

Preventing Cardiovascular Disease in Women

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Cardiovascular disease (CVD) has been the primary cause of death in women for almost a century, and more women than men have died of CVD every year since 1984. Although CVD incidence can be reduced by adherence to a heart-healthy lifestyle and detection and treatment of major risk factors, preventive recommendations have not been consistently or optimally applied to women. The American Heart Association guidelines for CVD prevention in women provide physicians with a clear plan for assessment and treatment of CVD risk and personalization of treatment recommendations. The emphasis of preventive efforts has shifted away from treatment of individual CVD risk factors in isolation toward assessment of a woman's overall or "global" CVD risk. In addition to accounting for the presence or absence of preexisting coronary heart disease or its equivalents (e.g., diabetes, chronic kidney disease), cardiovascular risk can be further calculated with the Framingham risk score, which is based on age, sex, smoking history, and lipid and blood pressure levels. Intervention intensity and treatment goals are tailored to overall risk, with those at highest risk receiving the most intense risk-lowering interventions. Women at high risk for CVD and without contraindications should receive aspirin, beta blockers, and an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker in addition to pharmacologic therapy for hyperlipidemia, hypertension, and diabetes. Women who already are at optimal or low risk for CVD should be encouraged to maintain or further improve their healthy lifestyle practices. Optimal application of these preventive practices significantly reduces the burden of death and disability caused by heart attack and stroke in women. (*Am Fam Physician* 2006;74:1331-40, 1342. Copyright © 2006 American Academy of Family Physicians.)

Patient information:

A handout on cardiovascular disease in women, written by Sumi Sexton, M.D., associate editor for *AFP*, and Jill Tremblay, B.S., is provided on page 1342.

See related editorial on page 1285.

Cardiovascular disease (CVD) remains the most common cause of death in women and men in the developed world, despite the multiple epidemiologic and interventional studies that demonstrate significant declines in CVD incidence and prevalence with adherence to a healthy lifestyle and identification and treatment of risk factors.¹ Women account for more than one half of the almost 1 million deaths caused by CVD in the United States annually²; yet historically, CVD risk factors in women have been insufficiently recognized, diagnosed, and treated.³⁻⁹

The basis for this lack of recognition and less aggressive management of cardiovascular risk in women has largely been a result of the misperception by women and physicians that women are at an inherently low risk for developing heart disease.^{10,11} A 2003 American Heart Association (AHA) survey found that only 13 percent of U.S. women (7 percent in 1997) believe heart disease is their major health threat.¹⁰ Black and Hispanic women are less likely than white women to be aware that heart disease is the

primary cause of death in women. Only about one third of women recall discussing heart-disease risk with their physician¹⁰; and women receive fewer preventive recommendations, such as lipid-lowering therapy, aspirin, and lifestyle advice, than do men with similar Framingham risk scores.^{11,12}

In 2004, the AHA published evidence-based guidelines for CVD prevention in women.¹ Several factors led to the development of these guidelines. First, much of the data used to develop previous prevention guidelines came from trials that enrolled few or no women, making it difficult to perform a meaningful analysis of results by sex. In practice, the response to this evidence gap has been to withhold preventive therapies from women because of the lack of sex-specific proof of benefit, or to provide "gender-blind" preventive care using data from studies involving men to guide treatment in women. Neither approach is evidence based and both have the potential for harm. In addition, new guidelines were necessitated by the publication of results from several large CVD prevention trials,

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most notably the Women's Health Initiative trial, which confirmed the lack of cardiovascular protection afforded by estrogen use in women after menopause.¹³⁻¹⁵ Finally, acceptance of the concept of "global risk," codified by the National Cholesterol Education Program—Adult Treatment Program III (NCEP—

Prophylactic aspirin use in women at low risk, anti-oxidants, and hormone therapy are categorized as ineffective and potentially harmful interventions

ATP III) report as a mechanism to assign CVD risk levels and guide the aggressiveness of preventive interventions using the Framingham risk score,¹⁶ provided a validated framework for the recommendations.

Methods of the AHA Guidelines

Systematic review topics of the AHA guidelines included dietary modification; physical activity; tobacco cessation; management of hyperlipidemia, blood pressure, weight, and diabetes; cardiac rehabilitation; angiotensin-converting enzyme (ACE) inhibitor/angiotensin receptor blocker (ARB), antiplatelet, and beta-blocker therapy; warfarin (Coumadin) for atrial fibrillation; aspirin for primary prevention; treatment for depression; hormone therapy; and antioxidant, omega-3 fatty acid, and folic acid supplementation.¹ Recent guidelines for treating hypertension,^{17,18} diabetes,¹⁹ hyperlipidemia,¹⁶ obesity,²⁰ tobacco dependence,²¹ and atrial fibrillation²² were incorporated where applicable.

