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Invited Review

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New and older proofs regarding the reliability of Automatic Blood Pressure Monitoring in the management of hypertension

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Abstract

Nowadays, there's an universal consensus that has been imposed by the reality: the casual/office determinations of blood pressure values are accompanied by numerous disadvantages: they cover only a small portion of the 24 hour values; the existence of many sources of error (including an important percentage of "white coat hypertension" [WCH]) and, more important than anything, the fact that it can not provide data regarding the nighttime evolution of BP values. On the other hand, ABPM is the only method by which we can obtain them, making it the most reliable method in determining cardiovascular prognosis of hypertensives. The data of important and reliable studies, including significant number of subjects: Dublin Outcome Study, MAPEC, IDACO, HYGIA have recently been confirmed by an impressive, considering the number of subjects and the duration of the monitoring, study, by Banegas et al., which examined the associations between the casual BP values and those determined by ABPM with mortality, either cardiovascular or any other cause. The conclusions highlight the necessity of addressing hypertensives by ABPM, as long as WCH proves to be not a benign condition and, and, on the other hand, demonstrated that "masked hypertension" MH is associated with a higher risk of death than sustained HBP. The SBP mean during sleep (the most significant predictor of cardiovascular events), as well as WCH and MH, can be demonstrated only by ABPM, considered currently the golden standard of HBP management.

Keywords: Hypertension (HT), systolic blood pressure (SBP), office blood pressure measurements (OBPM), automated blood pressure measurement (ABPM), white coat hypertension (WCH), masked hypertension (MH), golden standard

Hypertension (HT), the "silent killer" of present times continues to deserve this denomination because it represent the leading cause of cardio-vascular (CV) diseases and death [1], being the main reason of about 55% of haemorrhagic stroke and ischaemic heart disease, of about 50% of ischaemic stroke and of 58% of different CV diseases, and his prevalence continues to increase [1–3].

In 2005 about 9,2 million premature deaths were considered generated by hypertension and in the last decade this number increased to 11,7 million deaths. [2 , 4].

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But, unfortunately, although being highly prevalent, one can consider that it remains (due to the lack of symptoms in about 50% of cases and to the lack of active screening in many countries) under-recognised, and although the armamentarium of drugs is composed of over 100 different active anti-hypertensive substances, under-controlled. And, also unfortunately, those treated, with an optimal adherence, don't overcome a percentage of 40-50 of optimally treated. [5–17]. Why?

Recently, in 2017, the Nobel Prize in Physiology or Medicine was awarded to Jeffrey C. Hall, Michael Robash and Michael W. Young for their works on the molecular mechanisms regulating the circadian rhythms [18]. As we are living in an Universe with a predominant circadian rhythmicity (the alternance light/obscurity), our whole organism and probably all our organs share the same kind of rhythmicity.

How could we find what's happening during the night (sleeping period) to BP values if not by a device that would make possible to find them, without disturbing the sleep.

That's why this method is Automated Blood Pressure Monitoring (ABPM). ABPM is considered by many a mandatory requiring for the diagnosis and the management of hypertension.

But, another mandatory condition to remember when we are using ABPM is to use concomitantly an actigraph or a diary, because BP is a very variable haemodynamic phenomenon, that can be significantly influenced by many environmental factors (as an example: "non-dipper" vs. "non-sleeper": BP values that do not decrease during the night due to a poor quality of the sleep; on a scale from 1 to 10, for validation of an ABPM session, the quality of the sleep must be quoted > 7).

Using this valuable method, it became very clear, and nowadays it is universally accepted that BP shares this circadian rhythmicity and that not only the BP values evolution during the day (the active period) and during the night (the sleeping period) is different, but also there is a different impact on CV health (CV morbidity and mortality). And, most important, that the systolic BP (SBP) during the night represent the most important prognostic marker of CV risk, his decrease, with a concomitant "dipper" profile (between 10-20% decrease of BP values) becoming the main the main therapeutic target [19–42].

Many reliable, large trials: Dublin Outcome Study (DOS) [43, 44], MAPEC [29], IDACO [45–48] and HYGIA [49], as many others [50–62], documented clearly that ABPM-derived sleep BP mean and especially SBP evolution during the night is the strongest predictor of future C-V events.

DOS included 11,291 patients who were not on antihypertensive medication, with a median follow-up of 5.3 years, demonstrated that ABPM is superior to clinic or office blood pressure measurement in predicting cardiovascular mortality, and that nighttime blood pressure is the most potent predictor of outcome.

MAPEC: 2,156 patients with untreated or resistant hypertension that were followed for a median of 5.6 years with a primary composite endpoint of all-cause mortality and total cardiovascular events; highlighted the same conclusions.

The International Database of Ambulatory blood pressure in relation to cardiovascular Outcome (IDACO) [45–48] – the first study conceived and realised for the assessment of the absolute and relative CV risks, women vs. men – 9.357 subjects (statistically analyzed), in 11 centers (67, 6% europeans; 17, 8% asians; 14,7% South Americans) and studied hard end-points as: strokes, coronary and cardiac events, CV deaths. The data obtained proved that the nighttime SBP evolution is the most important predictor in CV morbidity and mortality.

HYGIA [49] – The first outcomes prospective study conducted within primary care-based in common clinical practice to assess the prognostic significance of BP data by repeated 48 h ABPM (due to the higher reproducibility) (the largest cohort so far): 18.078 subjects with baseline Ambulatory BP ranging from normotension to HT; a median follow-up of 5,1 years.

The asleep SBP mean was the most significant BP-derived risk factor for the primary outcome (from normotension to hypertension): hard end-points and the progressive decrease of asleep SBP was the most significant marker of event-free survival (regardless of changes in office or awake SBP mean) during follow-up.

