

**ORIGINAL RESEARCH**

How in-office and ambulatory BP monitoring compare: A systematic review and meta-analysis

Isolated office BP measurement is insufficient to confirm or rule out poorly controlled hypertension, and it increases the likelihood of under- or overestimating BP control.

ABSTRACT

Purpose ► We performed a literature review and meta-analysis to ascertain the validity of office blood pressure (BP) measurement in a primary care setting, using ambulatory blood pressure measurement (ABPM) as a benchmark in the monitoring of hypertensive patients receiving treatment.

Methods ► We conducted a literature search for studies published up to December 2013 that included hypertensive patients receiving treatment in a primary care setting. We compared the mean office BP with readings obtained by ABPM. We summarized the diagnostic accuracy of office BP with respect to ABPM in terms of sensitivity, specificity, and positive and negative likelihood ratios (LR), with a 95% confidence interval (CI).

Results ► Only 12 studies met the inclusion criteria and contained data to calculate the differences between the means of office and ambulatory BP measurements. Five were suitable for calculating sensitivity, specificity, and likelihood ratios, and 4 contained sufficient extractable data for meta-analysis. Compared with ABPM (thresholds of 140/90 mm Hg for office BP; 130/80 mmHg for ABPM) in diagnosing uncontrolled BP, office BP measurement had a sensitivity of 81.9% (95% CI, 74.8%-87%) and specificity of 41.1% (95% CI, 35.1%-48.4%). Positive LR was 1.35 (95% CI,

1.32-1.38), and the negative LR was 0.44 (95% CI, 0.37-0.53).

Conclusion ► Likelihood ratios show that isolated BP measurement in the office does not confirm or rule out the presence of poor BP control. Likelihood of underestimating or overestimating BP control is high when relying on in-office BP measurement alone.

A growing body of evidence supports more frequent use of ambulatory blood pressure monitoring (ABPM) to confirm a diagnosis of hypertension¹ and to monitor blood pressure (BP) response to treatment.² The Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure has long accepted ABPM for diagnosis of hypertension,³ and many clinicians consider ABPM the reference standard for diagnosing true hypertension and for accurately assessing associated cardiovascular risk in adults, regardless of office BP readings.⁴ The US Preventive Services Task Force (USPSTF) recommends obtaining BP measurements outside the clinical setting to confirm a diagnosis of hypertension before starting treatment.⁵ The USPSTF also asserts that elevated 24-hour ambulatory systolic BP is consistently and significantly associated with stroke and other cardiovascular events independent of office BP read-

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Likelihood ratios show that isolated in-office blood pressure measurement does not confirm or rule out poor BP control.

ings and has greater predictive value than office monitoring.⁵ The USPSTF concludes that ABPM, because of its large evidence base, is the best confirmatory test for hypertension.⁶ The recommendation of the American Academy of Family Physicians is similar to that of the USPSTF.⁷

■ The challenge. Despite the considerable support for ABPM, this method of BP measurement is still not sufficiently integrated into primary care. And some guidelines, such as those of the European Society of Hypertension, continue to restrict its use in diagnosis and in managing treatment.⁸

But ABPM's advantages are numerous. Ambulatory monitors, which can record BP for 24 hours, are typically programmed to take readings every 15 to 30 minutes, providing estimates of mean daytime and nighttime BP and revealing an individual's circadian pattern of BP.⁹⁻¹⁰ Ambulatory BP values usually considered the uppermost limit of normal are 135/85 mm Hg (day), 120/70 mm Hg (night), and 130/80 mm Hg (24 hour).⁸

Office BP monitoring, usually performed manually by medical staff, has 2 main drawbacks: the well-known white-coat effect experienced by many patients, and the relatively small number of possible measurements. A more reliable in-office BP estimation of BP would require repeated measurements at each of several visits.

By comparing ABPM and office measurements, 4 clinical findings are possible: isolated clinic or office (white-coat) hypertension (ICH); isolated ambulatory (masked) hypertension (IAH); consistent normotension; or sustained hypertension. With ICH, BP is high in the office and normal with ABPM. With IAH, BP is normal in the office and high with ABPM. With consistent normotension and sustained hypertension, BP readings with both types of measurement agree.^{8,9}

In patients being treated for hypertension, ICH leads to an overestimation of uncontrolled BP and may result in overtreatment. The cardiovascular risk, although controversial, is usually lower than in patients diagnosed with sustained hypertension.¹¹ IAH leads to an underestimation of uncontrolled BP and may result in undertreatment; its associated cardiovascular risk is similar to

that of sustained hypertension.¹²

■ Our research objective. We recently published a study conducted with 137 hypertensive patients in a primary care center.¹³ Our conclusion was that in-office measurement of BP had insufficient clinical validity to be recommended as a sole method of monitoring BP control. In accurately classifying BP as controlled or uncontrolled, clinic measurement agreed with 24h-ABPM in just 64.2% of cases.¹³

In our present study, we performed a literature review and meta-analysis to ascertain the validity of office BP measurement in a primary care setting, using ABPM as a benchmark in the monitoring of hypertensive patients receiving treatment.