Each major topic was reviewed for content, strength of recommendation, level of evidence, and generalizability to women (where data in women were insufficient). The classification of efficacy and level of evidence rating systems (*Table 1*) were based on methods used in AHA and American College of Cardiology (ACC) clinical practice guidelines.²³ Class I and IIa interventions are generally recommended and have adequate levels of evidence to support their implementation; class IIb interventions typically have potential benefit but are supported by weaker or conflicting data. The final recommendations were divided into five main categories: lifestyle interventions, major risk factor interventions, preventive drug interventions, atrial fibrillation and stroke prevention, and contraindicated (potentially harmful) interventions.

Dissemination and use of the guidelines was recognized as critical. Most women who could benefit from CVD preventive measures are not cared for by cardiovascular subspecialists until they develop symptoms or signs of CVD. Previous guidelines were published primarily in

cardiology journals, which limited knowledge and adoption of preventive practices by family physicians, gynecologists, and internists, who care for most women at risk.

Cardiovascular Risk Assessment

The first step in applying the guidelines to individual women is the assessment of overall CVD risk. The Framingham 10-year coronary heart disease (CHD) risk score is central to making appropriate CHD preventive recommendations.¹⁶ Risk level can be calculated using age, sex, total and high-density lipoprotein (HDL) cholesterol levels, smoking history, and blood pressure (*Figure 1*).¹ An online calculator is available at <http://hin.nhlbi.nih.gov/atpiii/calculator.asp?usertype=prof>. Persons at high risk have a greater than 20 percent 10-year CHD risk, and include women with established CVD as well as those

TABLE 1
AHA/ACC Recommendation Classifications and Levels of Evidence

	<i>Strength of recommendation</i>
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	Intervention is not useful/effective and may be harmful.
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
Generalizability index	
1	Very likely that results generalize to women
2	Somewhat likely that results generalize to women
3	Unlikely that results generalize to women
0	Unable to project whether results generalize to women

AHA = American Heart Association; ACC = American College of Cardiology.

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Framingham Point Score Calculator: Estimate of 10-Year CHD Risk for Women

Age	Points	Age	Points	Age	Points	
20-34	-7	50-54	6	65-69	12	
35-39	-3	55-59	8	70-74	14	
40-44	0	60-64	10	75-79	16	
45-49	3					Points ____
Total cholesterol (mg per dL)	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79	
<160	0	0	0	0	0	
160-199	4	3	2	1	1	
200-239	8	6	4	2	1	
240-279	11	8	5	3	2	
≥280	13	10	7	4	2	Points ____
Smoking	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79	
Nonsmoker	0	0	0	0	0	
Smoker	9	7	4	2	1	Points ____
HDL (mg per dL)	Points					
≥60	-1					
50-59	0					
40-49	1					
<40	2					Points ____
Systolic BP (mm Hg)	If untreated	If treated				
<120	0	0				
120-129	1	3				
130-139	2	4				
140-159	3	5				
≥160	4	6				Points ____
						Total points ____
Point total	10-year risk (%)	Point total	10-year risk (%)	Point total	10-year risk (%)	
<9	<1	14	2	20	11	
9	1	15	3	21	14	
10	1	16	4	22	17	
11	1	17	5	23	22	
12	1	18	6	24	27	
13	2	19	8	≥25	≥30	10-year risk ____%

Figure 1. Framingham point score calculator for the 10-year risk of CHD in women. Points from each category are added to calculate risk. (CHD = coronary heart disease; HDL = high-density lipoprotein cholesterol; BP = blood pressure.)

NOTE: An online risk calculator is available at <http://hin.nhlbi.nih.gov/atp/iii/calculator.asp?usertype=prof>.

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with CHD equivalents such as diabetes and chronic renal disease (Table 2).¹ Persons at intermediate risk have a 10 to 20 percent 10-year CHD risk, and persons at lower risk have a less than 10 percent 10-year CHD risk. “Optimal risk” is defined as optimal levels of all risk factors and adherence to a heart-healthy lifestyle. The guidelines or recommendations for each risk category based on a person’s risk score determine the intensity of intervention.

Final AHA Recommendations

The AHA CVD prevention recommendations for women are outlined in Tables 3 through 6.¹ Interventions categorized as ineffective and potentially harmful, including

prophylactic aspirin use in women at low risk, antioxidants,²⁴ and hormone therapy, are listed in Table 7.¹ A framework for applying the recommendations based on individual risk is given in Table 8,¹ which lists the recommended interventions for each level of CVD risk.

