

Brief Report: EAST Workshop on How to Build a Clinical Research Program

Authors: Stephen M. Cohn, MD¹, Timothy G. Buchman, MD², Martin A. Croce, MD³, Peter M. Rhee, MD⁴, Thomas M. Scalea, MD⁵, and Basil A. Pruitt, Jr., MD¹

From the Departments of Surgery, University of Texas Health Science Center San Antonio¹, Emory University², University of Tennessee Health Science Center Memphis³, University of Arizona⁴, University of Maryland⁵.

Corresponding Authors: Stephen M. Cohn, MD Department of Surgery, University of Texas Health Science Center San Antonio, cohn@uthscsa.edu

On January 25, 2011, a workshop was conducted at the 24th annual meeting of the Eastern Association for the Surgery of Trauma (EAST) in Naples, Florida. The workshop had the following objectives: 1) to describe the resources needed to develop a successful clinical research program; 2) to explain the amount of time necessary for developing and sustaining a clinical research program; and 3) to discuss the pitfalls that can hinder the development of a clinical research program.

I. Essential Ingredients and Potential Pitfalls of Building a Clinical Research Program

A. Departmental goals and incentives: Managing an academic or business unit is different from managing a clinical service. Section chiefs, division chiefs, chairs, and deans deal with competing priorities, all of which demand the allocation of limited resources. Successful execution involves people, strategy, and an operational plan. The closer your individual agenda aligns with the unit's priorities and execution plan, the better your chances of accessing limited resources and thereby advancing your personal agenda. It is crucial to understand the strategic plan of your department and division so

that you can ensure unanimity of purpose. Also, understanding how your research efforts and time will be funded will be as valuable as developing relationships with potential mentors and collaborators.

B. Protected time for faculty/trainees: Protected time for academic pursuits is essential if you and your group are to be successful in producing quality research. Remember that surgeons have great cash-generating abilities, and as you become busier clinically the desire to generate more income at the expense of academic pursuits often strongly influences leadership decisions (particularly in these challenging financial times). Essential ingredients of protected time are both time and resources. Time for surgeons must involve clinical coverage (or a reduced goal for clinical productivity) to permit them to design studies, conduct research, analyze data, and prepare abstracts, presentations, and manuscripts. Resources in the form of clinical research coordinators, laboratory assistants, and biostatistical support, as well as dollars to buy needed equipment, are a must. There must be a culture of research productivity that facilitates this type of protected work and a commitment from departmental and divisional leadership. There are many examples of failure to provide promised protected time. At the time of recruitment, statements such as the following may be made: “You can have two days off per week when we hire another faculty member” (but funding never comes through and the person is not hired); or “You can have Wednesdays as your academic day” (but you are made a member of the Institutional Review Board (IRB) or the admissions committee, and that membership occupies the entire academic day, or you are always performing surgery on that day); or “You can share my research coordinator” (but that person always has a full workload). The promise of protected time (and each essential ingredient) must be in writing, or it will not happen! Assume that your division chief or chair will be fired shortly after you arrive at your new position, and therefore every promise must be written down.

C. Research coordinators: Research is a business. Treat it like one. Create a real *infrastructure* with a clear hierarchy. Because nurses are task-oriented

and can think independently, they make the best coordinators. (Students probably do not have enough time or focus to do a superior job as a research coordinator, although many students do this job because they think it will help them get a better residency. Residents on a clinical service already have a full-time job and are easily distracted, but they may want to work as research coordinators because they believe that collecting data will get their name on a manuscript.) If you do not pay research coordinators, they will not take the job seriously. Achieving 24/7 coverage with research coordinators is difficult but possible and works infinitely better than any other system. It is important to give coordinators ownership of at least part of the project.

