Abstract—The National Heart, Lung, and Blood Institute convened a working group on outcomes research in cardiovascular disease (CVD). The working group sought to provide guidance on research priorities in outcomes research related to CVD. For the purposes of this document, “outcomes research” is defined as investigative endeavors that generate knowledge to improve clinical decision making and healthcare delivery to optimize patient outcomes. The working group identified the following priority areas: (1) national surveillance projects for high-prevalence CV conditions; (2) patient-centered care; (3) translation of the best science into clinical practice; and (4) studies that place the cost of interventions in the context of their real-world effectiveness. Within each of these topics, the working group described examples of initiatives that could serve the Institute and the public. In addition, the group identified the following areas that are important to the field: (1) promotion of the use of existing data; (2) facilitation of collaborations with other federal agencies; (3) investigations into the basic science of outcomes research, with an emphasis on methodological advances; (4) strengthening of appropriate study sections with individuals who have expertise in outcomes research; and (5) expansion of opportunities to train new outcomes research investigators. The working group concluded that a dedicated investment in CV outcomes research could directly improve the care delivered in the United States. (Circulation. 2005;111:3158-3166.)

Key Words: outcome assessment ■ cardiovascular diseases ■ patients ■ statistics

Outcomes research is a field directed to the study and eventual improvement of the end results of health care.1 “Outcomes research” can be defined as the study of the delivery and consequences of health care on outcomes from the perspective of patients, practitioners, and the healthcare system. Outcomes research focuses particularly on providing evidence to assess and promote the effectiveness of therapeutic interventions, enhancing the migration of best practice to clinical practice, improving decision making, elevating the quality of care, and supporting the optimal allocation of resources for all patients. Consequently, the research has a proximate and immediate connection to patient care and healthcare delivery.

Despite the accelerating pace of basic and traditional clinical research in cardiovascular disease (CVD), there remains ample opportunity to improve clinical practice and healthcare delivery. Clinicians and policy makers often lack knowledge about gaps in healthcare delivery, disparities and inefficiencies, ineffectiveness of seemingly “proven” strategies, and the cumulative impact of interventions on the lives of patients. There is also a dearth of knowledge about how best to promote CV health and healthcare delivery in practice.1-3 These gaps in knowledge hinder our ability to advance medical care even as our understanding of health and disease expands. We lack basic information about contemporary patterns of care and have a limited array of valid tools and...
strategies to quantify and improve clinical performance. We often demonstrate efficacy of treatments but commonly do not know the effectiveness of different clinical strategies in actual practice, as well as the impediments to achieving the true potential of the best interventions. We often do not know the impact of clinical and policy strategies on a broad range of patient outcomes, other than mortality and events. We lack basic information that would enhance clinical decision making from the patient’s perspective. We lack evidence about how to involve patients in decision making and translate scientific findings into clinical practice so that outstanding quality of care is universally available.

Outcomes research can generate knowledge about the effectiveness of clinical strategies; the health and healthcare experiences of patients (including measures of health status); quality of care; the balance of costs and effectiveness; and the best way to optimize clinical decision making. Outcomes research can be descriptive and prescriptive, focusing on current deficiencies in knowledge or interventions to improve clinical practice. Thus, outcomes research aims to inform patients, providers, healthcare systems, payers, and policy makers of the effects of health care and provide evidence to support the development of strategies (at the patient, provider, and system levels) that will help address universal health needs. CV outcomes research applies these aims and approaches specifically to the prevention or treatment of CVD.

Outcomes research is not defined by a particular methodology but rather by its objective to generate knowledge that can improve clinical decision making and healthcare delivery, leading to the best patient outcomes for the resources that are available. It can employ a variety of methodological approaches, including nonexperimental (observational) designs, as well as quasi-experimental or clinical trial approaches to test interventions, whichever is most suited to the specific research question. Outcomes research draws from the disciplines of clinical epidemiology, statistics, health services research, psychology, sociology, anthropology, economics, informatics, and management sciences.

