Traditionally, women with coronary heart disease (CHD) have been understudied, underrecognized, and undertreated, with consequently more adverse outcomes than men. Sex-based differences in CHD outcomes are a compelling basis for enhancing the representation of women in CHD clinical trials. A robust literature specifically identifies that younger women have more adverse outcomes with myocardial infarction and coronary artery bypass graft surgery than do their male peers.

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This has obtained despite the data that, since 2000, there has been a steady decline in cardiovascular mortality for US women, narrowing the gender gap (Figure 1). Half of this mortality decline is attributable to improved management of established cardiovascular disease, and the remainder, to preventive interventions. Sex-specific science (evidence) guides management decisions and has translated into these improved cardiovascular outcomes for women over the past decade, yet many important clinical outcomes differ by age, with young women selectively disadvantaged. Since 1984, more women than men continue to die annually of cardiovascular disease. Importantly, in recent years, there has been an increase in cardiovascular mortality for young women, those aged 35 to 54 years, reversing the favorable trend of the past 4 decades. Cardiovascular mortality continues to decline, albeit more slowly in women aged 55 to 64, 65 to 74, 75 to 84, and >85 years (Figure 2).

This highlights the prescience and creativity of the Variations in Recovery: Role of Gender on Outcomes of Young AMI Patients (VIRGO) investigators in designing, conducting, and analyzing this National Heart, Lung, and Blood Institute study to fill the knowledge gap, examining the role of sex in the outcome of young patients (18–55 years) with acute myocardial infarction. The VIRGO protocol design is worthy of commendation. At each research site, after every 2 women enrolled, the next consecutive male patient present was enrolled. Women were thus preferentially represented.

Overall, young women with ST-elevation myocardial infarction (STEMI) in VIRGO were less likely to receive reperfusion therapy and less likely to meet reperfusion time guidelines than their male peers. The low overall mortality rate precluded this outcome correlation, but identified greater sex disparities in reperfusion delays in patients transferred to percutaneous coronary intervention (PCI) institutions or receiving fibrinolytic therapy.

The 4 incremental models in this study provide an understanding of the specific contribution of female sex to suboptimal management strategies. Model 1 adjusted only for sex; model 2 added sociodemographic factors, previous CHD, and cardiovascular risk factors; model 3 added transfer status, ECG data, atypical symptoms, presenting within 6 hours of symptom onset and hemodynamic instability on arrival; and model 4 added receipt of fibrinolytic therapy. Female sex remained a significant determinant of delay in reperfusion therapy even after adjustment for the items serially added in these models.

Education of emergency department professionals is pivotal. The ECG changes of STEMI are not subtle, but there remains major dependence on emergency department professionals to have a high index of suspicion of myocardial infarction even for young women with atypical symptoms, to immediately obtain the ECG, and then to promptly address transfer to the cardiac catheterization laboratory or transfer to a PCI-capable facility because myocardial ischemia kills.

It is noteworthy in the VIRGO article in this issue of Circulation addressing the subset of patients with STEMI, n=1465 (557 men and 908 women) that the first author represents the Department of Emergency Medicine, a critical link in the implementation of STEMI guidelines.

Educational and organizational opportunities may also derive from this study. Community public education endeavors, such as the Go Red for Women and Heart Truth campaigns of the American Heart Association and National Heart, Lung, and Blood Institute, respectively, should target CHD awareness in young women, the importance of atherosclerotic cardiovascular disease risk factor control, and the appropriate response of women to typical and atypical symptoms (non-chest pain ischemic equivalents). Increased awareness of the CHD burden of young women and their atypical symptoms should be addressed to primary care (including obstetrics/gynecology) providers, emergency department staff, emergency medical services staff; with specific initial access components of the STEMI guidelines emphasized with emergency department and emergency medical services professionals.

Owing to the demography of the study participants, the difference within populations of young women is inadequately represented, but...
there should be the opportunity to compare the baseline variables, interventions, and outcomes for the young black and young white women. Do these racial and ethnic subgroups differ in presenting symptoms, in time to presentation, in interventions? Given the underrepresentation of Hispanic and Asian women, their information cannot be derived from the VIRGO study.

