8-5-2019

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Recommended Citation

Cheng, Y. B., Thijs, L., Zhang, Z. Y., Kikuya, M., Yang, W. Y., Melgarejo, J. D., Boggia, J., Wei, F. F., Hansen, T. W., Yu, C. G., Asayama, K., Ohkubo, T., Dolan, E., Stolarz-Skrzypek, K., Malyutina, S., Casiglia, E., Lind, L., Filipovský, J., Maestre, G. E., Imai, Y., … Staessen, J. A. (2019). Outcome-Driven Thresholds for Ambulatory Blood Pressure Based on the New American College of Cardiology/American Heart Association Classification of Hypertension. Hypertension (Dallas, Tex. : 1979), 74(4), 776–783. https://doi.org/10.1161/HYPERTENSIONAHA.119.13512

HHS Public Access

Author manuscript

Hypertension. Author manuscript; available in PMC 2020 October 01.

Published in final edited form as:

Hypertension. 2019 October ; 74(4): 776–783. doi:10.1161/HYPERTENSIONAHA.119.13512.

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Disclosures
None.

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International Database on Ambulatory Blood Pressure in Relation to Cardiovascular Outcome (IDACO) Investigators.

Abstract

The new ACC/AHA guideline reclassified office blood pressure (OBP) and proposed thresholds for ambulatory blood pressure (ABP). We derived outcome-driven ABP thresholds corresponding with the new OBP categories. We performed 24-h ABP monitoring in 11,152 participants (48.9% women; mean age 53.0 years) representative of 13 populations. We determined ABP thresholds resulting in multivariable-adjusted 10-year risks similar to those associated with elevated OBP (120/80 mm Hg) and stages 1 and 2 of office hypertension (130/80 and 140/90 mm Hg). Over 13.9 years (median), 2728 (rate per 1000 person-years, 17.9) people died, 1033 (6.8) from cardiovascular disease; furthermore, 1988 (13.8), 893 (6.0) and 795 (5.4) cardiovascular and coronary events and strokes occurred. Using a composite cardiovascular endpoint, systolic/diastolic outcome-driven thresholds indicating elevated 24-h, daytime and nighttime ABP were 117.9/75.2, 121.4/79.6 and 105.3/66.2 mm Hg. For stages 1 and -2 ambulatory hypertension, thresholds were 123.3/75.2 and 128.7/80.7 mm Hg for 24-h ABP, 128.5/79.6 and 135.6/87.1 mm Hg for daytime ABP and 111.7/66.2 and 118.1/72.5 mm Hg for nighttime ABP. ABP thresholds derived from other endpoints were similar. After rounding, approximate thresholds for elevated 24-h, daytime and nighttime ABP were 120/75, 120/80 and 105/65 mm Hg and for stages 1 and 2 ambulatory hypertension 125/75 and 130/80 mm Hg, 130/80 and 135/85 mm Hg, and 110/65 and 120/70 mm Hg. Outcome-driven ABP thresholds corresponding to elevated blood pressure and stages 1 and 2 of hypertension are similar to those proposed by the current ACC/AHA guideline.

Keywords

ambulatory blood pressure monitoring; cardiovascular events; hypertension; mortality; population science

INTRODUCTION

Recording the ambulatory blood pressure (BP) allows risk stratification over and beyond the office BP and is cost-effective in managing hypertension.[1–3] The recently published ACC/AHA guideline for the management of hypertension therefore recommended the application of ambulatory BP monitoring for diagnosing hypertension and adjusting antihypertensive drug treatment.[4] Based on the new classification of office BP, the ACC/AHA guideline suggested as ambulatory BP thresholds corresponding with office stage-1 hypertension, systolic/diastolic BP levels of 125/75, 130/80, and 110/65 mm Hg for the 24-h, daytime and nighttime BP, respectively. Similarly, the guideline also proposed ambulatory BP thresholds corresponding with office of elevated BP (120/80 mm Hg) and stage-2 and severe hypertension (140/90 and 160/100 mm Hg, respectively).[4] The objective of the current analysis was to determine outcome-driven diagnostic BP thresholds for ambulatory recordings, corresponding with the new cut-off levels proposed by ACC/AHA for office BP. To this effect, we analyzed the International Database on Ambulatory Blood Pressure in Relation to Cardiovascular Outcome (IDACO), which at the time of writing of this article included 13,654 people recruited from 13 populations.[5]

METHODS

The data that support the findings of this study are available from the corresponding author on reasonable request.

Study Population

Previous publications describe the IDACO database in detail.[5] Population studies qualified for inclusion, if information on the office and the ambulatory BP and cardiovascular risk factors was available at baseline and if follow-up included both fatal and nonfatal outcomes. All studies received ethical approval and adhered to the principles of the Declaration of Helsinki.[6] Participants gave written informed consent. Of the 13,654 people included in the database, we excluded 2502 because they were teenagers younger than 18 without events (n = 317), because their office blood pressure had not been measured (n = 223), because their use of antihypertensive drugs had not been recorded (n = 28), or because they had an ambulatory BP recording with fewer than 10 daytime and 5 nighttime readings (n = 1934). Thus, the number of participants analyzed was 11,152. Table S1 available in the online-only Data Supplement provides detailed information on where and how participants were enrolled.

