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The Increase in Blood Pressure with Age and Body Mass Index is Overestimated by Conventional Sphygmomanometry

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This cross-sectional study investigated whether the technique of blood pressure measurement used (conventional sphygmomanometry vs. ambulatory monitoring) affects the relation between blood pressure and both age and body mass index. Two independent data sets were analyzed. The first comprised 328 subjects (48% men) drawn from the population of a small Belgian town, and the second comprised 776 Irish bank employees (51% men). Age ranged from 17 years to 81 years, and body mass index (weight (kg)/height (m)^2) ranged from 16.6 to 40.2. Twenty-four-hour ambulatory blood pressure was lower than blood pressure measured by a nurse in both the Belgian population sample (118/71 mmHg vs. 122/73 mmHg) and the Irish employees (118/72 mmHg vs. 119/76 mmHg). When blood pressure was measured by an observer, the well-established relations between systolic and diastolic blood pressure and both age and body mass index were evident. When the analyses were repeated using 24-hour measurements, the increment (cross-sectionally assessed) in blood pressure with age was weaker, especially in young and middle-aged subjects (20–60 years), while the increase in blood pressure with body mass index was also reduced. The within-subject differences between the conventional and ambulatory blood pressure measurements increased with older age and greater body mass index. Several other relations with blood pressure as the response variable may require revision in light of the present findings. *Am J Epidemiol* 1992;136:450–9.

age factors; blood pressure; blood pressure determination; blood pressure monitors; body mass index

Most experts would agree that ambulatory blood pressure monitoring provides a better estimate of an individual's usual blood pressure than conventional measurement by an observer (1, 2). The relation between ambulatory blood pressure and age in normal subjects has been described as positive in most (3–7) but not all (8) reports (for a review, see reference 9). However, the increase in ambulatory blood pressure with

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age is generally less (3–9) than that expected on the basis of population studies, where blood pressure has been measured by conventional means (10, 11). This could possibly be attributed to the selection of healthy participants in studies of ambulatory blood pressure.

While selection bias may partially explain why, in some studies, ambulatory blood pressure does not increase with age or rises less, alternative mechanisms must also be considered. This cross-sectional study investigated whether measuring a subject's blood pressure by ambulatory monitoring, as opposed to conventional sphygmomanometry, affects the relation between blood pressure and both age and body mass index. The relations with age and body mass index were first examined in a Belgian population sample (12), and the findings were thereafter reproduced in a group of Irish bank employees (13).

MATERIALS AND METHODS

Study population

The relation between blood pressure and both age and body mass index was first cross-sectionally assessed in a population sample of 328 subjects (12). We randomly selected a total of 849 subjects from a small Belgian town (Hechtel-Eksel) after stratification of the population by sex and age in an attempt to recruit equal numbers of men and women in 10-year age groups from 20 years through 79 years. Subjects were excluded from participation if they did not live at the indicated address ($n = 111$, of whom 7 had died), they were taking antihypertensive drugs, diuretics, or nitrates ($n = 131$), or they could not move about freely ($n = 4$). Of the remaining 603 subjects, 55 percent ($n = 330$) agreed to participate. However, two subjects were excluded from the analyses because more than 20 percent of their programmed ambulatory blood pressure readings were missing.

A second independent data set was analyzed to investigate whether the findings in the Belgian population sample could be reproduced. It consisted of 776 current and retired Irish bank employees and their spouses, who volunteered for a study on ambulatory blood pressure monitoring (13). Body weight and height were recorded in only 416 subjects, because in its initial phase the Irish study did not include these anthropometric measurements.

Both the Belgian study and the Irish study were originally designed with the goal of determining reference values for ambulatory blood pressure. Neither the investigators who planned the studies nor the nurses involved in the field work nor the subjects participating in the studies anticipated the present analysis. Thus, bias with respect to the hypothesis under scrutiny during data collection is unlikely. In both studies, a self-administered questionnaire was used to inquire into each participant's personal and familial medical history, smoking habits, alcohol consumption, and use of medications.

Conventional blood pressure measurement

In both the Belgian study and the Irish study, a mercury sphygmomanometer was used in preference to the Hawskley sphygmomanometer, because a systematic tendency to underestimate pressure has been demonstrated with the random-zero machine (14). In both studies, cuff size was adjusted according to arm circumference for both the conventional blood pressure readings and the ambulatory measurements.

