AHA Policy Statement

Forecasting the Future of Cardiovascular Disease in the United States
A Policy Statement From the American Heart Association

Paul A. Heidenreich, MD, MS, FAHA, Chair; Justin G. Trogdon, PhD; Olga A. Khavjou, MA; Javed Butler, MD, MPH, FAHA; Kathleen Dracup, RN, DNSe; Michael D. Ezekowitz, MBChB, DPhil, FRCP, FAHA; Eric Andrew Finkelstein, PhD, MHA; Yuling Hong, MD, PhD, FAHA*; S. Claiborne Johnston, MD, PhD, FAHA; Amit Khera, MD, MSc; Donald M. Lloyd-Jones, MD, MSc, FAHA; Sue A. Nelson, MPA; Graham Nichol, MD, MPH, FRCP(C), FAHA; Diane Orenstein, PhD*; Peter W.F. Wilson, MD, FAHA; Y. Joseph Woo, MD, FAHA; on behalf of the American Heart Association Advocacy Coordinating Committee, Stroke Council, Council on Cardiovascular Radiology and Intervention, Council on Clinical Cardiology, Council on Epidemiology and Prevention, Council on Arteriosclerosis, Thrombosis and Vascular Biology, Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation, Council on Cardiovascular Nursing, Council on the Kidney in Cardiovascular Disease, Council on Cardiovascular Surgery and Anesthesia, and Interdisciplinary Council on Quality of Care and Outcomes Research

Background—Cardiovascular disease (CVD) is the leading cause of death in the United States and is responsible for 17% of national health expenditures. As the population ages, these costs are expected to increase substantially.

Methods and Results—To prepare for future cardiovascular care needs, the American Heart Association developed methodology to project future costs of care for hypertension, coronary heart disease, heart failure, stroke, and all other CVD from 2010 to 2030. This methodology avoided double counting of costs for patients with multiple cardiovascular conditions. By 2030, 40.5% of the US population is projected to have some form of CVD. Between 2010 and 2030, real (2008$) total direct medical costs of CVD are projected to triple, from $273 billion to $818 billion. Real indirect costs (due to lost productivity) for all CVD are estimated to increase from $172 billion in 2010 to $276 billion in 2030, an increase of 61%.

Conclusions—These findings indicate CVD prevalence and costs are projected to increase substantially. Effective prevention strategies are needed if we are to limit the growing burden of CVD. (Circulation. 2011;123:933-944.)

Key Words: AHA Scientific Statements ■ cardiovascular diseases ■ forecasting ■ US costs ■ cost analysis

*The findings and conclusions in this paper are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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 November 15, 2010. A copy of the statement is available at http://www.americanheart.org/presenter.jhtml?identifier=3033999 by selecting either the “topic list” link or the “chronological list” link (No. KB-0184). To purchase additional reprints, call 843-216-2533 or e-mail kelle.ramsay@wolterskluwer.com.


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.

© 2011 American Heart Association, Inc.

Circulation is available at http://circ.ahajournals.org DOI: 10.1161/CIR.0b013e31820a55f5
Circulating healthcare costs and their impact on the economy is critical to understand what the future might hold for cardiovascular disease (CVD) prevalence and cost in the United States. Currently, CVD is the leading cause of death in the United States, and constitutes 17% of overall national health expenditures.1–3 US medical expenditures are the highest in the world and rose from 10% of the Gross Domestic Product in 1985 to 15% of Gross Domestic Product in 2008.4 In the past decade, the medical costs of CVD have grown at an average annual rate of 6% and have accounted for ∼15% of the increase in medical spending.5 The growth in costs has been accompanied by greater life expectancy, suggesting that this spending was of value.6 Despite this trend, there are many opportunities to further improve cardiovascular health while controlling costs.7

To optimally plan for these opportunities, however, it is imperative to understand the future of CVD prevalence and costs. Previous projections have focused on disease states such as stroke8 or coronary heart disease (CHD),9 or have evaluated the implications of broadly defined “heart disease.”10,11 Systematic projections of prevalence and costs for all the major categories of CVD are not currently available. This study was undertaken to project the prevalence and medical costs of hypertension, CHD, heart failure, stroke, and all other CVDs from 2010 to 2030. We use a methodology that avoids double counting disease costs across categories.12 The projections assume no change in policy but do reflect changing demographics over time. The projections serve as an illustration of what is likely to happen to CVD prevalence and costs if no change to current policy is made and no further action is taken to reduce the disease and economic burden of CVD. These projections provide a useful baseline to gauge the success of current and future CVD policy.

Data and Methods

Overview

Projections of CVD prevalence and costs (direct and indirect) were built as follows. We generated estimates of CVD prevalence and average cost per person by age group (18 to 44 years, 45 to 64 years, 65 to 79 years, 80+ years), sex (men, women), and race/ethnicity (white non-Hispanic, white Hispanic, black, other). CVD prevalence was assumed to remain constant for each of the 32 age, sex, and race/ethnicity cells. Initial average CVD cost per person was estimated for each cell and allowed to grow in real terms based on the historical rate of growth of overall medical spending (direct and real wages (indirect), which assumes that drivers of medical spending such as rising prices and technological innovation will continue at the same rate for the next 20 years. We generated projections of the total CVD population and costs by multiplying prevalence rates and average costs by the Census-projected population of each demographic cell. Therefore, the projections reflect expected changes in population demographics but assume no change in policy that would affect prevalence and average relative cost within a demographic cell.

