Supplemental material

Smartphone application-assisted home blood pressure monitoring compared with office and ambulatory blood pressure monitoring in patients with hypertension: the AMUSE-BP study

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File S1 – Detailed description of study in- and exclusion criteria

Inclusion criteria

1. Age of 18 years or older.
2. Documented medical history of hypertension in local hospital electronic patient record.
3. Stable dose of anti-hypertensive medication for at least 2 months, includes no current antihypertensive medication, diagnosis hypertension is sufficient.
4. Systolic blood pressure (SBP) >90 and <180 mm Hg and diastolic blood pressure (DBP) >60 and <110mm Hg at screening obtained by attended automated office blood pressure (AOBP).
5. Dutch and/or English language capable for reading patient information folder and in-app instructions.
6. Smartphone or tablet. Operating system (OS) requirements: iOS 8.0 or higher, Android version 4.1 or higher.

Exclusion criteria

1. SBP >180 mm Hg and/or DBP >110mm Hg at screening (measured by attended AOBP method).
2. Any BP that according to the treating physician is not adequately controlled and needs medication adjustment < 2 months or within the study time period.
3. Recent (<2 months) anti-hypertensive medication changes (including diuretics). Includes no current antihypertensive medication, diagnosis hypertension is sufficient.
4. Recent start or change in dosing of alpha-blockers prescribed for other purpose than blood pressure control (for example benign prostate hypertrophy).
5. Unstable or uncontrolled endocrine disease (e.g. thyroid disease, Cushing's or Addison's disease) with the exception of diabetes mellitus.
6. Arrhythmias that prevent any BP measurement device to correctly measure BP during inclusion screening visit; such as supraventricular arrhythmias or atrial ventricular block. Known arrhythmias, but not clinically present during inclusion screening is not an exclusion criterion.
7. Heart failure grade 2 or higher on the New York Heart Association (NYHA) Functional Classification.
8. Documented missed outpatient clinic appointments (2 or more the last 6 months).
9. Documented therapy non-adherence (e.g. biochemically proven medication non-adherence, known or highly suspected medication non-adherence by treating physician, proven direct observed therapy effect in BP).
10. Participants cannot plan a measurement schedule with a minimum of 15 and a maximum of 29-day period participation or a minimum of 4 and maximum of 5 hospital visits due to logistical issues or scheduling issues of any kind.
11. Physical inability to perform an home BP measurement, use the Microlife A6 BT BP device or the EmmaHBPM app.
12. Active pregnancy or planning trying to get pregnant during the study period.

Table S1 – Mean BP values for each BP measurement method and the difference compared to daytime ABPM

	Daytime ABPM	**App-assisted HBPM**	**30-min BP**	**Attended OBP**	**Unattended OBP**
	n = 101	n = 109	n = 112	n = 112	n = 112
Systolic blood pressure (mm Hg)	130.4 ± 11.1	140.6 ± 13.6	133.5 ± 13.4	136.7 ± 16.0	135.3 ± 15.3
Mean difference (95%CI)	-	10.4 (8.2 – 12.7)	2.9 (0.7 – 5.2)	6.3 (4.0 – 8.5)	4.7 (2.5 – 7.0)
Diastolic blood pressure (mm Hg)	77.0 ± 8.1	81.5 ± 9.8	80.2 ± 9.1	81.3 ± 10.7	80.6 ± 9.7
Mean difference (95%CI)	-	4.5 (3.2 – 5.9)	2.9 (1.6 – 4.3)	4.3 (3.0 – 5.7)	3.4 (2.0 – 4.7)

All data in mean ± standard deviation or mean difference (95% confidence interval). Mean differences were obtained by fitting a linear mixed model. This model was adjusted for age, sex, body mass index (BMI), and smoking. ABPM = ambulatory blood pressure monitoring, HBPM = home blood pressure monitoring, OBP = office blood pressure.

