Heart Disease Prevention in Young Women: Sounding an Alarm

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We have come a long way in the past 50 years toward reducing death and disability from cardiovascular diseases (CVD). And yet, as articulated by Wilmot KA et al. in this edition of *Circulation*,¹ we still have a long way to go, especially for young women and some racial/ethnic groups. These new findings highlight the value of looking “behind the curtain” at health data, in particular teasing apart age- and sex-related outcomes.

Wilmot KA et al. now build on our understanding of CVD mortality by highlighting recent trends in sub-populations, including young women, and they are troubling. These investigators examined mortality data for U.S. men and women 25 years and older between 1979 and 2011 using U.S. National Vital Statistics data that focused on coronary heart disease (CHD).¹,² ICD-9 and ICD-10 codes were used to determine the underlying cause of CHD deaths. Analyses of mortality data within three age groups (<55 years, 55 to 64 years, and 65+ years) during three decades (1979 to 1989, 1990 to 1999, and 2000 to 2011) yielded an initial assessment of mortality trends. Regression modeling then further evaluated trends in the estimated annual percentage change (EAPC) in CHD mortality across the entire time period, permitting calculation of statistically significant differences in EAPC from year to year.

On one hand, the news is good. The impressive (68 percent) decline in age-adjusted CHD mortality rate for both men and women across the overall study period is nothing short of remarkable and validates progressive improvements in CVD prevention and treatment. Overall, since 2002, older men and women (>age 65) continue to experience large reductions in CHD mortality, which drives this overall mortality decline.

Yet, disaggregating the data and recalculating mortality rates by age, gender, race, and time period points to worrisome new information. For both men and women, the EAPC was greater in older individuals (> 55 years) compared with those younger (<55 years). In addition,
men exhibited greater reductions in CHD mortality than did women when compared within age groups <65 years. For example, women <55 years had the lowest decline in CHD mortality. Furthermore, when stratified by race, Caucasians exhibited greater rates of decline compared with African Americans. One bright note in the new data is that the disparity in CHD mortality between men and women in the earlier decades, before 2002, has narrowed in the most recent decade, as young women and men showed a similar declining trend, despite a low EAPC.

**How did we get to our current situation and where do we need to go next?**

Much of what we know about CVD risk and health outcomes was seeded by observational cohort studies launched in the mid-20th century. Conventional wisdom about CVD at that time, in the mid-1960s, shifted dramatically when apparently healthy men in their 40s and 50s — many of whom had just returned alive from World War II — succumbed to fatal acute myocardial infarctions (AMIs). Searching for scientific explanations behind this rise in CVD deaths, the then-National Heart Institute launched the Framingham Heart Study in 1948. The goal of this cohort study was to identify the common factors that contribute to CVD by following its development in residents of Framingham, Massachusetts, over many years. The Framingham Heart Study is ongoing, now involving third-generation participants.

The first description of the Framingham findings, “Factors of risk in the development of coronary heart disease,” ³ indicated that elevations in serum cholesterol levels and hypertension were associated with an increase in AMIs and coronary heart death. In short, this seminal publication introduced the notion that CVD was preventable. But interestingly, this report foreshadowed another topic of concern: a high frequency of AMIs among women, albeit occurring later in life than in men. That observation was not re-visited in earnest until the
Women’s Health Initiative (WHI) was launched in 1991, and which yielded important data about CVD and other health risks in older (postmenopausal) women.

In the 1970s and 1980s, upon identification of the pathologic CVD risk factors, The National Heart Institute (later renamed the National Heart, Lung and Blood Institute, NHLBI) responded by creating national education programs and treatment guidelines for hypertension (in 1972) and hypercholesterolemia (in 1985). These efforts, combined with knowledge gained from large-scale primary and secondary prevention clinical trials and technological advances (angioplasty, defibrillation, pacemakers, and imaging), contributed to dramatic improvements in age-adjusted cardiac death rates (Figure 1).

**Forward to the present: How do we account for the flattening of mortality rates in younger people during the past decade, especially in women?** Several explanations are feasible. First, risk factors and outcomes have been predominantly studied in older individuals (>55 years), without similar attention to younger people. Women, in particular, have been underrepresented. Although federal regulations in place since 1993 have increased the representation of women in clinical studies to approximately 50 percent on the whole, once again it is important to look beyond the aggregate data. Variability in clinical trial participation exists across fields of medicine and across age. Careful attention to specific populations and disease context is warranted, as Wilmot KA et al. have done in the current analysis.

To that end, although the primary Framingham study population demographics yielded guidelines for prevention, diagnosis, and treatment targeted to an older-age group, many additional Framingham-style cohorts exist today and continue to provide data on sub-populations. NHLBI has been a leader in assembling an array of population studies focusing on
unique cohorts. These include the WHI, the Jackson Heart Study, Atherosclerosis Risk in Communities, the Multi-Ethnic Study of Atherosclerosis, the Strong Heart Study, and many more.\textsuperscript{5} It will be important for these studies to disseminate their results broadly and to follow up on new hypotheses prompted by their ongoing investigations. Such findings may inform individualized care options for women and people of various ethnic/racial backgrounds, toward improving outcomes in these populations.