Blood Pressure Measurement

Experienced observers measured the office blood pressure with standard mercury sphygmomanometers or with validated auscultatory (USM-700F[7]) or oscillometric (OMRON HEM-705CP[8] or Dinamap 8100[9]) devices, using the appropriate cuff size, after the participants had rested for at least two minutes in the sitting or supine position. Office BP was the average of two consecutive readings.[10] We programmed validated portable monitors to obtain ambulatory blood pressure readings at 30-minute intervals throughout the

whole day, or at intervals ranging from 15 to 30 minutes during daytime and from 20 to 60 minutes at night. Methods used for office and ambulatory BP measurement are described for each cohort in Table S2 and S3, respectively. Daytime ranged from 10 AM to 8 PM in Europeans and South Americans and from 8 AM to 6 PM in Asians. The corresponding nighttime intervals ranged from midnight to 6 AM and from 10 PM to 4 AM, respectively. Using short fixed clock-time intervals eliminate the transition periods in the morning and evening, when blood pressure changes rapidly and produce daytime and nighttime blood pressure levels, which are within 1 mm Hg of the levels during wakefulness and sleep, respectively.[11] Participants were categorized according to their office and 24-h ambulatory BP. Normotension and elevated BP on office BP measurement were systolic levels of <120 mm Hg and 120–129 mm Hg and a diastolic level of <80 mm Hg. Stage-1 and stage-2 hypertension and severe hypertension were systolic or diastolic levels of 130–139/80–89 mm Hg, 140–159/90–99 mm Hg and ≥160/≥100 mm Hg, respectively. Considering the 24-h ambulatory BP, normotension and elevated BP were systolic levels of <115 mm Hg and 115–124 mm Hg and a diastolic level of <75 mm Hg. Stage-1 and stage-2 hypertension and severe hypertension on ambulatory monitoring were systolic or diastolic levels of 125–129/75–79 mm Hg, 130–144/80–89 mm Hg and ≥145/≥90 mm Hg, respectively. If systolic and diastolic BP were in different categories, the highest level was used to categorize people.

Ascertainment of Events

We ascertained vital status and the incidence of fatal and nonfatal diseases from the appropriate sources in each country, as described in previous IDACO publications.5 Outcomes were coded according to the international classification of diseases. Fatal and nonfatal stroke (ICD8/9 430–434 and 436, ICD10 I60–I64) did not include transient ischemic attacks. Coronary events encompassed death from ischemic heart disease (ICD8 411–412, ICD9 411 and 414, and ICD10 I20, I24–I25), sudden death (ICD8 427.2 and 795, ICD9 427.5 and 798, and ICD10 I46 and R96), nonfatal myocardial infarction (ICD8/9 410, and ICD10 I21–I22), and coronary revascularization. Cardiovascular events included all aforementioned endpoints plus cardiovascular mortality (ICD8 390–448, ICD9 390.0–459.9, and ICD10 I00-I79 and R96) and heart failure (ICD8 428, 427.0, 427.1, 427.2, 429, 5191, and 78214, ICD9 429, and ICD10 I50 and J81). In the Danish and Swedish cohorts, the diagnosis of heart failure required admission to hospital. In the other cohorts, heart failure was either a clinical diagnosis or the diagnosis on the death certificate. All events were validated against records held by family doctors or hospitals. In the outcome analyses, only the first event within each disease cluster was considered.

Statistical Analysis

For database management and statistical analysis, we used SAS software, version 9.4 (SAS Institute, Cary, NC). We compared means and proportions by the large sample z test or ANOVA and by the χ^2 test, respectively. Statistical significance was a two-sided probability of 0.05 or less. In exploratory analyses, we first plotted incidence rates of mortality and cardiovascular events by the BP categories proposed by the ACC/AHA guideline,[4] while standardizing by the direct method for cohort, sex and age (<40, 40–60, ≥60 years). Next, in multivariable-adjusted Cox regression, we accounted for cohort (random effect), sex, and baseline characteristics including age, body mass index, smoking and drinking, serum

cholesterol, antihypertensive drug intake, history of cardiovascular disease, and diabetes mellitus. To adjust for cohort, we pooled participants recruited in the framework of the European Project on Genes in Hypertension (Novosibirsk, Kraków, Gdańsk, Pilsen and Padova).[12] We checked the proportional hazards assumption by the Kolmogorov-type supremum test and by testing the interaction between follow-up duration and the BP variables.

We obtained diagnostic thresholds for ambulatory BP monitoring in five steps. First, we computed the 10-year incidence rates of mortality and cardiovascular events associated with normal and elevated BP or hypertension on office BP measurement. Second, we computed the 10-year incidence rates of death and cardiovascular events associated with ambulatory BP levels ranging from the 5th to the 95th percentile, using intervals of 0.1 mm Hg. In a third step, we selected the ambulatory BP levels that were associated with similar 10-year risks as the office BP thresholds. Next, we calculated the bootstrap distribution of the so-obtained ambulatory BP thresholds by randomly resampling the study population 1000 times with replacement, using the PROC SURVEY SELECT procedure, as implemented in the SAS package. For each new sample, we repeated the first three steps. We accounted for tied event times, caused by resampling with replacement, by the TIES = EXACT option in the PROC PHREG procedure. Finally, we calculated the bootstrap point estimates and 95% confidence intervals of the ambulatory BP thresholds as the mean ± 1.96 SEs of the bootstrap distribution.

