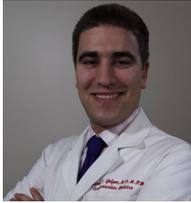


LEADERSHIP PAGE



The American College of Cardiology Ventures Into Medical Research and Innovation Policy



Benjamin Z. Galper, MD, MPH

Patrick T. O'Gara, MD, MACC, ACC Immediate Past-President

The American College of Cardiology's (ACC's) mission to transform cardiovascular (CV) care and improve heart health requires a willingness to examine current practices across all aspects of the care continuum, as well as the critical contributions of research and innovation to the cycle of quality improvement. Concerns have been raised that the U.S. research enterprise has become stagnant and that we have begun to lose our global leadership role in innovation and health care delivery. New technologies, devices, biological agents, and medications are often first available outside of the United States. There is growing recognition that we must advocate to ensure that CV patients in the United States can gain more timely access to medical, interventional, and surgical innovations shown to be effective and safe. In parallel, we need to advance comparative effectiveness and health services research.

To date, efforts by the College to engage federal policymakers in the area of medical research and innovation policy have been sporadic and focused on particular areas of interest. Given the current climate for research funding, and amid real concerns that the United States is lagging in its efforts, it is imperative that the College bring a strategic and organized approach to these issues. To effect change, it is important to identify key areas where the ACC can have the greatest impact, taking advantage of its member base, scientific expertise, and focus on quality improvement.

At the request of the Advocacy Steering Committee, we undertook an effort to identify strategic areas of interest to the College, its members, and patients. Based on interviews with experts from a range of professional backgrounds, we identified 3 major

objectives that will further the College's mission, along with the dual goals of promoting support for CV research and ensuring that U.S. patients have timely access to cutting-edge, high-quality, safe, and efficient CV care. These objectives include increasing the availability of funding for research, removing barriers to clinical research, and developing a learning health system.

OBJECTIVE 1: INCREASE THE AVAILABILITY OF FUNDING FOR RESEARCH

Funding sources are stressed. The National Institutes of Health budget has been stagnant for the past decade, and foundation and industry support is limited. The 2015 pay line for grants from the National Heart, Lung, and Blood Institute is 13% and has hovered between 10% and 13% for the last 5 years (1). Accordingly, a significant amount of important, high-quality research has not been funded from traditional sources. Between 1980 and 2013, the average age of investigators receiving their first Research Project Grant (R01) increased by 6 to 8 years. For PhD investigators, the average age increased from 36 to 42 years, whereas for MDs, the average age increased from 38 to 45 years. Individuals with MD-PhDs, on average, now wait until they are 44, rather than 36 years of age, to achieve their first R01 grant (2).

Increased funding for basic, translational, clinical, population, and health services research is critical to reinvigorate the enterprise, improve our ability to address critical questions, and promote investigation as a career opportunity for young investigators, all with the goal of advancing the understanding of CV disease and developing science-based strategies for

prevention, treatment, and follow-up. Clearly, alternative funding sources must be identified and vigorously pursued while the ACC continues its advocacy efforts to increase federal support.

OBJECTIVE 2: REMOVE BARRIERS TO RESEARCH

CV trials have become prohibitively expensive because of their size and scope, as well as numerous regulatory inefficiencies that often do not advance patient safety or applicability. There have been increasing calls for the design and execution of large-scale, pragmatic clinical trials (3). A recent example of a trial conducted more efficiently than the traditional randomized controlled trial is the HEAT-PPCI (Unfractionated Heparin Versus Bivalirudin in Primary Percutaneous Coronary Intervention) trial, a U.K. study with a unique design incorporating delayed, informed consent of research subjects (4). It is not clear that this trial could have been conducted in the United States given the issues surrounding informed consent and the differences across institutional review boards in the consistent application of policies and regulations. The TASTE (Thrombus Aspiration during ST-Segment Elevation Myocardial Infarction) trial, a multicenter, prospective, randomized trial of aspiration thrombectomy at the time of primary PCI conducted in Sweden, used the national comprehensive SCAAR (Swedish Coronary Angiography and Angioplasty Registry) as an online platform for randomization, case-record forms, and follow-up data (5). It was conducted more quickly and at a fraction of the cost of comparable trials of its type and was highly touted as an example of the next-generation clinical trial for the United States (6). A National Cardiovascular Data Registry (NCDR) registry-based trial, SAFE-PCI (Study of Access Site for Enhancement of PCI for Women) Trial, was conducted to assess the effect of radial artery access on outcomes of women undergoing PCI (7). It was terminated early because of a lower than expected event rate, but nevertheless, it highlighted the potential of the ACC’s patient registries to function as a platform for randomized trials.

