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Value of Primordial and Primary Prevention for Cardiovascular Disease

A Policy Statement From the American Heart Association

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on behalf of the American Heart Association Advocacy Coordinating Committee, Council on Cardiovascular Disease in the Young, Council on the Kidney in Cardiovascular Disease, Council on Epidemiology and Prevention, Council on Cardiovascular Nursing, Council on Arteriosclerosis, Thrombosis and Vascular Biology, Council on Clinical Cardiology, and Stroke Council

Abstract—The process of atherosclerosis may begin in youth and continue for decades, leading to both nonfatal and fatal cardiovascular events, including myocardial infarction, stroke, and sudden death. With primordial and primary prevention, cardiovascular disease is largely preventable. Clinical trial evidence has shown convincingly that pharmacological treatment of risk factors can prevent events. The data are less definitive but also highly suggestive that appropriate public policy and lifestyle interventions aimed at eliminating tobacco use, limiting salt consumption, encouraging physical exercise, and improving diet can prevent events. There has been concern about whether efforts aimed at primordial and primary prevention provide value (ie, whether such interventions are worth what we pay for them). Although questions about the value of therapeutics for acute disease may be addressed by cost-effectiveness analysis, the long time frames involved in evaluating preventive interventions make cost-effectiveness analysis difficult and necessarily flawed. Nonetheless, cost-effectiveness analyses reviewed in this policy statement largely suggest that public policy, community efforts, and pharmacological intervention are all likely to be cost-effective and often cost saving compared with common benchmarks. The high direct medical care and indirect costs of cardiovascular disease—approaching \$450 billion a year in 2010 and projected to rise to over \$1 trillion a year by 2030—make this a critical medical and societal issue. Prevention of cardiovascular disease will also provide great value in developing a healthier, more productive society. (*Circulation*. 2011;124:00-00.)

Key Words: AHA Scientific Statements ■ cardiovascular diseases ■ prevention

Cardiovascular disease (CVD), including heart disease and stroke, is the leading cause of death and disability in women and men in the United States.¹ The preclinical substrates for clinical CVD (eg, fatty streaks and atherosclerosis) begin early in life and are influenced over time by potentially modifi-

able risk factors, behaviors, and environmental exposures. Favorable risk factor levels in middle age are associated with a lower lifetime risk for CVD mortality, increased survival, and improved quality of life.² Population-based and clinical studies highlight the importance of primordial prevention, defined

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herein as prevention of the development of risk factors in the first place,³ and primary prevention, defined as interventions designed to modify adverse levels of risk factors once present with the goal of preventing an initial CVD event.^{4,5} Recently, the passage of the Patient Protection and Affordable Care Act (PPACA) (public law 111–148) has focused the attention of policy makers, providers, and consumers on the value and cost savings/cost-effectiveness of life-course primordial and primary prevention strategies.⁶

Although it is clear and accepted from clinical trial data that prevention is efficacious (ie, that prevention works within the scope of the trial), it is less well accepted that preventive community interventions are effective and provide value (ie, that prevention will work in the community and is worth what we will pay for it). This statement summarizes the rationale and available evidence that support a life-course approach to primordial and primary prevention, as well as the cost-effectiveness (ie, value) of, multilevel policy implications for, and fertile areas for future research of preventive intervention. A primer on cost-effectiveness is provided as an Appendix. Common terms used in cost-effectiveness analysis are defined in Table 1. Table 2 provides a summary of the various cost-savings/cost-effectiveness data for various primordial or primary prevention initiatives reviewed in this statement.

Rationale for Life-Course Approach to Primordial and Primary Prevention

The life course is generally divided into 5 stages: fetal development and the maternal environment, infancy and childhood, adolescence, adulthood, and older age.²⁹ Although these stages are distinctly identified, they merge into one another, and influences during each life stage can have subsequent impact throughout the course of life. Disturbing trends for chronic disease and conditions like obesity and diabetes mellitus are emerging in which the incidence rates not only are increasing but also are affecting people at an earlier age.²⁹ These trends highlight the important need for primordial and primary prevention across the lifespan. Prevention efforts targeted at one point during the life course may have a lasting impact later in life or even from one generation to the next. For example, smoking cessation programs targeted at pregnant mothers can influence not only maternal health but also fetal health and infant and childhood well-being, including the incidence of ear infections, asthma, sudden infant death syndrome, and respiratory infections.

No multidecade, population-based, longitudinal studies have been conducted linking absolute levels of risk factors in childhood to incident clinical CVD events in adult life. Moreover, no randomized clinical trials have demonstrated that reduction of risk factor levels in childhood prevents cardiovascular events in adult life. Such studies are difficult to undertake in light of the large sample sizes, multidecade follow-up, and costs of long-term interventions and monitoring that would be required. Large cohort studies are possible; in particular, the National Children's Study is just getting underway (in 2011). It will examine the effects of the environment, defined broadly, and genetics on the growth, development, and health of children across the United States.³⁰ The study will follow the cohort from before birth to

Table 1. Glossary of Terms in an Economic Analysis

Term	Definition
Cost-effectiveness analysis	A formal approach to assessing value in which the effectiveness and costs of a medical service are compared with a previous standard
Direct costs	Costs directly related to medical care provided such as the cost of a diagnostic test or a medication
Indirect costs	Costs that are incurred as a result of illness but not actually part of the medical service; lost income from missing time at work is a common example
Average costs	All costs related to a medical service, including both fixed and marginal costs
Fixed costs	Costs that will be spent regardless of the number of services, including the cost of developing the facility
Marginal cost	The cost of the next service of a particular type such as the next stress test, including the cost of equipment or pharmaceuticals that are used only once; the cost of a coronary stent would be a marginal cost
Utility	Overall evaluation of health status, generally with 1 meaning optimal health and functioning and 0 being death
QALYs	QALYs are calculated by multiplying survival by utility; if a patient is expected to live for 10 y at 0.8 utility, this would be 8 QALYs; QALYs are often used as a measure of effectiveness when calculating an ICER
ICER	An ICER is the most common measure of cost-effectiveness; cost-effectiveness always compares one service with another such as a new treatment for hypertension compared with the previous standard; the ICER is calculated by first determining the incremental cost-effectiveness of the new therapy compared with the standard; the ICER is then the incremental cost divided by the incremental effectiveness
Willingness-to-pay threshold	The amount of money that an individual or group of individuals will pay for a medical service; an ICER below the threshold would be considered cost-effective, whereas an ICER above the threshold is not cost-effective
Discounting	Both future cost and survival are generally discounted, which means that people value cost over a 1-y period or 1 y of survival at the present time more than costs or 1 y of survival in the future; thus, with a discount rate of 3%, next year's costs or survival is 3% less important than this year's costs or survival

QALY indicates quality-adjusted life-years; ICER, incremental cost and incremental effectiveness ratio.

21 years of age and will contribute to an understanding of the role that various factors have on health and disease.

Several lines of evidence support the need for and value of primordial and primary prevention beginning early in life. This evidence base includes pathology studies of child and adolescent decedents that demonstrate that the extent of atherosclerotic vascular change is associated with the number and intensity of premortem modifiable risk factors and behaviors.^{31–33} Further evidence comes from noninvasive imaging studies demonstrating that adverse levels of major risk factors for CVD measured in childhood and adolescence are associated with a prognostically significant early indicator of subclinical atherosclerosis, increased carotid intima-media

Table 2. Summary of Cost Savings or Value for Key Primordial and Primary Prevention Strategies in the United States

Intervention	Primordial or Primary Prevention	Cost Savings/Value	Source
Comprehensive prevention programs			
Community-based programs to increase physical activity, to improve nutrition, and to prevent smoking and other tobacco use	Primordial	A return on investment of \$5.60 for every \$1 spent within 5 y	7
Comprehensive worksite wellness programs	Primordial and primary	Within first 12 to 18 mo, medical costs fall by approximately \$3.27 for every \$1 spent on worksite wellness; absenteeism costs fall by about \$2.73 for every \$1 spent	8
Comprehensive school-based initiatives to promote healthy eating and physical activity	Primordial	Cost-effectiveness is \$900–\$4305 per QALY saved	9, 10
Physical activity			
Building bike and pedestrian trails	Primordial and primary	Nearly \$3 in medical cost savings is seen for every \$1 invested in building these trails	11
Physical activity interventions such as pedometer and walking programs	Primordial and primary	ICERs ranging from \$14 000–\$69 000 per QALY gained relative to no intervention, especially in high-risk groups	12–14
Diet/nutrition			
Reducing sodium in the food supply	Primordial and primary	It is estimated that reducing population sodium intake to 1500 mg/d would result in \$26.2 billion in healthcare savings annually	15
Obesity prevention			
Obesity management program	Primary	1-y interventions have shown reduction in risk categories such as poor eating and poor physical activity habits and in weight for a return on investment of \$1.17 for every \$1 spent	16
Tobacco control and prevention			
Excise taxes	Primary	A 40% tax-induced cigarette price increase would reduce smoking prevalence to 15.2% by 2025 with large gains in cumulative life-years (7 million) and QALYs (13 million) for a total cost savings of \$682 billion	17
Comprehensive smoke-free air laws in public buildings	Primordial	Eliminating exposure to second-hand smoke would save an estimated \$10 billion annually in direct and indirect healthcare costs	18
Tobacco cessation programs	Primary	ICERs for treatment programs range from a few hundred to a few thousand dollars per QALY saved	19
Comprehensive coverage for tobacco cessation programs in Medicaid programs	Primary	Comprehensive coverage led to reduced hospitalizations for heart attacks and a net savings of \$10.5 million or a \$3.07 return on investment for every \$1 spent; states offering comprehensive smoking cessation therapy to their employees or in their tobacco control and prevention programs save \$1.10–\$1.40 in healthcare expenditures and productivity for every \$1 spent	20, 21
Tobacco cessation programs for pregnant women	Primary for mother; primordial for fetus	These programs produce a cost-to-benefit ratio as high as 3:1 (ie, for every \$1 invested in cessation/relapse programs, \$3 are saved in downstream health-related costs)	22
Diabetes prevention			
Diabetes screening	Primordial	Targeted screening for T2DM based on age and risk was found to be far more cost-effective (ICERs ranging from \$46 800–\$70 500 per QALY gained) compared with universal screening (ICERs from \$70 100–\$982 000 per QALY gained); targeted screening for undiagnosed T2DM in blacks between 45 and 54 y of age was found to be the most cost-effective with an ICER of \$19 600 per QALY gained relative to no screening	23, 24
Lifestyle changes in diabetes prevention	Primary	Lifestyle changes reduced the incidence of diabetes mellitus by 58%, whereas metformin therapy reduced risk by 31%; in patients with impaired glucose tolerance, primary prevention in the form of intensive lifestyle modification has median ICERs of \$1500 per QALY gained	23, 25
Cholesterol screening and prevention			
Widespread use of statins	Primary	Full adherence to ATP III primary prevention guidelines would prevent 20 000 myocardial infarctions and 10 000 CVD deaths at a total cost \$3.6 billion or \$42 000 per QALY if low-intensity statins cost \$2.11 per pill (which is substantially higher than the cost of currently available, effective generic statins); at a \$50 000 willingness-to-pay threshold, statins are cost-effective up to \$2.21 per pill	26
Blood pressure			
Hypertension medication therapy	Primary	Approximate \$37 100 cost per life-year saved	27
Polypill administration	Primary	Polypill medication treatment in men was less expensive and more effective, with an average cost of \$70 000 compared with \$93 000 for no treatment, and resulted in 13.62 QALYs compared with 12.96 QALYs without treatment	28

