ORIGINAL ARTICLE

# Home Blood Pressure Compared With Office Blood Pressure in Relation to Dysglycemia

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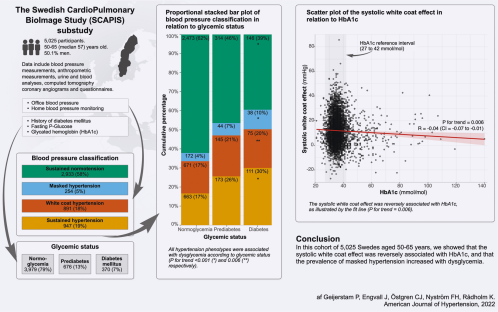
**BACKGROUND**
Masked hypertension is more common in individuals with type 2 diabetes than in individuals with normoglycemia. We aimed to explore if there is a discrepancy between office blood pressure (office BP) and home blood pressure monitoring (HBPM) in relation to HbA1c as well as glycemic status in 5,029 middle-aged individuals.

**METHODS**
HBPM was measured in a subsample of 5,029 participants in The Swedish CardioPulmonary BioImage Study (SCAPIS), a population-based cohort of 50–64 years old participants. Both office BP and HBPM were obtained after 5 minutes' rest using the semiautomatic Omron M10-IT oscillometric device. White coat effect was calculated by subtracting systolic HBPM from systolic office BP. Participants were classified according to glycemic status: Normoglycemia, prediabetes, or diabetes based on fasting glucose, HbA1c value, and self-reported diabetes diagnosis.

**RESULTS**
Of the included 5,025 participants, 947 (18.8%) had sustained hypertension, 907 (18.0%) reported taking antihypertensive treatment, and 370 (7.4%) had diabetes mellitus. Both systolic office BP and HBPM increased according to worsened glycemic status (*P* for trend 0.002 and 0.002, respectively). Masked hypertension was more prevalent in participants with dysglycemia compared with normoglycemia ($P = 0.036$). The systolic white coat effect was reversely associated with HbA1c ($P = 0.012$).

**CONCLUSIONS**
The systolic white coat effect was reversely associated with HbA1c, and the prevalence of masked hypertension increased with dysglycemia.

**GRAPHICAL ABSTRACT**




*Keywords:* blood pressure; cardiovascular disease; diabetes; dysglycemia; HbA1c; home blood pressure monitoring; hypertension; white coat effect.

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Hypertension is the major preventable cause of premature all-cause mortality globally, mainly through cardiovascular disease (CVD) such as ischemic heart disease and stroke.[1] The prevalence of hypertension is around 30%–45%, and is increasing.[1] However, detection and treatment of hypertension vary greatly, with evidence suggesting that few patients with hypertension worldwide have a controlled blood pressure (BP).[2] Hypertension and diabetes mellitus often coexist,[3] and both increase the risk of CVD so that the total risk is the combined or even multiplicative risk of each disease.[1,3] Lowering BP reduces both morbidity and mortality.[1]

Both elevated office BP and out-of-office BP are associated with independent and continuous increased risk of CVD.[1] There are several benefits with out-of-office BP over office BP measurements, where out-of-office measurements have been shown to significantly predict cardiovascular mortality,

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also when adjusted for office BP measurements. On the contrary, office BP measurements adjusted for out-of-office BP measurements have not been shown to predict cardiovascular mortality.[4] Neither home blood pressure monitoring (HBPM) nor ambulatory blood pressure monitoring (ABPM) is superior for predicting cardiovascular events.[4] HBPM has been shown to increase patient adherence to antihypertensive therapy.[4] Furthermore, the combination of office and out-of-office BP measurements allows for the diagnosis of intermediate hypertension phenotypes: white coat hypertension, in which office BP measurements are falsely elevated, and masked hypertension, in which office BP measurements are falsely normal.[5] Masked hypertension is more prevalent among patients with obesity and diabetes mellitus, and the prevalence increases with treatment (so-called masked uncontrolled hypertension).[6] Current guidelines consider out-of-office BP to be of decisive value in the diagnosis of hypertension.[7,8]

Diabetes mellitus is a heterogeneous group of metabolic diseases diagnosed by elevated fasting plasma glucose, elevated plasma glucose after oral glucose tolerance testing, and/or elevated glycated hemoglobin (HbA1c).[9,10] HbA1c is an indirect marker of prolonged elevation of plasma glucose levels, and a diagnostic threshold of 48 mmol/mol or higher is advised by most guidelines.[9,10] Prediabetes is defined as supernormal glucose levels that do not meet the criteria of diabetes mellitus, but the diagnostic criteria are not universally agreed upon. Furthermore, prediabetes is classified as impaired fasting glucose (IFG) and impaired glucose tolerance and this categorization is lacking consensus as well.[10–12] Prediabetes increases the risk of type 2 diabetes mellitus and the risk of CVD,[13] although the predictive significance of the various definitions of prediabetes differ.[14,15]

