Original Article

Ambulatory blood pressure monitoring in Australia: 2011 consensus position statement

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Objective: Although most national guidelines for the diagnosis and management of hypertension emphasize that the initiation and modification of blood pressure (BP)-lowering treatment should be related to absolute cardiovascular disease (CVD) risk, there is only limited information on how to incorporate ambulatory BP (ABP) monitoring into this framework. The objective of this initiative is to provide ABP equivalents for BP cut-points for treatment initiation and targets to be included into guidelines.

Methods: A critical analysis of the best available evidence from clinical trials and observational studies was undertaken to develop a new consensus statement for ABP monitoring.

Results: ABP monitoring has an important place in defining abnormal patterns of BP, particularly white-coat hypertension (including in pregnancy), episodic hypertension, masked hypertension, labile BP and nocturnal or morning hypertension. This consensus statement provides a framework for appropriate inclusion of ABP equivalents for low, moderate and high CVD risk patients. The wider use of ABP monitoring, although justified, is limited by its availability and cost due to the lack of medical subsidy in Australia. However, cost–benefit analysis does suggest a cost-saving in reduced numbers of inappropriate antihypertensive treatments.

Conclusion: Although clinic measurement of BP will continue to be useful for screening and management of suspected and true hypertension, ABP monitoring provides considerable added value toward accurate diagnosis and the provision of optimal care in uncomplicated hypertension, as well as for patients with moderate or severe CVD risk.

Keywords: blood pressure, cardiovascular risk, consensus, guidelines, masked hypertension, white-coat hypertension

Abbreviations: AASI, ambulatory arterial stiffness index; ABP, ambulatory blood pressure; BP, blood pressure; CVD, cardiovascular disease; ESH, European Society of Hypertension; HR, heart rate

INTRODUCTION

Like most international guidelines, existing national guidelines in Australia for the management of hypertension emphasize that the necessity, choice and intensity of blood pressure (BP)-lowering treatment should be determined by the individual's probability of an event within a given period [absolute cardiovascular disease (CVD) risk] [1]. The CVD risk is based on a thorough assessment of all major risk factors (e.g. age, sex, waist circumference and/or BMI, lifestyle, family history, blood lipids, glucose metabolism) and the presence of associated clinical conditions and/or end-organ damage [2]. Inherent in these guidelines is the determination of a patient's BP. Current management of hypertension strongly relies on clinic BP measurement, although increasing evidence suggests that measurement of BP outside the clinic by ambulatory BP (ABP) and/or home BP devices better represents patients' actual BP. However, there is only limited information of how to include ABP monitoring, as a stronger predictor of clinical outcomes, into the diagnosis and management of hypertension.

ABP monitoring provides a necessary adjunct to current practice and is particularly useful to detect white-coat and masked hypertension, as well as the extent of nocturnal dipping of BP, all of which are important prognostic factors. ABP equivalents for BP targets have recently been determined from a large Australian database [3] and, this together with recent outcome studies [4], has prompted the ABP monitoring 2011 consensus position statement update of the previous 2002 Australian position statement, 'Ambulatory blood pressure monitoring' [5]. The aim was to provide an expert up-to-date consensus opinion statement concerning the relevance, use and validity of ABP monitoring in clinical

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practice. This consensus statement outlines the rationale for the recommended upper limits for daytime, night-time and 24-h SBP/DBP (systolic and diastolic BP) levels determined by ABP monitoring. It also details specific indications for its use, interpretation of the measurements and potential areas of further research. The statement provides guidance for those who use or are considering using 24-h ABP monitoring and it supplements current guidelines for the diagnosis and management of hypertension in adults [2] and incorporates revised ABP thresholds for the diagnosis and management of hypertension [2,3]. Although the focus of the expert opinion is directed at ABP monitoring, comparatives to home BP monitoring are provided where relevant within the document. This consensus statement was developed by the Ambulatory Blood Pressure Monitoring Working Group which is a subcommittee of the National Heart Foundation of Australia (NHF) National Blood Pressure and Vascular Disease Advisory Committee and the High Blood Pressure Research Council of Australia (HBPRCA). The statement has been ratified by both parent groups together with the Royal Australian College of General Practitioners (RACGP).

WHAT DOES AMBULATORY BLOOD PRESSURE INVOLVE?

ABP monitoring involves a patient wearing a portable BP measuring device for a specified period (usually 24 h). This periodically measures BP (every 15–30 min during the day and every 30–60 min overnight) automatically via a cuff worn on the upper arm. The resulting SBP and DBP readings provide an assessment of the patient's BP during normal daytime activities and importantly during sleep. Once the measurements are downloaded to a computer, a report is generated that calculates the number of readings and the amount of time a patient's readings are above the hypertension threshold. The data can also be used to calculate a range of parameters associated with CVD risk, including BP variability, heart rate (HR) variability, BP load and morning BP (see section 'Interpreting ambulatory blood pressure').

RATIONALE FOR AMBULATORY BLOOD PRESSURE MONITORING IN CLINICAL PRACTICE

Box 1 Key points

Ambulatory blood pressure monitoring

- Provides BP readings for daytime (awake), night-time (asleep) and 24-h average.
- Provides more reliable assessment of actual BP than clinic BP.
- Enables detection of white-coat and masked hypertension.
- Identifies nocturnal 'nondippers' who have a worse prognosis.
- Enables better prediction of end-organ damage associated with elevated BP and risk of future cardiovascular events than clinic or occasional BP measurements.

Consensus view

Although clinic measurement of BP will continue to be useful for screening and management of suspected and true hypertension, ABP and home BP measurements provide considerable added value toward accurate diagnosis and the provision of optimal care. Importantly, there are specific situations (detailed in this document) in which information provided by ABP monitoring can be particularly useful.