Projections of CVD Prevalence

Prevalence estimates for hypertension, CHD, heart failure, and stroke were generated using data from the 1999 to 2006 National Health and Nutrition Examination Survey (NHANES) and Census Bureau projected population counts for the years 2010 to 2030. Additional details are provided in Appendixes A and B. Projected population counts for years 2010 to 2030 were obtained from the 2008 Population Projections of the United States resident population by age, sex, race, and Hispanic origin generated by the US Census Bureau based on Census 2000. The US Census Bureau generated these projections using a cohort-component method and assumptions about future births, deaths, and net international migration. We multiplied predicted prevalence of each CVD condition in each sex/age/race cell by the projected population counts in the corresponding cells for years 2010 to 2030 to project the number of people with CVD in each cell in each of the years. We then aggregated the number of people with CVD by sex, by age, and by race, and calculated the projected CVD prevalence overall and by each demographic characteristic.

Projections of Direct Medical Costs of CVD

The main data source for generating projections of medical costs of CVD was the 2001 to 2005 Medical Expenditure Panel Survey (MEPS).13 Details of the MEPS data and their use in estimating cost of care are described in Appendix B. In brief, projections of the direct medical costs of CVD were estimated in several steps. First, we estimated total annual medical expenditures for people by medical condition. Expenditures attributable to each CVD condition were calculated as the difference in predicted expenditures for a person with the specified condition and predicted expenditures for a similar person without the condition. We avoided double counting the expenditures resulting from individuals with multiple conditions by using a previously developed procedure (described in more detail in Appendix B).13 We then estimated total medical costs of CVD by multiplying the per person cost of each CVD condition by the projected number of people with the condition.

Projections of Indirect Costs of CVD

Two types of indirect costs were calculated: lost productivity from (1) morbidity and (2) premature mortality. Morbidity costs represent the value of foregone earnings from lost productivity due to CVD. Morbidity costs include 3 components: work loss among currently employed individuals, home productivity loss (defined as the value of household services performed by household members who do not receive pay for the services),14 and work loss among individuals too sick to work.15 Mortality costs represent the value of foregone earnings from premature mortality due to CVD. Details of indirect cost calculations are included in Appendix B.

Results

Table 1 describes the projected crude (not age-adjusted) CVD prevalence from 2010 to 2030. With the aging population, the prevalence of all CVD is projected to increase. People >65 years of age (especially >80 years of age) have a higher prevalence for all CVD, and this population segment will grow significantly in the next 2 decades. These increases translate to an additional 27 million people with hypertension, 8 million with CHD, 4 million with stroke, and 3 million with heart failure in 2030 relative to 2010. By 2030, 40.5% of the US population is projected to have some form of CVD.
Between 2010 and 2030, real (2008$) total direct medical costs of CVD are projected to triple, from $272.5 billion to $818.1 billion (Table 2). Because it has a higher prevalence than other CVD conditions, hypertension is the most expensive component of CVD. Annual costs directly attributable to hypertension are projected to increase to $130.4 billion (in real 2008$) in 2030 compared with 2010, for a total projected annual cost of $389.0 billion (in real 2008$) by 2030. If the costs of hypertension are expanded to include how much the presence of hypertension adds to the treatment of sequelae (ie, costs of hypertension as a risk factor), the increase in annual spending from 2010 to 2030 is $258.3 billion, with a projected annual total cost of $389.0 billion (in real 2008$) by 2030. Real medical costs of CVD and heart failure are projected to increase by approximately 200% over the next 20 years, and stroke is projected to have the largest relative increase in real annual medical costs of 238%.

Real indirect costs for all CVDs are estimated to increase from $171.7 billion in 2010 to $275.8 billion in 2030, an increase of 61% (Table 3). CHD has the highest indirect cost and is expected to continue to account for approximately 40% of all CVD indirect costs. Real indirect (lost productivity) costs of CVD are expected to grow over the next 20 years, but not as fast as the growth in direct medical costs (Figure 1). By 2030, the projected total cost of CVD, including direct and indirect costs, exceeds $1 trillion ($818.1 billion + $275.8 billion) (real 2008$).

The aging of the population combined with the growth in per capita medical spending are the primary drivers of increased CVD costs, which are expected to grow the fastest for ages 65 and over (Figure 2). The aging of the population has less of an impact on indirect costs than direct costs because of the lower rates of employment among the elderly. Annual CVD costs for people aged 65 to 79 years are projected to increase by 238%, from $135 billion to $457 billion per year. By 2018, CVD costs among those aged 65 to 79 years are expected to exceed CVD costs among those aged 45 to 64 years.

### Table 1. Projections of Crude CVD Prevalence (%), 2010–2030 in the United States

<table>
<thead>
<tr>
<th>Year</th>
<th>All CVD*</th>
<th>Hypertension</th>
<th>CHD</th>
<th>HF</th>
<th>Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>36.9</td>
<td>33.9</td>
<td>8.0</td>
<td>2.8</td>
<td>3.2</td>
</tr>
<tr>
<td>2015</td>
<td>37.8</td>
<td>34.8</td>
<td>8.3</td>
<td>3.0</td>
<td>3.4</td>
</tr>
<tr>
<td>2020</td>
<td>38.7</td>
<td>35.7</td>
<td>8.6</td>
<td>3.1</td>
<td>3.6</td>
</tr>
<tr>
<td>2025</td>
<td>39.7</td>
<td>36.5</td>
<td>8.9</td>
<td>3.3</td>
<td>3.8</td>
</tr>
<tr>
<td>2030</td>
<td>40.5</td>
<td>37.3</td>
<td>9.3</td>
<td>3.5</td>
<td>4.0</td>
</tr>
</tbody>
</table>

*This category includes hypertension, CHD, HF, and stroke.