RESULTS

Characteristics of Participants

Table 1 shows the baseline characteristics of the participants by ethnicity. The whole study population comprised 6958 Europeans (62.4%), 2167 Asians (19.4%) and 2027 South Americans (18.2%). Of the 11,152 participants, 5455 were women (48.9%), 6865 (61.6%) had hypertension on office BP measurement, and 2190 (19.6%) were taking antihypertensive drugs. Of 8962 untreated participants, 2848 (31.8%) and 1106 (12.3%) had a normal or elevated office blood pressure, respectively. Mean age was 53.0±15.9 years. At enrolment, 3059 participants (27.4%) were current smokers, and 5864 (52.6%) reported intake of alcohol.

The prevalence of elevated BP was highest among Asians (16.7%), stage-1 (26.4%) and stage-2 (23.8%) hypertension among Europeans, and severe hypertension among South Americans (25.9%) with treatment rates varying from 4.2% to 22.9% among people with normotension or elevated BP and from 13.8% to 46.2% among hypertensive patients (Table 1). Between-ethnicity differences were significant for all variables ($P \leq 0.006$), except for daytime diastolic BP ($P=0.11$) and treatment rates among severe hypertension ($P=0.14$).

In the whole study population, mean systolic/diastolic levels were 132.9/79.9 mm Hg for office BP and 123.8/74.0 mm Hg, 129.9/78.9 mm Hg and 112.9/65.0 mmHg for 24-h, daytime and nighttime BP, respectively. Systolic/diastolic BP were on average 2.9 mm Hg ($P<0.001$) and 1.0 mm Hg ($P<0.001$) higher on office than daytime measurement.

Incidence of Events in Relation to Blood Pressure

In the overall study population, median follow-up was 13.9 years (5th to 95th percentile interval, 3.6 to 24.9 years). Over 152,156 person-years, 2728 participants died (17.9 per 1000 person-years) and 1988 experienced a fatal or nonfatal cardiovascular event (13.8 per 1000 person-years). Mortality included 1033 and 1585 cardiovascular and noncardiovascular deaths and 110 from unknown causes. The number of endpoints was 893 for coronary events and 795 for stroke.

Figure 1 shows the increase in total mortality, cardiovascular and coronary events and stroke across categories of the office and 24-h ambulatory BP with standardization of the rates for cohort, sex and age. The number of events contributing to the incidence rates is presented in Table S4. With adjustments applied for cohort, sex, age, body mass index, serum cholesterol, smoking and drinking, history of cardiovascular disease and diabetes mellitus and antihypertensive drug treatment, blood pressure was a highly significant (P<0.001) and consistent predictor of all outcomes, irrespective of the type of measurement (Table 2). The standardized hazard ratios for total mortality in relation to the office, 24-h, daytime and nighttime BP were 1.14, 1.16, 1.11 and 1.18 systolic and 1.08, 1.14, 1.09 and 1.17 diastolic; the corresponding hazard ratios for fatal combined with nonfatal cardiovascular events were 1.25, 1.32, 1.26 and 1.29 systolic and 1.19, 1.28, 1.22 and 1.28, respectively.

Ambulatory Blood Pressure Thresholds

Using a bootstrap procedure with adjustments applied for the aforementioned covariates, ambulatory BP thresholds were calculated that yielded 10-year absolute risks of total and cardiovascular mortality, cardiovascular and coronary events and stroke similar to the risks associated with the ACC/AHA thresholds for office systolic (Table 3) and diastolic (Table 4) BP. The thresholds based on the full data set were similar to the means of the bootstraps. Excluding 2190 participants on antihypertensive treatment at enrolment (Tables S5 and S6) or using diary information (Table S7 and Table S8) to derive BP during wakefulness and sleep in 7196 participants (64.5%) produced results highly consistent with those reported in Tables 3 and 4. To obtain more easily recallable thresholds, in the last step of our analysis, we rounded the systolic (Table 3) and diastolic (Table 4) point estimates of the ambulatory BP thresholds for cardiovascular events to an integer value ending in 0 or 5. Table 5 lists the thresholds proposed by the ACC/AHA guideline as well as the rounded thresholds based on the current analysis. In sensitivity analyses, from which we excluded one cohort at a time, these diagnostic thresholds remained largely consistent.

DISCUSSION

Several studies established that out-of-office BP, measured by ambulatory[10,13] or home[14] monitoring, is a better predictor of mortality and cardiovascular complications than office BP is. The 2017 ACC/AHA guideline for the management of hypertension[4] and other directives[15] recommended that for the proper diagnosis and management of hypertension out-of-office BP measurement is a prerequisite. The new ACC/AHA guideline reclassified office BP and proposed thresholds for 24-h, daytime and nighttime BP corresponding to the new office BP categories.[4] Of these ambulatory thresholds, the 24-h systolic and diastolic

levels are prognostically most meaningful, because they are based on the largest number of readings. Using the IDACO database, we derived outcome-driven thresholds in 11,152 participants from 13 population studies. The key finding of our study was that we largely confirmed the validity of the ACC/AHA proposal for ambulatory BP thresholds in terms of mortality and cardiovascular complications. The thresholds derived by our analysis were identical with the ACC/AHA proposal with the exception of the systolic thresholds delineating elevated BP for 24-h and nighttime BP (ACC/AHA *vs.* IDACO, 115 *vs.* 120 mm Hg and 100 *vs.* 105 mm Hg, respectively). For severe hypertension, the ACC/AHA and IDACO thresholds differed by 5 mm Hg systolic or diastolic (Table 5) and by 10 mm Hg for the systolic nighttime BP (140 *vs.* 130 mm Hg).

