HHS Public Access

Author manuscript

Curr Hypertens Rep. Author manuscript; available in PMC 2018 October 25.

Published in final edited form as:

Curr Hypertens Rep. ; 19(12): 94. doi:10.1007/s11906-017-0792-4.

AN UPDATE ON MASKED HYPERTENSION

D. Edmund Anstey, MD[a], **Daniel Pugliese, MD**[a], **Marwah Abdalla, MD MPH**[a], **Natalie A. Bello, MD MPH**[a], **Raymond Givens, MD PhD**[a], and **Daichi Shimbo, MD**[a]

[a]Columbia University Medical Center, New York, New York

Abstract

Masked hypertension refers to the phenomenon of having a non-elevated clinic blood pressure (BP) despite having an elevated out-of-clinic BP. Masked hypertension is a common phenotype with a cardiovascular risk profile similar to that of sustained hypertension, defined as elevated clinic and out-of-clinic BP. Current guidelines offer little guidance on the best practices for detecting and treating masked hypertension. This is in part due to insufficient evidence upon which to base recommendations as many questions remain regarding the optimal clinical management of masked hypertension. In this review, we will discuss the recent literature on masked hypertension related to disease prevalence, diagnosis, screening strategies, adverse outcomes, and treatment, and will highlight critical areas for future research.

Keywords

Hypertension; masked hypertension; ambulatory blood pressure monitoring; home blood pressure monitoring; cardiovascular disease; prevalence

INTRODUCTION

Hypertension is typically diagnosed by detecting an elevated blood pressure (BP) in the clinic. However, BP levels measured in the clinic may differ substantially when measured in the out-of-clinic setting by ambulatory BP monitoring (ABPM) or home BP monitoring (HBPM). The phenomenon of white coat hypertension describes those individuals with elevated clinic BP, but non-elevated out-of-clinic BP.(1) Data have demonstrated that white coat hypertension is common and likely not associated with an increased risk of cardiovascular disease (CVD) events when compared to individuals with sustained normotension, defined as non-elevated clinic and out-of-clinic BP.(2–5) Masked hypertension is the inverse phenomenon: an elevated out-of-clinic BP despite a non-elevated clinic BP. First coined by Pickering in 2002,(6) masked hypertension has gained increasing recognition in research and clinical practice and is now known to be a high-risk BP phenotype, associated with an increased risk of CVD events and target organ damage.(5–10)

Address Correspondence and Reprint Requests: D. Edmund Anstey, MD, Columbia University Medical Center, 622 West 168th Street, PH 9-310, New York, NY 10032, Phone / Fax: (212) 342-4490 / (212) 342-3431, dea2123@cumc.columbia.edu.

HUMAN AND ANIMAL RIGHTS

This article does not contain any studies with human or animal subjects performed by any of the authors.

In this review, we will discuss the recent literature on masked hypertension including disease prevalence, controversies related to the use of ABPM versus HBPM to detect masked hypertension, potential approaches to screening for masked hypertension, adverse clinical outcomes associated with masked hypertension, recent perspectives on treating masked hypertension, and suggestions on future areas of research. The papers and topic areas are discussed with an emphasis on issues which may guide future research and the clinical management of masked hypertension.

DEFINITIONS

Originally, the term “masked hypertension” referred to individuals not taking antihypertensive medication who have a non-elevated clinic BP but have elevated out-of-clinic BP.(6) Several guidelines recommend using the daytime and/or the 24-hour periods to define masked hypertension(10–12) though more recent recommendations(10) propose the use of the nighttime period as well. The term “masked hypertension” can also be applied to individuals taking antihypertensive medication. For these individuals, the term “masked uncontrolled hypertension” has been used. Herein, for readability, we use the term “masked hypertension” for both individuals not taking and taking antihypertensive medication. Sustained hypertension will refer to individuals with both elevated clinic and out-of-clinic BP; and sustained normotension will refer to individuals with both non-elevated clinic and out-of-clinic BP.

