THE 10 Q REPORT

ADVANCING WOMEN'S HEART HEALTH THROUGH IMPROVED RESEARCH, DIAGNOSIS AND TREATMENT

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The 10 Q Report: Advancing Women's Heart Health Through Improved Research, Diagnosis and Treatment

By
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Introduction

Heart disease remains the number one killer of women in the United States, [1] yet a 2005 survey by the Society for Women's Health Research found that most women are more fearful of dying from breast cancer than heart disease. Although more women than men die each year of heart disease,[2] most people still think of it as a "man's disease". Information gaps related to the development, diagnosis and treatment of heart disease among women are enormous, in part because women continue to be underrepresented in heart–related research studies. As a result, women often face misdiagnosis, delayed diagnosis, undertreatment and mistreatment of their heart problems. Gender-based disparities in access to accurate diagnosis and appropriate cardiac treatment remain systemic but poorly understood.

A look at the current state of federal spending on women's health shows the economic impact of heart disease in women. The annual spending report in women's health, prepared by the U.S. Department of Health and Human Services (HHS) for the House of Representatives Committee on Appropriations shows that the Center for Medicare and Medicaid Services (CMS) accounts for the vast majority of spending on women's health. The highest expenditure at CMS in FY 2005 was in **cardiovascular/pulmonary services**, which constituted half of all CMS spending in women's health: **$36 billion of the nearly $72 billion** that CMS identified for women's health in FY 2005.

Despite this large expenditure of taxpayer's dollars to treat women with heart disease, relatively little funding is targeted at prevention or research that could lead to more science-based and effective cardiac diagnosis and treatment for women. For example, of the $8.2 billion non-CMS spending by HHS on women's health in

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FY 2005, less than six percent (less than $0.5 million) was focused on women and cardiovascular/pulmonary disease. Most of this non-CMS funding was for research funded by National Institutes of Health (NIH), which spent $419 million on cardiovascular/pulmonary research in women. Furthermore, at NIH, cardiovascular/pulmonary research generally receives significantly less funding than all cancers or even breast cancer alone.

A greater investment in research on heart disease in women – and how it differs from that in men – would both save women's lives and ensure that federal dollars that pay for women's cardiovascular care are spent on treatments that are effective and safe for women. Such research must encompass disease risk assessment, prevention and early intervention, in order to improve physician decision-making.

WomenHeart: the National Coalition for Women with Heart Disease, the nation's only patient advocacy organization serving the 8,000,000 American women living with heart disease, and the **Society for Women's Health Research**, a national organization whose mission is to improve the health of all women through research, education and advocacy, have joined forces to identify ten crucial questions that must be answered if women are to receive optimal cardiovascular care and treatment. The questions cover effectiveness of risk assessment and diagnostic tools, the differences in risk and in effectiveness of therapies for men and women, and the need for improved understanding of heart disease in women.

The 10 Q Report surveyed top cardiology experts and asked them to identify the top ten unanswered research questions concerning the development, diagnosis and treatment of heart disease in women. Together these questions comprise a powerful research agenda and a blueprint for reducing the number of women who die prematurely from heart disease by 50 percent over the next ten years.

WomenHeart and the Society for Women's Health Research believe that *The 10 Q Report* will serve as a powerful guide for the NIH, Agency for Healthcare Research and Quality (AHRQ), CMS and other health research agencies. In addition, it is critical that the development of a research agenda for women's heart health proceed with the full participation of women heart disease survivors. With this strategy, policymakers become partners with women living with heart disease to dramatically reduce women's cardiac disability and premature death in ten years and in the

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process of creating more effective treatments, also save American taxpayers hundreds of millions of dollars.

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1. Why do women receive significantly fewer referrals for advanced diagnostic testing and treatments for heart disease than men, and how can the referral rate for women be increased?

The American Heart Association (AHA) guidelines recommend initial evaluation of coronary heart disease (CHD) with exercise electrocardiographic (ECG) testing. Despite these guidelines, studies have demonstrated that men were more likely than women to undergo ECG testing, and more men who underwent ECG testing were more likely to report no cardiovascular disease (CVD) symptoms.[3, 4] An additional study showed that women younger than age 55 (both African American and Caucasian) were less likely to have this test than same-aged Caucasian men.[5] The lower ECG referral rate may be due to a lower suspicion of CVD in younger women. However, the diagnostic ability of this test may be limited in women for several reasons: lower prevalence of CHD in women, higher prevalence of single vessel disease, higher incidence of mitral valve prolapse, differences in exercise capacity, and the digoxin-like effects of estrogen.[6]

