

CMDManagement™

INSIGHTS AND INFORMATION ON **CARDIOVASCULAR AND METABOLIC DISEASES**

VOL. 11, NO. 2 SUMMER 2006

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LEARNING OBJECTIVES

After reading this issue of *CMDManagement™*, participants should be able to:

- Discuss the perceived "gender gap" inherent with the prevention, diagnosis, and management of CVD and identify strategies to diminish it based on recent clinical evidence
- Identify the advantages and potential limitations of current CVD risk-assessment algorithms, including the Framingham risk equation and coronary artery calcium scoring
- Recognize the importance of early, multifactorial risk-factor management as a means to reduce CVD risk, particularly in women
- Determine the extent to which social support systems influence adherence to lifestyle changes and therapeutic regimens

Target audience: primary-care physicians, cardiologists, endocrinologists

Release/End dates: 7/12/2006–7/12/2007

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STAFF DISCLOSURES: Sr Managing Editor Nancy Salerno, Managing Editor Danielle Gabriel, and Sr Medical Writer Mark Palangio have no relevant financial relationships to disclose.

The CCMD is supported by unrestricted educational grants from Pfizer Inc, Reliant Pharmaceuticals, Abbott Laboratories, and Takeda Pharmaceuticals North America, Inc.

CMDManagement™ is supported by an unrestricted educational grant from Pfizer Inc.

Women and Cardiovascular Disease: Strategies for Improved Prevention, Detection, and Treatment

Cardiovascular disease (CVD), which includes coronary heart disease (CHD), stroke, and other diseases related to the heart and vasculature, is the leading cause of death among women in the United States, accounting for more than 500,000 deaths per year.¹ Considering that the CVD mortality rate in women has remained relatively stable over the past 2 decades, several recent studies have focused on strategies for preventing, detecting, and treating CVD in women. This article reviews the latest research in this area.

Awareness, Prevention, and Barriers to Cardiovascular Health

Although the rate of awareness of CVD as the leading cause of death among women has nearly doubled in the past decade (30% in 1997 vs 55% in 2005)², it is uncertain whether this awareness translates into increased action by women to reduce their personal risk. In a recent women's-health study, 1,008 women were given a standardized questionnaire about awareness, preventive action, and barriers to CV health.² Awareness was significantly greater among white women than black and Hispanic women (62% vs 38% and 34%, respectively). In logistic regression models, awareness of CVD as the leading cause of death independently correlated with increased physical activity (odds ratio [OR], 1.35; 95% confidence interval [CI], 1.00–1.83) and weight loss (OR, 1.47; 95% CI, 1.14–2.02) for the previous year. Preventive action was also associated with perception of high- versus moderate- or low-risk status, and most women took action to lower risk in family members and in themselves. Commonly cited barriers to CV health were confusion in the media (49%), the belief that health is determined by a higher power (44%), and caretaking responsibilities (36%). These findings suggest that, although recent educational efforts underscoring CVD risk in women have been generally effective, better efforts targeting racial/ethnic minority women are needed.

Assessing CHD Risk

Framingham Risk Equation

CHD risk is commonly assessed using the Framingham risk equation (FRE), a method that categorizes asymptomatic adults and their primary-prevention needs for therapy according to 10-year risk for hard CHD events: low-risk, <10%; intermediate-risk, 10% to 20%; high-risk, ≥20%. The National Cholesterol Education Program (NCEP) has adopted FRE to target LDL-C.³ However, FRE does not incorporate several important risk factors (family history, exercise and diet, obesity, and metabolic syndrome) and, based on its estimates, few women under age 70 qualify for preventive pharmacotherapy despite relatively high lifetime risk.⁴ Therefore, current NCEP guidelines may fail to identify a large portion of women with subclinical atherosclerosis and underestimate cardiovascular risk in women.

Coronary Artery Calcium Scoring

Accumulating evidence suggests that coronary artery calcium (CAC) measurement using electron-beam or multidetector computed tomography to detect subclinical atherosclerosis may be a more accurate means than FRE for assessing CHD risk in women. A study evaluating the relationship between family history and CAC-measured

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Women and CVD

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Read about gender disparities in CVD on page 4

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subclinical atherosclerosis among 102 asymptomatic women (mean age 51±7 years; 40% African-American; sisters of a family member hospitalized with premature CHD) found that 40% had detectable CAC, 12% had at least moderate plaque burden (CAC scores >100 Agatston units), and 6% had extensive plaque burden (≥400 units) despite that 98% were classified as low risk according to FRE.⁴ Moreover, among low-risk patients, 32% demonstrated significant subclinical atherosclerosis (>75th percentile age-gender CAC score).

A more extensive study examined the adequacy of FRE for identifying CAC in 2,447 nondiabetic asymptomatic women (mean age 55±10 years).⁵ Although 90% of patients were classified as low risk by FRE, 33% had detectable CAC, 10% had CAC scores >100 Agatston units, and 3% had CAC scores ≥400. Significant CAC (>75th percentile) was apparent in 20% of participants. Furthermore, 84% of women with CAC were classified as low-risk, and 45% of low-risk women with ≥2 CHD risk factors and a family history of premature CHD had significant CAC. These results suggest that the selective use of CAC scoring in women aged ≥45 with either the metabolic syndrome or a family history of early CHD may provide incremental prognostic value over FRE. (See Figure 1.)

