Levels of Office Blood Pressure and Their Operating Characteristics for Detecting Masked Hypertension Based on Ambulatory Blood Pressure Monitoring

Anthony J. Viera,[1,2] Feng-Chang Lin,[2,3] Laura A. Tuttle,[1,2] Daichi Shimbo,[4] Keith M. Diaz,[4] Emily Olsson,[1,2] Kristin Stankevitz,[1,2] and Alan L. Hinderliter[2,5]

BACKGROUND
Masked hypertension (MH)—nonelevated office blood pressure (BP) with elevated out-of-office BP average—conveys cardiovascular risk similar to or approaching sustained hypertension, making its detection of potential clinical importance. However, it may not be feasible or cost-effective to perform ambulatory BP monitoring (ABPM) on all patients with a nonelevated office BP. There likely exists a level of office BP below which ABPM is not warranted because the probability of MH is low.

METHODS
We analyzed data from 294 adults aged ≥30 years not on BP-lowering medication with office BP <140/90 mm Hg, all of whom underwent 24-hour ABPM. We calculated sensitivity, false-positive rate, and likelihood ratios (LRs) for the range of office BP cutoffs from 110 to 138 mm Hg systolic and from 68 to 88 mm Hg diastolic for detecting MH.

RESULTS
The systolic BP cutoff with the highest +LR for detecting MH (1.8) was 120 mm Hg, and the diastolic cutoff with the highest +LR (2.4) was 82 mm Hg. However, the systolic level of 120 mm Hg had a false-positive rate of 42%, and the diastolic level of 82 mm Hg had a sensitivity of only 39%.

CONCLUSIONS
The cutoff of office BP with the best overall operating characteristics for diagnosing MH is approximately 120/82 mm Hg. However, this cutoff may have an unacceptably high false-positive rate. Clinical risk tools to identify patients with nonelevated office BP for whom ABPM should be considered will likely need to include factors in addition to office BP.

Keywords: ambulatory blood pressure monitoring; blood pressure; diagnosis; hypertension; masked hypertension; screening.

doi:10.1093/ajh/hpu099

The pairing of the average of blood pressure (BP) measurements derived from out-of-office BP monitoring with office BP measurements yields 4 possible diagnostic categories (Figure 1). White-coat hypertension refers to the scenario of elevated office BP with nonelevated out-of-office average. Based on cost-savings from not treating such patients, clinical guidelines recently developed by the National Institute for Healthcare and Clinical Excellence in the United Kingdom recommend ambulatory BP monitoring (ABPM) for patients with elevated office BP to confirm hypertension before initiating drug treatment.[1,2]

What is not considered in the National Institute for Healthcare and Clinical Excellence guidelines and most other guidelines, however, is that approximately 10% of the general population, and a high proportion of clinic patients, has masked hypertension (MH).[3,4] MH is defined as nonelevated office BP with elevated average out-of-office BP, and it conveys cardiovascular disease (CVD) risk approaching that associated with sustained hypertension.[5–8]

In current US practice, an initially elevated BP in the office (which can be considered a positive screening measurement) calls for follow-up office BP measurements to confirm or refute the presence of hypertension.[9] The follow-up office measurements could be considered the diagnostic measurements, and there is generally no further discerning diagnostic testing performed. Additionally, in current practice, a nonelevated office BP would not be an indication for further

Correspondence: Anthony J. Viera (anthony_viera@med.unc.edu).

Initially submitted January 7, 2014; date of first revision February 26, 2014; accepted for publication April 26, 2014; online publication June 4, 2014.

[1]Department of Family Medicine, University of North Carolina School of Medicine, Chapel Hill, North Carolina; [2]Hypertension Research Program, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina; [3]Department of Biostatistics, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina; [4]Department of Medicine, Center for Behavioral Cardiovascular Health, Columbia University Medical Center, New York, New York; [5]Department of Medicine, Division of Cardiology, University of North Carolina School of Medicine, Chapel Hill, North Carolina.

