Preventing Cancer, Cardiovascular Disease, and Diabetes

A common agenda for the American Cancer Society, the American Diabetes Association, and the American Heart Association

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Collectively, cardiovascular disease (including stroke), cancer, and diabetes account for approximately two-thirds of all deaths in the U.S. and about $700 billion in direct and indirect economic costs each year. Current approaches to health promotion and prevention of cardiovascular disease, cancer, and diabetes do not approach the potential of the existing state of knowledge. A concerted effort to increase application of public health and clinical interventions of known efficacy to reduce prevalence of tobacco use, poor diet, and insufficient physical activity—the major risk factors for these diseases—and to increase utilization of screening tests for their early detection could substantially reduce the human and economic cost of these diseases. In this article, the American Cancer Society, American Diabetes Association, and American Heart Association review strategies for the prevention and early detection of cancer, cardiovascular disease, and diabetes, as the beginning of a new collaboration among the three organizations. The goal of this joint venture is to stimulate substantial improvements in primary prevention and early detection through collaboration between key organizations, greater public awareness about healthy lifestyles, legislative action that results in more funding for and access to primary prevention programs and research, and reconsideration of the concept of the periodic medical checkup as an effective platform for prevention, early detection, and treatment.

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Cardiovascular disease, cancer, and diabetes account for nearly two of every three deaths in the U.S.—close to 1.5 million people in 2001 (1). These diseases undermine health, shorten life expectancy, and cause enormous suffering, disability, and economic costs. However, much of this disease burden could be avoided if there were systematic application of what is known about preventing the onset and progression of these conditions. By addressing the underlying causes of cardiovascular disease, cancer, and diabetes, and by improving the systems to detect and treat early stage disease when interventions are most effective, significant reductions in disability and premature mortality could be achieved.

Despite the incontrovertible evidence supporting the medical and economic benefits of prevention and early detection, current disease control efforts are underfunded and fragmented. While health care costs skyrocket, the national investment in prevention was estimated at less than 3% of the total annual health care expenditures (2). Last year, the National Center for Health Statistics (NCHS) issued its 27th report on the health status of the nation (3). The report emphasized that too many Americans still smoke cigarettes, are physically inactive, and that the prevalence of overweight and obesity in adults had risen to 65% in 1999–2000; all of these factors confer significant risk for developing cardiovascular disease, diabetes, and cancer.

The evidence base regarding the efficacy and cost-effectiveness of specific components of prevention and early detection is reviewed regularly by many health organizations, including the American Cancer Society (ACS), the American Diabetes Association (ADA), and the American Heart Association (AHA). *Healthy People 2010* provides the most current and comprehensive health agenda for the nation (4). It addresses 476 specific objectives in 28 focus areas that include nutrition and overweight, physical activity and fitness, tobacco use, cancer, diabetes, cardiovascular disease, and access to quality health services. The U.S. Preventive Services Task Force (USPSTF) periodically reviews more than 200 preventive services offered in primary care settings (5). The USPSTF presently recommends routine screening for cervical, breast, and colorectal cancers, hypertension and lipid disorders, obesity, and tobacco use, as well as the provision of treatment for tobacco addiction in adults. The Centers for Disease Control and Prevention (CDC) provides similar reviews concerning community, population, and health care system interventions related to cancer, cardiovascular disease, diabetes, and other chronic diseases (6). Criteria for evaluating the delivery of preventive services by managed care plans are provided by the National Committee for Quality Assurance (NCQA). The

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In these discussions, cardiovascular disease includes diseases of the heart, hypertension, stroke, and peripheral vascular diseases.

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Abbreviations: ACS, American Cancer Society; ADA, American Diabetes Association; AHA, American Heart Association; CDC, Centers for Disease Control and Prevention; FPG, fasting plasma glucose; HPV, human papilloma virus; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; OGTT, oral glucose tolerance test.

Table 1—*Burden of chronic diseases in the U.S.*

	Cardiovascular disease*	All cancers	Diabetes
Deaths†			
Number	931,108‡	553,768	71,372
Percent of total	38.5	22.9	3.0
New cases	2,450,000	1,368,030‖	1,300,000
Prevalent cases	64,400,000¶	9,600,000#	18,200,000
Total costs (billions)**	$351.8††	$189.5	$132.0

*The category of cardiovascular disease includes heart disease, stroke, and other cardiovascular diseases. †Number of deaths in 2001. ‡Includes 700,142 deaths from heart disease, 163,538 deaths from stroke, and 67,428 from other cardiovascular disease. §Includes coronary heart disease, stroke, and congestive heart failure only. ‖Number of newly diagnosed cancers in 2004, estimated by ACS. ¶Estimated by AHA and National Heart, Lung, and Blood Institute for 2001. Includes 13,200,000 cases of coronary heart disease and 4,800,000 cases of stroke. The National Health Interview Survey (NHIS) estimated a prevalence for all types of heart disease of 23,482,000 for 2001; however, we have not utilized the NHIS data as they are solely based on interview. #Number of prevalent cases in 2000, estimated by the National Cancer Institute. **Total direct and indirect costs in 2003, estimated by the National Institutes of Health. ††Includes $229.9 cost of heart disease and $51.2 cost of stroke.

Health Plan Employer Data and Information Set (HEDIS) measures a broad spectrum of preventive services including provision of breast, cervical, and colorectal cancer screening, blood pressure control, comprehensive care for diabetes, and treatment for tobacco dependence (7). Yet, despite the abundance of data, guidelines, and objectives, progress in the nation's health falls well short of its true potential, and some trends are worsening.

In this publication, we announce a new collaborative initiative by the ACS, AHA, and ADA to create a national commitment to the prevention and early detection of cancer, cardiovascular disease, and diabetes. Our goal is to stimulate substantial improvements in primary prevention and early detection through collaboration between key organizations, greater public awareness about healthy lifestyles, legislative action that results in more funding for and access to primary prevention programs and research, and reconsideration of the concept of the periodic medical checkup as an effective platform for prevention, early detection, and treatment.

