Reply to Chow et al

To the Editor—We thank Chow et al. [1] for their interest in our study and their analyses of the association of the Veterans Aging Cohort Study (VACS) index with coronary artery calcium (CAC). We are pleased to have others evaluate the index and agree that it is important to consider whether it predicts mortality due to coronary heart disease (CHD) in addition to that of all-cause mortality.

Although the association of CAC with CHD events has yet to be demonstrated among those with human immunodeficiency virus (HIV) infection, we agree that an association seems highly likely. Coronary artery calcium is associated with traditional CHD risk factors [2] and with conditions associated with increased inflammation, including diabetes, systemic lupus, rheumatoid arthritis, and obesity, in the general population [3–6].

There are many reasons to expect that the VACS index would predict CHD deaths. The index includes CD4 count, HIV-1 RNA, and eGFR, which are associated with CHD events among those with HIV infection [7–9]. Further, we demonstrate a strong association of VACS index scores with markers of inflammation (interleukin 6, D-dimer, and sCD14) [10]. Thus, we are surprised that Chow et al found no association beyond age with the VACS index score.

There are several possible explanations for this apparent contradiction. First, there may not be sufficient variation in other components of the VACS index in their dataset. If most people in the sample had an HIV-1 RNA <500 copies/mL, a CD4 cell count >500 cells/mL, and no evidence of organ injury, we would expect to see little additional association beyond age.

Second, as they mentioned, CAC is not a perfect surrogate for CHD. It would be a mistake to assume that the VACS index does not reflect risk of mortality from CHD simply because it is not correlated with CAC.

To explore this question directly, we ran an analysis using death certificate cause-of-death data from the National Death Index recently added to the VACS. We considered all HIV-infected subjects who had been on combination antiretroviral therapy for 12 months (n = 4932) and asked whether the VACS index is as good at predicting deaths attributed to CHD (codes 120.X–123.X and 125.X: 34 deaths) as all-cause mortality (755 deaths). The C statistic for CHD deaths (0.77; 95% confidence interval [CI], .70–.85) was similar to the C statistic for all-cause mortality (0.78; 95% CI, .76–.80). The C statistic for predicting CHD deaths using the restricted index (including only age, CD4 count, and HIV-1 RNA) was substantially lower (0.70; 95% CI, .61–.78), and that for age only was lower still (0.67; 95% CI, .58–.76). These data suggest that organ system injury as reflected in the VACS index is independently associated with CHD among those with HIV infection—beyond the association of age alone. It is possible that the strong association between the VACS index and both coronary heart disease and all-cause mortality would be enhanced by addition of CAC, but this remains to be established, and the added prognostic discrimination would need to counterbalance added complexity and cost [11].

Notes

Potential conflicts of interest. M. S. F. has received institutional grant support from the National Institutes of Health (NIH) Heart, Lung, and Blood Institute. A. C. J. and J. P. T. have received institutional grant support from NIH/National Institute on Alcohol Abuse and Alcoholism. M. C. R.-B. has received institutional grant support and support for travel to

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meetings from the NIH. R. T. has received institutional grant support from the Veterans Administration and the NIH.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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Clinical Infectious Diseases 2012;55(5):751–2
Published by Oxford University Press on behalf of the Infectious Diseases Society of America 2012.
DOI: 10.1093/cid/cis539