Cautionary Note on the Use of Pulse Pressure as a Risk Factor for Coronary Heart Disease

To the Editor:

Dr Franklin and others have reported a number of important findings from the Framingham data set. In the latest article, the authors have concluded that, among systolic, diastolic, and pulse pressures, pulse pressure is the strongest predictor of coronary heart disease (CHD) in persons 60 years of age and older. However, the relative importance of various blood pressure measures as predictors for CHD risk is not, in our opinion, tested properly. We believe that the statistical analyses comparing different measures of blood pressure are flawed in this and other studies.1–4

A common means of comparing different blood pressures for CHD prediction is to examine the relative risk (RR) or hazard ratio (HR) of a CHD event that would result from a change of 10 mm Hg in each pressure measure.1–4 However, comparing risks or hazards of two different continuous measures is only valid if the amount of change in one measure is comparable to the same amount of change in the other. For example, if pulse pressure has a smaller standard deviation than systolic pressure, using the same absolute value of change for both, such as 10 mm Hg, biases analyses of predictive strength in favor of pulse pressure. This is why researchers often use ±1 standard deviation (SD) to calculate RRs for continuous measures rather than some arbitrary absolute value, such as 10 mm Hg. Next, the question of relative importance for two predictors (eg, systolic and pulse pressure) must be tested by the −2 log likelihood (L) comparison statistic, which assesses increased variance explained when each measure is added to the same multivariate model.5

Many studies have now suggested that the pulse pressure is superior to systolic or diastolic blood pressure in predicting CHD. We believe that this conclusion cannot be accepted until data sets are reanalyzed using ±1 SD change for both, such as 10 mm Hg, biases analyses of predictive strength in favor of pulse pressure. This is why researchers often use ±1 standard deviation (SD) to calculate RRs for continuous measures rather than some arbitrary absolute value, such as 10 mm Hg. Next, the question of relative importance for two predictors (eg, systolic and pulse pressure) must be tested by the −2 log likelihood (L) comparison statistic, which assesses increased variance explained when each measure is added to the same multivariate model.5

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Response

We agree completely with Davidson et al that valid comparison of hazards ratios (HRs) for different continuous measures requires that the units of both variables are comparable. In our earlier paper,1 we reported HRs per 10 mm Hg and per 1-SD increment and found no appreciable difference in the prediction of coronary heart disease (CHD) risk by either method. In the recent paper,2 we reported only per 10 mm Hg, which we felt was more easily understood by clinicians.

We also agree that the question of relative importance cannot be addressed by the HRs, but should be addressed by comparison of test statistics, or significance levels, obtained when each variable is added to the same model. Whether one compares −2 log likelihood statistics, or the asymptotically equivalent Wald chi-squared statistics, makes little difference in large samples. From comparisons of chi-squared statistics in our 2001 paper2 (Table 2), we note that diastolic pressure is more “important” among subjects under 50 years old, whereas pulse pressure is (somewhat) more “important” than systolic pressure in subjects aged 60 years and older.

As for recalculation of HRs to 1-SD increment in our 2001 paper,2 data are shown in Table 1 that permit one to perform the calculations, albeit crudely, for each age group: multiply by SD/10 the β estimated per 10 mm Hg to obtain the estimate per 1 SD, then exponentiate. For subjects aged 60 years and older, one obtains HR = 1.40 for SBP, HR = 1.12 for DBP, and HR = 1.43 for PP. The test statistics are invariant to location and scale changes on the variables, so inference about relative importance is unaffected.

The conclusion that pulse pressure is superior to systolic blood pressure in predicting CHD risk in individuals 60 years and older requires further elaboration. Pulse pressure cannot replace systolic blood pressure as a single measure of CHD risk.3 The best clinical strategy for using blood pressure indices for the estimation of CHD risk in older persons is to first determine the level of SBP elevation and then adjust the overall risk upward if there is wide pulse pressure, ie, discordantly low diastolic blood pressure.3 However, it remains premature to change national treatment recommendations, because any new strategy of blood pressure assessment must first be tested directly in clinical trials.

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