Besides these very important data, universally accepted, ABPM offers also some others, until now considered not significantly reliable: regarding resistant HT, sodium sensibility and the possibility to diagnose secondary HT, and last, but not least,

the possibility to have meaningful data about the result of drug or non-drug HT treatment. [63–81], the "smoothness index": that means a decrease of BP values without huge variations (considered now an important target in HT management) [82–84].

The data of above mentioned studies have recently been confirmed by a reliable, very impressing study: data from 223 primary centres, within the Spanish National Health System (a registry-based, multicentre, national cohort), including 63.910 adults, within a median follow-up of 4, 7 years, comparing 24-hour and OBP, using two kind of devices: oscillometric type for OBP, Spacelabs model 90207, Space labs Healthcare. [85], which examined the associations between the casual and ABPM BP values with CV- or other any other cause of death.

They divided the subjects studied in the following hypertensive phenotypes, using the definitions and classification of OBP and 24-h BP:

Definitions and classification of office BP levels and out-of-office hypertension levels [66].:

- White-coat HT (clinic SBP ≥ 140 mm Hg; clinic DBP ≥ 90 mm Hg and 24-h SBP < 130 mm Hg; 24-h DBP < 80 mm Hg);
- Masked HT (clinic SBP < 140 mm Hg; clinic DBP < 80 mm Hg and 24-h SBP ≥ 130 mm Hg; 24-h DBP ≥ 80 mm Hg);
- Sustained HT (clinic SBP ≥ 140 mm Hg; clinic DBP ≥ 90 mm Hg and 24-h SBP ≥ 130 mm Hg; 24-h DBP ≥ 80 mm Hg);
- Normotension (clinic SBP < 140 mm Hg; clinic DBP < 90 mm Hg and 24-h SBP ≤ 130 mm Hg; 24-h DBP ≤ 80 mm Hg).

BP values: cut-off values for OBP and for ABPM [66]

Category	Systolic BP		Diastolic BP
Office BP			
Optimal	< 120	and	< 80
Normal	120–129	and/or	80–84
High normal	130–139	and/or	85–89
Grade 1 HT	140–159	and/or	90–99
Grade 2 HT	160–179	and/or	100–109
Grade 3 HT	>=180	and/or	>=110
Isolated Systolic HT	>=140	and	< 90
Ambulatory HT			
Daytime	>= 135		>= 85
Night-time	>= 120		>= 70
24-hour	>= 130		>= 80
Home HT	>= 135		>= 85

Of very important significance are the conclusions of this study that also recommend ABPM as a mandatory method in HT management), demonstrating that "white coat hypertension": (WCH) is not a benign condition (similar to normotension) and that "masked hypertension" (MH) has a worst prognosis than sustained HT.

The main conclusions of this study are considered the following:

- 24-h SBP mean was more strongly associated with all-cause mortality: [hazard ratio (HR) 1,56-1,60 after adjustment for clinic BP than the clinic SBP (HR 1,00-1,04 after adjustment for 24-hour BP];
- MH was more strongly associated with all-cause mortality than sustained HT (HR 2,83 vs. 1,80);
- MH was more strongly associated with all-cause mortality or WCH (HR, 1.79; 95% CI, 1.38 to 2.32).

HRs was calculated per 1-SD increment in BP. The reference group for hypertension phenotypes was untreated normotensives.

About 1/3 in this Spanish registry patients considered by office blood pressure measurement (OBPM) to have resistant HT, with normal ABPM data demonstrated a "white coat" effect (WCE) or "false" resistance (FR) [86].

The study demonstrated (a fact already mentioned by others) [87–110] that WCH is not a benign condition that may be a consequence of either their metabolic phenotype [2, 87, 88, 90-94] or to a higher BP load mean (higher mean BP over 24 h) [100-103, 106]. 15-30% of subjects had normal BP values, due to: measurement errors, systolic HT, WCH; 5-65% of patients with elevated office BP were not diagnosed with HT after an ABPM session.

Increased SBP as measured by ABPM was significantly associated with increased risk for fatal and

non-fatal stroke and CV events, independent of OBPM. Subjects with high normal BP, overweight or obese and afro-americans had a 2-fold increased incidence of HT on rescreening within 6 years than those without these risk factors. So, for these, and also for adults over 40 years or older, for those at increased risk for high BP is recommended an annual ABPM screening.

Some of the main reasons for ABPM use is represented by the desire to avoid misdiagnosing and over-treating of WCH. The overall estimated prevalence of WCH is between 18 and 40% [92, 94, 95, 100] and the increased usage of ABPM improved CV risk stratification and diminished the cost of HT management, creating a better benefit/cost ratio, in comparison to OBPM .[111–114]

And, very important, results for cardiovascular mortality were similar to those for all-cause mortality. Cumulative mortality, after full adjustment: the strongest predictor of risk is masked hypertension (MH), followed by masked uncontrolled hypertension (MUHT), that compared with the group of controlled HT. and making possible to discover "masked hypertension" (MH), that has been proven, by this study, to be associated with a higher risk of death than sustained HT. [78–110].

One can consider that the significant greater mortality associated with MH than with sustained HT is due to a delayed and sometimes postponed for ever diagnosis of HT having as cause only clinic BP data. [91, 93, 97, 98, 101, 115–117].

