**Chapter 44
EMS research basics**

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**Why prehospital research?**

In the early days of EMS, most clinical practices lacked objective supporting data from the field prior to implementation. Treatments and diagnostic modalities often were transferred from the hospital setting to the field or adopted with limited testing in a controlled setting. This resulted in widespread use of ineffective practices – for example, the first generation of esophageal obturator airways. Today EMS experts and providers agree that we have a duty to prove what works and what does not work using well-designed research methods.

In terms of direct benefits, the most important reason to do prehospital research is to improve patient care. This need exists not only for drug interventions (e.g. “Is drug A or drug B better for the prehospital treatment of disease X?”), but also for device use and other care opportunities, such as diagnostics and assessments, care algorithms, provider education, human interactions that can alter treatment, or unit deployment strategies. Classic experimental research designs examine a tightly focused question, using a small number of controlled observations in tightly monitored settings. EMS often has to rely on non-experimental approaches, surrogate settings, or systems research (involving complex interrelated questions, and large amounts of data from multiple agencies, collected in a poorly controlled environment [1]). Spaite and colleagues provide an excellent overview of how the concepts of systems research, as borrowed from such fields as engineering, public administration, and social sciences, can be applied to EMS [2].

Another direct benefit of conducting research is that the patients enrolled in studies often have better outcomes than patients not enrolled in studies. This often holds true even for the patients in placebo or “no treatment” study arms or when the study intervention is not proven to be advantageous [3]. There are a number of possible reasons for this: clinical information tends to be more closely followed, ancillary testing and care are optimized, and harm versus benefit is more closely monitored.

Research has a number of indirect benefits. First, the investigators and providers gain direct knowledge of the disease or issue being studied. By the time a study is designed, executed, presented, and published, the authors are experts on the topic. Second, both the researchers and the specialty gain academic recognition for well-done EMS research. Third, EMS physicians and field personnel who participate in a study may benefit from learning the scientific process and seeing how science can affect daily practice. Finally, research can facilitate improved teamwork within an EMS system. The interactions of EMS physicians, study coordinators, emergency department personnel, and field personnel can lead to an enhanced appreciation of the roles that each play and the problems each face.

**Getting started**

**Ask a simple question**

Although it sounds simple, asking the wrong question – one that has little interest or utility to others or one that is not clear and focused – is one of the most common errors in research. Simply put, every research question should pass the “So what?” test and be clear and focused. Although a study can involve some subtopics or smaller questions related to the main question, the researcher must be able to state clearly in one or two sentences the main study question. Asking colleagues or a research mentor to review the question before starting the study will help ensure that the question is important, clear, and understandable and may also lead to additional ideas for conducting the project.

It is important that the researcher ask an important and focused question first and then design an approach to answering it, rather than the other way around. Searching through a mound of data (e.g. numbers generated by a quality improvement project or dumped out of a computer-aided dispatch system) for a question that could be addressed can result in either misleading or uninteresting results. Large databases are tempting to explore because it seems there must be a study lurking in the numbers, but care must be taken to ask a clear question before analyzing the data.

**Write a hypothesis or a clear, simple objective**

Once a research question has been formulated, a hypothesis or a clear objective must be composed. A hypothesis is a declaration to be proved or disproved. There are several types of hypotheses, depending on the phrasing. A null hypothesis states that no difference exists between two (or more) groups being studied. An example from a published study states, “Our null hypothesis is no difference in survival exists between an EMS system using targeted response and one using a uniform or all advanced life support response model” [4]. The alternative hypothesis states that a difference between groups will exist. This difference can be directional, specifying a better/worse or higher/lower effect (e.g. “We hypothesized that 4-hour survival would be greater among patients randomized to load distributing band CPR compared with those randomized to manual CPR” [5]). It also can be non-directional, where no direction is specified for the sought-after difference.

It is important to recognize that not all studies can have traditional hypotheses, but every study should have a clear focus. For example, the following is a focused and clear objective: “The objective of the current study, the OPALS Respiratory Distress Study, was to assess the incremental benefit with respect to morbidity and mortality that results from the implementation of an advanced-life-support program for the evaluation and management of respiratory distress before patients arrive at the hospital” [6]. Many observational EMS studies observe patterns and operational features of systems rather than compare groups, and a formal hypothesis may not be appropriate. Such studies can refine a question and explore areas in need of future work rather than define an association.