Thresholds for the clinical application of ambulatory BP were initially based on the distribution of the ambulatory blood pressure in individuals with an office blood pressure in the normotensive range,[16,17] usually defined as a level of less than 140 mm Hg systolic and 90 mm Hg diastolic, or by regression of the ambulatory on the office BP.[18] In a meta-analysis of summary statistics from 23 studies,[17] the mean ambulatory BP plus two times the SD in 3476 normotensive people amounted to 139/87 mm Hg, 146/91 mm Hg, and 127/79 mm Hg for the 24-h, daytime and nighttime BP, respectively. In a participant-level meta-analysis of 7069 individual recordings from 24 clinical research groups, the thresholds were set at the 95th percentiles of the ambulatory BP distributions among 4577 individuals, who were normotensive on office measurement. The BP limits derived in this manner were 133/82 mm Hg, 140/88 mm Hg and 125/76 mm Hg for the 24-h, daytime and nighttime BP, respectively.[16] Head et al.[18] applied a least-product fit to regress ambulatory BP measurements on office BP in 8575 Australians. The thresholds for 24-h, daytime and nighttime ABP were 7/6 mm Hg, 4/3 mm Hg and 19/14 mm Hg lower than the 140/90 mm Hg threshold for office BP, 133/84 mm Hg, 136/87 mm Hg and 121/76 mm Hg, respectively.

The aforementioned studies relied heavily on the proportion and representativeness of individuals with office normotension in the studies analyzed and entirely on a distributional or statistical approach for setting the ambulatory BP thresholds, which ignores what matters most, i.e., the incidence of adverse health outcomes. Later studies therefore applied a more robust outcome-based approach.[19–21] According to the Ohasama investigators,[19] the 24-h BP associated with the lowest risk of all-mortality ranged from 120 to 133 mm Hg systolic and from 65 to 78 mm Hg diastolic. Using the same statistical methods as in the current manuscript, the IDACO consortium proposed as ambulatory BP thresholds corresponding with an optimal office BP (<120/<80 mmHg) levels of 116.8/74.2 mm Hg, 121.6/78.9 mm Hg and 100.9/65.3 mm Hg for 24-h, daytime and nighttime BP.[20] The corresponding thresholds for the ambulatory BP with a risk equivalent to normal office BP (<130/<85 mm Hg), were 123.9/76.8, 129.9/82.6, and 110.2/68.1 mm Hg, respectively, and the ambulatory thresholds yielding a risk equivalent to office hypertension (≥140/90 mm Hg) were 131.0/79.4 mm Hg, 138.2/86.4 mm Hg, and 119.5/70.8 mm Hg. Rounded upper limits for the 24-h, daytime and nighttime BP amounted to 115/75 mm Hg, 120/80 and 100/65 mm Hg for optimal BP, to 125/75 mm Hg, 130/85 and 110/65 for normal BP, and to 130/80 mm Hg, 140/85, and 120/70 mm Hg for ambulatory hypertension. In the Jackson Heart Study,[21] 1016 of 5306 African-American participants (19.2%) had their office and ambulatory BP measured. In an outcome-driven approach, the composite of all-cause mortality and

cardiovascular disease was used as endpoint. Diastolic was not related to outcome and therefore not analyzed. For systolic BP, the thresholds corresponding with an office BP of 140 mm Hg were 134 mm Hg, 138 mm Hg and 129 mm Hg for 24-h, daytime and nighttime, respectively.

The present study must be interpreted within the context of its potential limitations. First, rounded ambulatory BP thresholds are a compromise between accuracy and practicability. For instance, the 24-h systolic BP threshold for stage-1 hypertension was 117.9 mm Hg. The 95% confidence interval ranged from 116.0 and 119.8 mm Hg. We proposed a rounded value of 120 mm Hg, which was only 0.2 mm Hg higher than the upper limit of the 95% confidence interval. Rounding to 115 mm Hg might have been the alternative, but such threshold would have been 1.0 mm Hg lower than the lower limit of the confidence interval. Second, office BP was the average of only two readings, obtained on a single occasion, which is less than recommended by the 2017 ACC/AHA guideline,[4] which proposes that office BP be measured on at least two occasions. Office and ambulatory BP were measured in a consistent manner across all IDACO centers. Overall, the pooled correlation coefficient, weighted for sample size in each center, was 0.68 systolic and 0.62 diastolic. It is therefore unlikely that our definition of office BP as the average of two readings obtained on a single occasion distorted our results. Third, the ambulatory BP thresholds based on equivalent risk with office BP, as proposed in the current manuscript and in an earlier IDACO analysis,[20] are equally applicable to women and men and across the adult age range up to 80 years. This approach serves clinical practicability, but might disregard the relative and absolute risks associated with BP over a the course of life.[22] However, a participant-level meta-analysis addressing this issue for the self-measured home BP as modality of the out-of-the-office BP confirmed that the application of single BP targets in both sexes and across the adults age range is justifiable.[23] Finally, our analysis did not include African Americans or Blacks born and living in Africa, who are more susceptible to the complications of hypertension than other ethnic groups.[24,25] In this context, the systolic ambulatory BP thresholds generated by the Jackson Heart Study investigators are 4 mm Hg, 8 mm Hg and 9 mm Hg higher than those listed in Table 5 for the 24-h, daytime and nighttime BP, yielding equivalent risk with a systolic office BP of 140 mm Hg. If people of African descent were at higher risk than other ethnicities, one would actually have anticipated ambulatory BP thresholds slightly lower than those in Table 5. This underscores the concept that multi-ethnic cohort studies enhance generalizability.