The National Heart, Lung, and Blood Institute (NHLBI) convened a working group on outcomes research in CVD to provide advice on research priorities in this area. The goals of CV outcomes research are closely aligned with a number of existing federal initiatives:

- **Healthy People 2010** sets forth ambitious goals to reduce CVD risk, improve CVD outcomes, and eliminate health disparities. Attaining these goals will require effective programs that actively support the integration of existing knowledge and discoveries into communities and clinical practice.

- The Agency for Healthcare Research and Quality (AHRQ), the Centers for Disease Control and Prevention (CDC), the Centers for Medicare and Medicaid Services (CMS), the Department of Veterans Affairs, and the Department of Defense are all seeking to promote the best “real-world” strategies for the prevention and treatment of disease; to determine the success of healthcare strategies by assessing patient-centered outcomes; to measure adherence to “best practices” (usually representing those embodied in clinical practice guidelines); and to develop interventions to improve the performance of the healthcare system. Success in these endeavors will depend on research that can identify best clinical practices, evaluate different clinical strategies, identify wasteful resource utilization, explore the involvement of patients in decision making, and study the effects of clinical and policy-related decisions on CV health.

- The National Academy of Sciences’ Institute of Medicine (IOM) has published a “blueprint” for improving healthcare delivery in a document entitled “Crossing the Quality Chasm: a New Health System for the 21st Century.” This report identified 6 core goals for the future of American health care: safety, effectiveness, equity, efficiency, timeliness, and patient centeredness. There is an urgent need for research into how best to attain the IOM’s goals in patients with CVD and how these domains, which are not currently a focus of traditional CV clinical research, are important topics for investigation.

- Many federal organizations, including the NHLBI, have strategic plans to reduce health disparities, and the newly created National Center for Minority Health and Health Disparities is championing national efforts to identify and remediate disparities in CV care. Central to the elimination of health disparities is research that identifies disparities, assesses their consequences, and develops and evaluates the effectiveness of interventions to eliminate them. This research would also explore the causes of differences in outcomes between racial, ethnic, and vulnerable socioeconomic groups. The working group believes that the NHLBI can take a leading role in fostering research to support these and other efforts related to CVD care and outcomes through programmatic commitments to CV outcomes research that will ensure that health care at the patient, provider, and health system level is supported by a strong scientific foundation built on contemporary, patient-centered, clinician-relevant information.

**Process Used to Generate This Report**

Working group members, whose backgrounds cover a broad spectrum of experience within outcomes research, considered a range of possible research areas, current gaps in knowledge, and the expected CV trends in the nation. The group first reviewed ongoing programs and funded projects within the NHLBI. Related initiatives and priorities set by other National Institutes of Health (NIH) and federal agencies were also considered. The group met and held conference calls to reach consensus about the research recommendation priorities.

The working group sought to identify high-priority areas in CV outcomes research that deserve support and to provide examples of important areas for future investigation. The objective was not to provide a comprehensive list of topics in CV outcomes research but rather to identify research directions that the working group believes require the most immediate action, with particular attention given to the stated missions of the NHLBI and the NIH.
Having described specific priority research domains and topics, the working group concluded that directed programmatic commitments are needed to support the growth and development of CV outcomes research. These investments, which complement laboratory research, will accelerate the optimization of care and outcomes for individuals with or at risk for CVD.

Research Recommendations

The working group identified several priority areas, including the development of national surveillance projects for high-prevalence CV conditions, the promotion of patient-centered care, definition and implementation of best practice, and expansion of studies that consider the cost of interventions in the context of their effectiveness. Within each of these topics, the working group described examples of initiatives that could serve the Institute and the public. In addition, the group identified several areas critical to the success of CV outcomes research, including promoting the use of existing data and collaboration with other federal agencies, augmenting the methodology of outcomes research, training of new investigators, and increasing study section support.