The 2019 ESC Guidelines on Diabetes, Pre-Diabetes and Cardiovascular Diseases suggest that HBPM should be considered to evaluate antihypertensive treatment in patients with diabetes.[9] However, there is no evidence of greater benefits of HBPM for patients with diabetes compared with hypertensive patients without diabetes.[16]

To our knowledge, the relationship between HbA1c, office BP, and HBPM is not known. Thus, the aim of our study was to explore if there is a discrepancy between office BP and HBPM in relation to HbA1c as well as glycemic status.

## METHODS

### Study population

The Swedish CardioPulmonary BioImage Study (SCAPIS) is a prospective observational study of 30,000 randomly selected men and women aged 50–64 years.[17] In brief, the study participants were selected randomly from the Swedish population register, and the study includes data from anthropometric measurements, clinical physiology such as electrocardiogram and spirometry, urine and blood analyses, advanced imaging studies such as ultrasound of the carotid arteries and coronary computed tomography angiography, as well as 175 questionnaire questions in a broad range of topics including lifestyle.[17] In addition, in a subsample in Linköping, the 5,057 SCAPIS participants were evaluated with HBPM as well as regular office BP measurements.

### Measurement of BP and definition of BP classification

Office BP and HBPM measurement methodology has been previously described in detail.[18] Measurements were taken after 5 minutes' rest using the same semiautomatic Omron M10-IT oscillometric device (Omron, Kyoto, Kyoto prefecture, Japan) for both office BP and HBPM, with approximately 1 minute between each consecutive measurement. Participants were instructed to abstain from smoking, coffee and strenuous activity at least 1 hour prior to measurements. Office BP was measured in the supine position twice consecutively on each arm and a mean variable was calculated. The arm with the highest mean BP was designated as reference arm and used for further measurements. HBPM was measured in a sitting position in the morning and evening on 7 consecutive days, except for the first day for which only evening measurements were recorded. Each of these thirteen measurements was calculated as an average from 2 separate measurements.

An average office BP ≥140 mm Hg systolic and/or ≥90 mm Hg diastolic was labeled as hypertensive office BP. An average office BP below these limits was labeled as normotensive office BP. An average HBPM ≥135 mm Hg systolic and/or ≥85 mm Hg diastolic was labeled as hypertensive HBPM. An average below these limits was labeled as normotensive HBPM. Based on this categorization of office BP and HBPM, BP was classified as "sustained normotension," "white coat hypertension," "masked hypertension," or "sustained hypertension," Box 1.

### Glycemic measurements and definition of glycemic status

Fasting capillary glucose and venous HbA1c were measured on day 1 of participant inclusion. IFG and diabetes mellitus were classified according to guidelines from the World Health Organization (WHO).[11] In addition, elevated HbA1c was defined according to current recommendations.[19,20] Thus, glycemic status was classified as "known diabetes mellitus," "new diabetes mellitus," "prediabetes," or "normoglycemia," Box 2. If HbA1c was missing, fasting glucose was used to classify glycemic status. If fasting glucose was missing, classification was done if HbA1c was elevated, ≥42 mmol/mol, but if fasting glucose was missing and HbA1c was <42 mmol/mol, participants were classified as

**Box 1. Blood pressure classifications according to study measurements**

- Sustained normotension: normal office BP and HBPM.
- White coat hypertension: elevated office BP but normal HBPM.
- Masked hypertension: normal office BP but elevated HBPM.
- Sustained hypertension: elevated office BP and elevated HBPM.

**Box 2. Classification of glycemic status**

- Known diabetes mellitus: Diabetes stated in medical history interview or in subject questionnaire.
- New diabetes mellitus: Fasting glucose ≥7 mmol/l or HbA1c ≥48 mmol/mol and not diabetes stated in the medical history interview or questionnaire.
- Prediabetes:
  - IFG: fasting glucose ≥6.1 mmol/l but <7.0 mmol/l.
  - Elevated HbA1c: HbA1c ≥42 mmol/mol but <48 mmol/mol.
  - Normoglycemia: No diabetes stated in medical history interview or in the questionnaire, HbA1c <42 mmol/mol and fasting glucose <6.1 mmol/l.

missing due to the low sensitivity of HbA1c (Östgren CJ, Frick A. SCAPIS Variable specification, 2019). All chemistry measurements were performed at the Department of Clinical Chemistry at Linkoping University Hospital which is accredited according to SS-EN ISO/IEC 17025:2018.