Private, nonprofit health organizations are uniquely positioned to foster collaborative efforts between federal and state governments, private health care providers, insurers, policy makers, nonprofit organizations, and the American public. Enhanced collaboration is critical, because cancer, cardiovascular disease, and diabetes share numerous risk factors and opportunities for prevention, including the importance of assessing and regularly updating an individual's family history. Efforts to achieve the ambitious goals of Healthy People 2010 require new strategies for delivering primary and secondary prevention. Currently, preventive health receives only sporadic attention in the context of office visits for acute and chronic medical problems (8). Health care providers and medical organizations must transform this model into systems that provide preventive care and early detection as an integral part of standard medical practice. The ACS, AHA, and ADA are committed to a forward-looking collaboration that is dedicated to reducing morbidity and premature mortality from cancer, cardiovascular disease, and diabetes. The logic and potential for this collaboration is described below.

CURRENT BURDEN OF DISEASE

— Collectively, cardiovascular disease, cancer, and diabetes accounted for 65% of all deaths in the year 2000 (9). The total number of deaths, new cases, prevalent cases, and economic costs contributed by these conditions in the most recent year for which data are available are shown in Table 1. The data on and discussions of cardiovascular conditions throughout this document include diseases of the heart, hypertension, stroke, and peripheral vascular diseases.

Mortality and person-years of life lost

Cardiovascular disease accounts for over 930,000 deaths per year—approximately 38.5% of all deaths in 2001 (10). All cancers combined accounted for nearly 554,000 deaths in 2001, almost 23% of the total number of deaths (1). Another 71,372 deaths occurred in 2001 from diabetes, representing 3% of all deaths in the U.S. (3). Another measure of the burden of these diseases is their impact in years of life lost. In 2000, deaths from malignant neoplasms, cardiovascular disease, and diabetes cost Americans 18.8 million person-years of life lost (11).

Prevalence and economic costs

The prevalence and economic costs of the major chronic diseases are equally sobering. Approximately one in four adults is hypertensive, and the majority of individuals with hypertension do not have adequately controlled blood pressure (12). More than 100 million adults have elevated cholesterol levels; of this group, more than 35 million adults have cholesterol levels that qualify as high risk and that require aggressive medical intervention (4). Recent estimates from the Third National Health and Nutrition Examination Survey (NHANES III) indicate that among insured individuals, 28.6% of adults with hypertension and 51.2% of adults with hypercholesterolemia were undiagnosed (13). Based on extrapolations from NHANES III (10,14), about 64,400,000 Americans (22.6% of the population) had prevalent cardiovascular disease in 2001; between 1988 and 1994, approximately 1 in 10 individuals were hospitalized each year for treatment of a cardiovascular problem.

Approximately 9.6 million Americans who have been diagnosed with cancer were alive in 2000. This estimate includes individuals living with cancer as well as those who were cancer-free (11). The estimate does not include persons with cancers that have not yet been detected. Substantial numbers of adults are diagnosed with advanced cancers each year because of lack of screening. Approximately one-third of breast and cervical cancers and nearly two-thirds of colorectal cancers are diagnosed at an advanced stage (11).

An estimated 18.2 million Americans had diabetes in 2002 (15). This includes both individuals who had been diagnosed (13 million) and those who were as yet undiagnosed (5.2 million). According to the CDC, approximately 33.8% of the population have impaired fasting glucose (IFG) levels, 15.4% have impaired glu-

cose tolerance (IGT), and 40.1% have pre-diabetes (IFG, IGT, or both) (16).

The economic costs of cardiovascular disease, cancer, and diabetes in the U.S. in 2003 were estimated at $351.8 billion, $189.5 billion, and $132.0 billion, respectively (17,18). The combined costs of these three diseases thus comprises 32% of the 2,256.5 billion dollars in total illness costs (19). This amount includes both direct medical costs and indirect economic costs from lost productivity due to illness or death. The estimates for health care expenditures include the cost of physicians and other professionals, hospital and nursing home services, the cost of medications, and home health care. These medical care costs also include treatment for diseases resulting from diabetes. For example, patients with diabetes, particularly if poorly controlled, may develop blindness, end-stage renal disease, cardiovascular disease, neuropathy, and many other complications, each of which incur economic as well as personal costs (20–22).

TRENDS IN DISEASE BURDEN

— Trends in incidence, prevalence, and mortality for these chronic conditions are influenced by changes in the prevalence of risk factors, utilization of screening, trends in treatment, and demographic shifts in the U.S. population. The growth and aging of the population is especially important now because of aging of post–World War II birth cohorts and the strong relationship between chronic disease and age. Unless there are substantial reductions in the underlying risk factors or major improvements in the treatment of these diseases, the human and economic costs from cardiovascular disease, cancer, and diabetes can be expected to rise. This demographic effect will be exacerbated by adverse trends in risk factors, such as the large and continuing increase in obesity rates among children and adults.

Cardiovascular disease

Age-standardized death rates from stroke have decreased substantially since the 1940s, as have mortality rates from coronary heart disease since the mid-1960s (3). This progress is attributed to a combination of primary prevention (e.g., reductions in the prevalence of tobacco smoking and saturated fat intake), secondary prevention (the early detection and treatment of hypertension and high blood cholesterol), and improved treatments for heart attack and stroke (10,14). However, while the death rate from cardiovascular disease fell by 17% during the last decade of the 20th century, the number of deaths increased each year by 2.5% due to the growth in the size of the population above age 65 (23).

