FORMULATING A RESEARCH PROTOCOL

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Overview

- Parts of a protocol/research proposal
  - Structure, contents
- Parts of a thesis
  - Structure, contents, length
- Parts of a paper
  - Structure, contents, length

Parts of a Protocol …

Structure

1. Title page
2. Declaration
3. Introduction
4. Research question
5. Hypothesis
6. Review of literature
7. Aims and Objectives
8. Materials and methods
9. Bibliography
10. Annexures
    - Proforma
    - Research information sheet
    - Consent form

Parts of a protocol…

1. **Title page**
   - Title of thesis
   - Investigators
   - Head of department
   - Head of institute

Parts of a Protocol…… TITLE

- Must include
  - Hypothesis/ problem studied

    Administration of fluid boluses over 5 minutes versus 15 minutes in septic shock
- May include
  - Study population

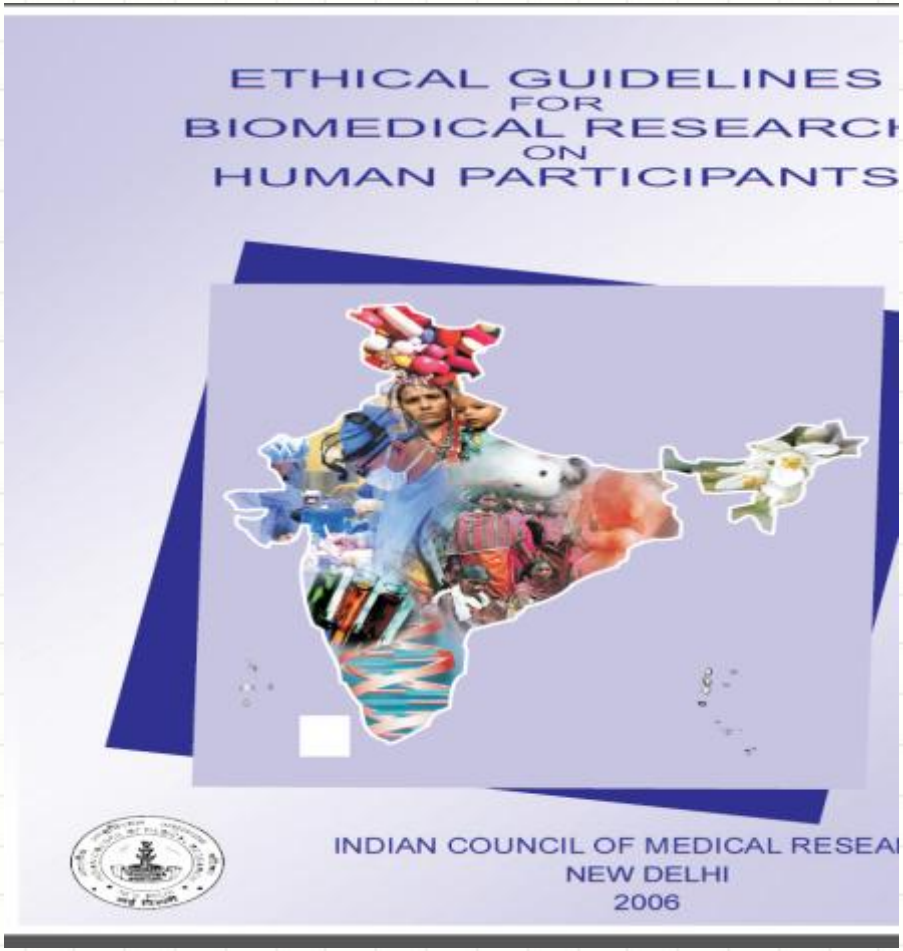
    Administration of fluid boluses over 5 minutes versus 15 minutes IN CHILDREN with septic shock
- Good to include
  - Research design

    Administration of fluid boluses over 5 minutes versus 15 minutes IN CHILDREN with septic shock – A RANDOMIZED CONTROLLED TRIAL

Parts of a Protocol……

2. DECLARATION

—ICMR guidelines on biomedical research



Parts of a protocol…

3. Introduction
   - Brief, relevant to the research question
   - Should address what has already been done and what is the need to do the study

Parts of a protocol…

4. Research Question

- Research attempts to answer questions
- First step in research- identifying the knowledge gap and developing a question to be answered
- The research question will guide the rest of the design process

Should be CLEAR, FOCUSSED, CONCISE and DEFENDABLE!

