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> Table of Contents > Section I - Basic Ingredients > 2 - Conceiving The Research Question

## 2

# Conceiving The Research Question

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The research question is the uncertainty about something in the population that the investigator wants to resolve by making measurements on her study subjects (Fig. 2.1). There is no shortage of good research questions, and even as we succeed in producing answers to some questions, we remain surrounded by others. Recent clinical trials, for example, have established that treatments that block the synthesis of estradiol (aromatase inhibitors) reduce the risk of breast cancer in women who have had early stage cancer (1). But now there are new questions: How long should treatment be continued, what is the best way to prevent the osteoporosis that is an adverse effect of these drugs, and does this treatment prevent breast cancer in patients with BRCA 1 and BRCA 2 mutations?

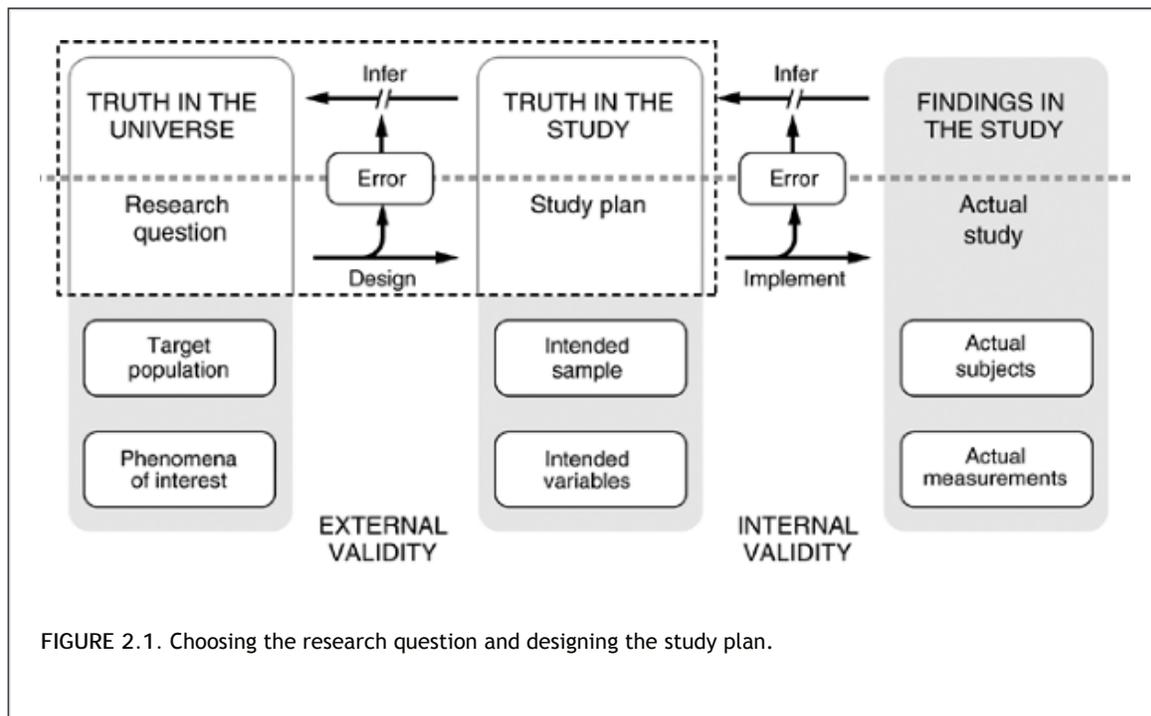


FIGURE 2.1. Choosing the research question and designing the study plan.

The challenge in searching for a research question is not a shortage of uncertainties; it is the difficulty of finding an important one that can be transformed into a feasible and valid study plan. This chapter presents strategies for accomplishing this in arenas that range from classical clinical research to the newly popular translational research.

## Origins of a Research Question

For an established investigator the best research questions usually emerge from the findings and problems she has observed in her own prior studies and in those of other workers in the field. A new investigator has not yet developed this base of experience. Although a fresh perspective can sometimes be useful by allowing a creative person to conceive new approaches to old problems, lack of experience is largely an impediment.

