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Masked Hypertension in the Elderly: Cross-Sectional Analysis of a Population-Based Sample

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BACKGROUND
Masked hypertension (MHT), defined as normal blood pressure (BP) at office associated with high BP at home, has been shown to be associated with an increased risk of vascular events. However, MHT is poorly known in the elderly, although this age segment is at high risk of hypertension-related vascular events. Our objectives were to assess frequency and determinants of MHT in the elderly.

METHODS
We studied MHT in a community-based sample of 1,814 participants aged 75 years or older, whose office BP and home BP measurements (HBPM) were both taken with the same device (Omron M6; Omron Healthcare, Kyoto, Japan).

Hypertension was defined as a systolic BP (SBP) ≥140 mm Hg and/or a diastolic BP (DBP) ≥90 mm Hg for office BP, and SBP ≥135 mm Hg and/or DBP ≥85 mm Hg for HBPM.

RESULTS
Frequency of MHT was 16% in the overall sample and 41% in participants with a normal office BP. Multivariable analyses revealed that male subjects, >80 years of age, with diabetes, on antihypertensive medication, and with office SBP >120 mm Hg were independently associated with a higher risk of MHT.

CONCLUSION
MHT is frequent in the elderly and is associated with a high vascular profile. These results should encourage a more widespread use of home BP monitoring in this age segment.

Keywords: *blood pressure; elderly; home blood pressure measurement; hypertension; masked hypertension; risk factors*

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Masked hypertension (MHT), defined as a normal clinic or office blood pressure (BP) and an elevated home BP, has been shown to carry a doubling of the risk of vascular events.[1] Indeed, in a large cohort of treated hypertensive patients, those with MHT had a risk of cardiovascular events approaching those with hypertension both at office and home.[1] Moreover, a recent meta-analysis based on data from eight studies gave similar results.[2]

Several studies have assessed the frequency of MHT[3–10] in various populations and settings. Yet, few results have been published in elderly persons, a segment of the population especially vulnerable to stroke, and none in a sample of the general population, the best target group to evaluate the actual extent of MHT. Few individuals in other age segments have used the same measuring device both at office and at home, even though doing so, as recommended, would limit this source of variability.[11]

Our objective was therefore to assess the prevalence of MHT in a large community-based sample of elderly individuals using the same BP device at office and at home. We also analyzed the characteristics of patients with MHT in order to identify the risk factors associated with it.

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METHODS

Study sample. The participants of this study were included in the Three-City Study (3C), a cohort study, whose aim is to evaluate the risk of dementia attributable to vascular factors. Study design and entry criteria for the 3C Study have been published in detail elsewhere.[12] To summarize, participants were recruited in three French cities (Bordeaux, Montpellier, and Dijon) between 1999 and 2000. The study population was randomly selected from the electoral rolls of each city. To be eligible for the study, subjects were required to be 65 years or older and noninstitutionalized. The study protocol was approved by the Ethical Committee of the University Hospital of Kremlin-Bicêtre and each participant signed an informed consent.

The 3C population at the Dijon center was asked to submit to a home BP measurement (HBPM) during the fifth follow-up exam, and 1,814 agreed to participate (participation rate = 87%). Nonparticipants were older (mean difference 1.5 years, $P < 0.0001$), more frequently had a low education level ($P = 0.002$) and lower cognitive function assessed by MMSE (Mini-Mental State Examination) (mean difference 0.6, $P < 0.0001$) (data not shown).

BP measurements

Office BP measurement: BP was measured at the study center by trained lay interviewers, after the subject had at least 5 min of rest in a seated position, with an appropriately sized cuff placed on the left arm, using a validated digital electronic

tensiometer (Omron M6, Omron Healthcare, Kyoto, Japan).[13] BP was measured three times at 2 min intervals, at the beginning of the interview and before cognitive testing. During this same visit, participants were given instructions on how to measure their own BP. They were given one supervised demonstration and assigned the same device (Omron M6) for use at home. A booklet with simplified instructions and a logbook to record their BP measures were also provided.

Among the 1,814 participants, office BP measure as described above was obtained from 1,499 of them in a seated position and 315 in supine position. We performed sensitivity analyses with and without the 315 patients' data, and as similar results were in both cases, we decided to keep them for all analyses.