Perspectives

The present study provides outcome-driven BP thresholds for the ambulatory BP that yield risks equivalent to those associated with the new ACC/AHA classification of hypertension. Our analysis supports the ACC/AHA recommendation for operational thresholds applicable to ambulatory BP. However, one caveat lies in the continuous nature of the association between cardiovascular complications and BP. Operational BP thresholds help clinicians in diagnosing and managing hypertension, but in addition to BP the complete clinical picture, including other risk factors and comorbidities, should always be considered as recommended in current guidelines.[4,15]

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgement

The authors gratefully acknowledge the clerical assistance of Vera De Leebeeck and Renilde Wolfs at the Studies Coordinating Centre in Leuven, Belgium.

Sources of Funding

The European Union (HEALTH-F7–305507 HOMAGE), the European Research Council (Advanced Researcher Grant 2011–294713-EPLORE and Proof-of-Concept Grant 713601-uPROPHET), the European Research Area Net for Cardiovascular Diseases (JTC2017–046-PROACT), and the Research Foundation Flanders, Ministry of the Flemish Community, Brussels, Belgium (G.0881.13) supported the Studies Coordinating Centre in Leuven. The European Union (grants LSHM-CT-2006–037093 and HEALTH-F4–2007–201550) also supported the research groups in Shanghai, Kraków, Padova, and Novosibirsk. The Ohasama Study was supported by: Grants for Scientific Research (16H05243, 16K09472, 16K11850, 16K15359, 17H04126, 17H06533, 17K15853, 17K19930, 18K09674, 18K09904, and 18K17396) from the Ministry of Culture, Sports, Science, and Technology, Tokyo, Japan; a Grant-in-Aid for Young Scientists of Showa Pharmaceutical University H28–4; the Japan Arteriosclerosis Prevention Fund; Comprehensive Research on Cardiovascular and Life-Style Related Diseases (H26-Junkankitou [Seisaku]-Ippan-001) and (H29–Junkankitou–Ippan–003) from the Ministry of Health, Labor, and Welfare, Tokyo, Japan; a Scheme to Revitalize Agriculture and Fisheries in Disaster Area through Deploying Highly Advanced Technology (NouEi 2–02) from the Ministry of Agriculture, Forestry and Fisheries, Japan. The Asociación Española Primera en Salud supported the research group in Montevideo. The Danish Heart Foundation (grant 01–2-9–9A-22914) and the Lundbeck Fonden (grant R32-A2740) supported the studies in Copenhagen. The JingNing study was supported by the National Natural Science Foundation of China (grants 81470533, 91639203 and 81770455), the Ministry of Science and Technology (2015AA020105–06, 2016YFC1300100 and 2018YFC1704902), Beijing, China, and by the Shanghai Commissions of Science and Technology (grants 14ZR1436200 and 15XD1503200) and the Shanghai Bureau of Health (15GWZK0802, 2017BR025 and a Grant for Leading Academics). The National Institutes of Health and the National Institute of Aging (5 R01 AG036469–05, 1R03AG054186) and FONACIT (G-97000726) supported the Maracaibo Aging Study. Follow-up of the Kraków cohort was supported by the Foundation for Polish Science.

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Novelty and Significance

What is new?

The new ACC/AHA guideline reclassified office blood pressure (BP) and proposed thresholds for ambulatory BP. We derived outcome-driven thresholds for ambulatory BP yielding risks equivalent to the new categories of office BP.

What is relevant?

- Rounded thresholds for elevated systolic/diastolic 24-h, daytime and nighttime ambulatory BP were 120/75, 120/80 and 105/65 mm Hg.
- Rounded thresholds for stage 1 of 24-h, daytime and nighttime ambulatory hypertension were 125/75, 130/80 and 110/65 mm Hg.
- Rounded thresholds for stage 2 of 24-h, daytime and nighttime ambulatory hypertension were 130/80, 135/85 and 120/70 mm Hg.

Summary

Outcome-driven thresholds for the ambulatory BP are similar to those proposed by the current ACC/AHA guideline. Our analysis supports the ACC/AHA recommendation for operational threshold applicable to ambulatory BP.