That's why in the European Society of Hypertension position paper on ambulatory blood pressure monitoring [66, 67] are mentioned the following reliable reasons for ABPM, not only regarding WC phenomena and WCH, MH, but also the possibility to discover abnormal 24-h blood pressure patterns, associated with (see below):

Clinical indications for ambulatory blood pressure monitoring [66]

- **Identifying white-coat HT phenomena:** WCH in untreated patients; WC effect in treated or untreated patients; false-resistant hypertension in treated patients.
- **Identifying masked hypertension phenomena**: MH in untreated patients; Masked uncontrolled hypertension in treated patients.
- **Identifying abnormal 24-h blood pressure patterns:** Daytime hypertension; Siesta dipping/postprandial hypotension; Nocturnal hypertension; Dipping status; Morning hypertension and morning blood pressure surge; Obstructive sleep apnea; Increased blood pressure variability; Assessment of treatment; Increased on-treatment blood pressure variability.

Due to these important and reliable qualities of the method, there is an agreement between ESH and ESC [68] regarding this tremendous method in HT management:

Biases of casual/office BP values: systematic over-estimation (in at least 1/3 of patients with WCH); no data of BP values evolution during the night; all values are obtained in artificial conditions: physical and psychical; lack of precision in estimating the hypotensive of the treatment; device-associated; observer-associated (even the presence of this one is generating WC effect).

Advantages of ambulatory blood pressure monitoring over clinic blood pressure [66-68]: gives a larger number of readings than office blood pressure measurement; provides a profile of blood pressure behavior in the patient's usual daily environment; allows identification of white-coat and masked hypertension phenomena; demonstrates nocturnal hypertension; assesses blood pressure variability over the 24-h period; assesses the 24-h efficacy of antihypertensive medication; is a stronger predictor of cardiovascular morbidity and mortality than office measurement. Also, by identifying those that besides being normotensives have a "non-dipping" circadian profile, it is possible, in the future, to consider, due to higher CV risk of the "non-dipping" profile (left ventricular hypertrophy, microalbuminuria, renal function damage, cerebro-vascular disease [associated with cognitive dysfunction], glucose intolerance, increased plasma fibrinogen (PIUMA – [118], Syst-Eur – [119], Ohasama study [87] are trials that document the deleterious impact of this circadian profile and trials as MAPEC [27, 29,30] and HYGIA [49] present the data of a test to therapeutically transformation of this deleterious profile to the normal one: "dipper" [27, 31].

Before presenting all the arguments that make us consider ABPM in HT management "**the golden standard**", keep in mind that only ABPM offer us

the mandatory data for "good practice" in that area: SBP mean during sleep, the presence of WCH or of MT.

Besides the aforementioned advantages in clinical practice, there are many important advantages of ABPM in clinical trials [120]: reduction of the mandatory number of studied subjects: for a "cross-over" trial: for detecting an effect of 8/5 mm Hg (16 vs. 88 subjects); for a trial with parallel groups for detecting an effect of 5 mm Hg (67 subjects for ABPM vs. 250 subjects for CBP); reduction/avoidance of the placebo effect; a better selection of the subjects; a reliable evaluation of the duration of anti-HT treatment; evaluation of the relation dose of drug/response; evaluation of the effects on the variability of BP values (circadian profile, "smoothness index").

The US Preventive Services Task Force (USPSTF) [October 2015] has issued a draft recommending the use of ABPM in adults to confirm the diagnosis of HT, excepting the cases where an immediate initiation of the therapy is necessary. There is impressive evidence that screening for and treatment of HT is not harmful, and the net benefit of screening is substantial; neither causal, nor automated measurement of BP values was superior to the other.

The Canadian Hypertension Education Program recommended using ABPM to diagnose HT since 2005 [121–124].

National Institute of health and Care Excellence (NICE) guidelines recommend that if office BP is 140/90 mm Hg or higher, ABPM should be performed to confirm the diagnosis of HT [125], considering that it's a cost-effective method, generating cost savings for the National Health System.

The increased usage of ABPM increases the diagnostic accuracy, improve CV risk stratification, diminish the cost of HT management and has a better benefit/cost ratio, compared to a OBPM (a reduction by 23% of overall costs) [111-114].

2011 – The United Kingdom National Health Service revised the National Institute for Health and Care Excellence BP screening guidelines to include the routine use of ABPM to confirm the diagnostic of HT in adults with increased values of CBP [126] and estimates a potential savings of 10 million pounds (16 million $) over 4-5 years mainly from the identification of WCH and subsequent reduction in treatment costs [113]

Hypertension is on the move! European, British, American and Canadian scientists recommend that ABPM is a mature and reliable method in HT diagnosis and management that should become mandatory, as a "golden standarad" of HT management [126–132], but underlining that the validation of the devices used must be a very thoroughly process [133–135].

The future will provide all the necessary for his implementation, for depassing his actual limitations.

Limitations of ambulatory blood pressure monitoring

Application: limited availability; may cause discomfort, particularly at night; reluctance to use by some patients, especially for repeat measurement; cost implications (although the cost of devices is reducing and possibly more cost-effective than office measurements).

Function: imperfect reproducibility; provision of intermittent measurements in sedentary rather than ambulatory conditions; possibility of inaccurate readings during activity; inability to detect genuine artefactual measurements [66].

Conflict of interest

The authors confirm that there are no conflicts of interest

References

1. Monique EAM van Kleef and Wilko Spiering - Hypertension: Overly important but under-controlled- European Journal of Preventive Cardiology 2017, Vol. 24(3S) 36–43 DOI: 10.1177/2047487317709116
2. Forouzanfar MH, Liu P, Roth GA, Ng M, Biryukov S, et al. Global burden of hypertension and systolic blood pressure of at least 110 to 115 mm Hg, 1990–2015. JAMA 2017; 317: 165–182.
3. Global Burden of Disease Risk Factors Collaborators. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet 2016; 388: 1659–1724.