Home BP measurement: Following the same protocol and with the same device, participants were asked to measure their home BP six times per day (3× in the morning and 3× in the evening) for three consecutive days within 2 weeks following the visit at the study center. They were instructed to measure their BP in the morning <1 h after awakening and before taking any drug. Evening measures had to be performed close to bedtime. Patients were asked to record all BP readings in their logbook, the study team assessed the reliability of the records of self-measured BP values[11,14] by comparing the values registered in the device's memory with those reported in the participants' logbooks.

As for previous studies, HBPM was considered successful when at least 12 measures out of the 18 were properly performed, that is, when the values recorded in the device matched those in the logbook.[15,16] HBPM success rate was 96% (n = 1,737), and 94% (1,708) of participants properly carried out all 18 measures. Office BP measurement was missing for five subjects.

Definition of high BP and hypertension. Mean BP was calculated taking into account all values measured. High office BP was defined as a mean systolic BP (SBP) ≥140 mm Hg or a mean diastolic BP (DBP) ≥90 mm Hg.[17,18] High home BP was defined as a SBP ≥130–135 mm Hg or a DBP ≥85 mm Hg.[18] Subjects were classified hypertensive when both office and home BPs were high. They were classified normotensive when both office BP and home BPs were normal. Subjects with normal office BP and high home BP were defined as having MHT.[18] Among the 1,733 subjects whose home and office BP measurement were both measured, 690 (40%) had a normal office BP (office SBP <140mm Hg and office DBP <90mm Hg); most of the analyses were performed on this working sample (**Figure 1**).

Other data and measurements. Demographic and socioeconomic characteristics, including age, sex, education, occupation, and income level, as well as medical history were

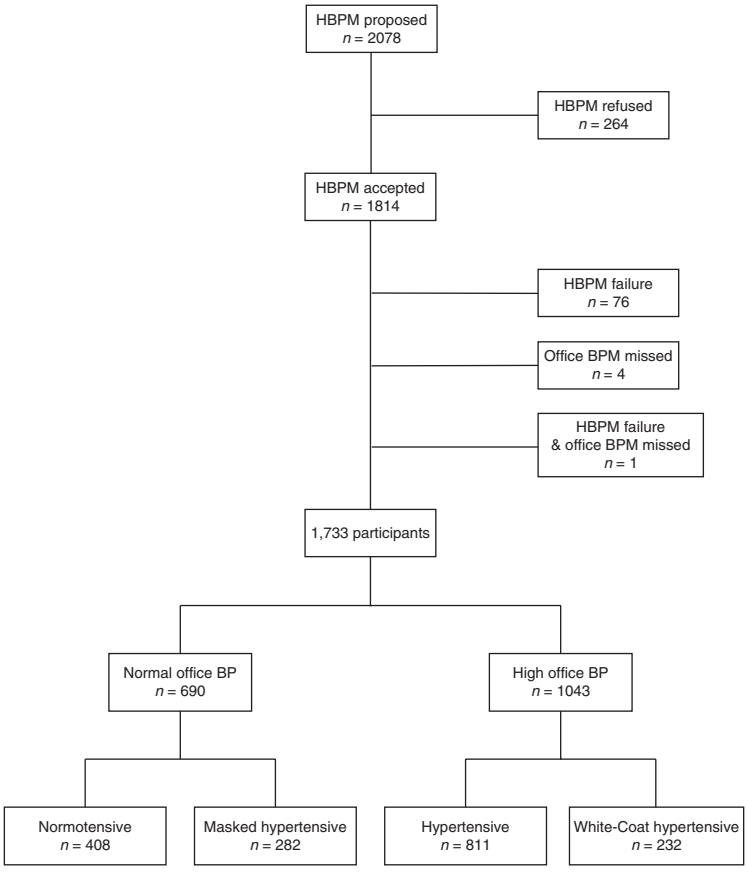

Figure 1 | Study flow diagram. BP, blood pressure; BPM, blood pressure measurement; HBPM, home blood pressure measurement.

