PRACTICE GUIDELINE

Effectiveness-Based Guidelines for the Prevention of Cardiovascular Disease in Women—2011 Update

A Guideline From the American Heart Association

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Substantial progress has been made in the awareness, treatment, and prevention of cardiovascular disease (CVD) in women since the first women-specific clinical recommendations for the prevention of CVD were published by the American Heart Association (AHA) in 1999 (1). The myth that heart disease is a "man's disease" has been debunked; the rate of public awareness of CVD as the leading cause of death among U.S. women has increased from 30% in 1997 to 54% in 2009 (2). The age-adjusted death rate resulting from coronary heart disease (CHD) in females, which accounts for about half of all CVD deaths in women, was 95.7 per 100,000 females in 2007, a third of what it was in 1980 (3,4). Approximately 50% of this decline in CHD deaths has been attributed to reducing major risk factors and the other half to treatment of CHD including secondary preventive therapies (4). Major randomized controlled clinical trials such as the Women's Health Initiative have changed the practice of CVD prevention in women over the past decade (5). The investment in combating this major public health issue for women has been significant, as have the scientific and medical achievements.

Despite the gains that have been made, considerable challenges remain. In 2007, CVD still caused ≈1 death per minute among women in the United States (6). These represent 421,918 deaths, more women's lives than were claimed by cancer, chronic lower respiratory disease, Alzheimer disease, and accidents combined (6). Reversing a trend of the past 4 decades, CHD death rates in U.S. women 35 to 54 years of age now actually appear to be increasing, likely because of the effects of the obesity epidemic (4). CVD rates in the United States are significantly higher for black females compared with their white counterparts (286.1/100,000 versus 205.7/100,000). This disparity parallels the substantially lower rate of awareness of heart disease and stroke that has been documented among black versus white women (2,6–8). Of concern is that in a recent AHA national survey, only 53% of women said the first thing they would do if they thought they were having a heart attack was to call 9-1-1. This distressing lack of appreciation by many women for the need for emergency care for acute cardiovascular events is a barrier to optimal survival among women and underscores the need for educational campaigns targeted to women (2).

CVD rates in the United States are significantly higher for black females compared with their white counterparts (286.1/100,000 versus 205.7/100,000), which parallels the substantially lower rate of awareness of heart disease and stroke that has been documented among black versus white women (2,6–8). Each year, 55,000 more women than men have a stroke. Atrial fibrillation is independently associated with a 4- to 5-fold increased risk of ischemic stroke and is responsible for 15% to 20% of all ischemic strokes. It has been shown that undertreatment with anticoagulants doubles the risk of recurrent stroke; therefore, the expert panel voted to include recommendations for the prevention of stroke among women with atrial fibrillation (6,9,10).

Adverse trends in CVD risk factors among women are an ongoing concern. After 65 years of age, a higher percentage of women than men have hypertension, and the gap will likely increase with the continued aging of the female population (6). The prevalence of hypertension in blacks in the United States is among the highest in the world, and it is increasing. From 1988 to 1994 through 1999 to 2002, the prevalence of hypertension in adults increased from 35.8% to 41.4% among blacks, and it was particularly high among black women at 44.0% (11).

A very ominous trend is the ongoing increase in average body weight, with nearly 2 of every 3 U.S. women >20 years of age now overweight or obese (6). The rise in obesity is a key contributor to the burgeoning epidemic of type 2 diabetes mellitus now seen in >12 million U.S. women. Furthermore, the rate of diabetes mellitus is more than double in Hispanic women compared with non-Hispanic white women (12.7% versus 6.45%, respectively) (6). The increasing prevalence of diabetes mellitus is concerning for many reasons, especially for its association with a greatly increased overall risk of myocardial infarction (MI) and stroke (12).

The challenge of CVD in women is not limited to the United States. Recent data document the global scope of the problem: Heart disease is the leading cause of death in women in every major developed country and most emerging economies (13).

Given the worldwide health and economic implications of CVD in women, there is strong rationale to sustain efforts to control major CVD risk factors and to apply evidence-based therapies in women.

In 2004, the AHA, in collaboration with numerous other organizations, expanded its focus on female-specific clinical recommendations and sponsored the "Evidence-Based Guidelines for Cardiovascular Disease Prevention in Women" and updated them in 2007 (14,15). Initially, the guidelines challenged the conventional wisdom that women should be treated the same as men, primarily related to concerns about the lack of representation of women in clinical trials. As more women have participated in CVD research studies and more gender-specific analyses have been published, data have become available to make more definitive recommendations. Evolving science suggests that the overwhelming majority of recommendations to prevent CVD are similar for women and men, with few exceptions. Notably, aspirin is routinely recommended for the primary pre-

vention of MI in men but not women (16,17). However, there is a growing appreciation that there may be gender differences in the magnitude of the relative and absolute potential benefits and risks of preventive interventions. The panel acknowledged unique opportunities to identify women at risk (e.g., pregnancy) and addressed concerns that women often have more comorbidities and are older than men when they experience CHD.

The current guidelines encompass prevention of the scope of atherosclerotic thrombotic cardiovascular outcomes in women. However, it should be noted that the majority of data used to develop these guidelines is based on trials of CHD prevention. Future guidelines should consider recommendations for specific outcomes of particular importance in women, such as stroke. Each year, 55,000 more women die of stroke than men, and before 75 years of age. Stroke accounts for a higher proportion of CVD events than CHD in females, whereas the ratio is the opposite for males. Women have unique risk factors for stroke such as pregnancy and hormone therapy, have a greater prevalence of hypertension in older ages, a major risk factor for stroke, and may have different benefits and risks associated with interventions to reduce stroke risk compared with men (6). Atrial fibrillation is independently associated with a 4- to 5-fold increased risk of ischemic stroke and is responsible for 15% to 20% of all ischemic strokes. It has been shown that undertreatment with anticoagulants doubles the risk of recurrent stroke; therefore, the expert panel voted to include recommendations for the prevention of stroke among women with atrial fibrillation (6,9,10).