Table S2 – Diagnostic performance of app-assisted home and automated office blood pressure monitoring in detecting hypertension diagnosed by daytime ambulatory blood pressure monitoring

	Sensitivity (%)	**Specificity (%)**	**PPV (%)**	**NPV (%)**	**Kappa coefficient**
Home blood pressure monitoring	86 (71 - 95)	42 (30 - 55)	46 (34 - 59)	84 (67 - 95)	0.24 (0.10 - 0.39)
30-min blood pressure	79 (64 - 91)	58 (45 - 70)	53 (40 - 67)	82 (68 - 92)	0.34 (0.17 - 0.51)
Attended office blood pressure	74 (58 - 87)	69 (57 - 80)	59 (44 - 73)	82 (69 - 91)	0.41 (0.24 - 0.59)
Unattended office blood pressure	64 (47 - 79)	80 (68 - 89)	66 (49 - 80)	78 (67 - 88)	0.44 (0.26 - 0.62)

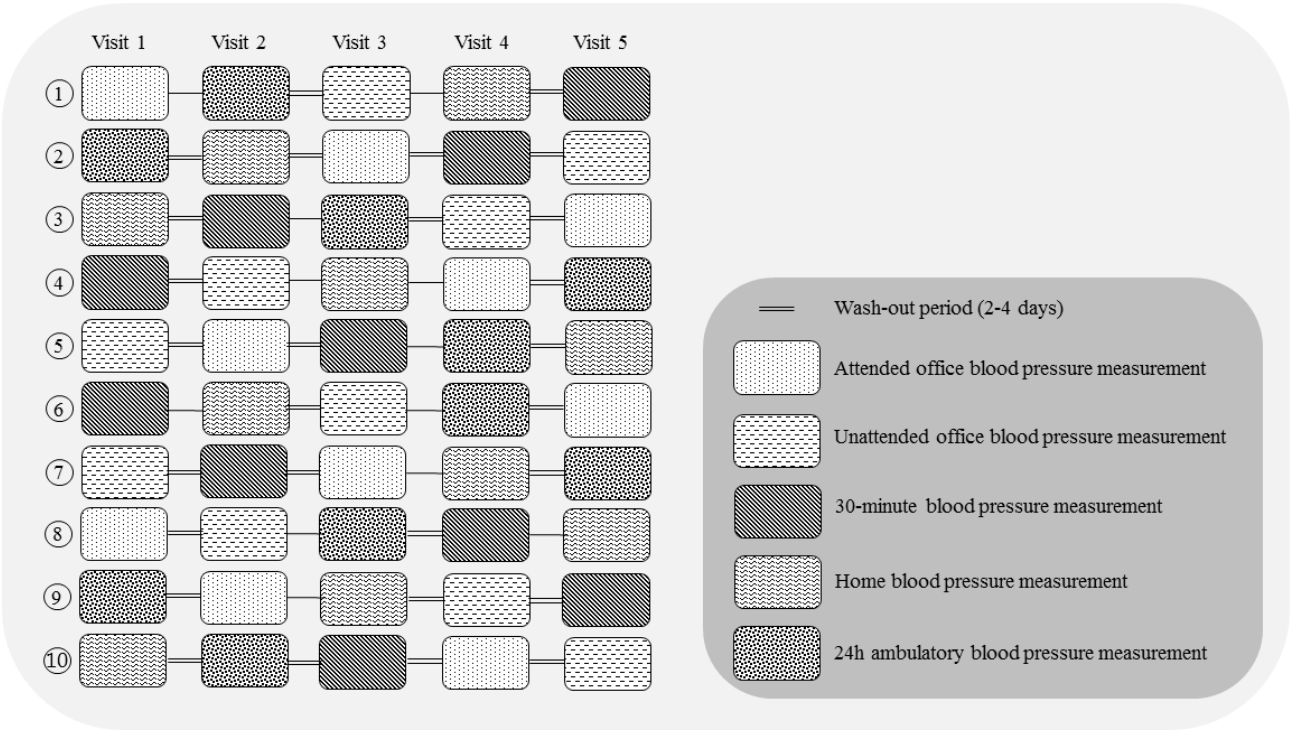
Values in the parentheses are 95% confidence interval. PPV = positive predictive value, NPV = negative predictive value. Cut-off values hypertension; daytime ABPM: : ≥135/85 mm Hg, HBPM: ≥135/85 mm Hg, 30-min BP: ≥135/85 mm Hg, attended OBP: ≥140/90 mm Hg, unattended OBP: ≥140/90 mm Hg.

