

Impact of ambulatory blood pressure monitoring on reclassification of hypertension prevalence and control in older people in Spain

Short title: Blood pressure reclassification by ABPM

Authors

José R. BANEGAS, MD†, Juan J. de la CRUZ, MSc, Auxiliadora GRACIANI, MD, Esther LÓPEZ-GARCÍA, PhD, Teresa GIJÓN-CONDE, MD, Luis M. RUILOPE, MD, Fernando RODRIGUEZ-ARTALEJO, MD

Authors affiliations

Department of Preventive Medicine and Public Health, School of Medicine, Universidad Autónoma de Madrid/IdiPAZ – CIBER in Epidemiology and Public Health (CIBERESP), Madrid, Spain.

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†Corresponding author:

José R. Banegas, MD.

Department of Preventive Medicine and Public Health, School of Medicine, Universidad Autónoma de Madrid, C/ Arzobispo Morcillo 2, 28029 Madrid, Spain.

E-mail: joseramon.banegas@uam.es Phone: +34 91 497 5425

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ABSTRACT-

Ambulatory blood pressure monitoring (ABPM) accurately classifies the blood pressure (BP) status, but its impact on the prevalence and control of hypertension is little known. We conducted a cross-sectional study in 2012 among 1047 individuals aged ≥ 60 years coming from the follow-up of a population cohort in Spain. Three casual BP measurements and 24-h ABPM were performed under standardized conditions. Some 68.8% were hypertensive based on casual BP ($\geq 140/90$ mmHg or current BP medication), and 62.1% under 24-h ABPM ($\geq 130/80$ or current BP medication) ($p=0.009$). The proportion of patients with treatment-eligible hypertension who met BP goals increased from 37.4% under casual BP target to 54.1% under the 24-h BP target (absolute difference 16.7%, $p<0.01$). These results were consistent across alternative BP thresholds. Therefore, compared with the casual BP, the 24-h ABPM led to a reduction in the proportion of older subjects recommended for hypertension treatment and a substantial increase in the proportion of those with hypertension control.

KeyWords: hypertension; control; prevalence; ambulatory blood pressure monitoring; epidemiology; aged.

High blood pressure (BP) poses a serious cardiovascular risk to the individual and a big burden to the population.¹⁻³ Casual BP determined in the office or clinic has been the standard of measurement during many decades. However, ambulatory BP monitoring (ABPM) can provide an estimate of the true, or mean, BP level and predicts clinical outcomes better than conventional BP measurements.⁴⁻⁷

Although there are many studies on the epidemiology of hypertension using both in-office and out-of-office BP measurements,⁸⁻¹² the consequences of using ABPM for surveillance of high BP in the general population have not been fully explored. In fact, it has been recently proposed that ABPM should be included in the National Health and Nutrition Examination Survey (NHANES) of the United States, to more accurately classify hypertension prevalence and control.¹³ Furthermore, the National Institute for Health and Clinical Excellence (NICE) in the United Kingdom recommends the use of ABPM to confirm the diagnosis of hypertension for all patients with an office BP $\geq 140/90$ mmHg.¹⁴

The introduction of ABPM in the follow-up of subjects aged over 60 years from the Spanish Nutrition and Cardiovascular Risk Survey¹⁵ has provided us with the opportunity to examine how many people would change their BP status by using this technology in this general population setting. Like some other population surveys,¹⁵⁻¹⁷ in this Spanish study casual BP was taken at subjects' home, thus providing a more real measurement of BP because it is not so much affected by the alert reaction.¹⁸ Given that home BP measurement is increasingly used,^{18,19} and likely to keep rising in the next few years, especially for monitoring BP control, this is a scenario in which measuring the impact of using ABPM makes also sense. Thus, we estimated the impact of the ABPM on the prevalence and control of BP in older adults in Spain, the population group where hypertension is more frequent and challenging. This information is relevant from both a clinic and public health viewpoint, since a more accurate classification of the BP status would allow for quantifying

over- or under-treatment, and obtaining a balanced view of the burden of hypertension in the population.

METHODS

Study design and participants

We conducted a cross-sectional analysis from the second wave of the Seniors-ENRICA study, a cohort set up in 2008-2010 with individuals selected through random sampling of the population aged ≥ 60 years in Spain.¹⁵ This second wave was conducted in 2012 among 2519 individuals alive and included a phone interview on health status, lifestyle and morbidity, as well as a home visit to record BP and anthropometry, habitual diet and prescribed medication.

Because of logistic and cost reasons, ABPM was offered to 1698 individuals, and ABPM was performed in 1328 subjects (response rate, 78.2%). Compared with subjects without ABPM, those who underwent it had similar age (71.8 vs. 71.7 years), proportion of males (47% vs. 49%), education level (63% vs. 61% with \leq primary studies), mean body mass index (27.8 vs. 27.5 kg/m²), proportion of diabetes (15.1% vs. 16.1%), current smoking (11.0% vs. 11.7%), and previous history of cardiovascular disease (5.7% vs. 4.5%).

Personnel involved in data collection received specific training in the study procedures. Study participants provided written consent and the study was approved by the clinical research ethics committee of the La Paz University Hospital in Madrid.

Study variables

Study participants reported their age, educational level, and smoking status. Weight and height were measured in each subject under standardized conditions. Body mass index (BMI) was calculated as weight in kg divided by height in m. Obesity was defined as BMI

$\geq 30 \text{ kg/m}^2$. Waist circumference (WC) was deemed to be located at the midpoint between the lowest rib and the iliac crest, and was measured with participants lightly clothed using a flexible, inelastic belt-type tape. Abdominal obesity was defined as WC >102 cm in men and >88 cm in women. Information on physical activity was obtained with the questionnaire used in the EPIC study that combines physical activity at work and at leisure time,²⁰ and physical inactivity was defined as being inactive or moderately inactive. Participants also reported if they had ever being diagnosed with cardiovascular disease (CVD), diabetes, or hypertension. Medication use was collected by a face-to-face interview and verified against drug packaging during the home visits.

Blood pressure measurement

BP was measured by certified examiners using standardized procedures and conditions.²¹ Casual BP was measured with validated automatic devices (Omron M6) and appropriate sized cuffs. BP was determined three times at 2-minute intervals, after resting 5 minutes in a seated position. In the analyses, casual BP was calculated as the mean of the last two of the three readings.

Thereafter, 24-h ABPM was performed with a validated automated non-invasive oscillometric device (Microlife WatchBPO3 monitor, Microlife Corp, Switzerland),²² programmed to register BP at 20-min intervals during the day and at 30-min during the night for the 24-h period. Appropriate cuff sizes were used. The majority of registries were performed on working days and the patients were instructed to maintain their usual activities but keeping the arm extended and immobile at the time of cuff inflation. The staff of the study returned to the patients' homes for device removal the following day. Valid ABPM registries had to fulfill a series of pre-established criteria, including 24-h duration and at least 70% successful recordings of systolic BP (SBP) and diastolic BP (DBP) during the day

and night.^{23,24} Daytime and night-time periods were defined individually according to the patient's self-reported time of going-to-bed and getting-up.

Based on casual BP, hypertension was defined as mean SBP ≥ 140 mm Hg, DBP ≥ 90 mm Hg, or currently taking prescribed antihypertensive medication.²³⁻²⁶ Treated hypertensive was defined as an affirmative answer to the following questions: "Were you prescribed an antihypertensive medication by your physician?" and "Are you currently taking this BP medication?" Among treated hypertensives, BP control was defined as SBP < 140 and DBP < 90 mm Hg, thresholds that were also used for identifying hypertension in untreated subjects. We chose this threshold since it corresponds to the universal definition of hypertension and BP target for all ages at the time of the survey,^{25,26} it is used in many population surveys,^{15-17,27} and has a consensus ABPM equivalent (130/80 mmHg for 24-h BP).²³⁻²⁵ Accordingly, ambulatory hypertension was defined as mean 24-h SBP ≥ 130 mmHg, DBP ≥ 80 mmHg, or on current BP medication; this same value also corresponded to the treatment target. Treatment-eligible hypertension was defined as either BP above target or at goal BP under drug treatment.

Statistical analyses

A total of 1047 individuals with $\geq 70\%$ valid ABPM readings and complete information on study's variables were used for analysis (78.8% of all with available ABPM).

We examined the relationship between casual and ambulatory BP through scatterplots supplemented with Bland-Altman plots.²⁸ Then we classified individuals according to casual BP using two criteria: 1) BP categories (720 subjects with hypertension and 327 with normotension), and 2) antihypertensive drug treatment (514 treated hypertensives and 533 untreated subjects; the latter including 206 untreated hypertensives and 327 normotensives). We then calculated the percentage (and 95% confidence intervals)

of hypertensive subjects according to casual BP and to ABPM. Likewise, we calculated the percentage of subjects at BP goal according to casual BP and ABPM thresholds.²³⁻²⁶ Although strictly speaking only treated subjects could meet BP goals, from a practical viewpoint untreated subjects were included in this definition since they could also be within (rather than achieve) the normal BP range. Next, we calculated the percentage of subjects reclassified from above casual BP goal to at 24-h BP goal, and those reclassified from at casual BP goal to above 24-h BP goal. Results were obtained for the total sample and also stratified by BP medication status. Lastly, we ran several sensitivity analyses to assess the robustness of the main results to alternative BP thresholds proposed by some authors for specific conditions. Thus, we used a casual BP threshold of 140/85 mmHg that some guidelines have recommended for people with diabetes.²³ Second, despite BP at home was only measured in 1-occasion, we also used the BP threshold of 135/85 mmHg suggested for definition of hypertension based on multiple BP readings at home over several days, and compared it with ambulatory daytime BP.¹⁸ Third, we made an additional sensitivity analysis using the recently proposed clinic BP goal of 150/90 mmHg for older people,^{23,29} and approaching its 24-h BP equivalent as 140/90 mmHg.³⁰

Data are presented as absolute frequencies and percentages for categorical variables and as mean \pm standard deviation for continuous variables. Differences in sample characteristics between groups were assessed with the χ^2 for categorical variables and the Student's *t* test for continuous data. McNemar's χ^2 test was used to compare the proportion of subjects classified according to casual versus ABPM methods. Analyses were performed using the SPSS version 21, and statistical significance was set at $P < 0.05$.