Cancer

The age-standardized death rate from all cancers combined decreased by 7.2% between 1991 and 2000, the most recent year for which statistics are available in the U.S. (11). The decline in the overall cancer mortality rate is attributed to a combination of reductions in cigarette smoking and improvements in early detection and treatment. As with cardiovascular disease, despite a decrease in the age-standardized death rate from cancer, the total number of people who develop or die from cancer each year continues to increase because of growth and aging of the population (24). From 1991 to 2000, the annual number of deaths from all cancers combined increased by 7.4% (about 38,400 deaths) over the 9-year period (25). However, this increase was smaller than would have occurred if the age-specific or age-adjusted death rates were not decreasing, since the population of the U.S. increased by nearly 10% (24 million), during the same period, with an even larger percentage rise in the number of people aged 65 years and older (24).

Diabetes

From 1990 to 2001, the prevalence of diabetes increased by 61%, with about 1.3 million Americans developing diabetes each year (15). This overall increase in diabetes prevalence reflects an increase in type 2 diabetes (which accounts for 90–95% of all diagnosed cases) due to the epidemic increase in excess body weight occurring in the U.S. population during that period (26). Based on current trends in childhood and adult obesity, the prevalence of type 2 diabetes and its complications will continue to increase (27).

OPPORTUNITIES FOR PRIMARY AND SECONDARY PREVENTION

— Cancer, cardiovascular disease, and diabetes share common risk factors, and all of these diseases can also be prevented or treated more effectively if they are diagnosed early. This section reviews the rationale for collaboration of ACS, ADA, and AHA, to focus primary prevention efforts toward reducing tobacco use and obesity, improving nutrition, and increasing physical activity. The next section presents the rationale for improved screening and early detection of chronic disease. Both sections also consider the benefits of reducing known risk factors or improving screening in relation to the disease burden and economic costs.

Primary prevention

Tobacco. Tobacco use is the single, largest preventable cause of disease and premature death in the U.S. Approximately 440,000 Americans die each year from illnesses related to active smoking; an additional 38,000 nonsmokers die as a result of exposure to environmental tobacco smoke (28). The CDC estimates that tobacco use accounted for an estimated $157.7 billion in health-related economic losses each year from 1995 to 1999 (28). The great majority of deaths from tobacco could be prevented by reducing the uptake of tobacco use by children and adolescents and increasing tobacco cessation among adults.

Nearly 20% of all deaths from cardiovascular disease are attributed to tobacco use (29), including more than 148,000 deaths from active smoking, and an additional 35,000 deaths caused by secondhand smoke. Among people who quit smoking, the risk of death from coronary heart disease is 50% lower than that of people who continue to smoke after 1 year of abstinence (30). The total economic cost from lost productivity due to smoking attributable cardiovascular disease was estimated as $35.6 billion in 2000 (31).

Approximately 30% of all deaths from cancer in the U.S. are attributable to active smoking (25,28,32). Tobacco smoking is causally related to at least 16 types of cancer (33), including cancers of the lung, colon and rectum, oral cavity, nasal cavities and nasal sinuses, pharynx, larynx, esophagus (squamous cell carcinoma and adenocarcinoma), stomach, pancreas, liver, urinary bladder, kidney (adenocarcinoma and transitional cell carcinoma), uterine cervix, and myeloid leukemia. Among these, the strongest association is with lung cancer, the most common type of fatal cancer among both

men and women in the U.S. (25). Cigarette smoking causes an estimated 85–90% of lung cancer deaths. Environmental tobacco smoke is responsible for an additional 3,000 lung cancer deaths among nonsmokers (29). Other forms of tobacco, such as snuff, chewing tobacco, cigars, pipes, and bidis also increase the risk of certain cancers (33). The extent to which these products contribute to the uptake of cigarette smoking by adolescents or delay cessation among persons attempting to quit is unclear.

Recent cohort studies suggest that smoking may also be an independent and modifiable risk factor for the development of type 2 diabetes. Among participants in the ACS Cancer Prevention Study cohort, men and women who smoked two packs per day at baseline had a 45 and 74% (respectively) higher diabetes mellitus incidence rate than men and women who had never smoked (34). In that same cohort, quitting smoking reduced the rate of incidence diabetes to that of nonsmokers after 5 years in women and after 10 years in men (34). Women in the Nurses' Health Study who smoked 15 cigarettes or more per day had a 30–40% higher risk compared with never smokers (22). A similar association between smoking and type 2 diabetes was observed among U.S. male physicians (35), other health professionals (36), and middle-aged men in Britain (37) and Japan (38). Tobacco use may also exacerbate the complications of diabetes (39–41).

Much is known about strategies that can prevent the initiation of tobacco use among young people (42) and promote successful cessation (43). Despite this, vigorous advocacy is needed to create and sustain effective tobacco control programs. Comprehensive tobacco control programs include restrictions on advertising and promotion of tobacco, increases in excise taxes, measures to reduce access to tobacco by minors, education and counter-advertising, clean air laws, and readily available treatment for tobacco dependence (44). States such as California and Massachusetts that have created strong tobacco control programs have seen accelerated declines in smoking prevalence (45,46), cardiovascular mortality (47), and lung cancer incidence at younger ages (48).

Counseling by medical caregivers can profoundly increase smokers' motivation to stop using tobacco (43). Advice from a physician to stop smoking should be accompanied by informed guidance in the use of prescription and nonprescription nicotine replacement products and other pharmacological and behavioral therapies (5,49). There are well-defined guidelines to assist the healthcare provider in treating tobacco dependence. A "teachable moment" may occur during hospitalization for ischemic heart disease or other morbidity potentially related to smoking (5). However, counseling and pharmacological interventions are currently underutilized. There is a need for further training of individual clinicians and for changes in health systems in order to require and reward appropriate treatment for tobacco dependence (43,50,51).

