Outcome-Driven Thresholds for Home Blood Pressure Measurement

International Database of HOme blood pressure in relation to Cardiovascular Outcome

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Abstract—The lack of outcome-driven operational thresholds limits the clinical application of home blood pressure (BP) measurement. Our objective was to determine an outcome-driven reference frame for home BP measurement. We measured home and clinic BP in 6470 participants (mean age, 59.3 years; 56.9% women; 22.4% on antihypertensive treatment) recruited in Ohasama, Japan (n=2520); Montevideo, Uruguay (n=399); Tsurugaya, Japan (n=811); Didima, Greece (n=665); and nationwide in Finland (n=2075). In multivariable-adjusted analyses of individual subject data, we determined home BP thresholds, which yielded 10-year cardiovascular risks similar to those associated with stages 1 (120/80 mm Hg) and 2 (130/85 mm Hg) prehypertension, and stages 1 (140/90 mm Hg) and 2 (160/100 mm Hg) hypertension on clinic measurement. During 8.3 years of follow-up (median), 716 cardiovascular end points, 294 cardiovascular deaths, 393 strokes, and 336 cardiac events occurred in the whole cohort; in untreated participants these numbers were 414, 158, 225, and 194, respectively. In the whole cohort, outcome-driven systolic/diastolic thresholds for the home BP corresponding with stages 1 and 2 prehypertension and stages 1 and 2 hypertension were 121.4/77.7, 127.4/79.9, 133.4/82.2, and 145.4/86.8 mm Hg; in 5018 untreated participants, these thresholds were 118.5/76.9, 125.2/79.7, 131.9/82.4, and 145.3/87.9 mm Hg, respectively. Rounded thresholds for stages 1 and 2 prehypertension and stages 1 and 2 hypertension amounted to 120/75, 125/80, 130/85, and 145/90 mm Hg, respectively. Population-based outcome-driven thresholds for home BP are slightly lower than those currently proposed in hypertension guidelines. Our current findings could inform guidelines and help clinicians in diagnosing and managing patients. **(*Hypertension*. 2013;61:27-34.)** ● **Online Data Supplement**

Key Words: home blood pressure measurement ■ blood pressure ■ hypertension ■ epidemiology ■ thresholds

Self-measurement of blood pressure (BP) at home offers specific advantages over conventional clinic measurement because it allows identifying patients with white-coat, masked, and sustained hypertension with readings taken under standardized home conditions, little measurement variability, and good reproducibility.[1] Home BP measurement is also appealing to most patients.[2] It can lead to better BP control by increasing awareness of hypertension and adherence to and persistence of drug treatment.[3] More importantly, some studies,[4–7] although not all,[8,9] suggested that home BP might be a stronger predictor of cardiovascular events than clinic BP. In addition to its benefits, home BP measurement is currently widely available to the general public because of the availability of affordable and reliably operating automatic devices. In 2005, 64% of American hypertensive patients owned a home BP monitor.[10]

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Despite the numerous advantages of home BP measurement, the diagnosis and treatment of hypertension are still mainly based on the clinic BP. One reason for the limited use of home BP measurement is the lack of a generally accepted reference frame and operational thresholds for initiating and adjusting treatment. Currently offered diagnostic thresholds for the home BP rely mainly on statistical parameters derived from cross-sectional analyses of reference populations instead of outcome data.[11–16]

We therefore built a new resource of prospective population studies based on individual participant data. The main objective of this collaboration was to generate outcome-driven diagnostic thresholds for home BP.

Methods

Study Participants

The International Database on HOme blood pressure in relation to Cardiovascular Outcomes (IDHOCO) includes studies involving a random population sample and longitudinal follow-up of both fatal and nonfatal cardiovascular outcomes. Details of the methodology of the project have been previously published.[17]

For the present analysis, we considered 2777 inhabitants of Ohasama, Japan[7]; a nationwide sample of 2075 Finns[6]; 836 inhabitants of the Tsurugaya district, Sendai, Japan[18,19]; 665 residents of Didima, Greece[8]; and 400 inhabitants of Montevideo, Uruguay.[20] Thus, the number of participants available for analysis totaled 6753. All studies contributing to the IDHOCO database received ethical approval and have been described in detail in peer-reviewed publications. All participants gave informed written consent. Of the 6753 participants, we excluded 283 because their clinic (n=267, 257 from Ohasama) or home (n=18) BPs had been measured <2 times. Thus, the number of participants included in the present analyses totaled 6470.