Table S3 – Diagnostic performance of app-assisted home against daytime ambulatory blood pressure monitoring in detecting different hypertension phenotypes

	Sensitivity (%)	**Specificity (%)**	**PPV (%)**	**NPV (%)**	**Kappa coefficient**
Sustained hypertension	86 (71 - 95)	42 (30 - 55)	46 (34 - 59)	84 (67 - 95)	0.24 (0.10 - 0.39)
White-coat hypertension	27 (12 - 46)	97 (90 - 100)	80 (44 - 97)	76 (66 - 84)	0.30 (0.11 - 0.48)
Masked hypertension	70 (35 - 93)	84 (74 - 90)	32 (14 - 55)	96 (89 - 99)	0.35 (0.12 - 0.57)

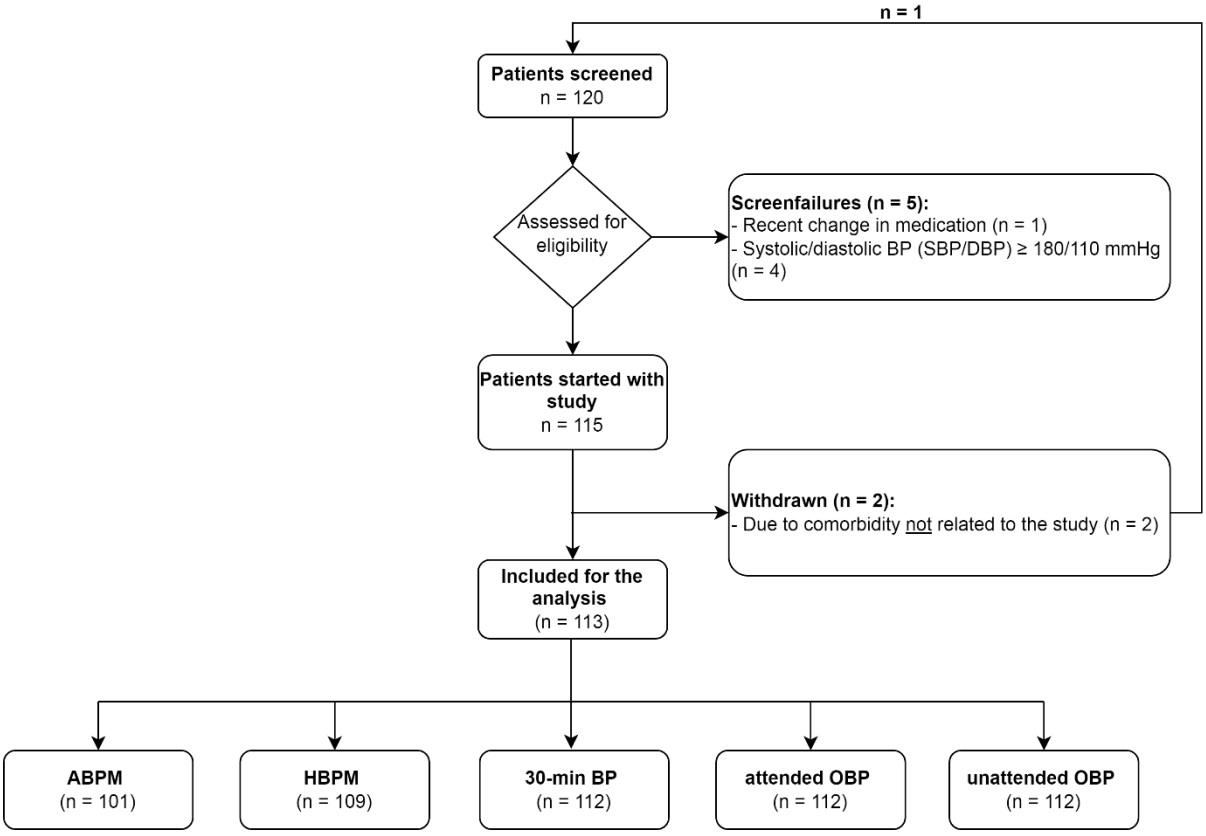
Values in the parentheses are 95% confidence interval. PPV = positive predictive value, NPV = negative predictive value.Cut-off values hypertension; daytime ABPM: : ≥135/85 mm Hg, HBPM: ≥135/85 mm Hg

