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Hypertension in Children: A Comprehensive Review of Contemporary Knowledge and Future Perspectives

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Abstract:
Introduction: Hypertension is one of the most common, well-documented and potentially reversible risk factors of cardiovascular incidents in the adult population. However, studies are much scarcer when it comes to children. With the obesity epidemic on the rise around the world, clinicians must try and ensure the best possible care is given to the patients in order to avoid potential unfavourable outcomes.
Aim of the Study: This study aims to evaluate and summarise current knowledge regarding arterial hypertension in the paediatric population, especially emerging trends, causes, risk factors, and long-term outcomes and outline possible future avenues of research.
Materials and Methods: A systemic search of currently available literature was conducted through databases such as PubMed, Google Scholar, ResearchGate, and the Cochrane Library using combinations of keywords such as "paediatric hypertension," " treatment," "screening," "epidemiology," and "complications." The current guidelines by associations around the world, such as the American Academy of Pediatrics (AAP), European Society of Hypertension (ESH) and the Canadian Cardiovascular Society (CCS) were also reviewed.

Conclusions: Arterial hypertension has emerged as a condition of growing prevalence within the paediatric population. Research indicates that it is prevalent among individuals with a Body Mass Index (BMI) equal to or exceeding 25. Furthermore, the potential complications associated with this condition are numerous, and prompt diagnosis alongside effective treatment, through lifestyle modifications or pharmacotherapy, is essential to mitigate these risks. Nonetheless, numerous avenues for further research remain available to enhance understanding and treatment strategies of paediatric hypertension.

Keywords:
Paediatrics; Hypertension; Risk factors; Complications; Treatment; Screening;

Introduction

Hypertension is one of the most common, well-documented and potentially reversible risk factors of cardiovascular incidents in the adult population. However, good quality studies are much scarcer when it comes to the paediatric population. With the prevalence of obesity on the rise around the world, clinicians must try and ensure the best possible care is given to children to avoid potential unfavourable outcomes. This review aims to summarize the available knowledge regarding paediatric HTN, including its many causes, possible complications and treatments. We focus on the latest guidelines from the American Academy of Paediatrics, European Society of Hypertension and Canadian Cardiovascular Society, as well as the latest research and recent epidemiological studies. Lastly, we outline avenues and topics that require conducting further research in the future.

The definitions of Arterial Hypertension

The international consensus is that HTN should be defined as ABP of or above the 95th percentile. However, the guidelines differ when it comes to normative tables required for arterial blood pressure (ABP) assessment. In all cases, these tables are scaled using the age, height and sex of the child. However, this is where the similarities end. ESH recommends using normative tables up to the 16th year of the child's life and only then switching to constant ABP values, similar to those used in the adult population. On the other hand, the AAP recommends using scaled tables up to the age of 13. In its most recent 2017 guidelines, the AAP excluded children with a BMI above the 95th percentile when creating the normative ABP values. This will most likely lead to a significantly increased diagnosis rate, although at the cost of lower specificity; however, the exact result of this change remains to be seen. [1-4] This change was demonstrated by Dong et al. in their 2018 study where they compared the diagnosis rate using the updated 2017 AAP diagnosis criteria and the previous one from the 2004 AAP's fourth report in a group of 50 336 children. Using the 2017 diagnosis criteria of HTN in this group, 16.7% of children aged 6-12 and 7.9% of those aged 13-17 had HTN in contrast to 10.8% and 6.3%, respectively, when using the previous criteria. [55]

In a 2022 consensus document on HTN by European Cardiology associations, HTN is further divided into subgroups depending on the patients' ABP values: stage 1 and stage 2 HTN. Stage 1 HTN is defined as ABP equal to or greater than the 95th percentile but lower than the 99th percentile + 5mmHg. Stage 2 HTN is defined as ABP equal to or greater than 99th percentile + 5 mmHg. [4]

Another important aspect of abnormal ABP is Elevated Blood Pressure (EBP), previously referred to as prehypertension (pre-HTN), with the new term being introduced in the 2017 AAP guidelines. It is diagnosed in patients with ABP values in the 90th to 94th percentile range. Similarly to established HTN, it's not an occurrence that can be ignored, and it requires as much clinical attention. [4]

Furthermore, when discussing HTN, there are several distinct subtypes and phenomena concerning HTN that clinicians must remember. These include: White Coat Syndrome (WCS), Masked HTN (MHTN), Isolated Systolic HTN (ISH), Isolated Diastolic HTN (IDH), and Pseudohypertension.

White Coat Syndrome (WCS) is a phenomenon which takes its name from the characteristic medical white coat. It occurs when solely the fact of being in a medical facility or the presence of a medical professional causes an increase in the adrenergic system's activity, which in turn results in a rise in ABP, taking it outside the recommended range. [9]

Masked HTN (MHTN) is a situation opposite to that of WCS. Contrary to WCS, where ABP is increased when measured by a medical professional, in MHTN, it is elevated in ambulatory ABP measurements (ABPM) but normal when measured in a medical facility [7]

Isolated Systolic HTN (ISH), defined as elevated DBP with SBP in the normal range, was initially believed to be a spurious, benign condition in children, caused by exaggerated pressure amplification in healthy, tall, physically active men. However, further research into this topic has shown otherwise and has demonstrated an association between ISH and increased central and brachial SBP, suggesting that these patients may be at an increased cardiovascular risk. Research also shows that isolated systolic HTN may be a very early step in the clinical development of HTN, although further research is required regarding the evolution of the condition, best course of treatment and the patients' prognosis. [73-76]

Isolated Diastolic HTN (IDH), defined as elevated DBP with SBP in the normal range. Although many studies have shown it to be artifactual and benign, new evidence in the adult population presents a likely association with greater cardiovascular risk. Furthermore, the Framingham Heart Study suggests that IDH is likely a precursor of HTN as

well as a good predictor of future coronary heart disease events, contradicting the theory of it being a benign condition. Children suffering from IDH are typically female, younger, leaner and have a higher resting heart rate. Further long-term follow-up research in the paediatric population is required to better understand the pathogenesis, progression and long-term outlook in children's IDH. [73,77, 78]

Pseudohypertension is a condition where ABP is elevated in an indirect assessment using a sphygmomanometer and within normal range once measured intra-arterially. Its pathogenesis is often associated with the stiffening of the arteries. It is most commonly reported in elderly patients; however, it can also present itself in children, although considerably rarely. One such case was reported by Narasimhan et al., where pseudohypertension presented itself in a 5-year-old child with Williams syndrome. [73, 79]

Epidemiology of Paediatric Hypertension

Over the years, the number of children and adolescents suffering from HTN and EBP has significantly increased. As reported by Song et al., over the last two decades, a relative increase of 75% to 79% has occurred. [5] In various studies, it has been reported that between 2.7% and 11.2% of children globally suffer from HTN [6, 13]. However, it must be noted that in many conducted studies, the prevalence of HTN decreased with each additional ABP measurement that was carried out. In their meta-analysis, Song et al. concluded the mean number to be 4%. However, it is important to note that the reported prevalence changes relatively to the patient's age, from 4.32% in the age group of 6 years old, peaking at 14 years with a value of 7.89% and later lowering to 3.28% at the age of 19 years. [5] However, it is also important to note that the increase in these values may be affected by significant underdiagnosing. As reported by Hansen et al. in their study on HTN underdiagnosis, of all the children included, only 26% of those suffering from HTN had a proper diagnosis in their medical records. [8]

The change in diagnosis criteria brought about by the 2017 AAP guidelines was certain to increase the frequency of HTN diagnosis in children. This problem was studied by Sharma et al. in their 2018 study of 15647 children. The initial HTN prevalence of 11.8% when using the previous guidelines increased to 14.2% when the new guidelines were applied. They also noticed that a total of 5.8% of included children were impacted by the change, either by diagnosing HTN or moving to a more advanced stage. Those affected by the change were more likely to be overweight or obese, with higher weight-for-age scores, waist circumference and BMI. It is estimated that due to the change of the diagnosis criteria, approximately 795,000 children in the US have been reclassified as having HTN. [70, 83]