Clinic and Home BP Measurement

Clinic BP was measured with a standard mercury sphygmomanometer or an automated device, using the appropriate cuff size, after the subjects had rested for ≥2 minutes in the sitting or supine position.[17] Clinic BP was the average of 2 consecutive readings obtained at an examination center. We used the thresholds proposed by the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure,[14] the Japanese Society of Hypertension,[15] and the European Societies of Cardiology and Hypertension[16] to classify participants according to their clinic BP. We divided prehypertension into 2 categories, stage 1 prehypertension, which ranged from 120 to 129 mm Hg systolic and from 80 to 84 mm Hg diastolic, and stage 2 prehypertension, which ranged from 130 to 139 mm Hg systolic and from 85 to 89 mm Hg diastolic. Stage 1 hypertension ranged from 140 to 159 mm Hg systolic and from 90 to 99 mm Hg diastolic, and stage 2 hypertension was a conventional clinic BP of ≥160 mm Hg systolic or ≥100 mm Hg diastolic. Patients on antihypertensive treatment were classified according to the above-mentioned BP thresholds.

Home BP measurements were obtained at the participants' homes after 2–5 minutes of rest with a validated, oscillometric device in the sitting position.[17] The mean of all available measurements was used as home BP.

Other Measurements

In all cohorts, a questionnaire was used to obtain detailed information on each participant's medical history, intake of medications, and smoking and drinking habits. We defined smoking as the current use of smoking materials. Body mass index was body weight in kilograms divided by height in meters squared. Previous cardiovascular disease included cardiac and cerebrovascular disorders and peripheral vascular disease. Serum total cholesterol and blood glucose were determined by automated enzymatic methods on venous blood samples. Diabetes mellitus was a self-reported diagnosis, a fasting or random blood glucose level of ≥7.0 mmol/L (126 mg/dL) or ≥11.1 mmol/L (200 mg/dL), respectively, or the use of antidiabetic drugs.[17,21] Information on serum total cholesterol level was unavailable for the Didima population and was extrapolated from data provided by the Attica study investigators by sex and 10-year age strata.[22] The Attica study population[22] was a large population cohort examined at the same time (2001–2002) and in the same geographical area as the Didima cohort.

Ascertainment of Events

We ascertained vital status and incidence of fatal and nonfatal diseases from the appropriate sources in each country, as described in detail in a previous publication.[17] Fatal and nonfatal stroke did not include transient ischemic attacks. Coronary events encompassed death because of ischemic heart disease, sudden death, nonfatal myocardial infarction, and surgical and percutaneous coronary revascularization. Cardiac events were composed of coronary end points, fatal and nonfatal heart failure, pacemaker implantation, and other cardiac deaths. The composite cardiovascular end point included cerebrovascular and cardiac end points and cardiovascular mortality. In all outcome analyses, we only considered the first event per participant within each category.

Statistical Methods

For database management and statistical analysis, we used SAS software, version 9.3 (SAS Institute, Cary, NC). We compared means and proportions by the large-sample z test or ANOVA and by the χ^2 test, respectively. To explore the plausibility of the Cox model, we plotted incidence rates by fifths of the BP distributions, while standardizing by the direct method for cohort, sex, and age (<40, 40–59, and ≥60 years). In line with large cohort studies, we included BP as a continuous linear term in the Cox regression model, but we also tested whether the addition of a quadratic term of BP improved the fit. We calculated hazard ratios, while adjusting for cohort, sex, age, body mass index, smoking, history of cardiovascular disease, diabetes mellitus, treatment with antihypertensive drugs, and serum total cholesterol. We compared the hazard ratios in treated and untreated participants by including a cross-product term between BP and antihypertensive treatment status. We adjusted for cohort by introducing 4 design variables in the Cox models.

