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Management of high blood pressure in children: Similarities and differences between US and European guidelines

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Abstract

Over the last several decades many seminal longitudinal cohort studies have clearly shown that the antecedents to adult disease have their origins in childhood. Hypertension (HTN), which has become increasingly prevalent in childhood, represents one of the most important risk factors for cardiovascular diseases (CVD) such heart disease and stroke. With the risk of adult HTN much greater when HTN is manifest in childhood, the future burden of CVD worldwide is therefore concerning. In an effort to slow the current trajectory, professional societies have called for more rigorous, evidence-based guideline development to aid primary care providers and subspecialists in improving recognition, diagnosis, evaluation and treatment of pediatric HTN. In 2016 the European Society of Hypertension and in 2017 the American Academy of Pediatrics published updated guidelines for prevention and management of high blood pressure (BP) in children. While there are many similarities between the two guidelines, important differences exist. These differences, along with the identified knowledge gaps in each, will hopefully spur clinical researchers to action. This review highlights some of these similarities and differences, focusing on several of the more important facets regarding prevalence, prevention, diagnosis, management and treatment of childhood HTN.

Keywords

High blood pressure; Hypertension; Cardiovascular Disease; Children; Childhood; Adolescent; Clinical Practice Guideline; Prevalence; Management

Introduction

Due to the accumulating wealth of knowledge gained from multiple landmark cohort studies, it is now clear that the antecedents to adult disease originate in childhood. Hypertension (HTN), one of the biggest risk factors for heart disease and the number one

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cause of mortality worldwide [1], has increased almost 4-fold in prevalence among children since the 1970s. Knowing that the risk of adult HTN increases when HTN is diagnosed in childhood, this increasing prevalence of pediatric HTN has significant implications for the future burden of cardiovascular diseases (CVD) worldwide, particularly as 40% of adults 25 years and older across the globe *currently* have a diagnosis of HTN [2]. In an effort to slow the present trajectory, professional societies have called for more rigorous, evidence-based guideline development to aid primary care providers and subspecialists in improving recognition, diagnosis, evaluation and treatment of pediatric HTN. In 2016 the Scientific Council and the Working Group on Hypertension in Children and Adolescents of the European Society of Hypertension (ESH) published guidelines to "increase(d) efforts toward prevention and management of HTN in the pediatric age, thus also helping relieving the burden of CVD in adults" [3]. In 2017 the American Academy of Pediatrics (AAP) and its Council on Quality Improvement and Patient Safety published clinical practice guidelines "to provide an update on topics relevant to the diagnosis, evaluation, and management of pediatric HTN published guidelines" [4]. Both guidelines were developed after review of the available literature, employing consensus based recommendations when evidence was lacking. And while there are many similarities between the latest guidelines published by each professional society, there are several notable differences. These differences highlight the fact that there is still much work that needs to be done to prevent and treat HTN in childhood and ultimately decrease the burden of adult CVD.

Prevalence and comorbidities of arterial HTN in the US and Europe

Despite the differences in geography, there are many epidemiologic similarities in pediatric HTN between the United States (US) and Europe. Current estimates suggest that approximately 3.5% of US children have HTN and between 2.2–3.5% of US children have elevated blood pressure (BP), an entity referred to as prehypertension in earlier US guidelines [5]. In the US, the burden of high BP is greater among males and certain racial/ethnic groups (Hispanic and non-Hispanic African American children). This is not much different than what is found in Europe. The prevalence of pediatric HTN in central European countries is estimated to be between 2.2–4.9%, with higher prevalences in males overall and among children living in Southern and Western Europe (9–13%). And, notably, in both the US and Europe the rate of HTN is greater among children with co-morbid overweight or obesity.

The impact of HTN on target organ damage is also similar in the US and Europe, with studies estimating that 30–40% of children with HTN have coronary artery disease with accelerated vascular aging and left ventricular hypertrophy (LVH) [6–8], a pathological remodeling of the heart thought to occur in response to an increased afterload as is seen with HTN. The most robust data regarding other intermediate outcomes such as arterial stiffness and function (determined by measuring carotid intima media thickness and pulse wave velocity) and measures of renal disease (microalbuminuria) remain limited to European children. As with LVH, these data suggest that HTN increases the risk of these manifestations of subclinical CVD and that successful treatment can ameliorate these findings [9–12].