The prevalence of HTN varies depending on age, with a steep increase being reported around the age of 13-14 years old, when children begin to reach puberty. Secondary HTN is the more frequent type of paediatric HTN up until the age of 13-14 years old, with the biggest disparity visible in those below 6 years old. In younger children (<12 years old), secondary HTN can constitute up to 70-85% of all HTN cases in that age group. However, as the children grow older (≥12 years old), those numbers change in favour of primary HTN, with it being said to constitute 85-95% of HTN cases. [5, 27, 63, 85]

When it comes to MHTN, as reported by Chung et al. it has a prevalence of approximately 10.4% in the general paediatric population. However, in patients with various comorbidities, this number is further increased. [7]

Research such as the Enigma study in the UK and the National Health and Nutrition Examination has shown that ISH affects between 2% and 8% of the population. However, most of these studies included only or predominantly the adult population, and thus, definitive conclusions regarding its prevalence in children shouldn't be drawn. [76

IDH has previously been reported to affect between 0.7-4.5% of generally healthy children. In their 2021 study, which included 17,362 American children, Alsaeed et al. calculated the prevalence of IDH to be 1.9%. (95% CI 1.5-2.2) [77]

Blood Pressure measurements

As described in the available guidelines, to properly measure the patient's ABP, they should be placed in a quiet environment, remaining calmly in a sitting position for a few minutes before the measurement is taken. When taking the measurement, the patient should be sitting comfortably, legs uncrossed and feet on the floor, their arm supported in front of them at heart level. Using an appropriate size cuff is not a detail that can be neglected; its bladder length should be 80-100% of the circumference of the arm, and the width should be at least 40% of the distance between the acromion and the olecranon. Likewise, the circumference should be measured in the middle between the acromion and the olecranon. [1-4] As shown by multiple publications, a too-small cuff will result in falsely elevated ABP values, while one that is too big will measure ABP results that are lower than the actual ABP value. [10, 11] Once a cuff of appropriate size has been selected, it should be placed on an unclothed arm about 3cm above the popliteal fossa. The measurement, preferably using an aneroid sphygmomanometer, should be taken 3 times in intervals of about 1-2 minutes each, especially if the first reading measures above the 90th percentile; after that, the first value should be discarded, and the remaining values averaged. As shown by Bovet et al., this should be done in order to reduce the amount of false positive measurements. [14] It is important to note that during a child's first visit, during which an ABP is measured, the measurement should be taken on both arms and one leg to rule out potential coarctation of the aorta. [4,26] There is a consensus that the best way of taking the measurement is by the auscultatory technique using an adequately calibrated aneroid sphygmomanometer. [1-4] In their study, Duncombe et al. concluded that oscillometric devices, on average, return a measurement 2.53 mmHg higher than their mercury counterparts. However, they also discovered that oscillometric sphygmomanometers that “passed” validation protocols by organizations such as the “European Hypertension Society, International Protocol” or “Association for the Advancement of Medical Instrumentation” returned results of only 1.76 mmHg higher than mercury sphygmomanometers. Because of that, they concluded that verified oscillometric sphygmomanometers can be used as a substitute for aneroid sphygmomanometers for the initial ABP screening in the paediatric population. [12]

Diagnosis of Arterial Hypertension

The guidelines emphasize the importance of precise history and physical examination when suspecting HTN. Some of the key points to ascertain include: the family history of HTN, comorbidities, the child’s birth weight and gestational age, environmental factors such as smoking (as well as second hand smoking) and diet, physical activity, and possible symptoms including, but not limited to headaches, vertigo, chest pain or epistaxis. [1-4]

In order to diagnose a patient with HTN or EBP, a singular instance of ABP above the cutoff point of 95th and 90th percentile, respectively, is not sufficient. The required number of independent measurements differs in various sources. De Simone et al. recommend two separate visits, while Sun et al. report that measurements during three individual visits are required. They report that measuring ABP during three separate visits results in a decrease of 77.7% in potential HTN prevalence. Unfortunately, this requirement may result in a lack of follow-up and potentially lead to a greatly delayed diagnosis and development of complications. In the case of stage 2 HTN or organ damage, only one abnormal ABP measurement is required. [4, 13]

It is also recommended that all potential HTN diagnoses be further confirmed via ABPM to negate the possibility of measurement falsification by WCS. [1-4, 15]

Clinicians must also remember that when suspecting the monogenic nature of HTN, the diagnosis process should begin by carrying out a serum electrolyte test (most importantly sodium and potassium cations), as well as renin and aldosterone levels. However, a definitive diagnosis can only be made after genetic testing has been conducted. [30, 80-82]

Blood pressure screening in the paediatric population

As recommended by the AAP guidelines, ABP measurements should be carried out in all children over the age of 3 during every appointment with a medical professional. As aforementioned, these results should be checked against an appropriate normative table. In a 2022 statement from the American Heart Association, Flynn et al. conclude that consistent with the 2017 AAP guidelines, they recommend ABPM to be used in order to confirm the diagnosis before starting pharmacotherapy. [84] Measuring ABP in children younger than 3 is usually not recommended unless HTN risk factors are present. The AAP guidelines outline these as: a history of prematurity (<32 week's gestation, small for gestational age or other neonatal complications requiring intensive care), congenital heart disease (repaired or unrepaired), recurrent urinary tract infections, haematuria or proteinuria, known renal disease or urologic malformations, family history of renal disease, solid organ transplant, malignancy or bone marrow transplant, treatment with drugs known to raise ABP, systemic illnesses such as neurofibromatosis, tuberous sclerosis or sickle cell disease which are associated with HTN, evidence of elevated intracranial pressure. In children with CKD, regular APBM checks are suggested if secondary causes of HTN are suspected or present. [1, 26, 27] All acquired measurements should be compared to the normative percentile tables standarded by sex, age and height. [1, 26, 27] This has been and, in all likelihood, will continue to be the go-to procedure for many years. However, it is a task that bears a high probability of human error, especially taking into consideration the high number of patients and the limited time for each one of them. Fortunately, nowadays, along with the progress of technology, numerous websites and applications exist, for example, websites such as "mdcalc.com" and "jakicentyl.pl", which allow clinicians to quickly and without error ascertain the exact percentile of the patient's ABP.

As aforementioned, ABPM remains a key clinical tool in the management of hypertensive patients. In the case of patients with WCS, further ABPM monitoring is vital, as demonstrated by Miyashita et al. in their study. Of all the patients included, during the follow-up, 61% progressed to either ambulatory HTN (23% of patients) or ambulatory EBP (38% of patients). [9] However, even in the case of seemingly normotensive patients, clinicians must remain vigilant. As concluded by Seeman et al., when a child presents with prehypertension, a positive family history of HTN, obesity, chronic kidney disease (CKD), diabetes or obstructive sleep apnoea syndrome, regular ABPM checks should be performed regularly due to a potential for MHTN. [16]

It is worth noting that in the 2020 recommendation statement on screening for high blood pressure in children and adolescents by the US Preventative Services Task Force, it was concluded that there is insufficient evidence to unambiguously recommend HTN screening as the balance of benefits and harms couldn't be determined. However, AAP, in its 2017 guidelines, recommends regular ABP screening in children between the ages of 3 and 18 years old. [1, 63]

Primary Hypertension and its Risk Factors

Primary HTN can be defined as HTN in which no singular causative factor can be determined. As mentioned before, the prevalence of primary HTN in the paediatric population

is rising across all age groups. In his review study, Prof. Litwin describes primary HTN as a complex issue with numerous pathophysiological mechanisms and risk factors. Most notably, the factors included in the revised version of the Page's mosaic, such as salt sensitivity and salt resistance, autonomic nervous system abnormalities, disturbed body composition (predominantly excessive visceral adipose tissue), hyperkinetic function of the left ventricle, vascular remodelling, metabolic abnormalities (predominantly hyperinsulinemia and insulin resistance), immune abnormalities and intestinal dysbiosis are considered to be of vital importance in the development of this disease. He proposes that factors such as age and perinatal factors (for example, preterm birth or neonates small for gestational age) should also be included in the next revision of the mosaic for childhood HTN. However, a detailed review of the pathophysiology of primary HTN is beyond the scope of this review. [18]

