#### **ORIGINAL PAPER**

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# Performance of blood pressure measurements at an initial screening visit for the diagnosis of hypertension in children

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#### Abstract

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Hypertension in children is defined as sustained elevated blood pressure (BP) over several visits. For the screening of hypertension, it is standard to obtain several BP readings at the initial visit. There is however no recommendation on the minimum number of readings needed. We evaluated the performance of BP readings obtained at one initial screening visit to predict the diagnosis of hypertension in children. In a school-based study conducted in Switzerland, BP was measured three times on up to three visits in 5207 children. Sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) of elevated BP at the initial screening visit for the identification of hypertension were estimated using the 1st, 2nd, and 3rd BP readings (R1, R2, R3), as well as (R1 + R2)/2 and (R1 + R2 + R3)/3). These performance indices were compared with the reference method (R2 + R3)/2. The ability of BP readings to discriminate children with and without hypertension was evaluated with receiver operating characteristic curve analysis. The prevalence of systolic/diastolic hypertension was 2.2%. The greatest performance to identify children with hypertension was obtained with R2 (sensitivity: 97%; specificity: 88%; PPV: 15%; NPV: 100%) and the reference method, (R2 + R3)/2 (sensitivity: 100%; specificity: 90%; PPV: 18%; NPV: 100%). The ability to discriminate using R1, R2, (R1 + R2)/2, and (R2 + R3)/2 for the identification of hypertension was strong (AUC: 0.89, 0.93, 0.92, and 0.95, respectively). Obtaining two BP readings and using only the second one at a screening visit may be sufficient as initial step for the identification of hypertension in children.

### 1 | INTRODUCTION

Hypertension is a major cardiovascular risk factor and a major cause of morbidity and mortality worldwide.<sup>1.2</sup> Children and adolescents with hypertension are at increased risk of hypertension later in life.<sup>3-5</sup> Further, markers of hypertensive target organ damage, such as left ventricular hypertrophy and thickening of the carotid vessel wall, are more frequent in children and adolescents with elevated blood pressure (BP).<sup>4,5</sup> Therefore, and despite major controversies,<sup>5</sup> screening and treatment of elevated BP has been recommended in children and adolescents by several health professional and scientific agencies, including the US National Heart, Lung, and Blood Institute and the European Society of Hypertension.  $^{6,7}$ 

However, one major challenge of BP screening in children is that the identification of hypertension is difficult.<sup>1,5,8</sup> One of these difficulties stems from the high variability of BP over time.<sup>9-14</sup> Indeed, BP varies from 1 minute to the other, from one day to the other, and over a longer period of time. In general, BP decreases over repeated readings both within and between visits.<sup>9,10,14</sup> In adults as in children, the decrease in BP over time can be explained by an accommodation effect due, partly, to a reduction of anxiety as patients become more familiar with the procedure. It is therefore recommended to assess hypertension in children based on multiple BP measurements taken on several visits and to base clinical decision on some averages of several readings.<sup>3,6,7,15</sup>

Currently, there is no recommendation on the exact number of measurements needed at each visit for the identification of hypertension in children. Yet, it is commonly acknowledged, mostly based on adults studies, that multiple BP measurements have a better predictive power than a single reading.<sup>5,15,16</sup> However, while taking too few readings can lead to overestimate BP, multiplying the number of readings is cumbersome for both the patients and healthcare providers.<sup>9,13,16</sup> Using data from a large study of children whose BP was measured several times on up to three separate visits, we assessed the performance of different combinations of BP readings taken on the initial screening visit to identify the risk of hypertension in children. More specifically, we examined which measurement scheme at the initial screening visit was the most efficient to maximize the identification of cases of hypertension.

#### 2 | METHODS

#### 2.1 | Study population and measurement methods

We conducted a secondary analysis of data collected among 5207 children of the 6th grade of all schools of the canton de Vaud (Switzerland).<sup>1,17-19</sup> The study was approved by the ethics research committee of the Faculty of Biology and Medicine, University of Lausanne. Consent was sought from the directors of all schools. Signed consent of one of the parents and of the child was obtained.

At the initial visit, weight, height, and BP were measured in all participants. Children were measured without shoes and in light garments in a quiet and tempered room by trained clinical officers or school nurses. Weight and height were measured with precision electronic scales (to the nearest 0.1 kg) and fixed stadiometers (to the nearest 0.1 cm). Blood pressure was measured on the right arm (to the nearest 1 mm Hg), after a rest of at least 3 minutes, with the child in a seated position. The mid-arm circumference was measured and the cuff width adapted accordingly (ie, pediatric or normal cuff for a mid-arm circumference of 17.0-21.9 cm or 22.0-32.0 cm, respectively). At each visit, three measurements of BP and of heart rate were taken on the right arm at 1-minute intervals after a rest of at least 3 minutes, in a seated position. Blood pressure was measured with a clinically validated oscillometric device (Omron M6; Omron Healthcare Europe BV). Each device was checked for accuracy by comparing BP values obtained with a mercury sphygmomanometer using a Y tube connected to the automated device.