### Table 2. Projected Direct (Medical) Costs of CVD, 2010–2030 (in Billions 2008$) in the United States

<table>
<thead>
<tr>
<th>Year</th>
<th>All CVD*</th>
<th>Hypertension</th>
<th>CHD</th>
<th>HF</th>
<th>Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>$272.5</td>
<td>$69.9</td>
<td>$35.7</td>
<td>$24.7</td>
<td>$28.3</td>
</tr>
<tr>
<td>2015</td>
<td>$358.0</td>
<td>$91.4</td>
<td>$46.8</td>
<td>$32.4</td>
<td>$38.0</td>
</tr>
<tr>
<td>2020</td>
<td>$470.3</td>
<td>$119.1</td>
<td>$61.4</td>
<td>$42.9</td>
<td>$51.3</td>
</tr>
<tr>
<td>2025</td>
<td>$621.6</td>
<td>$155.0</td>
<td>$81.1</td>
<td>$57.5</td>
<td>$70.0</td>
</tr>
<tr>
<td>2030</td>
<td>$818.1</td>
<td>$200.3</td>
<td>$106.4</td>
<td>$77.7</td>
<td>$95.6</td>
</tr>
</tbody>
</table>

% Change: 9.9 9.9 16.6 25.0 24.9

*This category includes hypertension, CHD, HF, and stroke.

### Table 3. Projected Indirect (Lost Productivity) Costs of CVD, 2010–2030 (in Billions 2008$) in the United States

<table>
<thead>
<tr>
<th>Year</th>
<th>All CVD*</th>
<th>Hypertension</th>
<th>CHD</th>
<th>HF</th>
<th>Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>$171.7</td>
<td>$23.6</td>
<td>$73.2</td>
<td>$9.7</td>
<td>$25.6</td>
</tr>
<tr>
<td>2015</td>
<td>$195.7</td>
<td>$27.2</td>
<td>$82.8</td>
<td>$11.3</td>
<td>$28.7</td>
</tr>
<tr>
<td>2020</td>
<td>$220.0</td>
<td>$31.0</td>
<td>$92.0</td>
<td>$13.0</td>
<td>$34.0</td>
</tr>
<tr>
<td>2025</td>
<td>$246.1</td>
<td>$35.1</td>
<td>$101.5</td>
<td>$15.1</td>
<td>$38.9</td>
</tr>
<tr>
<td>2030</td>
<td>$275.8</td>
<td>$39.8</td>
<td>$112.3</td>
<td>$17.4</td>
<td>$44.4</td>
</tr>
</tbody>
</table>

% Change: 61 69 53 80 73 69

*This category includes hypertension, CHD, HF, and stroke.

### Commentary

The current study found that the prevalence of CVD will increase by approximately 10% over the next 20 years under status-quo CVD prevention and treatment trends (ie, assuming no change to current policy), whereas the direct costs will increase almost 3-fold. Direct costs of CVD will continue to account for a relatively stable and large share of overall medical expenditures. By 2030, we estimate that >40% of US adults, or 116 million people, will have one or more forms of CVD.

Potential Impact of CVD Prevention

Although these projections are sobering, they need not become reality, because CVD is largely preventable. Several...
studies have demonstrated that individuals with favorable levels of major atherosclerotic risks have a marked reduction in the onset of CHD and heart failure. Similarly, people who follow a healthy lifestyle experience a comparably reduced risk of CHD and stroke. Therefore, a greater focus on prevention may alter these CVD projections in the future.

Improving population-level risk factors has clearly had a dominant impact on the decline in CVD death rates in the United States in the past. Smoking rates have declined since the first Surgeon General’s report on adverse effects of smoking in 1964. In addition, efforts to reduce dietary fat intake in the 1960s and 1970s, treat hypertension in the 1970s and 1980s (National High Blood Pressure Education Program), and improve blood lipid levels in the 1980s and 1990s (National Cholesterol Education Program) have likely contributed to dramatically reduced CVD death rates through declines in risk factors in the population. In addition to population-based strategies, individual interventions to treat high-risk individuals have a valuable complementary role in CVD risk reduction. Unfortunately, the adverse trends in obesity threaten to undermine the progress made from declining smoking rates.

Emerging evidence suggests that CVD prevention should begin earlier in life. In the Coronary Artery Risk Development in Young Adults (CARDIA) study, initial risk factor levels in those under age 30 years were predictive of established subclinical atherosclerosis at 15 years follow-up, and those with risk factors above optimal levels were 2- to 3-fold more likely to have subclinical disease. It is noteworthy that individuals who reach middle age with optimal levels of all major risk factors, the remaining lifetime risk of developing CVD is only 6% to 8%. Modest improvements in risk factors earlier in life can have a greater impact than more substantial reductions later in life. In one study, a genetic variant resulting in a modest 28% reduction in low-

Figure 1. Projected direct and indirect costs of all CVD, 2010 to 2030 (in billions 2008$).