A New Algorithm

In light of such findings, a risk-assess-

ment algorithm incorporating CAC scoring with FRE was recently proposed for better identification of high-risk individuals needing aggressive treatment; those with no or very mild CHD requiring a more conservative LDL-C goal; and women and young adults, who are more likely to be classified as low risk in the presence of multiple risk factors.⁶

In this model, 10 years are added to chronological age for CAC scores from the 75th to 90th percentile, and 20 years are added for CAC scores above the 90th percentile. Additionally, among those in whom a positive CAC score is the norm (men ≥55 years; women ≥65 years), a CAC score of 0 will yield an age point score that corresponds with the age group whose median CAC score is 0 (ie, 40–44 years for men; 55–59 years for women). (See Figure 2.)

Additional Research

Further studies have examined the classification of cardiovascular risk in women and young individuals according to NCEP Third Adult Treatment Panel (ATP III) guidelines across a continuum of CAC scores in 1,611 asymptomatic patients (67% men; mean age 53±10 years).⁷ In this study, participants were categorized as low (46%), intermediate (36%), moderately high (16%), and high (2%) risk. A high CAC score percentile (≥75th) and a high CAC score (≥400 Agatston units) were noted in 26% and 9% of patients, respectively. Based on these guidelines,

Figure 1: CHD Risk Assessment: NCEP Classification According to CAC Burden

CAC Score (Agatston units)	Intermediate-risk FRE	Low-risk FRE
<100 (n=2,200)	180 (8%)	2,020 (92%)
<400 (n=2,364)	219 (9%)	2,145 (91%)
<75th percentile (n=1,958)	168 (9%)	1,790 (91%)
>100 (n=247)	69 (28%)	178 (72%)
>400 (n=83)	30 (36%)	53 (64%)
≥75th percentile (n=489)	81 (16%)	408 (84%)

CAC = coronary artery calcium; FRE = Framingham risk equation; NCEP = National Cholesterol Education Program

73% and 59% of patients with a high CAC score percentile and CAC score, respectively, were not identified as high risk or candidates for pharmacotherapy. These differences were especially evident for women and young patients. The results suggest that NCEP guidelines may underestimate cardiovascular risk in women and young, asymptomatic individuals. Evaluation of plaque burden for such patients may provide added value to global risk assessment.

Familial predisposition to CAC and the presence of multiple metabolic risk factors have also been linked.⁸ A cross-sectional study of 6,141 consecutive, asymptomatic, nondiabetic patients found that those with a family history of premature CHD were more likely to have a higher burden of CAC (prevalence of any CAC, CAC score ≥ 100 Agatston units, and CAC ≥ 75 th age-gender percentile) in the presence of ≥ 2 metabolic risk factors than those without any family history for CHD.

Risk-Factor Management

Obesity, Physical Inactivity, and Hypertension

Although obesity and physical inactivity are recognized as CHD risk factors, the relative predictive importance of each is unclear, particularly among women. Li et al followed 88,393 women (aged 34–59) without CVD in the Nurses’ Health Study from 1980

to 2000, demonstrating that physical activity and adiposity were independent CHD risk factors.⁹ Adjusting for CV risk factors through multivariate analysis confirmed that overweight and obesity (BMI ≥ 30 kg/m²) were significantly associated with increased CHD risk, whereas increasing levels of physical activity were associated with a graded reduction in CHD risk ($P < 0.001$). The lowest risk was found in women who were both lean and physically active, although neither characteristic eliminated the risks associated with being sedentary or obese. Using women who were at a healthy weight (BMI 18.5–24.9 kg/m²) and were physically active (exercise ≥ 3.5 hr/wk) as the reference group, analysis confirmed CHD relative risks were 3.44 (95% CI, 2.81–4.21) for women who were obese and sedentary (exercise < 1 hr/wk), 2.48 (95% CI, 1.84–3.34) for women who were active but obese, and 1.48 (95% CI, 1.24–1.77) for women who were at a healthy weight but were sedentary. Furthermore, waist-to-hip ratio was shown to be a significant predictor of CHD. Remarkably, even a modest weight gain (9–22 lb) was associated with a 27% (95% CI, 12%–45%) increased CHD risk.

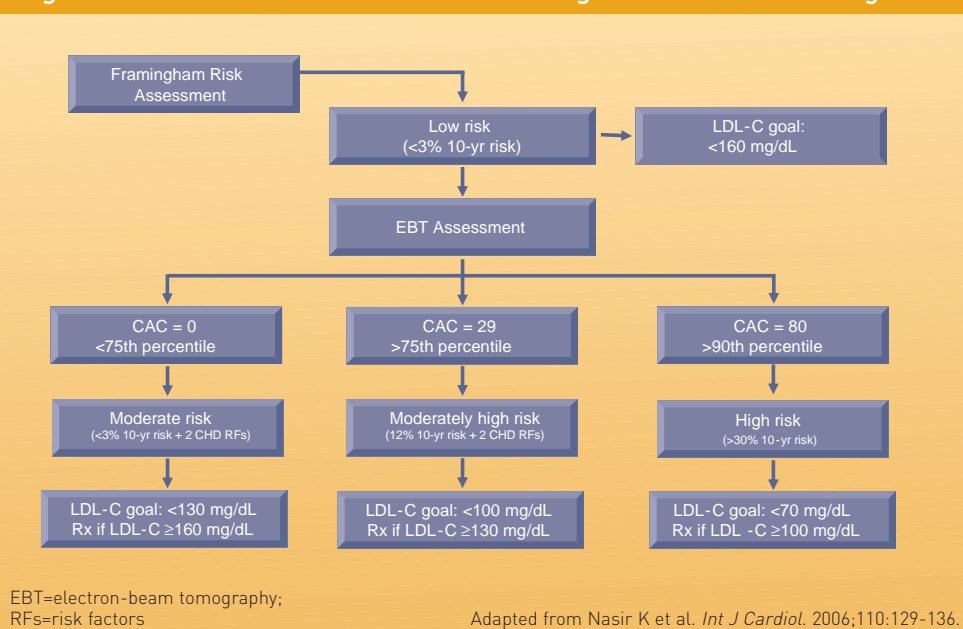
Along with obesity and physical inactivity, hypertension is a major risk factor for CVD development and an

