
DR. HUI FAN (Orcid ID : 0000-0003-3920-0600)

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Validation of recommended definition in identifying elevated blood pressure in adolescents

Hui Fan PhD,¹ Yudan Liu MS,¹ Xingyu Zhang PhD²

Affiliations:¹Department of Preventive Medicine, North Sichuan Medical College, Nanchong, Sichuan, China;²Applied biostatistics laboratory, University of Michigan School of Nursing, Ann Arbor, USA

Correspondence to: Hui Fan PhD, Department of Preventive Medicine, North Sichuan Medical College, No. 234 Fujiang Road, Shunqing District, Nanchong 637000, China. Telephone: 86-817-3352113, Fax: 86-817-3352113. Email: 1577371399@qq.com.

Short Title: Definition of elevated blood pressure in adolescents

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Keywords: adolescent, blood pressure, identify

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Email: Hui Fan, 1577371399@qq.com; Yudan Liu, 303644536@qq.com; Xingyu Zhang, zhangxyu@umich.edu.

Abbreviations: BMI, body mass index; BP, blood pressure; CVD, cardiovascular disease; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride.

Abstract

Recently, the American Academy of Pediatrics (AAP) recommended 120/80 mm Hg as thresholds for identifying elevated blood pressure (BP) in adolescents aged 13-17 years. We aimed to compare the performance of the new definition in identifying elevated BP with traditional percentile-based definition. Data were obtained from the National Health and Nutrition Examination Survey 1999–2014, which included 7485 adolescents aged 13 to 17.

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Elevated BP was defined using the recommended ($\geq 120/80$ mm Hg) and traditional definition (≥ 90 th percentile for sex, age and height or 120/80 mm Hg) presented in AAP guideline. The prevalence of elevated BP was 15.7% and 17.2% using the recommended and traditional definition, respectively ($P < 0.001$). The recommended definition had high sensitivity (90.9%), perfect specificity (100.0%), perfect positive predictive value (100.0%) and very high negative predictive value (98.1%) compared with the traditional definition. The Kappa correlation coefficient between two definitions was 0.94 ($P < 0.001$). Similar results can be observed in subgroups across sex, age and sex- and age-specific height percentile except both genders with young age and low height percentile. Generally, our results supported the use of the recommended definition for identifying elevated BP in adolescents.

Keywords: adolescent, blood pressure, identify

1. Introduction

Adult hypertension is an important public-health challenge worldwide due to its high prevalence and its risk for cardiovascular disease (CVD).^{1,2} Blood pressure (BP) levels in children and adolescents have been increasing alarmingly during the past decades.^{3,4} Elevated BP in children and adolescents may result in target organ damage, and increase the risks of adult hypertension and consequent subclinical CVD.⁵⁻⁸ Consequently, the early detection of elevated BP in children and adolescents is crucial to promote cardiovascular health and reduce the future CVD risk.

The US Fourth Report recommended the sex-, age-, and height-specific 90th BP percentiles to define pediatric elevated BP, which was accepted worldwide.⁹ However, the percentile-based definition included hundreds of abnormal BP cutoff values, which resulted in a complex and cumbersome decision process. Elevated BP in children and adolescents was frequently undiagnosed in the clinical practice.^{10,11} As a solution for this problem, the American Academy of Pediatrics (AAP) recommended 120/80 mm Hg as thresholds to

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identify elevated BP in adolescents aged 13-17 years.¹² The new definition of elevated BP in adolescents was consistent with adult hypertension definition released recently by American College of Cardiology/American Heart Association.^{12,13} To our best knowledge, data are presently limited to compare the performance of the new definition in identifying elevated BP and concomitant cardiometabolic risks with the revised sex-, age- and height-specific pediatric BP standard presented in AAP guideline. The aim of this study was to evaluate this using the National Health and Nutrition Examination Survey (NHANES) from 1999 to 2014.

2. Methods

2.1 Study population

NHANES, which has been described in detail elsewhere, is a ongoing, nationally representative, and time-series cross-sectional survey to evaluate health and nutritional status of the resident civilian noninstitutionalized US population.¹⁴ It has been conducted by the US National Center for Health Statistics of the Centers for Disease Control and Prevention since 1999 in 2-year cycle. It consists of questionnaire survey, physical examination and laboratory tests in each cycle. The protocols for NHANES were approved by the National Center for Health Statistics of the Centers for Disease Control and Prevention Institutional Review Board. All the participants and their guardians provided signed informed consent.

