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Clinical Research and Critical Care Transport: How to Get Started

Editors' note: This is the first in a multipart series designed to improve the knowledge base of our readers, particularly novices, in the area of clinical research. A better understanding of these principles should help in reading and understanding the application of published studies. It should also help those involved in beginning their own research projects.

Though we often do not consciously acknowledge it, most of our clinical decisions have their basis in previous published research studies. Melnyk and Fineout-Overholt[1] identify seven levels in a hierarchy of evidence to support clinical practice. All but one level relies on evidence generated from original research. Thus, research provides an important foundation for the provision of care during critical care transport. Clinical studies are potentially powerful tools for shaping the way in which care is delivered. Even a single article can radically change clinical practices or understanding of a disease process. It can influence clinical care on the other side of the country, or even the world.

Unfortunately, simply because a study is published within the medical literature does not ensure the quality of the research. Errors in design, data analysis, or author interpretation can slip through even with the best of editorial review. In other cases, a study may be of high quality but not applicable to your clinical care environment. The reader who has a solid understanding of the research process has a distinct advantage in best understanding a given study and applying the findings appropriately to their practice.

The trend toward evidence-based practice has made the ability to read and understand research an even more important skill, because all members of the medical team are expected to apply research findings to their practice. This includes those involved in critical care transport.

The articles in this series represent a revision of a series initially begun in 1995. The original articles are over 10 years old and will be updated with new knowledge and examples. When possible the original authors will be involved in the publication. In some cases, however, authorship will be reassigned.

The emphasis of the original publications was on the basics of conducting clinical research. The republication will continue to discuss the process of conducting research but will also add information relevant to the interpretation of research and the application of findings to practice. As with the originals, these articles will be directed at the novice. The series will cover the entire research process. It will start with formulating a research question, and continue through selecting a research design, fleshing out a protocol, understanding the basics of statistics, and, ultimately, presenting or publishing the results.

It is hoped that this series of articles will bring a better appreciation for the difficulty of doing research properly, while helping novices to avoid some of the known pitfalls. We also hope that novices will become more comfortable reading the research literature and making appropriate application to their practice.

There is certainly more than one way to approach a research project. This is obvious when reading multiple articles or textbooks on the subject. Different textbooks often have varying recommendations and sometimes even use different systems for categorizing the basic research designs. The important point is not to focus on a single classification system or approach but to understand the basic underlying principles and to learn to use the tools that are most relevant to your setting, background, and experience. Regardless of the system used, a systematic approach to research is important, and some fundamental "rules" have stood the test of time. This series of articles presents a relatively common accepted framework for approaching research and emphasizes a practical approach.

How Research Begins

A great irony of research is that at the beginning of one's career, one has the greatest amount of extra time because of fewer administrative responsibilities. However, novices also tend to have fewer good research ideas, because most clinical research ideas come from direct clinical experiences. As one becomes more experienced, often numerous research ideas appear, but there usually is not enough time to pursue even the most important ones. Properly performed research is much more work than most people anticipate and takes much longer than usually anticipated.

All research begins with a research question. The question reflects a desire to know something, a desire to know the truth, for example, to know whether Drug A truly works better than Drug B in patients with condition Y, or whether it works as well to measure a parameter (eg, blood pressure) using technique C versus technique D. No research project should begin without a clear understanding of the research question to be answered. Every published research study should make their purpose—the research question they attempted to answer—very apparent. In publications reporting the results of research studies, that purpose is usually stated in the last paragraph of the introduction section of the article. It is worth reading those sentences very carefully, because the rest of the manuscript should be considered in the context of the question being addressed.

Sources of Research Questions

Where do research questions come from? Everywhere! When we bring an evidence-based approach to our profession, we realize that clinical questions are all around us. This includes each of the following:

1.Our own clinical practice. This is usually the best source. Every day we encounter gaps in our medical knowledge. For example:

a. Clinical observations or experiences that do not fit the textbook.
b. Frustrations felt when confronted with a patient condition for which available treatment is unsatisfying.
c. Treatment protocols that "everyone uses" but no one can provide adequate evidence or efficacy or rationale for their use.