AMBULATORY BLOOD PRESSURE REFLECTS ACTUAL BLOOD PRESSURE MORE CLOSELY THAN CLINIC MEASUREMENTS

The three common methods to measure a patient's BP are within the clinic, during an ambulatory recording session and with self-measurement at home. Each has advantages and disadvantages and provides complementary information (Table 1) [6]. Clinic BP measurements are mostly too few in number to provide an accurate measure of BP due to considerable variation within a patient's day-to-day BP [7]. They are also affected by a number of factors which can lead to an overestimation or underestimation of the true BP in addition to errors related to defective instruments, improper techniques or observer bias [8,9]. It is well established that clinic BP measurements are lower when taken by trained nonmedical staff compared with a doctor [3] and when measurements are made automatically with the patient alone [10]. The higher readings measured by the doctor are referred to as the white-coat effect and in untreated individuals can result in white-coat hypertension (isolated clinic hypertension) (see section 'White-coat effect and suspected white-coat hypertension'). Conversely, approximately 10% of patients have lower BP measurements in the clinic compared with ABP which is referred to as masked hypertension (see section 'Suspected masked hypertension'). Importantly, clinic BP measurements provide limited information about the individual's actual BP profile and do not provide information about the circadian BP pattern which is influenced by a variety of factors (e.g. ambient temperature and humidity, physical activity, consumption of alcohol, caffeine and food, emotional states, such as anxiety and anger, and sleep–wake routine) [8].

Thus, ABP has long been recognized as a valid method for reducing errors associated with clinic measurements [11] and provides a BP profile of the individual with measures of

TABLE 1. Comparison of clinic, home and ambulatory measures of blood pressure

	Clinic	Home[a]	Ambulatory
Parameter[b]			
Screening for hypertension	Yes	No	No
Diagnosis of hypertension	Yes	Yes	Yes
Evaluation of antihypertensive therapy	Yes	Yes	Yes
Prediction of cardiovascular events	Yes	Yes	Yes
White-coat hypertension	No	Yes (limited)	Yes
Masked hypertension	No	Yes (limited)	Yes
Presence/absence of nocturnal dipping	No	No	Yes
Morning hypertension	No	Yes (limited)	Yes
Short-term day and night BP/HR variability	No	No	Yes
Long-term BP variability (if repeated)	Yes	Yes	Yes (limited)
BP load	No	No	Yes

ABP, ambulatory blood pressure; HR, heart rate. Adapted from [6].
[a]Self-measured BP.
[b]Parameters measured or clinical conditions that can be detected by properly interpreted ABP monitoring.

not only daytime but, importantly, the night-time BP [8]. Increasingly, home BP measurement is advocated due to its convenience and perceived lower cost to the patient, that it promotes patient involvement and provides a means of assessing BP over the long term [12]. However, a recent systematic review of home BP suggests only modest diagnostic agreement between home BP and ABP [13].

AMBULATORY BLOOD PRESSURE IS A BETTER PREDICTOR OF CLINICAL OUTCOMES AND END-ORGAN DAMAGE

Prospective studies have convincingly shown that ABP is a stronger predictor of clinical outcomes than conventional clinic BP measurements [4,14–30]. End-organ damage associated with elevated BP, such as left ventricular hypertrophy (LVH), is more strongly correlated with ABP than with clinic BP measurements [31–34]. ABP also correlates more closely with renal and vascular surrogate markers of end-organ damage, such as microalbuminuria and carotid artery wall thickness [35]. Of the ABP measures, night-time BP is a stronger predictor of end-organ damage than daytime BP [29]. Thus, ABP measurement is a better predictor of outcomes than clinic BP. The use of ABP can result in less intensive therapy to preserve BP control and therapy based on ABP can be as effective as that based on clinic BP in reducing end-organ damage [36].

AMBULATORY BLOOD PRESSURE MONITORING CAN DETECT ABSENCE OF NOCTURNAL BLOOD PRESSURE DIPPING

ABP monitoring is the most commonly used practical method to determine the presence or absence of nocturnal BP dipping (see section 'Interpreting ambulatory blood pressure'). Most studies investigating the significance of night-time hypertension have reported that night-time (sleeping) BP is more important in predicting clinical outcomes than daytime (awake) BP [22,29,37,38], particularly in people with hypertension who do not show normal BP reduction ('dipping') during sleep. Nocturnal nondipping is associated with increased risk of stroke, end-organ damage and cardiovascular events including death [20,37,39,40]. A nondipping status should also raise the suspicion of obstructive sleep apnoea [41,42] or diabetes [43].

COST-EFFECTIVENESS OF AMBULATORY BLOOD PRESSURE MONITORING

ABP monitoring costs more than conventional clinical measurements to perform. In Australia, the costs to the patient are not currently reimbursed by the national insurance scheme Medicare; however, for eligible patients, reimbursement is available from the Department of Veterans Affairs. However, there is consistent evidence that the additional cost of testing is offset by more reliable diagnosis of hypertension and, hence, a more precise quantification of CVD risk [44–47]. ABP is also highly cost-effective in children in the initial evaluation of hypertension [48]. The cost of providing good control of hypertension in an individual can be up to four times higher using conventional clinic BP measurements [49]. Thus, prescribing of antihypertensive treatment based on accurate BP assessment may lead to cost-savings by avoiding unnecessary drug therapy in the follow-up period or by deferring treatment in patients with white-coat hypertension (although they require monitoring and lifestyle management of BP) [50,51]. The cost–benefit ratio would be expected to increase, as the cost of managing hypertension rises with increasing rates of diagnosis and prescribing of new, more expensive antihypertensive agents.

WHEN IS AMBULATORY BLOOD PRESSURE MONITORING USEFUL?

Box 2

Key points

ABP monitoring is indicated for the following conditions:

- Suspected white-coat effect (including suspected white-coat hypertension).
- Suspected masked hypertension.
- Suspected lack of nocturnal dipping.
- Patients with a high risk of future cardiovascular events.
- Hypertension despite appropriate treatment (including isolated systolic hypertension in older patients).
- Known or suspected episodic hypertension.