We obtained diagnostic thresholds for home BP measurement in 5 steps.[17,23] First, we computed the 10-year incidence rates of cardiovascular end points associated with the cutoff points for stage 1 prehypertension, stage 2 prehypertension, stage 1 hypertension, and stage 2 hypertension on clinic BP measurement. Second, we computed the 10-year incidence rates of cardiovascular end points associated with home BP levels ranging from the fifth to 95th percentiles, using intervals of 0.1 mm Hg. We calculated these incidence rates from the Cox regression model with the clinic or home BP entered as independent variable and while adjusting for cohort only. In the third step, we selected the home BP levels that were associated with similar 10-year risks as the clinic BP thresholds. Next, we calculated the bootstrap distribution of the so-obtained home diagnostic thresholds by randomly resampling the study population 1000 times with replacement. The bootstrap method estimates the distribution of a sample statistic by resampling the data.[24] The method does not make any assumptions about the distribution of the sample statistic. Finally, we calculated the bootstrap point estimates and 95% CIs of the home thresholds as the mean±1.96 SEs of the bootstrap distribution.

Results

Baseline Characteristics of Participants

Table 1 shows the baseline characteristics of each cohort. The 6470 participants included 3680 women (56.9%), 2516 patients (38.8%) with hypertension on clinic measurement, and 1452 patients (22.4%) taking BP-lowering drugs. Of 5018 untreated participants, 1016 (20.3%), 1040 (20.7%), 1130 (22.5%), and 494 (9.8%) had stage 1 or 2 prehypertension, or stage 1 or 2 hypertension, respectively. Systolic and diastolic BPs were on average 6.7 mm Hg

Table 1. Baseline Characteristics by Cohort

Characteristic	Ohasama	Finn-Home	Tsurugaya	Didima	Montevideo	All Cohorts
No. of participants	2520	2075	811	665	399	6470
Women, n (%)	1524 (60.5)	1113 (53.6)	444 (54.8)	387 (58.2)	212 (53.1)	3680 (56.9)
Age, y	59.9 (12.3)	57.1 (8.5)	75.3 (4.6)	54.3 (17.6)	41.9 (12.7)	59.3 (13.5)
Range	35.0–97.0	42.2–78.6	69.2–91.5	18.5–90.9	20.4–81.3	18.5–97.0
Body mass index, kg/m^2	23.5 (2.9)	27.4 (4.5)	23.9 (3.3)	27.1 (4.2)	26.0 (4.5)	25.3 (4.2)
Clinic blood pressure, mm Hg						
Systolic	131.3 (18.1)	137.4 (20.3)	145.2 (20.2)	127.3 (21.4)	120.2 (19.5)	133.9 (20.5)
Diastolic	74.6 (11.3)	83.7 (10.6)	83.4 (10.6)	76.4 (11.0)	77.7 (11.7)	79.0 (11.8)
Home blood pressure, mm Hg						
Systolic	123.6 (14.5)	129.9 (18.7)	140.1 (19.4)	124.3 (19.8)	114.9 (14.1)	127.2 (18.2)
Diastolic	73.8 (9.5)	80.3 (9.2)	77.1 (10.2)	73.6 (9.1)	71.3 (10.7)	76.1 (10.0)
Serum total cholesterol, mg/dL	193.2 (34.4)	237.4 (43.1)	204.2 (33.2)	198.9 (16.6)	214.3 (39.8)	210.6 (41.1)
Diabetes mellitus, n (%)	245 (9.7)	130 (6.3)	123 (15.2)	30 (4.5)	18 (4.5)	546 (8.4)
Current smoking, n (%)	499 (19.8)	482 (23.2)	98 (12.1)	169 (25.4)	104 (26.1)	1352 (20.9)
Previous cardiovascular disease, n (%)	84 (3.3)	251 (12.1)	129 (15.9)	59 (8.9)	34 (8.5)	557 (8.6)
Antihypertensive drug treatment, n (%)	510 (20.2)	470 (22.7)	335 (41.3)	94 (14.1)	43 (10.8)	1452 (22.4)

Data are expressed as mean (SD) unless otherwise noted. All between-cohort differences were significant (P<0.001). To convert cholesterol to mmol/L, multiply by 0.0259.

