CHAPTER 1

Aspects of research specific to acute care

Jarrod M. Mosier[1] and Peter Rosen[2]

[1] *Department of Emergency Medicine, University of Arizona, USA*

[2] *Emergency Medicine, Harvard University Medical School, USA*

Responsibility of the academic physician

The power to save lives, and the knowledge which forms that power, is a sacred art entrusted to every physician. One can debate about whether knowledge is discovered or invented (we think it may be both), but regardless of the means of acquisition, new knowledge falls into the realm of research and, thus, of the book that you are holding. It is the responsibility of the academic physician to uncover and disseminate this knowledge. Enthusiastic young physicians commonly enter academic medicine after inspiration in seeing their accomplished mentors' body of work, only to find it frustrating that it is not easy and that it may not be possible to hit the ground running smoothly.

Indeed, many young physicians are both puzzled and dissuaded by the responsibilities faced in academic medicine. They are often willing to participate in the dissemination of knowledge, especially when this involves synthesizing others' research, giving a lecture or supervising residents and students in the clinical setting. When it comes to research and storage (i.e., the preservation of that knowledge through articles, books, etc.) many find these areas too difficult or discouraging. Both research and storage are activities that can be learned and become easier with experience. However, neither is a customary part of the student or resident curriculum and both are, therefore, very intimidating to the young physician. This chapter reflects on research as an academic responsibility for acute care and Emergency Medicine (EM) physicians and, hopefully, will give some clues on how to make it less painful and intimidating for the inspired academic physician.

Asking the right questions

> The first research effort of one of the second author in medical school was an effort to produce an animal model of emphysema in rats. This was studied by building the rat a helmet with a one-way valve that it had to breathe against. The theory was that the increased pulmonary pressures would produce emphysema, but the experiment was a dismal failure. The only thing derived from the experience was an unswerving hatred of rats, which bit frequently and painfully as they were put into their helmets. The net result was that it was twenty years before the author tried any more animal research, and never again with rats.

One of the areas of intimidation is the thought that the best research (i.e., the research most likely to be funded, recognized, rewarded, and acknowledged with promotion) involves basic science. While this is partially true, it is also true that basic science is not the only form of research that is useful, funded, or desirable. Clinical and translational science is concerned with the improved quality of the practice of medicine based on evidence, and the acquisition of that evidence is of critical importance. It has become increasingly evident that the best practice of clinical medicine is based on posing the right questions (see, for example, Chapter 3). The answers to those questions are dependent both upon the quality of data that create the evidence as well as how long the evidence can be relied upon. For example, in the presence of abdominal pain, last year's pregnancy test result, no matter how well performed, is not going to help

Doing Research in Emergency and Acute Care: Making Order Out of Chaos, First Edition. Edited by Michael P. Wilson, Kama Z. Guluma, and Stephen R. Hayden.

with sorting out the etiology of this year's pain. Similarly, in the presence of chest pain, how long is last year's negative stress test result helpful and, moreover, does it matter which stress test was performed?

Yet we are taught that we must obtain certain tests to be complete, thorough, or prudent, but no one gives any information on how long information lasts to be useful, nor what to do if the test is negative when only a positive test has any useful meaning. Thus, while the basic science questions regarding the best assay for determining pregnancy or detecting at-risk myocardium while stressed are of interest, a clinical scientist is most interested in the clinical questions that guide the practice of emergency medicine. (See, for example, Chapter 4, "Evidence-based medicine: Finding the knowledge gap.")

Challenges with acute care research

How then should one commence a research project in acute care? There are many challenges to carrying out research in acute care settings, whether it is prehospital research, the emergency department (ED), or the intensive care unit (ICU). Some considerations include major hurdles such as:

- Consent: How are you going to obtain informed consent on the subjects of your study? If you want to carry out a study on resuscitation related measures, how are you expected to truly obtain informed consent when they are in respiratory distress, cardiac arrest, or are altered? Are you going to be there night and day to enroll and obtain consent from these participants?
- Where are you going to do this study? It may seem like an easy question to answer, but let us say you want to carry out a study on prehospital intubations with a new device. Are you going to put the device on every ambulance? If you want to carry out a study in the emergency department regarding a new device for an emergent procedure, where are you going to keep it? Are all the patients requiring that procedure going to go to the same place, or are they going to be spread out all over your 60 bed emergency department?
- Specialists: If you want to carry out a study with a new therapy in acute coronary syndrome, you are going to have to get buy-in from the cardiologists. Our time with these patients in the emergency department is limited, so obtaining agreements to participate from admitting services and specialists is very important and can be incredibly challenging based on your relationships with those services.
- Outcomes: What are the outcomes of your study going to be and how are you going to show that your limited time with this patient population made a difference in those outcomes?
- Blinding: How will you keep the participants and raters in your experiment blinded to their true treatment condition?
- Funding: The answer to many of the questions above is to have resources in place, but resources require funding. How and where will you obtain funding, which is increasingly harder to obtain?