### Pulse wave velocity

Carotid–femoral pulse wave velocity (PWV) was measured by trained biomedical scientists using an applanation tonometer according to a previously published protocol.[21] In brief, measurements were made twice using the SphygmoCor XCEL device (from Atcor Medical, Sydney, NSW, Australia). The average of these measurements was used for analysis, and calculated using a correction factor of 0.8 in accordance with current international guidelines.[22]

### Statistical analyses

A Kolmogorov–Smirnov test as well as visual assessment was used to determine distribution. Continuous variables with normal distribution were shown as the mean and standard deviation, and differences in trend were tested using a 1-way ANOVA test. Continuous variables with skewed distribution were shown as the median and interquartile range (except for BP measurements that were shown as mean and standard deviation), and differences in trend were tested using the Jonckheere–Terpstra test. Categorical variables were shown as the frequency and percentage, and differences in trend were tested using the Cochran–Armitage test.

Baseline characteristics according to glycemic status were evaluated for all participants as well as separately for men and women, respectively. For participants with dysglycemia, waist circumference was tested against the WHO cutoff point[23] for substantially increased risk of metabolic complications using the Wilcoxon signed-rank test. The systolic white coat effect was calculated for each individual by subtracting systolic HBPM from systolic office BP. Low-density lipoprotein (LDL) was calculated using Friedwald's formula (LDL = total cholesterol − high-density lipoprotein − 0.45 × triglycerides). Estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation,[24] but without including race since that was not recorded. Coronary artery calcium score (CACS) was presented as a dichotomous variable of a total score of less than 100, or a total score of 100 or above.

Subgroup analyses were made comparing white coat hypertension with sustained hypertension and masked hypertension with sustained normotension, in participants without current antihypertensive medication. Analyses were made using logistic regression, and were crude (model 1), adjusted for age and sex (model 2), adjusted for age, sex, smoking status, prescribed lipid-lowering medication, waist circumference, eGFR, hemoglobin, LDL/high-density lipoprotein ratio, and total CACS ≥100 (model 3) and adjusted for PWV in addition to the variables in model 3 (model 4). Further subgroup analysis was made comparing masked hypertension with sustained normotension, in participants without current antihypertensive medication and with PWV in the highest quartile, using logistic regression.

Analyses of systolic white coat effect in relation to HbA1c were made using linear regression with the same adjustments as in models 1–4, but with the addition of including prescribed medication for diabetes and prescribed antihypertensive medication in the adjusted models (models 3 and 4). Furthermore, sensitivity analyses were done for the relationship between the systolic white coat effect and HbA1c in participants without known antihypertensive medication.

Analysis of the difference between morning and evening mean systolic HBPM in relation to antihypertensive medication was made using linear regression.

Statistical tests were 2 tailed and $P$ values of <0.05 were considered statistically significant. IBM SPSS Statistics version 26 and R 4.1.2 and RStudio 2021.09.1 were used for data analyses.

### Ethical considerations

The SCAPIS study was approved by the Regional Ethical Review board in Umeå (Dnr 2010-228-31M) and the Regional Ethical Review board in Linköping (Dnr 2018/478-31) and adheres to the Declaration of Helsinki.

## RESULTS

Of 5,057 included participants, 5,029 participated in the HBPM measurements. Four of these had a hemoglobin level below 90 g/l (range 76–86 g/l), hence their HbA1c (range 33–44 mmol/mol) was considered invalid, and the participants were excluded. Thus, a total of 5,025 individuals were included in our analysis. The median age was 57.3 (53.5–61.3) years, and 2,520 (50.1%) of the participants were men. Of participants, 907 (18.0%) reported taking medication for hypertension, 363 (7.2%) reported taking medication for hyperlipidemia, and 181 (3.6%) reported taking medication for diabetes mellitus, Table 1. The prevalence of diabetes was 370 (7.4%), of which 126 (34.1%) were previously undiagnosed. Among all participants with diabetes, 172 (46.5%) reported taking antihypertensive medication. In those with previously known diabetes, 131