Top-Tier Priorities

National Surveillance of CV Care and Outcomes

Background

Large-scale, NHLBI-funded, population-based epidemiological studies, such as the Framingham Heart Study and the Cardiovascular Health Study, have helped define the prevalence, determinants, incidence, and consequences of CVD. However, there is a paucity of resources directed to assess the quality of CV care and health outcomes of community-based populations with or at risk for CVD. For example, the Worcester Heart Attack Study has provided important insights but is geographically limited and does not include long-term outcomes aside from mortality. The Atherosclerosis Risk in Communities surveillance identified myocardial infarction (MI) and coronary heart disease death in 4 communities (Minneapolis, Minn, suburbs; Forsyth County, NC; Washington County, Md; and Jackson, Miss) by review of hospital-discharge diagnosis codes, medical record abstraction, and death certificates. It has no follow-up component except for linking, when appropriate, of patients’ events occurring within 30 days of one another. The Minnesota Heart Survey identified MI and coronary heart disease mortality in the Minneapolis/St Paul area by review of hospital-discharge diagnosis codes, medical record abstraction, and death certificates. It also had an out-of-hospital sudden cardiac death autopsy component. It did not involve any patient interviews.

Other agencies have databases and projects that are relevant to surveillance, but they also have their limitations. The administrative databases of AHRQ provide information about hospitalizations but lack clinical detail and data on long-term outcomes. The CDC conducts national surveys of risk factors and behaviors but does not focus on clinical CV conditions. Similarly, the surveys by AHRQ provide important insights about access and health behaviors but do not focus on clinical conditions. The National Health and Nutrition Examination Survey, conducted by the CDC’s National Center for Health Statistics, collects information concerning general population health and diet but does not address CV-specific quality of care or a wide range of patient outcomes.

Thus, despite rapid changes in CV knowledge, efficacious treatments, and technical capabilities, we have no established national capacity to assess how technologies and treatments are used or to measure their performance when implemented in real-world conditions. The generalizability of randomized, controlled trials and other efficacy studies is rarely formally assessed but often presumed. Answers to questions concerning population- and patient-level effects of health care across a broad spectrum of outcomes, including mortality, events, quality of life, and cost, are not available. For example, how will drug-eluting stents be adopted and perform in practice? What determines the adoption of internal defibrillators, are there disparities in their use, and what is their impact on patients’ lives in actual clinical practice? Similarly, the identification of problems with medications or devices often comes through the fortuitous reporting of individual cases rather than an existing systematic process of evaluation.

Given the substantial commitment of resources to improving CV health and health care, a national CV surveillance system could provide the infrastructure to develop new insights into improving practice and target future efforts to improve care and outcomes. The CMS Cooperative Cardiovascular Project (CCP) was a limited example of such a system. The CCP was developed as a large, 1-time, cross-sectional evaluation of acute MI care in elderly patients. This clinically rich database has supported many studies addressing the clinical management of acute MI in the elderly. The CCP was able to produce such research because it generated a database that included a representative national sample and detailed medical record abstraction of information about processes of care and clinical events, supplemented by additional physician and hospital data. Despite the immense value of the CCP, the study had notable limitations, including its limited time frame (1994–1996), the lack of data on quality of life or functional status, the exclusive focus on Medicare fee-for-service patients, and the absence of information on outpatient treatment patterns.

Other groups have also sought to provide data on CV care and outcomes. The Veterans Administration has studied the relationship between patterns of healthcare delivery and outcomes through its Quality Enhancement Research Initiative (QUERI) groups. The heart failure QUERI has used administrative data to identify a national cohort of veterans with heart failure, and efforts are under way to link this resource to clinical and outcomes data. Professional medical societies have also initiated CV procedure registries, including the Society for Thoracic Surgeons’ National Cardiac Surgery Database and the American College of Cardiology’s National CVD Registry for percutaneous coronary interventions. Finally, there are clinical registries funded by pharmaceutical and medical device companies or nonprofit organizations. Such condition- or procedure-specific registries have
added substantially to the medical literature, but most of these current efforts are limited by their focus on the treatment of hospitalized patients. Moreover, the databases frequently lack follow-up information, information on posthospitalization outcomes or utilization of care, and reliable assessment of detailed patient-centered outcomes and are often restricted to limited geographic areas, age groups, or other selected patient populations. They also collect information only from hospitals that volunteer to participate. In addition, health services researchers frequently have limited access to these proprietary commercial databases, and their use is commonly aligned with company interests.18,19

Another example of such a proposed surveillance system has been developed in the area of cancer research, with the National Cancer Institute’s Cancer Care Outcomes Research and Surveillance (CanCORS) Consortium (http://www.healthservices.cancer.gov/cancors/).20 The CanCORS Consortium is collecting detailed primary data from medical records and surveys of patients and providers to understand variations in the treatment and outcomes of lung cancer and colorectal cancer in 5 states and regions, 5 large health plans, and the Veterans Administration system. Finally, the Canadian approach of supporting national outcomes research teams may also serve as a template.

