Centers for Cardiovascular Outcomes Research
Defining a Collaborative Vision

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Background—Recognizing the value of outcomes research to understand and bridge translational gaps, to establish evidence in clinical practice and delivery of medicine, and to generate new hypotheses on ongoing questions of treatment and care, the National Heart, Lung, and Blood Institute of the National Institutes of Health established the Centers for Cardiovascular Outcomes Research program in 2010.

Methods and Results—The National Heart, Lung, and Blood Institute funded 3 centers and a research coordinating unit. Each center has an independent project focus, including (1) characterizing care transition and predicting clinical events and quality of life for patients discharged after an acute coronary syndrome; (2) identifying center and regional factors associated with better patient outcomes across several cardiovascular conditions and procedures; and (3) examining the impact of healthcare reform in Massachusetts on overall and disparate care and outcomes for several cardiovascular conditions and venous thromboembolism. Cross-program collaborations seek to advance the field methodologically and to develop early-stage investigators committed to careers in outcomes research.

Conclusions—The Centers for Cardiovascular Outcomes Research program represents a significant investment in cardiovascular outcomes research by the National Heart, Lung, and Blood Institute. The vision of this program is to leverage scientific rigor and cross-program collaboration to advance the science of healthcare delivery and outcomes beyond what any individual unit could achieve alone. (Circ Cardiovasc Qual Outcomes. 2013;6:00-00.)

Key Words: cross-collaboration ■ outcomes research ■ translation of knowledge

The National Heart, Lung, and Blood Institute (NHLBI) convened a Working Group on Outcomes Research in Cardiovascular Disease in 2004 to establish priorities for future research.1 As a direct output from this working group, the NHLBI established various key initiatives, including the Cardiovascular Research Network, which focused on surveillance in cardiovascular disease in its early phases of funding; the Trials Assessing Innovative Strategies to Improve Clinical Practice Through Guidelines in Heart, Lung and Blood Diseases, which tested innovative interventions to improve adherence to guidelines; and the Implementation Research program, which focused on translating best practice into clinical care.

To further promote outcomes research in cardiovascular disease, the NHLBI initiated the Centers for Cardiovascular Outcomes Research (CCOR) program, funding 3 centers and a Research Coordinating Unit (RCU) to conduct outcomes research that examines strategies of clinical decision making, healthcare policy, and the consequences of health care; compares the effectiveness of clinical tests or treatments on outcomes; examines contemporary patterns of care; and generates evidence to inform quality of care and to promote clinically appropriate choices by patients.2-3

Program Overview and Vision
The centers in the NHLBI CCOR program have the following components: a unifying research theme and structural core, support for research projects, and faculty development. The 3 centers include the following:

1. Transitions, Risks, and Actions in Coronary Events Center for Cardiovascular Outcomes Research and Education (TRACE-CORE), University of Massachusetts Medical School, Worcester, Massachusetts.

2. Improving Cardiovascular Care and Outcomes in Regions and States (ICCOORS), University of Washington, Seattle, Washington.

3. Massachusetts Health Outcomes Research Institute (MHI), Boston University, Boston, Massachusetts.

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2. Center for Cardiovascular Outcomes Research at Yale University, New Haven, CT (principal investigators: Jeptha Curtis, MD, and Harlan M. Krumholz, MD, SM; U01HL105270)

3. Center for Health Insurance Reform, Cardiovascular Outcomes and Disparities, Boston Medical Center, Boston, MA (principal investigator: Nancy R. Kressin, PhD; U01HL105342)

The RCU facilitates coordination of research activities and communications between and among awardees and the NHLBI. The unit reviews CCOR research proposals and seeks to establish data standardization and sharing when appropriate; convenes meetings and maintains communications; promotes the cross-center development of early-stage outcomes investigators; fosters collaboration both across the centers and with the larger outcomes research community; and provides programmatic evaluation. The RCU is located at Duke Clinical Research Institute at Duke University School of Medicine, Durham, NC (principal investigator: Eric Peterson, MD, MPH; U01HL107023).

The overall CCOR vision is to innovate the science of cardiovascular healthcare delivery and patient outcomes while aiming for the program to be more than the sum of its individual parts. The program seeks to achieve this goal through (1) collaboration within the CCORS and other scientific groups engaged in cardiovascular outcomes research; (2) methodological innovation; and (3) development of future cardiovascular outcomes researchers.