We pooled data based on NHANES 1999–2014. The present study was restricted to 9039 individuals aged 13 to 17 years. Participants with incomplete data on age, sex, race, and height were excluded (n=78). Participants who did not have 3 consecutive BP values were also excluded (n = 1476). After these exclusions were conducted, a total of 7485 participants were included in the current analyses.

2.2 General examinations

In the mobile examination center, BP measurements were conducted in the sitting position after 5 minutes resting. BP was measured by auscultation by trained officers. The Korotkoff first and fifth phases were used to define systolic BP (SBP) and diastolic BP (DBP), respectively. Three consecutive BP readings were recorded and the mean of the last two readings was used in the analysis. Height was measured without shoes by trained staff using calibrated equipment. Weight was measured using standard and calibrated equipment. The questionnaire survey was conducted to collect information on demographic data including sex,

age, and race.

2.3 Definition of elevated BP in adolescents

Childhood BP values were classified as normal BP, elevated BP, hypertension stage 1 and stage 2 in the AAP guideline.¹² In the present study, we consider children with elevated BP, hypertension stage 1 and stage 2 identified by the AAP guideline as having “elevated BP”.

2.3.1 Recommended definition

Elevated BP in adolescents was defined as $BP \geq 120/80$ mm Hg.¹²

2.3.2 Traditional definition

Elevated BP in adolescents was defined as $BP \geq 90$ th percentile for sex, age and height (or $\geq 120/80$ mm Hg) according to new normative pediatric BP tables issued by the AAP guidelines.¹² The new normative pediatric BP tables were developed based on normal-weight children, and the details of the development process have been described elsewhere.¹⁵

2.4 Cardiometabolic risks

The cardiometabolic risks assessment included body mass index (BMI), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglyceride (TG) and glycated hemoglobin. BMI was calculated as weight divided by height squared (kg/m^2). Laboratory data consisted of TC, HDL-C, LDL-C, TG and glycated hemoglobin were available for adolescents aged 13-17 years. NHANES Laboratory Procedures Manual released information about sample collection, preservation, measurement procedures and method.¹⁶

2.5 Statistical analysis

Through the use of traditional definition, BPs were classified as normal and elevated BP. Then, BP categories were conducted as defined in the recommended definition. We will report data as means (SEs) and frequencies as appropriate stratified by BP category, which were weighted to represent the US population.

Compared with the traditional definition, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated to assess the performance of the recommended definition for identifying pediatric elevated BP. The Kappa correlation coefficient was calculated to evaluate the agreement between two aforementioned definitions.

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Height percentiles were calculated according to the US Centers for Disease Control and Prevention data.¹⁷ Subgroup analyses were conducted by demographics characteristics (gender, age) , and sex- and age-specific height percentile.

Participants were categorized into 4 groups based on the combinations of the recommended and traditional definitions: participants with normal BP identified by both two definitions, participants with elevated BP detected by the traditional definition but normal BP reclassified by the recommended definition, participants with normal BP detected by the traditional definition but elevated BP reclassified by the recommended definition, and participants with elevated BP diagnosed by both two definitions. The differences were tested for age, sex, height, and race using the univariate linear regression models or χ^2 test between groups. Meanwhile, multiple linear regressions after adjusted for sex, age and height were used to test the differences of cardiometabolic risks between groups (coded as the dummy variables). The analyses were adjusted for sampling weights, primary sampling units and strata to account for the complex survey design of NHANES 1999–2014.¹⁸ All data analyses were conducted with the SAS version 9.2 (SAS Institute, Cary, NC). Statistical significance was inferred at a 2-tailed $P < 0.05$.

3. Results

A total of 7485 participants were included in the present study. The prevalence of elevated BP was 15.7% and 17.2% using the recommended and traditional definitions, respectively ($P < 0.001$). Characteristics of the participants stratified by BP category as defined in the recommended and traditional classifications are presented in Table S1 and S2. Table 1 summarizes the demographic and cardiometabolic characteristics of all participants considering the weight for survey.

Table 2 shows the performance of the recommended definition for identifying elevated BP. Compared with the traditional definition, the recommended definitions had high sensitivity (90.9%), perfect specificity (100.0%), perfect PPV (100.0%) and very high NPV (98.1%). The Kappa correlation coefficient between two definitions was 0.94 ($P < 0.001$). Similar results can be obtained in subgroup across sex and age. Both specificity and PPV were perfect (both 100%) in all subgroups across sex, age and sex- and age-specific height percentile. Sensitivity differed substantially comparing data at low vs. high height percentile

among both sexes with young age.

