Task Force II: Ambulatory blood pressure monitoring in population studies

Giuseppe Mancia, Eoin O'Brien[a], Yutaka Imai[b] and Joseph Redon[c]

Ambulatory blood pressure (ABP) has only rarely been employed in population studies because of the difficulty posed by the greater complexity of this technique. The cross-sectional studies that have been published, however, have allowed a number of conclusions to be drawn. One, 24 h average blood pressure of populations is significantly but not closely related to office blood pressure, which thus can not predict accurately daily-life values of blood pressure. Two, 24 h average blood pressure is usually less than office blood pressure, the discrepancy increasing with the increase in office values and being of magnitude several mmHg at the office blood pressure of 140/90 mmHg (systolic/diastolic) Three, ABP in women is somewhat less than that in men and ABP for both sexes increases less with aging than does office blood pressure. Four, a circadian profile of blood pressure consisting in values that are much lower at night than are those during daytime characterizes both sexes and all ages with the possible exception of individuals aged 75 years and more, in whom the nocturnal hypotension appears to be attenuated. A similar attenuation has been found for blacks in comparison with whites. The upper limit of normality of ABP has not yet been defined conclusively, although 24 h average values ≤ 125/80 mmHg are almost invariably regarded as normal. Normality of ABP should be defined, however, by longitudinal population studies in which ambulatory values are related to prognosis. One of these studies has already been published and others will be completed in the near future. *Blood Press Monit* 4:295–301 © 1999 Lippincott Williams & Wilkins.

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University of Milan-Bicocca, S. Gerardo Hospital, Monza, Milan, Italy, [a]The Blood Pressure Unit, Beaumont Hospital, Dublin, Ireland, [b]The Second Department of Internal Medicine, Tohoku University School of Medicine, Sendai, Japan and [c]Hypertension Clinic, Hospital of Sagunto, Sagunto, Spain.

Correspondence and requests for reprints to Professor Giuseppe Mancia, Università di Milano-Bicocca, Ospedale S. Gerardo, Via Donizetti 106, I 20052 Monza (Milano), Italy.

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Introduction

Ambulatory blood pressure (ABP) monitoring has only rarely been employed in population studies because the difficulty posed by the greater complexity of this procedure *vis-à-vis* office measurements is magnified. Furthermore, the consumption of time inherent to measurements during a long ambulatory period is a limiting factor when, as in populations, most of the individuals involved are normotensive and thus less interested in and compliant with procedures to do with collecting information on blood pressure. Finally, the purely epidemiologic nature of population studies makes getting financial support from drug companies (which are the major sources of research funding in many countries) more difficult.

Nevertheless, the few population studies published have provided adequate data on a number of issues: one, the relationship of office blood pressure to ABP and the presumptive normality of ABP values in the population as a whole; two, ABP values for some segments of the population; three, the values and the prevalence of control of blood pressure in the hypertensive fraction of the population, based on ambulatory data rather than on the conventional approach involving office blood pressure. These three sets of data will be reviewed below. Then we will give some consideration on the methodologic problems posed by population studies on ABP as well as discussing the knowledge that would be important to obtain in future population studies.

Office versus 24 h average blood pressure and normality of 24 h average blood pressure in cross-sectional population studies

Authors of cross-sectional population studies agree that 24 h average systolic and diastolic blood pressures for the population correlate to the corresponding office values [1,2]. The correlation coefficients are around 0.6–0.7, which indicate, however, that there is a discrepancy between these two measures and hence that information on office blood pressure does not allow daily-life blood pressure of populations to be known precisely. Authors of cross-sectional population studies also agree that 24 h average systolic and diastolic blood pressures are distributed over a considerably narrower range than are office blood pressures [1,2] (Fig. 1). More importantly, these studies [1–9] have provided information on normality of ABP after earlier

