Current Hypertension Reports (2019) 21: 18
https://doi.org/10.1007/s11906-019-0922-2

HYPERTENSION AND METABOLIC SYNDROME (JOHN SPERATI, SECTION EDITOR)

Real-World Strategies to Treat Hypertension Associated with Pediatric Obesity

Edem Binka[1] · Tammy M. Brady[2]

Published online: 12 February 2019

Abstract

Purpose of Review To review the most recent literature on current strategies for the treatment of hypertension associated with pediatric obesity.

Recent Findings Over the last three decades, childhood and adolescent overweight and obesity prevalence in the USA has continued to rise. Unsurprisingly but rather disturbingly, this rising prevalence has been paralleled by an increase in cardiovascular disease (CVD) risk factors in childhood such as hypertension, dyslipidemia, and diabetes that become manifest earlier than previously reported. These childhood CVD risk factors are not only associated with target organ damage in childhood but also track into adulthood, increasing the risk of long-term CVD morbidity and mortality.

Summary There have been several mechanisms proposed to explain the role of obesity on the development of hypertension in childhood. However, central to the management of obesity-related hypertension is a multifaceted approach targeting lifestyle modifications and weight loss. Effective treatment often also requires a pharmacologic approach and rarely bariatric surgery.

Keywords Obesity · Adiposity · Blood pressure · Hypertension · Cardiovascular disease risk factors · Weight management · Lifestyle modifications · Pharmacotherapy

Introduction

The prevalence of childhood and adolescent obesity has tripled in the past three decades in the USA and increased tenfold worldwide [1]. In the USA alone, nearly 12.7 million children meet the criteria for obesity. This statistic of increased adiposity prevalence in the USA dramatically increases to almost 30 million when children who are overweight are included [2]. This epidemic is not isolated to the USA: in 2016, 50 million girls and 74 million boys worldwide were considered obese [3]. The implications of this rise are significant, as it has coincided with an increase in cardiovascular disease (CVD) risk factor prevalence at this early age. In the 1970s and 1980s, 0.3–1.2% of children and adolescents were estimated to have hypertension [4, 5]. Currently, this estimate of hypertension prevalence among all children has tripled to approximately 3.5% and is as high as 25% among children with overweight and obesity [6••]. The important role of obesity in pediatric CVD risk factor development is further illustrated by the concurrent rise in the prevalence of left ventricular hypertrophy (LVH) among youth with overweight and obesity. Left ventricular hypertrophy, a form of end-organ damage associated with cardiac dysfunction and ventricular arrhythmias and associated with myocardial infarction in adulthood [2, 7•], is independently and strongly associated with obesity, even in the absence of hypertension [8•, 9]. Even before the development of LVH and other clinical signs of cardiac dysfunction, microvascular and macrovascular impairments have been associated with childhood obesity and hypertension [10]. While often clinically silent in the pediatric age group, we now know that these childhood CVD risk

This article is part of the Topical Collection on *Hypertension and Metabolic Syndrome*

✉ Edem Binka
ebinka1@jhmi.edu

Tammy M. Brady
tbrady8@jhmi.edu

[1] Pediatric Cardiology, Johns Hopkins University, Bloomberg Children's Center, 1800 Orleans Street, M2303, Baltimore, MD 21287, USA

[2] Division of Pediatric Nephrology, Johns Hopkins University, David M. Rubenstein Child Health Building, 200 N. Wolfe Street, Baltimore, MD 21287, USA

factors persist long into adulthood, increasing the long-term risk of CVD-related morbidity and mortality [9, 11, 12].

Mechanisms and Pathophysiology of Obesity-Related Hypertension

Obesity contributes to the development of hypertension and increased CVD risk via several interconnected and complex pathways. The overall premise is that with obesity, one not only has an excess of adipose tissue but that this adipose tissue becomes dysfunctional, leading to a cascade of events resulting in the elevation in blood pressure (BP) [13], and increase in comorbid CVD risk factors. Adipose tissue is no longer considered an inert energy source but is instead known to be an active endocrinological cell [2, 14], secreting cytokines, acute-phase reactants, and chemotactic agents, collectively known as adipokines. One of those adipokines, leptin, upregulates the sympathetic nervous system (SNS) activity which can lead to hypertension by direct vasoconstriction or by increasing renin-angiotensin-aldosterone (RAAS) activity [2]. RAAS hormones are also directly secreted by adipocytes, and studies have linked increased urinary and serum levels of aldosterone with obesity and obesity-related risk factors such as arterial hypertension, dyslipidemia, and pro-inflammatory states [15]. Aldosterone, a human mineralocorticoid, is thought to affect BP regulation as a result of its effect on sodium homeostasis and plasma volume expansion [16•]. However, aldosterone can also increase SNS activity by inducing oxidative stress, thus contributing to another pathway to arterial hypertension [2, 15].