independent risk factor for death after acute coronary syndrome (ACS). However, little is known about its effects in women and men presenting with ACS. To that end, Frazier and colleagues examined the prevalence and treatment of hypertension among 15,904 ACS patients. The overall prevalence of hypertension among individuals in the United States was determined to be 54%, with more women than men being diagnosed with hypertension (63% vs 50%). Use of calcium-channel blockers and diuretics was higher in women, whereas men were more likely to receive treatment with beta-blockers; use of angiotensin-converting enzyme inhibitors was similar for both. Women were treated with multiple antihypertensive agents more frequently than men were (2 agents, 35% vs 30%; ≥ 3 agents, 16% vs 13%). Diuretics were the only class in which female sex independently predicted drug-class use (OR, 2.1; 95% CI, 1.6–2.7). Results indicate that hypertension management varies by sex, and that opportunities exist to improve outcomes in women.

Management of Stable Angina

Although women are more likely than men to present with stable angina, they are treated less aggressively.¹¹ This apparent gender bias in managing angina prompted Daly and colleagues to evaluate differences in the management and outcome of stable angina between men and women at 1 year among 3,779 patients enrolled in the Euro Heart Survey of Stable Angina.¹¹ They found that women presenting with stable angina were less likely to undergo an exercise electrocardiogram (OR, 0.81; 95% CI, 0.69–0.95) or to be referred for coronary angiography (OR, 0.59; 95% CI, 0.48–0.72). Both at initial assessment and at 1 year, women received antiplatelet and statin therapies significantly less frequently than men, even upon coronary disease detection. Furthermore, women were less likely to be revascularized and twice as likely to suffer death or nonfatal myocardial infarction during the 1-year follow-up period (hazard ratio [HR], 2.09; 95% CI, 1.13–3.85).

Figure 2: CHD Risk Assessment: Combining FRE and CAC Scoring



CASE STUDY

Gender Disparities in the Diagnosis, Treatment, and Prevention of Coronary Heart Disease—Are Men and Women Treated Equally?



FEMALE PATIENT

INITIAL

Physical Exam:

- ◆ Height: 5'2"
- ◆ Weight: 206 lb
- ◆ Body mass index (BMI): 37.7 kg/m²
- ◆ Waist circumference: 39"
- ◆ Hip circumference: 35"
- ◆ Waist-to-hip ratio (WHR): 1.11
- ◆ Average sitting blood pressure (BP): 148/86 mm Hg (on medication; two readings)

Lab Findings:

- ◆ Fasting blood glucose (FBG): 102 mg/dL
- ◆ TC: 263 mg/dL
- ◆ TG: 121 mg/dL
- ◆ LDL-C: 183 mg/dL
- ◆ HDL-C: 56 mg/dL
- ◆ Chem-8: within normal limits
- ◆ Hematocrit (HCT): 32%

The following cases were provided by CCMD Education Council Member Thomas A. Pearson, MD, MPH, PhD, and Laurie A. Kopin, MS, RN, ANP. Dr. Pearson is the Albert D. Kaiser Professor and Chair of the Department of Community and Preventive Medicine, and a Professor of Medicine at the University of Rochester Medical Center (URMC) in New York. Ms. Kopin is an Associate Professor of Nursing and Senior Instructor of Medicine at URMC. She is also the Senior Nurse Manager and Nurse Practitioner for the Strong Heart Cardiac Rehabilitation and Preventive Cardiology Program, also at URMC.

Disclosure information for Dr. Pearson: speakers bureau for Abbott Laboratories, AstraZeneca, Bristol-Myers Squibb (BMS); Kos Pharmaceuticals, Inc., Pfizer Inc, Merck/Schering Plough (M/SP) Pharmaceuticals; retained consultant for BMS, Bayer, Forbes/Medi-Tech Inc., Johnson & Johnson-Merck, M/SP, Sanofi Aventis; grant/research support from Kos Pharmaceuticals, Inc., Merck & Co., Inc., Pfizer Inc, Sanofi Aventis.

Ms. Kopin has no relevant financial relationships to disclose.



Is there a “gender bias” in the diagnosis, treatment, and prevention of coronary heart disease (CHD)? This case study aspires to address that vital question by chronicling two patients—one female, the other male—with a similar coronary disease presentation and examining how each is diagnosed and treated to provide insights into the prevention of cardiovascular disease (CVD) in women. CVD is the leading cause of death for similar proportions of women and men (51% and 48%, respectively).¹ Still, cardiology clinics, cardiac rehabilitation programs, and risk-factor management programs consists largely of male patients. Why?