Elevated BP (EBP) was defined for systolic or diastolic BP  $\ge$  95th sex-specific, age-specific, and height-specific percentiles, using the European guidelines of 2016, based on American normative data (or, equivalently, for a *Z*-score of this sex-, age-, and height-specific distribution of BP  $\ge$  1.64).<sup>6.7</sup> Sex- and age-specific height percentiles (necessary to determine BP thresholds for EBP) were derived from the Centers for Disease Control and Prevention (CDC) growth charts. If children had EBP at the initial visit, based on the average of the last two BP readings (ie, (R2 + R3)/2, the reference method

to identify EBP at the initial visit), BP was measured on up to two additional visits, separated by at least 1 week and using the same BP measurement method. Children with sustained EBP at the three visits were defined to have hypertension, with the reference method used at each visit to identify EBP.

Body mass index (BMI) was calculated as weight divided by height squared (kg/m<sup>2</sup>). "No excess weight," "overweight," and "obesity" were defined, respectively, for a BMI less than the 85th percentile, between the 85th and 94th percentiles, and of at least the 95th percentile of the US reference data, which are often used to define excess body weight in children.

#### 2.2 | Statistical analyses

To define EBP at the initial screening visit, we used either the 1st (R1), the 2nd (R2), or the 3rd (R3) BP readings; or the averages of the 1st and the 2nd BP readings (R1 + R2)/2), or of the 2nd and 3rd BP readings (R2 + R3)/2, the reference method; or the average of the three readings (R1 + R2 + R3)/3.

For each combination of readings to define EBP, we built two-bytwo tables crossing EBP at the initial visit (yes/no) with hypertension (yes/no). Using each of these two-by-two tables, we estimated the sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) of EBP at the initial screening visit for the identification of hypertension.

# **TABLE 1** Characteristics of the participants (N = 5207, 2621boys and 2586 girls)

Characteristics	Mean	SD	Min	Max
Age (y)	12.3	0.5	10.1	14.9
Weight (kg)	44.3	9.4	18.2	106.0
Height (cm)	153.5	7.6	127.0	183.2
Systolic R1 (mm Hg)	116.3	10.9	76.0	164.0
Systolic R2 (mm Hg)	113.4	10.3	72.0	161.0
Systolic R3 (mm Hg)	112.3	10.1	71.0	163.0
Systolic (R1 + R2)/2 (mm Hg)	114.9	10.2	81.5	161.0
Systolic (R2 + R3)/2 (mm Hg)	112.9	9.9	72.0	160.5
Systolic (R1 + R2 + R3)/3 (mm Hg)	114.0	9.9	81.3	161.7
Diastolic R1 (mm Hg)	67.4	7.7	39.0	139.0
Diastolic R2 (mm Hg)	66.0	7.6	39.0	136.0
Diastolic R3 (mm Hg)	65.6	7.5	30.0	120.0
Diastolic (R1 + R2)/2 (mm Hg)	66.7	7.1	42.0	109.0
Diastolic (R2 + R3)/2 (mm Hg)	65.8	7.1	37.0	102.0
Diastolic (R1 + R2 + R3)/3 (mm Hg)	66.3	6.9	39.0	96.7

*Note*: Mean blood pressure (BP) level at the initial visit, with standard deviation (SD), minimum (Min), and maximum (Max), are reported using the 1st (R1), the 2nd (R2), and the 3rd (R3) readings or average of different set of readings.

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	Reading(s) used to esti- mate BP	Number (proportion)
Elevated systolic BP	R1	1062 (20.4%)
	R2	656 (12.6%)
	R3	547 (10.5%)
	(R1 + R2)/2	802 (15.4%)
	(R2 + R3)/2 <sup>a</sup>	568 (10.9%)
	(R1 + R2 + R3)/3	672 (12.9%)
Elevated diastolic BP	R1	177 (3.4%)
	R2	130 (2.5%)
	R3	124 (2.4%)
	(R1 + R2)/2	172 (3.3%)
	(R2 + R3)/2 <sup>a</sup>	130 (2.5%)
	(R1 + R2 + R3)/3	141 (2.7%)
Elevated systolic/diastolic BP	R1	1104 (21.2%)
	R2	693 (13.3%)
	R3	594 (11.4%)
	(R1 + R2)/2	849 (16.3%)
	(R2 + R3)/2 <sup>a</sup>	604 (11.6%)
	(R1 + R2 + R3)/3	708 (13.6%)

**TABLE 2** Number and proportion of children with elevated blood pressure (EBP) at the initial screening visit based on different combinations of readings (N = 5207, 2621 boys and 2586 girls)

Note: R1, R2, R3: reading 1, 2, and 3; (R1 + R2)/2, (R2 + R3)/2, and (R1 + R2 + R3)/3: average of the

readings.