Figure S1 – Schematic overview of randomization clusters



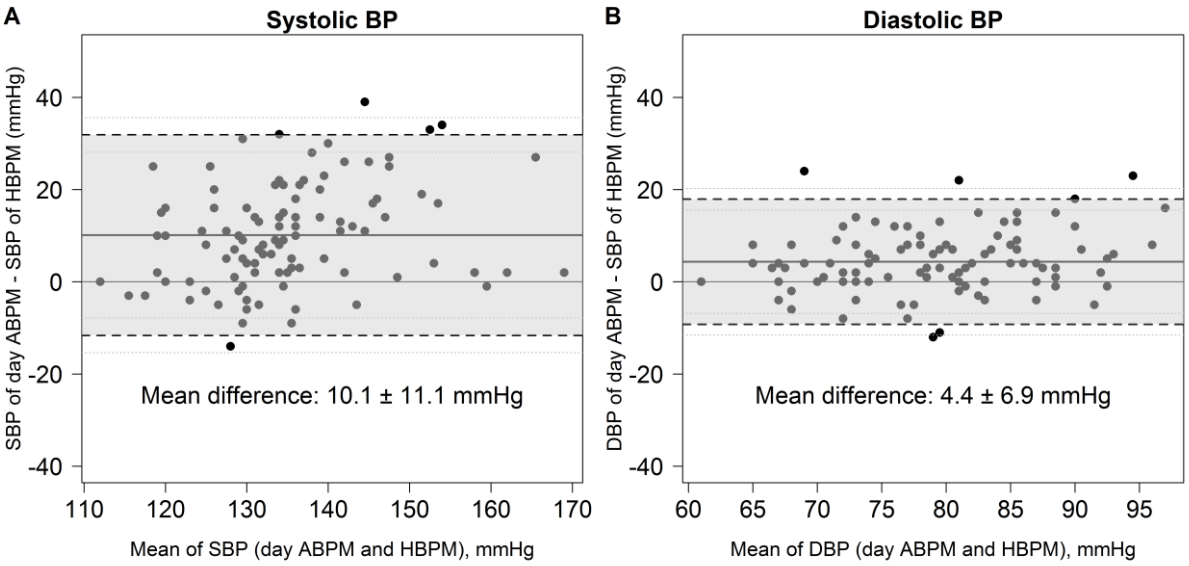
Overview of all 10 randomization clusters. Each patient underwent all five BP measurement methods. To minimize the carry-over effect, a wash-out period of 2 - 4 days was incorporated before and after each out-of-office BP measurement (ABPM and HBPM).