Case Study—Female Patient

JC is 45-year-old African-American woman who works as a caseworker for her state’s unemployment department. For the past several months, she has experienced increasing lethargy associated with heavier-than-normal vaginal bleeding and lower-back discomfort during her menstrual cycles. Assuming these symptoms were due to premenstrual syndrome and potential perimenopause, JC saw her gynecologist and PCP, both of whom diagnosed anemia.

Over the next 3 months, JC received oral iron supplementation and two units of packed red blood cells. She was also given dietary advice regarding her hypercholesterolemia, although no lipid-lowering medications were prescribed. Despite the transfusions and subsequent increase of her HCT to 40%, her back discomfort and lethargy persisted over the next few months.

One evening while cooking dinner after a stressful workday, JC’s back pain exacerbated, radiating up between her shoulder blades and causing her to

become nauseated and diaphoretic. One of her sons noticed her slumped over the kitchen table nearly unresponsive. JC was taken via ambulance to a local emergency department, where she was found to have ST-segment elevations in her inferior and lateral leads. She was given morphine sulfate for pain relief and transported to the Invasive Cardiology Laboratory. Her angiogram revealed severe triple-vessel disease requiring emergency coronary artery bypass grafting (CABG) x 4. She ruled in for an inferolateral myocardial infarction (MI) by troponin level and electrocardiography. Her left ventricular ejection fraction (LVEF) was moderately reduced at 40%.

For the past 8 years, JC has had pharmacologically treated hypertension (amlodipine 10 mg qd and hydrochlorothiazide 25 mg qd). Her mother died from stroke at age 52 and her father of an MI at age 38. She has 9 brothers and 4 sisters, among whom one or more carries a diagnosis of hypertension, diabetes, hypercholesterolemia, cardiomegaly, coronary artery disease (CAD) with CABG and

percutaneous coronary intervention, MI, peripheral vascular disease, or limb amputations. JC is married with three teenage sons. She has never smoked, nor does she drink alcohol or caffeine.

Case Study—Male Patient

DH is a 31-year-old Caucasian male with known hyperlipidemia since age 24, at which time his TC was 450 mg/dL; he was prescribed lovastatin 20 mg qd and given dietary counseling. DH has always been very physically active and, in fact, was training for his second triathlon when he began to experience shortness of breath while exercising. He attributed this to his exercise asthma, which he has had for a number of years, initially ignoring the symptoms and using only his inhalers for relief. At age 28, while playing basketball at the high school where he teaches English, he began to experience typical shortness of breath accompanied by a dull chest pressure that seemed to radiate to his neck. He became lightheaded and experienced a syncopal episode. Shortly after, he regained consciousness and insisted on seeing his PCP the next morning rather than immediately going to the emergency department.

After a thorough evaluation, DH was referred for a cardiology consultation. One week later, he underwent a stress echocardiogram, which revealed both anterior and lateral ischemic defects with a well-preserved LVEF of 55%. The next day, an emergency angiogram identified severe triple-vessel disease. Subsequently, DH underwent CABG x 3.

DH has no history of hypertension and is now taking atorvastatin 40 mg qd for hypercholesterolemia. His paternal grandfather died from an MI at age 40, and his maternal grandfather suffered an MI while in his 40s, eventually undergoing CABG at age 76. DH has one brother (34-years-old) who also has hypercholesterolemia. DH is married with two young sons. He has never smoked and drinks two beers on the weekend and one cup of coffee daily.

1-Year Follow-Up: Male Versus Female

After their CABG surgeries, JC and DH were referred to a cardiac rehabilitation center, where they received intensive lifestyle counseling to encourage appropriate dietary, exercise, and stress-management changes as part of a secondary CHD prevention effort. Beyond this, their individual courses of therapy differed significantly.

DH's Treatment Course

DH faithfully attended cardiac rehabilitation three times per week for 3 months, completing an outpatient Phase II Program. With his wife's support, he participates in a Phase III Maintenance Program, working closely with his registered dietitian, exercise physiologist, and psychologist. He continues to exercise at a local health club and frequently fits in a midday workout at the school where he works. Semi-annually, he reports to the Preventive Cardiology Clinic and continues to maintain his weight and high fitness level, as demonstrated on his annual exercise tolerance test. DH closely adheres to his pharmacologic treatment regimen, which includes a statin, beta-blocker, angiotensin-converting enzyme inhibitor, and aspirin. Additionally, his current lipid profile (TC 119 mg/dL, TG 63 mg/dL, LDL-C 76 mg/dL, HDL-C 30 mg/dL) is consistent with targets set forth by the Third Adult Treatment Panel of the National Cholesterol Education Program (NCEP ATP III), with the exception of his low HDL-C, which is likely genetically determined.

JC's Treatment Course

JC attended cardiac rehabilitation for just 2 weeks before abandoning the program, citing her work and family obligations and inability to afford co-pays. The program staff suggested she exercise before or after work and offered her a full financial scholarship to assist with co-pay coverage. Despite these efforts, JC did not return the program's calls.