In the Belgian population study, all conventional blood pressure readings were obtained between 10:00 a.m. and 8:00 p.m. Trained nurses measured each participant's sitting blood pressure five times consecutively on each of two separate home visits (12). The observers involved in the study were tested for the accuracy of their blood pressure measurements at 6-month intervals. They had to first record the pressures from a film showing a falling mercury column with Korotkoff sounds ("Measuring Blood Pressure"; production no. B-132, The Audio-Visual Centre, University of London, 11 Bedford Square, London WC1, England, 1973). Thereafter, they were tested using live subjects and stethoscopes with double ear-

pieces. The blood pressure readings of the observers were within 5 mmHg of those of experienced medical staff.

Because, in many published epidemiologic studies, blood pressure is measured on only one occasion, only the five blood pressure readings recorded at the first home visit were used to calculate the conventionally measured blood pressure in the Belgian study. However, the correlations with age and body mass index were not materially altered when the blood pressure readings of the second home visit or of both home visits were averaged.

In the Irish sample, blood pressure was measured at medical clinics during regular working hours (13). After the subjects had rested for a few minutes in the sitting position, a trained nurse obtained two readings according to the recommendations of the British Hypertension Society (15). The majority of the subjects had the first and second office blood pressure measurements performed at the first visit, before and after completing the questionnaire. In some subjects, however, the first office blood pressure measurement was separated from the second by an interval of some days. The mean of the two office measurements was used in the present analysis.

Ambulatory blood pressure measurement

In both studies, ambulatory blood pressure was registered with SpaceLabs 90202 devices (SpaceLabs, Inc., Redmond, Washington) (16). The recorders were calibrated before use in the studies, and the calibration was checked at at least 3-month intervals.

In the Belgian study, the recordings were started on one of the home visits (13); the recorders were programmed to obtain measurements at intervals of 20 minutes from 8:00 a.m. until 10:00 p.m. and every 45 minutes from 10:00 p.m. to 8:00 a.m. In the Irish study, the ambulatory readings were programmed at intervals of 30 minutes.

The ambulatory blood pressure recordings were truncated so that their total duration did not exceed 24 hours. The following exclusion criteria (17, 18) were considered prior to analysis: 1) a recorded systolic pressure lower than the diastolic pressure; 2) a systolic pressure >240 mmHg or <50 mmHg; 3) a diastolic pressure >140 mmHg or <40 mmHg; 4) a pulse pressure of <10 percent of the systolic pressure; and 5) a pulse rate faster than 150 beats per minute or slower than 40 beats per minute. Because these five criteria together excluded less than 1 percent of the readings and because they did not affect the computed average levels of ambulatory blood pressure or the correlations with age and body mass index, only the results for unedited recordings are presented.

Statistical methods

Data base management and statistical analyses were performed with the Statistical Analysis System (19, 20). The intra-individual ambulatory blood pressure means were weighted by the time interval between successive blood pressure readings. The daytime period was defined as the time interval from 10:00 a.m. to 8:00 p.m., because previous studies (13, 21) have shown that this definition excludes the rapid blood pressure changes that occur in the morning and evening.

Statistical methods used included Student's t test and linear regression. Multivariate analysis of variance was performed to test the null hypothesis of no differences between the parameters of the regression equations (20).

RESULTS

Characteristics of the Belgian subjects

The 328 participants, 159 men and 169 women, were 49 ± 14 years old (mean ± standard deviation) (range, 20–81 years). Their mean body mass index (weight (kg)/height $(m)^2$) was 25.2 ± 3.5 (range, 17.0–40.2). Ninety-six subjects were smokers, and 60 reported daily intake of alcohol. Thirty women were taking oral contraceptives. Four subjects reported a history of myocardial infarction, three had experienced a tran-

sient ischemic attack, and one subject had both conditions, but none of these subjects had symptoms at the time they were asked to participate.

The blood pressure measurements in the Belgian subjects are summarized in table 1. Systolic blood pressure measured at home was 4 ± 11 mmHg higher ($p < 0.001$) than that obtained on 24-hour ambulatory measurement, and the conventionally measured diastolic pressure was 2 ± 7 mmHg higher ($p < 0.001$). The factors determining the differences between the conventional and ambulatory measurements were identified by stepwise multiple regression, terminating when all regression coefficients in the model were significant at the 5 percent probability level. Sex, age (linear and quadratic terms), body mass index, arm circumference, regular alcohol consumption (coded 0 for absent or 1 for present), and smoking (coded 0 for nonsmoker or 1 for current smoker) were considered for entry into the regression model. For the differences in systolic blood pressure (conventional minus 24-hour measurement, keeping the sign of the difference), the regression model was $y = -20.8 + 0.181(\text{age}) + 0.631(\text{body mass index})$ ($R^2 = 0.11$). For the differences in diastolic blood pressure, it was $y = -6.0 + 0.339(\text{body mass index}) - 1.405(\text{being a smoker})$ ($R^2 = 0.05$).