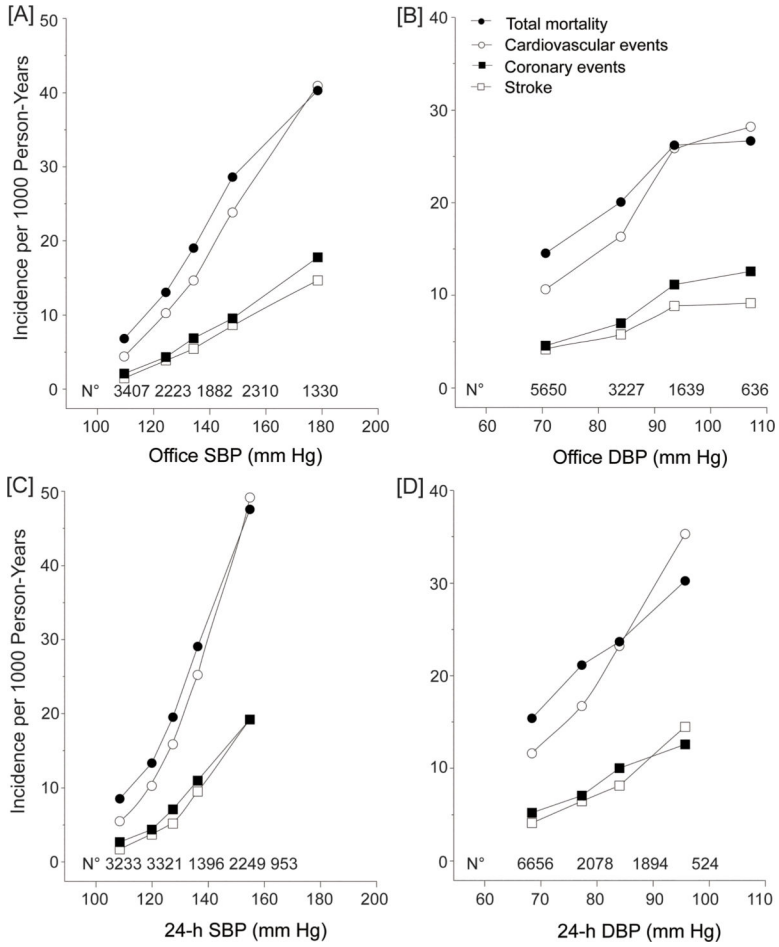

Figure 1.

Incidence of total mortality, cardiovascular and coronary events and stroke by ACC/AHA categories of office systolic (A) and diastolic (B) blood pressure (SBP: <120, 120–129, 130–139, 140–159, ≥160 mm Hg – DBP: <80, 80–89, 90–99, ≥100 mm Hg) and by ACC/AHA categories of 24-h systolic and diastolic blood pressure (SBP: <115, 115–124, 125–129, 130–144, ≥145 mm Hg – DBP: <75, 75–79, 80–89, ≥90 mmHg) blood pressure. Incidence rates were standardized by the direct method for cohort, sex, and age (<40, 40–60, and >60 years). N° indicates the number of participants at risk within each blood pressure category. The number of events contributing to the incidence rates is presented in Table S4.

Table 1.

Baseline Characteristics of Participants

Characteristic	All	Characteristics by Ethnicity			
		Europeans	Asians	South Americans	*P*
N° with characteristic (%)	11,152	6958	2167	2027	
Women	5455 (48.9)	2936 (42.2)*	1343 (62.0)†	1173 (57.9)‡	<0.001
Smokers	3059 (27.4)	2171 (31.2)*	468 (21.6)	420 (20.7)‡	<0.001
Drinking alcohol	5864 (52.6)	4531 (65.1)*	714 (33.0)	619 (30.5)‡	<0.001
Diabetes mellitus	847 (7.6)	329 (4.7)*	245 (11.3)†	273 (13.5)‡	<0.001
History of CV disease	1256 (11.3)	652 (9.4)*	96 (4.4)†	508 (25.1)‡	<0.001
Hypertension status					
Normotension	3012 (27.0)	1952 (28.1)*	528 (24.4)	532 (26.3)	0.002
On treatment	164 (5.4)	81 (4.2)*	56 (10.6)†	27 (5.1)	<0.001
Elevated blood pressure	1275 (11.4)	770 (11.1)*	362 (16.7)†	143 (7.1)‡	<0.001
On treatment	169 (13.3)	71 (9.2)*	83 (22.9)†	15 (10.5)	<0.001
Stage-1 hypertension	2739 (24.6)	1835 (26.4)	534 (24.6)†	370 (18.3)‡	<0.001
On treatment	449 (16.4)	254 (13.8)*	143 (26.8)†	52 (14.1)	<0.001
Stage-2 hypertension	2560 (23.0)	1658 (23.8)*	444 (20.5)†	458 (22.6)	0.005
On treatment	738 (28.8)	437 (26.4)*	174 (39.2)†	127 (27.7)	<0.001
Severe hypertension	1566 (14.0)	743 (10.7)*	299 (13.8)†	524 (25.9)‡	<0.001
On treatment	670 (42.8)	325 (43.7)	138 (46.2)	207 (39.5)	0.14
Mean characteristic (±SD)					
Age, y	53.0±15.9	51.0±16.2*	57.0±13.3†	55.4±16.0‡	<0.001
Body mass index, kg/m^2	25.4±4.3	25.7±4.2*	23.1±3.1†	26.8±4.9‡	<0.001
Serum cholesterol, mmol/L	5.55±1.14	5.71±1.14*	4.96±0.92†	5.66±1.17‡	<0.001
Blood pressure, mm Hg					
Office systolic	132.9±23.4	130.2±19.7*	133.7±22.2†	141.3±32.4‡	<0.001
Office diastolic	79.9±12.1	80.2±11.1*	76.8±12.7†	82.3±13.6‡	<0.001