4. Wilkins E, Wilson L, Wickramasinghe K, Bhatnagar P, Leal J, et al. European Cardiovascular Disease Statistics 2017. European Heart Network, Brussels.
5. Ogden LG, He J, Lydick E, , Whelton PK. Long-term absolute benefit of lowering blood pressure in hypertensive patients according to the JNC VI risk stratification. Hypertension 2000; 35: 539–543.
6. Lewington S, Clarke R, Qizilbash N, Peto R, Collins R; Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet 2002; 360: 1903–1913.
7. Kjeldsen SE, Lund-Johansen P, Nilsson PM, Mancia G. Unattended blood pressure measurements in the Systolic Blood Pressure Intervention Trial: implications for entry and achieved blood pressure values compared with other trials. Hypertension 2016; 67: 808–812.
8. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, et al. The Task Force for the management of arterial hypertension of the European Hypertension Society (ESH) and of the European Society of Cardiology (ESC). 2013 ESH/ESC Guidelines for the management of arterial hypertension. J Hypertens 2013; 22:193–278.
9. Pickering TG, Hall JE, Appel LJ, Falkner BE, Graves J, 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.
10. Ogihara T, Kikuchi K, Matsuoka H, Fujita T, Higaki J, et al. Japanese Society of Hypertension Committee. The Japanese Society of Hypertension Guidelines for the Management of Hypertension (JSH 2009). Hypertens Res 2009; 32:3–107.
11. Calhoun DA, Jones D, Textor S, Goff DC, Murphy TP, et al. - American Heart Association Professional Education Committee. Resistant hypertension: diagnosis, evaluation, and treatment – a scientific statement from the American Heart Association Professional Education Committee of the Council for High Blood Pressure Research. Circulation 2008; 117:e510–e526.
12. Fagard RH, Van Den Broeke C, De Cort P. Prognostic significance of blood pressure measured in the office, at home and during ambulatory monitoring in older patients in general practice. J Hum Hypertens 2005; 19:801–807.
13. European Medical Agency, Committee for Medicinal Products for Human Use. Guideline on clinical investigation of medicinal products in the treatment of hypertension. London, 18 November 2010 EMA/238/1995/Rev. 3. http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2010 /12/WC500100191
14. Mancia G, Parati G, Bilo G, Maronati A, Omboni S, et al. Assessment of long-term antihypertensive treatment by clinic and ambulatory blood pressure: data from the European Lacidipine Study on Atherosclerosis. J Hypertens 2007; 25:1087–1094.
15. Stergiou GS, Myers MG, Reid JL, Burnier M, Narkiewicz K, et al. Setting-up a blood pressure and vascular protection clinic: requirements of the European Society of Hypertension. J Hypertens 2010; 28:1780–1781.
16. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts). Eur Heart J 2016; 37: 2315–2381.
17. Olsen MH, Angell SY, Asma S, Boutouyrie P, Burger D, et al. A call to action and a lifecourse strategy to address the global burden of raised blood pressure on current and future generations: the Lancet Commission on hypertension. Lancet 2016; http://dx.doi.org/10.1016/S0140-6736 (16)31134-5.
18. The Nobel Prize in physiology or medicine 2017. Nobelprize.org. August 2, 2018. Source Accessed August 3, 2018
19. O'Brien E, Sheridan J, O'Malley K. Dippers and nondippers. Lancet 1988; 2:397.
20. Ohkubo T, Hozawa A, Yamaguchi J, Kikuya M, Ohmori K, et al. Prognostic significance of the nocturnal decline in blood pressure in individuals with and without high 24-h blood pressure: the Ohasama study. J Hypertens 2002; 20:2183–2189.
21. Kario K, Shimada K. Risers and extreme-dippers of nocturnal blood pressure in hypertension: antihypertensive strategy for nocturnal blood pressure. Clin Exp Hypertens 2004; 26:177–189.
22. Metoki H, Ohkubo T, Kikuya M, Asayama K, Obara T, et al. Prognostic significance for stroke of a morning

