

Title:

From detection early in life to the primordial prevention of elevated blood pressure

Authors:

Adina Mihaela Epure MD¹, Arnaud Chiolero MD, PhD^{1,2,3}

Affiliations

¹Department of Epidemiology and Health Services, Center for Primary Care and Public Health (UNISANTÉ), University of Lausanne, Lausanne, Switzerland

²Institute of Primary Health Care (BIHAM), University of Bern, Bern, Switzerland

³Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montréal, Canada

Email: Adina Mihaela Epure: adina-mihaela.epure@unisante.ch; Arnaud Chiolero: arnaud.chiolero@biham.unibe.ch.

Correspondence to: Professor Arnaud Chiolero, Institute of Primary Health Care (BIHAM), University of Bern, Mittelstrasse 43, 3012, Bern, Switzerland; arnaud.chiolero@biham.unibe.ch

Short title: Early-life prevention of elevated blood pressure

Statement of Financial Disclosure: This work was funded by the Swiss National Science Foundation (SNSF; funding reference number 32003B-163240).

Statement of Conflict of Interest: The authors have no conflict of interest to disclose.

Other information: Invited commentary in relation to accepted manuscript number JCH-19-0113.R1

Keywords: blood pressure; children; adolescent; primordial prevention; screening

Abbreviations: BP, blood pressure; CVD, cardiovascular disease

Body of the text

Elevated blood pressure (BP) in children and adolescents is a public health concern. Childhood BP tracks into adulthood and is associated with cardiac and vascular damage, such as left ventricular hypertrophy and increased carotid intima-media thickness during both childhood and adulthood^{1,2}. In the view of this evidence, prevention of adult cardiovascular disease (CVD) starting early in life, e.g., during childhood, is advocated. One approach is the primordial prevention of CVD, which aims to prevent the development of elevated BP and other CVD risk factors since conception, for example, through improving maternal nutrition during pregnancy or reduction in salt intake among children^{3,4}. Another approach, more clinically oriented, is through screening and treatment of elevated BP. However, the medical community remains divided on whether and when recommending screening in children and adolescents, mainly due to complex screening tools and a lack of evidence on the benefits and harms of universal screening⁵⁻⁷.

In the effort to simplify screening tools in children and align to standards in adults, in the current issue of the Journal of Clinical Hypertension, Fan et al evaluated the performance of a simplified BP threshold ($\geq 120/80$ mmHg) in identifying elevated BP in individuals aged 13-17 years⁸. Using a rich dataset from the National Health and Nutrition Examination Survey, authors concluded that the simplified threshold performed well in identifying elevated BP compared to traditional thresholds based on age-, sex-, and height-specific percentiles. Indeed, the simplified threshold had perfect specificity overall and across subgroups defined based on age, sex, or age- and sex-specific height percentiles, thus attenuating the risks related to false-positives and overdetection (e.g. anxiety, stress, extra time and financial resources for diagnosis confirmation). Sensitivity varied from 40% to 100%, depending on age and height. However, the positive predictive values and negative predictive values of the simplified threshold were

above 90% in all age- and height-specific subgroups. The strengths of this paper are notably the population-based large sample size, which facilitates generalizability of findings, and the good quality BP measurement based on multiple readings.

We congratulate Fan and al for their study, which advances the knowledge on the development and accuracy of user-friendly tools to help improve recognition of elevated BP in the pediatric age group. Simplifying the screening process and agreeing on simple, easy to remember, hypertension thresholds will indeed facilitate the uptake of screening in practice, assuming that screening in children is useful. However, when a child has elevated BP, pediatricians face a series of questions regarding what other investigations should be conducted (e.g. ambulatory BP measurement, etiology assessment, cardiac or vascular echography) or which therapy would be most effective and safest on the long-term (e.g. lifestyle measures, drug therapy or combination of both) to decrease adult BP, subclinical, or manifest CVD⁶. Further, universal screening of elevated BP starting in childhood remains highly challenged. According to the US Preventive Services Task Force (USPSTF) “current evidence is insufficient to assess the balance of benefits and harms of screening for primary hypertension in asymptomatic children and adolescents to prevent subsequent cardiovascular disease in childhood or adulthood”⁹. Until more evidence becomes available, targeted screening of at-risk individuals, such as those exposed to prematurity or obesity, rather than universal screening, is probably preferable⁵.

Considering these open questions on early screening, should we rather concentrate our efforts toward the primordial prevention of elevated BP? From a public health perspective, several arguments exist in favor of this shift in paradigm. Firstly, acting early in life, when diet and other lifestyle preferences are formed, may influence CVD risk behaviors across the life course^{3,10}. Secondly, health promotion and primordial prevention strategies can target multiple CVD

risk factors simultaneously. Thirdly, within a Developmental Origins of Health and Disease (DOHaD) framework, interventions during critical periods of development may have long-term impact on programming BP trajectories and cardiometabolic health¹¹. Nonetheless, as for screening, stronger evidence is needed to guide primordial prevention policy.

Statement of Financial Disclosure: This work was funded by the Swiss National Science Foundation (SNSF; funding reference number 32003B-163240).

Statement of Conflict of Interest: The authors have no conflict of interest to disclose.

REFERENCES

1. Urbina EM, Lande MB, Hooper SR, Daniels SR. Target Organ Abnormalities in Pediatric Hypertension. *J Pediatr* 2018; **202**: 14-22.
2. Epure AM, Leyvraz M, Mivelaz Y, Di Bernardo S, da Costa BR, Chiolero A, Sekarski N. Risk factors and determinants of carotid intima-media thickness in children: protocol for a systematic review and meta-analysis. *BMJ open* 2018; **8**(6): e019644.
3. Gillman MW. Primordial prevention of cardiovascular disease. *Circulation* 2015; **131**(7): 599-601.
4. Leyvraz M, Chatelan A, da Costa BR, Taffe P, Paradis G, Bovet P, Bochud M, Chiolero A. Sodium intake and blood pressure in children and adolescents: a systematic review and meta-analysis of experimental and observational studies. *Int J Epidemiol* 2018; **47**(6): 1796-1810.
5. Chiolero A, Bovet P, Paradis G. Screening for elevated blood pressure in children and adolescents: a critical appraisal. *JAMA pediatrics* 2013; **167**(3): 266-273.
6. Ide N, Thompson M. Screening children for hypertension: the case against. *Pediatr Nephrol* 2018; **33**(1): 93-100.
7. Taylor-Zapata P, Baker-Smith CM, Burkart G, Daniels SR, Flynn JT, Giacoia G, Green D, Kelly AS, Khurana M, Li JS, Pratt C, Urbina EM, Zajicek A. Research Gaps in Primary Pediatric Hypertension. *Pediatrics* 2019; **143**(5).
8. Fan H, Liu Y, Zhang X. Validation of recommended definition in identifying elevated blood pressure in adolescents. *J Clin Hypertens* 2019.
9. Moyer VA. Screening for primary hypertension in children and adolescents: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med* 2013; **159**(9): 613-619.
10. Vaduganathan M, Venkataramani AS, Bhatt DL. Moving Toward Global Primordial Prevention in Cardiovascular Disease: The Heart of the Matter. *J Am Coll Cardiol* 2015; **66**(14): 1535-1537.
11. Hanson M, Gluckman P. Developmental origins of noncommunicable disease: population and public health implications. *Am J Clin Nutr* 2011; **94**(Suppl 6): 1754S-1758S.