Hypertension Research (2013) 36, 285–292

www.nature.com/hr

REVIEW

# Ambulatory and home blood pressure monitoring in children and adolescents: diagnosis of hypertension and assessment of target-organ damage

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**The prevalence of elevated blood pressure in children and adolescents is more common than previously believed and often represents the early onset of essential hypertension, particularly in adolescents. The definition of hypertension in children is based on distribution criteria and normalcy tables that provide blood pressure percentiles for each measurement method (office, ambulatory and home) according to the individual's age, gender and body size. Owing to the white coat and masked hypertension phenomena, ambulatory blood pressure monitoring is indispensable for the diagnosis of hypertension in children. Home blood pressure monitoring in children has been less well studied, and at present, treatment decisions should not be based solely on such measurements. Hypertension-induced preclinical target-organ damage (mainly echocardiographic left ventricular hypertrophy) is not uncommon in children and should be evaluated in all hypertensive children. Other indices of target-organ damage, such as carotid intima-media thickness, pulse wave velocity and microalbuminuria, remain under investigation in pediatric hypertension.**
*Hypertension Research* (2013) **36,** 285–292; doi:10.1038/hr.2012.220; published online 24 January 2013

**Keywords:** diagnosis; masked hypertension; pediatric; white coat hypertension

## INTRODUCTION

In the last two decades, accumulating evidence has considerably altered the awareness and understanding of pediatric hypertension. Recent studies demonstrate that particularly among adolescents, hypertension is not as uncommon as previously believed, and in most cases represents the early onset of essential rather than secondary hypertension. Therefore, current guidelines recommend that all children older than 3 years seen in a medical setting should have their blood pressure (BP) measured unless there are special conditions that justify earlier screening.[1,2]

Several studies have estimated the prevalence of elevated BP in children and adolescents to be ~1–2%, which is largely affected by differences in protocols and methodology for BP assessment and by differences in ethnic background.[3–8] More importantly, there is evidence that the average BP in children and adolescents is rising.[8,9] The US National Health and Nutrition Examination Surveys (NHANES) demonstrated in the 1999–2000 survey that the average BP in children was 1.4/3.3 mm Hg (systolic/diastolic) higher than the average BP in the 1988–94 survey, after adjustment for age, gender and race/ethnicity.[9]

The obesity epidemic appears to be the major contributor to the increasing trends in childhood hypertension, given that a strong association between body mass index and BP levels has been reported.[9,10] Other factors of the modern lifestyle, such as sedentary behavior assessed by screen use time (television and computer) and adverse dietary habits, also appear to be associated with increased BP in children and adolescents.[8,11–13] A cohort study following 166 children 5–12 years old for 7 years revealed that the risk of developing high BP during adolescence can be predicted by BP and body mass index at childhood.[14] Elevated BP in children and adolescents has been shown to induce preclinical target-organ damage, as assessed by echocardiographic left ventricular hypertrophy, microalbuminuria and carotid artery thickness.[15–18]

The assessment of hypertension typically relies on conventional office or clinic BP measurements taken by the doctor or nurse using a classic mercury sphygmomanometer and the auscultatory method. However, as in the case in adults, the phenomena of white coat and masked hypertension are not uncommon in children and are missed without out-of-office BP assessment.[5]

## OFFICE BP MEASUREMENT AND HYPERTENSION CLASSIFICATION

As with several other measurements and diseases, the thresholds for BP classification and hypertension diagnosis in the pediatric population exhibit fundamental differences compared with adults. The hypertension recommendations for adults are largely supported by

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Received 11 August 2012; revised 27 October 2012; accepted 5 November 2012; published online 24 January 2013

observational and interventional, large long-term outcome studies with hard endpoints of morbidity and mortality, which have been meta-analyzed and demonstrate the cardiovascular risk associated with elevated BP,[19] and the protective effects of treatment-induced BP reduction. These data permitted the estimation of BP thresholds for hypertension diagnosis and intervention. In contrast, in children and adolescents, large outcome hypertension trials are lacking and are unlikely to be available due to the very long follow-up required and the multiple infiltrating, confounding factors. Thus, recommendations for hypertension management in children and adolescents are based on statistical considerations and assumptions or on extrapolation from evidence obtained in adults.