PREVALENCE

Systematic reviews of population-based studies have reported a prevalence of masked hypertension ranging from 15% to 30% among individuals with non-elevated clinic BP, with out-of-clinic BP measured on ABPM or HBPM.(13, 14) This wide range in part reflects the sampling of different populations as well as the use of different time periods (i.e. daytime, 24-hour, nighttime periods) to define masked hypertension. A recent analysis by Melgarejo et al. demonstrated that the prevalence of masked hypertension also varies by geographic region.(15) Examining ABPM data from 10 cohorts over 3 continents, the authors found that the prevalence of masked hypertension defined using the daytime, 24-hour, and/or nighttime periods on ABPM ranged from 8.8% in Belgium (in the Belgian Population Study) to 30.5% in China (the JingNing Population Study) among individuals with non-elevated clinic BP. Significant variation by geographic region was also observed in an analysis of the ARTEMIS registry, an international network of clinics performing ABPM, where the prevalence of masked hypertension was observed to range from 9% in Europe to 16% in Asia and 17% in Africa with masked hypertension defined using 24-hour ABPM.(16) A recent study from the US highlights racial differences in the prevalence of masked hypertension. In an analysis by Wang et al., a community sample of employed adults from the Masked Hypertension Study was used to model daytime BP on ABPM in National Health and Nutrition Examination Survey (NHANES, 2005 – 2010). The authors estimated a prevalence of masked hypertension in the US population of 12.3% which ranged from 10.6% among Hispanics and 11.8% among Non-Hispanic whites, to 15.7% among African Americans.(17)

Individuals taking antihypertensive medication have also been found to have an increased prevalence of masked hypertension as compared to those not taking antihypertensive medication. Among 6,432 individuals with non-elevated clinic BP in the International Database of Ambulatory Blood Pressure in relation to Cardiovascular Outcomes (IDACO), the prevalence of masked hypertension using daytime BP on ABPM was ~1.7 times higher for individuals taking versus not taking antihypertensive medication (31.9% treated versus 19.2% untreated).(18) Similarly, an analysis of the Jackson Heart Study demonstrated among African Americans the prevalence of masked hypertension using daytime BP on ABPM was 1.5 times greater for individuals on treatment compared to those not taking antihypertensive medication (32.8% versus 21.5% respectively).(19)

The prevalence of masked hypertension also varies when different ABPM periods (daytime, 24-hour, and nighttime) are used to define out-of-clinic hypertensions status. Examining data from the IDACO cohort, Asayama et al. determined that the prevalence of masked hypertension among individuals with non-elevated clinic BP ranged from 13.8% when out-of-clinic hypertension was defined only using the 24-hour BP to 27.9% when using the daytime, 24-hour, and/or nighttime BP.(5) In the Jackson Heart Study, the prevalence of masked hypertension defined separately using the daytime, 24-hour, and nighttime periods was 22.1%, 26.6% and 41.7%, respectively.(20) When all three periods were used – having elevated daytime, 24-hour and/or nighttime BP – the overall prevalence was 44.1%. Therefore, it is possible that, in some populations, using only daytime BP or 24-hour period to define masked hypertension would considerably under-estimate the prevalence of masked hypertension. Which period should be used to define masked hypertension, and if the same criteria are appropriate for all populations, is an important area of ongoing and future research.

OUT-OF-CLINIC BLOOD PRESSURE MEASUREMENT STRATEGIES TO DEFINE MASKED HYPERTENSION

Multiple studies have demonstrated that out-of-clinic BP, as measured by ABPM or HBPM, is a better predictor of target organ damage(21, 22) and fatal and nonfatal cardiovascular events(23–25) than clinic BP. ABPM are wearable, portable devices which are worn continuously and measure BP automatically at predetermined intervals (typically every 15–30 minutes over a 24-hour period) usually with the oscillometric method. In contrast, HBPM typically includes the use of a patient-initiated oscillometric BP measurement device. As compared to ABPM, almost all home BP devices record measurements only during the awake period. However, HBPM may be more practical than ABPM as it is less cumbersome for the patient, less expensive, and more widely available.(13, 19, 26)

The question of which method should be used to detect masked hypertension is complicated by the question of which method is superior for measuring out-of-clinic BP. Multiple studies have examined whether ABPM or HBPM better predicts CVD events and mortality.(27) A systematic review by Shimbo et al. found 9 articles including 7 unique cohorts where both ABPM and HBPM were used and CVD events and/or mortality outcomes were reported.(27) The authors found that both ABPM and HBPM were independently associated with

CVD events and mortality, however, there was insufficient evidence to consider either modality superior for predicting CVD events and/or mortality.

