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*For Debate . . .*

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**Does change in blood pressure predict heart disease?**

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**Abstract**

Whether a change in blood pressure is related to the occurrence of cardiovascular disease, independent of blood pressure level, was investigated using data collected in the Framingham heart study on 5209 subjects. The follow up period of 26 years was divided into a first period of 12 years in which the blood pressure change was computed for each individual and a subsequent period of 14 years in which the risk of cardiovascular disease was determined. Blood pressure change was positively related to risk of cardiovascular disease. This association remained when blood pressure level at the start of the study was taken into account but disappeared when the level attained after the first 12 years was taken into consideration. For the clinician this suggests that the decision to treat high blood pressure is best guided by the actual level of pressure and not by its long term trend in the past.

**Introduction**

Although many studies have shown a strong relation between the level of blood pressure and atherosclerotic diseases,<sup>1-5</sup> it is not known whether it is the actual level of blood pressure or the rate of increase of blood pressure over time that is the most important predictor of cardiovascular events.

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We studied the relation between rise of blood pressure and the occurrence of cardiovascular events, coronary heart disease, and death from all causes using data collected in the Framingham heart study. The yearly increase of blood pressure was obtained for each individual from five to seven blood pressure readings over a 12 year observation period and related to incidence of cardiovascular events, coronary disease, and death from all causes in a subsequent 14 year period of follow up.

**Subjects and methods**

In the Framingham heart study a cohort of residents of Framingham, Massachusetts, USA, aged 30-62 years at the start of the study, has been followed for 26 years since 1948, as described in detail elsewhere.<sup>5</sup> In brief, a sample of 3074 men and 3433 women was invited, of whom 2024 men and 2445 women took part in the study; 740 volunteers (312 men) were added to the respondents, so that the study cohort comprised 2336 men and 2873 women. They were examined every two years and follow up data were obtained over a period of 26 years for essentially the entire cohort. Blood pressure was measured by a doctor on the subject's left arm while sitting. Diastolic pressure was based on the fifth Korotkoff sound. A standard mercury sphygmomanometer with a 14 cm cuff was used.

**DIAGNOSTIC CRITERIA**

Diagnostic criteria for the diseases under study have been given elsewhere.<sup>5</sup> Here we consider only all cardiovascular events (including coronary heart disease, intermittent claudication, congestive heart failure, cerebrovascular accidents), coronary heart disease (excluding angina pectoris), and death from all causes. All events were reviewed by a panel of investigators.

**OBSERVATION PERIOD**

For this analysis the 26 years of follow up were divided into an observation period of 12 years on which the rate of increase of blood pressure for each individual was computed and a subsequent period of 14 years during which the incidence of cardiovascular events, coronary

disease, and death from all causes was determined. This gives estimates of the 14 year risk of these events. The men and women in the cohort were aged 42-74 years at the start of the 14 year follow up period.

### ELIGIBILITY FOR ANALYSIS

Eligible for this analysis were the 1460 men and 1890 women who attended the seventh biennial examination (12 years after entry in the study), were free of cardiovascular disease at that time, were not taking antihypertensive drugs, and had at least five (out of a maximum of seven) readings during the observation period of 12 years. Of the original cohort, 876 men were not eligible for one (or more) of the following reasons: 253 died (149 of a cardiovascular event) and 430 suffered a cardiovascular event before the seventh biennial examination, 136 were taking antihypertensive drugs at the seventh biennial examination, and 296 had fewer than five blood pressure readings. Similarly, 983 women were not eligible: 152 died (63 of a cardiovascular event) and 267 had a cardiovascular event, 356 were taking antihypertensive drugs, and 284 had fewer than five blood pressure readings.

### DATA ANALYSIS

The rate of increase in blood pressure was determined by least squares regression of pressure on time for each individual. The slope obtained in this regression serves as an estimate of the yearly increase of pressure.

We analysed the predictive value of the rise in blood pressure for cardiovascular disease conditional on initial pressure and conditional on attained pressure. Initial and attained levels were recorded at the beginning and the end respectively of the 12 year observation period over which the yearly increase of blood pressure was obtained. Within each of four strata of initial and attained blood pressure readings the subjects were divided according to the median of the yearly change of pressure (medians are given in table I). We compared the proportions of subjects suffering a cardiovascular event among those with a small increase in blood pressure (below the median) and those with a large

increase (above the median). In addition, we performed logistic regression<sup>6</sup> with cardiovascular events, coronary disease, or death from all causes as the outcome variable and the yearly change of blood pressure and initial or attained level of pressure as independent variables. We added potential confounders of the relation between blood pressure change and cardiovascular disease to the model, notably age (years), total serum cholesterol (mmol/l), obesity (Framingham relative weight), diabetes mellitus (yes, no), and cigarette smoking (yes, no). These covariates were measured at the start of the 14 year follow up (together with the attained level of blood pressure).