**Table 1.** Baseline characteristics according to glycemic status

| | Normoglycemia (*n* = 3,979) | Prediabetes (*n* = 676) | Diabetes (*n* = 370) | Total (*N* = 5,025) | *P* for trend |
|---|---|---|---|---|---|
| Sex, men, *n* (%) | 1,926 (48.4) | 352 (52.1) | 242 (65.4) | 2,520 (50.1) | <0.001 |
| Age (y), median (Q1–Q3) | 56.9 (53.2–60.9) | 58.4 (54.6–61.9) | 59.8 (55.8–62.8) | 57.3 (53.5–61.3) | 0.002 |
| Ever-smokers, *n* (%) | | | | | <0.001 |
| Previous | 1,200 (30.2) | 241 (35.7) | 136 (36.8) | 1,577 (31.4) | |
| Current | 343 (8.6) | 81 (12.0) | 46 (12.4) | 470 (9.4) | |
| BMI (kg/m$^2$), median (Q1–Q3) | 26 (24–28) | 28 (25–31) | 30 (27–33) | 26 (24–29) | 0.002 |
| Waist circumference (cm), median (Q1–Q3) | 91 (82–99) | 98 (89–105) | 104 (97–113) | 92 (84–101) | 0.002 |
| Fasting glucose (mmol/l), median (Q1–Q3) | 5.4 (5.2–5.7) | 6.2 (5.9–6.5) | 7.7 (6.8–9.4) | 5.6 (5.2–5.9) | 0.002 |
| HbA1c (mmol/mol), median (Q1–Q3) | 35 (33–37) | 37 (35–40) | 48 (42–58) | 35 (33–38) | 0.002 |
| Hemoglobin (g/l), mean (SD) | 142.7 (11.2) | 142.0 (11.4) | 143.8 (11.7) | 142.7 (11.3) | 0.052 |
| eGFR (CKD-EPI) (ml/min/1.73 m$^2$), median (Q1–Q3) | 82 (73–92) | 84 (74–93) | 88 (77–96) | 82 (74–92) | 0.002 |
| Total cholesterol (mmol/l), median (Q1–Q3) | 5.5 (4.9–6.2) | 5.3 (4.6–6.0) | 4.6 (3.7–5.4) | 5.4 (4.8–6.1) | 0.002 |
| LDL (mmol/l), median (Q1–Q3) | 3.3 (2.7–3.9) | 3.1 (2.5–3.7) | 2.4 (1.8–3.2) | 3.2 (2.6–3.9) | 0.002 |
| HDL (mmol/l), median (Q1–Q3) | 1.6 (1.3–2.0) | 1.5 (1.2–1.8) | 1.3 (1.0–1.6) | 1.6 (1.3–1.9) | 0.002 |
| Triglycerides (mmol/l), median (Q1–Q3) | 1.0 (0.8–1.4) | 1.1 (0.8–1.5) | 1.3 (1.0–2.1) | 1.0 (0.8–1.5) | 0.002 |
| LDL/HDL ratio, median (Q1–Q3) | 2.0 (1.5–2.7) | 2.1 (1.5–2.7) | 1.9 (1.3–2.6) | 2.0 (1.5–2.7) | 0.022 |
| Total CACS ≥100, *n* (%) | 390 (9.8) | 102 (15.1) | 100 (27.0) | 592 (11.8) | <0.001 |
| PWV (m/s), median (Q1–Q3) | 8.6 (7.9–9.6) | 8.9 (8.2–9.9) | 9.6 (8.6–10.6) | 8.7 (7.9–9.7) | 0.002 |
| Current medication, *n* (%) | | | | | |
| Hypertension | 564 (14.2) | 171 (25.3) | 172 (46.5) | 907 (18.0) | <0.001 |
| Hyperlipidemia | 166 (4.2) | 76 (11.2) | 121 (32.7) | 363 (7.2) | <0.001 |
| Diabetes mellitus | 0 (0) | 0 (0) | 181 (48.9) | 181 (3.6) | <0.001 |
| Office BP, mean (SD), mm Hg | | | | | |
| Systolic | 131 (17) | 137 (18) | 139 (17) | 133 (17) | 0.002 |
| Diastolic | 83 (10) | 85 (11) | 85 (10) | 83 (10) | 0.002 |
| HBPM, mean (SD), mm Hg | | | | | |
| Systolic | 119 (14) | 124 (14) | 129 (13) | 121 (14) | 0.002 |
| Diastolic | 77 (9) | 80 (9) | 81 (8) | 78 (9) | 0.002 |
| Systolic white coat effect (mm Hg), mean (SD) | 12.0 (11.4) | 12.4 (12.1) | 9.9 (12.6) | 11.9 (11.6) | 0.282 |

