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The Impact of Multiple Single Day Blood Pressure Readings on Cardiovascular Risk Estimation: The Atherosclerosis Risk in Communities Study

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Abstract

Aims—To determine the magnitude of change in estimated cardiovascular disease risk when multiple same day blood pressure measurements are used in estimating coronary heart disease (CHD), heart failure (HF) and stroke risks.

Methods and Results—11,129 black and white participants enrolled in the Atherosclerosis Risk in Communities (ARIC) study (mean age 53.9 ± 5.7 (SD) years) were included. Each participant had 3 sitting, 5 supine, and 6 standing BP measures during one day. Main outcome measures were changes in estimated CHD, HF and stroke risk when using the different BP measures. Mean sitting, standing and supine SBP of the study population were 120.8 ± 18.6 , 124.9 ± 20 and 124.7 ± 19.6 mmHg respectively. The substitution of the second sitting SBP with the third sitting SBP (taken ~5 minutes later) in two separate CHD risk models reclassified 3.3% to 5.1% of study participants. Similar substitutions for HF and stroke risk prediction models led to reclassification of 1.9 and 2.7% of participants respectively. When mean sitting SBP was replaced with mean standing SBP 5.4% to 11.6% of the participants were reclassified. Maximum upward and downward change in an individual's estimated risk was 31%, and 26% respectively.

Conclusions—Estimated risks of CHD, HF and stroke for an individual can change significantly within a day due to changes in SBP. Given recommendations to use estimated risk for therapeutic decisions, our study has implications for the use of a single SBP in cardiovascular risk estimation.

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Keywords

Blood pressure; ARIC; CVD risk reclassification; ASCVD

Introduction

Systolic blood pressure (SBP) measurements are used in addition to hypertension status in all established coronary heart disease (CHD), heart failure (HF) and stroke risk prediction models including the Framingham CHD Risk Score (FRS), ¹ Atherosclerosis Risk in Communities (ARIC) Coronary Risk Score (ACRS), ² ARIC Heart failure Risk Score (HFRS), ³ ARIC Stroke Risk Score (ASRS), ⁴ European Systematic Coronary Risk Evaluation (SCORE) ⁵ and the pooled cohorts Atherosclerotic Cardiovascular Disease (ASCVD) risk equations⁶. However, BP is dynamic and subject to short-term changes secondary to external and internal factors such as posture, physical activity, diet, and changes in endocrine and nervous system functions. ^{7–10} Examples of such changes include "white coat hypertension" (raised BP occurring only in the presence of the physician or nurse) or the "alerting phenomenon" (repeating BP immediately leading to lower values). ^{11,12} However, in daily practice, a single sitting BP is used in estimating an individual's cardiovascular risk. Given that BP varies through the day, one would predict that a spectrum of risk estimates would result depending on the SBP values.

While studies have reported on the impact of BP readings performed across clinic visits on estimated CV risk, ^{13–15} to our knowledge, none has evaluated the effect of multiple single day BP readings on estimated CV risk except for one preliminary report from Dallas Heart Study that suggested averaging multiple single day BP readings may improve prediction of target organ damage from hypertension. ¹⁶ However, this preliminary analysis did not investigate the magnitude in change in estimated risk. Our aim therefore was to 1. Quantify changes in the estimated CHD, HF and stroke risk using different measurements of BP, obtained on the same day and 2. Compare the various systolic BP (SBP) measures with respect to prediction of incident CHD, HF and stroke risk; in addition we also evaluated the potential value of using hypertension as a categorical variable without the SBP value in risk prediction models.

Methods

The ARIC study, a population based study of 15792 individuals was used for our analysis.¹⁷ Please see supplemental methods for details about the study participants and risk factor definition.

Blood pressure measurement

Trained technicians measured BP in the sitting, supine and standing positions on the same day. Following a rest period, three manual sitting BP measurements were made within a 10–15 minutes period, using a random zero sphygmomanometer. Subsequently, other BP measurements were made during the ultrasound examination using a Dinamap-SX oscillometric machine with a dedicated microcomputer. Five automated BP measurements

were made in the supine position at 5 minutes intervals, while 6 standing BP measurements were taken at 20-second intervals in a two-minute period immediately following the supine measurements. ¹⁸ Additional details are provided in the supplemental methods.

Cardiovascular risk score calculations

We studied 3 CHD risk scores (ACRS, FRS and pooled cohort risk equation), 1 stroke and 1 HF risk score (ARIC scores).

