

Guidelines

Hypertension Canada's 2017 Guidelines for the Diagnosis, Assessment, Prevention, and Treatment of Pediatric Hypertension

Janis M. Dionne, MD,^a Kevin C. Harris, MD, MHSc,^b Geneviève Benoit, MD,^c
Janusz Feber, MD,^d Luc Poirier, BPharm, MSc,^e Lyne Cloutier, RN, PhD,^f
Meranda Nakhla, MD, MSc,^g Doreen M. Rabi, MD, MSc,^h Stella S. Daskalopoulou, MD, PhD,ⁱ
and Anne Fournier, MD;^j for the Hypertension Canada Guideline Committee

^a Division of Nephrology, Department of Pediatrics, University of British Columbia, Vancouver, British Columbia, Canada; ^b Division of Cardiology, Department of Pediatrics, University of British Columbia, Vancouver, British Columbia, Canada; ^c Service de néphrologie, Centre Hospitalier Universitaire Sainte-Justine, Université de Montréal, Montréal, Québec, Canada; ^d Division of Nephrology, Department of Pediatrics, Children's Hospital of Eastern Ontario, University of Ottawa, Ottawa, Ontario, Canada; ^e Centre Hospitalier Universitaire de Québec et Faculté de Pharmacie, Université Laval, Québec, Québec, Canada; ^f Department of Nursing, Université du Québec à Trois-Rivières, Trois-Rivières, Québec, Canada; ^g Department of Endocrinology and Metabolism, Montreal Children's Hospital, McGill University Health Centre, Montreal, Quebec, Canada; ^h Departments of Medicine, Community Health, and Cardiac Sciences, University of Calgary, Calgary, Alberta, Canada; ⁱ Divisions of General Internal Medicine, Clinical Epidemiology and Endocrinology, Department of Medicine, McGill University, McGill University Health Centre, Montreal, Quebec, Canada; ^j Service de cardiologie, Centre Hospitalier Universitaire Sainte-Justine, Université de Montréal, Montréal, Québec, Canada

ABSTRACT

After the 2016 guidelines for blood pressure measurement, diagnosis, and investigation of pediatric hypertension, we now present evidence-based guidelines for the prevention and treatment of hypertension in children. These guidelines were developed by Hypertension Canada's Guideline Committee pediatric subgroup after thorough evaluation of the available literature. Included are 10 guidelines specifically addressing health behaviour management, indications for drug therapy in children with hypertension, choice of therapy for children with primary hypertension, and goals of therapy for children with hypertension. Although the pediatric literature is inherently limited by small numbers of participants, fewer trials, and a prolonged latency to the development of vascular outcomes, this report reflects the current and highest level of evidence and provides guidance for primary care practitioners on the management of pediatric hypertension. Studies of therapeutic lifestyle modifications in children are available to guide

RÉSUMÉ

Après la publication, en 2016, des lignes directrices concernant la mesure, le diagnostic et l'évaluation de l'hypertension chez l'enfant, nous vous présentons maintenant les lignes directrices fondées sur des données probantes portant sur la prévention et le traitement de l'hypertension chez l'enfant. Ces lignes directrices ont été élaborées par le sous-groupe de médecine pédiatrique du comité des lignes directrices d'Hypertension Canada après une revue détaillée de la littérature médicale publiée à ce sujet. On retrouve 10 lignes directrices traitant des saines habitudes de vie, des indications de pharmacothérapie chez l'enfant atteint d'hypertension, du choix du traitement chez l'enfant atteint d'hypertension primaire et des objectifs thérapeutiques pour ce groupe de patients. Bien que la littérature médicale concernant les enfants comporte des limites inhérentes au faible nombre d'études disponibles, au peu de participants prenant part

The prevalence of hypertension in children is 1%-2% in Canada and is closely associated with childhood obesity and sedentary activity patterns in youth.^{1,2} Fortunately, there are

encouraging data suggesting that the prevalence of obesity is stabilizing and that the prevalence of elevated blood pressure (BP) in children is decreasing, especially in overweight or obese adolescents in the United States.³ These findings underscore the importance of a continued and evidence-based approach toward improving the cardiovascular health of Canadian children.

Health behaviour modification lies at the foundation of hypertension prevention and management in children. The use of pharmacotherapy in hypertensive children has been increasingly studied over the past 2 decades, and more evidence is currently available to inform therapeutic

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Corresponding author: Dr Janis M. Dionne, Division of Nephrology, Department of Pediatrics, BC Children's Hospital and University of British Columbia, 4480 Oak St, Vancouver, British Columbia V6H 3V4, Canada. Tel.: +1-604-875-2272; fax: +1-604-875-3649.

E-mail: jdionne@cw.bc.ca

See page 583 for disclosure information.

current management and more antihypertensive drugs have been studied in children since the Food and Drug Administration Modernization Act. Consistent with Hypertension Canada's guideline policy, diagnostic and therapeutic algorithm tools will be developed and the guidelines will be reviewed annually and updated according to new evidence.

decision-making in pediatric populations. However, there are important limitations, compromising the quality of this evidence, including: small numbers of participants, short follow-up, the use of surrogate outcomes (ie, BP change), industry funding, and absence of traditional placebo control.