D. Electronic data-collection system: A Web-based electronic case report form (CRF) is essential for trauma trials (particularly multicenter trials). Available software programs eliminate the need for developing extensive software and also eliminate the myriad of glitches that are inevitably encountered. Any electronic data-collection system must be based on a framework that provides a monitoring/query component for completing the medical monitoring and quality assurance component required by many sponsors. The system must also meet all HIPAA-required security requirements. One such system is the Informatics Data Exchange and Acquisition System (IDEAS), which was developed with the support of a large Department of Defense grant. This system was subsequently used in five clinical trials and required only relatively simple incremental changes. Data are made available in standardized reports (one report for each data collection page) that can be saved to Excel or to a statistical package such as SAS, or in text-delimited format. IDEAS has been operational for more than 9 years and has undergone multiple audits. It is scanned annually and protected by multiple firewalls. It is available, at minimal cost to anyone who wants to use it, through the University of Texas Health Science Center, San Antonio, Department of Epidemiology and Biostatistics. Contact Brad Pollock, PhD, at bpollock@uthscsa.edu.

E. Biostatisticians: Statistical methods are an essential component of the research process. Involve a biostatistician in the planning process for the study. Involving a biostatistician after the study has been completed is a case of “too little, too late.” Occasionally, a research study may yield differences so large that the validity of the findings can be established without statistical tests, although sometimes even large differences may not be statistically significant. To claim “a trend toward significance” when the P value is close to the predetermined level of significance is a statistical no-no.

II. Organization

A. Time Management: Aspiring academic surgeons should eventually declare a “research major”. Know what various scientific meetings want. Each one has a flavor.

1. Infrastructure support resources (such as statisticians) cannot help everyone on the day before a deadline. You need to plan for time to use these resources. If you have a large organization, it is wise to investigate nontraditional trauma meetings and journals. Posters are fine, but they should still be turned into manuscripts.
2. No abstract, manuscript or set of slides goes out until the senior person sees it. With few exceptions, every presentation should be vetted before it is presented. It is fine to plan to shoot for the moon; you may get lucky. But even if you don't succeed in having your paper accepted in journals such as the *New England Journal of Medicine*, these journals typically reject manuscripts quickly. It is best, however, not to waste a substantial amount of resources on submissions for which the likelihood of publication is low.

B. Weekly meetings: Develop a meeting agenda with the *goals* of the meeting in mind. The agenda of research meetings should contain a mix of preplanned topics and open discussion. Shepherd the meeting effectively. Preparation is key.

1. The moderator should ensure that the meeting stays on schedule and on track, prioritize the discussion, encourage participation, and look for a product or accomplishment. After the meeting, review its effectiveness.
2. The reason for the meeting must be clear. Meetings can be used for disseminating information, gathering information, brainstorming, providing feedback, tracking progress, generating ideas, or achieving congruence.
3. Don't meet merely to meet, but meet when necessary. Research meetings must be regularly scheduled if they are to work. These meetings may not always work or be productive, but their priority should be high enough that they are held regularly.
4. Academic research meetings should be open, and attendance should be encouraged. For certain meetings, specific attendees can be invited.
5. Meetings that provide lunch are typically better attended.
6. Develop and distribute a list of projects. Advertise these projects and keep people informed by reporting on projects that are ongoing and projects that need additional researchers.
7. Maintain a balance between basic science meetings, clinical meetings, meetings for preparing presentations, journal clubs, and didactic meetings.

C. *IRB review process*: KISS—keep it simple, stupid. More writing is not necessarily better. In the IRB application, do not regurgitate a protocol (industry or non-industry) and do not refer to the external protocol. Summarize the important points. Do not exaggerate any potential benefits to society. Most studies will not actually affect society at large. Outline the study interventions and differentiate them from the standards of care. Create charts, timelines, spreadsheets, etc.—whatever is necessary to concisely illustrate the procedures. Clearly state the risk-benefit ratio. If the study procedures do not impart “more than minimal risk” (the key phrase), simply say so. If the study does pose more than a minimal risk, explain why (and the explanation had better be good!). Try to become a member of your local IRB; serving on this committee will help you when you are writing your own protocols. (Because such membership is very time consuming, it may be ideal not to serve on the IRB until you reach Associate Professor status.)