RESULTS

Sample characteristics

Table 1 shows the participants characteristics. Mean age of the 1047 individuals was 71.7 years, 50.8% were males, mean BMI was 28.1 kg/m², 14.9% had diabetes, and 5.7% had had previous CVD. **Figure 1** displays the distribution of casual and ambulatory BP. Mean casual BP was 137.8/74.0 mmHg, mean 24-h BP was 123.6/69.8 mmHg, and mean daytime BP was 127.0/72.4 mmHg (**Table 1**). Both SBP and DBP distributions were bell-shaped. However, as expected in an old population, diastolic BP figures contributed much less than systolic to elevated BP. For example, 47.9% of subjects had casual SBP \geq 140 mmHg, 26.9% had 24-h SBP \geq 130, and 23.2% had daytime SBP \geq 135. The corresponding percentage of subjects with casual DBP \geq 90 mmHg, 24-h DBP \geq 80, and daytime DBP \geq 85 were 10.9%, 7.4% and 4.5%, respectively.

Hypertensive patients were older, with higher prevalence of obesity and diabetes than normotensives. Also, treated hypertensives were older, with higher mean BMI and higher frequency of obesity, diabetes and previous history of CVD than untreated subjects (Table 1). Mean casual and ambulatory SBP was higher in treated hypertensives than untreated participants (Table 1). However, compared with the 514 treated hypertensive patients, the 206 untreated hypertensive patients had higher mean casual and ambulatory BP (data not shown). Among treated patients, 36% were taking angiotensin-receptor blockers, 23.9% ACE inhibitors, 17.3% calcium-channel blockers, 20% diuretics, 20.8% beta-blockers, and 4.7% alpha-blockers. Overall, 56% of treated patients were on monotherapy, 31% on 2 drugs, and 13% on 3 or more drugs.

Relationship between casual and ambulatory blood pressure

The scatter diagrams showed only moderate fitting to the regression line (**Figure 2, panel a and b**). Pearson correlation coefficients were also moderate: 0.62 (0.65 for untreated subjects and 0.56 for those treated) for the association between casual and 24-h SBP, and

0.56 for the association between casual and daytime SBP. Corresponding coefficients for DBP were similar (data not shown). The Bland-Altman plots of mean ambulatory SBP against the difference between casual and ambulatory SBP showed a marked overestimation bias (**Figure 2, panel c and d**). Mean difference between casual and 24-h SBP was 14.3 mmHg (13.5 in untreated subjects and 15.1 in treated subjects), and 4.17 mmHg (4.18 in untreated and 4.16 in treated) for mean difference in casual vs 24-h DBP. Mean difference between casual and daytime SBP was 9.9 mmHg (1.6 for DBP).

Prevalence of hypertension according to blood pressure measurement

Based on only casual BP, the prevalence of hypertension was 68.8% (95% CI 66.0-71.6%), and it was 62.1% based on 24-h ABPM (95% CI 59.2-65.0%) (**Table 2**). The difference in hypertension prevalence between casual and 24-h BP generally remained across sociodemographic and cardiovascular risk factors like education level, obesity, physical inactivity, diabetes, smoking, and previous CVD (data not shown).

Blood pressure reclassification according to treatment status

A total of 206 (38.6%) untreated participants were above casual BP normal value, and 103 of these (19.3% of all subjects) were above the 24-h normal value. Thus, 103 or 19.3% of all participants were above normal values under casual BP measurement and would be reclassified as at normal BP under ABPM (**Table 3**). Similarly, 245 (47.7%) treated subjects were above casual BP goal, and 121 of these (23.5% of all subjects) were above the 24-h goal. Thus, 124 (24.1% of all subjects) were above the goal under casual BP and would be reclassified as at BP goal under ABPM (Table 3).

Likewise, 33 (6.2%) untreated participants had normal BP according to casual BP but would be reclassified as at above normal BP with ABPM, and 41 (8.0%) treated patients

were at goal under casual BP and would be reclassified as at above BP goal with ABPM (Table 3).

Total reclassifications were 21.7% from above normal casual BP to at normal 24-h BP, and 7.1% from at normal casual BP to above normal 24-h BP (Table 3).

Casual and 24-h blood pressure control

A total of 596 subjects were within casual BP normal range, for either being normotensive or at treatment goal (56.9%, 95% CI 53.9%-59.9%), and 749 were at 24-h BP normal range or goal (71.5%, 95% CI 68.8-74.2%; absolute difference 14.6%, $p < 0.001$). A breakdown by treatment status showed 327 untreated subjects at normal casual BP range (61.4%, 95% CI 57.3-65.5%), and 397 at normal 24-h BP range (74.5%, 95% CI 70.8-78.2%; difference 13.1%, $p < 0.001$). On the other hand, 269 treated hypertensive patients were at casual BP goal (52.4%, 95% CI 48.1-56.7%), and 352 at 24-h BP goal (68.5%, 95% CI 64.5-72.5%; difference 16.1%, $p < 0.001$).

Lastly, 522 or 49.9% of all subjects (55.2% of untreated and 44.4% of treated) were within both normal casual and ambulatory BP ranges (Table 3).

Treatment eligible hypertension and blood pressure control

The 720 casual-BP-based hypertensives and the 650 24h-BP-based hypertensives were eligible for treatment. BP control among these patients with treatment-eligible hypertension increased from 37.4% (95% CI 33.9%-40.9%) under casual BP target to 54.1% (95% CI 50.3%-57.9%) under 24-h ABPM target (absolute difference 16.7%, $p < 0.01$) (**Figure 3**).

Lastly, among subjects with BP above goal under casual BP target, 206 (45.7%) were not receiving antihypertensive medication treatment. Among subjects with BP above

goal under the 24-h ABPM target, 136 (45.6%) were not treated with antihypertensive medication.

Sensitivity analyses

Under the 140/85 mmHg casual BP threshold only for people with diabetes, main results remained materially unchanged (data not shown). Results were also similar when comparing casual BP (140/90 threshold) with ambulatory daytime target (135/85 mmHg) (**Table 4**). Interestingly, when using the 135/85 mmHg threshold for both casual and ambulatory daytime BP, we obtained an even greater difference in the frequency of hypertension between both measurement methods (74.5% vs 60.6%, or 13.9%) as compared with the difference based on main targets (6.7%), BP control among treated-eligible patients would double (26.3% vs 59.7%), and the total reclassification proportions (15.9% and 2%) would be moderately lower than those based on main targets (Table 4). Lastly, according to casual BP goal of 150/90 mmHg for older people (and 140/90 as 24-h BP equivalent), the difference in hypertension frequency based on casual BP (58.9%) versus 24-h BP (52.0%) was practically identical to that based on main thresholds used (6.7%), and the total reclassification proportions would then be 26.0% and 3.6%, close to those from the main targets considered (Table 4); however, control among treatment-eligible patients was much higher, thus a much larger number of patients would be seen as reaching target.

DISCUSSION

This contemporary population-based study has comprehensively quantified the proportion of older patients potentially affected by ABPM targets. It has shown that, the impact of using ABPM is appreciable. First, the prevalence of hypertension would be overestimated had BP status been assessed with casual BP instead of ABPM. Specifically, 6.7% or one in 15

hypertensive patients according to casual BP would not be considered hypertensive had ABPM been used, suggesting a considerable overdiagnosis when clinic BP is used alone. Extrapolating this 6.7% reduction to the older population of Spain in 2012,³¹ it would represent a reduction of approximately 700,000 older subjects classified as needing BP medication (7.5 million under casual BP and 6.8 million under the 24-h BP targets). In addition, the percentage of patients with treatment-eligible hypertension who met BP goals increased by 16.7% in absolute terms (one in 6 patients, or about 900,000 patients).

Also, there was a considerable gap between the percentage of hypertensive patients at BP goal with ambulatory versus casual BP (16.1% or one additional hypertensive actually controlled in 6 treated patients). This conveys an optimistic message to physicians because when BP is measured more accurately, the degree of BP control achieved is clearly higher. However, overall only half of all subjects were at BP goal under both BP measurement techniques, which is important since some studies have shown that the ability to predict mortality was increased by the combination of in-office and out-of-office BP values.³²

Discordance between casual and ambulatory BP. Clinical and public health implications

Given the scarce concordance between casual and ambulatory BP, two main BP phenotypes emerge: white-coat (only casual BP above goal) and masked hypertension (only 24-h BP above goal) among untreated patients, and “office or casual resistance” and masked uncontrolled hypertension among treated patients.^{4,19,23-25,32} Nevertheless, we prefer to place the emphasis on patient reclassification to better appreciate the impact of using ABPM. One in 5 untreated subjects would be reclassified as not treatment-eligible, a concept that is consistent with the generally benign prognosis and conservative therapeutic approach in subjects with only casual BP elevated, at least in the absence of additional risk factors.^{23,25,34}

Likewise, one in 4 treated patients would be reclassified as BP at goal, and thus might not need treatment intensification. Methodological differences aside, these proportions are moderately higher than those in other population-based studies,^{8,19,23,25} as corresponds to an older population.^{19,23,25} Interestingly, these proportions were lower than those obtained in Spanish older patients attending clinical settings,³⁵ probably reflecting the minimization of the alert reaction in our study. On the other hand, assuming that only-24h BP elevated has a more serious prognosis and thus could deserve a more aggressive management,^{23,25,34} one in 16 untreated subjects would be reclassified as treatment-eligible, and one in 12 treated patients would be reclassified as possibly needing intensification of treatment. The proportion of isolated ambulatory hypertension in this study is at the lower end of the range reported in other population studies,^{8,9,12,19,23,25} which is consistent with generally lower frequency in the elderly.^{19,33,36} Given the lack of clear indications for treatment of these discordant clinical entities,^{23,25,34,37,38} the therapeutic implications of reclassification have been presented only as an illustration of the potentially significant over- or under-treatment if using only a more inaccurate technique of measuring BP.