There also is substantial disagreement in the diagnosis of masked hypertension when using ABPM versus HBPM. In a study by Stergiou et al.,(28) among individuals who underwent both ABPM and HBPM to make the diagnosis of masked hypertension, only 44% were diagnosed as having masked hypertension on both modalities; 34% were diagnosed on only ABPM and 22% diagnosed on only HBPM. A separate study by Viera et al. found daytime ABPM and HBPM to agree 72.1% of the time (kappa 0.36) for diagnosing masked hypertension.(29) As different diagnoses can be reached when using alternate out-of-clinic BP measurement modalities, the preferred method for clinical practice remains uncertain.

Additionally, the optimal methodology to measure clinic BP is also an ongoing area of investigation. In most studies, clinic BP has been measured using either a mercury sphygmomanometer or an automated oscillometric device by trained medical staff. However, there is recent interest in the use of a fully automated oscillometric device that is able to obtain multiple clinic measurements without an observer present (i.e. unattended clinic BP).(30–33) Compared to attended clinic BP, unattended measurements obtained with an automated device are lower(33, 34) and correlate more strongly with daytime BP on ABPM ($r = 0.145$ versus 0.571).(31) It has been suggested that routine use of an unattended automated device could decrease the prevalence of white coat hypertension.(11, 33) However, measuring lower BP levels in the clinic may have the unintended effect of increasing the prevalence of masked hypertension as individuals who would have previously been identified as having sustained hypertension will now have masked hypertension because clinic BP is no longer elevated. The consequences of using the unattended clinic BP method on the diagnosis of masked hypertension should be considered if such strategies for clinic BP measurement become standard practice.

WHOM TO SCREEN

ABPM and HBPM are recommended by many guidelines, scientific statements, and position papers for excluding white coat hypertension among those with elevated clinic BP.(10–12, 35) The optimal approach for the detection of masked hypertension is unknown.(36) Screening all individuals with non-elevated clinic BP for masked hypertension is impractical. For example, Booth et al. determined that such an approach in the US would require 118.6 million adults undergo ABPM.(37) Consequently, several studies have now examined the utility of using clinic BP thresholds to identify populations at increased risk for having masked hypertension with varying success. A higher clinic BP including BP levels in the prehypertensive range (120–139 / 80–89 mmHg) is associated with a higher prevalence of masked hypertension. However, in a US population screening individuals with clinic BP in the prehypertension range was found to have a sensitivity for detecting masked hypertension of 82.5%(37) and would still require 59.3 million adults to be referred for ABPM. Among individuals with clinic BP in the prehypertension range Viera et al. tried to identify a clinic BP threshold above which masked hypertension may be more likely and individuals should be referred for ABPM.(38) Although, in this cohort, a clinic BP cutoff of 120/82 mmHg would have the best operating characteristics for detecting masked

hypertension, they determined that it would result in high false positive rates as approximately 40% of individuals meeting this BP cutoff would not have masked hypertension.(38) The authors concluded that clinic BP alone may not be a sufficient screening tool to guide decisions on whom to screen for masked hypertension.

A CVD risk-based approach, limiting the use of out-of-clinic BP measurement to those individuals with multiple risk factors for masked hypertension, has similarly been examined.(39, 40) Prior studies have identified risk factors such as male sex, smoking, diabetes, and higher clinic BP to be associated with masked hypertension.(13) One theorized approach for identifying masked hypertension is therefore to screen individuals with metabolic syndrome as components of the metabolic syndrome have been associated with masked hypertension and higher out-of-clinic BP.(41) However, studying the association between metabolic syndrome and masked hypertension, Colantonio et al. found that using metabolic syndrome, which includes clinic BP, to identify individuals at risk for having masked hypertension would not provide additional predictive information beyond clinic BP alone.(39) A strategy with more promise may be to focus masked hypertension screening on those individuals at increased baseline CVD risk. We previously found that higher 10-year predicted CVD risk, using the pooled cohort risk equations, was associated with a higher prevalence of masked hypertension.(42) Although 10-year predicted risk was not superior to clinic BP for predicting masked hypertension, the majority of individuals with masked hypertension had a 10-year predicted CVD risk ≥10%. Risk prediction equations may therefore help identify individuals with masked hypertension who would derive the most benefit from antihypertensive treatment. Whether this finding can be applied to all populations, and how such a strategy may impact CVD outcomes, is unknown.

