

The American Heart Association's Principles for Comparative Effectiveness Research

A Policy Statement From the American Heart Association

Raymond J. Gibbons, MD, FAHA, Co-Chair; Timothy J. Gardner, MD, FAHA, Co-Chair;
Jeffrey L. Anderson, MD, FAHA; Larry B. Goldstein, MD, FAHA; Neil Meltzer, MPH;
William S. Weintraub, MD, FAHA; Clyde W. Yancy, MD, FAHA;
on behalf of the American Heart Association Advocacy Coordinating Committee

Determining the comparative effectiveness of different treatment modalities provides a potentially useful approach for improving clinical decision making and patient outcomes. There are, however, differing views of the definition, scope, and application of comparative effectiveness research that have led to considerable controversy. As a mission-driven volunteer organization that focuses on optimal cardiovascular health for all Americans and on the best interests of patients with cardiovascular diseases and stroke, the American Heart Association offers the following principles on comparative effectiveness research.

A. Conducting and interpreting comparative effectiveness research according to fundamental scientific principles

1. Comparative effectiveness research should ideally build on the data provided by randomized clinical trials by evaluating medical interventions in more diverse populations and in broader clinical contexts.
2. Comparative effectiveness research should be conducted according to established scientific principles and processes, focusing on unambiguous, meaningful clinical end points and quality-of-life measures.
3. The methods, results, and applications of comparative effectiveness research need to be transparent, well validated, and adequately communicated to patients, healthcare providers, and policy makers.

B. Defining value for patients through comparative effectiveness research

1. Comparative effectiveness research may include estimates of cost and cost-effectiveness, but comparative

effectiveness research should focus on enhancing value for patients rather than minimizing costs.

2. Although comparative effectiveness research provides opportunities to address important gaps in knowledge relatively quickly, its most dramatic effects will occur over longer time frames.

3. Comparative effectiveness research is not intended to impede the development of new approaches (pharmaceuticals, devices, and diagnostic methods) but rather to facilitate the application of new technologies to those areas in which they will provide the greatest incremental benefit and value.

C. Applying comparative effectiveness research to patient treatment decisions

1. Comparative effectiveness research should focus on conditions with important public health consequences, with priority given to addressing existing gaps in scientific evidence in current clinical practice guidelines.

2. Comparative effectiveness research is not a substitute for the exercise of clinical judgment in the care of individual patients, particularly for patients at the end of life, those of advanced age, and those with multiple comorbidities.

3. Comparative effectiveness research should provide important information to guide decision making by patients and healthcare providers, but ongoing challenges will remain in the optimal delivery of high-

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

This statement was approved by the American Heart Association Advocacy Coordinating Committee on March 27, 2009. A copy of the statement is available at <http://www.americanheart.org/presenter.jhtml?identifier=3003999> by selecting either the "topic list" link or the "chronological list" link (No. LS-2046). To purchase additional reprints, call 843-216-2533 or e-mail kelle.ramsay@wolterskluwer.com.

The American Heart Association requests that this document be cited as follows: Gibbons RJ, Gardner TJ, Anderson JL, Goldstein LB, Meltzer N, Weintraub WS, Yancy CW; on behalf of the American Heart Association Advocacy Coordinating Committee. The American Heart Association's principles for comparative effectiveness research: a policy statement from the American Heart Association. *Circulation*. 2009;119:2955-2962.

Expert peer review of AHA Scientific Statements is conducted at the AHA National Center. For more on AHA statements and guidelines development, visit <http://www.americanheart.org/presenter.jhtml?identifier=3023366>.

Permissions: Multiple copies, modification, alteration, enhancement, and/or distribution of this document are not permitted without the express permission of the American Heart Association. Instructions for obtaining permission are located at <http://www.americanheart.org/presenter.jhtml?identifier=4431>. A link to the "Permission Request Form" appears on the right side of the page.

(*Circulation*. 2009;119:2955-2962.)

© 2009 American Heart Association, Inc.

Circulation is available at <http://circ.ahajournals.org>

DOI: 10.1161/CIRCULATIONAHA.109.192518

quality care and the elimination of racial and ethnic disparities.

D. Funding and oversight of comparative effectiveness research

1. The funding for comparative effectiveness research should be complementary to, and not competitive with, existing federal support for biomedical research through the National Institutes of Health.
2. Increased levels of funding will be required for comparative effectiveness research to achieve meaningful goals.
3. Any entity overseeing comparative effectiveness research should possess sufficient independence to promote credibility, efficiency, and the ability to reach controversial decisions. Such independence should be coupled with sufficient safeguards that promote accountability, fairness, and transparency.

