# Fat-free mass may play a dominant role in the association between systolic blood pressure and body composition in children and adolescents

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### Abstract

Systolic blood pressure (SBP) is significantly associated with body composition in children and adolescents. However, which one of the components of body composition is the dominant contributor to SBP in children and adolescents remains unclear. We, therefore, aimed to determine the dominant contributor to SBP among components of body composition in a large cohort of American children and adolescents derived from the National Health and Nutrition Examination Survey with cross-sectional analysis. In total, 13 618 children and adolescents (median age 13 years; 6107 girls) with available data on whole-body dual-emission X-ray absorptiometry measurements were included. Multiple linear regression showed that SBP was associated with higher total fat-free mass in boys ( $\beta = 0.49$ , P < 0.001) and girls ( $\beta = 0.47$ , P < 0.001) and with higher total fat mass only in boys ( $\beta = 0.12$ , P < 0.001) after adjustment for covariates. When taking fat distribution into consideration, SBP was associated with higher trunk fat mass (boys:  $\beta = 0.28$ , P < 0.001; girls:  $\beta = 0.15$ , P < 0.001) but negatively associated with leg fat mass (Boys:  $\beta = -0.14$ , P < 0.001; Girls:  $\beta = -0.11$ , P < 0.001), in both boys and girls. Dominance analysis showed that total fat-free mass was the dominant contributor to SBP (boys: 49 %; girls: 55.3 %), followed by trunk fat mass (boys: 32.1%; girls: 26.9%); leg fat mass contributed the least to SBP in boys (18.9\%) and girls (17.8\%). Our findings indicated that total fat-free mass was not only associated with SBP but also the most dominant contributor to SBP variation in American children and adolescents.

Keywords: Systolic blood pressure: Children and adolescents: Body composition: Fat-free mass: Fat mass

Elevated blood pressure (BP) in childhood and adolescence tracks into adulthood and is associated with incident hypertension and increased cardiovascular risk later in life<sup>(1-3)</sup>. Understanding the mechanisms underlying BP elevation in children and adolescents is thus of great importance for preventing the development of hypertension and other related CVD.

Rapid body growth and development lead to an increase in body size and changes in body composition and is one of the important determinants of age-related BP elevation during childhood and adolescence<sup>(4–6)</sup>. Increases in fat-free mass and fat mass (two components of body composition) are both related to elevated metabolic need and thus drive an elevation in cardiac output which is one major haemodynamic determinant of BP elevation<sup>(6,7)</sup>. However, which one of the components of body composition is the dominant factor in driving the BP elevation in children and adolescents remains unclear.

From the perspective of physiology and pathophysiology, the metabolic need is mainly determined by fat-free mass or muscle mass<sup>(8)</sup>, and fat-free mass of minors increases more dramatically than fat mass along with growing up from childhood to early adulthood<sup>(6,9)</sup>; therefore, fat-free mass is supposed to play a major role on the association between the BP level and body composition in children and adolescent. Limited data in previous published studies provided preliminary support for this speculation<sup>(7)</sup>. Based on 201 subjects aged 6 to 17 years, Daniels et al. showed that only fat-free mass was significantly associated with systolic BP (SBP) after adjustment for potential covariates<sup>(7)</sup>. However, in a large cohort of 9-year-old children, Brion et al. reported a relatively greater regression coefficient for fat mass, although both fat-free mass and fat mass were significantly associated with SBP<sup>(10)</sup>. More investigations are undoubtedly needed to further confirm whether fat-free mass plays an important role in determining SBP in children and adolescents. Besides, in our previous study<sup>(11)</sup> and other groups'

Abbreviations: BP, blood pressure; DXA, dual-emission X-ray absorptiometry; NHANES, National Health and Nutrition Examination Survey; SBP, systolic blood pressure.

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studies<sup>(12-14)</sup>, leg fat mass was found to be negatively associated with BP and played a protective role in cardiometabolic profile in adults. Whether these findings could be extrapolated to the children and adolescents who have less ageing and exposure to cardiovascular risk factors is unknown.

Therefore, in the present study, we aimed to determine the dominant contributor among components of body composition to SBP and the impact of fat mass in various depots on SBP in a large cohort of American children and adolescents derived from the National Health and Nutrition Examination Survey (NHANES).