Overweight and obesity. The percentage of Americans who are overweight or obese has increased rapidly over the past 25 years. Nearly two-thirds (64%) of U.S. adults, age 20 years or older, met the criteria for overweight or obesity in 1999–2000 (52), while 30.5% qualified as obese. These categories were defined by the World Health Organization as representing a body mass index (BMI; calculated as body weight in kilograms divided by height in meters squared) of 25.0–29.9 for overweight and >30 for obesity (53). The percentage of overweight children and adolescents also increased dramatically since the late 1980s (54). The trends among children will influence future adult rates, since individuals who become overweight as children or adolescents are more likely to be overweight or obese as adults (55,56). The estimated direct and indirect annual costs from obesity are approximately $117 billion (57).

Excess body weight is an independent risk factor for cardiovascular diseases as well as causing other risk factors such as hypertension, dyslipidemia, and type 2 diabetes (58–62). Several studies highlight the relationship between obesity and risk of stroke. In one study, the percentage of patients hospitalized for ischemic stroke increased from 10 to 30% with an increase of 3 kg/m^2 in BMI (63). The pattern of obesity may also influence stroke risk. Individuals with a waist-to-hip ratio equal to or greater than the median had an overall odds ratio (OR) of 3.0 (95% CI 2.1–4.2) for ischemic stroke even after adjustment for other risk factors and BMI (64). Modest weight loss and increases in physical activity have been demonstrated to reduce cardiovascular risk factors such as hypertension, dyslipidemia, and type 2 diabetes (65–69). Using mathematical modeling, it has been estimated that a sustained 10% weight loss among obese individuals would reduce the expected lifetime incidence of CHD and stroke by 12–38 cases per 1,000 and 1–13 cases per 1,000, respectively (70).

Epidemiological and animal studies have shown that overweight and obesity are associated with increased risk for cancers at numerous sites, including breast (among postmenopausal women), colon, endometrium, esophagus, gallbladder, liver, prostate, ovarian, pancreas, and kidney (71–74). A recent study of approximately 900,000 individuals suggests that obesity may account for 14% of cancers in men and 20% of cancers in women, and in this cohort the heaviest men and women were 52 and 62%, respectively, more likely to die of cancer (75).

While it is not clear whether losing weight reduces the risk of cancer, there are physiological mechanisms that suggest weight loss may be beneficial, since overweight or obese individuals who lose weight intentionally have reduced levels of circulating glucose, insulin, bioavailable estrogens, and androgens (76). Despite some uncertainty about weight loss and cancer risk, it is nonetheless clear that individuals who are overweight or obese should be strongly encouraged and supported in their efforts to reduce their weight.

The epidemiological associations of obesity and type 2 diabetes, and the underlying pathophysiologic mechanisms, have been the subject of extensive research (77,78). It has been estimated that 70% of type 2 diabetes risk in the U.S. is attributable to overweight and obesity, and that each kilogram of weight gain over 10 years increases risk by 4.5% (79). Weight reduction, often achieved by the combination of reduced caloric intake and increased physical activity, has been shown to reduce the risk of diabetes and decrease insulin resistance, as well as improve measures of glycemia and dyslipedmia in diabetic individuals (80–85). Based on evidence from studies in Finland and the U.S., 30 min of daily physical activity has been endorsed as part of a healthy lifestyle to reduce the risk of diabetes (18,80–82). The consistency of this recommendation along with similar recommendations for reducing cancer and

cardiovascular risks suggests the potential for simplified health education messages about physical activity and disease prevention. The proven benefit of weight loss and physical activity strongly suggests that lifestyle modification should be the first choice to prevent or delay diabetes, as well as contribute to more effective management of disease in individuals with diabetes. Even modest weight loss (5–10% of body weight) and modest physical activity (30 min daily) can have a positive impact on diabetes risk and management (81).

Nutrition

While much remains to be learned about the role of specific nutrients or combination of nutrients in decreasing the risk of chronic disease, dietary patterns are emerging as an important consideration. Dietary patterns that emphasize whole grain foods and legumes, vegetables and fruits, and that limit red meat, full-fat dairy products, and foods and beverages high in added sugars are associated with decreased risk of a variety of chronic diseases (86,87). It also is critically important that individuals limit their overall caloric intake and become physically active to help maintain a healthy body weight. Despite evidence of the importance of nutritional factors for health, the American diet has shifted unfavorably, especially over the past decade. Vegetable and fruit consumption of both adults and youth continues to be below recommended levels: only 24.5% of adults and 21.4% of youth consume at least five servings each day (88). Dietary fat, which had remained stable since the mid 1980s, also increased by 6% in 2000.

Estimates by the Economic Research Service of the U.S. Department of Agriculture (USDA) of adult caloric intake in the U.S. suggest that daily intake in 2000 was approximately 300 calories greater than in 1985 (89). The largest percentage of the increase in calories consumed since the 1980s has been from refined grains and foods high in added sugar (90,91). This level of overnutrition, in addition to physical inactivity (38% of adults report no leisure time physical activity) (88) has contributed to the alarming increase in the levels of obesity and overweight over the past decade (92). If the increasing trend of overweight is not reversed over the next few years, poor diet and inactivity may soon overtake tobacco as the leading cause of death (27). While there is widespread confusion about how the public should achieve energy balance, it is clear that balance between caloric intake and expenditure is the critical factor in maintaining a healthy BMI.

Cardiovascular diseases. It is difficult to obtain randomized, controlled data on the long-term effects of nutritional components or even patterns, but there is good evidence that following a healthful eating plan can reduce a number of the recognized risk factors for cardiovascular diseases. While it is rarely possible to precisely define the contribution of single nutrients, with notable exception, such as sodium, there is good evidence that a nutritionally balanced diet plays an important role in maintaining a healthy weight, and can have a favorable impact on blood pressure (12) and plasma lipids (93). Increased consumption of fiber, fruit, vegetables and calcium, combined with sodium restriction, was more effective than sodium restriction alone in reducing hypertension in the DASH (Dietary Approaches to Stop Hypertension) study (94). Excessive intake of fat, saturated fat, *trans* fats, or cholesterol is associated with an increased risk for coronary artery disease and should be avoided (86).