pressor surge and a nocturnal blood pressure decline: the Ohasama study. Hypertension 2006; 47:149–154.
23. Fagard RH. Dipping pattern of nocturnal blood pressure in patients with hypertension. Expert Rev Cardiovasc Ther 2009; 7:599–605.
24. Hermida RC, Smolensky MH. Chronotherapy of hypertension. Curr. Opin. Nephrol.Hypertens. 2004; 13:501-505
25. Hermida RC, Ayala DE, Calvo C. Administration time-dependent effects of antihypertensive treatment on the circadian pattern of blood pressure. Curr. Opin. Nephrol. Hypertens. 2005; 14:453–459
26. Hermida RC, Ayala DE, Calvo C, Portaluppi F, Smolensky MH. Chronotherapy of hypertension: Administration-time dependent effects of treatment on the circadian pattern of blood pressure. Adv. Drug Deliv. Rev. 2007; 59:923–939
27. Hermida RC, Ayala DE, Mojón A, Fernández JR. Influence of circadian time of hypertension treatment on cardiovascular risk: Results of the MAPEC study. Chronobiol. Int. 2010; 27:1629–1651.
28. Hermida RC, Ayala DE, Fernández JR, Portaluppi F, Fabbian F, Smolensky MH. Circadian rhythms in blood pressure regulation and optimization of hypertension treatment with ACE inhibitor and ARB medications. Am. J. Hypertens. 2011; 24:383–391.
29. Portaluppi F, Smolensky MH. Perspectives on the chronotherapy of hypertension based on the results of the MAPEC study. Chronobiol. Int. 2010; 27:1652–1667.
30. Portaluppi F, Tiseo R, Smolensky MH, Hermida RC, Ayala DE, Fabbian F. Circadian rhythms and cardiovascular health. Sleep Med. Rev. 2012; 16:151–166.
31. Smolensky MH, Hermida RC, Ayala DE, Tiseo R, Portaluppi F. Administration-timedependent effect of blood pressure-lowering medications: Basis for the chronotherapy of hypertension. Blood Press. Monit. 2010; 15:173–180
32. Smolensky MH, Siegel RA, Haus E, Hermida R, Portaluppi F. Biological rhythms, drug delivery, and chronotherapeutics. In: Siepmann J, Siegel RA, Rathbone MJ (eds). Fundamentals and Applications of Controlled Release Drug Delivery. Heidelberg (Germany): Springer Verlag, 2012; 359–4432012
33. Parati G, Lombardi C, Hedner J, Bonsignore MR, Grote L, et al. European Respiratory Society; EU COST ACTION B26 members. Position paper on the management of patients with obstructive sleep apnea and hypertension: joint recommendations by the European Society of Hypertension, by the European Respiratory Society and by the members of European COST (COoperation in Scientific and Technological research) ACTION B26 on obstructive sleep apnea. J Hypertens 2012; 30:633–646.
34. Verdecchia P, Schillaci G, Guerrieri M, Gatteschi C, Benemio G, et al. Circadian blood pressure changes and left ventricular hypertrophy in essential hypertension. Circulation 1990; 81:528–536.
35. Hoshide S, Kario K, Hoshide Y, Umeda Y, Hashimoto T, et al. Associations between nondipping of nocturnal blood pressure decrease and cardiovascular target organ damage in strictly selected community-dwelling normotensives. Am J Hypertens 2003; 16:434–438.
36. Sega R, Corrao G, Bombelli M, Beltrame L, Facchetti R, et al. Blood pressure variability and organ damage in a general population: results from the PAMELA study (Pressioni Arteriose Monitorate E Loro Associazioni). Hypertension 2002; 39:710–714.
37. Verdecchia P, Angeli F, Mazzotta G, Garofoli M, Ramundo E, et al. Day-night dip and early-morning surge in blood pressure in hypertension: prognostic implications. Hypertension 2012; 60:34–42.
38. Parati G, Lombardi C, Hedner J, Bonsignore MR, Grote L, et al. EU COST Action B26 members. Recommendations of the management of patients with obstructive sleep apnea and hypertension. Eur Respir J 2013; 41:523–538.
39. Lurbe E, Redon J, Kesani A, Pascual JM, Tacons J, et al. Increase in nocturnal blood pressure and progression to microalbuminuria in type 1 diabetes. N Engl J Med 2002; 347:797–805.
40. Fagard RH, Thijs L, Staessen JA, Clement DL, De Buyzere ML, De Bacquer DA. Prognostic significance of ambulatory blood pressure in hypertensive patients with history of cardiovascular disease. Blood Press Monit 2008; 13:325–332.
41. Liu M, Takahashi H, Morita Y, Maruyama S, Mizuno M, et al. Nondipping is a potent predictor of cardiovascular mortality and is associated with autonomic dysfunction in haemodialysis patients. Nephrol Dial Transplant 2003; 18:563–569.
42. Timio M, Venanzi S, Lolli S, Lippi G, Verdura C, et al. 'Nondipper' hypertensive patients and progressive renal insufficiency: a 3-year longitudinal study. Clin Nephrol 1995; 43:382–387.
43. Dolan E, Stanton A, Thijs L, Hinedi K, Atkins N, et al. Superiority of ambulatory over clinic blood pressure

measurement in predicting mortality: the Dublin Outcome Study. Hypertension 2005;46:156–61.