In the presence of obesity, adipokines are upregulated, ultimately becoming dysregulated with an imbalance of pro- vs. anti-inflammatory adipokine secretion. When the release of pro-inflammatory adipokines (i.e., leptin, resistin, and IL-6) exceed the secretion of anti-inflammatory adipokines (i.e., adiponectin), the dysfunctional adipose tissue promotes a chronic pro-inflammatory state, leading to inappropriate neuro-hormonal activation of the SNS and/or RAAS activity, resulting in elevated BP.

Furthermore, comorbid CVD risk factors such as dyslipidemia and insulin resistance, while a consequence of obesity, also contribute to the vicious cycle of metabolic dysfunction. Elevated LDL-cholesterol can induce chronic inflammation and hence perpetuate this cycle, and insulin resistance can inhibit adipose tissue lipolysis which accelerates the release of free fatty acids (FFA) into circulation [17]. Elevated levels of FFA increases alpha-adrenergic vascular effects leading to increased arterial tone [13].

The pathophysiology of obesity-related hypertension is clearly complex but involves two central tenets: dysregulation of adipocyte metabolism and neuro-hormonal activation of the SNS. This has implications for the management of obesity-related hypertension as many therapeutic approaches have targeted specific aspects of these interconnections.

Hypertension Evaluation for Children with Comorbid Obesity

All children with elevated blood pressure should undergo repeated BP measurements to confirm that the elevation is sustained prior to being diagnosed with hypertension. Obtaining an accurate BP measurement in children with obesity can be particularly challenging, with barriers to proper measurement potentially leading to misdiagnosis [18]. For example, pediatric practices may not have access to cuffs that are the appropriate size for larger arm circumferences, forcing them to "undercuff" (use a cuff that is too small for the arm) during the measurement. In this scenario, when the cuff used does not meet the American Heart Association (AHA) recommendations of a bladder length of 80 to 100% and a width of 45 to 55% of the patient's mid-arm circumference [6••], BP measurements can be artificially elevated (by an average of 6.9 mmHg systolic and 4.0 mmHg diastolic) [19]. In fact, based on NHANES data of more than 13,000 children evaluated from 1999 to 2000, 6–7% of those aged 3–19 years had an arm circumference that would require a large adult cuff, and 0.2–0.4% had an arm circumference that would require a thigh cuff for upper extremity BP measurement [20]. This data provides strong evidence to support routine assessment/measurement of the mid-arm circumference in all patients prior to BP measurement to ensure the proper-sized cuff is applied.

Another impediment to proper BP measurement in children with obesity is that many have a conically shaped arm, meaning that their proximal arm circumference is significantly larger than their distal arm circumference. This difference is often quite large, ranging from 1 to 20 cm (average 8.7 cm) [21]. With this difference, it can be challenging to achieve equal brachial artery occlusion, a necessary step in BP measurement. Having the patient extend their arm out to the side while placing the cuff on can be helpful in optimizing cuff placement in this situation.

In the fall of 2017, the American Academy of Pediatrics (AAP) published updated clinical practice guidelines for the evaluation and treatment of hypertension in children. As with earlier guidelines, these guidelines include age-sex-height-specific BP thresholds to define elevated BP. However, these percentile-based definitions are exclusively for children younger than 13 years of age. For adolescents and young adults, the AHA/ACC guideline definitions apply. This important update (Table 1) was made to simplify BP classification and hypertension diagnosis in children and to make the pediatric hypertension guidelines consistent with the AHA and ACC guidelines for those 13 years of age and older. Despite this change, the approach to elevated BP remains the same: any BP that is > 90th percentile in those under 13 years of age or > 120/80 (regardless of age) should be repeated. If the BP

Table 1 Updated BP classifications based on the 2017 Clinical Practice Guidelines

Age group	Normal BP	Elevated BP	Stage 1 HTN	Stage 2 HTN
1 to < 13 years	< 90th percentile	≥ 90th percentile or 120/80 to < 95th percentile	≥ 95th percentile or 130/80 to < 95th percentile + 12 mmHg or 139/89 mmHg	≥ 95th percentile + 12 mmHg or ≥ 140/90 mmHg
≥ 13 years	< 120/< 80 mmHg	120/< 80 to 129/< 80 mmHg	130/80 to 139/89 mmHg	≥ 140/90 mmHg

elevation persists, then several measurements obtained by manual auscultation at that visit need to be performed, with the average measurement used to determine future steps.

Another major difference in the new pediatric hypertension guidelines is that the data informing these percentile-based definitions are now only based on data from children without overweight and obesity (body mass index < 85 percentile). The normative data used to calculate the BP tables in earlier hypertension guidelines (fourth report) included BP data from over 13,000 children with overweight or obesity [22•]. By eliminating the data from these children, the BP thresholds for normal, elevated, and hypertensive range BP are several millimeters of mercury lower across all age and height percentiles, with clear implications for hypertension diagnosis and management.