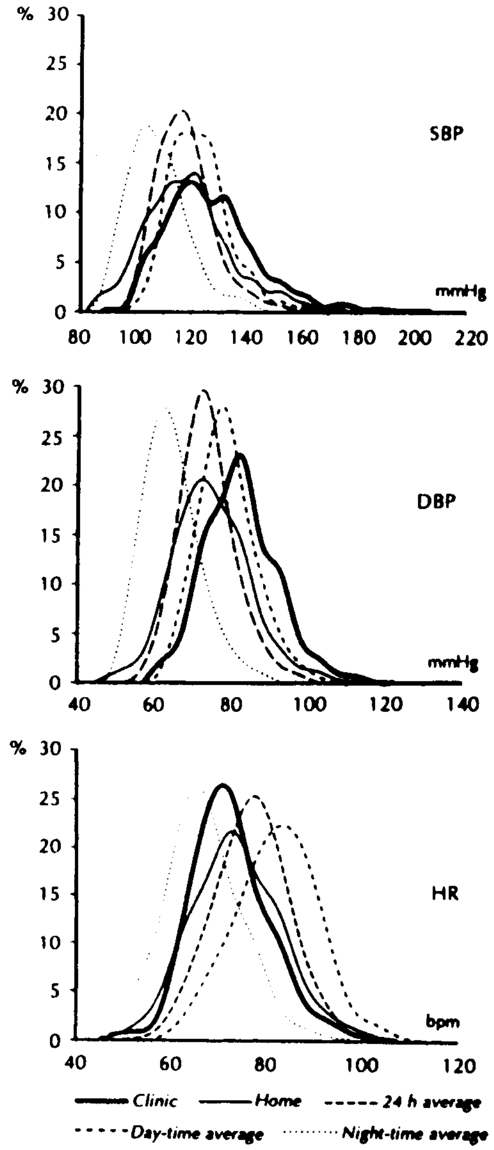
Table 1 **Average office and 24 h blood pressure systolic/diastolic blood pressure in population studies**

Study	n	Age (years)	Office blood pressure (mmHg)	24 h blood pressure (mmHg)
Danish [2]	1854	41–71	127/81	122/72
PAMELA [1]	1438	25–64	128/82	118/74
Belgian [6]	718	20–88	–	119/71
Japanese [8]	474	20–80	127/72	119/70
PAMELA Elderly [9]	248	65–74	148/83	123/73

attempts to determine it by a meta-analysis of studies on individuals defined as normotensive after a visit to a hypertension clinic [10,11] or from a survey of the employees of a bank [12] in which the aim was to avoid the potential selection bias involved in the above approaches [13]. With the exception of the value of systolic blood pressure in a Danish study [2] the results are consistent with the fact that 24 h average systolic and diastolic blood pressures in the population as a whole are lower than office blood pressures (Table 1). They [1–9] are also consistent with the fact that the differences between office and 24 h average blood pressures increase progressively as office blood pressure increases, thereby being less for the average population values than they are for the greater values of blood pressure that correspond to the accepted upper limits of normality of office blood pressure (i.e. 140/90 mmHg; Fig. 2) [1,8].

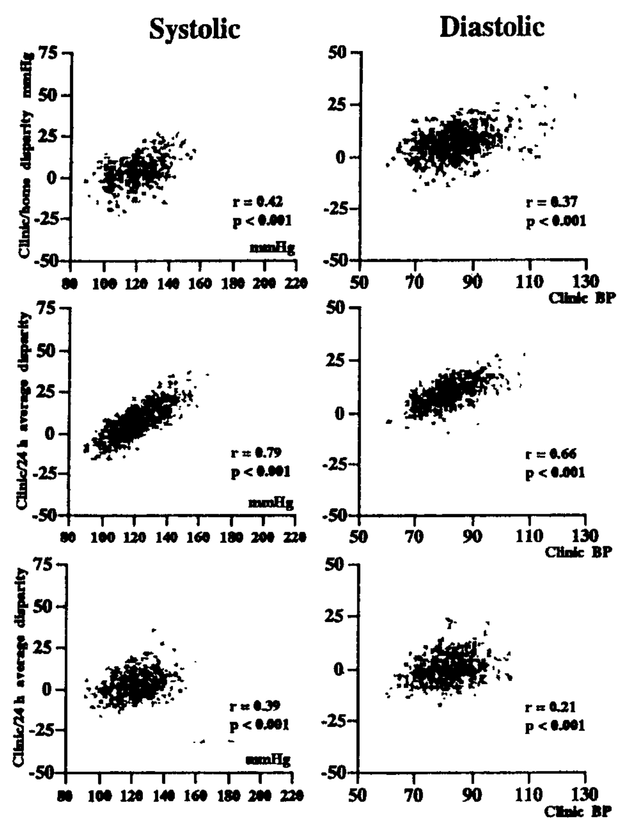
On the other hand, there is some disagreement about which values reflect the upper limit of normality of 24 h

Fig. 1



Frequency distribution of clinic and ambulatory values of blood pressure in the PAMELA population of subjects aged 25–64 years. Data for systolic blood pressure (SBP) and diastolic blood pressure (DBP) as well as for heart rate (HR) are shown separately. Ambulatory blood pressure values are shown as 24 h, daytime and night-time averages. (From [1] with permission).