Important similarities between guidelines

The ESH and AAP guidelines both take a similar stance regarding BP measurement technique when screening for and diagnosing HTN.

HTN is defined in both guidelines as the sustained elevation in BP, and both recognize the utility and limitations of automated devices when screening for HTN. They stress that at least three BP measurements obtained at rest by manual auscultation, utilizing the first and fifth phase Korotkoff sound as the systolic and diastolic measurement, respectively, are essential when diagnosing a child or adolescent with HTN. If the average BP is elevated, repeated measurements obtained in a similar manner are required to confirm the elevation.

Both guidelines also utilize age/sex/height-based definitions of HTN until a period in adolescence when a standard definition is used (13 years in the US guidelines, 16 years in the ESH guidelines), which is equivalent to the respective adult definitions of HTN. This aspect to each guideline was included to allow for a seamless transition into adult care, where HTN thresholds can differ markedly from the age/sex/height-based 95th percentile for older children. In both sets of guidelines, many of the 95th percentile BPs for adolescents 16 and 17 years of age were well below the adult cutpoints for HTN. As these teens age into adulthood, this difference would practically result in a hypertensive adolescent “becoming” normotensive at 18 years of age just based on the different definitions.

An additional motivation for a unified threshold for HTN diagnosis among all adolescents in the US guidelines was to simplify identification of abnormal BP and diagnosis of HTN. Many studies in the US have demonstrated a significant degree of underrecognition of elevated BP and HTN [13–15] thought to be related to the many complex steps required to determine BP percentiles. By simplifying diagnosis through this unified threshold for adolescents, those at greatest CVD risk should be more easily identifiable. The concern, however, is the issue raised above: this standardized threshold for HTN diagnosis in adolescents is markedly higher than the 95th percentile BP cutoffs for many teens. In Europe, where HTN is defined as a sustained elevation in BP >140/90 for all children 16 years and above, this threshold is higher than the 95th percentile BP for all children except for the tallest 17-year-old males who have a 95th percentile BP cutoff of 140/89. In the US, possibly more concerning is that this unified threshold for HTN diagnosis has disparate implications based on sex. Starting at age 13 years, the 95th percentile systolic BP starts to include the unified threshold for HTN diagnosis (130 mmHg) for some US males, and at 17 years of age the 95th percentile systolic BP is >130 mmHg for all males. This is in direct contrast to the 95th percentile cutoffs for US adolescent females, where at no point does the 95th percentile systolic BP reach 130 mmHg. In fact, the difference in 95th percentile BP threshold and the unified threshold for HTN diagnosis is as great as 9 mmHg for the youngest, shortest teen girls. By raising this cutoff not only will many children previously considered hypertensive and at increased CVD risk now be classified as “normotensive”, we have potentially lost an opportunity for earlier intervention and prevention of adult CVD. The European guidelines limit this approach to those 16 and 17 years of age, thereby minimizing the potential missed opportunity for prevention and treatment in their population.

Finally, both guildelines take a similar treatment approach to the recommended therapeutic lifestyle change, with expanded recommendations regarding activity level provided in the European guidelines. They also both agree on the approach to the initial pharmacologic regimen.

Important differences between guidelines

Perhaps one of the more striking differences between the two guidelines is the reported methodology of scientific review and guideline development. The European guidelines describe their methods in a single paragraph, noting that “the text was finalized over approximately 12 months, during which the members corresponded intensively” [3]. In contrast, the US guidelines dedicate more than one page to the methodology employed and promise the future publication of a technical report to describe the scientific methodology in greater detail. The US guideline used a structured format for research of the literature (Patient, Intervention/Indicator, Comparison, Outcome, and Time (PICOT) format), evaluated the evidence quality based on an AAP grading matrix. and conducted a systematic review per established Institute of Medicine recommendations. The 17 member writing team included experts in the field across various clinical disciplines (general pediatrics, pediatric nephrology, pediatric cardiology, pediatric endocrinology, internal medicine), a parent representative and an epidemiologist. The epidemiologist was charged with creating the detailed content outline, serving as a mediator when expert interpretation differed, and participating in the literature review. Similarly, the European guideline appointed HTN experts to their writing group. While these experts included leaders in pediatric nephrology and pediatric cardiology, a significant proportion of the writing group were adult medicine physicians (adult cardiology, adult endocrinology, adult CVD, internal medicine), a notable difference in the composition of the groups.

