



# Paradigm shifts in the approach to women's health care

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Women's health care has traditionally focused on the screening, diagnosis, and treatment of conditions unique to women. However, the recent recognition of significant differences in risk factors, disease manifestations, and responses to treatments in women also affects the best evidence-based management options to optimize treatment outcomes for many conditions not unique to women. As with all patients, ethnicity, culture, education, social and economic status, and access to medical care are important determinants of overall health. These health-related issues are especially important for women for several reasons, including, among others, their lower earning power, their higher incidence of chronic disease, and their lower likelihood of seeking health care when needed.<sup>1</sup> Thus, gender-based women's health care not only incorporates the roles and expectations of the culture and society specific to one woman at a given point in her life but also necessarily includes awareness of biological and physiologic differences between females and males.

This report focuses on a shift in the approach to gender-based medicine using results from recent research and evidence-based recommendations regarding evaluation and treatment of women that are specifically different from those for men. Physician assistants can and should be learning new information about gender-based differences in diseases and conditions in order to provide the highest possible level of expertise and the most appropriate health care for women of all ages.

## Research, past and present

Although women represent approximately half of the adult population,<sup>2</sup> they spend a greater share of health care dollars. According to one study, the total mean annual charges per capita expenditure was \$7,104 for women and \$5,050 for men. These charges included pri-

mary care visits, specialty care, emergency department care, hospitalizations, and diagnostic services.<sup>3</sup>

Yet not until 1993 did the National Institutes of Health (NIH) Revitalization Act require that both women and minorities be included in all NIH-supported clinical research studies.<sup>4</sup> That same year, the FDA published the Guideline for the Study and Evaluation of Gender Differences in the Clinical Evaluation of Drugs that lifted the restriction against including women of childbearing age in clinical trials.<sup>5</sup> This exclusion of

## The quality care perspective

### From the AAPA Quality Care Committee

The National Healthcare Disparities Reports (NHDR), published by the Agency for Healthcare Research and Quality, can provide PAs with important insights into the areas where women may not have optimal or accessible health care. The 2004 NHDR included a section focused specifically on women.

This CSAC Special Report identifies some important areas of concern for women regarding cardiovascular disease (CVD). The NHDR tracks several measures of quality care for heart disease in women, including screening and counseling for cardiovascular risk factors, acute treatment of MI and heart failure, and chronic management of hypertension and heart failure. Although major risk factors for CVD can be controlled by lifestyle changes, health care professionals are less likely to counsel women about diet, exercise, and weight reduction.

The NHDR identifies quality gaps in other diseases as well, including cancer, diabetes, osteoporosis, maternity care, and access to care. Another resource, called Quick Health Data Online, is available through the Office on Women's Health. It offers comprehensive health data, for both women and men, at national, regional, state, and county levels. Data can be stratified by gender, race/ethnicity, and age concurrently. This easy-to-use database allows health care providers to identify important indicators of health status in their communities. The database can be accessed through [www.4woman.gov](http://www.4woman.gov).

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TABLE 1

**Summary of recommendations**

**American Heart Association recommendations\* for preventing cardiovascular disease in women**

Pharmacotherapy is indicated when BP is >140/90 mm Hg, or even lower in the setting of BP-related target-organ damage or diabetes. Thiazide diuretics should be part of the drug regimen for most patients unless contraindicated.

Initiate LDL-cholesterol-lowering therapy (preferably a statin) if the LDL cholesterol level is >130 mg/dL on lifestyle therapy for patients with intermediate risk (defined as a 10-year absolute coronary heart disease risk of 10% to 20%).

Aspirin therapy (75-162 mg daily), or clopidogrel if patient is intolerant to aspirin, should be used in high-risk (defined as a coronary heart disease risk >20%) women unless contraindicated.

Beta-blockers should be used indefinitely in all women who have had an MI or who have chronic ischemic syndromes unless contraindicated.

ACE inhibitors should be used (unless contraindicated) in high-risk women.