ABP monitoring may also be useful for the following:

- Titrating antihypertensive therapy.
- Syncope or other symptoms suggesting orthostatic hypotension, where this cannot be demonstrated in the clinic.
- Suspected or confirmed sleep apnoea.
- Hypertension detected early in pregnancy.

Although ABP monitoring is generally recommended for reliable assessment of 24-h BP pattern, it is particularly valuable in the following clinical situations:

WHITE-COAT EFFECT AND SUSPECTED WHITE-COAT HYPERTENSION

In some patients, the BP measurement process itself can induce an increase in BP (known as the white-coat effect). This effect is particularly noticeable when BP is measured by a doctor, and much less pronounced when BP is measured by a nurse or another trained staff member within the clinic [3]. Recent studies suggest that the magnitude of white-coat effect can be reduced by taking clinic BP measurements using a validated automated device while the patient is alone in a quiet room [10].

White-coat hypertension (isolated clinic hypertension) refers to the condition in which an untreated individual meets criteria for hypertension when measured in the clinic, but shows normal BP levels when measured at home or by ABP monitoring [52,53]. It occurs in approximately 10–13% of the general population [54–56]. Factors that make white-coat hypertension more likely in a patient with raised clinic BP include [57]

1. female sex,
2. nonsmoker,
3. few recorded clinic BP measurements,

4. borderline hypertension,
5. recent onset hypertension, and
6. no evidence of end-organ damage.

When white-coat hypertension is suspected in a patient otherwise at low risk of CVD, ABP monitoring should be performed to provide a more comprehensive and reliable assessment of the patient's BP levels during daily activities (Fig. 1). It is preferable to home BP measurement because it can avoid a self-induced pressor effect [58].

White-coat hypertension has been associated with the following:

1. Higher anxiety scores [59].
2. Increased (approximately double) risk of hypertension within 8–10 years, compared with those with normal BP [60,61].
3. Increased risk of developing impaired fasting glucose or diabetes [62].

Accordingly, white-coat hypertension confirmed on ABP monitoring warrants careful assessment, including thorough investigation for end-organ damage and the management of other CVD risk factors (including glucose intolerance and lifestyle risk factors). The diagnosis should be confirmed by repeat ABP monitoring [63] or self-monitoring using home BP, and repeated every 1–2 years.

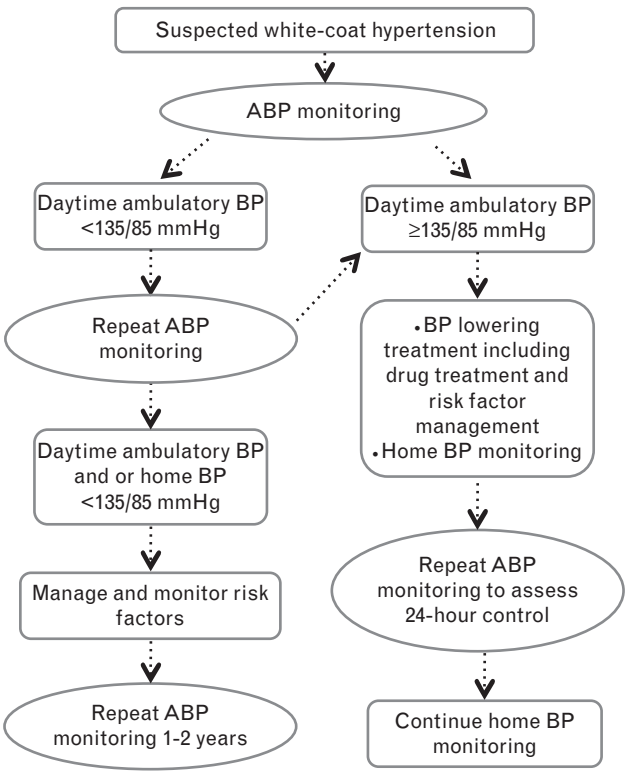

FIGURE 1 Flow diagram for ambulatory blood pressure (ABP) monitoring in the management of BP in patients with suspected white-coat hypertension, who are otherwise thought to be at low risk of cardiovascular disease. Risk scores are based on clinic measurements and, therefore, require the use of clinic measure equivalents (see Table 2 and S3, http://links.lww.com/HJH/A138). Schema includes management of lifestyle risk factors and monitoring glucose tolerance as required by the current National Heart Foundation of Australia (NHF) hypertension management guidelines.

SUSPECTED MASKED HYPERTENSION

Masked hypertension refers to untreated individuals in whom clinic measurements are normal, but ABP measurements are elevated which occur in up to 10% of the general population [64,65]. Possible reasons for failure to detect BP elevation on clinic measurements (particularly in the morning) include evening alcohol consumption and the use of short-acting antihypertensive agents [66]. Obstructive sleep apnoea is another important cause of masked hypertension [41] which is resolved in the majority of cases with continuous positive airway pressure treatment [67].

Masked hypertension should be suspected in people with normal clinic BP readings [41,57,68] and any of the following:

1. LVH or evidence of other target organ damage.
2. A history of hypertension in both parents.
3. Multiple risk factors for CVD.
4. Obstructive sleep apnoea [42].
5. Occasional high BP readings.
6. Chronic kidney disease [65].
7. Significant job stress [69].
8. Excessive or exaggerated hypertensive response to exercise [70,71].

Although the full clinical implications of masked hypertension and its appropriate management are uncertain, this condition has been associated with a worse prognosis than consistent normotension [64,72,73], including increased risk of the following:

1. A major cardiovascular event [72] (equal to sustained hypertension).
2. Developing hypertension within 10 years [61].
3. Developing impaired fasting glucose, or diabetes [62].

When masked hypertension is suspected, ABP should be performed to provide a more comprehensive and reliable assessment of the patient's BP during daily activities and during the night. The detection of masked hypertension can also be made from multiple home measurements in the morning and afternoon with moderate sensitivity and high specificity [74]. However, the long-term reproducibility of the classification with home measurements has been questioned by several studies which have suggested that ABP is superior [75,76].