- D. *Grant review process:* The grant application must be relevant to the topic of interest of the potential grantor. Remember that you must respond to the question or topic stated in the grant request. Therefore, early communication with the grant's Program Director is essential. Prepare the grant in time for leisurely review and revision before submission. Be neither too brief nor too ambitious. Identify endpoints and define what will be considered a positive result. Enhance the application with preliminary data, if available. Expunge all grammatical, typographical, and syntactical errors. Have a senior scientific colleague review the grant. Ensure that the budget and the duration of the study are appropriate for the work proposed. Requests for funds to be used for equipping an investigator's new laboratory will be viewed with skepticism. Revise as necessary to address as definitively as possible all of the reviewers' concerns. Do not argue with the reviewers unless they are really off-base, and even then an application to an alternative funding source should be considered.
- E. *Research program/grant administrator and accountant:* Administering grants is not an intuitive process. The consequences of errors in grant administration may lead to requests for return of funds to the funding agency and associated penalties . It is essential that an experienced person administer your grants and maintain a strict accounting process. You cannot rely on institutional accounting practices because they often lag behind your use of funds. Depending on the number and size of grants involved, you may require a considerable infrastructure to help keep accurate financial records and efficiently use your grant dollars.
- F. *Medical editor:* Consulting a medical editor for assistance with writing and publishing should be no different from consulting a specialist in a different field of medicine. Using an editor doesn't mean that the author can't write; it simply means that the author recognizes that someone else may have a different knowledge base and, therefore, can contribute a different kind of expertise to the project. A medical editor can save the author a good bit of time and can help to ensure the clarity of the material. Typically, the draft is

sent to the medical editor by e-mail with a reasonable expected date for completion (usually about two weeks). Payment is based on work required (\$60-75/hour in 2010); the typical manuscript requires 6 to 8 hours of work (perhaps 8 to 10 hours for a book chapter). Experienced medical editors can review 4 to 6 double-spaced pages per hour. The American Medical Writers Association (www.amwa.org) is an excellent initial contact point; the association maintains a directory of freelance medical editors. (see Acknowledgment).

- G. *Recruiting students, residents, fellows:* There must be a research question. Having a resident, student, or fellow merely review your experience will probably not yield data for a publishable paper.
1. Create a forum for peer review and discussion of new projects. Every trainee must have a faculty research mentor. Be clear about expectations for both the faculty member and the trainee. Enthusiasm at the top creates enthusiasm in the ranks.
 2. Create realistic projects for trainees. A prospective trial does not happen in a year. The trial should be good for trainees, not just for you. Students, residents, and fellows need to know the rules. Remember that you will pay the price for their “honest” mistakes. Sending residents or fellows to classes to learn research methodology, statistics, or both costs some money but makes the experience much better for them. As soon as you are successful, you will be inundated with e-mail messages from foreign doctors or residents. This attention will seem very attractive, but choose carefully. Match students, residents, or fellows with subjects that they actually like. Forcing a round peg into a square hole means that the project will probably fail.
- H. *MSCI/MPH/PhD programs:* The additional credential is yours and therefore portable. The investment to gain the additional credential is yours—and someone else’s. You must answer two questions: what is the cost of the investment, and what is the return? The advantages of an advanced degree include time to focus on an additional body of knowledge, mastering that body of knowledge, and joining the “invisible college” of people in the field (“street

cred”; learning “what’s hot” and “what’s not). If you choose to pursue a degree program, you need to determine whether you have sufficient time and support (especially financial).

Remember, there are differences between programs.

