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IMPLEMENTATION TO INCREASE BLOOD PRESSURE CONTROL: WHAT WORKS? (JEFFREY BRETTLER AND KRISTI REYNOLDS, SECTION EDITORS)

Masked Hypertension: Whom and How to Screen?

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Abstract
Purpose of Review To review issues regarding the practical implementation of screening strategies for masked hypertension.
Recent Findings Masked hypertension has been associated with an increased risk of cardiovascular disease events and all-cause mortality. Recent guidelines have encouraged practitioners to use out-of-clinic monitoring to detect masked hypertension in some situations. However, it is unclear from these guidelines who should be screened or how to best measure out-of-office blood pressure. In this review, challenges to screening strategies for masked hypertension, and factors that should be considered when deciding to screen using ambulatory or home blood pressure monitoring.
Summary Masked hypertension is an important clinical phenotype to detect. Future research is needed in order to develop optimal screening strategies, and to understand population level implications of using ambulatory or home blood pressure monitoring on blood pressure control.

Keywords Hypertension · Masked hypertension · Out-of-office monitoring · Blood pressure · Blood pressure control · Population health

Introduction

Hypertension is typically diagnosed in the clinical setting after one or more blood pressure (BP) readings reach an established threshold. However, as many as 1 in 4 untreated individuals with a clinic BP below the hypertensive range will have hypertensive range BPs outside the clinical setting, a phenotype known as "masked hypertension." [1, 2, 3••, 4••] Masked hypertension is a known risk factor for subclinical cardiovascular disease (CVD) and, compared to normotension, is associated with a greater than 2-fold risk for stroke or myocardial infarction [2, 5, 6•]. Recent guidelines acknowledge the importance of using out-of-clinic BP monitoring to detect masked hypertension and avoid undertreatment of individuals at increased CVD risk [3••, 4••, 7, 8]. Such recognition is a significant achievement and a result of years of collaborative research. Yet, despite these recommendations, a fundamental challenge persists: how to translate the guidelines into practice.

A significant barrier to routine masked hypertension screening is that it is unclear who should be screened. Screening all individuals without clinic measured hypertension may be challenging. For example, an analysis by Booth et al. estimates that screening all US adults with non-elevated clinic BP would require that approximately 120 million individuals undergo out-of-clinic BP monitoring [9]. A feasible alternative was recently suggested by the European Society of Cardiology/European Society of Hypertension (ESC/ESH) and the American College of Cardiology/American Heart Association (ACC/AHA) guidelines: screen those populations most likely to have masked hypertension (Table 1) [3••, 4••]. One such proposal is to screen based on the clinic BP as higher clinic BP levels are associated with an increased prevalence of masked hypertension. This was demonstrated in a recent analysis by Brguljan-Hitij et al. of the International Database of Ambulatory Blood Pressure in relation to Cardiovascular Outcome (IDACO) cohort where the prevalence of masked hypertension among individuals with optimal BP (< 120/80 mmHg) was 7.5%, compared to 29.3% among those with prehypertension (130–139/

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Table 1 Recommendations regarding which individuals without hypertension should be considered for masked hypertension screening according to the 2017 American college of Cardiology/American Heart Association (ACC/AHA) [4••] and the 2018 European Society of Cardiology/European Society of Hypertension (ESC/ESH) [3••] blood pressure guidelines

2017 ACC/AHA	Populations to screen
	•Individuals with repeated office systolic blood pressure 120–129 mmHg or diastolic blood pressure 75–79 mmHg after 3-month trial of lifestyle modification and suspected masked hypertension.
	Method of out-of-clinic monitoring
	•Either daytime ambulatory blood pressure monitoring or home blood pressure monitoring.
2018 ESC/ESH	Populations to screen
	• Individuals with office systolic blood pressure 130–139 mmHg or diastolic blood pressure 85–89 mmHg
	• Individuals with hypertension related target organ damage (arterial stiffening, peripheral vascular disease, retinopathy, proteinuria, chronic kidney disease, left ventricular hypertrophy)
	• Individuals at high cardiovascular disease risk (e.g., a calculated 10-year Systematic COronary Risk Evaluation of > 5%)
	Method of out-of-clinic monitoring
	•Either ambulatory blood pressure monitoring or home blood pressure monitoring. Ambulatory blood pressure monitoring is specifically indicated for assessment of nighttime blood pressure values and dipping status (e.g., suspicion of nocturnal hypertension, such as in sleep apnea, chronic kidney disease, diabetes, endocrine hypertension, or autonomic dysfunction)

80–89 mmHg) [10]. Another strategy suggested by the ESC/ESH guidelines is to limit screening to individuals with unexplained end-organ damage—such as proteinuria, left ventricular hypertrophy, or peripheral vascular disease [3••]. This approach could identify individuals most in need of treatment while minimizing unnecessary testing. However, this would inevitably mean that the detection and treatment of masked hypertension is deferred until after the onset of end-organ damage, with subclinical end-organ damage going undetected and untreated which may limit the opportunities for benefit. A more ideal, preventative strategy would detect high-risk individuals before they develop hypertension-related comorbidities, ensuring that those most at risk for CVD events receive the greatest benefit and risk reduction from antihypertensive therapy.