		Office BP average	
		≥140/90 mm Hg	<140/90 mm Hg
Out-of-office BP average	≥135/85* mm Hg	Sustained hypertension	Masked hypertension
	<135/85* mm Hg	White-coat hypertension	Sustained normotension

Note that classification is based on either systolic, diastolic, or both

*<130/80 mm Hg if sleep measurements from 24-hour ambulatory BP data included

Figure 1. Categories of blood pressure (BP) based on pairing office and out-of-office measurements. Note that classification is based on either systolic, diastolic, or both. The asterisk (*) indicates that <130/80 mm Hg was used if sleep measurements form 24-hour ambulatory BP data were included.

testing outside of routine office screening at periodic health checkups. Unfortunately, this approach leads to misclassification (i.e., misdiagnosis) of many people when compared with measurements obtained from ABPM, which provides the best assessment of someone's true BP status.[10] Patients with an elevated office BP may have normal ambulatory BP (a false-positive office screen), and patients with a normal office BP may have elevated ambulatory BP (a false-negative office screen).

It likely would not be feasible or cost-effective to perform ABPM on all patients with nonelevated office BP (to rule out MH) in addition to the suggested strategy of performing ABPM on all patients with elevated office BP (to rule out white-coat hypertension).[2] Therefore, it would be valuable to have a strategy to guide clinical decision-making about which patients with nonelevated office BP ought to have ABPM. Previous studies have shown that MH is more likely among patients with office prehypertension, particularly in the upper (borderline) range (e.g., 130–139/85–89 mm Hg).[4,11] An approach that uses screening office BP level to guide ABPM testing decisions for persons with nonelevated office BP should be considered. There is likely a BP level below which very few people have MH. Using diagnostic out-of-office measurements (e.g., ABPM) for people with a BP above such a level may enable those with MH to be identified while minimizing excess testing. The goal of this analysis is to begin to define the office BP level above which ABPM should be considered for detecting MH.

METHODS

Study recruitment and setting

For a larger BP measurement study, we recruited 420 primary care patients aged ≥30 years with no diagnosis of hypertension and not taking any BP-lowering medications. The most recent BP measured in the outpatient clinic had to be between 120 and 149 mm Hg systolic or 80 and 95 mm Hg diastolic and not >149/95 mm Hg. Exclusion criteria included pregnancy, dementia, any condition that would preclude wearing an ambulatory BP monitor, and persistent atrial fibrillation or other arrhythmia. We also excluded potential enrollees if the initial office BP at the research visit was ≥160/100 mm Hg. All study procedures took place in a clinical research center. For this analysis, only the 294 participants with a research visit office BP average <140/90 mm Hg were included.

Office BP

After check-in procedures at the study visit, participants were placed in an exam room in the clinical research center. After at least a 5-minute rest, same-arm BP was measured 3 times with the subject appropriately prepared and positioned[9] using a validated office-type oscillometric device (Welch Allyn Vital Signs Welch Allyn, Skaneateles Falls, NY)[12] equipped with an appropriately sized cuff. The second and third measurements were averaged to determine the participant's office BP for the visit.

Ambulatory BP monitoring

At the conclusion of the study visit, participants were fitted with an Oscar 2 oscillometric monitor (Suntech Medical, Morrisville, NC) with an appropriately sized cuff for 24-hour ambulatory BP monitoring. The Oscar 2 has been validated for use in adults by both the British Hypertension Society protocol and the International Protocol for the validation of BP measuring devices.[13,14] The monitors were programmed to measure BP at 30-minute intervals from 6 AM to 10 PM and at 1-hour intervals from 10 PM to 6 AM. We chose these intervals rather than more frequent intervals to minimize participant burden. For most participants, we used a diary to define sleep and awake periods. For those missing a diary (n = 95), we defined awake as 10 AM to 10 PM and the sleep period as midnight to 6 AM. Maximum BP measurement time was limited to <140 seconds, and the monitors were set for a maximum pressure of 220 mm Hg. Participants were encouraged to leave the cuff on during the entire monitoring period and to hold their cuffed arm as still as possible during cuff inflation and deflation to ensure that the monitor would acquire an accurate reading and were informed that faulty readings would trigger a repeat measurement. A minimum of 14 awake and 6 sleep readings were required for an ABPM session to be considered adequate.[15]

Additional variables

We collected demographic information, including age, self-reported race, education level, and insurance status. We asked participants to rate their health using a standard question with answers ranging from poor to excellent.[16] We measured height and weight and calculated body mass index.