HEALTHY LIFESTYLE

Counseling on lifestyle interventions, including smoking cessation, physical activity, a heart-healthy diet, and weight maintenance, is important for all women, regardless of risk level, even if only to reinforce established healthy behaviors (Table 3).¹ Women at higher risk may need additional consultation with a dietitian and prescription

of a therapeutic diet or professional guidance in designing an exercise program. All women should be encouraged to perform at least 30 minutes of moderate-intensity physical activity (e.g., brisk walking) every day; to maintain or achieve a healthy weight; and to eat a diet low in saturated fat, cholesterol, *trans*-fatty acids, and sodium, and one that is rich in a variety of fruits, vegetables, whole grains, low-fat and nonfat dairy products, legumes, and fish.

RISK FACTOR MANAGEMENT

Risk factor interventions such as control of blood pressure and treatment of hyperlipidemia apply to all risk groups. The treatment targets and intensity of interventions are based on established guidelines as outlined in the Seventh Report of the Joint National Committee

on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure and the NCEP-ATP III report (Table 4¹).^{16,17} Ideal blood pressure is defined as less than 120/80 mm Hg. If weight loss, dietary modification, and exercise are insufficient to control blood pressure, pharmacologic therapy should be considered when blood pressure is 140/90 mm Hg or greater, or 130/80 mm Hg or greater in women with diabetes or chronic kidney disease.¹⁷

The ideal low-density lipoprotein (LDL) cholesterol level in women is less than 100 mg per dL (2.59 mmol per L), and the ideal HDL cholesterol level is greater than 50 mg per dL (1.29 mmol per L). The primary target for lipid-lowering therapy is LDL cholesterol. Women at high risk whose LDL cholesterol level is greater than 100 mg per dL should receive statin therapy to reach the goal level, and those at very high risk (e.g., multiple uncontrolled risk factors) should be considered for a target LDL cholesterol level of less than 70 mg per dL (1.81 mmol per L).^{25,26} Consideration also should be given to initiating pharmacologic therapy in women at high risk whose LDL cholesterol level is less than 100 mg per dL, because these women may benefit from further reduction. Pharmacologic therapy should be considered in women at intermediate risk whose LDL cholesterol levels are 130 mg per dL (3.36 mmol per L) or greater and in those at lower risk whose LDL cholesterol levels are 160 mg per dL (4.14 mmol per L) or greater. In women who have no more than one risk factor, a treatment threshold of LDL cholesterol 190 mg per dL (4.91 mmol per L) or greater should be used. Triglyceride levels should be less than 150 mg per dL (1.69 mmol per L), and combination therapy with niacin or a fibrate should be considered in women whose triglyceride levels remain elevated after LDL cholesterol level goals have been met.

Tight control of diabetes (i.e., normalized A1C level) is associated with a reduction in CVD events compared with less-stringent glucose control.²⁷ Although the current A1C goal for most persons with diabetes is less than 7 percent, recent data suggest that normalization of A1C level (i.e., less than 6 percent) is associated with better outcomes and should be considered in patients who do not experience frequent hypoglycemic episodes.²⁸

TABLE 2
Spectrum of Cardiovascular Risk in Women

<i>Risk group</i>	<i>Framingham global risk (10-year absolute CHD risk)</i>	<i>Clinical examples</i>
High risk	>20%	Established CHD Peripheral arterial disease Abdominal aortic aneurysm Diabetes mellitus Chronic kidney disease
Intermediate risk	10 to 20%	Subclinical CVD* (e.g., coronary calcification, carotid stenosis) Metabolic syndrome (e.g., obesity, hypertension, hyperlipidemia) Multiple risk factors Markedly elevated levels of a single risk factor First-degree relative with early-onset (i.e., younger than 55 years in men and younger than 65 years in women) atherosclerotic disease
Lower risk	<10%	Modest or mild elevation of one or more risk factors; may include women with metabolic syndrome or no risk factors
Optimal risk	<10%	Optimal levels of risk factors and heart-healthy lifestyle

*—Some patients with subclinical CVD have a greater than 20 percent 10-year CHD risk and should be elevated to the high-risk category.

CHD = coronary heart disease; CVD = cardiovascular disease.

Adapted with permission from Mosca L, Appel LJ, Benjamin EJ, Berra K, Chandra-Strobo N, Fabunmi RP, et al., for the American Heart Association. Evidence-based guidelines for cardiovascular disease prevention in women. *Circulation* 2004;109:673.