The gold standard method for hypertension diagnosis and decision making in children has always been the conventional office BP measurement. The 2004 US Task Force of the National High BP Education Program Working Group on High BP in Children and Adolescents published normalcy tables for office BP based on a large database of children and adolescents (Table 1).[1] Tables of the 50th, 90th, 95th and 99th BP percentiles for each year of age and according to height percentiles (based on the growth charts of the Center for Disease Control and Prevention) are provided for boys and girls. The US Task Force recommended the use of the 90th and 95th office BP percentiles to diagnose prehypertension and hypertension.[1] It should be noted, however, that although this database was developed from single-visit BP measurements, current guidelines recommend that the diagnosis of hypertension should be based on BP values from at least three visits.[1,2]

For office BP measurement in children, the use of a mercury sphygmomanometer and the auscultatory method are recommended or, if not available, a calibrated aneroid device, with first (K1) and fifth (K5) Korotkov sounds, defining systolic and diastolic BP, respectively, is recommended. BP measurements obtained by oscillometric devices that exceed the 90th percentile should be confirmed by auscultation,[1] because normative data have been based on auscultation and because of concerns about the accuracy of measurements obtained by oscillometric devices in children.

Attempts to define normative data for office BP in children and adolescents in Europe were made in 1991 in 28 043 children from six Northwest European countries and in 1999 in 11 519 Italian schoolchildren,[22] both using the auscultatory technique. The oscillometric technique has been used in subsequent studies, which also provided normative data for office BP.[22–25] Owing to the large database that was used to define the US Task Force normalcy tables, these normative data were adopted from the 2009 European Society of Hypertension (ESH) recommendations for the management of high BP in children and adolescents (Table 1).[2] However, physicians who use these tables in the evaluation of children with elevated BP in Europe should be aware that these are not based on a European population and that the BP values in the European studies appear to be several mm Hg higher than those in the US (the 90th and 95th BP percentiles were 3–8 mm Hg higher for systolic and diastolic BP in both sexes for children between 5 and 12 years of age and 2–3 mm Hg higher in older males[26]).

According to both the US Task Force and the ESH guidelines, hypertension in children and adolescents is defined as an average systolic and/or diastolic BP that is above the 95th percentile for gender, age and height on at least three separate occasions. High-normal BP in the ESH guidelines[2] or prehypertension in the US guidelines[10] is defined as an average BP above the 90th percentile but lower than the 95th percentile or as a BP over 120/80 mm Hg in adolescents with BP lower than the 90th percentile. Both the ESH and the US guidelines categorize hypertension into stage 1 and 2 using the 99th percentile plus 5 mm Hg as the threshold (Table 2).

## OUT-OF-OFFICE BP MEASUREMENT

The conventional office or clinic BP measurement exhibits a number of important disadvantages that are due to the technique itself, the involvement of an observer, the statistical issue of regression to the mean and the white coat and masked hypertension phenomena.[5,27]

With conventional auscultatory office BP measurement, the observer error is classified into 'systematic error', which leads to both intra- and interobserver error, 'terminal digit preference' with the observer

**Table 1 Cross-sectional studies that defined the currently recommended normative tables for office, home and ambulatory blood pressure measurements in children and adolescents.[1,2]**

| *Blood pressure* | *Country year* | N *of subjects* | *Age (years)* | *Boys (%)* | *Method device* | N *of readings* |
|---|---|---|---|---|---|---|
| Office[1] | US 2004 | 63 227 | 1–17 | 51 | auscultatory mercury | single occasion |
| Ambulatory[20] | Germany 1997 | 949 | 5–20 | 49 | oscillometric SpaceLabs 90 207 | day 36–48 night 7–12 |
| Home[21] | Greece 2007 | 778 | 6–18 | 46 | oscillomertric Omron 705 IT | 12 |