Figure 2. Projected total (direct and indirect) costs of all CVD by age, 2010 to 2030 (in billions 2008$).
density lipoprotein cholesterol from birth resulted in 88% reduction in the risk of CHD,\textsuperscript{28} which is in contrast to the 20% to 30% reduction seen with a 30% reduction in low-density lipoprotein with statin medications initiated at middle and older ages.\textsuperscript{29}

Overall, hypertension has the greatest projected medical cost. The increased prevalence of hypertension is in part attributable to the aging of the population. However, analyses from the NHANES surveys from the years 1988 to 1991 to 1999 to 2000 revealed a 15% relative increase in the prevalence of hypertension after age adjustment\textsuperscript{40} and this prevalence has continued to increase through more recent NHANES surveys.\textsuperscript{31} Increasing body mass index contributed to >50% of the increase in hypertension. Reversing the obesity epidemic will play a pivotal role in favorably impacting the projected hypertension trends.

Hypertension accounts for 18% of CVD deaths in Western countries and is a major risk factor for stroke, CHD, and heart failure.\textsuperscript{32} Thus, the total medical costs for hypertension inclusive of these downstream diseases are approximately double the cost of hypertension itself, making hypertension a particularly valuable target to modify the future total costs of CVD.

A reduction in sodium intake is a promising goal for prevention and treatment of hypertension. A recent analysis using the Coronary Heart Disease Policy Model estimated that reducing dietary salt by 3 g per day per person would reduce the annual number of new cases of CHD by 60 000 to 120 000, stroke by 32 000 to 66 000, and myocardial infarction by 54 000 to 99 000 and reduce the annual number of deaths from any cause by 44 000 to 92 000.\textsuperscript{33}

Interest is growing in more personalized approaches to CVD prevention that can involve the assessment of genetic variants, biomarkers (eg, C-reactive protein) and imaging modalities (eg, coronary artery calcium scoring) to refine risk assessment and individually tailor prevention recommendations. Whether and how these will improve prevention or treatment of CVD and alter their future projections is yet to be realized. Despite the great enthusiasm for personalized medicine, further studies are needed to determine whether these personalized approaches are superior (or complementary) to population-based approaches to CVD prevention.\textsuperscript{34}

**Will the Provider Workforce Be Adequate?**

Changes in access to CVD providers and services may alter these projections in the future.\textsuperscript{2} Primary and secondary prevention of CVD requires a team approach with professionals prepared in medicine, nursing, pharmacy, nutrition, social work, and other disciplines. The projected lack of US healthcare professionals in the fields of nursing, pharmacy, and medicine are of particular concern.

The shortage in nursing has been well described\textsuperscript{35} and is projected to grow to 260 000 registered nurses by 2025.\textsuperscript{36} Although the percentage of nurses working exclusively with individuals with heart disease is unknown, the projected shortage is double that of any nursing shortage experienced since the mid-1960s and will likely negatively affect patient care. This shortage will be fueled by a rapidly aging workforce; a large segment of the registered nurse population is scheduled to retire over the next decade.\textsuperscript{37} Furthermore, as our healthcare system adopts a team-based approach to care, the demand for nurses with advanced education to fill managerial and quality improvement roles will increase substantially.\textsuperscript{38}

Pharmacists are also critical to the care of patients with cardiac disease. Currently, >8000 vacancies exist in retail pharmacies, hospitals, clinics, and other industry sectors, and these figures are expected to worsen over time.\textsuperscript{39} Finally, a looming shortage of physicians prompted the Council on Graduate Medical Education to recommend a 15% increase in 2003.\textsuperscript{40} More recently, the president of the Association of American Medical Colleges recommended that US medical schools increase the annual number of graduates by 30%.\textsuperscript{41} However, a large fraction of new US physicians come from non-US medical schools and it is unclear whether their numbers can be increased based on needs. Another barrier to increasing the number of physicians is the current Medicare payment program that limits the number of residency training positions funded annually.

Although primary care physicians are already in short supply, a significant shortage is growing in cardiac specialty care. A recent report estimated that there is a shortage of 1600 general cardiologists and 2000 interventional cardiologists.\textsuperscript{42} The current number of cardiologists would need to double by 2050 to erase the expected shortage of 16 000 cardiologists, if current trends continue. An even more marked shortfall is looming for cardiac surgery. Since 1975, the American Board of Thoracic Surgery has certified 4500 cardiothoracic surgeons. In recent years, this rate has dropped to ~100 new cardiothoracic residents completing training annually. At this rate, and taking into account death, retirement, and attrition, it is estimated that only 3000 practicing cardiothoracic surgeons will be in practice in the year 2030.\textsuperscript{43,44} Thus, the overall access of the population to cardiovascular care will likely be significantly limited without an active effort to enhance the recruitment of personnel into the various health professions responsible for prevention and treatment of CVD.

**Future Disparities in Care**

Disparities in incidence and outcomes for CVD,\textsuperscript{45–50} are observed across socioeconomic gradients and across geographic regions. Non-Hispanic blacks bear a disproportionate burden of morbidity and mortality attributable to CVD.\textsuperscript{51} Our projections indicate that the aging of the population will not change this pattern; blacks, averaged over age and sex cells, are projected to have continued higher prevalence rates for CVD (not reported).

Primary\textsuperscript{52} or secondary prevention of CVD is less common in disadvantaged individuals and communities. Such differences could be reduced by implementation of systems of care for such patients.\textsuperscript{53} Thus, there is a great opportunity to improve the health of the disadvantaged populations by dissemination and implementation of effective prevention strategies. For example, an average 3 g per person reduction in daily salt (1200 mg of sodium) intake is expected to reduce CHD by 15% among black men and women compared with a 10% reduction for nonblack men and women.\textsuperscript{53} Similar reductions (greater in blacks than nonblacks) would be expected for stroke and total mortality.

