The Problem of Diabetes and Cardiovascular Disease: Include Women in the Solution

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Do men and women with diabetes fare equally in cardiovascular disease (CVD) prevention and mortality? It appears that they do not. Although mortality from CVD is on the decline,[1] women with diabetes are 2.5 times more likely to develop CVD and 2.2 times more likely to die from CVD than nondiabetic women.[2] The favorable reductions in all-cause and CVD mortality among individuals with diabetes during the past few decades have not been shared equally by men and women.[3] From 1971 to 2000, mortality rates from CVD and all-cause mortality declined significantly among men with diabetes, but not among women with diabetes. The same study showed that all-cause mortality for women with diabetes was double that of women without diabetes.[3]

The gender gap may be narrowing, however. In a recent study, there was an equal reduction in CVD mortality in men and women with diabetes between 1997 and 2006.[4,5] The mortality gap between hospitalized myocardial infarction (MI) patients with and without diabetes also narrowed during this time period, with the greatest improvements in women with diabetes.[6]

Despite the substantially increased CVD risk in both men and women with diabetes, 30–50% of individuals with diabetes do not meet individual targets for risk modification.[7] The prevalence of suboptimal glycemic, blood pressure, and lipid control and smoking remains high.[7] Furthermore, more than three out of four adults with diabetes are overweight,[7] and nearly half are obese.[8]

Sex differences in the effects and rates of control of CVD risk factors have been identified in numerous studies, but the significance and impact on recommended practice are not always clear. The relative and absolute impact of diabetes on CVD risk is greater in women than in men,[9,10] and several CVD risk factors have been shown to affect women more than or differently from men and thus should receive more attention in clinical practice. For example, women with diabetes have been shown to derive even greater adjusted risk reduction than men from interventions to control blood pressure and cholesterol levels.[11] However, they are less likely than men to receive counseling or treatment[12,13] or to achieve target LDL cholesterol and blood pressure goals.[14] Obese women with diabetes also have a greater lifetime risk of CVD than nonobese women.[15] Sex-based disparities in CVD and diabetes care and outcomes are apparent across the age spectrum. The prevalence of diabetes is higher in women than men > 60 years of age, and premenopausal women with diabetes do not enjoy the relative "cardio-protection" that their nondiabetic counterparts do. In fact, women with diabetes who are < 60 years of age are as likely as men without diabetes to have CVD.[16]

Glycemic control remains a subject of interest and controversy as it relates to CVD mortality in people with diabetes. Given the evidence that sex differences exist in diabetes outcomes and the provision of optimal care, recent multi-site clinical trials evaluating the impact of glycemic control on CVD outcomes have included more women. In the ACCORD (Action to Control Cardiovascular Risk in Diabetes)

trial,[17] 38% of study participants were women. No sex differences were reported in the effect of intensive glucose control on nonfatal heart attack, nonfatal stroke, or CVD death. The ADVANCE (Action in Diabetes and Vascular disease: preterAs and diamicroN-MR Controlled Evaluation) trial,[18] in which 42% of participants were women, similarly did not find sex differences. The Look AHEAD (Action for Control for Health in Diabetes) trial,[19] which included 60% women, failed to demonstrate reduction in CVD events among men or women randomized to an intensive lifestyle intervention for sustained weight loss.

Sex differences have also been observed in studies evaluating the impact of glycemic control on outcomes for women with established CVD. Although the DIGAMI (Diabetes Mellitus Insulin-Glucose Infusion in Acute Myocardial Infarction) 2 study[20] did not reveal differences in death, stroke, or nonfatal MI between men and women, it did identify a heavier risk factor burden in women. It has also been observed that the risk of 30-day CVD re-hospitalization was 8.5 times higher among women with diabetes who were hospitalized for CVD and had poor glycemic control (A1C > 7%) than for those with good glycemic control (A1C < 7%); there was no similar association in men.[9]

So, where do we go from here? To continue to understand the gender gap in care and outcomes, more research is needed on women with diabetes who are at risk for or diagnosed with CVD. Women often have not been "at the table" in CVD research, despite their disproportionate burden of diabetes and CVD.[21] They must be better represented in clinical research, and furthermore, the resulting data must be stratified, analyzed, and reported by sex to determine optimal care for both women and men.[22] Clinicians, investigators, industry leaders, funders, and regulatory agency staff should be held accountable for increasing the participation of women in trials in proportion to their population burden of CVD and diabetes. Medical journal editors should require sex-specific reporting (or the provision of a legitimate rationale for not including such data) as a condition of publishing research.

Consistently applied, these efforts to fully include women in research will provide a greater quality and quantity of evidence and will better inform sex-specific treatment and risk factor modification for individuals with diabetes. Parallel concerted efforts are needed to increase awareness of CVD risk among women with diabetes and to encourage clinicians to better identify and more aggressively treat CVD risk factors.

We can and must do more to improve women's heart health and understand its relationship with diabetes. Systematic changes in how we study these conditions have the potential to provide better evidence-based care. Including women in research and appropriately applying what we already know to their care will reduce disparities in morbidity and mortality for women with diabetes.

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Electronically published ahead of print on 24 June 2013 (DOI: 10.1056/NEJMoa1212914)

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