Analysis

We used the research visit office BP measurements and the corresponding 24-hour ABPM session to calculate the prevalence of MH among the study participants. We defined MH as office BP average <140/90 mm Hg with 24-hour ABPM average ≥130 mm Hg systolic or ≥80 mm Hg diastolic. We then calculated sensitivity and specificity for levels of office systolic BP from 110 mm Hg to 138 mm Hg and diastolic BP from 68 mm Hg to 88 mm Hg for diagnosing MH. From these data, we report sensitivity, false-positive rate (1 – specificity), positive likelihood ratio, and negative likelihood ratio. Sensitivity represents the proportion of people with MH who would be detected. Specificity represents the proportion of people without MH who would be classified as such; therefore 1 – specificity (i.e., false-positive rate) represents the proportion of people with normal ambulatory BP who would screen positive (and be tested unnecessarily). A likelihood ratio represents how many times more likely the screening result would be found in those with the outcome than without it. A likelihood ratio of 1 means the test is not helpful at all, in this case in distinguishing people who did and did not have MH.

We also present the receiver operator characteristic curves for both systolic and diastolic office BP measurements for detecting MH. Receiver operator characteristic curves plot the sensitivity against the false-positive rate across all levels of the screening test (in this case the office BP levels). We also created a scatterplot depicting the cutoff for which the optimal classification is reached based on the maximum positive likelihood ratio in systolic and diastolic office BP.

Study approval

This study was approved by the Office of Human Research Ethics at the University of North Carolina at Chapel Hill.

RESULTS

Participant characteristics

The mean ± SD age of the study sample participants was 47 ± 12 years. Most participants were aged 30–44 years (46%) or 45–64 years (43%) (Table 1). A small proportion was aged ≥65 years (11%). Approximately 22% were black. Nearly three-fourths were college graduates (74%), and nearly all (94%) reported good to excellent health. Most were overweight (30%) or obese (41%) and nonsmokers (92%). The majority were married or living with a partner. Most participants (72%) had >20 awake ambulatory BP measurements and at least 6 sleep measurements during their ABPM session. Only 1 participant did not have sufficient awake ambulatory BP monitor readings.

BP and prevalence of MH

The mean ± SD office BP average of participants at the initial research visit was 123/78 ± 8/7 mm Hg. The overall prevalence of MH based on the research office BP average and corresponding ABPM session average was 69% (95% confidence interval (CI) = 64%–75%) (Table 2). Among the subset of participants with systolic BP of 110–119 mm Hg, the prevalence was 51% (95% CI = 39%–62%). The prevalence increased to approximately 80% among the groups with systolic BP of 120–129 mm Hg and 130–139 mm Hg. A similar pattern was seen when participants were stratified by diastolic BP levels.

Sensitivity and specificity of systolic BP cutoffs

The sensitivity and false-positive rates (1 – specificity) for detecting MH in the study sample based on increasing levels of office systolic BP cutoffs from 110 mm Hg to 138 mm

Table 1. Participant characteristics (n = 294)

Characteristic	No.	%
Age group, y		
30–44	135	46
45–64	127	43
>65	32	11
Female sex	178	61
Race		
Black	66	22
White	217	74
Other	11	4
Hispanic ethnicity	14	5
Education level		
Some high school	5	2
High school graduate	16	5
Some college	56	19
College graduate	127	74
Insurance status		
Private	207	71
Public	38	13
Both	29	10
Uninsured	18	6
Self-reported health		
Excellent/very good	109	68
Good	77	26
Fair or poor	18	6
Nonsmoker	271	92
Drink alcohol	200	68
BMI		
Normal (<25 kg/m^2)	86	29
Overweight (25–29 kg/m^2)	88	30
Obese (≥30 kg/m^2)	120	41
Married or living with partner	183	62

Abbreviation: BMI, body mass index.

Hgmm are shown in Table 3 and depicted in Figure 2. Above the lowest included cutoff of 110 mm Hg, 97% of participants with MH would be detected, but the false-positive rate would be 87%. At the highest included cutoff of 138 mm Hg, there are very few false positives (1%), but the sensitivity drops to <1%. The cutoff of 120 mm Hg has a sensitivity of 76% with a false positive rate of 42%, yielding a positive likelihood ratio of 1.79.

Sensitivity and specificity of diastolic BP cutoffs

The sensitivity and false-positive rates (1 – specificity) for detecting MH in the study sample based on increasing levels of office diastolic BP cutoffs from 68 mm Hg to 88 mm Hg are shown in Table 4 and depicted in Figure 2. At the lowest included cutoff of 68 mm Hg, 95% of participants with MH would be detected, but the false-positive rate would be 82%. At the highest included cutoff of 88 mm Hg, there are very few false positives (1%), but the sensitivity is also very low (3%). A cutoff of 82 mm Hg has a sensitivity of 39% with a false positive rate of about 17%. The cutoff of 82 mm Hg yielded the best positive likelihood ratio based on a sensitivity of 39% and false-positive rate of 17%.

