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Review Article
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Developing a Hypothesis and Statistical Planning

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WITH A SURPLUS OF questions and a desire to find meaningful answers, understanding the basics of performing clinical research is crucial. The first step is to develop a research question, which serves as the objective of a study. A concise question will give a clear aim to a study, narrow the vast amount of literature on the subject, and aid in developing a hypothesis.[1] When choosing a question, it is imperative to focus on a topic that is novel, interesting, and/or provides scientific value (see Table 1 and Fig 1).[2] Among topics already well researched, a good research question may add new cohorts, further expanding upon generalizability of the findings for the population with that condition.[3]

A thorough literature search is necessary to gain an understanding of what is already known, which areas need further investigation, and which areas have not been examined at all. This initial search can narrow down a research question that would add value to the scientific community. However, it is important to keep in mind that a literature search may not reveal all studies performed. Studies with negative results may not always be as well represented in the literature as positive studies (ie, they may be less likely to get published), and studies with positive results still may need further investigation. Furthermore, it is possible that a study with negative results may be due to issues related to lack of power or small number of subjects rather than the actual hypothesis being false.

After examining the current literature, clinicians may choose to expand or improve upon a question that already has been asked, or they may choose a question that is entirely novel. For example, interest in studying the use of dexmedetomidine in cardiac surgery would require a literature search that would lead to the study by Cheng et al, *The Effects of Dexmedetomidine on Outcomes of Cardiac Surgery in Elderly Patients*,[4] which found decreases in operative and in-hospital mortality as well as postoperative stroke and delirium after perioperative dexmedetomidine infusion. While reviewing this and other articles on this topic would elucidate the areas that already have been studied, they also may inspire further inquiry in an area that may need further investigation or that has not been well examined, such as the effects of intraoperative clonidine use in similar patient populations, or differences in anesthetic costs after dexmedetomidine use in cardiac surgery.

Although interest in a specific topic often leads to a search in the literature, at times, reviewing medical literature subsequently may lead to discovery of a topic of interest. Case reports may present novel treatments or management that can be invaluable in leading to further high-quality research questions in that area.[5] In the case report by Gutsche et al, *Treatment of Ventricular Assist-Device-Associated Gastrointestinal Bleeding with Hormonal Therapy*,[6] the authors described a case in which the use of ethinyl estradiol and norethindrone may have aided in the cessation of gastrointestinal bleeding in a patient with a ventricular assist device. The case report may lead to a research question: does hormone therapy with ethinyl estradiol and norethindrone assist in

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Table 1
Characteristics of a High-Quality Research Question

Concise with clear aim
Novel or improving on prior research
Adds value to the current literature
Clinically relevant/meaningful
Feasible costs, patient variables, ethics

cessation of gastrointestinal bleeding in patients with ventricular assist devices?

A literature search will aid in creating a research question that is desired by or would benefit the scientific community. However, a novel question may not lead necessarily to clinically meaningful results. Inquiring on the incidence of preoperative hiccups and postoperative outcome, although not studied before, may not yield a change in perioperative care by the patient's anesthesiologist or surgical team. What defines clinically meaningful remains subjective in nature, but must add value to the topic at hand, whether by increasing awareness on an important subject, by leading to a change in practice, or by inspiring further inquiry about a topic that may be fruitful after additional study.

Lastly, studies must be feasible to perform; not every relevant research question will lead to a study that is feasible. For instance, a study examining vapocoolants and lidocaine infiltration for pain control in radial artery cannulation performed by Rusch et al[7] involved careful consideration of patient population when designing the study. This prospective trial was performed on patients undergoing *elective* cardiac surgery or carotid endarterectomy, which allowed for proper patient enrollment and blinding. A similar study designed to examine this question in patients receiving emergent ruptured aneurysm repair would be difficult to perform. Feasibility of a study carries an element of subjectivity, but requires that a study question will be able to be examined properly in the population desired, considering costs, patient variables, and ethical factors.

Developing a Hypothesis

Transforming a research question into a hypothesis is the next step in designing a research study. In a study by Haanschoten et al titled *Use of Postoperative Peak Arterial Lactate Level to Predict Outcome After Cardiac Surgery,*[8] a research question may postulate, "do peak postoperative lactate levels aid in predicting mortality after cardiac surgery?" This question then can be transformed into the research hypothesis: the peak postoperative lactate level is a predictive factor of mortality for patients undergoing cardiac surgery.

A research hypothesis compares what is observed in the data to what would be expected if the null hypothesis (H_0) is true. The goal of hypothesis testing is to measure the consistency of the observed data with the null hypothesis.[9,10] The null hypothesis (Ho) assumes that there is no association between exposure (or treatment) and the outcome.[11] In the current example, the null hypothesis may be: there is no association between the postoperative lactate level and mortality in

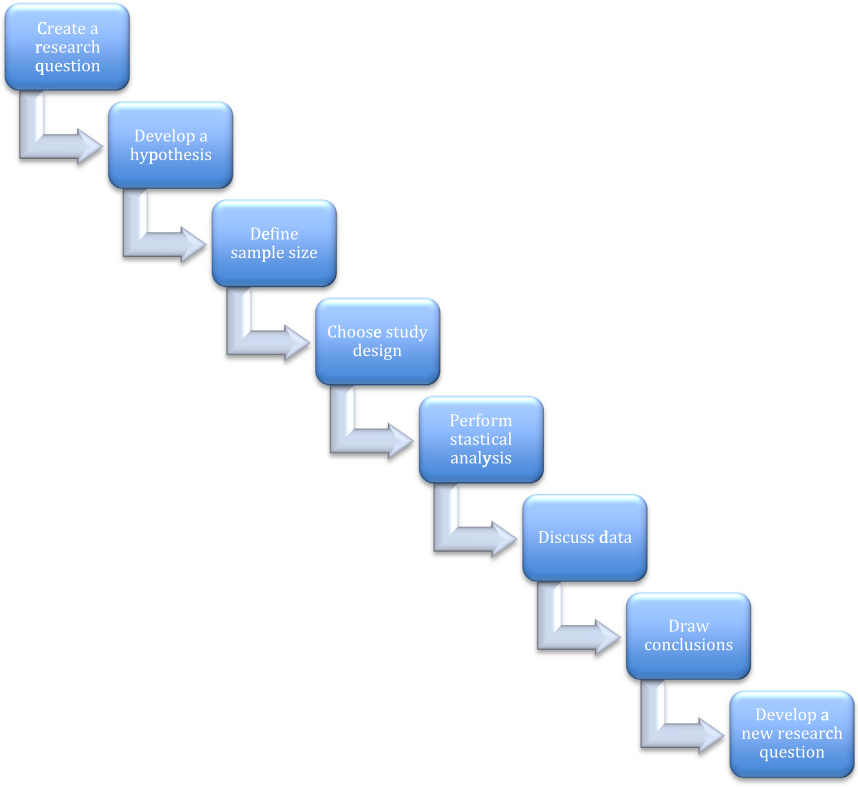

Fig 1. Steps for creating and designing a study.

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