ADVERSE OUTCOMES

Masked hypertension has also been associated with target-organ damage. Prior studies have found masked hypertension to be associated with renal dysfunction (reduced estimated glomerular filtration ratio: eGFR, proteinuria) and vascular dysfunction (increased pulse wave velocity).(43–45) Masked hypertension has also been associated with increased left ventricular mass index. In a recent meta-analysis by Cuspidi et al., as compared to individuals with sustained normotension, individuals with masked hypertension had an increased left ventricular mass index (79.2 ± 0.35 g/m^2 versus 91.6 ± 4.0 g/m^2, respectively) and an increased prevalence of left ventricular hypertrophy (3.7% versus 14.1%, respectively).(46) A separate meta-analysis found masked hypertension to be associated with increased carotid intima-media thickness, a presumed measure of early carotid atherosclerosis.(47)

At present, multiple studies have found masked hypertension to be associated with an increased risk for CVD events including stroke or myocardial infarction. Compared to sustained normotension, the hazard ratio (HR) for CVD events for masked hypertension approached that of sustained hypertension (2.09, 95% confidence interval (CI) 1.55 – 2.81 and 2.59, 95% CI 2.0 – 3.35 respectively).(8) Studies included in this meta-analysis used ABPM, and masked hypertension was defined based on elevated daytime BP in all but one study which examined mean 24-hour BP; none of the studies defined masked hypertension

by nighttime BP measurements. More recently, masked hypertension based on nighttime readings is also associated with an increased risk of CVD events. In a study by Booth et al., masked hypertension based on nighttime readings was associated with a greater than 2-fold increased risk of CVD events among African Americans.(20) There is also evidence that masked hypertension identified using HBPM is associated with increased CVD risk. Using data from the International Database of HOme blood pressure in relation to Cardiovascular Outcome (IDHOCO), Stergiou et al. found, among 6,458 participants who had undergone HBPM, risk for CVD events was higher for those with masked hypertension (HR 1.55, 95% CI 1.12 – 2.14) compared to sustained normotension.(48)

As previously mentioned, there is often disagreement between ABPM and HBPM when diagnosing masked hypertension. It is unknown if individuals with masked hypertension on ABPM but not HBPM have the same risk of CVD events as individuals with masked hypertension on HBPM but not ABPM. Studying Japanese adults in the Ohasama cohort, Satoh et al. looked at the association of stroke with masked hypertension diagnosed on ABPM only (using daytime, 24-hour, and/or nighttime periods), HBPM only, or on both out-of-clinic BP measurement modalities.(49) They found that masked hypertension detected on both ABPM and HBPM was associated with an increased risk of stroke (HR 2.05, 95% CI 1.23 – 3.41) compared to sustained normotension defined as having non-elevated clinic BP, non-elevated BP on ABPM, and non-elevated BP on HBPM. Further, this risk was also elevated among individuals with masked hypertension diagnosed only on ABPM but not on HBPM (HR 1.93, 95% CI 1.15 – 3.24); and when diagnosed on HBPM but not ABPM (HR 2.26, 95% CI 1.32 – 3.89). There were no direct statistical comparisons made between individuals with masked hypertension on only ABPM versus those with masked hypertension on only HBPM.(49) Future studies aimed at contrasting how masked hypertension diagnosed by ABPM versus HBPM relates to outcomes is an important area for research with substantial implications for guidelines.

TREATMENT

Few studies have examined masked hypertension treatment and none have examined how treatment may affect CVD events. The European Society of Cardiology/European Society of Hypertension is the only major society to recommend pharmacologic treatment or lifestyle measures for the treatment of masked hypertension and acknowledges that there is minimal evidence (Level of Evidence C) to support this Class IIa recommendation.(10) When considering management strategies for masked hypertension and related phenotypes, important questions remain including: (1) what out-of-clinic BP target should clinicians use to monitor treatment response, (2) if out-of-clinic BP is used, should it be monitored via ABPM (using daytime, 24-hour, or nighttime BP values) or HBPM, and (3) what may be the effect of treatment of masked hypertension on CVD events.

Lifestyle modifications may be an appropriate and effective intervention for the treatment of masked hypertension. A study by Bromfield et al. categorized participants in the Jackson Heart Study as having poor, intermediate, or ideal factors of cardiovascular health as defined by the American Heart Association's "Life's Simple 7" – a composite measure that includes body mass index, physical activity, diet, cigarette smoking, blood pressure, cholesterol and

glucose.(50) In multivariable adjusted analysis, masked hypertension based on daytime BP was less common among participants with a healthier lifestyle. Specifically, masked hypertension was less common among those individuals who had ideal versus poor scores for physical activity and cigarette smoking, ideal versus poor scores for diet, and ideal versus intermediate scores for blood pressure. The finding that better cardiovascular health is associated with a lower prevalence of masked hypertension suggests that lifestyle modifications may reduce the risk of masked hypertension. Further studies are required to support this hypothesis.

