Change Viewed on the Level

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Readers of the Journal will have seen two contributions on the question of whether change in blood pressure is related to coronary heart disease, independent of the level of blood pressure. An analysis of data collected in the Seven Countries study led Farchi et al. to suggest that change of blood pressure is a predictor of heart disease independent of blood pressure level. Woodbury et al. reported a similar finding based on data collected in the Framingham Heart study. However, in a recently published report also using Framingham data, we found no evidence for an independent contribution of blood pressure change in predicting the risk of coronary heart disease, all cardiovascular diseases, and total mortality. It is the purpose of this article to discuss the reasons for these contrasting inferences, even arising from the same study. But first we have to make sure that the matter is worth talking about.

The issue of whether blood pressure change is an independent predictor of disease risk has a bearing upon three basic questions.

(1) At a certain level of blood pressure, does it matter what the future level is? This is a major question from the public health viewpoint, and its answer may be the rationale for interventive measures to keep the pressure from rising.

(2) At a certain level of pressure, does it matter what the original level was in the past? This seems to be an important question from the clinician's position. It addresses the internist or GP, who is wondering whether a 50 year old man with a systolic pressure of 160 mmHg all his adult life should be treated differently from a man of the same age who had a rise of systolic pressure from 130 to 160 mmHg in recent years.

(3) Does change of blood pressure play a part in the causation of heart disease, or is it merely a certain level of blood pressure that causes the trouble? This question may be of interest to students of the aetiology of coronary heart disease, curious as they are about the mechanisms of athero-and thrombogenesis.

The contrasting opinions mentioned above are not a matter of the findings, but of the inference based upon them. The major problem in the data-analytical approach to these questions is that it is hard to disentangle change and level in observational studies. Blood pressure change has always to be considered conditional on a certain level of blood pressure because of the strong association between level and change. The two major options are depicted in Figure 1: blood pressure change might be viewed given an initial level, or given an attained level of blood pressure. As to the analysis of change conditional on initial level the findings are unequivocal. All reports suggest that change of blood pressure predicts heart disease risk given a certain initial level. Farchi et al. have concluded that this means that blood pressure change is a predictor of heart disease, but we do not entirely agree with their view and have suggested that this observation might simply be a manifestation of the impact of blood pressure level on cardiovascular risk. Inference about any independent contribution of blood pressure change in the prediction of disease must be based on analyses conditional on attained blood pressure level. Our report, based on the latter analysis, presents no evidence for an independent contribution of blood pressure change to disease risk. Thus, our first question may be answered positively: at a certain level of blood pressure, it does matter what the future level is. But, as an answer to the second one, it does not matter what the level was in the past. And, as far as the aetiology of heart disease is concerned it seems that the intuitively appealing view that rise in blood pressure is related to the amount of atherosclerosis and thereby to heart disease risk, is not supported.

Why is the interpretation of the analysis conditional on attained level completely different from the one conditional on initial level? And why does a true indepen-

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dent effect of blood pressure change manifest itself as being only conditional on attained level? Imagine a population in which blood pressure level is associated positively with the occurrence of heart disease and in which change in blood pressure is not associated with heart disease. Consider first only those subjects who have the same initial blood pressure. Subjects with a large rise in blood pressure will suffer more cardiac events than those with a small rise, although there is no true association between change in blood pressure and heart disease. Blood pressure change determines the attained level of blood pressure and thereby the risk of suffering a cardiac event. In a statistical model with cardiac events as the outcome variable and initial level and change of blood pressure as determinants, the coefficient of blood pressure change will be positive. But consider now in the same population only those with the same attained blood pressure. In this case subjects with a large rise of pressure will have the same incidence of cardiac events as those with a small rise, since only blood pressure level is a determinant of the disease. In a statistical model blood pressure change will (in principle) have a coefficient of zero.

What are the more general implications of this reasoning? This approach may also have merit in other areas of epidemiological research where concern is with the effect of change with age of a certain characteristic on disease risk. For example, when the relation between the rate of decrease in cognitive function and the occurrence of senile dementia is studied, or change in pulmonary function and the incidence of chronic nonspecific lung disease, or the relation between change in serum cholesterol concentrations and cardiovascular diseases. And as for blood pressure and coronary heart disease, one wonders what other prospective follow-up studies with repeated blood pressure measurements would show when analysed along the lines suggested above.*

REFERENCES

*Postscript: At a recent meeting of the European Society of Cardiology, Farchi et al. presented an analysis of data collected in the Seven Countries Study that closely confirmed our Framingham findings. (Farchi G, Capocaccia R, Menotti A, Verdecchia A. Spontaneous risk factor changes as predictors of coronary events [Abstract]. Eur Heart 1983; 4 (suppl E): 7).