Framingham Risk Score (FRS) and ARIC Coronary Risk Score (ACRS) for 10year CHD risk prediction—The FRS algorithm includes age, sex, race, cigarette smoking, SBP, total cholesterol and HDLc levels as variables ¹ while the ACRS includes age, sex, smoking status, SBP, total cholesterol, HDLc, hypertension medications use and diabetes status. ²

ARIC Heart Failure Risk Score (HFRS) and ARIC Stroke Risk Score (ASRS) for 10-year risk prediction—The HFRS algorithm includes age, sex, smoking status, SBP, heart rate, BMI, previous CHD, use of hypertension medications and diabetes status. ³ The ASRS includes age, sex, smoking status, SBP, electrocardiographic evidence of left ventricular hypertrophy, previous CHD and diabetes status. ⁴ Further details regarding both the HFRS and ASRS have been described. ³, ⁴

AHA/ACC Pooled Cohort Atherosclerotic Cardiovascular Disease (ASCVD) Risk Score for 10-year CVD risk prediction—The recently introduced Pooled Cohort Risk calculator provides 10 year estimates for atherosclerotic cardiovascular disease (ASCVD) risk for African American and non-Hispanic White men and women aged 40–79 years. Variables used include subject's race, age, sex, total cholesterol, HDLc, SBP, antihypertensive medication use, as well as diabetes and smoking status.⁶

Finally, for each of the ARIC models (which would represent the best models in the ARIC study) we created a model that excluded the SBP variable and treated hypertension as a categorical variable (present/absent).

Statistical Analysis

Please see supplemental methods for additional details. Briefly, intra-class correlation coefficients were determined (see supplementary information). Then, hazard ratios (HR) and 95% confidence intervals (CI) were estimated for the FRS, ACRS, HFRS, ASRS and ASCVD risks using the various BP measurements taken and published β coefficients for the ARIC cohort. Then the 10-year risk was estimated for each individual for the various SBP measures and risk scores. Using the following risk groups [5%, >5–10%, >10–20% and >20% (5, >5–7.5% and >7.5% for the pooled cohort score)], reclassification tables were constructed to assess number of individuals who would be reclassified to different risk groups when two sitting BP measures (2nd and 3rd sitting SBP readings) were compared. Then, similarly, mean sitting and standing BP, and mean sitting and supine BP were compared. Additional analyses were then conducted using hypertension as a categorical variable (present/absent) rather than using both hypertension status and SBP as currently

done. Finally, we also assessed reclassification using alternate risk groups 10%, >10–20% and >20% for all the risk scores except for the pooled cohort score where we used 7.5 and >7.5% (Supplemental results table 1). Using incident events until December 31, 2009 (See Supplemental methods for description of incident events) risk prediction metrics including area under the receiver operating characteristics curve (AUC), net reclassification index (NRI), integrated discrimination index (IDI) and model calibration using the Hosmer Lemeshow test statistic were determined for ARIC CHD, HF and stroke prediction models by comparing standing, supine blood pressures, as well as one having hypertension (present/absent) with a model using sitting SBP. Confidence intervals were furnished by bootstrapping (1000 bootstraps).

Results

The mean age of the study participants was 53.9 ± 5.7 years, (55.9% women). Fifty seven percent had a history of any smoking (current and former), 31% were hypertensive, and 10% had a history of diabetes (Table 1). Mean sitting, standing and supine SBP were 120.8 ± 18.6 mmHg, 124.9 ± 20 mmHg and 124.7 ± 19.6 mmHg, respectively. Table 2 provides the hazards ratios for the various CHD, HF and stroke risk prediction models using the various SBP readings. We observed a consistently higher numerical HR when supine SBP was used. For example, using the ACRS algorithm, estimated HR for CHD was 1.14 (95% CI: 1.12, 1.17) when mean supine SBP was used, compared to 1.11 (95% CI: 1.08, 1.14) and 1.09(95% CI: 1.06, 1.12) when mean sitting and standing BP measurements were used respectively.

Risk Reclassification with SBP Substitutions

1. CHD Risk Reclassification—Using the ACRS classification system, 5.1% of all participants were reclassified when the 2nd sitting SBP measure was replaced by 3rd sitting SBP with 2.4% being reclassified to a higher and 2.7% to a lower risk group. Similarly, with the FRS, 3.3% were reclassified with 1.6% being reclassified to a higher and 1.7% to a lower risk group. The highest percentage of reclassification was seen when mean sitting SBP was compared to mean standing SBP measures with 10.7% and 7% of subjects being reclassified in the ACRS and FRS models, respectively. The maximum observed absolute change in estimated risk (upward and downward) in any individual was 29%, 25% for the ACRS and 19%, 16% for the FRS risk score (Table 3).

