Review of the American Heart Association's guidelines for cardiovascular disease prevention in women

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Cardiovascular disease (CVD) is the leading cause of death of women in the United States and most of the developed world. The latest available data from the World Health Organization indicate that 16.6 million people around the globe die of CVD each year. World deaths from coronary heart disease (CHD) in 2002 totalled 7.2 million. One in seven women in Europe will die of CHD; in the United Kingdom > 1.2 million women are living with CHD. Despite advances in diagnosing and treating CHD, the disease accounts for the majority of CVD deaths in women in the United States, with more than 240 000 dying annually. Although coronary heart disease is the predominant cause of mortality for adult women in the United States, screening for coronary risk factors and coronary risk reduction interventions remains underused in women. In February of 2004, the American Heart Association published the first evidence-based guidelines for CVD prevention in women, consisting of a set of clinical recommendations tailored to a woman's individual level of risk.

Cardiovascular disease (CVD) is the leading cause of death of women in the United States and most of the developed world.^{1,2} The latest available data from the World Health Organization (WHO) indicated that 16.6 million people around the globe die of CVD each year. World deaths from coronary heart disease (CHD) in 2002 totalled 7.2 million. One in seven women in Europe will die of CHD; in the United Kingdom > 1.2 million women are living with CHD.^{3,4} Despite advances in diagnosing and treating CHD, the disease accounts for the majority of CVD deaths in women in the United States, with more than 240 000 dying annually.¹

Emerging data have reinforced important sex-related differences in the pathophysiology of CHD, its clinical presentation, diagnostic procedures, response to treatments, and adverse outcomes. Therefore, attention to specific features of CHD in women offers the potential to improve clinical outcomes and the heart health of women. Although coronary heart disease is the predominant cause of mortality for adult women in the United States, screening for coronary risk factors and coronary risk reduction interventions remains underused in women.⁵ In February 2004, the American Heart Association (AHA) published the first evidence-based guidelines for CVD prevention in women, consisting of a set of clinical recommendations tailored to a woman's individual level of risk.⁵ In an effort to educate health care professionals and raise awareness about methods for primary and secondary prevention of CVD, these evidence-based guidelines highlight recommendations for incorporation into clinical practice based on a literature review of 399 published clinical studies. The complete details of the process involved in the creation of the

guidelines for CVD prevention in women have been published.⁶

The following is a summary of the important highlights related to CHD as presented in the AHA's evidence-based guidelines for cardiovascular disease prevention in women.

CONCEPTS AND SPECTRUM OF RISK

The main concepts of the guidelines for CVD prevention in women were: (1) to provide a strategic plan for physicians to treat women with CVD based on a spectrum of CVD risk (table 1); (2) to empower women to take charge of their cardiovascular health by increasing awareness and providing educational tools with the emphasis on the fact that favourable lifestyle changes can decrease the CVD risk factors and prevent CVD and CHD; and (3) behavioural changes by women and the reshaping of clinical practice patterns by health care professionals can decrease dramatically the number of women disabled and killed by CHD. The guidelines link the aggressiveness of treatment based on the risk of developing one of the following: angina pectoris, myocardial infarction, or coronary disease death in the next 10 years, based on a standardised heart risk scoring method developed by the Framingham heart study.⁷ Women are stratified into three risk categories of high, intermediate and lower risk based on clinical diagnoses and the absolute Framingham risk score for women of a 10 year probability of a coronary event. Table 1 provides a summary of the risk classification. Women at high risk are those with a calculated 10 year CHD risk of > 20% and/or established CHD, diabetes, vascular disease or chronic kidney disease. Women at intermediate risk have a 10 year risk of 10–20% and may have multiple risk factors, metabolic syndrome, a first degree relative with CVD and may have subclinical coronary atherosclerosis as evidenced by coronary calcification. Women at lower risk are those with a 10 year risk of < 10% and may have a variable number of risk factors or metabolic syndrome. The optimal risk group is defined as women who lead a heart-healthy lifestyle and have desirable levels of risk factors.

