Hypothesis Writing in Clinical Research

PoCoG Biostatistical Clinic Series

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Introduction

› Aims (Objectives)
› Research Questions
› Research Hypotheses
› An overarching statement about how the study will answer the research question.

› EXAMPLE: To investigate the effect of a mindfulness intervention on Quality of Life.
The research question arises out of a perceived knowledge deficit in a particular subject area.

Must understand what has already been studied in order to further the knowledge in a subject area.

Knowledge can be obtained from systematic reviews of the literature, interviews and focus groups with patients, and from subject matter experts.

Should be driven by hypotheses not data.

EXAMPLE: How does a mindfulness intervention compare with an attention control in improving QOL in patients with cancer?
Criteria for a Good Research Question

FINER

› F Feasible
  • Adequate number of subjects
  • Affordable in time and money
  • Manageable in scope

› I Interesting
  • Intrigues investigator, peers and community

› N Novel
  • Confirms, refutes or extends previous findings

› E Ethical
  • Amenable to approval by institutional review board

› R Relevant
  • To scientific knowledge
  • To clinical and health policy
  • To future research
Research Hypothesis

› Developed from the research question before the start of the study.

› A well-designed research hypothesis guides
  - Decisions on study design
  - Population
  - Data to be collected
  - Data analysis

› EXAMPLE: QOL as measured by the SF-36 Mental Component Score is improved in patients with cancer who receive the mindfulness intervention compared to those in the control group at 12 weeks.
Criteria for a good research hypothesis

PICOT

› P Population
  • What specific patient population are you interested in?

› I Intervention
  • What is your investigational intervention?

› C Comparison Group
  • What is the main alternative to compare with the intervention?

› O Outcome
  • What do you intend to accomplish, measure, improve or affect?

› T Time
  • What is the appropriate follow-up time to assess the outcome?
Research Hypothesis

› Intervention A will improve distress in patients with cancer

› Does this meet the PICOT criteria?
  - Population: Patients with cancer
  - Intervention: Intervention A
  - Comparison Group: ?
  - Outcome: Distress
  - Time: ?

New Hypothesis: Intervention A will improve distress in patients with cancer at 12 weeks compared to the control intervention.
But inclusion criteria states that patients with clinical levels of depression and anxiety will be recruited.

New Hypothesis: Intervention A will improve distress in cancer patients with clinical levels of depression and anxiety at 12 weeks compared to the control intervention.
But the methods section doesn’t have distress described as an outcome. The only outcome measurement listed is HADS which is collected at baseline and every 3 months for 12 months.

New Hypothesis: Intervention A will improve distress (as measured by HADS) in cancer patients with clinical levels of depression and anxiety at 3, 6, 9 and 12 months compared to the control intervention.

Best to choose one time point as primary, but provide rationale for why data is collected every 3 months elsewhere in the grant or protocol.

New Hypothesis: Intervention A will improve distress (as measured by HADS) in cancer patients with clinical levels of depression and anxiety at 3 months compared to the control intervention.
But HADS has two subscales: one for anxiety and one for depression.

New Hypothesis: Intervention A will improve distress (as measured by the HADS depression and anxiety subscales) in cancer patients with clinical levels of depression and anxiety at 3 months compared to the control intervention.
But this is actually 2 hypotheses:

Hypothesis A: Intervention A will improve anxiety (as measured by the HADS anxiety subscale) in cancer patients with clinical levels of anxiety at 3 months compared to the control intervention.

Hypothesis B: Intervention A will improve depression (as measured by the HADS depression subscale) in cancer patients with clinical levels of depression at 3 months compared to the control intervention.

The study will have to be repowered to accommodate 2 primary hypotheses and the Type 1 error rate should be reduced from 5% to 2.5% (requiring more participants).

The study population has also changed from clinical levels of anxiety AND depression to clinical levels of anxiety for Hypothesis A and clinical levels of depression for Hypothesis B thus reducing the analysis population for each hypothesis (thereby reducing power).

Have the PICOT criteria now been satisfied?
But will HADS Anxiety and HADS Depression subscales be analysed as continuous or discrete? This should be described in the Statistical Methods section, but is good practice to include in the hypothesis as well.

For continuous:
- Hypothesis A: Intervention A will improve anxiety (as measured by the mean change from baseline in the HADS anxiety subscale) in cancer patients with clinical levels of anxiety at 3 months compared to the control intervention.

For discrete:
- Hypothesis A: Intervention A will improve the proportion of cancer patients with clinical levels of anxiety at baseline (as measured by the HADS anxiety subscale) at 3 months compared to the control intervention.
TIPS

Tips for developing research questions, hypotheses and objectives

› Perform a literature review
› Keep up with current trends and advances on the topic
› Seek input from experts, colleagues and collaborators to refine the research question
› Use the FINER criteria to develop the research question
› Develop a research hypothesis from the research question
› Ensure the hypothesis includes the PICOT criteria
› Ensure the research questions are answerable, feasible and clinically relevant
Practical Considerations

› Limit the number of primary hypotheses.
› The study should be designed to answer the primary hypotheses.
› The study should be powered to the primary hypotheses.
› All measures included in the primary and secondary hypotheses should be described in the methods section.
› The statistical methods section should include the analysis techniques for all primary and secondary hypotheses.
REFERENCES

For additional reading:

