## HCFA'S ADDITIONAL PERTINENT ARTICLES

| Author / Title / Journal / Year | Type of Study | Outcomes Studied | Patient Characteristics | Results | HCFA Comments |
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| Boley E, Pickering T, James G, de Simone G, Roman M, Devereux R / Relations of ambulatory blood pressure level and variability to left ventricular and arterial function and to left ventricular mass in normotensive and hypertensive adults / Blood Pressure Monitoring / 1997 | Case-series | Outcomes studied were clinic and ambulatory BP levels, left ventricular systolic function, left ventricular wall thickness, and left ventricular wall mass. These outcomes were assessed through use of a sphygmomanometer, an ABPM, and echocardiographic measurements.<br><br>Objective of study was to assess the relation of blood pressure measured through ABPM to left ventricular and arterial function. | n=280; 106 women and 107 men<br>Mean age was 50+/-14<br><br>The study population consisted of both normotensive (predominately hospital workers and participants in community outreach programs) patients and hypertensive subjects who had not previously been treated for their hypertension.<br><br>Information about smoking, alcohol consumption, family medical history, previous treatment, duration of high blood pressure, plasma renin levels, and cholesterol levels was obtained.<br><br>No mention was made about the length of the study.<br><br>Hypertensives were older on average and drank alcohol more. They were similarly 90% white and 60% men. No significant differences existed in height, weight, body surface area, cholesterol, or plasma renin activity. | On echocardiography there were no differences detected on LV chamber size, Cardiac Output, Mean Wall Stress, or circumferential end-systolic stress but were present and significant in wall thickness, relative wall thickness, LV mass index, and total peripheral resistance.<br><br>Authors concluded that, for a population of predominately hypertensive, unmedicated adults, ambulatory blood pressures during waking hours and at home are related to left ventricular and arterial function. | No health outcomes studied. Study focuses on surrogate outcome such as left ventricular and arterial function.<br><br>Results may not be generalizable to the Medicare population due to the mean age of the study population. |

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| Imai Y, Ohkubo T, Sakuma M, et al / Predictive power of screening blood pressure, ambulatory blood pressure and blood pressure measured at home for overall and cardiovascular mortality: a prospective observation in a cohort from Ohasama, northern Japan / Blood Pressure Monitoring / 1996 | Prospective Cohort | Outcomes studied were overall and cardiovascular mortality. Cardiovascular mortality was confirmed by death certificates.<br><br>Objective of study was to investigate the risks of high and low BP levels determined by ABPM and home BP measurements. | All subjects were residents of Ohasama north-eastern Japan.<br><br>People aged 20 years and older were asked to participate in the ABPM program<br><br>n=1192 for ABPM group; n=1962 for home BP measurement<br><br>n=1556 for subjects >50 years of age. Of these 1556 subjects, 1057 were measured by screening (casual) BP, 893 by ABP, and 1226 by home BP recording.<br><br>Max period of observation was 6.2 years. | Both groups were stratified into quintiles. The screening group only showed apparent decrease in survival rate in the highest quintile of SBP. The ABPM group showed decreased survival in the highest quintile of SBP and in the highest and lowest quintiles of DBP.<br>No significant risk ratio was observed in any quintile of casual blood pressure level. A significant risk ratio was observed for the highest and lowest quintiles of DBP and the lowest quintile of SBP.<br><br>Cerebrovascular and cardiovascular mortalities were higher in the highest and lowest quintiles of ABPM that was not similarly recognized by casual blood pressure levels.<br><br>Authors proposes that there is a significant risk associated with low BP levels that can be determined only by ABPM and home BP measurements, not by casual BP measurements. | Study may not be generalizable to Medicare population because of possible variation due to ethnic differences (all Japanese subjects) and because of the age of the subjects (non-specific aging except for that about half were >50 years of age).<br><br>Stated that no significant risk ratio was observed in any quintile of casual blood pressure level but that a significant risk ratio was observed for the lowest quintile of ambulatory systolic BP and diastolic BP but not for the highest quintiles. |