**Recommendation**

The first is to establish a national surveillance program for CV care and outcomes. We recommend a series of national or multiregional clinical cohort studies that would bridge the gap between evidence and practice and provide information on practice, care, and outcomes. These studies should be undertaken for several key CVD conditions, designed to describe, with longitudinal data and adequate clinical detail, population-based patterns of care across the United States and their short- and long-term consequences. We recommend that initial priority conditions be acute coronary syndromes, heart failure, and atrial fibrillation. We also recommend that selected CV procedures (eg, percutaneous coronary intervention, coronary artery bypass surgery, and implantable cardioverter-defibrillators) be studied on the basis of their high prevalence, impact on patients and healthcare systems, and variations in clinical strategies and outcomes.

These studies will provide descriptions of current practice patterns and their associations with patient outcomes, support the development of performance measures for quality, allow the identification of best practices from which quality improvement initiatives may be developed and tested, stimulate discussion about best practice, generate evidence about the effect of national healthcare policies, and identify topics for future research. Those studies that enroll patients by condition (rather than procedure) can also provide the foundation for the development and testing of risk-stratification models and the ability to appreciate which patient subsets benefit most from procedures and other interventions. Finally, registries of this type can lay the foundation for the existence of an established network of investigators to describe, refine, and test novel strategies that will accelerate the translation of new scientific knowledge into clinical practice.21

Because of the urgency in addressing known and suspected healthcare disparities, the working group suggests that racial and ethnic minority groups, individuals in poverty, older persons, and/or other vulnerable subgroups should be well represented to permit appropriate comparisons across subpopulations.

**Promoting ‘Patient-Centered’ Care**

**Background**

Recently, the IOM emphasized the need for more patient-centered care as a critical step toward improving the quality of American health care.3 Patient-centered care is that which helps clinicians “in attending to their patients’ physical and emotional needs, and maintaining or improving their quality of life” and gives patients the opportunity to be “the locus of control” in medical decision making. Key components of patient-centered care include the assessment of patient-centered health-status outcomes (eg, symptom burden, functional limitation, and health-related quality of life) and the incorporation of patients’ views about treatment into clinical decision making.

During the last 2 decades, however, valid and reliable tools have been developed to measure patient health status, including both generic and disease-specific questionnaires.22–25 Despite these advances in health-status measurement, there remain at least 3 important opportunities to improve the application of the measures. First, little is known about the impact of cardiac therapies on patients’ health status, and there is a significant gap in our understanding of the determinants of health-status outcomes in patients with CVD. Second, it has been shown that health-status measures predict subsequent mortality and morbidity in CV populations.26–28 And finally, the application of health-status measures in facilitating “shared decision making” has not been fully evaluated.29,30 Studies are needed to improve our understanding of the impact of various CVDs and therapies on patient health status, to evaluate interventions designed to improve health-status outcomes for patients with CVD31 and understand the use of these interventions in disease management, and to assess the utility of health-status measurement and elicitation of patient preferences in clinical practice to maximize patient outcomes.