44. Dolan E, Staessen JA, O'Brien E. Data from the Dublin outcome study**.** Blood Press Monit. 2007 Dec; 12(6):401–3. doi: 10.1097/MBP.0b013e328244df74.
45. Boggia J, Thijs L, Hansen TW, Li Y, Kikuya M, et al., on behalf of the International Database on Ambulatory blood pressure in relation to Cardiovascular Outcomes (IDACO) Investigators. Ambulatory blood pressure monitoring in 9357 subjects from 11 populations highlights missed opportunities for cardiovascular prevention in women. Hypertension 2011; 57:397–405.
46. Boggia J, Li Y, Thijs L, Hansen TW, Hansen TW, Kikuya M, et al. International Database on Ambulatory blood pressure monitoring in relation to Cardiovascular Outcomes (IDACO) Investigators. Prognostic accuracy of day versus night ambulatory blood pressure: a cohort study. Lancet 2007; 370:1219–1229.
47. Fan HQ, Li Y, Thijs L, Hansen TW, Boggia J, et al. International Database on Ambulatory Blood Pressure In Relation to Cardiovascular Outcomes Investigators. Prognostic value of isolated nocturnal hypertension on ambulatory measurement in 8711 individuals from 10 populations. J Hypertens 2010; 8:2036–2045.
48. Hansen TW, Kikuya M, Thijs L, Björklund-Bodegård K, Kuznetsova T, et al. IDACO Investigators. Prognostic superiority of daytime ambulatory over conventional blood pressure in four populations: a meta-analysis of 7030 individuals. J Hypertens 2007; 25:1554–1564
49. Hermida R.C. Sleep-time ambulatory blood pressure as a prognostic marker of vascular and other risks and therapeutic target for prevention by hypertension chronotherapy; rationale and design of the Hygia Project – Chronobiol. Int. 2016; 33: 906–936.
50. Fagard RH, Celis H, Thijs L, De Cort P. Daytime and nighttime blood pressure as predictors of death and cause-specific cardiovascular events in hypertension. Hypertension 2008;51:55–61.
51. Hansen TW, Li Y, Boggia J, Thijs L, Richart T, Staessen JA. Predictive role of the nighttime blood pressure. Hypertension 2011;57:3–10.
52. Mancia G, Verdecchia P. Clinical value of ambulatory blood pressure: evidence and limits. Circ Res 2015;116:1034–45.
53. Staessen JA, Li Y, Hara A, Asayama K, Dolan E, O'Brien E. Blood pressure measurement Anno 2016. Am J Hypertens 2017;30:453–63.
54. Boggia J, Li Y, Thijs L, Kikuya M, Björklund-Bodegård K, et al. Prognostic accuracy of day versus night ambulatory blood pressure: a cohort study. Lancet 2007;370:1219–29.
55. Mancia G, Fagard R, Narkiewicz K, Redón J, Zanchetti A, Task Force Members.et al. 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.
59. Sega R, Facchetti R, Bombelli M, Cesana G, Corrao G, 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: 1777–83.
60. Kikuya M, Ohkubo T, Asayama K, Metoki H, Obara T et al. Ambulatory blood pressure and 10-year risk of cardiovascular and noncardiovascular mortality: the Ohasama study. Hypertension 2005;45:240–5.
61. Hansen TW, Jeppesen J, Rasmussen S, , Ibsen H, Torp-Pedersen C. Ambulatory blood pressure and mortality: a population-based study. Hypertension 2005;45: 499–504.
62. Staessen JA, Thijs L, Fagard R, O'Brien ET, Clement D, et al. Predicting cardiovascular risk using conventional vs ambulatory blood pressure in older patients with systolic hypertension. JAMA 1999;282:539–46.
63. Clement DL, De Buyzere ML, De Bacquer DA, de Leeuw PW, Duprez DA, et al.et al. Prognostic value of ambulatory blood-pressure recordings in patients with treated hypertension. N Engl J Med 2003;348:2407–15.
64. Mancia G, Facchetti R, Bombelli M, Grassi G, Sega R. Long-term risk of mortality associated with selective and combined elevation in office, home, and ambulatory blood pressure. Hypertension 2006;47:846–53.
65. Gorostidi M, Banegas JR, de la Sierra A, Vinyoles E, Segura J, Ruilope LM. Ambulatory blood pressure monitoring in daily clinical practice—the Spanish ABPM Registry experience. Eur J Clin Invest 2016;46:92–8.
66. O'Brien E, Parati G, Stergiou G, Asmar R, Beilin L, et al. European Society of Hypertension position paper on ambulatory blood pressure monitoring. J Hypertens 2013;31:1731–68.
67. Parati G, Stergiou G, O'Brien E, Asmar R, Beilin L, et al. European Society of Hypertension practice guidelines for ambulatory blood pressure monitoring. J Hypertens 2014;32: 1359–66.
68. Authors/Task Force Members Giuseppe Mancia, Robert Fagard, Krzysztof Narkiewicz, Josep Redon, Alberto

Zanchetti et al. 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). Eur Heart J 2013;34:2159–219.
69. O'Brien E. Ambulatory blood pressure measurement. The case for implementation in primary care. Hypertension 2008; 51:1435–1441.
70. 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 Int Med 2011; 269:478–495.
71. Pickering TG, Shimbo D, Haas D. Ambulatory blood pressure monitoring. N Engl J Med 2006; 354:2368–2374.
72. Dolan E, Stanton A, Thijs L, Hinedi K, Atkins N, et al. Superiority of ambulatory over clinic blood pressure measurement in predicting mortality. The Dublin outcome study. Hypertension 2005; 46:156–161.
73. Parati G, Bilo G, Mancia G. Prognostic and diagnostic value of ambulatory blood pressure monitoring. In: Oparil S, Weber MA, editors. Hypertension. Philadelphia, PA: Elsevier Inc; 2005. pp. 305–317.
74. Parati G, Bilo G, Mancia G. Blood pressure measurement in research and clinical practice: recent evidence. Curr Opin Nephrol Hypertens 2004; 13:343–357.
75. Kikuya M, Hansen TW, Thijs L, Björklund-Bodegård K, Kuznetsova T, et al. International Database on Ambulatory blood pressure monitoring in relation to Cardiovascular Outcomes Investigators. Diagnostic thresholds for ambulatory blood pressure monitoring based on 10-year cardiovascular risk. Circulation 2007; 24:2145–2152.
76. Head GA, Mihailidou AS, Duggan KA, Beilin LJ, Berry N, et al. for the 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; 40:c1104.
77. O'Brien E. The value of 24-h blood pressure monitoring to assess the efficacy of antihypertensive drug treatment. Hot Topics in Hypertens 2011; 4:7–23.
78. O'Brien E. Why ABPM should be mandatory in all trials of blood pressure-lowering drugs. Drug Inform J 2011; 45:233–239.
79. Staessen JA, Byttebier G, Buntinx F, Celis H, O'Brien ET, Fagard R Antihypertensive treatment based on conventional or ambulatory blood pressure measurement. A randomized controlled trial. Ambulatory Blood Pressure Monitoring and Treatment of Hypertension Investigators. JAMA 1997; 278:1065–1072.
80. Clement DL, De Buyzere M, De Bacquer DA, de Leeuw PW, Duprez DA, et al. for the Office Versus Ambulatory BP (OvA) Study Investigators. Prognostic value of ambulatory blood-pressure recordings in patients with treated hypertension. N Engl J Med 2003; 348:207–215.
81. Palatini P, Dorigatti F, Mugellini A, Spagnuolo V, Van N, et al. Ambulatory versus clinic BP for the assessment of antihypertensive efficacy in clinical trials: insights from the Val-Syst Study. Clin Ther 2004; 26:1436–1445.
82. Omboni S, Parati G, Mancia G. The trough:peak ratio and the smoothness index in the evaluation of control of 24 h blood pressure by treatment in hypertension. Blood Press Monit 1998; 3:201–204.
83. Parati G, Schumacher H, Bilo G, Mancia G. Evaluating 24-h antihypertensive efficacy by the smoothness index: a meta-analysis of an ambulatory blood pressure monitoring database. J Hypertens 2010;28:2177–2183.
84. Verdecchia P, Angeli F, Borgioni C, Gattobigio R, Reboldiet G Ambulatory blood pressure and cardiovascular outcome in relation to perceived sleep deprivation. Hypertension 2007; 49:777–783.
85. J.R. Banegas, L.M. Ruilope, A. de la Sierra, Vinyoles E, Gorostidi M., et al. Relationship between Clinic and Ambulatory Blood-Pressure Measurements and Mortality - N Engl J Med 2018;378:1509–20.DOI: 10.1056/NEJMoa1712231
86. Banegas JR, Ruilope LM, de la Sierra A, de la Cruz JJ, Gorostidi M, et al. High prevalence of masked uncontrolled hypertension in people with treated hypertension. Eur Heart J 2014;35: 3304–12.
87. Ohkubo T, Kikuya M, Metoki H, Asayama K, Obara T, et al. et al. Prognosis of "masked" hypertension and "white-coat" hypertension detected by 24-h ambulatory blood pressure monitoring 10-year follow-up from the Ohasama study. J Am Coll Cardiol 2005;46:508–15.
88. Khattar RS, Senior R, Lahiri A. Cardiovascular outcome in white coat versus sustained mild hypertension: a 10-year follow-up study. Circulation 1998; 98:1892–1897.
89. Uallachain GN, Murphy G, Avalos G. The RAMBLER study: the role of ambulatory blood