Third, many awareness and education programs that are indeed targeted to women, such as the Heart Truth campaign, Go Red for Women and Women Heart, were initially focused on older women. After several years of experience, however, this focus has shifted to younger women. Time will tell how effective these awareness programs are reaching their target audiences, but such activities must continue given the serious health situation at hand.

A fourth issue speaks to behavioral and cultural factors that shape human activities. Older individuals tend to seek more medical care and are more likely to be evaluated for CVD risk, compared to younger people. Additionally, compared to men, women at any age tend to be underdiagnosed and undertreated. Some of this is attributable to individual behaviors, but another element is the broader societal context in which women are often, still, the primary caretaker in a family, who may forego their own health needs for a variety of reasons.

**Where do we go from here?**

The data speaks to us loudly and clearly. Framingham risk scores for women ages 35 to 54 years with AMI have increased, likely due to a range of influences, some of which are mentioned above. These elevated Framingham scores in younger women provide a clarion call for prioritized research toward understanding the basis of worse risk factor profiles in this
population. Lest we forget, these are women in the prime of life, and their health is often central to that of their families and their communities. By addressing women’s health at this stage, we are also extending benefit to the children and men in a woman’s life.

Improving primary prevention strategies is a good place to start. Given the results reported in Wilmot et al., requiring CVD screening in women, and in men, over age 25 years seems warranted. Evidence should guide such prevention efforts, and data collection – aggregated by sex and age – should be ongoing to assess the value of screening on both quantitative and qualitative outcomes. Reaching young women relies on a group of health professionals: our primary care physicians, obstetricians, gynecologists, family practitioners, and other health providers who care for women routinely. Specialists, such as endocrinologists, can play an important role in CVD diagnosis and treatment by considering co-morbidities such as diabetes, which has risen dramatically in young women over the past few decades along with a concomitant increase in overweight and obesity.6-9

We should also continue to pursue novel CVD prevention and treatment modalities that are based on new mechanistic findings about CVD pathology. Over the past few years, it has become clear that PCSK9 monoclonal antibodies that lower blood LDL may offer some advantages over statins.10 Continued basic research on the fundamental mechanisms of CVD at various life stages and in both sexes may offer additional valuable insights into new approaches that might be tailored specifically to individuals.

A common theme in the parlance of biomedicine today is that the era of personalized medicine is upon us. Beyond genomic and molecular foci, there is much more to consider. Physicians have a responsibility to meet the needs of their patients on an individual level that is person-centric. Thus, personalized medicine addresses a patient’s context, including the web of

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biological and psychosocial factors that contribute to risk and health outcomes in an individual. It also employs communication strategies that meet people where they are: at work and at play, well beyond periodic health care visits. Communication to younger women through the wide range of social media outlets with which they interact frequently is an enormous opportunity to reach this group, who may not recognize vulnerability until it is validated by their peers.

Finally, the current seismic shifts in health care access and affordable preventive care have important implications for considering health in different populations, including women. In keeping with changes in health care that involve team care and that focus on prevention, enlisting the contributions of behavioral health specialists will go a long way toward both recognizing and mitigating CVD risk factors.

We are at a crossroads. In spite of the considerable gains in cardiovascular health in this country over the past 50 years, considerable work is still ahead. We must refocus our efforts on better understanding CVD risk, particularly in younger women and men; we should routinely screen younger individuals for CVD risk; and where warranted, we should engage in primary prevention – including concrete, evidence-based lifestyle changes that promote good cardiovascular health. The promise of a life free from CVD should be within reach of all Americans.

Conflict of Interest Disclosures: None.

References:


Figure Legend:

**Figure 1.** Decline in Deaths from Cardiovascular Disease in Relation to Scientific Advances. The timeline shows the steady decline in cardiovascular deaths over the late 20th and early 21st centuries, along with major advances in cardiovascular science and medicine. ALLHAT denotes Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial, CASS Coronary Artery Surgery Study, GISSI Italian Group for the Study of Streptokinase in Myocardial Infarction, HMG-CoA 1-hydroxy-3-methylglutaryl coenzyme A, ISIS-2 Second International Study of Infarct Survival, MI myocardial infarction, NCEP National Cholesterol Education Program, NHBPEP National High Blood Pressure Education Program, PCI percutaneous coronary intervention, SAVE Survival and Ventricular Enlargement, and TIMI 1 Thrombolysis in Myocardial Infarction 1. From Nabel EG, Braunwald E. A tale of coronary artery disease and myocardial infarction. *N Engl J Med.* 2012 Jan 5;366(1):54-63.
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