

A REVIEW ON HEALTH RESEARCH PROTOCOL

Ujjaliya Nitin^{1*}, Shrivastav Sumit² and Bhatt Dharmpal³

¹Lecturer, Dept of Dravyaguna, Govt. Ayurvedic College, Patiala, Punjab, India.

² Associate Prof. Dept of Roga Nidan, Shri Dhanwantry Ayurvedic College & Hospital,
Chandigarh.

³Lecturer, Dept of Kriya Sharira, Govt. Ayurvedic College, Patiala, Punjab, India.

Article Received on
17 Aug 2015,

Revised on 07 Sep 2015,
Accepted on 28 Sep 2015

***Correspondence for
Author**

Dr. Ujjaliya Nitin

Lecturer, Dept of
Dravyaguna, Govt.
Ayurvedic College,
Patiala, Punjab, India.

ABSTRACT

A research protocol is the detailed plain which helps the investigator to carry out the study in an authentic and systematic way. Every research study should have a protocol. Research involving humans should be scientifically justified and described in a clear detailed protocol. A well written protocol can be judged according to three main criteria.

1. It should answer the research question question (s), and achieve the study objective.
2. Feasible in the particular set up for the study.
3. It should provide enough detail that can allow another investigator to do the same study and arrive at comparable conclusions.

KEYWORDS: Research protocol, Medical research, Study design, Good clinical practice

INTRODUCTION

A precise and detailed plan for a scientific experiment medical trail or other piece of research that describes the objective(s), rationale, design methodology, statistical considerations, organization and background of a trial. It evolves as the study evolves.

Type

A Clinical research protocol can be designed based on international standards.

1. International Conference on Harmonization (ICH).
2. WHO Good Clinical Practice (GCP) Standards.

Advantages of a research protocol

- It gives us a clear idea regarding all aspects of study.
- It is a necessary guide especially if a team is working on the research.
- It is essential for getting an ethical approval, if the study involves research on human subjects or experimental animals.
- This is an essential component of a research proposal submitted for financial assistance.
- Operations manual, essential in a detailed study could be developed from a research protocol.

Format for research protocol

Part-A

The research protocol is generally written according to the following format.^[1]

1. General information.
2. Project title.
3. Project summary.
4. Project description:
 - a) Rationale and background information.
 - b) General and specific objectives.
 - c) Statement of research hypothesis:
 - a. Rationale and background information.
 - b. General and specific objectives.
 - c. Statement of research hypothesis.
 - d. Methodology.
 - e. Follow up and expected outcome.
 - f. Data management and statistical analysis.
5. Ethical considerations.
6. Informed consent.
7. Gender issues.
8. References.

1. GENERAL INFORMATION

Protocol identifying number (if any) and date.

- Name and address of the sponsor/funder. Number (s) of research site (s), including responsibilities of each.

- Name (s) and address (es) of the clinical laboratory (ies) and other medical and/or technical department(s) and/or insitiutions involved the research.

2. PROJECT TITLE

The title should be descriptive, concise and clearly stated.

3. PROJECT SUMMARY

The summary should be concise with not more than 150 words but with all the central elements of the protocol.

4. PROJECT DESCRIPTION

a) Rationale and background information

- Rationale specifies the reasons for conducting the research in light of current knowledge. It should include a well documented statement of the need/problem that is the basis of the research, the cause of this problem and its possible solutions. It should answer the questions like, why the research needs to be done and what will be its relevance.
- Background information specifies name and description of the investigational product along with summary of the known and potential risks and benefits, to human subjects. Description of and justification for the route of administration dosage, dosage regimen, and treement period should also be mentioned.
- Any study done previously if available can be included here.

b) General and specific objectives

General objectives are broad statements of what the proposal hopes to accomplish. Specific objectives-are statements of the research question(s). Objectives should be simple specific and stated in advance. After statement of the primary objective secondary objectives may be mentioned.

(c) Statement of research hypothesis

Hypothesis are carefully constructed statement about a phenomenon in the population which, when tested, will lead to identification of the most likely causes of disease or changes in the condition being observed.

(d) Methodology

The methodology implies a system of methods and principles used for carrying out the research. This is the most important part of a protocol and has to be written in full detail. It

should include information on the research design research subjects, sample size, study period, interventions used observations to be made, and a description of the measures taken to minimize like randomization blinding etc. to avoid bias.^[1]

I. Study design

The choice of the design should be explained in relation to the study objectives. The design of the study should include information on the type of study, the research population or the sampling frame (with inclusion and exclusion criteria, withdrawal criteria etc.) and the expected duration of the study. The same study can be described in several ways. For example a study may be described as being a basic science research epidemiologic or social science research it may also be described as observational or interventional if observational, it may be either descriptive or analytic, if analytic it could either be cross-sectional or longitudinal etc. If experimental, it may be described as a controlled or a non controlled study.^[2]

II. Study setting

Research setting includes all important factors of study such as study population, place and time of study with ethical considerations.