Table 3 presents the comparison of demographic and cardiometabolic characteristics between groups classified by the combinations of 2 definitions. There are 1172, 117, 6196 and 0 participants with elevated BP diagnosed by both two definitions, elevated BP detected by the traditional definition but normal BP reclassified by the recommended definition, normal BP identified by both two definitions, and normal BP detected by the traditional definition but elevated BP reclassified by the recommended definition, respectively. A total of 117 reclassified participants were younger, shorter and had lower proportion of male than 6196 participants who remained in the normal BP category (all $P_s < 0.05$). Between these 2 groups, the cardiometabolic risk (ever BMI, TC, HDL-C, LDL-C, TG and glycated hemoglobin) was not significantly different with adjustment for sex, age and height (all $P_s > 0.05$).

4. Discussion

The present study showed that recommended definition performed well in identifying elevated BP in adolescents aged 13-17 years, with high sensitivity, perfect specificity, perfect PPV and high NPV. Sensitivity differed greatly comparing data at low vs. high height percentile among both genders with young age. This study also demonstrated that the differences of cardiometabolic risks were not significant between the participants with elevated BP detected by the traditional definition but normal BP reclassified using the recommended definition and those with normal BP identified using both two definitions.

To improve the detection of pediatric elevated BP, several simplified definitions were developed.¹⁹⁻²² Cross-sectional studies suggested that those simplified definitions had high sensitivities and moderate specificities in comparison with the Fourth Report.¹⁹⁻²¹ These results were also confirmed by a recent meta-analysis showing many simplified definitions as the accurate screening tools.²² Of note, several previous studies emphasized the importance of BP reassessment using the Fourth Report after identifying children with elevated BP by the simplified definition.¹⁹⁻²²

In 2017, AAP updated the Fourth Report.¹² To use friendly and align with adult hypertension guidelines, the most prominent change in the AAP updated guideline was the recommendation of absolute BP thresholds (120/80 mm Hg) on the diagnosis of elevated BP in adolescents aged 13 to 17 years. In other words, the simplified definition ($\geq 120/80$ mm Hg)

replaced traditional percentile-based definition for identifying elevated BP in adolescents.¹² There were limited data regarding the difference between the recommended and traditional percentile-based definition revealed by AAP guidelines for adolescents. Our findings showed that the recommended definition had high sensitivity, perfect specificity (100%), perfect PPV (100%), and very high NPV compared with the traditional definition. Additionally, the agreement between two definitions was high.

Good performance of the recommended definition can be expected. Considering the characteristics of the recommended ($\geq 120/80$ mm Hg) and traditional definition (\geq sex-, age-, and height-specific 90th BP percentiles or 120/80 mm Hg, whichever is lower), the reclassification of BP category can only be observed among participants whose BP was $>$ corresponding sex-, age-, and height-specific 90th BP percentiles and $< 120/80$ mm Hg. Consequently, only 117 (1.6%) of all participants, who were detected as elevated BP by the traditional definition, were reclassified as normal BP by the recommended definition. Meanwhile, there were 0 participants with normal BP detected by the traditional definition but elevated BP reclassified by the recommended definition.

Previous simplified tools did not have perfect specificity/PPV, and very high sensitivity/NPV.¹⁹⁻²² Due to many diagnostic thresholds, these tools had the relatively low simplified degree.¹⁹⁻²² On the contrary, 120/80 threshold was simple and user-friendly. Clinicians can use the recommended definition to quickly identify elevated BP. Of note, sensitivity differed greatly comparing data at low vs. high height percentile among both genders with young age. The recommended definition was used with caution among younger (e.g. 13years) and shorter (e.g. $<$ sex- and age-specific 25th height percentiles) participants, whose 90th BP percentiles for sex, age and height, as described in the AAP guidelines,¹² were obviously lower than 120/80 mm Hg.