Figure S2 – Flow diagram of patients enrolled in the study



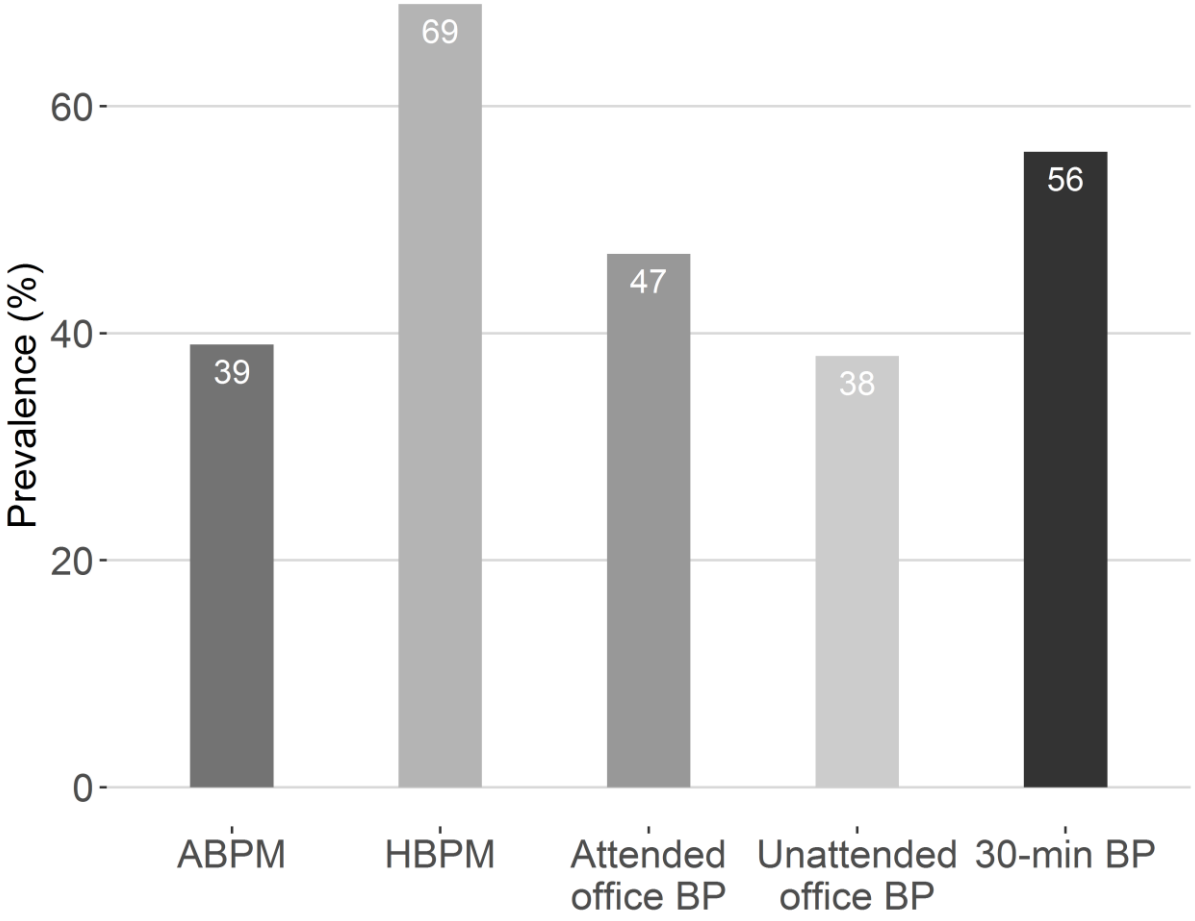
ABPM = Ambulatory Blood Pressure Monitoring, HBPM = Home Blood Pressure Monitoring, OBP = Office Blood Pressure

Figure S3 – Bland-Altman plots of agreement between home and daytime ambulatory systolic (a) and diastolic blood pressure (b).