QALY indicates quality-adjusted life-years; ICER, incremental cost and incremental effectiveness ratio; T2DM, type 2 diabetes mellitus; ATP III, Adult Treatment Panel III; and CVD, cardiovascular disease.

thickness, in adulthood.^{34–37} Results from a population-based prospective cohort study, the Young Finns Study, are particularly noteworthy because risk factor exposures (including low-density lipoprotein cholesterol [LDL-C], body mass index, cigarette smoking, and systolic blood pressure) in 12- to 18-year-old adolescents predicted increased carotid intima-media thickness in adulthood independently of the risk factors for CVD present in adulthood.³² More recently, in a cross-sectional comparative study of lean and obese children and youth with type 2 diabetes mellitus (T2DM), those with T2DM had significantly greater carotid intima-media thickness and stiffer carotid arteries than their leaner counterparts.³⁸ The presence of either T2DM or obesity contributed independently to adverse changes in carotid structure and function.³⁸ Moreover, a combined data analysis from 4 cohorts comprising 4380 patients showed that risk factors from 9 years of age were predictive of carotid intima-media thickness in adulthood.³⁹

Additional evidence supporting the need for primordial and primary prevention beginning early in life comes from population-based epidemiological studies indicating that major risk factors for and adverse health behaviors associated with CVD in adulthood, including cigarette smoking, dyslipidemia (high levels of LDL-C and low levels of cardioprotective high-density lipoprotein cholesterol), elevated blood pressure, physical inactivity, and obesity, are prevalent in childhood and adolescence^{1,40–42} and are potentially modifiable.^{43,44} The US Surgeon General's office reported that "overweight adolescents have a 70% chance of becoming overweight or obese adults. This increases to 80% if one or more parent is overweight or obese. Overweight or obese adults are at risk for a number of health problems including CVD, T2DM, high blood pressure, and some forms of cancer."⁴⁵ Tracking of risk factors from childhood to young adulthood and intraindividual clustering of risk factors and adverse health behaviors have been well documented in clinical and population-based studies in the United States and globally.^{46–48} Finally, the efficacy and safety of modifying major CVD risk factors in early life with therapeutic lifestyle change and, although data on safety are more limited, the efficacy of pharmacological interventions have also been demonstrated.^{49–53} More data in large populations are needed to establish the safety of pharmacological therapy begun in the young and continued long term.

Collectively, these data have led to the development of primordial and primary prevention of CVD guidelines in children and youth^{4,54–56} and throughout the life course.^{57,58} With emphasis on the development of healthy lifestyle behaviors as the cornerstone of both primordial and primary prevention, the ultimate goal is to promote optimal cardiovascular health beginning in childhood and adolescence and continuing throughout the life course to reduce the risk and burden of CVD and its sequelae.

Prevention Framework in the United States

The framework for health in the United States is the Healthy People framework. Healthy People 2020 is the current iteration.⁵⁹ The US Preventive Health Services Task Force and the Task Force on Community Preventive Services, sponsored by the Agency for Healthcare Research and Quality and the Centers for

Disease Control and Prevention, respectively, have attempted to evaluate the evidence for the effectiveness of preventive services.⁶⁰

Healthy People 2020 lays out a set of objectives for optimizing the health of America. The most relevant categories of Healthy People 2020 objectives include diabetes mellitus, heart disease and stroke, nutrition and weight status, physical activity and fitness, and tobacco use.⁵⁹ However, it is clear that there are substantial deficiencies and disparities in the delivery of preventive services.⁶¹ The PPACA tried to address some of these deficiencies in clinical and community-based prevention in several programs created by the new law.^{6,62}

The PPACA mandates that clinical preventive services graded A or B by the US Preventive Health Services Task Force will be offered to people with insurance at no out-of-pocket cost. Among the CVD-related A or B services are aspirin counseling, blood pressure screening, cholesterol screening, healthy diet counseling, obesity screening and counseling, and tobacco cessation counseling.⁶⁰ The National Commission on Prevention Priorities, before the PPACA, ranked 25 US Preventive Health Services Task Force A and B–graded services according to health impact and cost-effectiveness.⁶³ The CVD services favorably ranked when cost-effectiveness was included as a criterion were aspirin counseling, blood pressure screening, cholesterol screening, and tobacco use counseling.

The PPACA also strengthens the Community Guide, which addresses health improvement and disease prevention at the community level by conducting systematic reviews to determine effective program and policy interventions and grading the interventions.^{64,65} Nutrition, obesity, physical activity, and tobacco are among the Community Guide topics.

The Economic Burden of Cardiovascular Disease and Potential to Reduce Cost

The direct and indirect costs of CVD in the United States have been projected by the American Heart Association to increase from \$272.5 and \$171.7 billion in 2010 to \$818.1 and \$275.8 billion in 2030, respectively.⁶⁶ Most of the cost of CVD is related to short- and long-term care, not prevention.⁶⁷ In addition, these cost estimates do not include all costs related to obesity, diabetes mellitus, and tobacco use. Despite the fall in overall mortality, the prevalence of disease is expected to increase, largely as a result of the aging of the population. This troubling scenario is not inevitable; most CVD is preventable or at least can be delayed until old age with less chronic morbidity, with the potential for fewer events, less disability, and even lower costs.

Challenges in Determining the Cost-Effectiveness of Primordial and Primary Prevention

Cardiovascular disease remains a serious medical problem that can be associated with death and disability on one hand and considerable resource use on the other. Clinical efficacy remains the primary driver for the use of any service. Once efficacy is established and despite its many limitations, cost-effectiveness analysis has an important role in assessing value. Properly applied, cost-effectiveness analysis not only offers a ratio and its distribution but also renders explicit the assumptions underlying the analysis (ie, costs of therapy,

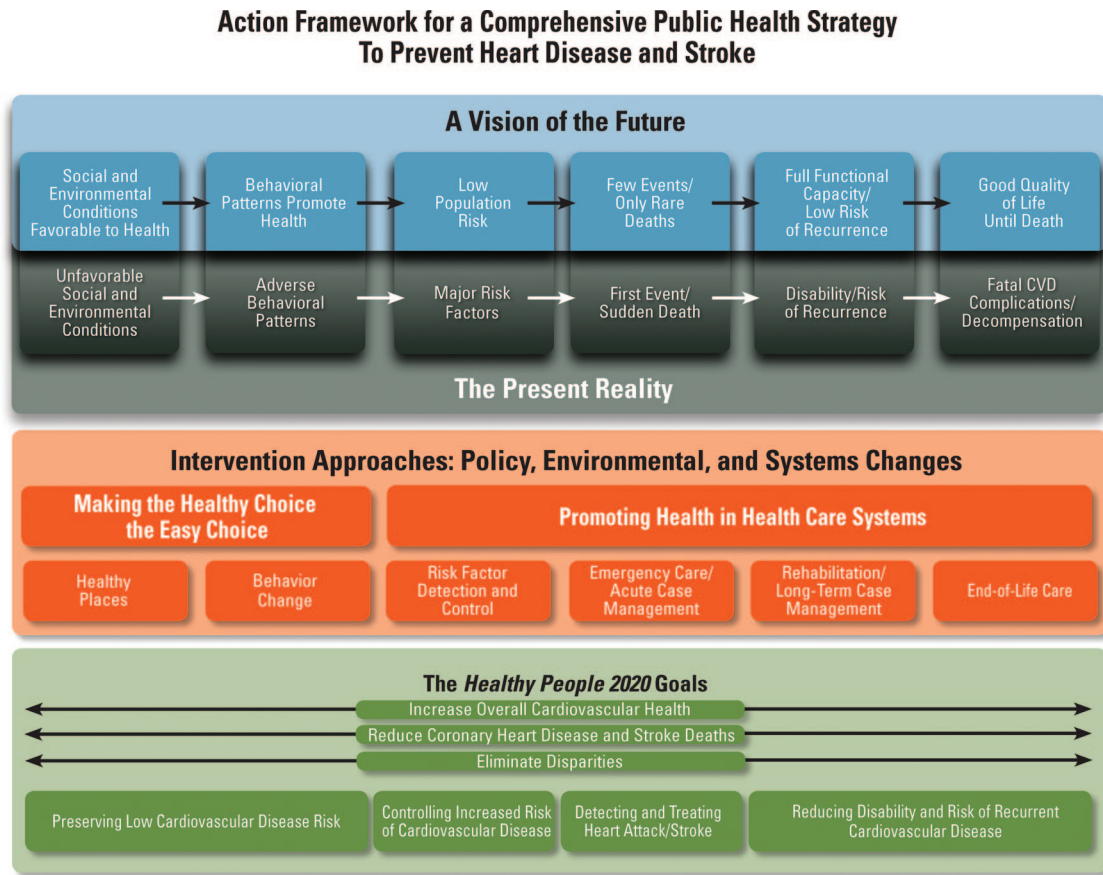


Figure 1. A framework for a comprehensive health strategy to prevent cardiovascular diseases (CVD), including policy, environmental, and systems changes to achieve Healthy People 2020 goals. Reprinted from Labarthe et al⁶⁹ with permission of the publisher. Copyright © 2005, Elsevier.

disease outcomes, and complications), thus helping patients and society evaluate the choices they make. However, in the evaluation of the value of primordial and primary prevention, formal cost-effectiveness analysis may not be realistic and may fail to evaluate value properly.

Assessing the value of prevention in apparently healthy patients is generally more difficult than evaluating therapy for established disease because the time horizon to the clinical manifestation of disease is generally long—many decades in the young. Thus, it is difficult, perhaps impossible, to assess long-term effectiveness in terms of survival or quality-adjusted life-years (QALYs) or associated costs because of increasing uncertainty about outcome the further one tries to look into the future. Furthermore, discounting (see the economics primer in the Appendix and the glossary in Table 1) works to the disadvantage of prevention because costs may accrue in the present and the benefit may become apparent only in the distant future. Thus, the costs will not be discounted but the benefit will be. Cost-effectiveness in prevention is also at a disadvantage because of the rule of rescue; for example, we will spend what it takes to save the child who falls down a well, but we will not finance the routine building of fences around wells. The rule of rescue is a fundamental, human emotional response to people in distress to which we all can respond. The decision not to build fences would be based on avoiding the costs at present to build fences around many wells to prevent 1 child from falling down

a specific well perhaps years in the future, discounting the costs of rescue. Both uncertainty about value and the rule of rescue may, in part, explain why society spends most of its healthcare resources on therapy for established, often advanced, disease and comparatively little on primordial and primary prevention.