**Table 2 Thresholds for the diagnosis of hypertension in children and adolescents.[1,2]**

| | *Blood pressure measurement method* | | | | |
|---|---|---|---|---|---|
| *Hypertension phenotype* | *Office/ Clinic* | | *Ambulatory* | | *Home* |
| Normal blood pressure | <90th centile | | — | | — |
| High-normal blood pressure or pre-hypertension | 90th–<95th centile or ⩾120/80 mm Hg | | — | | — |
| Hypertension | Stage 1: 95–99th centile + 5 mm Hg<br>Stage 2: >99th centile + 5 mmHg | | ⩾95th centile | | ⩾95th centile |
| White coat hypertension | >95th centile | and | <90th centile | or | <90th centile[a] |
| Masked hypertension | <90th centile | and | ⩾95th centile | or | ⩾95th centile[a] |

[a]At present not adequately investigated.

rounding off the pressure reading to a certain terminal digit (usually 0 or 5) and 'observer prejudice and bias', whereby the observer adjusts the recorded BP according to his/her expectation.[28] These phenomena can be minimized by careful observer training but cannot be eliminated. A century after applying the technique, these phenomena remain common, even in specialized BP clinics, and significantly affect the accurate diagnosis of hypertension.[27]

For environmental reasons, the European Community has recently banned all mercury devices, including the sphygmomanometer.[29] Reliable alternative solutions for auscultatory office BP measurement appear to include the validated aneroid devices or the hybrid devices that have digital, LED or LCD display.[30] An alternative yet still debatable solution is the use of automated oscillometric devices in the pediatric population. The oscillometric method measures mean BP at the level of the maximal oscillation and then uses a manufacturer- and device-specific algorithm to estimate systolic and diastolic BP. Children often have different and typically shorter or smaller oscillations, which might lead to inaccurate BP assessment.[31] Furthermore, as mentioned above, the normalcy thresholds for office BP measurement are based on data using auscultatory measurements; therefore, the use of oscillometry in the office is questionable, even when regarded as accurate.

It should be realized, however, that oscillometry is already widely applied for out-of-office BP assessment and is used almost exclusively for 24-hour ambulatory BP monitoring and in most cases of self-home BP monitoring. In addition, the normalcy tables for these methods (ambulatory and home BP) have been based on measurements obtained by oscillometric devices. However, the use of oscillometric devices that have been specifically validated in pediatric populations using established protocols, such as the British Hypertension Society protocol, the American Association for the Advancement of Medical Instrumentation protocol or the ESH International Protocol, is recommended.[32–37] Unfortunately, very few oscillometric devices for office, home or ambulatory BP measurement have been successfully validated in children and adolescents.[38] Owing to these problems with the oscillometric method, the diagnosis of hypertension in children detected using such measurements should be confirmed using the auscultatory method.[1]

Out-of-office monitoring is indispensable for the detection of white coat hypertension (elevated office BP and normal out-of-office BP, ambulatory or home) and masked hypertension (normal office BP and elevated out-of-office BP). The diagnosis of hypertension in children based exclusively on office BP measurements can lead to either overtreatment (in cases of white coat hypertension) or undertreatment (in masked hypertension).[2,5] In 2004, the US Task Force recommended that a diagnosis of white coat hypertension should be made when office BP is higher than the 95th percentile but normal outside the clinical setting.[1]

The first report on the white coat hypertension phenotype in children was published in 1991 and found that 44% of 159 children with a positive family history of hypertension exhibited white coat hypertension.[39] Subsequent studies reported a prevalence of white coat hypertension ranging from 10–60% according to the office BP measurement methodology, the diagnostic thresholds for office and ambulatory BP and the population studied (healthy, referred for elevated BP, or other).[40–46] As in adults, white coat hypertension appears to be more common in children with mild elevation of office BP compared with those with higher BP levels.[45] The relationship of white coat hypertension and target-organ damage in children and adolescents remains controversial. Some studies report the association of target-organ damage, most of them referring to left ventricular mass index, with white coat hypertension,[46–48] whereas others do not report such a correlation.[49]