<sup>a</sup>Reference method

The ability of these BP readings to discriminate children with and without hypertension was further evaluated with receiver operating characteristic (ROC) curve analyses, also known as C-statistic.<sup>20,21</sup> We computed the area under the ROC curve (AUC) statistic based on different sets of readings (R1; R2; R3) or their averages ((R1 + R2)/2; (R2 + R3)/2, the reference method; (R1 + R2 + R3)/3). The AUC ranges from 0.5 (random discrimination) to 1.0 (perfect discrimination), and values of 0.8 and above are traditionally considered as indicating a strong discrimination power.<sup>20,21</sup>

#### 3 | RESULTS

Characteristics of the participants are shown in Table 1. Of the 6873 eligible children, 5207 participated (participation rate: 76%; 2621 boys, 2586 girls). Mean BP decreased across readings at the 1st visit. Proportions of children with EBP at the initial visit using different readings are shown in Table 2. Depending on the readings used, the proportion of children with elevated systolic/diastolic BP ranged between 11.4% and 21.2%. The prevalence of systolic/diastolic, systolic, and diastolic hypertension, that is, sustained elevated BP at the three visits, was 2.2%, 2.1%, and 0.4%, respectively.

Table 3 shows the performance of different reading combinations to identify children with either systolic/diastolic hypertension (sustained elevated systolic BP or sustained elevated diastolic BP), systolic hypertension (sustained elevated systolic BP), or diastolic hypertension (sustained elevated diastolic BP). For systolic/diastolic hypertension, based on the reference method, that is, using (R2 + R3)/2, the sensitivity and specificity were high (100% and 90%, respectively), and the PPV was 18%. By comparison, using R1 solely, the sensitivity was high (98%), but the specificity (80%) and PPV (10%) were lower. Using R2 solely, the sensitivity (97%), the specificity (88%), and the PPV (15%) remained elevated. Using R3 solely, the sensitivity decreased substantially (91%). Using (R1 + R2)/2 or (R1 + R2 + R3)/3, the sensitivity was high, but the specificity was relatively low. Whatever the readings used, the NPV was high (100%).

For systolic hypertension, sensitivity, specificity, and PPV were also high using R2 solely (96%, 89%, 16%) and close to the performance achieved using the reference method, that is, (R2 + R3)/2 (100%, 91%, 19%). Using R3 solely, the sensitivity decreased substantially (91%). Whatever the readings used, the NPV was high (100%).

For diastolic hypertension, whatever the readings used, the sensitivity was low (20%-35%) and the specificity was high (97%-98%). A relatively high PPV was reached with the averages of readings (R1 + R2)/2 (22%), (R2 + R3)/2 (24%), and (R1 + R2 + R3)/3 (24%). Whatever the readings used, the NPV was high (98%-99%).

The highest AUC for the identification of systolic/diastolic hypertension was obtained using R2 solely and the averages of readings (R1 + R2)/2, (R2 + R3)/2 and (R1 + R2 + R3)/3 (0.93, 0.92, 0.95, 0.94, respectively). For the identification of systolic hypertension, the AUC was the highest with R2 solely and the averages of readings (R1 + R2)/2, (R2 + R3)/2, (R1 + R2 + R3)/3 (0.93, 0.92, 0.95, **TABLE 3** Sensitivity (SE), specificity (SP), positive predictive value (PPV), negative predictive value (NPV), and AUC statistic for different combinations of BP readings (R) at the initial screening visit to identify children with systolic hypertension, diastolic hypertension, and systolic/diastolic hypertension at the third visit

	SE	SP	PPV	NPV	AUC
R1					
Systolic/diastolic hypertension	98%	80%	10%	100%	0.89
Systolic hypertension	97%	81%	10%	100%	0.89
Diastolic hypertension	28%	97%	17%	98%	0.63
R2					
Systolic/diastolic hypertension	97%	88%	15%	100%	0.93
Systolic hypertension	96%	89%	16%	100%	0.93
Diastolic hypertension	23%	98%	19%	98%	0.61
R3					
Systolic/diastolic hypertension	91%	90%	16%	100%	0.90
Systolic hypertension	91%	91%	18%	100%	0.91
Diastolic hypertension	20%	98%	17%	98%	0.59
(R1 + R2)/2					
Systolic/diastolic hypertension	99%	85%	13%	100%	0.92
Systolic hypertension	98%	86%	13%	100%	0.92
Diastolic hypertension	35%	97%	22%	99%	0.66
(R2 + R3)/2 <sup>a</sup>					
Systolic/diastolic hypertension	100%	90%	18%	100%	0.95
Systolic hypertension	100%	91%	19%	100%	0.95
Diastolic hypertension	29%	98%	24%	99%	0.64
(R1 + R2 + R3)/3					
Systolic/diastolic hypertension	100%	88%	15%	100%	0.94
Systolic hypertension	100%	89%	16%	100%	0.94
Diastolic hypertension	31%	98%	24%	99%	0.64