Table 2. Prevalence of masked hypertension among the study participants (n = 294) stratified by office blood pressure average

Office blood pressure	n/N (%)	(95% CI)
Overall	204/294 (69)	(64–75)
Systolic BP 110–119 mm Hg	39/77 (51)	(39–62)
Systolic BP 120–129 mm Hg	97/118 (82)	(74–88)
Systolic BP 130–139 mm Hg	63/82 (77)	(66–85)
Diastolic BP 75–79 mm Hg	50/73 (68)	(56–79)
Diastolic BP 80–84 mm Hg	63/76 (83)	(72–90)
Diastolic BP 85–89 mm Hg	41/50 (82)	(68–91)

Masked hypertension was defined as office blood pressure (BP) average <140/90 mm Hg with 24-hour ambulatory blood pressure monitoring average ≥130 mm Hg systolic or ≥80 mm Hg diastolic.
Abbreviation: CI, confidence interval.

Maximum positive likelihood ratio

As shown in Figure 3, the maximum positive likelihood ratio for an office systolic BP cutoff to detect MH is approximately 120 mm Hg. The maximum positive likelihood ratio for an office diastolic BP cutoff to detect MH is approximately 82 mm Hg. Using a cutoff that defines a positive screen as either a systolic BP >120 mm Hg or a diastolic BP >82 mm Hg, the sensitivity is 78% and false positive rate is 47%. The positive likelihood ratio is 1.68, which is slightly lower than the optimal positive likelihood ratio using only systolic BP.

DISCUSSION

Our data suggest that the office BP cutoff with the best operating characteristics to identify patients with MH is approximately 120/82 mm Hg (Tables 3 and 4; Figure 3). However, at this cutoff, the false-positive rate may be unacceptably high. That is, many of these patients would have a nonelevated ambulatory BP. The amount of excess testing would depend on the prevalence of MH in the population. For example, a prevalence of 69% MH (as observed in this analysis) would mean that out of 100 people with a systolic BP <140 mm Hg, 70 would screen positive (Figure 4), but 18 would be false positive (i.e., their ABPM average would not be elevated). The number of missed diagnoses also needs to be considered. Of the 30 who would screen negative, 17

Table 3. Diagnostic properties of varying screening systolic office blood pressure cutoffs to diagnose masked hypertension

Office systolic blood pressure (mm Hg)	Sensitivity	False-positive rate (1 − specificity)	Positive likelihood Ratio	Negative likelihood ratio
110	96.6%	86.7%	1.11	0.26
112	94.6%	76.7%	1.23	0.23
114	92.2%	73.3%	1.26	0.29
116	89.2%	62.2%	1.43	0.29
118	83.8%	52.2%	1.61	0.34
120	75.5%	42.2%	1.79	0.42
122	64.7%	38.9%	1.66	0.58
124	57.4%	34.4%	1.67	0.65
126	50.0%	28.9%	1.73	0.70
128	34.8%	25.6%	1.36	0.88
130	28.9%	21.1%	1.37	0.90
132	23.0%	14.4%	1.60	0.90
134	13.7%	8.9%	1.54	0.95
136	3.9%	5.6%	<1	1.02
138	0.5%	1.1%	<1	1.01

