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The research question: a first, essential step in study design

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Dear Editor,

The process of building and refining a research question is the first and most important step in the study design, since a research question that is not well considered makes the subsequent work a waste of time.[1] The research question consists of a short sentence that summarizes the aim of the investigation. It could also be defined as the specific query the investigator seeks to answer, and it serves as the cornerstone of any research project.[2] A well-crafted question provides the foundation for study design, guides the selection of appropriate outcomes, and shapes the analytical approach. In its absence, even the most sophisticated methodologies or extensive datasets may lead to results that are unfocused or lack clinical relevance.

In order to build an answerable and well-structured research question, it is of utmost importance to know the topic of interest in detail, as this helps to identify knowledge gaps or clinical uncertainties.[1] To this end, Haynes wrote that, when formulating a research question, it is important to know "where the boundary between current knowledge and ignorance lies".[3] It is essential to collect all the available knowledge about the topic to be studied, which can be achieved in different ways, including clinical experience, discussions with experts, and systematic literature searches using databases such as PubMed or Embase, among others.[2,4] Accordingly, practice traditions with poor or no evidence to support them are worthy of scrutiny and may represent a good basis to build a research question upon (Figure 1). For this reason, a research question should be driven by the hypothesis rather than the data, meaning that both the hypothesis and research question must precede the start of the study. In fact, from a database created for a study, it is possible to perform multiple statistical comparisons of data to find a statistically significant association; however, such spuriously positive findings might occur for the play of chance and lack true clinical relevance when not guided by a pre-specified question.[2,4]

Although it may occur that while collecting knowledge on a specific subject, multiple questions arise, each question should be answered through a single study.[4] It is then recommended to keep the research question concise and avoid addressing many questions in one study. For this reason, the FINER and PICO frameworks are tools helping formulate and refine research questions (Table 1). The use of the FINER criteria could help develop a good research question, where key aspects are feasibility, interest, novelty, ethics, and relevance[2], as summarized in Table 1. While the FINER criteria list the essential concepts of the question, a helpful tool to develop a specific research question is the PICO format, where "P" stands for the population of interest, "I" for the intervention to be investigated, "C" for the control group, and "O" for the outcome of interest. Sometimes, a "T" could be added, referring to the time frame across which the time takes place (Table 2).[3] By using such tools, the investigator will be able to design an extremely specific research question. Indeed, stringent inclusion and exclusion criteria provide a greater effect on the interpretation and generalization of the study findings, thus limiting bias.

Once a research question is defined, this should be transformed into a testable hypothesis, *i.e.*, a prediction that responds to the research question. To this end, the research hypothesis should be formulated as a "null" hypothesis that allows for an inference about the population of interest based on a random sample from that population.[5] The null hypothesis states that there is no difference between the two interventions tested in the study. At the end of the study, if the results are not statistically significant (*i.e.*, no statistical difference between the two interventions), the null hypothesis cannot be rejected, and no conclusion can be drawn in favor of the alternative hypothesis. Conversely, when study findings are statistically significant, the null hypothesis can be refused and the alternative hypothesis accepted. This means that testing the hypothesis will confirm or refute that the study findings did not occur by chance alone, but because there was a true difference between the two interventions.[4] Importantly, a 2-sided hypothesis should always be considered, meaning that there is a difference between the experimental group and the control group, although the expected direction of the difference is not specified in advance.[4,6]

In conclusion, building an appropriate and sound research question is the pivotal step of a research project, although a number of issues may arise. However, if well refined, a good research question

will guide the investigators through a successful research project. Tools, such as the FINER and the PICO criteria, could help shape a well-structured, ethical, and practical research question.

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Table 1. FINER criteria according to Hulley *et al.*[2]

F	Feasibility	• Number of enrolled subjects • Availability of techniques and equipment, Adequate technical expertise • Available time and money
I	Interest	• Capability to create interest in the investigators and in the medical community
N	Novelty	• Capability of advancing knowledge by confirming, refusing or expanding previous findings
E	Ethics	• Respect for ethical principles • Approval by Institutional Review Board
R	Relevance	• For scientific community • For patients • For future research in the field

Table 2. PICOT criteria.[3]

P	Patients	• What patients are you interested in?
I	Intervention	• What is the intervention you want to investigate?
C	Control group	• What is the alternative to compare with the intervention?
O	Outcome of interest	• What is the outcome? What do you want to measure?
T	Time	• What is the follow-up time to assess the outcome?

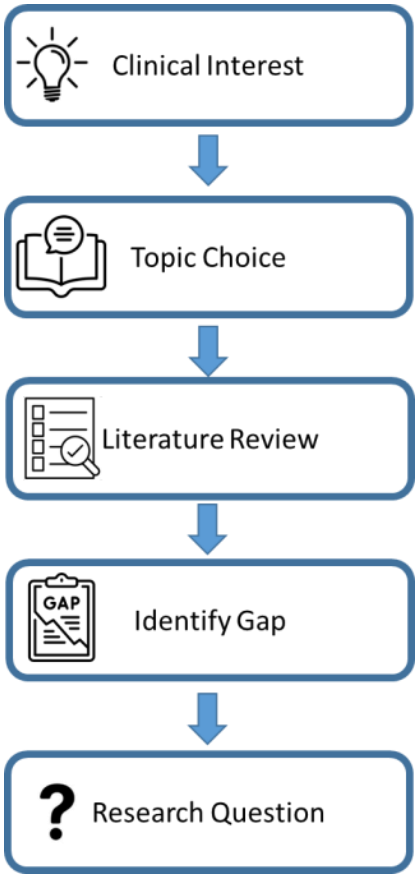

Figure 1. Steps to formulate a research question.