Characteristic	All	Characteristics by Ethnicity			
		Europeans	Asians	South Americans	*P*
24-h systolic	123.8±14.4	124.2±13.8 *	123.2±14.7	123.4±16.1 ‡	0.006
24-h diastolic	74.0±8.7	73.6±8.1 *	74.4±9.5	74.8±9.5 ‡	<0.001
Daytime systolic	129.9±15.2	131.0±14.7 *	128.6±15.3 †	127.5±16.4 ‡	<0.001
Daytime diastolic	78.9±9.3	79.1±8.7 *	78.6±10.1	78.8±10.4	0.11
Nighttime systolic	112.9±15.6	112.4±14.6	112.8±16.3 †	114.6±18.1 ‡	<0.001
Nighttime diastolic	65.0±9.6	64.1±9.0 *	66.5±10.4	66.6±10.5 ‡	<0.001

Body mass index was body weight in kilograms divided by height in meters squared. Diabetes mellitus was the use of antidiabetic drugs, fasting blood glucose of ≥7.0 mmol/L, random blood glucose of ≥11.1 mmol/L, a self-reported diagnosis, or diabetes documented in practice or hospital records. The *P*-value denotes significant overall between-group differences. Symbols indicate significant ethnic differences:

* between Europeans and Asians

† between Asians and South Americans

‡ between Europeans and South Americans.

For the calculation of the prevalence of antihypertensive drug treatment, the number of people with a given blood pressure status was used as denominator; otherwise the column totals.

Table 2.

Hazard Ratios for Mortality and Cardiovascular Events in Relation to Baseline Blood Pressure

Blood Pressure	Mortality		Fatal and Nonfatal Cardiovascular Events		
	Total	Cardiovascular	All	Coronary	Stroke
Endpoints, n (%)	2728 (24.5)	1033 (9.3)	1988 (17.8)	893 (8.0)	795 (7.1)
Systolic					
Office	1.14 (1.09–1.20)	1.25 (1.16–1.34)	1.25 (1.18–1.31)	1.16 (1.08–1.26)	1.37 (1.26–1.49)
24-Hour	1.16 (1.12–1.21)	1.34 (1.26–1.41)	1.32 (1.27–1.38)	1.25 (1.17–1.33)	1.44 (1.35–1.54)
Daytime	1.11 (1.07–1.16)	1.26 (1.19–1.33)	1.26 (1.20–1.31)	1.21 (1.13–1.29)	1.35 (1.26–1.45)
Nighttime	1.18 (1.14–1.22)	1.32 (1.25–1.39)	1.29 (1.24–1.34)	1.24 (1.17–1.31)	1.38 (1.30–1.46)
Diastolic					
Office	1.08 (1.04–1.13)	1.16 (1.09–1.25)	1.19 (1.13–1.25)	1.11 (1.03–1.19)	1.25 (1.16–1.35)
24-Hour	1.14 (1.09–1.18)	1.28 (1.20–1.36)	1.28 (1.23–1.34)	1.16 (1.09–1.25)	1.39 (1.30–1.50)
Daytime	1.09 (1.05–1.14)	1.21 (1.14–1.29)	1.22 (1.17–1.28)	1.12 (1.05–1.20)	1.31 (1.22–1.41)
Nighttime	1.17 (1.12–1.22)	1.30 (1.22–1.38)	1.28 (1.22–1.34)	1.18 (1.10–1.26)	1.38 (1.28–1.48)

Hazard ratios (95% CI) express the risk associated with 1-SD increases in blood pressure. Hazard ratios were adjusted for cohort, sex, age, body mass index, smoking and drinking, serum cholesterol, history of cardiovascular disease, diabetes mellitus and treatment with antihypertensive drugs. All hazard ratios were significant (P<0.001).

Table 3.

Systolic Ambulatory Blood Pressure Levels Yielding Similar 10-Year Risk as Office Thresholds