Values for sex, age, body mass index (BMI), estimated glomerular filtration rate (eGFR), cholesterol, high-density lipoprotein (HDL), triglycerides, and all blood pressure variables were calculated based on all 5,025 participants. Values for other variables were calculated based on 97%–99% of the total population. BMI was calculated as weight (kg) divided by the square of height (m). Low-density lipoprotein (LDL) was calculated using Friedwald's formula (LDL = total cholesterol − high-density lipoprotein − 0.45 × triglycerides). Estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation,[24] but without including race since that variable was not recorded. For HBPM, mean values were calculated from the sum of all measurements. CACS was presented as a dichotomous variable of a total score of less than 100, or a total score of 100 or above. Pulse wave velocity (PWV) was measured according to a previously published protocol,[21] and calculated using a correction factor of 0.8 in accordance with current international guidelines.[22] Difference between glycemic statuses was tested using 1-way ANOVA for continuous variables with normal distribution, Jonckheere–Terpstra test for trend for continuous variables with skewed distribution and Cochran–Armitage test for trend for categorical variables. Abbreviations: BP, blood pressure; CACS, coronary artery calcium score; HbA1c, glycated hemoglobin; HBPM, home blood pressure monitoring; N/A, not applicable.

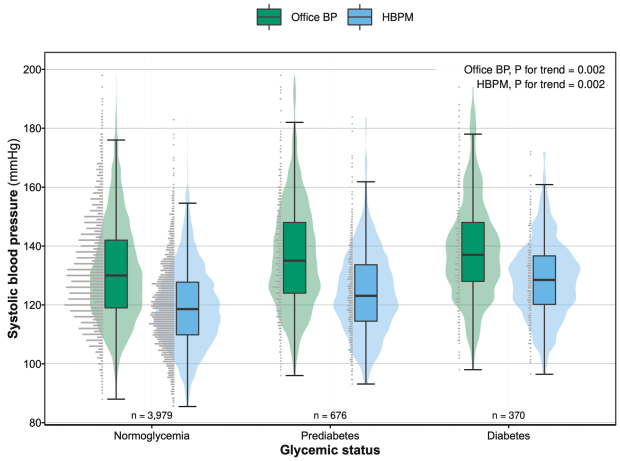


**Figure 1.** Boxplot of mean systolic office BP and HBPM, respectively, according to glycemic status. Difference between systolic office BP and systolic HBPM, respectively, and glycemic status, was tested using Jonckheere–Terpstra test for trend. The boxplot includes the median, the box extending between the 25th and the 75th percentile (the interquartile range, IQR) and its whiskers extending between the IQR times 1.5; the violin plot illustrates the relative distribution of observations; and the left-sided vertical bar plot shows the actual observations. Abbreviations: BP, blood pressure; HBPM, home blood pressure monitoring.

(53.7%) reported taking antihypertensive medication. The number of participants with a CACS ≥100 increased with dysglycemia, from 390 (9.8%) of participants with normoglycemia to 100 (27.0%) of participants with diabetes mellitus, $P$ for trend <0.001, Table 1. Overall, 439 (17.4%) of men and 153 (6.1%) of women had a CACS value of ≥100, Supplementary Tables S1 and S2 online. Both systolic office BP and HBPM increased with increased dysglycemia according to glycemic status ($P = 0.002$ for both), Table 1 and Figure 1. Of participants, 947 (18.8%) had sustained hypertension, Table 2. Waist circumference was more often above the WHO cutoff point[23] for substantially increased risk of metabolic complications for participants with diabetes (both men and women, $P < 0.001$ and $P < 0.001$, respectively) and prediabetes (only women, $P < 0.001$), compared with participants with normoglycemia, not shown.

The systolic white coat effect was reversely associated to HbA1c in models 1–3 ($P = 0.006$, $P = 0.002$, and $P = 0.012$), but not in model 4 ($P = 0.291$), Figure 2. However, there was no such association in the sensitivity analysis of only participants without current antihypertensive medication ($P = 0.793$ in model 1, not shown). Systolic white coat effect was not associated with glycemic status when analyzed for trend ($P = 0.282$, Table 1).

The prevalence of all classes of hypertension increased with worsened glycemic status ($P$ for trend = 0.006 for white coat hypertension, <0.001 for sustained hypertension, and <0.001 for masked hypertension), Table 1 and Figure 3.

In the sensitivity analysis of participants without current antihypertensive medication and elevated office BP, the prevalence of white coat hypertension compared with sustained hypertension was not associated with glycemic status (in models 1–4 $P = 0.092$, $P = 0.092$, $P = 0.058$, and $P = 0.112$, respectively), Table 3. In those without current antihypertensive medication and normal office BP, the prevalence of masked hypertension compared with sustained normotension was associated with dysglycemia in models 1–3 ($P = 0.005$, $P = 0.005$, and $P = 0.036$, respectively) but not in model 4 ($P = 0.181$), Table 3. However, in a subgroup analysis of those without current antihypertensive medication and PWV in the highest quartile ($n = 596$), the association was no longer significant ($P = 0.218$ for model 1), not shown.