Where do I start?

The initial responsibility is to define a question that needs examination. This can come from any source of inspiration, but the most useful way to begin is to think about a question from your clinical practice for which you do not know the answer. In fact, the less you know about the answer the better. If you do not know anything about the question, then any data you derive in the examination of the question will be interesting. If any data are interesting, you will be less likely to bias the results in trying to find a particular answer (see, for example, Chapter 10).

Think about cases you have seen in the emergency department. Your question may come from an observation of a dogmatic clinical practice that you do not understand the need to perform. For illustrative purposes, we will use the example of cricoid pressure during intubation. No matter how many people tell you it makes intubation safer, do we really know that to be true? If it is well studied, if the available evidence is valid, and if that evidence suggests that cricoid pressure does, in fact, increase the safety of intubation, then move on to another question. If the quest is not studied adequately, then you are on the right path. While computerized databases have made it much easier to carry out a literature search, they have a finite origin for the database, and your failure to find any literature in the computerized database does not mean that there might not have been some successful studies carried out prior to computerization. You may have to do an old-fashioned hand search. Suppose that all you have been able to find are papers on how cricoid pressure helps or hinders intubation but that there is no valid evidence that it increases safety. This suggests that the practice applying cricoid pressure to increase the safety of intubation is based on theory, which no matter how logical does not constitute evidence. You have found your propositus: the reason for doing your study. (Chapter 3, "How do I formulate a research question," gives more information.)

Roadblocks, errors, and things to avoid

The next step is to consider how to acquire the evidence. This is where most research momentum fizzles out before it even starts. In this example, the hypothesis you wish to test is whether cricoid pressure actually improves intubation safety. It would seem easy to simply set up a prospective study of intubation, where you randomize the use of cricoid pressure. If you do so, however, you will quickly encounter many of the traps of clinical research that can destroy a project.

Firstly, it is likely that very few of your faculty or colleagues will be comfortable in challenging dogma by attempting intubation without cricoid pressure. That is how they learned the technique of intubation and they are sure that it is safer than not using it. Secondly, even if they were willing to change their practice, you are dependent upon other people to acquire your data; this is fraught with error because you all are very busy clinically, such as when you work in an emergency department. Unless others share your enthusiasm for the clinical question, no one is going to be motivated to perform the additional work. Hiring research assistants to help with your study will cost a significant amount of funding that you are unlikely to get in today's economic climate. Thirdly, you will have to get Institutional Review Board approval, and even if you stimulate the curiosity of the members of that committee as to the outcome of your proposed study, they will most likely demand you have informed consent prior to each intubation. Challenges of obtaining consent for emergency procedures aside, this is an instantaneous oxymoron since, if there is no evidence whether the procedure is safe, what constitutes informed consent? Asking the subject to agree to either arm of the study, both of which might be unsafe, is not likely to get an informed consent so much as a transfer to another institution where the physicians know better what they are doing, as they do not scare their subjects before mandatory procedures.

Welcome to the world of acute care research. You found a question you are genuinely interested in, and would truly like to know the answer, but the project simply cannot be done. You might try to compromise the ideal study of a randomized prospective trial of intubation with and without cricoid pressure by doing a retrospective analysis of a group of patients who had cricoid pressure versus a control group that did not (assuming of course that you could find a group of intubations before cricoid pressure became popularized, and that there exists sufficient data to compare the two). Then you have the nightmare of analyzing records that were not completed with your study question in mind, trying to decide if your intubators represent a similar group of physicians whose intubation skills are constant, whether your subjects are a similar group of patients, and whether new equipment or technology has modified your techniques enough so that the question is no longer relevant (e.g., your colleagues now intubate with a video laryngoscope). (More information is given in Chapter 2 and Chapter 14.)