TABLE 3
Clinical Recommendations for Lifestyle Interventions for the Prevention of CVD in Women

<i>Lifestyle intervention</i>	<i>AHA/ACC class, level</i>	<i>GI</i>	<i>References</i>
Cigarette smoking			
Consistently encourage women not to smoke and to avoid environmental tobacco.	I, B	1	21
Physical activity			
Consistently encourage women to accumulate a minimum of 30 minutes of moderate-intensity physical activity (e.g., brisk walking) on most, and preferably all, days of the week.	I, B	1	
Cardiac rehabilitation			
Women with a recent acute coronary syndrome or coronary intervention, or new-onset or chronic angina should participate in a comprehensive risk-reduction regimen, such as cardiac rehabilitation or a physician-guided home- or community-based program.	I, B	2	
Heart-healthy diet			
Consistently encourage an overall healthy eating pattern including a variety of fruits, vegetables, grains, low-fat or nonfat dairy products, fish, legumes, and sources of protein low in saturated fat (e.g., poultry, lean meats, plant sources). Limit saturated fat intake to less than 10 percent of calories, limit cholesterol intake to less than 300 mg per day, and limit intake of <i>trans</i> -fatty acids.	I, B	1	18
Weight maintenance/reduction			
Consistently encourage weight maintenance/reduction through an appropriate balance of physical activity, caloric intake, and formal behavioral programs when indicated to maintain or achieve a body mass index between 18.5 and 24.9 kg per m ² and a waist circumference less than 35 inches.	I, B	1	20
Psychosocial factors			
Women with CVD should be evaluated for depression and referred or treated when indicated.	Ila, B	2	29
Omega-3 fatty acids			
As an adjunct to diet, omega-3 fatty acid supplementation may be considered in women at high risk.	Ilb, B	2	
Folic acid			
As an adjunct to diet, folic acid supplementation may be considered in women at high risk (except after revascularization procedure) if a higher-than-normal level of homocysteine has been detected.	Ilb, B	2	

CVD = cardiovascular disease; AHA = American Heart Association; ACC = American College of Cardiology; GI = generalizability index.

NOTE: For definitions of risk categories, see Table 2.

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Women at high risk, especially those with overt CHD, should be screened and treated for depression (Table 3).¹ Depression confers a significantly increased risk of adverse outcome after a diagnosis of heart disease and is a major barrier to adoption of healthy lifestyle behaviors. It is associated with a higher risk for first and recurrent myocardial infarction and is more prevalent in women than in men. Diagnosing and treating depression is critical, because treatment with selective serotonin reuptake inhibitors is safe and effective and may

be associated with a reduced risk of adverse outcomes in women and men with heart disease.^{29,30}

Except for generally higher levels of evidence to support CVD risk-lowering interventions in men, differences in treatment goals and recommendations for men and women are slight. For example, the desirable level of HDL cholesterol for men is 40 mg per dL (1.0 mmol per L) or greater. As in women, the goal levels of lipids, blood pressure, and diabetes control for men are dependent on estimated CVD risk, calculated using a separate

TABLE 4
Clinical Recommendations for Major Risk Factor Interventions for Prevention of CVD in Women

<i>Risk factor intervention</i>	<i>AHA/ACC class, level</i>	<i>GI</i>	<i>References</i>
Blood pressure—lifestyle			
Encourage an optimal blood pressure of less than 120/80 mm Hg through lifestyle approaches.	I, B	1	17
Blood pressure—drugs			
Pharmacotherapy is indicated when blood pressure is 140/90 mm Hg or greater, or lower in patients with blood pressure–related target-organ damage or diabetes. Thiazide diuretics should be part of the drug regimen for most patients unless contraindicated.	I, A	1	17
Lipid, lipoproteins			
Optimal levels of lipids and lipoproteins in women are LDL cholesterol less than 100 mg per dL (2.59 mmol per L), HDL cholesterol greater than 50 mg per dL (1.29 mmol per L), triglycerides less than 150 mg per dL (1.69 mmol per L), and non-HDL cholesterol (total cholesterol minus HDL cholesterol) less than 130 mg per dL (3.36 mmol per L); these should be encouraged through lifestyle approaches.	I, B	1	16
Lipids—diet therapy			
In women at high risk or with elevated LDL cholesterol, saturated fat intake should be reduced to less than 7 percent of calories, cholesterol should be reduced to less than 200 mg per day, and <i>trans</i> -fatty acid intake should be reduced.	I, B	1	16
Lipids—pharmacotherapy—high risk			
Initiate LDL cholesterol–lowering therapy (preferably a statin) simultaneously with lifestyle therapy in women at high risk with LDL cholesterol 100 mg per dL or greater.	I, A	1	16, 26
Initiate statin therapy in women at high risk with an LDL cholesterol less than 100 mg per dL unless contraindicated.	I, B	1	16, 26
Initiate niacin or fibrate therapy when HDL cholesterol is low, or non-HDL cholesterol is elevated in women at high risk.	I, B	1	16, 26
Lipids—pharmacotherapy—intermediate risk			
Initiate LDL cholesterol–lowering therapy (preferably a statin) if LDL cholesterol level is 130 mg per dL or greater even with lifestyle therapy.	I, A	1	16
Initiate niacin or fibrate therapy when HDL cholesterol is low or non-HDL cholesterol elevated after LDL cholesterol goal is reached.	I, B	1	16
Lipids—pharmacotherapy—lower risk			
Consider LDL cholesterol–lowering therapy in women at low risk with no more than one risk factor when LDL cholesterol level is 190 mg per dL (4.91 mmol per L) or greater, and in women with multiple risk factors when LDL cholesterol is 160 mg per dL (4.14 mmol per L) or greater; consider niacin or fibrate therapy when HDL cholesterol is low or non-HDL cholesterol elevated after LDL cholesterol goal is reached.	Ila, B	1	16
Diabetes			
Lifestyle and pharmacotherapy should be used to achieve near-normal A1C levels (i.e., less than 7 percent) in women with diabetes.	I, B	1	19