Fig. 2



Relationship between clinic systolic and diastolic blood pressure and clinic 24 h average or disparity between clinic and home blood pressures. Data are from the PAMELA study for subjects aged 65–74 years. (From [9] with permission).

average systolic and diastolic blood pressures because of the different methods employed when extracted from the raw population data. The issue is the object of a continuing debate [1,14] which has emphasized, however, that no method is devoid of limitations and inconvenience. This is the case, for example, for the method by which the upper limit of normality of 24 h average blood pressure has been determined as the value on the regression line corresponding to the office blood pressure of 140 mmHg systolic and 90 mmHg diastolic [1] because the relationship between office and ambulatory values, although it is highly statistically significant, is compatible with individual discrepancies (see above). It is also the case for the attempt to determine the upper limit of normality as the value 2SD above the mean of the group as a whole because this is a statistical normality that does not take into account that individuals definable as hypertensive on prognostic grounds correspond to much more than the 4% left uncovered by use of 2SD and can hardly be related to the upper limit of normality of office blood pressure (i.e. 140/90 mmHg), which includes only about 80% of the population. This is finally the case for the use of values 2SD above the mean for the normotensive fraction of the population only, both because exclusion of hypertensive individuals makes this distribution of values of blood pressure not normal (a limitation for which one can correct by use of the 95% confidence interval) [15] and, more importantly, because this exclusion is based on criteria derived from office blood pressure (i.e. the very criteria which are regarded as inadequate for distinguishing ABP normotension from hypertension).

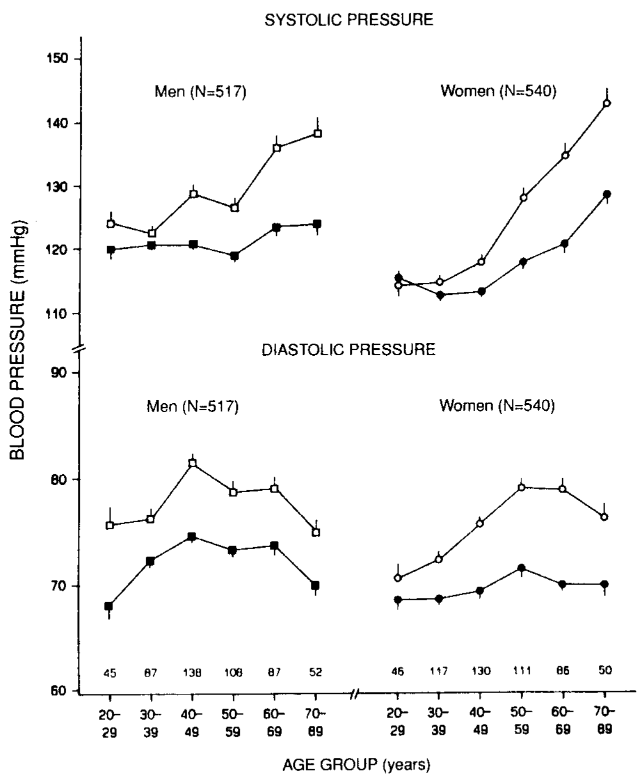
Despite this disagreement the calculated upper limit of normality of 24 h average blood pressure does not differ substantially among results of most studies, with values of 125–130 mmHg for systolic and 80–85 mmHg for diastolic blood pressure. A more recent proposal is to classify individuals' 24 h average blood pressures as probably elevated if they are ≥ 135/85 mmHg, and probably normal if they are ≤ 120/80 mmHg, thus leaving undefined the values in between [16]. More importantly, there is agreement on the need to regard values from population studies as merely orientative because, for it to be clinically meaningful, normality of ABP should be defined on the basis of prognostic criteria, for which we will have to await publication of large-scale population studies on ABP with longitudinal designs [17].