There are technical and practical limitations to studies of the cost-effectiveness of prevention. Given the difficulties of conducting long-term clinical trials, many cost-effectiveness analyses about prevention are based on mathematical models or simulations. Such models are dependent on assumptions about both overall construction and input variables and thus must be assessed with some skepticism. Because of the difficulties involved in establishing the value of prevention with formal cost-effectiveness analyses, less quantitative approaches are often appropriate and must suffice.

There are also theoretical problems with cost-effectiveness analyses of prevention. Typically, cost-effectiveness analysis considers direct medical benefit to an individual patient and both direct medical care costs and indirect costs such as lost time at work. However, it is difficult to establish the overall benefit and reduced costs that society accrues by having a healthier population and more productive workforce. The benefit is one of both preventing early death and compressing morbidity until the end of life.⁶⁸ Thus, the focus on individual benefits in the distant future and direct medical care costs incurred immediately underestimates the economic and other value to society

Table 3. American Heart Association 2010 to 2013 Strategic Policy Recommendations That Address Primordial and Primary Prevention Efforts in the United States

Federal level

Overall policy

Preserve the prevention and public health fund in the Patient Protection and Affordable Care Act

Increase funding for Centers for Disease Control and Prevention state-based heart disease and stroke prevention programs

Nutrition and dietary guidance

Develop and finalize robust nutrition standards for school meals and foods sold in schools outside the meal program; ensure schools adopt robust wellness policies that are implemented, disseminated, and evaluated

Improve food labeling to minimize consumer confusion and to increase knowledge and awareness especially about calories, sodium, saturated fat, *trans* fat, and added sugar

Effectively implement restaurant menu labeling

Address food marketing and advertising to children

Physical activity

Fit Kids Act: hold schools accountable for providing students with high-quality physical education and facilitate the integration of physical activity throughout the school day

Require that the Physical Activity Guidelines for Americans be regularly updated every 5 y in coordination with the Dietary Guidelines for Americans

Support funding for the Safe Routes to School program in the Surface Transportation Reauthorization Act, helping children walk and bike to school safely

Help implement the US National Physical Activity Plan

Tobacco

Implement Food and Drug Administration tobacco regulation in a strong and timely manner in the Family Smoking Prevention and Tobacco Control Act

Support efforts to increase access to tobacco cessation services

State level

Overall policy

Provide adequate prevention, diagnosis, treatment of overweight and obesity in the healthcare environment

Provide robust surveillance and monitoring

Implement comprehensive worksite wellness programs

Implement and monitor strong local wellness policies in all schools

Provide adequate funding and implementation of coordinated school health programs

Develop comprehensive obesity prevention strategies in early childhood and daycare programs

Provide adequate funding for state heart disease and stroke prevention programs

Nutrition

Work to eliminate food desserts and to improve access and affordability of healthy foods (community gardens, farmers' market expansion, incentives, Healthy Food Financing Initiative)

Strengthen nutrition standards in schools for meals and competitive foods and in all government nutrition assistance or feeding programs

Implement menu labeling in restaurants

(Continued)

Table 3. Continued

Continue to monitor and pass legislation/regulation for the removal of industrially produced *trans* fats from the food supply and to ensure the use of healthy replacement oils

Implement robust procurement standards for foods purchased by employers or government feeding programs

Physical activity

Address the built environment and support efforts to design workplaces, communities, and schools around active living; integrate physical activity opportunities throughout the day

Fund and develop walking/biking trails that connect key aspects of the community

Increase Safe Routes to School

Implement zoning/building ordinances that encourage walking/using stairs

Advocate for implementation of Complete Streets policies that allow biking and walking and are pedestrian friendly with appropriate cross-walks, sidewalks, traffic lights, and slower speed limits in walking/biking areas

Implement shared use of school facilities within the community and support the construction of school fitness facilities

Increase sports, recreational opportunities, parks, and green spaces in the community

Increase the quantity and improve the quality of physical education in schools

Support 60 min/d of supervised, moderate-to-vigorous physical activity integrated throughout the school day

Tobacco

Pass and implement comprehensive clean indoor air laws

Increase excise taxes on tobacco products

Increase/sustain funding for state tobacco control/prevention programs

Implement clinical guidance and monitor health claims around smokeless tobacco products

Advocate for comprehensive smoking cessation benefits in Medicaid, Medicare, and other healthcare plans

Eliminate tobacco sales in pharmacies and other health-related institutions

and to individuals of prevention, which offers the prospect of a healthier, more productive society at all times.

Evidence Base for the Value of Cardiovascular Disease Prevention: Societal Change

The Cost-Effectiveness/Value of Prevention: The Impact of Environment and Policy Change

The conceptual basis for implementing primordial and primary prevention is an environmental model that maintains that an individual's behavior is influenced by his or her surrounding physical, social, and cultural environments (Figure 1).⁶⁹ In other words, policy change makes the greatest impact when it optimizes the environments where people live (ie, workplaces, schools, homes, and communities), making healthier behaviors and healthier choices the norm by default or by design and putting individual behavior in the context of multiple-level influences. This environmental model represents a shift away from prioritizing individual behavior change that focuses on individual-level or intrapersonal influences. For example, passing comprehensive clean indoor air laws,⁷⁰ raising tobacco excise taxes,⁷¹ or reducing sodium from the food supply¹⁹ can have a profound impact on a large segment of the population and may contribute to marked improvements

in cardiovascular health. State-level policies have been shown to reduce junk food in vending machines and school stores.⁷² These population-based strategies are a critical complement to preventive services and treatment programs in which practitioners and patients are working together to foster important individual behavior and lifestyle changes.⁷³ In fact, research continues to demonstrate that environment and policy change is one of the most impactful ways to improve public health, providing the counterargument to those policy makers who argue that government has no role, that health is largely an individual's responsibility.^{74–77} Many policy strategies to affect environmental change are relatively new, and evidence continues to emerge on their cost-effectiveness and economic value. This article summarizes many of them and underscores the important role that policy change has in affecting public health. Table 3 summarizes the American Heart Association's 2010 to 2013 specific strategic policy priorities that address primordial and primary prevention. These priorities certainly do not encompass all of the policy strategies that are underway in prevention efforts, but they are the priorities of one major nonprofit organization working in collaboration with coalitions and partners in public health.

Communities

Community leaders are beginning to understand the preventive value of environment and policy changes that facilitate a healthy diet, increased physical activity, and elimination of tobacco use. Three recent landmark reports have highlighted policy strategies at the community level to address cardiovascular health, sensitizing community leaders, policy makers, and organizations to a range of policy options such as access to and affordability of healthy foods; opportunities for active living through the built environment and parks, recreational spaces, and walking/biking trails; increased consumer knowledge with approaches like menu labeling in restaurants; and strengthened nutrition standards and physical education/physical activity opportunities in schools for children.^{78–80} Cities across the United States are debating the best ways to convert vacant lots or brown fields in the context of economic development. Community gardens, small parks, and open green spaces are excellent options for these areas that positively impact surrounding residential properties, increase rates of home ownership, and spur economic redevelopment.⁸¹ Other studies have shown the direct cost-benefit of building bike/pedestrian trails by reducing healthcare costs associated with physical inactivity. A study based on a simulation model found that for every \$1 invested in building these trails, nearly \$3 in medical cost savings may be achieved.¹¹ Linking different parts of the community with trails and walkways spurs community integration, more efficient land use, lower traffic congestion, and better quality of life.

Other initiatives like the Healthy Food Financing Initiative address the importance of making healthy, affordable foods available in low-income urban, rural, and minority communities. The Healthy Food Financing Initiative provides critical loan and grant financing for food retailers to renovate existing stores or to develop new stores to provide healthy foods.⁸² Concurrently, the Healthy Food Financing Initiative reduces health disparities, creates jobs, and stimulates local economic development. One example is the Pennsylvania Fresh Food

Financing Initiative, a public-private partnership created in 2004 that led to 83 new or renovated supermarkets and fresh-food outlets, providing 400 000 residents with access to healthy food while creating or maintaining 5000 jobs. Essentially, \$190 million was leveraged as a result of \$30 million in state seed money. A recent report by Trust for America's Health showed that an investment of \$10 per person per year in proven community-based prevention programs could save the country more than \$16 billion annually within 5 years.⁷ This report is based on a model developed by researchers at the Urban Institute that assessed medical cost savings only, not additional gains from worker productivity, reduced absenteeism, or quality-of-life measures. The researchers made low-end assumptions for the drops in disease rates and high-end assumptions on costs of programs based on a comprehensive review of the literature.

New York City and several other major cities have been on the forefront of public health policy change with initiatives such as smoking bans in public buildings and workplaces, *trans* fat bans in restaurants, restaurant menu labeling, the Green Kart initiative, and healthy corner store initiatives. Most recently, the New York City Department of Health has led the National Sodium Reduction Initiative, a partnership of ≈64 cities, states, and national health organizations, in establishing target levels for sodium reduction by food categories and soliciting pledges from food companies to meet these targets. The many benefits of lowering sodium intake underscore the need for a comprehensive, coordinated public health strategy to lower the amount of salt in the food supply to 1500 mg/d by 2020. It is estimated that if the US population moved to an average intake of 1500 mg/d sodium, there would be a 25.6% overall decrease in high blood pressure and \$26.2 billion in healthcare savings.¹⁵ Such a national effort would result in fewer coronary heart disease events, strokes, heart attacks, and deaths.⁸³

Worksites

The worksite is an important environment for policy implementation and program intervention. More than 130 million Americans are employed across the United States annually, and workplace wellness programs have been shown to prevent the major shared risk factors for CVD and stroke.⁸⁴ Comprehensive worksite wellness programs are aimed at improving employees' cardiovascular and general health and should include the following: tobacco cessation and prevention; regular physical activity; stress management/reduction; early detection/screening; nutrition education and promotion; weight management; disease management; CVD education, including cardiopulmonary resuscitation and automated external defibrillator training; and changes in the work environment to encourage healthy behaviors and to promote occupational safety and health.⁸⁴ An estimated 25% to 30% of companies' medical costs per year are spent on employees with obesity, hypertension, dyslipidemia, and diabetes mellitus and those who use tobacco products.⁸⁵ A recent meta-analysis showed that medical costs fell by ≈\$3.27 and absenteeism costs fell by \$2.73 for every dollar spent on worksite wellness programs.⁸ These savings are most often realized within the first 12 to 18 months.⁸⁵ Average reduc-

tions in sick leave absenteeism, healthcare costs, and workers' compensation and disability management claims were 28%, 26%, and 30%, respectively.^{86,87} Productivity outcomes are harder to measure in today's postmanufacturing economy, and many employers do not have the resources or expertise to conduct such assessment.^{88,89} Most productivity estimates are based on questionnaires that often yield varied estimates of on-the-job productivity gains or losses even when administered in the same setting.^{90,91} Overall, however, considerable data now suggest that health-related productivity losses from employees with health risk factors or chronic disease cost US employers \$225.8 billion a year or \$1685 per employee per year, of which 71% is due to reduced performance at work.⁹² Currently, the low level of intervention provided in the US workforce for many at-risk employees offers the opportunity to recuperate substantial productivity gains by initiating evidence-based health promotion programs, activities, and policy change in the worksite environment.^{84,93}

Healthcare Systems

Healthcare systems are increasingly a target of policy intervention concerning healthy food and beverage offerings, worksite health promotion, and tobacco-free environments because they are often leading employers and role models within the community. Many hospital systems have established tobacco-free environments and are providing healthier foods and beverages in their cafeterias, food service, and vending machines⁹⁴; improving their procurement strategies; and/or making their worksite wellness programming and health promotion efforts more robust.