**Recommendations**

The first goal is to identify determinants of patient-centered health status. We recommend studies to identify the key determinants of patient-centered health status, such as quality of life and functional status, in populations with CVD. Such studies will require the collection of longitudinal data on clinical and health-status outcomes. The knowledge generated from these studies can lead to the development of interventions to improve health status for patients with CVD and to the development of studies focused on the use of health-status data to guide clinical decision making. This recommendation overlaps with the aim stated earlier for “National Surveillance of CV Care and Outcomes.” Thus, as mentioned previously, we recommend a focus on high-prevalence conditions, such as acute and chronic ischemic heart disease, heart failure, and atrial fibrillation. In addition,
such studies should address high-risk and underserved populations, including older persons, women, and racial/ethnic minorities, as well as patients in poverty, those with multiple comorbid conditions (eg, diabetes, chronic obstructive pulmonary disease, or depression), and those in high-risk settings (eg, nursing homes).

Evaluate Patient-Centered Tools and Interventions
The working group recommends studies to evaluate the utility of patient-centered tools or interventions in clinical care. The measurement and explicit use of patient preferences to promote shared decision making and the measurement and integration of health-status information to guide management of CVD are promising approaches to increase the appropriateness and optimize the impact of clinical interventions. For example, CV health-status measures may be provided to clinicians to help identify patients at particularly high risk for subsequent adverse outcomes who may benefit from more intensive management. As another example, potentially modifiable aspects of health status (eg, depression) may be targeted for intervention. Patient-level interventions, such as patient activation and/or patient training and interventions aimed at the hospital, healthcare system, or community, are also important. Where possible, studies should include explicit evaluation of the impact of these interventions on a broad range of patient outcomes (eg, mortality, morbidity, satisfaction, and health status). Longitudinal studies will be needed to demonstrate the value of the interventions over time. A focus on high-risk and/or underserved populations should be encouraged. Studies that include a focus on chronic disease management, coordination and integration of care, access to care, and/or transitions between healthcare environments would be particularly valuable. Studies are needed in all CV populations, but those with marked health-status deficits, such as heart failure, ischemic heart disease, atrial fibrillation, peripheral arterial disease, and cerebrovascular disease, are of particular interest.

Include Patient-Centered Health-Status Outcomes in Clinical Trials
The NHLBI has been committed to the inclusion of health-status outcomes in clinical trials. The working group recommends that the NHLBI continue this support and continue considering the inclusion of CV health-status measures (ie, formal measures of symptom burden, functional status, and health-related quality of life) in all relevant CV clinical trials that it sponsors. A workshop on integrating health status into CV studies might be an appropriate approach to pursue this recommendation.

Translating Best Practice Into Clinical Practice
Translating best practice into clinical practice requires that best practice in the real world be defined, that we generate evidence about how to implement best practice, and that we ensure patients’ involvement in their own care.

Defining Best Practice
Background
Many clinical decisions lack a strong evidence base, resulting in uncertainty about what constitutes optimal care. Thus, data are needed concerning the comparative safety and effectiveness of different clinical strategies in real-world settings.

Also critical to improving care is defining best practice based on the scientific literature. This effort requires the impartial, methodologically rigorous synthesis of the research literature into evidence-based guidelines for care. Importantly, this effort should also include rapid integration of new evidence on a real-time basis. What is currently lacking is a professionally recognized core group of multidisciplinary experts, such as those found in the AHRQ Evidence-Based Practice Centers, to provide a rigorous synthesis of the evidence to support the continuous integration of new evidence. The effort could directly support the development and revision of CV clinical practice guidelines, conducted by professional societies such as the American College of Cardiology and the American Heart Association.

Recommendations
A major goal should be to evaluate the effectiveness of CV treatments and strategies. We propose that the NHLBI enhance its current portfolio of studies to evaluate further the safety and effectiveness of CV treatments and clinical strategies. An effectiveness study is one that tests an intervention in an applied (real-world) setting, where the effects of the intervention are affected by both efficacy and adherence/delivery. Studies consistent with this aim may be observational or experimental. Randomized trials have the particular strength of allocating measured and unmeasured factors among the various study groups. Observational study designs can provide important evidence to guide practice based on real-world experience.32 They also may have particular utility in quantifying the risks of interventions as they are applied beyond the original efficacy studies.