The new pediatric hypertension guidelines now also highlight the need for more frequent hypertension screening for youth with obesity. While children without comorbidities are recommended to undergo annual BP measurement to screen for hypertension, children with obesity and other risk factors are recommended to undergo BP measurement at all health care encounters.

After the diagnosis of hypertension has been confirmed, an evaluation for secondary causes of hypertension should be completed. This evaluation should include a thorough history and physical exam and a fasting laboratory evaluation [6••]. Specific attention to comorbidities such as sleep-disordered breathing/obstructive sleep apnea, diabetes mellitus, mood disorders, orthopedic diagnoses such as arthritis and slipped capital femoral epiphysis, dyslipidemia, and thyroid disease should be made not only to determine potential etiologies for hypertension but also to identify comorbidities and potential barriers to effective treatment and/or weight loss (Table 2). A child with overweight or obesity and depression or anxiety is not only more likely to have hypertension [23], but may also find it more challenging to implement and adhere to the heart healthy lifestyle changes necessary for weight loss and hypertension control. A child with untreated OSA may present with resistant hypertension and persistent LVH and may also find it more challenging to be successful with weight loss. It is for these reasons that, once identified, appropriate management of these comorbidities should be prioritized as failure to do so has been shown to impede effective treatment of obesity-related hypertension.

While it may be tempting to attribute hypertension to overweight and obesity, and this may be the ultimate diagnosis, all children less than 6 years of age and those older than 6 years of age with an abnormal urinalysis or renal function should undergo renal ultrasonography [6••].

Management of Obesity-Related Hypertension

Non-Pharmacologic Management

Non-pharmacologic approaches should be the focus of initial management strategies. Integral to the management of obesity-related hypertension is the attainment of a healthy weight and maintenance of a healthy lifestyle—this should be considered first-line treatment. According to the AAP, weight management in children should focus on weight loss for obese children 6 years and older and weight maintenance for overweight children [2]. The AAP currently recommends a staged approach to the management of childhood obesity (Fig. 1).

Prevention typically emphasizes lifestyle changes including dietary modifications and increased physical activity. The cornerstone of dietary recommendations is the Dietary Approaches to Stop Hypertension (DASH) diet, a diet that

Table 2 Comorbidities associated with childhood obesity and recommended testing

Comorbidity	Laboratory testing
Diabetes mellitus	Fasting plasma glucose 2-h plasma glucose HbA1c
Dyslipidemia	Fasting lipid panel
Thyroid disease	Thyroid-stimulating hormone
Polycystic ovary syndrome (PCOS)	Sex hormone–binding globulin (SHBG) testosterone levels (free and total)
Non-alcoholic fatty liver disease (NAFLD)	Aspartate transaminase (AST), alanine transaminase (ALT)
Obstructive sleep apnea (OSA)	Sleep history • possible polysomnography
Slipped capital femoral epiphysis (SCFE)	X-rays of the pelvis, hip, and thigh
Psychiatric	Appropriate screening for mood disorders • possible mental health referral toxicology screen

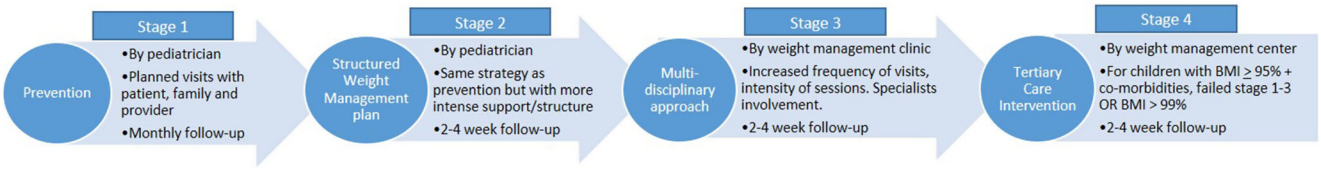

Fig. 1 Staged approach to management of childhood obesity per AAP guidelines [24••]

emphasizes consumption of fruits and vegetables, whole grains, low-fat dairy, and reduction of sodium, fat, processed sugar, and fat content. According to the Dietary Guidelines for Americans, salt intake should be limited to < 2300 mg in children ≥ 14 years and < 1500 mg for children 1–3 years of age [2]. The new pediatric hypertension Clinical Practice Guidelines recommends sodium reduction as one of the key lifestyle changes that should be emphasized to those with hypertension. A systematic review by Bricarello et al. regarding the effects of the DASH diet on blood pressure in overweight and obese adolescents showed that, overall, this diet leads to a decrease in body mass index (BMI) and systolic BP. The cohort studies included in this review also showed a decrease in diastolic BP [25•]. Similarly, a systematic review and meta-analysis of the effect of the DASH diet on obese adults showed that the DASH diet significantly reduced systolic BP by 6.7 mmHg and diastolic BP by 3.54 mmHg [26•]. Sodium reduction may be particularly beneficial to children and adolescents with obesity. An NHANES study of 6235 children 8–18 years of age with an average sodium intake of 3387 mg/day found that sodium intake was significantly associated with SBP among children with BMI > 85 percentile. This finding was not present among children with normal BMI [27].