Cancer. Doll and Peto (32) first estimated that 35% (10–70%) of cancer deaths in the U.S. were attributable to diet, with no specific reference to obesity or physical inactivity. Doll (95) later narrowed the range of the estimate attributable to diet to 35% (20–60%), still largely considering macro- and micronutrients rather than energy balance. In another analysis, McGinnis and Foege (96) reviewed the literature on the actual causes of death in the U.S. and attributed 14% of all deaths occurring in 1990 to diet and physical activity.

Many important questions concerning nutrition and chronic disease remain, especially with respect to cancer. There is incomplete evidence on how single nutrients, combinations of nutrients, overnutrition and energy imbalance, or the amount and distribution of body fat at particular stages of life can influence risk for specific cancers. However, epidemiological studies also have shown that populations whose diets are high in vegetables and fruits and low in animal fat, meat, and/or calories have a reduced risk of some of the most common types of cancer (97–100). Until more is known about the specific components of diet that influence cancer risk, current recommendations are to consume a mostly plant-based diet that includes at least five servings of vegetables and fruits each day, to chose whole grain carbohydrate sources over refined sources, and to limit saturated fat, alcohol, and excess calories.

Diabetes. Achieving energy balance and maintaining a healthy body weight are critical for the prevention and treatment of type 2 diabetes, and limiting saturated fat intake can help to prevent the vascular complications of diabetes. Higher consumption of whole grains and dietary fiber are associated with reduced risk of diabetes in some studies (22). The evidence that micronutrients influence the risk of diabetes is limited, although some studies suggest that certain micronutrients may affect glucose and insulin metabolism (101).

Physical activity

Supporting evidence continues to accumulate that physical activity reduces chronic disease risk, both directly through its impact on hormones and indirectly through its impact on weight control.

Cardiovascular disease. Prospective epidemiological studies of occupational and leisure-time physical activity have consistently documented a reduced incidence of coronary artery disease and stroke in the more physically active and fit individuals (102–105). Conversely, physical inactivity has been recognized as an important risk factor for cardiovascular disease. While it interacts with other risk factors, e.g., by increasing the tendency to overweight, its effect is independent of other risk factors. While the beneficial effect of exercise is "dose-related," increasing with the duration and energy expended, increasing physical activity by even the modest amount of 30 min at least 5 days/week has been documented to reduce risk of cardiovascular events (106). Since this exercise can be moderate in effort and can be broken up into smaller time periods, it is within the reach of nearly everyone (107,108). However, creating the habit of seeking more exercise in our increasingly sedentary population will be challenging and will require a concerted, ongoing effort.

Cancer. Physical activity reduces the risk of breast and colon cancers and may reduce the risk of several other types of cancer (109–113).

There are a variety of mechanisms by which physical activity is thought to impact cancer risk. Regular activity plays an important role in helping to maintain a healthy body weight; excess body weight increases amounts of circulating estrogen, androgens, and insulin, all of which are associated with cell and tumor growth (114). Physical activity may also help to prevent certain cancers both directly and indirectly. For colon cancer, physical activity causes food to move more quickly through the intestine, reducing the length of time that the bowel lining is exposed to potential mutagens (111). For breast cancer, vigorous physical activity may decrease the exposure of breast tissue to circulating ovarian hormones. Physical activity may also reduce cancer risk by reducing circulating concentrations of insulin and insulin-like growth factors and by improving energy metabolism. Physical activity also helps to prevent type 2 diabetes, which has been associated with increased risk of cancers of the colon, pancreas, and possibly other sites (115–118).

Many questions regarding the impact of physical activity on cancer risk remain unanswered. Research continues to clarify the optimal intensity, duration, and frequency needed to impact cancer risk. Presently, it is recommended that individuals be at least moderately active for 30 min or more on 5 or more days per week. Moderate to vigorous activity for at least 45 min on 5 or more days per week may further reduce the risk of breast and colon cancers and also may reduce the risk of kidney, endometrial, and esophageal cancers (110,111,113,119,120).

SCREENING AND SECONDARY PREVENTION —

Since reducing risk of disease does not eliminate risk of disease, early detection of some chronic conditions has the potential to alter the natural history of disease. For cancer, cardiovascular disease, and diabetes, screening for risk or early manifestations of disease can reduce incidence and mortality through recommendations for altered lifestyles, pharmacological interventions, treatment of precursor lesions, or earlier treatment of the disease itself.

Cardiovascular disease

Hypertension. Approximately one in four American adults have high blood pressure, defined as systolic pressure ≥140 mmHg or a diastolic pressure ≥90 mmHg (12). An additional estimated 45 million fall into the "prehypertensive" range of 120–139/80–89 (17). Elevated blood pressure is associated with a two to three times higher risk of developing congestive heart failure and substantially increases the risk of stroke, with blood pressures of 160 mmHg systolic and/or 90 mmHg diastolic or greater associated with a relative risk of stroke that has been estimated at four times greater than in individuals without hypertension. And in terms of total impact, the role of hypertension is increasing. For example, while the age-adjusted death rate from coronary heart disease has decreased, reflecting multiple improvements in treatment, the age-adjusted death rate attributable to hypertension as a primary or contributing cause of death actually rose by 36.4% over the past decade (data from 1991 to 2001), with the actual number of deaths increasing even more, by an alarming 53%. The prevalence of hypertension is increasing, and an estimated 30% of those with hypertension are unaware that they have it (12). Only about 34% are on medication and well-controlled; 25% are on medication, but have inadequate control (12). There are important disparities in the prevalence of hypertension, with blacks both developing elevated blood pressure at an earlier age and having higher pressures on average. This translates into increased rates of stroke, heart disease death, and a 4.2 times greater rate of end-stage kidney disease. This important risk factor is easily assessed in the office, and there is a panoply of medications that can provide excellent control. As a preventive measure, it is critical and must be addressed more effectively.