Structure of the Program

If you want to be incrementally better: be competitive.
If you want to be exponentially better: be cooperative.

—Unknown

Similar to other collaborative programs, the structure of the CCOR program facilitates cooperation (Figure). Although projects do not use a common study protocol, the program encourages investigators to forge cross-program collaborations and to share knowledge to foster a potentially synergistic outcome from these individually funded grants. The participating centers are linked to each other through meetings, idea exchanges, and networking and development opportunities for early stage investigators (ESIs) and trainees. These activities are facilitated by the NHLBI Project Office, the RCU, and the Steering Committee, which oversees the development of collaborative operating policies. An External Advisory Board provides guidance and recommendations to the CCOR Steering Committee with the hope of enhancing the impact of the research conducted, as well as promoting collaboration in the overall program.

Faculty Development and Training

A key area of focus for the CCOR program is developing ESIs to become independently funded cardiovascular outcomes researchers. Activities in the CCOR program are complementary to local institutional efforts and provide practical experience and preliminary data for future grant applications. Center leadership identified several ESIs to have significant roles in center projects and established a plan for mentorship and career development. Cross-institutional mentorship in the CCOR program aims to provide a broad perspective, diverse expertise, and new collaborations. ESIs participate in cross-program workshops with invited experts focused on selected topics relevant to their research; works-in-progress sessions and steering committee meetings to interact with senior investigators who provide feedback and input on manuscripts and grant proposals; and ESI network meetings to review mentorship relations and provide peer support. ESIs across programs collaborate to present findings from their research at national meetings (eg, recent session at the 2012 annual scientific meeting of the Gerontological Society of America).

Program Evaluation

To elucidate the value of the research being conducted across the Centers, the CCOR program is detailing inputs (ie, how many and what kind of scientists, participants, and...
funding) and outputs (ie, knowledge, products, better health) that validate accountability to funding agencies and stakeholders. The evaluation includes center-specific metrics (eg, project milestones) and metrics related to cross-program collaboration (eg, cross-program publications and presentations). Center milestones focus on tasks needed to complete specific aims, as well as overall metrics for monitoring performance. For example, the University of Massachusetts center is recruiting participants. Its metrics include quarterly recruitment and retention goals, as well as the number of ancillary studies submitted and graduate theses completed by ESIs. Importantly, the program as a whole will be collectively evaluated by all entities of the network with an emphasis on establishing collaborative activities across the centers and the RCU. Examples of cross-program metrics include cross-center manuscripts, editorials, and presentations; the number of cross-center applications to funding agencies; and the establishment of mentoring relationships across centers for ESIs.

Center Research Interests

University of Massachusetts Medical School

TRACE-CORE has 2 overall goals: (1) advancing the science of cardiovascular disease outcomes by providing critical new knowledge on quality measurement and health disparities and (2) training the next generation of cardiovascular outcomes researchers.

TRACE-CORE focuses on acute coronary syndromes (ACS), for which ≈1.5 million Americans are hospitalized annually. Although in-hospital and 30-day mortality for ACS has markedly declined, evidence-based interventions are often underprescribed or prescribed but not followed by patients. Furthermore, analysis of Medicare claims data finds that 20% of patients hospitalized with an acute myocardial infarction are rehospitalized within 30 days. Pharmacological and lifestyle-based interventions have proven successful in preventing recurrent ACS events that require rehospitalization. High-quality care during transition from hospital to home may reduce rehospitalization rate. Currently, there are no tools to comprehensively measure ACS transition quality. Furthermore, there is insufficient understanding of the complex relation between transition quality and repeatedly documented ACS health disparities. Project 1 of TRACE-CORE, The Transitions Project, is directed at these gaps.

Project 2: The Action Scores Project

ACS decisions depend on accurate risk assessment. Predictive indices, such as the Framingham Risk Score for general populations and the Global Registry of Acute Coronary Events Risk Score for hospitalized ACS patients, are widely used in research but less frequently used in routine care. Use is limited because these scores (1) place limited emphasis on modifiable factors; (2) exclude patient-centered factors such as symptoms; (3) exclude patient complexity, such as cognitive impairment; and (4) focus on clinical end points (eg, mortality, readmission) without considering quality of life. The TRACE-CORE Action Scores Project builds on the Framingham Risk Score tradition, separating modifiable from nonmodifiable risk while considering patient-centered measures, such as quality of life.