In addition to improved diet quality and sodium reduction, exercise or increased physical activity is a key component of obesity management and hypertension treatment. It is recommended that screen time be limited to less than 2 h per day and moderate to vigorous physical activity (MVPA) or exercise be performed for at least 60 min daily [28••]. It has been shown that television watching in childhood and low levels of physical activity in adolescence are predictive of metabolic syndrome in adulthood whereas increased levels of aerobic activity in childhood are associated with decreased metabolic syndrome in adulthood [17]. While some pediatric studies have shown no effect of MVPA on BP, the majority have shown an association between MVPA and lower BP [6••, 29].

Ultimately, a combination of dietary modifications and MVPA yields the best results. When individual attempts at lifestyle modifications fail, referral to a weight loss clinic or program that utilizes a multidisciplinary approach to weight management, focusing not just on methods to improve diet and increase physical activity, but also on how to modify eating behaviors and improve familial dynamics that exacerbate adverse dietary habits, may be warranted. Many of these clinics/programs are primarily run on an outpatient basis with variable success. A novel approach has been to adopt a similar multidisciplinary approach but in an inpatient setting. Taylor et al. recently reported results of such a program, the CHANGES Health and Wellness Program, conducted at the Healthbridge Children's Hospital in Houston, Texas [30]. Eighteen patients between 2 and 21 years of age with BMI ≥ 95th percentile were given treatment goals of 25% weight reduction. The structure of the program included a detailed initial assessment including evaluation of prior eating habits, fitness testing, and any indicated psychological testing. Patients were given individualized exercise programs and were provided with structured days that included regular therapy sessions and scheduled mealtimes. The average length of hospitalization was 76 days with an average weight loss of 14.98% and a mean decrease in BMI *z*-score of 8.6%. Remarkably, systolic BP and diastolic BP decreased by 7.2% and 10.3%, respectively.

Both outpatient and inpatient programs can be effective for weight management but the burden of childhood obesity in the USA surpasses the availability of programs to meet this need. As a result, interventions delivered via the internet and mobile technology have become adjuncts to these aforementioned weight management programs, with varying degrees of utilization and efficacy [31–33]. Many adolescents today have access to mobile phones which are now inundated with a variety of applications, some of which have weight management purposes. Many such apps provide access to dietary information and allow adolescents to set daily goals in terms of physical activity, water, nutrient, and caloric intake. Adolescents are also able to track their daily activity with smartphones and with use of accessories such as smart watches, receiving real-time feedback on progress made throughout the day. Websites also offer a similar functionality, with assessment and feedback on progress sent via emails or short message service (SMS). Few pediatric randomized controlled trials have evaluated the effect of these interventions on childhood obesity and hypertension. A systematic review by Turner et al. described three randomized clinical trials (RCTs) that investigated the effect of websites/SMS feedback on physical activity and measures of adiposity such as BMI and BMI *z*-score [31]. While technology-based interventions are promising in a pediatric population, where many children are early, avid adapters to this format, adherence to the interventions in these three RCTs was poor and none of the trials demonstrated an effect on BMI [31]. Further robust studies are clearly needed to determine the effect of behaviorally based technologic interventions on childhood obesity and CVD risk factors as the ubiquitous nature of these technologies could potentially be an invaluable tool in combatting this concerning epidemic.

Pharmacologic Management

Hypertension

Antihypertensive medications may ultimately be needed for children and adolescents with obesity and persistent hypertension despite non-pharmacologic treatment. Importantly, it should be emphasized that any pharmacologic management should be initiated in conjunction with lifestyle modifications. As described previously, one of the proposed mechanisms of obesity-related hypertension is the activation of RAAS and children with obesity may be more sensitive to the effects of sodium intake on BP. As such it naturally follows that angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs), agents that block the RAAS and decrease sodium reabsorption in the kidney are ideal agents for treating obesity-related hypertension [2, 6••, 13]. Furthermore, ACEIs and ARBs provide additional benefit to children with obesity-related hypertension. These agents provide renal protection, which can help counteract obesity-related hyperfiltration and may be important in those with comorbid diabetes, and they have a favorable metabolic side effect profile which is particularly important for those with type 2 diabetes and dyslipidemias [2, 6••, 13]. These benefits should be considered along with the known adverse effects of increasing creatinine and potassium and the risk of teratogenicity.