METHODS

Most published studies comparing conventional office BP measurement with ABPM have been conducted with patients not taking antihypertensive medication. We excluded these studies and conducted a literature search for studies published up to December 2013 that included hypertensive patients receiving treatment in a primary care setting.

We searched Medline (from 1950 onward) and the Cochrane Database of Systematic Reviews. For the Medline search, we combined keywords for office BP, hypertension, and ambulatory BP with keywords for outpatient setting and primary care, using the following syntax: (((“clinic blood pressure” OR “office blood pressure” OR “casual blood pressure”))) AND (“hypertension” AND (((“24-h ambulatory blood pressure”) OR “24 h ambulatory blood pressure”) OR “24 hour ambulatory blood pressure”) OR “blood pressure monitoring, ambulatory”[Mesh]) AND ((((((“outpatient setting”) OR “primary care”) OR “family care”) OR “family physician”) OR “family practice”) OR “general practice”)). We chose studies published in English and reviewed the titles and abstracts of identified articles.

With the aim of identifying additional candidate studies, we reviewed the reference lists of eligible primary studies, narrative reviews, and systematic reviews. The studies were generally of good quality and used

appropriate statistical methods. Only primary studies qualified for meta-analysis.

Inclusion and exclusion criteria

Acceptable studies had to be conducted in a primary care setting with patients being treated for hypertension, and had to provide data comparing office BP measurement with ABPM. We excluded studies in which participants were treated in the hospital, were untreated, or had not been diagnosed with hypertension.

The quality of the studies included in the meta-analysis was judged by 2 independent observers according to the following criteria: the clear classification and initial comparison of both measurements; explicit and defined diagnostic criteria; compliance with the inclusion/exclusion criteria; and clear and precise definition of outcome variables.

Data extraction

We extracted the following data from each included study: study population, number of patients included, age, gender distribution, number of measurements (ambulatory and office BP), equipment validation, mean office and ambulatory BP, and the period of ambulatory BP measurement. We included adult patients of all ages, and we compared the mean office BP with those obtained by ABPM in hypertensive patients.

STATISTICAL ANALYSIS

For each study, we summarized the diagnostic accuracy of office BP with respect to ABPM in terms of sensitivity, specificity, and positive and negative likelihood ratios (LRs), with the 95% confidence interval (CI), if available. If these rates were not directly reported in the original papers, we used the published data to calculate them.

We used the R v2.15.1 software with the “mada” package for meta-analysis.¹⁴ Although a bivariate approach is preferred for the meta-analysis of diagnostic accuracy, it cannot be recommended if the number of primary studies to pool is too small,¹⁴ as happened in our case. Therefore, we used a univariate approach and pooled summary statistics for positive LR, negative LR, and the

diagnostic odds ratio (DOR) with their 95% confidence intervals. We used the DerSimonian-Laird method to perform a random-effect meta-analysis. To explore heterogeneity between the studies, we used the Cochran’s Q heterogeneity test, I² index, and Galbraith and L’Abbé plots.

RESULTS

Our search identified 237 studies, only 12 of which met the inclusion criteria and contained data to calculate the differences between the means of office and ambulatory BP measurements (TABLES 1 AND 2).¹⁵⁻²⁶ Of these 12 studies, 5 were suitable for calculating sensitivity, specificity, and LR (TABLE 3),^{16,18,22,24,26} and 4 contained sufficient extractable data for meta-analysis. The study by Little et al¹⁸ was not included in the meta-analysis, as the number of true-positive, true-negative, false-positive, and false-negative results could not be deduced from published data.