ADDITIONAL INDICATIONS FOR AMBULATORY BLOOD PRESSURE MONITORING

ABP monitoring can be useful as a guide to the requirement for BP-lowering treatment in patients with high-normal BP on clinic measurements, for patients with intermediate (with additional risk factors) or high CVD risk as assessed by an absolute risk calculator. Thus, variability in clinic BP fails to identify a significant group of patients who should be treated [76].

RESISTANT HYPERTENSION

Resistant hypertension is defined as BP that remains above target despite appropriate doses of antihypertensive agents from at least three different classes (including a diuretic), good adherence to treatment and appropriate management of lifestyle risk factors [77]. Measurement of ABP is indicated in these patients to assess the daytime BP pattern and assess the degree to which any white-coat effect is contributing to apparent resistance [78]. About a quarter of patients with apparent resistant hypertension have controlled BP when assessed by ABP monitoring [79].

OLDER PATIENTS

Daytime and night-time values from ABP monitoring in older individuals are valid and reproducible [80] and have better long-term prognostic value for cardiovascular events than clinic BP [81,82].

SYNCOPE OR OTHER SYMPTOMS SUGGESTING ORTHOSTATIC HYPOTENSION

ABP monitoring can be useful to document syncope or other symptoms, suggesting orthostatic (postural) hypotension (particularly when this cannot be confirmed in the clinic) [83]. ABP monitoring can also be used to document fluctuating and unstable BP patterns in patients with autonomic failure [83], or asymptomatic postprandial hypotension [83] which is more common in older patients [84]. The incidence of orthostatic hypotension is particularly high (68%) in older patients with diabetes [85]. ABP monitoring has been recommended to detect the high incidence of masked hypertension in patients with cardiac autonomic neuropathy resulting from type 2 diabetes [86].

HYPERTENSION IN PREGNANCY

ABP monitoring can be used as an adjunct to clinical BP measurements in pregnancy and is usually well tolerated (see section 'Practical considerations').

Normal mean daytime (awake) ABP values are [87]

1. less than 132/79 mmHg at up to 22 weeks gestation,
2. less than 133/81 mmHg at 26–30 weeks gestation, and
3. less than 135/86 m mHg at more than 30 weeks gestation.

A major role for ABP monitoring is to identify white-coat hypertension in early pregnancy [88–90]. The use of BP-lowering treatment can be avoided in pregnant women with white-coat hypertension, provided that BP is monitored throughout pregnancy using ABP or home BP monitoring to ensure early detection of preeclampsia or true hypertension in later pregnancy [88].

In women with preeclampsia or gestational hypertension, ABP monitoring enables the detection of night-time (sleeping) hypertension (see Table S1, http://links.lww.com/HJH/A138, BP more than 120/75 mmHg) which is associated with higher daytime (awake) BP, increased risk of maternal renal and hepatic dysfunction and lower birth weight [79]. At this time, there is no evidence that targeting nocturnal hypertension in these women alters pregnancy outcomes.

As a group, women who later develop preeclampsia show higher average daytime ABP in early pregnancy. However, ABP monitoring in an individual pregnant woman cannot be used to assess woman's risk of preeclampsia, progression from gestational hypertension to preeclampsia or baby's risk of low birth weight [90,91]. ABP monitoring has currently no role in the management of established preeclampsia or gestational hypertension. A Cochrane analysis (updated in 2005 and 2011) has found no randomly controlled studies comparing ABP with conventional BP monitoring during pregnancy [92].

TITRATING ANTIHYPERTENSIVE MEDICINES

Antihypertensive therapy based on ABP monitoring, rather than regular clinic measurements, provides better management with more appropriate adjustment of medication doses required to achieve target BP [78,93–97]. There is good evidence that when used to manage antihypertensive therapy, ABP is equally effective as clinic BP in reducing end-organ damage, but with less intensive therapy to preserve BP control [36]. ABP monitoring may also be used as a sensitive indicator of loss of BP control [96] and to ensure that treatment is effective for a full 24 h [98]. We also recommend that home BP measurements are combined with ABP monitoring as described in Figs 1 and 2.

EPISODIC HYPERTENSION

Episodic hypertension (e.g. in patients with phaeochromocytoma) may escape detection with clinic BP measurements. ABP monitoring for at least 24 h increases the likelihood of capturing bouts of episodic hypertension that otherwise could be missed.

SUSPECTED SLEEP APNOEA

Because ABP monitoring permits BP measurements during sleep, it can be useful for demonstrating lack of nocturnal dipping in patients with suspected sleep apnoea [41,42].

PATIENTS AT HIGH CARDIOVASCULAR DISEASE RISK

Detection of hypertension and treatment to target are critical in those at high CVD risk identified by existing CVD (e.g. a history of stroke or myocardial infarction), the presence of end-organ damage (e.g. LVH or microalbuminuria) or associated conditions that increase CVD risk (e.g. diabetes or chronic kidney disease). ABP monitoring may be useful in assessing treatment effects and guiding dose titration in these patients (Fig. 2) [98]. Note that ambulatory SBP readings cannot automatically be substituted for clinic SBP in an absolute risk calculation and, therefore, corrected equivalents are provided in Supplement Appendix B (Table S3, http://links.lww.com/HJH/A138).