The first study on masked hypertension in children was published in 2004;[50] therefore, the 2004 US Task Force Report did not mention this condition.[1] A study in 136 normotensive (on the basis of office BP) subjects aged 6–25 years in Japan revealed the prevalence of masked hypertension to be 11% (19% in boys and 5% in girls), without differences in the prevalence between participants $<15$ and $>15$ years old.[50] However, the study population consisted of a mixture of children, few of them healthy, many in the recovery phase after acute illness and some with chronic illnesses.[50]

A study by Lurbe *et al.*[51] in Spain in 592 children and adolescents aged 6–18 years old who attended an outpatient clinic for a routine health checkup established the existence and clinical significance of masked hypertension in children. On the basis of office and ambulatory BP monitoring, 90% of the children were normotensive, 0.8% were hypertensive, 1.2% exhibited white coat hypertension and a remarkable 7.6% exhibited masked hypertension. These data were confirmed in a school study of 765 children in Greece that used office and home BP measurements to demonstrate that masked hypertension (4.2%) is more common than sustained (2.1%) or white coat hypertension (1.8%).[52] In the Spanish study, children with masked hypertension were more likely to have a parental history of hypertension than normotensive children (18 and 7%, respectively) and a consistently higher ambulatory pulse rate throughout the entire 24-hour period than normotensive controls, suggesting overactivation of the sympathetic nervous system.[51] It is worth mentioning, however, that the diagnosis of masked hypertension was not particularly reproducible; approximately half of these children exhibited normal ambulatory BP after 12 months.[51] These data suggest that more than one 24-hour ambulatory BP recording is needed to make an accurate diagnosis of masked hypertension. More importantly, 8.8% of subjects with masked hypertension developed sustained hypertension during the study follow-up, and subjects with persistent masked hypertension exhibited an increased prevalence of left ventricular hypertrophy compared with normotensive subjects.[51] A more recent study using ambulatory BP monitoring in 85 children and adolescents referred for elevated BP reported that the prevalence of hypertension, white coat hypertension and masked hypertension was 25%, 13% and 9.4%, respectively.[48] Therefore, in children and adolescents referred for elevated BP, masked hypertension and white coat hypertension are common phenomena. The data for target-organ damage in children with masked hypertension, although based on small groups of children in the abovementioned two studies,[48,51] are in agreement with findings in adults that demonstrate that masked hypertension is associated with increased left ventricular mass[53] and greater cardiovascular risk compared with normotensive adults.[54] Thus, as in the adult population, there is a need to make a precise diagnosis of white coat, masked and sustained hypertension in children.

## AMBULATORY BP MONITORING

In adults, the application of 24-hour ambulatory BP monitoring is supported by sufficient data indicating its superiority over office BP measurements, both in terms of its association with target-organ damage and its prediction of cardiovascular morbidity and mortality.[27] Furthermore, ambulatory monitoring has important clinical applications, including the detection of the white coat and masked phenomena and the assessment of nocturnal hypertension.[27] In the last two decades, ambulatory BP monitoring has been increasingly

used in children and adolescents with elevated BP, and in the recent ESH guidelines, ambulatory BP monitoring is regarded as indispensable for the management of pediatric hypertension.[1,2,10]

Several studies have indicated that ambulatory BP monitoring is feasible in children,[55] even in infants[56] and is useful for the assessment of pediatric hypertension.[55] Lurbe *et al.*[57] reported BP measurements nearly 90% valid in 333 children aged 3–18 years, with the proportion depending on the age and the systolic BP level. Furthermore, ambulatory BP is more reproducible than office measurements, a criterion with high clinical relevance,[58–61] and appears to be cost-effective when applied in the initial evaluation of pediatric hypertension.[62] Interestingly, studies in normotensive children and adolescents have demonstrated that awake ambulatory BP is significantly higher than office BP,[20] which has been attributed to the high level of physical activity of the young subjects during the day (Figure 1).[63]