Current systematic and critical review of the literature continues to update the guidelines, which have become the foundation to inform national educational programs for healthcare professionals and women consumers of healthcare. A major evolution from previous guidelines to the 2011 update is that effectiveness (benefits and risks observed in clinical practice) of preventive therapies was strongly considered and recommendations were not limited to evidence that documents efficacy (benefits observed in clinical research); hence, in the transformation from "evidence-based" to "effectiveness-based" guidelines for the prevention of cardiovascular disease in women, the panel voted to update recommendations to those therapies that have been shown to have sufficient evidence of clinical benefit for CVD outcomes. Class III recommendations from prior guidelines that are not recommended for use for the prevention of CVD (Table 1) were retained as no new evidence has become available to alter the recommendations. The list of Class III recommendations is not exhaustive, and therapies that were previously searched were based on those preventive interventions commonly believed to have a potential benefit for the prevention of CVD in women despite a lack of definitive clinical trial evidence of benefit. Uses of medications for indications beyond the prevention of ischemic CVD are not addressed in this document. Some interventions (e.g., screening for depression) were recognized to lack data on direct CVD outcomes benefit but were included in an algorithm for approaches to the evaluation of women because they may indirectly impact CVD risk through

Table 1. Class III Interventions (Not Useful/Effective and May Be Harmful) for the Prevention of CVD in Women

Menopausal therapy
Hormone therapy and selective estrogen-receptor modulators (SERMs) should not be used for the primary or secondary prevention of CVD *(Class III, Level of Evidence A).*

Antioxidant Supplements
Antioxidant vitamin supplements (e.g., vitamin E, C, and beta carotene) should not be used for the primary or secondary prevention of CVD *(Class III, Level of Evidence A).*

Folic Acid*
Folic Acid, with or without B6 and B12 supplementation, should not be used for the primary or secondary prevention of CVD *(Class III, Level of Evidence A).*

Aspirin for MI in women <65 years of age
Routine use of aspirin in healthy women <65 years of age is not recommended to prevent MI *(Class III, Level of Evidence B).*

CVD indicates cardiovascular disease; MI, myocardial infarction.
*Folic acid supplementation should be used in the childbearing years to prevent neural tube defects.

adherence to prevention therapies or other mechanisms (Figure 1). The expert panel also recognized that cost-effectiveness, which may differ by sex, needed to be addressed; thus, a comprehensive review of current literature on the topic has been added. The guidelines continue to prioritize lifestyle approaches to the prevention of CVD, likely the most cost-effective strategy. The panel also acknowledged that difficulty in adhering to lifestyle and medical recommendations limits effectiveness; therefore, new sections were added on guideline implementation.

CVD Risk Assessment

In the 2007 update, a new algorithm for risk classification in women was adopted that stratified women into 3 categories: "at high risk," based on the presence of documented CVD, diabetes mellitus, end-stage or chronic kidney disease, or 10-year predicted risk for CHD >20%; "at risk," given the presence of ≥1 major CVD risk factors, metabolic syndrome, evidence of subclinical vascular disease (e.g., coronary calcification), or poor exercise tolerance on treadmill testing; and "at optimal risk" in the setting of a Framingham risk score <10%, absence of major CVD risk factors, and engagement in a healthy lifestyle. This approach to risk classification in women was based on several observations: 1) The lifetime risk for CVD is high in almost all women and approaches 1 in 2 on average, so prevention is important in all women (18); 2) most clinical trial data used to formulate the recommendations included either women at high risk because of known CVD or apparently healthy women with a spectrum of risk, which allowed the scheme to align the guidelines with the evidence; and 3) the appreciation of the limitations of standard risk stratification schemes such as the Framingham risk score is growing. These limitations include the narrow focus on only short-term (10-year) risk and on only MI and CHD death, the lack of inclusion of family history, overestimation or underestimation of risk in nonwhite populations, and the fact that subclinical CVD can have relatively high

Evaluation of CVD Risk:

- Medical history/family history/pregnancy complication history
- Symptoms of CVD
- Depression screening in women with CVD
- Physical examination including blood pressure, body mass index, waist size
- Laboratory tests including fasting lipoproteins and glucose
- Framingham risk assessment if no CVD or diabetes

Implement Class I Lifestyle Recommendations (for all):
- Smoking cessation
- DASH–like diet
- Regular physical activity
- Weight management

History of Paroxysmal Atrial Fibrillation?

No   Yes

Is Woman at High Risk of CVD (having ≥1 of the following)?
- Clinically established CHD
- Cerebrovascular disease
- Peripheral arterial disease
- Abdominal aortic aneurysm
- Diabetes mellitus
- Chronic kidney disease
- 10-year predicted CVD risk ≥10%

Implement Class I Recommendations:
- Warfarin or
- Aspirin or
- Dabigatran

Yes

No

Implement Class I Recommendations:
- Blood pressure control
- LDL-C–lowering therapy if ≥190 mg/dL

Recent cardiovascular event, procedure, or congestive heart failure symptoms?

Yes   No

Refer to cardiac rehabilitation

Implement Class I Recommendations:
- Blood pressure control
- LDL-C–lowering therapy (goal <100 mg/dL)
- β-Blocker
- Angiotensin-converting enzyme inhibitor/ angiotensin receptor blocker

Consider Class II Recommendations:
- Therapy for high LDL-C, non–HDL-C and triglycerides and/or HDL-C in select women
- Aspirin

Consider Class II Recommendations:
- LDL-C–lowering therapy (goal <70 mg/dL in very high-risk women)
- Non–HDL-C–lowering therapy (goal <130 mg/dL in very high-risk women with recent ACS or multiple poorly controlled cardiovascular risk factors)
- Glycemic control in diabetics
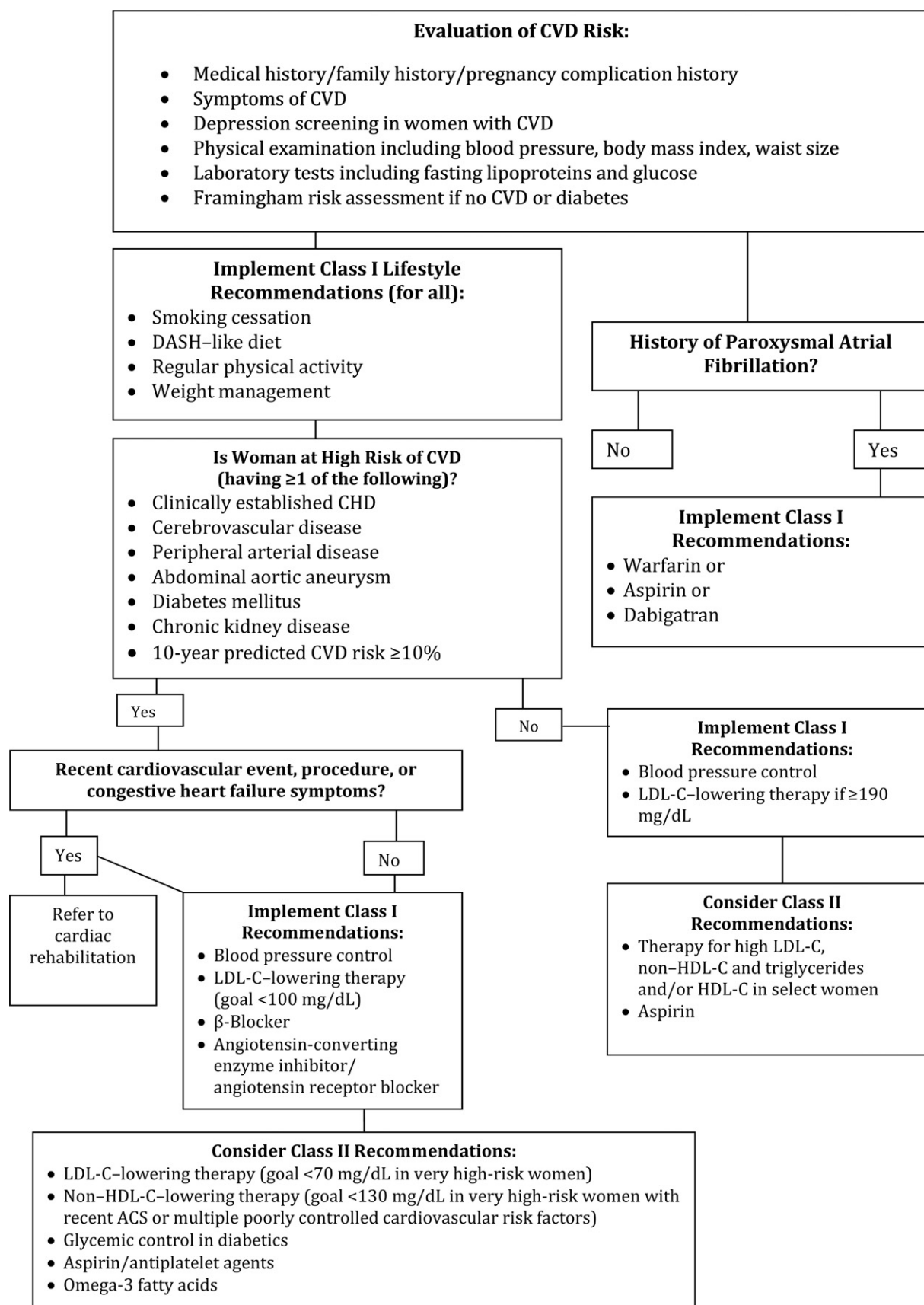- Aspirin/antiplatelet agents
- Omega-3 fatty acids