Support Evidence-Based Reviews of CV Treatments
We propose that the NHLBI provide support for CV evidence-based centers, perhaps in collaboration with AHRQ and the professional societies, which would be specifically charged to provide research and analytical support for the development of empirical, unbiased evidence reviews according to accepted evidence synthesis and meta-analytical methods. The evidence-based centers would provide adequate resources to conduct systematic literature searches needed to support scientifically based national CV care guidelines that are being conducted by professional societies. They would also continuously monitor the published literature and provide real-time updates to specific guidelines as needed. The topics identified through the systematic reviews as having insufficient evidence for clinical care recommendations should then be referred back to the NHLBI and disseminated to potential investigators as topics for future research. This effort should be synergistic, not redundant, with current AHRQ efforts.

Implementing Best Practices
Background
Numerous studies have documented a large gap between evidence-based care recommendations and the actual care delivered in community practice.16,33–36 These “lost opportunities” have real consequences for patients.37 Thus, there is a
need to generate knowledge concerning the means by which to improve physicians’ adoption of optimal therapies in routine CV care. To date, intervention studies designed to increase physician compliance with practice guidelines have often lacked adequate controls and have tended to assess single rather than multimodal interventions. Such assessments also have generally focused on hospital-based treatment rather than the outpatient setting. Furthermore, nearly all of the studies have assessed changes in provider behavior over a limited time period, creating uncertainty about the durability of these approaches. Finally, there have been limitations in terms of the studies’ power and scope, affecting both their internal and external validity. Although these early demonstration projects were important first steps for the field, there remains much to do in terms of identifying optimal strategies for implementing best practices.

**Recommendations**

There is a need to identify factors associated with provider delivery of effective therapies. We propose a call for observational qualitative and quantitative research to identify strategies to evaluate and promote physicians’ adherence to evidence-based guidelines, as well as to characterize key structure and process features of successful implementation of best practices. These efforts would investigate potential causes for the wide national variation in guideline adherence. Studies may employ existing data sources, utilize the surveillance initiative proposed earlier, or alternatively, gather new additional data on structure and/or process variables that explain variations in treatment. The goal of this research is to identify successful practices and/or organizational features that can be applied widely. Study of existing “leading centers” could generate novel, potential approaches for improving provider adherence that could then be rigorously tested.

**Test Interventions to Improve Provider Delivery of Effective Therapies**

We recommend the continuation and expansion of programs such as NHLBI-RFA HL-01-011 (Trials Assessing Innovative Strategies to Improve Clinical Practice Through Guidelines in Heart, Lung, and Blood Diseases), which was a 1-time call for research “to evaluate interventions that represent innovative strategies that can be employed in clinical practice to improve implementation of national, evidence-based clinical practice guidelines.” Areas of highest impact would include primary and secondary prevention interventions, acute coronary syndromes, and heart failure. Particular interest should be focused on the transition from inpatient to outpatient settings and longitudinal care. Although unique interventions in a particular setting are of interest, priority should be given to those interventions that can be applied broadly, ideally on a regional or national level.

**Involving Patients in Care**

**Background**

Advances in the prevention and treatment of CVD are often not fully realized because of limited involvement by patients in their own care. Rates of nonadherence to prescribed regimens of pharmacotherapy, exercise, diet, smoking cessation, and self-monitoring often range from 30% to 50%. Patient adherence is also diminished by discontinuities in the long-term management of therapeutic regimens, including the paucity of systems to facilitate feedback to patients about their progress in achieving therapeutic goals. The issue of patient adherence becomes even more salient as management guidelines advocate extensive combination therapy for many conditions.

Previous research has predominantly focused on hospitals and primary care practices. Critical opportunities for improvement in patient adherence exist for self-management at the transition from the home setting to hospital or emergency department care and from hospital care to the outpatient setting. Maximizing the benefits of pharmacotherapy and lifestyle approaches will require a sustained and substantial commitment to research initiatives on patient adherence that will focus on the patient as well as on the provider and the healthcare environment.