In the face of the worldwide obesity epidemic, the most frequent and most important risk factor of HTN is excessive fat tissue. Over the last decades, there has been a substantial increase in the prevalence of overweight and obesity worldwide. Among children and adolescents, the global age-standardised prevalence of obesity increased from 0.7% in girls and 0.9% in boys in 1975 to 5.6% and 7.8%, respectively, in 2016. [19] According to the data collected by the WHO, in the year 2022, over 390 million children and adolescents worldwide were overweight (BMI ≥ 25), of which 160 million were obese (BM I≥ 30). [20] This rise is often correlated with the increasing frequency of primary hypertension among children, as high BMI and especially excessive amounts of adipose tissue have been linked to hypertension. Many researchers reported that as the patient's BMI increases, so does the prevalence of hypertension. This correlation can be observed in all age groups, even in those as young as 2 years old. [21-24, 54] Ji et al. conclude that puberty is a vital moment for HTN development, and appropriately controlling the BMI then will significantly reduce the risk for HTN. Many methods, such as BMI, skin fold calipers and fat mass measured using bioimpedance, have been developed for the purpose of estimating and tracking obesity and adipose tissue contents, with BMI being the one most widely used. However, as reported by Drozdz et al., fat mass estimated using bioimpedance analysis is superior to BMI for tracking the amount of adipose tissue as it better correlates with ABP. [23]

In their study, Levy et al. identified tobacco exposure (both primary and secondary) as an additional risk factor associated with elevated ambulatory blood pressure (ABP). Their analysis included a cohort of 8,520 children with a mean age of 13.1 years, with 51% of participants being male. Children with documented tobacco exposure demonstrated a 1.31-fold increased likelihood of elevated ABP (95% CI: 1.06–1.61). [50]

As reported by Belfort et al., another factor associated with paediatric HTN is a rapid increase in weight for length in the first 6 months of the child's life, as it correlates to an increase in the child's adipose tissue content. This association was pronounced the strongest, especially in children who were in the lowest quartile of weight at birth of those included in the study. [51]

Affiliation with different ethnic groups has also been proven to impact patients' ABP values. An analysis by Dekkers et al. conducted on 745 young participants revealed that children who identified as Black had significantly higher SBP and DBP values when

compared to those who identified as White (P<0.01). In boys, these differences became apparent upon reaching adolescence, whereas in girls, they were evident earlier in childhood. The authors have also concluded that these differences could not be attributed to differences in adiposity or height. [65]

Furthermore, many gene loci that increase the risk of developing HTN have been identified. According to studies, these include, but are not limited to, single-nucleotide polymorphisms in CACNB2(3′) rs1813353, ULK4 (rs3774372), ZNF831 (rs6015450), and ZNF652 (rs12940887) genes. [67]

Secondary Hypertension

Secondary HTN can be defined as a clinical situation in which a tangible cause for the HTN can be identified. Once thought of as the main type of paediatric HTN, nowadays, secondary HTN is being overtaken by primary HTN when it comes to prevalence. However, despite this change, in the youngest of patients, especially those under the age of 6, it is still secondary HTN that is the main cause of HTN and must be ruled out when a young patient presents themselves with HTN. [53]

Many diseases can lead to the development of secondary HTN, with the most common ones being renal diseases, coarctation of the aorta (CoA) and reno-vascular diseases. In children up to the age of 6 years old, renal disease and CoA are the most frequent causes, whereas in those aged 6 to 10 years, renal parenchymal disease is the leading etiology. The most common reno-vascular causes of secondary HTN include renal artery stenosis, fibromuscular dysplasia, arteritides, extrinsic compression of a renal artery, renal artery dissection or infarction, radiation fibrosis, and obstruction from the aortic endovascular graft. Less commonly, secondary HTN may be caused by genetic arteriopathies, such as Williams-Beuren Syndrome (WBS), caused by a deletion located on the long arm of the 7th chromosome. This mutation causes the loss of function of the elastin gene, leading to supravalvular aortic stenosis, stenosis of pulmonary artery branches, supravalvular pulmonary stenosis, and stenosis of other vascular territories, including the thoracic or abdominal aorta, renal arteries, intracranial arteries, and potentially others, ultimately leading to systemic HTN. Other less prevalent causes of secondary HTN include systemic arteritis, renal tumours, and various endocrine and neurological disorders. [26, 27]

Chronic kidney disease, mainly congenital anomalies of the kidneys and urinary tract, is the most common cause of secondary HTN in children. As reported by Taha et al., patients with decreased kidney size, proteinuria, additional kidney anomalies and chronic kidney disease are more likely to develop HTN. Additionally, HTN further increases the risk of CKD. [28]

There are reports that Wilms tumour (WT), one of the most prevalent kidney tumours in the paediatric population, can both directly and indirectly result in secondary HTN. As described by Hsiao et al. WT often presents with HTN, which resolves after nephrectomy. However, due to a reduction in nephron mass, combined with potential additional nephrotoxic effects of therapies and radiotherapy, HTN may develop. They also report that WT survivors frequently suffer from MHTN, which would make additional ABPM measurements beneficial for these patients. [29]

One of the rarer causes of secondary HTN is monogenic HTN [30]. Monogenic HTN is a group of diseases in which a mutation of a single gene (usually inherited in an autosomal dominant way) disrupts the renal or adrenal physiological mechanisms of ABP regulation. They can be divided into two groups: kidney-dependent (with low, normal or excessive aldosterone levels) and kidney-independent (adrenergic or sympathetic excess or disorders of

vascular smooth muscle). Many of these mutations result in increased renal sodium retention, leading to total body volume expansion, which in turn results in the suppression of renin levels. Possible monogenic disorders which can lead to HTN include, but are not limited to: Liddle syndrome, type 2 pseudohypoaldosteronism (Gordon's syndrome), familial hyperaldosteronism, and congenital adrenal hyperplasia due to 11-beta-hydroxylase deficiency, apparent mineralocorticoid excess, Bilginturan syndrome, as well as pheochromocytomas and paragangliomas caused by hereditary syndromes such as MEN2A and VHL syndrome. In all instances when the genetic cause of HTN is suspected, family history is a vital part of the investigation, as it will likely be present in close family members. Clinicians should also remember that when a very young child presents with HTN, a monogenic mutation could be the underlying cause. They should also be suspected in children in whom more common causes of HTN have not been identified, especially in children who present with electrolyte abnormalities, such as hyper- or hypokalaemia, metabolic acidosis or alkalosis. In these rare conditions, a precise diagnosis is crucial, as treatment strategies are specific and differ depending on the causative condition. [30, 80-82]

Treatment

Research has shown that children with EBP or HTN are more likely to suffer from EBP or HTN once they reach adulthood. As reported by Kelly et al., participants had their ABP measurements taken in childhood and followed up 20 years later. For tracking of ABP into adulthood, they calculated the Spearman correlation coefficients for SBP to be 0.31 ($P < 0.001$) and 0.16 ($P < 0.001$) for DBP. On the 20-year follow-up, those with elevated ABP in childhood had a higher risk of elevated ABP in adulthood, when compared to normotensive children (RR(95%CI, 1.35 (1.18-1.55)); red <0.001; PAF (95% CI, 10.2% (3-18%))) However, they also report that adopting a healthy lifestyle potentially lowers the risk of HTN tracking into adulthood. [46] Because of that, instances of elevated ABP in children should not be ignored, as any potential delay can result in more complications in the future.