According to the current guidelines, the diagnosis of ambulatory hypertension is defined by an average 24-hour, daytime or nighttime systolic and/or diastolic ambulatory BP greater than or equal to the 95th percentile for gender and height or age (Table 2).[1,2,10] The BP load, which is defined as the percentage of BP readings above the 95th percentile, has been used in the staging of ambulatory BP.[10] The normalcy tables for ambulatory BP measurements are also based on cross-sectional studies. The tables endorsed by both the US and ESH guidelines[2,10] are those by Soergel *et al.*,[20] which included 1141 children and adolescents in Germany. The study initially provided a normative table that reported the 90th and 95th percentiles, stratified according to age and height (Table 1). Later publications from the same study provided percentiles by age (5–16 years) and percentiles for daytime (0800–2000 hours) and nighttime (0000–0600 hours).[64]

However, there are still some issues regarding the application of ambulatory BP monitoring in children. First, only a few manufacturers have developed the necessary pediatric cuffs for ambulatory monitors. Second, the devices are almost exclusively oscillometric, with several issues in children as mentioned above. Third, only a few ambulatory monitors have been tested in children[38,65–68] using established protocols,[32–37,69] and most of these monitors have been shown to have questionable accuracy. It should be noted that the Spacelabs 90207 ambulatory monitor, which has been used in the study that defined the currently recommended normalcy tables for ambulatory BP in children and is extensively used in practice,[20] did not satisfy the validation criteria.[38,65]

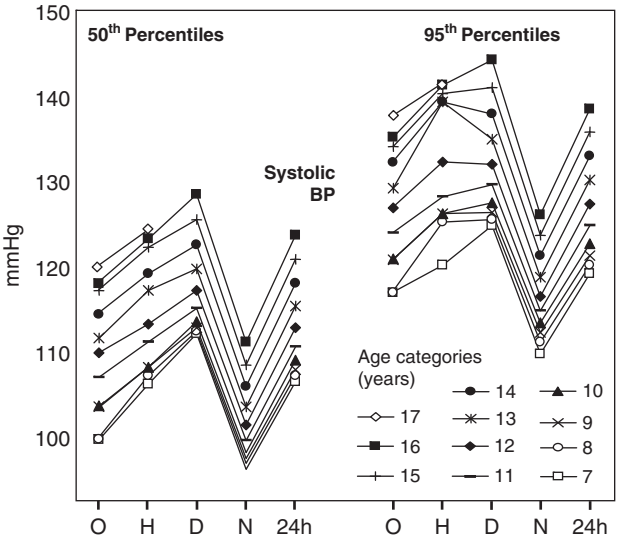


**Figure 1** Comparison of the 50th and 95th percentiles for office, ambulatory and home systolic blood pressure in boys by age (modified from Stergiou *et al.*[63]). O, Office blood pressure; H, Home blood pressure; D, Daytime ambulatory blood pressure; N, Nighttime ambulatory blood pressure; 24 h, 24-hour ambulatory blood pressure.

In addition to the diagnosis of hypertension and the detection of white coat and masked hypertension, 24-hour ambulatory BP monitoring is a unique tool for the evaluation of nocturnal hypertension and the identification of impaired nocturnal dipping, which are often seen in children with secondary hypertension, renal disease and diabetes.[70–72] The detection of impaired nocturnal dipping is clinically important, as impaired nocturnal dipping has been shown to precede microalbuminuria in children with type 1 diabetes; in those children with normal nocturnal BP dipping, the development of microalbuminuria is less likely.[72] Therefore, based on established evidence in adults, more strict control of BP in children with diabetes could be recommended.[2] Studies in the general pediatric population have demonstrated that the non-dipping phenomenon is not uncommon in hypertensive children and is present in almost half of children with primary hypertension, two-thirds of children with secondary hypertension and approximately one-third of children with white coat hypertension.[73] Impaired nocturnal dipping and nocturnal systolic hypertension have been shown to be the most frequent forms of hypertension in obese children and are correlated with the degree of obesity and insulin resistance as well as with obstructive sleep apnea.[74]