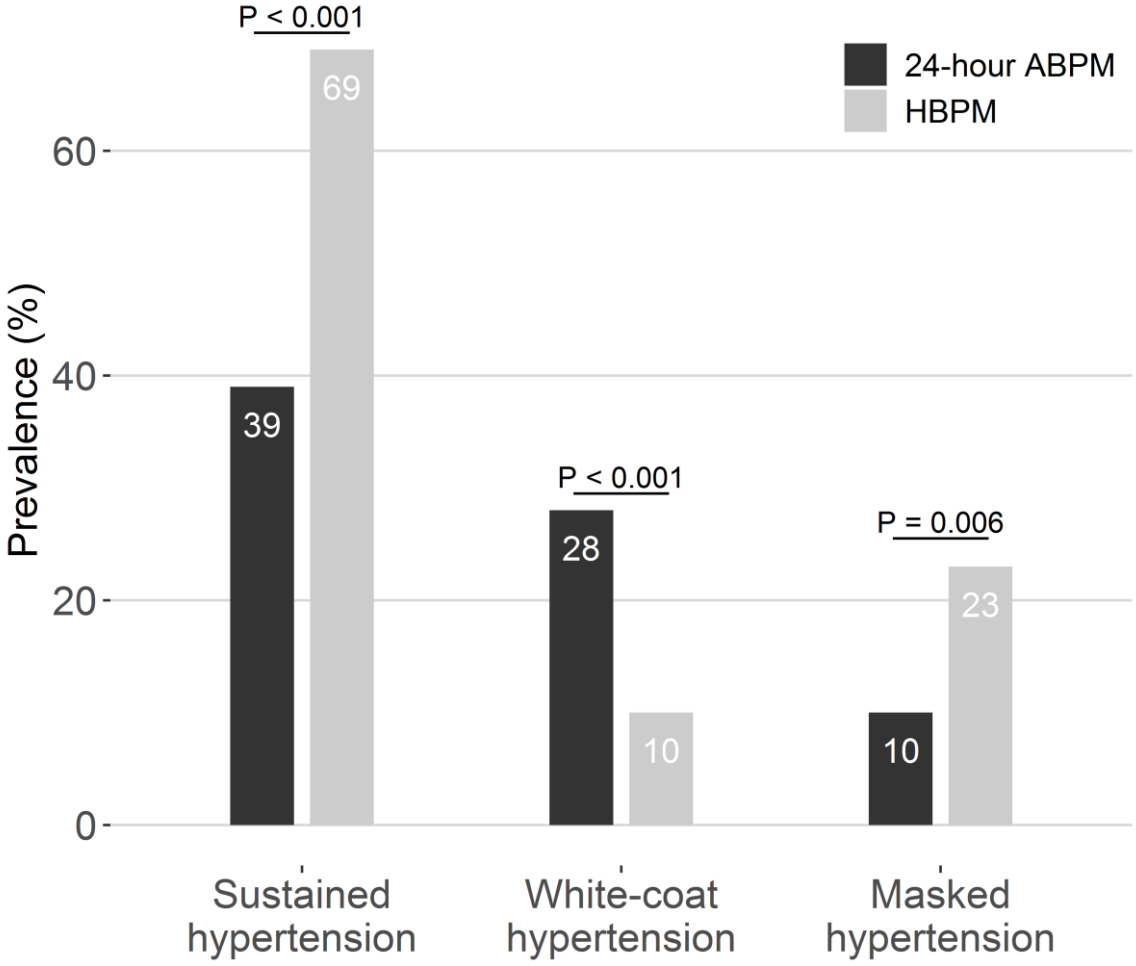
Plots comparing the difference between app-assisted HBPM and daytime ABPM systolic (A) and diastolic (B) BP on the y-axis with the mean of the two methods on the x-axis.

Figure S4 – Prevalence of hypertension according to different BP measurement methods