### Results

The yearly rise in systolic blood pressure was positively associated with cardiovascular events, coronary disease, and death from all causes. When the initial level of pressure was taken into account this association remained (table II). Within each category of initial pressure subjects with a large increase in blood pressure suffered considerably more cardiovascular events than those with a small increase (fig 1). After adjustment for other potential predictors of disease risk the yearly rise of systolic blood pressure remained associated with cardiovascular events, coronary disease, and death from all causes in both men and women (table III). The interaction between age and change of blood pressure in the logistic model was not significantly different from zero. We obtained essentially the same results for diastolic pressure.

When instead of initial level the attained level of systolic blood pressure was taken into account the increase in systolic pressure was not related to disease risk (table II). Within each stratum of attained systolic pressure subjects with a large increase in blood pressure before they reached the attained level experienced about the same number of cardiovascular events as those with a small rise (fig 2). A separate analysis showed this also to be the case for those with an

TABLE I—Median yearly change in systolic blood pressure (mm Hg) over a 12 year period according to initial and attained systolic blood pressures. (Number of subjects is given in parentheses)

Systolic blood pressure	Men (n = 1460)		Women (n = 1890)	
<i>Initial level</i>				
≤ 119	0.64	(291)	0.76	(518)
120-129	0.22	(358)	0.43	(473)
130-139	0.20	(383)	0.41	(387)
≥ 140	-0.26	(428)	0.07	(512)
<i>Attained level</i>				
≤ 119	-0.54	(317)	-0.29	(445)
120-129	-0.06	(316)	0.17	(379)
130-139	0.21	(317)	0.64	(372)
≥ 140	1.14	(510)	1.32	(694)

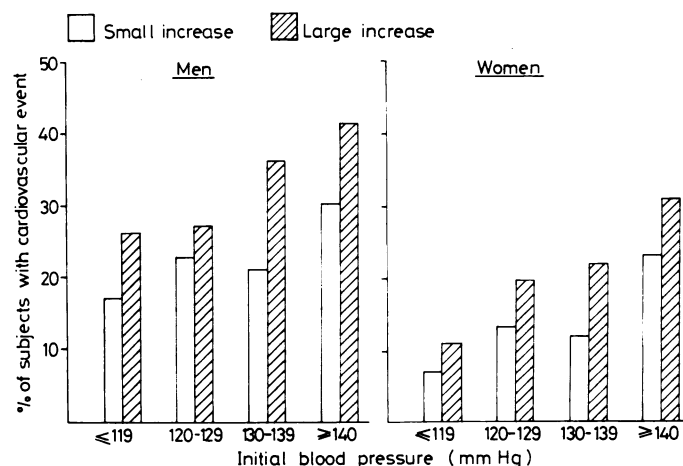


FIG 1—Proportion of small increasers and large increasers suffering a cardiovascular event conditional on initial blood pressure.

TABLE II—Percentage of events among subjects with small increases in blood pressure (S) and those with large increases (L) according to initial and attained systolic blood pressures (mm Hg). (Percentage of fatal cardiovascular events are given in parentheses)

Systolic blood pressure	Men (n = 1460)						Women (n = 1890)					
	Cardiovascular disease*		Coronary heart disease†		Death		Cardiovascular disease*		Coronary heart disease†		Death	
	S	L	S	L	S	L	S	L	S	L	S	L
<i>Initial level</i>												
≤ 119	7	16	8	12	16 (5)	19 (9)	7	11	2	4	6 (1)	11 (3)
120-129	23	27	13	16	13 (7)	25 (10)	13	19	3	8	7 (1)	12 (5)
130-139	21	36	13	20	16 (5)	25 (9)	12	22	5	6	11 (3)	12 (5)
≥ 140	30	41	18	22	24 (12)	31 (18)	23	30	10	11	24 (9)	25 (14)
<i>Attained level</i>												
≤ 119	23	15	13	12	7 (7)	12 (0)	9	10	2	2	10 (2)	7 (1)
120-129	23	21	14	14	21 (9)	17 (6)	13	12	4	3	7 (2)	9 (3)
130-139	23	23	14	11	18 (7)	23 (6)	15	12	6	5	12 (3)	12 (3)
≥ 140	41	42	25	21	26 (13)	34 (15)	28	26	11	11	24 (12)	17 (8)

\* All cardiovascular diseases, including coronary heart disease, angina pectoris, intermittent claudication, congestive heart failure, cerebrovascular accidents.  
† Coronary heart disease, not including angina pectoris.

attained systolic blood pressure of 160 mm Hg or over. Logistic regression with the attained level in the model gave coefficients which were not significantly different from zero, although they were all negative (table III). This was the case for systolic and diastolic pressure.