In 2016, Hypertension Canada's Guidelines Committee (GC) published their first pediatric guidelines for BP measurement, diagnosis, and investigation of pediatric hypertension.⁴ Having provided guidance on identification of hypertension in children, the next crucial step is to provide guidance for management of hypertension. Following the highly structured Hypertension Canada's guideline process, the pediatric subgroup systematically evaluated existing literature to construct guidelines for the prevention and treatment of pediatric hypertension. Specifically, guidelines were developed for health behaviour management, indications for drug therapy in children with hypertension, choice of therapy for children with primary hypertension, and goals of therapy for children with hypertension.

Together these guidelines aim to guide primary care practitioners and pediatricians to identify, investigate, and manage hypertension in children and adolescents and also provide recommendations on when referral to experts in pediatric hypertension is appropriate. Health behaviour modification might be beneficial to hypertensive children of all ages. Medications need to be dosed on a milligram per kilogram basis in children and dosing ranges might differ from those for adults so familiarity with the drugs is important for treating physicians. Our guidelines for pharmacologic treatment of pediatric hypertension by primary care practitioners apply to children 12 years of age and older with primary hypertension. As is standard practice with Hypertension Canada guidelines, diagnostic and therapeutic algorithm tools will be developed and guidelines will continue to be reviewed annually and updated as new evidence becomes available.

Methods

Hypertension Canada's GC is a multidisciplinary panel of content and methodological experts comprised of 1 Chair, 1 Chair of the Central Review Committee (CRC), a CRC, and 15 subgroups. Each subgroup addresses a distinct content area

aux études et à l'importante période de latence entre le diagnostic et l'apparition de problèmes vasculaires, notre rapport s'appuie sur les plus récentes et les meilleures données probantes actuellement disponibles pour offrir aux intervenants de première ligne des indications sur la prise en charge de l'hypertension chez l'enfant. Diverses études sur la modification du mode de vie à des fins thérapeutiques chez l'enfant permettent désormais de guider les intervenants à ce chapitre et nous disposons également d'information sur un plus grand nombre d'antihypertenseurs ayant été étudiés chez l'enfant à la suite de l'adoption de la *Food and Drug Administration Modernization Act* aux États-Unis. Conformément à la politique sur les lignes directrices d'Hypertension Canada, nous élaborerons des algorithmes de diagnostic et de traitement de l'hypertension chez l'enfant et nous reverrons annuellement les lignes directrices en fonction des données probantes émergentes.

([Supplemental Appendix S1](#) presents the current GC membership list). Members of the Canadian Task Force on Preventive Health Care, the Canadian Diabetes Association GC, the Canadian Society of Nephrology, the Canadian Stroke Network, the Canadian Cardiovascular Society, and the Canadian Cardiovascular Harmonized National Guideline Endeavour Initiative regularly collaborate with Hypertension Canada members to facilitate harmonization of hypertension-related guidelines across organizations. In many cases, Hypertension Canada GC members serve as volunteers for multiple organizations.

A systematic literature search of MedLine/PubMed from January 2004 to December 2015 was performed by a highly trained research librarian. Search terms included hypertension and BP; these were combined with relevant topic-specific terms and age limited to children (birth to 18 years). References of identified articles were also reviewed to identify additional works. Details of search strategies and retrieved articles are available on request.

The pediatric subgroup reviewed the search results. Study characteristics and quality were assessed using prespecified standardized algorithms developed by Hypertension Canada's GC for the critical appraisal of studies.⁵ Recommendations were graded according to the strength of their underlying evidence (details in [Supplemental Table S1](#)) from grade A (strongest evidence, on the basis of high-quality studies) to grade D (weakest evidence, on the basis of low-powered imprecise studies or expert opinion). Although Hypertension Canada's GC does not use the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) recommendation scheme (www.gradeworkinggroup.org), it should be noted that all GC guidelines are considered to be "strong" in nature.

Pediatric subgroup members are hypertension specialists in pediatric nephrology, pediatric cardiology, pharmacology, and nursing. The pediatric subgroup was responsible for reviewing abstracts, critically appraising the literature, and drafting the guidelines. An independent CRC consisting of methodological experts with no industry affiliations independently reviewed, graded, and refined the proposed guidelines, which were then presented at a consensus conference of the GC in Montreal, Quebec, Canada on October 19, 2016. Present at the meeting were the Chair of the Hypertension Canada's

GC, the CRC Chair, the CRC, and members of all subgroups. Further revisions to proposed guidelines were on the basis of these discussions.

Members with potential conflicts of interest recused themselves from voting on specific guidelines (a list of conflicts is available in [Supplemental Appendix S2](#)). After the consensus meeting, the guidelines that were supported by the majority of the consensus conference attendees were finalized and submitted electronically to all 81 voting members of the Hypertension Canada GC for final approval. Guidelines receiving > 70% approval passed. The Hypertension Canada guidelines process is in accordance with the **Appraisal of Guidelines for Research and Evaluation (AGREE) II** guidelines and has been externally reviewed.⁶ A summary of how the Hypertension Canada guidelines process aligns with AGREE II can be found online at <http://guidelines.hypertension.ca/about/overview-process>. Materials to assist with patient and public education on the basis of these guidelines are available at <http://www.hypertension.ca>.

Hypertension Canada's 2017 Guidelines for Diagnosis and Assessment of Hypertension in Children

I. Accurate measurement of BP in children

Background. There are no changes to these guidelines⁴ for 2017.