CLINICAL RECOMMENDATIONS

The guidelines are prioritised based on strength of the recommendation divided into class, level of evidence, and generalisability index (G) (table 2). The clinical recommendations on lifestyle, risk factor and preventive drug interventions are based on the evidence rating system based on

Abbreviations: ACE, angiotensin converting enzyme; AHA, American Heart Association; ARB, angiotensin receptor blocker; CHD, coronary heart disease; CVD, cardiovascular disease; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; WHO, World Health Organization

Table 1 Spectrum of CVD risk in women (adapted from Mosca *et al*⁵)

Risk : based on Framingham global risk (10 year absolute CHD)	Clinical events
High risk: >20%	Established CHD, diabetes mellitus, peripheral arterial disease, abdominal aortic aneurysm, chronic renal disease*, cerebrovascular disease†
Intermediate risk: 10–20%	Subclinical CVD‡ (e.g. coronary calcification), multiple risk factors, markedly elevated levels of a single risk factor§, metabolic syndrome, family history of CVD (first degree relative(s) with early onset of CVD age <55 in men, <65 in women)
Lower risk: <10%	May include women with multiple risk factors, metabolic syndrome or one or no risk factors
Optimal risk: < 10%	Optimal level of risk factors and heart-healthy lifestyle

*The risk of CVD increases as chronic renal disease progresses to end stage kidney disease.

†If the affected vasculature is above the carotid arteries, the risk of CHD may not be high in patients with cerebrovascular disease. Carotid artery disease (>50% stenosis) confers a high risk of CHD.

‡In the setting of subclinical CVD, some patients will have >20% 10 year CHD risk and should be elevated to the high risk category.

§Most women with a single, severe risk factor will factor a 10 year risk <10%.

CHD, coronary heart disease; CVD, cardiovascular disease.

methods used in previous American College of Cardiology/ AHA guidelines.⁸

The AHA evidence-based cardiovascular prevention guidelines for women focused on the following:

- lifestyle interventions
- major risk factor interventions
- preventive drug interventions
- class III interventions.

A synopsis of the above interventions is presented below.

LIFESTYLE INTERVENTIONS

The following are the class I (useful and effective) supporting evidence B, recommended lifestyle interventions:

- G1: All women should be advised and encouraged:
 - **Cigarette smoking:** avoid smoking and environmental tobacco.
 - **Physical activity:** minimum of 30 minutes of moderate intensity physical activity (for example, brisk walking) on most days, preferably every day.
 - **Heart-healthy diet:** healthy eating pattern to include a variety of fruits, vegetables, grains, low-fat or non-fat dairy products, fish, legumes, and sources of protein low in saturated fat (for example, poultry, lean meats, plant sources). Limit saturated fat intake to < 10% of calories, cholesterol intake to < 300 mg/day, and limit intake of trans fatty acids.
 - **Weight maintenance/reduction:** Consistently encourage weight maintenance/reduction through an appropriate balance of caloric intake, physical activity, and formal behavioural programmes as needed to maintain/achieve a body mass index (BMI) between 18.5–24.9 kg/m² and a waist circumference < 35 inches.

Table 2 Classification and levels of evidence (reproduced from Mosca *et al*⁵ with permission)

Classification	Description
Class I	Intervention is useful and effective
Class IIa	Weight of evidence/opinion is in favour 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 randomised trials
B	Limited evidence from single randomised trial or other non-randomised studies
C	Based on expert opinion, case studies, standard of care
Generalisability index	
1	Very likely that results generalise to women
2	Somewhat likely that results generalise to women
3	Unlikely that results generalise to women
0	Unable to project if results generalise to women

- G2: Select group of women

- **Cardiac rehabilitation:** Women with a recent acute coronary syndrome or coronary intervention, 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 programme.

Other lifestyle interventions that may be recommended for women at high risk include the following class II, level B, G2 interventions:

- Class II a: **psychosocial factors:** Women with CVD should be evaluated for depression and refer/treat when indicated.
- Class II b: (1) **omega 3 fatty acids:** As an adjunct to diet, omega 3 fatty acid supplementation may be considered in high-risk women; and (2) **folic acid:** As an adjunct to diet, folic acid supplementation may be considered in high-risk women (except after revascularisation procedure) if a higher-than-normal level of homocysteine has been detected.