Twenty-four-hour average blood pressures for subgroups of the population

Twenty-four-hour average blood pressures in women have been found to be slightly less than those in men [1,2], reflecting data obtained for office blood pressures over a large age range. It has also been found that the increase of systolic and, to a lesser extent diastolic blood pressure with aging is much less evident for 24 h average blood pressures than it is for office blood pressures for subjects aged about 20–75 years, as can be seen from data concerning the population as a whole [1] or men and women separately (Fig. 3) [6]. This is likely to originate, in part, from the fact that 24 h mean values for the populations are distributed over a narrower range than are office values (see above). It is also possible, however, that, for technical reasons, conventional blood pressure measurements do overestimate the age-related increase in blood pressure [18]. Or that daytime blood pressure in the elderly is maintained relatively low by physical activity or standing, or both [19], because their depressor effects are less effectively counteracted by the baroreflex whose function undergoes progressive impairment with aging [20]. Finally, one can not exclude the possibility that this phenomenon results also from a selection bias (e.g. from a greater mortality rate of elderly patients in whom ABP is high), because ABP in elderly patients appears to have a greater prognostic value than does office blood pressure [21].

Definition of normality of ABP in pregnant women and blacks [22–24] has also been attempted without entirely fitting the criteria for population studies. Population studies on normality of ABP in children and adolescents have, on the other hand, been published [25–27]. The

Fig. 3



Increases in clinic and 24 h average blood pressures in men and women with age. Values are means ± SEM. (From [6] with permission).

results indicate that ABP increases with the increases in body weight and height with aging (although less so for diastolic than for systolic and differently in boys and girls), thereby exhibiting a similar relationship to growth to that of office blood pressure. They also indicate that, within these age ranges, 24 h average blood pressures are lower than the values in adults, with no substantial difference from office blood pressures, both when the comparison is made with average population values and when it is made with the upper limit of normality, defined as the 95th percentile. It should be emphasized that it is particularly difficult to perform population studies on children and adolescents adequately because artifactural readings may be more common and behavioral activity is highly diversified. This might at least in part account for differences among ABP values of different populations [27]. Furthermore, although the results of published studies indicate that ABP in children and adolescents is characterized by a tracking phenomenon, as is office blood pressure, the significance of ABP values for predicting future appearance of office or ambulatory hypertension, or both, has not yet been established. Results of ongoing studies on adolescents may fill this gap [28] while other studies may provide information on normality of 24 h blood pressure in individuals over 75 years of age, which is limited at the present time.

