Insights and implications of new blood pressure guidelines in children and adolescents

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Data on childhood blood pressure (BP) have increased substantially from 1977, when the National High Blood Pressure Education of the National Heart Lung and Blood Institute convened a Task Force and consequently published the first Report on BP control in children [1]. Prior to this publication, there was no consistent definition of hypertension (HTN) in childhood, and BP was not commonly measured in asymptomatic children or adolescents. Afterwards, several guidelines on this issue have been released [2–5].

The broad present interest in clinical guidelines about HTN in children and adolescents stems from the desire of healthcare professionals to offer, and of patients to receive, the best possible care, that is, a care that is consistent, efficient, and closes the gap between what clinicians do and what scientific evidence supports. The guidelines that have been published over the years have importantly expanded knowledge to the field and have boosted the interest, not only of epidemiologists, but also of pediatricians and basic researchers.

An important issue in this field is the normative values of BP. The definition of HTN in children and adolescents is still based on the normal distribution of BP in healthy children and not on the cardiovascular morbidity and mortality or on the risk to develop early organ damage associated with a certain level of BP. Diagnostic criteria for elevated BP in children are based on the concept that BP in children increases with age and body size, making it impossible to utilize a single-BP level to define HTN, as done in adults. Clinicians can use the available pediatric normative BP data to determine whether BP is within the normal range or is at a level that warrants attention or preventive intervention. Recognition that HTN can be present in otherwise apparently healthy children and that the early increment of BP tracks into adult life raised the interest and the necessity to include BP measurements in the regular healthcare of children and adolescents. It has also become possible to refine BP-derived parameters and to identify subclinical organ damage through measures and markers now far more sensitive than those available decades ago. In the meantime, the increasing prevalence of HTN in children and adolescents has become a significant public health issue as a consequence of the obesity epidemic. The early recognition of the roots of HTN is crucial for introducing early interventions and thereby reducing cardiovascular morbidity and mortality among adults.

Two new guidelines have been published over the past 2 years [6,7]. The Scientific Council and the Working Group on Hypertension in Children and Adolescents of the European Society of Hypertension (ESH) acknowledged the need for an update of the 2009 guidelines because of the large body of new information acquired during the 7-year lapse between publications [5,6]. In the United States, it was also considered that the pediatric HTN guidelines needed to be updated. The American Academy of Pediatrics (AAP) became the new sponsors of the Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents 2017 [7].

Both the ESH and the AAP guidelines [6,7] agree on a number of issues, which include:

1. Screening: BP should be measured in children and adolescents at least 3 years of age and in younger children with increased risk to develop HTN.
2. BP devices and measurement: The auscultatory method is recommended, and phase I and V Korotkoff sounds are used to identify SBP and DBP, respectively. However, oscillometric devices may be used for BP screening in children and adolescents. Whenever doing so, providers should use a device that has been validated in the pediatric age group [8]. If elevated BP is suspected on the basis of oscillometric

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readings, confirmatory measurements should be obtained by auscultatory readings.
3. Ambulatory blood pressure monitoring: it should be used during diagnosis and evaluation of antihypertensive drug treatment in high-risk individuals.
4. Treatment: once HTN has been diagnosed, the ESH and AAP guidelines agree that the procedures to adopt are, in sequence, to repeat BP measurements, to implement lifestyle changes, and finally to make use of pharmacological therapy, unless BP is at a level that implies life-threatening risk, in which case pharmacological therapy should be started immediately.

Despite their agreement on these essential issues, the two guidelines differ on several aspects that impact, to a nonmarginal degree, on clinical practice, that is, the BP threshold that defines HTN, the classification of the BP categories, and as a consequence, the therapeutic BP targets. This is because of changes in the normative data of childhood BP values, as well as the different ages adopted by the two guidelines at which adult BP classification replaces the childhood and adolescent ones. Normative BP values derive from the same source in both guidelines (4), with, however, a difference. Although the ESH still uses the same population as the 2009 guidelines, the AAP guidelines calculated the percentiles based only on normal weight children of the original 2004 cohort. The AAP excluded children who were overweight or obese because there were concerns that they would skew the normal range data in an upward direction, resulting in under-diagnosis of HTN.