CVD = cardiovascular disease; AHA = American Heart Association; ACC = American College of Cardiology; GI = generalizability index; LDL = low-density lipoprotein; HDL = high-density lipoprotein.

NOTE: For definitions of risk categories, see Table 2.

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Framingham risk table to reflect sex-based differences in risk intensity.

PHARMACOTHERAPY

In addition to pharmacologic therapy for hyperlipidemia, hypertension, and diabetes, all women at high risk for CVD should receive aspirin, beta blockers, and an ACE

inhibitor or ARB unless contraindicated (Table 5).^{31,32} The use of omega-3 fatty acid and folic acid supplementation also should be considered in women at high risk, but there is insufficient evidence to support universal recommendations (Table 3).¹

Aspirin has proven benefit and is recommended for all women at high risk without contraindications

TABLE 5
Clinical Recommendations for Pharmacologic Interventions for Prevention of CVD in Women

<i>Pharmacologic intervention</i>	<i>AHA/ACC class, level</i>	<i>GI</i>	<i>References</i>
Aspirin—high risk			
Aspirin (75 to 162 mg per day), or clopidogrel (Plavix) if intolerant to aspirin, should be used in women at high risk unless contraindicated.	I, A	1	33
Aspirin—intermediate risk			
Consider aspirin therapy (75 to 162 mg per day) in women at intermediate risk if blood pressure is controlled and benefit is likely to outweigh the risk of gastrointestinal side effects.	Ila, B	2	33
Beta blockers			
Beta blockers should be used indefinitely in all women who have had a myocardial infarction or who have chronic ischemic syndromes unless contraindicated.	I, A	1	
ACE inhibitors			
ACE inhibitors should be used in women at high risk unless contraindicated.	I, A	1	31
ARBs			
ARBs should be used in women at high risk with clinical evidence of heart failure or an ejection fraction less than 40 percent who are intolerant of ACE inhibitors.	I, B	1	32

CVD = cardiovascular disease; AHA = American Heart Association; ACC = American College of Cardiology; GI = generalizability index; ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker.

NOTE: For definitions of risk categories, see Table 2.

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and for select women at intermediate risk (Table 5).¹ Previously, there were few data on the use of aspirin for primary prevention of CVD in women. Earlier recommendations were based on extrapolation from large, men-only studies that demonstrated a reduction in risk for myocardial infarction but not stroke in men of middle age or older at intermediate or high risk. Data from the aspirin arm of the Women's Health Initiative, released subsequent to the AHA guidelines, support the practice of not recommending aspirin to women at lower risk.³³ In that study, almost 40,000 women were randomized to receive low-dose aspirin (100 mg every two days) or placebo. The overall risk of significant bleeding complications was increased by 40 percent in those taking aspirin, whereas ischemic stroke incidence was reduced by 24 percent. In contrast to the effects of aspirin for primary prevention of CVD in men, the risks of fatal and nonfatal myocardial infarction were not reduced in women except in those older than 65 years. A meta-analysis of five major aspirin primary prevention trials had similar findings.³⁴ As a result, widespread use of aspirin is not recommended for women at low risk because of the excess risk of cerebral and gastrointestinal hemorrhage and the lack of definite benefit for prevention of CVD (Table 7).¹

TABLE 6
Clinical Recommendations for Prevention of Stroke in Women with Atrial Fibrillation

<i>Pharmacologic intervention</i>	<i>AHA/ACC class, level</i>	<i>GI</i>	<i>References</i>
Warfarin—atrial fibrillation			
Warfarin (Coumadin) should be used in women with chronic or paroxysmal atrial fibrillation to maintain an International Normalized Ratio of 2 to 3 unless they are at low risk of stroke (i.e., less than 1 percent per year) or at high risk of bleeding.	I, A	1	22
Aspirin—atrial fibrillation			
Aspirin (325 mg per day) should be used in women with chronic or paroxysmal atrial fibrillation who have a contraindication to warfarin or are at low risk of stroke (i.e., less than 1 percent per year).	I, A	1	22

AHA = American Heart Association; ACC = American College of Cardiology; GI = generalizability index.