The studies differed in sample size (40-31,530), patient ages (mean, 55-72.8 years), sex (percentage of men, 31%-52.9%), and number of measurements for office BP (1-9) and ABPM (32-96) (TABLE 1),¹⁵⁻²⁶ as well as in daytime and nighttime periods for ABPM and BP thresholds, and in differences between the mean office and ambulatory BPs (TABLE 2).¹⁵⁻²⁶

In general, the mean office BP measurements were higher than those obtained with ABPM in any period—from 5/0 mm Hg to 27.4/10.1 mm Hg in the day, and from 7.9/6.3 mm Hg to 31.2/13.7 mm Hg over 24 hours (TABLE 2).¹⁵⁻²⁶

Compared with ABPM in diagnosing uncontrolled BP, office BP measurement had a sensitivity of 55.7% to 91.2% and a specificity of 25.8% to 61.8% (depending on whether the measure was carried out by the doctor or nurse¹⁸); positive LR ranged from 1.2 to 1.4, and negative LR from 0.3 to 0.72 (TABLE 3).^{16,18,22,24,26}

For meta-analysis, we pooled studies with the same thresholds (140/90 mm Hg for office BP; 130/80 mm Hg for ABPM), with diagnostic accuracy of office BP expressed as pooled positive and negative LR, and as pooled DOR. The meta-analysis revealed that the pooled positive LR was 1.35 (95% CI, 1.32-1.38), and the pooled negative LR was



The likelihood of under- or overestimating BP control is high when relying on in-office measurement alone.

TABLE 1

Methods of primary-care studies in ambulatory vs office monitoring of blood pressure

Study	N	Age (years); mean ± SD (if available)	Men (%)	Study population	No. of measurements		Equipment validation
					Ambulatory	Office	
Myers 1995 ¹⁵	147	64 ± 1	38.1	Primary care	>56 (x2)	2 (N)	Yes
Imai 1996 ¹⁶	285*	66.5 ± 9.2	31+	General population	46.5 ± 3.8*	2	Yes
Taylor 1998 ¹⁷	40			Primary care	96	1	Yes
Little 2002 ¹⁸	200	>65: 33%	46	Primary care	32	9	Yes
Bur 2002 ¹⁹	736	55 ± 14	49.1	Hypertension unit, hospital	64	3	Yes
Lindbæk 2003 ²⁰	107	60.3 ± 10.5	51	Primary care	N/A	2	N/A
Martinez 2006 ²¹	225	61.8 ± 10.5	51.1	Primary care	40	6 (D)	Yes
Sierra 2007 ²²	31530	♂ 57.2 ± 13.6	52.9	Primary care and hospital	>48	2	Yes
		♀ 61 ± 13.6					
Gómez 2008 ²³	241	63.7 ± 12.2	46.9	Primary care	>48	2 (D)	Yes
Banegas 2008 ²⁴	♂15212 ♀13936	60.1 ± 12.4	52.2	Primary care	72	2	Yes
		63.9 ± 12.4					
Zaninelli 2010 ²⁵	1768	61.1 ± 12	47.7	Primary care	78	3 (D)	Yes
Llisterri 2011 ²⁶	1028	72.8	47.3	Primary care and hypertension unit, hospital	>48	2	Yes

D, doctor office readings; N, nurse office readings; N/A, not available; SD, standard deviation; ♂, male; ♀, female.

*In Imai, N is treated patients only, and the mean number of measurements was 46.5 ± 3.8; percentage of men is taken from whole sample, including treated and untreated patients.

0.44 (95% CI, 0.37-0.53). The pooled DOR was 3.47 (95% CI, 3.02-3.98). Sensitivity was 81.9% (95% CI, 74.8%-87%) and specificity was 41.1% (95% CI, 35.1%-48.4%).

One study¹⁶ had a slightly different ambulatory diagnostic threshold (133/78 mm Hg), so we excluded it from a second meta-analysis. Results after the exclusion did not change significantly: positive LR was 1.39 (95% CI, 1.34-1.45); negative LR was 0.38 (95% CI, 0.33-0.44); and DOR was 3.77 (95% CI, 3.31-4.43).

In conclusion, the use of office-based BP readings in the outpatient clinic does not correlate well with ABPM. Therefore, caution must be used when making management decisions based solely on in-office readings of BP.