During her 12-month follow-up visit to the Preventive Cardiology Clinic (she missed her 6-month follow-up appointment), JC was quick to note that after a



MALE PATIENT

INITIAL

Physical Exam:

- ◆ Height: 5'9"
- ◆ Weight: 171 lb
- ◆ BMI: 35.2 kg/m²
- ◆ Waist circumference: 34"
- ◆ Hip circumference: 31"
- ◆ WHR: 1.10
- ◆ Average sitting BP: 124/80 mm Hg (two readings)

Lab Findings:

- ◆ FBG: 90 mg/dL
- ◆ TC: 178 mg/dL
- ◆ TG: 115 mg/dL
- ◆ LDL-C: 130 mg/dL
- ◆ HDL-C: 25 mg/dL
- ◆ Chem-8: within normal limits

Women and CVD

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Ischemic Heart Disease Assessment

In assessing gender differences in the presentation, evaluation, and outcomes for ischemic heart disease (IHD), data from the Women's Ischemia Syndrome Evaluation (WISE) have confirmed that evaluating IHD is more difficult in women than in men because of greater symptom burden, higher functional disability rate, and lower prevalence of obstructive CAD by coronary angiography.¹²

Furthermore, women with IHD have more adverse outcomes despite evidence of lower angiographic disease burden than men. Most notably, WISE data showed that women evaluated for symptoms of myocardial ischemia had low rates of obstructive CAD at angiography. Nearly 50% of women referred for evaluation of suspected myocardial ischemia did not have obstruction, and the prognosis for future cardiac events and persistent symptoms among these women was intermediate.¹³

It has been suggested that women may have a unique risk profile characterized by hypoestrogenemia and a dysmetabolic state that induces symptoms and ischemia in the setting of nonobstructive CAD. As such, chest pain symptoms are less accurate predictors of obstructive CAD in women than in men, and clinicians should not disregard nonobstructive coronary angiograms in women. Such findings point to the need for new paradigms in assessing women for IHD.

Hormone Replacement Therapy and CVD

Women's Health Initiative (WHI) trials have compared the risks and benefits of hormone replacement therapy with estrogen plus progestin and estrogen alone in postmenopausal women. The WHI estrogen plus progestin trial was terminated early after a mean follow-up of 5.2 years due to increased CHD, stroke, and venous thromboembolic

disease risk. Despite the halting of this trial, the estrogen-alone trial continued with increased vigilance.¹⁴ A total of 10,739 mostly healthy, postmenopausal women (aged 50–79 years) with prior hysterectomy were randomly assigned either 0.625 mg qd of conjugated equine estrogen (CEE) or placebo. Over an average of 6.8 years, CEE was found to increase stroke risk (HR, 1.39; 95% CI, 1.10–1.77), decrease hip fracture risk (HR, 0.61; 95% CI, 0.41–0.91), and not significantly affect CHD incidence (HR, 0.91; 95% CI, 0.75–1.12) or total mortality (HR, 1.04; 95% CI, 0.88–1.22). The data also suggest a possible reduction in breast cancer risk (HR, 0.77; 95% CI, 0.59–1.10). Because the burden of incident disease events was comparable among women treated with CEE or placebo, the WHI Steering Committee recommends that estrogen replacement therapy should not be used for chronic disease prevention in postmenopausal women. The WHI results are consistent with current US Food and Drug Administration recommendations for postmenopausal women to use CEE only for menopausal symptoms at the smallest effective dose for the shortest possible time.

Conclusions

Mounting evidence suggests a gender bias for CVD based on recent studies revealing a greater decrease in CHD mortality in men than in women over the past 2 decades. CVD diagnosis is a greater challenge in women than in men, in whole or in part due to the perceived failure of traditional risk-factor assessment to accurately and reproducibly identify a large portion of women who are at increased CVD risk. Moreover, the clinical literature indicates that quality of care for dyslipidemia, stable angina, and hypertension is seen as substandard among women. Thus, an urgent need exists for improved strategies in preventing, detecting, and treating CVD in women. ♥

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Considering... Heart Disease and Women

What You Need to Know to Reduce Your Risk

SUMMER 2006

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Report From the
Committee on Cardiovascular and Metabolic Diseases™

What's So Important About Heart Disease?

Although *coronary heart disease (CHD)* is the leading cause of death for US women—killing 500,000 each year, which amounts to about one death per minute—a surprising amount of women (just 13%) view it as their greatest health threat. *Cardiovascular disease (CVD)* includes many deadly conditions, including *heart attack* and *stroke*. Understanding your risk for these diseases and what you can do to prevent them can truly mean the difference between life and death.

Isn't CHD a "Man's Disease"?

No! Although women develop CHD about 10 years later than men do, women of all ages should be aware of their risk. *Consider this:* women are *six times* more likely to die of CHD than breast cancer. Plus, after having a severe, sudden event, such as a heart attack, women are more likely than men to die within 1 year. By age 65, a woman's risk is usually the same as a man's.

What Are the Risks for CHD in Women?

They're the same for men and women. Some are *controllable*, meaning they can be treated and sometimes even reversed with appropriate *lifestyle changes*, including a healthy diet and exercise. Prescription medications may also be used to help patients reach their goals. Other risk factors, such as family history and age, cannot be controlled. With your doctor's help, you can find out your risk and create a prevention plan that's right for you.

Are There Any Symptoms of CHD and Stroke to Look Out For?

Although chest pain is not always caused by CHD, it should still be a cause for concern. *Consider this:* 64% of women who died suddenly of CHD had no previous symptoms.