The definition of hypertension: According to the ESH guidelines [6], HTN is present when SBP and/or DBP are persistently at or above the 95th percentile for sex, age, and height, measured on at least three separate occasions. For individuals aged at least 16 years, ESH uses the adult criteria to diagnose HTN, at least 140/90 mmHg [9]. Furthermore, stage-1 HTN is defined by ESH as a value between the 95th and 99th percentiles plus 5 mmHg, and stage-2 HTN as the value greater than 99th percentile plus 5 mmHg. In contrast, AAP define HTN as SBP and/or DBP persistently at or above the 95th percentile for sex, age, and height until 13 years of age. For children aged at least 13 years, AAP uses the guidelines for adulthood recently released by ACC/AHA, which have lowered the criteria to define HTN to at least 130/80 mmHg [10]. As a consequence of this new threshold, the definition of stages 1 and 2 also differ between the American and the European guidelines.

In addition to the change in the normative data, the other important difference between the APP and the ESH guidelines is, as mentioned above, 'the age at which the adult criteria should be applied.' The ESH guidelines [6] recommend that youths aged 16 years or older be evaluated according to the BP thresholds for HTN used for adults. This was based on the consideration that a 16-year-old boy in the 95th percentile for height would be defined as hypertensive by an office SBP of 137–140 mmHg, whereas in a 16-year-old girl with the same height percentile, a diagnosis of HTN would be made at an office SBP of only 132 mmHg. However, when 1 or 2 years later, these individuals will no longer be seen by a pediatrician, the girl will now be diagnosed as normotensive or having a high-normal BP by the family physician on the basis of adult guidelines. Even greater differences in diagnosis will occur in adolescents below the 95th height percentile. Due to these differences in diagnosis, a consensus has been reached that for boys and girls aged 16 or older, the definition of HTN should no longer be based on the 95th percentile but on the absolute cut-off BP values used for adults. Therefore, at this age, a high-normal BP is defined as 130–139/85–89 mmHg, a stage-1 HTN as 140–159/90–99 mmHg, and a stage-2 HTN as 160–179/100–109 mmHg.

The AAP [7] consider 13 years as the age above which the normative data of adults should be used. As in the American College of Cardiology/American Heart Association (ACC/AHA) Guidelines, the threshold for HTN definition has been reduced by 10 mmHg [10], this will result in an increase in the number of children that will be labelled as hypertensive, with a likely overburden on the primary care workload. It must be highlighted that the new definition of HTN of the ACC/AHA guidelines [10] relies not only on BP values but also on the calculation of the risk of atherosclerosis and related diseases at the time of the diagnosis, a factor that may have a rationale in adults, but that is not possible to consider in children and adolescents.

Along with the prevalence of HTN, the new guidelines will markedly increase the number of children who will require 24-h ambulatory BP because of the recommendation that 'ABPM should be performed for the confirmation of hypertension in children and adolescents with office BP measurements in the elevated BP category for one year or more or with Stage 1 hypertension over three clinic visits (Grade C, moderate recommendation). ' In both the ESH [6] and AAP [7] guidelines, ABPM is recognized as being useful in the identification of white coat and masked HTN, and the only reliable method for the diagnosis of nocturnal HTN, which confers a cardiovascular risk independent of office and daytime ambulatory BP. The reported frequency of white-coat and masked HTN varies, perhaps as a result of the different office and ambulatory BP criteria used to establish the diagnosis. In this context, the reduced office BP value for office HTN definition adopted by the AAP guidelines will lead to a marked increase of the percentage of white-coat individuals, even if the thresholds to define HTN by ambulatory BP are maintained as the reference values obtained from the European population [11].