pressure measurement in routine clinical practice – a cross-sectional study. Ir Med J 2006; 99:276–279.
90. Fagard RH, Cornelissen VA. Incidence of cardiovascular events in white-coat, masked and sustained hypertension versus true normotension: a meta-analysis. J Hypertens 2007;25:2193–8.
91. Pierdomenico SD, Cuccurullo F. Prognostic value of white-coat and masked hypertension diagnosed by ambulatory monitoring in initially untreated subjects: an updated meta analysis. Am J Hypertens 2011;24:52–8.
92. Franklin SS, Thijs L, Asayama K, Li Y, Hansen TW, et al. The cardiovascular risk of white-coat hypertension. J Am Coll Cardiol 2016;68: 2033–43.
93. Verdecchia P, Angeli F, Gattobigio R, Borgioni C, Castellani C, et al. The clinical significance of white coat and masked hypertension. Blood Press Monit 2007;12:387–9.
94. Franklin SS, Thijs L, Hansen TW, O'Brien E, Staessen JA. et al. White-coat hypertension: new insights from recent studies. Hypertension 2013;62:982–7.
95. Mancia G, Grassi G. The heterogeneous nature of white-coat hypertension. J Am Coll Cardiol 2016;68:2044–6.
97. Asayama K, Thijs L, Li Y, Gu YM, Hara et al. Setting thresholds to varying blood pressure monitoring intervals differentially affects risk estimates associated with white-coat and masked hypertension in the population. Hypertension 2014;64:935–42.
98. Franklin SS, O'Brien E, Staessen JA. Masked hypertension: understanding its complexity. Eur Heart J 2017;38:1112–8.
99. Verdecchia P, Reboldi GP, Angeli F, Schillaci G, Schwartz JE Short- and long-term incidence of stroke in white-coat hypertension. Hypertension 2005;45:203–8.
100. Briasoulis A, Androulakis E, Palla M, Papageorgiou N, Tousoulis D. et al. White-coat hypertension and cardiovascular events: a meta-analysis. J Hypertens 2016;34:593–9.
101. Stergiou GS, Asayama K, Thijs L, Kollias A, Niiranen TJ, et al. Prognosis of white-coat and masked hypertension: International Database of Home blood pressure in relation to Cardiovascular Outcome. Hypertension 2014; 63:675–82.
102. Huang Y, Huang W, Mai W, Cai X, An D, et al. White-coat hypertension is a risk factor for cardiovascular diseases and total mortality. J Hypertens 2017;35:677–88.
103. Verdecchia P, O'Brien E, Pickering T, Staessen JA, Parati G, et al. European Society of Hypertension Working Group on Blood Pressure Monitoring. When to suspect white coat hypertension? Statement from the Working Group on Blood Pressure Monitoring of the European Society of Hypertension. Am J Hypertens 2003; 16:87–91.
104. Pickering TG, James GD, Boddie C, Harshfield GA, Blank S, Laragh JH. How common is white coat hypertension? JAMA 1988; 259:225–228.
105. Myers MG, Valdivieso M, Kiss A. Use of automated office blood pressure measurement to reduce the white coat response. J Hypertens 2009; 27:280–286.
106. Fagard RH, Cornelissen VA. Incidence of cardiovascular events in white-coat, masked and sustained hypertension versus true normotension: a meta-analysis. J Hypertens 2007; 25:2193–2198.
107. Mancia G, Bombelli M, Facchetti R, Madotto F, Quarti-Trevano F, et al. Long-term risk of sustained hypertension in white-coat or masked hypertension. Hypertension 2009; 54:226–232.
108. Pierdomenico SD, Cuccurullo F. Prognostic value of white-coat and masked hypertension diagnosed by ambulatory monitoring in initially untreated subjects: an updated meta analysis. Am J Hypertens 2011; 24:52–58.
109. Ugajin T, Hozawa A, Ohkubo T, Asayama K, Kikuya M, et al. White-coat hypertension as a risk factor for the development of home hypertension: the Ohasama study. Arch Int Med 2005; 165:1541–1546.
110. Myers MG. Pseudoresistant hypertension attributed to white-coat effect. Hypertension 2012; 59:532–533.
111. Omboni S, Gazzola T, Carabelli G, Parati G. Clinical usefulness and cost effectiveness of home blood pressure telemonitoring: metaanalysis of randomized controlled studies. J Hypertens 2013; 31:455–468.
112. CMS. Centers for Medicare & Medicaid Services. Medicare PolicyDecisions. ABPM Monitoring(#CAG-00067N); 2001. http://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.
113. Krakoff LR. Cost-effectiveness of ambulatory blood pressure: a reanalysis. Hypertension 2006; 47:29–34.
114. Fischer MA, Avorn J. Economic implications of evidence-based prescribing for hypertension: can better care cost less? JAMA 2004; 291:1850–1856.
115. Pickering T, Davidson K, Gerin W, et al. Masked hypertension. Hypertension 2002; 40:795–796.
116. Stergiou GS, Salgami EV, Tzamouranis DG, Roussias LG Masked hypertension assessed by