Contact your doctor immediately if you experience:

- pressure, heaviness, or a sensation of tightness/squeezing in your chest
- pain in your shoulder, neck, or jaw
- sudden shortness of breath, indigestion, palpitations, or nausea and/or vomiting
- numbness/weakness in the face, arm, or leg (usually on one side of the body)
- confusion or trouble speaking, understanding, or seeing in one or both eyes
- difficulty walking or a feeling of dizziness or loss of balance
- severe headache without cause

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Controllable Risk Factors

What You Can Do

High cholesterol

- Your level should be *less than 100 mg/dL*
- Limit dietary cholesterol by replacing lean meats like chicken (roasted or baked without skin) for red meats; also opt for fat-free/low-fat dairy products and egg substitutes

High blood pressure

- Your blood pressure should be *less than 120/80 mm Hg*
- Always look for *sodium* (salt) content on nutrition labels; your daily intake should be *less than 2,400 mg*
- Use a salt substitute and eliminate salty foods like potato chips from your diet

Overweight/Obesity

- Avoid *saturated* and *trans* fats (found in red meats, high-fat dairy products, and processed or "junk" foods)
- Keep fat calories to *30% or less* of your total daily calories
- Get moving! Exercise for 15 to 30 minutes on most days (remember to check with your doctor before starting an exercise routine)

Smoking

- If you smoke, quit; if you don't smoke, don't start! Quitting can lower your heart attack risk by one-third within 2 years!
- Try an over-the-counter nicotine product or ask your doctor about prescription medications that can help you to stop

Diabetes

- Schedule and keep regular check-ups with your doctor
- Exercise regularly and eat a low-fat diet as recommended by your doctor
- Always take the diabetes medicines that your doctor has prescribed

CASE STUDY continued from page 5

long day of work with few or no breaks, she is burdened with family and home responsibilities. She stated that she “has no time” for herself and feels exhausted “all of the time.” Upon further questioning, JC admitted to having experienced ongoing anginal symptoms during the past year and, for the past 6 months, to not taking her cardiac medications once the refills expired. She has gained 15 lbs and is suffering from depressive-type symptoms. Her previsit exercise tolerance test reveals new 1- to 2-mm ST-segment depression, and her LDL-C is well above goal at 169 mg/dL.

Why Such Different Outcomes?

Although both patients experienced and underwent similar coronary events and procedures, they look very dissimilar 1 year later. Could their disparities be due to the so-called “gender gap”? Differences in minority and socioeconomic status (SES)? Lack of social support? Challenges with adherence and the resultant “treatment gap” that frequently plague healthcare providers? Importantly, has JC’s nonadherence to lifestyle changes contributed to the progression of her disease and, hence, her less favorable prognosis? To what extent do social support systems influence adherence to lifestyle changes and therapeutic regimens?

The Gender Gap

Significant attention has focused on the adequacy of cardiovascular care for women, specifically regarding the presentation, diagnosis, and treatment of acute coronary syndromes (ACS). For example, the Red Dress Campaign, a population-wide effort spearheaded by the American Heart Association, has identified CHD as a disease for which women often have atypical symptoms.¹

Gender-based differences in the vascular wall, metabolic alterations, or atherosclerotic plaque deposition may be associated with poor outcomes in women.² Evidence also suggests that women display substantial delay in healthcare-seeking behavior, less intensive resource-use patterns, and longer times to diagnosis when compared with men.³ This so-called “gender gap” in the

presentation, diagnosis, and treatment of CHD in women alludes to an underutilization of medical services. As a result, a recent upward trend toward referrals for invasive procedures (eg, surgical revascularization) for women has been noted.⁴ Conversely, it has also been shown from the Women’s Ischemia Syndrome Evaluation (WISE) study database that nearly 60% of women undergoing invasive evaluation for investigation of chest pain or abnormal noninvasive tests do not have flow-limiting coronary stenoses at angiography.⁵ However, these women also suffered persistent (or worsening) symptoms, were often chronically disabled, used tremendous healthcare resources, and, most importantly, experienced adverse cardiovascular events over 4 to 5 years.

Further compounding the gender gap is the frequency, persistence, and intensity of anginal symptoms in women, resulting in more hospitalizations than in men. Women also report more frequent symptoms of anxiety, depression, and physical-exertion limitations than men, which feeds the challenge of equal and appropriate medical resource utilization.^{6,7} Underappreciation of presenting symptoms among female patients has resulted in misdiagnoses and under- or overuse of invasive and noninvasive testing. The question remains whether the reduced intensity of care and underdiagnosis of

CHD in women is due in part to atypical clinical presentation, symptoms, and lower acuity level contributing to poor outcomes.^{8,9}

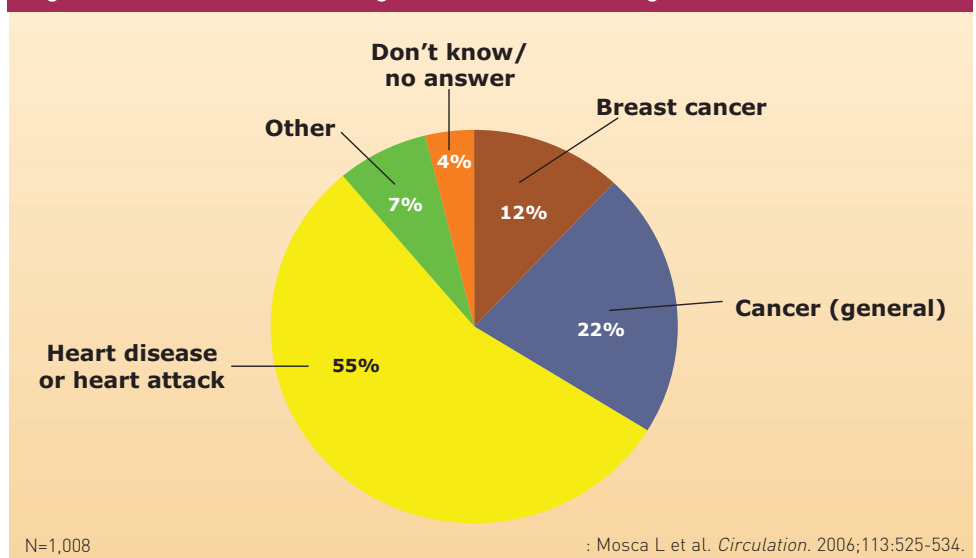
Based on abnormal HCT and Hgb (not included in initial lab frame) values, JC’s healthcare providers diagnosed anemia rather than a cardiac-related condition. This is not unusual. Anemia has recently been linked to worsening outcomes in women who present with low Hgb values with suspected ischemia.¹⁰ Adverse outcomes have been noted in these women, many of whom have suspected acute MI or heart failure.

