REPLY: Poor Sensitivity and Specificity of Electrocardiographic Estimation of Myocardial Mass

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patients in this cohort, then this adjustment may in fact strengthen these associations.

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REPLY: Poor Sensitivity and Specificity of Electrocardiographic Estimation of Myocardial Mass

We thank Drs. Ormerod and Rider for their interest in our study (1). Although we would agree that the electrocardiograph (ECG) is an imperfect measure for estimating myocardial mass and that QRS indices "might also reflect electrical remodeling of the action potential and not mass per se" (1), we are mindful of the fact that more sophisticated measures such as those based on magnetic resonance scanning (2,3) would have yielded a much smaller sample size compared with our study (N = 73,518) or other ECG-based analyses (4,5). From our perspective, the key advantage of the ECG is that it has been associated repeatedly with outcomes and is used universally across worldwide biobanks and population cohorts. We acknowledge that a genome-wide association study is only a first step toward a better understanding of the heritable factors underlying cardiac function in general. We note that, even if the 4 QRS measures used in our study capture myocardial mass imperfectly, this should not lead to an increased type 1 error (false-positive genotype-phenotype associations); there was no evidence of an inflated test statistic. With regard to the effect of body mass index on our ECG measures, we agree with Ormerod and Rider, and that is exactly why we did adjust for age, sex, height, and body mass index, as described in the Supplementary Materials.

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Please note: Dr. de Bakker is currently an employee of Vertex Pharmaceuticals; and owns Vertex Pharmaceuticals equity. Dr. van der Harst has reported that he has no relationships relevant to the contents of this paper to disclose.

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Heart Rate Reduction and Cardiovascular Outcome in Hypertension

I read with great interest the paper by Messerli et al. (1) on the effects of heart rate (HR) reduction in hypertension (1). The authors affirm that HR lowering in hypertension has been documented to progressively increase cardiovascular mortality. This statement was mainly based on a meta-analysis of 9 clinical trials encompassing more than 60,000 hypertensive patients (2). I suggest caution is needed when interpreting these findings for several reasons, but particularly for the possible fallacy of meta-analyses based on aggregate data. Using averages or proportions of patient data often leads to misinterpretation of the effect of patient characteristics on outcomes. Indeed, the analyses of individual patient data made in the 3 main