In their research, Kaelber et al. have proven that up to 48% of cases of paediatric HTN and 70% of cases of EBP will resolve themselves without intervention. [25] A similar problem is touched upon by Juhola et al. In their research, encompassing 4210 participants, they report that out of all children with elevated ABP, only about 40% will be able to avoid elevated ABP in adulthood. [66] It is an important discovery; however, despite that, clinicians cannot allow children with HTN to go untreated. There is a consensus among medical societies and their guidelines that the first-line treatment of HTN in children, especially those without end-organ damage, should be non-pharmacological interventions, predominantly in the form of lifestyle changes. These include various recommendations, for example, weight reduction and, more importantly, fat tissue mass reduction, dietary changes and an increase in the patient's physical activity frequency and intensity, a reduction of sedentary time, cessation of smoking, and a reduction of alcohol consumption. This intervention should last no less than 6 months. [1-4, 26]

Several studies have demonstrated that reductions in BMI or adipose tissue are associated with significant reductions in ABP. However, as described by MacLean et al., weight loss causes changes in adipose tissue that predispose it to store ingested energy. This mechanism, aimed at restoring the body's initial weight, can result in rebound weight gain. [31] In their 2014 review and meta-analysis, Cai et al. concluded that "obesity prevention programs have a moderate effect on reducing BP, and those targeting both diet and physical activity seem to be more effective". They calculated the mean reduction of SBP to be -1.64mmHG and DBP -1.44mmHg. [49] In patients with severe obesity or those failing to reach established weight goals, pharmacotherapy can be introduced. Drugs such as

semaglutide, liraglutide, metformin, sibutramine, and orlistat have been proven to exert a positive effect on BMI in the paediatric population, however, as Mead et al. have concluded in their metanalysis, further research on the topic is required due to poor quality of the available trials and lacking drug registrations in paediatric populations. [59-61]

Increasing the weekly amount of physical activity has been proven to exert a beneficial effect on ABP. Anaerobic exercises, performed in the amount of 3 to 5 sessions per week, for 30 to 60 minutes per session, are recommended. Studies have demonstrated that such a regimen effectively reduces cardiovascular risk and is associated with lower SBP values. Mark et al. report a dose-response relation between physical activity and both SBP and DBP values. Furthermore, as described by Gidding et al. in their study of 663 youths with an active lifestyle, children who engaged in regular physical activity had lower SBP values, as well as reduced concentrations of low-density lipoprotein (LDL) cholesterol. Further evidence for the importance of physical activity in paediatric obesity is provided by Cao et al. in their systemic review and meta-analysis of 8 trials involving 197 total participants with obesity and metabolic syndrome. They demonstrated that aerobic exercise alone can have a positive effect on patients' lipid profiles, as well as SBP values (standardised mean difference -6.90; 95% CI -10.46 - -3.35; $p<0.01$), BMI and waist circumference. However, it should be noted that children diagnosed with stage 2 HTN should refrain from participating in high-static sports (e.g., lifting, boxing and wrestling) until their ABP values are within the normal range, even in the absence of end-organ damage such as left ventricular hypertrophy. [1, 47, 48, 52, 53]

Another vital aspect of lifestyle changes are dietary modifications. Reports suggest that a DASH (Dietary Approach to Stop Hypertension) diet, fitting the patients' caloric needs, is the most beneficial. The DASH diet is rich in fresh fruits and vegetables, low-fat dairy, whole grains and lean protein sources. Additionally, a restriction of dietary salt by reducing or eliminating foods such as chips or French fries and highly processed products in which sodium chloride contents tend to be especially high is proven to be beneficial. In its 2017 guidelines, the AAP recommends that daily sodium intake be kept below 2300 mg/day. Furthermore, a limitation of added dietary sugars is recommended. Most commonly found in foods most popular with the paediatric populace, such as sweets and sugar-sweetened beverages, they can significantly increase the daily caloric intake, resulting in weight gain and excessive accumulation of adipose tissue. [1, 26]

Smoking is a known cardiovascular risk factor, as well as being proven to be a modifiable risk factor for developing HTN. With the substantial rise in the popularity of e-cigarettes, alternative forms of combustible tobacco (such as heat-not-burn cigarettes) and smokeless tobacco among the youth, clinicians must be ready to counteract this situation. [37] Every patient, especially those suffering from HTN or having other cardiovascular risk factors, should be advised to quit smoking and then adequately supported in their efforts. At first, the patient should be assessed for the symptoms of nicotine dependency, and they should be given the Fagerstrom questionnaire to assess the strength of their addiction. It is recommended that interventions aimed at the cessation of smoking be carried out according to the "five A's" approach. It consists of: Ask, Advise, Assess, Assist and Arrange. A recommended first-line treatment option, besides counselling, is nicotine replacement therapy in the form of patches, gum, or nasal spray. Second-line pharmacological options include drugs such as bupropion and varenicline. Their effectiveness has been proven in the adult population; however, in children, only small-scale randomised control trials are available and have yielded mixed results regarding their effectiveness. The specifics of interventions aimed at the cessation of smoking are beyond the scope of this review. [32-34]

Patients suffering from HTN should be recommended to limit alcohol consumption. As described by Algharably et al. in their review paper, even low to moderate daily alcohol intake (10-20g of pure ethanol, which corresponds to one to two drinks, 125- 250ml of wine, 250- 500ml of beer or 40- 80ml of vodka) results in an increased risk of HTN. What is more, keeping abstinence associated with SBP and DBP lowering by 3.3 and 2.0 mmHg respectively. [35] This correlation is highly dose-dependent; the higher the initial alcohol consumption was, the greater the possible reduction in BP. A meta-analysis of 36 trials with a total of 2865 adult participants, conducted by Roerecke et al., has shown that in those who initially consumed 6 or more units of alcohol per day SBP and DBP has lowered by 5.50 mmHg (95% CI -6.70 to -4.30) and 3.97 mmHg (95% CI -4.70 to -3.25) respectively once they reduced their alcohol intake by 50% or more. At the same time, in people who initially consumed two units of alcohol per day or less, no significant reduction in ABP was reported. [36]

If the patient additionally presents with dyslipidaemia, it should be treated without delay, as it further increases the patient's CVD risk. Therapy goals should be established based on the patient's CVD risk category, and the treatment should begin by implementing lifestyle modifications similar to those listed above. The diet should be rich in fibre from sources such as fresh fruits, vegetables and whole grains, as well as polyunsaturated and monounsaturated fats due to their positive impact on cardiovascular health. Conversely, the intake of saturated and trans fats should be minimised. Patients should be advised to engage in regular, daily physical activity. In the case of obese and overweight patients, weight reduction should also be recommended and actively encouraged. If, through lifestyle modification alone, the patient does not achieve the desired therapeutic goals, pharmacological treatment may be considered. Agents such as statins, ezetimibe, bile acid sequestrants, and fibric acid derivatives have been shown to be effective in managing dyslipidemia. [43-45] A comprehensive report on pharmacotherapy of paediatric dyslipidaemia, including specific treatment targets, falls outside the scope of this review.

Research conducted in the adult population has shown that insufficient sleep duration and poor sleep quality increase cardiovascular morbidity and can lead to an increase in ABP values. Because of that, patients suffering from HTN should be advised regarding sleep hygiene and other possible treatments to reduce CVD risk. Relatively common conditions, such as obstructive sleep apnoea, can lead to impaired sleep quality and have been shown to contribute to the development of hypertension. In these patients, therapeutic interventions such as nasal continuous positive airway pressure therapy (nCPAP) or targeted causal treatment can be implemented. A comprehensive report on this topic lies beyond the scope of this review. [38-42]

In patients without end-organ damage, pharmacotherapy should be recommended if the introduced lifestyle changes do not yield the desired results, or in case of symptomatic HTN, organ damage, diabetes, CKD, left ventricular hypertrophy or stage 2 HTN without modifiable risk factors. Unfortunately, research regarding the efficacy, safety and long-term results of anti-HTN pharmacotherapy in children is limited, and so much of the knowledge must be transferred from research carried out in adult populations. Pharmacotherapy of HTN in children should begin with angiotensin receptor blockers (ARB), angiotensin-converting enzyme (ACE) inhibitors, dihydropyridine calcium channel blockers, and diuretics should be used as first-line treatment options, there is no evidence available that would single out one of these as the best first choice. Therapy should begin with the lowest effective dose, which then can be gradually up-titrated if the therapy goals are not reached and the patient's tolerance of treatment is good. Alternatively, if the ABP target is not reached, therapy can be switched to a different drug, or an additional drug from a different class can be introduced. The authors of

the guidelines unanimously agree that a stepped-care approach is advised. A network meta-analysis conducted by Burello et al., which included 13 studies with a total of 2378 patients, indicates that ACE inhibitors (such as lisinopril and enalapril) and ARBs (such as losartan) could potentially be the best choice in paediatric HTN treatment. However, as the authors themselves acknowledge, the amount of available data is limited and, due to heterogeneity, small sample sizes and short follow-up time of existing randomized control trials, reaching definitive conclusions would require carrying out additional trials. [1-4, 26, 58, 62]