2. HF Risk Reclassification—Substitution of the third for the second sitting SBP in the HFRS led to the reclassification of 1.9% of participants (0.8% to a higher and 1.1% to a lower risk group). Again, the highest number of reclassified participants was seen for the mean sitting SBP vs. mean standing SBP risk score comparisons with a total of 4.6% being reclassified (1.5% to a higher risk group and 3.1% to a lower risk group). The maximum upward change in risk scores observed in an individual within the study cohort was 14%, and the maximum observed reduction in risk score was 16% (Table 3).

3. Stroke Risk Reclassification—For the ASRS algorithms, 2.1% of participants were reclassified when the third sitting BP measures was included instead of the second sitting

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SBP. In all, 0.9% of participants were reclassified to higher risk groups and 1.2% to lower risk groups. Substitution of the mean supine SBP for mean sitting SBP again resulted in the reclassification of the highest number of with an estimated 5.4% being reclassified (1.7% to a higher, and 3.7% to a lower risk group). The maximum observed upward change in any individual was 31% and the maximum downward change in risk score estimate was 24% (Table 3).

4. ASCVD Pooled Cohort Risk Reclassification—When the second sitting SBP is replaced with the third sitting SBP measurement, 5.8% of study participants were reclassified (2.6% to a higher risk group, and 3.2% to a lower one). Approximately 11.6% of study participants were reclassified from one risk group to another (8.1% to a higher, and 3.5% to a lower risk category) when the mean sitting SBP was replaced with the mean standing SBP. The maximum upward change in risk scores observed in any individual was 31%, and the maximum reduction in risk was 26% (Table 3).

5. Risk prediction metrics using the various SBP measures (Supplemental

Table 2)—When comparing the AUC, NRI and IDI values for different ARIC CVD risk prediction models using sitting SBP as the base model, we found that the model utilizing supine SBP performed marginally better than the models based on sitting SBP. For example, in the prediction of CHD risk, the AUC difference between the model based on supine SBP and the base (sitting SBP) model was 0.004 (CI: 0.002, 0.007). AUC differences between the models based on standing SBP and hypertension versus the base model were -0.001 (CI: -0.003, 0.0001) and -0.004 (CI: -0.007, -0.002) respectively. Similar observations were made when HF and stroke risks prediction were evaluated. With respect to NRI estimates for CHD and stroke risks prediction, there were no significant differences between the different models. However, for HF risk prediction, the model using supine SBP performed marginally better than the model based on sitting SBP (NRI% 3.99%, CI: 0.11, 7.54) No significant differences existed in the NRI values of the standing SBP and hypertension status models compared to the base model (-0.47, CI: -3.83%, 2.77 and -2.75, CI: -6.57, 0.21 respectively).

Discussion

Risk estimation and institution of preventive therapies based on estimated risk remains the cornerstone of preventive medicine. SBP is a variable used in most (if not all) cardiovascular risk scores, and is in fact among the strongest predictors of stroke. Short term variations in SBP have been well described and documented; however, its effect on estimated risk and its potential clinical impact has not been studied. In this analysis, we demonstrate the significant impact of different BP readings obtained on a single day on estimated risk and demonstrate how, in ~2–11% of the participants, the estimated risk categories (low, medium or high) can change within a day. In fact, in some individuals (although rare) the estimated risk went from low to high and in others, from high to low. Such changes have clear clinical implications. We then showed that substituting the various SBP measures and removing SBP from the risk prediction equation resulted in comparable algorithms for the most part although supine SBP measures were statistically marginally better.

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In clinical practice, consideration of 'risk' versus 'benefit' is critically important. Physicians routinely weigh the risks of a proposed intervention against its potential benefit and guide the patient in the management of his/her health. Clearly, the higher the baseline risk, the greater the potential benefit of an intervention, and hence greater willingness to tolerate potential side effects. Treatment guidelines therefore factor in 'baseline risk' and suggest risk thresholds at which one should consider therapy in the prevention of diseases including CHD.⁶ As an example, most clinicians would recommend statin therapy for an individual with an LDL-c of 110 mg/dL and an estimated 10-year CHD risk of 22% based upon the high estimated risk (using either the Adult Treatment Panel III or the new Lipid Guidelines). In this situation, despite the 0.2–0.3% increased risk of diabetes, the negligible risk of rhabdomyolysis and minimal risk of liver dysfunction, statin therapy holds the potential for benefit. On the other hand, if the patient's estimated 10-year CHD risk is 3–4%, the managing physician is likely to re-evaluate the risk/benefit of starting statin therapy for this low risk individual.