Regarding the clinical recommendations, differences between the two sets of guidelines begin with the recommended frequency of screening for HTN, with those at low risk (under 3 years of age with no risk factors, those normotensive on screening with no risk factors) generally recommended to undergo screening at a reduced frequency while those at higher risk (those with “prehypertension”, entitled “high-normal BP” in the European guidelines and “elevated BP” in the US guidelines; those with risk factors) recommended to be screened more frequently. The screening schedule is delineated in Table 1.

While easier for primary care providers to implement screening less frequently for those deemed at lower CVD risk, the minimized screening schedule endorsed by the European guidelines presents another missed opportunity for early diagnosis and treatment of HTN. Blood pressure measurement is an easy screening test with little to no adverse effects. While it has been argued that the potential need for repeated BP measurements at the same and subsequent visits to follow up on an elevated BP measurement should be considered a “potential harm” [16], there is no published evidence to substantiate this claim. Further, individuals with elevated BP that normalizes when repeated are at greater risk for the development of HTN over time [17]. These individuals, with potentially only one elevated BP, will have had the opportunity to identify themselves as one in whom closer attention should be paid to their CVD risk, including their BP measurements.

As introduced above, while the rationale underlying the HTN definitions and BP thresholds are the same for each guideline, the actual definitions are different (Table 2). The impact of these differences are not as obviously significant for children less than 13 years of age when compared to those 13 years of age and above. Percentile based definitions continue to be recommended for the diagnosis of HTN in children and pre-adolescents in both guidelines. The BP percentile cut-offs recommended by the ESH guidelines are practically the same as the percentiles recommended in the US guidelines (the 95th percentile + 12 mmHg threshold that defines stage II HTN in the US guidelines is essentially equivalent to the 99th + 5 mmHg threshold that defines Grade II HTN in the European guideline). However, one of the more significant changes to the US guidelines involves the normative table that provides the actual BP measurements that correspond to the age/sex/height-based BP percentiles. The data used to develop the original tables published in the 2004 Fourth Report was based on BP measurements of over 60,000 healthy children in the US who participated in 1 of 11 research studies conducted over several decades. Twenty-one percent of the children in this database had a body mass index in the overweight or obese category, and removal of their BP measurements resulted in BP norms that were several mmHg lower for each age/sex/height strata. Wanting to avoid this impact of overweight and obesity on BP norms, the new US guidelines have revised the BP tables to only reflect normative data from children who were of healthy weight (BMI < 85th percentile) at the time of data collection. Therefore, the 95th percentile BP in the US will correspond to a BP measurement several mmHg lower than the 95th percentile BP in the ESH guidelines, as the European guidelines continue to reference the normative tables published in the 2004 Fourth Report [5].

Several notable differences also exist regarding the role of out–of–office BP measurements in the diagnosis of HTN. The US guidelines go to great effort to recommend against home and school BP measurements when diagnosing children and adolescents with HTN. The US expert group determined that there was a dearth of quality evidence in this area, making it difficult to recommend its use in the diagnosis of HTN. While not recommended for diagnosis, the guidelines do make concessions regarding the usefulness of these measurements in the ongoing management of children with established HTN.

The European guidelines take a different stance on this topic. Not only is home BP monitoring recommended as a useful adjunct to the diagnosis and treatment of children with HTN, but it delivers specific guidance on how to properly conduct home BP monitoring. The European guidelines also provide normative data specifically tailored to home BP monitoring [18–20]. This approach allows for more practical application of the guidelines, as completing the required in-clinic BP measurement for HTN diagnosis can be a barrier for some patients and providers. The provision of guidance regarding the proper methodology for reliable home measurement in the European guidelines could help identify more children at increased CVD risk and has the potential to move the field forward.