1. Master of Science in Clinical Investigation (MSCI): These programs are about clinical investigation, not basic science or theoretical biology. Thus, the programs are limiting in that sense. Determine whether you want a career in clinical investigation.
 2. Master of Public Health (MPH): These programs generally include clinical epidemiology and study design but with a broader focus on population-based research, including environmental science. Executive or distance-learning programs are available.
 3. Doctor of Philosophy (PhD): These programs allow you to demonstrate your ability to identify, address, struggle with, and solve a challenge not previously addressed. They are open-ended in scope, resources, and time.
- I. *Faculty requirements when applying for jobs*
1. Dean: Get a feel for how important research and faculty advancement are to the dean. It is doubtful that the dean will be able to provide you directly with money and space. However, the question is whether the dean places a priority on research rather than clinical work load, medical school, or financial issues.
 2. Chair: If you are applying for a position as chief of a division, most negotiations will involve the department chair. If you are starting out with a fellowship position, most negotiations will involve the division chief. You should be able at least to get an idea of whether the department is financially secure; if it is, there may be financial support for research. If the department’s financial status is marginal or in the red, it is unlikely that there will be any direct financial support for research. You should also get a sense of whether the chair has the luxury of building an academic program or whether such a program is just talk while the chair is trying to keep the department afloat financially.

3. Division chief: Everyone wants protected time for research, but does the system support protected time? If there is to be protected time, there must be enough surgeons to support the clinical workload. If this number is not sufficient, you will be supporting the workload during your “time off.”
4. Space: Everyone needs more space. Next to money, space is the second most important issue. There must be laboratory space for basic scientists but also space for the clinical research infrastructure, which includes coordinators, a research nurse, research fellows, and residents. There must also be an animal facility for courses and translational research.
5. Money: Some surgeons may be able to negotiate start-up funds, but such finding is improbable for anyone other than associate or full professors. Some guarantee of space and money is possible, but this guarantee is very limited in amount and duration. You will need money for laboratory technicians, supplies, etc. You will probably begin with scholarships and intramural grants.
6. Troops: Does the department provide ancillary support? If the chair or chief laughs when you ask this question, you have your answer. Some programs do provide grant writing support, statistical support, editorial support, laboratory technicians, research nurses, and research administrators.
7. Bottom line: Very few chairs or chiefs can afford to give you support and time, so you will have to carve them out on your own. If the department, division, or section has no outside support other than clinical dollars, you will find it difficult to get sufficient long-term dollar commitments. The division chief and chair must have a track record of research and productivity in academia.

III. Identifying Research Focus and Developing Collaborators

A. Identifying funding sources

1. Internal departmental funding: Ask someone in the Grants and Contracts office about various institutional options. These are usually posted on your institution’s Web site.

2. Become involved in industry-sponsored studies. Lists of such studies can be found at www.clinicaltrials.gov.
3. Budget appropriately.
4. Use residual funds to fund small pilot projects.
5. Start with smaller clinical projects. Use these pilot data to apply for other grants.

B. Society Research grants: Some society grants are competitive, but they offer one way to obtain funding early in your career because their applications do not require preliminary data. If you have an idea, apply. These grants can be the best way to fund clinical research. They are prestigious, and they provide start-up funding. The application process is usually less arduous than that for NIH grants or intramural funding: the typical application is approximately 6 pages long.

1. American College of Surgeons (ACS) grants: Four fellowships are available. The key is to have your junior staff apply early or they will miss the opportunity.
2. American Association for the Surgery of Trauma (AAST): Various scholarships are available, including scholarships for medical students, travel awards to allow residents to attend meetings, technology-driven awards from the Center for the Integration of Medicine and Innovative Technology, basic science research awards, and KCI Wound Care awards.
3. EAST: This association offers the EAST Foundation Research Scholarship and the Templeton Injury Prevention Scholarship.
4. Western Trauma Association (WEST): The Western Trauma Association Foundation for Education and Research, established in 2002, funds the Earl G. Young Resident Research Prize and provides support for research projects.
5. Surgical Infection Society (SIS): The society offers the SIS Foundation Resident Award, the SIS/Pfizer Evaluative Research Junior Faculty Fellowship, and the SIS Junior Faculty Fellowship Award.

6. Society of Critical Care Medicine (SCCM): Available are SCCM Vision Grants for junior faculty and the Norma J. Shoemaker Research Grant for critical care nurses.
7. North American/US Shock Society: The society offers the Shock Society Research Fellowship for Early Career Investigators.
8. Society of University Surgeons (SUS): Several awards are available: the Ethicon-SUS Surgical Research Fellowship Award, the SUS Foundation Junior Faculty Award, the Wyeth-SUS Foundation Clinical Scholar Award, and the SUS Translational Research Award.
9. American Surgical Association (ASA): The ASA offers the American Surgical Association Foundation Fellowship Research Award and the ASA Flance-Karl Award.