Figure 1. Flow diagram for CVD preventive care in women. CVD indicates cardiovascular disease; DASH, Dietary Approaches to Stop Hypertension; CHD, coronary heart disease; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; and ACS, acute coronary syndrome.

prevalence among women who are scored as being at low risk (6,19).

The 2007 panel believed that a Framingham 10-year predicted risk for CHD >20% could be used to identify a woman at high risk but that a lower score was not sufficient to ensure that an individual woman was at low risk. Thus, the algorithm included consideration of factors beyond the 10-year predicted risk for CHD used in current National Cholesterol Education Panel guidelines of lipid management (20). The panel emphasized that healthcare professionals should take several factors into consideration beyond just the Framingham risk score, including medical and lifestyle history, family history of CVD, markers of preclinical disease, and other conditions, as they make decisions about the intensity of preventive therapy.

Since the 2007 update, a number of lines of evidence have emerged to support the risk classification algorithm adopted in 2007. Hsia et al. (21) directly evaluated the algorithm in 161,808 women 50 to 79 years of age who were enrolled in the Women's Health Initiative and followed up for a mean of 7.8 years. When the 2007 update categories were applied, 11% of women were found to be at high risk, 72% were at risk, and 4% were at optimal risk (21). Of note, 13% of women could not be classified by the 2007 algorithm because, although they lacked risk factors, they did not adhere to a healthy lifestyle.

Among high-risk, at-risk, optimal risk, and unclassified women, the rates of MI, CHD death, or stroke were 19.0%, 5.5%, 2.2%, and 2.6% per 10 years, respectively (p for trend <0.0001) (20). Although absolute event rates differed among women of different race/ethnic groups, the 2007 risk classification algorithm appropriately ordered event rates in all groups, with a 7- to 20-fold difference in event rates between optimal-risk and high-risk women. The 2007 update algorithm discriminated those who experienced coronary events with accuracy similar to current National Cholesterol Education Panel Adult Treatment Panel III risk categories (<10%, 10% to 20%, and >20%) based on Framingham 10-year predicted risks (20).

Therefore, the current panel elected to continue this general approach to risk classification in women for the 2011 guidelines with some modifications (Table 2). First, the AHA recently defined a new concept of "ideal cardiovascular health" defined by the absence of clinical CVD and the presence of all ideal levels of total cholesterol (<200 mg/dL), blood pressure (<120/80 mm Hg), and fasting blood glucose (<100 mg/dL), as well as adherence to healthy behaviors, including having a lean body mass index (<25 kg/m^2), abstinence from smoking, participation in physical activity at recommended levels, and pursuit of a Dietary Approaches to Stop Hypertension–like eating pattern (22). When achieved or maintained into middle age, the overall pattern of ideal cardiovascular health is associated with greater longevity; dramatic reductions in short-term, intermediate-term, and lifetime risks for CVD events; greater quality of life in older ages; and lower Medicare costs at older ages (22). It should also be noted that several factors, which have been associated with an increased risk of CVD in women, have been identi-

Table 2.   Classification of CVD Risk in Women

Risk Status	Criteria
High risk (≥1 high-risk states)	Clinically manifest CHD
	Clinically manifest cerebrovascular disease
	Clinically manifest peripheral arterial disease
	Abdominal aortic aneurysm
	End-stage or chronic kidney disease
	Diabetes mellitus
	10-y Predicted CVD risk ≥10%
At risk (≥1 major risk factor[s])	Cigarette smoking
	SBP ≥120 mm Hg, DBP ≥80 mm Hg, or treated hypertension
	Total cholesterol ≥200 mg/dL, HDL-C <50 mg/dL, or treated for dyslipidemia
	Obesity, particularly central adiposity
	Poor diet
	Physical inactivity
	Family history of premature CVD occurring in first-degree relatives in men <55 y of age or in women <65 y of age
	Metabolic syndrome
	Evidence of advanced subclinical atherosclerosis (e.g., coronary calcification, carotid plaque, or thickened IMT)
	Poor exercise capacity on treadmill test and/or abnormal heart rate recovery after stopping exercise
	Systemic autoimmune collagen-vascular disease (e.g., lupus or rheumatoid arthritis)
	History of preeclampsia, gestational diabetes, or pregnancy-induced hypertension
Ideal cardiovascular health (all of these)	Total cholesterol <200 mg/dL (untreated)
	BP <120/<80 mm Hg (untreated)
	Fasting blood glucose <100 mg/dL (untreated)
	Body mass index <25 kg/m^2
	Abstinence from smoking
	Physical activity at goal for adults >20 y of age: ≥150 min/wk moderate intensity, ≥75 min/wk vigorous intensity, or combination
	Healthy (DASH-like) diet (see Appendix)

CVD indicates cardiovascular disease; CHD, coronary heart disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C; high-density lipoprotein cholesterol; IMT, intima-media thickness; BP, blood pressure; and DASH, Dietary Approaches to Stop Hypertension.

fied, but their utility for screening and improving clinical outcomes has not been determined.

