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### REPLY: Association Between Migraine Headache and Cardiac Syndrome X



We appreciate the interest in our State-of-the-Art Review on nonobstructive coronary artery disease (CAD) (1) and the interesting data about migraine, and are pleased to add our comments.

In a previous report from the original Women's Ischemia Syndrome Evaluation (WISE) cohort, among 905 women, mean age 58 years, 220 reported a migraine history (2). They had lower angiographic CAD severity scores and less severe ( $\geq 70\%$  stenosis) angiographic CAD versus women without migraine history ( $n = 685$ ). These differences remained significant after adjustment for important cardiac risk factors. We prospectively followed 873 of the WISE cohort and found that migraine was not associated with a significant increase in adverse outcomes after 4.4 years. In addition, a preliminary analysis of that cohort concluded migraine was not linked to alterations in endothelial function (unpublished observations).

We have since reported WISE 10-year outcomes that now included a National Death Registry search (3). In response to this letter we updated our prior analyses, and now note that of a total cohort of 902 women included in extended follow-up 177 women died. Among those reporting migraine headaches, 32 of 220 (14%) died (all-cause) versus 145 of 682 (21%) in those without migraine (hazard ratio: 0.66; 95% confidence interval: 0.45 to 0.96;  $p = 0.031$  [unadjusted]). However, when adjusted for age, diabetes, body mass index, smoking, family history of CAD, race, aspirin use, dyslipidemia, and CAD severity score, absence of migraine is no longer a significant predictor for either all-cause death (hazard ratio: 1.12; 95% confidence interval: 0.73 to 1.72;  $p = 0.60$ ) or cardiovascular death.

We also use this opportunity to reemphasize that it is no longer possible to support use of the term "cardiac syndrome X" for the rationale described in our recent article (1). A comprehensive review confirmed that there were no standard definitions for this terminology among published data (4). Furthermore, at least 1 pathophysiological mechanism present in many of these patients is attributable to coronary microvascular dysfunction, and therefore no longer "unknown" as implied by this term.

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## Caveat Emptor

### Antibiotics, Endocarditis, and Statistical Artifacts



In October 2007, the American Heart Association published guidelines that recommended against the use of prophylactic use of antibiotics before oral surgery among patients at moderate risk of adverse outcomes from infective endocarditis (IE) (1). Analyzing the Nationwide Inpatient Sample dataset for IE hospitalizations, Pant et al. (2) noted an increase in rates of streptococcal IE and "speculate(d) that this may be related to the decrease in the use of