To our knowledge, there are currently 3 clinical trials examining treatment of masked hypertension (www.clinicaltrials.gov; Table 1). These studies are investigating important unknown areas of masked hypertension management including how clinical strategies targeting clinic versus out-of-clinic BP and treatment with antihypertensive medications may affect masked hypertension, target organ damage, and cardiovascular events. The findings of these studies may have an important impact regarding the treatment of masked hypertension.

CONCLUSIONS

A recent study among US adults found that the majority of incident CVD events occur in individuals with non-elevated clinic BP.(51) Given the prevalence of masked hypertension and its association with cardiovascular outcomes, many of these individuals may have undetected and untreated masked hypertension. Improving outcomes for this prevalent BP phenotype should be a primary focus of future hypertension research. Despite recent advances in our understanding of masked hypertension, challenges remain which have implications for academic research and clinical care (Table 2). As we strive to improve public health outcomes and decrease cardiovascular disease burden, it is imperative that we continue to address these gaps in knowledge and work towards improving the management of individuals with masked hypertension.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

None.

SOURCES OF FUNDING

This work was supported by P01-HL047540 and K24-HL125704 from the National Heart, Lung, and Blood Institute at the National Institutes of Health (NIH), and 15SFRN2390002 from the American Heart Association. DEA receives support through 2T32HL007854-21. MA and NAB are supported by UL1TR001873 and KL2TR001874 from the National Center for Advancing Translational Sciences, NIH.

References

1. Pickering TG, James GD, Boddie C, Harshfield GA, Blank S, Laragh JH. How common is white coat hypertension? JAMA. 1988; 259(2):225–8. [PubMed: 3336140]

2. 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(11):2193–8. [PubMed: 17921809]

3. Hansen TW, Jeppesen J, Rasmussen S, Ibsen H, Torp-Pedersen C. Ambulatory blood pressure monitoring and risk of cardiovascular disease: a population based study. American journal of hypertension. 2006; 19(3):243–50. [PubMed: 16500508]

4. Pierdomenico SD, Lapenna D, Di Mascio R, Cuccurullo F. Short- and long-term risk of cardiovascular events in white-coat hypertension. Journal of human hypertension. 2008; 22(6):408–14. [PubMed: 18288127]

5. Asayama K, Thijs L, Li Y, Gu YM, Hara A, Liu YP, et al. Setting thresholds to varying blood pressure monitoring intervals differentially affects risk estimates associated with white-coat and masked hypertension in the population. Hypertension. 2014; 64(5):935–42. [PubMed: 25135185]

6. Pickering TG, Davidson K, Gerin W, Schwartz JE. Masked hypertension. Hypertension. 2002; 40(6):795–6. [PubMed: 12468559]

7. O'Brien E, Parati G, Stergiou G, Asmar R, Beilin L, Bilo G, et al. European Society of Hypertension position paper on ambulatory blood pressure monitoring. J Hypertens. 2013; 31(9):1731–68. [PubMed: 24029863]

8. Pierdomenico SD, Cuccurullo F. Prognostic value of white-coat and masked hypertension diagnosed by ambulatory monitoring in initially untreated subjects: an updated meta analysis. American journal of hypertension. 2011; 24(1):52–8. [PubMed: 20847724]

9. Franklin SS, O'Brien E, Thijs L, Asayama K, Staessen JA. Masked hypertension: a phenomenon of measurement. Hypertension. 2015; 65(1):16–20. [PubMed: 25287401]

10. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Bohm M, et al. 2013 ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). European heart journal. 2013; 34(28):2159–219. [PubMed: 23771844]

11. Leung AA, Daskalopoulou SS, Dasgupta K, McBrien K, Butalia S, Zarnke KB, et al. Hypertension Canada's 2017 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults. Can J Cardiol. 2017; 33(5):557–76. [PubMed: 28449828]

12. (UK) NCGC. National Institute for Health and Clinical Excellence: Guidance. London, UK: Royal College of Physicians; 2011. Hypertension: The Clinical Management of Primary Hypertension in Adults: Update of Clinical Guidelines 18 and 34.