Other modifications to the risk classification algorithm include acknowledgement of the availability of several 10-year risk equations for the prediction of 10-year global CVD risk such as the updated Framingham CVD risk profile and the Reynolds risk score for women (23,24). The panel considered that either of these scores would be appropriate for use, particularly given their inclusion of CVD events beyond just CHD, but did not endorse routine screening with high-sensitivity C-reactive protein (hsCRP), which would be required for use of the Reynolds risk score, because there are no data to support the association between a reduction in hsCRP and improved clinical outcomes. Numerous other

multivariable risk scores exist and may be clinically useful if based on a population and on end points relevant to the patient in question (25–27). In this context, the current guidelines recommend use of a new cut point for defining high risk as ≥10% 10-year risk for all CVD, not just CHD alone.

Recent analyses of clinical trial data suggest that at approximately this threshold statin therapy is associated with high cost-effectiveness (and possibly cost savings) in the era of generic statins (28). In addition, the recent Justification for Use of Statins in Prevention, an Intervention Trial Evaluating Rosuvastatin (JUPITER) in primary prevention populations demonstrated the efficacy of statin medications in lowering global CVD event risk, including among women, although the absolute benefit was small and the number needed to treat to prevent a major CVD event was greater than in men (29).

Several lines of evidence support the focus of women's guidelines on long-term risk for CVD rather than solely on 10-year risk for CHD. First, observational and clinical trial data indicate that women's risks for stroke and heart failure through middle and older age typically exceed their risk for CHD, in contrast to the pattern observed in men, for whom CHD risk increases earliest (30,31). Thus, the focus in the current National Cholesterol Education Panel Adult Treatment Panel III guidelines on 10-year CHD risk may substantially underestimate clinically relevant overall CVD risk and therefore tends to preclude the warranted, intensive preventive measures for most high-risk women (32).

Indeed, it is difficult for a woman <75 years of age, even with several markedly elevated risk factors, to exceed a 10% (let alone a 20%) 10-year predicted risk for CHD with the Adult Treatment Panel III risk estimator (33,34). Thus, few women qualify for aggressive CVD prevention when 10-year risk is used to determine its need. Fortunately, more recent Framingham equations are now available to predict 10- and 30-year risk for all CVD events (including CHD, stroke, heart failure, and claudication) (34–36).

A focus on long-term CVD risk, not solely on 10-year CHD risk, is also supported by recent data indicating that 56% of American adults (87 million people), including 47.5 million women overall and 64% of women 60 to 79 years of age, have a 10-year predicted risk for CHD of <10% but a predicted lifetime risk for CVD of ≥39% (37).

The role that novel CVD risk biomarkers (e.g., hsCRP or advanced lipid testing) and imaging technologies (e.g., coronary calcium scoring assessment) should play in risk assessment and in delineation of appropriate preventive interventions is not yet well defined. It should be noted that JUPITER did not test a strategy of routine screening with hsCRP to determine benefit of statin therapy because those with lower hsCRP levels were not studied (29). These approaches should not be used for routine screening of all women. Instead, the AHA and other national groups have recommended that the use of these novel modalities should be reserved for refining risk estimates in intermediate-risk patients when there is uncertainty about the need to start drug therapy (38–41). Further research is needed on added benefits, risks, and costs associated with such strategies. Although recent evidence suggests that using imaging modalities such as coronary

calcium scoring and carotid ultrasound to demonstrate the presence of advanced atherosclerosis has the greatest utility for reclassifying risk in those (including women) predicted to be at intermediate risk on the basis of short-term risk equations such as the Framingham risk score, their value in improving clinical outcomes has not been established (42,43). It should also be noted that several novel risk factors, which have been associated with an increased risk of CVD in women, have been identified, but their utility for screening and improving clinical outcomes has not been determined.

Because of its unique cardiovascular and metabolic stress, pregnancy provides a unique opportunity to estimate a woman's lifetime risk. For example, preeclampsia may be an early indicator of CVD risk (44,45). A recent large meta-analysis found that women with a history of preeclampsia have approximately double the risk for subsequent ischemic heart disease, stroke, and venous thromboembolic events over the 5 to 15 years after pregnancy (46). In these patients, the physiological "metabolic syndrome of pregnancy" may provoke pregnancy complications. The latter could be considered a "failed stress test," possibly unmasking early or preexisting endothelial dysfunction and vascular or metabolic disease (47). Therefore, appropriate referral postpartum by the obstetrician to a primary care physician or cardiologist should occur so that in the years after pregnancy, risk factors can be carefully monitored and controlled. Healthcare professionals who meet women for the first time later in their lives should take a careful and detailed history of pregnancy complications with focused questions about a history of gestational diabetes mellitus, preeclampsia, preterm birth, or birth of an infant small for gestational age (48–50).

Future research should evaluate the potential for exposures, events, or interaction with the medical system during periods of potential vulnerability across a woman's lifespan such as menarche, pregnancy, and menopause to identify women at risk and to determine the effectiveness of diagnostic and preventive interventions during these critical times.

Other factors that are more prevalent among women and/or may make special contributions to CVD risk in women need further clarification in the context of defining effective interventions to improve CVD outcomes, as well as functional outcomes and adherence to therapy. These include depression and other psychosocial risk factors, as well as autoimmune diseases. Systemic lupus erythematosus and rheumatoid arthritis may be unrecognized risk factors in women and have been associated with a significantly increased relative risk for CVD (51). Women with such conditions but without clinically evident CVD should be considered at risk and screened for CVD risk factors, whereas women with prior CVD events should be screened for these conditions to allow appropriate secondary CVD prevention efforts and to allow the autoimmune condition to be addressed.

Diversity, Disparities, and Population Representation

The changing demographics of the United States, and indeed the world, necessitate that healthcare professionals consider the diversity of the patients that they encounter. Diversity

may denote a variety of factors to each member of a healthcare team. In addition to the well-recognized classifications of race/geographic origin and ethnic origin, other facets of diversity need to be considered such as age, language, culture, literacy, disability, frailty, socioeconomic status, occupational status, and religious affiliation, among others. A better understanding of these aspects of diversity may help to reduce disparities in healthcare delivery. The Institute of Medicine defines disparity as a difference in treatment provided to members of ethnic or racial groups that is not justified by health condition differences or treatment preferences. The Institute of Medicine report also states that these disparities exist even when controlling for insurance status, socioeconomic status, and comorbidities (52). Disparities in cardiovascular health continue to be a serious public health issue in the United States. Despite the remarkable declines in cardiovascular mortality observed nationally over the past few decades, many population subgroups defined by race, ethnicity, gender, socioeconomic status, educational level, or geography, still show striking disparities in cardiovascular health. The pervasive nature of these disparities and compelling evidence of the adverse impact they have on clinical outcomes and quality of life in black and Hispanic women need to be recognized by clinicians. The root causes of disparities include variations and lack of understanding of health beliefs, cultural values and preferences, and patients' inability to communicate symptoms in a language other than their own, among other factors (53–55). During the past decade, the clinical research focus on innovative methods to eliminate healthcare disparities has demonstrated some promise in multiteam culturally tailored interventions such as those with nurse-led case managers and community health workers. Cultural competence, therefore, has emerged as a process that unites the assessment and recognition of cultural differences, cultural knowledge, and cultural skills (56). Culturally sensitive care includes the adaptation of healthcare delivery to meet the needs of a diverse patient population. Thus, diversity, as defined above, in the context of healthcare, is concerned with delivering equitable care for all individuals (57–59).