Among women with chronic or paroxysmal atrial fibrillation, warfarin should be used to maintain the international normalized ratio at 2.0 to 3.0 unless they are considered to be at low risk for stroke (<1%/yr) or at high risk for bleeding.

Aspirin (325 mg daily) should be used in women with chronic or paroxysmal atrial fibrillation with a contraindication to warfarin or at low risk for stroke (<1%/yr).

Combined estrogen plus progestin hormone therapy should not be initiated to prevent CVD in postmenopausal women.

**Partnership for Gender-Specific Medicine recommendations\* for the care of women with diabetes**

Avoid olanzapine for women with diabetes in whom obesity is a risk factor.

Discontinue the use of ACE inhibitors in women who might become or who are pregnant.

Coronary angioplasty should not be withheld from women with diabetes because of an increased risk of mortality or restenosis compared with men with diabetes.

\*These recommendations were found to be useful and effective and are supported by evidence from multiple randomized trials.

Data from Mosca L et al,<sup>16</sup> and Legato MJ, Gelzer A, Goland R, et al. Gender-specific care of the patient with diabetes: review and recommendations. *Gender Med.* 2006;3:131-158.

women had been justified based on the premise that hormonal changes could interfere with research results or because of the possibility that the subject might become pregnant during a study, putting the fetus at risk.

“Gender-neutral” research—in reality, research that ignored or was developed to assess potential differences between the sexes—had become the de facto norm, perpetuating disparities in many aspects of health care for women. Gender-based studies now hold an important place on national research agendas, as evidenced by the creation of the FY 2006 NIH Research Priorities for Women’s Health.<sup>6</sup> Furthermore, the results of research focused on women’s health, such as the Women’s Health Initiative study and others, have gained national attention.<sup>7,8</sup>

It can no longer be assumed that any given disease will manifest similarly or follow the same course in women and men or that women and men respond to treatments identically. Continued research is needed to explain differences and determine their level of medical significance.<sup>9</sup>

**Health care delivery and access**

Although factors such as career choice, education, income, and health insurance coverage create gender influences on health care outcomes, these environmental factors cannot fully explain the many differences between men and women with respect to disease etiology and pathophysiology, treatment responses, and outcomes.<sup>10</sup> If the quality of health care for women is to improve, other disparities, including access to care, cost of care, and allocation and utilization of resources, must be recognized and dealt with by policy makers and providers alike.<sup>11</sup> However, the approach to the treatment of women must have a fundamental paradigm shift to fully accomplish this very complicated task.

**Pharmacology issues**

A primary focus of gender-based medicine is examining differences in pharmacodynamics and pharmacokinetics between women and men. The FDA’s 1993 Guideline for the Study and Evaluation of Gender Differences in the Clinical Evaluation of Drugs required analysis of data for sex-related variations in response to drug treatment.<sup>12</sup> This guideline advised that when the clinical characteristics of a drug are studied, the influence of menstrual and menopausal status and of estrogen treatment or systemic contraceptives on pharmacokinetics should be considered.<sup>13</sup> Further recommendations emphasized that assessments of differences in drug action due to sex-specific variations, ethnicity, age, body size, hepatic and renal function, disease state, or enzyme activity be included in research studies.<sup>12</sup> Only some of these had been traditionally included in clinical trials.

There are male-female differences in response to pharmacologic agents that go well beyond the normal and expected variation seen from patient to patient. For example, the incidence of adverse events was statistically higher for women than for men in clinical trials of numerous drugs—especially agents that are potent inducers or inhibitors of the cytochrome P450 pathway.<sup>13,14</sup> Male-female differences in metabolic pathways and oxidative metabolism of certain drugs by the liver results in the clearance of many benzodiazepines more rapidly in men than in women.<sup>13,14</sup> Physiologic differences can affect male and female response to the same drug, and this dissimilarity becomes especially important for drugs with a narrow therapeutic range.<sup>13,14</sup> Women are more likely to develop drug-induced QT prolongation and torsades de pointes, for instance.<sup>13,15</sup> Women appear to have a greater response than men to selective serotonin reuptake inhibitors.<sup>14</sup> They appear to have more adverse events with antihypertensive medications, as well as more bleeding events when taking warfarin.<sup>13,14</sup>

### Women and cardiovascular disease

Many women do not recognize that heart disease is the leading cause of death for women in the United States. In fact, the American Heart Association (AHA) reported that approximately 500,000 American women die each year from cardiovascular disease (CVD)—more than die from the next seven causes of death combined.<sup>16,17</sup> It is a common misconception, not only among the lay population but among clinicians as well, that breast cancer is the biggest killer of women.