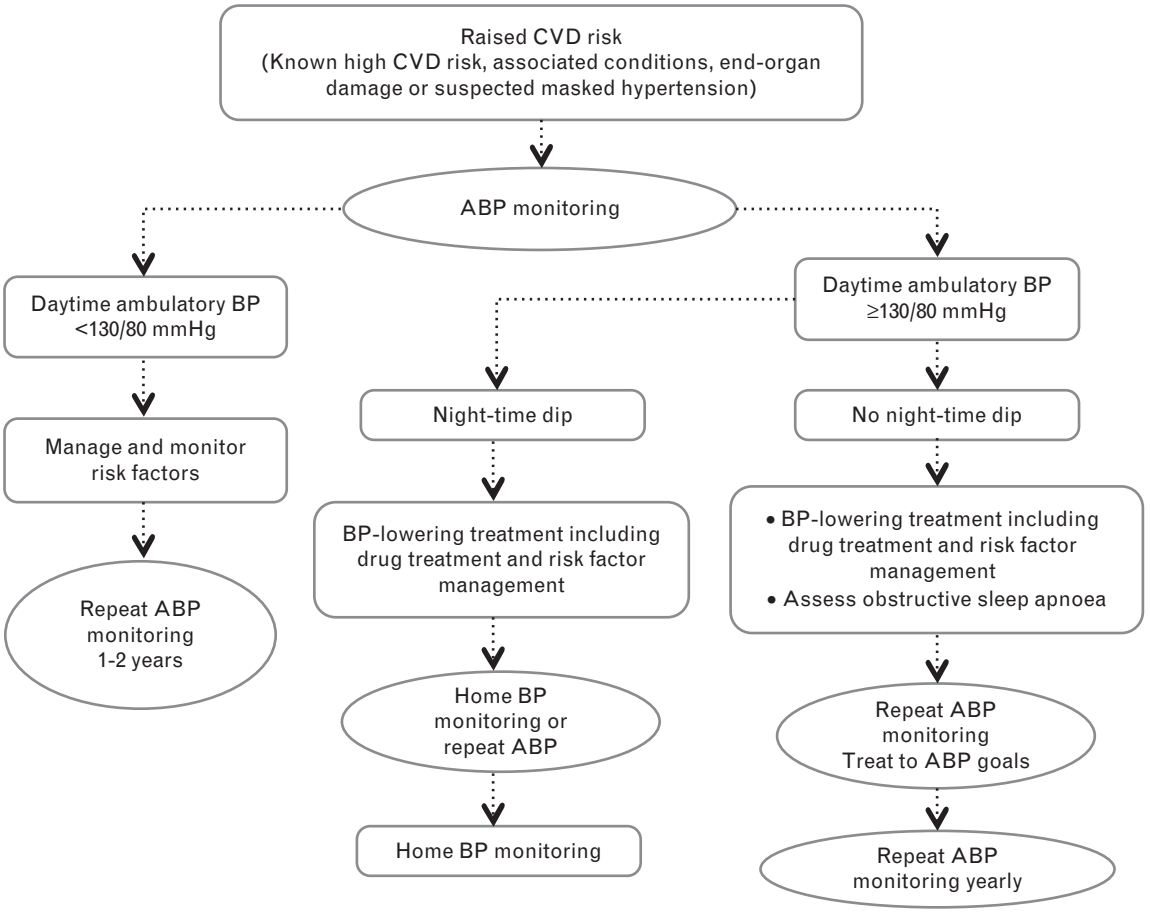

FIGURE 2 Flow diagram for management of blood pressure (BP) in patients at high risk of cardiovascular disease (CVD) or in whom masked hypertension is suspected. In these patients it is appropriate to perform ambulatory BP (ABP) monitoring, even if the clinic BP levels are not elevated and lifestyle factors have been assessed and modified as required. Raised CVD risk includes any of the following: existing CVD; high CVD risk as assessed using absolute CVD risk calculator, irrespective of BP; or presence of associated conditions or end-organ damage (any of the following: diabetes, cerebrovascular disease, coronary heart disease, chronic heart failure, chronic kidney disease, aortic disease, peripheral arterial disease, dyslipidaemia, family history of premature CVD or familial hypercholesterolaemia, left ventricular hypertrophy or microalbuminuria). Refer to current National Heart Foundation of Australia (NHF) hypertension management guidelines for details.

INTERPRETING AMBULATORY BLOOD PRESSURE

Box 3

Key points

- Measurements obtained from ABP monitoring must be interpreted carefully with reference to diary information and timing of medicines.
  Reference 'normal' ABP values for nonpregnant adults are as follows:
- Twenty-four hour average less than 115/75 mmHg (hypertension threshold 130/80 mmHg).
- Daytime (awake) less than 120/80 mmHg (hypertension threshold135/85 mmHg).
- Night-time (asleep) less than 105/65 mmHg (hypertension threshold 120/75 mmHg).
- ABP values above 'normal' and below thresholds for hypertension are considered 'high-normal'.
- Night-time (sleeping) average SBP and DBP should both be at least 10% lower than daytime (awake) average.
- BP load (percentage time during which BP readings exceed hypertension threshold over 24 h) should ideally be less than 20%.
- BP variability, maximum SBP and morning BP surge should also be taken into account (and targeted by treatment).
- Treatment targets based on ABP equivalents are lower than for clinic BP readings.

ABP readings should be interpreted with reference to patient diary records for sleep, medicines, posture, activity, symptoms and/or other events (see section 'Instructions for patients'). Actual times for day/night should be used rather than those defined by the software. Explanatory notes on the selection of thresholds are provided in (Supplementary Appendix B).

'NORMAL' BLOOD PRESSURE LEVELS IN ADULTS COMPARED WITH CLINIC BLOOD PRESSURE

Current Australian national guidelines for the diagnosis and management of hypertension define 'normal' BP for adults as clinic BP less than 120/80 mmHg [2]. This category corresponds to the following ABP readings (rounded to nearest 5 mmHg):

24-h average	<115/75 mmHg
Daytime average	<120/80 mmHg
Night-time average	<105/65 mmHg

CLASSIFICATION OF HYPERTENSION IN ADULTS COMPARED WITH CLINIC BLOOD PRESSURE

Current Australian national guidelines for the diagnosis and management of hypertension define hypertension in adults as clinic BP of at least 140/90 mmHg [2]. Note that the term 'hypertension' and classification cut-points are used for practical reasons, on the understanding that individual CVD risk assessment determines appropriate management in each patient [2]. They further emphasize that BP-related risk is a continuum with no defined lower cut-point [2]. Equivalent ABP thresholds for hypertension (rounded to nearest 5 mmHg) are as follows:

24-h average	130/80 mmHg
Daytime average	135/85 mmHg
Night-time average	120/70 mmHg

Equivalent ABP thresholds for the classification of hypertension are shown in Table 2 [3]. This classification may provide guidance on the appropriate intensity of antihypertensive therapy. For example, daytime ABP more than 168/105 mmHg corresponds to clinic BP more than 180/110 mmHg and should, therefore, trigger immediate initiation of antihypertensive therapy for the management of grade 3 hypertension according to current guidelines [2], including both pharmacological therapy (commencement of treatment or an increase in dose) and lifestyle risk factor modification regardless of other CVD risk factors.