**Review the current literature**

Reviewing the available literature on the topic to be studied is not glamorous or fun, but it is crucial. A review will confirm that the question is appropriate and important. If the question has already been studied, there may be no need for a trial. This is unlikely for a good clinical question – even if previous work exists, a confirmatory study or a study conducted in a different type of EMS system may be of value. More likely, a researcher will find work on a similar but different question. A review may also help identify problems that may be encountered or methods that may be better suited to the study question than those originally planned.

To ensure a comprehensive review of the literature, perform a computer search using at least two different databases. For the EMS literature, the MEDLINE and CINAHL (Cumulative Index to Nursing and Allied Health) databases are of particular value. MEDLINE is produced by the National Library of Medicine, indexes approximately 5,600 journals, and is generally considered to be the authoritative biomedical index. CINAHL indexes more than 5,400 journals and includes “emergency services” among the 17 allied health fields on which it focuses. On-line abstracts are given for the majority of citations, and these can help screen for articles that need to be located and reviewed in their entirety. Online Google Scholar searches may also assist in identifying relevant published research. No matter which search engine is used, computerized searches will miss some papers [7], making a manual search of cited references from all relevant articles found in the computer search essential, although frequently tedious.

After completing the literature review, the investigator should be an expert on the subject and have a clear idea of the direction the study is going to take. In fact, many investigators write review papers from this effort or are able to frame the introduction, methods, and even parts of the discussion section of the eventual study manuscript before beginning the study based on this gained expertise.

**Select a study design**

A study design is a general plan for testing the study hypothesis or approaching the objective. There are many designs, and the best choice will depend on the study question and available resources. The researcher must select a design that balances costs, time, feasibility, and ethics and will produce useful results.

Although often perceived as the “gold standard” from an evidentiary strength view, a randomized controlled trial (RCT) is not always possible or even desirable. For example, some outcomes may occur so far in the future that it is not practical to wait for them to occur; similarly, an RCT may be unethical if clear benefit, harm, or a lack of supporting data for a particular therapy exists. New questions may require background work to define the magnitude of the problem or identify potential solutions, usually best accomplished using non-RCT designs.

When choosing a study design, researchers must ask three questions.

1. Can they follow participants over time?
2. Can they intervene with participants (instead of simply observing)?
3. Will they look at events that have already occurred or as they occur?

The first question determines if the study will be cross-sectional or longitudinal. Cross-sectional studies are those that measure all the study variables at the same point in time (or during a brief interval, perhaps a week or a month), providing a “snapshot” of data. Most surveys are cross-sectional, in that they gather data regarding the state of a particular problem or variable across a number of respondents, all at approximately the same time. A survey of all 9-1-1 communication centers in the state of North Carolina regarding dispatcher training and protocols for stroke and myocardial infarction is an example [8].

In contrast, longitudinal studies examine variables over time by following patients. Longitudinal studies are challenging in EMS, where patients generally do not maintain contact with the EMS system after their encounters. Although many out-of-hospital cardiac arrest studies follow survivors out to 1 year [9], very few studies follow patients through multiple EMS encounters over time. Some studies seem to have characteristics of both types, as with a study of changes in out-of-hospital cardiac arrest survival rates over an 11-year period. In this example, the investigators assembled sequential 1-year snapshots (rather than individual patients being followed over time) over more than a decade [10].

The second question determines if the study will be observational or interventional. An observational study monitors what is happening but makes no attempt to influence outcome or otherwise intervene in the events being studied. By comparison, an interventional design imposes a change or perturbation and studies the effects. Contrasting examples are a study by Hostler and colleagues examining blood samples from out-of-hospital cardiac arrest patients for the presence of thrombin/antithrombin complexes (an observational trial) [11], and a randomized controlled trial by Rickard and colleagues comparing intranasal fentanyl to intravenous morphine for prehospital pain management (an interventional design) [12].

The third question determines if the study will be prospective or retrospective. In a prospective study, the events of interest have not yet occurred when the patient is identified. For example, in the analgesia study by Rickard and colleagues, patients were enrolled before any pain medication was given. After enrollment, each patient randomly received one of the two study drugs, which was then administered, followed by outcome assessment (the amount of change in the patient’s verbal rating score of the degree of pain). In a retrospective study, the events of interest have already occurred at the time of patient identification. A retrospective study might have reviewed the records of patients to see what pain medications they had received and compared outcomes.