**Clinicians have the ability and responsibility to ease the burden of disease and improve quality of life for women.**

Women present with coronary heart disease (CHD) at older ages than men. Women often do not have typical (or even atypical) chest pain or chest pain equivalents; instead, their presenting symptoms commonly include fatigue and shortness of breath.<sup>18,19</sup> Risk factor control is especially important for African-American women, who have the highest incidence among women of CHD as well as the highest incidence of uncontrolled hypertension, obesity, physical inactivity, and dyslipidemia.<sup>20</sup>

The diagnosis of heart disease is a greater challenge in women than men; interestingly, nearly two thirds of

### For more information

Detailed information about gender-based medicine is available from an online course, “The Science of Sex and Gender in Human Health,” established by the National Institutes of Health Office of Research in collaboration with the FDA Office of Women’s Health. The course outlines major physiologic differences between the sexes and their influence on illness and health outcomes, as well as providing guidance for policy, medical research, and health care. CME credit is available upon successful completion. See <http://sexandgendercourse.od.nih.gov/index.aspx>.

Information on diabetes and women’s health is available in Beckles GLA, Thompson-Reid PE, eds. *Diabetes and Women’s Health Across the Life Stages: A Public Health Perspective*. Atlanta, Ga: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Division of Diabetes Translation; 2001. See [www.cdc.gov/diabetes/pubs/english.htm](http://www.cdc.gov/diabetes/pubs/english.htm).

women who die suddenly from a cardiac cause did not have previous cardiac symptoms that were recognized.<sup>16,17</sup> In persons older than 65 years, low levels of HDL cholesterol are a stronger predictor of death from heart disease in women than in men. High levels of triglycerides may be a more important risk factor in women, especially in elderly women.<sup>17</sup> Women are less likely than men to receive diagnostic or therapeutic procedures and rehabilitation after their first MI.<sup>18,21,22</sup> Finally, women are more likely than men to die after their second MI.<sup>21</sup>

The majority of women are not aware of the risk factors for CHD in women or of differences in presenting symptoms, jeopardizing their chances for aggressive screening and risk factor control (see Table 1).<sup>16,17</sup> While awareness has grown since 2000, there is still a knowledge gap, especially for women who are younger than 45 years or in a minority group. According to a 1997 AHA survey, only 30% of women listed heart disease as the leading cause of death for women. By 2004, 46% acknowledged CHD as the number one cause of death.<sup>16,17</sup> Recent efforts to promote awareness of CHD in women through programs developed by the AHA and the NIH, such as the “Red Dress” campaign, seem to have been effective.

### Diabetes in women

Recent studies show that type 2 diabetes mellitus may be a stronger risk factor for heart disease in women than in men.<sup>17</sup> Diabetic women have a higher risk for stroke and MI than do diabetic men.<sup>23</sup> In comparing data from the National Health and Nutrition Examination Survey (NHANES) III 1988-1994 and NHANES

1999-2000, Ford and colleagues noted an increased prevalence of metabolic syndrome in women compared to men.<sup>24</sup> Studies have found that obese postmenopausal women develop reduced insulin sensitivity to a greater degree than premenopausal women do, which in turn increases their risk for development of metabolic syndrome as they age. This outcome may be due to obese women's increased abdominal fat and high levels of triglycerides.<sup>25</sup>