Guidelines

1. BP should be measured regularly in children 3 years of age and older by a health care professional using standardized pediatric techniques ([Supplemental Table S2](#); Grade D).
2. BP may be measured with a mercury sphygmomanometer, aneroid sphygmomanometer, or oscillometric device (Grade D). Abnormal oscillometric values should be confirmed with auscultation (Grade C).
3. BP varies with age, sex, and height in children, and BP values should therefore be compared with norms for age, sex, and height ([Supplemental Table S3](#); Grade D).

II. Criteria for diagnosis of hypertension in children

Background. There are no changes to these guidelines⁴ for 2017.

Guidelines

1. Using office BP measurements, children can be diagnosed as hypertensive if systolic BP (SBP) or diastolic BP (DBP) is at the 95th percentile or greater for age, sex, and height, measured on at least 3 separate occasions (Grade C).
2. If the BP is at the 95th percentile or greater, BP should be staged. Stage 1 is defined by BP between the 95th and 99th percentiles plus 5 mm Hg. Stage 2 is defined by BP > the 99th percentile plus 5 mm Hg (Grade D).
 - i. If BP is stage 1, BP measurements should be repeated on 2 more occasions within 1 month; if hypertension is confirmed, evaluation (as described in section *IV. Routine Laboratory Tests for the Investigation of Children*

- With Hypertension*) or appropriate referral should be initiated within 1 month, or both (Grade D).
 - ii. If BP is stage 2, prompt referral should be made for evaluation and therapy (Grade C).
3. All children with suspected or confirmed hypertension should undergo a hypertension-focused history and physical evaluation ([Supplemental Table S4](#); Grade C).

III. Assessment of overall cardiovascular risk in hypertensive children

Background. There are no changes to these guidelines⁴ for 2017.

Guidelines

1. Cardiovascular risk factors should be assessed in hypertensive children (Grade C).

IV. Routine laboratory tests for the investigation of children with hypertension

Background. There are no changes to these guidelines⁴ for 2017.

Guidelines

1. Routine tests that should be performed for the investigation of all children with hypertension include:
 - i. Blood chemistry (sodium, potassium, chloride, total CO₂, and creatinine; Grade D);
 - ii. Urinalysis (Grade D);
 - iii. Renal ultrasonography (Grade D).
2. Routine laboratory tests that should be performed for the assessment of cardiovascular risk in all children with hypertension include the following:
 - i. Fasting blood glucose (Grade C);
 - ii. Serum total cholesterol and high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and triglyceride levels (Grade C).
3. Routine tests that should be performed for the assessment of target organ damage in all children with hypertension include the following:
 - i. Echocardiography (Grade C);
 - ii. Retinal examination (Grade C);
 - iii. Albumin-to-creatinine ratio (first-morning determination; Grade D).

V. Ambulatory BP monitoring in children

Background. There are no changes to these guidelines⁴ for 2017.

Guidelines

1. For children with elevated office BP readings, ambulatory BP monitoring (ABPM) should be guided by a physician with expertise in pediatric hypertension; ABPM is useful to classify BP ([Supplemental Table S5](#); Grade C).
2. Physicians should use only ABPM devices that have been validated independently in children using established

protocols. A standard approach to obtaining ABPM readings should be used (Supplemental Table S6; Grade D).

3. ABPM levels should be interpreted with appropriate pediatric normative data for children 5 years of age or older or height of ≥ 120 cm (Grade D).

VI. Role of echocardiography

Background. There are no changes to these guidelines⁴ for 2017.

Guidelines

1. Routine echocardiographic evaluation in children with confirmed hypertension is recommended (Grade D).
2. The echocardiographic assessment should include measurements of left ventricular mass index (LVMI), systolic and diastolic left ventricular function, and evaluation of the aortic arch (Grade D).

Hypertension Canada's 2017 Guidelines for the Prevention and Treatment of Hypertension in Children

I. Health behaviour management

Background. In the Canadian Health Measures Survey, the strongest effect on BP in obese children and adolescents was BMI.¹ BMI, calculated by dividing weight in kilograms by the square of height in metres, should be determined for all children at routine health visits. Values need to be compared with pediatric normative curves with a BMI greater than the 85th percentile consistent with overweight and greater than the 97th percentile with obesity in children 5 years of age and older on the basis of World Health Organization data. Information and growth charts are available at www.cps.ca/tools-outils/who-growth-charts.

With the reported associations between childhood BP and BMI,^{1,2,7} diet,⁷⁻⁹ and physical activity,^{1,10} recent intervention studies to modify these risk factors have shown some improvements in markers of cardiovascular health.¹¹⁻¹⁶ One randomized controlled trial of exercise intervention including 60 minutes of physical activity 3 times a week for 3 months compared with no intervention showed reduction in office and ambulatory BP in the physical activity group.¹¹ In the no intervention group, the BPs increased so that the exercise intervention BP difference was 7 mm Hg for clinic SBP and DBP, and 11 mm Hg for 24-hour ambulatory SBP. They also showed improvements in carotid intima-media thickness and arterial stiffness in the intervention group at 6 months. A systematic review and meta-analysis of exercise intervention trials in children with obesity showed a small but significant pooled effect estimate for reduction in BP.¹² The analysis was likely affected by the heterogeneity in trial design with differences in duration of study intervention, frequency of intervention, length of time of activity during session, and total exercise time. These limitations make it challenging to offer specific evidence-based recommendations for amount and frequency of physical activity, and an individualized and patient-centred approach is likely to be the most successful.