The American Heart Association stands committed to seek input, engage in meaningful dialogue, and join in collaboration with other voluntary health organizations to help create a stronger consensus on how comparative effectiveness research can best serve the public interest.

Introduction

There are multiple challenges facing the healthcare system in the United States, and a variety of strategies and interventions will be required to effect meaningful reform. Determining the comparative effectiveness of different treatment modalities provides a potentially useful approach for improving clinical decision making and patient outcomes. There are, however, differing views of the definition, scope, and application of comparative effectiveness research that have led to considerable controversy. In this policy statement, the American Heart Association builds on its prior recommendations for healthcare reform,¹ describing the Association's principles for the conduct, purpose, application, and oversight of comparative effectiveness research.

The term *comparative effectiveness* generally refers to studies that evaluate and compare 2 or more interventions. The medical and scientific communities generally consider randomized clinical trials that use well-defined patient groups as the best way to compare treatments under controlled conditions. An important benefit of randomized trials is the ability to overcome treatment selection and other biases in the comparison of evaluation or treatment strategies; however, there are limitations to many randomized controlled trials, including the use of relatively small, homogeneous patient populations, short follow-up periods, and surrogate end points.

Many people hope that comparative effectiveness research, using meta-analyses as well as observational studies that are based on clinical registries or large databases, will provide additional information to supplement the efficacy data provided by randomized trials. Many such studies have been performed, and others are in progress. Nonetheless, there are substantial challenges in interpreting and using this information to guide clinical decisions and establish public policy.

The federal government of the United States has provided direct funding through the National Institutes of Health for a number of landmark clinical trials that fall within the definition of comparative effectiveness research. In the treatment of

cardiovascular disease and stroke, these landmark trials include the Coronary Artery Surgery Study (CASS),² the Thrombolysis In Myocardial Infarction trial (TIMI),³ the North American Symptomatic Carotid Endarterectomy Trial (NASCET),⁴ the Asymptomatic Carotid Atherosclerosis Study (ACAS),⁵ the Warfarin-Aspirin Symptomatic Intracranial Disease study (WASID),^{6,7} the Bypass Angioplasty Revascularization Investigation (BARI),⁸ and the Warfarin-Aspirin Recurrent Stroke Study (WARSS).⁹ Such clinical trials have helped shape clinical guidelines that the American Heart Association and the American Stroke Association have promulgated, often in collaboration with the American College of Cardiology and with the endorsement of other professional organizations.

As part of the American Recovery and Reinvestment Act of 2009 (commonly referred to as the "stimulus bill"), \$1.1 billion was dedicated to supporting comparative effectiveness research. The law states that the funding will be used for the conduct, support, or synthesis of research that compares the clinical outcomes, effectiveness, and appropriateness of items, services, and procedures used to prevent, diagnose, or treat diseases, disorders, and other health conditions and for encouraging the development and use of clinical registries, clinical data networks, and other forms of electronic health data that can be used to generate or obtain outcomes data.¹⁰

In the report that accompanied the stimulus bill, Congress indicated that this comparative research funding may not be used to mandate coverage determinations, provider reimbursement decisions, or other such policies for any public or private payer. The legislation, however, does not expressly prohibit Medicare or other payers from basing coverage and reimbursement policies on the findings of the comparative effectiveness research funded under this legislation. Congress also cautioned against a one-size-fits-all approach to the treatment of individual patients, which indicates that the comparative effectiveness research funded under this bill should consider the needs of patient subpopulations.¹¹

Identification and Discussion of Principles

The American Heart Association is a mission-driven volunteer organization that focuses on optimal cardiovascular health for all Americans and the best interests of patients with cardiovascular diseases and stroke. The Association believes that if used properly, comparative effectiveness research may provide important opportunities to enhance scientific knowledge, promote an emphasis on value and improved patient outcomes, and inform patient and healthcare provider decisions and communications. The American Heart Association offers its principles for comparative effectiveness research within the following 4 broad categories:

- Conducting and interpreting comparative effectiveness research according to fundamental scientific principles;
- Defining value for patients through comparative effectiveness research;
- Applying comparative effectiveness research to patient treatment decisions; and
- Funding and oversight of comparative effectiveness research.

A. Conducting and Interpreting Comparative Effectiveness Research According to Fundamental Scientific Principles

1. Comparative Effectiveness Research Should Ideally Build on the Data Provided by Randomized Clinical Trials by Evaluating Medical Interventions in More Diverse Populations and in Broader Clinical Contexts

Comparative effectiveness research should be based on the scientific knowledge gained from the randomized clinical trials that are typically used to assess the clinical efficacy of a new therapy. Randomized trials are generally designed to evaluate an intervention in well-defined patient populations by use of control groups, intervention protocols, and defined clinical end points. By avoiding selection and other biases between diagnostic or therapeutic options, a randomized design provides the highest level of evidence for evaluating the benefits and risks of a new diagnostic test or therapy. Randomized trials often provide critical scientific evidence for clinical guidelines and influence the coverage policies adopted by health insurers.

