Strategic research related to the prevention of cardiovascular disease (CVD) and improvement in quality of life encompasses a wide range of scientific disciplines. Experts from the fields of epidemiology, social sciences, health services and outcomes research, and preventive cardiology reached consensus with regard to five priority substantive areas of research to achieve the Healthy People 2010 objectives and to support the long-term goals and mission of the American Heart Association (AHA). The 2010 goals and objectives for heart disease and stroke are to guide the nation in achieving both increased quality and years of life and the elimination of health disparities among different segments of the population.

Broadly, the Healthy People 2010 goals are prevention of the risk factors, detection and treatment of the risk factors, early identification and treatment of heart attacks and strokes, and prevention of recurrent cardiovascular events. Specific objectives include (but are not limited to) reduction in coronary heart disease mortality by 20%, reduction in stroke mortality by 20%, reduction in hospitalization rates for congestive heart failure by 50%, reduction in prevalence of high blood pressure to 16%, and reduction in prevalence of high total blood cholesterol concentration to 17%. Attainment of these goals and objectives will require increased investment of resources at the population level, through such strategies as are outlined below.

Within each content area, the committee systematically identified specific research priorities using complementary scientific approaches:

Prevention Research Priority Content Areas

I. Methods to Improve Utilization and Quality of Preventive Services and Health Care
II. Disparities in Cardiovascular Risk in Subpopulations
III. Lifestyle and Metabolic Risk Factors
IV. Psychosocial Risk Factors
V. Population Genetics/Pharmacogenetics Related to Prevention

Subcategories of Priority Prevention Research

Within each of the following categories, highest priority should be given to aspects closest to delivery of science to the population.

- Effectiveness/outcomes research to determine the impact of interventions in real-world settings
- Efficacy research to evaluate interventions in controlled trials
- Early detection/subclinical measures
- Etiologic research/surveillance

I. Methods to Improve Utilization and Quality of Preventive Services and Health Care

Introduction

Well-established methods to reduce morbidity and mortality associated with CVD exist, including lifestyle approaches, lipid management, blood pressure control, smoking cessation, cardiac rehabilitation, and pharmacotherapy for the secondary prevention of CVD, including β-blockers, angiotensin-converting enzyme inhibitors, aspirin, and other antiplatelet therapy. Increasing evidence supports the ability to prevent high blood pressure and diabetes through nutritional/behavioral interventions. Despite the large evidence base in prevention, there is widespread documentation of underutilization in both primary and secondary prevention settings. For example, fewer than 10% of eligible patients in a national survey were referred to formal comprehensive secondary prevention programs after an acute coronary event or revascularization procedure, an intervention that has been shown to increase survival by 25%.

The reasons for lack of uniform application of AHA guidelines across diverse healthcare settings are poorly de-
fined. Moreover, there have been limited, controlled studies that have examined the role of the healthcare system in facilitating achievement of prevention goals. Because change at the level of the individual physician is slow, “systems” of prevention need to be developed and tested that are cost-effective and increase adherence to prevention guidelines in diverse clinical and community settings. Population-wide strategies, including policy and environmental change, are also in need of further development, evaluation, and dissemination so that research can be translated into effective practices.

Subcategories of Research/Funding Mechanisms

Effectiveness Research

(a) Studies that increase the science base with regard to communication between practitioners and patients
(b) Research about how risk information is understood and acted on by the public
(c) Cost-effectiveness analysis related to prevention
(d) Studies of the impact of policy and environmental change on behaviors related to reducing incidence and prevalence of CVD risk factors

Suggested Funding Mechanisms: Target AHA-Pharmaceutical Roundtable grants; investigator-initiated grants; and partnerships with media, industry, and ongoing AHA public educational programs.

Efficacy Research

(a) Meta-analyses of large-scale efficacy studies in prevention that permit an evaluation of important subgroups, such as the elderly, women, and minorities, that do not typically have the power in a single study to determine subgroup efficacy
(b) Feasibility/pilot studies of interventions to prevent high blood pressure in children, adolescents, and whole communities

Suggested Funding Mechanisms: New investigator awards and investigator-initiated grants.

Early Detection/Subclinical Measures

(a) Studies that examine the impact of complementary and alternative medical approaches on subclinical measures of atherosclerosis
(b) Research on the impact of nonpharmacotherapy and education on intermediate cardiovascular end points

Suggested Funding Mechanisms: Traditional investigator-initiated projects or ancillary studies of large-scale National Institutes of Health (NIH) projects that include subclinical end points.