Schools

More than 55 million children spend the majority of their day in schools across the United States. Accordingly, it is vitally important to offer healthy educational environments by providing opportunities for daily physical activity and/or physical education and healthy foods and beverages to create a foundation for learning the fundamentals of healthy living. School-based interventions can be effective in preventing the development of obesity in children, even in low-socioeconomic-level neighborhoods, although results are often modest and short term.^{95,96} Most research focuses on other types of outcomes such as academic performance, nutrition education, physical education, physical fitness, behavior in the classroom, and knowledge gain. For example, numerous studies have documented that children who are more physically fit perform better academically, have higher attendance, display fewer behavioral problems in the classroom, and improve the overall quality of the school environment.^{97–101} Schools can provide the knowledge base children need to practice healthy behaviors for a lifetime and the policy and environment changes that reinforce this prevention-related education. Providing healthier meals can also be cost-effective and may lead to better food choices at home and outside of school.^{102–104} Comprehensive school interventions to promote healthy eating and physical activity can be cost-effective, ranging from \$900 to \$4305 per QALY saved.^{9,10}

Further research is needed to determine the long-term effectiveness of policy and environment change in schools on nutrition, physical activity, obesogenic behaviors, and health

outcomes, especially in at-risk populations, and the associated impact on community and home, as well as the short- and long-term cost savings associated with these interventions.^{105,106}

Addressing Disparities

Lower socioeconomic and educational status are established risk factors for CVD.¹⁰⁷ Additionally, the obesity epidemic and risk factors for CVD such as smoking, physical inactivity, hypertension, and diabetes mellitus are disproportionately prevalent in certain populations, especially non-Hispanic blacks, American Indians, Hispanics/Latinos, and Pacific Islanders, compared with non-Hispanic whites.¹ Children also make up a vulnerable population, and their health statistics are worsening. To attenuate these disparities, policy work will have to prioritize opportunities to address social inequities, issues specific to vulnerable populations (ethnic and racial minorities, those with low income or less education, children, blue collar workers), and the importance of removing barriers and obstacles for risk reduction and behavior change. Often, the most disadvantaged members of the population have the greatest need for preventive screenings, health promotion, or programming and have the least access to or are the most reluctant to participate in these opportunities.¹⁰⁸ The fundamental causes of vulnerability are rooted in issues of daily life, most often beyond the scope of traditional public health. Thus, it will be important for the public health community to consider engaging with nontraditional partners to promote increased prevention strategies and to reduce health disparities in communities.¹⁰⁹ Additional research is needed to determine how best to reach and engage underserved populations and to optimize policy interventions for people of all races, ages, ethnicities, and education and income levels.

Ongoing research and evaluation of preventive interventions and policy change in community settings will provide additional data on cost-effectiveness and value. The Sydney Diabetes Prevention Program, for example, is a community-based translational study with >1500 participants who are at high risk of developing diabetes mellitus. The study will ascertain the reach, feasibility, effectiveness, and cost-effectiveness of delivering a lifestyle modification program in a community setting through primary health care.¹¹⁰ Too often, the difficulty in assessing the cost-effectiveness of these types of public health interventions is the lack of specific effectiveness data and insufficient sample sizes, inadequate follow-up, or different basic principles of analysis used by health promoters and economists.¹¹¹ To bridge the evidence gap and to provide a framework for informed decision making, it will be important to promote effective policy evaluation, optimal research design in real-world settings, and common outcome measures to assess the true value and economic impact of change and to incorporate individuals' broader perspective of well-being.

Evidence Base for the Value of Cardiovascular Disease Prevention: Behavior Change

As models suggest, the willingness for individuals to change their lifestyle behaviors is affected by a number of factors such as the different stages of readiness, perceived threat or

susceptibility of developing a health condition, concerns about the seriousness of the preventable condition, perceived benefits of changing behavior, and cues to action that might come from social networks and their surrounding environment.¹¹² This section outlines the cost-effectiveness of primordial and primary prevention concerning environment and policy change that affects behavior in the areas of tobacco use, physical activity, diet, and obesity.

Tobacco Use

Smoking costs the US economy more than \$301 billion per year, including workplace productivity losses of \$67.5 billion, premature death at \$117 billion, and direct medical expenditures of \$116 billion.²⁰ These costs to people's lives and their quality of living underscore the importance of primordial prevention such as state tobacco control and prevention programs and smoke-free air laws and primary prevention efforts such as adequate coverage for cessation therapy and tobacco excise taxes.

Tobacco Control and Prevention Programs

In 1998, the 4 largest US tobacco companies and the attorneys general of 46 states signed the Tobacco Master Settlement Agreement, settling the states' Medicaid lawsuits against the tobacco industry for recovery of their tobacco-related healthcare costs. Under the agreement, states received upfront payments of \$12.74 billion with the promise of an additional \$206 billion over the next 25 years. Ideally, states would use this money to fully fund tobacco control programs that follow Centers for Disease Control and Prevention "best practices." Unfortunately, as a result of the negative fiscal environment and competing priorities, only 1 state, North Dakota, currently funds its tobacco prevention programs at Centers for Disease Control and Prevention-recommended levels. Revenue from the settlement continues to flow toward other parts of state budgets despite the fact that state tobacco control program expenditures have been shown to be independently associated with overall reductions in smoking prevalence.¹¹³ States are sacrificing long-term health benefits and healthcare cost reductions for short-term budget fixes. If all states had funded their tobacco control programs at the minimum or optimal levels recommended by the Centers for Disease Control and Prevention, there could have been millions of fewer smokers a decade later.¹¹³

Smoke-Free Environments

Passing comprehensive smoke-free air laws in public places and work environments is a cornerstone of the public health strategy in tobacco control efforts. Although these efforts have been extremely effective in protecting a large segment of the US population from the deleterious effects of secondhand smoke, >88 million nonsmokers >3 years of age are still exposed, especially children in the home.¹¹⁴ The Institute of Medicine, backed by studies from around the world, published a report showing reduced incidence of acute myocardial infarction after implementation of clean indoor air laws in workplaces and communities.¹¹⁵ Lightwood et al¹¹⁶ developed a simulation to estimate the CVD event incidence and costs as a function of risk factor prevalence, including passive smoking. At 1999 to 2004 levels, passive smoking caused 21 800 to 75 100 CVD deaths

and 38 100 to 128 900 myocardial infarctions annually, with a yearly treatment cost of \$1.8 to \$6.0 billion. The Institute of Medicine estimates direct and indirect healthcare costs associated with disease incidence caused by secondhand smoke exposure at \$10 billion annually.¹⁸

There are other economic arguments for clean indoor air laws. The hospitality and tobacco industries often promote the idea that business will suffer after these laws are passed. However, increasing evidence from municipalities, states, and countries shows no significant impact on sales data, and in many instances, business actually increases after a short-term initial decline.¹¹⁷ Additional benefits for businesses are lower cleaning costs, lower worker absenteeism, and increased productivity.¹¹⁸

Several federal government initiatives¹¹⁴ are currently underway to address comprehensive smoke-free air policies and tobacco control, including funds from the American Recovery and Reinvestment Act that have been distributed to communities, territories, and states to address tobacco control. In 2009, the US Department of Housing and Urban Development issued notices encouraging public housing authorities to implement no-smoking policies. Moreover, the US Environmental Protection Agency conducts a national campaign that educates and encourages parents to make their homes smoke free to protect their children's health.

Tobacco Excise Taxes

Tobacco excise taxes are another pillar of the tobacco control movement. The federal government has imposed excise taxes, most recently with the expansion of the Children's Health Insurance Program. A cigarette tax increase of 61.66 cents per pack went into effect on April 1, 2009. There were also increases in the federal tax rates on other tobacco products such as smokeless products, "small cigars," roll-your-own tobacco, and regular cigars. At the same time, states have imposed tobacco excise taxes with a current nationwide average of \$1.45 per pack (as of July 2010). As a leader in public health initiatives, the state of New York (June 2010) raised its cigarette tax by \$1.60 to give it the highest cigarette tax in the nation at \$4.35 per pack.

A robust literature has examined the impact of cigarette tax increases on smoking prevalence, especially in youth. Most studies have found that higher taxes reduce consumption, especially via cessation rates in young smokers.^{71,119} Modeling techniques have estimated that a 40% tax-induced cigarette price increase would reduce smoking prevalence to 15.2% in 2025 with large gains in cumulative life-years (7 million) and QALYs (13 million) for a total cost savings of \$682 billion.¹⁷ Industry documents show, however, that the tobacco companies understand the impact of tax increases on consumption and have developed pricing strategies, including the development of lower-cost generics and price-related marketing efforts such as multipack discounts and couponing to reverse these effects.¹²⁰ The tobacco control movement has to continue to adapt to strategies to maintain the health impact and value of tobacco use prevention strategies.