Minority/Socioeconomic Status and Social Support

Disease and death rates for minority populations such as African-Americans are disproportionately high compared with their Caucasian counterparts with similar disease states (eg, cardio- and cerebrovascular disease, type 2 diabetes).¹ Notably, black women have a higher rate of first MI than white women between ages 45 and 74.

Interestingly, both the occurrence and progression of these diseases are partially attributable to risk factors that can be minimized or eliminated with therapeutic lifestyle changes and medications if appropriate. Much debate has centered on reasons for the apparent poor adherence to necessary lifestyle changes for risk reduction among

Figure 1: Awareness of Leading Cause of Death Among Women



minority populations, especially women. It has been suggested that SES influences on adherence include income level, educational status, unemployment (or employment type), literacy level, and health insurance.^{11,12}

JC, our female patient, is employed full time and paid on an hourly basis. She receives a 30-minute unpaid lunch break and usually eats take-out from a nearby fast-food restaurant, as her company does not have an onsite cafeteria. JC has little-to-no formal educational training and holds a general educational development (GED) degree. Although she has health insurance, her co-pays for participation in a formal cardiac rehabilitation program (post-CABG) were \$20/visit. At home, JC is the primary caregiver, leaving her little time to take care of herself. Unlike DH, our male patient, JC does not have a nurturer to whom she can turn, leading her to feel stressed, neglected, and “burned out.”

Conversely, DH is a salaried high-school English teacher who exercises during his paid lunch period between classes in his school’s fitness facility. Afterward, he eats lunch in the school cafeteria, which offers a full salad bar and many heart-healthy options. At the close of his day (2:30 PM), he attends a local health club where he combines resistive and aerobic training in his workout. DH holds a master’s degree in secondary education and is pursuing his doctorate in education. His health insurance, supported by his state’s Teachers Association, is superior and requires only a \$5 co-pay/visit for cardiac rehabilitation. Unlike JC, DH is able to return home after a busy day and relax; his wife is supportive and prepares heart-healthy meals for their family.

The Treatment Gap

In 1994, the Heart and Estrogen/progestin Replacement (HERS) study showed that only 47% of postmenopausal women with CHD were receiving lipid-lowering therapy.¹³ Further, just 37% attained an LDL-C \leq 130 mg/dL, and only 9% had an LDL-C \leq 100 mg/dL. During that time, the NCEP ATP II guidelines (formally

issued in 1988) advised healthcare providers to begin ACS patients on statin therapy before hospital discharge. Unfortunately, just 7% of the patients in HERS were started on statin therapy during their first year post-ACS. It’s also worth noting that undertreatment was more pronounced among black women than white women in HERS.¹⁴ These findings are consistent with the case of JC, our female patient. Interestingly, statin use and attainment of lipid goals were significantly less frequent among married compared with single or divorced women.

Lastly, data collected from 1998 to 1999 in the National Registry of Myocardial Infarction showed a consistent disparity between women and men receiving lipid-lowering therapy at hospital discharge, with women being less likely to receive statins.¹⁵ However, overall adherence with lipid-lowering therapy prescribed at discharge was dismally low: less than one-third across both genders.

Recent findings from cardiac rehabilitation programs indicate that such settings positively affect adherence and clinical outcomes among women, provided they participate in controlled programs that offer support and structure.¹⁶ The data indicate that 49% of women with CHD reached their LDL-C treatment goal of <100 mg/dL.

Where Do We Go From Here?

CHD is the leading cause of death in women over age 25 and kills more than 500,000 women in the US each year.¹ While women are less likely than men to develop CHD before age 60, their prognoses are similar or worse than that of men. Women suffer far more anginal symptoms, heart failure, and long-term disability. Further, they often have more comorbid conditions (eg, hypertension, dyslipidemia, type 2 diabetes) than do men. With this in mind, healthcare providers must embrace the importance of treating multiple risk factors early on. ♥

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- Stay tuned for challenging cases from Peter Ganz, MD, and John C. LaRosa, MD

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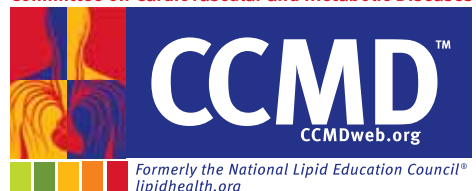
CURRENT LITERATURE OVERVIEW

Perspectives on Dyslipidemia and Coronary Heart Disease in Women

Vera Bittner, MD, MSPH
J Am Coll Cardiol. 2005;46:1628-1635.