**Using Guidelines to Improve Care**

Care can also be improved through either the development of new guidelines and technologies or improved use of the existing guidelines. In an effort to increase the use of evidence-based practices,
the American Heart Association has partnered with the American College of Cardiology and other professional societies to produce guidelines for the care and prevention of CVD.54–57 Other prevention-oriented guidelines have been produced by the National Institutes of Health (eg, the National Cholesterol Education Program Adult Treatment Panel III)58 and the European Society of Cardiology.59

Although some providers expressed concern about loss of autonomy and decreased satisfaction with medical practice early on, subsequent studies demonstrated that guidelines can improve care.60 However, the implementation of a new practice guideline is often slow and modest given the passive nature of dissemination and diffusion.

Many have recognized that focusing on a few of the most important care strategies of a guideline can have a clinical impact. Accordingly, select measures, often referred to as performance measures, have been identified by accrediting bodies (eg, The Joint Commission), and payers (eg, Center for Medicare and Medicaid Services in conjunction with the American Heart Association and the American College of Cardiology).61,62 By publicly reporting these measures, requiring a certain level of performance for accreditation, and, in certain cases, linking performance on these measures to the hospital director’s compensation (Veterans Administration Healthcare system), adherence has risen dramatically for many of these measures.

Performance measures are a key component of the Get With The Guidelines program of the American Heart Association. Not only have hospitals been shown to improve care dramatically over time,63 those providing the highest levels of care based on the performance measures have better patient survival rates than hospitals not performing at the highest level.64 These findings indicate that guidelines and performance measures can have a substantial impact on prevention and treatment and will be an important tool for limiting the burden of CVD.

Policy Implications and Future Opportunities
The US healthcare system often rewards practices that treat disease and injury rather than those that prevent them. This has resulted in a population health status that has remained relatively unchanged in this decade despite exponential increases in healthcare spending.1,2 As our nation debates healthcare reform policies, we must realize that a variety of policy- and practice-related measures will be necessary to affect real change in the healthcare system. Expanding access to affordable healthcare coverage may provide important benefits for individuals with CVD.65 We must reorient our healthcare system toward implementing effective health promotion and disease prevention. This metamorphosis is not unrealistic and provides an exciting opportunity and call to action. The Centers for Disease Control and Prevention is committed to strengthening our collective capacity to protect and improve the nation’s health by responding to increasingly complex challenges, in particular, our epidemic of chronic diseases. Prevention at the community level is one such avenue to reduce the projected burden of CVD. Community prevention efforts may include greater tobacco control, elimination of artificial trans fat, reducing dietary sodium intake, reducing air pollution, reducing obesity, and increasing physical activity with a focus on children and the design of new communities.

The increased use of electronic medical records is also recommended and could have a positive impact on the prevention of CVD. The ability to systematically identify all patients with risk factors for CVD, address their barriers to care, and hopefully provide improved access to preventive care should result in beneficial alterations in current trends.

It should be recognized that, although prevention will delay or even prevent the onset of CVD and the cost of cardiovascular treatment,66 patients will need medical care longer and the lifetime cost of care may not be reduced as patients live longer. Thus, prevention strategies should not be evaluated solely on their ability to reduce cost of care, but instead they should be valued based on a combination of cost and impact on patient well being, including the length and quality of life.

Limitations
The projections are subject to sampling error in the underlying surveys; however, the combination of such a large number of data sources prevented calculation of confidence intervals. The human capital approach, as implemented, did not include the time value of informal caregivers of those with CVD.67 In general, the human capital approach does not capture the psychological costs of morbidity and, therefore, probably undervalues the morbidity costs for those not in the labor force.68 Our analysis did not separate out arrhythmias from other types of CVD. Atrial fibrillation, one of the most common types of arrhythmia, is projected to more than double in the next 40 years.69 It is important to note that our analysis did not assume any change in the prognosis of disease once established. To the extent that adherence to recommended treatments increases, or new life-prolonging technologies are developed, the prevalence of CVD will increase because patients will live longer with disease. However, if a reduction in the level of risk factors occurs, the prevalence and associated costs will be overestimated. Our study also assumed a continued acceleration of healthcare spending for CVD based on historical trends. If investment in new CVD technologies wanes, fewer advances in care will occur and will impact costs.

The authors acknowledge that differences exist between CVD cost estimates for 2010 presented in this statement and those previously published in the Heart Disease and Stroke Statistics—2010 Update: A Report From the American Heart Association.2 For this study, we used more recent data and a different methodology for estimating medical (direct) costs of CVD that minimizes double counting disease costs across categories. We followed methodology used by Lloyd-Jones et al12 to estimate indirect costs of CVD but our estimates are based on more recently available data.