(P<0.0001) and 2.9 mm Hg (P<0.001) higher on clinic than on home measurement in the whole cohort. Between-cohort differences were significant for all variables (P<0.001). The median number of home measurements was 28 (fifth to 95th percentile interval, 2–56).

Incidence of End Points in Relation to BP

In the overall study population, median follow-up was 8.3 years (fifth to 95th percentile interval, 4.2–16.8 years). Across cohorts, median follow-up ranged from 5.5 years (fifth to 95th percentile interval, 2.5–5.6 years) in Tsurugaya to 11.9 years (fifth to 95th percentile interval, 3.7–16.9 years) in Ohasama. During 59 326 person-years of follow-up, there were 812 deaths (13.7 per 1000 person-years), of which 294 were cardiovascular, 513 were noncardiovascular, and 5 were because of unknown causes. During follow-up, a fatal or nonfatal cardiovascular end point occurred in 716 participants. The number of cardiovascular end points per cohort and in all cohorts is reported in Table S1 in the online-only Data Supplement. The unadjusted incidence of fatal and nonfatal cardiovascular complications was averaged 12.5 events per 1000 person-years, ranging from 5.0 in Montevideo to 17.1 in Tsurugaya.

The Figure shows the increase in cardiovascular events, stroke, and cardiac end points across fifths of the distributions of the conventional clinic and home systolic and diastolic BPs with standardization for cohort, sex, and age. With adjustments applied for cohort, sex, age, body mass index, smoking, history of cardiovascular disease, diabetes mellitus, treatment with antihypertensive drugs, and serum total cholesterol, BP was a significant predictor of cardiovascular outcome and stroke in the whole cohort, irrespective of the type of measurement (Table 2). Systolic home BP, however, was the sole significant predictor of cardiac and coronary events. The

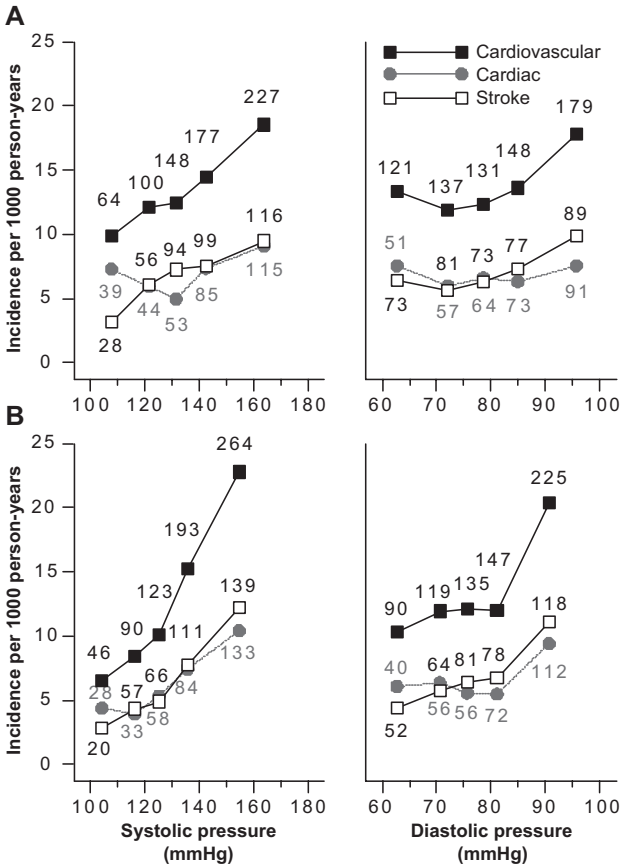

Figure. Incidence of cardiovascular events, stroke, and cardiac end points by fifths of the distributions of conventional clinic blood pressure (**A**) or home blood pressure (**B**). Incidence rates were standardized by the direct method for cohort, sex, and age (<40, 40–59, and ≥60 years). The number of events contributing to the incidence rates is presented.

addition of a quadratic term of BP to the 16 Cox models for the whole cohort listed in Table 2 did not improve the fit of the models, except slightly for diastolic home BP in relation to cardiac outcome (P=0.03). However, adding the quadratic term of BP did not materially alter the results (data not shown). Noncardiovascular mortality was weakly associated with systolic home BP (P=0.04/0.26 for systolic/diastolic), but not with clinic BP (P=0.99/0.79 for systolic/diastolic).