Characteristics of the Irish bank employees

The 776 participants, 396 men and 380 women, were aged 36 ± 11 years (range, 17–79 years). Body mass index was determined in 218 men and 198 women, and it averaged 23.6 ± 3.1 (range, 16.6–40.0). Forty-five subjects had a personal history of hypertension but were not on hypertension medication when examined. Smoking was reported by 123 subjects and alcohol consumption by 624. Thirty-five women were taking oral contraceptives, and four were on hormone replacement therapy.

The blood pressure measurements in the Irish employees are summarized in table 1. Conventional systolic blood pressure was 1 ± 12 mmHg higher ($p < 0.001$) than the ambulatory readings over 24 hours, and the conventionally measured diastolic blood pressure was 4 ± 8 mmHg higher ($p < 0.001$). In stepwise multiple regression (considering the same variables for entry into the model as in the Belgian sample), the within-subject differences in systolic blood pressure (clinic minus 24-hour measurement, keeping the sign of the difference) were correlated with age. The regression model was $y = -11.4 + 0.398(\text{age})$ ($R^2 = 0.11$; $n = 776$). For the differences in diastolic blood pressure, the regression model was $y = 0.8 - 0.393(\text{age}) + 0.00650(\text{age})^2 - 0.361(\text{body mass index})$ ($R^2 = 0.08$; $n = 416$).

TABLE 1. Blood pressure measurements in 328 Belgians (1989–1990) and 776 Irish bank employees (1988–1990)

	Belgians	Irish
Conventional blood pressure*		
Systolic	122 ± 17†	119 ± 17
	90–211‡	70–215
Diastolic	73 ± 9	76 ± 10
	52–103	50–132
Ambulatory blood pressure		
Whole-day (24 hours)		
Systolic	118 ± 11	118 ± 11
	97–155	96–182
Diastolic	71 ± 7	72 ± 7
	52–103	56–116
Daytime (10:00 a.m.–8:00 p.m.)		
Systolic	124 ± 11	125 ± 12
	97–166	98–187
Diastolic	76 ± 8	79 ± 8
	56–111	60–119
Nighttime (midnight–6:00 a.m.)		
Systolic	108 ± 11	107 ± 11
	84–151	86–172
Diastolic	62 ± 8	62 ± 8
	45–93	43–112

* Conventional blood pressure is the average of five blood pressure readings taken at home in the Belgian subjects and the average of two clinic readings in the Irish employees.
† Mean ± standard deviation.
‡ Range.

Relation between blood pressure and age

Blood pressure measured by conventional means showed a significant relation with age in both the Belgian subjects and the Irish

employees (figure 1). A quadratic term was required to describe the relation with age.

The increase in systolic blood pressure with age was significantly weaker when blood pressure was determined by ambulatory monitoring (complete 24-hour recordings). This was a consistent observation both when the Belgian subjects and the Irish employees were analyzed separately (table 2) and when the two samples were combined (table 2 and figure 1). From 20 years of age to 60 years of age, there was virtually no increase in the 24-hour systolic blood pressure (table 2 and figure 1). The increase in the 24-hour diastolic pressure with age was also significantly attenuated in the Irish employees (table 2) but not in the Belgian subjects when they were analyzed separately (table 2).

Relation between blood pressure and body mass index

Blood pressure measured by conventional means increased significantly and linearly with body mass index in both the Belgian subjects and the Irish employees (figure 2).

The slopes for the regression of blood pressure on body mass index were significantly attenuated when blood pressure was measured by ambulatory monitoring (complete 24-hour recordings). This was the case for most comparisons, regardless of whether the Belgian and Irish subjects were analyzed separately or combined (table 3 and figure 2); only for diastolic pressure in the Belgian men and diastolic pressure in the Belgian and Irish men combined did the attenuation, using complete 24-hour blood pressure

