The significantly increased life expectancy of Western Society in the past several decades has been attributed to 2 major successes in the prevention and treatment of human disease: (1) the elimination of the scourge of common infectious diseases thanks to public health measures, vaccines, and antibiotic drug development and (2) the decline in cardiovascular morbidity and mortality because of the advances in prevention and therapy. In the past 35 years alone, US age-adjusted mortality from cardiovascular disease declined 50%. This drastic reduction is largely because of breakthroughs in cardiovascular research and medicine. Greater understanding of the Cardiovascular Disease Continuum has led to the development of drugs targeting the various pathways of the Continuum resulting in improved clinical outcomes. Consider the development of life-saving targeted drugs such as β-adrenergic blocking agents, statins, angiotensin-converting enzyme inhibitors, thrombolytic agents, and others. More recently, we have seen another major advance with the introduction of PCSK9 inhibitors whose development is an impressive exemplar of the combined power of genetic and population studies, basic and translational research, and therapeutic development in cardiovascular medicine. In addition, we have witnessed significant advances in the development of innovative medical devices, which have resulted in effective interventions for cardiovascular disease.

Part 1 is available on p 20

Indeed, cardiovascular research is a poster child for the Discovery to Care Continuum paradigm. Many breakthroughs in cardiovascular medicine stemmed from basic science discoveries, which were successfully translated to the clinical arena. These advances would not have been possible without teams of scientists and clinicians working together and with support from organizations such as the American Heart Association, National Heart, Lung, and Blood Institute, the American College of Cardiology, and industry partners.

In addition to research excellence and innovation forming the basis of scientific advances and clinical progress, other important factors influence their trajectory, clinical translation, and implementation. These factors include guidelines and policy, regulation, and ethical considerations. It is imperative that the research community become more knowledgeable and engaged in these arenas, particularly in science policy. Why? Just consider the effect of politics and policy on research funding. Science and policy are becoming more interrelated. Scientists are increasingly asked to demonstrate the value of their work to society; likewise, policy makers are often asked to provide the scientific basis on which their policies are based.

As a result, the role of scientific academies, which bridge science and policy, has never been more important, especially in the biomedical research community. Indeed, society can benefit enormously from the activities of an independent scientific academy with the directive to mobilize the best minds to advance knowledge and accelerate progress in science, medicine, and policy.

How Can the National Academy of Medicine Work With the Cardiovascular Researchers to Advance Science and Medicine?

It is an incredible time for science and technology; there has been substantial progress in the fields of genomics, regenerative medicine, and gene editing, to name just a few. The scope is broad, and the potential is enormous for cardiovascular research and medicine. The National Academy of Medicine (NAM) is prepared to work with cardiovascular scientists and clinicians to provide advice and guidance, facilitate progress, and shape resources and policies.

Below are selected examples of major research and clinical areas for discussion:

Noncommunicable Chronic Diseases

An important area of cardiovascular research is addressing the increasing burden of noncommunicable diseases in the United States and globally. Once thought to be confined primarily to industrialized nations, cardiovascular disease (CVD) has emerged as a major health threat in low- and middle-income countries. In recognition of the growing burden of CVD, and at the request of National Heart, Lung, and Blood Institute, the National Academies released the report, Promoting Cardiovascular Health in the Developing World: A Critical Challenge to Achieve Global Health in 2010. The report recommended that the National Heart, Lung, and Blood Institute, development agencies, nongovernmental organizations, and governments work toward 2 essential goals: (1) creating environments that promote heart healthy lifestyle choices and help reduce the risk of chronic diseases and (2) building public
health infrastructure and health systems with the capacity to implement programs that will effectively detect and reduce risk and manage CVD. To meet these goals, the report recommended several steps, including public–private collaboration to reduce people’s consumption of salt, sugar, saturated fats, and trans fats and to make therapies, diagnostic tools, and preventive techniques for these diseases affordable and accessible in all nations. In addition, the report recommended that global health efforts include prevention and care for cardiovascular disease and other chronic diseases as a focus.