When untreated and treated participants were analyzed separately, clinic BP was not associated with cardiovascular outcome in the treated population. Furthermore, for clinic systolic BP, the association between cardiovascular end points was steeper (P<0.03 for all) in untreated than treated participants, whereas for the home systolic BP these associations were similar (P≥0.07; Table 2).

Diagnostic Thresholds for Home BP Measurement

Using a bootstrap procedure, we calculated the home BP levels that yielded 10-year absolute risks of cardiovascular, cerebrovascular, or cardiac events similar to those associated with stages 1 and 2 prehypertension, and stages 1 and 2 hypertension on clinic BP measurement. Table 3 shows the point estimates and 95% CIs for those risk thresholds adjusted for cohort in the whole study population. In sensitivity analyses, from which we excluded 1 cohort at a time, these diagnostic thresholds remained largely consistent (Table S2). When men and women were analyzed separately, the results did not differ considerably between sexes (Table S3).

As previously noted in Table 2, the associations between cardiovascular outcomes and clinic systolic BP were significantly stronger in the untreated population. To avoid the confounding effects of the time of BP measurement in relation to drug intake, the 1452 treated hypertensives at baseline were excluded from the analyses (Table 4). These systolic/diastolic thresholds differed slightly from those reported in Table 3 (whole population). To obtain easily recallable thresholds, in the last step of our analysis, we rounded the point estimates for cardiovascular events reported in Table 3 to an integer value ending in 0 or 5. After rounding, approximate thresholds for stages 1 and 2 prehypertension and stages 1 and 2 hypertension for home BP measurement amounted to 120/75, 125/80, 130/85, and 145/90 mm Hg, respectively.

Table 2. Hazard Ratios for Cardiovascular End Points in Relation to Clinic and Home Blood Pressure at Entry for the Whole Cohort and by Treatment Status

		Fatal and Nonfatal Cardiovascular End Points Combined		
Blood pressure index	Cardiovascular Death	All	Stroke	Cardiac
All subjects (n=6470)				
End points, n	294	716	393	336
Systolic blood pressure				
Clinic	1.11 (1.04–1.17)‡	1.09 (1.05–1.13)§	1.12 (1.06–1.17)§	1.05 (1.00–1.11)
Home	1.13 (1.05–1.21)†	1.19 (1.14–1.25)§	1.28 (1.20–1.37)§	1.10 (1.03–1.18)†
Diastolic blood pressure				
Clinic	1.05 (1.00–1.11)	1.07 (1.04–1.11)§	1.09 (1.04–1.14)‡	1.04 (0.99–1.10)
Home	1.04 (0.97–1.11)	1.13 (1.08–1.17)§	1.19 (1.13–1.25)§	1.05 (0.99–1.12)
Treated (n=1452)				
End points, n	136	302	168	142
Systolic blood pressure				
Clinic	1.02 (0.93–1.11)	1.01 (0.96–1.07)	1.07 (0.99–1.16)	0.94 (0.86–1.02)
Home	1.16 (1.04–1.29)‡	1.15 (1.08–1.24)§	1.31 (1.18–1.45)§	1.03 (0.93–1.14)
Diastolic blood pressure				
Clinic	1.00 (0.93–1.08)	1.03 (0.98–1.08)	1.04 (0.97–1.11)	1.00 (0.92–1.08)
Home	1.07 (0.97–1.19)	1.11 (1.04–1.17)†	1.19 (1.10–1.29)§	1.00 (0.91–1.11)
Untreated (n=5018)				
End points, n	158	414	225	194
Systolic blood pressure				
Clinic	1.19 (1.10–1.28)§	1.15 (1.09–1.20)§	1.15 (1.08–1.23)§	1.15 (1.07–1.23)‡
Home	1.10 (1.00–1.21)	1.21 (1.14–1.28)§	1.26 (1.16–1.37)§	1.16 (1.06–1.26)‡
Diastolic blood pressure				
Clinic	1.10 (1.02–1.18)*	1.11 (1.06–1.16)§	1.13 (1.07–1.20)§	1.08 (1.00–1.15)*
Home	1.00 (0.91–1.09)	1.14 (1.08–1.20)§	1.18 (1.09–1.27)§	1.08 (1.00–1.18)