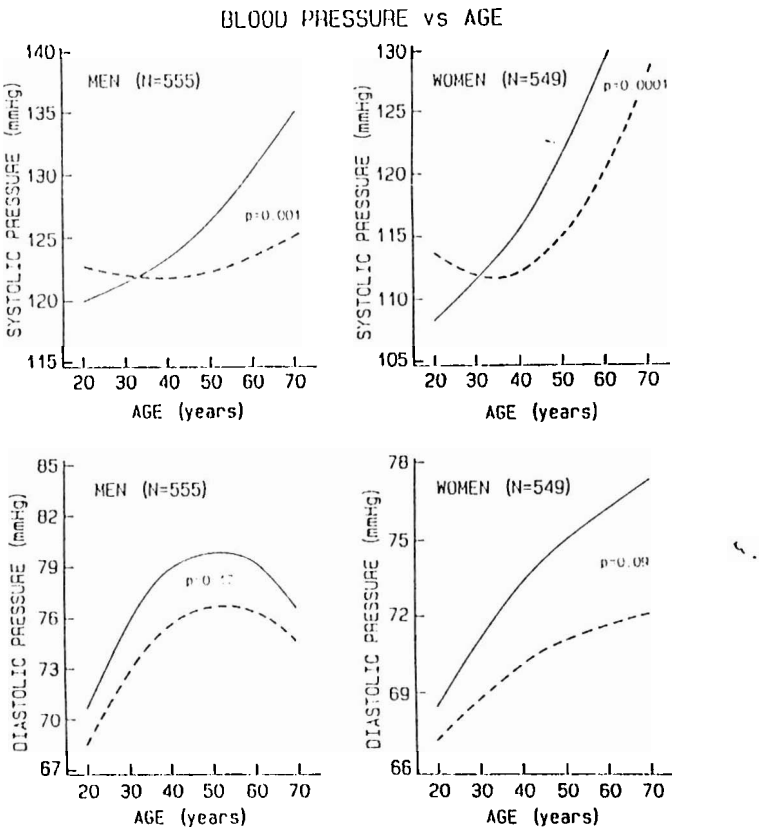

FIGURE 1. The relation between systolic (upper panels) and diastolic (lower panels) blood pressure and age in men (left panels) and women (right panels). The regression lines are shown for conventional (solid lines) and ambulatory (dashed lines) blood pressure measurements. The *p* values refer to the comparison of the regression lines (linear and quadratic regression slopes combined). Belgian and Irish subjects were pooled for this analysis.

TABLE 2. Difference in blood pressure (mmHg) associated with an increase in age from 20 years to 60 years in Belgian and Irish subjects

	CBP*	ABP*	Difference	p†
Belgians				
Men (n = 159)				
Systolic	+9.0	−3.1	12.1	0.007
Diastolic	+8.0	+9.1	−1.1	0.67
Women (n = 169)				
Systolic	+10.6	−1.6	12.2	0.0007
Diastolic	+4.4	+2.6	1.8	0.18
Irish employees				
Men (n = 396)				
Systolic	+16.9	+1.0	15.9	0.0001
Diastolic	+14.2	+8.6	5.6	0.006
Women (n = 380)				
Systolic	+28.1	+10.1	18.0	0.0001
Diastolic	+13.8	+7.6	6.2	0.0001
Both samples				
Men (n = 555)				
Systolic	+9.5	+0.7	8.8	0.0001
Diastolic	+6.5	+6.9	−0.4	0.55
Women (n = 549)				
Systolic	+16.9	+5.2	11.7	0.0001
Diastolic	+5.2	+3.4	1.8	0.002

* Blood pressure was measured by conventional and ambulatory methods. CBP, conventional blood pressure; ABP, ambulatory blood pressure.

† p values refer to the comparison between CBP and ABP for the predicted change (cross-sectionally assessed) in blood pressure from 20 years to 60 years.

recordings, not attain a level of statistical significance.

Additional analyses

In both data sets, the results with regard to the correlations with age and body mass index were reproduced when, instead of complete 24-hour blood pressure recordings, only the daytime (10:00 a.m. to 8:00 p.m.) or nighttime (midnight to 6:00 a.m.) ambulatory readings were used.

We computed standardized regression coefficients for the regression of blood pressure on age and body mass index to explore the influence of the range of the measurements on the comparison of the regression slopes. These additional calculations confirmed the present findings in both the Belgian subjects and the Irish subjects.

DISCUSSION

This cross-sectional study confirmed the well-established relations between systolic and diastolic blood pressure and both age (10, 11, 22) and body mass index (10, 11), at least when blood pressure was recorded by an observer in the conventional manner. With use of ambulatory monitoring, the increase in blood pressure with age was less pronounced, while the slope of ambulatory blood pressure values on body mass index was reduced. These observations were consistent in two independent data sets which represented populations that were of different national origins and were recruited and investigated in different ways. It remains to be seen, however, whether the present findings on the age-related differences between conventional and ambulatory blood pressure measurements would be reproducible in longitudinal studies.