Therefore, while BP is clearly a risk factor for various CVD, incorporation of a variable that has significant short-term variability, which can lead to clinically meaningful changes in estimated risk within a day, requires careful consideration and thought. BP estimations have been shown to demonstrate significant variability: Powers et al studied 444 Veterans with hypertension (111,181 SBP measures over an 18-month period), and reported that the mean within-patient coefficient of variation was 10%.¹⁹ They also reported that using multiple readings could decrease overall BP variability. Similarly, Velasco et al in a preliminary report from the Dallas Heart Study suggested that averaging several BP recordings is associated with the best improvements in risk prediction. ¹⁶ A recent study by Niiranen et al²⁰ suggests that ambulatory BP may offer improved prognostication of cardiovascular risk compared to home or office measurements. Other options such as the use of home BP measures have been investigated as well; however, again implementation of such ambulatory measurements has its challenges as well. Overall, due to these challenges, while averaging multiple readings may be the most scientific approach, in practice, physicians often use single BP measures for risk prediction. However, based on the wide variations in predicted risks shown in our analysis physicians need to strive to adhere to published guidelines on the measurement of BP to allow its better use in risk prediction. It is hoped that technological advancements make the inclusion of ambulatory measurements in risk prediction algorithms practicable on a population-wide scale in the near future. In the meantime, strict adherence to proper measurement of BP or options of just factoring in the presence or absence of hypertension or including a measure of variability in risk equations may need to be considered.

One may argue that the wide variation in estimated risk in our analysis was due to the use of SBPs obtained in different positions, irrespective of the duration of time between these readings. However, even simply substituting sitting BP measurements reclassified as many as 517, 614 and 503 participants for CHD, HF and stroke risk prediction, respectively. The implications of the change in estimated risk based solely on the substitution of BP measures in such a short time period are great. If such significant changes can be seen when the BP is measured under ideal conditions as exist in clinical studies such as the ARIC study, one can hypothesize that the changes will be greater in real world clinical practice. Similarly,

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arguments could also be made that the observed variability in BP is as a result of the 'alerting phenomenon' or 'white-coat hypertension'. ^{11, 12} However, if this were related to the alerting phenomenon, participants should have been reclassified down from higher risk groups to lower; but in our analysis, reclassification happened both ways. On the other hand, white coat hypertension is associated with stroke risk and end organ damage, ^{21, 22} and is not routinely considered in risk prediction algorithms.

Although previous studies have reported changes in BP and estimated risk across visits, ²³ we believe that our study is among the first to report on the same day changes of estimated risk based on different same day BP readings. Ye et al used data from the Third National Health and Nutrition Examination Survey and reported, using the pooled cohort risk equation, that several individuals (~10%) with estimated risks between 5–10%, had meaningful risk reclassification (i.e. across the threshold where the decision on initiation of statin therapy may change) when using BP measured a median of 17 days apart were compared.²³ Our study expands and complements the findings of Ye et al by examining the impact of same day changes in BP and further assessing the impact on heart failure and stroke risk scores as well using a larger population-based epidemiological study, thereby increasing the generalizability of these findings.

This study has several strengths and limitations. The study population is large and well characterized, with rigorous protocols followed to estimate BP. Our analysis also included the recently introduced AHA/ACC Pooled cohort ASCVD risk equation which has been incorporated into the most recent lipid guidelines. ⁶ Our analysis does have limitations. One limitation is that BP measurements were taken with different equipment, which may introduce some measure of systematic errors. Furthermore, both random zero sphygmomanometer and the Dinamap XP equipment used for these measurements in Visit 2 have been shown to be less accurate when compared to more modern equipment. However, the ARIC study employed rigorous protocols to ensure accurate data collection with the standard equipment available at the time of collecting the original data. Furthermore, in everyday practice, different BP monitors are used by clinicians to determine BP and this limitation may reflect existing realities of clinical practice.