Evidence for dietary improvements in reducing BP in children is increasing. Most children consume high amounts of salt and a meta-analysis of 10 controlled trials of salt reduction in children by 42% found a small but significant reduction in systolic (-1.2 to -2.5 mmHg) as well as diastolic (-1.3 mm Hg) BPs.¹³ In a longitudinal study of young girls followed for 10 years it was reported that a higher intake of potassium (≥ 2400 mg/d) was related to lower BP.¹⁴ Higher potassium foods are generally fruits and vegetables, as well as dairy products. The Dietary Approaches to Stop Hypertension (DASH) diet, which is high in fruits, vegetables, grains, low fat dairy, and low in fat, sugar, and sodium has shown some benefits in adult as well as pediatric populations. Specifically, in a randomized cross-over trial of DASH diet vs usual dietary advice in children with metabolic syndrome a reduction in the prevalence of elevated BP with the DASH diet was reported.¹⁵

The combination of dietary improvements as well as increased physical activity seems to amplify the beneficial effects. A systematic review and meta-analysis of 23 studies of obesity prevention programs in children found that combined diet and physical activity interventions led to a significantly greater reduction in SBPs and DBPs than either alone.¹⁶ Although healthy eating and physical activity is taught in most school systems, children with hypertension, obesity, or those at risk for either might benefit from specific advice from health care practitioners or allied health team members to improve these healthy behaviours. A patient- and family-centred approach to promote changes to the entire family diet and lifestyle might increase the probability of long-term beneficial change.¹⁷

Guidelines

1. Height and weight should be measured and body mass index (BMI) calculated for all children at routine health visits (Grade D).
2. Achieving a healthy body weight (BMI < 85 th percentile) is recommended for nonhypertensive individuals to prevent hypertension and for hypertensive children to reduce BP (Grade C).
3. A comprehensive approach should include dietary education and increased physical activity (Grade C).

II. Indications for drug therapy for children with hypertension

Background. The decision to initiate drug treatment of pediatric hypertension depends on many factors including the presence of symptoms of hypertension, level of BP elevation, presence of end-organ damage, response to nonpharmacologic therapy, and presence of comorbid conditions that confer increased cardiovascular risks. Symptoms of hypertension might include irritability, fatigue, dizziness, chest pain, abdominal pain, and headache. End-organ damage might be detected on echocardiogram as left ventricular hypertrophy (LVH), on fundoscopy as hypertensive retinopathy, or on urine analysis as albuminuria. These factors are not entirely exclusive because children with more severe hypertension might also have greater LVMI and albuminuria than those

with less significant hypertension and albuminuria has been correlated with LVMI.^{18,19}

In a retrospective cohort study, Kupferman et al. compared children treated with antihypertensive medications with untreated patients.²⁰ The indications for drug treatment included hypertensive symptoms, severe hypertension, risk factors such as chronic kidney disease, and target organ damage. They reported that 33% of treated patients with LVH had resolution of the cardiac anomaly by follow-up echocardiogram after more than 6 months of treatment.²⁰ Of untreated patients, 28% developed LVH by follow-up. The change in LVMI correlated with the change in SBP.²⁰ Additional evidence for pharmacologic intervention comes from the Effect of Strict Blood Pressure Control and ACE Inhibition on the Progression of CRF in Pediatric Patients (ESCAPE) trial. They showed that treatment of BP reduced LVMI in all treated and more so in those with LVH.²¹ The prevalence of LVH decreased from 38% to 25% after 1-2 years of treatment. In addition, intensified BP control reduced systolic dysfunction. Many factors, including side effects, need to be considered for initiation of pharmacologic management of hypertension in children but with treatment, cardiac target organ damage can be reduced.

Guidelines

1. Pharmacologic therapy should be initiated when patients have:
 - i. Symptomatic hypertension (Grade D);
 - ii. Hypertensive target organ damage (Grade C);
 - iii. Stage 2 hypertension (Grade D);
 - iv. BP is at or greater than the 90th percentile associated with diabetes mellitus type 1 or 2, chronic kidney disease, or heart failure (Grade D);
 - v. Stage 1 hypertension without target organ damage that persists (≥ 6 months) despite a trial of non-pharmacologic therapy (Grade D).
2. In children with proven secondary hypertension, specific treatment of the underlying disease must be initiated by an expert in pediatric hypertension (Grade D).

III. Choice of therapy for children with primary hypertension

Background. There are an increasing number of antihypertensive drugs approved for use in children since passage of the Food and Drug Administration Modernization Act in 1997. However, trials have primarily been limited to the newer medications, mostly ACE inhibitors and ARBs. Most of the drugs are approved for use only in children older than 6 years of age because of limited trials in the younger age groups. **In children, medications need to be dosed on a milligram per kilogram basis and dosing ranges might differ from those in adults because of differences in drug metabolism and body composition.**^{22,23} Younger children usually prefer suspension formulations if they are palatable. Targeting drug therapy to an underlying cause of hypertension should be directed by an expert in pediatric hypertension. The younger the child, the more likely they are to have a secondary cause identified for the hypertension. **For these reasons, we strongly recommend that the guidelines for pharmacologic**

treatment of pediatric hypertension by primary care practitioners should apply only to children 12 years of age or older. Younger children and those suspected of having a secondary cause for their hypertension should be referred to and managed by experts in pediatric hypertension. The pharmacologic guidelines apply to children with systolic and/or diastolic hypertension.