Conclusion
CVD prevalence and costs are projected to increase substantially in the future. It is fortunate that CVD is largely preventable; our healthcare system should promote prevention and early intervention. In the public health arena, more evidence-based effective policy, combined with systems and environmental approaches should be applied in the prevention, early detection, and management of CVD risk factors. Through a combination of improved prevention of risk factors, and treatment of established risk factors, the dire projection of the health and economic impact of CVD can be diminished.
Appendix A: Data Definitions

Table A1. Questions/Measures and ICD-9 Codes Used to Define CVD Conditions in NHANES and MEPS

<table>
<thead>
<tr>
<th>Condition</th>
<th>Qualifying Questions/Measures From NHANES</th>
<th>ICD-9 Codes From MEPS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>Were you told on 2 or more different visits that you had hypertension, also called high blood pressure? Are you now taking prescribed medicine for your high blood pressure? Average SBP ≥140 or average DBP ≥90</td>
<td>401, 403</td>
</tr>
<tr>
<td>CHD</td>
<td>Has a doctor or other health professional ever told you that you had coronary heart disease? Has a doctor or other health professional ever told you that you had angina, also called angina pectoris? Has a doctor or other health professional ever told you that you had a heart attack (also called myocardial infarction)? Rose Questionnaire</td>
<td>410, 411, 412, 413, 414</td>
</tr>
<tr>
<td>HF</td>
<td>Has a doctor or other health professional ever told you that you had congestive heart failure?</td>
<td>428</td>
</tr>
<tr>
<td>Stroke</td>
<td>Has a doctor or other health professional ever told you that you had a stroke?</td>
<td>430, 431, 433, 434, 436, 438</td>
</tr>
</tbody>
</table>

CVD indicates cardiovascular disease; NHANES, National Health and Nutrition Examination Survey; MEPS, Medical Expenditure Panel Survey; ICD-9, International Classification of Diseases, Ninth Revision; SBP, systolic blood pressure; DBP, diastolic blood pressure; CHD, coronary heart disease; HF, heart failure; NA, not applicable.

Appendix B: Detailed Data and Methods

Projections of CVD Prevalence

The prevalence of hypertension, CHD, heart failure, and stroke was estimated using data from the 1999 to 2006 NHANES. The NHANES is a survey of a nationally representative sample administered by the National Center for Health Statistics, which is part of the Centers for Disease Control and Prevention. The survey includes an interview and a physical examination component where the interview includes demographic, socioeconomic, dietary, and health-related questions and the examination component consists of medical, dental, and physiological measurements, as well as laboratory tests administered by highly trained medical personnel. The prevalence of hypertension was based on blood pressure measurements and the responses to interview questions about being told of having high blood pressure and taking blood pressure medications. The prevalence of CHD was based on patient self-report during an interview that asked about CHD, angina, or heart attack. The prevalence of heart failure and stroke was based on patient self-report. A list of qualifying measures and questions used to define each condition is presented in Table A1.

We estimated the prevalence of each CVD condition by use of logistic regression models controlling for survey year and demographics (age, sex, and race/ethnicity). Stepwise regressions were used to determine the significant interactions of the demographics to be included in the models. We predicted the prevalence of each condition in each sex/age/race cell for 2005 to 2006 using coefficients from the logistic regressions. Prevalence estimates were adjusted to account for the nursing home care population with use of data from the 2004 National Nursing Home Survey.

Prevalence estimates were then combined with Census projections of population counts for years 2010 to 2030 to generate the projected number of people with each CVD condition and projected CVD prevalence for years 2010 to 2030. Projected population counts for years 2010 to 2030 were obtained from the 2008 Population Projections of the United States resident population by age, sex, race, and Hispanic origin generated by the US Census Bureau. The 2008 projections are based on Census 2000 and were produced using a cohort-component method. The projections are based on assumptions about future births, deaths, and net international migration. We multiplied the predicted prevalence of each CVD condition in each sex/age/race cell by the projected population counts in the corresponding cells for years 2010 to 2030 to project the number of people with CVD in each cell in each of the years. We then aggregated the number of people with CVD by sex, by age, and by race and calculated the projected CVD prevalence overall and by each demographic characteristic.

Projections of CVD Direct (Medical) Costs

The main data source for generating projections of medical costs of CVD was the 2001 to 2005 MEPS. MEPS is a nationally representative survey of the civilian noninstitutionalized population administered by the Agency for Healthcare Research and Quality. MEPS provides data on participants’ utilization of medical services and the corresponding medical costs. Medical conditions are identified in MEPS Medical Condition files based on self-reports of conditions affecting the respondent within the interview year. Medical conditions are classified using International Classification of Diseases, Ninth Revision, Clinical Modifications codes based on self-reported conditions that were transcribed by professional coders. Conditions were defined using International Classification of Diseases, Ninth Revision, Clinical Modifications codes with a full list of the codes presented in Table A1 (Appendix A). The MEPS data measure total annual medical spending, including payments by insurers and out-of-pocket...
spending (copayments, deductibles, and payments for non-covered services). The costs captured by MEPS represent payments (not charges) from the payer to the provider. MEPS spending data are obtained through a combination of self-report and validation from payers (e.g., private insurers).

Projections of the direct medical costs of CVD were estimated in 5 steps. First, we estimated per person medical costs as a function of health conditions using a 2-part regression model. In the first part of the 2-part model, we used a logistic regression model to predict the probability of any expenditures. For the second part of the model, we used a generalized linear model with a gamma distribution and a log link to estimate total annual medical expenditures for people having any expenditures. We used an algorithm for choosing among alternative nonlinear estimators recommended by Manning and Mullahy and found that this type of model was the most appropriate for the data. Our model controlled for CVD conditions and other potentially costly or prevalent medical conditions and sociodemographic variables.

Second, expenditures attributable to each CVD condition were calculated as the difference in predicted expenditures for a person with the specified condition and predicted expenditures for a similar person without the condition. We estimated the per person cost attributable to each CVD condition for each age/sex/race cell based on coefficients from the national, pooled model.

