

When Can the Practicing Physician Suspect White Coat Hypertension? Statement From the Working Group on Blood Pressure Monitoring of the European Society of Hypertension

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The Centers for Medicare and Medicaid Services (CMS) in the United States have recently approved ambulatory blood pressure measurement (ABPM) for reimbursement, but only for "patients with suspected WCH (white coat hypertension)" in whom the CMS believes the information deriving from the technique "is necessary in order to determine the appropriate management of the patient."¹ This decision, which is likely to change the clinical management of hypertension in the United States, makes white coat hypertension a condition of major importance. The decision by the CMS begs the question as to how the practicing physician can select patients with white coat hypertension. It might indeed be argued that all patients with an elevated clinic blood pressure (BP) are candidates for ABPM. However, the CMS decision carries a few other stipulations. First, white coat hypertension should be defined as "office BP >140/90 mm Hg on at least three separate clinic/office visits with two separate measurements made at each visit." Second, in addition "there should be at least two BP measurements taken outside the office which are <140/90 mm Hg." Third, "there should be no evidence of end-organ damage." Fourth and last, patients selected for ABPM on the foregoing criteria who have "an ambulatory BP <135/85 (presumably average daytime pressure, although this is not stated) with no evidence of end-organ damage" are likely to be at normal risk, whereas those patients whose pressures are above this level "may be at

increased cardiovascular risk, and a physician may wish to consider antihypertensive therapies."¹

In anticipation of a considerable increase in the use of ABPM in clinical practice in the United States, it is timely to examine the CMS recommendations in the light of recent evidence from a number of studies on WCH.

Definition of White Coat Hypertension

The CMS decision is dependent on the definition of WCH,¹ which is a term used to denote individuals with abnormally elevated BP in the medical environment and normal BP during usual daily life.^{2,3} The most popular definition of white coat hypertension is that BP measured by conventional techniques in the office, clinic, or surgery exceeds 140 mm Hg systolic or 90 mm Hg diastolic, but when ABPM is performed the average BP is less than 135 mm Hg systolic and 85 mm Hg diastolic during the daytime period.⁴ Currently, an average daytime ABPM of less than 135 mm Hg systolic and 85 mm Hg diastolic is generally considered normal and levels less than 130/80 mm Hg are considered optimal.⁴⁻⁸ The CMS stipulations on definition of WCH are in line, therefore, with the evidence from the literature.

Although, the CMS decision does not mention self measurement of BP, this is implied in that a potential candidate for ABPM must not only have an office BP greater than 140/90 mm Hg measured twice on three

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separate clinic visits, but two measurements outside the office should be less than 140/90 mm Hg; these latter measurements would only be obtainable using a self-measurement technique. Self-measured home BP has been used to identify subjects with white coat hypertension,³ though its role in this regard remains to be validated in further clinical studies.⁹ Subject to this caveat a Report of the First International Consensus Conference on self-measured home BP recommended that the upper limit of normal home BP should be 135/85 mm Hg based on the average of two measurements in the morning and in the evening for at least 3 working days.¹⁰ So again, although there may be a little difference in the detail, the CMS stipulations in this regard are in line with current evidence.

Although on the issue of definition, it is important to be clear on the terms being used, and WCH should be distinguished from *white coat effect*, which is the difference between clinic BP and ABPM, regardless of the normality or otherwise of either BP. Therefore, white coat effect is present in virtually all hypertensive subjects,¹¹ whereas WCH is considered a normal or near-normal phenomenon. White coat effect has been the subject of several studies.^{11–16}

Clinical Significance of White Coat Hypertension

Another important stipulation in the CMS decision is that potential patients for ABPM should have no evidence of end organ damage.¹ However, the means whereby a practicing physician is to determine the end organ status of a patient is not stipulated. Perhaps this recommendation should be taken as a broad means of excluding those patients with severe hypertension, who will have had an electrocardiograph and echocardiograph as part of specialized work-up rather than a call for intensive and expensive investigations in patients with WCH in whom such investigations are likely to be negative.

The clinical significance of WCH has become clearer from a growing mass of data, including some event-based cohort studies,^{17–21} which suggest that subjects with elevated office/clinic BP, who have normal average daytime pressures on ABPM have a risk of major cardiovascular events comparable to that of clinically normotensive subjects and less than that of subjects with elevated daytime pressures.

In a study by Verdecchia and co-workers,¹⁷ event risk was comparable between clinically normotensive controls and subjects with white coat hypertension (defined as an average daytime ABPM of less than 130 mm Hg systolic and 80 mm Hg diastolic), whereas risk increased with higher ABPM values. Likewise, in a study by Kario and co-workers,¹⁹ the risk of stroke was comparable between clinically normotensive individuals and subjects with white coat hypertension (defined as an average daytime ABPM of less than 135 mm Hg systolic and 85 mm Hg diastolic). Fagard and co-workers,¹⁸ who analyzed the

Syst-Eur study dataset in older subjects with isolated systolic hypertension, found treatment more effective than placebo in preventing events in subjects with moderate sustained hypertension, defined by an average daytime ABPM ≥ 160 mm Hg, but not in those with white coat hypertension. On the other hand, some studies have suggested that patients with WCH may be at increased risk.^{20,21} The results of studies with large cohorts, which should include the elderly with isolated systolic hypertension, are needed to confirm these findings.^{5,6} Nonetheless, the CMS decision regarding risk is again in keeping with the evidence.