Although guidelines may be applied across all groups, it is important to remember the higher prevalence of risk factors in certain racial/ethnic groups such as hypertension among black women or diabetes mellitus in women of Hispanic descent (6). Notably, the highest coronary heart death rates and the highest overall CVD morbidity and mortality occur in black women. Furthermore, the mortality from coronary artery disease for black women is similar to that of white men (6). These disparities in the occurrence of CVD and established risk factors underscore the need for heightened preventive efforts in subpopulations of women.

Ethnic categorization often fails to recognize cultural differences such as within Hispanics. Although the broad term is "Latino" or "Hispanic," the actual definition includes people of Cuban, Mexican, Puerto Rican, or South or Central American origin. These cultures have distinct backgrounds, health behaviors, and beliefs, but they are often grouped together. Hispanics living in the United States may be faced with stresses of immigration, lower socioeconomic status,

and inadequate access to healthcare. Despite these adversities, Hispanics, with a burden of cardiovascular risk factors similar to that of non-Hispanic whites, have a lower mortality. This observation has been called the "Hispanic paradox" as confirmed in recent data released by the National Center for Health Statistics, which finds Hispanic life expectancy to be 80 years compared with 77.5 years for non-Hispanic whites and 72.3 years for non-Hispanic blacks (60,61). Although deaths from heart disease have decreased in all groups, Hispanics have the lowest percentage of cardiovascular deaths (21.7%) compared with non-Hispanics (26.3%) (62). The life expectancy for Hispanic women was the highest for all groups at 83.1 years compared with 80.4 years for non-Hispanic white women, 76.2 years for non-Hispanic black women, 77.9 years for Hispanic men, and 75.6 years for non-Hispanic white men. The lowest life expectancy was for non-Hispanic black men at 69.2 years (63).

In addition to racial and ethnic diversity, the healthcare professional should be familiar with the patient's socioeconomic status, which may make attaining healthy lifestyles and using medications more difficult. In this context, recommendations that are more appropriate to the life circumstances of the patient may have to be adapted. Age should also be considered in the context of diversity because in the life continuum of women, application of the guidelines may need adaptation to stages such as pregnancy or the frailty of the elderly. Thus, the recognition of all aspects of diversity and the delivery of culturally sensitive care must guide clinicians to apply these guidelines broadly to match the diversity of women patients they treat, avoiding disparity of care (64–66).

International Issues

The international applicability of these guidelines is a critical issue because CVD has become a global pandemic among women. Approximately 81% of all CVD deaths in women occur in low- and middle-income countries with limited capacity for guidelines development (67). International applicability can be defined as the desirability and capacity to adopt the recommendations proposed in this guidelines document "as is" or after appropriate adaptation by medical societies, clinicians, and patients in other countries.

The World Health Organization and other international organizations have proposed measures for evaluating the international applicability of a guidelines document (68–72). In the *Global Program on Evidence for Health Policy. Guidelines for WHO Guidelines*, 4 criteria were proposed for assessing the international applicability of guidelines: 1) efficacy and safety, 2) cost-effectiveness, 3) affordability, and 4) population benefits (68). The Appraisal of Guidelines Research and Evaluation project, an international collaboration, also designed an instrument to appraise clinical guidelines (69). The indicators for applicability assessment include potential organizational barriers in applying the guidelines, cost implications of applying the recommendations, and the presence of key review criteria for monitoring and audit purposes (70). Methods and tools are available for international users to determine whether recommendations provided

in guidelines are suitable for local applications or whether some modifications are needed before application of guidelines (70–75).

International applicability is an important feature of the updated women's guidelines because almost all of the recommendations can be used in most countries or regions, either directly or with slight modifications. The descriptions of the recommendations are easy to comprehend and apply in clinical practice. Risk classification is practical and should be feasible for clinicians and patients worldwide. Additionally, generic drugs are available for most of the therapies recommended in this guidelines document. Some modifications, however, may be required, depending on the specific demands of the countries or regions such as the definition of generalized overweight obesity and central obesity.

It is noteworthy that some of the recommendations in the guidelines for CVD prevention in women are based on studies with relatively small sample sizes of women, which is particularly problematic when considering women with different cultural and racial-ethnic backgrounds. Thus, the conclusions of meta-analyses based on these studies may not be generalizable to women worldwide.

Healthcare Professional Implementation

Achievement of both the desired degree and persistence of CVD preventive care has been disappointing in both women and men. Although improving, the level of public awareness and rates of treatment and control of lipids, hypertension, and diabetes mellitus remain suboptimal (76–78). For instance, ≈50% of Americans with hypertension are not treated to goal. Furthermore, ethnic/racial disparities in the management of hypertension, lipids, and diabetes mellitus persist (76).

By establishing scientific levels of evidence and desired treatment strategies, guidelines are fundamental to improving CVD preventive care. However, multiple patient, clinician, and systemic barriers limit adherence to CVD prevention guidelines for women (79,80). A meta-analysis of >100 medical adherence studies shows that women are as likely to be nonadherent to medical therapies as men (81). It is ironic that the level of scientific evidence incorporated in most guidelines is much more robust than the research available for practical implementation and maintenance of adherence to those guidelines. Multiple barriers hinder adoption of guidelines, including lack of access to primary care services and lack of knowledge and skill in guideline implementation on the part of internists, family practitioners, and gynecologists (82,83). For instance, in a study of impediments to CVD prevention, one half of obstetrician-gynecologists and one third of internists surveyed were unaware that tobacco use is the leading cause of MIs in younger women (84).

The physicians who reported time as a barrier were less likely to discuss smoking cessation with their women patients (83). Impediments to implementation of guidelines include time pressures, lack of organizational support, and patient resistance to behavioral change (84,85). Conclusions about the best methods for implementation of CVD prevention have been difficult to reach because of heterogeneity in interventions and outcomes between studies and other methodological

limitations (84,85). The preponderance of evidence suggests that unidimensional interventions such as brief initial patient education and traditional patient reminders are generally ineffective (84,85). The most robust interventions are multi-faceted, are interactive, and incorporate decision systems and feedback (84,85).

An intervention increasingly advocated improving guidelines adherence is "pay for performance." Performance measures are available for primary prevention of CVD, and the literature suggests some improvement in healthcare professional adherence to healthcare quality measures when pay-for-performance policies are implemented (86,87). Unfortunately, however, because of reliance on patient outcomes, such policies may also result in unintended detrimental consequences such as reduced access to care for sicker patients (87). Similar to the literature supporting guidelines adherence in general, much more research is needed on best practices, benefits, and hidden costs of pay-for-performance initiatives, including whether performance measures sometimes increase disparities in care.