Endpoints (n)	Office SBP, mm Hg	10-Year Absolute Risk, %	Ambulatory SBP (95% CI), mm Hg		
			24-Hour	Daytime	Nighttime
Total mortality (2728)	120	3.66	117.1 (113.8–120.3)	118.9 (113.8–124.1)	106.0 (102.7–109.2)
	130	3.91	123.0 (121.5–124.5)	127.7 (125.7–129.8)	111.9 (110.3–113.5)
	140	4.18	128.8 (128.1–129.6)	136.6 (135.0–138.1)	117.7 (117.0–118.5)
	160	4.79	140.6 (136.5–144.8)	153.7 (147.7–159.7)	129.5 (125.6–133.4)
Cardiovascular mortality (1033)	120	1.12	119.1 (116.0–122.1)	122.5 (118.4–126.6)	106.9 (103.3–110.5)
	130	1.24	124.1 (122.3–125.9)	129.1 (126.9–131.4)	112.6 (110.5–114.7)
	140	1.38	129.1 (128.1–130.1)	135.8 (134.6–137.0)	118.3 (117.1–119.5)
	160	1.72	139.1 (136.2–142.0)	149.1 (144.8–153.4)	129.7 (126.3–133.2)
Cardiovascular events (1988)	120	4.34	117.9 (116.0–119.8)	121.4 (118.8–123.9)	105.3 (102.8–107.7)
	130	4.84	123.3 (122.3–124.3)	128.5 (127.2–129.7)	111.7 (110.5–112.9)
	140	5.40	128.7 (128.2–129.2)	135.6 (134.8–136.3)	118.1 (117.5–118.8)
	160	6.71	139.5 (137.3–141.8)	149.7 (146.4–153.1)	131.0 (128.0–134.1)
Coronary events (893)	120	2.02	118.6 (115.4–121.8)	122.7 (119.1–126.4)	106.8 (102.6–111.0)
	130	2.18	123.3 (121.9–124.8)	128.6 (127.0–130.2)	112.2 (110.4–114.1)
	140	2.36	128.1 (127.1–129.0)	134.5 (133.4–135.6)	117.7 (116.6–118.8)
	160	2.76	137.5 (133.3–141.8)	146.3 (141.1–151.4)	128.6 (123.0–134.2)
Stroke (795)	120	1.58	117.2 (114.9–119.4)	120.6 (117.5–123.6)	103.9 (101.0–106.8)
	130	1.84	123.0 (121.9–124.1)	128.2 (126.7–129.6)	111.0 (109.6–112.4)
	140	2.15	128.9 (128.3–129.4)	135.7 (135.0–136.5)	118.1 (117.4–118.9)
	160	2.93	140.6 (138.1–143.2)	150.9 (147.1–154.6)	132.3 (128.9–135.8)

Table 4.

Diastolic Ambulatory Blood Pressure Levels Yielding Similar 10-Year Risk as Office Thresholds

Endpoints (n)	Office DBP, mm Hg	10-Year Absolute Risk, %	Ambulatory DBP (95% CI), mm Hg		
			24-Hour	Daytime	Nighttime
Total mortality (2728)	80	3.98	75.3 (74.7–76.0)	79.7 (78.8–80.7)	66.6 (65.9–67.3)
	90	4.34	80.8 (79.3–82.4)	87.9 (85.2–90.7)	71.8 (70.4–73.3)
	100	4.74	86.3 (83.0–89.7)	94.8 (91.5–98.2)	77.0 (73.8–80.2)
Cardiovascular mortality (1033)	80	1.25	76.3 (75.4–77.2)	80.7 (79.4–82.0)	67.6 (66.5–68.6)
	90	1.46	81.5 (80.1–82.9)	87.8 (85.8–89.8)	73.2 (71.6–74.7)
	100	1.71	86.6 (83.7–89.5)	94.4 (91.3–97.5)	78.7 (75.4–82.0)
Cardiovascular events (1988)	80	4.94	75.2 (74.7–75.7)	79.6 (79.0–80.2)	66.2 (65.6–66.8)
	90	5.86	80.7 (79.8–81.6)	87.1 (85.7–88.4)	72.5 (71.5–73.6)
	100	6.96	86.3 (84.2–88.3)	94.3 (91.9–96.8)	78.9 (76.6–81.3)
Coronary events (893)	80	2.21	74.4 (73.6–75.2)	78.7 (77.5–79.9)	65.5 (64.5–66.5)
	90	2.50	80.2 (78.2–82.2)	86.8 (83.6–89.9)	71.9 (69.5–74.4)
	100	2.82	86.0 (81.5–90.5)	93.9 (89.0–98.8)	78.3 (72.8–83.7)
Stroke (795)	80	1.95	75.7 (75.0–76.4)	80.2 (79.3–81.0)	66.7 (65.8–67.6)
	90	2.43	81.2 (80.1–82.3)	87.4 (85.9–88.9)	73.1 (71.8–74.3)
	100	3.03	86.7 (84.2–89.3)	94.4 (91.6–97.2)	79.4 (76.4–82.5)

Table 5.

Proposal for Outcome-Driven Thresholds for the Ambulatory Blood Pressure

Blood Pressure Category	ACC/AHA 2017 Thresholds				Ambulatory Thresholds Based on IDACO		
	OBP	24 H	Day	Night	24 H	Day	Night
Elevated blood pressure, mm Hg	120/80	115/75	120/80	100/65	120/75	120/80	105/65
Stage-1 hypertension, mm Hg	130/80	125/75	130/80	110/65	125/75	130/80	110/65
Stage-2 hypertension, mm Hg	140/90	130/80	135/85	120/70	130/80	135/85	120/70
Severe hypertension, mm Hg	160/100	145/90	145/90	140/85	140/85	150/95	130/80

Abbreviations: ACC/AHA, American College of Cardiology/American Heart Association; IDACO, International Database on Ambulatory Blood Pressure in Relation to Cardiovascular Outcome; OBP, Office blood pressure. Ambulatory thresholds based on IDACO were obtained by rounding the point estimates reported in Tables 3 and 4 for cardiovascular events to the nearest integer value ending in zero or five.