Overall, the number of subjects who were still considered to have above-goal BP (28.5% of all subjects) outnumbered the number of subjects reclassified as at goal under ABPM target (21.7%), and almost half of subjects with BP above goal under either casual or 24-h targets were untreated.

All this supports the NICE statement on offering ABPM for the diagnosis of hypertension after an initial raised reading in the clinic; ABPM would reduce misdiagnosis, ensure the right people are treated with antihypertensives, and reduce the number of patients treated for hypertension.^{14,39} Although not universally accepted,²⁴ this could save costs since the extra costs from ABPM are offset by cost savings from better targeted treatment.⁴⁰ Furthermore, ABPM is well tolerated by people, including the elderly.^{41,42} Likewise, given

these and other advantages of ABPM, some authors have proposed that the US Centers for Disease Control and Prevention include ABPM in the NHANES and that the US Food and Drug Administration (FDA) requires the use of ABPM as the gold standard for recording BP in randomized clinical trials.⁴³ Yet it is well known that ABPM is not available to most patients with hypertension, and we might as well wonder if it will not take a medico-legal challenge to make the technique universally available.

Methodological aspects

Given that this study was not strictly representative of the general older population of Spain, extrapolations should be interpreted with caution. Nevertheless, the baseline sociodemographic and clinical characteristics of the participants at the inception of the cohort were reasonably similar to those who did not participate (age, 68.6 vs. 69.4 years; males, 48.1% vs. 45.0%; mean casual BP, 139.7/77.5 vs. 139.2/77.1 mmHg; mean BMI, 28.6 vs. 28.6 kg/m²; diabetes, 15.2% vs. 18.0%; and previous CVD, 5.7% vs. 5.9%).

Of note, like in some other population surveys,¹⁵⁻¹⁷ casual BP was not measured in the office but in subjects' home, thus probably diminishing a reaction alarm and giving more realistic estimates. However, only a few BP readings were taken on a single occasion by observers which were not familiar to the subjects. No doubt other methods such as automated office BP monitoring with the patient alone can also minimize anxiety-related increases in BP,⁴⁴ and some population studies have used office, home, and ABPM measurements.^{8,9} Nevertheless, the present study was specifically focused on the direct comparison between the two out-of-office BPs individually, which may provide a more accurate classification of the BP status. Given that the present analyses suggest that casual BP measurements are a biased estimate of ambulatory BP, it is likely that having multiple BP measurements would have not minimized the beneficial impact of ABPM.

The issue of selecting BP threshold is far from settled. Nevertheless, despite our results being sensitive to different BP thresholds, their direction is consistent. Under all alternative thresholds, casual BP overestimates the true (ambulatory) hypertension prevalence, greatly underestimated the BP control among treatment-eligible subjects, and upward and downward BP reclassification is noticeable. All this suggests the potential benefit of ABPM as compared with casual BP.

Lastly, antihypertensive therapy was based on the participant's declaration and therefore may be imprecise. Also, treatment adherence was not assessed, but it has been reported to be relatively high in Spain (68%).⁴⁵

Conclusions

We estimated that the application of ABPM would potentially reduce the number of older persons for whom hypertension therapy would be recommended by approximately 7%. In addition, about 17% of treatment-eligible patients would no longer be classified as having their BP poorly controlled, but instead would be considered adequately managed. This surely makes the case for ABPM mandatory in this age group. However, even under the ABPM target, over one fourth of older subjects with hypertension still have uncontrolled BP, and approximately half of them remain untreated. Reclassification of patients based on ABPM illustrates the clinical and public health implications of targeting treatment at patients who have actually elevated BP and avoiding treatment in those who don't. All this supports the usefulness of measuring BP with ABPM.⁴⁶

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REFERENCES

- 1.-Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. *Lancet* 2005;365:217-223.
- 2.-Wolf-Maier K, Cooper RS, Banegas JR, et al. Hypertension prevalence and blood pressure levels in 6 European countries, Canada, and the United States. *JAMA* 2003;289:2363-2369.
- 3.-Lim SS, Vos T, Flaxman AD, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;380:2224-2260.
- 4.- Pickering TG, Shimbo D, Haas D. Ambulatory blood-pressure monitoring. *N Engl J Med* 2006;354:2368-2374.
- 5.- Hansen TW, Kikuya M, Thijs L, et al; IDACO Investigators. Prognostic superiority of daytime ambulatory over conventional blood pressure in four populations: a meta-analysis of 7,030 individuals. *J Hypertens* 2007;25:1554-1564.
- 6.-Burr ML, Dolan E, O'Brien EW, O'Brien ET, Mc Cormack P. The value of ambulatory blood pressure in older adults: the Dublin outcome study. *Age Ageing* 2008;37:201-206.
- 7.- O'Brien E. 24-h ambulatory blood pressure measurement in clinical practice and research: a critical review of a technique in need of implementation. *J Intern Med* 2011;269:478-495.
- 8.- Bombelli M, Toso E, Peronio M, et al. The Pamela study: main findings and perspectives. *Curr Hypertens Rep* 2013;15:238-243.
- 9.- Hozawa A, Ohkubo T, Kikuya M, et al. Blood pressure control assessed by home, ambulatory and conventional blood pressure measurements in the Japanese general population: the Ohasama study. *Hypertens Res* 2002;25:57-63.