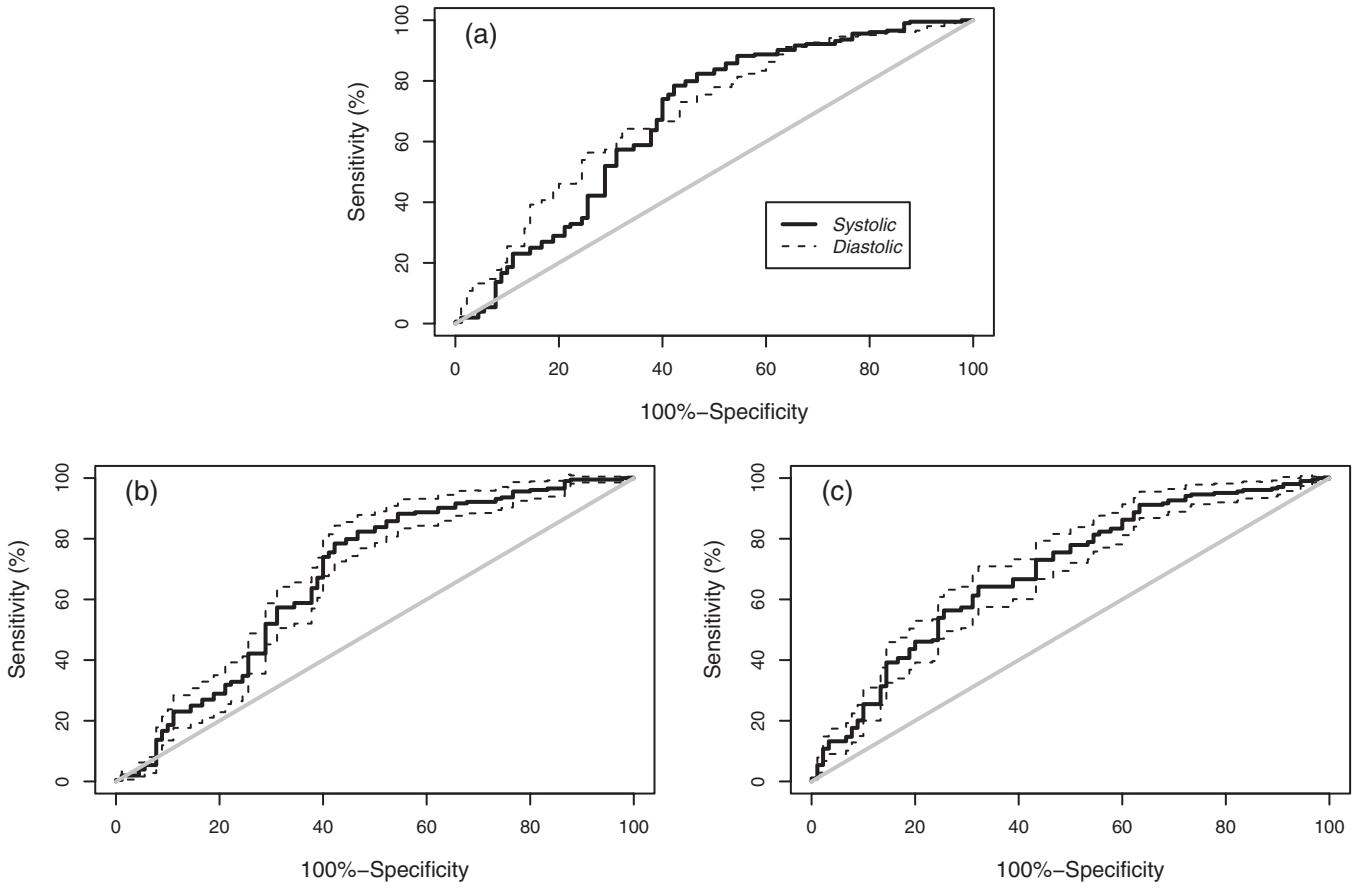

Figure 2. Receiver operator characteristic (ROC) curves for office blood pressure as a screening test for masked hypertension. (**a**) ROC curves for office systolic and diastolic blood pressure as a screening test for masked hypertension. (**b**) ROC curves for systolic office screening blood pressure levels. (**c**) ROC curves for diastolic office screening blood pressure levels. The dotted lines represent 95% confidence intervals.

Table 4. Diagnostic properties of varying screening diastolic office blood pressure cutoffs to diagnose masked hypertension

Office diastolic blood pressure (mm Hg)	Sensitivity	False-positive rate (1 − specificity)	Positive likelihood ratio	Negative likelihood ratio
68	95.1%	82.2%	1.16	0.28
70	91.7%	68.9%	1.33	0.27
72	83.3%	60.0%	1.39	0.42
74	77.9%	53.3%	1.46	0.47
76	66.7%	43.3%	1.54	0.59
78	56.4%	28.9%	1.95	0.61
80	46.6%	24.4%	1.91	0.71
82	39.2%	16.7%	2.35	0.73
84	25.5%	13.3%	1.91	0.86
86	13.2%	6.7%	1.99	0.93
88	3.4%	1.1%	3.09[a]	0.98

[a]This value is based on the ratio of two low percentages, so it has large variation.

would actually have MH that remains undetected (false negatives). If the prevalence of MH is lower, say 40%, 65 out of 100 would screen positive, more than half (35) of whom ultimately would not have MH. Of the 35 who would screen negative, 10 would have MH that remains undetected.