In general, longitudinal, interventional, and prospective studies are of greater value in assessing causal relationships – ”this affects/changes that” – than are cross-sectional, observational, or retrospective studies. This benefit comes at an expense: the more powerful designs are generally harder to perform, are often more expensive, and are usually more time consuming.

In making the final choice, a researcher must match the specific needs and maturity of the question with available resources and ability to complete the project. For example, before embarking on an RCT to evaluate two different methods of limiting needle-stick exposure in EMS providers, a cross-sectional or observational design might help define the magnitude of the problem with provider needle-sticks and measure the current prevention practices. These data are key to planning an interventional trial.

**Descriptive studies**

The simplest research designs are descriptive and include the correlational, case report, case series, and cross-sectional survey study designs. Their primary use is to formulate hypotheses for more advanced work [13]. These studies may not have hypotheses, but they should have clear and focused objectives.

One type of descriptive study is correlational, which can also be called aggregate or ecologic. Instead of comparing individuals, this design assesses rates for a population. For example, during the Vietnam War the survival rate for trauma patients increased and the average time to definitive care decreased when compared to the Korean War [14]. This did not prove a causal relationship between survival and time to definitive care, but it suggested potential benefit. A major limitation for correlational designs is that the researcher cannot determine if individuals with the exposure (i.e. independent variable, or the factor being studied as a possible cause of some outcome) actually developed the disease (i.e. dependent variable, or the outcome itself). Using the previous example, it is impossible to determine if those soldiers who survived actually had short transport times. This is known as the ecological fallacy, where group characteristics are assumed for individual subjects [15]. Another limitation of this design is the inability to control for any confounders in the analysis (e.g. injury severity, preexisting conditions, or ancillary care changes).

In contrast, the case report and case series are the simplest of study designs that analyze individuals. A case study looks at only one individual with a presentation or disease, whereas a case series looks at multiple patients with a presentation or disease. These studies describe in detail the identified individual(s), their treatment, and outcome. Although often seen as less valuable, case reports and series often give seminal insight into new diseases and treatments. For example, the 1981 case series by the Centers for Disease Control reporting on five homosexual men in Los Angeles who were diagnosed with *Pneumocystis carinii* pneumonia was the first published report of acquired immunodeficiency syndrome (AIDS) [16].

Case reports and case series may postulate a reason for the phenomenon that is being reported, but neither can be used to formally demonstrate an association [13]. Therefore, the primary purpose of these designs is education (regarding the clinical scenario) and hypothesis formulation (regarding a possible causal link). It is important to note that case reports are the experience of only one person or group and may not be generalizable to other situations or patient populations. In the EMS world, case reports and case series are frequently used to describe not just clinical entities, such as a mass gamma-hydroxybutyrate intoxication [17] or a perimortem Cesarean section by an air medical crew [18], but also operational issues such as a complex boat-dock collision rescue [19] or an urban search and rescue training exercise [20].

The last of the descriptive study types is the cross-sectional survey, also known as the prevalence study [21]. In these designs, the exposure (i.e. risk factor) and disease status (i.e. outcome) of the participants are measured at the same time. All measurements are made at one point in time, like taking a snapshot picture. The researcher only knows what happened at the time the question was asked and not what happened next. Surveys are the typical tool used for these analyses. The primary advantage of cross-sectional surveys is their ease because they are fast and inexpensive to conduct. The main disadvantage is that it is not usually possible to establish a cause–effect relationship, although data from this design can help guide the next investigation seeking to define that relationship. Further, this design is called a prevalence study because it will measure only the number of existing cases of a disease (i.e. prevalence) as opposed to the number of new cases of the disease over a set period (i.e. incidence) [21]. An example is a survey of prehospital personnel regarding the amount, format, and content of training they had received in the past year regarding chemical, biological, nuclear/radiological, and other mass casualty events [22].

**Analytical designs**

**Observational**

The two principal observational analytical study design types are case–control studies and cohort studies. A third variety, the before–after study, is an observational approach nested in a near- or “quasi-” experimental way.

The primary difference between the case–control and cohort studies is the method of subject identification. Using the hypothetical question of whether intubation improves survival for major trauma patients, in a case–control study patients are identified by their outcome (e.g. survivors versus non-survivors of major trauma), whereas in a cohort study they are selected by their exposure status (e.g. those intubated versus not intubated in the field [23]).