In addition, the National Academies have produced many reports addressing the risk factors for CVD. For instance, our Dietary Reference Intake series present dietary reference values for the intake of nutrients based on current available evidence, which have served as the basis of all federal and state food nutrition programs and policies. We called national attention to the obesity epidemic in 2005 with the report, Preventing Childhood Obesity: Health in the Balance, highlighting the need for cross-sector and multilevel action to address this problem. Since then we have produced many reports and workshops to inform policy and research and spur action to solve the obesity crisis. Furthermore, other reports have assessed the effects of tobacco control policies and the public health implications of raising the minimum age of legal access to tobacco products.

**Precision Medicine**

There has been much discussion about precision medicine, an approach which tailors “medical treatment to the individual characteristics of each patient...allowing preventative or therapeutic interventions to be concentrated on those who will benefit, sparing expense and side effects for those who will not”. Precision medicine has the potential to transform all fields of medicine, and cardiovascular medicine is poised to be an early leader. This approach could have significant impact on diagnosis, treatment, and prevention of heart disease while reducing healthcare costs. Using economic modeling, it has been estimated that an intervention reducing the incidence of heart disease by 50% in the United States would generate average $607 billion in savings over 50 years. However, many issues such as evidence generation, data sharing, security and privacy, adoption and implementation in clinical care, reimbursement and regulatory framework, and patient engagement and trust, need to be addressed for precision medicine to realize its full clinical potential.

**Cardiovascular Regeneration**

A key area of unmet need is cardiovascular regeneration. There has been significant progress in research on cardiac stem and progenitor cells. Clinical trials of cell-based therapy have yielded encouraging but modest results. The recent advances in tissue engineering, induced pluripotent stem cells, and direct reprogramming hold much promise as therapies in the future. The National Heart, Lung, and Blood Institute has recognized the importance of supporting basic and translational research to advance this field and has developed key initiatives, such as Cardiovascular Cell Therapy Research Network and Progenitor Cell Biology Consortium. However, many key issues must be explored to realize the full potential of cardiovascular regeneration and regenerative medicine broadly. A potential challenge for the field is the ethical, legal, and social issues posed by these new technologies. There is debate around the use of adult, embryonic, and induced pluripotent stem cells for research and therapy and concern about possible unanticipated consequences of these treatments and products. Guidelines for the safe and proper use of these advances will need to be developed, translational barriers identified, the regulatory environment clearly defined, and proper oversight of clinics offering stem cell therapies to assure patient safety will be needed.

**Gene Therapy and Gene Editing**

The possibility that cardiovascular genetic diseases can be cured by gene therapy, mitochondrial transfer therapy, and now gene editing is exciting. These techniques can also be used for somatic therapy to treat acquired cardiovascular diseases. Many preclinical and early-stage clinical studies have shown early signs of encouraging results for gene therapy. Furthermore, new mitochondrial transfer therapies have the potential to treat or prevent inherited mitochondrial diseases. Gene editing holds great promise for advancing science and improving cardiovascular health. Initial studies have shown that gene editing may be used to target genes, such as PCSK9 and ANGPTL3, and to treat Duchenne muscular dystrophy. However, gene editing—technologies also raise many ethical and social concerns. Of particular, controversy is the ability to make permanent modifications to human germline DNA and its use in gene enhancement.

The National Academies have ongoing activities in all these emerging scientific areas. We have convened experts in Forums and Roundtables to advance knowledge through scientific exchange, identify challenges, set standards, and facilitate collaboration. For example, we have a Roundtable on Genomics and Precision Health, which fosters cross-sector dialogue on global issues surrounding the translation of genomics and genetics research findings into medicine, public health, education, and policy. Our Forum on Regenerative Medicine brings stakeholders together to address the challenges and opportunities facing regenerative medicine. Our Forum on Drug Discovery, Development, and Translation brings stakeholders together to discuss important issues in the science and policy of drug development.