TREATMENT TARGETS IN ADULTS COMPARED WITH CLINIC BLOOD PRESSURE

Treatment targets based on ABP monitoring are lower than those based on clinic BP readings. Like clinic BP treatment targets, ABP targets depend on the individual's absolute risk of CVD (i.e. targets are lower for patients with or at elevated risk of CVD, including those with associated conditions or end-organ damage).

ABP treatment targets corresponding with current national guidelines are shown in Table 3 [3,99–101] (see Supplementary Appendix B, Table S2, http://links.lww.com/HJH/A138 for age-adjusted and sex-adjusted targets in patients with moderate-to-high CVD risk). For practical purposes, the clinic target BP can be simply used as the target for the mean daytime BP during ABP monitoring (e.g. for a patient with diabetes, the target goal for average daytime ABP is less than 130/80 mmHg) [3].

FACTORS TO CONSIDER WHEN INTERPRETING AMBULATORY BLOOD PRESSURE READINGS

Age and sex effects

The Italian and the Danish population studies of normal untreated individuals showed a similar 2/1 mmHg increase in mean 24 h BP per decade [102,103]. The recent Australian ABP study of untreated individuals from hypertension clinics with ages ranging from 18 to 80 showed SBP rising by 1.6 mmHg per decade, whereas DBP did not change with age [3]. Although these SBP age-related changes are relatively small, they are less than the 'apparent' age-related effect when measured within the clinic [102]. The impact of this age-related increase in white-coat effect is that the SBP treatment target thresholds (equivalent to clinic 140/90 mmHg) are 1 mmHg per decade lower in older age groups [3]. Calculated daytime diastolic ABP equivalents are not affected by age. Systolic and diastolic ABP equivalents for women are 3 and 2 mmHg lower, respectively, than for age-matched men (see Supplementary Appendix B).

Nocturnal dipping status

Physiologically, BP follows a diurnal pattern, with average night-time (asleep) BP levels substantially lower than daytime (awake) BP levels. There is wide interindividual variation in the magnitude of the nightly BP dip.

Nocturnal nondipping is defined as a fall of less than 10% in average night-time SBP or DBP (or both), compared with daytime averages [25]. Nondipping (or nocturnal BP increase) may indicate marked end-organ damage, autonomic dysfunction [33] or the presence of obstructive sleep apnoea [42]. Thus, it is not surprising that night-time BP predicts end-organ damage [20,95,104] and may be a better predictor of clinical outcomes than daytime BP [15,22,38,40]. For some people, BP readings during the night may result in unusually poor sleep in which case it may be necessary to repeat ABP monitoring, as sleep disturbance may reduce or even prevent dipping [105,106]. Thus, it is important to relate night-time readings with the patient's diary to confirm their reliability. Optimal BP control involves treating to targets for both daytime and night-time BP (e.g. an evening dose of an antihypertensive drug may be indicated if nondipping is detected) [107].

The converse of nondipping is known as extreme dipping where there is more than 20% reduction in BP at night.

TABLE 2. Classification of hypertension in adults

		ABP predicted from clinic BP (mmHg)		
Hypertension thresholds	Clinic BP (mmHg)	24 h	Night	Day
Grade 3 (severe)	180/110	163/101	157/93	168/105
Grade 2 (moderate)	160/100	148/93	139/84	152/96
Grade 1 (mild)	140/90	133/84	121/76	136/87

Predicted mean systolic/diastolic ABP values (not rounded) corresponding to specific clinic BP levels that are used in grading hypertension. Equivalents are based on clinic BP measured by trained staff other than doctors [3]. These equivalents differ slightly from the rounded recommended values shown in the text. ABP, ambulatory blood pressure. Adapted from [3].

TABLE 3. Treatment targets in adults

Patient group	Clinic BP (mmHg)	ABP equivalents (mmHg)		
		24 h	Night	Day
Uncomplicated hypertension[a]	140/90	133/84	121/76	136/87
People with associated clinical conditions or end-organ damage[b]	130/80	125/76	112/67	128/78
Hypertension with proteinuria >1 g per day	125/75	121/71	107/63	124/74

Predicted mean systolic/diastolic ABP levels (not rounded) for specific clinic BP targets (upper limits) in which BP is measured by trained staff other than doctors [99]. The clinic BP targets are based on overall cardiovascular risk assessment. These equivalents differ slightly from the rounded recommended values shown in the text. ABP, ambulatory blood pressure. Adapted from [3].
[a]People without any of the following: coronary heart disease, diabetes, chronic kidney disease, proteinuria (>300 mg/day), stroke or transient ischaemic attack.
[b]People without any conditions listed above. The exact clinic target of 130/80 mmHg has recently been questioned particularly for diabetic individuals [100,101].

This is not necessarily benign, as there is evidence that it may be associated with underperfusion of the brain and mild cognitive impairment in older patients [108], particularly if antihypertensive treatment results in a greater dipping [109].

Blood pressure load

The proportion of time during which BP readings exceed the hypertension threshold over a 24-h period, that is, 135/85 mmHg while awake and 120/75 mmHg during sleeping hours, can be defined as BP load. The measure is closely related to mean BP and BP variability and is a better predictor of end-organ damage than occasional clinic or mean ABP readings [110]. An estimate of BP load (expressed as percentage time or area under the BP–time curve) is often provided automatically by ABP analysis software. In a patient with an average 24-h SBP of 120 mmHg, a BP load of approximately 20% would be expected [110]. For an average 24-h SBP of 130 mmHg, BP load would be approximately 50%, whereas for an average 24-h SBP of 140 mmHg, BP load would be approximately 85%.