The purpose of comparative effectiveness research is not to determine whether an intervention is efficacious under ideal circumstances but rather to aid clinical decision making by determining whether the therapeutic effects and safety profiles found in randomized trials can be generalized to broader populations and to general clinical practice. For example, an initial randomized trial may include subjects in specific age groups and with limited chronic medical conditions (comorbidities). A comparative effectiveness study might provide information on how the therapy works in other age groups and in patients with greater comorbidity. To accomplish this goal, comparative effectiveness research may use clinical registries, clinical data networks, and other forms of electronic health information that can generate or obtain outcomes data.

2. Comparative Effectiveness Research Should Be Conducted According to Established Scientific Principles and Processes, Focusing on Unambiguous, Meaningful Clinical End Points and Quality-of-Life Measures

Although the study groups and data sources used in comparative effectiveness research may vary, the methodology for data analyses and interpretations should follow standard scientific principles and processes. There are growing efforts to establish clinical registries and to use administrative and other databases that employ new health information technologies. The potential to conduct meaningful comparative effectiveness research with large databases is significant. For example, there may be great value in exploring opportunities to analyze information on patient populations that are diverse with respect to gender, race, ethnicity, and genetic composition. For patients and healthcare providers to act on comparative effectiveness research findings, the highest possible standards of statistical analysis, validation, and evaluation must be used.

In some situations, only nonrandomized databases are large enough and sufficiently inclusive to identify small signals that indicate a potential safety concern that might be important (or even catastrophic) but that occur too infrequently to

be identified in randomized clinical trials performed during the development of a new intervention. In some cases, such risks may occur only in a specific, small subset of patients. Large databases can be particularly valuable in identifying these rare treatment risks.

There are, however, challenges in using large databases for comparative effectiveness research. These challenges include the following:

- *The play of chance*: When differences in outcomes of interest occur (including death and other events or measures of health status), statistical inference testing can help determine whether the differences are likely to be real or chance observations. When multiple outcomes are considered or when results are examined in multiple subgroups, there is an increased likelihood that some differences will be chance findings. This can be controlled with appropriate statistical analysis. In addition, even large databases may offer insufficient patient observations to ensure that there are no true differences between groups. This is especially problematic for rare events.
- *Bias*: There is a greater likelihood of clinically relevant biases in studies based on observational data than in well-conducted randomized trials. If unrecognized, such biases can lead to erroneous conclusions. Whenever non-randomized data are used in comparative effectiveness research, there should be a rigorous evaluation for bias and for the potential for such bias to skew the conclusions. Cohort studies generally will have varying degrees of selection bias, depending on the nature of the competing therapies or diagnostics and the outcomes measured. Case-control studies can suffer from additional biases, such as recall bias, in which patients with a particular outcome are more likely to recall an exposure than control patients. Case-control studies also can be confounded by protopathic bias, in which patients may experience the event before the exposure or in which the event may lead to the exposure. Observational studies also may suffer from uncertain degrees of exposure, such as uncertain drug dosing and varying degrees of misclassification of data.
- *Causality*: A statistical association does not establish causality. In the 1960s, Austin Bradford-Hill proposed 9 criteria (originally concerning cigarette smoking) to help determine whether an exposure caused an outcome. The Bradford-Hill criteria describe basic conditions for the establishment of scientifically valid causal relationships. By assessing factors such as the temporal relationship between 2 events (outcome always follows the exposure), the consistency of results when replicated in different settings, dose response, biological plausibility, and the potential for alternative explanations, the Bradford-Hill criteria offer a standard for determining whether an observed relationship is likely causal. In comparative effectiveness research, caution should be used in drawing conclusions regarding cause-and-effect from statistical associations.¹²

It is essential for patients and healthcare providers to understand these limitations when interpreting the findings of comparative effectiveness research.

Comparative effectiveness research should focus on clinically meaningful and unambiguous clinical end points (such as the incidence of death, myocardial infarction, or stroke) rather than surrogate measures whenever possible. In most instances, such objective measures of patient outcomes provide the most robust measures of the value of a particular medical therapy for the patient population served.

A primary goal of health care is to optimize quality of life. Assessment of quality of life is an important end point for comparative effectiveness research. The protocols used in such analyses should provide rigorous and reproducible standards for the collection of such data. This may be especially challenging (but important) in the context of comparative effectiveness research that involves large administrative databases.