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| Lantelme P, Milon H, Vernet M, Gayet C / Difference between office and ambulatory blood pressure or real white coat effect: does it matter in terms of prognosis? / Journal of Hypertension / 2000 | Case-series | Outcomes studied were left ventricular mass index, office BP and ABP. Outcomes were assessed through ABPM, electrocardiography, and echocardiography.<br><br>Aim of study was to compare the real white coat effect and the estimated white coat effect in terms of magnitude and consequences on target organs. | n=88 all with hypertension<br><br>Mean age was 50 +/- 13 years.<br><br>46 males, 42 females comprised the study population.<br><br>The majority of the population had never been treated for hypertension; 24 participants had been treated. | The estimated WC effect proved to be a bad index of the real response to the doctor's visit as assessed by:<br>1. difference of magnitude between the two<br>20 +/- 17 est, 12 +/- 12 avg, 30 +/- 14 mmHg max<br>2. loose correlations<br>r = 0.31, P = 0.004 est & avg, r = 0.27, P = 0.01 est & max<br>3. agreement in less than two-thirds of the patients for the categorization of WC response<br><br>No differences were detected in cardiac mass, diastolic function, arterial distensibility, renal function, cardiovascular risk profile when age and ABP were controlled.<br><br>Author states that this study confirms that the office BP minus ABP is a poor estimator of the real WC effect. Author suggests that the true white coat effect and its estimation are not equivalent and that the way in which the white coat response is defined does not alter its effect on target organs or cardiovascular risk profile. | Surrogate outcomes were studied.<br><br>White coat effect addressed. |

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| Lemne C, Lindvall K, Georgiades A, Fredrikson M, De Faire U / Structural cardiac changes in relation to 24-h ambulatory blood pressure levels in borderline hypertension / Journal of Internal Medicine / 1995 | Case-control | Outcomes studied were: left ventricular hypertrophy (assessed through echocardiography, insulin, and 24 ABPM levels).<br><br>Authors wanted to investigate left ventricular hypertrophy (LVH) in relation to 24-h ABPM and insulin levels in borderline hypertensives.<br><br>Hypothesis is that 24-h BP will be a better predictor of LVH in borderline hypertension than casual BP measurements. | All subjects were from Stockholm.<br><br>N=81 borderline hypertensives (cases); N=80 normotensives (controls)<br><br>All men; cases and controls were age-matched | Casual BP levels did not correlate with LVH indices, while ABPM systolic levels did in the borderline group but not the normotensive group. These asymmetric structural changes are detected with ABPM but not casual BP or trophic factors.<br>Insulin levels in the ABPM group correlate strongly with LVH indices in the normotensive group but not the borderline group.<br><br>The borderline group demonstrated increased septal thickness, peak systolic wall stress, a decreased LV ejection time, and a significantly higher septum versus posterior wall thickness ratio.<br><br>Authors concluded that the casual BP levels correlate poorly with the degree of LVH in borderline hypertension, while ABP levels, especially systolic BP, correlate much more closely with LV wall dimensions; p-values were noted. | Study looked at surrogate outcome. |

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| Lin J, Hsu K, Chian F, Tseng C, Tseng Y / Influence of isolated diastolic hypertension identified by ambulatory blood pressure on target organ damage / International Journal of Cardiology / 1995 | Case-series | Outcomes studied were isolated systolic and diastolic BP levels, target organ damage.<br><br>These groups were measured using ABPM and assessed with regard to end target organ damage including proteinuria, retinopathy, cardiomegaly, and EKG changes. | 130 patients and 41 healthy people were stratified into four groups:<br>1. normotensive<br>2. isolated diastolic hypertensive<br>3. isolated systolic hypertension<br>4. combined hypertension<br><br>Patients with mean ABP within normal limit (systolic BP<140 and diastolic BP<90) were excluded | Findings include:<br>1. lower incidence of damage in the normotensive group<br>2. incidence higher in isolated systolic than isolated diastolic<br>3. no significant difference in isolated systolic and combined hypertension<br><br>Authors propose that the results suggest the severity of hypertensive complications is more closely related to mean ambulatory systolic BP than mean ambulatory diastolic BP. | Study does not address clinical outcomes; only surrogate outcomes. |