TRACE-CORE is recruiting an inception cohort of 2500 patients enrolled at an index hospitalization for ACS and followed up for 12 to 24 months. The cohort is recruited from urban, suburban, and rural areas of Massachusetts and Georgia from 6 community teaching and nonteaching hospitals. TRACE-CORE (1) reviews inpatient medical records of the index ACS hospitalizations and conducts baseline in-person interviews; (2) conducts follow-up interviews at 1, 3, 6, and 12 months after discharge to collect data, including quality of life, cognitive impairment, medication adherence, and health behavior information, as well as patient-reported outcomes, such as shortness of breath; and (3) follows patient vital status and readmission status for up to 2 years through National Death Index and administrative data.

In the spirit of the CCOR program, TRACE-CORE represents a convergence of (1) standard principles of primary data collection for observational studies and their analyses and (2) outcomes and effectiveness research approaches directly relevant to healthcare delivery and health-related quality of life.

Yale University

The CCOR at Yale University is dedicated to the generation and dissemination of scientifically based knowledge that can be used by patients, practitioners, and policy makers to improve clinical decision making and healthcare policy. CCOR has developed 2 complementary projects that seek to elucidate organizational and regional patterns of care, to link them with outcomes, and to uncover relations that might assist in efforts to improve the effectiveness and efficiency of healthcare delivery. Furthermore, both projects provide opportunities for ESIs to participate substantively as the leaders of individual studies.

Project 1: Examining Novel Cardiovascular Outcomes and Regional Effects

The Examining Novel Cardiovascular Outcomes and Regional Effects (ENCORE) project leverages large existing databases and innovative analytic approaches to characterize hospital and regional performance and patient-level outcomes; to assess patient, organizational, and regional time trends; and to determine factors associated with performance and improvement. The effort includes a focus on short- and long-term clinical outcomes, as well as costs of care.

This project is developing methodological approaches to illuminate previously hidden patterns in the data, promoting the identification and determinants of disparities in performance that may be tracked by patient and regional characteristics, revealing associations that indicate factors necessary to excel in clinical effectiveness and efficiency, elucidating obstacles and opportunities to improve care, and establishing partnerships with organizations to facilitate the dissemination and appropriate adoption of new knowledge.

Project 2: Translating Outstanding Performance in Percutaneous Coronary Intervention

The Translating Outstanding Performance in Percutaneous Coronary Intervention (TOP PCI) project uses a mixed-methods approach, combining qualitative and quantitative research methods approach, combining qualitative and quantitative research
methodology to identify the enabling structures associated with outstanding hospital performance on 30-day mortality and readmission after percutaneous coronary intervention. During the first phase, the team conducts in-depth interviews of key informants at 10 to 15 high- and low-performing sites and uses this information to develop hypotheses regarding the organizational strategies (ie, structures, processes, hospital internal environments) associated with high and low hospital performance. During the second phase, the team tests these hypotheses using a Web-based survey administered to a sample of the >1000 percutaneous coronary intervention hospitals that currently participate in the CathPCI Registry. The knowledge generated will contribute to hospitals' performance improvement efforts and will be disseminated through collaboration with key partner organizations.

**Boston Medical Center/Boston University School of Medicine**

A central policy assumption in the United States today is that expanding health insurance coverage will improve access to health care and patient outcomes and make each more equitable. The state of Massachusetts is the site of a key policy-relevant natural experiment and is the ideal setting to examine the effects of gaining coverage on access to and use of care for cardiovascular conditions. The Center for Health Insurance Reform, Cardiovascular Outcomes, and Disparities is based on the Health/Care Disparities Research Program within the Department of Medicine of the Boston University School of Medicine and at Boston Medical Center, the largest urban safety net hospital in New England.