The timing of assessment for the presence of target organ damage has important clinical implications. Assessment of left ventricular mass remains a cornerstone whenever looking for target organ damage in sustained pediatric HTN. Children and adolescents with HTN may have left ventricular hypertrophy even in early stages of the disease [6,7], and delaying the assessment may misclassify their cardiovascular risk. Although ESH recommends evaluating target organ damage at the diagnosis of HTN, and to consider its presence as an indication for initiation of pharmacological treatment, AAP recommends assessment for left ventricular hypertrophy only at the time that the use of drugs enters the therapeutic decision. Thus, the ESH guidelines promote the concept that search and detection of early organ damage

may identify hypertensive children and adolescents at high risk who may need more intensive management both through lifestyle modification and pharmacological treatment. In addition, AAP endorses the adult criteria of left ventricular mass index greater than 51 g/m$^{2.7}$ for children older than 8 years. This leads to considerably higher values than a left ventricular mass index threshold based on the 95th percentile for age and sex, which is recommended by ESH (difference 10 g/m$^{2.7}$ and 15 g/m$^{2.7}$ for 8-year-old boys and girls, respectively) [12]. Unlike ESH, AAP does not include any recommendation on how to define left ventricular hypertrophy in children younger than 8 years, which is the group facing the most significant methodological problems with regard to left ventricular mass quantification. Searching for markers of hypertensive target organ damage, ESH recommends the quantitative measurement of albuminuria for routine clinical use in all children with HTN in order to enable early treatment and to improve long-term prognosis.

The continuing debate on the preferred BP targets is also reflected in the recommendations of the ESH and AAP guidelines. In children, evidence in favor of any specific BP goal is scarce and uncertainty prevails also on the drug-specific effects on cardiovascular and renal outcomes. In the absence of prospective long-term studies on the impact of different BP levels on intermediate or major cardiovascular and renal endpoints, the 95th percentile is considered as a cut-off for defining HTN in children and adolescents. This provides a rationale for targeting children and adolescents with essential HTN to a BP below the 95th percentiles for age, sex, and height, although aiming at a BP below the 90th percentile is probably safer, provided that this goal can be attained by a well tolerated treatment. In individuals aged 16 years or older the adult cut-off values for office BP, that is, less than 140/90 mmHg, are recommended as a target by ESH, but values of less than 130/80 mmHg are not excluded, thereby considering the same target that AAP recommends from 13 years of age. In patients with chronic kidney disease (CKD), a BP less than 75th percentile is recommended as a target in children with nonproteinuric CKD whereas a BP less than 50th percentile is recommended in those with proteinuric CKD. This is at variance from APP, which recommends to go to less than 50th percentile also in nonproteinuric patients, although there is no evidence that a low BP goal improves renal survival in nonproteinuric CKD patients [14]. Target values apply to office, home, and 24-h ambulatory BP based on the prospective randomized ESCAPE trial [13], which has provided evidence that a strategy that pursues reduction in these pressures improves long-term renal survival.

Finally, isolated systolic hypertension, namely the most frequent type of HTN in youth, has been considered by the ESH but not the AAP guidelines [6]. This issue is closely related to the understanding of the clinical value of central SBP in the assessment of adolescents with isolated systolic hypertension, because in a number of cases the elevation of brachial SBP is not accompanied by a central BP elevation. Central SBP may be especially relevant in asymptomatic children incidentally found to have isolated peripheral systolic HTN in the absence of target organ damage.

All guidelines acknowledge and lament the lack of solid, trial-based evidence for recommendations on diagnosis and management of pediatric HTN. To fill this gap, a commitment should be made to embark on a concerted action that will provide new important evidence over the next several years. To determine the usefulness and appropriateness of the new BP threshold, studies should examine their effects in both a short-term and a long-term perspective, the latter facing the difficulty of assessing the incidence of the cardiovascular complications of HTN over many years. However, a short-term judgment may be accomplished according to whether new strategies would improve BP control without substantially increasing the cost, workload, and side effects of treatment. Working for the future, the progress to date should provide an impetus for research advances that may translate into clinical practice.

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Conflicts of interest

There are no conflicts of interest.

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