Dyslipidemia. Elevated cholesterol levels have long been recognized as an important independent risk factor for coronary artery disease. While there are clear dietary approaches and highly effective medications available, 50.7% of the population had a total cholesterol of 200 mg/dl or greater in 2001 and 45.8% had an LDL cholesterol of 130 mg/dl or higher. And this is not simply a problem of the adult population. With the rising prevalence of obesity, 10% of children 12–19 now also have total cholesterol that exceeds 200 mg/dl (28). While cholesterol screening increased from 67.3% in 1991 to 70.8% in 1999, awareness of this as a risk factor, even among those who had been screened, was only 28.6% in 1999. Awareness of the adverse effects of LDL and triglycerides (especially in women) and the beneficial effects of HDL is even lower (121).

Equally important, of individuals who would meet the criteria set out by the Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults for treatment aimed at lipid modification, fewer than 50% are actually receiving treatment (122). And this is true even for those who are at highest risk—those who have symptomatic coronary heart disease. An additional problem is that of compliance. Half of those prescribed lipid-lowering drugs stop taking them before 6 months have passed. Here, attention must be given not only to screening for this important risk factor, but also to increasing compliance with lipid-lowering regimens.

Novel risk factors. There has been considerable attention given to additional factors that may help in the prognostication of risk, including, but not limited to, the measurement of plasma homocysteine, high-sensitivity C-reactive protein, more detailed lipoprotein panels, as well as the imaging determination of vascular calcium. A number of newer markers have been shown in small studies to offer some further prognostic information about the imminent occurrence of cardiovascular events. While the utility of these risk factors is still being determined, it is important to realize that the conventional risk factors account for the great majority of the risk that can be determined, and that it is in fact unusual to find patients with cardiovascular disease and none of the established risk factors (123).

Early and global assessment of risk

Because many risk factors can be modified or even abolished by appropriate treatment, whether it is accomplished by the choice of a healthy lifestyle or by medications, early recognition of these risk factors is essential. The American Heart Association recommends that adults have risk assessed at age 20 and then at the intervals outlined in Fig. 1. In addition, since an individual's risk is determined by multiple factors, and the benefit of interventions depends on the level of risk, a global or multiple risk factor assessment is an even better guide to providing that individual the care that has the greatest

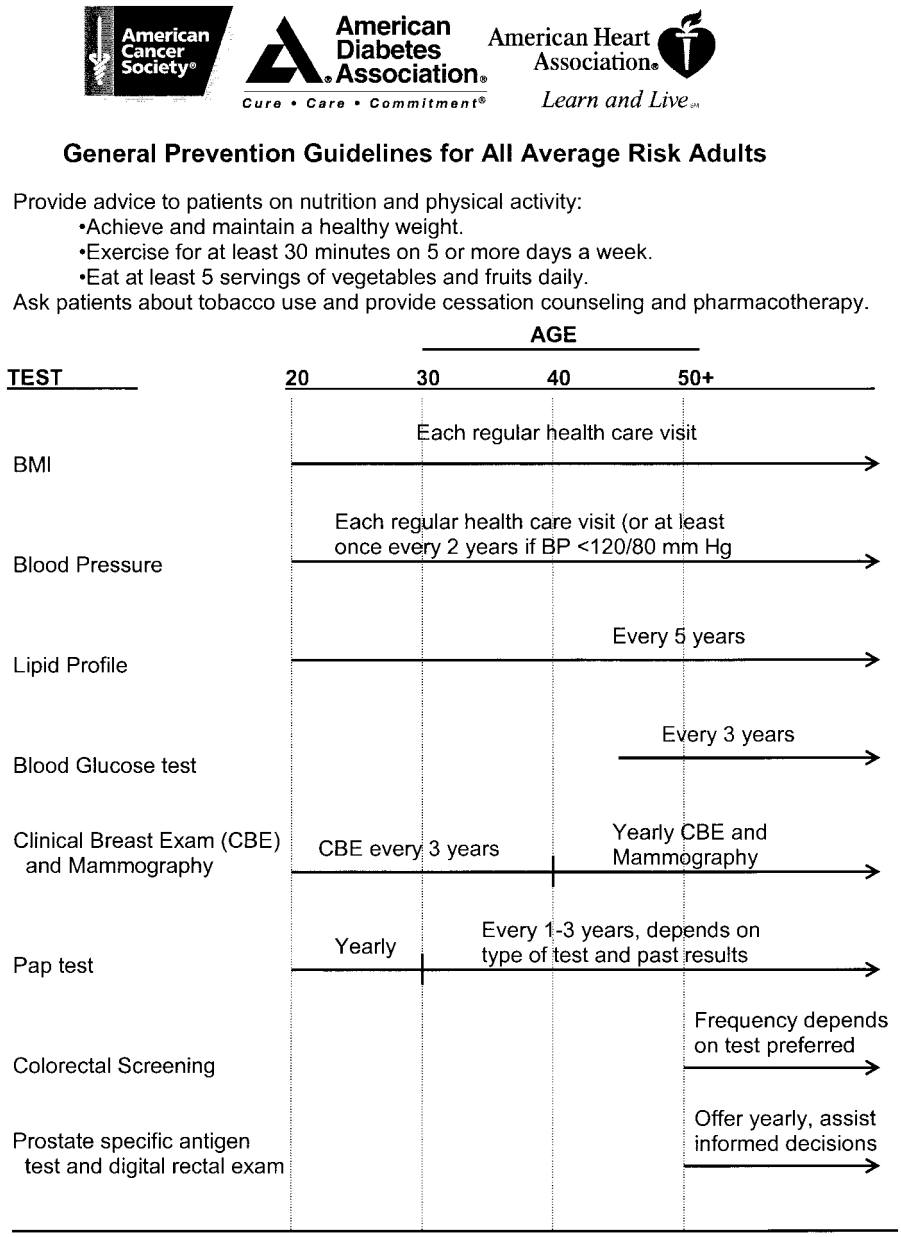

Figure 1

benefit and the lowest risk. The Framingham risk score is the best available current approach, and while it was derived from a specific geographic area and thus may not apply to all populations, its performance within subgroups has been assessed and is good (124,125).