*Note:* BP: blood pressure; R1, R2, R3: reading 1, 2, 3; (R1 + R2)/2, (R2 + R3)/2, (R1 + R2 + R3)/3: averages of the readings. <sup>a</sup>Reference method.

and 0.94, respectively). For diastolic hypertension, the AUC was low (<0.8), whatever the readings used. Among overweight children, the performance of difference readings was similar compared with per-

#### 4 | DISCUSSION

formance in the whole sample (data not shown).

Our study shows that hypertension, that is, elevated BP on three separate medical visits, is predicted similarly well based on the sole second BP reading made at the initial screening visit or the average of the 2nd and the 3rd readings made at the initial visit, the reference method. Therefore, obtaining two BP readings and using only the second one at a screening visit may be sufficient as an initial step for the identification of hypertension in children.

Only few studies among adults, and none among children to our knowledge, have examined the minimum number of readings needed to identify hypertension. In 2003, Bovet et al<sup>9</sup> have shown that hypertension, that is, elevated BP on four separate visits at a 6 weeks interval, was reliably identified using only the third reading, or the average of the second and third readings, made at the second visit. In 2013, Oladipo et al<sup>16</sup> have analyzed the optimal number of consecutive readings on a single visit needed for BP assessment, they found that using the averages of at least two readings could be sufficient in clinic BP monitoring. In 2017, Veloudi et al<sup>14</sup> have studied the impact of within-visit BP variability on the accuracy of BP measurements; they observed that in some children BP did not drop on consecutive readings, but they also highlighted the importance to standardize the protocols, particularly the number of BP readings needed to avoid misdiagnosis of hypertension.

Current guidelines are still evasive on the numbers of readings needed to reliably assess hypertension, despite the important practical significance of this issue to avoid under or overdiagnosis, and to minimize procedures to diagnose hypertension. Accurate measurement of BP is essential to accurately classify individuals (particularly to limit false-positive cases and unnecessary treatment) and to guide effective clinical management.<sup>9,13,15,22</sup> There is also only little incentive from the pharmaceutical industry to conduct these kinds of studies, as some overestimation of BP when hypertension is based on only few measurements favors drugs management<sup>23,24</sup> and may increase the apparent effect of treatment; that is, some of the

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normally occurring BP decrease over time is attributed to treatment when a treatment is given.

Nonetheless, aiming for an optimal accuracy in assessing hypertension remains a valid issue. Avoiding overdiagnosis of hypertension is important in view of potential side effects and substantial cost of treatment. As stated by some authors, the optimal trade-off between accurate BP determination which accrues from multiple readings and feasibility and cost issues related to the screening procedure (ie, measuring as few readings as possible) remains to be identified.<sup>5,14</sup>

The study has several strengths. It was based on a large school-based sample. Further, we used a standard definition of hypertension, based on elevated BP on three separate visits, and with BP measured by trained staff using a clinically validated device along a strict and predefined protocol. This study has some important limitations. First, children of a narrow age range were examined, and our findings may not be applied to older or younger children. Second, we only examined subjects with sustained elevated BP at or above the 95th percentile and did not take into consideration the children with prehypertension (systolic or diastolic BP  $\geq$  90th percentile but <95th percentile). Third, in order to assess definite hypertension (elevated BP on three visits), readings were measured in subsequent visits only if BP was elevated at the prior visit: This removed children who might have had normal BP at the first visit but high BP at the next visits, likely not a frequent situation. Fourth, we had no ambulatory BP measurements and could not confirm the diagnosis of hypertension with this method, as recommended by several guidelines.

To our knowledge, this is the first study that examined different combinations of readings on a first visit in order to predict hypertension among children (based on EBP on three successive visits). Our results suggest that obtaining solely two BP readings and using only the second one at an initial screening visit performs well to identify hypertension in children. Further studies in other age ranges and other populations should be conducted to guide recommendations for the diagnosis of hypertension in children in clinical practice.

#### CONFLICT OF INTEREST

None.

#### AUTHORS CONTRIBUTION

Z. Outdili, P. Bovet, and A. Chiolero conceived this study. Z. Outdili analyzed data under the supervision of A. Chiolero and P. Bovet. H. Marti Soler gave advice to conduct statistical analyses. Z. Outdili drafted the initial manuscript under the supervision of A. Chiolero. All authors provided critical feedback on the manuscript and approved the final version.

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