Day and night blood pressures and variability of blood pressure

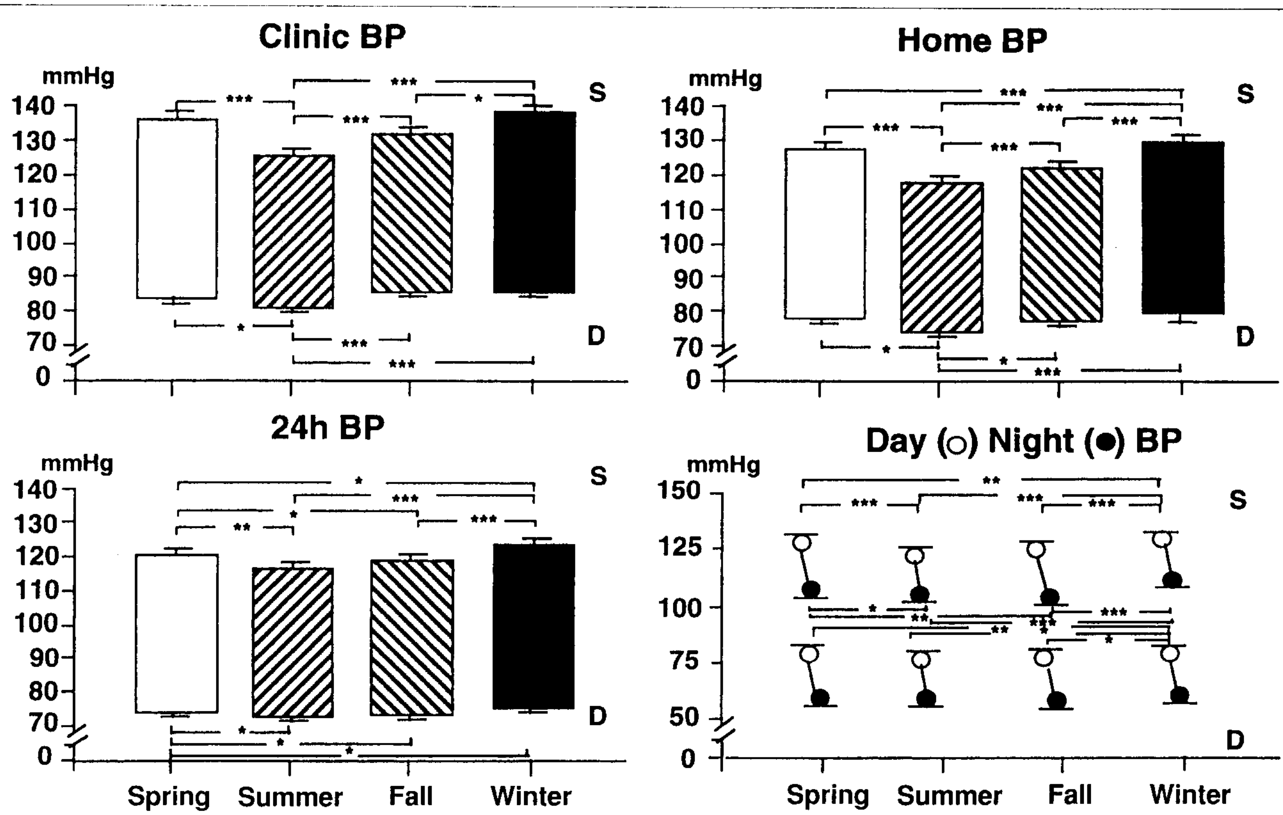
Cross-sectional population studies on ABP have also provided information on normality of day and night blood pressures. Daytime blood pressure has been reported to be much greater than night-time blood pressure for both sexes [1] as well as in childhood, adolescence, and adulthood [1–8,26–28]. Elderly individuals have also been reported to have a large night-time fall in blood pressure compared with the daytime values, although population data have so far been restricted mainly to individuals up to 75 years [9]. An attenuation of the night-time fall in blood pressure has been reported from analysis of an international data base on subjects aged 75 years and more [29]. Calculation of the upper limits of normality of daytime and night-time average blood pressure has met with the methodologic disagreement described for calculation of the upper limit of normality of 24 h average blood pressure. Yet the values reported do not differ substantially insofar as they identify as upper daytime normality values between 125 and 135 mmHg systolic, and between 80 and 85 mmHg diastolic, the corresponding night-time values being between 110 and 120 and 65 and 75 mmHg [1–12,29]. It should again be emphasized that these values are simply reference values. This is the case for the reasons mentioned for the upper limit of normality of 24 h average blood pressure (see above). It is additionally the case that the temporal correspondences between daytime wakefulness on one side and night-time and sleep on the other are difficult to assess precisely [30], particularly in population studies, in which behavior can differ so much among individuals as to include periods of sleep (and thus hypotension) [31] of various durations during the day (e.g. the siesta), and periods of being awake (and thus of a high blood pressure) during the night. Furthermore, night-time fall in blood pressure has been shown to have limited reproducibility in comparisons of different 24 h monitoring periods [32], probably because depth of sleep has between-night variations. This can make it more difficult also to determine whether there are differences in night-time blood pressure among different segments of the populations. However, although these studies were not based on population data, authors of several studies have consistently reported this to be the case for blacks, who appear to have greater night-time blood pressures than do whites [24], a phenomenon that could be involved in the greater hypertension-related morbidity observed in blacks.

Little attempt to quantify 24 h variability of blood pressure in the population as a whole has been made, except for the consistent report that, on a qualitative basis, there is a circadian profile of blood pressure in various subgroups. Quantification of 24 h variability of blood pressure is usually obtained by calculation of the SD or the coefficient of variation of the mean value of blood pressure [31], which measures the overall tendency of blood pressure to vary, although not the patterns of variation. This quantification, however, is less accurate when automatic rather than intra-arterial or beat-to-beat blood pressure monitoring devices are employed because automatic devices sample blood pressure intermittently, thereby missing variations in blood pressure in between samplings [33]. Because intra-arterial measurements and beat-to-beat noninvasive devices can hardly be used in population studies, definition of normal range of variability of blood pressure could be a difficult goal to pursue.