Cancer

Cancers that can be detected by screening account for half of all new cancer cases. The 5-year relative survival rate for these cancers is about 84%. If all of these cancers were diagnosed at a localized stage through regular screening, the 5-year relative survival rate would increase to about 95%. The following guidelines pertain to adults who are not measurably at elevated risk for one or more cancers due to known or suspected hereditary for familial cancer syndromes, prior history of cancer, or other risk factors that so significantly elevate risk that recommendations for average risk adults are inappropriate.

Breast cancer. Favorable results from randomized trials conducted in the U.S. and Europe have established the value of routine screening with mammography, and over the past three decades repeated analysis and updates of individual trial data, as well as meta-analyses, have demonstrated the efficacy of mammography to reduce breast cancer deaths in women ages 40–69 (126,127). Evaluation of modern mammography service screening programs have shown mortality reductions of approximately 50% in women who participate in regular screening (128).

Average-risk women should begin regular mammography at age of 40, and should have at least an annual mammogram thereafter (127). The American Cancer Society recommends that women ages 20–39 have a clinical breast examination (CBE) every 3 years and annual exams beginning at age 40. As long as a woman is in good health and would be a candidate for treatment, she should continue to be screened with mammography. The decision to stop screening should be individualized considering the potential benefits and risks of screening in the context of overall health status and longevity.

Cervical cancer. Guidelines for cervical cancer screening reflect the current understanding of the underlying epidemiology of cervical intraepithelial neoplasia (CIN) and offer alternative strategies based on new screening and diagnostic technologies that have emerged since the late 1980s (129).

The ACS recommends that cervical cancer screening should begin approximately 3 years after the onset of vaginal intercourse, but no later than 21 years of age (129). Cervical screening should be performed annually until age 30 with conventional cervical cytology smears or every 2 years until age 30 using liquid-based cytology. After age 30, screening may continue every 2–3 years for those women who have had three consecutive, technically satisfactory, normal/negative cytology results. Human papilloma virus (HPV) DNA testing with cytology also is reasonable for screening women 30 years of age and older as an alternative to cytology alone, with HPV DNA testing and conventional or liquid-based cytology done every 3 years. HPV testing any more frequently than every 3 years is discouraged. Women 70 and older with an intact cervix may choose to cease cervical cancer screening if they have had both three or more documented, consecutive, technically satisfactory, normal/negative cervical cytology tests and also have had no abnormal/positive cytology tests within the 10-year period before age 70.

Colorectal cancer. There is strong direct and inferential evidence that screening for colorectal cancer and adenomatous polyps reduces both mortality and incidence from this disease (130,131).

The ACS recommends that adults at average risk should begin colorectal cancer screening at age 50, utilizing one of the following five options for screening: *1*) annual fecal occult blood test (FOBT) or fecal immunochemical test (FIT), *2*) flexible sigmoidoscopy every 5 years, *3*) annual FOBT or FIT plus flexible sigmoidoscopy every 5 years, *4*) double-contrast barium enema (DCBE) every 5 years, or *5*) colonoscopy every 10 years (132). More intensive surveillance is recommended for individuals at increased or high risk due to personal history or inherited predisposition to colorectal cancer.

Prostate cancer. The ACS recommends that the prostate-specific antigen (PSA) test and digital rectal examination (DRE) should be offered annually in the context of shared decision making beginning at age 50 to men who have a life expectancy of at least 10 years (132). This recommendation is similar to recommendations presently issued by the American College of Physicians and the U.S. Preventive Services Task Force (5). Men at higher risk, including men of African descent (specifically, sub-Saharan African descent) and men with a first-degree relative diagnosed before at a younger age (i.e., <65) should begin testing at age 45.

Diabetes

Pre-diabetes. Combined with an aging population and continuing rise in the prevalence of obesity, projected trends indicate a rising incidence and prevalence of diabetes. Rising incidence has led to the initiation of studies in the last decade to determine the feasibility and benefit of various strategies to prevent or delay the onset of type 2 diabetes in individuals at very high risk (i.e., those with "pre-diabetes"), thus also measuring whether there was value in identifying individuals at elevated risk for diabetes. Pre-diabetes is diagnosed in an individual who has a fasting plasma glucose (FPG) between 100 and 125 mg/dl (i.e., IFG) or a 2-h value in the oral glucose tolerance test (OGTT) between 140 and 199 mg/dl (i.e., IGT).

There are now six large studies, including four randomized control trials, that tested whether the progression from pre-diabetes to diabetes could be delayed or prevented by intensive lifestyle modification (nutritional and exercise interventions) or by the use of commercially available glucose-lowering drugs such as metformin or acarbose (80,81,133–136). All of these interventions were effective to variable degrees. Of note, in the lifestyle modification studies, these results were obtained by a modest reduction in body weight and moderate exercise (e.g., walking).

Most of the diabetes prevention trials required that subjects have IGT as the main enrollment criterion. In the Diabetes Prevention Program (DPP), about 80% of the participants also had IFG. Thus, the FPG test or 2-h OGTT can be used to screen for pre-diabetes. None of the prevention studies explicitly addressed the age at which screening should begin, the optimal frequency of screening, or other indications for screening. In the Finnish, DPP, and STOP-IDDM trials, screening data suggested that individuals >45 years of age and who are overweight (i.e., BMI $\geq$25 kg/m^2) were most likely to have IGT (or IFG) (82,133,134). The prevalence of IFG or undiagnosed diabetes increases greatly between age 40 and 49 years and reaches a peak in people aged 60–74 years.