Coronary heart disease (CHD) remains the leading—and arguably most important—cause of death among women in the United States. Among CHD risk factors, dyslipidemia is associated with the initiation and progression of atherosclerosis and subsequent cardiovascular events. Numerous studies have identified a correlation between elevated LDL-C levels and decreased HDL-C levels with an increase in CHD risk. Moreover, available evidence suggests that lipid-lowering therapy with statins confers benefits with respect to coronary event risk in women with documented cardiovascular disease (CVD). Despite this, women remain undertreated. Furthermore, lipid-lowering clinical trials to date focus on lowering LDL-C, which may not be optimal among women in whom low HDL-C or high TG appear to be strongly (or more strongly) associated with CHD. The authors conclude that emphasis on a healthy lifestyle should start in early childhood and continue throughout life, and point to the need for additional data to determine appropriate cardiovascular prevention and treatment in this population. ♥

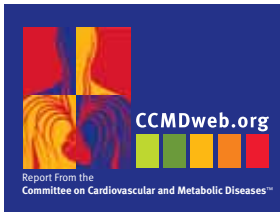
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Women and Heart Disease



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To upgrade to this version, please click on the Adobe Acrobat Reader icon on the *CMDManagement™* newsletter home page. Otherwise, please login to [CCMDweb.org](http://www.ccmdweb.org) and highlight and copy the provided links into your browser window.

The following links are relevant to the feature story highlighting strategies for improved prevention, detection, and treatment in women with CVD.

Current Literature:

Estrogen Plus Progestin and the Risk of Coronary Heart Disease
http://www.ccmdweb.org/content/currentliterature/cm_litshow.asp?a=145

Opportunity for Intervention to Achieve American Heart Association Guidelines for Optimal Lipid Levels in High-Risk Women in a Managed Care Setting
http://www.ccmdweb.org/content/currentliterature/cm_litshow.asp?a=222

Using the Coronary Artery Calcium Score to Predict Coronary Heart Disease Events
http://www.ccmdweb.org/content/currentliterature/cm_litshow.asp?a=186

Dynamic Slide Library:

Awareness and Preventive Action for Cardiovascular Health in Women
http://www.ccmdweb.org/content/dynamic_slide_library/middle.asp?sid=514&cid=19

ATP III Framingham Risk Scoring—Assessing CHD Risk in Women
http://www.ccmdweb.org/content/dynamic_slide_library/middle.asp?sid=67&cid=2

Leading Causes of Death for US Females, 2001
http://www.ccmdweb.org/content/dynamic_slide_library/middle.asp?sid=387&cid=19

CVD Mortality Trends for US Males and Females
http://www.ccmdweb.org/content/dynamic_slide_library/middle.asp?sid=386&cid=19

WISE: Prevalence of Angiographic CAD Based on BMI, Metabolic Status
http://www.ccmdweb.org/content/dynamic_slide_library/middle.asp?sid=399&cid=19

WISE Study: Review of Ischemic Heart Disease in Women
http://www.ccmdweb.org/content/dynamic_slide_library/middle.asp?sid=513&cid=19

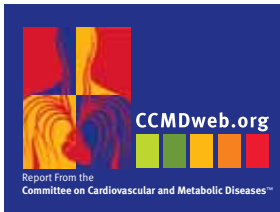
Awareness and Preventive Action for Cardiovascular Health in Women
http://www.ccmdweb.org/content/dynamic_slide_library/middle.asp?sid=514&cid=19

Outcomes in WHI Trial of Estrogen, Progestin
http://www.ccmdweb.org/content/dynamic_slide_library/middle.asp?sid=142&cid=19

Guidelines-at-a-Glance:

ATP III: Assessing CHD Risk in Women
<http://www.ccmdweb.org/content/guidelines/guide1.asp#1b>

Guide to Risk Reduction for Women
<http://www.ccmdweb.org/content/guidelines/guide5.asp>



The following links are relevant to the case study examining gender disparities in diagnosing, treating, and preventing CHD.

Current Literature:

Risk Factors and Secondary Prevention in Women with Heart Disease:
The Heart and Estrogen/progestin Replacement Study
http://www.ccmdweb.org/content/currentliterature/cm_litshow.asp?a=23

Use of Lipid-Lowering Medications at Discharge in Patients With Acute Myocardial Infarction:
Data From the National Registry of Myocardial Infarction 3
http://www.ccmdweb.org/content/currentliterature/cm_litshow.asp?a=33

Effects of Aggressive Cholesterol Lowering and Low-dose Anticoagulation on Clinical and
Angiographic Outcomes in Patients With Diabetes: the Post Coronary Artery Bypass Graft Trial
http://www.ccmdweb.org/content/currentliterature/cm_litshow.asp?a=36

Dynamic Slide Library:

WISE Study: Review of Ischemic Heart Disease in Women
http://www.ccmdweb.org/content/dynamic_slide_library/middle.asp?sid=513&cid=19

CVD Mortality Trends for US Males and Females
http://www.ccmdweb.org/content/dynamic_slide_library/middle.asp?sid=386&cid=19

HERS, HERS II: Relative Hazard of CHD Events
http://www.ccmdweb.org/content/dynamic_slide_library/middle.asp?sid=240&cid=19

Guidelines-at-a-Glance:

USDA Dietary Guidelines for Americans
<http://www.ccmdweb.org/content/guidelines/guide7.asp#7c>

Procedure for Implementing Therapeutic Lifestyle Changes (TLC)
<http://www.ccmdweb.org/content/guidelines/guide9.asp#fig9a>