# 2 Conceiving the Research Question

Steven R. Cummings, Warren S. Browner, and Stephen B. Hulley

The research question is the uncertainty about something in the population that the investigator wants to resolve by making measurements on her study subjects. There is no shortage of questions. Even as we succeed in producing good answers to some questions, we remain surrounded by others. Recent clinical trials, for example, have established that the estrogen-like drug tamoxifen reduces the risk of breast cancer during 4 years of use by women at high risk of breast cancer (1). But now there are new questions: Does tamoxifen reduce the risk of death due to breast cancer? How long should treatment be continued? Might other estrogen-like drugs have the same beneficial effects without tamoxifen's propensity for thromboembolism?

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.

## ■ 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 such as a meta-analysis of a question is a great first step in developing and establishing expertise, and the literature review can serve as a source of 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.

No amount of reading can substitute for firsthand experience in guiding the many judgments of clinical research. Therefore an essential strategy for a young

investigator is to apprentice herself to an experienced **mentor** who has the time and interest to work with her regularly. A good relationship of this sort also provides the tangible resources a young investigator needs—office space, computer facilities, support for supplies and laboratory tests, and so on. The choice of one or two senior scientists who will be her mentor is the single most important decision a new investigator makes.

## 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 very helpful to **attend conferences** in which recent work is presented. The discussion of the work in the meeting can be supplemented by 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.

A **skeptical attitude** about prevailing beliefs can stimulate good research questions. For example, in the past, surgery was recommended for patients with asymptomatic gallstones because studies indicated that up to 50% of such patients eventually developed symptoms or complications. However, one research group critically reviewed these studies and observed that some had included patients with symptomatic gallstones and others had counted symptoms that were probably not due to gallstones. Using better criteria for gallstone-related symptoms in a well-defined cohort of patients with asymptomatic gallstones, the investigators found that only 15% of the patients suffered any biliary pain during 15 years of follow-up (2).

The application of **new technologies** often generates new insights and questions about familiar clinical problems (3). Recent advances in imaging and in techniques for molecular and genetic analyses, for example, have spawned many new clinical research studies. 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. Higher levels of bone density, for example, have come to be seen as a marker that reflects a woman's lifelong exposure to estrogen. Investigators applied this technology to problems besides bone disease to demonstrate that women with low bone density have a lower risk of breast cancer (4) and higher rates of cognitive decline (5), 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 a notebook for future reference.

There is a major role for **creativity** in the process of conceiving research questions, imagining new answers to 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. The trick is to put an unresolved problem clearly in view and turn on the mental switch that lets the mind run freely toward it.

## ■ CHARACTERISTICS OF A GOOD RESEARCH QUESTION

The characteristics of a good research question are that it be feasible, interesting, novel, ethical, and relevant (which forms the mnemonic *FINER*; Table 2.1).

### 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. The first step is to make a preliminary estimate of the sample size requirements of the study (Chapter 6). The next step is to estimate 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 be very certain that there are enough willing subjects. It is sometimes necessary to carry out a pilot survey to be sure. If the number of subjects appears insufficient, the investigator can consider a number of strategies. These include 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 (Chapter 4), and using a different study design.

***Technical Expertise.*** The investigators must have the skills, equipment, and experience needed for recruiting the subjects, measuring the variables, and managing and analyzing the data. The easiest strategy is to use familiar and established approaches, because the process of developing new methods and skills is time-consuming and uncertain. When it is necessary to develop an approach such as a new questionnaire for the study, expertise in how to accomplish the innovation

■ **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** |
| To the investigator |
| **Novel** |
| Confirms or refutes previous findings |
| Extends previous findings |
| Provides new findings |
| **Ethical** |
| **Relevant** |
| To scientific knowledge |
| To clinical and health policy |
| To future research directions |

should be available. 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 as a coinvestigator. For example, it is often wise to include a statistician as a member of the research team from the beginning of the planning process.

***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 costs are prohibitive, the only options are to consider a less expensive design or to develop additional sources of funding. If the study will be too expensive or time-consuming, it is best to know this early, when the question can be modified or abandoned 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 will 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 seems 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 the interest of a question with mentors and outside experts before devoting substantial energy to developing a research plan or grant proposal that peers and funding agencies may find 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 by agencies. (See, for example, the NIH Computer Retrieval of Information on Scientific Projects [CRISP] website.) A question need not be totally original. It may 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 is particularly useful if it avoids the weaknesses of previous studies.

## Ethical

A good research question must be ethical. If the study poses unacceptable physical risks or invasion of privacy (Chapter 14), the investigator must seek other ways to answer the question. If there is uncertainty about whether the study is ethical, it is important to discuss it at an early stage with the institutional review board.

### Relevant

Among the characteristics of a good research question, none is more important than its relevance. A good way to decide about relevance is to imagine the various outcomes that are likely to occur and consider how each possibility might advance scientific knowledge, influence clinical management and health policy, or guide further research.

## ■ DEVELOPING THE RESEARCH QUESTION AND STUDY PLAN

It helps a great deal to write down the research question and a brief (one- or two-page) outline of the study plan at an early stage. This requires some self-discipline, but it forces the investigator to clarify her own ideas about the plan and to discover specific problems that need attention. The outline also provides a basis for colleagues to react to with specific suggestions.

### Problems and Solutions

The potential problems in choosing the research question and developing the study plan are recapped, with solutions, in Table 2.2. Two general kinds of solutions deserve special emphasis. The first is the importance of getting good advice.