- 10.- Banegas JR, Segura J, Sobrino J, et al. Effectiveness of blood pressure control outside the medical setting. *Hypertension* 2007;49:62-68.
- 11.- Franklin SS, Thijs L, Hansen TW, O'Brien E, Staessen JA. White-coat hypertension: new insights from recent studies. *Hypertension* 2013;62:982-987.
- 12.- Bobrie G, Clerson P, Ménard J, Postel-Vinay N, Chatellier G, Plouin PF. Masked hypertension: a systematic review. *J Hypertens* 2008;26:1715-1725.
- 13.-Giles TD, Black HR, Messerli F, White WB. Ambulatory blood pressure monitoring should be included in the National Health and Nutritional Examination Survey (NHANES). *J Am Soc Hypertens* 2012;6:364-366.
- 14.-National Institute for Health and Clinical Excellence. Hypertension: clinical management of primary hypertension in adults. London: NICE, 2011. Available at: <http://guidance.nice.org.uk/CG127> (Accessed 26 February 2014).
- 15.- Rodríguez-Artalejo F, Graciani A, Guallar-Castillón P, et al. Rationale and methods of the Study on Nutrition and Cardiovascular Risk in Spain (ENRICA). *Rev Esp Cardiol* 2011;64:876-882.
- 16.- Falaschetti E, Mindell J, Knott C, Poulter N. Hypertension management in England: a serial cross-sectional study from 1994 to 2011. *Lancet* 2014;383:1912-1919.
- 17.- Hajjar I, Kotchen TA. Trends in prevalence, awareness, treatment, and control of hypertension in the United States, 1988-2000. *JAMA* 2003;290:199-206.
- 18.- Parati G, Stergiou GS, Asmar R, et al. European Society of Hypertension practice guidelines for home blood pressure monitoring. *J Hum Hypertens* 2010;24:779-785.
- 19.- Mancia G, Bombelli M, Seravalle G, Grassi G. Diagnosis and management of patients with white-coat and masked hypertension. *Nat Rev Cardiol* 2011;8:686-693.

20.- Wareham NJ, Jakes RW, Rennie KL, et al Validity and repeatability of a simple index derived from the short physical activity questionnaire used in the European Prospective Investigation into Cancer and Nutrition (EPIC) study. *Public Health Nutr* 2003;6:407-413.

21.-Pickering TG, Hall JE, Appel LJ, et al. Recommendations for blood pressure measurement in humans and experimental animals: part 1: blood pressure measurement in humans: a statement for professionals from the Subcommittee of Professional and Public Education of the American Heart Association Council on High Blood Pressure Research. *Circulation* 2005;111:697-716.

22.- Ragazzo F, Saladini F, Palatini P. Validation of the MicrolifeWatchBP O3 device for clinic, home, and ambulatory blood pressure measurement, according to the International Protocol. *Blood Press Monit* 2010;15:59-62.

23.-Mancia G, Fagard R, Narkiewicz K, et al; Task Force Members. 2013 ESH/ESC Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens* 2013;31:1281-1357.

24.- O'Brien E, Parati G, Stergiou G, et al, on behalf of the European Society of Hypertension Working Group on Blood Pressure Monitoring. European Society of Hypertension position paper on ambulatory blood pressure monitoring. *J Hypertens* 2013;31:1731-1768.

25.- Mancia G, De Backer G, Dominiczak A, et al. Management of Arterial Hypertension of the European Society of Hypertension; European Society of Cardiology. 2007 Guidelines for the Management of Arterial Hypertension: the TaskForce for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens* 2007; 25:1105–1187.

- 26.- Chobanian AV, Bakris GL, Black HL, et al, and the National High Blood Pressure Education Program Coordinating Committee. Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of high blood pressure. *Hypertension* 2003;42:1206–1252.
- 27.- Egan BM, Zhao Y, Axon RN. US trends in prevalence, awareness, treatment, and control of hypertension, 1988-2008. *JAMA* 2010;303:2043-2050.
- 28.-Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986;1:307–310.
- 29.- James PA, Oparil S, Carter BL, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA* 2014;311:507-520.
- 30.- Head GA, Mihailidou AS, Duggan KA, et al; Ambulatory Blood Pressure Working Group of the High Blood Pressure Research Council of Australia. Definition of ambulatory blood pressure targets for diagnosis and treatment of hypertension in relation to clinic blood pressure: prospective cohort study. *BMJ* 2010;340:c1104.
- 31.-<http://www.ine.es/jaxiBD/tabla.do?per=01&type=db&divi=EPOB&idtab=1>. (Accessed 25 June2014.)
- 32.- Sega R, Facchetti R, Bombelli M, et al. Prognostic value of ambulatory and home blood pressures compared with office blood pressure in the general population: follow-up results from the Pressioni Arteriose Monitorate e Loro Associazioni (PAMELA) study. *Circulation* 2005;111:1777-1783.
- 33.-Banegas JR, Ruilope LM, Sierra A, et al. High prevalence of masked uncontrolled hypertension in people with treated hypertension. *Eur Heart J* 2014;35:3304-3312.

