

# Controversy and Agreement Among Guidelines Defining Ambulatory Hypertension in Children



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Hypertension is the strongest modifiable risk factor for cardiovascular disease, with origins in early life.<sup>1</sup> Identifying children following high-risk trajectories depends on accurate diagnosis and is important if we are to intervene before organ damage and clinical events occur. Yet, despite growing evidence about the prevalence and relative importance of high blood pressure (BP) in childhood, there remains a paucity of data on which to base the definition of hypertension in children. Hence, controversy persists, with discrepancies internationally, and between pediatric and adult guidelines.

Updated guidelines place an increasing emphasis on ambulatory BP monitoring (ABPM) in diagnosing and treating hypertension. This has been driven by strong evidence correlating ABPM with outcomes among adults, and growing data supporting an association

between ABPM and intermediate vascular phenotypes in childhood.<sup>2</sup> ABPM also allows us to better phenotype hypertension, differentiating diurnal and nocturnal components, average values and variability, including time spent above the 95th centile threshold (BP load). Although the relative value of these components has yet to be fully delineated, it seems likely there is at least utility in measuring nocturnal BP in addition to daytime measurements.<sup>3</sup>

Despite both the American Academy of Pediatrics (AAP) and European Society of Hypertension (ESH) using the 95th centile of BP for age, sex, and height to define hypertension, there are important differences between the guidelines.<sup>4,5</sup> The reference data when defining an elevated office BP differs between the two; pertinently, the most recent AAP guidelines removed overweight and obese children from their reference population. This serves to produce threshold curves that are congruent with the updated American Heart Association definition of hypertension in the United States but provides a lower

95th centile for office BP by the AAP guidelines compared with that by the ESH. With regard to ABPM, the AAP and ESH are congruent in the threshold values defining the 95th centile, both using common data from the German Working Group, as the best available pediatric reference data.<sup>6</sup> However, in contrast to a greater number of children being diagnosed with hypertension on office BP by the AAP guidelines, the opposite is true for ABPM. The AAP guidelines require the presence of an elevated BP load ( $\geq 25\%$  of measurements being  $\geq 95$ th percentile) and a mean 24-hour BP  $\geq 95$ th percentile (Figure 1). The inclusion of a BP load criterion is based on data demonstrating that this has an additive value to mean 24-hour BP in predicting left ventricular mass index, including among children.<sup>7</sup> However, despite its inclusion among earlier versions, this load criterion has since been removed from the American Heart Association guidelines, which now focus on daytime readings because of a greater amount of data on which to base threshold selection.<sup>8</sup> In contrast, the ESH guidelines do not include a load criterion, but do include a fixed threshold of a mean 24-hour BP  $\geq 130/80$  mm Hg that acts as a ceiling for the reference BP value among adolescents. This avoids the paradoxical situation in which an adolescent can meet criteria for hypertension by adult but not pediatric guidelines.

In light of these discrepancies, it is important to understand the impact of using different systems of classifying hypertension. Hence, the value of work by Sharma *et al.*<sup>9</sup> published in this issue of *Kidney International Reports*. They report a cross-sectional study that includes 159 children seen in a

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AAP	ESH
<ul style="list-style-type: none"> <li>• Mean 24-hour blood pressure <math>\geq</math>95th percentile for age, sex, and height</li> </ul>	<ul style="list-style-type: none"> <li>• Mean 24-hour blood pressure <math>\geq</math>95th percentile for age, sex, and height</li> </ul>
AND	OR
<ul style="list-style-type: none"> <li>• <math>\geq</math>25% of readings elevated (blood pressure load)</li> </ul>	<ul style="list-style-type: none"> <li>• Mean 24-hour blood pressure <math>\geq</math>130/80 mm Hg</li> </ul>

**Figure 1.** Diagnosing ambulatory hypertension. Among younger children, the main difference between guidelines is the requirement for an elevated blood pressure load in the guideline of the American Academy of Pediatrics (AAP). Among older children, the European Society of Hypertension (ESH) guideline includes a fixed 130/80 mm Hg threshold that prevents hypertension being diagnosed under adult but not pediatric criteria.

tertiary hospital hypertension clinic, using office BP and ABPM measurements to classify participants into normotensive, white-coat hypertension, masked hypertension, and hypertension categories according to both AAP and ESH guidelines. As anticipated, given common ABPM reference data defining the 95th centile, 85% of subjects were similarly classified by both guidelines. However, this leaves a substantial proportion of children classified differently dependent on the guideline used. Among the cohort overall, 9% more children were diagnosed as having hypertension or masked hypertension using the ESH guidelines, and this discrepancy increased to 13% among children  $\geq$ 13 years old because of the 130/80 mm Hg fixed threshold. Although the primary objective of the study was the impact of ABPM criteria defining hypertension, Sharma *et al.*<sup>9</sup> also examined the impact of using AAP compared with the previous standard, Fourth Report, guidelines to define an elevated office BP.<sup>S1</sup> They confirm more children were classified as hypertensive based on office BP measurements alone under the AAP guidelines, but given no change has occurred in the ABPM reference data used, most of these recategorized children were subsequently diagnosed with white-coat hypertension.