Furthermore, ambulatory BP monitoring is a valuable tool in children for the evaluation of antihypertensive drug treatment effects, assessment of refractory hypertension, evaluation of BP control in children with target-organ damage and evaluation of symptomatic hypotensive episodes.[2,10]

## HOME BP MONITORING

The evidence of the clinical utility of home BP monitoring in children is much weaker than that for ambulatory monitoring.[2,75,76] However, surveys among pediatric nephrologists in the US, Canada and Europe demonstrate that home BP monitoring is already widely used in children.[21,77] Owing to the limited evidence of its clinical relevance in children, home BP monitoring was not mentioned in the pediatric hypertension guidelines until 2009 when the ESH guidelines were published.[2] The normalcy tables by gender and height endorsed by the ESH guidelines[2,76] were obtained from a study in 768 healthy subjects aged 6–18 years in Greece (Arsakeion school study),[78] and a recent reanalysis of these data provided percentiles by age.[75] In contrast to adults, in whom average home BP does not differ from daytime ambulatory BP, daytime ambulatory BP in children is significantly higher than home BP (Figure 1),[63] which is likely due to the high level of daytime physical activity in young individuals.

Several recent studies have provided useful information on the clinical application of home BP monitoring in children.[60,76,78–81] This method appears to be feasible in the pediatric population, and the vast majority of children and adolescents are able to follow a several-day schedule and acquire an acceptable number of measurements at home, with or without (in older children and adolescents) the parents' assistance. In an early study in 43 children and adolescents with type 1 diabetes who were asked to perform home BP monitoring for 3 days, 61% of the participants provided all of the requested measurements and 88% provided at least one of the three requested days of measurements.[79] In the Arsakeion school study in Greece, 70% of the participants provided all of the requested home BP

readings (duplicate morning and evening measurements for 3 days), and 95% provided two-thirds or more of the requested readings.[78] However, as in adults, caution is needed, and devices with automated memory are preferred because misreporting (over- or under-reporting) of home BP values by patients is not uncommon.[76]

In line with findings in adults, two studies have demonstrated the reproducibility of home BP monitoring in children to be superior to that of office BP[60,80] and as good as that of ambulatory BP monitoring.[60] The optimal home BP monitoring schedule was investigated in a study of 100 children and adolescents and demonstrated that, as in adults, home BP monitoring for 3 days with duplicate morning and evening measurements is the minimum schedule required to provide a reliable assessment of the BP at home.[81]

Two studies suggested that, as in adults, home BP monitoring in children allows the accurate detection of the white coat and masked hypertension phenomena.[5] The ESCAPE (Effect of Strict Blood Pressure Control and ACE Inhibition on the Progression of CRF in PEdiatric Patients) study in 118 subjects with chronic renal failure aged 3–19 years demonstrated the ability of home BP measurements to diagnose hypertension.[82] By taking ambulatory BP as a reference method, the sensitivity of home BP was 41%, the specificity was 92%, the positive predictive value was 61% and the negative predictive value was 84%.[82] Another study that compared the diagnostic value of home versus ambulatory BP monitoring in 102 children and adolescents referred to a hypertension clinic for elevated BP concluded that the two methods are interchangeable in the detection of white coat or sustained hypertension, with clinically important disagreement between the two methods in the diagnosis of hypertension in only 8% of the cases.[83] By taking ambulatory BP as the reference method for the diagnosis of hypertension, the sensitivity, specificity and positive and negative predictive value of home BP was 55, 92, 74 and 82%, respectively; 89, 92, 70 and 98%, respectively, for the diagnosis of white coat hypertension and 36, 96, 50 and 93%, respectively, for the diagnosis of masked hypertension.[83]

## BP MEASUREMENT METHODS AND TARGET-ORGAN DAMAGE

In children and adolescents with essential hypertension, the presence of preclinical target-organ damage is of paramount importance in the assessment of the cardiovascular risk and decision-making. As discussed above, in the pediatric population, there are no alternative well-studied endpoints related to hypertension, due to the extremely long follow-up required for the determination of the predictive value of BP for cardiovascular events. Thus, the assessment of preclinical target-organ damage is part of the essential evaluation in every child with essential hypertension.