### *Mastering the Literature*

It is important to master the published literature in an area of study; scholarship is a necessary ingredient to good research. A new investigator should conduct a thorough search of published literature in the area of study. Carrying out a systematic review is a great first step in developing and establishing expertise in a research area, and the underlying literature review can serve as background for grant proposals and research reports. Recent advances may be presented at research meetings or just be known to active investigators in a particular field long before they are published. Thus, mastery of a subject entails participating in meetings and building relationships with experts in the field.

### *Being Alert to New Ideas and Techniques*

In addition to the medical literature as a source of ideas for research questions, all investigators find it helpful to attend conferences in which recent work is presented. As important as the presentations are the opportunities for informal conversations with other scientists during the breaks. A new investigator who overcomes her shyness and engages a speaker at the coffee break will often find the experience richly rewarding, and occasionally will find she has a new senior colleague. Even better, for a speaker known in advance to be especially relevant, it may be worthwhile to look up her recent publications and contact her in advance to arrange a meeting during the conference.

A skeptical attitude about prevailing beliefs can stimulate good research questions. For example, it has been widely believed that lacerations that extend through the dermis require sutures to assure rapid healing and a satisfactory cosmetic outcome. Alternative approaches that would not require local anesthetics and be faster, less expensive, and produce as good a cosmetic result were widely believed to be unachievable. However, Quinn et al. noted personal experience and case series evidence that wounds repair themselves regardless of whether wound edges are approximated. They carried out a randomized trial in which patients with hand lacerations less than 2 cm in length all received tap water irrigation and a 48-hour antibiotic dressing, but one group receive conventional sutures while the other did not. The group treated with sutures had a more painful and time-consuming treatment but subsequent blinded assessment revealed similar time to healing and cosmetic results (2).

The application of new technologies often generates new insights and questions about familiar clinical problems, which in turn can generate new paradigms (3).

P.19

Recent advances in imaging and in techniques for molecular and genetic analyses, for example, have spawned a large number of clinical research studies that have informed extraordinary advances in the use of these technologies in clinical medicine. Similarly, taking a new concept or finding from one field and applying it to a problem in a different field can lead to good research questions. Low bone density, for example, is widely recognized as a risk factor for fractures. Investigators applied this technology to other populations and found that women with low bone density have higher rates of cognitive decline (4), perhaps due to low levels of estrogen over a lifetime.

### *Keeping the Imagination Roaming*

Careful observation of patients has led to many descriptive studies and is a fruitful source of research questions. Teaching is also an excellent source of inspiration; ideas for studies often occur while preparing presentations or during discussions with inquisitive students. Because there is usually not enough time to develop these ideas on the spot, it is useful to keep them in a computer file or notebook for future reference.

There is a major role for creativity in the process of conceiving research questions, imagining new methods to

address old questions and having fun with ideas. There is also a need for tenacity, for returning to a troublesome problem repeatedly until a resolution is reached that feels comfortable. Some creative ideas come to mind during informal conversations with colleagues over lunch; others occur in brainstorming sessions. Many inspirations are solo affairs that strike while preparing a lecture, showering, perusing the Internet, or just sitting and thinking. Fear of criticism or seeming unusual can prematurely quash new ideas. The trick is to put an unresolved problem clearly in view and allow the mind to run freely toward it.

### *Choosing a Mentor*

Nothing substitutes for experience in guiding the many judgments involved in conceiving and fleshing in a research question. Therefore an essential strategy for a new investigator is to apprentice herself to an experienced mentor who has the time and interest to work with her regularly. A good mentor will be available for regular meetings and informal discussions, encourage creative ideas, provide wisdom that comes from experience, help ensure protected time for research, open doors to networking and funding opportunities, encourage the development of independent work, and put the new investigator's name first on grants and publications whenever appropriate. Sometimes it is desirable to have more than one mentor, representing different disciplines. Good relationships of this sort can also provide tangible resources that are needed—office space, access to clinical populations, datasets and specimen banks, specialized laboratories, financial resources, and a research team. Choosing a mentor can be a difficult process, and is perhaps the single most important decision a new investigator makes.