3. The Methods, Results, and Applications of Comparative Effectiveness Research Need to Be Transparent, Well Validated, and Adequately Communicated to Patients, Healthcare Providers, and Policy Makers

Transparency is critical for the application and acceptance of the results of comparative effectiveness research. However, the integrity of the research design, the dissemination of the results, and the need to study questions that may be controversial should take precedence over stakeholder opinions.

The need for transparency extends to the communication of research results to both healthcare consumers and providers. The impact of comparative effectiveness research will be limited in the absence of significant resources devoted to such dissemination efforts.

The findings of comparative effectiveness research should be communicated through an organized strategy that involves technical advisory documents for clinicians and user-friendly tools for the public to assist in healthcare decision making. There should be adequate funding for such communications to ensure that meaningful comparative effectiveness research is available to help guide care. In addition, innovative tools such as the American Heart Association's "Get With the Guidelines" program can be used to drive the translation of scientific discovery into day-to-day practice.

B. Defining Value for Patients Through Comparative Effectiveness Research

1. Comparative Effectiveness Research May Include Estimates of Cost and Cost-Effectiveness, but Comparative Effectiveness Research Should Focus on Enhancing Value for Patients Rather Than Minimizing Costs

The primary focus of comparative effectiveness research should be to inform clinical decision making by patients and their healthcare providers, with the overarching goal of optimizing outcomes and value for patients. Value is very broadly defined to include patient outcomes, safety, and satisfaction, adjusted for cost. For example, if 2 treatments or procedures achieve the same patient outcomes, safety, and satisfaction, but 1 option is only half as costly as the other, then the less costly option has greater value. Steps must be taken to address the legitimate concerns among some stakeholders that comparative effectiveness research has the po-

tential to overemphasize cost at the expense of providing optimal clinical care.

Comparative effectiveness research should not be undertaken for the purposes of cost minimization or the rationing of healthcare services but should be part of the quality and cost-of-care analysis that is necessary to promote an efficient, value-driven healthcare system in the United States. Comparative effectiveness research must not be used to restrict access to healthcare services but rather to provide additional scientific data to help determine the most preferred alternative tests or treatments.

Cost-effectiveness analysis provides methodologies to understand the interrelationship of outcomes and associated costs of one form of therapy or diagnostic testing compared with an alternative. These types of analyses can help stakeholders within society to understand the incremental value of one form of diagnostic testing or therapy versus another. When properly applied, cost-effectiveness analyses can offer insights into the choices made by society and can clarify the assumptions underlying such choices.

Cost-effectiveness analyses do, however, have inherent limitations. The same standards may not apply to both (1) common problems for which therapy is marginally effective at moderate cost and (2) uncommon but catastrophic problems for which therapy is more effective but expensive. As with other comparative effectiveness evaluations, cost-effectiveness requires a meaningful comparator group and is dependent on the quality of the data used for the analysis. Cost data may change over time as suppliers or providers adjust their prices. Cost-effectiveness research can suffer from the same biases as other studies. Cost-effectiveness analysis should be used to help inform public policy, but it should not be the primary guide. Cost-effectiveness research should not be about minimizing costs but rather about maximizing value.

Comparative effectiveness research should not be used in isolation to establish coverage and reimbursement policies. In particular, the needs of vulnerable patient populations, including the critically ill and individuals with rare diseases, must be taken into consideration when developing and applying comparative effectiveness research.

2. Although Comparative Effectiveness Research Provides Opportunities to Address Important Gaps in Knowledge Relatively Quickly, Its Most Dramatic Effects Will Occur Over Longer Time Frames

There are important short-term benefits that can be gained from comparative effectiveness research that is targeted to address gaps in the evidence base for common chronic diseases and other disorders. Through the use of meta-analyses and observational studies that use existing databases, gaps in current scientific knowledge can begin to be addressed and partially clarified.

There are many clinical conditions for which there is only limited evidence regarding which treatment among existing options is likely to be the most effective for an individual. There can be large differences in practice patterns in different regions of the United States for the same condition. Research involving Medicare beneficiaries suggests that differences in

clinical practice patterns that result in increased financial expenditure are often not associated with improvements in clinical outcomes, although the costs of care can differ markedly among different regions of the country.¹³

Comparative effectiveness research holds promise as a way to address such issues, providing patients and healthcare providers with opportunities to identify a preferred clinical approach for each patient. It is hoped that improvements in patient care will be associated with cost savings through fewer complications and targeting the use of clinical interventions that are considered more valuable in effectively treating each patient.

Investing resources in comparative effectiveness research is a prudent way to improve both patient care and the use of future resources. Nonetheless, a number of years will be required before the full impact of the application of the results of comparative effectiveness research on quality improvement and enhanced efficiencies becomes evident.