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| Musialik D, Kosicka T, Skohuda A, Boruczkowska A, Tronjnarska O, Tykarski A / Twenty-four hour ambulatory blood pressure monitoring in young and elderly hypertensive subjects / Journal of Human Hypertension / 1998 | Case-series | Outcomes studied were LVM index and BP levels/ratios. To assess the outcomes, ABP and echocardiography were used.<br><br>Purpose of study was to compare BP measured by 24h ABPM in young and elderly hypertensives and to relate left ventricular mass (LVM) and different BP ratios. | Two hypertensive groups:<br>Group 1: n=15, aged 22-45 years<br>Group 2: n=15, aged 65-79 years | Group I included 15 persons age 22 to 45 and group II had 15 persons aged 65 to 79. Groups were similar with regard to duration and degree of hypertension as well as body mass index.<br><br>Group I demonstrated 10 non-dippers (see article for definition) while group II had 7. LVM and LVMI were comparable in both groups.<br><br>Serum LDL-cholesterol was significantly higher in the elderly group. A negative correlation was demonstrated for both serum calcium and triglyceride in both the young and elderly hypertensives.<br><br>Authors concluded that more non-dippers are in the young hypertensives group and that being a non-dipper worsened their prognosis. Authors also concluded that there was a relation between mean BP at night and LVM. Also concluded that there was a relation between nocturnal BP load and LVM. | Study addressed surrogate outcomes and did not address clinical outcomes. |

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| Ohkubo T, Imai Y, Tsuji I, et al / Prediction of mortality by ambulatory blood pressure monitoring versus screening blood pressure measurements: a pilot study / Journal of Hypertension / 1997 | Cohort | Outcomes measured were survival rates; cardiovascular mortality and non-cardiovascular mortality. Outcomes were assessed through ABPM, death certificates along with cause-of-death classification, and computed tomography to diagnose cerebrovascular disease.<br><br>Aim of study was to compare ambulatory blood pressure monitoring and clinic blood pressure to see if one was a better predictor of mortality than the other.<br><br>Independent variables were: the baseline blood pressure, age, sex smoking status, and use of anti-hypertensive medication. | n=1542;<br>565 men (mean age 62.5)<br><br>977 women (mean age 61.2)<br><br>All subjects were living in Ohasama, Iwate Prefecture, Japan.<br><br>Followed for 8.1 years<br><br>Excluded non-hospitalized, non-bedridden, non-demented individuals. | The association between BP level and mortality was more distinctive with ABPM over casual screening. This risk increased significantly in the highest quintiles of 24 ABPM while there was no significant association between screening BP and cardiovascular mortality.<br><br>Using the Cox model only the systolic ABP relates significantly to increased risk of cardiovascular mortality.<br><br>Authors concluded that data from this study demonstrated ambulatory blood pressure monitoring was superior to casual (clinic) blood pressure measurements for prediction of mortality. | Generalizability to Medicare population may be problematic because of the demographic characteristics of the all-Japanese study group.<br><br>Clinical outcomes were studied. |

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| Palatini P, Canali C, Dorigatti F et al / Target organ damage and ambulatory blood pressure in stage I hypertension, The hypertension and ambulatory recording venetia study / Blood Pressure Monitoring / 1997 | Case-Series | Outcomes studied were left ventricular diastolic function, left ventricular mass, albumin excretion rate. Outcomes were assessed through echocardiogrpahy.<br><br>Aim of study was to investigate the prevalence of cardiac and renal changes among subjects with borderline-to-mild hypertension and to assess the relation of hypertensive target organ damage to office and ambulatory blood pressures. | n=1095<br><br>Stage 1 hypertensive subjects aged 18-45 who had never been administered anti-hypertensive therapy; mean BP at entry was 146/94 mmHg | White coat hypertensive patients defined as those with office BP >140/90 mmHg and mean day-time BP <140/90 mmHg (60% of subjects) showed significant differences for left ventricular wall thickness, albumin exretion rate, and left ventricular mass index.<br><br>Authors suggest that ABP is useful for identifying those subjects among a population of young patients with stage 1 hypertension who are at low risk (white coat hypertensive). | Study addresses surrogate outcomes and does not address clinical outcomes. |