In contrast, beta-adrenergic blockers (beta-blockers) are typically not considered first-line antihypertensive medications for youth with obesity-related hypertension. While beta-blockers decrease renin activity and block SNS activation, mechanisms implicated in obesity-related hypertension [2, 13] and their unfavorable side effect profile of dyslipidemia and increased weight make them less ideal agents for this population. Diuretics are also less ideal because, via their mechanism of action, they decrease intravascular volume and cardiac output leading to downstream effects of increasing SNS and RAAS activity. Furthermore, diuretics can worsen insulin resistance and can increase glucose, dyslipidemia, and uric acid, particularly among individuals with obesity. Both agents, beta-blockers and diuretics, may also be less ideal in physically active youth, presenting unintended barriers to weight management.

Calcium channel blockers may be good agents for children with obesity-related hypertension. While not specifically targeting the pathophysiological pathway to hypertension, these agents are well tolerated with a minimal side effect profile and no known metabolic side effects. Finally, unmasked observational studies suggest aldosterone antagonists such as spironolactone and eplerenone may be efficacious in lowering BP among individuals with obesity and resistant hypertension [34–38].

Obesity

In select instances, pharmacologic management for obesity-related hypertension can also include the use of anti-obesity medication for purposes of weight reduction. However, the European Society of Endocrinology and the Pediatric Endocrine Society have suggested that these medications should only be considered after intensive lifestyle modification programs have failed [39••]. They recommend against using obesity medications in overweight but not obese pediatric patients < 16 years unless done within the context of a clinical trial [39••]. Currently, orlistat is the only Food and Drug Administration (FDA)–approved pharmacotherapy for the treatment of obesity in children > 12 years of age [11, 39••, 40••]. Orlistat is a lipase inhibitor that reduces the absorption of fat in the gut [11, 39••]. Orlistat modestly reduces BMI in adolescents by about 0.7 to 1.7 kg/m^2 but is associated with gastrointestinal side effects including abdominal pain, fecal incontinence, and fatty stools [11, 39••, 40••]. Metformin is another medication used as an anti-obesity medication in pediatrics but is not FDA approved for this purpose. It is a biguanide insulin-sensitizing agent and is FDA approved for treating type 2 diabetes in children ≥10 years of age. Metformin affects hepatic glucose metabolism and may reduce appetite but there is no clear mechanism by which it reduces weight. It reduces BMI by about 1.16 kg/m^2 over a 6–12-month period [39••]. Metformin does have the added benefit of treating obesity-related comorbidities such as PCOS and type 2 diabetes. However, there is insufficient data from pediatric studies to determine the long-term outcomes of orlistat and metformin in this population.

Adjunctive Management Approaches to Obesity-Related Hypertension

Bariatric Surgery

Bariatric surgery to address severe obesity is another therapeutic approach to CVD risk reduction. This treatment for obesity can reduce BP and other CVD comorbidities as weight decreases. While this approach can be successful for populations at greatest risk, specific requirements need to be met prior to considering this procedure. Specifically, the European Society of Endocrinology and the Pediatric Endocrine Society state that bariatric surgery should only be considered for patients who (1) have attained Tanner 4 or 5 pubertal development and have either a BMI of > 40 kg/m^2 or a BMI > 35 kg/m^2 with significant comorbidities; (2) have persistent extreme obesity despite implementing intensive lifestyle modifications with or without medications; (3) have a stable family situation based on psychological evaluation; (4) have shown ability to adhere to recommended dietary and activity habits; and (5) are able to have the surgery performed

by an experienced surgeon in a reputable pediatric bariatric surgical center with the ability to provide appropriate follow-up [39••].

Laparoscopic sleeve gastrectomy (LSG) and Roux-en-Y gastric bypass (RYGB) are the most common forms of bariatric surgery performed in the USA. According to the National Patient-Centered Clinical Research Network (PCORnet) bariatric study, adolescents who underwent LSG and RYGB had a significant reduction in BMI that persisted at 1- and 3-year follow-ups [41]. This was a retrospective study of adolescents who underwent bariatric surgery from 2005 to 2015 at one of 56 healthcare systems. Overall, 544 adolescents (aged 12–19 years) were studied with the majority of the patients undergoing LSG. RYGB and LSG were associated with BMI loss of 31.4% and 28%, respectively, at 1-year follow-up compared with a 24.7% and 29.4% loss at the 3-year follow-up, respectively [41]. In addition to weight loss, bariatric surgery has shown improvements in CVD risk factors and resolution of obesity-related comorbidities such as T2DM and sleep apnea [39••]. However, these procedures are not without considerable risk including perioperative complications such as wound infections, small bowel obstruction, venous thromboembolic events, and even death [11, 41]. Pediatric bariatric surgery remains a controversial procedure and has been met with many critics.