NOTE: For definitions of risk categories, see Table 2.

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TABLE 7
Contraindicated Interventions for Prevention of CVD in Women

<i>Intervention</i>	<i>AHA/ACC class, level</i>	<i>GI</i>	<i>References</i>
Hormone therapy			
Combined estrogen/progestin hormone therapy should not be initiated to prevent CVD in postmenopausal women.	III, A	NA	13, 14
Combined estrogen/progestin hormone therapy should not be continued to prevent CVD in postmenopausal women.	III, C	NA	14
Other forms of menopausal hormone therapy (e.g., unopposed estrogen) should not be initiated or continued to prevent CVD in postmenopausal women pending the results of ongoing trials.	III, C	NA	15
Antioxidant supplements			
Antioxidant vitamin supplements should not be used to prevent CVD pending the results of ongoing trials.	III, A	1	24
Aspirin—lower risk			
Routine use of aspirin in women at lower risk is not recommended.	III, A*	2	33

CVD = cardiovascular disease; AHA = American Heart Association; ACC = American College of Cardiology; GI = generalizability index; NA = not applicable.

*—Based on results from trials published after 2004.

NOTE: For definitions of risk categories, see Table 2.

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TABLE 8
Recommendations for Prevention of CVD in Women

<i>High risk (>20%)</i>	<i>Intermediate risk (10 to 20%)</i>	<i>Lower risk (<10%)</i>
Strength of recommendation* A		
Smoking cessation	Smoking cessation	Smoking cessation
Physical activity/cardiac rehabilitation	Physical activity	Physical activity
Diet therapy	Heart-healthy diet	Heart-healthy diet
Healthy weight	Healthy weight	Healthy weight
Blood pressure control	Blood pressure control	Treatment of individual CVD risk factors as indicated
Cholesterol control/therapy	Cholesterol control	
Aspirin therapy		
Beta-blocker therapy		
ACE inhibitor therapy (or ARB therapy if contraindicated)		
Management of diabetes		
Strength of recommendation* B		
Evaluation/therapy for depression	Aspirin therapy	
Omega-3 fatty acid supplementation		
Folic acid supplementation		

CVD = cardiovascular disease; ACE = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker.

*—A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence. For information about the SORT evidence rating system, see page 1263 or <http://www.aafp.org/afpsort.xml>.

NOTE: For definitions of risk categories, see Table 2.

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TABLE 9

ALOHA: CVD Prevention Strategies

- Assess and stratify women into high, intermediate, lower, or optimal risk categories.
- Lifestyle approaches (i.e., smoking cessation, regular exercise, weight management, and heart-healthy diet) to prevent CVD are AHA/ACC class I (SORT A*) recommendations for all women and a top priority in clinical practice.
- Other CVD risk-reducing interventions should be prioritized on the basis of strength of recommendation and level of evidence, with the exception of lifestyle, which is a top priority for all women.
- Highest priority is intervention in women at high risk.
- Avoid interventions designated as AHA/ACC class III (e.g., hormone therapy, antioxidants; see Table 7).

CVD = cardiovascular disease; AHA = American Heart Association; ACC = American College of Cardiology; SORT = strength of recommendation taxonomy.

*—A = consistent, good-quality patient-oriented evidence. For information about the SORT evidence rating system, see page 1263 or <http://www.aafp.org/afpsort.xml>.

NOTE: For definitions of risk categories, see Table 2.

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STROKE PREVENTION IN ATRIAL FIBRILLATION

Women with atrial fibrillation, paroxysmal or permanent, are at significantly increased risk for stroke; although systemic anticoagulation, particularly in older women, reduces this risk,²² women are less likely than men to receive it.³⁵⁻³⁷ As with other interventions, the decision to treat depends on risk level, and treatment guidelines are similar for women and men (Table 6).¹ Women with atrial fibrillation who are at low risk for stroke (i.e., less than 1 percent per year) should be treated with aspirin at a dosage of 325 mg per day. Women at low risk include those younger than 60 years without heart disease or risk factors (e.g., hypertension, congestive heart failure, left ventricular dysfunction) and select older women with no risk factors for thromboembolism.²² Those at high or intermediate risk (i.e., 1 percent per year or greater) should receive warfarin anticoagulation with a goal International Normalized Ratio of 2 to 3. Persons with contraindications to warfarin anticoagulation should receive aspirin.

MANAGING HEALTH

Women must become more actively informed and work with physicians to manage their health, not just their illnesses. The mnemonic ALOHA can help physicians and women use the new guidelines effectively (Table 9).^{1,38} Several useful patient education pieces also

have been developed.^{38,39} With wider dissemination and adoption of the AHA guidelines,¹ CVD prevention practices in women may be enhanced, and CVD incidence and prevalence may decline. The gaps in sex-specific data identified in the systematic review process serve as a guide for researchers of future clinical trials to identify opportunities for reducing CVD risk in women.