Whether the participants with elevated BP as defined in the traditional definition but normal BP as reclassified in the recommended definition had the increased risks of CVD compared to those with normal BP diagnosed by both two definitions has not been clarified. In the current study, our findings indicated that the differences of cardiometabolic risks were not significant between these two groups, suggesting that participant from these two groups may exhibit the similar risks of future CVD. Our results was partly supported by a cohort

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study with 27.1-year follow-up, which demonstrated that the recommended definition (120/80 mm Hg) performed equally with the Fourth Report in predicting adult hypertension and subclinical CVD.⁸ Similarly, previous publications summarized the convincing evidence and underscored the importance of conserving optimal BP (<120/80 mm Hg) in primordial prevention of CVD for adolescents.²³

The strengths of this study included the nationally representative data from NHANES, the large sample size, and the high quality of data measurement (trained examiners and calibrated instruments), which made our results convincing and generalizable to US adolescents aged 13-17 years. Several limitations should be noted in the current study. First, NHANES was conducted in the US population, which limits the generality of our results to other population. Second, due to unavailable long-term follow-up data, we cannot assess whether adolescents whose BP was reclassified as normal BP had increased risk of CVD compared with those with normal BP detected by both two definitions. Further cohort studies are necessary to bridge this gap. Finally, the small number of participants who underwent BP reclassification and laboratory assessment did not allow us to perform further analysis by abnormal cutoffs of cardiometabolic risks. Further studies should fill in this gap.

In summary, our study suggested that the recommended definition performed well in identifying elevated BP in adolescents compared with the traditional standard. Our results supported the use of the recommended definition for identifying elevated BP in adolescents aged 13-17 years.

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Table 1. Characteristics of the study participants by BP category weighted for survey

	All participants	Normal BP		Elevated BP	
		Traditional definition	Recommended definition	Traditional definition	Recommended definition
No. of participants	7485	6196	6313	1289	1172
Demographic characteristics					
Age (years)	15.5(0.02)	15.4(0.02)	15.4(0.02)	15.8(0.1)	15.9(0.1)
Male (%)	49.3	46.0	45.7	66.8	70.4
Height (cm)	166.5(0.2)	165.9(0.2)	165.8(0.2)	169.5(0.4)	170.5(0.4)
Race					
White (%)	59.8	60.2	60.2	57.8	57.5
Black (%)	14.3	13.5	13.5	18.5	18.9
Mexican American (%)	12.2	12.1	12.1	12.8	13.0
Hispanic (%)	6.5	6.7	6.7	5.4	5.3
Other (%)	7.2	7.5	7.5	5.6	5.3
SBP (mm Hg)	108.7(0.2)	106.0(0.1)	106.1(0.1)	122.8(0.4)	124.0(0.3)
DBP (mm Hg)	61.1(0.3)	60.3(0.3)	60.6(0.3)	65.6(0.6)	64.5(0.6)
Cardiometabolic characteristics					
BMI (kg/m ²)	23.3(0.1)	22.9(0.1)	22.9(0.1)	25.7(0.2)	26.0(0.2)
Total cholesterol (mg/dl)	157.1(0.5)	156.1(0.5)	156.2(0.5)	161.8(1.3)	162.0(1.3)

HDL cholesterol (mg/dl)	50.5(0.2)	50.9(0.2)	50.9(0.2)	48.7(0.5)	48.3(0.5)
LDL cholesterol (mg/dl)	88.4(0.6)	87.2(0.6)	87.2(0.6)	95.1(2.2)	95.7(2.4)
Triglyceride (mg/dl)	83.1(1.3)	80.8(1.3)	80.9(1.3)	94.9(3.6)	95.9(3.9)
Glycated hemoglobin (%)	5.2(0.01)	5.2(0.01)	5.2(0.01)	5.2(0.03)	5.2(0.02)

BP, blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Data are presented as means (SEs) or frequencies (%) as appropriate.

Some data were missing for cardiometabolic variables, and available data were showed on the supplemental Table S2.

Table 2. Performance of the recommended definition for identifying elevated BP

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Kappa coefficient*
All participants	90.9	100	100	98.1	0.94
Gender					
Boys	95.5	100	100	98.7	0.97
Girls	81.1	100	100	97.7	0.88
Age					
13 years	79.9	100	100	97.1	0.87
14 years	85.5	100	100	97.7	0.91
15 years	94.8	100	100	99.0	0.97
16 years	94.2	100	100	98.5	0.96
17 years	94.8	100	100	98.6	0.97
Height percentiles among boys aged 13 years					
< 25	40.0	100	100	92.4	0.54
25~	71.4	100	100	94.5	0.81
50~	80.0	100	100	97.2	0.88
≥75	100	100	100	100	1
Height percentiles among boys aged 14 years					
< 25	64.7	100	100	94.3	0.76
25~	96.8	100	100	99.3	0.98
50~	86.8	100	100	96.8	0.91
≥75	97.8	100	100	99.5	0.99
Height percentiles among boys aged 15 years					
< 25	95.8	100	100	99.1	0.97
25~	100	100	100	100	1
50~	100	100	100	100	1
≥75	100	100	100	100	1