III. sampling.

Sampling is a process of choosing a section of the population for observation and study. The sampling frame consists of a list of elements (units) of the population. In population surveys, this is a list of people and in clinical trials for a disease; it is a list of patients with that disease. Two common approaches are employed in research studies the empirical and the analytical. The empirical approach involves using sample sizes that have been used in similar studies.^[3]

- The analytical (scientific) approach to determining the appropriate of the sample to be included in the study depends on the assessment of errors of inference and a desire to minimize sampling error.

Sample size

The should be information regarding basis on which sample size is calculated. The sample should be of sufficient size to produce meaningful results and to allot tests of statistical

significance to be applied. Samples should be representative and reliable to minimized sampling errors.

Controls

Use of controls increase validity of the conclusions.

IV. Duration of the project

The protocol should specify the time that each phase of the project is likely to take along with a detailed month by month timeline for each activity to be undertaken.

V. Interventions

A description must be given of the drugs or devices to be used and whether they are already commercially available or in phase of experimentation.

For drugs and devices that are commercially available the protocol must state their proprietary names, manufacturer, chemical composition, dose and frequency of administration. For drugs and devices that are still in the experimental stage (or that are commercially available but are being used for a different indication or in a different mode of administration). additional information should be provided on available pre clinical investigations in animals and/or results of studies already conducted on humans. In such cases the approval of the drug regulatory agency in the country is generally needed before implementing the study.

VI. Observations

Information should provided on the observations to be made how they will be made and how frequently will they be made. If the observation is made by a questionnaire this should be appended to the protocol. (a note on questionnaire preparation is added at the end of this chapter) Laboratory or other diagnostic and investigative procedures should be described. For established procedures reference to appropriate published work is enough. For new or modified procedures an adequate description is needed with a justification for their use.

e) Follow-Up and Expected Outcomes of the Study

The research protocol must give a clear indication of what follow up will be provided to the research participants and for how long. This may include a follow up, especially for adverse events, even after data collection for the research study is completed.

The protocol should indicate how the study will contribute to advancement of knowledge, how the results will be utilized, not only in publications but also how they will likely affect health care, health systems, or health policies.

f) Data management and statistical analysis

The protocol should provide information on how the data will be managed, including data coding for computer analysis, monitoring and verification information should also be provided on the available computer facility.^[3]

Statistical methods proposed to be used for the analysis of data should be clearly outlined, including reasons for the sample size selected, power of the study, level of significance to be used, spurious data etc. for projects involving qualitative approaches, sufficient details of how the data will be analyzed also should be added.

5. ETHICAL CONSIDERATIONS

Written approval of the appropriate ethics review committee- Clinical trials should be conducted in accordance with the ethical principles that have their origin in the declaration of Helsinki, and that are consistent with GCP (good clinical practices).

A special section, preferably in the format of a checklist, to address all possible ethical concern including safety measures, quality assurance should be added.

6. INFORMED CONSENT FORMS

The approved version of the protocol must have copies of informed consent forms (ICF), both in English and the local language in which they are going to be administered.

7. GENDER ISSUES

Ensure, where indicate, that clinical trials of pharmaceuticals, medical devices and other medical products include women, with their full knowledge and consent and assure that the resulting data is analyzed for sex and gender differences.

8. REFERENCES

The protocol should end with relevant bibliography references on which researcher depend for carrying out the study. An epidemiological study of vasectomy and atherosclerotic disease.

1) Statement of Problem

Studies in experimental study of vasectomy and atherosclerotic. This raised concern among vasectomy provides whether the alleged association applied to human beings.

2) Relevance of the problem national or local health objectives

In view of the negative impact on vasectomy programmes as evidence by the animal, there are both programmatic and scientific reasons for conducting epidemiological and scientific reasons for conducting epidemiological studies. Prevalence of vasectomies incidence of atherosclerotic disease, number of years that vasectomy has been widely available, general access to medical services and consistency of diagnostic skills were considered while undertaking the study.

3) Field of application of proposed research design

The study results will be useful in assisting family planning policy makers and health scientists to implement vasectomy programmes in a more effective and safe way.

4) Review of literature and other existing information

Twelve epidemiological studies were conducted in different countries none of which has detected casual relation between vasectomy and cardiovascular morbidity and/or mortality in men. Major references: (eg: Wallace, R. B., Lee, J., Gerber, W.L., Clarke, W.R. and Lauer, R.M. (1981) Vasectomy and coronary disease in men.