In summary, the current evidence suggests that opportunistic screening to detect pre-diabetes (IFG or IGT) should be considered in individuals $\geq$45 years of age, particularly in those with a BMI $\geq$25 kg/m^2. Screening should also be considered for people who are <45 years of age and who are overweight if they have another risk factor for diabetes (e.g., family history, hypertension, dyslipidemia). Asian Americans should be considered for screening at lower levels of BMI (e.g., 23 kg/m^2). There are no data that support screening of children for IFG or IGT, although there are recommendations for screening children for diabetes (137).

Screening should be performed using either the FPG test or a 2-h OGTT, although the former is the preferred test (138). If possible, the FPG test should be given in the morning because afternoon values tend to be lower (139). Given the age-related incidence of diabetes and the rate of progression to diabetes in normoglycemic middle-aged subjects, repeat testing in 3-year intervals seems reasonable.

The case for screening is strengthened by the fact that screening will not only detect cases of IFG or IGT, but also cases of undiagnosed diabetes. Thus, policies to identify individuals for whom it is appropriate to initiate a diabetes prevention strategy will also identify individuals who should receive treatment for diabetes. Furthermore, because individuals with IFG, IGT, or undiagnosed diabetes are at high risk for cardiovascular disease, their identification should herald increased surveillance and treatment for hypertension, dyslipedmia, and tobacco use.

THE OFFICE VISIT — Although the underlying science supporting recommendations for behaviors and interventions in chronic disease prevention and control has many unanswered questions, there is considerable evidence to support the importance of avoiding tobacco use, promotion of physical activity, maintenance of BMI <25 kg/m^2, eating a nutritionally balanced diet, screening for risk factors for diabetes and cardiovascular disease, and regular cancer screening. While the importance of prevention and early detection is generally understood, inadequacies in the structure and organization of health care delivery, along with competing societal influences, detract from the adequate delivery of, and reimbursement for, preventive services. As a result, the delivery of preventive care emphasizes the use of opportunities for prevention during acute and chronic illness encounters, i.e., opportunistic preventive care. This model of opportunistic prevention has emerged as a replacement for the annual physical exam, which several evidence-based reviews determined had little empirical evidence of value (140–144). While the opportunistic model acknowledges the important role of the primary care provider as the most influential factor in preventive care, the need to treat illness(es) in an encounter and simultaneously identify and prioritize opportunities for prevention counseling and early detection results in disappointing and erratic opportunities for adherence with recommended guidelines. The weak accomplishments of the encounter-based approach to prevention have been documented in numerous studies (8,145).

While the logic for the annual checkup may have been successfully challenged, the unintended consequence has been that there presently are no recommendations for intervals for periodic preventive health encounters among asymptomatic adults. If the traditional an-

nual checkup cannot be supported, then it is important to identify which preventive health tests and counseling (based on age/gender/risk) for otherwise healthy individuals, would contribute to greater progress toward preventive health goals. For example, as noted above, since essential hypertension is manifest at varying ages and is usually asymptomatic, an otherwise healthy patient needs regular and ongoing screening of blood pressure to determine when and if they become hypertensive, especially if opportunistic visits are infrequent. If prehypertension is identified, lifestyle modification should be instituted and follow-up is needed to judge effectiveness. If a blood pressure of 140/90 mmHg or greater is found, frequent office visits will be needed early in treatment for adjustment of lifestyle modifications and or medications until an optimal blood pressure is reached.

The time has come to identify age- and gender-appropriate models for periodic health maintenance visits, and the delineation of a visit schedule based on age, gender, and other relevant considerations (8). It also is important to recognize that clinicians must be fairly reimbursed for encounter-based preventive care, for visits devoted exclusively to prevention and early detection, and for the costs of office systems that improve efficiency and adherence with preventive care. The ambitious health promotion/disease prevention goals set by our organizations simply cannot be met unless we acknowledge the critically important and influential role of an individual's primary care provider and provide the incentive, guidance, and opportunity for regular periodic preventive health examinations.

CONCLUSION — The collaboration between the ADA, ACS, and AHA offers several unique new opportunities to advance a collective cause for prevention and early detection of cancer, heart disease, and diabetes. First, and foremost, this collaboration holds the potential to achieve greater progress in health promotion and disease prevention. Second, against the background of what is often decried as a bewildering, inconsistent, and competing number of messages about health, the joint promotion of a set of core recommendations that could reduce individual and collective risk could be a unifying force for action and advocacy for individuals, families, communities, health care professionals, and other organizations. In particular, the common themes outlined above provide a new opportunity for clinicians to focus on important risk factors that, if avoided or modified, could have beneficial effects for reducing incidence and premature mortality for the leading chronic conditions. Third, we see an opportunity to stimulate new initiatives that could improve health care delivery, such as a greater emphasis on the importance of taking detailed family histories in order to identify familial patterns of disease or to stimulate new directions in health promotion. For example, it is time that the U.S. population was directly informed that being overweight is hazardous to your health. Fourth, this collaboration offers new opportunities for collective advocacy by our organizations at the local level, with the potential for being more influential in local policies such as smoke-free ordinances, enforcing restriction in tobacco sales to minors, promoting good nutrition and physical activity in schools and throughout their communities, and promoting safe venues for physical activity, etc. Finally, national and statewide goals for health are rarely proscriptive, and thus progress toward those goals rarely results in a deliberate, mission-oriented, collective effort. Indeed, for some health indicators, the goals serve only as a reminder of how little progress we're making or how much ground we're losing. With this collaboration we seek to set an ambitious agenda, one that serves to consistently remind us that by working together we can achieve greater progress in health promotion and disease prevention than by working alone.

APPENDIX

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