Physical Activity

The benefits of regular exercise and cardiorespiratory and general physical fitness are numerous and contribute signif-

icantly to health impact and cost savings, including lower risk for CVD and diabetes mellitus, improved musculoskeletal health, better weight management, reduced risk for hypertension, less dyslipidemia, preserved cognitive function, reduced symptoms of depression, and improved overall quality of life.^{121–125} The majority of children, adolescents, and adults do not achieve the recommended levels of physical activity each day, spending a majority of their time in sedentary activities.^{126,127} The proportion of adults who meet the physical activity guidelines varies by education level: 46% of people with a college degree or higher are regularly active compared with only 21.4% of adults with less than a high school diploma.¹²⁸ When assessed with actual accelerometer data from the National Health and Nutrition Examination Survey rather than self-reported physical activity, the data are much more sobering: Only 3.8% of adults engage in moderate to vigorous physical activity at least 5 days a week.¹²⁹ Globally, ≈ 1.9 million deaths per year are attributed to physical inactivity.¹²⁷ There is a strong, positive relationship between physical inactivity and QALYs lost in the obese population.¹³⁰

The Task Force on Community Preventive Services recommends physical activity interventions under 4 major strategies: community-wide campaigns, individually adapted healthy behavior change, community social-support interventions, and the creation of or enhanced access to physical activity information and opportunities.¹² Studies that have examined the cost-effectiveness of community-based physical activity interventions show some reduction of chronic disease incidence and incremental cost and incremental effectiveness ratios (ICERs) ranging from \$14 000 to \$69 000 per QALY gained relative to no intervention, especially in high-risk groups.^{12–14} These interventions can also be successfully implemented in a cost-effective way in primary care settings to reduce CVD risk and to improve quality of life.¹³¹ Pedometer programs and mass media-based community campaigns have been found to be the most cost-effective, whereas general practitioner referral to an exercise physiologist was the least cost-effective because of travel costs and the associated time spent on consultation and screening.¹²⁷ A behavior-based intervention in which participants were taught to integrate daily moderately vigorous physical activity into their lives was found to be more cost-effective than a structured exercise program for improving physical activity and cardiovascular health.¹³² A report from the National Institute for Clinical Excellence in the United Kingdom found that when the costs of health care avoided are included, exercise programs are dominant (ie, offer better outcome at a lower cost).¹³³

Despite accumulating evidence on the cost-effectiveness of exercise promotion and intervention in various settings, there is significant heterogeneity in study quality, intervention strategies used, and measured health and behavior outcomes. Further research and cost-effectiveness analyses are needed to determine sustainability, long-term outcomes, impact on various population subgroups, wide-ranging appeal, and perceived value that people place on the time they spend exercising.^{134,135}

Diet and Obesity

The centerpiece of a healthy lifestyle is a diet and physical activity pattern that follows the evidence-based recommen-

dations put forward by several agencies, including the US Department of Agriculture, the American Diabetes Association, and the American Heart Association. A growing body of evidence supports the benefits of following the established dietary guidelines. Compared with those who did not follow the guidelines, those who reported adherence to the dietary guideline had a lower prevalence of the metabolic syndrome,¹³⁶ and among women, there was a lower prevalence of insulin resistance,¹³⁷ a lower odds of carotid atherosclerosis,¹³⁸ and slower progression of atherosclerosis.¹³⁹ Moreover, adherence to the dietary guidelines was associated with reduced CVD mortality, significantly smaller waist circumference, and lower levels of serum insulin and C-reactive protein concentration.¹⁴⁰ Numerous clinical trials have demonstrated the benefits of reduced sodium intake^{141–143} and the benefits of healthy eating patterns such as the Mediterranean-style diet.^{144–147} However, despite the cumulative evidence supporting the benefits of a healthy diet on blood pressure, lipids, insulin sensitivity, and body weight, the majority of the population does not meet several of the public health targets set forward in the dietary guidelines. It has been estimated that $>50\%$ of global deaths can be attributed to diet.¹⁴⁸ Clearly, the cost of these unnecessary deaths and the comorbidity preceding the deaths is astronomical.

Today, one of the most significant and prevalent conditions associated with nonadherence to the dietary guidelines is obesity. Overall, the economic impact of obesity in the United States is substantial.¹⁴⁹ In 2011, $\approx 66\%$ of adults in the United States are overweight, including 33% who are obese.¹⁵⁰ Among children, the prevalence of obesity in recent years has increased 2- to 3-fold.¹⁵¹ Research examining the costs of obesity has focused on 3 areas of impact: direct medical costs, productivity costs, and human capital costs.

Direct Medical Costs

Obesity is associated with myriad comorbid conditions; for example, hypertension, diabetes mellitus, CVD, arthritis, and sleep disorders.^{152–154} As the medical conditions associated with obesity increase, so do the associated medical costs—from diagnosis to treatment of these disorders. The methods used and the populations studied in examining the cost of overweight and obesity vary widely; however, there is widespread agreement that the medical costs are substantial.¹⁵⁵ One example of costs attributed to overweight and obesity comes from a study of a managed-care population between 35 and 64 years of age that was followed up for 9 years. On average, obese patients accumulated annual costs that were 36% higher than the healthy-weight group, which included 105% higher costs for prescriptions and 39% higher primary care costs. When the overweight group was compared with the healthy-weight group, prescription costs were 37% higher and primary care costs were 13% higher.¹⁵⁶ Others have used regression analysis of nationally representative surveys such as the 1998 and 2006 Medical Expenditure Panel surveys and the National Health Expenditure accounts data to derive cost estimates of obesity of \$147 billion in 2008.¹⁵⁷ A recently published article reported that almost 17% of US medical costs can be attributed to the treatment of obesity and suggested that the obesity problem in the United States may

be having close to twice the impact on medical spending as previously estimated.¹⁵⁸ Estimates of medical costs for childhood obesity in the United States are ≈\$14.3 billion.¹⁵⁹

Productivity

Costs of lost productivity are substantial and have been studied extensively. Distinct subcategories of productivity exist, for example, absenteeism, or reduced productivity because the person is absent from work for obesity-related health reasons, and presenteeism, or decreased productivity while the person is at work. Other sequelae include premature mortality, impaired quality of life, increased rates of disability benefit payments, and increased medical care costs. It is difficult to compare the magnitude of absenteeism across studies because of the different methodologies used; however, a study reported that compared with a normal-weight employee, an overweight/obese employee lost an additional 3.73 days of work per year, with 36% of illness-related absences resulting from body habitus.¹⁶⁰ Nationwide, annual estimates of this loss in productivity range from \$3.38 billion to \$6.38 billion.¹⁶¹ One investigator examined disability and reported that for men, being obese increased the probability of receiving disability income by 6.92%; for women, the increased probability was 5.64%. Premature mortality or reduced QALYs is another form of lost productivity associated with obesity. One study reported that the largest effect of obesity on morbidity was among white men; a 20-year-old white man with a body mass index >45 kg/m² could be expected to have a 22% reduction in remaining life-years, the equivalent of 13 years of life lost.¹⁶² Obese people have reported lower quality of well-being, which at the national level translates into 2.93 million QALYs lost in the United States.¹⁶³

Human Capital

Human capital is defined as the both the quantity and quality of education an individual is able to attain. The accumulation of human capital is inversely related to overweight/obesity. There is an association between body mass index and days of school missed¹⁶⁰ and the number of school years completed¹⁶⁴; moreover, there is a consistent negative relationship between weight and grade point average among female students.¹⁶⁵ Among nonwhites, the relationship exists for both male and female students. These findings emphasize the impact of childhood obesity on not only educational attainment but also other related aspects of life.

The research examining the economic impact of obesity varies widely in the data sources and methodologies used. The data thus far confirm that there is a substantial cost to obesity in direct medical costs and productivity; however, further research is needed in the area of accumulation of human capital and in policy development that addresses these significant costs.¹⁴⁹

Considering the negative economic impact of obesity, it would seem logical that interventions to reduce obesity would be beneficial in terms of lowering an organization's medical costs and improving worker productivity. Return-on-investment models have been used to forecast program savings in several large organizations; the most costly employees for employers were those with certain modifiable risk factors. Applying a predictive return-on-investment model,

another group of investigators tested whether an obesity management program would result in reduced health risks at 119 employer sites.¹⁶ The program included four 30-minute telephone-based coaching sessions each month for a year, plus access to educational materials, exercise planning support, nutrition education, stress management, and Web-based health tracking. Of the 1542 participants enrolled, 890 (57.7%) completed the program. At 1 year, there was a statistically significant reduction in 7 of the 10 risk categories monitored, with sizable reductions in body weight and poor eating and poor physical activity habits. On the basis of the return-on-investment analysis, compared with no changes occurring, there was a reduction in total employer expenses by \$311 755. Additionally, 59% of the total projected expense reductions were attributed to a 4.3% reduction in healthcare expenditures and 41% were attributed to enhanced productivity.¹⁶ Other investigators have reported findings consistent with these results, supporting the association between health risk reductions, absenteeism, and presenteeism.^{86,157,158}

Researchers in Switzerland developed a Markov model to evaluate the lifetime effect of a 3-year lifestyle intervention and compared it with standard care among overweight and obese adults.¹⁶⁶ Lifestyle intervention increased both survival and quality of life and dominated standard care in borderline obese and obese men and women. In the overweight group with an average body mass index of 27 kg/m², costs were higher with lifestyle intervention but were offset by the reduced risk of developing obesity-related complications and comorbidities.

Another group in Europe examined published studies to determine how cost-effective dietary changes were compared with other measures targeting CVD risk reduction.¹⁶⁷ Although the comprehensive studies available were limited in number and quality, findings suggested that health-promoting strategies that targeted healthy eating were more cost-effective than strategies that included pharmacotherapy for lipid reduction or nurse screening and adjunctive lifestyle counseling.

Between 2005 and 2007, the Partnership for Prevention evaluated the relevant evidence to support the ranking of the health impact and cost-effectiveness of 25 clinical preventive services that had been recommended by the US Preventive Health Services Task Force and the Advisory Committee on Immunization Practices. This ranking, based on the clinically preventable burden, measures the health impact on the affected population and the cost-effectiveness of each service; each of these received a score between 1 and 5. A score of 5 for clinically preventable burden was given to the services that produced the most health benefits; a 5 was also given to the service deemed most cost-effective. Included in this list of services was obesity screening with high-intensity lifestyle counseling for obese patients, which had clinically preventable burden and cost-effectiveness scores of 3 and 2, respectively. Diet counseling, which included intensive behavioral counseling for patients with hyperlipidemia and other risk factors for CVD and diet-related chronic diseases, received clinically preventable burden and cost-effectiveness scores of 1, suggesting that these services, at least in their present format, did not appear warranted.¹⁶⁸ These rankings are considerably lower than those for such activities as tobacco counseling or screening for hypertension or hyperlipidemia.

Changing Diet

Although the evidence suggests that dietary counseling for CVD and diet-related disorders has limited impact on health, a diet that is high in fruits and vegetables can reduce the risk of several major causes of death and contribute to weight management.^{137–139} Objectives of Healthy People 2010 included related targets such as having 75% of the population >2 years of age consume ≥ 2 fruit servings daily and 50% consume ≥ 3 vegetable servings daily. According to the latest update on progress in meeting these objectives, which was based on Behavioral Risk Factor Surveillance System data, $\approx 32.5\%$ of adults consumed ≥ 2 servings of fruit per day and 26.3% consumed ≥ 3 servings of vegetables per day.¹⁶⁹ These results demonstrate not only that the population is far short of meeting these objectives but also that there has been a slight but significant decline in fruit consumption since 2000. Collectively, these findings emphasize the serious need for interventions at multiple levels (eg, point of purchase, schools, worksites, and community settings) that will improve access to affordable fruits and vegetables. Recently, an intensive lifestyle intervention that focuses on diet and physical activity has been shown to be successful in achieving weight loss in severely obese adults.¹⁷⁰ Moreover, a commercial weight loss program with free prepared meals and incentivized weight loss can effect weight loss and prevent weight regain.¹⁷¹ These findings may extend the potential reach of this treatment approach to weight loss.^{172,173}

Evidence Base for the Value of Cardiovascular Disease Prevention: Therapeutic Areas

Several diseases and chronic health states are associated with CVD risk: diabetes mellitus, hyperlipidemia, hypertension, and tobacco use. This section focuses on the cost-effectiveness of primary prevention in the clinical environment or community setting that is therapeutic in nature to initiate behavior change or to prevent the onset of chronic disease.

