

# Taking an idea to a research protocol

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## Abstract

We present a nine-step process to assist with developing an idea into a research protocol. This process ensures that evidence-based medicine practice is followed to prevent redundant research questions. The first step is to identify broad research ideas with a potentially “weak” evidence base, rather than starting with a specific research question. The second step is to identify the knowledge gap within the intended field of research by examining the background literature. Thirdly, the focus will be on the “foreground knowledge” needed to frame a potential research question. The fourth step uses this potential research question to conduct a comprehensive literature research, and aims to determine whether or not the question has been asked before. The fifth step entails writing a study one-page summary which provides a succinct summary of what is intended. The sixth step involves writing the protocol. The rigid process of protocol writing will ensure that a number of important practical study issues are dealt with timeously. The seventh step is to discuss the protocol with experts. Their input will make the protocol more robust. The eighth step necessitates making a “social contract” that requires public commitment to the project. The final step is to write a grant application for the study. This serves to allow the researcher to identify the funding priorities of potential grant-funding agencies, thereby allowing the researcher to frame his or her research in such a manner that the financial support necessary for the success of the project will hopefully be ensured.

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## Introduction

A young researcher wanting to develop an idea into a research protocol is often overwhelmed by issues that arise in what is initially perceived to be a simple process. In this review, we present pragmatic considerations that will assist in making this process successful.

The format of this paper is shaped by the belief that evidence-based medicine principles should underpin all research endeavours. Therefore, it is important to avoid conducting unnecessary or redundant research which may place additional study participants at risk, while simultaneously denying the public the health benefit that should have already been identified. An example of this is the use of beta blockers for secondary prevention following myocardial infarction. Had cumulative meta-analyses been conducted earlier, this pharmacological intervention could

have been identified as an effective therapy as early as 1977. Instead, multiple studies continued to unnecessarily conduct research on this question for over a decade.<sup>1</sup> In summary, a researcher should not conduct research for the sake of research alone, but rather with the intention of contributing to the greater body of existing knowledge. We believe that robust investigator-initiated and investigator-led research is necessary to drive evidence-based medicine practice.

## Suggested steps from the idea to the protocol

In this review, we present a nine-step process (Table I) which focuses on the first-time researcher, e.g. a registrar embarking on a Master's degree, and individuals with aspirations of developing a research career.

**Table I:** The nine steps to a successful research protocol

| Step | First-time researcher                          | Researcher with long-term research aspirations  |   |
|------|--|---|---|
| 1    | Start with an idea                             | Do what interests you   | Take a proactive approach to idea generation. Aim to “link” research ideas to create long-term research agendas   |
| 2    | Identify the “knowledge gap”                   | Read narrative reviews  | Write a narrative review  |
|      |  | Read with a critical frame of mind  | Actively develop critical reading skills  |
| 3    | Frame a potential research question            | <ul style="list-style-type: none"> <li>• FINER potential question screening</li> <li>• Write a PICOT research question</li> </ul> | <ul style="list-style-type: none"> <li>• FINER potential question screening</li> <li>• Write a PICOT research question</li> </ul>   |
| 4    | Ensure your question has not been asked before | Look for meta-analyses  | Conduct a meta-analysis   |
| 5    | Write a one-page summary                       | -   | -   |
| 6    | Write a protocol                               | Consider using similar published studies as templates   | Consider using similar published studies as templates   |
| 7    | Discuss the protocol with experts              | They will help you to improve the protocol  | <ul style="list-style-type: none"> <li>• Build relationships with experts</li> <li>• Use their knowledge to develop your skills and understanding of relevant issues</li> </ul> |
| 8    | Make a social contract                         | Make a public declaration of your research intentions   | Make a public declaration of your research intentions   |
| 9    | Write a grant application                      | -   | This provides insight into the funding priorities of potential funding agencies   |

FINER: feasible, interesting, novel, ethical and relevant, PICOT: population, intervention, comparison, outcome and time

### Step 1: Start with a broad idea

Most ideas start as general and rather nonspecific concepts or involve a broad area of interest, as opposed to a specific research question. The broad idea usually provides the setting in which the research will be conducted, but not the specifics of the research. For example, a potential investigator may express the desire to conduct research in vascular anaesthesia, rather than starting with a specific question, such as: “Should all vascular surgical patients receive preoperative acute beta blockade to prevent major adverse cardiac events within 30 days of surgery?”