The one form of out-of-office BP measurement endorsed by the US guidelines is 24-hour ambulatory BP monitoring (ABPM). This diagnostic tool has a substantially expanded role in the US HTN guidelines, being recommended for all hypertensive children at initial diagnosis and all children with elevated BP for 1 year or longer. Additionally, 24-hour ABPM should be considered for children with high risk conditions, medical diagnoses with

a large potential breadth: obesity, diabetes, prematurity, kidney disease, obstructive sleep apnea, and history of solid organ transplantation, among others. While ABPM has many advantages over clinical and other out-of-office BP measurements, the scope of this recommendation in the US guideline is not practical for universal implementation. Limited availability of 24-hour ABPM monitors and personnel with expertise in interpretation; limited feasibility in many at-risk populations; and lack of reliable reimbursement for this service all contribute to the difficulty providers will face when trying to comply with this strong recommendation in the US guideline.

The European guidelines also recommend 24-hour ABPM but not in such an explicitly extensive manner as the US guidelines. Specifically, while ABPM is recommended for all children at initial diagnosis in the US guidelines, the European guidelines only recommend this monitoring when considering antihypertensive medication initiation. Another notable difference is the addition of having a hypertensive response during the treadmill test to the list of indications for ABPM. Treadmill testing is not addressed in the US guidelines. Finally, the two guidelines differ in how the data gleaned from ABPM should be interpreted. The European guidelines recommend using the lower of either the 95th percentile from normative ABPM data or the accepted criteria for adults (24-hour mean 130/80mmHg; daytime mean 135/85mmHg; nocturnal mean 125/75mmHg). US guidelines solely recommend use of the ABPM 95th percentile cutoffs [21].

Once a child is diagnosed with HTN, he or she should undergo an initial evaluation to investigate for secondary causes of HTN. Both guidelines agree on this, as secondary HTN is much more common in children than adults, and is particularly more likely the younger the age and the higher the BP at diagnosis. The US guidelines, in response to the growing obesity epidemic and the resultant increase in primary HTN, have proposed a more streamlined approach to the initial evaluation of children with HTN. Many tests that were previously endorsed have been eliminated for *all* children at initial diagnosis, reserving these tests for those at greater CVD risk [22]. This is in contrast to the recommendations in the European guidelines which present a more extensive initial evaluation for hypertensive children and adolescents (Table 3).

An essential component of the evaluation of the hypertensive child is screening for the presence of target organ damage. This aspect to hypertensive management also differs between the two guidelines, both in type of organ damage and how such organ damage is defined [23–25] (Table 4). Both guidelines advocate for echocardiography among children being treated with pharmacologic therapy but, as with BP thresholds, they differ in left ventricular mass index (LVMI) threshold for diagnosis of LVH. The European guidelines maintain the 95th percentile LVMI cutoff to diagnose LVH, whereas the US guidelines adopted a much stricter definition of LVH, requiring LVMI ≥51 g/m$^{2.7}$ for diagnosis in all children older than 8 years of age. This cutpoint is much higher than the 95th percentile (95th percentile LVMI is 41 g/m$^{2.7}$ for 8–10 year-old boys and is 36 g/m$^{2.7}$ for 8–10 year-old girls as an example) [26], and has been associated with a four-fold increase in CV morbidity in adults [22]. The US guideline acknowledges the large evidence gaps regarding the role of echocardiography in hypertensive children and that more data is needed in this area.

Both HTN guidelines stress the importance of lifestyle modification in the treatment of pediatric HTN and both stress the importance of weight loss on achieving normotension and cardiovascular health. The European Guidelines, however, provide considerably more guidance regarding these recommended changes. They also provide specific goals regarding weight loss for each BMI category. This is not a prominent part of the US HTN guidelines.

Each guideline provides specific treatment goals, with specific caveats for those at greater CVD risk. As with the BP definitions, the European guidelines have different BP goals for those 16 years of age and above, and the US guidelines have different BP goals for those 13 years of age and older (Table 5). The BP targets are in line with the BP thresholds for HTN diagnosis, with European targets higher than the US targets. The US guidelines have streamlined therapeutic targets for all children by abandoning separate BP goals for those at higher risk (those with chronic kidney disease, diabetes and target organ damage, for example) and instead recommend the same clinic BP treatment target for all children. There remains a need for intermediate outcome data in children to inform recommended treatment targets. Without this essential pediatric data, extrapolating from recent evidence provided by the SPRINT trial [27], the lower treatment goals in the US guideline compared to the European guideline may be more beneficial in decreasing CVD risk among children and adolescents.

