



Clinical research

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Clinical research refers to any kind of study that involves patients. Clinical research studies range from case reports and case series at one end of the spectrum to randomized clinical trials at the other end. As surgery and medicine are transformed to evidence-based practice, clinical studies gain importance, especially randomized clinical trials. Participating in clinical studies is an important endeavor for all surgeons, whether they are in academic or private practice. Many large randomized trials in surgery have depended and will continue to depend on private surgeons to recruit and enroll patients. Reviewing one's own outcomes in a clinical study (usually a retrospective case series) is emerging as an important part of clinical practice, whether for recertification or for acquiring patient referrals.

For some academic surgeons, clinical trials are the main focus of their scholarly pursuits. Such studies may take long periods of time to complete. For example, the large Veteran's Affairs (VA) multicenter hernia trial required 2 years to plan, 5 years to execute, and more than 2 years to analyze and publish all the results; it produced a total of 14 publications.

Getting Started

Many methods and opportunities are available to acquire skills as a clinical trialist. It is possible to work in an already established laboratory, but this is not generally a key component of surgical clinical trials (unlike the basic sciences).

At Your Institution

Participation in the Human Subjects Committee or Institutional Review Board (IRB) requires a significant commitment of time, but holds certain advantages. It is a good way to learn about clinical trials, the institution's interpretation

of the regulations, and it also keeps participants informed as to which trials are ongoing and who the most active researchers are at the institution (which can provide a potential source for a collaborator or mentor). Being known to the members of the IRB can be of assistance in getting your own proposals approved, and you will be more likely to be called if a question arises regarding your protocol, rather than the committee relying on their own interpretation of areas they may not understand fully.

It is advantageous to enroll patients into ongoing studies. Departmental research nurses or coordinators usually are knowledgeable about existing studies and can be helpful. If no pertinent studies are ongoing at your institution, consider participating in some that do not require your institution to be a funded center, such as American College of Surgeons (ACS) Oncology Group Trials. Details are available at the ACS Web site: <http://www.acosog.org/>.

Training

Human subjects training

Certification of human subjects training now is required on a yearly basis for all those involved in human research. Courses are available on-line, such as the Collaborative IRB Training Initiative (CITI), licensed to the University of Miami (<http://www.miami.edu/citireg>), or the Human Participant Protections Education for Research Teams sponsored by the National Cancer Institute (<http://www.cancer.gov/clinicaltrials>). Furthermore, many institutions, such as the VA, have their own specific requirements. VA training can be accessed from the following Web site: <http://vaww.ess.aac.gov>.

Web resources

There is a wealth of information about conducting clinical trials on the Web and information about ongoing clinical trials (eg, the National Cancer Institute site: <http://www.cancer.gov/clinicaltrials>).

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Courses on conducting clinical trials

Consider enrolling in the ACS (www.facs.org) or VA (www.va.gov) Clinical Trials Courses. These courses have almost the same curriculum, except the ACS course is focused on surgeons/surgical trials. It requires an intensive 5 to 6 days (usually from 7:00 am to midnight), but the course gets great reviews and you will learn more in that week than you would in a year or more of trial and error. The ACS has developed a Clinical Methods course lasting an intensive 5 days. It is given in Chicago, has limited enrollment, and next will be offered in November of 2007. More information is available at www.facs.org. These courses are expensive so it is desirable to seek funding from your institution or from a grant. For information about the VA course, contact your VA Research Office.

Master's degrees

It is possible to tailor a program emphasizing clinical studies by working through a School of Public Health or other institution offering a Master of Public Health (MPH) or Master of Health Administration. Several medical schools have training grants from the National Institutes of Health (NIH) to train clinical investigators; inquire at the medical school research office. Most MPH programs teach epidemiology research. Master's-level training in a subject allows one to converse more knowledgeably with PhD health services researchers and presents opportunities to collaborate that would not otherwise be available.

A unique program is available through the University of Michigan School of Public Health On the Job/On Campus program, which allows pursuit of a Master's degree while working. Master of Health Services Administration, MPH, and Master of Science in Clinical Research Design and Statistical Analysis degrees are offered. These programs take almost 2 years and require a number of intensive 4-day weekend class sessions in Ann Arbor, Michigan. Course work includes classes in statistics, survey design, study design, human subjects' protection, and more. The program is excellent and has a high success rate of its graduates achieving funding. Details are available at: http://www.sph.umich.edu/exec_ed/ojoc/index.html.