While research ideas may occur to anyone, a proactive approach to idea generation is recommended for individuals who are interested in research. Research ideas can be generated from a number of different areas. Observing your own practice may identify anomalies or personal quandaries with regard to appropriate patient management. Observing the practice of colleagues will further identify differences in opinion and management. Discussion with colleagues may identify unsubstantiated generalisations, opinions and reasonable concerns. A different perspective on relevant issues is often revealed by having discussions about your own practice with colleagues who are involved in different subspecialties, or having conversations with colleagues from different geographical backgrounds or institutions, when at congresses, for example. Attending poster sessions at congresses has the potential to alert the researcher to areas of considerable interest and clinical uncertainty. These proactive approaches to idea generation may identify broad areas with a “weak” evidence base

for the researcher with long-term research aspirations. Furthermore, it is essential to consider whether or not these areas have long-term research potential. Potential research ideas which systematically address weak areas in a field are desirable, and may contribute to the creation of a research agenda.

### Step 2: Identify the knowledge gap

In order to understand what potential questions may exist within a field or setting, it is important to understand the “background knowledge” within the field of intended research.<sup>2</sup>

This is carried out to identify potential “gaps” within the knowledge or evidence-based practice<sup>3</sup> relating to the field of the idea. Undertaking this step can be daunting, and it is best to undertake this in a structured and logical manner. Reading narrative reviews around the potential broad idea is essential for the first-time researcher. Great success can be found by writing a critical narrative review of the literature within the field by researchers with longer-term ambitions.

This allows you to personally identify areas:

- Which have not been examined critically.
- Where the evidence (or even literature) is non-existent.
- Where there is equipoise with regard to possible therapeutic interventions.

It is also possible that a “junior” reviewer may be more likely to give an accurate summary of the evidence, than an older, more senior and potentially biased reviewer of current controversies.

Although a narrative review provides the researcher with background knowledge to a research field and is invaluable in identifying “knowledge gaps”, it is important that the researcher is aware that these narrative reviews are prone to bias. It should be kept in mind that if something has not been formally and rigorously tested, then any comment on the efficacy of the intervention must be seen to be potentially biased. As an example, the assertion is made in perioperative literature that acute perioperative beta blockade that is started many weeks before surgery is associated with less perioperative hypotension and therefore strokes, than that when beta blockers are started on the day of surgery.<sup>4</sup> In reality, this has not been tested, is potentially biased, and could be a reasonable research question.

It is important for the researcher with long-term research aspirations to learn how to read the literature objectively. There are some excellent, simple books on this topic.<sup>2,5</sup> This skill makes it easier to identify the limitations of current studies and the “background knowledge” that would allow identification of further research ideas. In addition, conducting a critical review will ensure that resources are not wasted on redundant research, and that the question being asked is relevant to the field of research.

### **Step 3: Focus on the “foreground knowledge” to frame a potential research question**

Once a “knowledge gap” has been identified through the use of “background knowledge”, it is appropriate to phrase a potential research question. Posing a question that will potentially result in the generation of new clinical knowledge means that the clinician is now working within the realms of “foreground knowledge”<sup>2</sup> within a field. When considering potential “foreground questions”, the FINER (feasible, interesting, novel, ethical and relevant) screening tool should be used to determine whether or not it is worth pursuing this research question.<sup>6</sup>

If the FINER tool suggests that it is acceptable to do so, the question should be framed using the PICOT (population, intervention, comparison, outcome and time) format.<sup>6</sup> This question framework ensures the development of a detailed and specific research question. Spending time to understand what is meant by each of the PICOT components will ensure that the question is specific with well-defined boundaries which will leave little room for ambiguity about the intentions of the research.