Etiologic Research/Surveillance Studies

(a) Studies that systematically assess adherence to AHA prevention goals in diverse primary care and hospital settings
(b) Research to understand barriers to achieving prevention goals at the level of the individual, the physician, the health system and society
(c) Methodological studies to validate hospital discharge data related to congestive heart failure and acute coronary syndromes
(d) Pilot surveillance studies of CVD trends in priority populations (those segments of a population deemed to have disproportionate burdens of risk or disease) and diverse communities in need of intervention

Suggested Funding Mechanisms: Research support through the AHA-Pharmaceutical Roundtable or investigator-initiated grants. Partnerships with the Centers for Disease Control and Prevention (CDC) and Agency for Healthcare Research and Quality.

Importance

AHA research dollars have contributed substantially to discovery in the field of prevention science, yet much of this new knowledge has not been applied. We are often better at discovering information than using it to reduce death and disability caused by CVD. This is attributable in large part to the deficiency of funding for research on the dissemination and application of this knowledge, an area that the AHA can impact importantly through its new research direction.

A unique and timely research opportunity is to invest in the developing field of applied preventive cardiology. Methods to determine effective mechanisms to communicate risk and to develop infrastructure in primary and secondary prevention settings to enhance compliance with guidelines that already have an established science base should be a top priority of the AHA. Corresponding guidelines for community preventive strategies should be devised, evaluated, and disseminated. The AHA can play a key role in this process, in collaboration with CDC and other partners. Although it is important to continue to invest in new discoveries, it is critical that the public be given an optimal chance to benefit from previous discoveries.

II. Disparities in Cardiovascular Risk in Subpopulations

Introduction

Disparities associated with race and ethnicity are among the most prominent ones in the burden of CVD and stroke in the nation. Disparities in CVD account for >25% of the relative reduction in life expectancy between blacks and whites in the United States. Disparities in prevalence of high blood pressure (~35% in blacks versus 25% in whites—versus a target of 16% for all by 2010) underscore the deep-rooted challenges to attaining the goals in mortality from coronary heart disease and stroke by 2010. Furthermore, behavioral determinants, risk factors, and conditions such as physical inactivity, obesity, and diabetes are also more prevalent in both blacks and Mexican Americans than among non-Hispanic whites. New approaches to risk factor prevention and risk factor detection and treatment must be rapidly devised, evaluated, and disseminated for widespread application if we are to attain the goals to which we are committed.

At a recent National Conference on CVD Prevention, alarming disparities in trends in CVD occurrence and risk factors were noted among several subpopulations. Despite an
overall decrease in the rate of CVD over the past several decades, there appears to be a slowing of the decline in rates of CVD, which is more significant in blacks than whites and is greater for women than men. The gap has also widened between low and high socioeconomic status groups. Stroke mortality rates are higher in blacks. Adverse risk factor trends were noted to parallel morbidity/mortality trends for blacks and whites. Minorities and women are less likely to be at target AHA prevention goals and less likely to receive cardiovascular interventions.

Reasons for disparities in CVD among subpopulations remain unclear but may be related to lack of awareness of CVD risk/symptoms, access to medical care, less aggressive risk factor management, referral bias for cardiovascular interventions/therapy, and differential response to standard therapy, as well as many other possibilities. A clearer understanding about the reasons for disparities in cardiovascular care and rates of CVD is fundamental to developing strategies to reduce the observed gaps. Because many cardiovascular research studies have not included diverse populations, the efficacy of many “standard interventions” in subpopulations is not known. Moreover, the effectiveness of preventive interventions outside of traditional clinical trials is also poorly defined because of lack of information about side effects and barriers to compliance in subpopulations.

Subcategories of Research/Funding Mechanisms

**Effectiveness Research**

(a) Studies to determine methods to ensure uniform application of proven therapies to reduce CVD among subpopulations through health system approaches to prevention

(b) Studies to determine best methods to increase awareness of CVD signs and symptoms (with a decrease in time to call 9-1-1) among blacks

*Suggested Funding Mechanisms: AHA-Pharmaceutical Roundtable outcomes request for proposals (RFP) and partnerships with Robert Wood Johnson Foundation and the Agency for Health Policy Research. AHA affiliate grants are generally funded through the NIH; however, funds to do race/ethnicity- and sex-specific analyses are reasonable for AHA to fund in the form of career development grants and grants-in-aid.*

**Efficacy Research**

(a) Studies to determine if preventive interventions (eg, diet, angiotensin-converting enzyme inhibitors) have a different impact on outcomes of interest (eg, blood pressure control, cardiovascular events) in subpopulations