Also, we did not examine reclassifications using the SCORE risk classification although the results would not have been any different. As an illustration, one subject was a 59 year old male non-smoker with diabetes, an HDL-c of 40 mg/dL (~1.03 mmol/L), total cholesterol of 216 mg/dL (5.6 mmol/L) who had a sitting SBP of 200 mmHg and a standing SBP of 135 mmHg; using the SCORE (high risk countries) chart his risk was estimated to be between 4 to 6% when the standing SBP was used as opposed to >13% or greater when the sitting SBP was used suggesting a big difference in estimated risk. Similarly when sitting BP alone is used, a 61 year old woman smoker whose total cholesterol was 306 mg/dL (i.e. ~7.9 mmol/L), HDL-c was 37 mg/dL (i.e. ~0.9 mmol/L) and sitting BPs were 116 and 142 mmHg respectively had her estimated risk change from ~4% (orange zone) to 6–9% (red zone).

Other limitations that should be considered include that this analysis was based on multiple BP measurements taken in 1 day and hence participant fatigue, changes in ambient

temperature and timing of anti-HTN meds may have impacted the BP measurements, but we feel that such factors are also likely to be present in everyday clinical practice. Finally, heart failure and stroke risk scores do not have low/intermediate/high-risk groups as CHD risk scores; we therefore used similar cut-points to categorize risk groups for these outcomes.

Conclusion

We demonstrate that significant changes in an individual's estimated cardiovascular risk can occur within a day on account of short term BP changes, and that CHD prediction models based on supine BP measures perform modestly better. Given that estimated cardiovascular risk is an important factor that guides preventative therapies and goals in current day clinical practice, further consideration of our findings and improvement in the way BP is utilized in risk prediction scores is needed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Translational Perspectives

A single sitting blood pressure is the standard measure used in everyday practice for estimating an individual's cardiovascular risk; however blood pressure is dynamic and changes through the day and careful measurements are essential.

Changes in same day blood pressure readings lead to reclassifications in CVD risk using the ARIC, FRS, HFRS, ASRS and the pooled cohort risk algorithms.

Blood pressure variability and incorporation of the same into CVD risk prediction models should be considered and addressed as we refine CVD risk prediction

Table 1

Baseline Characteristics of ARIC Study Visit 1 Participants

Participants' Characteristics	Blacks (N = 2856)	Whites (N = 8273)	Total (N = 11129)
Age (years), mean (SD)	53.4 (5.8)	54.1 (5.7)	53.9 (5.7)
Gender, n (%)			
Male	1087 (38.1)	3818 (46.2)	4905 (44.1)
Female	1769 (61.9)	4455 (53.9)	6224 (55.9)
Systolic Blood Pressure (mmHg), mean (SD)			
Sitting	128.6 (21.1)	118.2 (16.8)	120.8 (18.6)
Standing	135.5 (22.5)	121.2 (17.6)	124.8 (20.0)
Supine	134.3 (22.7)	121.3 (17.2)	124.7 (19.6)
Body Mass Index (kg/m ²), mean (SD)	29.3 (6.0)	26.8 (4.7)	27.5 (5.2)
^a Total Cholesterol (mg/dl), mean (SD)	213.7 (44.5)	213.7 (40.2)	213.7 (41.3)
<i>b</i> High Density Lipoprotein (mg/dl) mean (SD)	55.7 (17.8)	51.1 (16.9)	52.2 (17.2)
^C Low Density Lipoprotein (mg/dl), mean (SD)	136.3 (42.3)	136.5 (37.4)	136.4 (38.7)
Diabetes, n (%)	507 (17.8)	654 (7.9)	1161 (10.4)
Hypertension, n (%)	1469 (51.4)	1998 (24.2)	3467 (31.2)
Left Ventricular hypertrophy n (%)	150 (5.3)	67 (0.8)	217 (2.0)
Heart rate per minute, mean (SD)	66.4 (10.9)	66.0 (9.7)	66.1 (10.0)
d Glucose, mean (SD)	117.2 (57.0)	104.3 (29.1)	107.6 (38.7)
Smoking, n (%)			
Current	850 (29.8)	1984 (24.0)	2834 (25.5)
Former	682 (23.9)	2859 (34.6)	3541 (31.8)
Hypertension medications, n (%)	1086 (38.0)	1710 (20.7)	2796 (25.1)
Statins, n (%)	7 (0.3)	45 (0.6)	52 (0.5)
Family History of CHD, n (%)	808 (35.5)	3552 (46.8)	4360 (44.2)

a, b&c. To convert cholesterol, high density lipoprotein (HDL) and low density lipoprotein (LDL) to mmol/L, multiply values by 0.0259.

