Clinical Investigation . . . An Impending Crisis?

Anthony N. DeMaria, MD, MACC
Editor-in-Chief, Journal of the American College of Cardiology

In an earlier Editor’s Page I indicated that nearly two-thirds of submissions to JACC originated from outside of the U.S. These manuscripts now receive an acceptance rate similar to papers from within the country. There are a number of possible explanations for the predominant number of international submissions, including an increasing quantity and quality of research overseas, advantageous circumstances for patient recruitment, and perhaps the desire to publish in U.S. journals having a world-wide readership. However, one possible explanation is diminished productivity of clinical research within the U.S.

The National Institutes of Health (NIH) defines “clinical research” to include: patient oriented research including mechanisms of human disease, clinical trials, and new technology development; epidemiologic and behavioral studies; and outcomes and health services research. That significant difficulties plague clinical research in the U.S. has been recognized since 1979 when then NIH Director, James Wyngaarden, described clinical investigators as “an endangered species” (1). However, the recent stunning advances in basic science have, by contrast, brought the problems in clinical research into sharp focus.

Anxiety regarding clinical research has reached a sufficient level that several groups have addressed the problem. Representatives of government, private funders of research, and health care payers met for over a year to issue a Clinical Research Summit Report, frequently referred to as the “Graylyn Report” (2). Concern has been expressed that the lack of major obstructions to converting new scientific knowledge into enhanced human health: translation of basic science discoveries into new preventive, diagnostic, and therapeutic modalities; and implementation of these new modalities into standard patient care. Clearly, neither barrier can be overcome without a thriving clinical research enterprise. The CRR recognized a number of obstacles confronting clinical research in the U.S., including rising costs and increased regulatory burdens. However, four problems were of particular importance: lack of patients, inadequate information systems, insufficient funding, and the need for well-trained clinical investigators. Although all are important, my own familiarity and concern is greatest for the plight of clinical investigators.

Recent years have witnessed our increasing appreciation for the courage and altruism of individuals volunteering for clinical research. However, as detailed in the CRR report, only 5% of the subjects screened for clinical trials actually complete the protocol, and by 2005 nearly 20 million individuals will have to be screened to fulfill the need of industry trials alone. Enrollment has surely been hurt by the potential conflict of interest of some investigators widely disseminated in the media. Research participants must have more understanding and ownership of the process. Getting patients to appreciate the importance of evidence-based medicine and how evidence is acquired could go a long way in this regard. However, it is also incumbent upon all cardiologists to encourage, facilitate, and even direct their patients to participate in clinical studies. The U.S. lacks the medical regionalization of most of the rest of the world, and the health care system fosters a strong sense of preserving our own patient population. For clinical investigation to thrive in the U.S., the active participation of all cardiovascular specialists will be required, whether in academia, private practice, or in other settings.

Just as medical records often continue to be generated manually and stored on paper, informatics have not made great inroads into the process of clinical investigation. Obviously, application of modern information technology could markedly reduce the time and effort in clinical research. Sophisticated information systems would, of course, require substantial increase in funding, another of the major challenges identified for clinical research. However, nowhere is the need for increased support more important than with respect to clinical investigators.

Clinical investigators are the base upon which the clinical research enterprise is built. However, the number of physicians pursuing a career in research has declined since the mid-1980s, as has the number of medical students planning a career in clinical research (4). A 47% decrease in physicians applying for research fellowships has occurred between 1995 and 2001, and currently only 8% of principal investigators conducting industry-sponsored clinical trials are un-
nder age 40 (3). The pool of clinical investigators may not only be unable to translate the new basic science discoveries into better care, but may not even be sufficient to continue the present level of efforts. This will be particularly true in cardiovascular medicine, where a significant shortage of specialists is projected to occur as early as 2010.

A number of impediments confront physicians contemplating a career in clinical research. Many physicians face a heavy debt upon graduation, and the prospect of spending additional years of training required for a research career at a relatively low pay scale is unappealing and often prohibitive. Although “on the job training” was the rule for producing clinical investigators in previous years, the need for specialized training is now well recognized, and there is a pressing need for more such training programs. Debate continues as to whether clinical investigators are born or can be produced, but all recognize that inquisitiveness, innovation, and imagination are traits that are difficult to teach. Accordingly, leakage from the system of productive clinical researchers is particularly painful.

The lack of academic prestige is often cited as a strong disincentive to embark on or continue in a clinical research career. Clinical investigation is often regarded as a tier below basic science, although all admit that the variables involved in studying humans are often much more difficult than those encountered in the experimental laboratory. The criteria for promotion at most medical schools emphasize independence and originality, although much clinical research involves collaborative efforts to address existing unresolved issues. Compared to basic science, the criteria for excellence in clinical research are more difficult to define. Even when promotion is accorded, it is often in a different appointment series than basic scientists. When financial disincentives—including a lesser pay than colleagues in practice—are added to the above impediments, it is not surprising that many of the “best and brightest” physicians choose clinical practice. We are fortunate that the thrill of discovery, pride of mentorship, and satisfaction of defining best care for other physicians are sufficient to keep so many excellent individuals in clinical research.

A special word seems in order about the role of mentors. As one whose career shifted from private practice to clinical research due to role models, I can attest to the importance of mentors in attracting and creating new clinical investigators. Today there is a progressively diminishing number of mentors, and they often function under very difficult circumstances. Clinical investigators are very often expected to generate the bulk of their salary from patient care collections. Although in the past one could generate an academic salary with part-time practice, reduced reimbursement and underinsured patients now require virtually full-time commitment. Since grant funding for clinical research is scarce, patient-based investigation must often be piggybacked onto clinical services. Reduced house staff and fellow numbers now require more direct faculty coverage of patient care than was previously required. Current requirements for documentation are now likewise much more time consuming. Thus, the clinical researcher is often left with little time and financial support to devote to investigation—much less for mentoring. Confronted with teachers who appear stressed, it is not surprising that trainees will choose alternate career paths. In my opinion, we will not be able to sustain a productive clinical research enterprise until the challenges confronting mentors are addressed.

The problems facing clinical investigation are not new, nor is their recognition. However, with the passage of time they have become more severe, so that the term “impending crisis” is likely not too strong a description. The voices recognizing the problem and recommending solutions have grown progressively louder. I believe that most responsible agencies will heed the chorus issuing a call to action. It is clear that measures should be instituted to ensure greater patient participation, that regulatory burdens will need to be reduced, that state-of-the-art information technology should be implemented, and that increased funding must be directed to the effort. Most importantly, these measures as well as others must serve to attract and nurture clinical investigators. Absent such an effort, society will not realize the health benefits available from the basic science research in which it has successfully invested.

Address correspondence to: Anthony N. DeMaria, MD, MACC, Editor-in-Chief, Journal of the American College of Cardiology, 3655 Nobel Drive, Suite 400, San Diego, California 92122.

REFERENCES