There are 3 good-quality randomized controlled trials of ACE inhibitors in children with hypertension. The drugs studied include enalapril, lisinopril, and fosinopril and each showed a good BP response to the medication (-6 to -16 mm Hg) and difference from placebo in the withdrawal phase ($4-6$ mm Hg).²⁴⁻²⁶ Meta-analysis of all ACE inhibitor trials in children submitted to the Food and Drug Administration showed that black patients experienced less BP reduction than other races with these drugs.²⁷ Side effects are uncommon but are similar to those in adult patients with the potential for hypotension, increased serum creatinine, acute kidney injury, hyperkalemia, and angioedema.^{23,28} Cough seems to be less common in children with ACE inhibitors and not different than placebo in trials.²⁹ Interval monitoring of kidney function and electrolytes should be practiced and caution should be used when considering these drugs in children prone to dehydration. Counselling on risks of teratogenicity should be done in female patients of child-bearing age.

Several randomized controlled trials of ARBs in children with hypertension have shown a good BP response to the medication (-6 to -13 mm Hg) and a difference from placebo ($3-7.5$ mm Hg).³⁰⁻³³ Good-quality trials have been completed with losartan, candesartan, olmesartan, and valsartan. Most of the studies report a lesser BP response in black patients. Side effects are not common and potentially might include hypotension, hyperkalemia, and acute kidney injury.²³ Similar to ACE inhibitors, caution should be used with these medications in children prone to dehydration; kidney function and electrolytes should be monitored, and counselling on risks of teratogenicity should be done in female patients of child-bearing age. One comparison trial, in which hypertensive children were randomized to either ARB (valsartan) or ACE inhibitor (enalapril) reported similar significant reductions in BP in both groups.³⁴

β -Blockers are less well studied in children. Only 1 trial in the literature has been completed using extended-release metoprolol showing a BP reduction significantly different from placebo.³⁵ With potential for bronchospasm, β -blockers are not recommended in children with asthma.²³ They also cause bradycardia because of their mechanism of action, and are therefore not preferred in high-performance athletes and β -blockers might mask symptoms of hypoglycemia in children with diabetes mellitus.²³ More recent studies in adults suggest an increased risk of insulin resistance and new diabetes onset with β -blockers making them a less desirable choice in children with or at risk for diabetes mellitus.^{28,36}

Other medications studied for pediatric hypertension have had less consistent results. Trials of the long-acting dihydropyridine calcium channel blockers amlodipine and felodipine have shown modest differences from placebo in BP response but the trials were confounded by lack of adjustment for body weight, low drug dosing, and inadequate time during the dose titration phase.^{37,38} Benefits of calcium channel

blockers include good tolerance of the drug with uncommon side effects including edema and gingival hyperplasia, and no need for bloodwork monitoring.²⁸ Only a single trial of a combination antihypertensive drug has been completed in children with a β -blocker/thiazide combination but the BP reduction was not significantly different from placebo.³⁹ Unlike in adult populations, diuretics alone have not been systematically studied in children for hypertension. In practice, diuretics are used in combination with other antihypertensive agents but caution must be taken because of the potential for electrolyte disturbances or dehydration with minor illness in children.^{19-21,23,28} The lack of trials of single-pill combination drugs and diuretics limits our ability to provide guidance regarding the efficacy of these medications for the treatment of pediatric hypertension.

A recent Cochrane systematic review of randomized placebo controlled trials of antihypertensive drugs in children found a limited number of positive trials with most trials of very low-quality evidence by their strict criteria.⁴⁰ Simonetti et al. completed a systematic analysis of data from 27 antihypertensive drug trials in children and reported that all drug classes (ACE inhibitors, ARBs, and calcium channel blockers) reduced BP by a similar amount with a mean of just > 10 mm Hg.⁴¹ Our recommendations are on the basis of the best available evidence for practitioners who are comfortable in prescribing antihypertensive medications to children and adolescents. Referral to an expert in pediatric hypertension for BP management is always an acceptable alternative.

Guidelines

1. Initial therapy should be monotherapy.
 - i. Recommended monotherapy choices are:
 - a. An angiotensin-converting enzyme (ACE) inhibitor (Grade C);
 - b. An angiotensin receptor blocker (ARB) (Grade C); or
 - c. A long-acting dihydropyridine calcium channel blocker (Grade D).
 - ii. An alternate option is a β -blocker (Grade D) although they are less preferable because of the side effect profile in children.
 - iii. If there are adverse effects, another drug from this group should be substituted.
2. If BP goals are not achieved with standard-dose monotherapy for ≥ 6 months, children should be referred to an expert in pediatric hypertension (Grade D).
3. ACE inhibitors (Grade C) and ARBs (Grade D) are not recommended as first-line agents in black patients and β -blockers are not recommended as first-line agents in children with asthma, diabetes (type 1 or type 2), or in high-performance athletes (Grade D).