Studies in high-risk pediatric populations, such as children with type 1 diabetes or renal failure, have revealed the close association of hypertension with target-organ damage.[84,85] More recently, research has focused on the relationship of BP with target-organ damage in essential hypertension. The main indices of target-organ damage in the pediatric population include left ventricular hypertrophy (mass and index), increased carotid intima media thickness, microalbuminuria, proteinuria and decreased glomerular filtration rate. Among these indices, left ventricular hypertrophy appears to be the most extensively studied index of preclinical target-organ damage in the pediatric population.

Echocardiography is widely available in most countries, and established criteria exist for left ventricular hypertrophy in children and adolescents based on the 95th percentiles for left ventricular mass corrected for body surface area.[86] In addition, specific left ventricular geometric patterns in children with essential hypertension have been described (for example, concentric left ventricular hypertrophy), which might be associated with higher risk.[16] Several studies have reported the prevalence of left ventricular hypertrophy in young hypertensive individuals ranging from 10% to 47% according to the methodology and the criteria applied.[16,87–89]

In addition to the average ambulatory BP values, several other parameters of the 24-hour BP profile have been associated with left ventricular hypertrophy. In particular, 24-hour, daytime and nighttime systolic ambulatory BP levels, 24-hour systolic ambulatory BP load and index, 24-hour pulse pressure and 24-hour heart rate have all been demonstrated to be more closely associated with left ventricular mass index than the conventional office BP measurements.[90–93] Furthermore, in children with nephropathy who are on dialysis, left ventricular hypertrophy has been demonstrated to be associated with a decreased nocturnal decline in systolic BP, which can only be assessed by 24-hour ambulatory BP monitoring.[94]

Carotid intima media thickness in children is a recently studied index and appears to be determined by adiposity and ambulatory BP, specifically 24-hour pulse pressure, 24-hour systolic ambulatory BP index and load.[92,95] Nighttime systolic ambulatory BP has also been reported to be more closely correlated with creatinine clearance in apparently healthy children.[18] Moreover, in a study of 82 children and adolescents (20% with essential hypertension), 24-hour pulse pressure was correlated with carotid-femoral pulse wave velocity, which is an established index of arterial wall stiffness in adults.[96] It should be noted that in the abovementioned studies, ambulatory BP was consistently correlated with indices of preclinical target-organ damage more strongly than office BP measurements.[18,92,96]

The association between BP monitoring methods and microalbuminuria has been investigated in children with diabetes mellitus, prehypertension or chronic nephropathy. A multicenter study in 2105 diabetic children revealed a close association of microalbuminuria with nocturnal diastolic BP and diastolic dipping.[97] Moreover, in prehypertensive children, the BP load appeared to be associated with a reduced glomerular filtration rate and increased proteinuria, but the cause-and-effect relationship remains uncertain.[98] These data underscore the importance of ambulatory BP monitoring due to its ability to assess the nocturnal BP and the BP load. Although left ventricular hypertrophy and microalbuminuria are often associated in children with essential hypertension,[99] the role of microalbuminuria in the general pediatric population and in non-diabetic children with essential hypertension remains unclear. However, it has been suggested that microalbuminuria might be used as a signal to begin BP-lowering interventions to prevent overt proteinuria.[2]

With respect to home BP monitoring, there is only one study in healthy children and adolescents referred to a hospital clinic for elevated BP (20% with essential hypertension) that demonstrated close association with left ventricular mass and pulse wave velocity, comparable to those of ambulatory BP.[100] Moreover, both methods were superior to clinic BP measurements in terms of their association with target-organ damage.

## TARGET-ORGAN DAMAGE IN WHITE COAT AND MASKED HYPERTENSION

The management of children with white coat hypertension is questionable because the prognostic significance of this phenomenon is not fully clarified. Studies in adults have demonstrated that white coat hypertension is associated with cardiovascular risk comparable to that of normotensive individuals;[101] however, data from prospective studies demonstrated that in the long term, this phenotype of

hypertension might be associated with a higher cardiovascular event rate[102,103] than that of normotension. No data are available regarding the long-term follow-up of children found to have white coat hypertension upon initial diagnostic procedures to indicate with confidence that this is an innocent phenomenon without future adverse cardiovascular consequences.