Hazard ratios (95% CIs) reflect the risk associated with 10- and 5-mm Hg increases in systolic and diastolic blood pressure, respectively. Hazard ratios were adjusted for cohort, sex, age, body mass index, smoking, history of cardiovascular disease, diabetes mellitus, treatment with antihypertensive drugs, and serum total cholesterol. The associations between clinic systolic blood pressure and cardiovascular end points were markedly steeper in the untreated as compared with the treated population (P<0.05 for all comparisons).

Significance of the hazard ratios: *P≤0.05; †P≤0.01; ‡P≤0.001; §P≤0.0001.

Table 3. Home Blood Pressure Levels Yielding 10-Year Risks Similar to Those Associated With Prehypertension or Hypertension on Clinic Measurement in All Participants

End Point (n)	Category	Clinic BP, mm Hg	10-Year Absolute Risk, %	Home BP (95% CI), mm Hg
Cardiovascular (716)	Stage 1 PHT			
	Systolic	120	8.4	121.4 (119.6–123.2)
	Diastolic	80	11.2	77.7 (77.3–78.0)
	Stage 2 PHT			
	Systolic	130	10.3	127.4 (126.3–128.4)
	Diastolic	85	13	79.9 (79.3–80.6)
	Stage 1 HT			
	Systolic	140	12.6	133.4 (132.9–133.9)
	Diastolic	90	14.2	82.2 (80.9–83.6)
	Stage 2 HT			
	Systolic	160	18.7	145.4 (143.8-146.9)
	Diastolic	100	16.7	86.8 (84.0-89.6)
Stroke (393)	Stage 1 PHT			
	Systolic	120	3.4	123.5 (121.1–126.0)
	Diastolic	80	5.1	78.0 (77.5–78.5)
	Stage 2 PHT			
	Systolic	130	4.3	128.9 (127.4–127.4)
	Diastolic	85	5.6	80.3 (79.6–80.9)
	Stage 1 HT			
	Systolic	140	5.3	134.3 (133.5–135.1)
	Diastolic	90	6.3	82.6 (81.2–83.9)
	Stage 2 HT			
	Systolic	160	8.3	145.1 (143.3-146.9)
	Diastolic	100	7.7	87.1 (84.3-89.9)
Cardiac (336)	Stage 1 PHT			
	Systolic	120	4.0	120.1 (117.4–122.8)
	Diastolic	80	5.6	77.3 (76.8-77.8)
	Stage 2 PHT			
	Systolic	130	4.9	126.5 (125.0–128.0)
	Diastolic	85	5.9	79.1 (77.3-81.0)
	Stage 1 HT			
	Systolic	140	5.9	132.9 (132.4–133.5)
	Diastolic	90	6.2	81.0 (77.4–84.5)
	Stage 2 HT			
	Systolic	160	8.5	145.8 (143.3–148.3)
	Diastolic	100	6.9	84.6 (77.7–91.5)

The analyses were adjusted for cohort. Point estimates and 95% CIs were obtained from the bootstrap distribution of 1000 random samples of the study population with replacement (for further details, see Methods). BP indicates blood pressure; PHT, prehypertension; HT, hypertension.