A risk-based approach, where screening focuses on individuals with elevated CVD risk, may be a practical alternative and has been suggested by some [3••], but not all [4••, 7, 8], guidelines and societies. There is evidence to suggest that there is an increased prevalence of masked hypertension among individuals with high 10-year predicted atherosclerotic CVD risk. Examining a cohort of African Americans in the Jackson Heart Study, we found that among individuals not taking antihypertensive medication and with clinic BPs < 140/90 mmHg, the majority (63.4%) of individuals with a predicted atherosclerotic CVD risk ≥ 7.5% had masked hypertension [11•]. If similar findings can be demonstrated in other populations, risk-based strategies may be useful to efficiently identify those individuals who not only have masked hypertension but who also would be most likely to have CVD events and to benefit from antihypertensive treatment.

After determining who should be screened, the next hurdle to overcome will be how to screen. Current guidelines recommend using either ambulatory BP monitoring (ABPM) or home BP monitoring (HBPM) to measure out-of-clinic BP (Table 1) [3••, 4••, 7, 8]. However, there is little evidence to guide whether ABPM or HBPM should be preferred. ABPM is conducted using continuously worn portable devices which automatically measure BP over a 24-h period, providing assessments of BP during regular activity as well as sleep. In contrast, HBPM is conducted using a patient-triggered oscillometric device which provides BP measurements at rest. While both ABPM and HBPM are prognostically superior to clinic BP, and may complement each other in achieving long-term BP control, they have important differences and it is unknown if either method is superior to the other for predicting CVD events or mortality [3••, 12]. HBPM may be more practical for routine use as there are few available ABPM centers, HBPM devices cost as little as 1% of the cost of ABPM devices, and HBPM devices are increasingly available in US households, even among patients without hypertension [3••, 13•, 14]. However, a limitation to HBPM is that obtaining clinically reliable and actionable data requires proper patient training and adherence [3••, 4••]. Furthermore, most HBPM devices approved in the USA are unable to evaluate for nighttime hypertension, a potentially crucial component of masked hypertension that predicts CVD events. There is growing research that nighttime hypertension (sleep BP ≥ 120/70 mmHg) is present in 30% to 45% of adults [15–17] and confers increased risk of CVD events and target organ damage independent of clinic BP and awake BP [6•, 18–20].

Whether ABPM or HBPM should be used for screening is further complicated by the discordance between ABPM and HBPM for the diagnosis of masked hypertension. In a recent study of adults not taking antihypertensive medication in the

New York area who underwent both ABPM and separately HBPM, we found the prevalence of masked hypertension was 11.1% when using HBPM, but 25.8% when out-of-clinic BP was examined on ABPM [21]. Among participants with masked hypertension detected with either device, only 29.5% had masked hypertension on both ABPM and HBPM; the majority had masked hypertension detected only on ABPM (61.1%) while few had masked hypertension only on HBPM (9.4%). This suggests that screening strategies which rely on HBPM may misclassify many untreated individuals with masked hypertension as true normotensives. This may be particularly true for populations with a high prevalence of nighttime hypertension such as individuals with obstructive sleep apnea, diabetes, chronic kidney disease, or of African or Asian ancestry [3••, 7, 17, 22]. Therefore, clinicians and healthcare systems are faced with a dilemma regarding the best strategy to screen for masked hypertension in their populations. Given the low availability of ABPM, high cost for ABPM devices, and lack of reimbursement for using ABPM to detect masked hypertension [3••, 13•], using HBPM may be the most pragmatic option until ABPM becomes more widely accessible. However, enthusiasm for such a strategy must be tempered as protocols only involving HBPM, even if practical to implement, may be inadequate if they fail to identify many individuals at increased CVD risk.

Conclusions

There is consensus from major hypertension societies that masked hypertension as an important BP phenotype that warrants detection [3••, 4••, 7, 8]. Future research, including cost-effectiveness analysis, is needed to elucidate who should be screened for masked hypertension, in particular considering risk-based approaches. In addition, research is needed to consider how best to implement out-of-clinic screening, including identifying ways to improve the specificity of HBPM for masked hypertension or identifying who would best be served by being screened by HBPM versus ABPM. Finally, clinicians and investigators should attempt to better understand the impact of treating masked hypertension. Thus far, there are no randomized clinical trials evaluating the efficacy of antihypertensive treatment in this patient population. With this, individual patients, clinicians, and health care systems may be better informed on how we may best align guidelines with practice and achieve BP control for this under-detected and under-treated phenotype.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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