The difference between morning and evening mean systolic HBPM was associated with antihypertensive medication, such that it was higher in the evening for participants without current treatment, but higher in the morning for participants with current treatment ($P < 0.001$ in all 4 models, not shown).

## DISCUSSION

Our study showed that the systolic white coat effect decreases with dysglycemia, both in terms of increased HbA1c, and known vs. not known diabetes mellitus. In line with these findings, masked hypertension (hypertensive BP at home but not at the office) was more prevalent than sustained normotension in participants with dysglycemia compared with participants with normoglycemia. The inverse correlation between the systolic white coat effect and the level of dysglycemia was no longer significant in the multivariate model, and this may have several explanations. For example, the positive correlation between arterial stiffness and both the white coat effect and dysglycemia, as well as its correlation with measurements such as PWV and CACS.[25–27] Arterial stiffness has previously been shown to precede both diabetes mellitus and hypertension, however whether this relationship is a result of confounding or causal is not yet known.[28]

BP is a complex measurement that has been studied in many different aspects: choice of parameter (diastolic, systolic, pulse pressure, mean BP, and mid-BP), location of measurement (at the office [attended or unattended] or out-of-office), and time of measurement (morning vs. evening, day vs. night, rest vs. activity).[1,7,8] Furthermore, results are known to vary depending on potential underlying medical conditions,[1,7,8] as well as possible antihypertensive treatment and if the patient takes the treatment in the morning or evening.[29] Systolic BP is of stronger predictive value than diastolic.[30]

Masked hypertension has previously been shown to be more prevalent among patients with obesity and diabetes mellitus, and the prevalence also increases with antihypertensive treatment (so-called masked uncontrolled hypertension).[6] One explanation for this is nocturnal hypertension,[6] but our findings indicate that this may only partially explain this difference as our study did not include BP measurements during the night. Another potential explanation is that current antihypertensive treatments have a greater effect on office BP as opposed to out-of-office BP.[3] Further possible explanations could be that patients with diabetes are less affected by stress when visiting their healthcare provider because of its regularity,[31] or that their

**Table 2.** Blood pressure measurements, classifications, and subtypes according to glycemic status

| | Normoglycemia (*n* = 3,979) | Prediabetes (*n* = 676) | Diabetes (*n* = 370) | Total (*N* = 5,025) | *P* for trend |
|---|---|---|---|---|---|
| Office blood pressure | | | | | <0.001 |
| Normotensive, *n* (%) | 2,645 (66.5) | 358 (53.0) | 184 (49.7) | 3,187 (63.4) | |
| Hypertensive, *n* (%) | 1,334 (33.5) | 318 (47.0) | 186 (50.3) | 1,838 (36.6) | |
| Home blood pressure monitoring | | | | | <0.001 |
| Normotensive, *n* (%) | 3,144 (79.0) | 459 (67.9) | 221 (59.7) | 3,824 (76.1) | |
| Hypertensive, *n* (%) | 835 (21.0) | 217 (32.1) | 149 (40.3) | 1,201 (23.9) | |
| Blood pressure classifications | | | | | |
| Sustained normotension, *n* (%) | 2,473 (62.2) | 314 (46.4) | 146 (39.5) | 2,933 (58.4) | <0.001 |
| Sustained hypertension, *n* (%) | 663 (16.7) | 173 (25.6) | 111 (30.0) | 947 (18.8) | <0.001 |
| White coat hypertension, *n* (%) | 671 (16.9) | 145 (21.4) | 75 (20.3) | 891 (17.7) | 0.006 |
| Masked hypertension, *n* (%) | 172 (4.3) | 44 (6.5) | 38 (10.3) | 254 (5.1) | <0.001 |
| Hypertension subtypes | | | | | |
| Combined hypertension, *n* (%) | 914 (23.0) | 225 (33.3) | 122 (33.0) | 1,261 (25.1) | <0.001 |
| Diastolic hypertension, *n* (%) | 260 (6.5) | 56 (8.3) | 37 (10.0) | 353 (7.0) | 0.004 |
| Systolic hypertension, *n* (%) | 332 (8.3) | 81 (12.0) | 65 (17.6) | 478 (9.5) | <0.001 |

Blood pressure classification was done according to the definitions specified in Box 1. Thus, sustained normotension was defined as normal office blood pressure (OBP) and normal home blood pressure monitoring (HBPM); white coat hypertension as elevated OBP but normal HBPM; masked hypertension as normal OBP but elevated HBPM; and sustained hypertension as elevated OBP and elevated HBPM. Difference between glycemic statuses was tested using Cochran–Armitage test for trend. For blood pressure classifications and hypertension subtypes, each class was tested against all other participants.