Tobacco Cessation Therapy

In general, tobacco cessation treatment remains highly cost-effective, even though a single application of any treatment for tobacco dependence may be successful in only a minority of smokers long term.¹⁷⁴ There is a strong relationship between the length of behavior counseling sessions, provider-to-person contact, and successful treatment outcomes.¹⁹ Available forms of nicotine replacement therapy (gum, transdermal patch, nasal spray, inhaler, and lozenges) increase quit rates by 50% to 100% over placebo; however, fewer than 1 in 5 smokers who are trying to quit take advantage of these products. The reasons for lower use are the inadequacies of dosing strength, formulations of existing medications, perceptions about the high cost of the drugs, and smokers' concerns about the safety and efficacy of nicotine medications. The ICERs for treatment programs range from a few hundred to a few thousand dollars per QALY saved.¹⁹

In July 2006, the Massachusetts healthcare reform law mandated tobacco cessation coverage for the Massachusetts Medicaid population. On implementation of the benefit, MassHealth subscribers were allowed two 90-day courses per

year of Food and Drug Administration–approved medications for smoking cessation, including over-the-counter medications like nicotine replacement therapy, and up to 16 individual or group counseling sessions. A total of 70 140 unique MassHealth subscribers used the newly available benefit between July 1, 2006, and December 31, 2008 (ie, $\approx 37\%$ of all Medicaid smokers). Before July 2006, there had been no significant change in smoking prevalence among the MassHealth population because smoking rates remained relatively high in this state. However, after implementation, in just over 2 years, 26% of MassHealth smokers quit smoking, and there was a decline in the use of other costly healthcare services (38% decrease in hospitalizations for heart attacks, 17% drop in emergency room and clinic visits for asthma, and a 17% drop in claims for adverse maternal birth complications, including preterm labor).¹⁷⁵ Additional research showed that comprehensive coverage led to reduced hospitalizations for heart attacks and a net savings of \$10.5 million or a \$3.07 return on investment for every dollar spent.^{21,175} A study by the American Lung Association showed that economic benefits to states offering comprehensive smoking cessation therapy to their employees in their public health or tobacco control programs can save \$1.10 to \$1.40 in healthcare expenditures and productivity for every dollar spent.¹⁷⁶

The health benefit of cessation and relapse therapy during pregnancy is even more apparent, minimizing low birth weight, placental abruption, sudden infant death syndrome, and other illnesses and life-threatening conditions for mother and child.¹⁷⁷ Moreover, a systematic review of the literature revealed a cost-to-benefit ratio as high as 3:1 (ie, for every \$1 invested in cessation/relapse programs, \$3 were saved in downstream health-related costs).²²

The PPACA requires state Medicaid programs to cover comprehensive tobacco cessation treatments, with no copayments, for pregnant women as of October 1, 2010. States have a tremendous opportunity to save even more lives by applying tobacco cessation treatments to all smokers in Medicaid. Nationwide, 36.6% of people in Medicaid smoke compared with 22.6% of the general population.¹⁷⁸ Ideally, comprehensive tobacco cessation services should be offered in all public and private healthcare plans.

Diabetes Mellitus

People with diabetes mellitus have CVD mortality rates that are 2 to 4 times higher than those for people without diabetes mellitus. Moreover, the estimated cost of diabetes mellitus in the United States in 2007 was \$174 billion, with 28% of expenditures attributed to cardiovascular complications of diabetes mellitus.¹⁷⁹ Current projections suggest that 1 of 3 people born in 2000 will develop diabetes mellitus over his or her lifespan.²³ A critical aspect of CVD and stroke prevention is screening for diabetes mellitus, along with early interventions, including behavioral modification, drug therapy, or both.

Diabetes Mellitus Screening

The American Diabetes Association (2010) recommends universal screening for T2DM in adults at 45 years of age that is repeated at least every 3 years.¹⁸⁰ Asymptomatic adults who are overweight or obese and who have 1 or more risk

factors (physical inactivity, cigarette smoking, family history in first-degree relative, history of CVD or hypertension, high-density lipoprotein <35 mg/dL, triglycerides >250 mg/dL, impaired glucose tolerance, impaired fasting glucose, or hemoglobin A_{1c} ≥5.7%; women with polycystic ovary syndrome or who delivered a baby >9 lb; blacks; and Latinos, Native Americans, Asian Americans, or Pacific Islanders) should be considered for screening regardless of age.¹⁸⁰ A recent systematic review of cost-effectiveness interventions to prevent and control both diabetes mellitus and the resulting complications found that targeted screening for T2DM based on age and risk was found to be far more cost-effective (ICERs ranging from \$46 800 to \$70 500 per QALY gained) compared with universal screening (ICERs from \$70 100 to \$982 000 per QALY gained).²⁴ Targeted screening for undiagnosed T2DM in blacks between 45 and 54 years of age was the most cost-effective, with an ICER of \$19 600 per QALY gained relative to no screening. For people with T2DM, statin therapy for the prevention of CVD was supported by strong evidence of cost-effectiveness.

Other studies examined the cost-effectiveness of more targeted screening, whether by age or risk factors. A recent study using a mathematical model based on a representative sample of the US population found that screening for T2DM at 30 and 45 years of age, repeated every 3 to 5 years, is cost-effective, with ICERs of ≈\$10 500 or less per QALY gained.¹⁸¹ There was a significant reduction in the incidence of myocardial infarction (5 to 7 events prevented per 1000 people screened) compared with no screening. Similar findings were shown for screening those with a diagnosis of hypertension, either annually or every 5 years, with a reduction in the incidence of myocardial infarction (3 events per 1000 people screened), although there was little or no effect on the incidence of stroke. The authors suggested that their results differed from other cost-effectiveness analyses because their model included the most recent treatment recommendations for more aggressive use of glucose-lowering drugs for T2DM.

Diabetes Mellitus Prevention and Treatment

The Finnish Diabetes Prevention Study demonstrated that lifestyle modification could delay or prevent the development of T2DM, and this approach has subsequently been implemented throughout Finland.^{182,183} The US Diabetes Prevention Program (2002) demonstrated that lifestyle modification and treatment with metformin could delay or prevent the development of T2DM.¹⁸⁴ Of interest, the lifestyle changes reduced the incidence of diabetes mellitus by 58%, whereas metformin therapy reduced the risk by 31%.²⁵ In patients with impaired glucose tolerance, a systematic review of the literature revealed that primary prevention, in the form of intensive lifestyle modification, is unequivocally cost-effective compared with standard lifestyle recommendations or no intervention, with a median ICER of \$1500 per QALY gained.²⁴ The intensity of intervention required to improve glycemic control remains unclear. One study postulated that in adults with T2DM, an additional 23.6 contact hours in diabetes mellitus self-management education would be required to produce a hemoglobin A_{1c} decrease of 1% (95% confidence interval, 13.3 to

105.4).¹⁸⁵ Other cost-effectiveness analyses outside the United States have also found both drug and lifestyle interventions to be cost-effective, although it is difficult to extrapolate those results to the United States because healthcare and reimbursement systems vary significantly.^{184,186}

Mathematical models evaluating the cost-effectiveness of community-based diabetes mellitus prevention programs using lifestyle interventions show conflicting results. A community-based modified Diabetes Prevention Program intervention designed to reduce risk factors for T2DM decreased metabolic syndrome risk by 16.2% at 12 months compared with 12.1% for usual care at an increased cost of \$3420 per QALY gained.¹⁸⁷ However, a 10-year community intervention study in Sweden of lifestyle changes to prevent diabetes mellitus offered equivocal results that were not as favorable as the Diabetes Prevention Program model.¹⁸⁸ In diabetes mellitus prevention programs from a societal perspective, model estimates may vary, depending on the intervention approach and lifetime projections.^{189,190} One study showed that cost per QALY of lifestyle intervention was much less than with metformin, whereas another study found that Diabetes Prevention Program treatment with metformin or delaying lifestyle intervention until after diagnosis was more cost-effective than earlier Diabetes Prevention Program lifestyle intervention.^{189,190}

Because of the improvement in risk factor control, patients who have been newly diagnosed with diabetes mellitus since 2005 have a better prognosis than their counterparts who were diagnosed 11 years earlier.¹⁹¹ Once a patient is diagnosed with T2DM, there is strong evidence that it is cost-saving to implement multicomponent interventions (standard antidiabetic care, education, angiotensin-converting enzyme inhibitors, and screening for microvascular complications) compared with standard antidiabetic care.²⁴ Intensive glycemic control resulted in a median ICER of \$12 400 per QALY gained. More intensive control of glycosylated hemoglobin (to a goal of <6%) was not shown to further reduce CVD events and was associated with increased mortality in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial.¹⁹² However, a meta-analysis of ACCORD, Action in Diabetes and Vascular Disease (ADVANCE), United Kingdom Prospective Diabetes Study (UKPDS), and VA Diabetes Trial (VADT) data showed a benefit of tight glycemic control on macrovascular outcomes and no increase in mortality.¹⁹³ Bariatric surgery, an emerging treatment strategy for diabetic patients who are severely obese, has also been found to be relatively cost-effective, with ICERs ranging from \$7000 to \$13 000, depending on the type of procedure (banding versus bypass) and length of time since diabetes mellitus diagnosis.¹⁹⁴

The ability to compare results of current studies is limited by marked differences in methodologies and intervention descriptions, including the lack of sufficient detail describing lifestyle interventions. Overall, more economic evaluations of diabetes mellitus intervention are needed to evaluate the cost-effectiveness for both prevention and treatment.