Disease-attributable expenditures are typically calculated by predicting expenditures using observed diseases and subtracting from that predicted expenditures setting the disease of interest (e.g., CHD) to zero and leaving all other covariates and diseases as they are in the data. However, in previous work, we have shown that, in nonlinear models, such as that the model used here, this approach will lead to double counting of expenditures for co-occurring diseases, regardless of whether one disease causes the other. Double counting of expenditures is a particular problem in cases where more than one condition is treated during a single office visit or hospitalization. We used a technique, termed “complete classification” and described in an earlier study, to ensure that no double counting occurs. Using the parameters of the econometric model, we specifically treated each disease and combination of diseases observed in the data as its own separate entity when calculating the attributable costs. For example, CHD alone and CHD with hypertension would be treated as 2 different diseases in the attributable expenditure calculation described above. We then divided the total expenditures attributable to the combinations of diseases back to the constituent diseases using the parameters from the model to construct shares for each constituent disease within a combination (i.e., a share of all CHD with hypertension disease costs that are attributable to CHD). The shares attribute a greater share of the joint expenditures to the disease with the larger coefficient in the main effect. The formula to construct the shares is given in Trogdon, Finkelstein, and Hoerger.

Our third step in calculating projections of direct medical costs was to adjust the per person cost estimates to account for nursing home spending by use of data from the 2004 National Nursing Home Survey and National Health Accounts. We assumed that per person, non-nursing home expenditures attributable to CVD were the same for the nursing home population as for the noninstitutionalized population.

Fourth, to estimate projected costs, we first followed recommendations from the Agency for Healthcare Research and Quality to inflate dollar values in the MEPS data to 2008. We then multiplied the per person cost of each CVD condition in each sex/age/race cell by the projected number of people treated for each disease in the corresponding cells for years 2010 to 2030 and summed across CVD conditions to estimate total medical costs of CVD. The projected number of people treated for each disease was calculated by using similar methodology as outlined in the Prevalence Section. However, instead of the NHANES data, we used 1996 to 2005 MEPS to predict the treated prevalence of each condition, because only those patients who receive treatment incur medical costs within a certain year.

Finally, we used Congressional Budget Office assumptions for future healthcare cost growth above and beyond growth due to population growth and aging. We assumed that the costs of CVD would increase at the same rate as overall medical expenditures between 2010 and 2030: an average annual rate of 3.6%.

Projections of Indirect Costs of CVD

Two types of indirect costs were calculated: lost productivity from (1) morbidity and (2) premature mortality.

Morbidity Costs of CVD

Morbidity costs represent the value of foregone earnings from lost productivity due to CVD. Morbidity costs include 3 components: work loss among currently employed individuals, home productivity loss, and work loss among individuals too sick to work. Per capita work lost days due to CVD by age, sex, and race/ethnicity were estimated by use of 2001 to 2005 MEPS. We estimated a negative binomial model for annual days of work missed because of illness or injury as a function of CVD, other comorbid conditions, and sociodemographic variables. Per capita work days lost because of CVD for each age/sex/race cell were based on coefficients from the national, pooled model. As for medical expenditures, we avoided double counting of costs resulting from individuals with multiple conditions by using the previously cited procedure. We generated total work loss costs by multiplying per capita work days lost owing to CVD by (1) prevalence of CVD (by age, sex, and race/ethnicity) from MEPS, (2) the probability of employment given CVD (by age, sex, and race/ethnicity) from MEPS, (3) mean per capita daily earnings (by age and sex) from the 2008 Current Population Survey, and (4) Census population projections counts (by age, sex, and race/ethnicity).

Home productivity loss was estimated by valuing days spent in bed because of CVD at the replacement cost of housekeeping services. Per capita days in bed because of CVD by age, sex, and race/ethnicity were estimated by using 2001 to 2005 MEPS and the same strategy as outlined above for work days lost. We generated total home productivity loss
costs by multiplying per capita bed days due to CVD by (1) prevalence of CVD (by age, sex, and race/ethnicity) from MEPS, (2) dollar value of a day of house work (by age and sex), and (3) Census population projections counts (by age, sex, and race/ethnicity).

To estimate work loss among individuals too sick to work because of CVD, we first estimated the number of people too sick to work who would have been employed, with the exception of their CVD. For the noninstitutionalized population, we multiplied the number of people not in the labor force because of illness/disability by age from the Current Population Survey by the percentage of all work loss because of CVD based on the MEPS regression analysis for work loss days described above. The assumption was that the percentage of work days missed because of CVD was the same for days missed by being out of the labor force and for days missed conditional on working. For the institutionalized population, we multiplied the number of people with a primary diagnosis of CVD from the 2004 National Nursing Home Survey (as percentage of total population) by Census population counts and the probability of employment given CVD (by age, sex, and race/ethnicity) from MEPS. The last component accounts for individuals with CVD who might not work even if they had not been institutionalized. Finally, the sum of the number of noninstitutionalized and institutionalized people too sick to work because of CVD was multiplied by 250 work days per year and mean annual earnings from the 2008 Current Population Survey.

**Mortality Costs of CVD**

Mortality costs represent the value of foregone earnings from premature mortality due to CVD. We began with estimates of lifetime earnings by sex and age provided by the National Heart, Lung, and Blood Institute to the American Heart Association (unpublished). We then expressed these 2003 values in real 2008 dollars using the Census price deflator and adjusted the values based on observed changes in real earnings between 2003 and 2008.