Types of research questions

- **How frequent is the disease?**
- **What are the features of diseased pts?**
- **Can one identify risk factors of the disease?**
- **Can an intervention prevent/treat?**

Parts of a protocol…

4. Research question (Prototype – RCT)

   Must contain the following

   – P- population being studied
   – I- Intervention
   – C- Control
   – O- Outcome

Parts of a protocol…

4. Research Question (examples)

Q 1. Does administration of fluid bolus over 15-20 (I) minutes as compared to 5-10 minutes (C) decrease the requirement of mechanical ventilation (O) in children with septic shock (P)

Q 2. Is the prevalence of diastolic dysfunction (O) in first 24 hours of admission significantly higher in children with septic shock (P-S) as compared to those without (P-C)?

Parts of a protocol…

5. Research hypothesis

Must contain the following

- Exactly who is being studied? (incl controls, if any)
- Exactly what is the predictor variable, if any?
  - risk factor in a CCS or cohort study;
  - drug in an RCT
  - positive test in a diagnostic tests study
- Exactly what is the outcome variable?
  - disease occurrence, death, gold std +veity etc
- What is the anticipated effect size/frequency of outcome and observed over what time?
  - prevalence/incidence in a descriptive study,
  - O.R. in a CCS,
  - difference in proportions in a cohort or RCT

Hypothesis…

Research hypothesis examples

Administration of fluid boluses over 15-20 minutes (STUDY GROUP) when compared to administration over 5-10 minutes (CONTROL GROUP) in the first hour of resuscitation in children with septic shock (POPULATION STUDIED) would reduce the composite outcome of need for mechanical ventilation and/or impaired oxygenation (i.e. decrease in peak oxygenation index by 5) (EFFECT SIZE) in the first 6 hours after initiation of fluid resuscitation (OBSERVED OVER WHAT TIME?)

Hypothesis

Research hypothesis examples

The prevalence of Ascariasis in children aged 1-5 yrs presenting to out-patient hospital services with pica (geophagia) is 25%

Among children aged 10-15 yrs with primary gastro-intestinal Non Hodgkin's Lymphoma, the odds of having celiac disease are 2.5 times that in age matched controls with extra-intestinal Non Hodgkin's Lymphoma

Children aged 5-10 yrs with moderate to severe iron deficiency anemia for a duration of > 6 months have mean IQ scores higher by 10 points compared to non-anemic age-matched controls

Parts of a protocol…

5. Review of literature

Must contain

- Progressive description from an overview to a focused account relevant to the research hypothesis
- Should lead up to the research hypothesis
  - Example
    - Study on myocardial dysfunction should not elaborate too much on anatomy and physiology of the heart
    - Should not include all studies on myocardial dysfunction
    - Should only include studies in septic shock and not MI

Parts of a protocol…

5. Review of literature …

- “A reference should not be cited simply because it has been found”
- Avoid sentences like: “It has been demonstrated that…”; or “Blah, blah, blah and Blah in 1990 showed that…”

Parts of a protocol…

5. AIMS and OBJECTIVES

- Start with the primary research hypothesis
- Aims include
  - Determining whether the hypothesis was true
  - Determing whether sub-hypotheses were true
  - Exploratory analyses

Parts of a protocol…

5. AIMS and OBJECTIVES

- Start with the primary research hypothesis
- **Aims include**
  - Determining whether the hypothesis was true
  - Determining whether sub-hypotheses were true
  - Exploratory analyses
- **Objectives should include**
  - All components of research hypothesis including population, intervention, effect size, period of observation and outcome
  - Two types
    - Primary- main aim/goal of the study
      - Used to calculate the sample size
      - Determines study design
    - Secondary
      - For determining sub-hypotheses
      - Adverse events/ drug reactions
      - Subgroup analyses

Parts of a protocol…

5. AIMS

Examples

1. Hypothesis- Among children admitted to ICU, PIM and PIM-2 scores predict mortality better if calculated after an initial period of stabilization – i.e. at 4 hours – when compared to calculation within the first hour of admission
2. The aim of our study is to compare the performance of the PIM and PIM-2 scores assigned at four hours with that assigned within one hour after admission

Parts of a protocol…

5. AIMS and OBJECTIVES

Example 2.