### **Step 4: Determine if the proposed “foreground question” has been asked before**

The “foreground” PICOT question can now be used to identify whether or not any data exist on the proposed research question. Components of the PICOT question can now be used as medical subject heading (MeSH) terms for comprehensive literature search. The researcher

should specifically attempt to identify the following potential publications on the proposed question, in descending order of priority: meta-analyses, clinical trials and then reviews. Identification of published meta-analyses on the proposed topic is a key process for the first-time researcher. If a meta-analysis on the topic does not exist for the aspiring career researcher, this presents an opportunity to conduct a meta-analysis prior to embarking on the research project. In order to do this, the researcher needs to identify appropriate studies or trials.

The role of identifying or conducting meta-analyses on the proposed research is to confirm that there is either equipoise regarding the proposed research, or that the data do not currently exist. Either of these findings would suggest that the proposed study would be appropriate.

Finally, should a meta-analysis exist which is similar to the proposed research, it is still possible that attempting to answer the research question may be potentially valid. The validity of the meta-analysis should be evaluated using the “external validation of a measurement tool to assess systematic reviews” or assessment of multiple systematic reviews (AMSTAR) recommendations.<sup>7</sup> The AMSTAR tool assesses 11 factors that assess the validity of a meta-analysis. These include an “a priori” review design, duplication of the study selection and data extraction, comprehensive literature research, publication status, list of included and excluded studies, characteristics of the included studies, the scientific quality of the included studies and the risk of bias, the appropriateness of the methods used to combine the findings, whether or not the potential for publication bias was assessed, and a declaration of potential conflicts of interest.<sup>7</sup>

Data from meta-analyses may aid the researcher in understanding the potential research question. This would then provide an opportunity to refine the PICOT question, while simultaneously providing an evidence-base for the question to be tested.<sup>3</sup>

### **Step 5: Write a one-page summary of the proposed study**

Writing a one-page summary provides an opportunity to make a succinct statement of intent. It is an opportunity to present a clear précis of the proposed research.

It should specifically cover:

- The background to the study.
- The study objectives.
- The preparatory work that has been carried out.
- The proposed study design.
- The reasons for the importance of this research.

This one-page summary can be used to “advertise” the research project, either through the basic education of

colleagues about the research, to “whetting the appetite” of desirable potential collaborators.

**Step 6: Write the protocol**

By writing a protocol, the investigator moves through a number of important processes. First and foremost, the researcher takes ownership of the study. This is important as it creates a personal imperative to ensure the success of the project.

Furthermore, the rigidity of the protocol process means that a number of important issues have to be dealt with timeously. These include:

- The aims and objectives.
- The study design.
- Inclusion and exclusion criteria.
- Powering and sample size.
- Statistical analyses.

It is useful to revert to your literature review at this time in order to identify other studies which may be similar to your proposed study. Such studies provide valuable information on a number of these important protocol considerations. The basic structure of a research protocol is shown in Table II.

**Table II:** The basic structure of a good research protocol

|   |
|---|
| <b>Introduction</b>   |
| <b>Background and rationale</b>   |
| <b>Aims and objectives</b>  |
| <b>Method</b>   |
| <ul style="list-style-type: none"> <li>• Design</li> <li>• Study outcomes</li> <li>• Definitions of study outcomes</li> <li>• <i>Eligibility criteria:</i> Inclusion and exclusion criteria</li> <li>• Outcome assessment</li> <li>• Follow-up and data collection</li> </ul> |
| <b>Statistical methods</b>  |
| <ul style="list-style-type: none"> <li>• Sample size, statistical power and variable selection</li> <li>• Statistical analyses plan</li> </ul>  |
| <b>Methodological challenges</b>  |
| <ul style="list-style-type: none"> <li>• Selection bias</li> <li>• Loss to follow-up</li> </ul>   |
| <b>Ethics</b>   |
| <b>Feasibility</b>  |
| <ul style="list-style-type: none"> <li>• Recruitment</li> <li>• Study team</li> <li>• Participating centres</li> <li>• Study funding and progress</li> </ul>  |
| <b>Study organisation and ensuring data quality</b>   |
| <ul style="list-style-type: none"> <li>• Organisation and management</li> <li>• Investigator responsibilities</li> <li>• Central coordination</li> <li>• Ethical considerations</li> <li>• Ensuring data quality</li> </ul>   |
| <b>Study significance</b>   |