DISCUSSION

The European Society of Hypertension still regards office BP measurement as the gold

standard in screening for, diagnosing, and managing hypertension. As previously mentioned, though, office measurements are usually handled by medical staff and can be compromised by the white-coat effect and a small number of measurements. The USPSTF now considers ABPM the reference standard in primary care to diagnose hypertension in adults, to corroborate or contradict office-based determinations of elevated BP (whether based on single or repeated-interval measurements), and to avoid over-treatment of individuals displaying elevated office BP yet proven normotensive by ABPM.^{4,7} The recommendation of the American Academy of Family Physicians is similar to that of the USPSTF.⁷ Therefore, evidence supports ABPM as the reference standard for confirming elevated office BP screening results to avoid misdiagnosis and over-treatment of individuals with isolated clinic hypertension.⁷

TABLE 2

Results of studies comparing ABPM with in-office blood pressure monitoring in hypertensive patients

Study	Mean office BP, systolic/diastolic (mm Hg)	Period of ambulatory BP	Mean ambulatory BP, systolic/diastolic (mm Hg)	Difference: mean office BP – mean ambulatory BP, systolic/diastolic (mm Hg)
Myers 1995 ¹⁵	137/78 (N)	Daytime	132/78	5/0 (N)
	146/87 (D)			14/9 (D)
Imai 1996 ¹⁶	139/76	24 h	128/74	11/2
Taylor 1998 ¹⁷	150/90	24 h	131/79	19/11
		Daytime*	137/83	13/7
		Nighttime*	116/70	34/20
Little 2002 ¹⁸	N/A	Daytime (07-23 h)	N/A	18.9/11.4 (D)
				9/9.8 (N1)
				5.2/8.3 (N2)
Bur 2002 ¹⁹	149/87	Daytime (06-22 h)	135/79 (24 h)	14/8
Lindbæk 2003 ²⁰	169.6/96.4	24 h	141.1/85.6	28.6/10.8
Martinez 2006 ²¹	156/91	Daytime (10-20 h)	139/82	17/9
Sierra 2007 ²² (Primary care and hospital units)	149.6/87.8	24 h	130.7/77.1	18.9/10.7
		Daytime*	133.8/80	15.8/7.8
		Nighttime*	121.8/69	27.8/18.8
Gómez 2008 ²³	155.8/87.6	24 h	124.6/73.9	31.2/13.7
		Daytime*	128.4/77.5	27.4/10.1
		Nighttime*	115.4/65.5	40.4/22.1
Banegas 2008 ²⁴	♂149.7/87.6 ♀152/86.2	24 h	♂ 131.6/78.2	♂ 18.1/9.4
			♀ 129.8/73.3	♀ 22.2/12.9
		Daytime*	♂ 134.4/80.8	♂ 15.3/6.8
			♀ 132.5/76	♀ 19.5/10.2
		Nighttime*	♂ 123.2/70.6	♂ 26.5/17
			♀ 122.4/66.1	♀ 29.6/20.1
Zaninelli 2010 ²⁵	144/85.8	24 h	136.1/79.5	7.9/6.3
		Daytime (7-22 h)	139.4/81.8	4.6/4
		Nighttime (22-7 h)	124.2/71.2	19.8/14.6
Llisterri 2011 ²⁶ (≥65 years)	146.7/81.1	24 h	128.5/70.8	18.2/10.3
		Daytime*	129.9/72.4	16.8/8.7
		Nighttime*	122.2/64.5	24.5/16.6

ABPM, ambulatory blood pressure monitoring; BP, blood pressure; CI, confidence interval; D, doctor office readings; N, nurse office readings; N1, nurse, mercury sphygmomanometers, visit 1; N2, nurse, mercury sphygmomanometers, visit 2; N/A, not available; SD, standard deviation; ♂, male; ♀, female.

*Daytime and nighttime periods were calculated based on participants' diary reports.

How office measurements stack up against ABPM

Checking the validity of decisions in clinical practice is extremely important for

patient management. One of the tools used for decision-making is an estimate of the LR.

We used the LR to assess the value of office BP measurement in determining controlled

TABLE 3

Sensitivity, specificity, and likelihood ratios for office monitoring compared with ABPM

Study	Diagnostic thresholds, systolic/diastolic (mm Hg)		Sensitivity (95% CI)	Specificity (95% CI)	Likelihood ratio (95% CI)	
	Ambulatory	Clinic			Positive	Negative
Imai 1996 ¹⁶	133/78	140/90	55.66 (45.71-65.2)	61.45 (53.87-68.53)	1.44 (1.12-1.86)	0.72 (0.57-0.92)
Little 2002 ¹⁸		140/90	91.2*	25.8*	1.2*	0.3*
			83.3 [†]	41.2 [†]	1.4 [†]	0.4 [†]
			80.8 [‡]	61.8 [‡]	2.1 [‡]	0.3 [‡]
Sierra 2007 ²²	135/85	140/90	88.5 (88-88.9)	33.3 (32.6-34.1)	1.33 (1.31-1.34)	0.35 (0.33-0.36)
	130/80		86.57 (86.1-87.02)	39.4 (38.4-40.3)	1.43 (1.41-1.45)	0.34 (0.33-0.36)
Banegas 2008 ²⁴	130/80	140/90	87.73 (87.22-88.23)	35.6 (34.8-36.4)	1.36 (1.34-1.38)	0.34 (0.33-0.36)
Llisterri 2011 ²⁶	130/80	140/90	75.2 (71.1-78.9)	45.4 (41.1-49.8)	1.4 (1.3-1.5)	0.6 (0.5-0.6)