*Suggested Funding Mechanisms: Partner with industry to conduct sex- and ethnicity-specific analysis of pharmacotherapies related to prevention or fund through investigator-initiated grants.*

**Early Detection/Subclinical Measures**

(a) Studies to evaluate if utilization and information obtained from technologies to detect CVD at its earliest stages is different, or if results are associated with disparate risk factor management in subpopulations

(b) Studies to determine differences in age at appearance of major CVD risk factors by race/ethnicity

*Suggested Funding Mechanisms: Support for analysis of existing registries of subclinical measures or through AHA-Pharmaceutical Roundtable outcomes RFP.*

**Etiologic Research/Surveillance**

(a) Studies to evaluate etiologic factors related to disparities in CVD occurrence and risk factor trends among race/ethnic groups

(b) Ongoing and expanded, community-based surveillance of trends in behaviors, risk factors, and CVD mortality and morbidity by sex and race/ethnic group

*Suggested Funding Mechanisms: Possible partnerships with the CDC for large-scale studies or support of pilot studies related to surveillance of CVD among diverse populations. Support for secondary analysis of ethnically diverse, large-scale, long-term cohort studies through investigator-initiated grants. Data collection for prospective studies are generally funded through the NIH; however, funds to do race/ethnicity- and sex-specific analyses are reasonable for AHA to fund in the form of career development grants and grants-in-aid.*

**Importance**

The substantial disparities in CVD risk and burden by race/ethnicity in the United States have been noted above. That these differences among groups have persisted for decades and in recent years have intensified clearly calls for new approaches to complement the best of those already effectively in place. The AHA can have a significant impact in the area by supplementing the scarce resources presently being invested. Minorities, women, and the elderly are growth areas of our population and contribute substantially to the burden of CVD in the United States. Because rates of CVD and heart failure have been rising (or slowing to a lesser degree) in these important subpopulations, studies that address disparities in cardiovascular care that may be contributing to adverse trends in risk factors and rates of disease are urgently needed. The gap in knowledge related to the efficacy and effectiveness of interventions that have been shown to reduce CVD in traditional populations cannot be overstated.

**III. Lifestyle and Metabolic Risk Factors**

**Introduction**

Research strongly supports the fact that several risk factors contribute to the development of CVD and its sequelae (eg, heart failure). Furthermore, aggressive risk factor management improves patient survival, reduces recurrent events and the need for interventional procedures, and improves quality of life.

Although some risk factors are not modifiable (eg, family history, ethnicity, and sex), most are amenable to modification, principally through lifestyle changes and/or compliance with pharmacological therapy.

Risk factor identification has been an ongoing focus of cardiovascular research. Although several risk factors have been shown to have causal links (“major risk factors”):
cigarette smoking, hypertension, hypercholesterolemia [LDL], low HDL, and high plasma glucose], many others have been identified, but not causally linked. These so-called conditional risk factors include elevated triglycerides, lipoprotein (a), small LDL particles, homocysteine, coagulation factors, and C-reactive protein. Additionally, there are several “predisposing” risk factors; although their association with CVD is complex, they probably contribute in some significant way to the major causal factors. These include obesity, diabetes/insulin resistance/metabolic syndrome, physical inactivity, and behavioral/socioeconomic factors. The combination of obesity and diabetes has recently received significant attention when epidemiological studies showed concurrent increases in the incidence of obesity and diabetes to epidemic levels.

Although both pharmacological and nonpharmacological strategies appear to be effective, research suggests that patient compliance with these therapies (short and long term) is lacking. Reasons for noncompliance remain unclear.

Subcategories of Research/Funding Mechanisms

Effectiveness Research

(a) Investigate ethnic and cultural influences that affect individuals’ lifestyle modification and compliance with recommended therapies
(b) Identify predictors of clinician compliance with recommendations to incorporate tested strategies to enhance lifestyle modification (eg, smoking cessation)
(c) Evaluate the impact of policy and environmental changes in risk factor management in clinical settings, workplaces, and whole communities

Suggested Funding Mechanisms: Focus on social sciences-type research; AHA affiliate grants, AHA-Pharmaceutical Roundtable outcomes RFP, Agency for Health Policy Research, Robert Wood Johnson Foundation.