The clinical and statistical methods used in this study were robust when compared with other studies of BP among children and included a standardized protocol to measure office BP with confirmation of elevated oscillometric readings using a calibrated aneroid device. Unfortunately, although commonly used in clinical practice and research, the Spacelabs 90207 ABPM device used (Space Labs Inc., Redmond, WA) may be inaccurate in children. A validation study rated the systolic/diastolic performance of the device, a C/D by British Hypertension Society, and Pass/Fail by Advancement of Medical Instrumentation, protocols.<sup>S2</sup> This problem highlights issues surrounding the development of ABPM devices in children and lack of validation data confirming that proprietary algorithms are applicable to young patients. For the purposes of this study, the accuracy of the monitor should not have resulted in differential bias between the AAP and ESH guidelines for younger children, but a higher mean systolic BP by the Spacelabs 90207 device may have exacerbated the impact of the 130/80 mm Hg fixed threshold among adolescents. Another caveat when interpreting the study results is that the study population was selected from a tertiary hypertension clinic, excluding patients with secondary hypertension.

Although the selection criteria served to create a homogeneous study population for analysis, they limit generalizability to other settings, such as primary care. Similarly, most of the study participants were Caucasian, further limiting generalizability.

Regardless of these limitations, the results are likely valid for the population included and have potentially important implications for patient care. They are similar to those reported among mostly overweight and obese Spanish children, among whom white-coat hypertension and masked hypertension were more common by AAP and ESH guidelines, respectively.<sup>S3</sup> Both the AAP and ESH guidelines recommend antihypertensive medication for hypertension or masked hypertension unresponsive to a 1-year trial of nonpharmacologic therapy, regardless of signs of end-organ damage. This article confirms that although the AAP guidelines will identify more children as hypertensive based on office BP alone, subsequent ABPM measurements will lead to more children being treated under the ESH guidelines. In the absence of outcome data to guide threshold selection, we are left to consider the potential impact of applying a more or less sensitive approach to identify hypertension among children. Perhaps a more sensitive approach is appropriate, given the cumulative cardiovascular risk among patients with hypertension from an early age.<sup>S4</sup> However, this needs to be balanced against exposing children to unnecessary investigations and pharmacotherapy.

Long-term clinical outcome studies would be the next step in understanding the practical significance of discrepancies between these guidelines. Clearly, the 2 subgroups that will be most

affected are the overweight and obese patients and the adolescent patients. Hypertension is increasingly common among these 2 populations, and unsurprisingly these subgroups comprised 54% and 57% of the Sharma *et al.*<sup>9</sup> cohort, respectively. These groups are in urgent need of further data to guide care. An increased concurrence of additional cardiometabolic risk factors, and shortened time-to-event compared with other children, makes them an enriched population for the purposes of clinical trials, for whom to study the net-benefit of recommended interventions. Other areas for further research include the classification of children with a mean 24-hour ABPM  $\geq$ 95th centile and a BP load  $<$ 25%, who are currently unclassified under the AAP guidelines, and the derivation of reference data for shorter, or compliant younger, children.<sup>55</sup>

Pediatric hypertension continues to emerge as an increasingly prevalent condition worldwide, and accurate diagnosis is essential if we are to prevent downstream morbidity and mortality. Work such as that published by Sharma *et al.*<sup>9</sup> brings us closer to understanding what might constitute a reference standard defining hypertension. Clearly, ABPM will continue to occupy a more significant position in the diagnostic toolkit of pediatricians, and hence the question of how best to define

ambulatory hypertension is not one confined to the realm of the researchers, or the subspecialty clinic, and will become an increasingly widespread and pressing clinical concern. For now, we can be reassured that use of either the AAP or ESH guidelines provide mostly synonymous results. That is, unless they don't, such as for high-risk subgroups, in which case the jury remains out, and one may be forced to rely on clinical judgment, including the presence or absence of other known cardiovascular risk factors.

### DISCLOSURE

All the authors declared no competing interests.

### SUPPLEMENTARY MATERIAL

Supplementary File (Word)

Supplementary References.

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