In South Africa, differentiation is often made between study “aims” and “objectives”. An aim is what you “hope to achieve in your research project” and objectives are the “actions you need to undertake in order to achieve your aims”.<sup>8</sup>

Remember that basic study designs are usually easily determined by the proposed research question (Table III).<sup>8</sup>

**Table III:** The research question and the study design<sup>8</sup>

| Research                       | Question            | Study design                |
|--------------------------------|---------------------|-----------------------------|
| Observational (descriptive)    | Prevalence          | Cross-sectional             |
|                                | Incidence           | Cohort                      |
| Observational (analytical)     | Prevalence (rare)   | Case-control                |
|                                | Prevalence (common) | Cross-sectional             |
|                                | Incidence           | Cohort                      |
| Interventional or experimental |                     | Randomised controlled trial |

**Step 7: Discuss the protocol**

It is important to discuss the protocol with experts in fields allied to your study. For example, this may include cardiology or haematology in a study on perioperative cardiovascular outcomes. It is useful to present your protocol and your argument as to why there is a need for the proposed study. This provides a unique opportunity to view your protocol through the eyes of others. They will identify areas where your explanation is poor, where you are being misinterpreted, and where you have made mistakes or errors in the interpretation or presentation of salient issues. Finally, it provides an opportunity to develop your understanding of the equipoise in the research question, a crucial part to the future success of your research project.

Discussion will also provide insight into how other “experts” have managed potentially similar projects.<sup>3</sup> This will help to determine the feasibility of the proposed research design and the methods employed.<sup>3</sup>

These personal interactions provide the opportunity for researchers to build relationships that are vital to the successful implementation and completion of research endeavours. These individuals provide access to relevant skills and knowledge. For example, it is particularly beneficial to develop a working relationship with a biostatistician.<sup>3</sup> Asking questions and trying to repeat the analyses oneself develops competence going forward. Simple biostatistics are not difficult. Currently, there are a number of relatively easy-to-use statistics packages. What is more important is knowledge of the appropriate required statistical analysis. It is here that close interaction with a biostatistician will provide invaluable insight.

In summary, consultation with experts will help to make your research project more robust. High-quality researchers improve research productivity,<sup>9</sup> and consultation with experts indirectly “recruits” quality researchers into the development of your project.

### Step 8: Make a social contract

At this point it is important to tell people what you intend to do. This social contract equates to a public declaration of your research intentions, and provides a catalyst for personal commitment to the project.

### Step 9: Write a grant application

Research success and productivity have been associated with grant funding.<sup>10-12</sup> Indeed, this association appears to correlate with both the number of successful grant applications and the financial value of these grants.<sup>13</sup> Therefore, it is now desirable for the researcher with long-term aspirations to write a grant application. This is an important step as it provides insight into the funding priorities of different grant funding agencies. A clear understanding of these funding priorities will allow the researcher to frame his or her research in such a manner that the funding priorities of grant funding bodies, such as universities, the Medical Research Council and the National Research Foundation, are addressed. As a result, long-term access to funding streams will hopefully be secured.

## Supervisors and mentors

While this paper has focused on the process of generating a protocol from an idea, the importance of a young researcher working with a mentor or supervisor cannot be overestimated. Generally, senior researchers have vast knowledge of their field of interest, and are able to rapidly provide insight into the relevance and feasibility of the research question. In addition, they are able to assist with study design aspects, statistical insight and accessing research infrastructure. A research supervisor is able to adequately fulfil this role

for the first-time researcher, but someone with long-term research aspirations should seek a mentor with whom he or she can develop a stronger relationship, with the goal of ultimately becoming colleagues.

## Conclusion

It is hoped that following these nine simple steps will provide aspiring researchers with the tools to initiate meaningful research within South Africa.

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