C. *Department of Defense (DOD) funding*: The budget has increased in recent years.

1. Topics of interest are posted in Calls for Proposals or in Broad Agency Announcements, Congressionally Directed Medical Research Programs, and the Defense Health Program.
2. Instructions for grant format and timelines are available online.
3. The review process resembles that of the NIH, but some programs, eg, National Trauma Institute (NTI) grants, have instituted a two-part process that includes the initial screening of a preliminary brief proposal.
4. The current emphasis of DOD grants is on clinical studies related to hemorrhage and hemorrhage control.
10. Budgetary reductions, if not outright cessation of earmarks, are anticipated to reduce DOD combat casualty care support by 40% in FY 2011.

D. *National Institutes of Health (NIH) funding*

1. K awards: These awards are also known as Career Development Awards. They are not merely awards; they are a cost share.
 - a. These awards require a 75% time commitment.
 - b. The expectation is that everyone has “skin in the game”: you, your department, your university, your professional society, your family.

- c. Your mentor(s) must demonstrate the following:
 - 1) Credibility
 - 2) Interest in your research area
 - 3) Rate of conversion of award recipients to R01 or other higher-level funding
 - 4) Excellent interpersonal relationships with mentees
 - 5) Confining or expanding your scope of vision
- d. Your career will be evaluated in the following areas:
 - 1) How does research generally fit into your career—past, present, and future? Is the trajectory obvious?
 - 2) What is the likelihood that you will continue your research—at your present institution or anywhere?
 - 3) How will research career development enhance your teaching or your clinical activity?
- 2. T32 programs: Only approximately 33 surgery departments in the United States have a T32 training grant. These grants have the following requirements:
 - a. Collaborative research with a general theme, which ideally is well developed both within and between departments.
 - b. Demonstrated commitment of leadership (translated, this requirements means that resident research years will be financially supported even if the Institution does not receive the T32 grant).
 - c. Track record on the part of the principal investigator and the faculty in successful mentorship of residents in research and in successful applications for Federal grants (NIH grants are best, but DOD grants are also important).
 - d. A 2-year training period, which can be combined with an NIH loan repayment program (which provides the recipient with \$70,000 of tax-free funding).
 - e. Combination with a MSCI/MPH (or PhD) degree program is optimal.

- f. A recruitment process that begins during the interview process and lines up mentorship during the early part of the intern year. The resident should submit a proposal for an F32 or similar award.
- g. An emphasis on diversity (this requirement may be challenging).
- h. Ethics in research training is required.
- i. T32 criteria for success: The trainee becomes an academic surgeon with NIH funding; the trainee becomes an academic surgeon; or the trainee engages in productive research during the research years. Communication with Scott Somers, PhD (somerss@nigms.nih.gov), the current T32 program director, is essential, at the National Institute of General Medical Sciences (NIGMS); he can provide advice and guidance throughout the application process. Program information can be found at <http://www.nigms.nih.gov/Training/InstPostdoc/>.

E Budgeting

1. Hard or soft dollars: All budgets are negotiable. All of them.
2. Minimize budgeted hard dollars as much as possible: negotiate with the laboratory, radiology, etc.
3. Maximize budgeted soft dollars from funding source as much as possible: charge for IRB filings, protocol revisions, medical supervision, etc.
4. Use residual funds for research nurse salaries, smaller pilot projects, or educational endeavors.
5. Never use residual funds for personal use. Ever.
6. Indirect costs: Assume that none of these grant dollars will be returned to you (but rather will go to your institution). Also, note that industry often includes these dollars in the total amount allotted (different from federal grants, which add indirect dollars over and above the amount of the grant), so you must add indirect costs within the limits set by the sponsor.

Acknowledgement: Medical editor, Flo Witte, PhD, ELS (flo.witte@roadrunner.com) assisted in the preparation of this document.