Patients taking antihypertensive drugs were not eligible for participation in the present studies (12, 13). However, it is unlikely that the present analyses were biased by the selection of the participants, because both the Belgian study (12) and the Irish

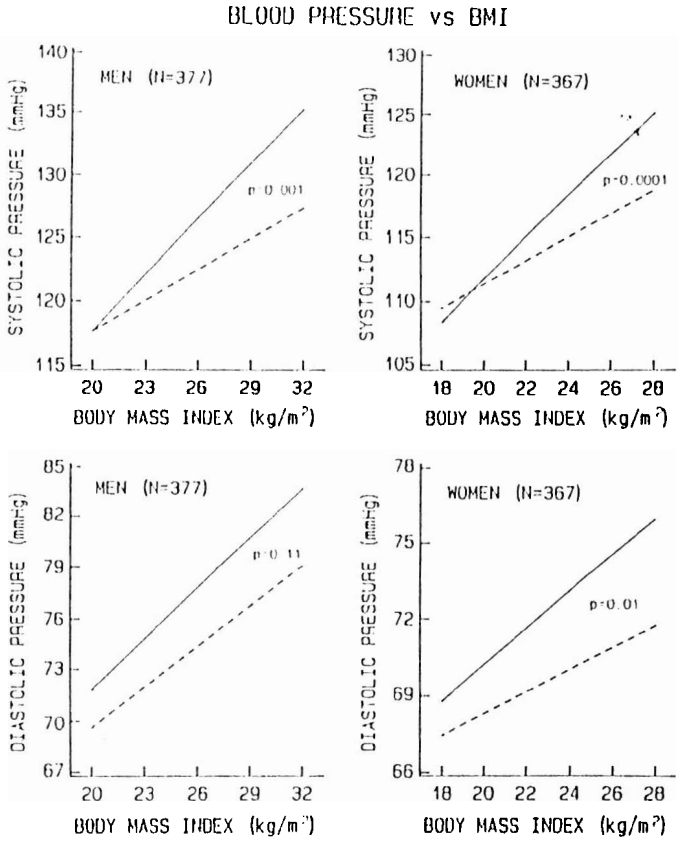

FIGURE 2. The relation between systolic (upper panels) and diastolic (lower panels) blood pressure and body mass index (weight (kg)/height (m)^2) in men (left panels) and women (right panels). The regression lines are shown for conventional (solid lines) and ambulatory (dashed lines) blood pressure measurements. The p values refer to the comparison of the linear regression slopes. Belgian and Irish subjects were pooled for this analysis.

study (13) included 10–12 percent untreated hypertensive patients (a systolic pressure >140 mmHg or a diastolic pressure >90 mmHg). In addition, selection bias should have affected the correlations with the conventional and ambulatory blood pressure readings equally. The present findings also could not be attributed to the differences in the ranges between the conventional and ambulatory blood pressure measurements. The possibility of confounding resulting from the fact that older and obese persons are usually less physically active and may therefore have lower ambulatory blood pressures than younger and leaner persons can probably be discounted. Indeed, in the two data sets, daytime (from 10:00 a.m. to 8:00 p.m.) and nighttime (from midnight to 6:00 a.m.) ambulatory recordings gave the same results as complete 24-hour recordings.

It is unlikely that the present findings are due to artifacts introduced by the SpaceLabs monitors. Indeed, age-related discrepancies between conventional and automated blood pressure readings have not been observed during the validation of this oscillometric device (16, 23). In these validation studies (16, 23), simultaneous conventional and automated measurements were obtained in the presence of an observer. A recent report (24) demonstrated that systolic blood pressure was, on average, 5.6 mmHg higher upon conventional measurement by two technicians than upon simultaneous registration by the auscultatory Accutracker II recorder (model 104; Suntech Medical Instruments,

TABLE 3. Difference in blood pressure (mmHg) associated with a 5-kg/m² increase in body mass index* in Belgian and Irish subjects