Table 4. Home Blood Pressure Levels Yielding 10-Year Risks Similar to Those Associated With Prehypertension or Hypertension on Clinic Measurement in 5018 Participants Untreated at Baseline

End Point (n)	Category	Clinic BP, mm Hg	10-Year Absolute Risk, %	Home BP (95% CI), mm Hg
Cardiovascular (414)	Stage 1 PHT			
	Systolic	120	6.2	118.5 (116.3–120.6)
	Diastolic	80	9.0	76.9 (76.5–77.3)
	Stage 2 PHT			
	Systolic	130	7.9	125.2 (124.0–126.3)
	Diastolic	85	10.0	79.7 (78.7–80.6)
	Stage 1 HT			
	Systolic	140	10.0	131.9 (131.3–132.5)
	Diastolic	90	11.1	82.4 (80.5–84.3)
	Stage 2 HT			
	Systolic	160	15.8	145.3 (143.1–147.6)
	Diastolic	100	13.6	87.9 (84.2–91.6)
Stroke (225)	Stage 1 PHT			
	Systolic	120	2.5	120.5 (117.8–123.3)
	Diastolic	80	3.6	77.1 (76.6–77.6)
	Stage 2 PHT			
	Systolic	130	3.2	126.5 (124.9–128.0)
	Diastolic	85	4.1	80.0 (79.0–80.9)
	Stage 1 HT			
	Systolic	140	4.1	132.4 (131.5–133.2)
	Diastolic	90	4.7	82.8 (80.9–84.6)
	Stage 2 HT			
	Systolic	160	6.6	144.2 (141.5–146.8)
	Diastolic	100	6.1	88.4 (84.8–92.1)
Cardiac (194)	Stage 1 PHT			
	Systolic	120	3.1	116.4 (112.8–119.9)
	Diastolic	80	4.5	76.6 (75.6–77.5)
	Stage 2 PHT			
	Systolic	130	3.9	124.0 (122.3–125.8)
	Diastolic	85	4.8	78.9 (75.9–81.9)
	Stage 1 HT			
	Systolic	140	5.0	131.7 (131.1–132.3)
	Diastolic	90	5.2	81.2 (76.2–86.3)
	Stage 2 HT			
	Systolic	160	8.0	147.0 (143.2–150.8)
	Diastolic	100	6.0	85.8 (77.0–94.5)

The analyses were adjusted for cohort. Point estimates and 95% CIs were obtained from the bootstrap distribution of 1000 random samples of the study population with replacement (for further details, see Methods). BP indicates blood pressure; PHT, prehypertension; HT, hypertension.

Discussion

In line with the research of Pickering and other investigators, home BP measurement is now recommended for all v with hypertension in the United States,[25] Japan,[15] and Europe.[26] However, until now, the widespread clinical use of home BP measurement has been limited by the lack of generally

accepted operational thresholds based on prognostic data. The existing guidelines[15,25,26] have proposed that levels of the self-measured BP at home of 135 mm Hg systolic or 85 mm Hg diastolic or higher indicate stage 1 hypertension and have made no recommendation on the thresholds for prehypertension and stage 2 hypertension. This article provides, for the first time, an outcome-driven reference frame for home BP measurement based on individual participant data that includes all existing population cohorts with fatal and nonfatal outcomes available for analysis. On the basis of our results, the rounded thresholds for stages 1 and 2 prehypertension and stages 1 and 2 hypertension on home BP measurement amounted to 120/75, 125/80, 130/85, and 145/90 mm Hg, respectively.

The results of this study should be carefully interpreted. The relation between cardiovascular outcomes and BP is continuous without any clear evidence of a threshold down to <115/75 mm Hg on clinic measurement.[27] Thresholds such as 140/90 mm Hg on clinic measurement for hypertension are therefore fairly arbitrary and only serve the need of clinicians to use cutoff limits for the diagnosis and management of hypertension. In addition, rounding of the point estimates for cardiovascular events unfortunately results in loss of precision, but is needed to obtain easily recallable thresholds and to send a clear message to physicians.

The classification of conventional clinic BP into prehypertension or hypertension is not sex or age specific. We, therefore, only adjusted for cohort and disregarded sex, age, and other cardiovascular risk factors. However, the association between cardiovascular outcome and BP was markedly stronger in the untreated participants. In hypertensive patients, BP-lowering treatment can be a confounder with too large an impact to adjust for. Indeed, in the Systolic Hypertension in Europe trial, systolic BP did not significantly predict cardiovascular end points in the active-treatment group, regardless of whether clinic or ambulatory BP measurement was used.[28] The use and dosing times of antihypertensive drugs also have a marked confounding effect on the relation between clinic and home BP.[29] We, therefore, chose to use the untreated population of 5018 participants for defining the finally recommended thresholds.