Conclusion

The epidemic of childhood obesity in the USA and worldwide shows no signs of waning. Consequently, the development of CVD risk factors that have previously been considered diseases of adulthood is now occurring earlier in childhood. Several mechanisms have been proposed to explain the pathophysiology behind obesity-related hypertension. Central to these theories is dysregulation of adipocyte homeostasis and activation of the SNS. The cornerstone of management remains lifestyle modifications and weight loss. The development of new technologies that are now ubiquitous among children and adolescents presents opportunities for newer, innovative ways to tackle both childhood obesity and hypertension. Unfortunately, while lifestyle modification is the first-line treatment for obesity-related hypertension, as this targets the primary cause for increased CVD risk, this alone is often not sufficient. Therefore, a multifaceted team-based approach that may include pharmacologic therapy and in some instances bariatric surgery is essential for effective management of obesity-related hypertension.

Compliance with Ethics Guidelines

Conflict of Interest Dr. Brady reports grants from NIH/NHLBI, grants from NIH/NIMH, grants from AHRQ, and grants from RESOLVE to Save Lives, during the conduct of the study. Dr. Binka reports grants from NIH/NHLBI during the conduct of the study.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

References

Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance

1. Turer CB, Brady TM, De Ferranti SD. Obesity, hypertension, and dyslipidemia in childhood are key modifiable antecedents of adult cardiovascular disease: a call to action. Circulation. 2018;137(12):1256–9. https://doi.org/10.1161/CIRCULATIONAHA.118.032531.
2. Brady TM. Obesity-related hypertension in children. Front Pediatr. 2017;5:1–7. https://doi.org/10.3389/fped.2017.00197.
3. Abarca-Gómez L, Abdeen ZA, Hamid ZA, Abu-Rmeileh NM, Acosta-Cazares B, Acuin C, et al. 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):2627–42. https://doi.org/10.1016/S0140-6736(17)32129-3.
4. Fixler DE, Laird WP, Fitzgerald V, Stead S, Adams R. Hypertension screening in schools: results of the Dallas study. Pediatrics. 1979 Jan;63(1):32-6. http://pediatrics.aappublications.org/content/63/1/32.short.
5. Sinaiko AR, Gomez-Marin O, Prineas RJ. Prevalence of "significant" hypertension in junior high school-aged children: The Children and Adolescent Blood Pressure Program. *J Pediatr*. 1989;114(4 PART 1):664–9. https://doi.org/10.1016/S0022-3476(89)80718-8.
6. •• Flynn JT, Kaelber DC, Baker-Smith CM, et al. Clinical practice guideline for screening and management of high blood pressure in children and adolescents. Pediatrics. 2017;140(3):e20171904. https://doi.org/10.1161/HYPERTENSIONAHA.117.10050. **A comprehensive guideline statement with current recommendation s for the screening and management of high blood pressure in children and adolescent, with important differences from the previous pediatric guidelines. This document has many useful tables and figures to facilitate implementation of the guidelines into clinical practice, and includes links to several online resources.**
7. • Morrison JA, Friedman LA, Gray-McGuire C. Metabolic syndrome in childhood predicts adult cardiovascular disease 25 years later: the Princeton lipid research clinics follow-up study. Pediatrics. 2007;120(2):340–5. https://doi.org/10.1542/peds.2006-1699. **Twenty-five year longitudinal follow up study that demonstrated childhood metabolic syndrome increases the risk of cardiovascular disease in adulthood 8. Association between adiposity and left ventricular mass in children with hypertension**
8. • Brady TM, Appel LJ, Holmes KW, Fivush B, Miller ER. Association between adiposity and left ventricular mass in children

with hypertension. J Clin Hypertens. 2016;18(7):625–33. https://doi.org/10.1111/jch.12717. **One-year prospective observational study which demonstrated a strong independent association between adiposity and LVH. Specifically, children with persistent overweight/obesity had a greater LVMI increase than children who remained at a healthy weight over the course of the study and baseline body mass index z-score independently predicted the change in LVMI**.