**Project 1: The Effects of Massachusetts Health Reform on Cardiovascular Outcomes and Disparities**

There has been little research using objective measures of healthcare utilization and outcomes related to the coverage expansion in Massachusetts. Changes in access to outpatient care under the reform can be examined indirectly in the absence of an all-payer outpatient data source. Investigators assess 3 measures of access to outpatient care: (1) changes in the use of referral-sensitive procedures; (2) hospitalizations for ambulatory care sensitive conditions (those believed to be preventable by access to ambulatory care within the weeks before admission)\(^1\); and (3) 30-day hospital readmissions, which are believed to be a marker of access to outpatient care because post-hospital discharge access to follow-up outpatient care is critical to avoiding rehospitalizations. The center will use inpatient administrative data on adults age 21 to 64 from 4 states, including Massachusetts, that have nearly complete race and ethnicity indicators, sizable minority populations, and diagnosis and cost data for each admission. Data from 2004 to 2010 will be analyzed, encompassing the years before and after the 2006 Massachusetts health reform implementation, to compare changes in outcomes.

**Project 2: Did Massachusetts Health Reform Reduce Disparities in Outcomes After Venous Thromboembolism, and at What Cost?**

Venous thromboembolism (VTE) is common, costly, and often fatal. Blacks have higher rates of VTE and worse prognoses,\(^2\) with a higher mortality after pulmonary embolus\(^3\) and higher rates of complications\(^2\) and readmissions\(^3\) after VTE. Warfarin anticoagulation is the mainstay of VTE therapy, but limitations in accessing quality anticoagulation care likely contribute to disparities in outcomes. Comprehensive insurance coverage may enhance access to community-based pharmacies, dedicated anticoagulation clinics, primary care, and home-care services that may contribute to improved outcomes. The team will use a data set comprising a diverse and high-risk population to examine outcomes (ie, recurrent VTE, major hemorrhage, mortality, quality of life, and costs) and disparities in outcomes, before and after health insurance reform. The analysis will use disease simulation, an integrative analysis technique that synthesizes acute- and subacute-phase outcomes in subpopulations tracked by a clinical database with long-term sequelae data from longitudinal studies of VTE.

The 2 projects at the center are led by general internist ESIs with expertise in health services and disparities research who will develop further proficiency in cardiovascular outcomes research through these activities.

**Cross-program Collaboration**

The CCOR program was designed to conduct research at each center and to facilitate collaboration to support methods innovation, ESI development, and overall synergy. Attaining these goals is challenged by different themes and independent projects at each individual center. The CCOR program has taken several steps to overcome these challenges and to promote collaborative opportunities.

Perhaps the greatest strengths of the program are the breadth of methodologic approaches, the differences among protocols, and the diverse expertise across the network. Open discussion of challenges and ongoing progress at each center at steering committee meetings and meetings of the External Advisory Board have resulted in creative solutions, enhanced analyses, and new mentoring opportunities. These collaborations have been achieved through the sharing of protocols, regular meetings both in person and by teleconference, and a Web site to support communication. Some specific examples include a collaboratively planned and executed concurrent session at the American Heart Association Quality of Care and Outcomes Research 2012 Scientific Sessions. The centers have convened brainstorming sessions with External Advisory Board members and investigators from the RCU to develop strategies to overcome center-specific research challenges that have arisen. Future plans include a State of the Science meeting, engaging other key cardiovascular outcomes research expertise; collaborative methodological research projects conducted by statisticians across the centers to deal with issues of confounding, missing data, and so on; and rotating conferences dedicated to broaden cross-center mentorship for ESIs.

**Limitations of the Research Portfolio**

Centers focus on specific cardiovascular conditions, and thus the portfolio is limited to conditions studied and is
not comprehensive in the field of cardiovascular outcomes research. Projects also have select populations, which limit generalizability. Lastly, most studies are observational. Although this observational work has the potential to lay the foundation for future clinical trials, such designs are not represented in the current CCOR program. Trials remain a crucial design for testing novel interventions in the field of outcomes research.

Conclusions

With the continuing evolution of healthcare policy and the rapid pace of clinical discovery, high-quality outcomes research is playing an increasingly important role in the generation of knowledge necessary to improve clinical decision making and healthcare delivery to optimize patient outcomes. The CCOR program encourages both scientific rigor and cross-program collaboration. Centers conduct innovative research while working with each other, the RCU, and the NHLBI to capitalize on the multidisciplinary, cross-institutional, and intellectual network in hopes of advancing the science of care delivery and outcomes beyond what any individual unit could achieve alone.

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