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| Prisant L, Carr A / Ambulatory blood pressure monitoring and echocardiographic left ventricular wall thickness and mass / American Journal of Hypertension / 1990 | Case-series | Outcomes studied were various echocardiographic indices of hypertensive cardiac target organ damage (left atrial diameter, left ventricular end diastolic diameter, posterior wall thickness, combined wall thickness, relative wall thickness, left ventricular mass and mass index, and combined wall thickness/left ventricular diastolic diameter ratio).<br><br>Aim of study was to examine whether twenty-four hour ABPM measurement is a better predictor of echocardiographic left ventricular wall thickness than either isolated or multiple averaged office visits. | n=55 hypertensive patients<br><br>Mean age was 44.7+/- 13.7 years.<br><br>41.8% of patients were women, 58.2% were men.<br><br>Exclusion criteria were recent or past myocardial infarction, echocardiographic wall motion abnormalities, unstable angina, congestive heart failure, valvular heart disease, mitral valve prolapse, chronic renal insufficiency, a cerebrovascular accident, insulin-requiring diabetes mellitus, claudication, current alcohol abuse, athletic trainman, or known secondary hypertension. | 24 Hr average ABP was more strongly associated with various echocardiographic indices of cardiac target organ damage in stable hypertensive patients than multiple or single office visit average BP. Diastolic ABPM was a significantly better predictor of echocardiographic posterior wall thickness, combined wall thickness, and relative wall thickness. | Surrogate outcomes were studied; no clinical outcomes studied. |

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| Redon J, Campos C, Narciso M, et al / Prognostic value of ambulatory blood pressure monitoring in refractory hypertension: a prospective study / Hypertension / 1998 | Cohort | Outcomes studied were fatal and nonfatal cardiovascular events.<br>Office BPs were measured in a quiet environment with a mercury sphygmomanometer. ABPM was performed with the use of an oscillometric monitor. Presence of end-organ damage was determined with the use of data derived from each patient's history, physical examination, ECG, chest radio-graph, fundus oculi, urinalysis, and plasma creatinine.<br><br>Objective was to investigate whether ABP offers a better estimate of cardiovascular risk than does its clinical BP counterpart in resistant (refractory) hypertension | n=86<br><br>Inclusion criteria: clinical diastolic BP>100 for 3 month visits at 1 month intervals during the same anti-hypertensive treatment; preserved renal function, glomerular filtration rate estimated by endogenous creatinine clearance >60mL/min.<br><br>Exclusion criteria: patients with diabetes mellitus or with secondary hypertension<br><br>Average follow-up period=49 months<br><br>Divided patients into tertiles of BP levels; low, medium, and high. | ABPM allowed for the stratification of patients with resistant hypertension (based on conventional BP measurement). The differences in BP were not identifiable with conventional BP (perhaps due to "white coat" effect).<br><br>Patients who had higher ABP at the time of inclusion had a higher risk of a cardiovascular event.<br><br>The authors conclude that ABPM is useful in stratifying the risk in patients with refractory hypertension measured by conventional (office or clinic) BP. | Study addressed refractory hypertension.<br><br>Sample size was small.<br><br>Needed to control for additional variables; anti-hypertensive drugs and their combinations were variable during the follow-up; a lipid profile might help to explain the study findings.<br><br>The exclusion of patients with diabetes mellitus and secondary hypertension may be problematic because they represent a large portion of those with hypertension.<br><br>Says that although they found ABPM to be beneficial in prognosis of cardiovascular events in patients with refractory hypertension, more studies are needed to better assess the prognostic value of ABPM for refractory hypertensives and in general. |