In a case–control study, after selecting the cases (i.e. those with the disease or outcome) and controls (i.e. those without the disease or outcome), the researcher looks to determine who was exposed to the risk factor of interest (e.g. to determine which patients had been intubated in the field) [24]. These studies are generally retrospective, but in some cases data can be gathered prospectively. This design is efficient in cost and time, especially for diseases with long latency periods, because it is not necessary to wait for the outcome [13]. It is also the best design to use when studying a rare outcome, such as survival from out-of-hospital asystolic arrest, because participants are selected based on an outcome that has already happened. However, it is a poor choice for studying rare exposures (e.g. cricothyrotomy), because large numbers of subjects are needed to have enough participants who had the exposure of interest.

Case–control studies also have the advantage of allowing the researcher to look at several exposures at once. However, care must be taken to develop a hypothesis prior to analyzing the data. Conducting a data-driven analysis by testing multiple exposures without a specific hypothesis is an excellent way to develop new hypotheses, but it may result in spurious findings that are due solely to chance.

The other major disadvantages of case–control studies are sampling and measurement bias [21]. Sampling bias can occur when cases and controls are selected. Theoretically, cases should be selected from all patients with the disease. However, in practice subjects are usually identified through a single source (e.g. trauma patients from a single hospital trauma registry). This method may miss cases who do not present to that source (e.g. patients who die on the scene or are transported to another facility). Even more difficult is the identification of controls, who must be drawn from the same population as the cases and be at the same risk for the disease. Stated differently, controls should be the same as cases in all respects *except* presence of the disease. Another potential bias is measurement bias, where the presence of the disease influences the retrospective assessment of exposure. For instance, cases may be more likely to remember an exposure than controls because they are sick (known as recall bias). A final disadvantage of the case–control design is difficulty establishing a temporal sequence (i.e. the exposure came before the disease) because the cases may have had unidentified disease prior to the exposure.

In a cohort study, patients are selected based on their exposure (e.g. field intubation). Two groups of patients are selected: one with and one without the exposure. The groups should be the same aside from the exposure – this is often a challenge and cannot be known with certainty, confounding observations [25]. Also, none of the potential participants should have the outcome of interest at the time of selection. These subjects are followed to determine if they develop the outcome of interest (e.g. survival from major trauma). The military use of the word cohort, a group of soldiers who all march forward together, can be helpful in remembering the difference: in a cohort study, the group starts out together (with or without the exposure) and moves forward through time toward an objective (the outcome). Although usually prospective, cohort studies can also be done retrospectively.

The principal advantages of a cohort study are that the temporal sequence can typically be determined and all can be sure that the exposure came before the outcome [21]. Further advantages are that the researcher can look at the exposure’s effect on multiple outcomes, albeit with the same caution regarding data-driven analyses noted earlier. If done prospectively, the cohort design limits the bias being introduced into the measurement of the exposure or the outcome, as compared to a case–control design. Cohort studies are good for studying rare exposures, because participants are selected based on exposure, but are best when the latency period is short. These studies can be expensive because contact with the subjects must be maintained throughout the follow-up period, and there is a risk of bias if participants are lost during the follow-up period. This design is a poor choice for rare outcomes because a large number of subjects is needed to have enough who develop the disease of interest.

An example of an EMS cohort study is one by Burstein and coworkers examining refusal of care [26]. The study population was patients who refused EMS transport, the exposure was the level of assertiveness of the physician providing direct medical oversight who spoke directly to the patient, and the outcome was patient acceptance of hospital transport.

The before–after study design is widely used in EMS research to study both clinical and operational topics. In this design, data are collected in two phases: before some sort of change is implemented in the system and after. The largest study of prehospital advanced life support, the Ontario Prehospital ALS Study (OPALS), utilized the before–after design in several phases to study whether ALS improves patient outcomes overall and for a variety of clinical entities [6,27–29].

This design may be considered purely observational if the researchers have no role in implementing the change being studied. For example, a group of researchers may study motor vehicle crash fatalities before and after the implementation of a state-wide trauma system [30]. However, if the researchers have some role in the change being implemented, this design can be considered quasi-experimental because the study will examine the effects of the changes that the researchers themselves implemented. As an example, a group of researchers participated in developing and implementing a dispatch protocol and then used the before–after design to study the effects of this protocol on first responder utilization [31].

**Experimental**

Experimental or clinical trials are constructed similarly to cohort studies, except that the researcher specifically assigns the exposure status in an experimental design. After identifying potential participants, measuring baseline characteristics, and checking to be certain the outcome does not already exist, the participants are each assigned to either receive or not receive the study treatment or intervention. Participants are followed over time to see which develop the outcome or disease of interest.