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REFERENCES

- Mosca L, Appel LJ, Benjamin EJ, Berra K, Chandra-Strobus N, Fabunmi RP, et al., for the American Heart Association. Evidence-based guidelines for cardiovascular disease prevention in women. *Circulation* 2004; 109:672-93.
- Thom T, Haase N, Rosamond W, Howard VJ, Rumsfeld J, Manolio T, et al. Heart disease and stroke statistics—2006 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee [Published correction appears in *Circulation* 2006;113:e696]. *Circulation* 2006;113:e85-151.
- Hajjar I, Kotchen TA. Trends in prevalence, awareness, treatment, and control of hypertension in the United States, 1988-2000. *JAMA* 2003;290:199-206.
- Meigs JB, Stafford RS. Cardiovascular disease prevention practices by U.S. physicians for patients with diabetes. *J Gen Intern Med* 2000; 15:220-8.
- Qureshi AI, Suri MF, Guterman LR, Hopkins LN. Ineffective secondary prevention in survivors of cardiovascular events in the U.S. population: report from the Third National Health and Nutrition Examination Survey. *Arch Intern Med* 2001;161:1621-8.
- Persell SD, Baker DW. Aspirin use among adults with diabetes: recent trends and emerging sex disparities. *Arch Intern Med* 2004;164: 2492-9.
- Centers for Disease Control and Prevention. Missed opportunities in preventive counseling for cardiovascular disease—United States, 1995. *MMWR Morb Mortal Wkly Rep* 1998;47:91-5.
- Schrott HG, Bittner V, Vittinghoff E, Herrington DM, Hulley S, for the HERS Research Group. Adherence to National Cholesterol Education Program Treatment goals in postmenopausal women with heart disease. The Heart and Estrogen/Progestin Replacement Study (HERS). *JAMA* 1997;277:1281-6.
- Blomkalns AL, Chen AY, Hochman JS, Peterson ED, Trynosky K, Diercks DB, et al., for the CRUSADE Investigators. Gender disparities in the diagnosis and treatment of non-ST-segment elevation acute coronary