Improvement in adherence to CHD guideline has been documented in centers implementing the Get With The Guidelines program of the AHA (88). Of note, disparities in MI guidelines adherence by gender, age, ethnicity, and race appeared to narrow over time in hospitals instituting this program (88,89). The AHA is now initiating a Get With The Guidelines–Outpatient program, and the American College of Cardiology has embraced quality improvement activities in implementation of CVD prevention guidelines.

The evidence base for practical methods for improving guideline adherence by effectively addressing substantive patient, clinician, and system-level barriers is generally lacking; however, there is some cause for optimism. There is increasing patient and clinician knowledge of the importance of CHD in women, and there have been improvements in CVD risk factor awareness, treatment, and control (89).

Achieving the goal of improving cardiovascular health while reducing death and disability from CVD and stroke in women will require concerted efforts toward further research and the dissemination and implementation of lifestyle and treatment interventions. In the interim, quality improvement efforts can focus on incorporating multidimensional, interactive systems to increase accountability among payers, healthcare professionals, and patients for cardiovascular preventive care in women (90).

Patient and Public Education

In 2000, it was estimated that only 7% of people with CHD adhered to prescribed treatments for CVD lifestyle risk factors (91). Studies evaluating adherence to medical therapies for CVD prevention also show similarly low rates of persistence. In addition, it is estimated that people with chronic illnesses may see up to 16 different physicians annually, making adherence reinforcement even more challenging for patients and healthcare professionals (92,93). Thirty percent to 70% of all hospital admissions for medication-related illness are attributed to poor adherence, resulting in billions of dollars in additional healthcare costs

annually. Addressing adherence to recommendations in guidelines is of utmost importance (94,95). Effective implementation of national guidelines for the primary prevention of CVD will require a team-based approach to education that includes the patient, the family, and key healthcare professionals (93).

The Joint Commission emphasizes the importance of patient education that is directed at improving patient outcomes, including quality of life (96). National guidelines for the primary prevention of CVD rely on patient education to support the importance of lifestyle change and medication adherence to reduce acute MI and stroke (32,97). Providing successful patient education is challenging for clinicians because of many factors, including limited time for healthcare visits, patients with complex comorbidities, lack of staff for teaching and follow-up, lack of training in counseling patients about behavior change, and lack of reimbursement for prevention in general and patient education in particular (98). Patient-related nonadherence is common and is most prevalent in several circumstances, including low socioeconomic status, low literacy level, depression and other psychiatric illnesses, older age, poor hearing or vision, poor cognitive function, and lack of fluency in English, as well as in certain cultures and religions in which confidence in and cooperation with Western medicine may be limited.

Understanding effective educational theories/practices can improve the ability of clinicians to effect behavior change and adherence to therapies. Well-recognized approaches include behaviorally based individual counseling, "motivational interviewing," "self-efficacy," and "stages of readiness for change" (99–101). Self-monitoring (e.g., food records, blood pressure/blood glucose logs), group sessions/shared medical visits (e.g., for newly diagnosed diabetes mellitus), computer-assisted reminders, and other electronic communication to support behavioral change have been shown to improve both lifestyle and medication adherence (102–106). Involving the patient and the patient's family in setting appropriate short-term achievable goals with frequent follow-up will also enhance success.

These guidelines call for a renewed focus on health education, including systematic follow-up to assess effectiveness of medical and lifestyle therapies. Assessment of barriers to adherence and interventions to address them must be integrated into clinical practice, and barriers specific for women must be considered. Barriers hindering adherence to CVD prevention recommendations are common among women and include family and caretaking responsibilities, stress, sleep deprivation, fatigue, and lack of personal time. Educational efforts are critically important, because increased awareness of personal cardiovascular risk factors has been associated with improved health and lifestyles for women and their family members (107).

Methods

Selection of Expert Panel

The AHA Manuscript Oversight Committee commissioned the update of the guidelines and approved the writing group chair, the executive writing committee members with specific

expertise (methods and cost-effectiveness, risk assessment, healthcare professional implementation, patient and consumer education, diversity and population representation, and international issues), and expert panel members to review the literature for updates to the recommendation topic areas. The leadership of each AHA scientific council was asked to nominate a recognized expert in CVD prevention who had particular knowledge about women.

Major professional or government organizations with a mission consistent with CVD prevention were solicited to serve as cosponsors and were asked to nominate 1 representative with full voting rights to serve on the expert panel. Each executive writing committee and expert panel member completed a conflict of interest statement and was asked to abstain from discussion or voting on any recommendations deemed to be a potential conflict of interest. Panelists also suggested diverse professional and community organizations to endorse the final document after its approval by the AHA Science Advisory and Coordinating Committee and cosponsoring organizations.

Selection of Topics and Systematic Search

The expert panel reviewed the list of recommendations in the 2007 guidelines and suggested additional topics to be searched to determine if they warranted discussion or a clinical recommendation. The search terms for the systematic search were similar to those conducted in 2007 and previously described (14,15). The databases searched for this update were PubMed, Embase, and Cochrane. The timeframe for the updated search was January 2006 through January 2010. Briefly, studies were included if they were randomized clinical trials or large prospective cohort studies (>1,000 subjects) of CVD risk–reducing interventions, meta-analyses that used a quantitative systematic review process, or surrogate end-point studies with at least 10 cases of major clinical CVD end points reported. The systematic search was conducted by the AHA librarian. Class III recommendations

Table 3.   Classification and Levels of Evidence

Classification and Level of Evidence	Strength of Recommendation
Classification	
Class I	Intervention is useful and effective
Class IIa	Weight of evidence/opinion is in favor of usefulness/efficacy
Class IIb	Usefulness/efficacy is less well established by evidence/opinion
Class III	Procedure/test not helpful or treatment has no proven benefit
	Procedure/test excess cost without benefit or harmful or treatment harmful to patients
Level of evidence	
A	Sufficient evidence from multiple randomized trials
B	Limited evidence from single randomized trial or other nonrandomized studies
C	Based on expert opinion, case studies, or standard of care

Table 4.   Guidelines for the Prevention of CVD in Women

Lifestyle Interventions

Cigarette smoking

Women should be advised not to smoke and to avoid environmental tobacco smoke. Provide counseling at each encounter, nicotine replacement, and other pharmacotherapy as indicated in conjunction with a behavioral program or formal smoking cessation program *(Class I; Level of Evidence B)*.

Physical activity

Women should be advised to accumulate at least 150 min/wk of moderate exercise, 75 min/wk of vigorous exercise, or an equivalent combination of moderate- and vigorous-intensity aerobic physical activity. Aerobic activity should be performed in episodes of at least 10 min, preferably spread throughout the week *(Class I; Level of Evidence B)*.

Women should also be advised that additional cardiovascular benefits are provided by increasing moderate-intensity aerobic physical activity to 5 h (300 min)/wk, 2 1/2 h/wk of vigorous-intensity physical activity, or an equivalent combination of both *(Class I; Level of Evidence B)*.

Women should be advised to engage in muscle-strengthening activities that involve all major muscle groups performed on ≥2 d/wk *(Class I; Level of Evidence B)*.