In the case of patients diagnosed with stage 2 HTN or coinciding organ damage, diabetes, CKD, or ventricular hypertrophy, treatment should begin with the simultaneous implementation of pharmacotherapy and lifestyle modifications. [26, 58] If the patient presents with acute symptoms, such as headaches, altered mental status, or papilledema, urgent evaluation and treatment should take place. If secondary HTN is diagnosed, a key part of treatment is treating the underlying condition leading to HTN. Chaturvedi et al. conducted a meta-analysis regarding pharmacological interventions in hypertensive children. They analysed 21 trials with a total number of 3454 participants. Not insignificant reductions in ABP in comparison to the placebo group were reported for all included pharmaceutical agents: angiotensin receptor blockers (candesartan and high-dose telmisartan), beta-blockers (metoprolol), beta blocker and thiazide diuretic dual therapy (bisoprolol + hydrochlorothiazide), and calcium channel blockers (extended-release felodipine). They calculated mean values by which different pharmaceutical compounds affected the ABP measurements, with high-dose telmisartan exerting the biggest impact, lowering the SBP by -8.50 (95% CI; -13.79 - -3.21). Many agents proved capable of reducing SBP values but did not have a significant effect on DBP values. Unfortunately, as the authors themselves have stated, there is a significant lack of data regarding antihypertensive drugs in the paediatric population (with the biggest amount of data available regarding candesartan), and much of the data included in this meta-analysis was low-quality evidence. [57] Furthermore, there is also a noticeable lack of long-term studies regarding the safety of HTN pharmacological agents in children. In the short term, all aforementioned pharmacological groups appear safe for use. Contraindications to their usage are the same as in the adult population, for example, pregnancy in the case of ACE inhibitors and angiotensin receptor blockers.

Based on available research regarding FGF23 and its function and interaction with the renin-angiotensin-aldosterone axis, in their 2020 study, Chrysaidou et al. theorise that in the case of HTN secondary to CKD, FGF23 may be a new therapeutic target for HTN treatment. [27]

Treatment of patients suffering from monogenic HTN is widely dependent on the specific mutation and syndrome they suffer from. Such an approach is crucial to enhancing patient outcomes. Because of that, as mentioned before, a swift, specific diagnosis is of vital importance. Due to pathogenesis being most commonly associated with increased sodium reabsorption, thiazide diuretics and aldosterone antagonists are some of the most common routes of pharmacotherapy. However, in Geller syndrome, for example, aldosterone antagonists should not be prescribed as they lead to symptom exacerbation. [30, 80-82]

The guidelines suggest that the goal of the treatment should be lowering the patient's ABP below the 90^{th} percentile for age and height, as organ damage can occur even in children with ABP values between the 90^{th} and 94^{th} percentile. According to ESH, consistent with adult guidelines, in children aged 16 and above, the first goal of treatment should be lowering the patient's ABP to <130/85 mmHg, with the ultimate goal of lowering it to <120/75 mmHg. However, in the case of children suffering from CKD, lowering the ABP values beneath the 50^{th} percentile is recommended. [1-4, 26]

After implementing lifestyle modifications, the follow-up visits should take place every 3-6 months. In the case of patients undergoing antihypertensive pharmacotherapy, examinations every 4-8 weeks are recommended. In the case of patients who demonstrated WCE, follow-up using ABPM is recommended. [1-3]

Complications

Childhood HTN is one of the strongest predictors of HTN in adulthood ($P<0.0001$), as well as being a substantial, well-proven, but also potentially reversible risk factor of cardiovascular events, avoiding, or introducing incorrect treatment risks the development of complications in the form of target organ damage (TOD), most notably impacting the heart, kidneys and the vascular bed. These include left ventricular hypertrophy (LVH), increased left ventricular mass index (LVMI), increased pulse wave velocity (PWV), and increased carotid intima-media thickness (cIMT). [65, 68]

Assessment of hypertension-mediated organ damage is vital in arranging the correct clinical management as well as assessing the potential patient outcome. The main measurable markers of TOD include assessment of the left ventricular mass, carotid intima-media thickness, arterial stiffness (assessed using pulse wave velocity), and assessment of microcirculation. Clinicians must remember that the recorded values must be checked against referential values normative for age and sex. As summarized by Pac et al., the main methods currently used to assess TOD include the estimation of left ventricular mass index (LVMI) using Echocardiography, ECG, examination of the eye fundus, evaluation of kidney function and microalbuminuria. Furthermore, measuring cIMT using ultrasonography and PWV is recommended. [72] Results of a study conducted by Sorof et al. suggest that 24h-SBP measurements are crucial for the assessment of children with HTN as they correlate more strongly with TOD, such as LVMI ($r=0.43$, $P=0.008$). [69] Another study by the same authors suggests that SBP correlates with LVH more strongly than DBP; thus, in order to avoid this possible complication, SBP normalization should be prioritized, even if DBP values are within normal range. [74]

In a meta-analysis of 38 studies, including a total of 3609 children, Chung et al. have found a non-insignificant association between ambulatory HTN and these pathologies. When compared to normotensive children, the risk of TOD was: LVH – 4.69 (odds ratio(95% CI, 2.69-8.19)), LVMI – 5.13 $g/m^{2.7}$ (pooled difference (95% CI, 3.78-.49)), PWV – 0.04mm (pooled difference, 0.39m/s (95% CI, 0.2-0.58)) and cIMT (pooled difference, (95% CI, 0.02-0.05)). Furthermore, they concluded that when compared to non-hypertensive children, hypertensive children may have a higher risk of future cardiovascular diseases and mortality. [64, 67] It is also worth noting that in many children, TOD is already present at the time of HTN diagnosis. A study by Litwin et al., which included 72 children with newly diagnosed HTN, left ventricular mass > 95^{th} percentile was present in 41.6% of patients and cIMT >2 SDS of normal values in 38.8% of patients. They also report that left ventricular mass and arterial injury, estimated using markers such as AproteinA1, AproteinB and C-reactive protein, correlate with SBP values, biochemical and perinatal cardiovascular risk factors. [68]

A study by Juhola et al. with a 23-year follow-up has shown that patients with elevated ABP in childhood have an increased risk of atherosclerosis (estimated using cIMT) once they reach adulthood. However, it has also shown that normalising ABP values allows to mitigate that risk, with the risk of having cIMT ≥ 90^{th} percentile being 0.66 (relative risk(95% CI (0.50-0.88))) when compared to those who had elevated ABP values both in childhood and adulthood. In those with persistently elevated ABP, the risk of cIMT ≥ 90^{th} percentile when compared to normotensive individuals is significantly increased 1.82 (relative risk (95% CI,

(1.47-2.38))). They also report that of those with elevated ABP in childhood, only 40% were able to avoid HTN in adulthood. [66]

Obrycki et al., in their study "Hemodynamic Patterns and Target Organ Damage in Adolescents With Ambulatory Prehypertension", have shown that patients with EBP have the same cardiovascular adaptations as those with HTN, with cIMT being significantly higher in both groups when compared to normotensive patients ($P<0.001$). Similarly, hemodynamic patterns and LVMI ($P<0.001$) in EBP patients were higher than in those with normal ABP. They conclude that considering these adaptations, EBP patients, similarly to HTN patients, may also have an increased risk of cardiovascular events. [71]

Increased risk of cardiovascular events due to HTN can lead to potentially lead to serious, life-threatening events. Kupferman et al., in their review paper, suggest that it may be associated with an increased risk of childhood stroke; however, further research is needed to confirm this link. [17]

Clinicians should also remember that in patients with monogenic HTN, due to a typically early onset of the disease, complications are more common and can be identified in even younger patients. [80]

Areas for Further Research

In recent years, as the topic of paediatric hypertension has gained traction in the medical community, more and more research has been done on the subject. Unfortunately, as scientific research on the paediatric population is much scarcer, much of the knowledge has to be imported from studies done exclusively in the adult population. Further research of areas such as pathogenesis of HTN, its evolution and risk factors, as well as predisposing gene mutations, could potentially lead to positive developments in the management of paediatric HTN. We believe that future work should concentrate on carrying out epidemiological research regarding the prevalence of HTN and all of its subtypes across differing age groups and paediatric populations to combat the problem of underdiagnosing and improve the screening process for HTN. Further research regarding screening for HTN should be conducted to definitively determine the long-term balance of benefits and harms to unambiguously determine the appropriate procedure. Specific research should be conducted regarding different subtypes of HTN, such as MHTN, ISH, and IDH, to determine their significance, predisposing factors, long-term outcomes, and appropriate management. To the best of our knowledge, there are no randomized controlled trials on the topic of MHTN treatment in children. ESH and AAP also do not address the issue of MHTN treatment. Seeman et al. recommend that lifestyle modifications be carried out in the case of children with MHTN who are obese or overweight, consume too much sodium and do not have sufficient physical exercise. Furthermore, they recommend pharmacotherapy be implemented in all children with MHTN if they have HTN-mediated organ damage, secondary HTN, diabetes or symptomatic HTN.