2. Discussion with professional colleagues. Often discussions of an individual patient or general clinical practices identify areas of disagreement that would be appropriate for clinical investigation.

3. Inspiration from other investigators at professional meetings. Research presentations commonly end with a discussion of future directions for research or questions not yet answered. Even when the investigator claims to already be working on these questions, the reality is that rarely do they have enough time to pursue all of these research ideas. Feel free to seek out these individuals and further discuss areas of mutual interest. Most researchers enjoy discussing their studies and related ideas worthy of further investigation. They are often willing to collaborate on projects.

4. Gaps in the medical literature. While performing a literature search or review on a given subject, it generally becomes apparent that aspects of the topic are well known and in other areas knowledge is lacking or absent. Indeed, studies have shown that most of our clinical practices are supported by anecdote or experience, not by empirical evidence. This means that most of our clinical practices are in need of investigation.

After some practice, appropriate research questions can be identified from almost every one of our patient encounters. What is required is an inquisitive mind, a willingness to question dogma, some knowledge of the medical literature, and an adequate base of experience from which to make observations.

Defining the Research Question

Research questions can take many forms. Generating rules that will cover every potential research question or area of investigation is not possible. However, most clinical research questions will fit one of the following categories:

1. An evaluation of the accuracy or usefulness of a diagnostic test
2. An evaluation of the effectiveness of a therapy or device
3. An attempt to establish the cause of a clinical condition
4. A description of the natural course, prognosis, or outcome of a medical condition
5. An analysis of clinical decision-making or cost-effectiveness
6. A feasibility description of new practices or emerging trends or a new observation that is not previously described

Once you have initially identified an area of research interest or a preliminary research question, the experience of a stream of ideas is very common. Instead of just one research question, several related questions may come to mind. Should you look at the research question this way or that way, in this patient population or in that patient population? Is it more important to look at prior history and potential cause or natural course and outcome? For an evaluation of Drug A, should it be at high dose or standard dose? Alternatively, should it be in combination with another medication, or alone? Several related or "tagalong" type research questions may occur to you. This process is important in helping to sort through options, better understanding the basis of interest in the topic, and further defining the exact nature of the research question.

At this stage you may experience a great temptation to broaden the research question, and this should be resisted. Sorting through competing research ideas is important and helps to focus the research question on a specific area. Too often researchers start out with an ill-defined project, which lacks a clear research question and therefore has no testable hypotheses. If this is not rectified in the early stages, the entire study will tend to wander without a clear focus. It will waste precious investigator time and resources.

Another potential obstacle, at this point, is the inability to proceed from a general area of interest/concern and convert it into a specific research question. For example, one has a general interest in studying emergency airway management. Before further research efforts can proceed, the study must have a single, primary focus. One way to achieve this is to break the topic area into constituent parts. Separately write down each aspect of the topic and transform each of those into individual questions. Then rank the questions in order of importance or greatest interest. Early in their career, researchers should concentrate on studies with a single, primary question. One or two secondary questions may occasionally be identified, but maintaining the quality of the study is easiest if the investigator has a single focus for the investigation. Secondary questions, if chosen, are meant to be complementary and should not be allowed to detract from the primary research question itself.

Table 1. Using a PICO Format to Generate a Properly Formatted Research Question

Patients (or subjects)	Intervention (or independent *variable)*	Comparison (to what)	Outcome (dependent variable)

Now, combine each of these four elements together into a research question:

Writing the Research Question

After the initial brainstorming about your research question, it is time to become more structured. At this point, prepare to write down the exact proposed research question in a single, understandable sentence. If you cannot do this, you do not yet have a clear understanding of the purpose of the proposed study. The research question is the objective of the study, the gap in medical knowledge that one hopes to resolve. Writing a properly formatted research question can be much harder than anticipated. It is not simply any sentence with a question mark on the end. This is a formidable stumbling block for many novice researchers.

One approach to help with this process is the "PICO" approach. It breaks the research question down into four common elements. By first defining these elements, the investigator can better focus on the intent and purpose of the study. The four elements are then combined into a single sentence. Table 1 lists these elements and provides a template for generating research questions.