The potential clinical importance of detecting MH is evident from a number of studies demonstrating a high prevalence of target-organ damage in patients with this condition. For example, in 1 study, left ventricular mass index and carotid plaque among people with MH were compared with

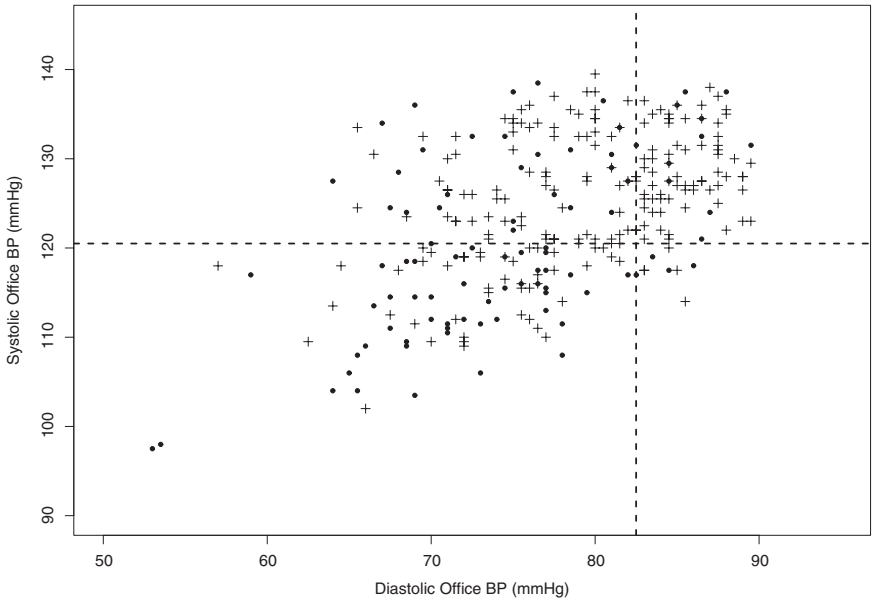

Figure 3. Scatterplot of systolic and diastolic office blood pressure (BP) for detecting masked hypertension. The + symbol indicates subjects who have masked hypertension. The • symbol indicates subjects who are normotensive. Horizontal and vertical dashed lines indicate the cutoff for which the maximum positive likelihood ratio is reached based on systolic office BP and diastolic office BP, respectively.

MH by ABPM

		Yes	No	Total
Office BP	**Positive**	52	18	70
	Negative	17	13	30
	Total	69	31	100

A. Using 69% prevalence of MH, 52 (0.75*69) screen true positive and 17 false negative; 13 (0.42*31) screen true negative and 18 screen false positive. The positive predictive value in this situation is 74% (52/70) and the negative predictive value is 43% (13/30).

MH by ABPM

		Yes	No	Total
Office BP	**Positive**	30	35	65
	Negative	10	25	35
	Total	40	60	100

B. Using 40% prevalence of MH, 30 (0.75*40) screen true positive and 10 false negative; 25 (0.42*60) screen true negative and 35 screen false positive. The positive predictive value in this situation is 46% (30/65) and the negative predictive value is 71% (25/35).

Figure 4. Examples of predictive values using cutoff of 120 mm Hg based on 2 different prevalence rates of masked hypertension (MH). (**a**) Using 69% prevalence of MH, 52 (0.75×69) screen true positive and 17 screen false negative; 13 (0.42×31) screen true negative and 18 screen false positive. The positive predictive value in this situation is 74% (52/70), and the negative predictive value is 43% (13/30). (**b**) Using 40% prevalence of MH, 30 (0.75×40) screen true positive and 10 screen false negative; 25 (0.42×60) screen true negative and 35 screen false positive. The positive predictive value in this situation is 46% (30/65), and the negative predictive value is 71% (25/35). Abbreviations: ABPM, ambulatory BP monitoring; BP, blood pressure.

those factors among people with true normotension and people with sustained hypertension.[5] The left ventricular mass index was 73 g/m^2 in the true normotensives, 86 g/m^2 in the masked hypertensives, and 90 g/m^2 in the sustained hypertensives. Carotid plaque was present in 15% of true normotensives and in 28% of both the masked and sustained hypertensives. In another study, left ventricular mass index in people with MH was 91 g/m^2, compared with 79 g/m^2 in true normotensives and 94 g/m^2 in people with sustained hypertension.[6] Thus, MH is associated with target-organ damage that is similar in magnitude to that observed in patients with sustained hypertension.