**■ TABLE 2.2**
The Research Question and Study Plan: Problems and Solutions

| Potential Problem | Solutions |
|---|---|
| A. The research question is not FINER | |
| 1. Not feasible | |
| Too broad | Specify a smaller set of variables<br>Narrow the question |
| Not enough subjects available | Expand the inclusion criteria<br>Eliminate or modify exclusion criteria<br>Add other sources of subjects<br>Lengthen the time frame for entry into study<br>Use strategies to decrease sample size (Chapter 6) |
| Methods beyond the skills of the investigator | Collaborate with colleagues who have the skills<br>Consult experts and review the literature for alternative methods<br>Learn the skills |
| Too expensive | Consider less costly study designs<br>Fewer subjects and measurements<br>Less extensive measurements<br>Fewer follow-up visits |
| 2. Not interesting, novel, or relevant | Consult with mentor<br>Modify the research question |
| 3. Uncertain ethical suitability | Consult with institutional review board<br>Modify the research question |
| B. The study plan is vague | Write the research question at an early stage<br>Get specific in the one- to two-page study plan<br>How the subjects will be sampled<br>How the variables will be measured |

We recommend a research team that includes representatives of each of the major aspects of the study and that includes at least one senior scientist. In addition, it is a good idea to consult with specialists who can guide the discovery of previous research on the topic and the choice and design of measurement techniques. Sometimes a local expert will do, but it is often useful to contact individuals in other institutions who have published pertinent work on the subject. A new investigator may be intimidated by the prospect of writing or calling someone she knows only as an author in the *Journal of the American Medical Association*, but most scientists respond favorably to such requests for advice.

The second thing to emphasize is the way the study plan should gradually emerge from an iterative process of designing, reviewing, pretesting, and revising (Chapter 17). Once the one- to two-page study plan is written, advice from colleagues will usually result in important changes. As the protocol gradually takes shape, a small pretest of the number and willingness of the potential subjects may lead to changes in the recruitment plan. The preferred imaging test may turn out to be prohibitively costly and a less expensive alternative may be sought. And so on.

### Primary and Secondary Questions

Many studies have more than one research question. Experiments often address the effect of the intervention on several outcomes; for example, the Women's Health Initiative was designed to determine whether reducing dietary fat intake would reduce the risks of coronary heart disease, of breast cancer, and of fractures (6). The advantage of designing a study with several research questions is the efficiency that can result, with several answers emerging from a single study. The disadvantages are the increased complexity of designing and implementing the study and of drawing statistical inferences from a study with multiple hypotheses (Chapter 5). A sensible strategy is to establish a single primary research question around which to focus the development of the study plan and sample size estimate. This can be supplemented with secondary research questions that may also produce valuable conclusions.

## ■ SUMMARY

1. All studies should start with a **research question** that addresses what the investigator would like to know. The goal is to find an important one that can be developed into a feasible and valid study plan.
2. One key ingredient for developing a research question is **scholarship** that is acquired by a thorough and continuing review of the work of others, both published and unpublished. Another key ingredient is **experience,** and the single most important decision a new investigator makes is her choice of one or two senior scientists who will be her **mentor.**
3. Good research questions arise from medical articles and conferences, from critical thinking about clinical practices and problems, from applying new concepts or methods to old issues, and from ideas that emerge from teaching.
4. Before committing much time and effort to writing a proposal or carrying out a study, the investigator should consider whether the research question and study plan are "FINER": **feasible, interesting, novel, ethical,** and **relevant.**
5. Early on, the research question should be developed into a brief **written study plan** that specifically describes how many subjects will be needed, and how the subjects will be selected and the measurements made.

6. Developing the research question and study plan is an **iterative process** that includes consultations with advisors and friends, a growing familiarity with the literature, and pilot studies of the recruitment and measurement approaches. The qualities needed in the investigator are **judgment, tenacity,** and **creativity.**
7. Most studies have more than one question, but it is useful to focus on a **single primary question** in designing and implementing the study

## EXERCISES

**1.** Consider the following research questions. First, write each question in a single sentence that specifies a predictor, outcome, and population. Then discuss whether it meets the FINER criteria (feasible, interesting, novel, ethical, relevant). Rewrite the question in a form that overcomes any problems in meeting their criteria.

**a.** What is the relationship between depression and health?
**b.** Does eating red meat cause cancer?
**c.** Does lowering serum cholesterol prevent heart disease?
**d.** Can a relaxation exercise decrease the anxiety associated with the mammography?
**e.** Do contraceptive vaginal sponges prevent HIV infection?

## References


1. Fisher B, Costantino JP, Wickerham DL, et al. Tamoxifen for prevention of breast cancer: report of the National Surgical Adjuvant Breast and Bowel Project P-1 Study. *J Natl Cancer Inst* 1998;90:1371–88.
2. Gracie WA, Ransohoff DF. The natural history of silent gallstones: the innocent gallstone is not a myth. *N Engl J Med* 1982;307:798–800.
3. Kuhn TS. *The structure of scientific revolutions*. Chicago: University of Chicago Press, 1962.
4. Cauley JA, Lucas FL, Kuller LH, et al. Bone mineral density and risk of breast cancer in older women: the study of osteoporotic fractures. Study of Osteoporotic Fractures Research Group. *JAMA* 1996;276:1404–8.
5. Yaffe K, Browner W, Cauley J, Launer L, Harris T. Association between bone mineral density and cognitive decline in older women. *J Am Geriatr Soc* 1999;47:1176–82.
6. Design of the Women's Health Initiative clinical trial and observational study. The Women's Health Initiative Study Group. *Control Clin Trials* 1998;19:61–109.