PICO stands for "patients," "intervention," "comparison," and "outcome." *Patients* means the intended study subjects, for example, "adults with acute chest pain" or "pediatric patients with blunt trauma" Epidemiologists refer to these as "subjects" rather than patients, because often they are looking at large population-based studies. *Intervention* generally means the aspect of those patients that is the main object of the study. It should be interpreted broadly as the independent variable, that is, simply the parameter of interest between the two study groups. It could be an active intervention (eg, giving a blood transfusion to one group, but not to the other) or it could be a passive characteristic (eg, the group that has pre-hospital hypotension vs. those that do not). Epidemiologists commonly refer to this as the "exposure." It could be exposure to cigarette smoke or to cocaine use or even to a gunshot wound. Either way, when two groups are being compared in a study, it is that characteristic, or parameter that varies between the two groups. *Comparison* refers to the other group being compared with the main study group. In the examples above, it is the group that does not get the blood transfusion or does not have prehospital hypotension. *Outcome* is fairly straightforward. It is the resultant measure (ie, the outcome) that is being used to assess the effect of the intervention. It is often referred to as the "dependent variable." It could be death rates, admission rates, hospital length-of-stay, changes in mean blood pressure, etc. With an understanding of the four PICO elements, they can be combined into a research question. For example, "In blunt trauma patients with hypotension, does pre-hospital blood transfusion, versus standard intravenous fluid, result in lower mortality rates?"

The question should be relatively simple, a single sentence, and written in the present tense.[2] Although the PICO format works for most research questions, it is not universally applicable. Sometimes investigators desire a simple descriptive summary of observations. For example, summarizing the county emergency medical services (EMS) transport experience for the year. How many were pediatric versus adult, trauma versus medical, etc.? Such observations can have investigative value. However, even such studies should have some underlying research question. Otherwise, what is the point? The investigator should have a purpose for taking the time and energy to collect and analyze the observations. For a research study, that purpose must be stated in a research question.

Research questions may be categorized many ways, but the system is not as important as understanding the general principles. In one classification system, Burns and Grove[2] identify four types of research questions: those that are descriptive, those that identify differences, those that examine relationships, and those that attempt to predict outcomes. See Table 2 for examples of each of these types of research questions.

Refining the Research Question

Once you have defined your research question, the next step is to "refine" it and determine whether it is a practical project to undertake. An investigator could have an absolutely brilliant and properly formatted research question, but one that is not appropriate for an actual research project. Several aspects must be considered at this stage. The characteristics of a good research question, appropriate for a research project, have been well described by Drs Stephen Hulley and Steven Cummings[3] in their book, Designing Clinical Research, in which they use the acronym of a FINER research question (Table 3):

1. Feasible. Can the project be completed? Does your clinical practice setting have an adequate number of potential research subjects? Are the appropriate resources available to perform the project? This could include personnel, equipment, or money. Are the end points measurable and reliable? For example, if you need central venous pressure measurements, is that a routine practice in your setting? Is the study manageable in scope, financial costs, and in terms of your own time? Will you need patient consent to perform the study and is your study population capable of giving informed consent?

2. Interesting. Is this a topic that truly interests you and for which you have a "passion to know"? Research projects tend

Table 2. Examples of Types of Research Questions

What is the average ground time for neonatal transport? (Description)
Is there a difference in satisfaction with transport team performance by parents who accompany their child on the transport versus those that travel separately? (Difference)
What is the relationship between ground time and the number and complexity of procedures performed before transport? (Relational)
Does the lowest systolic blood pressure during transport or the length of transport predict the incidence of decubiti 3 days posttransport for those transported on a wooden backboard? (Prediction)

Table 3. The FINER Elements of a Research Question

F Feasible
I Interesting
N Novel
E Ethical
R Relevant

to be full of enthusiasm at the beginning and excitement at the end. However, in between there is inevitable drudgery. If the investigator does not have a passion for the project, it can easily die an early death during the boring data collection phase. Do not embark on a project that is not interesting.

