

What's Different about Women's Health?

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What's different about women's health? Does the biology of women differ enough from that of men to warrant separate studies and comparative analysis? Until recently, much of the medical literature that was published focused predominantly on male populations. Slowly, we have come to appreciate the differences in normal physiology, as well as disease pathology, between men and women. In this special issue, which focuses on "Advancing Women's Health," we explore recent studies involving determinants and detection of health outcomes that uniquely affect women, as well as the differences in risk between males and females for shared diseases.

For instance, cardiovascular disease (CVD) is the leading cause of death for both men and women in the US. According to the CDC, 25.2% of deaths in men and 24% of deaths in women in 2009 were attributable to heart disease (Table 1) (1, 2). CVD generally manifests clinically for women in the sixth decade of life. The widespread belief was that this was due to menopausal loss of estrogens and, hence, hormone replacement therapy would help to prevent heart disease. However, landmark studies from the Women's Health Initiative indicated that combined estrogen and progestin therapy actually increased the risk of heart disease, blood clots, and strokes, among other disorders! These risks were particularly high in older women. The incidence of stroke in women, although lower than that in men before the age of 80 years, thereafter exceeds the incidence



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in men. This results in a higher lifetime risk of stroke for women than men (6.3% vs 4.3%, respectively) (1, 2). CVD risk associated with diabetes and smoking is also higher in women than in men and is particularly concerning given the epidemic rise in the prevalence of diabetes. These observations illustrate the need for inclusion of a sufficient number of women in CVD studies to assess the utility of biomarkers to predict risk and guide treatment decisions in women. In this issue, Paynter et al. (3) review biomarkers to assess the risk of CVD in women, and Bassuk and Manson (4) review their use to guide menopausal hormone therapy. Other articles assess the performance of emerging cardiovascular biomarkers such as fetuin-A and high-sensitivity troponin (5–7).

Cancer is the second leading cause of death in both men and women, with lung cancer causing the most malignancy-related deaths (1, 2). In 2012, the 3 most commonly diagnosed cancers in women were breast, lung and bronchus, and colorectum (8). Breast cancer accounted for 29% of all new cancer cases among women. Men had a slightly higher lifetime probability of being diagnosed with an invasive cancer than women (45% vs 38%) (8). However, because of the earlier age at diagnosis for breast cancer, women have a higher chance of developing cancer before the age of 60 years. The genomics of breast, cervical, and endometrial cancers are reviewed in this issue (9–11). It is clear that new biomarkers are needed for cancer screening, prognosis, and disease monitoring. To this end, new methods for the early detection and prognosis of breast cancer, including circulating proteolytic products of



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Table 1. Leading causes of death by sex for all races in the US, 2009.

Rank	Males		Females	
1	Heart disease	25.2%	Heart disease	24%
2	Cancer	24.4%	Cancer	22.2%
3	Unintentional injuries	6.2%	Stroke	6.3%
4	Chronic lower respiratory diseases	5.3%	Chronic lower respiratory diseases	5.9%
5	Stroke	4.3%	Alzheimer disease	4.5%
6	Diabetes	2.9%	Unintentional injuries	3.5%
7	Suicide	2.4%	Diabetes	2.8%
8	Influenza and pneumonia	2.1%	Influenza and pneumonia	2.3%
9	Kidney disease	2%	Kidney disease	2%
10	Alzheimer disease	2%	Septicemia	1.6%

Data from the CDC (2).

carboxypeptidase N, viable circulating tumor cells, and metastasis-related miRNA, are presented in this issue (12–14).

Psychological problems (such as depression, anxiety, and eating disorders) are among the top 10 chronic diseases affecting women (15). Women are almost twice as likely to suffer from major depression as men. Married women and mothers are especially vulnerable to depression, especially in their childbearing and rearing years. Approximately 10%–16% of pregnant women fulfill diagnostic criteria for depression and up to 70% of pregnant women report symptoms of depression (16). Furthermore, only approximately 30% of patients with major depressive disorders achieve symptomatic remission with their initial treatment, and rates of noncompliance are high. Recent data suggest genetic variation in treatment response. The ability to identify an optimal treatment for a particular patient could shorten the time to remission and improve long-term outcomes. Recent advances in the pharmacogenomics of depression are reviewed by Perlis (17).

In addition to differences between men and women in their risk for disease, women face different healthcare issues. First, women are disproportionately impacted by chronic disease (15). In the US, women utilize more healthcare services than men. This is a result, in part, of their more complex reproductive healthcare needs, lon-

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ger life expectancies, and increased rates of chronic diseases such as diabetes, depression, heart disease, and osteoporosis. Yet, women often have lower mean incomes and greater difficulty affording care. In developing countries, women lack basic healthcare and hence have increased rates of death during pregnancy and childbirth, obstetric fistulas, HIV/AIDS, malaria during pregnancy, and cervical cancer (owing to lack of screening). They are also subject to social and cultural customs and behaviors such as female genital cutting. The United Nations has developed 8 “Millennium Development Goals,” an action plan to meet the needs of the world’s poorest people (18). Several of these goals are highly relevant to women’s health, including: promoting gender equality and empowering women; improving maternal health; and combating HIV/AIDS, malaria, and other diseases. In this issue, Nour examines the progress of women’s healthcare globally (19), and Johnson et al. review the implications of the Affordable Care Act for women’s healthcare in the US (20).

Pregnancy presents significant health risks to women. Each year 10–20 million women worldwide suffer complications during pregnancy. The most common complications include ectopic pregnancy, preterm labor, gestational diabetes, hyperemesis gravidarum, hypertensive states including preeclampsia, and anemia. Each of these complications can result in death, and approximately

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300 000 women worldwide die each year from pregnancy-related causes. Almost all of these deaths occur in resource-limited settings. However, pregnancy-related deaths are not limited to third world countries. The number of reported pregnancy-related deaths in the US has steadily increased from 7.2 deaths per 100 000 live births in 1987 to a high of 17.8 deaths per 100 000 live births in 2009 (21). Although the reasons for this increase are not clear, it may result in part from enhanced surveillance and from the greater numbers of women with chronic health conditions such as hypertension, obesity, diabetes, and chronic heart disease, because they increase the risk of adverse outcomes. More studies are needed that address the health needs of women during and immediately following pregnancy. The urgent need for universal guidelines for the diagnosis of gestational diabetes is discussed by Sacks (22).

Much research has been conducted on biomarkers that can be used for the prenatal screening of trisomies and other chromosomal abnormalities. In this issue, Wald takes a look back at the birth of “the triple test” (23) and Bianchi and Wilkins-Haug look forward to the future of noninvasive DNA testing (24). We also examine the ethics of preimplantation genetic diagnosis (25).

So, what is different about women’s health? Women have a unique physiology and set of health conditions that arise from different reproductive organs as well as pregnancy. They also may differ in their risk for developing, and their response to, diseases that

are common to both men and women. This disparity in risk is multifactorial and arises from difference in genetics, access to healthcare, social behaviors, and other factors. It is clear that more research is needed to understand these differences so that the screening, treatment, and monitoring of health outcomes in women may be optimized. In this special issue we have examined the impact of biomarkers and genomics on the current state of women’s health.

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