EMERGING AMBULATORY BLOOD PRESSURE PARAMETERS THAT COULD ALSO BE CONSIDERED

Morning blood pressure surge

The risk of stroke, sudden cardiac death or myocardial infarction is highest in the morning, [111] during which there are increases in BP, HR, circulating catecholamines, other hormones and hypercoagulability [112]. The magnitude and rate of morning BP surge is exaggerated in people with hypertension [113]. Morning SBP measured by ABP monitoring is a strong independent predictor of stroke and other CVD outcomes [114,115]. Morning BP can also be measured using home BP measurement [116,117]. In older patients with hypertension, morning BP surge (difference between morning BP and nadir during sleep) measured by ABP monitoring is strongly correlated with the risk of stroke, independent of mean BP and nocturnal BP [118].

Blood pressure and heart rate variability

ABP monitoring provides information on the following:

1. Short-term BP and HR variability (SD for daytime or night-time readings).
2. Circadian BP and HR variability (day–night difference).
3. Long-term BP and HR variability (when ABP monitoring repeated 6 monthly or yearly).

BP variability should be taken into account when interpreting BP profiles as evidenced by the following:

1. Short-term night-time and daytime BP variability has been correlated with risk of end-organ damage [119] and daytime SBP variability has been correlated with CVD mortality risk [120].
2. Long-term (between-visit) clinic SBP variability in patients receiving antihypertensive treatment and maximum daytime ambulatory SBP are predictors of stroke risk, independent of mean SBP [121,122].

Smoothness index

Smoothness Index is a measure of optimal 24-h BP control. It is defined as the ratio between the effect of treatment on average hourly BP for the 24-h period [change in BP (Δ^H)] and the SD, the effect of treatment on average hourly BP (SD of average Δ^H) [119,123]. It may be a better predictor of reduction of left ventricular mass index during treatment than trough : peak ratio [123].

Ambulatory arterial stiffness index

Ambulatory arterial stiffness index (AASI) has been suggested to be a measure of arterial wall stiffness [124], although this is still controversial [125]. AASI is based on the concept that in stiffer vessels SBP will rise to a greater extent than DBP, as BP changes from lowest (sleeping) levels to highest daytime levels. It is calculated as one minus the regression slope of DBP over SBP. Normal AASI is typically less than 0.5 for younger adults and less than 0.7 for older adults [124]. AASI is correlated with other measures of arterial stiffness, is a better predictor of mortality than other risk factors [126] and is associated with subclinical organ damage in hypertensive patients irrespective of treatment [127]. A symmetrical version of AASI has recently been developed to improve prediction of CVD risk, independent of BP [128].

PRACTICAL CONSIDERATIONS

Box 4

Key points
- Ideally, ABP monitoring should be performed by professionals trained in BP measurement and ABP monitoring.
- Only appropriately calibrated devices should be used for ABP monitoring.

- Arm circumference should be measured to select the correct cuff size.
- BP should be measured in both arms to select the correct arm in which to measure ABP (see below).
- Patients should be given written information and instructed to keep a diary (see section on instructions to patients).
- ABP readings should be validated against readings taken using a calibrated sphygmomanometer.
- ABP readings may not be accurate when taken during exercise, movement or driving or when the cardiac rhythm is irregular.

WHO SHOULD PERFORM AMBULATORY BLOOD PRESSURE MONITORING?

ABP monitoring is a specialized technique that requires training, skills and experience, validated and well calibrated monitors, the use of correct cuff sizes and appropriate protocols. The insight provided by experienced professionals in interpreting ABP is of considerable value to the clinical management of hypertension.

AMBULATORY BLOOD PRESSURE MONITORING DEVICES

ABP monitors use cuff oscillometry which relies on detection of cuff pressure oscillations and defines the maximal oscillations as mean arterial BP and then uses an algorithm to calculate SBP and DBP [129]. As different algorithms are used by different manufacturers, there is some variation between devices. Mean BP is the most reliable measurement by oscillometric devices [129]. Studies assessing day-to-day variability in ABP profiles have generally reported good reproducibility. Regimens for quality control, including continual training and assessment, calibration testing and regular evaluation of equipment, are essential. Devices should be calibrated regularly (e.g. twice yearly) using a calibrated reference pressure device. Only devices validated and approved (reaching grade A) by international standards (British Hypertension Society [130] or American Association for the Advancement of Medical Instrumentation [131]) should be used for ABP monitoring. Lists of validated devices can be obtained from the websites of the European Society of Hypertension (ESH) and British Hypertension Society [132]. As the criteria specified in these protocols are difficult to fulfil, the working group on BP monitoring of the ESH has developed a simplified protocol to facilitate validation of devices to be used in clinical practice [133].

IMPORTANCE OF CORRECT CUFF SIZE

It is essential to choose the correct cuff size, because BP obtained from oscillometric devices may vary, depending on cuff size and cuff–arm compliance [134]. Selection of the correct cuff is best determined by measurement of the arm circumference. This can be aided by the manufacturer's labelling on the cuff and lines that indicate whether the wrap-round is within the cuff's dimensions. People with a large upper arm (particularly obese people) may need cone-shaped cuffs.

ASSESSING THE QUALITY OF AMBULATORY BLOOD PRESSURE DATA

As a guide, a recording is usually considered successful when at least 85% of readings are suitable for analysis. ABP profiles should be interpreted cautiously, with reference to activity and sleep patterns. ABP readings may not be accurate when taken during exercise, movement or driving or when the cardiac rhythm is irregular (e.g. atrial fibrillation). Incorrect readings can be due to improper cuff fitting (e.g. patients with cone-shaped arms), movement artefact, tremor and weak or irregular pulse.