We also believe that studies regarding possible complications of HTN and its long-term outcomes both in childhood as well as later on in adulthood should take place. Lastly, we believe large randomised control trials should be carried out regarding the efficacy of treatment and safety of individual pharmacotherapeutics in children. In our opinion, all these aforementioned points are vital for the benefit of children worldwide.

Conclusions

Due to its increasing prevalence, the significance of HTN in the paediatric population is rising exponentially, especially considering its many possible complications if the condition is left unnoticed or untreated. Many new studies have been conducted in recent years,

emphasising the problem and shedding new light on it. However, as aforementioned, much of the knowledge is transferred from studies carried out exclusively in adults, and those in children are still lacking. Many more venues requiring further research and development remain to enhance the care available for children and prevent long-lasting, possibly debilitating complications both during childhood as well as later in their adult life.

Disclosure

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References:

1. Flynn JT, Kaelber DC, Baker-Smith CM, et al. Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents [published correction appears in Pediatrics. 2017 Dec;140(6):e20173035. doi: 10.1542/peds.2017-3035.] [published correction appears in Pediatrics. 2018 Sep;142(3):e20181739. doi: 10.1542/peds.2018-1739.]. *Pediatrics*. 2017;140(3):e20171904. doi:10.1542/peds.2017-1904
2. Lurbe E, Agabiti-Rosei E, Cruickshank JK, et al. 2016 European Society of Hypertension guidelines for the management of high blood pressure in children and adolescents. *J Hypertens*. 2016;34(10):1887-1920. doi:10.1097/HJH.0000000000001039
3. Rabi DM, McBrien KA, Sapir-Pichhadze R, et al. Hypertension Canada's 2020 Comprehensive Guidelines for the Prevention, Diagnosis, Risk Assessment, and

Treatment of Hypertension in Adults and Children. *Can J Cardiol*. 2020;36(5):596-624. doi:10.1016/j.cjca.2020.02.086
4. de Simone G, Mancusi C, Hanssen H, et al. Hypertension in children and adolescents. *Eur Heart J*. 2022;43(35):3290-3301. doi:10.1093/eurheartj/ehac328
5. Song P, Zhang Y, Yu J, et al. Global Prevalence of Hypertension in Children: A Systematic Review and Meta-analysis. *JAMA Pediatr*. 2019;173(12):1154-1163. doi:10.1001/jamapediatrics.2019.3310
6. de Moraes ACF, Lacerda MB, Moreno LA, Horta BL, Carvalho HB. Prevalence of high blood pressure in 122,053 adolescents: a systematic review and meta-regression. *Medicine (Baltimore)*. 2014;93(27):e232. doi:10.1097/MD.0000000000000232
7. Chung J, Robinson C, Sheffield L, et al. Prevalence of Pediatric Masked Hypertension and Risk of Subclinical Cardiovascular Outcomes: A Systematic Review and Meta-Analysis. *Hypertension*. 2023;80(11):2280-2292. doi:10.1161/HYPERTENSIONAHA.123.20967
8. Hansen ML, Gunn PW, Kaelber DC. Underdiagnosis of hypertension in children and adolescents. *JAMA*. 2007;298(8):874-879. doi:10.1001/jama.298.8.874
9. Miyashita Y, Hanevold C, Faino A, et al. White Coat Hypertension Persistence in Children and Adolescents: The Pediatric Nephrology Research Consortium Study. *J Pediatr*. 2022;246:154-160.e1. doi:10.1016/j.jpeds.2022.03.036
10. Bovet P, Hungerbuhler P, Quilindo J, Grettve ML, Waeber B, Burnand B. Systematic difference between blood pressure readings caused by cuff type [published correction appears in Hypertension 1995 Apr;25(4 Pt 1):660]. *Hypertension*. 1994;24(6):786-792. doi:10.1161/01.hyp.24.6.786
11. Linfors EW, Feussner JR, Blessing CL, Starmer CF, Neelon FA, McKee PA. Spurious hypertension in the obese patient. Effect of sphygmomanometer cuff size on prevalence of hypertension. *Arch Intern Med*. 1984;144(7):1482-1485.
12. Duncombe SL, Voss C, Harris KC. Oscillometric and auscultatory blood pressure measurement methods in children: a systematic review and meta-analysis. *J Hypertens*. 2017;35(2):213-224. doi:10.1097/HJH.0000000000001178
13. Sun J, Steffen LM, Ma C, Liang Y, Xi B. Definition of pediatric hypertension: are blood pressure measurements on three separate occasions necessary?. *Hypertens Res*. 2017;40(5):496-503. doi:10.1038/hr.2016.179
14. Bovet P, Gervasoni JP, Ross AG, et al. Assessing the prevalence of hypertension in populations: are we doing it right?. *J Hypertens*. 2003;21(3):509-517. doi:10.1097/00004872-200303000-00016
15. Parati G, Mancia G. Assessing the white-coat effect: which blood pressure measurement should be considered?. *J Hypertens*. 2006;24(1):29-31. doi:10.1097/01.hjh.0000198041.47128.05
16. Seeman T, Šuláková T, Stabouli S. Masked Hypertension in Healthy Children and Adolescents: Who Should Be Screened? [published correction appears in Curr Hypertens Rep. 2023 Nov;25(11):421. doi: 10.1007/s11906-023-01271-3.]. *Curr Hypertens Rep*. 2023;25(9):231-242. doi:10.1007/s11906-023-01260-6
17. Kupferman JC, Lande MB, Stabouli S, Zafeiriou DI, Pavlakis SG. Hypertension and childhood stroke. *Pediatr Nephrol*. 2021;36(4):809-823. doi:10.1007/s00467-020-04550-2
18. Litwin M. Pathophysiology of primary hypertension in children and adolescents. *Pediatr Nephrol*. 2024;39(6):1725-1737. doi:10.1007/s00467-023-06142-2

19. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128·9 million children, adolescents, and adults. *Lancet*. 2017;390(10113):2627-2642. doi:10.1016/S0140-6736(17)32129-3
20. Obesity and overweight (2024, March 1). Retrieved from https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight. (Accessed on 17.03.2025)
21. Wang L, Ren L, Wang Y, et al. Effect of body mass index trajectory on hypertension among children and adolescents aged 5-18 years: a retrospective cohort study. *Ann Med*. 2023;55(2):2267572. doi:10.1080/07853890.2023.2267572
22. Ji Y, Zhao X, Feng Y, et al. Body mass index trajectory from childhood to puberty and high blood pressure: the China Health and Nutrition Survey. *BMJ Open*. 2021;11(11):e055099. Published 2021 Nov 25. doi:10.1136/bmjopen-2021-055099
23. Drozdz D, Kwinta P, Korohoda P, Pietrzyk JA, Drozdz M, Sancewicz-Pach K. Correlation between fat mass and blood pressure in healthy children. *Pediatr Nephrol*. 2009;24(9):1735-1740. doi:10.1007/s00467-009-1207-9
24. Wühl E. Hypertension in childhood obesity. *Acta Paediatr*. 2019;108(1):37-43. doi:10.1111/apa.14551
25. Kaelber DC, Localio AR, Ross M, et al. Persistent Hypertension in Children and Adolescents: A 6-Year Cohort Study. *Pediatrics*. 2020;146(4):e20193778. doi:10.1542/peds.2019-3778
26. Bassareo PP, Calcaterra G, Sabatino J, et al. Primary and secondary paediatric hypertension. *J Cardiovasc Med (Hagerstown)*. 2023;24(Suppl 1):e77-e85. doi:10.2459/JCM.0000000000001432
27. Chrysaidou K, Chainoglou A, Karava V, Dotis J, Printza N, Stabouli S. Secondary Hypertension in Children and Adolescents: Novel Insights. *Curr Hypertens Rev*. 2020;16(1):37-44. doi:10.2174/1573402115666190416152820
28. Taha K, Catapang M, Becknell B, Matsell DG. Hypertension in children with congenital anomalies of the kidney and urinary tract. *Pediatr Nephrol*. 2024;39(4):1185-1192. doi:10.1007/s00467-023-06207-2
29. Hsiao W, Denburg M, Laskin B. Hypertension in Wilms tumor. *Pediatr Nephrol*. 2024;39(1):15-24. doi:10.1007/s00467-023-06011-y
30. Singh V, Van Why SK. Monogenic Etiology of Hypertension. *Med Clin North Am*. 2024;108(1):157-172. doi:10.1016/j.mcna.2023.06.005
31. MacLean PS, Higgins JA, Giles ED, Sherk VD, Jackman MR. The role for adipose tissue in weight regain after weight loss. *Obes Rev*. 2015;16 Suppl 1(Suppl 1):45-54. doi:10.1111/obr.12255
32. Tobacco Use and Dependence Guideline Panel. Treating Tobacco Use and Dependence: 2008 Update. Rockville (MD): US Department of Health and Human Services; 2008 May. Available from: https://www.ncbi.nlm.nih.gov/books/NBK63952/1 (Accessed on 17.03.2025)
33. Gray KM, Baker NL, McClure EA, et al. Efficacy and Safety of Varenicline for Adolescent Smoking Cessation: A Randomized Clinical Trial. *JAMA Pediatr*. 2019;173(12):1146-1153. doi:10.1001/jamapediatrics.2019.3553
34. Gray KM, Rubinstein ML, Prochaska JJ, et al. High-dose and low-dose varenicline for smoking cessation in adolescents: a randomised, placebo-controlled trial. *Lancet Child Adolesc Health*. 2020;4(11):837-845. doi:10.1016/S2352-4642(20)30243-1

35. Algharably EA, Meinert F, Januszewicz A, Kreutz R. Understanding the impact of alcohol on blood pressure and hypertension: From moderate to excessive drinking. *Kardiol Pol*. 2024;82(1):10-18. doi:10.33963/v.kp.98704
36. Roerecke M, Kaczorowski J, Tobe SW, Gmel G, Hasan OSM, Rehm J. The effect of a reduction in alcohol consumption on blood pressure: a systematic review and meta-analysis. *Lancet Public Health*. 2017;2(2):e108-e120. doi:10.1016/S2468-2667(17)30003-8
37. WHO report on the global tobacco epidemic 2021: addressing new and emerging products (published 27 July 2021), retrieved from https://www.who.int/publications/i/item/9789240032095 (Accessed on 17.03.2025)
38. Knutson KL, Van Cauter E, Rathouz PJ, et al. Association between sleep and blood pressure in midlife: the CARDIA sleep study. *Arch Intern Med*. 2009;169(11):1055-1061. doi:10.1001/archinternmed.2009.119
39. Sabanayagam C, Shankar A. Sleep duration and cardiovascular disease: results from the National Health Interview Survey. *Sleep*. 2010;33(8):1037-1042. doi:10.1093/sleep/33.8.1037
40. Hoevenaar-Blom MP, Spijkerman AM, Kromhout D, Verschuren WM. Sufficient sleep duration contributes to lower cardiovascular disease risk in addition to four traditional lifestyle factors: the MORGEN study. *Eur J Prev Cardiol*. 2014;21(11):1367-1375. doi:10.1177/2047487313493057
41. Friedman O, Logan AG. The price of obstructive sleep apnea-hypopnea: hypertension and other ill effects. *Am J Hypertens*. 2009;22(5):474-483. doi:10.1038/ajh.2009.43
42. Pepperell JC, Ramdassingh-Dow S, Crosthwaite N, et al. Ambulatory blood pressure after therapeutic and subtherapeutic nasal continuous positive airway pressure for obstructive sleep apnoea: a randomised parallel trial. *Lancet*. 2002;359(9302):204-210. doi:10.1016/S0140-6736(02)07445-7
43. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents; National Heart, Lung, and Blood Institute. Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: summary report. *Pediatrics*. 2011;128 Suppl 5(Suppl 5):S213-S256. doi:10.1542/peds.2009-2107C
44. Gidding SS, Dennison BA, Birch LL, et al. Dietary recommendations for children and adolescents: a guide for practitioners [published correction appears in Pediatrics. 2006 Sep;118(3):1323. Gilman, Matthew W [corrected to Gillman, Matthew W]]. *Pediatrics*. 2006;117(2):544-559. doi:10.1542/peds.2005-2374
45. McCrindle BW, Urbina EM, Dennison BA, et al. Drug therapy of high-risk lipid abnormalities in children and adolescents: a scientific statement from the American Heart Association Atherosclerosis, Hypertension, and Obesity in Youth Committee, Council of Cardiovascular Disease in the Young, with the Council on Cardiovascular Nursing. *Circulation*. 2007;115(14):1948-1967. doi:10.1161/CIRCULATIONAHA.107.181946
46. Kelly RK, Thomson R, Smith KJ, Dwyer T, Venn A, Magnussen CG. Factors Affecting Tracking of Blood Pressure from Childhood to Adulthood: The Childhood Determinants of Adult Health Study. *J Pediatr*. 2015;167(6):1422-8.e2. doi:10.1016/j.jpeds.2015.07.055

47. Mark AE, Janssen I. Dose-response relation between physical activity and blood pressure in youth. *Med Sci Sports Exerc*. 2008;40(6):1007-1012. doi:10.1249/MSS.0b013e318169032d
48. Gidding SS, Barton BA, Dorgan JA, et al. Higher self-reported physical activity is associated with lower systolic blood pressure: the Dietary Intervention Study in Childhood (DISC). *Pediatrics*. 2006;118(6):2388-2393. doi:10.1542/peds.2006-1785
49. Cai L, Wu Y, Wilson RF, Segal JB, Kim MT, Wang Y. Effect of childhood obesity prevention programs on blood pressure: a systematic review and meta-analysis. *Circulation*. 2014;129(18):1832-1839. doi:10.1161/CIRCULATIONAHA.113.005666
50. Levy RV, Brathwaite KE, Sarathy H, Reidy K, Kaskel FJ, Melamed ML. Analysis of Active and Passive Tobacco Exposures and Blood Pressure in US Children and Adolescents. *JAMA Netw Open*. 2021;4(2):e2037936. Published 2021 Feb 1. doi:10.1001/jamanetworkopen.2020.37936
51. Belfort MB, Rifas-Shiman SL, Rich-Edwards J, Kleinman KP, Gillman MW. Size at birth, infant growth, and blood pressure at three years of age. *J Pediatr*. 2007;151(6):670-674. doi:10.1016/j.jpeds.2007.05.010
52. Cao Y, Zhu L, Liu J. Effects of aerobic exercise on obese children with metabolic syndrome: a systematic review and meta-analysis. *J Pediatr Endocrinol Metab*. 2021;34(9):1069-1079. Published 2021 Jul 22. doi:10.1515/jpem-2021-0295
53. Ekelund U, Luan J, Sherar LB, et al. Moderate to vigorous physical activity and sedentary time and cardiometabolic risk factors in children and adolescents [published correction appears in JAMA. 2012 May 9;307(18):1915. Sardinha L [corrected to Sardinha, L B]; Anderssen, S A [corrected to Anderson, L B]]. *JAMA*. 2012;307(7):704-712. doi:10.1001/jama.2012.156
54. Falkner B, Gidding SS, Ramirez-Garnica G, Wiltrout SA, West D, Rappaport EB. The relationship of body mass index and blood pressure in primary care pediatric patients. *J Pediatr*. 2006;148(2):195-200. doi:10.1016/j.jpeds.2005.10.030
55. Dong Y, Song Y, Zou Z, Ma J, Dong B, Prochaska JJ. Updates to pediatric hypertension guidelines: influence on classification of high blood pressure in children and adolescents. *J Hypertens*. 2019;37(2):297-306. doi:10.1097/HJH.0000000000001903
56. Burrello J, Erhardt EM, Saint-Hilary G, et al. Pharmacological Treatment of Arterial Hypertension in Children and Adolescents: A Network Meta-Analysis. *Hypertension*. 2018;72(2):306-313. doi:10.1161/HYPERTENSIONAHA.118.10862
57. Chaturvedi S, Lipszyc DH, Licht C, Craig JC, Parekh R. Pharmacological interventions for hypertension in children. *Cochrane Database Syst Rev*. 2014;2014(2):CD008117. Published 2014 Feb 1. doi:10.1002/14651858.CD008117.pub2
58. Mainieri F, Tagi VM, Chiarelli F. Treatment of Hypertension in Children. *Curr Hypertens Rev*. 2024;20(2):80-89. doi:10.2174/0115734021305332240712103602
59. Mead E, Atkinson G, Richter B, et al. Drug interventions for the treatment of obesity in children and adolescents. *Cochrane Database Syst Rev*. 2016;11(11):CD012436. Published 2016 Nov 29. doi:10.1002/14651858.CD012436
60. Weghuber D, Barrett T, Barrientos-Pérez M, et al. Once-Weekly Semaglutide in Adolescents with Obesity. *N Engl J Med*. 2022;387(24):2245-2257. doi:10.1056/NEJMoa2208601