IV. Goals of therapy for children with hypertension

Background. The overall goals of therapy for children with hypertension are to achieve a BP level that reduces the risk of target organ damage in childhood, and ultimately reduces the risk of hypertension and cardiovascular disease in adulthood. The International Childhood Cardiovascular Cohort Consortium has shown that adult carotid intima-

media thickness is significantly higher in adults who had elevated BP during childhood that persisted to adulthood compared with those whose BP normalized in adulthood.⁴² In addition, several longitudinal studies provide evidence that elevated BP in childhood increases the risk up to 5-fold for developing adulthood hypertension and metabolic syndrome.⁴³⁻⁴⁵

Limited evidence exists on assessment of goals of pharmacologic treatment of pediatric hypertension to guide hypertension management. In a prospective controlled trial of 12-month antihypertensive treatment of children with hypertension, 80% were able to achieve the goal clinic BP of less than the 95th percentile at 1 year.¹⁹ With treatment, LVMI decreased by 32% and albuminuria decreased by 45%. A study of pharmacologic treatment of pediatric hypertension to an ABPM goal BP less than the 95th percentile or BP load < 25% showed that the prevalence of LVH was lower in children with controlled hypertension than in those with uncontrolled hypertension (13% vs 46%, respectively).⁴⁶ In other ABPM studies, treatment of pediatric hypertension was able to reduce BP to less than the 95th percentile in 53%-74% of children, and LVH reduced from 42%-46% at baseline to 11%-28% at 6-12 months.^{18,47} Although these studies show that targeting a BP less than the 95th percentile reduces LVH, achievement of the goal does not seem to eliminate the end-organ damage in all. Therefore, it seems reasonable to target less than the 90th percentile clinic or ambulatory BP in children with current target organ damage or concurrent cardiovascular risk factors including diabetes mellitus type 1 and 2, chronic kidney disease, or a structural or functional cardiac anomaly. This is in keeping with current practice of most pediatric nephrologists in North America.⁴⁸

Guidelines

1. The treatment goal is office BP (systolic and diastolic) less than the 95th percentile (Grade D). The goal for ABPM is BP (systolic and diastolic) less than the 95th percentile (Grade D).
2. For patients with risk factors or target organ damage the goal is BP (systolic and diastolic) less than the 90th percentile (Grade D).

Summary/Future Directions

These evidence-based guidelines represent the second report of Hypertension Canada's GC pediatric subgroup. Building on the previous guidelines for BP measurement, diagnosis and investigation of hypertension, the current guidelines on prevention and treatment of pediatric hypertension aim to guide primary care practitioners in providing initial evidence-based care to children and adolescents with hypertension. Although the etiology, implications, and management considerations of hypertension in children might differ from that in adults, we appreciate that primary care practitioners might be evaluating and managing patients of most age groups. We have therefore provided a table that highlights the major guideline recommendations for BP assessment and management from the pediatric as well as adult guidelines for comparison (Table 1).⁴⁹ Diagnostic and

Table 1. Comparison of Hypertension Canada's 2017 pediatric and adult guidelines for blood pressure measurement and hypertension diagnosis, assessment, and management

	Pediatric guidelines	Adult guidelines ⁴⁹
Measurement	<ul style="list-style-type: none"> Use standardized pediatric techniques and validated equipment (Supplemental Table S2) Oscillometric device or auscultation method for initial measurement Elevated oscillometric values should be confirmed with auscultation BP values should be compared with norms on the basis of age, sex, and height (Supplemental Table S3) ABPM should be guided by experts in pediatric hypertension 	<ul style="list-style-type: none"> Use standardized measurement techniques and validated equipment Oscillometric devices are preferred over auscultation. Automated office blood pressure is the preferred method of performing in-office BP measurement Elevated office BP measurements should be confirmed with out-of-office BP measurements including ABPM (preferable) or home BP monitoring where available
Diagnosis	<ul style="list-style-type: none"> Diagnose according to BP percentile on the basis of norms for age, sex, and height and: <ul style="list-style-type: none"> level of BP elevation number of visits and measurements see the section, <i>II. Criteria for Diagnosis of Hypertension in Children</i> 	<ul style="list-style-type: none"> Diagnose according to absolute BP value according to: <ul style="list-style-type: none"> level of BP elevation number of visits and measurements method of BP measurement see Figure 1 in Leung et al.⁴⁹
Assessment	<ul style="list-style-type: none"> History and physical examination Cardiovascular risk factor assessment Routine investigations for: <ul style="list-style-type: none"> secondary causes of hypertension cardiovascular risk factors target organ damage 	<ul style="list-style-type: none"> History and physical examination Cardiovascular risk factor assessment Routine investigations for: <ul style="list-style-type: none"> secondary causes of hypertension cardiovascular risk factors target organ damage
Management	<ul style="list-style-type: none"> Dietary education and increased physical activity Initial pharmacologic therapy for primary hypertension is monotherapy with choice of ACE inhibitor, ARB, or CCB If BP is not controlled with monotherapy, refer to an expert in pediatric hypertension 	<ul style="list-style-type: none"> Dietary education, increased physical activity, alcohol limitation, and stress management Initial pharmacologic therapy with either thiazide/thiazide-like diuretic, β-blocker, ACE inhibitor, ARB, or CCB monotherapy or single pill combination with ACE inhibitor and CCB, ARB and CCB, or ACE inhibitor/ARB and diuretic*

ABPM, ambulatory blood pressure monitoring; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BP, blood pressure; CCB, calcium channel blocker.