Research on cutoff limits for the self-measured BP has been ongoing for the past 30 years.[30] The currently recommended threshold of 135/85 mm Hg for elevated home BP mainly originated from 2 meta-analyses that were based on aggregate data extracted from published articles[11] and on individual patient data, respectively.[12] In analysis of aggregate data, the reference values for the self-recorded systolic/diastolic BP as derived from the mean+2 SDs and the 95th percentile of the distribution in normotensive participants were 137/89 and 135/86 mm Hg, respectively.[11] However, when the cutoff points were derived using the regression and percentile methods they were considerably lower, that is, 129/84 and 125/79 mm Hg, respectively.[11] In analysis of individual patient data,[12] the reference values determined from the 95th percentiles of the distributions for normotensive participants were 137 mm Hg systolic and 85 mm Hg diastolic. However, all these analyses were cross-sectional in design, applied selection criteria based on BP values, and did not necessarily use validated home monitors, which reduces the reliability and generalizability of these previous meta-analyses.[11,12] In fact, both meta-analyses concluded that establishing operational thresholds for the self-measured home BPs would require prospective studies to clarify the link between cardiovascular disease and the home BP.[11,12]

In addition to cross-sectional data, limited evidence on home BP thresholds is available from prospective studies. Although the risk associated with various home BP categories has been reported in several articles, only the Ohasama study investigators have suggested a prognosis-based threshold for hypertension based on home BP measurements.[5,13,30] The Ohasama research initially proposed 137 mm Hg systolic and 85 mm Hg diastolic as acceptable upper limits for the home BP on the grounds that the risk of death increased above these thresholds.[13] Later, the Ohasama investigators published a subgroup analysis performed in high-risk patients that showed that prehypertension (home BP 115–135/75–85 mm Hg) carried a 2-fold higher risk of stroke compared with normotension.[5] These observations suggested that the thresholds of the home BP applicable to high-risk patients might be <135/85 mm Hg.

Despite all advantages, the results of our analyses must be interpreted within the context of their potential limitations. First, the anthropometric characteristics and the time of recruitment differed between cohorts. Second, the clinic and home BP measurements were not standardized in terms of device type, number of measurements, and intervals between readings. Third, the availability of end point data differed between cohorts. Fourth, serum cholesterol levels were unavailable for the Didima population. However, the Didima cohort accounted for only 10% of the total study population. We also compensated for this shortcoming by excluding the Didima cohort in sensitivity analyses and by extrapolating total cholesterol values from a large Greek population cohort examined in the same time period and the same geographic area as the Didima cohort.[22] Moreover, our main analyses were only adjusted for cohort. In our view, this was the optimal approach, because within each cohort, at the level of individual participants, risk factor profiles were the same for clinic and home BPs. Fifth, the clinic BP in the present study was the average of 2 readings obtained at a single examination, which can lead to an overestimation of clinic BP because of the white-coat effect.

Perspectives

The present report provides an outcome-driven reference frame for self-measured home BP. Our findings suggest that outcome-driven thresholds for hypertension defined by home BP are slightly lower than those currently proposed by hypertension guidelines. The present findings could inform guidelines and be of help to clinicians in diagnosing and managing patients.

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Disclosures

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Novelty and Significance

What Is New?

- Current diagnostic thresholds for home blood pressure rely mainly on statistical parameters derived from cross-sectional analyses.
- The objective of our study was to determine for the first time an outcome-driven reference frame for home blood pressure measurement.

What Is Relevant?

- Rounded home blood pressure thresholds for clinic stages 1 (blood pressure 120/80 mm Hg) and 2 (130/85 mm Hg) prehypertension and stages 1 (140/90 mm Hg) and 2 (160/100 mm Hg) hypertension were uniformly lower with levels of 120/75, 125/80, 130/85, and 145/90 mm Hg, respectively.

Summary

The present report provides an outcome-driven reference frame for home blood pressure. These findings could inform guidelines and be of help to clinicians in diagnosing and managing patients.