13. Peacock J, Diaz KM, Viera AJ, Schwartz JE, Shimbo D. Unmasking masked hypertension: prevalence, clinical implications, diagnosis, correlates and future directions. Journal of human hypertension. 2014; 28(9):521–8. [PubMed: 24573133]

14. Bobrie G, Clerson P, Menard J, Postel-Vinay N, Chatellier G, Plouin PF. Masked hypertension: a systematic review. J Hypertens. 2008; 26(9):1715–25. [PubMed: 18698202]

15. Melgarejo JD, Maestre GE, Thijs L, Asayama K, Boggia J, Casiglia E, et al. Prevalence, Treatment, and Control Rates of Conventional and Ambulatory Hypertension Across 10 Populations in 3 Continents. Hypertension. 2017; 70(1):50–8. [PubMed: 28483916]

16. Omboni S, Aristizabal D, De La Sierra A, Dolan E, Head G, Kahan T, et al. Hypertension types defined by clinic and ambulatory blood pressure in 14143 patients referred to hypertension clinics worldwide. Data from the ARTEMIS study. Journal of Hypertension. 2016; 34(11):2187–98. [PubMed: 27512964]

17. Wang YC, Shimbo D, Muntner P, Moran AE, Krakoff LR, Schwartz JE. Prevalence of Masked Hypertension Among US Adults With Nonelevated Clinic Blood Pressure. Am J Epidemiol. 2017; 185(3):194–202. [PubMed: 28100465]

18. Franklin SS, Thijs L, Li Y, Hansen TW, Boggia J, Liu Y, et al. Masked hypertension in diabetes mellitus: treatment implications for clinical practice. Hypertension. 2013; 61(5):964–71. [PubMed: 23478096]

19. Redmond N, Booth JN 3rd, Tanner RM, Diaz KM, Abdalla M, Sims M, et al. Prevalence of Masked Hypertension and Its Association With Subclinical Cardiovascular Disease in African

Americans: Results From the Jackson Heart Study. Journal of the American Heart Association. 2016; 5(3)

20. Booth JN 3rd, Diaz KM, Seals SR, Sims M, Ravenell J, Muntner P, et al. Masked Hypertension and Cardiovascular Disease Events in a Prospective Cohort of Blacks: The Jackson Heart Study. Hypertension. 2016; 68(2):501–10. [PubMed: 27354424]
21. Gaborieau V, Delarche N, Gosse P. Ambulatory blood pressure monitoring versus self-measurement of blood pressure at home: correlation with target organ damage. J Hypertens. 2008; 26(10):1919–27. [PubMed: 18806615]
22. Bliziotis IA, Destounis A, Stergiou GS. Home versus ambulatory and office blood pressure in predicting target organ damage in hypertension: a systematic review and meta-analysis. J Hypertens. 2012; 30(7):1289–99. [PubMed: 22499289]
23. Conen D, Bamberg F. Noninvasive 24-h ambulatory blood pressure and cardiovascular disease: a systematic review and meta-analysis. J Hypertens. 2008; 26(7):1290–9. [PubMed: 18550999]
24. Boggia J, Li Y, Thijs L, Hansen TW, Kikuya M, Bjorklund-Bodegard K, et al. Prognostic accuracy of day versus night ambulatory blood pressure: a cohort study. Lancet. 2007; 370(9594):1219–29. [PubMed: 17920917]
25. Fagard RH, Celis H, Thijs L, Staessen JA, Clement DL, De Buyzere ML, et al. Daytime and nighttime blood pressure as predictors of death and cause-specific cardiovascular events in hypertension. Hypertension. 2008; 51(1):55–61. [PubMed: 18039980]
26. Shimbo D, Abdalla M, Falzon L, Townsend RR, Muntner P. Role of Ambulatory and Home Blood Pressure Monitoring in Clinical Practice: A Narrative Review. Ann Intern Med. 2015; 163(9):691–700. [PubMed: 26457954]
27. Shimbo D, Abdalla M, Falzon L, Townsend RR, Muntner P. Studies comparing ambulatory blood pressure and home blood pressure on cardiovascular disease and mortality outcomes: a systematic review. Journal of the American Society of Hypertension : JASH. 2016; 10(3):224–34. e17. [PubMed: 26822864]
28. Stergiou GS, Salgami EV, Tzamouranis DG, Roussias LG. Masked hypertension assessed by ambulatory blood pressure versus home blood pressure monitoring: is it the same phenomenon? Am J Hypertens. 2005; 18(6):772–8. [PubMed: 15925734]
29. Viera AJ, Lin FC, Tuttle LA, Olsson E, Stankevitz K, Girdler SS, et al. Reproducibility of masked hypertension among adults 30 years or older. Blood Pressure Monitoring. 2014; 19(4):208–15. [PubMed: 24842491]
30. Myers MG. A Short History of Automated Office Blood Pressure-- 15 Years to SPRINT. J Clin Hypertens (Greenwich). 2016; 18(8):721–4. [PubMed: 27038200]
31. Beckett L, Godwin M. The BpTRU automatic blood pressure monitor compared to 24 hour ambulatory blood pressure monitoring in the assessment of blood pressure in patients with hypertension. BMC Cardiovasc Disord. 2005; 5(1):18. [PubMed: 15985180]
32. Myers MG, Godwin M, Dawes M, Kiss A, Tobe SW, Grant FC, et al. Conventional versus automated measurement of blood pressure in primary care patients with systolic hypertension: randomised parallel design controlled trial. Bmj. 2011; 342:d286. [PubMed: 21300709]
33. Myers MG, Valdivieso M, Kiss A. Use of automated office blood pressure measurement to reduce the white coat response. J Hypertens. 2009; 27(2):280–6. [PubMed: 19155785]
34. Wohlfahrt P, Cífková R, Movsisyan N, Kunzová S, Lešovský J, Homolka M, et al. Threshold for diagnosing hypertension by automated office blood pressure using random sample population data. Journal of Hypertension. 2016; 34(11):2180–6. [PubMed: 27512968]
35. Siu AL. Force USPST. Screening for high blood pressure in adults: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2015; 163(10):778–86. [PubMed: 26458123]
36. Anstey DE, Shimbo D. Masked hypertension-what lies ahead? Journal of human hypertension. 2017; 31(9):545–6. [PubMed: 28790438]
37. Booth JN 3rd, Muntner P, Diaz KM, Viera AJ, Bello NA, Schwartz JE, et al. Evaluation of Criteria to Detect Masked Hypertension. Journal of clinical hypertension (Greenwich, Conn). 2016; 18(11):1086–94.