	CBP†	ABP†	Difference	p‡
Belgians				
Men (*n* = 159)				
Systolic	+9.3	+5.5	3.8	0.02
Diastolic	+5.7	+4.5	1.8	0.16
Women (*n* = 169)				
Systolic	+8.8	+4.7	4.1	0.0001
Diastolic	+4.5	+2.4	2.1	0.005
Irish employees				
Men (*n* = 218)				
Systolic	+6.0	+3.2	2.8	0.04
Diastolic	+5.7	+3.9	1.8	0.05
Women (*n* = 198)				
Systolic	+8.4	+4.7	3.7	0.03
Diastolic	+5.5	+3.1	2.4	0.02
Both samples				
Men (*n* = 377)				
Systolic	+7.4	+4.1	3.3	0.001
Diastolic	+5.0	+4.0	1.0	0.11
Women (*n* = 367)				
Systolic	+8.4	+4.7	3.7	0.001
Diastolic	+3.6	+2.1	1.5	0.01

* Weight (kg)/height (m)².
† Blood pressure was measured by conventional and ambulatory methods. CBP, conventional blood pressure; ABP, ambulatory blood pressure.
‡ *p* values refer to the comparison between CBP and ABP for the predicted change (cross-sectionally assessed) in blood pressure associated with a 5-kg/m² increase in body mass index.

Inc., Raleigh, North Carolina) and that conventional diastolic blood pressure was 6.3 mmHg higher. After sex and race were controlled, the systolic blood pressure differences in the latter study (24) increased with age (0.15 mmHg per year of age) but not with body mass index, while the differences in diastolic pressure were not related to age or body mass index. An artifact of similar magnitude would be insufficient to completely explain the present findings on the correlations with age. In addition, if the differences between conventional and automated readings published for the Accutracker II are real (24), this device fails to fulfill the British Hypertension Society criteria for accuracy (25).

The present study suggests that older and obese subjects are more susceptible to the "white coat effect" (26–28), i.e., to increasing their blood pressures in response to the presence of an observer. However, age and body mass index explained less than 12 percent of the differences between the two techniques of blood pressure measurement; thus, additional factors must be considered. The variability of blood pressure measurements increases with the level of blood pressure (29, 30) and age (29–31). Older subjects tend to have impaired baroreflexes (29, 31) and older hypertensives are more susceptible to placebo effects (32) when blood pressure is measured by an observer.

The sympathetic system could play an important role in the explanation of the present findings, because the white coat effect is a mainly sympathetically mediated alerting reaction (26–28). In keeping with the present findings, plasma norepinephrine levels rise with aging (33), and responses of plasma norepinephrine to mental stress are larger in elderly subjects (34). Along similar lines, overfeeding is associated with an increased sympathetic tone and turnover of norepinephrine (35, 36). In addition, smoking, which in the Belgian subjects was a

minor factor involved in the age-related differences in diastolic blood pressure between conventional and ambulatory measurements, causes acute sympathetic stimulation (37, 38). Finally, the white coat effect (30–32) could be less well buffered in older persons as a consequence of impaired baroreflexes (29, 31) and the greater stiffness of their arteries (22, 39).

A phenomenon analogous to the present findings has been described as occurring when blood pressure is the independent variable used to predict the incidence of cardiovascular complications (40–42). The blood pressure readings obtained at baseline in longitudinal studies are subject to random variation, because of the imprecision of the measurement process and temporary deviations of blood pressure from the usual level (40, 43). When a linear model is applicable, this results in a systematic underestimation of the slope of the real association between usual blood pressure and the incidence of cardiovascular complications. This phenomenon, termed "regression dilution bias" (40–42), can be alleviated by plotting the incidence of cardiovascular complications against an unbiased estimate of the usual blood pressure. The latter may be obtained by ambulatory blood pressure monitoring (1, 2, 44).

The present findings may have implications for clinical and epidemiologic studies in which blood pressure is the response variable. Ambulatory blood pressure monitoring, by providing an estimate of a subject's usual blood pressure, may be particularly useful for determining the true effect of an effector variable on blood pressure. For instance, it is possible that the rise in conventional blood pressure with age (10, 11, 22) reflects mainly an age-related increase in the alerting reaction to the observer (26–28) and that the true effect of aging on usual blood pressure is less pronounced. Sympathetic stimulation not only increases blood pressure but also lowers serum potassium (45, 46). This may explain why plasma potassium is negatively correlated with blood pressure when blood pressure is measured in the conventional manner (47). Similarly, studies reporting weak associations between blood pressure as the response variable and other measurements, such as blood lead (48) or sodium intake (11, 49), may need to be reevaluated to investigate whether the presumed effects on blood pressure can be confirmed when the observer effect is avoided by ambulatory blood pressure monitoring.

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