There also appears to be a difference between men and women in terms of the preferred time to measure blood glucose levels. A recent study shows that for women, blood glucose levels after meals are better predictors for development of heart and blood vessel disease; thus, it is important for women with diabetes to closely monitor themselves using after-meal glucose levels.<sup>26</sup> Women with gestational diabetes have a 20% to 50% chance of developing diabetes in the next 5 to 10 years.<sup>23</sup> The children of women who had gestational diabetes have a higher risk of obesity later in life. However, recent studies have shown increasing evidence that breast-feeding has a protective effect against obesity in adulthood.<sup>27</sup>

## Conclusion

Clinicians have the ability and responsibility to ease the burden of disease and improve quality of life for women. They can achieve these goals by remaining vigilant to gender differences in how diseases develop, manifest themselves, and are treated and by tailoring treatment strategies to improve outcomes. PAs should be aware of gender differences when caring for women and develop preventive strategies to decrease the risks of CVD and diabetes, among other conditions. To be most effective, these efforts should begin as early as adolescence.

The teaching and practice of women's health care can no longer concentrate on contraception, pregnancy, and menopause to the exclusion of other concerns. Future research must consider differences in men's and women's roles and responsibilities, information about access to and use of resources, and the best ways to address inequalities between men and women's health care. It is crucial that culturally competent providers

and researchers strive to develop and provide appropriate services that respond to the health care needs of all women of all ages. □

