

## Response to Letter Regarding Article, “Dietary Fish and $\omega$ -3 Fatty Acid Consumption and Heart Rate Variability in US Adults”

Drs Jong and colleagues raise important issues on assessment and use of heart rate variability (HRV) for scientific and clinical evaluation of preventive treatment strategies. They note that pharmacological, biobehavioral, and exercise interventions modestly increase time-domain and frequency-domain HRV, with average effects equivalent to  $\approx$ 16% increase in SDNN (standard deviation of all N-N intervals).<sup>1</sup> We also found modest differences in time-domain and frequency-domain HRV with fish consumption,<sup>2</sup> such as 11%-higher SDNN on 12-lead ECGs, and 6%-higher SDNN index and 12%-higher normalized high frequency and very low frequency power on 24-hour Holter, suggesting that fish consumption may have effects on these HRV indices of similar magnitude to those of pharmacological and other interventions. Notably, we were also able to assess prospectively the relationships of these modest HRV differences with future clinical outcomes: modest but significant differences in coronary heart disease mortality were seen. We therefore agree with Dr Jong and colleagues that such modest differences in HRV are likely to be clinically relevant and appropriate for assessment of preventive strategies. We also agree that detection of such differences will require appropriately large numbers of participants and that insufficient statistical power likely accounted, at least in part, for inconsistent results of prior trials of fish oil and HRV.

However, our findings also highlight 2 other critical points related to scientific and clinical evaluation of HRV. Not all increased HRV is healthy: greater erratic (noncyclical) HRV, as quantified by nonlinear HRV indices such as short-term fractal scaling exponent and Poincaré ratio, reflects abnormal sinus firing and predicts higher clinical risk.<sup>2-4</sup> Increases or decreases in erratic sinus firing can confound certain time-domain and frequency-domain indices and must be accounted for when evaluating the effects of specific interventions on HRV. Additionally, whereas such nonlinear HRV indices are uncommonly evaluated in clinical studies, our findings suggest that differences in these indices may be both easier to detect (in terms of numbers of participants required) and more strongly associated with clinical outcomes, at least among older adults. Thus, clinical studies of HRV should routinely assess nonlinear HRV measures to account for confounding effects of erratic heart rate

patterns on time-domain and frequency-domain indices and to determine how changes in nonlinear HRV indices may affect clinical outcomes.

## Disclosures

None.

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