Efficacy Research

(a) Evaluate the importance of modification of conditional risk factors in well-designed trials.
(b) Determine how the predisposing risk factors interact with major risk factors. Is it due to intensification of major causal risk factors? Is it due to the effect on conditional risk factors? Is it due to something as yet unidentified?
(c) Design and test interventions to enhance long-term compliance.
(d) Design and test interventions to prevent development of major CVD risk factors among those predicted to progress beyond desirable levels, eg, blood pressure or blood cholesterol concentration.

Suggested Funding Mechanisms: Experimental pilot studies; partner with NIH/National Heart, Lung and Blood Institute.

Early Detection/Subclinical Measures

(a) Evaluation of noninvasive technologies in children at risk for CVD to detect atherosclerosis at its earliest stages, and research to determine how this information is used to alter clinical management and improve lifestyle
(b) Studies to identify groups especially likely to develop major CVD risk factors, as predicted, for example, by demographic characteristics, family history, individual levels of body mass index, blood pressure, blood lipids, glucose or insulin, or genetic markers

Suggested Funding Mechanisms: Investigator-initiated grants and/or training grants.

Etiologic Research/Surveillance

(a) Surveillance studies to document initial and long-term compliance levels of pharmacological and nonpharmacological methods to reduce metabolic risk factors and CVD-prone lifestyles. What are the pathogenic factors that contribute to compliance?
(b) Investigate predictors of obesity in young children and intervention strategies to attenuate potential risk factors for childhood obesity.

Suggested Funding Mechanisms: Support secondary analyses of existing databases to identify potential predictors. Support prospective longitudinal studies using predictors identified in secondary analyses. Partner with groups such as American Academy of Pediatrics or American Diabetes Association to identify and pilot test intervention strategies (primarily nonpharmacological, lifestyle). Other potential partners include such groups as the CDC; the National Center for Health Statistics; National Institute of Nursing Research; and the National Heart, Lung and Blood Institute.

Importance

Improvements in lifestyle have accounted for a major proportion of the decline in CVD over the past 3 decades. However, recent ominous trends in risk factors, especially an alarming rise in obesity in the young and a dramatic increase in the prevalence of diabetes, may lead to a further slowing of this decline that has been observed in recent years. Research to identify predictors of adverse patterns of behavior, and studies to determine the most effective interventions to improve lifestyle and prevent or reduce metabolic risk factors will have both an immediate and a long-term impact on rates of CVD.

IV. Psychosocial Risk Factors

Introduction

Epidemiological data show that an individual’s social environment can affect health. Exposure to stressful life events, eg, to bereavement or disasters such as earthquakes or terrorism, can trigger myocardial infarction and sudden death in susceptible individuals. Long-term exposure to occupational stress, such as the strain of a demanding job or lack of job security, increases risk for coronary heart disease, hypertension, and stroke. Having few social connections and social resources are linked to all-cause and CVD mortality, especially in men. A recent report showed that the socioeconomic status of a neighborhood was a predictor of coronary heart disease incidence, even when the participants’ own socioeconomic status was taken into consideration.

Individual psychological traits including hostile attitudes, anger proneness, anxiety, and depression have been related to CVD morbidity and mortality. Less clear is the extent to which psychiatric illnesses related to these traits, eg, major
depression and anxiety disorders, contribute to the development of atherosclerosis. Large cardiovascular responses to acute psychological stress may be characteristic of those who tend to be hostile and anxious and has been proposed as a possible risk factor for CVD. Moreover, few studies have evaluated the impact of psychosocial interventions on reducing morbidity and mortality due to CVD.

Previous research in this area has been limited by including only select populations (e.g., middle-aged, white men). Studies have often not been designed explicitly to test psychosocial hypotheses or have not examined separately measures of the social environment and traits and their interaction. Psychosocial measures have often not been standardized or validated in diverse populations. Women are now in the labor force in ever-increasing numbers and, as such, are exposed to occupational stressors that previously preferentially affected men. Most psychosocial measures have been standardized on male samples, have not undergone rigorous psychometric testing, including ascertaining the relationships among the measures, and have not taken into account some of the recent advances in stress research. Finally, available studies have had to rely on relatively crude, albeit important, clinical outcomes to evaluate psychosocial hypotheses. Clinical outcomes are affected by subgroup differences in symptom presentation, physician and patient biases, long incubation period, and comorbidity.

**Subcategories of Research/Funding Mechanisms**

**Effectiveness Research**

(a) Studies to determine cost-effective mechanisms to screen and intervene for psychosocial risk factors in practice

*Suggested Funding Mechanisms:* AHA-Pharmaceutical Roundtable research related to psychosocial risk and outcomes.