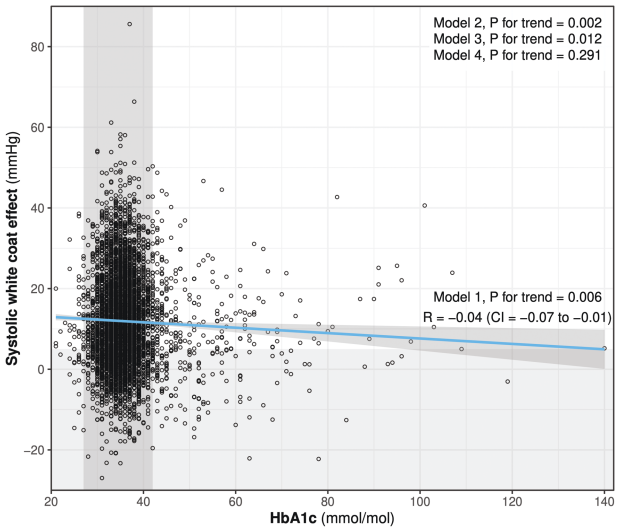


**Figure 2.** Scatter plot of systolic white coat effect (mm Hg) in relation to HbA1c (mmol/mol). The systolic white coat effect decreases as the HbA1c increases, as illustrated by the fit line. The vertical gray area corresponds to the reference interval of HbA1c from 27 to 42 mmol/mol. The horizontal gray area corresponds to an OBP <5 mm Hg above the HBPM, i.e., an area in which plotted values could match the clinical criteria of masked hypertension, if the HBPM was also ≥135 mm Hg and the OBP was <140 mm Hg, and the corresponding diastolic BP measurements aligned with the diagnosis as well. *P* for trend was calculated using linear regression. Model 1: crude. Model 2: adjusted for age and sex. Model 3: adjusted for age, sex, smoking status, prescribed lipid-lowering medication, prescribed antihypertensive medication, prescribed medication for diabetes, waist circumference, eGFR, hemoglobin, LDL/HDL ratio, and total CACS ≥100. Model 4: adjusted for model 3 and PWV. Abbreviations: BP, blood pressure; CACS, coronary artery calcium score; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; HBPM, home blood pressure monitoring; HDL, high-density lipoprotein; LDL, low-density lipoprotein; OBP, office blood pressure; PWV, pulse wave velocity.

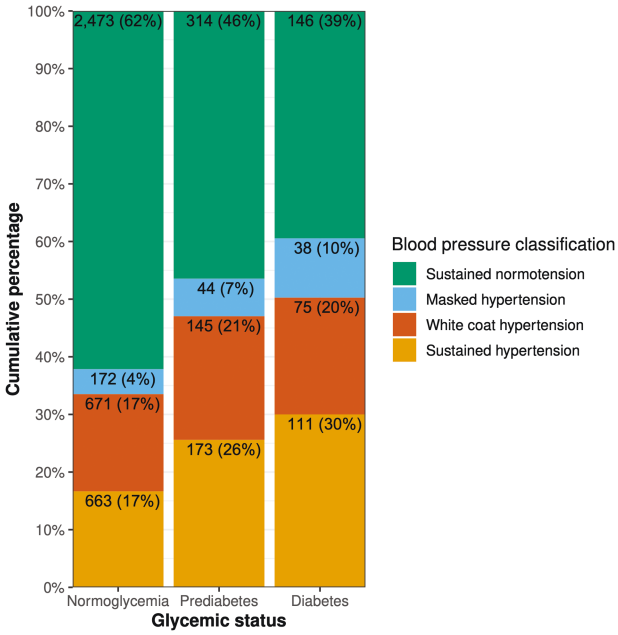


**Figure 3.** Proportional stacked bar plot of blood pressure classification in relation to glycemic status in all participants. *P* for trend was calculated using a Cochran–Armitage test for trend, with *P* for trend for sustained hypertension <0.001, white coat hypertension = 0.006, masked hypertension <0.001, and sustained normotension <0.001.

compliance to antihypertensive treatment may be increased ahead of healthcare visits compared with the compliance at home.[32]