The book "Fundamentals of Clinical Trials" by Friedman et al [1] is an excellent resource and is used in the ACS Clinical Trials course.

Society membership

The Society for Clinical Trials has an annual meeting, during which researchers of all types involved in clinical trials can attend. This meeting provides networking opportunities and discussions of pitfalls of clinical trials. Details are available at: <http://www.sctweb.org/>.

Getting the Help You Need

After acquiring the appropriate education to become a clinical trialist, further support is needed. Most clinical trials require at least a research assistant if not a research nurse. A PhD-level biostatistician also often is needed and may be available through your department. Usually, whether within your department or not, the clinical trialist becomes responsible for the cost of this appropriate support. Other specialty help may be needed. For example, a study involving cost analysis should use the expertise of a health economist and a systems analysis requires a health sciences researcher. This partly explains why clinical research is so expensive.

Where to Seek Funding

One way to get started is by participating in industry-sponsored drug trials. Most companies pay a certain amount for enrolling each patient. Carefully evaluate the requirements (paperwork, follow-up evaluation, and so forth) before enrolling patients so that the cost-per-patient does not exceed reimbursement and hopefully allows for some overage. Try to keep the funds in a research account you control so that the resources are directed to support your research program. Participating in these trials to some extent provides experience. If you have an idea about a project that involves a drug or device, research this area carefully to ensure no one else is working on it and present it to the appropriate company. However, it can be challenging to get to the right person.

The VA is an excellent environment in which to acquire funding for a clinical trial. To be eligible for the funding the researcher must have at least a 5/8 appointment (8/8 means a full-time appointment) at the VA. The VA has a Cooperative Studies Program (details are available at: <http://www.va.gov/resdev/csp.cfm>). If you have an idea for a trial, prepare a 5-page letter of intent and send it to the head of Cooperative Studies in Washington, DC, who will send it out for review. If the reviewers believe it is a reasonable project to pursue, the Cooperative Studies Office will assign your proposal to one of the Cooperative Studies Centers staffed with biostatisticians, health services researchers, health economists, data managers, and so forth. The appropriate personnel will be assigned to help plan the study (although you can suggest a few other surgeons from the VA to participate), prepare the grant, and, if and when the grant is approved and funded, they will help you with the trial. The Cooperative Studies Centers have vast experience with clinical trials in the VA so they provide a huge resource. Another avenue to pursue is the Health Services Research and Development Service geared primarily toward systems and health services research. Details are available at: <http://www.hsrp.research.va.gov/>.

The NIH has a somewhat similar, albeit much smaller scale, program called *Clinical Research Centers*, which

might be funded at your institution and is related more to space than personnel. However, the Director of that center is knowledgeable regarding the most NIH-funded clinical research at your institution and has contacts with biostatisticians. In addition, the Director probably will have experience with the funding of clinical trials through the NIH.

Private foundations also should be considered. They are not likely to fund a multicenter trial, but may fund a pilot study at your institution. Many of the surgical associations have foundations that fund such research projects.

How to be a Successful Clinical Trialist

Regarding research, it is important to acquire good help at the appropriate level and type. Completing all the forms for patients enrolled in the trial is time consuming, not to mention the many hours required to complete the IRB approval process. While working on the IRB process, consider asking your departmental representative to the IRB to review your application and proposal and make suggestions. They review many proposals each month and can advise you of the important factors involved in the ever-changing world of IRBs.

Funds are needed to hire the appropriate help. If you try to do it all yourself, you either will have to give up the operating room or sleep, or sometimes both. Do not ignore

or skimp on the paperwork either because that could become a problem and, in some instances, put patient safety at risk. As in the rest of your work, you have to be attentive to detail. When a serious adverse event occurs in a clinical trial, respond immediately, making sure the appropriate authorities on local and national (if it is a multicenter trial) levels are informed fully.

Should the protocol require additional investigators other than the PI and the study nurse or coordinator to recruit patients, diligence for details of the protocol and its requirements must be exercised throughout the conduct of the trial. Try to find people who can be trusted.

As far as making this effort an academic success, the good news is that clinical trials are expensive (ie, lots of grant funding listed by your name), but they take several years (often 5 or 6) to complete. Therefore, do not rely alone on the trials to provide the information needed for publications required for promotion unless the acceptable timeline is longer than 7 years. Other avenues for publications will need to be written in the meantime.

References

- [1] Friedman L, Furberg C, DeMets D. *Fundamentals of Clinical Trials*. 3rd ed. New York: Springer, 1998.