Height percentiles among boys aged 16 years

< 25	93.6	100	100	98.1	0.96
25~	100	100	100	100	1
50~	100	100	100	100	1
≥75	100	100	100	100	1

Height percentiles among boys aged 17 years

< 25	95.3	100	100	98.4	0.97
25~	100	100	100	100	1
50~	100	100	100	100	1
≥75	100	100	100	100	1

Height percentiles among girls aged 13 years

< 25	70.0	100	100	96.4	0.81
25~	72.7	100	100	97.3	0.83
50~	63.6	100	100	97.9	0.77
≥75	84.6	100	100	97.3	0.90

Height percentiles among girls aged 14 years

< 25	50.0	100	100	96.4	0.65
25~	81.8	100	100	97.9	0.89
50~	91.7	100	100	98.9	0.95
≥75	81.0	100	100	97.2	0.88

Height percentiles among girls aged 15 years

< 25	82.6	100	100	97.8	0.89
25~	70.0	100	100	96.6	0.81
50~	100	100	100	100	1
≥75	94.4	100	100	99.2	0.97

Height percentiles among girls aged 16 years

< 25	83.3	100	100	97.9	0.90
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25~	77.4	100	100	96.0	0.85
50~	80.0	100	100	97.8	0.88
≥75	94.1	100	100	99.3	0.97

Height percentiles among girls aged 17 years

< 25	82.6	100	100	98.2	0.90
25~	84.2	100	100	98.1	0.91
50~	75.0	100	100	96.3	0.84
≥75	93.8	100	100	99.2	0.96

BP, blood pressure; PPV, positive predictive value; NPV, negative predictive value.

* all Ps<0.001

Table 3. Comparison of the characteristics between groups classified by the combinations of 2 definitions

	Group 1	Group 2	Group 3	P	
				Group 1 vs 3	Group 2 vs 3
Demographic characteristics*					
No.	1172	117	6196		
Age (years)	15.9(0.1)	15.0(0.2)	15.4(0.02)	<0.001	0.009
Male (%)	70.4	30.8	46.0	<0.001***	0.012***
Height (cm)	170.5(0.4)	159.3(0.7)	165.9(0.2)	<0.001	<0.001
Race				0.503***	0.994***
White (%)	57.5	60.0	60.2		
Black (%)	18.9	13.9	13.5		
Mexican American (%)	13.0	11.2	12.1		
Hispanic (%)	5.3	6.4	6.7		
Other (%)	5.3	8.5	7.5		
Cardiometabolic characteristics**					
BMI (kg/m ²)	26(0.2)	23.2(0.7)	22.9(0.1)	<0.001	0.293
Total cholesterol (mg/dl)	162(1.3)	160.6(3.3)	156.1(0.5)	<0.001	0.686
HDL cholesterol (mg/dl)	48.3(0.5)	53.5(2.3)	50.9(0.2)	0.036	0.567

LDL cholesterol (mg/dl)	95.7(2.4)	88.3(3.9)	87.2(0.6)	<0.001	0.649
Triglyceride (mg/dl)	95.9(3.9)	85.3(11.7)	80.8(1.3)	0.001	0.648
Glycated hemoglobin (%)	5.2(0.02)	5.5(0.2)	5.2(0.01)	0.570	0.145

BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Data are presented as means (SEs) or frequencies (%) as appropriate. Some data were missing for cardiometabolic variables.

Group 1: participants with elevated BP diagnosed by both two definitions; Group 2: participants with elevated BP detected by the traditional definition but normal BP reclassified by the recommended definition; Group 3: participants with normal BP identified by both two definitions. There are 0 participants with normal BP detected by the traditional definition but elevated BP reclassified by the recommended definition.

* Comparison of demographic characteristics between groups was performed using univariate linear regression models or χ^2 test.

** Comparison of cardiometabolic characteristics between groups (coded as the dummy variables) was performed using multiple linear regressions after adjusted for sex, age and height.

*** Compared with adjusted alpha levels (0.05/2) due to multiple comparisons