recorded. Two educational levels were defined: High (12 or more years of formal education) and Low (<12 years of formal education). All prescribed drugs taken during the preceding month were recorded. To avoid under-reporting, participants were asked to show all their medical prescriptions and drug packages. The trade names of all drugs were recorded. Drug names were coded according to the Anatomic Therapeutic Chemical classification recommended by the World Health Organization.[19] Use of antihypertensive drugs was classified according to the number and the type of antihypertensive drugs taken (diuretics, β-blockers, angiotensin-converting enzyme inhibitors, among others).[20] The total number of medications and the use of psychotropic drugs were also recorded in this study. Data on past and present tobacco consumption were collected. Participants were classified as nonsmokers if they had never smoked or if they had stopped smoking at least last 6 months prior to study entry. Blood samples were collected and assayed for fasting cholesterol, triglycerides, and glucose levels. Diabetes mellitus was defined as either a current intake of glucose-lowering drugs or a fasting glycemia ≥7 mmol/l. Hypercholesterolemia was defined as either a current use of lipid-lowering therapy or a fasting total cholesterol ≥6.2 mmol/l.

Participants were classified as having a history of cardiovascular events if they had experienced a past history of stroke, bypass, angioplasty, myocardial infarction, angina, or heart surgery.

Height, weight, and arm circumference were measured. Body mass index (BMI) was computed as the weight divided by the square of the height and obesity was defined as a BMI ≥30 kg/m^2.

Physical activity was defined as a summed score evaluating daily activities and usual activities. The test scores ranges from 0 to 49, higher scores indicating higher level of activity. Two groups were defined using the median. Subjects with a lower score than the median were classified as having a "low degree of activity" and those with a higher score than the median were classified as having a "high degree of activity."

Cognition level was assessed with the MMSE which is a summed score evaluating various dimensions of cognition (memory, calculation, orientation in space and time, language, and word recognition). Test scores range from 0 to 30; higher scores indicating better cognitive status.

Depression was assessed with the Center for the Epidemiologic Study-Depression (CES-D) scale. This scale, a 20-item self-administered instrument that provides total scores ranging from 0 to 60[21] has been validated for use in studies that include elderly individuals.[22–24] The CES-D rates the frequency of reported depressive symptoms experienced in the past week. The CES-D scores were considered dichotomously (yes/no) using recommended cutoff values. Clinically significant depressive symptoms were defined as CES-D scores of 17 or greater in men and 23 or greater in women.[24]

Statistical analysis. Among those with normal office BP, we first compared baseline characteristics of those with a normal home BP (normotensive) and those with a high home BP (masked hypertensive) using χ^2 test for categorical variables and analysis of variance for continuous variables.

Frequency of MHT was estimated in the whole sample and among those with a normal office BP. These analyses carried out using the two high home BP thresholds defined by the European Society of Hypertension (ESH)[18] (SBP ≥135 mm Hg or DBP ≥85 mm Hg; and, SBP ≥130 mm Hg or DBP ≥85 mm Hg).

Frequency of MHT was also estimated and compared in strata of age, sex, office SBP level, diabetes, BMI, and intake of antihypertensive medication. We tested differences of MHT prevalence across these strata, and we estimated the risk of MHT using a logistic regression model adjusted for age and sex. Three age groups were used based on tertiles: ≤76 years, 76–80 years, and >80 years.

For the purpose of determining the factors associated with MHT, we used multivariable logistic regression analysis. Model 1 was a simple age and sex adjusted model. In model 2 we added variables that were found to be associated with the risk of MHT in univariate analyses (age, sex, BMI, office SBP, diabetes, and BP-lowering medication). These analyses were performed in the whole sample.

We also performed multivariable analyses in the participants treated and not treated with antihypertensive medication.

Statistical analyses were performed using SAS statistical software version 9.1 (SAS Institute, Cary, NC). A P value of <0.05 was considered as statistically significant.

RESULTS

Frequency of MHT and sample description

Using the usual threshold to define high home BP (SBP ≥135 mm Hg and/or DBP ≥85 mm Hg), we found that the frequency of MHT was 16% in the overall sample and 41% in participants with a normal office BP (**Figure 1**). Using the alternative SBP cutoff value suggested by ESH[18] to define high home BP (SBP ≥130 mm Hg and/or DBP ≥85 mm Hg), the frequency of MHT was 23% (404/1,733) in the entire sample and 59% (404/690) among participants with a normal office BP.