9. Wade K, Chiesa ST, Hughes AD, et al. Assessing the causal role of BMI on cardiovascular health in young adults. Circulation. 2018;138:2187–201. https://doi.org/10.1161/CIRCULATIONAHA.117.033278.
10. Köchli S, Endes K, Steiner R, et al. Determine vascular phenotype in young children the EXAMIN YOUTH study. 2018;1–9. doi: https://doi.org/10.1161/HYPERTENSIONAHA.118.11872.
11. Kumar S, Kelly AS. Review of childhood obesity: from epidemiology, etiology, and comorbidities to clinical assessment and treatment. Mayo Clin Proc. 2017;92(2):251–65. https://doi.org/10.1016/j.mayocp.2016.09.017.
12. Li L, Pérez A, Wu L-T, Ranjit N, Brown HS, Kelder SH. Cardiometabolic risk factors among severely obese children and adolescents in the United States, 1999–2012. Child Obes. 2016;12(1):12–9. https://doi.org/10.1089/chi.2015.0136.
13. Leggio M, Lombardi M, Caldarone E, Severi P, D'Emidio S, Armeni M, et al. The relationship between obesity and hypertension: an updated comprehensive overview on vicious twins. Hypertens Res. 2017;40:947–63. https://doi.org/10.1038/hr.2017.75.
14. Kidambi S, Kotchen TA. Treatment of hypertension in obese patients. Am J Cardiovasc Drugs. 2013;13(3):163–75. https://doi.org/10.1007/s40256-013-0008-5.
15. Vecchiola A, Lagos CF, Carvajal CA, Baudrand R, Fardella CE. Aldosterone production and signaling dysregulation in obesity. Curr Hypertens Rep. 2016;18(3):1–9. https://doi.org/10.1007/s11906-016-0626-9.

16.• Schütten MTJ, Houben AJHM, de Leeuw PW, Stehouwer CDA. The link between adipose tissue renin-angiotensin-aldosterone system signaling and obesity-associated hypertension. Physiology. 2017;32(3):197–209. https://doi.org/10.1152/physiol.00037.2016. **Comprehensive review paper on the association of the renin-angiotensinaldosterone system (RAAS) with obesity-related hypertension**.

17. Mameli C, Zuccotti GV, Carnovale C, Galli E, Nannini P, Cervia D, et al. An update on the assessment and management of metabolic syndrome, a growing medical emergency in paediatric populations. Pharmacol Res. 2017;119:99–117. https://doi.org/10.1016/j.phrs.2017.01.017.
18. Muhamed PK, Olsen MH, Holm JC, Ibsen H, Hvidt KN. Cuff size influences blood pressure measurement in obese children and adolescents. Dan Med J. 2016;63(1):A5183.
19. Mourad JJ, Lopez-Sublet M, Aoun-Bahous S, Villeneuve F, Jaboureck O, Dourmap-Collas C, et al. Impact of miscuffing during home blood pressure measurement on the prevalence of masked hypertension. Am J Hypertens. 2013;26(10):1205–9. https://doi.org/10.1093/ajh/hpt084.
20. Ostchega Y, Zhang G, Kit BK, Nwankwo T. Factors associated with home blood pressure monitoring among US adults: National Health and Nutrition Examination Survey, 2011–2014. Am J Hypertens. 2017;30(11):1026–32. https://doi.org/10.1093/ajh/hpx101.
21. Palatini P, Benetti E, Fania C, Malipiero G, Saladini F. Rectangular cuffs may overestimate blood pressure in individuals with large conical arms. J Hypertens. 2012;30(3):530–6. https://doi.org/10.1097/HJH.0b013e32834f98a0.

22.• The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. *Pediatrics*. 2004;114(2 Suppl 4th Report):555–576. http://www.ncbi.nlm.nih.gov/pubmed/15286277. Accessed August 19, 2014. **Previous guideline statement on the screening and management of high blood pressure in children and adolescents**.

23. Medrano L, Amatya K, Vizthum D, Fadrowski JJ, Brady TM. Association of mood disorders with cardiovascular disease risk factors in overweight and obese youth with elevated blood pressure. J Clin Hypertens. 2018;20(9):1268–75. https://doi.org/10.1111/jch.13348.

24.•• Barlow SE. Expert committee recommendations regarding the prevention, assessment, and treatment of child and adolescent overweight and obesity: summary report. Pediatrics. 2007;120(Supplement):S164–92. https://doi.org/10.1542/peds.2007-2329C. **Summary report by an expert committee, consisting of a multidisciplinary group with representation across medicine, nutrition, nursing, psyc hology, and epidemiology, on guidelines for assessment and treatment of overweight and obesity among children and adolescents**.

25.• Paula Bricarello L, Poltronieri F, Fernandes R, Retondario A, de Moraes Trindade EBS, de Vasconcelos FAG. Effects of the dietary approach to stop hypertension (DASH) diet on blood pressure, overweight and obesity in adolescents: a systematic review. Clin Nutr ESPEN. 2018;28:1–11. https://doi.org/10.1016/j.clnesp.2018.09.003. **An important systematic review of published literature through March 2018 describing the likely beneficial effects of the DASH diet on blood pressure, overweight and obesity in adolescents. This review included results from cross-sectional studies, cohort studies and randomized clinical trials**.