- 34.-Fagard RH, CornelissenVA. Incidence of cardiovascular events in white-coat, masked and sustained hypertension versus true normotension: a meta-analysis. *J Hypertens* 2007;25:2193-2198.
- 35.- Llisterri JL, Alonso FJ, Gorostidi M, et al; en representación de los investigadores del Proyecto CARDIORISC-MAPAPRES. Sociedad Española de Hipertensión-Liga Española para la Lucha contra la Hipertensión Arterial (SEH-LELHA). Differences between office and ambulatory control of hypertension in very elderly patients. The CARDIORISC - MAPAPRES project. *Med Clin (Barc)* 2009;133:769-776.
- 36.- Ben-Dov IZ, Ben-Arie L, Mekler J, Bursztyn M. In clinical practice, masked hypertension is as common as isolated clinic hypertension: predominance of younger men. *Am J Hypertens* 2005;18(5 Pt 1):589-693.
- 37.-Verdecchia P, Angeli F, Gattobigio R, et al. The clinical significance of white-coat and masked hypertension. *Blood Press Monit* 2007;12:387-389.
- 38.-Pierdomenico SD, Cuccurullo F. Prognostic value of white-coat and masked hypertension diagnosed by ambulatory monitoring in initially untreated subjects: an updated metaanalysis. *Am J Hypertens* 2011;24:52-58.
- 39.-Mayor S. Hypertension diagnosis should be based on ambulatory blood pressure monitoring, NICE recommends. *BMJ* 2011;343:d5421.
- 40.-Lovibond K, Jowett S, Barton P, et al. Cost-effectiveness of options for the diagnosis of high blood pressure in primary care: a modelling study. *Lancet*. 2011;378:1219-1230.
- 41.-Ernst ME, Bergus GR. Favorable patient acceptance of ambulatory blood pressure monitoring in a primary care setting in the United States: a cross-sectional survey. *BMC Fam Pract* 2003;4:15.
- 42.-McGreevy C, Mulrooney J, O'Keeffe ST, Mulkerrin EC. Do older people tolerate ambulatory blood pressure monitoring? *J Am Geriatr Soc* 2004;52:1780-1781.

43.-Giles TD, Sander GE. Diastolic blood pressure and hypertension phenotypes: the US Food and Drug Administration has it right. *J Clin Hypertens (Greenwich)* 2013;15:145-146.

44.- Myers MG. Eliminating the human factor in office blood pressure measurement. *J Clin Hypertens* 2014;16:83-86.

45.-Márquez Contreras E, Gil Guillén V, Casado Martínez JJ, et al. Analysis of studies published on hypertension treatment non-compliance in Spain between 1984 and 2005. *Aten Primaria* 2006;3:325-332.

46.-O'Brien E. First Thomas Pickering Memorial Lecture: ambulatory blood pressure measurement is essential for the management of hypertension. *J Clin Hypertens* 2012;14:836-847.

TABLE 1.Characteristics of the study participants.

Variable	All	Hypertension status		P*	Treatment status		P**
	N=1047	Normotensive N=327	Hypertensive N=720		Untreated N=533	Treated N=514	
Age, years	71.7±6.3	70.5±5.8	72.2±6.4	<0.001	70.9±6.3	72.5±6.3	<0.001
Males, %	50.8	48.0	52.1	0.222	51.2	50.4	0.788
≤Primary studies, %	61.4	61.8	61.3	0.872	59.3	63.6	0.150
Casual SBP, mmHg	137.8±18.7	124.1±9.8	144.0±18.5	<0.001	135.5±18.2	140.2±18.9	<0.001
Casual DBP, mmHg	74.0±10.3	70.1±8.2	75.8±10.6	<0.001	74.1±10.2	73.9±10.4	0.765
24-h SBP, mmHg	123.6±11.4	117.3±9.9	126.4±10.9	<0.001	122.1±11.6	125.2±11.0	<0.001
24-h DBP, mmHg	69.8±7.0	67.7±6.4	70.8±7.1	<0.001	69.9±7.2	69.7±6.8	<0.001
Daytime SBP, mmHg	127.0±11.5	121.6±10.4	129.4±11.2	<0.001	126.1±11.8	127.9±11.2	0.012
Daytime DBP, mmHg	72.4±7.5	70.7±6.9	73.2±7.6	<0.001	72.8±7.7	72.0±7.2	0.073
BMI, kg/m ²	28.1±4.6	27.1±4.1	28.6±4.7	<0.001	27.2±4.0	29.1±4.9	<0.001
BMI ≥30 kg/m ² , %	30.9	23.5	34.2	<0.001	23.5	38.5	<0.001
WC ≥102/88cm, %	57.6	49.2	61.4	<0.001	50.3	65.2	<0.001
Physical inactivity, %	41.0	39.1	41.8	0.417	40.3	41.6	0.670
Diabetes mellitus, %	14.9	10.4	16.9	<0.001	10.9	19.1	<0.001
Current smoking, %	11.1	11.6	10.8	0.762	13.3	8.8	0.06
Previous CVD, %	5.7	6.1	5.6	0.718	4.1	7.4	0.023

Abbreviations: BMI, body mass index; WC, waist circumference; CVD, cardiovascular disease.
For definition of hypertension and treatment status, see the Methods section.