While this review is not meant to be an exhaustive description of all of the differences between the two sets of HTN guidelines, there are several other notable differences between the two that are worth mentioning. The European guidelines discuss additional methods to assess CVD risk and also give a deeper explanation of the treatment in heart failure, metabolic syndrome and dyslipidemia. They delineate the various benefits and limitations related to oscillometric BP measurement and provide needed guidance on how to best use these devices in clinical practice They define malignant HTN. The US guidelines address the unique aspects regarding the importance of a psychosocial history when evaluating a child with HTN; the care of the hypertensive athlete, the pediatric transplant recipient, and the adolescent transitioning to adulthood; the impact of environmental exposures, prematurity and low birth weight; cognitive impairment as a comorbid condition; and the economic impact of a HTN diagnosis.

Discussion and conclusion

Pediatric providers increasingly recognize that contemporary children are at a much greater risk for CVD, both in childhood and as they reach adulthood, than those born several decades ago. With this knowledge, there has been a greater urgency to improve the diagnosis and treatment of hypertensive children so that the CVD burden in adults may at least plateau if not decrease over time. In this context, European and North American experts in CVD prevention and treatment recognized the need for reevaluation of the literature to provide relevant updates to guidelines and improve best clinical practices. While there are many commonalities to the resulting guidelines, important differences exist. These differences, along with the identified knowledge gaps in each, will hopefully spur clinical researchers to action. By answering these persistent questions and striving to achieve consensus, the global

community will get much closer to decreasing the CVD burden of our most vulnerable population.

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Summary points

1. In an effort to slow the current trajectory of increasing HTN and CVD prevalence in children and adults, in 2016 the European Society of Hypertension and in 2017 the American Academy of Pediatrics published updated evidence-based guidelines for prevention and management of high BP in children.
2. Both European and US guidelines agree that at least three BP measurements obtained at rest by manual auscultation, utilizing the first and fifth phase Korotkoff sound as the systolic and diastolic measurement, respectively, are essential when diagnosing a child or adolescent with HTN. If the average BP is elevated, repeated measurements obtained in a similar manner are required to confirm the elevation.
3. The new US guidelines have revised the normative BP tables utilized in the diagnosis of HTN for children to only reflect normative data from children who were of healthy weight (BMI $<85^{th}$ percentile) at the time of data collection. This has resulted in BP thresholds being several mmHg lower than in previous guidelines.
4. While home and school monitoring is not recommended for the diagnosis of HTN in the US guidelines, these are recognized as useful adjuncts for the management of HTN. The European guidelines, however, do recommend home BP measurements for the diagnosis and management of HTN and provides specific guidance on how to properly conduct home BP monitoring along with normative data specifically tailored to home BP monitoring.
5. Ambulatory blood pressure monitoring remains an essential component of the evaluation and management of pediatric HTN.

Table 1

Screening office BP measurement schedule for children 3 years of age and older

Clinical Scenario	European Guidelines	US Guidelines
Normotensive BP	Remeasure BP in 2 years	Remeasure BP in 1 year
High normal/Elevated BP	Remeasure BP in 1 year *	Remeasure BP in 6 months
History of: obesity, renal disease, diabetes, or aortic arch coartation. Taking medications that are known to increase BP	Not addressed.	Measure BP at each health care encounter