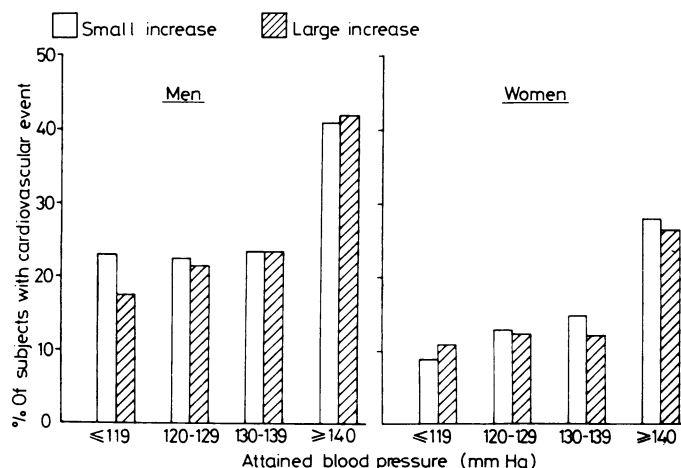


FIG 2—Proportion of small increasers and large increasers suffering a cardiovascular event conditional on attained blood pressure.

TABLE III—Coefficients of logistic regression\* of events on rate of increase in systolic blood pressure conditional on initial and attained systolic pressures

Event	Men (n = 1427)†			Women (n = 1760)		
	b	SEb	p <sub>2</sub>	b	SEb	p <sub>2</sub>
Conditional on initial level						
Cardiovascular disease‡	0.150	0.046	0.001	0.190	0.048	0.0002
Coronary heart disease	0.129	0.056	0.018	0.164	0.071	0.022
Death	0.177	0.051	0.001	0.128	0.052	0.015
Conditional on attained level						
Cardiovascular disease‡	-0.074	0.057	0.194	-0.042	0.056	0.453
Coronary heart disease	-0.082	0.067	0.219	-0.125	0.081	0.126
Death	-0.049	0.062	0.435	-0.109	0.060	0.070

SE = Standard error.

\* Adjusted for total serum cholesterol, smoking, diabetes mellitus, Framingham relative weight, and age.

† Slightly different from table I owing to missing values of covariates.

‡ All cardiovascular diseases, including coronary heart disease, angina pectoris, intermittent claudication, congestive heart failure, and cerebrovascular accidents.

## Discussion

The findings in this study suggest that blood pressure rise predicts cardiovascular disease conditional on initial level of blood pressure, but not on attained level. In other words, given a certain level of blood pressure, what matters is where you go to, and not where you came from (fig 3). This seems paradoxical, but it has to be borne in mind that the relation between

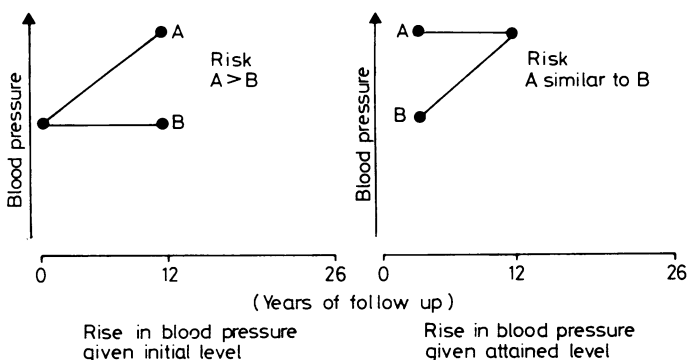


FIG 3—Diagram of observations in this study.

blood pressure rise and cardiovascular disease, given initial level, might simply reflect the change of level over time. Contrary to what has been suggested<sup>7,8</sup> we cannot infer from this that change in blood pressure by itself contributes to cardiovascular risk. A true independent effect of blood pressure change should manifest itself conditional on attained level, and we found no evidence of such an effect.

Blood pressure change was estimated by linear regression of blood pressure on time. This entailed making the assumption, undoubtedly unwarranted in some subjects, of a linear increase in blood pressure over time. The inadequacy of the model might dilute a true relation between rise of pressure and disease risk and therefore the true coefficients conditional on attained level might be (more) negative. Since the study population was between 42 and 74 years old and free of cardiovascular disease at the start of follow up our analysis does not address the question whether blood pressure change earlier in life plays an important role in determining cardiovascular risk. Furthermore, we consider here only the long term change in pressure and the current findings reflect average trends in the population. A separate analysis showed that the variability of blood pressure over the 12 year observation period, as measured by the residuals of individual linear regression of pressure on time, was not a predictor of cardiovascular disease, whether conditional on initial or attained level. This confirms a previous report from the Framingham study.<sup>9</sup>

From a clinician's viewpoint these findings suggest that decisions concerning the treatment of "borderline" or high blood pressure might be best guided by the actual level of pressure and not by its trend in the past. For example, the risk for a 50 year old man with a systolic pressure of 160 mm Hg is similar whether his pressure has risen from 130 mm Hg or has remained at 160 mm Hg over the past 12 years.

From a public health viewpoint the finding that the rate of change in blood pressure, given a certain initial level, predicts occurrence of cardiovascular disease indicates that there might be merit in preventing blood pressure from rising. This seems to apply to the whole range of initial levels and underscores the idea that preventive measures affecting the population as a whole,<sup>10</sup> as well as "high risk" groups, might be effective.

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