Women who need to lose weight or sustain weight loss should be advised to accumulate a minimum of 60 to 90 min of at least moderate-intensity physical activity (e.g., brisk walking) on most, and preferably all, days of the week *(Class I; Level of Evidence B)*.

Cardiac rehabilitation

A comprehensive CVD risk-reduction regimen such as cardiovascular or stroke rehabilitation or a physician-guided home- or community-based exercise training program should be recommended to women with a recent acute coronary syndrome or coronary revascularization, new-onset or chronic angina, recent cerebrovascular event, peripheral arterial disease *(Class I; Level of Evidence A)* or current/prior symptoms of heart failure and an LVEF ≤35% *(Class I; Level of Evidence B)*.

Dietary intake

Women should be advised to consume a diet rich in fruits and vegetables; to choose whole-grain, high-fiber foods; to consume fish, especially oily fish, at least twice a week; to limit intake of saturated fat, cholesterol, alcohol, sodium, and sugar; and avoid *trans*-fatty acids. See Appendix *(Class I; Level of Evidence B)*.

Note: Pregnant women should be counseled to avoid eating fish with the potential for the highest level of mercury contamination (e.g., shark, swordfish, king mackerel, or tile fish).

Weight maintenance/reduction

Women should maintain or lose weight through an appropriate balance of physical activity, caloric intake, and formal behavioral programs when indicated to maintain or achieve an appropriate body weight (e.g., BMI <25 kg/m^2 in U.S. women), waist size (e.g., <35 in), or other target metric of obesity. *(Class I; Level of Evidence B)*.

Omega-3 fatty acids

Consumption of omega-3 fatty acids in the form of fish or in capsule form (e.g., EPA 1800 mg/d) may be considered in women with hypercholesterolemia and/or hypertriglyceridemia for primary and secondary prevention *(Class IIb; Level of Evidence B)*.

Note: Fish oil dietary supplements may have widely variable amounts of EPA and DHA (likely the only active ingredients).

Major risk factor interventions

Blood pressure: optimal level and lifestyle

An optimal blood pressure of <120/80 mm Hg should be encouraged through lifestyle approaches such as weight control, increased physical activity, alcohol moderation, sodium restriction, and increased consumption of fruits, vegetables, and low-fat dairy products *(Class I; Level of Evidence B)*.

Blood pressure: pharmacotherapy

Pharmacotherapy is indicated when blood pressure is ≥140/90 mm Hg (≥130/80 mm Hg in the setting of chronic kidney disease and diabetes mellitus). Thiazide diuretics should be part of the drug regimen for most patients unless contraindicated or if there are compelling indications for other agents in specific vascular diseases. Initial treatment of high-risk women with acute coronary syndrome or MI should be with β-blockers and/or ACE inhibitors/ARBs, with addition of other drugs such as thiazides as needed to achieve goal blood pressure *(Class I; Level of Evidence A)*.

Note: ACE inhibitors are contraindicated in pregnancy and ought to be used with caution in women who may become pregnant.

Lipid and lipoprotein levels: optimal levels and lifestyle

The following levels of lipids and lipoproteins in women should be encouraged through lifestyle approaches: LDL-C <100 mg/dL, HDL-C >50 mg/dL, triglycerides <150 mg/dL, and non–HDL-C (total cholesterol minus HDL) <130 mg/dL *(Class I; Level of Evidence B)*.

Lipids: pharmacotherapy for LDL-C lowering, high-risk women

LDL-C–lowering drug therapy is recommended simultaneously with lifestyle therapy in women with CHD to achieve an LDL-C <100 mg/dL *(Class I; Level of Evidence A)* and is also indicated in women with other atherosclerotic CVD or diabetes mellitus or 10-year absolute risk >20% *(Class I; Level of Evidence B)*.

A reduction to <70 mg/dL is reasonable in very-high-risk women (e.g., those with recent ACS or multiple poorly controlled cardiovascular risk factors) with CHD and may require an LDL-lowering drug combination *(Class IIa; Level of Evidence B)*.

(Continued)

Table 4. Continued

Lipids: pharmacotherapy for LDL-C lowering, other at-risk women

LDL-C–lowering with lifestyle therapy is useful if LDL-C level is ≥130 mg/dL, there are multiple risk factors, and the 10-y absolute CHD risk is 10% to 20% *(Class I; Level of Evidence B)*.

LDL-C lowering is useful with lifestyle therapy if LDL-C level is ≥160 mg/dL and multiple risk factors even if 10-y absolute CHD risk is <10% *(Class I; Level of Evidence B)*.

LDL-C lowering with lifestyle therapy is useful if LDL 190 mg/dL regardless of the presence or absence of other risk factors or CVD *(Class I; Level of Evidence B)*.

In women >60 y of age and with an estimated CHD risk >10%, statins could be considered if hsCRP is >2 mg/dL after lifestyle modification and no acute inflammatory process is present *(Class IIb; Level of Evidence B)*.

Lipids: pharmacotherapy for low HDL-C or elevated non–HDL-C

Niacin or fibrate therapy can be useful when HDL-C is low (<50 mg/dL) or non–HDL-C is elevated (>130 mg/dL) in high-risk women after LDL-C goal is reached *(Class IIb; Level of Evidence B)*.

Diabetes mellitus

Lifestyle and pharmacotherapy can be useful in women with diabetes mellitus to achieve an HbA$_{1C}$ <7% if this can be accomplished without significant hypoglycemia *(Class IIa; Level of Evidence B)*.

Preventive drug interventions

Aspirin: high-risk women

Aspirin therapy (75–325 mg/d) should be used in women with CHD unless contraindicated *(Class I; Level of Evidence A)*.

Aspirin therapy (75–325 mg/d) is reasonable in women with diabetes mellitus unless contraindicated *(Class IIa; Level of Evidence B)*.

If a high-risk woman has an indication but is intolerant of aspirin therapy, clopidogrel should be substituted *(Class I; Level of Evidence B)*.

Aspirin: other at-risk or healthy women

Aspirin therapy can be useful in women ≥65 y of age (81 mg daily or 100 mg every other day) if blood pressure is controlled and benefit for ischemic stroke and MI prevention is likely to outweigh risk of gastrointestinal bleeding and hemorrhagic stroke *(Class IIa; Level of Evidence B)* and may be reasonable for women <65 y of age for ischemic stroke prevention *(Class IIb; Level of Evidence B)*.

Aspirin: atrial fibrillation

Aspirin 75–325 mg should be used in women with chronic or paroxysmal atrial fibrillation with a contraindication to warfarin or at low risk of stroke (<1%/y or CHADS2 score of <2) *(Class I; Level of Evidence A)*.

Warfarin: atrial fibrillation

For women with chronic or paroxysmal atrial fibrillation, warfarin should be used to maintain the INR at 2.0 to 3.0 unless they are considered to be at low risk for stroke (<1%/y or high risk of bleeding) *(Class I; Level of Evidence A)*.