38. Viera AJ, Lin FC, Tuttle LA, Shimbo D, Diaz KM, Olsson E, et al. Levels of office blood pressure and their operating characteristics for detecting masked hypertension based on ambulatory blood pressure monitoring. American Journal of Hypertension. 2015; 28(1):42–9. [PubMed: 24898379]

39. Colantonio LD, Anstey DE, Carson AP, Ogedegbe G, Abdalla M, Sims M, et al. Metabolic syndrome and masked hypertension among African Americans: The Jackson Heart Study. Journal of clinical hypertension (Greenwich, Conn). 2017

40. Sheppard JP, Fletcher B, Gill P, Martin U, Roberts N, McManus RJ. Predictors of the Home-Clinic Blood Pressure Difference: A Systematic Review and Meta-Analysis. American journal of hypertension. 2016; 29(5):614–25. [PubMed: 26399981]

41. Hanninen MR, Niiranen TJ, Puukka PJ, Jula AM. Metabolic risk factors and masked hypertension in the general population: the Finn-Home study. Journal of Human Hypertension. 2014; 28(7): 421–6. [PubMed: 24384630]

42. Anstey DE, Booth JN 3rd, Abdalla M, Spruill TM, Min YI, Muntner P, et al. Predicted Atherosclerotic Cardiovascular Disease Risk and Masked Hypertension Among Blacks in the Jackson Heart Study. Circ Cardiovasc Qual Outcomes. 2017; 10(7)

43. Drawz PE, Alper AB, Anderson AH, Brecklin CS, Charleston J, Chen J, et al. Masked Hypertension and Elevated Nighttime Blood Pressure in CKD: Prevalence and Association with Target Organ Damage. Clin J Am Soc Nephrol. 2016; 11(4):642–52. [PubMed: 26912547]

44. Hanninen MR, Niiranen TJ, Puukka PJ, Kesaniemi YA, Kahonen M, Jula AM. Target organ damage and masked hypertension in the general population: the Finn-Home study. J Hypertens. 2013; 31(6):1136–43. [PubMed: 23466942]