5) Statement of objectives**a) General objectives**

To determine whether there is casual association between vasectomy and atherosclerotic diseases. If so whether vasectomy potentiates the risk of atherosclerotic diseases in subjects with other predisposing risk factors.

b) Specific objectives

- To estimate the relative risk of vasectomy with other risk factors for atherosclerotic diseases in men.
- To estimate the independent effect of vasectomy on atherosclerosis.
- To test the possible duration of the effect of vasectomy on risk for atherosclerosis
- To examine synergistic effect between vasectomy, cigarette smoking and hypertension.

6) Variables

Atherosclerotic diseases will be identified according to the WHO criteria.

- A. Atherosclerotic diseases will be identified according to the who criteria.
- B. Patient characteristics: age, Birth, date religion, education, occupation, family history, marital status.
- C. Reproductive history: number and sex distribution of living children, wife's reproductive status.
- D. Lifestyle: smoking status. Alcohol intake, dietary habits, salt intake, coffee drinking, physical activity.
- E. Medical history: diseases or operation that might have affected sterility .Hypertension, diabetes or hypercholesterolemia.

7) Statement of research hypothesis

Animal studies suggest that vasectomy may accelerate the progress of atherosclerosis.

We wish to investigate whether this finding applies to human beings.

8) Research methodology^[2]**a) Summary of methodology**

A hospital-based case control study will be conducted to examine the possible relationship between vasectomy and atherosclerotic morbidity in men. 500 men aged 35-64 yrs (cases) diagnosed for the first time with atherosclerotic disease will be compared with 1000 matched non-atherosclerotic patients (controls) hospitalized with a diagnosis considered to be unrelated to vasectomy.

b) Research design**1) Selection of research strategies.**

Cases and controls will be interviewed by using a pre constructed questionnaire.

2) Selection of research settings

Case will be married male patients aged 35- 64 yrs, with at least one living child and diagnosed with the first episode of atherosclerotic disease controls will be males with no history of atherosclerotic disease. Controls will be males with no history of atherosclerosis and who were admitted with a disease not suspected of being related to vasectomy. Study period: September 1988-March 1990.

3) Sampling

Sample will be selected by a non randomized method. Sample size: 500 cases and 1000 controls. Attempt will be made to avoid or diminish potential sources of bias and errors that are frequently encountered in case control studies.

4) Use of controls Two controls will be matched with each case by

- 1) Hospital (same)
- 2) Age(\pm 5yrs)
- 3) Number of living children (At least one son)
- 4) ADMISSION DATE (Closest)
- 5) Study instruments

The questionnaire will be structured to minimize interviewer and respondent bias. It will include questions on: (i) patient characteristics; (ii) family health history; (iii) reproductive history, (iv) habits; (v) personality type; (vi) medical history (including questions on vasectomy); and (vii) clinical information (from medical charts).

6) Short description of plans for collecting data. Recruitment of cases: interviewer reviews daily inpatient status. If diagnosis falls into study category, refer case to chief cardiologist for review. Doctor decides on eligibility of case. Interviewer checks eligibility of patient's background. If the patient meets the eligibility criteria for diagnosis and background, interviewer performs interview and fills in questionnaire. On completion of a batch of five cases and ten matched controls, interviewer contacts research headquarters staff for review of questionnaires and repeats above procedure. Recruitment of controls: interviewer reviews admission log and selects potential controls per case who fulfill matching criteria and have appropriate admission diagnosis. Checks eligibility criteria of patient's background. If selected as eligible control, performs interview.

7) Short description of plans for analysis of data and interpretation of results. Data analysis and interpretation of results will be done as follows. Independent variables like age, education, etc. will be divided as follows.

Age: 35-54 Yrs versus 55-64 yrs. Education: Upto 12 yrs versus above 12 yrs. Occupation: Administrative others. Cigarette smoking: Ever versus never. Coffee drinking: Everyday versus less often /never. History of diagnosed disease: Present versus absent.

8. Statistical analysis

Odd's ratio will be calculated from matched triplets (one case, two controls) to estimate the overall relative risk of vasectomy as well as other risk factors. Independent effect of vasectomy on atherosclerosis will be evaluated by adjusted odd's ratios. Effect of time elapsed since vasectomy on risk for atherosclerosis will be tested with atherosclerosis as the dependent variable and interval since vasectomy as the independent variable.^[3]

REFERENCE

1. Isaac Stephen, Michel, William B. Handbook in research and evaluation, Robert R. Knapp, California,
2. A framework for the development and evaluation of RCTs for intervention to improve health. Medical research council, London: MRC, 2000.
3. Kjell benson, Arthar J Hartz. A comparison of observational studies and randomized controlled trials. N Engl J Med, 2000; 342: 1878-1886|june, 22, 2000.
4. Campbell M, Donner A, Klar N. Developments in cluster randomized trials and statistics in medicine. Star Med, 2007; 26: 2-19.
5. Peter craig, Paul Dieppe, Sally macintyre. Developing and evaluation complex intervention: the new medical research council guidelines. BMJ, 2008; 337: a1655.