In particular, initial funding needs to be devoted to developing the infrastructure necessary to support the national capacity to conduct comparative effectiveness research. This includes initial funding for the development of electronic health records, the linking of databases, the development of new registries, and the establishment of a universal patient identification system. Initial funding also is needed to expand the pool of scientists and biostatisticians with the skill sets necessary to conduct comparative effectiveness research, as well as to develop methodologies to define best practices for conducting comparative effectiveness research. Multiyear stability in funding for comparative effectiveness research is required to maintain this infrastructure (including technological and human resources) and to reap the long-term benefits of the investments made in comparative effectiveness research activities.

To best address clinical issues within the country, comparative effectiveness research should focus on studies conducted within the United States, because studies performed in other healthcare systems may have limited applicability in American populations and settings. Steps must be taken to eliminate barriers to the conduct of comparative effectiveness research. This includes addressing some of the underlying problems that more broadly affect the performance of research studies within the country, such as the lack of a universal patient identifier and barriers to the accrual of patients within study protocols. The American Heart Association endorses the conclusions and recommendations reflected in the recent Institute of Medicine report focused on the impacts on research programs of the rules promulgated under the Health Insurance Portability and Accountability Act (HIPAA). The Institute of Medicine concluded that “as currently implemented, the HIPAA Privacy Rule impedes important health research” and recommended specific revisions to the HIPAA Privacy Rule and associated guidance to reduce variation in interpretation by institutional review boards and privacy boards.¹⁴ At the same time, there remains an overarching need to protect the confidentiality of patient information.

3. Comparative Effectiveness Research Is Not Intended To Impede the Development of New Approaches (Pharmaceuticals, Devices, and Diagnostic Methods) but Rather to Facilitate the Application of New Technologies to Those Areas in Which They Will Provide the Greatest Incremental Benefit and Value

Although some stakeholders have expressed concern that comparative effectiveness research will have a chilling effect on the development of new technologies, the role of comparative effectiveness research is not to replace the initial efficacy studies used to evaluate new diagnostic or treatment approaches. Rather, comparative effectiveness research can be used to compare therapies that already are established and are being used in the care of patients. For these reasons, comparative effectiveness research should not create barriers to the development and introduction of novel therapies in the United States. It may, however, appropriately limit the widespread use of high-cost products with very marginal benefits.

C. Applying Comparative Effectiveness Research to Patient Treatment Decisions

1. Comparative Effectiveness Research Should Focus on Conditions With Important Public Health Consequences, With Priority Given to Addressing Existing Gaps in Scientific Evidence in Current Clinical Practice Guidelines

There have been only limited public resources allocated to support comparative effectiveness research. With the availability of substantial federal funding through the American Recovery and Reinvestment Act of 2009, optimal use of these funds argues for the prioritization of conditions that have the greatest public health implications. For example, research should focus initially on high-volume, high-cost chronic conditions in which the results could offer patients and healthcare providers insights regarding which interventions provide the best value for patients. In addition, comparative effectiveness research should be prioritized for the evaluation of treatments in subpopulations in which healthcare disparities are known or suspected to be an ongoing challenge, as well as to address gaps in evidence-based clinical guidelines. The prioritization of questions to be addressed through comparative effectiveness research should be undertaken in consultation with expert stakeholders representing patients, healthcare providers, and researchers.

2. Comparative Effectiveness Research Is Not a Substitute for the Exercise of Clinical Judgment in the Care of Individual Patients, Particularly for Patients at the End of Life, Those of Advanced Age, and Those With Multiple Comorbidities

As advocated by the Institute of Medicine, the healthcare delivery system should be patient centered,¹⁵ and clinical decisions should be based on the needs of each individual. Healthcare decisions should be based on consideration of the clinical evidence and, as applicable, evidence-based clinical guidelines such as those promulgated by the American Heart Association and the American Stroke Association.

The practice of medicine, including the application of comparative effectiveness research, must take into consider-

ation each patient's values and goals. Clinical guidelines and the results of comparative effectiveness research should not be used to supplant physicians' clinical judgment regarding the most appropriate treatment approach for an individual patient.

For those instances in which competing efficacious interventions are available, comparative effectiveness research can offer guidance to clinicians and patients regarding the relative risks and benefits of each option. Use of comparative effectiveness research in these circumstances can help advance a value-driven, patient-centered healthcare system that respects the integrity of the provider-patient relationship.