**Recommendations**

**Study New Approaches to Improving Patient Adherence**

The working group proposes support for research that characterizes and enhances patients’ adherence to medication and lifestyle regimens, with the consideration of incorporating proven models of behavioral change. Research on patient adherence has tended to be disease-specific, without sufficient attention to behavioral and cultural factors that may differ among racial, ethnic, and socioeconomic groups and modify the effectiveness of preventive and treatment regimens. The best strategies will be those that mobilize not only the resources and capabilities of individual patients but also their network of family and friends. As part of this research, there is a need for improved approaches for measuring adherence. These efforts would build on recent NHLBI initiatives that focused on understanding and promoting patient adherence. For example, HL-01-005 (Overcoming Barriers to Treatment Adherence in Minorities and Persons Living in Poverty) sought to evaluate interventions in clinical care settings designed to improve adherence to medically prescribed lifestyle and medication regimens. However, it was limited to specific groups and required a randomized study design. Future initiatives built on this effort could be less restrictive and include other study designs that might be useful in addressing this topic.

**Study Novel Approaches to Enhance Patient Self-Management**

The working group proposes that the NHLBI foster research on the development and clinical implementation of technologies and systems that enhance patients’ participation in monitoring and management of chronic CV conditions. Devices for self-monitoring parameters such as symptoms, health status, blood pressure, anticoagulation, and blood glucose in the home environment are available, yet these devices are not well integrated into treatment practice. Likewise, interactive technologies such as Web-based instruction and feedback that can support patient responses to these data are infrequently utilized. Innovative ways of organizing healthcare personnel and systems of care to empower patients
and enhance their involvement in care are also needed. Research support should be directed to evaluate the effectiveness of advanced interactive technologies and systems that incorporate not only instruction but also ongoing monitoring and corrective feedback.

Studies That Place the Cost of Interventions in the Context of Their Real-World Effectiveness

Background

In an era in which healthcare costs are rapidly increasing, society is demanding that health care offer good value by providing good outcomes at a fair price. Thus, it is no longer sufficient to show that a test predicts outcome, that a therapy is efficacious, or that a pattern of practice can be proven to be effective. It is also critically important to demonstrate that these services justify their associated costs.

Recommendation

A major aim is to study cost-effectiveness of clinical strategies. The working group recommends that the NHLBI continue including cost-effectiveness analyses in relevant CV clinical trials that it sponsors. Establishing cost-effectiveness in real-world settings is equally important to the efficacy evaluations in clinical trials. We recommend that the NHLBI consider fostering investigations of the economic consequences of alternative clinical strategies to reduce risk and diagnose and treat disease in real-world settings. These investigations, funded by nonindustry sources, are important for guiding reimbursement policies and resource allocation.

Areas That Are Critical to the Success of CVD Outcomes Research

Several areas are critical to the success of CVD outcomes research. These include promotion of the use of existing data, development and refinement of analytical tools in outcomes research, support of trainees and young investigators, and expansion of study sections’ expertise in outcomes research.

Promotion of Research by Using Existing Databases

The investment in studies by the NHLBI and other federal agencies has produced several detailed datasets that have tremendous potential to yield important insights even after the specific aims of the project have been addressed. The NHLBI has done an excellent job of making datasets available to investigators, and support for access to this national resource should be continued. In addition, we propose that mechanisms be expanded to provide funding support for proposals that make appropriate use of existing data to address important research questions. This mechanism ideally would have a rapid evaluation cycle and be directed specifically toward data analysis. There are also opportunities for collaboration with other federal agencies in the collection and dissemination of data to provide important insights that can advance clinical science. These partnerships could have a substantial impact on the ability of researchers to produce knowledge that can guide practice and policy.

Development and Refinement of Analytical Tools in Outcomes Research

We need to promote the development of advanced analytical tools from other disciplines that can be applied to outcomes research. Such disciplines include statistics, economics, and the behavioral sciences. Examples of powerful tools used in these disciplines but generally not supported in CV research efforts are hierarchical linear models (for nested study designs, such as group-randomized trials of physician-level interventions); propensity scores and instrumental variables (for causal inferences from observational evaluation); and structural equation modeling (for the study of unobservable categories underlying observed phenomena, such as components of CV quality of care). Basic methodological work also needs to be undertaken to quantify potential differences among providers in their quality of care; to develop and refine tools to assess patient-centered data (eg, preferences and health status), including strategies to overcome barriers to the use of these data in clinical practice; and to advance the methodology of the handling of missing data. Finally, research methods are needed to enhance appropriate interpretation of data on health status and resource use. If CV researchers are to use these advanced tools, methodological research to further develop the tools should also be supported. To support the interdisciplinary work in this area, the NHLBI could consider program project grants in outcomes research.