Lipid Screening and Primary Prevention

Elevated LDL-C is a major risk factor for CVD.¹⁹⁵ Multiple major clinical trials and national clinical guidelines support

screening for adverse levels of cholesterol and offer recommendations for treatment, including both lifestyle and pharmacological therapy.⁶⁰ Several meta-analyses have addressed the effectiveness of statin therapy for primary prevention. Ray et al¹⁹⁶ found a trend toward reduced all-cause mortality. A 2011 Cochrane review found reduced risk of all-cause mortality (relative risk, 0.83; 95% confidence interval, 0.73 to 0.95) and nonfatal events with statin therapy.¹⁹⁷ Although there is general agreement about the value of statins to reduce elevated LDL-C in high-risk individuals, research varies as to what constitutes a “normal” range of LDL-C, when to initiate statin therapy, and the best therapeutic range for primary and secondary reduction of cardiovascular events.^{198–200}

Manuel et al²⁰¹ noted that the effectiveness and efficiency of algorithms for statin treatment based on 6 different national or international guidelines on statin treatment to prevent deaths from CVD varied widely. When applied to a Canadian population, Australian and British guidelines were most effective, potentially preventing the most deaths over 5 years (>15 000 deaths). The New Zealand guideline was most efficient, potentially preventing almost as many deaths (14 700) while recommending treatment to the fewest number of people (12.9% versus 17.3% with Australian and British guidelines). If “optional” recommendations are included, US guidelines recommend treating about twice as many people as New Zealand guidelines (24.5% of the population), with almost no additional decrease in mortality. Similarly, studies conducted outside the United States found that targeted screening based on risk is less costly and can identify up to 84% of high-risk individuals compared with mass screening.²⁰²

The public health impact of widespread use of statins was evaluated with a Markov model analysis for the US population from 35 to 85 years of age.²⁶ Full adherence to Adult Treatment Panel III primary prevention guidelines would require starting statins in 9.7 million and increasing the dose in 1.4 million Americans. This strategy would prevent 20 000 myocardial infarctions and 10 000 CVD deaths at a total cost \$3.6 billion or \$42 000 per QALY if low-intensity statins cost \$2.11 per pill (which is substantially higher than the cost of currently available, effective generic statins). At a \$50 000 willingness-to-pay threshold, statins are cost-effective up to \$2.21 per pill.

Multiple studies using mathematical models have evaluated the cost-effectiveness of statins for primary prevention of CVD within specific populations. One study reported that statin therapy is likely to be cost-effective in the prevention of CVD among Koreans ≥ 45 years of age, with an estimated ICER of \$12 612 per QALY gained (based on 1200 Korean won per US \$1), although it may be difficult to translate the findings to the United States because of differences within healthcare systems.²⁰³ In the US population, statin therapy has been found to be cost-effective in individuals with T2DM who have LDL-C levels between 100 and 129 mg/dL, where cost and effectiveness vary among type of statin used.²⁰⁴

Blood Pressure Screening and Treatment

Hypertension is a major risk factor for coronary artery disease, stroke, heart failure, and renal failure.^{205,206} As with lipids, multiple major clinical trials and national clinical guidelines support screening and treatment for hypertension,

including both lifestyle and pharmacological therapy. The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) study (2002) reported that thiazide-type diuretics (chlorthalidone) are at least as effective in preventing CVD as a calcium channel blocker (amlodipine) or an angiotensin-converting enzyme inhibitor (lisinopril). Thiazide-type diuretics have also been shown to be less expensive.^{207,208} In an extension of the ALLHAT study, chlorthalidone was found to be more cost-effective than amlodipine and lisinopril.

Lipid and Blood Pressure Treatment

Several studies have evaluated the cost-effectiveness of the treatment of dyslipidemia and hypertension for primary prevention of coronary heart disease. In an extension of the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT), lifetime cost-effectiveness of atorvastatin plus amlodipine was the most expensive but also the most effective treatment compared with amlodipine-based therapy alone (ICER of €8591 per QALY in Sweden and €11 965 per QALY gain in the United Kingdom).²⁰⁹ In Canada, both lipids and hypertensive therapy were found to be cost-effective (ICER of \$16 700 and \$37 100 per life-years saved, respectively), although statin treatment was less effective among women <50 years of age, as was hypertension treatment for men and women <50 and 60 years of age, respectively.²⁷

Evidence is emerging on the use and cost-effectiveness of fixed-dose medication combinations (“polypill”) for CVD prevention. Coadministration of atorvastatin and amlodipine for hyperlipidemia and hypertension has been found to be well tolerated and without adverse pharmacological interaction.²¹⁰ This combination was shown to be cost-effective in preventing CVD in a subgroup of Koreans ≥ 45 years of age without a history of myocardial infarction or stroke, with an approximate ICER of \$6000 per QALY gained.²¹¹ Newman et al²⁸ used a mathematical model to evaluate whether a fixed-dose medication (statin, angiotensin-converting enzyme inhibitor, thiazide diuretic, and β -blocker) would be cost-effective in the primary prevention of CVD in men ≥ 55 years of age without coronary heart disease, hypertension, or dyslipidemia. The decision model, which compared treatment and no treatment, considered medication costs and side effects, as well as direct medical costs and age-related health states, including morbidity and mortality from CVD. The fixed-dose medication treatment was less expensive and more effective, with an average cost of \$70 000 compared with \$93 000 for no treatment, and resulted in 13.62 QALYs compared with 12.96 QALYs without treatment. The authors concluded that the use of a fixed-dose polypharmacy approach to CVD prevention in men >55 years of age may be cost-effective.

Making the Case for Prevention to Policy Makers

The policy landscape for CVD prevention is active with considerable potential to improve health. The challenge is how to translate biological science, economic analysis, and behavioral science into policy that supports the promotion of heart health and the prevention of CVD. Brownson et al²¹² describe the parallel worlds of researchers and policy makers and the diffi-

culty in connecting the two. One of the challenges described is timing. Whereas researchers' time frame is longer term with studies and analysis and publishing, the time frame of the policy maker is related to election cycles. With regard to primordial and primary prevention of CVD, the tyranny of the urgent, the acute stroke or myocardial infarction that evolves over minutes, can seem more important than the much slower, but potentially far more substantial, benefits of effective prevention strategies (ie, the rule of rescue). However, targeted population-level prevention policies can have a measurable impact even in the short time frame of policy makers.

Convincing policy makers of the importance of prevention has less to do with whether they believe prevention works and more to do with whether they believe prevention programs are effective and provide value. As previously discussed, standard cost-effective analyses are difficult to conduct, with considerable uncertainty about outcomes that occur over a period of decades. And certain types of savings are difficult to measure accurately. The interventions selected must provide evidence of improved outcome at an acceptable cost (ie, that they provide value). The assessment of cost and benefits must include the cost of intervention and anticipated reductions in medical care costs, as well as value in the workplace and society by having a healthier population and workforce.

From a government policy perspective, support for prevention policies and the necessary appropriations that support prevention can be difficult to garner when resources are limited. Congressional Budget Office scoring does not reflect long-term savings or savings that cannot be accurately measured.²¹³ In addition, the Congressional Budget Office considers only costs or savings to the federal government, so a program with a broader societal benefit, fiscal or otherwise, may not seem to show a positive return on investment. The Congressional Budget Office has outlined the challenges in assessing the cost savings of prevention, noting that achieving substantial savings in healthcare spending or federal outlays from prevention initiatives may take years of costly intervention and a variety of approaches to succeed; even if these initiatives change people's behavior, the resulting health benefits may take a long time to emerge, so the immediate impact on health spending may be limited; and the long-term savings on health care from reductions in the incidence of illnesses and disabilities may be substantial, but any savings to the federal government could be offset at least partially by additional expenditures as healthier individuals live longer. For example, Medicare costs could rise for the treatment of other diseases and conditions during those extra years of life, and expenditures for programs that are not directly related to health (such as Social Security) could also increase as lifespans are extended.²¹³ The challenge is to convince policy makers that although there may not be significant net cost savings in the short term to society (or even long term to the federal government), there is value in making an important investment in the health of our nation.

Another challenge is that the healthcare system responsible for public medical care (eg, Medicare and Medicaid) and private medical care is seen as distinct from public health rather than as an integrated system. Furthermore, the healthcare system separates the biological from the psychosocial in

the socioecological model that takes into account the influence of social, cultural, and physical environments on individual and population health.

Translating evidence into policy is not as simple as knowing the science. At least 4 requirements must be satisfied to effect policy change. The policy maker has to be convinced that there is a theoretical basis for successful outcomes, that the policy is a practical one to pursue, that it is an affordable or a worthy investment, and that it is reasonable politically to pursue the new policy. In addition, in an environment of limited resources, activities undertaken must be viewed as an appropriate role of government versus the individual.

Those hoping to effect policy change must be able to articulate a rationale for policy change that, in the case of the primordial and primary prevention of CVD, adheres to the following principles: a robust evidence base on quality of life and/or prevention of future events, the impact of the health of the population on healthcare costs and medical care delivery, and the positive influence on the nation's productivity and long-term national security. In summary, the practical benefits of policies that should be adopted will promote health and prevent disease and disability with benefits accruing to both individuals and society.

Future Research Directions

By several indexes, healthcare expenditures continue to rise at the fastest rate in our history. According to a recent projection, total healthcare spending will approximate \$4 trillion in 2015, or 20% of the gross domestic product, corresponding to \$1 of every \$5 spent in the United States.²¹⁴ This growth in healthcare spending is clearly not sustainable, making cost-effective prevention of disease a national priority. Future research in prevention should routinely include economic studies. Potential areas include the following:

- Serial assessment of participants in behavioral or multi-component trials to confirm maintenance of the treatment effect and to assess longer-term outcomes
- Evaluation of the role of technology in facilitating and supporting lifestyle change interventions
- Assessment of motivational interviewing and related behavior-change techniques, including the impact of motivational interviewing strategies delivered in primary care settings
- Clarification of the independent and additive benefits of lifestyle modification on cardioprotective pharmacotherapies and vice versa
- Evaluation of the effects of moderate versus vigorous physical activity, with specific reference to the associated benefits, risks, and long-term compliance
- Evaluation of the advantages and limitations of selected environments to deliver primordial and primary preventive interventions, including the home, community, worksite, school, and healthcare system
- Clarification of the impact of excise taxes on the consumption/use of unhealthy foods, sugary beverages, and tobacco products
- Testing of the thesis that we are initiating treatment of hypercholesterolemia (and other risk factors) too late in life, particularly among adolescents and young adults with

high lifetime risk, clarifying the potential benefits, harms, and costs of initiating lifestyle modification interventions, drug therapy, or both early in life^{199,200}

- Research on the role of genetic testing in developing more personalized approaches to prevention
- Methodological research on better approaches to evaluating value of preventive services

The medical and research communities are challenged to further clarify the effectiveness and sustainability of cost-effective preventive cardiovascular services so that proven interventions can be provided in home-, work-, school-, and community-based settings to save lives, money, and resources. Legislators, public health and planning professionals, and community representatives can help to facilitate this objective by supporting selected advocacy initiatives and empowering localities to embrace a lifestyle culture of physical activity, healthy nutrition options, smoking bans, and affordable access to health care for all Americans. The American Heart Association has developed initiatives to foster the development of a healthier population, including Go Red for Women, Power to End Stroke, Alliance for a Healthier Generation, and Start!

Cardiovascular disease is largely preventable. The mortality from CVD has fallen by two thirds since the peak in the 1960s, resulting in an unprecedented increase in longevity.²¹⁵ Approximately 55% of this decrease has been attributed to primary and secondary prevention because of improved management of cholesterol, blood pressure, and tobacco use. These gains have been offset in part by increases in obesity and diabetes mellitus.²¹⁵ These improvements have occurred despite a relatively modest investment in prevention compared with the management of acute disease. Much is yet to be accomplished to optimize the health and productivity of our nation by the economically advantageous development of healthy lifestyles, including diet, tobacco avoidance, and physical activity, and appropriate pharmacological therapy for hypertension, hyperlipidemia, tobacco cessation, and diabetes mellitus. A population with optimal health will be developed through the sustained and coordinated efforts of an informed citizenry, community participation, and the medical care system. Given the high cost of treating acute and chronic disease, prevention offers the potential of both improving health and decreasing costs.