The scope of comparative effectiveness research should include the concept of personalized medicine, ie, the evaluation of strategies customized to characteristics of individual patients, including the application of genetic analysis and pharmacogenetics, to optimize response to therapy and minimize side effects. "Personalized medicine is the practice of clinical decision-making such that the decisions made maximize the outcomes that the patient most cares about and minimizes those that the patient fears the most, on the basis of as much knowledge about the individual's state as is available."¹⁶ Identification of predictive risk factors, including genomic markers, may allow implementation of effective, patient-specific preventive measures that delay or prevent manifestation of a disease. Although much discussed in recent years, advanced personalized medicine has yet to be adequately tested or widely applied.

3. Comparative Effectiveness Research Should Provide Important Information to Guide Decision Making by Patients and Healthcare Providers, but Ongoing Challenges Will Remain in the Optimal Delivery of High-Quality Care and the Elimination of Racial and Ethnic Disparities

Americans currently receive care recommended by evidence-based clinical guidelines only approximately half of the time. Although many barriers to adherence are related to inappropriate incentives, lack of physician time, and inadequate access, comparative effectiveness research can help to identify interventions that can help patients best comply with clinical guidelines. A national comparative effectiveness research agenda should give priority to identifying and closing the knowledge gaps that impede comprehensive adoption of and compliance with clinical guidelines.

One example is that only approximately half of all patients with atrial fibrillation, a condition that increases the risk of stroke, receive recommended therapy, without any documentation of a rationale for withholding treatment.¹⁷ Programs such as the American Heart Association's Get With the Guidelines are designed to address such problems with the translation of clinical guidelines into practice, and studies are under way to assess the program's effectiveness.

Comparative effectiveness research as done in broader patient populations has the potential to identify the depth of disparate care that affects certain racial and ethnic groups. Although solutions to eliminate disparate care may not arise from comparative effectiveness research, the data provided

may better target other initiatives intended to reduce or eliminate disparate care.

D. Funding and Oversight of Comparative Effectiveness Research

1. Funding for Comparative Effectiveness Research Should Be Complementary to, and Not Competitive With, Existing Federal Support for Biomedical Research Through the National Institutes of Health

Comparative effectiveness research has promise as a means to address gaps and ambiguities in existing medical knowledge. It is not a replacement for the traditional forms of research that are supported through the National Institutes of Health, other public agencies, and the private sector. In particular, the federal government should continue to expand its support for traditional clinical trials. Funding for biomedical research through the National Institutes of Health should not be diverted to comparative effectiveness studies to the extent that such funding is otherwise needed to support and expand the current commitment to ongoing biomedical research.

2. Increased Levels of Funding Will Be Required for Comparative Effectiveness Research to Achieve Meaningful Goals

The funding recently appropriated by Congress for comparative effectiveness research is to be used over a 2-year period. Higher levels of sustained funding will be required to reach the full potential of comparative effectiveness research to address gaps in scientific knowledge and to promote improved patient outcomes.

In the area of cardiovascular disease and stroke alone, the opportunities for application of comparative effectiveness research are significant. There are many examples within current clinical guidelines for cardiovascular disease and stroke in which topics have been identified for additional research, and there are numerous other examples where recommendations based on expert opinion could be studied further through the use of comparative effectiveness research methodology.

3. Any Entity Overseeing Comparative Effectiveness Research Should Possess Sufficient Independence to Promote Credibility, Efficiency, and the Ability to Reach Controversial Decisions; Such Independence Should Be Coupled With Sufficient Safeguards That Promote Accountability, Fairness, and Transparency

One of the challenges in implementing a government-funded initiative to pursue comparative effectiveness research involves the interplay between the governmental entity overseeing this research, academic interests, clinical practice champions, industry, and the political process. There are many stakeholders who have important and legitimate interests in providing input regarding the selection, design, interpretation, and application of comparative effectiveness research. These interests must be considered and balanced against the need to focus society's resources on the unresolved scientific questions that are most likely to improve patient outcomes, as well as the need to address scientific questions that may be controversial.

There has been a challenging history involving the federal oversight of studies evaluating the relative efficacy of diagnostic and therapeutic interventions.¹⁸ For example, the National Center for Health Care Technology was created in 1978 to support assessments of “any discreet and identifiable regimen or modality used to diagnose and treat illness, prevent disease, maintain patient well-being, or facilitate the provision of health services.” It was eliminated in December 1981 as a result of opposition from the Health Industry Manufacturers Association.^{19,20} Similarly, the decision by the US Congress to withdraw funding for the Office of Technology Assessment in 1995 has been attributed in part to efforts by healthcare industry stakeholders.²¹ Congress also reduced the budget and limited the mission of the Agency for Health Care Policy and Research in the mid-1990s after criticism by stakeholders that disagreed with the recommendations published in a set of Agency for Health Care Policy and Research clinical guidelines regarding the treatment of low back pain.^{18,22}

These examples suggest that when comparative effectiveness research is conducted, the financial and professional stakes for industry and providers are high. Concerns arise regarding whether and how medical interventions will be

covered by public and private health insurance plans depending on the outcomes of these studies.