61. Kelly AS, Auerbach P, Barrientos-Perez M, et al. A Randomized, Controlled Trial of Liraglutide for Adolescents with Obesity. *N Engl J Med*. 2020;382(22):2117-2128. doi:10.1056/NEJMoa1916038
62. Burrello J, Erhardt EM, Saint-Hilary G, et al. Pharmacological Treatment of Arterial Hypertension in Children and Adolescents: A Network Meta-Analysis. *Hypertension*. 2018;72(2):306-313. doi:10.1161/HYPERTENSIONAHA.118.10862
63. US Preventive Services Task Force, Krist AH, Davidson KW, et al. Screening for High Blood Pressure in Children and Adolescents: US Preventive Services Task Force Recommendation Statement. *JAMA*. 2020;324(18):1878-1883. doi:10.1001/jama.2020.20122
64. Chung J, Robinson CH, Yu A, et al. Risk of Target Organ Damage in Children With Primary Ambulatory Hypertension: A Systematic Review and Meta-Analysis. *Hypertension*. 2023;80(6):1183-1196. doi:10.1161/HYPERTENSIONAHA.122.20190
65. Dekkers JC, Snieder H, Van Den Oord EJ, Treiber FA. Moderators of blood pressure development from childhood to adulthood: a 10-year longitudinal study. *J Pediatr*. 2002;141(6):770-779. doi:10.1067/mpd.2002.128113
66. Juhola J, Magnussen CG, Berenson GS, et al. Combined effects of child and adult elevated blood pressure on subclinical atherosclerosis: the International Childhood Cardiovascular Cohort Consortium. *Circulation*. 2013;128(3):217-224. doi:10.1161/CIRCULATIONAHA.113.001614
67. Juhola J, Oikonen M, Magnussen CG, et al. Childhood physical, environmental, and genetic predictors of adult hypertension: the cardiovascular risk in young Finns study. *Circulation*. 2012;126(4):402-409. doi:10.1161/CIRCULATIONAHA.111.085977
68. Litwin M, Niemirska A, Sladowska J, et al. Left ventricular hypertrophy and arterial wall thickening in children with essential hypertension. *Pediatr Nephrol*. 2006;21(6):811-819. doi:10.1007/s00467-006-0068-8
69. Sorof JM, Cardwell G, Franco K, Portman RJ. Ambulatory blood pressure and left ventricular mass index in hypertensive children. *Hypertension*. 2002;39(4):903-908. doi:10.1161/01.hyp.0000013266.40320.3b
70. Sharma AK, Metzger DL, Rodd CJ. Prevalence and Severity of High Blood Pressure Among Children Based on the 2017 American Academy of Pediatrics Guidelines. *JAMA Pediatr*. 2018;172(6):557-565. doi:10.1001/jamapediatrics.2018.0223
71. Obrycki Ł, Feber J, Derezinski T, Lewandowska W, Kułaga Z, Litwin M. Hemodynamic Patterns and Target Organ Damage in Adolescents With Ambulatory Prehypertension. *Hypertension*. 2020;75(3):826-834. doi:10.1161/HYPERTENSIONAHA.119.14149
72. Pac M, Obrycki Ł, Koziej J, Skoczyński K, Starnawska-Bojsza A, Litwin M. Assessment of hypertension-mediated organ damage in children and adolescents with hypertension. *Blood Press*. 2023;32(1):2212085. doi:10.1080/08037051.2023.2212085
73. Franklin SS, Wilkinson IB, McEniery CM. Unusual hypertensive phenotypes: what is their significance?. *Hypertension*. 2012;59(2):173-178. doi:10.1161/HYPERTENSIONAHA.111.182956
74. Sorof JM. Systolic hypertension in children: benign or beware?. *Pediatr Nephrol*. 2001;16(6):517-525. doi:10.1007/s004670100586
75. McEniery CM, Franklin SS, Cockcroft JR, Wilkinson IB. Isolated Systolic Hypertension in Young People Is Not Spurious and Should Be Treated: Pro Side of the Argument. *Hypertension*. 2016;68(2):269-275. doi:10.1161/HYPERTENSIONAHA.116.06547

76. Lurbe E, Redon J. Isolated Systolic Hypertension in Young People Is Not Spurious and Should Be Treated: Con Side of the Argument. *Hypertension*. 2016;68(2):276-280. doi:10.1161/HYPERTENSIONAHA.116.06548
77. Alsaeed H, Metzger DL, Blydt-Hansen TD, Rodd C, Sharma A. Isolated diastolic high blood pressure: a distinct clinical phenotype in US children. *Pediatr Res*. 2021;90(4):903-909. doi:10.1038/s41390-021-01369-x
78. Franklin SS, Pio JR, Wong ND, et al. Predictors of new-onset diastolic and systolic hypertension: the Framingham Heart Study. *Circulation*. 2005;111(9):1121-1127. doi:10.1161/01.CIR.0000157159.39889.EC
79. Narasimhan C, Alexander T, Krishnaswami S. Pseudohypertension in a child with Williams syndrome. *Pediatr Cardiol*. 1993;14(2):124-126. doi:10.1007/BF00796994
80. Ostrowska-Czyżewska A, Szwed D, Barcińska J. Monogenic hypertension — state-of-the-art knowledge. Arterial Hypertens 2024;28:160-170. DOI: 10.5603/ah.102778
81. Park SJ, Shin JI. Diagnosis and Treatment of Monogenic Hypertension in Children. *Yonsei Med J*. 2023;64(2):77-86. doi:10.3349/ymj.2022.0316
82. Gallegos FR, Delahunty MP, Hu J, et al. Decoding Monogenic Hypertension: A Review of Rare Hypertension Disorders. *Am J Hypertens*. Published online January 13, 2025. doi:10.1093/ajh/hpaf005
83. Jackson SL, Zhang Z, Wiltz JL, et al. Hypertension Among Youths - United States, 2001-2016. *MMWR Morb Mortal Wkly Rep*. 2018;67(27):758-762. Published 2018 Jul 13. doi:10.15585/mmwr.mm6727a2
84. Flynn JT, Urbina EM, Brady TM, et al. Ambulatory Blood Pressure Monitoring in Children and Adolescents: 2022 Update: A Scientific Statement From the American Heart Association. *Hypertension*. 2022;79(7):e114-e124. doi:10.1161/HYP.0000000000000215
85. Viera AJ, Neutze DM. Diagnosis of secondary hypertension: an age-based approach. *Am Fam Physician*. 2010;82(12):1471-1478.