Clinical trials of the future must be more efficient and less costly, but also address a broad array of critical questions in populations more representative of those with or at risk of the condition under study. To address these concerns, the “pragmatic clinical trial” must consider streamlining patient enrollment; incorporating data from a variety of sources, including clinical registries and electronic health records, wearable technologies, and “-omics” writ large; engaging affected patients and their caregivers;

and ensuring adequate representation of special populations, including women, racial and ethnic minorities, the elderly, and the young. There are additional considerations for smaller populations affected by less common diseases. This effort will require examination of current practices, methodologies, and requirements, such as those in the Common Rule and the Food and Drug Administration’s research regulations that conflict, complicating the use of registry data for product label expansion (8). The ultimate goal is to incorporate clinical research into practice in ways that are seamless for both the patient and the clinical provider.

The government plays a substantial role in medical research and innovation; it funds research and defines the processes by which patients gain access to new therapies. Although it is the role of government to ensure that patients receive timely access to safe and effective therapies, it is also incumbent upon government to implement policies and processes that are free of unnecessary burdens and complexities, obstacles that ultimately only serve to delay access to lifesaving technologies and increase the cost of those therapies. Some of these concerns could be reflected in the delay of access to transcatheter aortic valve replacement (TAVR) in the United States. The United States was the 44th country to approve TAVR for commercial use (9). Last, it is essential that these processes to streamline clinical and health systems research provide opportunities for patients, caregivers, and the public to participate.

OBJECTIVE 3: DEVELOP AND IMPLEMENT A LEARNING HEALTH SYSTEM

As data become easier to collect and are increasingly mobile, they can be used for a wider variety of purposes. To date, health systems research has been sorely neglected. Research into improving quality and reducing costs is essential. It is equally important to ensure that the results of any comparative effectiveness research project are provided to clinicians and health systems to improve care delivery and patient outcomes. We need more initiatives like Door-to-Balloon (D2B), which was developed based on research indicating that timeliness of reperfusion therapy for patients with myocardial infarctions was key to improving outcomes (10). Additionally, we need greater ability to use data gathered on patient care to further improve and refine that care. It is encouraging that the Food and Drug Administration decided to expand the label indication for the Edwards Sapien transcatheter aortic valve (Edwards Lifesciences, Irvine, California) using prospectively

acquired and vetted Society of Thoracic Surgeons/ACC TVT (Transcatheter Valve Therapy) Registry data (11). The use of previously collected data for multiple purposes is encouraged. Importantly, patients must be fully engaged at each step and must be provided transparent information regarding the many ways their participation in research, even as an entrant in a registry, can help close our knowledge gaps.

CONCLUSIONS

Much work lies ahead and the actions of many others will be needed to achieve our aims. The identification

of these 3 objectives is just the first step in the process. Among the next steps are the further refinement of the College's priorities, the development of policy positions, and the identification of partners with similar agendas and goals. We look forward to achieving the ultimate goal of better outcomes for CV patients.

ADDRESS CORRESPONDENCE TO: Dr. Benjamin Z. Galper OR Dr. Patrick T. O'Gara, Brigham & Women's Hospital, 75 Francis Street, Boston, Massachusetts 02115. E-mail: bgalper@partners.org OR pogara@partners.org.

REFERENCES

1. National Heart, Lung, and Blood Institute, National Institutes of Health. FY 2015 funding and operating guidelines. Available at: <https://www.nhlbi.nih.gov/research/funding/general/current-operating-guidelines>. Accessed November 18, 2015.
2. National Institutes of Health. New investigator update 1980-2013. Available at: http://grants.nih.gov/grants/new_investigators/New%20Investigator%20Update%201980%20-%202013.pptx. Accessed November 18, 2015.
3. The National Patient-Centered Clinical Research Network. ADAPTABLE Aspirin Study. Available at: <http://www.pcornet.org/aspirin/>. Accessed November 18, 2015.
4. Shahzad A, Kemp I, Mars C, et al. Unfractionated heparin versus bivalirudin in primary percutaneous coronary intervention (HEAT-PPCI): an open-label, single centre, randomised controlled trial. *Lancet* 2014;384:1849-58.
5. Fröbert O, Lagerqvist B, Olivecrona GK, et al. Thrombus aspiration during ST-segment elevation myocardial infarction. *N Engl J Med* 2013;369:1587-97.
6. Lauer MS, D'Agostino RB Sr. The randomized registry trial—the next disruptive technology in clinical research? *N Engl J Med* 2013;369:1579-81.
7. Rao SV, Hess CN, Barham B, et al. A registry-based randomized trial comparing radial and femoral approaches in women undergoing percutaneous coronary intervention. *J Am Coll Cardiol Intv* 2014;7:857-67.
8. 45 CFR 46.116. 21 CFR 50. 21 CFR 812 (CFR is Code of Federal Regulations).
9. Mack MJ, Holmes DR, Webb J, et al. Patient selection for transcatheter aortic valve replacement. *J Am Coll Cardiol* 2013;62 Suppl 17:S1-10.
10. American College of Cardiology. About D2B. Available at: <http://cvquality.acc.org/en/Initiatives/D2B/About-D2B.aspx>. Accessed November 18, 2015.
11. U.S. Food and Drug Administration. FDA news release: FDA approval expands access to artificial heart valve for inoperable patients. Available at: <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm369510.htm>. Accessed November 18, 2015.