Policy makers should consider ways in which the management of comparative effectiveness research can be insulated from the ongoing pressure of special interests. This might be accomplished, for example, by insulating the agency from the annual funding cycle, such as by providing multiyear funding or securing partial funding from the private sector.^{23,24}

Conclusions

Comparative effectiveness research offers great promise for improving clinical decision making and patient outcomes. As the recent public attention and policy dialogue have shown, however, there are concerns regarding the potential scope of such research and how it may be used to influence healthcare delivery. The American Heart Association offers these principles on comparative effectiveness research to advance its mission of “building healthier lives free of cardiovascular diseases and stroke.” As an association, we stand committed to seek input, engage in meaningful dialogue, and join in collaboration with other voluntary health organizations to help create stronger consensus on how comparative effectiveness research can best serve the public interest.

Disclosures

Writing Group Disclosures

Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honoraria	Expert Witness	Ownership Interest	Consultant/Advisory Board	Other
Raymond J. Gibbons	Mayo Clinic	TherOx†; King Pharmaceuticals†	None	None	None	None	Cardiovascular clinical studies (WOMEN study)*; TherOx*; Medscape*; Molecular Insight Pharmaceuticals*	None
Timothy J. Gardner	Christiana Care Health System	None	None	None	None	None	None	None
Jeffrey L. Anderson	Intermountain Health Care	None	None	None	None	None	None	None
Larry B. Goldstein	Duke University/ Durham VA Medical Center	AHA-Bugher Foundation Center for Stroke Prevention Research†; AGA Medical, RESPECT Trial*; Schering-Plough, TIMI 50*; NC Department of Health and Human Services*; El Centro Hispanico (KB Reynolds Foundation)*	None	Pfizer*	None	None	Pfizer*; AGA Medical*; Schering Plough*; Johnson & Johnson*; Abbott Vascular*	None
Neil Meltzer	Sinai Hospital of Baltimore	None	None	None	None	None	None	None
William S. Weintraub	Christiana Care Health System	To his institution: AstraZeneca†; Abbott†; CVT†; Otsuka†; Bristol-Myers Squibb†; Sanofi Aventis†	None	None	Expert witness/testimony and other financial incentives: AstraZeneca†; Bayer†; Pfizer†	None	Bristol Myers Squibb*; Sanofi Aventis*; Eli Lilly*; CVT*	None
Clyde W. Yancy	Baylor University Medical Center	None	None	None	None	None	Advisory board, “Heart Failure,” Theheart.org*	None

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be “significant” if (1) the person receives \$10 000 or more during any 12-month period, or 5% or more of the person’s gross income; or (2) the person owns 5% or more of the voting stock or share of the entity, or owns \$10 000 or more of the fair market value of the entity. A relationship is considered to be “modest” if it is less than “significant” under the preceding definition.

*Modest.

†Significant.

Reviewer Disclosures

Reviewer	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honoraria	Expert Witness	Ownership Interest	Consultant/Advisory Board	Other
Loren F. Hiratzka	Cardiac Surgery, TriHealth	None	None	None	None	None	None	None
William J. Scanlon	Health Policy R&D	None	None	None	None	None	None	None
Vincent Bufalino	Midwest Heart Specialists; Edward Heart Hospital	None	None	None	None	None	United Health Care Scientific Advisory Board*	None
Daniel Jones	University of Mississippi Medical Center	None	None	None	None	None	None	None

This table represents the relationships of reviewers that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all reviewers are required to complete and submit. A relationship is considered to be "significant" if (1) the person receives \$10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (2) the person owns 5% or more of the voting stock or share of the entity, or owns \$10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