* assuming no organ damage

BP=blood pressure; US = United States

Table 2

Definition of normotension and hypertension

	European Guidelines		**US Guidelines**		
	<16 years	**≥16 years**		**<13 years**	**≥13 years**
Normotension	<90th %ile	<130/85	*Normotension*	<90th %ile *	<120/80
High-normal BP	≥90th %ile–<95th %ile	130–139/85–90	*Elevated BP*	≥90th%ile *–<95th %ile	120–130/80
Grade I HTN	≥95th %ile–99th %ile + 5mmHg	140–159/90–99	*Stage I HTN*	≥95th %ile–<95th %ile +12mmHg £	130/80–139/89
Grade II HTN	>99th %ile + 5mmHg	160–179/100–109	*Stage II HTN*	≥95th%ile + 12mmHg €	≥140/90
Isolated Systolic HTN	SBP>95th% ile and DBP < 90th %ile	SBP >140 and DBP<90	*Isolated Systolic HTN*	Not addressed	Not addressed
Immediate Referral to ED	Severe HTN ± associated with life threatening condition.	Severe HTN ± associated with life threatening condition.	*Immediate Referral to ED*	>95th %ile + 30mmHg ¥	>180/120 ¥

* or 120/80, whichever lower;

£ or 130/80–139/89, whichever lower;

€ or 140/90, whichever lower;

± Defined by some as 20% above Grade II limit

¥ Or stage II with symptoms

US=United States; BP=blood pressure; SBP=systolic blood pressure; DBP=diastolic blood pressure; HTN=hypertension; ED=emergency department

Table 3

Recommended Initial Screening Tests for the Evaluation of Pediatric Hypertension

	European Guidelines		US Guidelines	
Children	***All***	***Selected group***	***All***	***Selected group***
Physical Examination				
- 4 limb BP			X	
Laboratory Evaluation				
- Urea and Creatinine	X		X	
- Electrolytes	X		X	
- Urinalysis	X		X	
- Lipids	X (fasting)		X	(fasting in obesity)
- Fasting glucose	X			X (high risk DM)
- Urine culture	X			
- Urine microalbumin	X			
- Uric acid	X			
- Hemoglobin A1c				X (obesity)
- AST/ALT				X (obesity)
Imaging Tests				
- Renal Ultrasound	X			X (children < 6 years or ≥ 6 years with concern for renal disease)
- Echocardiography	X			X (at medication initiation)
24-hour ABPM		X (at medication initiation or if clinical condition warrants)	X	

US=United States; BP=blood pressure; ABPM=ambulatory blood pressure monitoring; AST=aspartate transaminase; ALT=alanine transaminase

Table 4

Target Organ Damage Definitions

	European Guidelines		US Guidelines	
	Screening	***How defined?***	***Screening***	***How defined?***
Electrocardiography	No		No	
Echocardiography				
* LVH	Yes	LVMI ≥ 95th %ile	Yes	LVMI ≥ 51 g/m$^{2.7}$ for children > 8 years (boys and girls) or LVM > 115g/BSA for boys and LVM > 95g/BSA for girls
* LV Wall Thickness	Yes	RWT ≥ 95th %ile	Yes	RWT >0.42 cm, LV wall thickness >1.4
* Ejection Fraction	No		Yes	EF<53%
Measures of Arterial Stiffness: Pulse Wave Velocity	No		No	
Measures of Arterial Structure: Carotid intima media thickness	Yes	cIMT ≥95th %ile by age and sex		

US=United States; LVH = left ventricular hypertrophy; LVM=left ventricular mass; LVMI=left ventricular mass index; LV=left ventricular; PWV=pulse wave velocity; RWT=relative wall thickness; EF=ejection fraction; cIMT=carotic intima media thickness

Table 5

Hypertension treatment goals

	European Guidelines		US Guidelines	
	BP Goal <16 years	**BP Goal ≥ 16 years**	**BP Goal < 13 years**	**BP Goal ≥ 13 years**
HTN without co-morbidities	<95th %ile	<140/90	<90th %ile*	<130/80
HTN + Diabetes Mellitus Type 1 or 2	<90th %ile	<130/80	<90th %ile *	<130/80
HTN + CKD				
**Without proteinuria*	<75th %ile	<130/80	<50th %ile MAP by ABPM	<50th %ile MAP by ABPM
**With proteinuria*	<50th %ile	<125/75	<50th %ile MAP by ABPM	<50th %ile MAP by ABPM

* Or <130/80, whichever lower.

US=United States; BP=blood pressure; CKD=chronic kidney disease; MAP=mean arterial pressure; ABPM=ambulatory blood pressure monitoring