* For adults with diastolic with or without systolic hypertension, without compelling indications for specific agents.

therapeutic algorithm tools to complement the Pediatric Guidelines will be developed by Hypertension Canada's Implementation Task Force in collaboration with the pediatric subgroup. We will continue to systematically review the literature annually and update guidelines as new evidence emerges.

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The Hypertension Canada GC is operated and funded by Hypertension Canada. The members of the GC are unpaid volunteers who contribute their time and expertise to the annual development and dissemination of the guidelines. To maintain professional credibility of the content, the process for the development of the guidelines is fully independent and free from external influence. External partners assist with the dissemination of the approved guidelines.

Disclosures

A complete list of author disclosures is available in Supplemental Appendix S2.

References

- Shi Y, Groh M, Morrison H. Increasing blood pressure and its associated factors in Canadian children and adolescents from the Canadian Health Measures Survey. *BMC Public Health* 2012;12:388.
- Statistics Canada. Blood pressure of children and youth, 2012 to 2013. Available at: www.statcan.gc.ca/pub/82-625-x/2014001/article/14102-eng.htm. Accessed December 7, 2016.
- Yang Q, Zhong Y, Merritt R, Cogswell ME. Trends in high blood pressure among United States adolescents across body weight category between 1988 and 2012. *J Pediatr* 2016;169:166-73.
- Harris KC, Benoit G, Dionne J, et al. Hypertension Canada's 2016 Canadian Hypertension Education Program Guidelines for blood pressure measurement, diagnosis, and assessment of risk of pediatric hypertension. *Can J Cardiol* 2016;32:589-97.
- McAlister FA. The Canadian Hypertension Education Program – a unique Canadian initiative. *Can J Cardiol* 2006;22:559-64.
- Brouwers MC, Kho ME, Browman GP, et al. AGREE II: advancing guideline development, reporting and evaluation in health care. *CMAJ* 2010;182:E839-42.
- Rosner B, Cook NR, Daniels S, Falkner B. Childhood blood pressure trends and risk factors for high blood pressure: the NHANES experience 1988-2008. *Hypertension* 2013;62:247-54.
- Yang Q, Zhang Z, Kuklina EV, et al. Sodium intake and blood pressure among us children and adolescents. *Pediatrics* 2012;130:611-9.
- Colin-Ramirez E, Castillo-Martinez L, Orea-Tejeda A, et al. Waist circumference and fat intake are associated with high blood pressure in Mexican children aged 8 to 10 years. *J Am Diet Assoc* 2009;109:996-1003.