Over the years, the NAM has played a key role in assessing how science and technology developments can be advanced to confer maximal benefits to health and society. More recently, we have undertaken major initiative to provide guidance on research involving Human Gene Editing. In December 2015, we held an international summit in collaboration with the National Academy of Sciences, the Chinese Academy of Sciences, and the Royal Society of the UK, to convene global experts to discuss the scientific, ethical, and governance issues associated with human gene—editing research. Importantly, we are currently conducting a comprehensive study by a multidisciplinary, international committee to examine the scientific underpinnings and clinical, ethical, legal, and social implications of Human Gene Editing. The committee will issue a report with definitive findings and recommendations to the scientific community and government regulators on the responsible conduct and application of human gene—editing research.
Clinical Research Data
Cardiovascular research has been at the vanguard in the development of multicenter mega-randomized controlled trials as a means of obtaining robust evidence for the adoption of new diagnostics and treatments. In addition, many major epidemiology studies, such as the Framingham Heart Study, have influenced cardiovascular medicine and health. Indeed, cardiovascular research success has been built on the impressive generation of data and evidence. Going forward, it will be important to develop new approaches for data and evidence generation. The rise of computing technologies and electronic communication technology has facilitated the collection of an unprecedented amount of information, big data, which brings tremendous possibilities, particularly in the realm of health and biomedical research. However, there are many scientific, policy, and social questions that must be addressed to realize the transformative potential of big data. The National Academies have worked closely with clinical researchers and data scientists in charting the course for the future of data science. In 2015, we released a report Sharing Clinical Trial Data: Maximizing Benefits, Minimizing Risk, which called on different stakeholders to work together to create both the culture and infrastructure needed to maximize the benefits and minimize the risks of sharing data.

These types of reports will only grow in importance as the use of big data and analytics expands. Our work on “learning health systems” has laid out a vision in which “science, informatics, incentives, and culture are aligned for continuous improvement and innovation, with best practices seamlessly embedded in the care process, patients and families active participants in all elements, and new knowledge captured as an integral by-product of the care experience.” In the future, cardiovascular research will be embedded into practice. Already, there are early indications that this new approach will transform cardiovascular research. The National Institutes of Health initiated the Health Care Systems Research Collaboratory to foster innovative approaches to integrating research with care delivery. For chronic diseases, such as heart failure or hypertension, it will be important to integrate registry data with data from electronic health records and the growing array of patient-reported outcome measures. Initial experiences in the United States (SAFE-PCI [Study of Access the growing array of patient-reported outcome measures. Initial grate registry data with data from electronic health records and such as heart failure or hypertension, it will be important to inte-

Future Directions
It is becoming increasingly clear that current health and biomedical challenges will require solutions that cut across disciplines. Indeed, the emerging field of Convergence Science is considered by many as the future of health. The National Academies have provided leadership in this important field since 2009, when we released A New Biology for the 21st Century: Ensuring the United States Leads the Coming Biology Revolution, which discussed the need for increasing interconnection among disciplines to better understand complex biological systems, and called for interdisciplinary research programs jointly administered across federal agencies. In 2014, we released Convergence: Facilitating Transdisciplinary Integration of Life Sciences, Physical Sciences, Engineering, and Beyond, which outlined the challenges of a siloed research infrastructure and provided examples of institutional practices to foster increased disciplinary integration. In addition to these reports, the National Academies have already taken steps as an organization to facilitate cross-cutting solutions. In July 2015, the National Academies underwent a broad reorganization in an effort to improve collaboration and coordination across the academies. Indeed, our reports and program activities are now uniformly labeled under the umbrella of the National Academies of Sciences, Engineering and Medicine.

Finally, leaders and the public in the United States and worldwide need aspirational and audacious goals to generate excitement around the idea that collectively we can do more—much more—to change the course of health. To do this, we are planning a Grand Challenges in Health and Medicine initiative. In the first phase of this initiative, NAM and its partners will identify the most important global challenges through a transparent process informed by many perspectives. In the second phase, NAM will catalyze action toward solutions—moonshots—by stewarding collective strategies from stakeholders in policy, business, philanthropy, academia, and the general public through public–private partnerships. Imagine a world without CVD. What if we could eliminate conditions such as hypertension, diabetes mellitus, or dyslipidemia?

Conclusions
To assist the field of cardiovascular science reach its full potential, the NAM is prepared to work closely with clinicians and the research community. The NAM can provide a national platform to elevate the issues of most importance to cardiovascular research. Our mutual goal is to improve cardiovascular health and eliminate cardiovascular disease; at the NAM, we aim to do so by advancing research for policy and policy for research.

Disclosures
None.

References


Cardiovascular Research and the National Academy of Medicine: Advancing Progress in Science and Medicine: Part 2: What We Do
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