Many studies have demonstrated that women are less likely to receive cardiac catheterization and revascularization procedures such as coronary artery bypass surgery (CABG) and percutaneous coronary intervention (PCI; angioplasty).[4, 7-11] A recent study found that women with acute coronary syndromes are nearly one-third less likely to receive invasive diagnostic procedures than men.[12] The difference was almost entirely due to women not being referred for diagnostic cardiac catheterization. Women who did have the diagnostic procedure were thirty-five percent less likely to have a subsequent therapeutic procedure such as angioplasty or CABG. Another study demonstrated sex differences in the type of revascularization procedure offered; older women were less likely to undergo CABG and more likely to undergo PCI than older men.[13] Studies of women who underwent CABG found that they were older and more likely to have diabetes, high cholesterol, hypertension, unstable, congestive heart failure

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(CHF), depression and lower physical function than men.[14, 15] Lower referral rates for these procedures may result from the increased hemorrhagic complications after CABG and the poorer recovery after revascularization in women compared to men.[6]

Studies concluded that considering both sexes have comparable outcomes after similar angioplasty-based treatments, sex alone should not be a factor in the decision to perform angioplasty.[16] Other factors that should be considered include age, co-morbidities, risk factors, patient preferences, and current health status.[4] However, another study found that elderly patients, particularly women, were less likely to receive angiography and to see a heart specialist after an MI than younger patients.[17]

2. What are the best tools and methods for assessing women's risk of heart disease?

The current methods used to assess risk of heart disease have not been independently validated for women. For example, one recent study at Johns Hopkins University found that the Framingham Risk Estimation (FRE),[19] a commonly used method for calculating 10-year risk of a cardiovascular event, underestimates risk in women with a family history of early heart disease.[20] In addition, the FRE does not include components of the metabolic syndrome, the incidence of which is increasing in women.

Physicians' beliefs about women's risk for heart disease also influence risk evaluations. In one study, doctors were given profiles of patients who had the same risk levels but were described as either male or female. The physicians were asked to make recommendations for reducing the patients' risk of CVD, including medications and lifestyle changes. Even when a woman's risk factors were the same as a man's, the physicians were more likely to evaluate her at a lower risk level than a comparable man. The majority of physicians in the sample did not know that in the U.S. more women than men die of heart disease each year.[21]

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3. What are the best strategies for preventing heart disease in women?

In 2004, the AHA published its guidelines for CVD prevention in women.[22] The guidelines were developed by an expert panel that evaluated all relevant studies available in the medical literature. The list of clinical recommendations that emerged included thirty specific recommendations for preventing CVD in women. However, only nine of those recommendations were supported by the highest level of evidence, "A," meaning sufficient evidence from multiple randomized trials.

Nineteen of the thirty recommendations had an evidence rank of "B"– limited evidence from single randomized trial or other nonrandomized studies. Two of the recommendations had the lowest evidence rank of "C"– based on expert opinion, case studies or standard of care. The gaps in evidence identified by this expert panel demonstrate that more research is needed to determine the best preventive strategies for women.

4. What treatments for heart disease work best for women?

Research on the effectiveness of drugs that reduce CVD risk such as lipid-lowering drugs and blood pressure medications has been almost entirely in men. When women have been included, the results have not been evaluated separately for men and women. Similarly, the initial studies looking at lifestyle factors such as diet and exercise were conducted done entirely with men, although in recent years some of these studies have been repeated with women.

5. What are the most effective evaluation methods and treatments for diastolic heart failure, which is the most common form of CHF in women?

Compared to men who suffer more from systolic dysfunction, a higher proportion of women suffer from diastolic heart failure, which is the inability of the left ventricle to fill properly with oxygenated blood.[23-25] Women who present with CHF are more likely to be older, obese, inactive and have a higher rate of c-morbid diabetes and hypertension than men.[25, 26] According to the AHA, in 2001, 62.5 percent of the CHF deaths were in women.[1]

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Although CHF affects both women and men, women have been a minority in CHF clinical trials,[25] and most studies of CHF that have been conducted have focused on systolic heart failure, which is more common in men. In addition, diastolic heart failure is understudied for both sexes, and comparative studies of treatments have not been performed using a uniform diagnosis for diastolic heart failure. Some studies on CHF have indicated that women do not receive pharmacologic treatments for CHF as often as men in both the ambulatory and hospital settings.[26] One study found modest sex differences in treatment, with women receiving therapies less often than men. Although the results were modest, the authors claim that considering nearly one million people are hospitalized for CHF each year in the U.S., the group of female patients who do not receive appropriate treatment is likely to be sizable. In order to ensure that women receive appropriate diagnostics and treatments for CHF, future studies must be performed that address the specific characteristics of CHF in women.