**Efficacy Research**

(a) Studies to determine if preventive interventions (e.g., diet, medications) have a different impact on outcomes of interest according to psychosocial traits and life circumstances

(b) Studies to evaluate the impact of widespread use of antidepressants on rates of CVD

*Suggested Funding Mechanisms:* Secondary analysis of existing data sets. Partner with CDC and National Center for Health Statistics in conducting ecological analyses of data collected elsewhere.

**Early Detection/Subclinical Measures**

(a) Studies to evaluate psychosocial hypotheses related to subclinical disease measures

(b) Studies aimed at understanding how psychosocial traits place young people at risk for the development of CVD or major CVD risk factors

*Suggested Funding Mechanisms:* Support for ancillary psychosocial studies in already existing large-scale human studies.

**Etiologic Research/Surveillance**

(a) Studies to evaluate psychosocial hypotheses related to development of CVD using state-of-the-art measurement of psychosocial variables

(b) Studies to identify psychobiological mechanisms that may link psychosocial variables with disease outcomes

*Suggested Funding Mechanisms:* Support to develop a psychometric battery for use in ongoing NIH- or AHA-funded projects. Partner with CDC to develop survey methodology for use in various activities. Preferential funding of career awards in this area.

**Importance**

Although psychosocial risk factors do predict CVD outcomes, how early in the disease process, in which groups, and the precise underlying mechanisms are not clear. Furthermore, the method of assessment has not been validated in diverse populations. Psychosocial risk factors are highly prevalent and poorly understood, and the methodology of assessment is at a very rudimentary stage. Improved understanding of the measurement of these factors, how they interact with other risk factors, and how they affect compliance with proven strategies to lower risk is a timely research opportunity that has the potential to have a significant and far-reaching impact on CVD burden as our social environments become even more complex.

**V. Population Genetics/Pharmacogenetics Related to Prevention**

**Introduction**

The draft sequence of the human genome is now available, and an enormous effort is underway to identify variations in genetic sequence across individuals of varying ethnic origins. There are also available resources, tools, and technologies to allow high-throughput genotyping and resequencing of candidate genes. Translation of this knowledge into population research is urgently needed. It is important to determine the relevance of sequence variation and mutations in disease onset and disease progression across population groups with various levels of genetic heterogeneity.

For CVD prevention, more information is needed to characterize the variation in disease, modifier, and susceptibility genes across different environments. This information will allow us to evaluate the influence of environmental factors responsible for differing levels of risk factors and disease in different populations. An important area that has yet to be adequately explored is genetic effects on age-related changes in subclinical disease measures and risk factors, and investigation of whether specific genes may have a greater or lesser impact at different ages (genotype by age interaction) or in accordance with other characteristics (e.g., sex). Importantly, the effectiveness of interventions may differ across different genetic subgroups, thus allowing the tailoring of interventions on an individual level.

**Subcategories of Research/Funding Mechanisms**

**Effectiveness Research**

Not yet applicable to genetics, although screening tools may soon be available to predict which patient will respond to a
particular drug and which patient is susceptible to development of risk factors.

**Efficacy Research**

(a) Studies to determine if preventive interventions (eg, diet, lipid-lowering drugs) have different effects on outcomes of interest (eg, lipid lowering, cardiovascular events).

*Suggested Funding Mechanisms:* Partner with industry to conduct pharmacogenomic studies or fund through investigator-initiated grants.

**Early Detection/Subclinical Measures**

(a) Subclinical measures may provide a more sensitive tool to assess the relevance of genetic variation in CVD onset and progression. Incorporate DNA collection, development of cell lines, and genetic testing for ongoing, large studies.

*Suggested Funding Mechanisms:* Funds could be provided through investigator-initiated grants to collect or process DNA and to conduct analyses.

**Etiologic Research/Surveillance Studies**

(a) Studies to allow for characterization of genetic variation and environment, and their interaction, in existing cohort studies.

*Suggested Funding Mechanisms:* Large studies are needed to effectively evaluate gene-environment interaction, and the NIH typically funds these. However, funds provided by the AHA could support the genotyping efforts and scientist development grants in this area.

**Importance**

Although genetic factors have been shown to account only for a small variation in the burden of CVD at the population level, it is likely that genes significantly interact with the environment and the response to preventive interventions. Information about the utility of genetic information to tailor individual treatment and the potential impact on population rates of disease is greatly needed.

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Task Force on Strategic Research Direction: Population/Outcomes/Epidemiology/Social Science Subgroup Key Science Topics Report
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