Objectives:

1. Primary objective

To compare the discriminative ability and calibration of PIM and PIM-2 scores calculated at 4 hours with that calculated at 1 hr after admission

2. Secondary objective

- To assess the performance of these two scores in a resource restricted setting
  - For the entire cohort of children admitted and
  - Across different age and diagnostic subgroups

Methods

6. Materials and methods

- Future tense in protocol, past tense in thesis
- Includes
  - Subject characteristics
  - Place & time
  - Protocol of events
  - Procedures/ apparatus/ standard curves/ list of names & sources of drugs, reagents, chemicals
  - Techniques
    - Standard ones: referenced
    - Novel ones: describe in detail

Subject characteristics

- Eligibility criteria of cases & controls
  - Too stringent exclusions compromise external validity
  - Too liberal inclusions compromise internal validity
- Decide eligibility criteria of controls
  - Descriptive studies: have no controls
  - RCT: controls get allocated automatically (by a random process)
  - Cohort: selection of controls crucial
  - Case controlled study: selection of controls is critical

Controls

- Rules in Cohort & Case controlled study
  - The controls should be subjects who would have otherwise qualified to be cases had it not been for their exposure status (cohort) or their disease status (case control)
- The control should ideally resemble the group that would have emerged from a RCT (if an RCT were ethically allowable)

Examples

- Example 3. Fluid bolus over 15 -20 minutes versus 5-10 minutes
- Inclusion criteria
  - Children < 18 years of age with features of septic shock with or without hypotension would be included
- Exclusion criteria
  - Severely malnourished (Indian Academy of Pediatrics classification for malnutrition -grade 4)
  - Primary cardiac illness
  - Contraindication to central venous catheter insertion
  - Children with features of fluid overload at presentation
  - Children whose parents refuse to give an informed consent

Parts of a protocol…

7. Bibiliography

- References in vancouver style

1. CenevivaG, Paschall JA, Maffei F, Carcillo Goldstein B, Giroir B, Randolph A. International pediatric sepsis consensus conference: definitions for sepsis and organ dysfunction in pediatrics. Pediatr Crit Care Med 2005; 6:2–8.
2. James A. Russell. Management of Sepsis. N Engl J Med 2006; 355:1699-713
3. Irazuzta J, Sullivan KJ, Garcia PC, Piva JP. Pharmacologic support of infants and children in septic shock. J Pediatr (Rio J). 2007; 83:S36-45
4. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B,et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med. 2001;345:1368-77

Parts of a protocol…

8. Annexures

- Proforma
- Research information sheet
- Consent form

Parts of a protocol…

8. Annexures

- Proforma
  - Screening form
  - All variables related to demographic characteristics, hospital course/ relevant information, interventions, outcome

Proforma

PROFORMA

SCREENING FORM -1

1. Form Filled by Dr. ☐☐☐☐☐☐☐☐☐☐☐
2. Date of Birth ☐☐ ☐☐ ☐☐☐☐
3. Age ☐☐ . ☐
4. CR No. ☐☐☐☐☐☐☐☐☐☐☐☐
5. Sex (male =1, female – 2) ☐
6. Father's name ☐☐☐☐☐☐☐☐☐☐
7. Address ☐☐☐☐☐☐☐☐☐☐
8. Phone No. ☐☐☐☐☐☐☐☐☐☐
9. Weight (in kgs) ☐☐☐☐

SCREENING FORM -II

This form is for checking the eligibility for enrolment in the study (to be filled in all patients for whom FORM-1 is filled)

1. Patient requires PICU admission *(Yes= 1, No=2)* ☐

If the answer is 1, then proceed further.