MAJOR RISK FACTOR INTERVENTIONS

The focus of the class I major risk factor interventions are hypertension, diabetes mellitus and dyslipidaemia.

Hypertension

Level of evidence A: G1 Blood pressure—drugs

Pharmacotherapy is indicated when blood pressure is $\geq 140/90$ mm Hg or an even lower blood pressure in the setting of blood pressure related target organ damage or diabetes. Include thiazide diuretics as part of the drug regimen for most patients unless contraindicated.

Level of evidence B: G1

Blood pressure: lifestyle

Encourage an optimal blood pressure of < 120/80 mm Hg through lifestyle approaches, including the dietary approaches to stop hypertension diet. (DASH).⁹

Diabetes mellitus

Class I level B: G1

For women with diabetes mellitus, lifestyle and pharmacotherapy should be used to achieve near normal HbA1c (< 7%).

Lipid management

Lifestyle modification and pharmacotherapy should be used to achieve ideal lipid values.

Class I, G1: women with high and intermediate risk

Optimal values of lipids and lipoproteins in women are low density lipoprotein cholesterol (LDL-C) < 100 mg/dl (< 2.6 mmol/l), high density lipoprotein cholesterol (HDL-C) > 50 mg/dl (> 1.3 mmol/l), triglycerides < 150 mg/dl (< 1.7 mmol/l), and non-HDL-C (total cholesterol minus HDL cholesterol) < 130 mg/dl (< 3.4 mmol/l) and should be encouraged through lifestyle approaches.

Women at high risk: class I, G1

- **Level B:** In high-risk women or when LDL-C is raised, saturated fat intake should be reduced to < 7% of calories, cholesterol to < 200 mg/day, and trans fatty acid intake should be reduced.
- **Level A:** Pharmacotherapy—initiate LDL-C lowering treatment (preferably a statin) simultaneously with lifestyle therapy in high-risk women with LDL-C $\geq$ 100 mg/dl ($\geq$ 2.6 mmol/l).
- **Level B:** Initiate statin treatment if LDL-C < 100 mg/dl (< 2.6 mmol/l) unless contraindicated and initiate niacin or fibrate treatment when HDL-C is low, or non-HDL-C is raised in high-risk women.

Women at intermediate risk: class I, G1

- **Level A:** Pharmacotherapy—initiate LDL-C lowering treatment (preferably a statin) if LDL-C is $\geq$ 130 mg/dl ($\geq$ 3.4 mmol/l) on lifestyle therapy.
- **Level B:** Niacin or fibrate therapy when HDL-C is low or non-HDL-C is raised after LDL-C goal is reached.

Women at lower risk: class II, G1

- **Class II a, level B:** Pharmacotherapy—consider LDL-C lowering therapy in low-risk women with 0 or 1 risk factor when LDL-C is $\geq$ 190 mg/dl ($\geq$ 4.9 mmol/l) or if multiple risk factors are present when LDL-C is $\geq$ 160 mg/dl ($\geq$ 4.1 mmol/l) (class IIa, level B) or niacin or fibrate therapy when HDL-C is low or non-HDL-C is raised after LDL-C goal is reached.

PREVENTIVE DRUG INTERVENTIONS

The guidelines include several pharmacologic interventions for women at high cardiovascular risk.

Women at high risk

Class I level A, G1 indications

- **Aspirin** (75–162 mg), or clopidogrel if intolerant to aspirin, should be used unless contraindicated.
- **β blockers** should be used indefinitely in all who have had a myocardial infarction or chronic ischaemic syndromes unless contraindicated.
- **Angiotensin converting enzyme (ACE) inhibitors** should be used (unless contraindicated).

Class I, level B

- **Angiotensin receptor blockers** (ARBs) should be used if there is clinical evidence of heart failure or an ejection fraction < 40% in patients who are intolerant to ACE inhibitors.