6. How can the heart disease diagnosis and care disparities between white women and women of color be eliminated?

In the U.S., women of color have a worse prognosis following a cardiac event than white women.[1] The reasons for these disparities are complex, and include lower physician referral rates for aggressive care and rehabilitation as well as socioeconomic factors that act as barriers to obtaining appropriate care when it is prescribed.[27, 28] One recent study pointed out the need for new theoretical models that explain why such disparities exist and that can drive the development, testing, and implementation of empirically based interventions to reduce these disparities.[29]

7. What are the biological differences between men and women in the location, type, and heart disease risk level associated with fat deposits, and what determines these differences?

There is increasing evidence that the amount of adipose tissue is less significant than its location. Very little is known about what determines where fat is deposited. A role for gondal hormones has been proposed, based on the knowledge that pre-menopausal women deposit fat preferentially in subcutaneous depots, and men deposit fat

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preferentially in the visceral depot. After menopause, women who gain weight begin to preferentially deposit fat in the visceral depot.[30]

8. How do sex differences in the regulation of heart rhythm affect risk of heart disease and response to treatment?

Women are more likely than men to develop a potentially fatal abnormal heart rhythm, or arrythmia. This is because in women, the heart takes longer to "recharge" following a heartbeat compared to the time this takes in men. The longer the recharge period, called the QT interval, the easier it is for the heart to develop arrhythmia. Ironically, when some women take the currently available medications used to prevent arrythmias, they develop a particular type of arrhythmia, *torsades de pointes*, caused when the medication makes the QT interval too long.[31] More research is needed to understand these effects and to develop safer, effective medications for women with arrhythmia.

9. What is the role of inflammation in heart disease in women?

A number of studies have found evidence for a role of inflammation in athero-sclerosis and CVD. Sex differences in the inflammatory response and the immune system are likely to affect the degree of risk. One study at the Mayo Clinic found that patients with rheumatoid arthritis were at higher risk of CVD independent of other risk factors.[32] Rheumatoid arthritis is an autoimmune disorder and 75 percent of patients with rheumatoid arthritis are women.

10. Why are women ages 50 and younger more likely to die following a heart attack than men of the same age?

There is increasing evidence, including analysis of data from the National Registry of Myocardial Infarction database and others, that women age 50 and younger, compared with the same age men, have significantly higher rates of death during hospitalization following a heart attack.[1, 32, 33] This difference diminishes and ultimately disappears

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with advancing age. It is not known how much of this difference is due to differences in physiology, how much is due to differences in the blockage that caused the heart attack and how much is due to differences in diagnosis in and appropriateness of treatment provided to younger women. If the higher mortality in younger women is due to differences in physiology, more research is needed to determine what those differences are and how they can be addressed to reduce the post-MI mortality in younger women.

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Number of Women in the U.S. with Heart Disease Aged 45 and Over, 2003 by State[1]

State	Number	State	Number
Alabama	145,000	**Missouri**	182,355
Alaska	13,108	**Montana**	29,810
Arizona	158,108	**Nebraska**	54,323
Arkansas	88,547	**Nevada**	59,364
California	943,685	**New Hampshire**	39,140
Colorado	116,583	**New Jersey**	276,460
Connecticut	115,364	**New Mexico**	54,775
Delaware	25,562	**New York**	614,282
Dist. of Columbia	17,327	**North Carolina**	252,818
Florida	619,903	**North Dakota**	21,105
Georgia	223,164	**Ohio**	369,127
Hawaii	39,864	**Oklahoma**	109,778
Idaho	37,454	**Oregon**	110,075
Illinois	374,430	**Pennsylvania**	443,665
Indiana	187,327	**Rhode Island**	36,207
Iowa	99,944	**South Carolina**	128,298
Kansas	83,714	**South Dakota**	24,521
Kentucky	127,669	**Tennessee**	182,042
Louisiana	132,103	**Texas**	556,440
Maine	45,423	**Utah**	49,563
Maryland	163,376	**Vermont**	20,182
Massachusetts	208,673	**Virginia**	215,653
Michigan	306,671	**Washington**	174,717
Minnesota	148,848	**West Virginia**	65,435
Mississippi	86,646	**Wisconsin**	170,106
		Wyoming	15,143

[1]Includes the District of Columbia. Source: Population Division, U.S. Census Bureau. Incidence of women with heart disease calculated according to ratios set forth by the National Heart, Lung, and Blood Institute: 1:10 among women aged 45-64 and 1:4 among women 65+.

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