TABLE 2. Prevalence of hypertension^a according to casual and 24-h ambulatory blood pressure among older adults from the general population of Spain.

Characteristics	N	Based on casual blood pressure	Based on 24-h blood pressure	Absolute difference	P value
		Percentage (95% CI)	Percentage (95% CI)		
Total*	1047	68.8 (66.0-71.6)	62.1 (59.2-65.0)	-6.7	0.009
Gender					
Male	532	70.5 (66.6-74.4)	63.3 (59.2-67.4)	-7.2	0.113
Female	515	67.0 (62.9-71.1)	60.8 (56.6-65.0)	-6.2	0.138
Age					
<70years	470	63.2 (58.8-67.6)	54.7 (50.2-59.2)	-8.5	0.101
≥70 years	577	73.3 (69.7-76.9)	68.1 (64.3-71.9)	-5.2	0.325

Abbreviations. CI, confidence interval; CVD, cardiovascular disease. ^aHypertension: casual blood pressure (BP) ≥140/90 mmHg or on current BP medication, or 24-h BP ≥130/80 mmHg or on current BP medication.

TABLE 3. Reclassification of blood pressure control status according to ambulatory monitoring, by treatment status.

Casual blood pressure		24-h blood pressure		Total
		<130/80 mmHg	≥130/80 mmHg	
<140/90 mmHg	Total	At casual and 24-h BP goal 522 (49.9%)	Reclassified to above 24-h BP goal 74 (7.1%)	Not hypertensive or at casual BP goal 596 (56.9%)
	Untreated	294 (55.2%)	33 (6.2%)	327 (61.4%)
	Treated	228 (44.4%)	41 (8.0%)	269 (52.3%)
≥140/90 mmHg	Total	Reclassified to at 24-h BP goal 227 (21.7%)	Above casual and 24-h BP goal 224 (21.4%)	Above casual BP goal 451 (43.1%)
	Untreated	103 (19.3%)	103 (19.3%)	206 (38.6%)
	Treated	124 (24.1%)	121 (23.5%)	245 (47.7%)
Total	Total	749 (71.5%)	298 (28.5%)	1047 (100.0%)
	Untreated	397 (74.5%)	136 (25.5%)	533 (100.0%)
	Treated	352 (68.5%)	162 (31.5%)	514 (100.0%)

Abbreviations. BP, blood pressure. Untreated: normotensive and untreated hypertensive individuals. Treated: hypertensive patients on current BP medication.

Table 4. Impact of different blood pressure thresholds on the prevalence and control of hypertension.

Blood pressure criteria	Prevalence of hypertension^a	Blood pressure at goal^b	Reclassified to at ambulatory BP goal^c	Reclassified to above ambulatory BP goal^d
Casual BP (140/90 mmHg)	720 (68.8%)	269 (37.4%)	227 (21.7%)	74 (7.1%)
24-h BP (130/80 mmHg)	650 (62.1%)	352 (54.1%)		
Casual BP (140/90 mmHg)	720 (68.8%)	269 (37.4%)	266 (25.4%)	71 (6.8%)
Daytime BP (135/85 mmHg)	635 (60.6%)	379 (59.7%)		
Casual BP (135/85 mmHg)	780 (74.5%)	205 (26.3%)	166 (15.9%)	21 (2.0%)
Daytime BP (135/85 mmHg)	635 (60.6%)	379 (59.7%)		
Casual BP (150/90 mmHg)	617 (58.9%)	301 (48.8%)	272 (26.0%)	38 (3.6%)
24-h BP (140/90 mmHg)	544 (52.0%)	462 (84.9%)		

^aHypertension: casual blood pressure (BP) above goal or on current BP medication, or 24-h BP above goal or on current BP medication.

^bPercentage of subjects with treatment-eligible hypertension with BP at goal, according to casual and ambulatory BP. Medication-eligible hypertension is defined as receiving treatment or above goal for each casual BP and ambulatory BP target.

^cReclassification of individuals from above goal under casual BP to at goal under ambulatory BP.

^dReclassification of individuals from at goal under casual BP to above goal under ambulatory BP.

Figures legends.

FIGURE 1. Distribution of casual, 24-hour, and daytime systolic blood pressure.

FIGURE 2. Scatterplots (panel a and b) and Bland-Altman plots (panel c and d) for the association between casual and ambulatory systolic blood pressure.

In panel a and b, solid circles represent treated subjects, and unfilled circles represent untreated subjects. In panel c and d, the solid line indicates the mean SBP difference, and dashed lines indicate the 95% limits of agreement (two standard deviations around the mean difference).

FIGURE 3. Number of subjects eligible for medication treatment, and percentage of subjects with treatment-eligible hypertension with BP at goal, according to casual and 24-h BP.

Medication-eligible hypertension is defined as receiving treatment or above goal for each casual BP and 24-h BP target. Bars: 95% confidence intervals for percentage estimates of BP at goal.

Casual BP at goal: <140/90 mmHg. 24-h BP at goal: <130/80 mmHg.