3. Novel. Is this a new idea or would it simply be reinventing the wheel? Does it add to or refute previous findings or provide new observations? Does it help confirm previous studies that remain controversial or expand the findings to a new population of patients? If the research question has already been addressed, well answered, and the answer makes sense, then it is done. Valuable resources should not be spent on the question again. However, even if studied before, if the results of previous studies do not make sense or are contradictory, it may be worth pursuing. Also, the medical community generally likes to see confirmatory studies, performed in a different setting, before accepting a new therapy or device. However, in general, your proposed study should be relatively novel. This is determined by researching the topic, including performing a literature search.

4. Ethical. Would performing this project represent ethical clinical and investigative practices? A number of regulations, codes, and policies are relevant here. Some of them are federal; others vary by state and institution. All investigators should become familiar with relevant research codes and ethics. However, even if individual investigators do not understand these issues, each institution has an Institutional Review Board (IRB) that reviews all proposed study protocols for ethical considerations to protect the rights of study subjects. All study projects must be first approved by the IRB before beginning the study.

5. Relevant. Would the results of this project be relevant in terms of impacting current medical care or the direction of future research? Imagine your study is completed and the results are the best you could have hoped for. You describe them to your professional colleagues. If, regardless of the results of your study, the response of most of your peers would be "So what?", it is probably not a project worthy of your time and efforts. It may not be relevant. An applicable saying is "a difference, to be a real difference, has to make a difference." Would your study make a difference?

Finalizing the Research Question

If you have not already done so, after defining your proposed research question, applying the FINER criteria, and deciding that you are headed in the right direction, it is time to discuss it with experienced and respected colleagues. Are they able to understand your question? Can they correctly identify the main variables that you will measure? Is a specific research design suggested by your question? If the answer to any of these questions is "no," work with your colleagues to clarify and strengthen your questions.

Having a proper research question, as discussed, is sufficient to move forward with developing a research project. However, defining the research-related hypotheses is also useful at this stage. A hypothesis is an intellectual exercise that predicts the outcome of the research, that is, the predicted answer to the research question. A research hypothesis may not be appropriate for studies that are entirely descriptive. However, it is always helpful in studies that are examining differences or relationships, or that attempt to predict outcomes. It helps organize the investigator's understanding of the project and forms the basis for subsequent classical statistical testing. Hypotheses can be tested, using statistical tests, whereas questions generally cannot be directly tested.

A research hypothesis may predict the presence or absence of a relationship. When a presence is predicted, it also may predict the direction of a relationship, or not. Hypotheses also may provide additional information such as the sample in which the relationship will be found and specific details regarding the circumstances under which the relationship will be demonstrated. An example of a non-directional hypothesis would be: There will be a relationship between family satisfaction with a transport and time spent with the family before the transport. An example of a similar hypothesis, but one that is directional, would be: Family satisfaction with transport will increase as time spent with the family before the transport increases.

These hypotheses are often referred to as the "alternative" hypothesis when they predict a relationship or that an inter-

vention will have an effect. In contrast, a "null" hypothesis proposes no relationship. For example: Family satisfaction with transport will not increase with an increase in time spent with the family before transport.

The null hypothesis is an important statistical concept and is used as the basis for the statistical analysis to be used at the conclusion of the study. This will be discussed in greater detail in a future part of this series.

Taking the Next Step

Now you have a research question that is well defined, refined, and highly specific. However, it may not be completely finalized. You have started the planning process that is the most important part of any research study. In research endeavors, more time should be spent on planning rather than rushing into actually performing the study. The next step is to research the topic further, including a systematic review of the literature relevant to your focused research question. The process of reviewing the literature will be discussed in an upcoming part in this series.

Congratulations on taking the first and most important step to better understanding the medical literature, or to becoming a researcher yourself. Although there are many roadblocks in the research process, there is tremendous personal satisfaction in performing credible research. This series will try to help with each of the steps and point out some of the pitfalls. In addition, if you want to read about this subject in greater depth, a number of excellent textbooks are available. Listed below are some of the best for the beginning researcher.

References

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1067-991X/$32.00

doi:10.1067/j.amj.2006.02.004