You therefore give up altogether and decide to pick a different propositus, hopefully one that will avoid similar kinds of procedural problems. It quickly becomes clear, however, that your first project needs to be very simple, easy to carry out with a small number of researchers, not dependent upon the cooperation of colleagues or another specialty, and modest in its labor and financial demands. For example, when California passed a mandatory seat belt law, one emergency medicine (EM) resident was surprised at the sudden public health claims for reduced automotive crash mortality. She picked her research team (herself), went to the nearest bridge over the freeway during some spare hours, and counted the number of cars with belted drivers. With only about 5% of the drivers wearing their seatbelts, she did not have to worry about a control group. However, she could conclude that, at that point in time, the new law had not had much impact upon the compliance of most drivers, and that the reduced mortality was merely wish-fulfillment fantasy.

Some other common errors in clinical research: It is often difficult to derive the propositus for the study. It should be clear what the original observation was that gave rise to the study other than that the authors did not have enough publications to get promoted. A clear propositus gives much greater understanding to what hypothesis is being tested.

Science, as demonstrated helpfully by Karl Popper, is based on the falsification of a hypothesis. It is not, as many lay people believe, the finding of examples of the proof of your hypothesis. The falsification is based on a study of the question in which the variance in the answer is greater than chance alone. This is not the accuracy that most people associate with science, but it is the best we can do since the observations of any differences obscure the results.

> For example, suppose you are trying to determine the boiling point of water. You take a calorimeter of some kind, heat it in some way, and measure the temperature at which you spot bubbles in the water. Yet, the very act of measuring the temperature of the water during the bubbling changes the temperature of the water. Depending upon the rigor with which you wish to perform the experiment, your thermometer may be more or less sensitive to slight changes in water temperature. Since it adds little utility to the answer you are seeking, a thermometer that measures temperatures to a thousandth of a temperature degree is probably wasteful precision. Yet if you use a thermometer that only measures to a tenth of a degree, you may find a different boiling point every time you try the experiment. That is why we believe the boiling point to be 212°F, but when we actually try to prove it, we get 211, 213, 212.5, and so on and realize that the boiling point can only be the average of all the measurements.

The reason we choose a hypothesis to falsify is that it is virtually impossible to prove any hypothesis by simply finding examples of its positive presence. Thus, if the question being studied is whether cooling improves survival from cardiac arrest, you cannot just take patients in arrest, cool them, and say that your survival is better. You have to have a control group that is tested by the hypothesis that cooling is not useful, and falsify that hypothesis by showing that the cooled group did much better than the uncooled group by more than chance alone. Finding adequately matched controls can be a very difficult part of research. Case–control studies are appealing, as they solve a lot of ethical and work problems, but the evidence produced is much less compelling because causation cannot be proven. Rather, only an association can be inferred (Chapter 11).

Another very common error in acute care research is studying too small a population. This is often done because the time required to get a sufficiently large population is too great, the disease of interest is too rare, there are ethical difficulties in varying the study population, or because funding is insufficient to continue the study. It takes time to perform good research and almost nothing in our present system of doing and funding science is patient with long-term results.

We have observed an ever-increasing reliance on statistical significance, but it must also be accompanied by clinical relevance. For example, one study examined the complications of central line insertion by comparing subclavian to femoral sites. The total number of complications was not statistically different between the two locations. Does this mean the two procedures are equally safe? There was one death following a complication of the femoral line insertion. This was not statistically significant, but it is certainly clinically relevant and needs to be part of your decision making when choosing one site over another.

The converse error is reporting "trends." This comes from the difficulties presented in trying to publish negative results or in trying to obtain continued funding for a project. If the difference between the two groups is not significant, it does not matter that the difference would have been significant with only one or two more positive results. That is not a trend towards significance as much as it is a wish-fulfillment fantasy. Statistically, there is a greater probability that if the study were carried out longer, the difference would be less, not greater, because what was shown is that the difference occurred by chance alone.

We will not talk about how to get funding for projects other than to state that for initial small projects funding is probably not necessary. It is the success of pilot projects that will help one to obtain funding. Most universities have seed grants for young investigators and those sources should be looked into whenever possible. Additionally, there are also seed grants available from the specialty societies for small pilot projects (Chapter 36).

KEY POINTS

- Have a propositus that is driven by a clinical question to which you do not know the answer but are curious.
- Derive a study hypothesis that can be falsified.
- Do not depend upon colleagues, other departments or specialties, or non-academicians for data collection.
- Start small, be patient, and do not think that your first project will win a National Institute of Health grant and be published in the *New England Journal of Medicine*.
- Rather than hitting the ground running smoothly, it is like learning how to walk; we all have to start by crawling. Do not be afraid to have fun!