In **Table 1**, participants with MHT are compared to normotensive participants. Compared to normotensives, participants with MHT were more frequently males, were older, had a higher BMI and a higher office SBP (+3.7 mm Hg). They were more frequently diabetic, and more frequently on antihypertensive drugs (64% vs. 47%) (**Table 1**). No difference was found between these two groups for cardiovascular events history, smoking status, hypercholesterolemia, education level, and depressive symptoms. Similarly, no difference was found regarding income level, amount of physical activity, and alcohol consumption (data not shown).

Factors associated with a higher frequency of MHT

Table 2 displays the frequency of MHT in different variables, as well as the sex and age-adjusted odds ratios (OR). MHT frequency increased with age and was the highest in partici-

Table 1 | Baseline characteristics of the sample overall and by home BP status

	Normal office BP participants			
	Total	Normotensive (normal HBP)	Masked HT (high HBP)	*P*[a]
	(*N* = 690)	(*N* = 408)	(*N* = 282)	
Age, mean (s.d.), years	78.8 (3.9)	78.3 (3.7)	79.6 (4.0)	<0.0001
Age >80 years, % (*n*)	31.7 (218)	25.6 (104)	40.4 (114)	<0.001
Male, % (*n*)	35.1 (242)	31.1 (127)	40.8 (115)	0.009
Mean office SBP (s.d.), mm Hg	127.4 (9.2)	125.9 (9.8)	129.6 (8.0)	<0.0001
Mean office DBP (s.d.), mm Hg	69.8 (7.7)	70.0 (7.3)	69.4 (8.2)	0.34
Mean home SBP (s.d.), mm Hg	133.2 (14.1)	123.9 (8.0)	146.6 (9.4)	<0.0001
Mean home DBP (s.d.), mm Hg	70.9 (7.7)	68.0 (6.3)	75.1 (7.8)	<0.0001
Office SBP, mm Hg, % (n)				
<120	19.3 (133)	25.5 (104)	10.3 (29)	<0.0001
120–129	29.9 (206)	29.4 (120)	30.5 (86)	
130–139	50.9 (351)	45.1 (184)	59.2 (167)	
BMI, mean (s.d.), kg/m^2	25.2 (3.7)	24.9 (3.8)	25.6 (3.6)	0.02
Obesity, % (*n*)	9.7 (67)	9.3 (38)	10.3 (29)	0.02
Cardiovascular events, % (*n*)	3.9 (27)	3.7 (15)	4.3 (12)	0.71
Diabetes, % (*n*)	6.1 (41)	3.5 (14)	9.7 (27)	<0.001
Hypercholesterolemia, % (*n*)	37.4 (257)	35.5 (144)	40.1 (113)	0.19
Depressive symptoms, % (*n*)	12.7 (87)	11.8 (48)	13.9 (39)	0.42
High education level, % (*n*)	39.1 (270)	41.2 (168)	36.2 (102)	0.19
BP lowering medication, % (*n*)	53.6 (369)	46.6 (189)	63.8 (180)	<0.0001
Tobacco consumption, % (n)				
Non smoker	61.8 (425)	61.8 (251)	61.7 (174)	0.96
Past smoker	35.2 (242)	35.0 (142)	35.5 (100)	
Current smoker	3.1 (21)	3.2 (13)	2.8 (8)	
MMSE score, mean (s.d.)	27.2 (2.2)	27.4 (2.3)	27.0 (2.0)	0.04

Obesity, BMI ≥30 kg/m^2; Cardiovascular events, past history of either stroke, bypass, angioplasty, myocardial infarction, angina, or heart surgery; Diabetes, blood sugar ≥7mmol/l or hypoglycemic medication; Hypercholesterolemia, cholesterol ≥6.2mmol/l or hypocholesterolemic medication; Depressive symptom, CES-D total ≥17 for men and ≥23 for women; High education level, 12 or more years of formal education.
BMI, body mass index; BP, blood pressure; CES-D, Center for Epidemiological Studies-Depression scale; DBP, diastolic blood pressure; HBP, home blood pressure; HT, hypertensive; MMSE score, Mini Mental State Examination score; SBP, systolic blood pressure.
[a]*P* value compares difference between normotensive and masked hypertensive using Pearson test with categorical variables and variance analysis with continuous variables.

pants older than 80 years of age (52%). This translated into a more than doubling of the risk of MHT in this age category (OR = 2.2; 95% confidence interval (CI) = 1.5–3.2). Male sex and a BMI ≥25 kg/m^2 were associated with an increased frequency of MHT. Frequency of MHT increased sharply with the level of office SBP ranging from 22% among those with a SBP <120 mm Hg to 48% among those with a SBP ≥130 mm Hg. Related to this observation, there was a tripling of risk of MHT in this last category compared to the first ($OR_{SBP \geq 130}$ = 3.1; 95%CI = 1.9–4.9). Participants with diabetes and those taking antihypertensive drugs had a doubling of the risk of MHT.