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- syndromes: large-scale observations from the CRUSADE (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of the American College of Cardiology/American Heart Association Guidelines) National Quality Improvement Initiative. *J Am Coll Cardiol* 2005;45:832-7.
10. Mosca L, Ferris A, Fabunmi R, Robertson RM. Tracking women's awareness of heart disease: an American Heart Association national study. *Circulation* 2004;109:573-9.
 11. Mosca L, Linfante AH, Benjamin EJ, Berra K, Hayes SN, Walsh BW, et al. National study of physician awareness and adherence to cardiovascular disease prevention guidelines. *Circulation* 2005;111:499-510.
 12. Abuful A, Gidron Y, Henkin Y. Physicians' attitudes toward preventive therapy for coronary artery disease: is there a gender bias? *Clin Cardiol* 2005;28:389-93.
 13. Rossouw JE, Anderson GL, Prentice RL, LaCroix AZ, Kooperberg C, Stefanick ML, et al., for the Writing Group for the Women's Health Initiative Investigators. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. *JAMA* 2002;288:321-33.
 14. Manson JE, Hsia J, Johnson KC, Rossouw JE, Assaf AR, Lasser NL, et al., for the Women's Health Initiative Investigators. Estrogen plus progestin and the risk of coronary heart disease. *N Engl J Med* 2003;349:523-34.
 15. Anderson GL, Limacher M, Assaf AR, Bassford T, Beresford SA, Black H, et al., for the Women's Health Initiative Steering Committee. Effects of conjugated equine estrogen in postmenopausal women with hysterectomy: the Women's Health Initiative randomized controlled trial. *JAMA* 2004;291:1701-12.
 16. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation* 2002;106:3143-421.
 17. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, et al.; Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; National High Blood Pressure Education Program Coordinating Committee. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension* 2003;42:1206-52.
 18. Bray GA, Vollmer WM, Sacks FM, Obarzanek E, Svetkey LP, Appel LJ, for the DASH Collaborative Research Group. A further subgroup analysis of the effects of the DASH diet and three dietary sodium levels on blood pressure: results of the DASH-Sodium Trial. *Am J Cardiol* 2004;94:222-7.
 19. American Diabetes Association. Implications of the diabetes control and complications trial. *Diabetes Care* 2003;26(suppl 1):S25-7.
 20. Poirier P, Giles TD, Bray GA, Hong Y, Stern JS, Pi-Sunyer FX, et al. Obesity and cardiovascular disease: pathophysiology, evaluation, and effect of weight loss: an update of the 1997 American Heart Association Scientific Statement on Obesity and Heart Disease from the Obesity Committee of the Council on Nutrition, Physical Activity, and Metabolism. *Circulation* 2006;113:898-918.
 21. Fiore MC, Bailey WC, Cohen SJ, Dorfman SF, Goldstein MG, Gritz ER, et al. Treating tobacco use and dependence. Clinical practice guideline. Rockville, Md.: U.S. Department of Health and Human Services Public Health Service, 2000.
 22. Fuster V, Ryden LE, Asinger RW, Cannon DS, Crijns HJ, Frye RL, et al. ACC/AHA/ESC guidelines for the management of patients with atrial fibrillation: executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines and Policy Conferences (Committee to Develop Guidelines for the Management of Patients with Atrial Fibrillation): developed in collaboration with the North American Society of Pacing and Electrophysiology. *J Am Coll Cardiol* 2001;38:1231-66.
 23. Gibbons RJ, Smith S, Antman E. American College of Cardiology/American Heart Association clinical practice guidelines: Part I: where do they come from? *Circulation* 2003;107:2979-86.
 24. Miller ER III, Pastor-Barriuso R, Dalal D, Riemersma RA, Appel LJ, Guallar E. Meta-analysis: high-dosage vitamin E supplementation may increase all-cause mortality. *Ann Intern Med* 2005;142:37-46.
 25. Grundy SM, Cleeman JI, Merz CN, Brewer HB Jr, Clark LT, Hunninghake DB, et al. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III Guidelines. *J Am Coll Cardiol* 2004;44:720-32.
 26. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. *Lancet* 2002;360:7-22.
 27. Nathan DM, Cleary PA, Backlund JY, Genuth SM, Lachin JM, Orchard TJ, et al., for the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Study Research Group. Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. *N Engl J Med* 2005;353:2643-53.
 28. American Diabetes Association. Standards of medical care in diabetes—2006 [Published correction appears in *Diabetes Care* 2006;29:1192]. *Diabetes Care* 2006;29(suppl 1):S4-42.
 29. Glassman AH, O'Connor CM, Califf RM, Swedberg K, Schwartz P, Bigger JT Jr, et al., for the Sertraline Antidepressant Heart Attack Randomized Trial (SADHEART) Group. Sertraline treatment of major depression in patients with acute MI or unstable angina [Published correction appears in *JAMA* 2002;288:1720]. *JAMA* 2002;288:701-9.
 30. Taylor CB, Youngblood ME, Catellier D, Veith RC, Carney RM, Burg MM, et al., for the ENRICH Investigators. Effects of antidepressant medication on morbidity and mortality in depressed patients after myocardial infarction. *Arch Gen Psychiatry* 2005;62:792-8.
 31. Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, Dagenais G. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators [Published corrections appear in *N Engl J Med* 2000;342:748, 1376]. *N Engl J Med* 2000;342:145-53.
 32. Dahlof B, Devereux RB, Kjeldsen SE, Julius S, Beevers G, de Faire U, et al., for the LIFE Study Group. Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. *Lancet* 2002;359:995-1003.
 33. Ridker PM, Cook NR, Lee IM, Gordon D, Gaziano JM, Manson JE, et al. A randomized trial of low-dose aspirin in the primary prevention of cardiovascular disease in women. *N Engl J Med* 2005;352:1293-304.
 34. Berger JS, Roncaglioni MC, Avanzini F, Pangrazzi I, Tognoni G, Brown DL. Aspirin for the primary prevention of cardiovascular events in women and men: a sex-specific meta-analysis of randomized controlled trials [Published correction appears in *JAMA* 2006;295:2002]. *JAMA* 2006;295:306-13.
 35. Humphries KH, Kerr CR, Connolly SJ, Klein G, Boone JA, Green M, et al. New-onset atrial fibrillation: sex differences in presentation, treatment, and outcome. *Circulation* 2001;103:2365-70.
 36. Fang MC, Singer DE, Chang Y, Hylek EM, Henault LE, Jensvold NG, et al. Gender differences in the risk of ischemic stroke and peripheral embolism in atrial fibrillation: the Anticoagulation and Risk factors In Atrial fibrillation (ATRIA) study. *Circulation* 2005;112:1687-91.
 37. Friberg J, Scharling H, Gadsboll N, Truelsen T, Jensen GB. Comparison of the impact of atrial fibrillation on the risk of stroke and cardiovascular death in women versus men (The Copenhagen City Heart Study). *Am J Cardiol* 2004;94:889-94.
 38. Mosca L. Cardiology patient page. Heart disease prevention in women. American Heart Association. *Circulation* 2004;109:e158-60.
 39. Johnson PA, Manson JE. Cardiology patient page. How to make sure the beat goes on: protecting a woman's heart. *Circulation* 2005;111:e28-33.