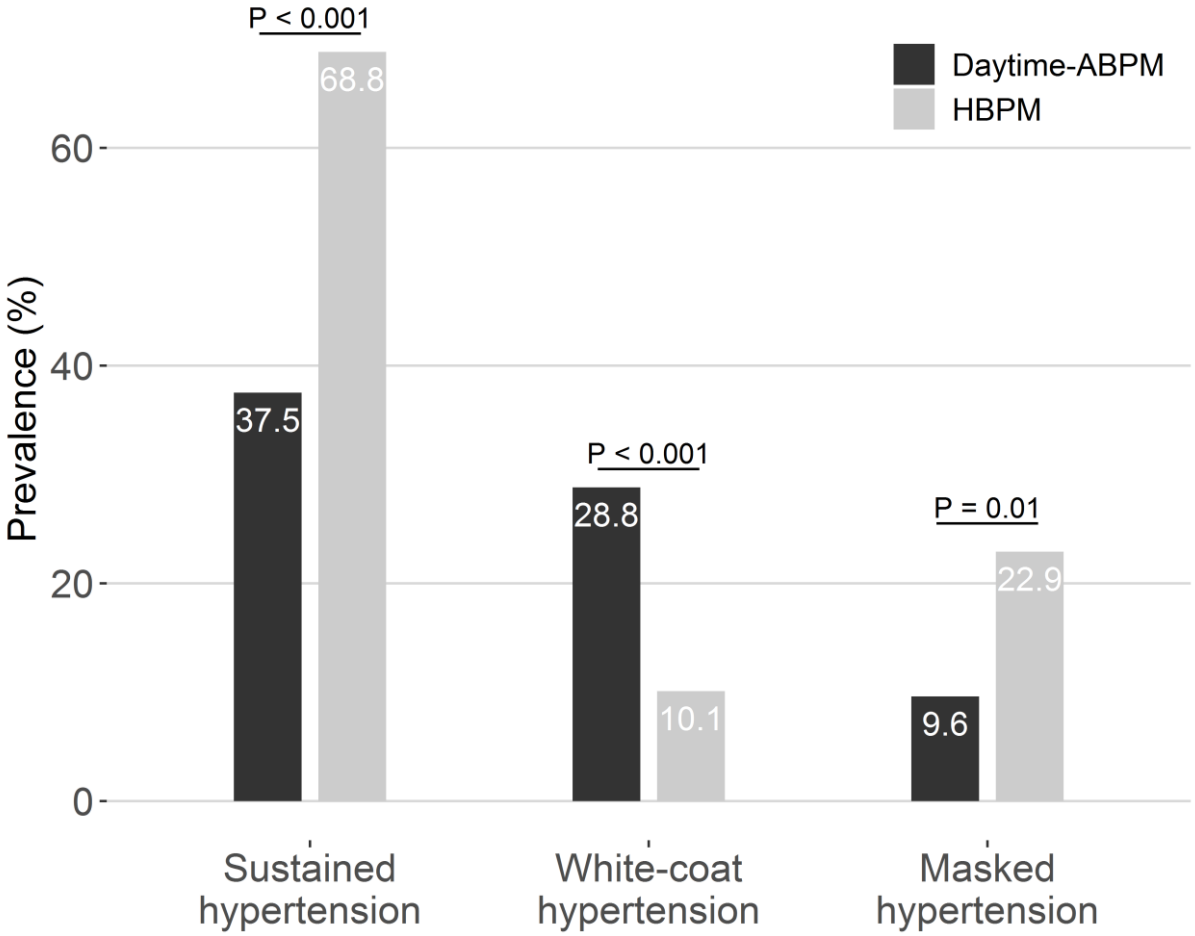
ABPM = Ambulatory Blood Pressure Monitoring, HBPM = Home Blood Pressure Monitoring. Cut-off values hypertension; HBPM: ≥135/85 mm Hg, 30-min BP: ≥135/85 mm Hg, attended OBP: ≥140/90 mm Hg, unattended OBP: ≥140/90 mm Hg.

Figure S5 – Prevalence of sustained, white-coat, masked hypertension according to 24-hour ambulatory or home BP monitoring.



Sustained hypertension = consistently elevated BP on office and home or 24-hour ambulatory measurements. White-coat hypertension = an elevated BP in the office and a normal home or 24-hour ambulatory BP. Masked hypertension = an elevated home or 24-hour ambulatory BP with normal office BP. McNemar's test was used to test the difference in prevalence for each hypertension phenotype.

Figure S6 – Prevalence of sustained, white-coat, masked hypertension according to daytime ambulatory or home blood pressure monitoring.



Sustained hypertension = consistently elevated BP on office and home or daytime ambulatory measurements. White-coat hypertension = an elevated BP in the office and a normal home or daytime ambulatory BP. Masked hypertension = an elevated home or daytime ambulatory BP with normal office BP. McNemar's test was used to test the difference in prevalence for each hypertension phenotype.