10. Lobelo F, Pate RR, Dowda M, Liese AD, Daniels SR. Cardiorespiratory fitness and clustered cardiovascular disease risk in U.S. adolescents. *J Adolesc Health* 2010;47:352-9.
11. Farpour-Lambert NJ, Aggoun Y, Marchand LM, et al. Physical activity reduces systemic blood pressure and improves early markers of atherosclerosis in pre-pubertal obese children. *J Am Coll Cardiol* 2009;54:2396-406.
12. Garcia-Hermoso A, Saavedra JM, Escalante Y. Effects of exercise on resting blood pressure in obese children: a meta-analysis of randomized controlled trials. *Obes Rev* 2013;14:919-28.
13. He FJ, MacGregor GA. Importance of salt in determining blood pressure in children: meta-analysis of controlled trials. *Hypertension* 2006;48:861-9.
14. Buendia JR, Bradlee ML, Daniels SR, Singer MR, Moore LL. Longitudinal effects of dietary sodium and potassium on blood pressure in adolescent girls. *JAMA Pediatr* 2015;169:560-8.
15. Saneei P, Hashemipour M, Kelishadi R, Rajaei S, Esmailzadeh A. Effects of recommendations to follow the Dietary Approaches to Stop Hypertension (DASH) diet vs. usual dietary advice on childhood metabolic syndrome: a randomised cross-over clinical trial. *Br J Nutr* 2013;110:2250-9.
16. Cai L, Wu Y, Wilson RF, et al. Effect of childhood obesity prevention programs on blood pressure: a systematic review and meta-analysis. *Circulation* 2014;129:1832-9.
17. Schwandt P, Bertsch T, Haas GM. Sustained lifestyle advice and cardiovascular risk factors in 687 biological child-parent pairs: the PEP Family Heart Study. *Atherosclerosis* 2011;219:937-45.
18. Sladowska-Kozłowska J, Litwin M, Niemirska A, et al. Change in left ventricular geometry during antihypertensive treatment in children with primary hypertension. *Pediatr Nephrol* 2011;26:2201-9.
19. Assadi F. Effect of microalbuminuria lowering on regression of left ventricular hypertrophy in children and adolescents with essential hypertension. *Pediatr Cardiol* 2007;28:27-33.
20. Kupferman JC, Paterno K, Mahgerefteh J, et al. Improvement of left ventricular mass with antihypertensive therapy in children with hypertension. *Pediatr Nephrol* 2010;25:1513-8.
21. Matteucci MC, Chinali M, Rinelli G, et al. Change in cardiac geometry and function in CKD children during strict BP control: a randomized study. *Clin J Am Soc Nephrol* 2013;8:203-10.
22. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents. *Pediatrics* 2004;114(suppl 2):555-76.
23. Meyers RS, Siu A. Pharmacotherapy review of chronic pediatric hypertension. *Clin Ther* 2011;33:1331-56.
24. Wells T, Frame V, Soffer B, et al. A double-blind, placebo-controlled, dose-response study of the effectiveness and safety of enalapril for children with hypertension. *J Clin Pharmacol* 2002;42:870-80.
25. Soffer B, Zhang Z, Miller K, et al. A double-blind, placebo-controlled, dose-response study of the effectiveness and safety of lisinopril for children with hypertension. *Am J Hypertens* 2003;16:795-800.
26. Li JS, Berezny K, Kilaru R, et al. Is the extrapolated adult dose of fosinopril safe and effective in treating hypertensive children? *Hypertension* 2004;44:289-93.
27. Li JS, Baker-Smith CM, Smith PB, et al. Racial differences in blood pressure response to angiotensin-converting enzyme inhibitors in children: a meta-analysis. *Clin Pharmacol Ther* 2008;84:315-9.
28. Chu PY, Campbell MJ, Miller SG, Hill KD. Anti-hypertensive drugs in children and adolescents. *World J Cardiol* 2014;6:234-44.
29. Baker-Smith CM, Benjamin DK, Califf RM, et al. Cough in pediatric patients receiving angiotensin-converting enzyme inhibitor therapy or angiotensin receptor blocker therapy in randomized controlled trials. *Clin Pharmacol Ther* 2010;87:668-71.
30. Shahinfar S, Cano F, Soffer B, et al. A double-blind, dose-response study of losartan in hypertensive children. *Am J Hypertens* 2005;18:183-90.
31. Trachtman H, Hainer JW, Sugg J, et al. Efficacy, safety, and pharmacokinetics of candesartan cilexetil in hypertensive children aged 6 to 17 years. *J Clin Hypertens (Greenwich)* 2008;10:743-50.
32. Hazan L, Hernandez Rodriguez OA, Bhorat AE, et al. A double-blind, dose-response study of the efficacy and safety of olmesartan medoxomil in children and adolescents with hypertension. *Hypertension* 2010;55:1323-30.
33. Wells T, Blumer J, Meyers KE, et al. Effectiveness and safety of valsartan in children aged 6 to 16 years with hypertension. *J Clin Hypertens* 2011;13:357-65.
34. Schaefer F, Litwin M, Zachwieja J, et al. Efficacy and safety of valsartan compared to enalapril in hypertensive children: a 12-week, randomized, double-blind, parallel-group study. *J Hypertens* 2011;29:2484-90.
35. Batsky DL, Sorof JM, Sugg J, et al. Efficacy and safety of extended release metoprolol succinate in hypertensive children 6 to 16 years of age: a clinical trial experience. *J Pediatr* 2007;150:134-9.
36. Poirier L, Tobe SW. Contemporary use of beta-blocker: clinical relevance of subclassification. *Can J Cardiol* 2014;30:S9-15.
37. Flynn JT, Newburger JW, Daniels SR, et al. A randomized, placebo-controlled trial of amlodipine in children with hypertension. *J Pediatr* 2004;145:353-9.
38. Trachtman H, Frank R, Mahan JD, et al. Clinical trial of extended-release felodipine in pediatric essential hypertension. *Pediatr Nephrol* 2003;18:548-53.
39. Sorof JM, Cargo P, Graepel J, et al. B-blocker/thiazide combination for treatment of hypertensive children: a randomized double-blind, placebo-controlled trial. *Pediatr Nephrol* 2002;17:345-50.
40. Chaturvedi S, Lipszyc DH, Licht C, Craig JC, Parekh R. Pharmacological interventions for hypertension in children. *Cochrane Database Syst Rev* 2014:CD008117.
41. Simonetti GD, Rizzi M, Donadini R, Bianchetti MG. Effects of anti-hypertensive drugs on blood pressure and proteinuria in childhood. *J Hypertens* 2007;25:2370-6.
42. 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;128:217-24.
43. Sun SS, Grave GD, Siervogel RM, et al. Systolic blood pressure in childhood predicts hypertension and metabolic syndrome later in life. *Pediatrics* 2007;119:237-46.
44. Theodore RF, Broadbent J, Nagin D, et al. Childhood to early-midlife systolic blood pressure trajectories: early-life predictors, effect modifiers, and adult cardiovascular outcomes. *Hypertension* 2015;66:1108-15.

45. Tirosh A, Afek A, Rudich A, et al. Progression of normotensive adolescents to hypertensive adults: a study of 26980 teenagers. *Hypertension* 2010;56:203-9.
46. Seeman T, Dostalek L, Gilik J. Control of hypertension in treated children and its association with target organ damage. *Am J Hypertens* 2012;25:389-95.
47. Seeman T, Gilik J, Vondrak K, et al. Regression of left-ventricular hypertrophy in children and adolescents with hypertension during Ramipril monotherapy. *Am J Hypertens* 2007;20:990-6.
48. Woroniecki RP, Flynn JT. How are hypertensive children evaluated and managed? A survey of North American pediatric nephrologists. *Pediatr Nephrol* 2005;20:791-7.
49. Leung AA, Daskalopoulou SS, Dasgupta K; for Hypertension Canada. Hypertension Canada's 2017 guidelines for diagnosis, risk assessment, prevention, and treatment of hypertension in adults. *Can J Cardiol* 2017;33:557-76.

Supplementary Material

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