ABPM, ambulatory blood pressure monitoring; CI, confidence interval.

*In Little:¹⁸ measurements taken by doctor (only systolic BP); [†]measurements taken by nurse (visit 1) (only systolic BP); [‡]measurements taken by nurse (visit 2) (only systolic BP).

or uncontrolled BP. A high LR (eg, >10) indicates that the office BP can be used to rule in the disease (uncontrolled BP) with a high probability, while a low LR (eg, <0.1) could rule it out. An LR of around one indicates that the office BP measurement cannot rule the diagnosis of uncontrolled BP in or out.²⁷ In our meta-analysis, the positive LR is 1.35 and negative LR is 0.44. Therefore, in treated hypertensive patients, an indication of uncontrolled BP as measured in the clinic does not confirm a diagnosis of uncontrolled BP (as judged by the reference standard of ABPM). On the other hand, the negative LR means that normal office BP does not rule out uncontrolled BP, which may be detected with ABPM. Consequently, the measurement of BP in the office does not change the degree of (un)certainly of adequate control of BP. This knowledge is important, to avoid overtreatment of white coat hypertension and undertreatment of masked cases.

As previously mentioned, we reported similar results in a study designed to deter-

mine the validity of office BP measurement in a primary care setting compared with ABPM.¹³ In that paper, the level of agreement between both methods was poor, indicating that clinic measurements could not be recommended as a single method of BP control in hypertensive patients.

The use of ABPM in diagnosing hypertension is likely to increase as a consequence of some guideline updates.² Our study emphasizes the importance of their use in the control of hypertensive patients.

Another published meta-analysis¹ investigated the validity of office BP for the diagnosis of hypertension in untreated patients, with diagnostic thresholds for arterial hypertension set at 140/90 mm Hg for office measurement, and 135/85 mm Hg for ABPM. In that paper, the sensitivity of office BP was 74.6% (95% CI, 60.7-84.8) and the specificity was 74.6% (95% CI, 47.9-90.4).

In our present study carried out with hypertensive patients receiving treatment, we obtained a slightly higher sensitivity

value of 81.9% (within the CI of this meta-analysis) and a lower specificity of 41.1%. Therefore, the discordance between office BP and ABPM seems to be similar for the diagnosis of hypertension and the classification of hypertension as being well or poorly controlled. This confirms the low validity of the office BP, both for diagnosis and monitoring of hypertensive patients.

Strengths of our study. The study focused on (treated) hypertensive patients in a primary care setting, where hypertension is most often managed. It confirms that ABPM is indispensable to a good clinical practice.

Limitations of our study are those inherent to meta-analyses. The main weakness of our study is the paucity of data available regarding the utility of ABPM for monitoring BP control with treatment in a primary care setting. Other limitations are the variability in BP thresholds used, the number of measurements performed, and the ambulatory BP devices used. These differences could contribute to the observed heterogeneity.

Application of our results must take into account that we included only those studies performed in a primary care setting with treated hypertensive patients.

Moreover, this study was not designed to evaluate the consequences of over- and undertreatment of blood pressure, nor to address the accuracy of automated blood pressure machines or newer health and fitness devices.

Implications for practice, policy, or future research. Alternative monitoring methods are home BP self-measurement and automated 30-minute clinic BP measurement.²⁸ However, ABPM provides us with unique information about the BP pattern (dipping or non-dipping), BP variability, and mean nighttime BP. This paper establishes that the measurement of BP in the office is not an accurate method to monitor BP control. ABPM should be incorporated in usual clinical practice in primary care. Although the consequences of ambulatory monitoring are not the focus of this study, we acknowledge that the decision to incorporate ABPM in clinical practice depends on the availability of ambulatory devices, proper training of

health care workers, and a cost-effectiveness analysis of its use.

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➤ See the related PURL on ambulatory BP monitoring at <http://bit.ly/2i24hoi>.

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