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| Staessen J, Byttebier G, Buntinx F, Celis H, O'Brien E, Fagard R / Anti-hypertensive treatment based on conventional or ambulatory blood pressure measurement: a randomized controlled trial / Journal of the American Medical Association / 1997 | Randomized clinical trial | Outcomes studied were: clinical BP and ABP; intensity of drug treatment; electrocardiographic and echocardiographic left ventricular mass, symptoms reported by questionnaire; cost. (conventional and ambulatory BPs were assessed in addition to self-administered questionnaires, electrocardiograms, imaging, and Doppler echocardiography).<br><br>Objective of study was to compare conventional blood pressure measurement and ABP measurement in the management of hypertensives. | n=419<br><br>Age >18 years whose untreated diastolic BP on clinic measurement averaged 95 mmHg or higher, randomized to clinic or ambulatory BP arms | Adjustment of anti-hypertensive treatment based on ABPM instead of conventional BP measurement led to less intensive drug treatment with preservation of BP control, general well-being, and inhibition of left ventricular enlargement but did not reduce the overall costs of anti-hypertensive treatment over a six month period.<br><br>Author concludes that ABPM instead of clinic measurement may lead to less intensive drug treatment with preservation of BP control and general well-being, however, ABPM does not seem to reduce the short-term costs of anti-hypertensive treatment. Author says that whether these conclusions would still hold true in the long term, especially after accounting for morbidity and mortality, remains to be elucidated. | Surrogate outcomes were measured. |

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| Staessen J, Thijs L, Fagard R et al / Predicting cardiovascular risk using conventional vs ambulatory blood pressure in older patients with systolic hypertension / Journal of the American Medical Association / 1999 | Sub-study to a double-blind placebo-controlled trial | Outcomes studied were total and cardiovascular mortality, all cardiovascular end points, fatal and nonfatal stroke, and fatal and nonfatal cardiac end points. (All major end-points were ascertained by reviewing the local patient files and other source documents). Cardiac endopoints included fatal and nonfatal heart failure, fatal and nonfatal myocardial infarction, and sudden death).<br><br>Aim of study was to compare the prognostic significance of conventional and ABP measurement in older patients with systolic hypertension. | n=808<br><br>Mean age of 69.6 +/- 6.2 years<br><br>BP level on clinic measurement at baseline was 160-219 mmHg for systolic and <95 mmHg for diastolic | Authors concluded that in untreated older patients with isolated systolic hypertension, ambulatory systolic BP was a significant predictor of cardiovascular risk over and above conventional BP.<br><br>At randomization, the cardiovascular risk conferred by a conventional systolic BP of 160 mmHg was similar to that associated with a 24hr, daytime, and nightime systolic BP of 142, 145, and 132 mmHg respectively. | Clinical outcomes were studied (example: cardiovascular mortality). |

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| Verdecchia P / Prognostic significance of the white coat effect / Hypertension / 1997 | Case-series | Outcomes studied were fatal cardiovascular morbidity and mortality (outcomes assessed through clinic BP measurements, ABP measurements, echocardiography, and electrocardiography)<br><br>Analyzed the PIUMA study database to investigate correlates and the prognostic significance of the difference between clinic and ambulatory BPs before treatment, taken as a surrogate measure of the white coat effect.<br><br>Observation period was up to 9 years | n=1522, 51% males, 49% females<br>All subjects were enrolled in PIUMA study (details of PIUMA study were not described in this article)<br><br>Mean age was 52 years<br><br>All subjects had clinic systolic BP of 140 mmHg or higher and/or diastolic of 90 mmHg or higher.<br><br>Inclusion criteria: no previous treatment for hypertension or withdrawal from anti-hypertensive drugs at least 4 weeks before the study; no clinic or laboratory evidence of heart failure, coronary heart disease, valvular defects, or secondary causes of hypertension; at least one valid BP measurement per hour over the 24hours. | Author proposed that cardiovascular morbidity and mortality rates did not differ among the four quartiles of the distribution of the difference between clinic BP and average daytime ambulatory BP.<br><br>Author concluded that clinic-ambulatory difference (a measure of white coat effect) does not predict cardiovascular morbidity and mortality in subjects with essential hypertension. | Health outcomes were studied.<br><br>Important to note that author makes a distinction between the definition of white coat effect and white coat hypertension. They are not synonymous. Hypertensive patients (who by definition do not have white coat hypertension) can display white coat effects.<br><br>It is unclear whether subjects with BP below threshold for hypertension when measured by ABP (white coat hypertensives) were included in the study. |