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## LETTER

*The Reply:*

We thank Halberg, Cornelissen, and Schwartzkopff for their interest in the article.[1] They are correct to point out that blood pressure measurements in the Atherosclerosis Risk in Communities study, the cohort used in our analysis, are obtained on conventional spot checks of blood pressure after 5 minutes of rest on 4 occasions 3 years apart. Indeed, most epidemiologic studies, ranging from the Framingham cohort[2] to National Health and Examination Surveys[3] and the Coronary Artery Risk Development in Young Adults,[4] use similar blood pressure readings.

Because conventional blood pressure measurements are prone to nonsystematic measurement error, they have a tendency to bias the results toward the null hypothesis and underestimate the effect of the exposure.[5] The authors suggest "a more demanding" approach for the measurement of blood pressure. This approach involves a half-hourly around-the-clock record of blood pressure and heart rate for 7 days that is then fitted into a best-fitting cosine curve adjusted for age and gender, and called circadian hyperamplitude-tension (CHAT). They present interesting data from a relatively small cohort of individuals suggesting that individuals with excessive CHAT have an increased risk of cardiovascular disease.

The approach suggested by authors is novel and likely speaks to the underlying pathophysiology of vascular tone, heart rate variability, and neuroendocrine factors on the development of cardiovascular disease. Yet before the implementation of this approach to the general public, some important theoretic and practical issues require clarification.

First, does this methodology add any incremental information to existing ways of measuring cardiovascular risk? The data illustrated in Figure 1 suggest that CHAT may be predictive of cardiovascular disease events independently of heart rate variability and pulse pressure, but does it add to a risk prediction model that incorporates multiple traditional cardiovascular risk factors? Furthermore, 24-hour ambulatory blood pressure monitoring (24-ABPM) is currently available as an alternative methodology to conventional blood pressure measurement and adds additional prognostic information, such as nocturnal dipping. It seems that 24-ABPM would be easier to perform than the method suggested by the authors. The authors imply that CHAT may precede an increase in 24-ABPM midline estimating statistic of rhythm, yet a comparison of CHAT and ABPM would be useful to determine which one is more effective at profiling subsequent cardiovascular disease risk.

Second, how could measurement of CHAT be practically implemented in the prehypertensive and hypertensive population? The methodology is not widely available and, thus, issues of reproducibility and standardized interpretation would arise. Furthermore, would it be acceptable to patients? The parameters typically assessed to predict cardiovascular risk (weight, physical activity, tobacco exposure, family history, serum creatinine, lipids, glucose, and blood pressure) can be measured with minimal discomfort or inconvenience to patients at a relatively small cost. CHAT requires measurements for 7 days. The prehypertensive population currently outnumbers the hypertensive population, and together they probably make up more than 100 million individuals and affect more than 60% adults in the United States alone.[6,7] Clinicians are constantly being asked to increase productivity and decrease costs. Measuring CHAT in all of these individuals would undoubtedly be time-consuming and expensive, and may not be tolerated by patients.

Third, does treatment aimed at reducing CHAT improve patient outcomes? The authors note that specific behavioral and pharmacologic therapies are effective in minimizing circadian blood pressure variability, but this may not translate into a lower risk of cardiovascular events. Indeed, the Controlled Onset Verapamil Investigation of Cardiovascular End Points Trial[8] demonstrated that controlled-onset, extended-release verapamil (dosed to minimize the early morning surge in blood pressure) was no more effective than conventional diuretic or beta-blocker treatment in reducing cardiovascular disease.

In summary, CHAT is a novel method of profiling blood pressure. In the future, it may have a place among the battery of clinical and laboratory measurements used to assess cardiovascular risk. Currently, its practical applicability is at best uncertain, and it remains unclear whether it will enhance the ability of the clinician to optimally manage patients to reduce the risk of cardiovascular disease.

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