Women at intermediate risk

Class II, level B, G2

- **Aspirin:** Consider aspirin treatment (75–162 mg) in intermediate risk women as long as blood pressure is controlled and benefit is likely to outweigh risk of gastrointestinal side effects.

CLASS III LIFESTYLE INTERVENTIONS: NOT RECOMMENDED

The inclusion of a list of class III interventions which are not be used in women at risk represents a unique, clinically useful aspect of the guidelines for CVD disease prevention in women.

At the time of guideline publication, the evidence did not support the use of hormone therapy and antioxidant supplements for CVD prevention. Routine use of aspirin is not recommended for CVD prevention in lower risk women.

LIMITATIONS

Adhering to evidence-based guidelines is an important step toward improving women's healthcare and decreasing CVD mortality in women.¹⁰ However, as discussed in the guidelines for CVD prevention in women, there are several limitations in the development of any clinical guideline.⁵ Specific for these guidelines the following limitations are noteworthy:

- While the Framingham risk score performs well within subgroups at risk for CHD, it may not apply equally for all populations.
- Data selected to establish the guideline recommendations may not be a reflection of the individual patient being

Table 3 Summary of the priorities for prevention in clinical practice based on Framingham risk classification (adapted from Mosca *et al*⁶)

Women at high risk (>20% risk)	Women at intermediate risk (10–20% risk)	Women at lower risk (<10% risk)
Class I: Smoking cessation, diet therapy, weight maintenance, physical activity/cardiac rehabilitation, blood pressure control, lipid control/statin treatment. Pharmacotherapy of: aspirin, β blocker, ACE inhibitors (ARBs if contraindicated), glycaemic control in the setting of diabetes mellitus	Class I: Smoking cessation, heart healthy diet, physical activity, blood pressure and lipid control, weight reduction.	Class I: Smoking cessation, heart healthy diet, physical activity, weight reduction and treatment of individual risk factors for CVD
Class IIa: Evaluation and treatment for depression Class IIb: Dietary supplementation with omega 3 fatty acids and folic acid	Class IIa: Aspirin treatment	

ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; CVD, cardiovascular disease.

treated and there can be variation in individual patient responses.

- The clinical cardiovascular end points included in the guidelines may not be an adequate reflection of clinically important and relevant end points, such as quality of life, symptoms, functional status and hospitalisations.

Overall, it must be remembered that the guidelines for CVD prevention in women are not a substitute for good clinical practice.⁵

CONCLUSION

Overwhelming evidence suggests that CVD can be prevented in both women and men.⁵ Clinical presentations of CHD and management strategies differ between the sexes. Underutilisation of proven beneficial treatments is a contributor to less favourable outcomes in women. The increased application of appropriate contemporary diagnostic, therapeutic, and interventional managements has favourably altered the prognosis for women, particularly when the data are adjusted for baseline characteristics. Table 3 represents a modified summary of the priorities for prevention in practice according to risk group as stated in the evidence-based guidelines for CVD prevention in women.⁵

Although not included in the official publication of the evidence-based guidelines for CVD prevention in women,⁵ the guideline summary which was published for a lay audience included a simplified approach. The factors of awareness, knowledge and action were incorporated into the mnemonic “ALOHA” in saying “goodbye” to CVD.¹¹ As outlined below, ALOHA can be a useful tool in empowering women to take charge of their cardiovascular health.

THE ALOHA: SAY FAREWELL TO HEART DISEASE

- **A:** Assess and stratify women into high, intermediate, lower, or optimal risk categories
- **L:** Lifestyle approaches (smoking cessation, regular exercise, weight management, and heart-healthy diet) are a top priority to prevent CVD (class I)
- **O:** Other CVD risk reducing interventions should be prioritised on the basis of strength of recommendation (class I > class IIa > class IIb) and within each class of recommendation on the basis of the level of evidence, with the exception of lifestyle, which is a top priority for all women (A > B > C)
- **H:** Highest priority for risk intervention in clinical practice is based on risk stratification (high risk > intermediate risk > lower risk > optimal risk)
- **A:** Avoid interventions designated as class III.

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