follow-up schedule, treatment strategy plan, comparison between new and already-in-use drugs, dose and dosage of the treatment in case of a pharmacological study. This part can be enhanced by flowcharts or algorithms that allow a more immediate comprehension and interpretation of the study strategy.

This section may result more complete if one more subsection, illustrating the expected results, is included. Considering the idea at the base on the project, the endpoints and the pre-arranged objectives, the author can explain how its research project will

- Contribute to optimize the scientific knowledge in that specific field
- Give real successive implications in clinical practice
- Pave the way for future scientific research in the same or similar area of interest, etc.

The study population must be specified in detail, starting from inclusion criteria (including age and gender if it is planned to be restricted) and exclusion criteria: the more precise are the lists, the more accurate the enrollment of the subjects will be to avoid selection biases. This will also help to raise the success rate of the project and to reduce the risks of statistical error during the successive analysis of the data. The sample size should be planned and justified on the base of a statistic calculation considering the incidence and prevalence of the disease, frequency of use of a drug, etc., and possibly also indicating if the study considers a minimal or maximal number of subjects for each enrollment center (in case of multicentric studies).

This section of the protocol should end with some indications regarding timing and duration of the study: Starting and end of enrollment date, starting and end of inclusion date, potential frequency of control examinations, and timing of the analysis of the acquired data. If already settled, it can be useful to indicate also the type of statistical analysis that the investigators will apply to the data.

It is always necessary to prepare an informed consent to be proposed to the patient where premises, methods, and aims of the research together with advantages (e.g., some visits or diagnostic examinations for free) and possible risks derived from the participation to the study.

Section three: Additional features of the study

In this short section, various pieces of information regarding safety of the study must be added (a classification is fundamental in case of studies that expect the use of invasive procedures or drugs use). Usually, for nonobservational studies, an insurance coverage must be considered.

If the investigators have requested or plan to request funding or financial support, all the obtained resources must be listed to avoid conflicts of interest.

Conclusion

Writing a complete and detailed document is a paramount step before starting a research projects. The protocol, as described in this paper, should be simply and correctly written but must clarify all the aspects of the protocol. The document could be divided into three different sessions to give all the parts the appropriate attention.

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