More important, there is also evidence of increased CVD events (stroke, myocardial infarction, cardiovascular mortality) in people with MH. A meta-analysis of 7 studies that included a total of 11,502 subjects followed over a mean of

8 years showed a 2-fold higher incidence of CVD events (hazard ratio (HR) = 2.00; 95% CI = 1.58–2.52) in people with MH compared with those with true normotension.[7] This risk approaches the risk conferred by sustained hypertension (HR = 2.28; 95% CI = 1.87–2.78).

Similar to our findings, other investigators have found that people with office BPs in the prehypertension range have a high prevalence (i.e., pretest probability) of MH. In a study of a community sample of 813 adults with prehypertension, the subset with BP in the 120–129/80–84 mm Hg range had a prevalence of MH of 27%, and those with BP in the 130–139/85–89 mm Hg range had a prevalence of MH of 52%.[12] Much of the elevated CVD risk of office prehypertension is attributable to MH.[17,18] Such findings suggest that office BP level may be an important factor in considering who to test for the presence of MH. However, our data indicate that office BP alone may not perform efficiently enough to guide these clinical decisions.

One critical question remaining to be answered is whether treatment of people identified with MH leads to a reduction in CVD morbidity and mortality. To move this area of hypertension research forward and permit testing to determine whether treatment of MH reduces CVD events, efficient strategies for identifying people with MH need to be developed. Our study suggests that no office BP level alone has an adequate sensitivity and specificity tradeoff. Therefore, other factors should be considered, such as age, sex,[19] and race. In addition, measures such as stress,[20] high pulse rate,[19] and smoking[21] could potentially be incorporated into a model to better define the group for whom testing is warranted. Further research is needed to develop and confirm such models using prospective studies.

Our measurements of office BP were taken in a research setting as opposed to a clinical setting. Research BPs tend to be lower than clinical measurements,[22] which may result in some participants being classified as having MH as opposed to sustained hypertension. However, we repeated the analyses using the eligibility office BP (the most recent BP taken in the clinic) and saw little differences. The prevalence of MH may be higher in our sample than in a general sample of primary care patients. However, although prevalence would affect the positive and negative predictive values of a screening test, it would not affect the actual operating characteristics (sensitivity and specificity) of the screening test itself.

An office BP level alone may not be sufficiently sensitive or specific to be used as a screening test to guide clinical decision-making about using ABPM in patients with nonelevated office BP. Further research might identify other easily measured clinical variables that could be incorporated, along with office BP, in predictive models to streamline diagnostic ABPM use. Additional cost-effectiveness analyses comparing strategies for accurately diagnosing ambulatory hypertension would also be informative.

ACKNOWLEDGMENTS

This work was supported by grant R01 HL098604 (to A.J.V.) from the National Heart Lung and Blood Institute. K.M.D. was supported by National Institutes of Health Diversity Supplement P01-HL047540-19S1.

DISCLOSURE

Dr. Viera serves on the Medical Advisory Board of Suntech Medical, manufacturer of the Oscar 2 ambulatory BP monitor.