### **Characteristics of a Good Research Question**

The characteristics of a good research question, assessed in the context of the intended study design, are that it be feasible, interesting, novel, ethical, and relevant (which form the mnemonic FINER; Table 2.1).

**Table 2.1 FINER Criteria for a Good Research Question**

**Feasible**

- Adequate number of subjects
- Adequate technical expertise
- Affordable in time and money
- Manageable in scope

**Interesting**

- Getting the answer intrigues the investigator and her friends

**Novel**

- Confirms, refutes or extends previous findings
- Provides new findings

**Ethical**

- Amenable to a study that institutional review board will approve

**Relevant**

- To scientific knowledge
- To clinical and health policy
- To future research

### *Feasible*

It is best to know the practical limits and problems of studying a question early on, before wasting much time and

effort along unworkable lines.

- *Number of subjects.* Many studies do not achieve their intended purposes because they cannot enroll enough subjects. A preliminary calculation of the sample size requirements of the study early on can be quite helpful (Chapter 6), together with an estimate of the number of subjects likely to be available for the study, the number who would be excluded or refuse to participate, and the number who would be lost to follow-up. Even careful planning often produces estimates that are overly optimistic, and the investigator should assure that there are enough eligible willing subjects. It is sometimes necessary to carry out a pilot survey or chart review to be sure. If the number of subjects appears insufficient, the investigator can consider several strategies: expanding the inclusion criteria, eliminating unnecessary exclusion criteria, lengthening the time frame for enrolling subjects, acquiring additional sources of subjects, developing more precise measurement approaches, inviting colleagues to join in a multicenter study, and using a different study design.
- *Technical expertise.* The investigators must have the skills, equipment, and experience needed for designing the study, recruiting the subjects, measuring the variables, and managing and analyzing the data. Consultants can help to shore up technical aspects that are unfamiliar to the investigators, but for major areas of the study it is better to have an experienced colleague steadily involved as a coinvestigator; for example, it is wise to include a statistician as a member of the research team from the beginning of the planning process. It is best to use familiar

P.21

and established approaches, because the process of developing new methods and skills is time-consuming and uncertain. When a new approach is needed, such as a questionnaire, expertise in how to accomplish the innovation should be sought.

- *Cost in time and money.* It is important to estimate the costs of each component of the project, bearing in mind that the time and money needed will generally exceed the amounts projected at the outset. If the projected costs exceed the available funds, the only options are to consider a less expensive design or to develop additional sources of funding. Early recognition of a study that is too expensive or time-consuming can lead to modification or abandonment of the plan before expending a great deal of effort.
- *Scope.* Problems often arise when an investigator attempts to accomplish too much, making many measurements at repeated contacts with a large group of subjects in an effort to answer too many research questions. The solution is to narrow the scope of the study and focus only on the most important goals. Many scientists find it difficult to give up the opportunity to answer interesting side questions, but the reward may be a better answer to the main question at hand.

## *Interesting*

An investigator may have many motivations for pursuing a particular research question: because it will provide financial support, because it is a logical or important next step in building a career, or because getting at the truth of the matter is interesting. We like this last reason; it is one that grows as it is exercised and that provides the intensity of effort needed for overcoming the many hurdles and frustrations of the research process. However, it is wise to confirm that you are not the only one who finds a question interesting. Speak with mentors and outside experts before devoting substantial energy to develop a research plan or grant proposal that peers and funding agencies may consider dull.

## *Novel*

Good clinical research contributes new information. A study that merely reiterates what is already established is not worth the effort and cost. The novelty of a proposed study can be determined by thoroughly reviewing the literature, consulting with experts who are familiar with ongoing research, and searching lists of projects that have been funded using the NIH Computer Retrieval of Information on Scientific Projects (CRISP). Although novelty is an important criterion, a research question need not be totally original—it can be worthwhile to ask whether a previous observation can be replicated, whether the findings in one population also apply to others, or whether improved measurement techniques can clarify the relationship between known risk factors and a disease. A confirmatory study