Using multivariable adjusted logistic regression in subjects with normal office BP (model 2), five variables remained independently associated with a higher frequency of MHT: age >80 years, male sex, office SBP ≥120 mm Hg, diabetes, and antihypertensive medication (**Table 2**). **Figure 2** shows the level of these independent risk factors of MHT according to antihypertensive treatment. Overall, there was no significant difference of risk pattern in those treated with antihypertensive drug and in those not treated. In both strata, the variable of age >80 years, male sex, and office SBP ≥120 mm Hg were independently associated with an increased risk of MHT. However, these associations appeared stronger in participants not treated for hypertension.

Further adjustments on for tobacco and alcohol consumption, physical activity, and anxiety did not change alter the main results (data not shown).

We performed the same analyses using the second cutoff value to define high home BP (130/85 mm Hg) and found that factors associated with MHT were the same. Renal function was not associated with MHT (data not shown).

DISCUSSION

In this large sample of elderly individuals 75 years of age and older drawn from the general population, we found that 41%

Table 2 | Frequency and factors associated with masked hypertension

	Frequency of MHT		Model 1[a]			Model 2[b]		
Variable	**% (*n*)**	***P*[c]**	**OR**	**95% CI**	***P***	**OR**	**95% CI**	***P***
Age, years								
≤76	33.7 (84)	<0.001	1	—		1	—	
[76; 80]	37.8 (84)		1.2	0.8–1.8	0.31	1.1	0.8–1.7	0.53
>80	52.1 (114)		2.2	1.5–3.2	<0.0001	2.0	1.3–3.0	<0.001
Gender								
Female	37.3 (167)	0.009	1	—		1	—	
Male	47.5 (115)		1.6	1.1–2.1	0.008	1.4	1.0–2.0	0.05
SBP office, mm Hg								
<120	21.8 (29)	<0.0001	1	—		1	—	
[120; 130]	41.7 (86)		2.6	1.6–4.3	<0.001	2.7	1.6–4.5	<0.001
[130; 140]	47.6 (167)		3.1	1.9–4.9	<0.0001	3.1	1.9–5.0	<0.0001
BMI, kg/m²								
Normal <25	36.0 (134)	0.02	1	—		1	—	
Overweight [25; 30]	47.4 (119)		1.5	1.1–2.1	0.02	1.3	0.9–1.9	0.14
Obesity ≥30	43.3 (29)		1.5	0.9–2.5	0.16	1.0	0.6–1.8	0.93
Diabetes								
No	39.7 (252)	<0.001	1	—		1	—	
Yes	65.9 (27)		2.9	1.5–5.7	0.002	2.1	1.1–4.3	0.04
BP lowering medication								
No	32.0 (102)	<0.0001	1	—		1	—	
Yes	48.8 (180)		1.9	1.4–2.6	<0.0001	1.8	1.3–2.5	<0.001

Diabetes, blood sugar ≥7mmol/l or hypoglycemic medication.
BP, blood pressure; BMI, body mass index; CI, confidence interval; MHT, mask hypertension; OR, odds ratio; SBP, systolic blood pressure.
[a]Age and sex adjusted model. [b]Multivariable (age, sex, SBP, BMI, diabetes, BP lowering drug) adjusted model. [C]Unadjusted χ^2 *P* value.