We estimated death rates for each CVD category by age, sex and race/ethnicity with use of 2006 National Vital Statistics data. Assuming that the death rates remain constant within the age, sex, and race/ethnicity cell, we multiplied the death rates by Census population projections to project the number of CVD deaths by age, sex, race/ethnicity, and year through 2030. Finally, we multiplied age- and sex-specific remaining lifetime earnings by the projected number of deaths in the corresponding age/sex cells to get projections of total mortality costs. The real value of indirect costs (morbidity and mortality) were assumed to grow at the Congressional Budget Office average annual growth rate of real earnings (1.4%) through 2030.

### Disclosures

#### Writing Group Disclosures

<table>
<thead>
<tr>
<th>Writing Group Member</th>
<th>Employment</th>
<th>Research Grant</th>
<th>Other Research Support</th>
<th>Speakers' Bureau/ Honoraria</th>
<th>Expert Witness</th>
<th>Ownership Interest</th>
<th>Consultant/ Advisory Board</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paul A. Heidenreich</td>
<td>VA Palo Alto Health Care System</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Javed Butler</td>
<td>Emory University</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Kathleen Dracup</td>
<td>University of California, San Francisco School of Nursing</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Michael D. Ezekowitz</td>
<td>Lankenau Institute for Medical Research</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>ARX Therapeutics; Sanofi; Bristol-Myers Squibb; Medtronics</td>
<td>None</td>
</tr>
<tr>
<td>Eric Andrew Finkelstein</td>
<td>Duke-NUS (Singapore); limited consulting with RTI</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Yuling Hong</td>
<td>Centers for Disease Control and Prevention</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>S. Clbourne Johnston</td>
<td>University of California San Francisco Medical Center</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Olga A. Khavjou</td>
<td>Research Triangle Institute International</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Amit Khera</td>
<td>University of Texas Southwestern Medical Center</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Donald M. Lloyd-Jones</td>
<td>Northwestern</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Sue A. Nelson</td>
<td>American Heart Association</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>
### Writing Group Disclosures, Continued

<table>
<thead>
<tr>
<th>Writing Group Member</th>
<th>Employment</th>
<th>Research Grant</th>
<th>Other Research Support</th>
<th>Speakers’ Bureau/ Honoraria</th>
<th>Expert Witness</th>
<th>Ownership Interest</th>
<th>Consultant/ Advisory Board</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Graham Nichol</td>
<td>University of Washington</td>
<td>†Resuscitation Outcomes Consortium (NIH U01 HL077863-05) 2004–2010; Co-PI</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>Unpaid collaborator, Soteria Wireless Inc., San Diego, CA*; Unguarded collaborator, Gambro Renal Inc., Lakewood, CO*; Unguarded collaborator, Lifebridge USA Inc., San Antonio, TX*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>†Evaluation of Video Self-Instruction in Compressions-Only CPR (Asmund S. Laerdal Foundation for Acute Medicine) 2007–2010; PI</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>†Randomized Trial of Hemofiltration After Resuscitation from Cardiac Arrest (NHBLI R21 HL089341-01A1) 2009–2011; PI</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>†Randomized Field Trial of Cold Saline IV After Resuscitation from Cardiac Arrest (NHBLI R01 HL089554-03) 2007–2012; Co-I</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>†Endovascular therapy for Advanced Heart Failure Trial (RAFT) (200211UC-T105607) 2003–2010; Co-I</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>†Cascade Recombinant Human insulin in LV Dysfunction (PARR 2) 5 Year Follow-Up (162502) 2007–2010; Co-I</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>†Novel Methods of Measuring Health Disparities (K22HL101759-01) 2009–2011; Co-I</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Diane Orenstein</td>
<td>Centers for Disease Control and Prevention</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Justin G. Trogdon</td>
<td>Research Triangle Institute International</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Peter W.F. Wilson</td>
<td>Emory University</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Y. Joseph Woo</td>
<td>University of Pennsylvania</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td></td>
</tr>
</tbody>
</table>

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 (a) the person receives $10,000 or more during any 12-month period, or 5% or more of the person’s gross income; or (b) 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

<table>
<thead>
<tr>
<th>Reviewer</th>
<th>Employment</th>
<th>Research Grant</th>
<th>Other Research Support</th>
<th>Speakers’ Bureau/ Honoraria</th>
<th>Expert Witness</th>
<th>Ownership Interest</th>
<th>Consultant/ Advisory Board</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vincent J. Bufalino</td>
<td>Midwest Heart Specialists</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Lynn V. Doering</td>
<td>UCLA</td>
<td>NIH†</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Mark A. Hitakky</td>
<td>Stanford University</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Daniel Mark</td>
<td>Duke University</td>
<td>Alexion Pharmaceuticals, Inc.;† Eli Lilly &amp; Company;† Proctor &amp; Gamble;† Pfizer;† Medtronic, Inc.;† Medicare;† Innocoll;† St. Jude†</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Christopher O’Donnell</td>
<td>NHLBI</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Barbara Riegel</td>
<td>University of Pennsylvania</td>
<td>NIH†</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Veronique L. Roger</td>
<td>Mayo Clinic</td>
<td>NHBLI†</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Frank W. Sellke</td>
<td>Beth Israel Deaconess Medical Center</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>William Weintraub</td>
<td>Christiana Hospital</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

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 (a) the person receives $10,000 or more during any 12-month period, or 5% or more of the person’s gross income; or (b) 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.
References