References

- Gibbons RJ, Jones DW, Gardner TJ, Goldstein LB, Moller JH, Yancy CW. The American Heart Association's 2008 Statement of Principles for Healthcare Reform. *Circulation*. 2008;118:2209–2218.
- Coronary Artery Surgery Study (CASS): a randomized trial of coronary artery bypass surgery: survival data. *Circulation*. 1983;68:939–950.
- TIMI Study Group. The Thrombolysis in Myocardial Infarction (TIMI) trial: phase I findings. *N Engl J Med*. 1985;312:932–936.
- North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. *N Engl J Med*. 1991;325:445–453.
- Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. Endarterectomy for asymptomatic carotid artery stenosis. *JAMA*. 1995;273:1421–1428.
- Chimowitz MI, Kokkinos J, Strong J, Brown MB, Levine SR, Silliman S, Pessin MS, Weichel E, Sila CA, Furlan AJ, Kargman DE, Sacco RL, Wityk RJ, Ford G, Fayad PB, and the Warfarin-Aspirin Symptomatic Intracranial Disease Study Group. The Warfarin-Aspirin Symptomatic Intracranial Disease Study. *Neurology*. 1995;45:1488–1493.
- The Warfarin-Aspirin Symptomatic Intracranial Disease (WASID) Study Group. Prognosis of patients with symptomatic vertebral or basilar artery stenosis. *Stroke*. 1998;29:1389–1392.
- The Bypass Angioplasty Revascularization Investigation (BARI) Investigators. Comparison of coronary bypass surgery with angioplasty in patients with multivessel disease [published correction appears in *N Engl J Med*. 1997;336:147]. *N Engl J Med*. 1996;335:217–225.
- Mohr JP, Thompson JL, Lazar RM, Levin B, Sacco RL, Furie KL, Kistler JP, Albers GW, Pettigrew LC, Adams HP Jr, Jackson CM, Pullicino P; Warfarin-Aspirin Recurrent Stroke Study Group. A comparison of warfarin and aspirin for the prevention of recurrent ischemic stroke. *N Engl J Med*. 2001;345:1444–1451.
- The American Recovery and Reinvestment Act of 2009. Pub L No. 111-5, 123 Stat 115.
- H. Rept. 111-16. Conference report to accompany H.R. 1. February 13, 2008.
- Rothman KJ, Greenland S. *Causation and Causal Inference in Modern Epidemiology*. Rothman KJ, Greenland S, eds. Philadelphia, Pa: Lippincott-Raven; 1998:7–28.
- Wennberg JE, Fisher ES, Goodman DC, Skinner JS. *Tracking the Care of Patients With Severe Chronic Illness: The Dartmouth Atlas of Health Care 2008*. Lebanon, NH: Dartmouth Institute for Health Policy and Clinical Practice, Center for Health Policy Research; 2008.
- Nass SJ, Levit LA, Gostin LO, eds. *Beyond the HIPAA Privacy Rule: Enhancing Privacy, Improving Health Through Research*. Washington, DC: National Academies Press; 2009.
- Institute of Medicine. *Crossing the Quality Chasm: A New Health System for the 21st Century*. Washington, DC: National Academies Press; 2001.
- Kohane IS. The twin questions of personalized medicine: who are you and whom do you most resemble? *Genome Med*. 2009;1(1):4.
- Jencks SF, Cuerdon T, Burwen DR, Fleming B, Houck PM, Kussmaul AD, Nilasena DS, Ordin DL, Arday DR. Quality of medical care delivered to Medicare beneficiaries: a profile at state and national levels. *JAMA*. 2000;284:1670–1676.
- Skeen J, ed. *Research on the Comparative Effectiveness of Medical Treatments: Issues and Options for an Expanded Federal Role*. Washington, DC: Congressional Budget Office; December 2007.
- Perry S, Eliastam M. The National Center for Health Care Technology. *JAMA*. 1981;245:2510–2511.
- Perry S. Special report: the brief life of the National Center for Health Care Technology. *N Engl J Med*. 1982;307:1095–1100.
- Eisenberg JM, Zarin D. Health technology assessment in the United States: past, present, and future. *Int J Technol Assess Health Care*. 2002;18:192–198.
- Iglehart JK. Politics and public health. *N Engl J Med*. 1996;334:203–207.
- Medicare Payment Advisory Commission. Report to the Congress: Reforming the Delivery System. Washington, DC: MedPAC; June 2008: chapter 5.
- Wilensky GR. Developing a center for comparative effectiveness information. *Health Aff (Millwood)*. 2006;25:w572–w585.

KEY WORDS: AHA Scientific Statements ■ outcomes assessment ■ outcomes research

The American Heart Association's Principles for Comparative Effectiveness Research: A Policy Statement From the American Heart Association

Raymond J. Gibbons, Timothy J. Gardner, Jeffrey L. Anderson, Larry B. Goldstein, Neil Meltzer, William S. Weintraub and Clyde W. Yancy
on behalf of the American Heart Association Advocacy Coordinating Committee

Circulation. 2009;119:2955-2962; originally published online May 11, 2009;
doi: 10.1161/CIRCULATIONAHA.109.192518

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2009 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the
World Wide Web at:

<http://circ.ahajournals.org/content/119/22/2955>

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Circulation* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the [Permissions and Rights Question and Answer](#) document.

Reprints: Information about reprints can be found online at:
<http://www.lww.com/reprints>

Subscriptions: Information about subscribing to *Circulation* is online at:
<http://circ.ahajournals.org/subscriptions/>