ambulatory blood pressure versus home blood pressure monitoring: is it the same phenomenon? Am J Hypertens 2005; 18:772–778.
117. Bobrie G, Clerson P, Menard J, Postel-Vinay N, Chatellier G, Plouin PF. Masked hypertension: a systematic review. J Hypertens 2008; 26:171
118. Verdecchia P, Schillaci G, Reboldi G, Santeusanio F, Porcellati C Relation Between Serum Uric Acid and Risk of Cardiovascular Disease in Essential Hypertension: The PIUMA Study - Hypertension. 2000;36:1072–1078
119. Amery A., Birkenhager W., Bulpitt C.J. Clément D, De Leeuw P et al. – Syst-Eur. A multicenter trial on the treatment of isolated systolic hypertension in the elderly: objectives, protocol, and organization – Aging (Milano) 1991 Sep; 3 (3): 287–302.
120. Pickering T., Alpert B.S., De Swiet M. et al. – Ambulatory blood pressure – Biophysical measurement series, 1994
121. Drouin D, Campbell NR and Kaczorowski J. Implementation of recommendations on hypertension: the Canadian Hypertension Education Program. Can J Cardiol 2006; 22: 595–598.
122. Feldman RD, Campbell NR and Wyard K. Canadian Hypertension Education Program: the evolution of hypertension management guidelines in Canada. Can J Cardiol 2008; 24: 477–481.
123. Schiffrin EL, Campbell NR, Feldman RD, Kaczorowski J, Lewanczuk R, et al. Hypertension in Canada: past, present, and future. Ann Glob Health 2016; 82: 288–299.
124. Canadian Hypertension Education Program (CHEP) Recommendations for the Management of Hypertension; 2011. http://www.hypertension.ca/images/ 2012_CHEPRecsFullVersion_EN_HCP1000.pdf.
125. National Institute for Health and Clinical Excellence (NICE). Hypertension. The clinical management of primary hypertension in adults. Clinical Guideline 127; 2011. www.nice.org.uk/guidance/CG127.
126. Bloch MJ and Basile JN. UK guidelines call for routine 24-hour ambulatory blood pressure monitoring in all patients to make the diagnosis of hypertension – not ready for prime time in the United States. J Clin Hypertens (Greenwich) 2011; 13: 871–872.
127. Agarwal R, Bills JE, Hecht TJ, Light RP Role of home blood pressure monitoring in overcoming therapeutic inertia and improving hypertension control: a systematic review and meta-analysis. Hypertension 2011; 57: 29–38.
128. Leung AA, Nerenberg K, Daskalopoulou SS, McBrien K, Zarnke KB, et al. Hypertension Canada's 2016 Canadian hypertension education program guidelines for blood pressure measurement, diagnosis, assessment of risk, prevention, and treatment of hypertension. Can J Cardiol 2016; 32: 569–588.
129. Gorostidi M, Banegas JR, de la Sierra A, Vinyoles E, Segura J, Ruilope LM. Ambulatory blood pressure monitoring in daily clinical practice — the Spanish ABPM Registry experience. Eur J Clin Invest 2016;46:92–8.
130. Calhoun DA, Jones D, Textor S, Goff DC, Murphy TP, et al. American Heart Association Professional Education Committee. Resistant hypertension: diagnosis, evaluation, and treatment – a scientific statement from the American Heart Association Professional Education Committee of the Council for High Blood Pressure Research. Circulation 2008; 117:e510–e526.
131. International Ambulatory Blood Pressure Monitoring Registry – ARTEMIS http://www.artemisnet.org
132. Mancia G, Verdecchia P. Clinical value of ambulatory blood pressure: evidence and limits. Circ Res 2015;116:1034–45.
133. Noninvasive sphygmomanometers Part 2: Clinical validation of automated measurement type. American National Standards Institute. ANSI/AAMI/ISO 81060-2, 2009. http://webstore.ansi.org.
134. Noninvasive sphygmomanometers: clinical validation of automated measurement type. International Organization for Standardization (ISO) 81060-2, 2009. www.iso.org.
135. Omboni S, Costantini C, Pini C, Bulegato R, Manfellotto D, Rizzoni D, et al. PA.NET International Quality Certification Protocol for blood pressure monitors. Blood Press Monit 2008; 13:285–289.