2. Look for the following exclusion criteria: *(Yes=1, No=2)*
   1. Received steroids for 10 days in previous month ☐
   3. Children whose parents refuse to give an informed consent ☐

If none is 1, move further

FORM – III

To be filled only if patient satisfies inclusion criteria and does not have any exclusion criteria

Name _____ Fathers Name _____

Age _____ Sex_____ weight_____ CR No _____

DOB_____DOA_____Date of discharge_____

1. History

Duration of illness prior to admission in days: _____

Nature of illness severe sepsis/septic shock/meningitis/ pneumonia/seizure disorder/ cardiogenic shock/ any other_____

Source of infection (GIT/ Cardiac/ Pulmonary/ CNS/ Skin/ urinary tract/liver/ other)_____

Presenting complaints and duration of the same

_____

_____

Past history:_____

Chronic underlying illness: [(1) chronic kidney disease, 2) congenital heart disease, 3) chronic liver failure, 4) nephrotic syndrome, 5) genetic/ neurometabolic disorders, 6) tubercular meningitis and 7) others including autoimmune disorders/underlying immunodeficiency disorders] *(please enter the appropriate number in the bracket in this space)* _____

Birth and Development history _____

Immunization history

Parts of a protocol…

8. Annexures

- Research information sheet
  - Relevant information about intervention and why you are doing this study
  - Risks involved in participation (procedural/emotional)
  - Back up measures in place in case of any adverse events
  - Contact information
  - Bilingual

Parts of a protocol…

8. Research information sheet
   - Example

सूचना पत्र

विषयः– "अर्ली गोल डारेक्टिड थेरेपी वर्सस स्टैंडर्ड प्रोटोकॉल गाईडिड थेरेपी इन पिडियाट्रिक सेप्टिक शौक"।

हम बच्चों में एक अध्ययन करने जा रहे है। आपको इस अध्ययन में भाग लेने के लिए आमंत्रित किया जा रहा है। कृपया इस सूचना को ध्यानपूर्वक पड़े और अगर चाहें तो सलाह कर लें।

जैसा कि आप जानते हैं कि आपके बच्चे का रक्तचाप (ब्लडप्रेशर) कम है जो कि इन्फेकशन के कारण हो सकता है। मेडिकल भाषा में इस को "सेप्टिक शौक" कहते हैं। ये एक गम्भीर बिमारी है जिसका जल्द से जल्द इलाज होना चाहिए क्योंकि अगर ऐसे नही किया गया तो इसके बुरे परिणाम हो सकते हैं।

हाल ही में एक अध्ययन किया गया था जो कि लक्ष्य निर्धारित भी हैं। इससे इलाज में देरी होने की सम्भावना कम है।

इस अध्ययन को बड़ों में सफलता मिलती हैं पर बच्चों में यह अध्ययन अभी तक नही हुआ हैं। हम अपने अस्पताल में इस अध्ययन को बच्चों में शुरु करने जा रहे हैं। इस अध्ययन के परिणाम से आने वाले समय में इस तरह के बीमार बच्चों में लाभ सिद्ध

Parts of a Thesis …

1. Title page-
2. Acknowledgements
3. List of contents-
4. List of figures and tables-
5. List of abbreviations-
6. Summary/abstract (?)-
7. Introduction-
8. Aims-
9. Methods-
10. Results-
11. Discussion-
12. Conclusion-
13. Bibliography-
14. Appendices-

(British Standard Institution's "Recommendations for the presentation of theses and dissertations", 1990)

Plan

- First draw up a rough plan
- Headings, sub-headings, paragraphs etc of intro, methods, results & discussion
- Discuss with guide
- Fill in details of plan
- Include
  - What to cover where: avoid overlaps between intro & discussion; results & discussion
  - Extent of describing a method
  - Which result by table/ figure/ graph

Length & organization

- Summary: < 1000 words
- Total length, excluding biblio: <50,000 words
- Adopt a convention that gives a heirarchical structure to text
  - Eg. 1 Section title, 1.1 heading, 1.1.1 sub-heading
  - Eg. SECTION, **Heading,** *Sub-heading*
  - Paras within sub-headings need no numbering

Organization of a paper

- IMRAD
  - Introduction, Methods, Results and Discussion
- Plus
  - Title, abstract, authors, acknowledgements, declarations, references
  - Tables and figures; legends
- Length-
  - 2500- 5000 words/ no limit

IMRAD Structure

- Title
- Abstract

- Introduction
- Methods
- Results

- Discussion
- References

QUESTIONS?