 $d_{\rm TO}$ convert glucose to mmol/l, multiply values by 0.0555 All measurements are reported as mean (SD) or N (%)

Table 2

Multivariable-adjusted hazard ratios (HR) in cardiovascular disease outcomes using systolic blood pressure measurements taken in different positions. HRs shown for every 10 mmHg increase in SBP

Risk Score	SBP Reading	HR
^a ACRS (N= 11,129)	Sitting	1.11 (1.08, 1.14)
	Standing	1.09 (1.06, 1.12)
	Supine	1.14 (1.12, 1.17) HR for CHD
^b FRS (N= 11,129)	Sitting	1.11 (1.08, 1.14)
	Standing	1.09 (1.06, 1.11)
	Supine	1.14 (1.12, 1.17) HR for CHD
^c HFRS (N= 11,129)	Sitting	1.14 (1.11, 1.17)
	Standing	1.12 (1.09, 1.14)
	Supine	1.18 (1.15, 1.21) HR for CHF
^d ASRS (N= 11,129)	Sitting	1.18 (1.14, 1.23)
	Standing	1.17 (1.13, 1.23)
	Supine	1.22 (1.18, 1.26) HR for Stroke
^e ASCVD Pooled Cohort Equation (N= 11,129)	Sitting	1.13 (1.11, 1.16)
	Standing	1.11 (1.09, 1.14)
	Supine	1.16 (1.14, 1.19) HR for ASCVD

^aARIC Coronary Risk Score (race, sex, age, SBP, smoking, total cholesterol, high density lipoprotein cholesterol, use of antihypertensive, diabetes),

^bFramingham Coronary Risk Score (sex, age, smoking, SBP, total cholesterol, and high density lipoprotein cholesterol),

^CARIC Heart Failure Risk Score (age, sex, smoking, SBP, heart rate, BMI, previous CHD, use of hypertension medications, and diabetes),

 $^d\mathrm{ARIC}$ Stroke Risk Score (age, sex smoking, SBP, ECG-LVH, previous CHD, and diabetes),

^ePooled Cohort Risk Assessment Equations (race, sex, age, SBP, smoking, total cholesterol, high density lipoprotein cholesterol, use of antihypertensive medications, and diabetes.

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Magnitude of reclassification for various risk prediction scores using different measures of systolic blood pressure

Outcome	* Risk comparison	% participants reclassified	% reclassified to a lower risk group	% reclassified to a higher risk group	Maximum % change in risk
² CHD (ACRS)	Sitting 3 SBP vs. Sitting 2 SBP	5.1	2.7	2.4	↑17 ↓12
	Mean Standing SBP vs. Mean Sitting SBP	10.7	3.2	7.5	↑29 ↓24
	Mean Supine SBP vs. Mean Sitting SBP	9.6	2.7	7.2	↑27 ↓25
bCHD (FRS) (N= 11,129)	Sitting 3 SBP vs. Sitting 2 SBP	3.3	1.7	1.6	↑11 ↓16
	Mean Standing SBP vs. Mean Sitting SBP	7.0	2.1	4.9	↑19 ↓16
	Mean Supine SBP vs. Mean Sitting SBP	6.7	1.9	4.8	↑16 ↓19
CHF (HFRS) (N= 11,129)	Sitting 3 SBP vs. Sitting 2 SBP	1.9	1.1	0.8	↑5 ↓9
	Mean Standing SBP vs. Mean Sitting SBP	4.6	1.5	3.1	↑14 ↓16
	Mean Supine SBP vs. Mean Sitting SBP	4.1	1.2	2.9	↑12 ↓15
dStroke (ASRS) (N= 11,129)	Sitting 3 SBP vs. Sitting 2 SBP	2.1	1.2	6.0	↑11 ↓12
	Mean Standing SBP vs. Mean Sitting SBP	5.4	1.7	3.7	↑31 ↓22
	Mean Supine SBP vs. Mean Sitting SBP	5.0	1.3	3.7	↑21 ↓24
ASCVD	Sitting 3 SBP vs. Sitting 2 SBP	5.8	3.2	2.6	↑16 ↓20
	Mean Standing SBP vs. Mean Sitting SBP	11.6	3.5	8.1	↑31 ↓24
	Mean Supine SBP vs. Mean Sitting SBP	10.5	2.9	7.6	↑30 ↓26

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 a,b Coronary Heart Disease,

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 $^{\mathcal{C}}_{\mathrm{Heart Failure,}}$

d Stroke; 0–5, >5–7.5, >7.5 risk cut-off for ° pooled cohort atherosclerotic cardiovascular disease.

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