The CMS decision makes the important recommendation that treatment may not be required in patients shown to have WCH with ABPM. Overall, evidence to date, however, does not allow us to make firm recommendations regarding drug treatment in subjects with white coat hypertension. Antihypertensive drug treatment would seem to be unnecessary in most subjects with uncomplicated white coat hypertension.²² However, intervention studies are needed to determine whether subjects with white coat hypertension might benefit from treatment to prevent the future development of organ damage and risk of cardiovascular events. In a study by Staessen and co-workers,²³ adjustment of antihypertensive treatment based on either ABPM or clinic BP resulted in less intensive drug treatment in the ABPM group despite comparable BP control in both groups, and importantly, patients in the ABPM group, who received less drug treatment were not disadvantaged as judged by left ventricular mass on echocardiography. At least on the basis of this study, the CMS suggestion that patients with WCH may not need antihypertensive medication, is reasonable.

A further point deserves mention. The ABPM levels in subjects defined as having white coat hypertension could represent, by chance, a sample taken at the low extreme of their random distribution. Consequently, day-to-day reproducibility of white coat hypertension might be impaired by a regression-to-the-mean phenomenon. In one study, diagnosis of white coat hypertension was not reproducible in as many as 58% of the subjects.²⁴ More data are needed, therefore, to elucidate the issue of reproducibility of white coat hypertension.

Identification of Subjects With White Coat Hypertension

Several hypertension guidelines^{25–27} stipulate that suspected WCH is an indication for ABPM, and this presumably influenced the CMS decision. However, the guidelines do not elaborate as to how the practicing physician may “suspect” WCH, and in fairness it has to be admitted that data allowing an estimate of the probability of WCH according to the clinical characteristics of subjects are very scarce.

In a study carried out in 292 subjects with office diastolic BP between 90 and 104 mm Hg, female gender, young age, and hypertension of short duration were independent predictors of WCH.² The analysis of a large international database composed of 2492 subjects with office BP more than 140 mm Hg systolic or 90 mm Hg diastolic showed that the probability of having WCH (defined as an average 24-h ABPM below the 95th centile of a normotensive control group) was greater in women, directly associated with age and inversely associated with office BP and the number of BP measurements in the office.²⁸ Thus, the role of age as a predictor of WCH is controversial. In another analysis of 1333 subjects in the Progetto Ipertensione Umbria Monitoraggio Ambulatoriale (PIUMA) database,¹¹ prevalence of white coat hypertension was 33.3% in Joint National Committee Stage I (systolic 140 to 159 mm Hg or diastolic BP 90 to 99 mm Hg), 11.8% in stage II (systolic 160 to 179 mm Hg or diastolic BP 100 to 109 mm Hg) and 3% in stage III (systolic \geq 180 mm Hg or diastolic BP \geq 110 mm Hg). These data indicate the higher probability of white coat hypertension in stage I hypertensive subjects. Recent studies in children have confirmed the findings in adults that WCH is more frequent in patients with milder (stage I) hypertension.²⁹

Recently, a joint analysis of the Hypertension and Ambulatory Recording Venetia Study and PIUMA databases examined 1564 subjects with uncomplicated stage I hypertension³⁰ from which subjects with diabetes mellitus, hypertension greater than stage I, renal failure, and previous cardiovascular events were excluded. Multivariate logistic regression analysis showed that lower values of office diastolic BP ($P = .0002$), female gender ($P = .002$), and nonsmoking status ($P = .038$) were the sole independent predictors of WCH. In the subjects with adequate echocardiographic tracings, a smaller value of left ventricular mass was a further independent predictor ($P = .002$) of WCH.

In a recent study, a lower body mass index and a more favorable lipid profile characterized subjects with future (after 20 years) development of white coat hypertension as opposed to those with future sustained hypertension.³¹ Left ventricular mass and prevalence of microalbuminuria did not differ between subjects with white coat hypertension, a clinically normotensive control group, whereas circulating glucose and insulin levels were higher in the white coat hypertension group than in the normotensive group.³¹

Overall, these data indicate that in untreated subjects with essential hypertension, the probability of WCH increases in subjects with 1) office systolic BP 140 to 159 mm Hg or diastolic BP 90 to 99 mm Hg, 2) female gender, 3) nonsmokers, 4) hypertension of recent onset, 5) limited number of BP measurements in the office, and 6) small left ventricular mass.

Conclusions

Taking account, therefore, of the CMS recommendations,¹ can this analysis of the available evidence give additional help to the practicing physician in deciding which subject with elevated office BP and suspected WCH should or should not have ABPM? In truth, it must be admitted that it is difficult to escape the conclusion that all patients in whom a diagnosis of hypertension is being contemplated based on office/clinic BP, should have ABPM to exclude WCH, but there are at least some features that may make it more likely that an elevated office BP is due to WCH. First, subjects (they are not necessarily patients) with office systolic BP between 140 and 159 mm Hg or diastolic BP between 90 and 99 mm Hg should have ABPM to exclude WCH, because about 33% of these subjects may have the condition.¹² In contrast, ABPM will only identify a small number of subjects with WCH when office BP is higher. Thus, if resources are limited ABPM should not be used in these subjects solely to identify WCH. Second, there is some evidence to suggest that the likelihood of identifying WCH is increased in subjects with at least one of the following conditions: female sex, non-smoking status, recent diagnosis of hypertension, limited number of BP measurements in the doctor's office, and small left ventricular mass at echocardiogram. Third, many patients may already be aware that their BP is higher in the physician's office than outside it, and the likelihood of WCH^{11,12} makes them candidates for ABPM for suspected WCH.

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