Support Trainees/Young Investigators

Ultimately, CV outcomes research will be defined by the investigators who are dedicated to this field. As the field grows and matures, an essential component will be the specific training and career development of young investigators. Training needs to include the development of skills necessary to conduct high-level outcomes research and provision of strong mentorship from established outcomes researchers. To this end, we recommend the formation of career development awards (KO8/K23) within the NHLBI specifically dedicated to CV outcomes research. The review panel for applications should consist of established outcomes investigators with multidisciplinary representation. In addition to the standard requirements for KO8/K23 applicants, key components to career development awards in CV outcomes research would include the following:

- Requirement of a formal educational plan, with emphasis on the attainment of an advanced degree (eg, PhD, MPH) in an appropriate field (eg, health services research, epidemiology, statistics, public health), unless already attained. Career development awardees would be required to obtain or document prior formal didactic training in topics such as clinical epidemiology, biostatistics, health services research methods, health policy, health economics, and health systems.
- Strong local and national mentorship, including demonstration of strong local support for the development of the awardee, with commitment of protected clinical time and administrative resources.
- Local mentorship in outcomes research by one or more investigators who are established, independent outcomes researchers (ie, those with active funding and a publication track record in the field, as defined in this document) and can offer significant time commitment to the development of the awardee.
• National collaborative mentorship with established outcomes researchers in areas that will complement the applicant’s interests and promote further career development.
• Multidisciplinary mentorship and collaboration.
• An outcomes research application by the awardee that addresses one or more important outcomes research domains (eg, the priorities outlined in this document or one or more of the IOM domains of quality) and demonstrates the applicant’s increasing independence as an investigator.
• A detailed career plan from the awardee, demonstrating strong commitment to an academic career as an independent outcomes researcher and clear short- and long-term career goals.

The formation of dedicated career development awards in CV outcomes research would directly support many of the key recommendations of the NHLBI research training and career development report (November 1999), including expansion of existing training programs to address new/emerging areas, the inclusion of and emphasis on advanced education of the awardees, a strong emphasis on mentorship plans, and a multidisciplinary approach to research and mentorship.38

There is also a need for support for midcareer awards. The NIH has K18 awards (1–2 years of support for “retooling and gaining laboratory experience” for midcareer investigators who want to broaden or redirect their research). These awards are usually targeted toward a specific area of NIH interest (eg, genetics, stem cells, etc) but would also be a good mechanism for the midcareer clinician or scientist who wants to learn outcomes research methodology. We believe that the implementation of career development awards in CV outcomes research will help ensure that the NHLBI trains the future leaders in this field.

Expansion of Study Sections’ Expertise in Outcomes Research
The working group recommends that efforts be undertaken to ensure that study sections that review outcomes research applications include experts who appreciate the role of outcomes research, understand the methods employed, and understand the strengths and weaknesses of different types of research designs common to this type of work. Ensuring that study sections have appropriate representation of outcomes research investigators is crucial to the fair evaluation of applications responsive to the research priorities described in this report.

Conclusions
CV outcomes research holds great promise for providing evidence that will guide the evolution of healthcare delivery and promote a healthcare system that is safe, effective, efficient, timely, equitable, and patient centered. CV outcomes research seeks to discover new knowledge about the prevention, diagnosis, and treatment of CVD through a focus on the end results of health care and seeks to ensure the translation of best practice into clinical practice. It places emphasis on the patient and real-world settings, with the intention of addressing the practical needs of clinicians, clinical policy makers, healthcare purchasers, and patients/consumers. This document provides a road map to support investigations that are directly relevant to clinical care and complement the longer-term investments of the Institute. We believe that a dedicated investment in CV outcomes research could directly improve the care delivered in the United States.

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References
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