Control of ABP in the hypertensive population

Authors of studies performed in various countries have consistently reported that many hypertensive patients are not aware of their hypertensive condition or do not seek or maintain treatment. They have also consistently reported, that only a limited percentage of treated hypertensive patients have office blood pressure values ≤ 140/90 mmHg [34]. Results of population studies on ABP, however, have complemented this information by showing that what is true for office blood pressure is also true for 24 h, day and night time average blood pressures, thereby demonstrating that previous findings were not due to the elevation of blood pressure in treated hypertensive individuals that could be produced by the alerting reaction elicited by measurements of blood pressure in the clinic environment (i.e. the white-coat effect) [35–37] but rather reflect a truly poor control of blood pressure in daily life [9,38]. This is the case for young, middle-aged and elderly hypertensive

Fig. 4



Several changes in clinic, home and 24 h average systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) for the PAMELA population. Open symbols, daytime blood pressure; closed symbols, night-time blood pressure. (From [1,9] with permission).

subjects, in only few of whom treatment reduced systolic and diastolic 24 h average blood pressures at least to the level identified in the same population studies as the upper limit of 24 h normality of blood pressure. The population approach to ABP thus provides scientific support for the opinion that optimization of effective antihypertensive treatment is a major goal to be pursued at population levels in the next few years in order to improve the prevention of cardiovascular disease.

Advantages and problems of population studies on ABP

It has been mentioned previously that population studies on ABP might meet with problems such as high cost, lesser chances of receiving funding and limited compliance of the recruited subjects, which could raise doubts about the representativeness for the population as a whole of the sample on which the study has been performed. Additional problems should be mentioned, however. One of them can be the greater heterogeneity of the environmental and behavioral situations in which ABP monitoring is performed compared with those in more restricted studies, in which the 'experimental' conditions can be more easily standardized. An example is offered by seasonal variations in blood pressure that have recently been shown to affect not only office but also ambulatory blood pressures [39,40]. The 24 h average systolic and diastolic blood pressures in temperate climates are several mmHg lower in summer than they are during winter months (Fig. 4) [39]. To minimize these problems, population studies on ABP should always be planned in such a way as to be completed within a limited time with no preponderance of ambulatory recordings in one season over those in another. Additionally, no mismatching between recordings performed during working days and those obtained during the weekend periods, for which blood pressures may differ. Other possible forms of mismatching should be considered, among which are those related to job type, socio-economic status [41], menopausal state [42,43] and female hormone treatment [44,45], because all are potentially able to affect blood pressure. Finally, particular attention should be given to the quality of the recordings, which should be ensured by use of validated devices [46] and by acceptance only of recordings in which the number of valid readings is above a certain preselected threshold (e.g. 70% of all 24 h readings) with most of the 24 h represented. This will allow the advantages of these studies (e.g. large size, ability to perform subgroup analyses, avoidance of selection bias, etc.) to fully emerge.

Longitudinal studies on ABP

We have previously emphasized that cross-sectional studies can provide only provisional data on normality of ABP, whose clinical definition can be obtained only by performing longitudinal studies that will show which ambulatory values correspond to minimal risk and best prognosis. To date, authors of only one population study on ABP have added longitudinal data to the initial cross-sectional ones. This is the study conducted on a sample of 1542 subjects (565 men, aged ≥ 40 years) from the general population of Ohasama, Japan. Data were obtained first over a follow-up period of 6.2 years with 117 deaths and then over a follow-up period of 8 years with 166 deaths [47]. After exclusion from consideration of the noncardiovascular deaths, 24 h average blood pressure at baseline was linearly and significantly related to the risk of cardiovascular mortality, the relationship persisting even after adjustment for possible confounding factors (age, sex, smoking, use of antihypertensive medication at baseline, history of cardiovascular disease, diabetes, hypercholesterolemia) and after additional adjustment for conventional baseline blood pressure. For increases in 24 h average systolic and diastolic blood pressures of 10 mmHg the relative risks were 1.326 and 1.436, respectively, compared to the reference risk value.

It will be desirable that future population studies on ABP also have a longitudinal design in order to determine the prognostic value of ABP over and above that of office blood pressure in populations. It will also be desirable that authors of these studies obtain information on ABP not just at baseline but rather at regular intervals over the follow-up period, as was done in classic epidemiologic studies on office blood pressure [48]. Prospective morbidity and mortality data from the Belgian ABP monitoring population study will be available in 2001.

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