Appendix

Primer on Cost-Effectiveness Analysis

Background on Economic Analyses

In evaluating societal choices concerning prevention, the initial and long-term direct costs and induced costs or saving of services are important considerations (see Table 1 for a glossary of terms). Given that society cannot afford unlimited medical services, all forms of care should compete for resources on the basis of effectiveness and cost. In choosing services, whether preventive or therapeutic, consumers will look to obtain value (ie, that the service is worth what is paid for it). The perspective in economic analyses will have an important impact on the assessment of value. For instance, an analysis from the perspective of a health system might not include the long-term consequences of a particular clinical strategy, whereas this issue may be vital to patients. In addition, the indirect, or nonmedical, costs or consequences are not always factored into the cost analysis. The perspective of all of the various stakeholders may be viewed in aggregate as "society." To be most useful in serving

societal goals, economic analyses should be performed from a societal perspective in which an attempt to measure all of the costs and effectiveness measures associated with a particular treatment is made.²¹⁶ These costs should include those incurred by the patient, the costs of medical resources that could have been used for other patients, and any loss of income that the patient sustained because of poor health, as well as the loss of income for those who may have provided informal care to the patient. Outcomes should include events, quality of life, and survival. By evaluating the sum of all of these costs in relation to outcomes, a policy maker could decide, for example, whether the public good benefited more by allocating limited healthcare resources to preventive services or to new therapies for incident or prevalent diseases.

Determining Costs

Costs may be considered from one of several possible perspectives.²¹⁷ For hospitals, costs are their expenses related to providing a service. For payers, cost is the funds transferred to a provider or providers for services rendered plus administrative expenses. In principle, cost studies generally seek to determine societal costs, which can be used in cost-effectiveness analyses to gain the widest perspective. However, societal costs are never directly measurable; thus, combinations of cost proxies from one or several stakeholders, when measurable, are used as estimates.

Costs are often classified as direct or indirect.²¹⁸ Theoretically, direct costs are those incurred by a stakeholder for a therapy or test, and indirect related costs are those incurred by other societal groups. More commonly, direct costs relate to the provision of medical care, whereas indirect costs are nonmedical costs such as travel and related societal costs. Indirect costs reflect lost patient or business opportunity and may be referred to as productivity costs.²¹⁹

Another issue involved in measuring hospital costs is average versus marginal or incremental cost.²²⁰ Average cost is calculated by dividing all costs for a service by the total number provided. In contrast, the marginal cost is the cost of the next similar procedure. Average costs include all resources used, including overhead, with associated costs that would not be decreased if not used. Marginal costing accepts fixed costs as a given and focuses only on variable costs or those additional resources consumed by each additional patient. Variable costs are analytically separated from fixed costs by establishing the perspective and time frame as fixed. Because of difficulties in assessing marginal cost, most cost and cost-effectiveness studies use average costs.

Future costs should be discounted to reflect the opportunity costs of current dollars; that is, future costs should be expressed at their present value.²¹⁶ For instance, if a policy maker were given the alternative of spending \$1000 now or \$1000 in 5 years to treat a given condition and obtain the same outcome, the decision would always be the latter. Costs are generally discounted at a rate of 3%/y to 5%/y.²¹⁶

Determination of Patient Utility and QALYs

In the treatment of CVD, it is unusual for 1 measurement of outcome to be of sufficient clinical importance that all other outcome measures may be ignored in clinical decision making. Although death generally overwhelms all other outcome measures in importance, patients may also suffer from considerable disability. Thus, a therapy may be justified on the basis of improved health status alone, even if not lifesaving. To incorporate health status measures into a cost-effectiveness analysis, an overall measure of health status is needed. In principle, this task may be accomplished through the determination of patient utility. The utility of a therapy or test is the sum of effects, both positive and negative, that accrue to a patient over time as the result of the procedure.²²¹ More technically, utility is a measure of patients' preferences for one health state over another.

Utility may be measured indirectly using either a validated survey such as the Health Utilities Index²²² or the EQ-5D²²³ or by directly assessing patient preference. The patient preference methods, Standard Gamble and Time Trade-Off,²²⁴ ask patients to directly evaluate their current state of health and what they would give up or risk to achieve optimal health. The patient preference methods are probably superior to surveys because the evaluation of a patient's view of his/her own state

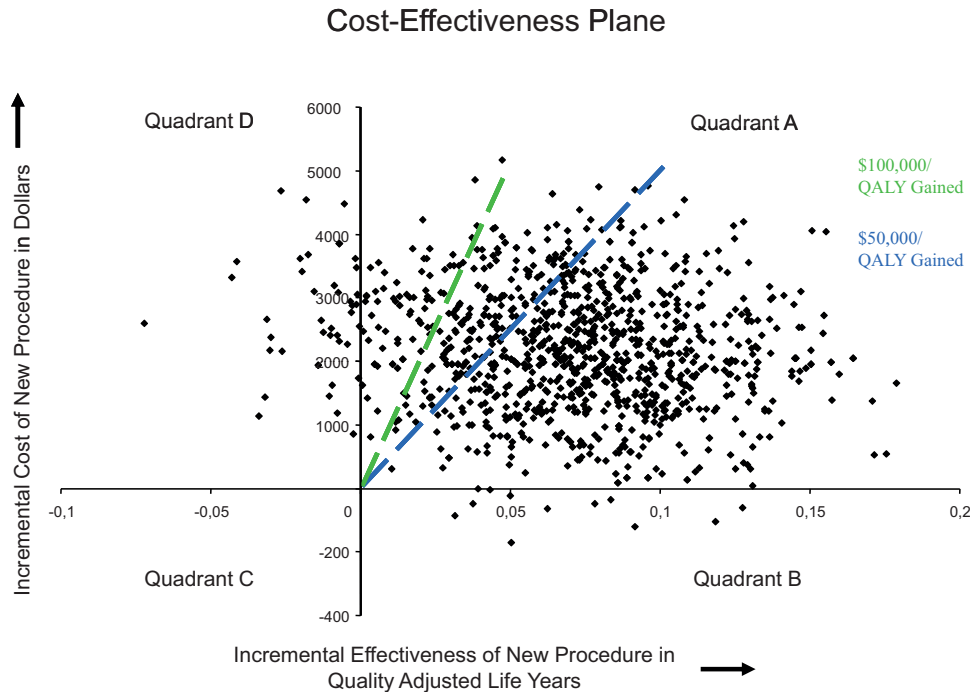


Figure 2. The distribution of cost-effectiveness in the cost-effectiveness plane. Each point represents an estimate of the incremental cost-effectiveness ratio based on dual bootstrap of cost and efficacy. Potential \$50 000 and \$100 000 per quality-adjusted life-year (QALY) gained threshold lines are noted. Estimates of the incremental cost-effectiveness ratio below those benchmarks would be considered cost-effective.

of health is measured directly; however, they are more difficult to administer. In the Time Trade-Off approach, patients weigh the fraction of expected survival they are willing to give up to achieve optimal health. With the Standard Gamble, patients weigh what risk of death they are willing to take to achieve optimal health. The Standard Gamble is probably superior because it includes the element of risk.

Utility alone does not provide a final summary measure of outcome because it does not include life expectancy. A summary measure can be created by combining utility and survival to obtain QALYs.²²⁵ Survival, as with cost presented above, is generally discounted, which means that patients value a year of survival at the present time more than a year of survival in the future. The “true” discount rate for survival is unknown. Values in the literature for the discount rate have varied from 2% to 10%, with 3% being the most popular, and it should be discounted at the same rate as cost.²¹⁶ Thus, with a discount rate of 3%, next year’s survival is 3% less important than this year’s survival. The QALY is the best summary measure of outcome in a cost-utility analysis because it incorporates patient value, risk aversion, expected survival, and a discount rate.

Cost-Effectiveness and Cost-Utility Analysis

Cost-effectiveness analysis is by its nature incremental. Thus, it is necessary to evaluate both added cost and effectiveness compared with a control group. At times, the appropriate control is no procedure or test (eg, a placebo in pharmaceutical trials); at times, the current standard procedure (ie, the appropriate control) depends on the clinical question being asked. It is also necessary to consider the time horizon of a study. In principle, a lifetime horizon is preferred because it incorporates all downstream resource use and events.

When additional costs and incremental measures of effectiveness of a new form of therapy are available, along with description of the distribution of each, then an ICER may be calculated, along with its own distribution.²²⁶ An ICER is a ratio of the incremental cost of the new therapy divided by the incremental measure of benefit. When the measure of benefit is expressed in life-years or QALYs, then the ICER will be measured in cost per life-year or QALYs gained.

The ICER should not be viewed only as a single number because of the uncertainty about measures of both cost and effectiveness. The first

level of uncertainty is based on chance or sampling error alone. This may best be considered when patient-level data are available. The distribution of an ICER based on sampling error of the numerator and denominator is somewhat complicated because the 95% confidence interval of a ratio is not easily defined. A popular approach to this problem is to examine the confidence interval of cost and effectiveness by sampling from the distribution of each, an approach called bootstrap analysis. By sampling from both the cost and effectiveness distributions concurrently, one can make multiple estimates of the ICER.²²⁷ The distribution of the ICER may then be displayed in a plane (Figure 2), where each point is an estimate of the ICER. In quadrant A, the new therapy is more effective but more costly than the previous standard. In quadrant B, the new therapy dominates the standard, being more effective and less expensive, whereas in quadrant D, the new therapy is dominated by the standard, being less effective and more expensive.

Cost-effectiveness analysis will almost always include a series of assumptions because it is generally not possible to accurately measure all variables necessary for a definitive analysis. In addition, even when measurements are available, they may not adequately represent values appropriate for the analysis at hand. Thus, cost-effectiveness analysis generally includes sensitivity analyses in addition to the stochastic estimates of variation discussed. With sensitivity analysis, the input variables for assessing both cost and effectiveness are varied between reasonable limits, and the ICER and its distribution are recalculated.

An ICER is an assessment of the cost-effectiveness of one treatment or test versus another; it does not say whether a service is cost-effective, and there is no scientific basis for a threshold below which an ICER must be for a new therapy to be considered cost-effective. The \$50 000 per QALY threshold has been widely used because it is based on renal dialysis, and in the United States, there is general (political) agreement that there is willingness to pay for renal dialysis. Although a threshold gives cost-effectiveness studies a benchmark that may be used to compare studies, there is no scientific justification for selection of any one threshold; indeed, the optimal threshold for cost-effectiveness is a sociopolitical decision. A cost-effectiveness threshold then is an assessment of value that might vary by payer, patient, or provider.

Disclosures

Writing Group Disclosures

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*Modest.

†Significant.



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*Modest.

†Significant.

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