## REFERENCES

- 2001 Kaiser Women's Health Survey. Women's Health in the United States: Health Coverage and Access to Care. The Henry J. Kaiser Family Foundation. Available at: <http://www.kff.org/womenshealth/20020507a-index.cfm>. Accessed September 6, 2006.
- US Census Bureau. National intercensal estimates (1990-2000). Available at: <http://www.census.gov/popest/archives/EST90INTERCENSAL/US-EST90INT-02.html>. Accessed September 6, 2006.
- Bertakis KD, Azari R, Helms LJ, et al. Gender differences in the utilization of health care services. *J Fam Pract*. 2000;49(2):147-152.
- US Department of Health and Human Services. National Institutes of Health. National Institutes of Health Revitalization Act of 1993. Subtitle B: Clinical Research Equity Regarding Women and Minorities. Available at: <http://orwh.od.nih.gov/inclusion/revitalization.pdf>. Accessed September 6, 2006.
- National Institute of Health. The Science of Sex and Gender in Human Health. Online Course Site. Lesson 1: Sex and Gender in Biomedical Research. Available at: <http://sexandgendercourse.od.nih.gov/lesson1/index.aspx>. Accessed September 6, 2006.
- Office of Research on Women's Health (ORWH). FY 2006. NIH research priorities for women's health. Available at: [orwh.od.nih.gov/research/FY06research\\_priorities.pdf](http://orwh.od.nih.gov/research/FY06research_priorities.pdf). Accessed September 6, 2006.
- Hulley S, Grady D, Bush T, et al. Randomized trial of estrogen plus progestin for secondary prevention of coronary heart disease in postmenopausal women. *JAMA*. 1998;280:605-613.
- Manson JE, Hsia J, Johnson KC, et al. Estrogen plus progestin and the risk of coronary heart disease. *N Engl J Med*. 2003;349(6):523-534.
- Culliton BJ. Sex matters: gender-based medical research. *Genome News Network*. 2000. Available at: [http://www.genomenewsnetwork.org/articles/04\\_00/comment\\_sexmatter.shtml](http://www.genomenewsnetwork.org/articles/04_00/comment_sexmatter.shtml). Accessed September 6, 2006.
- Correa-de-Araujo R, Clancy CM. Catalyzing quality of care improvements for women [commentary]. *Women's Health Issues*. 2006;16(2):41-43.
- Taylor AK, Larson S, Correa-de-Araujo R. Women's health care utilization and expenditures. *Women's Health Issues*. 2006;16(2):66-79.
- Department of Health and Human Services. Guideline for the Study and Evaluation of Gender Differences in the Clinical Evaluation of Drugs. *Federal Register*. 58(139):39406-16 (July 22, 1993). Available at: <http://www.fda.gov/cder/guidance/old036fn.pdf>. Accessed September 6, 2006.
- National Institute of Health. The Science of Sex and Gender in Human Health. Online Course Site. Lesson 5: Pharmacodynamics and Pharmacokinetics. Available at: <http://sexandgendercourse.od.nih.gov/lesson5/index.aspx>. Accessed September 6, 2006.
- Society for Women's Health Research. Sex differences in response to pharmaceuticals, tobacco, alcohol and illicit drugs. Available at: [http://www.womenshealthresearch.org/site/PageServer?pagename=hs\\_facts\\_dat](http://www.womenshealthresearch.org/site/PageServer?pagename=hs_facts_dat). Accessed September 22, 2006.
- Correa-de-Araujo R, Clancy CM. Improving the use and safety of medications in women through sex/gender and race/ethnicity analysis: introduction. *J Wom Health*. 2005;14(1):12-15.
- Mosca L, Appel LJ, Benjamin EJ, et al; American Heart Association. Evidence-based guidelines for cardiovascular disease prevention in women. *Circulation*. 2004;109:672-693.
- American Heart Association. Facts about women and cardiovascular diseases. Available at: <http://www.americanheart.org/presenter.jhtml?identifier=2876>. Accessed September 6, 2006.
- Society for Women's Health Research. Sex differences in cardio/cerebrovascular diseases. *Epidemiology*. Available at: [http://www.womenshealthresearch.org/site/PageServer?pagename=hs\\_facts\\_cardio](http://www.womenshealthresearch.org/site/PageServer?pagename=hs_facts_cardio). Accessed September 6, 2006.
- AMA Feature Report: Women's Health: Sex and Gender-Based Differences in Health and Disease. CSA Report 4 at the 2000 interim AMA meeting. Available at: <http://www.ama-assn.org/ama/pub/category/13607.html>. Accessed September 6, 2006.
- Huggins S. The role of the advanced practice nurse in reducing coronary heart disease in African-American women. *Topics in Advanced Practice Nursing eJournal*. 2006;6(2). Available at: <http://www.medscape.com/viewarticle/533898>. Accessed September 6, 2006.
- Correa-de-Araujo R. A wake-up call to advance women's health. Article originally published in *Women's Health Issues*. 2004;14:31-34. Agency for Healthcare Research and Quality, Rockville, Md. Available at: <http://www.ahrq.gov/research/wrmwakeup.htm>. Accessed September 6, 2006.
- Agency for Healthcare Research and Quality (AHRQ). Women's health care in the United States: Selected findings from the 2004 national healthcare quality and disparities reports. Fact Sheet. AHRQ Publication No. 05-P021. May 2005. Rockville, Md. Available at: <http://www.ahrq.gov/qual/nhrqwomen/nhrqwomen.htm>. Accessed September 6, 2006.
- Society for Women's Health Research. Sex differences in diabetes. Available at: [http://www.womenshealthresearch.org/site/PageServer?pagename=hs\\_facts\\_diabetes](http://www.womenshealthresearch.org/site/PageServer?pagename=hs_facts_diabetes). Accessed September 6, 2006.
- Ford ES, Giles W, Mokdad Ali. Increasing prevalence of metabolic syndrome among U.S. adults. *Diabetes Care*. 2004;27(10):2444-2449.
- Karelis AD, Henry JF, St-Pierre DH, et al. Degradation in insulin sensitivity with increasing severity of the metabolic syndrome in obese postmenopausal women. *Diabetes, Obesity and Metabolism*. 2006;8(3):336-341.
- Cavalot F, Petrelli A, Traversa M, et al. Postprandial blood glucose is a stronger predictor of cardiovascular events than fasting blood glucose in type 2 diabetes mellitus, particularly in women: lessons from the San Luigi Gonzaga Diabetes Study. *J Clin Endocrinol Metab*. 2006;91:813-819.
- Schaefer-Graf UM, Hartmann R, Pawliczak J, et al. Association of breast-feeding and early childhood overweight in children from mothers with gestational diabetes mellitus. *Diabetes Care*. 2006;29:1105-1107.

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