The best method for dealing with outlying values is a matter of considerable debate but, as a general rule, editing should be kept to a minimum [135] or the modified Casadei method used to eliminate artefactual readings [136]. Clearly, physiologically impossible pressures (e.g. such as when the diastolic pressure equals the systolic pressure) should be removed. Some devices feature in-built accelerometer to detect movement, but this still needs to be validated.

USE OF AN AMBULATORY BLOOD PRESSURE MONITOR

Initial validation of readings in the clinic

At the time the ABP monitoring device is fitted, at least three readings should be recorded simultaneously using a calibrated sphygmomanometer connected to the ABP monitoring device by a Y-connector. Average readings for ABP and sphygmomanometer should not differ by more than 5 mmHg. BP should be measured in both arms. If the SBP difference between arms is less than 10 mmHg, use the nondominant arm. If the SBP difference is greater than 10 mmHg, the arm with the higher pressure should be used [57].

Frequency of measurements

ABP monitoring devices are usually programmed to take readings at set intervals of 20–30 min during the day and every 30–60 min at night in order to avoid interfering with activity or sleep. However, measurements can be made more frequently; some centres use intervals of 15–20 min during the day and 30 min during the night, whereas others take readings at 30-min intervals throughout the entire 24-h period [137]. The latter is sufficient to obtain correct mean values, but high-recording frequency may be required for measures related to short-term variability.

Instructions for patients

Patients should be given information and instructions about the procedure in order to minimize fear and anxiety. A written set of instructions to take home is recommended after the initial verbal description (in the patient's first language, if possible). Patients should be informed which activities may interfere with the device and instructed to keep a diary to record timing of activities, sleep, taking of medicines, posture and symptoms (e.g. dizziness) that may be related to BP. A normal work day should be chosen rather than a rest day to obtain a typical BP profile that better predicts end-organ damage.

Although modern devices are quiet, lightweight and relatively easy to wear, inflation of the cuff may cause discomfort, particularly in people with hypertension or when multiple repetitions of the reading are triggered due to errors in measurement. In one study conducted among pregnant women, up to 15% discontinued ABP monitoring due to discomfort [138].

ABP monitoring is safe and not usually associated with complications, but occasionally petechiae of the upper arm or bruising under the inflating cuff may occur, and there may be sleep disturbances. Discomfort and sleep disturbance should be taken into account when interpreting the readings (including the presence or absence of nocturnal dipping) acquired by ABP monitoring.

Box 5

Key messages for patients

- The monitor will automatically inflate and record BP and pulse rate periodically throughout the 24-h period.
- Continue with typical daily activities throughout the monitoring period, but avoid vigorous exercise during monitoring.
- When the cuff starts inflating, keep the cuff at heart level, temporarily stop moving or talking for about 1 min, keep the arm immobilized and relaxed and try to relax and breathe normally.
- Some monitors give a warning tone prior to measurement.
- Do not kink tubing, but do retighten connections if a leak occurs.
- Occasionally, the device may repeat the measurement a moment later at a higher pressure. This is quite common and does not mean there is a problem.
- Keep the device on during sleep and do not switch it off.
- During monitoring, do not shower or bathe (sponge baths only) because the cuff should not be removed.
- Make diary entries as requested.
- Avoid napping during the day.
- Call phone number provided if you have technical difficulties or other concerns during the monitoring period.

HOW REPRODUCIBLE AND RELIABLE IS A SINGLE AMBULATORY BLOOD PRESSURE RECORDING?

The reproducibility and reliability of ABP has been extensively studied with the consensus indicating sufficient reliability in mean 24 h values to diagnose hypertension [139,140], to assess the efficacy of drug treatment with a single before and after assessment [93,94] or to detect nocturnal dipping [141,142]. Reproducibility is less for daytime and night-time values than 24 h estimates [143], although one study suggests that daytime is equal to 24 h for diagnosing hypertension [140]. Repeated ABP recordings are generally recommended to correctly detect white-coat hypertension [63]. Also, there is a small pressor effect of wearing the ABP monitor in most patients which lasts for the first few hours and would be expected to add 1–2 mmHg to the average [144,145]. Reproducibility is expected to be better with a shorter interval (a few weeks) between recordings [139].

HOW OFTEN SHOULD AMBULATORY BLOOD PRESSURE MONITORING BE REPEATED?

When and how often ABP monitoring is repeated depends on clinical judgement [1] and should take into consideration whether the patient is at high risk of CVD [1] and whether BP treatment targets have been met (Fig. 2). Repeated ABP monitoring should be considered to guide treatment in people with masked hypertension, 'nondippers' and people with markedly increased BP variability. Suspected white-coat hypertension should be confirmed by ABP monitoring repeated several weeks later [63]. ABP monitoring (or home BP monitoring) should be repeated every 1–2 years in patients with white-coat hypertension (Fig. 1).

FUTURE RESEARCH

The potential benefits of normalization of the circadian BP variability in people with hypertension, particularly by using chronotherapy aimed at optimizing nocturnal BP, will become an important area of research. The recent findings of the Ambulatory Blood Pressure Monitoring and Cardiovascular Events (MAPEC) study are encouraging. This study found that taking antihypertensive medication at night led to better 24 h control, lower rates of nondipping and lower levels of cardiovascular risk markers [146,147].

Although there has been one randomized controlled study comparing outcomes in 419 patients with hypertension who were treated on the basis of ABP monitoring versus clinic BP measurements [36], this needs to be confirmed with larger trials possibly with the addition of home measurement as well. The 'power' of the morning BP surge is a mathematically derived measure of the morning rate–amplitude product. Currently, this parameter cannot readily be calculated from data output provided by standard ABP analysis software. Power of the morning surge may become a useful standard diagnostic measure, because it has been shown to be almost double in people with hypertension or white-coat hypertension, compared with normotensive people [3].

Another measure to consider for further research is AASI which is associated with subclinical organ damage in hypertensive patients [127]. A comparative study could be to measure AASI in white-coat hypertension, masked hypertension and normotensive individuals to determine whether AASI correlates with target organ damage.

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Conflicts of interest

There are no conflicts of interests.

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