Dabigatran: atrial fibrillation

Dabigatran is useful as an alternative to warfarin for the prevention of stroke and systemic thromboembolism in patients with paroxysmal to permanent AF and risk factors for stroke or systemic embolization who do not have a prosthetic heart valve or hemodynamically significant valve disease, severe renal failure (creatinine clearance 15 mL/min), or advanced liver disease (impaired baseline clotting function) *(Class I; Level of Evidence B)*.

β-Blockers

β-Blockers should be used for up to 12 mo *(Class I; Level of Evidence A)* or up to 3 y *(Class I; Level of Evidence B)* in all women after MI or ACS with normal left ventricular function unless contraindicated.

Long-term β-blocker therapy should be used indefinitely for women with left ventricular failure unless contraindications are present *(Class I; Level of Evidence A)*.

Long-term β-blocker therapy may be considered in other women with coronary or vascular disease and normal left ventricular function *(Class IIb; Level of Evidence C)*.

ACE inhibitors/ARBs

ACE inhibitors should be used (unless contraindicated) in women after MI and in those with clinical evidence of heart failure, LVEF ≤40%, or diabetes mellitus *(Class I; Level of Evidence A)*.

In women after MI and in those with clinical evidence of heart failure, an LVEF ≤40%, or diabetes mellitus who are intolerant of ACE inhibitors, ARBs should be used instead *(Class I; Level of Evidence B)*.

Note: ACE inhibitors are contraindicated in pregnancy and ought to be used with caution in women who may become pregnant.

Aldosterone blockade

Use of aldosterone blockade (e.g., spirololactone) after MI is indicated in women who do not have significant hypotension, renal dysfunction, or hyperkalemia who are already receiving therapeutic doses of an ACE inhibitor and β-blocker and have LVEF ≤40% with symptomatic heart failure *(Class I; Level of Evidence B)*.

LVEF indicates left ventricular ejection fraction; BMI, body mass index; EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; CHD, coronary heart disease; CVD, cardiovascular disease; ACS, acute coronary syndrome; hsCRP, high-sensitivity C-reactive protein; HbA$_{1C}$, hemoglobin A$_{1C}$; MI, myocardial infarction; CHADS2, Congestive Heart Failure, Hypertension, Age, Diabetes, Prior Stroke; and INR, international normalized ratio.

from the 2007 guidelines update were not searched because of consensus by the expert panel members that data remained insufficient for modification (ie, menopausal therapy, antioxidants, and folic acid supplementation). Some topics were not included in the systematic search if they were covered in recent guidelines (e.g., treatment of atrial fibrillation for stroke prevention) (10).

Evidence Rating and Recommendation Procedures

Subcommittees were organized by subtopic and were charged with preparation of summary evidence tables based on the updated literature review. These tables were then reviewed in series of conference calls, after which the subcommittee modified or retained the current recommendation on the basis of the discussions. Each recommendation was assigned both a strength of recommendation (Class I, IIa, IIb, or III) and a Level of Evidence (A, B, or C) as outlined in Table 3. The updated recommendations were voted on by the expert panel by individual ballot to determine by a majority vote the final rating of evidence, the strength of the recommendation, and its wording. Further minor modifications to text and clinical recommendations were based on peer review comments and cosponsor reviews. The guidelines were then finalized and approved by the expert panel (Table 4).

Cost-Effectiveness

Cost-effectiveness analyses reviewed were published between 2000 and 2010, focusing on randomized controlled trials and observational studies of omega-3 use, dietary intake, β-blocker and aspirin therapy, and management of obesity, smoking, and hypertension in secondary and primary prevention of CVD (108–125). Few of these studies included gender-stratified or gender-specific analyses (119,122); however, some cost-effectiveness analyses with Markov or sim-

ulation modeling presented gender-specific or women-only data (126–138).

Often the cost inputs and methodologies were insufficiently described or used resource consumption as a surrogate for cost. On the basis of these analyses, aspirin appears cost-effective in women ≥65 years of age with moderate to severe CVD risk (133–135). Antihypertensive treatments and smoking cessation treatments appear cost-effective for women (126–132). Weight management approaches, including drug therapy and gastric bypass surgery, appear effective for weight loss but add costs, with decision analytic approaches noting favorable cost-effective ratios in younger and middle-aged obese women (123,137,138).

The expert panel emphasized the need for more cost-effective analyses according to gender. Consistent with a recent Institute of Medicine report on women's health research, the expert panel recommends adequate participation of women and reporting of gender-stratified analyses in health research (139). The panel also emphasized the need for reporting of gender-specific analyses for *both* efficacy and adverse effects of preventative interventions to inform the development of future gender-specific guidelines.

Appendix.　Specific Dietary Intake Recommendations for Women

Nutrient	Serving	Serving Size
Fruits and vegetables	≥4.5 cups/d	1 cup raw leafy vegetable, 1/2 cup cut-up raw or cooked vegetable, 1/2 cup vegetable juice; 1 medium fruit, 1/4 cup dried fruit, 1/2 cup fresh, frozen, or canned fruit, 1/2 cup fruit juice
Fish	2/wk	3.5 oz, cooked (preferably oily types of fish)
Fiber	30 g/d (1.1 g/10 g carbohydrate)	Bran cereal, berries, avocado, etc.
Whole grains	3/d	1 slice bread, 1 oz dry cereal, 1/2 cup cooked rice, pasta, or cereal (all whole-grain products)
Sugar	≤5/wk (≤450 kcal/wk from sugar-sweetened beverages)	1 tablespoon sugar, 1 tablespoon jelly or jam, 1/2 cup sorbet, 1 cup lemonade
Nuts, legumes, and seeds	≥4/wk	1/3 cup or 1 1/2 oz nuts (avoid macadamia nuts and salted nuts), 2 tablespoons peanut butter, 2 tablespoon or 1/2 oz seeds, 1/2 cup cooked legumes (dry beans and peas)
Saturated fat	<7%/total energy intake	Found in fried foods, fat on meat or chicken skin, packaged desserts, butter, cheese, sour cream, etc.
Cholesterol	<150 mg/d	Found in animal meats, organ meats, eggs, etc.
Alcohol	≤1/d	4 oz wine, 12 oz beer, 1.5 oz of 80-proof spirits, or 1 oz of 100-proof spirits
Sodium	<1,500 mg/d	
Trans-fatty acids	0	0

Note: The recommended serving amounts are based on a 2,000-kcal diet, and recommendations vary according to individual preference and needs (141).

Note for Vitamin D: It is expected that ongoing research regarding the role of vitamin D supplementation in the prevention of cardiovascular disease will shed further light on this issue for future versions of this guideline (142).

Disclosures

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Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honoraria	Expert Witness	Ownership Interest	Consultant/Advisory Board	Other
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This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10,000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10,000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

    *Modest.
    †Significant.

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(Continued)

Reviewer Disclosures, *Continued*

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This table represents the relationships of reviewers that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all reviewers are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10,000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10,000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.
†Significant.

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