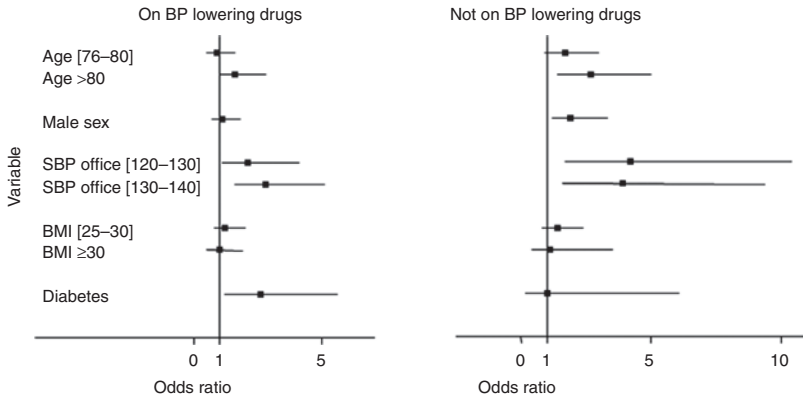

Figure 2 | Factors associated with masked hypertension by antihypertensive medication consumption status. BP, blood pressure; BMI, body mass index; SBP, systolic blood pressure.

of individuals with a seemingly normal office BP had indeed a high home BP and were thus classified as MHT.

So far, few studies have estimated the frequency of MHT in elderly individuals and no studies have done so in the general population.[25] Two studies, SHEAF[1] and J-HOME[26], which were performed in elderly hypertensive patients, also found a high frequency of MHT among patients with normal office BP (40% for the SHEAF study and 55% for the J-HOME study). In our study, the frequency of MHT in the restricted sample of participants taking antihypertensive treatment was 49%, an estimate that is consistent with these previous studies mentioned. However, even among participants without antihypertensive treatment, roughly one third (32%) had MHT. In another study performed in individuals ≥40 years in the general population, MHT frequency was 17% in the whole sample and 23% among those with a normal office BP.[27] These estimates are lower than

in our sample but are nevertheless consistent as we found that age is associated with a higher risk of MHT. Consistent frequencies were also found in a sample of 282 untreated Japanese men (frequency of MHT = 37% among those with a normal office BP)[28] and in a group of 602 elderly individuals, also not receiving antihypertensive treatment (frequency of MHT 30% among those with a normal office BP).[29]

Regarding factors associated with MHT, office SBP was one of the factors most strongly related to the risk of MHT. This was expected, as participants with office SBP values close to the 140 mm Hg threshold are more likely to have a home SBP over surpassing this threshold by the simple play of variability. Overall, the age-related deterioration of the baroreflex and the increased BP variability may partly explain the high frequency of MHT observed in this sample of elderly individuals.[30]

Apart from a high office SBP, other factors independently associated with MHT were older age, male sex, diabetes, and antihypertensive medication. As these variables are well-known to be associated with an increased risk of vascular events, participants with MHT have therefore a profile of higher vascular risk. Previous studies performed in younger individuals with hypertension also reported an association between MHT and age, male sex, antihypertensive treatment, diabetes, cholesterol level, BMI and waist circumference[25,26,31–34] although not consistently.[35] This pattern could at least partly explain why MHT has been shown to carry a risk of vascular events similar to hypertension.[1]

The strengths of our study lie in the large sample size, the community-based setting, and the age range of our participants, variables that have been previously little-examined. We notably used the same automatic electronic device for both office and home measurements, thus limiting the variability induced by the use of different devices.

Some limitations should also be taken into account. Compared with the general population of the same age, the 3C-Dijon-HBPM study participants have higher education and socioeconomical levels, and they are overall healthier. We cannot exclude the fact that our participant selection criteria may have an impact on the frequency of MHT, which may be actually higher in a truly representative sample. Furthermore, HBPMs in the evening were performed close to bedtime, rather than before dinner.[36] This timing could have affected evening home BP and resulting MHT frequency. However, they were no major differences observed in MHT frequency based strictly on morning BP measurements (18% in the whole sample, 46% in those with a normal office BP), or based strictly on evening BP measurements (15% and 39%). This suggests that this measurement bias may have a very limited impact, if any. Because of the cross-sectional nature of our study, we cannot infer causality from the associations observed. Cross-sectional analyses are exposed to biases such as temporal bias, as we do not know which came first, diabetes or MHT. Or there may be incidence-prevalence bias, since those with a higher prevalence of MHT might survive better with MHT, not those necessarily a higher incidence of MHT, and this distinction thus limits the interpretation on causality.

Overall, these data suggest that MHT is frequent in elderly individuals in the general population, and that this particular form of hypertension is therefore probably underdiagnosed in elderly individuals during their routine medical exam. Indeed, out of five subjects apparently normotensive during medical consultation, two were actually hypertensive. These results should encourage the widespread use of HBPM among elderly individuals.

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