26.• Saneei P, Salehi-Abargouei A, Esmaillzadeh A, Azadbakht L. Influence of dietary approaches to stop hypertension (DASH) diet on blood pressure: a systematic review and meta-analysis on randomized controlled trials. Nutr Metab Cardiovasc Dis. 2014;24(12):1253–61. https://doi.org/10.1016/j.numecd.2014.06.008.

27. Yang Q, Zhang Z, Kuklina EV, Fang J, Ayala C, Hong Y, et al. Sodium intake and blood pressure among US children and adolescents. Pediatrics. 2012;130(4):611–9. https://doi.org/10.1542/peds.2011-3870.

28.•• US Department of Health and Human Services. Physical Activity Guidelines for Americans, 2nd edition. Washington, DC: US Department of Health and Human Services; 2018. **Essential resource from the Department of Health and Human Services with comprehensive physical activity guidelines to promote health**.

29. Poitras VJ, Gray CE, Borghese MM, et al. Systematic review of the relationships between objectively measured physical activity and health indicators in school-aged children and youth [1]. Appl Physiol Nutr Metab. 2016;41(6 (Suppl. 3)):S197–239. https://doi.org/10.1139/apnm-2015-0663.
30. Taylor SJA, Rennie K, Jon C. Clinical outcomes of an inpatient pediatric obesity treatment program in the USA. Int J Adolesc Med Health. 2017. https://doi.org/10.1515/ijamh-2016-0141.
31. Turner T, Spruijt-Metz D, Wen CKF, Hingle MD. Prevention and treatment of pediatric obesity using mobile and wireless technologies: a systematic review. Pediatr Obes. 2015;10(6):403–9. https://doi.org/10.1111/ijpo.12002.
32. Ashrafian H, Toma T, Harling L, Kerr K, Athanasiou T, Darzi A. Social networking strategies that aim to reduce obesity have achieved significant although modest results. Health Aff. 2014;33(9):1641–7. https://doi.org/10.1377/hlthaff.2014.0370.
33. Rivera J, McPherson AC, Hamilton J, et al. User-centered design of a mobile app for weight and health management in adolescents with complex health needs: qualitative study. J Med Internet Res. 2018;20(4):1–15. https://doi.org/10.2196/formative.8248.
34. Weinberger MH, Roniker B, Krause SL, Weiss RJ. Eplerenone, a selective aldosterone blocker, in mild-to-moderate hypertension.

Am J Hypertens. 2002;15(8):709–16. https://doi.org/10.1016/S0895-7061(02)02957-6.

35. Chapman N, Dobson J, Wilson S, Dahlöf B, Sever PS, Wedel H, et al. Effect of spironolactone on blood pressure in subjects with resistant hypertension. Hypertension. 2007;49(4):839–45. https://doi.org/10.1161/01.HYP.0000259805.18468.8c.
36. Václavík J, Sedlák R, Plachý M, Navrátil K, Plášek J, Jarkovský J, et al. Addition of spironolactone in patients with resistant arterial hypertension (ASPIRANT): a randomized, double-blind, placebo-controlled trial. Hypertension. 2011;57(6):1069–75. https://doi.org/10.1161/HYPERTENSIONAHA.111.169961.
37. Václavík J, Sedlák R, JarkovskÝ J, Kociánová E, TáborskÝ M. Effect of spironolactone in resistant arterial hypertension. Med (United States). 2014;93(27):1–9. https://doi.org/10.1097/MD.0000000000000162.
38. Calhoun DA, White WB. Effectiveness of the selective aldosterone blocker, eplerenone, in patients with resistant hypertension. J Am Soc Hypertens. 2008;2(6):462–8. https://doi.org/10.1016/j.jash.2008.05.005.
39.•• Styne DM, Arslanian SA, Connor EL, et al. Pediatric obesity-assessment, treatment, and prevention: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2017;102(3):709–57. https://doi.org/10.1210/jc.2016-2573. **A guideline statement from the European Society of Endocrinology and the Pediatric Endocrine society on the assessment, treatment and prevention of pediatric obesity**.
40.•• Grossman DC, Bibbins-Domingo K, Curry SJ, et al. Screening for obesity in children and adolescents us preventive services task force recommendation statement. JAMA. 2017;317(23):2417–26. https://doi.org/10.1001/jama.2017.6803. **Statement from the US Preventive Services Task Force with guidelines for screening for obesity in children and adolescents**.
41. Inge TH, Coley RY, Bazzano LA, Xanthakos SA, McTigue K, Arterburn D, et al. Comparative effectiveness of bariatric procedures among adolescents: the PCORnet bariatric study. Surg Obes Relat Dis. 2018;14(9):1374–86. https://doi.org/10.1016/j.soard.2018.04.002.