In a study by Stabouli *et al.*,[45] children with white coat hypertension tended to exhibit higher left ventricular mass index and carotid intima media thickness than normotensive subjects but lower values than hypertensive subjects suggesting that this phenotype in children may represent an intermediate phenotype. In a case-control study of 163 adolescents, the prevalence of left ventricular hypertrophy differed between normotensive, hypertensive, white coat and masked hypertensive individuals, with the greatest risk for hypertrophy observed among those subjects with stage II hypertension. Although these differences did not reach statistical significance after adjusting for body mass index, the left ventricular mass index in the subjects with white coat hypertension was between that of normotensives and hypertensives.[88] In another case-control study, three groups (normotension, white coat and essential hypertension group) were compared with respect to their left ventricular mass index, which, in the white coat hypertensives, was observed to be between that of normotensives and hypertensives.[47] In a small study of 52 children with essential hypertension and with white coat hypertension, an increased prevalence of microalbuminuria was observed in the essential hypertension group, whereas children with white coat hypertension exhibited no signs of renal damage.[104]

In contrast with white coat hypertension, masked hypertension appears to be more closely associated with cardiovascular risk and may significantly contribute to the burden of target-organ damage in the pediatric population. As mentioned above, masked hypertension is not uncommon in the young, exhibiting a prevalence of up to 7.6% in children 6–18 years old.[48] Children with masked hypertension exhibit a higher left ventricular mass index compared with normotensive children.[51] In a study by Stabouli *et al.*,[48] 85 children were evaluated with clinic and ambulatory blood pressure and were investigated for target-organ damage. In children with masked hypertension, left ventricular mass index was similar to that in hypertensive subjects and significantly higher than normotensives.[48] This was also the case for carotid intima media thickness, which was higher in children with masked hypertension than in normotensives but lower than in hypertensive subjects, though this difference did not reach statistical significance.[48] In a case-control study in 163 adolescents, the risk of left ventricular hypertrophy among subjects with masked hypertension was similar to those with stage I hypertension, and for both of these groups, the risk tended to be lower than that of stage II hypertension.[88] Moreover, in a study of 226 children (median age 12 years) with chronic kidney disease, the likelihood of having left ventricular hypertrophy was four-fold higher in children with masked hypertension than in those with normal clinic and ambulatory BP.[105]

Further prospective studies with long-term follow up are needed to establish the cardiovascular risk burden of white coat and masked hypertension in the pediatric population. Until such data become available, children with white coat hypertension and especially those with masked hypertension should be evaluated with special care. Confirmation of these diagnoses with repeated office and ambulatory monitoring is required, as well as evaluation of subclinical target-organ damage. Subjects with white coat hypertension and no evidence of target-organ damage should be followed with non-pharmacological measures, whereas treatment initiation should be considered in children with target-organ damage or persistent masked hypertension.

## CONCLUSIONS

The prevalence of elevated BP in children and adolescents is more common than previously believed and often represents the early onset of essential hypertension, particularly among adolescents. The definition of hypertension in children is based on normalcy tables that provide BP percentiles for each measurement method (office, ambulatory, home) according to the individual's age, gender and body size. Owing to the white coat and masked hypertension phenomena, ambulatory BP monitoring is indispensable for the diagnosis of hypertension in children. Home BP monitoring in children has been less well studied, and at present, treatment decisions should not be based solely on such measurements. Hypertension-induced preclinical target-organ damage (mainly echocardiographic left ventricular hypertrophy) is not uncommon in children and should be evaluated in all hypertensive children. Given that outcome trials with cardiovascular morbidity and mortality endpoints are not feasible in children, long-term follow-up studies to validate the BP thresholds of hypertension on the basis of preclinical target-organ damage are required.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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