## Study limitations

Our SCAPIS substudy had a low missing rate of less than 3% for all baseline variables, and less than 0.6% for all BP measurements. We used the same BP monitoring devices and intervals in the office and at home, something that previous studies have been criticized for not doing.[33] A limitation is that participants had their BP measured in a supine position at the office and in a sitting position at home. However, a previous study with a similar measurement protocol showed no significant difference comparing supine and sitting systolic BP.[34] Furthermore, the same study found no association between diabetes and the difference between systolic supine and sitting BP.[34] Another limitation is that we did not have access to data on prescribed medications, and participants' current medication for diabetes and hypertension were reported via the questionnaires. Our study did not include the parameter of race for calculation of eGFR as included in the original formula for CKD-EPI, which is another limitation.[24] The use of race however is also debated based on its origins as a social rather than biological concept,[35] and studies have shown that the use of race in calculating eGFR may not be clinically relevant outside of the United states.[36] To further increase our knowledge on the correlation between HBPM and dysglycemia, it would be of interest to combine our data with more detailed information on antihypertensive medication, including substance, dosage, and time of intake.

## Conclusion and future studies

In conclusion, decreased systolic white coat effect as well as increased prevalence of masked hypertension was associated with dysglycemia. However, these associations were highly dependent on PWV which implies linkage with the degree of aortic stiffness to glycemic control. Our findings suggest that for patients with diabetes or prediabetes, a combination of office and home blood pressure measurements could aid clinicians in their risk evaluation of this large group of patients, already at increased cardiovascular risk.

There are currently no studies investigating the prevalence of masked hypertension depending on the type of out-of-office BP measurements used, which would be relevant since only ABPM measures nighttime BP. Masked hypertension could then be further categorized as occurring during the day, during the night or both. In that context, it would also be highly relevant to investigate the timing of antihypertensive treatments in relation to these diagnoses.

## SUPPLEMENTARY MATERIAL

Supplementary data are available at *American Journal of Hypertension* online.

**Table 3.** Intermediate hypertension phenotypes according to glycemic status in participants without current antihypertensive medication

| | Normoglycemia ($n$ = 3,415) | Prediabetes ($n$ = 505) | Diabetes ($n$ = 198) | Total ($N$ = 4,118) | $P^a$ | $P^b$ | $P^c$ | $P^d$ |
|---|---|---|---|---|---|---|---|---|
| White coat hypertension, $n$ (%) | 539 (15.8) | 103 (20.4) | 40 (20.2) | 682 (16.6) | 0.092 | 0.092 | 0.058 | 0.112 |
| Masked hypertension, $n$ (%) | 134 (3.9) | 24 (4.8) | 14 (7.1) | 172 (4.2) | 0.005 | 0.005 | 0.036 | 0.181 |

Blood pressure classification was done according to the definitions specified in Box 1. Thus, sustained normotension was defined as normal office blood pressure (OBP) and normal home blood pressure monitoring (HBPM); white coat hypertension as elevated OBP but normal HBPM; masked hypertension as normal OBP but elevated HBPM; and sustained hypertension as elevated OBP and elevated HBPM. Difference between glycemic statuses, comparing white coat hypertension with sustained hypertension, and comparing masked hypertension with sustained normotension, was tested using logistic regression. Abbreviations: CACS, coronary artery calcium score; eGFR, estimated glomerular filtration rate; HBPM, home blood pressure monitoring; HDL, high-density lipoprotein; LDL, low-density lipoprotein; OBP, office blood pressure; PWV, pulse wave velocity.

[a]Crude model (model 1).

[b]Adjusted for age and sex (model 2).

[c]Adjusted model (model 3) for age, sex, smoking status, prescribed lipid-lowering medication, waist circumference, eGFR, hemoglobin, LDL/HDL ratio, and total CACS ≥100.

[d]Adjusted model (model 4) for age, sex, smoking status, prescribed lipid-lowering medication, waist circumference, eGFR, hemoglobin, LDL/HDL ratio, total CACS ≥100, and PWV.


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## AUTHORS' CONTRIBUTIONS

P.a.G., F.H.N., and K.R. contributed to the concept and rationale for the study, interpretation of the results, and drafted the manuscript. P.a.G. conducted statistical analysis with advice from F.H.N., P.a.G., J.E., C.J.Ö., F.H.N., and K.R. contributed to discussion and reviewed and edited the manuscript. F.H.N. and K.R. are the guarantors of this work and, as such, had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

## DISCLOSURE

The authors declared no conflict of interest.

## DATA AVAILABILITY

The data underlying this article will be shared on reasonable request to the corresponding author.

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