The participants in a clinical trial are typically assigned their exposure status randomly. Randomized assignment means that at the time each potential candidate is identified, he or she has an equal chance of being assigned to any treatment arm based on a non-systematic process, such as a random number genera- tor. When done correctly, randomization to a study arm can limit the effect of both known and unknown factors that may influence the study outcome by distributing them equally between the groups. This process attempts to ensure that each group is similar at the start of the study.

Alternatives to randomization exist and are used to simplify logistics, especially in the prehospital setting. These pseudo-randomization techniques include “every other time interval” (e.g. every other day), use of end digits of a Social Security number, or other perceived non-systematic features [32]. These alternatives often achieve the goal of each group having similar characteristics at the start of the study, but they may ultimately fail and produce groups that differ for a reason distinct from the exposure. For example, a study of intubation that gives group assignment based on day of the week may measure the skill differences of the providers (if EMS personnel work certain fixed schedules) or enroll varying populations (because injury and illness patterns often differ by day of week), rather than the target intervention (intubation).

Blinding is used in clinical trials to limit assessment bias (beliefs held prior to or outside the experimental question that influence judgment regarding the subject’s outcome). Specifically, blinding attempts to eliminate the distortions in variable measurement caused by the participant, care provider, or outcome assessor knowing which treatment arm the participant has been assigned. Single-blind studies generally try to ensure that the study subjects cannot tell which therapy is being used. Double-blind studies shroud both the subject and outcome assessor from the participant’s group assignment. Triple-blind studies require the subject, assessor, and care provider to be unaware of the participant’s group assignment.

Placebos or shams are substances or devices that are intended to be physiologically or functionally inactive but appear identical to the active therapy that is being studied. Using a placebo can allow the researcher to blind the participant, assessor, and caregiver to the participant’s group assignment. The use of placebos also allows the researcher to separate the perceived effect of treatment from the actual effect of the specific treatment that is being studied. Placebos are generally used only when an accepted standard of care does not exist. In studies where a standard of care exists, it is unacceptable to use a placebo because the control subjects should receive the standard therapy, unless there are substantial questions regarding the effectiveness of that standard therapy. Blinding – whether the researchers or patients can distinguish between two active agents/interventions or a placebo and an active agent/intervention – can be unrealistic or difficult if there are obvious differences (e.g. color, smell, appearance).

There are several clinical trial design variations for assigning treatments. Clinical trials can range from simple two-arm studies (e.g. a study comparing active compression–decompression CPR to standard CPR) [33] to more complex designs with multiple arms (e.g. a study comparing intravenous diazepam, lorazepam, or placebo for adults with prolonged or repetitive seizures) [34,35]. Another option is to have each participant serve as his or her own control in a cross-over trial. In this design, each participant gets the treatment for a certain period of time and, after a washout period (i.e. a period of time where the effects of the treatment are removed), each enters the other arm of the study. An example is a 1998 study looking at the effect of melatonin on night-shift paramedics. Each paramedic in the study was randomly assigned to receive either melatonin or placebo for the first week of the study. After a washout period of several weeks where no treatment was given, each paramedic was given the opposite treatment. In this way, each subject was in each arm of the study and could serve as his or her own control [36]. This design can also be used without a washout period. An example is a study by Woollard and colleagues examining the ability of field personnel to use two different types of airway devices. Each paramedic student randomly used one of the two devices, then was tested on the other device [37].

One advantage of clinical trials is that they can account for both known and unknown factors that might affect outcome. However, these studies are costly and time consuming, so they are typically only used after a hypothesis has been examined and refined using simpler study designs. Further, there may be ethical barriers to randomly assigning patients to a treatment group. To ethically conduct a randomized trial, a researcher must have clinical equipoise; in other words, he or she must be confident that there is not a clear benefit or harm from receiving the study intervention based on current knowledge (recognizing the trial may detect said difference).

**Conclusion**

High-quality research is important to the field of EMS. To conduct a meaningful study, the researcher must ask a clear and focused question, review the literature to determine what has been done in the past, and identify an appropriate study design. Typically when investigating a new area it is best to start simple and observe the phenomenon (case report or case series), review the past to see if there is a pattern (case–control), watch the future to see if that pattern can be predicted (cohort), and finally manipulate participants to see if that pattern can be created (experimental).

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