REFERENCES

1. Lovibond K, Jowett S, Barton P, Caulfield M, Heneghan C, Hobbs FD, Hodgkinson J, Mant J, Martin U, Williams B, Wonderling D, McManus RJ. Cost-effectiveness of options for the diagnosis of high blood pressure in primary care: a modelling study. *Lancet* 2011; 378:1219–1230.
2. Krause T, Lovibond K, Caulfield M, McCormack T, Williams B; Guideline Development Group. Management of hypertension: summary of NICE guidance. *BMJ* 2011; 343:d4891.
3. Verberk WJ, Kessesl AG, de Leeuw PW. Prevalence, causes, and consequences of masked hypertension: a meta-analysis. *Am J Hypertens* 2008; 21:969–975.
4. Viera AJ, Hinderliter AL, Kshirsagar AV, Fine J, Dominik R. Reproducibility of masked hypertension in adults with untreated borderline office blood pressure: comparison of ambulatory and home monitoring. *Am J Hypertens* 2010; 23:1190–1197.
5. Liu JE, Roman MJ, Pini R, Schwartz JE, Pickering TG, Devereux RB. Cardiac and arterial target organ damage in adults with elevated ambulatory and normal office blood pressure. *Ann Intern Med* 1999; 13:564–572.
6. Sega R, Trocino G, Lanzarotti A, Carugo S, Cesana G, Schiavina R, Valagussa F, Bombelli M, Giannattasio C, Zanchetti A, Mancia G. Alterations of cardiac structure in patients with isolated office, ambulatory, or home hypertension: data from the general population (Pressione Arteriose Monitorate E Loro Associazioni [PAMELA] Study). *Circulation* 2001; 104:1385–1392.
7. 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.
8. Pierdomenico SD, Pannarle G, Rabbia F, Lapenna D, Licitra R, Zito M, Campanella M, Gaudio C, Veglio F, Cuccurullo F. Prognostic relevance of masked hypertension in subjects with prehypertension. *Am J Hypertens* 2008; 21:879–883.
9. Chobanian AV, Bakaris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr, Roccella EJ; National Heart, Lung, and Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; National High Blood Pressure Education Program Coordinating Committee. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension* 2003; 42:1206–1252.
10. Pickering TG, Shimbo D, Haas D. Ambulatory blood-pressure monitoring. *N Engl J Med* 2006; 354: 2368–2374.
11. Jones CR, Taylor K, Poston L, Shennan AH. Validation of the Welch Allyn Vital Signs oscillometric blood pressure monitor. *J Hum Hypertens* 2001; 15:191–195.
12. Shimbo D, Newman JD, Schwartz J. Masked hypertension and prehypertension: diagnostic overlap and interrelationships with left ventricular mass: the masked hypertension study. *Am J Hypertens* 2012; 25:664–671.
13. Jones SC, Bilous M, Winship S, Finn P, Goodwin J. Validation of the Oscar 2 oscillometric 24-hour ambulatory blood pressure monitor according to the International Protocol for the validation of blood pressure measuring devices. *Blood Press Monit* 2004; 9:219–223.
14. Goodwin J, Bilous M, Winship S, Finn P, Jones SC. Validation of the Oscar 2 oscillometric 24-hour ambulatory blood pressure monitor according to British Hypertension Society protocol. *Blood Press Monit* 2007; 12:113–117.
15. Viera AJ, Zhu S, Hinderliter AL, Shimbo D, Person SD, Jacobs DR Jr. Diurnal blood pressure pattern and development of prehypertension or hypertension in young adults: the CARDIA study. *J Am Soc Hypertens* 2011; 5:48–55.

16. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992; 30:473–483.
17. Pierdomenico SD1, Pannarale G, Rabbia F, Lapenna D, Licitra R, Zito M, Campanella M, Gaudio C, Veglio F, Cuccurullo F. Prognostic relevance of masked hypertension in subjects with prehypertension. *Am J Hypertens* 2008; 21:879–883.
18. Brguljan-Hitij J, Thijs L, Li Y, Hansen TW, Boggia J, Liu YP, Asayama K, Wei FF, Bjorklund-Bodegard K, Gu YM, Ohkubo T, Jeppesen J, Torp-Pedersen C, Dolan E, Kuznetsova T, Katarzyna SS, Tikhonoff V, Malyutina S, Casiglia E, Nikitin Y, Lind L, Sandoya E, Kawecka-Jaszcz K, Filipovsky J, Imai Y, Wang J, O'Brien E, Staessen JA; on behalf of the International Database on Ambulatory blood pressure in relation to Cardiovascular Outcome Investigators. Risk stratification by ambulatory blood pressure monitoring across JNC classes of conventional blood pressure. *Am J Hypertens*, published online 26 February 2014 (doi:10.1093/ajh/hpu002).
19. Ben-Dov IZ, Ben-Arie L, Mekler J, Bursztyn M. In clinical practice, masked hypertension is as common as isolated clinic hypertension: predominance of younger men. *Am J Hypertens* 2005; 18:589–593.
20. Lindquist TL, Beilin LJ, Knuiman MW. Influence of lifestyle, coping, and job stress on blood pressure in men and women. *Hypertension* 1997; 29:1–7.
21. Mann SJ, James GD, Wang RS, Pickering TG. Elevation of ambulatory systolic blood pressure in hypertensive smokers. A case-control study. *JAMA* 1991; 265:2226–2228.
22. Myers MG, Godwin M, Dawes M, Kiss A, Tobe SW, Kaczorowski J. Measurement of blood pressure in the office: recognizing the problem and proposing the solution. *Hypertension* 2010; 55:195–200.