45. Tientcheu D, Ayers C, Das SR, McGuire DK, de Lemos JA, Khera A, et al. Target Organ Complications and Cardiovascular Events Associated With Masked Hypertension and White-Coat Hypertension: Analysis From the Dallas Heart Study. J Am Coll Cardiol. 2015; 66(20):2159–69. [PubMed: 26564592]

46. Cuspidi C, Sala C, Tadic M, Rescaldani M, Grassi G, Mancia G. Untreated Masked Hypertension and Subclinical Cardiac Damage: A Systematic Review and Meta-analysis. American journal of hypertension. 2015; 28(6):806–13. [PubMed: 25468808]

47. Cuspidi C, Sala C, Tadic M, Rescaldani M, De Giorgi GA, Grassi G, et al. Untreated masked hypertension and carotid atherosclerosis: a meta-analysis. Blood Press. 2015; 24(2):65–71. [PubMed: 25608631]

48. Stergiou GS, Asayama K, Thijs L, Kollias A, Niiranen TJ, Hozawa A, et al. Prognosis of white-coat and masked hypertension: International database of home blood pressure in relation to cardiovascular outcome. Hypertension. 2014; 63(4):675–82. [PubMed: 24420553]

49. Satoh M, Asayama K, Kikuya M, Inoue R, Metoki H, Hosaka M, et al. Long-Term Stroke Risk Due to Partial White-Coat or Masked Hypertension Based on Home and Ambulatory Blood Pressure Measurements: The Ohasama Study. Hypertension. 2016; 67(1):48–55. [PubMed: 26527046]

50. Bromfield SG, Shimbo D, Booth JN, Correa A, Ogedegbe G, Carson AP, et al. Cardiovascular Risk Factors and Masked Hypertension. The Jackson Heart Study. 2016

51. Tajeu GS, Booth JN 3rd, Colantonio LD, Gottesman RF, Howard G, Lackland DT, et al. Incident Cardiovascular Disease Among Adults with Blood Pressure< 140/90 mm Hg. Circulation. 2017

Table 1

A summary of current clinical trials examining the impact of treatment of masked hypertension (www.clinicaltrials.gov)

Name of Trial	Study Sample and Target Enrollment	Intervention and Study Design	Outcomes
"Treatment of Masked Hypertension"	Country: United States Sample: Adults with masked hypertension, age 18–75 years, chronic kidney disease Target Enrollment: 50	Randomized, open label study comparing optimization of antihypertensive treatment based on office BP and 24-hour ABPM versus usual care	Primary: Percentage of participants with masked hypertension Secondary: Change in urine albumin/creatinine ratio, pulse wave velocity, and 24-hour BP
"MASked and masked-unconTrolled hypERtension managed based on Office BP or Out-of-office (Ambulatory) BP Measurement"(MASTER)	Country: Italy Sample: Adults with masked hypertension, age 35–80 years Target Enrollment: 1240	Randomized, open-label, blinded-endpoint study comparing optimization of antihypertensive treatment based on office BP versus 24-hour ABPM	Primary: Changes in target organ damage (left ventricular mass index and urine albumin/creatinine ratio)
"Antihypertensive Treatment in Masked Hypertension for Target Organ Protection" (ANTI-MASK)	Country: China Sample: Adults with masked hypertension, age 30–70 years, with target-organ damage Target Enrollment: 300	Randomized, double-blind study comparing treatment with Allisartan Isoproxil versus Placebo	Primary: Changes in target organ damage (left ventricular hypertrophy, large arterial stiffness, and microalbuminuria) Secondary: Electrocardiogram evidence of left ventricular hypertrophy, microalbuminuria/ creatinine ratio, 24-hour BP, brachial-ankle pulse wave velocity, incidence rate of all cause death and CVD events

Table 2

Future areas of masked hypertension research

• Who is at risk for developing masked hypertension?
• Which individuals with masked hypertension are at the highest risk for adverse events?
• What time periods (daytime, 24-hour, and/or nighttime) should be used to diagnose masked hypertension and is it appropriate to use the same criteria for all populations
• What strategies should be used to monitor out-of-clinic BP (ABPM, HBPM or both)?
• What are cost-effective screening strategies to diagnose masked hypertension and monitor response to treatment?
• Should subclinical cardiovascular disease or target organ damage be a screening criteria for masked hypertension prior to conducting ABPM or HBPM?
• What are the effects of lifestyle and/or pharmacologic treatment on reducing target organ damage, CVD events and mortality in persons with masked hypertension?