Figure 1. Cardiovascular disease (CVD) mortality trends for males and females (United States: 1979–2011). Reprinted from Mozaffarian et al5 with permission of the publisher. Copyright © 2015, the American Heart Association.

Figure 2. Trends in age-specific mortality rates from coronary heart disease. Reprinted from Ford and Capewell6 with permission of the publisher. Copyright © 2007, the American College of Cardiology,
Risk factor control and patient education may relate to character-
istics of the patient’s primary care provider. A number of reports document more frequent primary care, especially for young women, by an obstetrician/gynecologist versus a general internist; was that evident in VIRGO? In a study from the Montefiore Medical Center presented at the Scientific Sessions of the American College of Cardiology in San Francisco in March 2013, young minority women were more likely to have their primary care needs met by an obstetrician/gynecologist. However, only 33% said they discussed heart disease with their obstetrician/gynecologist, despite the fact that 31% of the women experienced pregnancy-related diseases such as pre-
ceclampsia, gestational diabetes mellitus, which increase the risk of heart disease. About 30% of the women surveyed reported having chronic conditions such as diabetes mellitus, obesity, or hypertension. In another study, 35% of women reported that their obstetrician/gynecologist discussed heart health, and less than half were asked about smoking, weight management, exercise, and diet. Only 4% of both women and men had no identifi-
able risk factors; their risk factors are presented in Table 1 of the article, but sex-specific adequacy of risk factor control would provide added insight. Sixteen percent and 10%, respectively, of women and men reported atypical or no symptoms, predominating in women. In the National Registry of Myocardial Infarction database,10 young patients with atypical symptoms had more adverse outcomes. Were the primary care providers aware of the importance of cardiovascular risk reduction for women? Were they aware of the atypical symptom presentation of myocardial ischemia in women, and did they educate their patients? Lack of CHD research regarding women, with lack of disaggregation of data by sex even when women were enrolled in CHD studies, limited the ability to identify sex differences in care and outcomes, such that many providers remained uncertain of the risks and benefits of CHD interventions for their female patients. Given that the low mortality rate in VIRGO did not enable correlation with survival, medical record review and telephone interviews of VIRGO participants could ascertain outcomes of importance in the interval following STEMI hospital discharge and the 12-month mortality follow-up. Was there difference in the occurrence/severity of postinfarction angina? Was there difference in the occurrence of symptomatic heart failure, of arrhythmias? Was there difference in rehospitalizations, need for repeat revascularization, late survival? Were there differences in imaging data for ventricular function?

Several retrospective studies had suggested potential eti-
ologies for the sex disparities in STEMI outcome. This article documents a number of remediable features that characterize the suboptimal therapy of young women with STEMI, raise awareness of this problem, and mandate approaches to solu-
tions. Remediable clinical, organizational, and educational variables have the potential to maximize health outcomes for young women, and young men, as well, with STEMI. These include clinical appreciation that atypical symptoms delay time to presentation. To be clinically emphasized is the need to control cardiovascular risk factors and to intensively manage major comorbidities to lessen the likelihood of STEMI occurrence. Prehospital management requires coordination of community resources, ie, organizational systems of care. Community emergency medical services should focus on STEMI ECG recognition in the field, direct ECG transmission, and transport to a PCI-capable facility. Non-PCI facilities require algorithms to facilitate rapid communication and transfer to a PCI-capable center. Education remains pivotal. Community endeavors are requisite to increase heart disease awareness among women, appreciation of their atypical symptoms, and need for preven-
tive strategies to avert STEMI. All healthcare providers, both in ambulatory care settings and in emergency departments, must be alert to the aspects of prevention, recognition, and rapid response characteristics of optimal STEMI care, particularly for women.

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References

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Disparities in ST-Elevation Myocardial Infarction Management for the Young Goose and Young Gander: Clinical, Organizational, and Educational Challenges
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