# Materials and methods

# Study population

The NHANES is a continuous population-based survey conducted by the Centers for Disease Control and Prevention (CDC) and the National Center for Health Statistics (NCHS) of the USA and used to assess the health and nutritional status of the civilian and non-institutionalised population in the USA. Details and information about the NHANES can be found on the website (https://wwwn.cdc.gov/nchs/nhanes/default.aspx) and on ClinicalTrials.gov (Identifier: NCT00005154). Protocol of NHANES has been approved by the NCHS Research Ethics Review Board in accordance with the Declaration of Helsinki. All participants had signed informed consent. The present study analysed the NHANES data collected from eight cycles (1999– 2006 and 2011–2018) with whole-body dual-emission X-ray absorptiometry (DXA) measurements.

In total, there were 14 414 boys and girls with DXA data derived from the eight cycles of NHANES. For the purpose of the present analysis, we further excluded 608 participants without BP measurements or taking antihypertensive drugs, sixty-six participants with self-reported history of diabetes and 122 participants with missing data on covariates. Finally, a total of 7511 boys and 6107 girls (age range 8–17 years for both sexes) were included in the present analysis.

# Anthropometry and measurements of body composition

Body height, weight and waist circumference were directly measured by trained health technicians using standardised protocols. BMI was calculated by dividing an individual's weight in kilograms by the square of height in metres. Total and regional body composition measurements were collected by DXA using a Hologic QDR-4500A fan-beam densitometer (Hologic, Inc.) by trained and certified technologists, following the instructions provided by the manufacturer. The details of the original data of DXA are represented on the NHANES website (https://wwwn.cdc.gov/nchs/nhanes/default.aspx). In the present study, we were mainly interested in whole-body fat mass, fat-free mass and regional fat mass in the legs and trunk.

# Blood pressure measurement

Trained physicians measured BP at a mobile examination centre according to a standard protocol (details shown on the official

website of NHANES: https://wwwn.cdc.gov/Nchs/Nhanes/ 2017–2018/BPXO\_J.htm). BP was repeatedly measured three times, and we took the average of the three BP readings for analysis.

# Assessment of covariates

Information on age, sex and race/ethnicity was obtained by selfreport during the household interview. Race/ethnicity was categorised into five groups (non-Hispanic White, non-Hispanic Black, Mexican American, other Hispanic group and other ethnic groups). Obesity for children and adolescents was defined as BMI for age at or above the 95<sup>th</sup> percentile according to the CDC growth chart<sup>(15)</sup>.

#### Statistical analysis

The continuous variables were presented as mean and standard deviation, or median and interquartile range, whenever it is suitable. The categorical variables were presented as absolute numbers and the corresponding percentages in parentheses. For continuous variables, the differences in characteristics between the sexes were detected using a two-sample Student's t test or Mann–Whitney Utest when appropriate, and the  $\chi^2$  test was used for categorical variables. Multiple linear regression of SBP on components of body composition with and without adjustment for age, race/ethnicity and height were conducted in the entire population and subgroups stratified by obesity. Significant multicollinearity among various independent variables was evaluated by variation inflation factor > 10. By this definition, multicollinearity was acceptable in all regression models constructed in the present study. Additionally, dominance analysis (also called relative importance analysis) was performed to quantify the proportionate contribution of each component of body composition (variables reached statistical significance in multiple linear regression models) to SBP, using calc.relimp function in R language.

Considering the significant impact of age and height on BP and body composition of children and adolescents, we adjusted age and body height in the above-mentioned multiple regression models; on the other hand, we also conducted regression analyses using Z-score values of SBP and components of body composition. SBP Z-score and diastolic BP Z-score for different ages and sexes were calculated based on the study by Stavnsbo and collaborators<sup>(16)</sup>. Hypertension was defined as SBP Z-score and/or diastolic BP Z-score  $\geq 1.96$ . The BMI Z-score and height Z-score for different ages and sexes were calculated according to the method provided by the CDC (https://www.cdc.gov/ nccdphp/dnpao/growthcharts/resources/sas.htm). The total fat-free mass Z-score, total fat mass Z-score, trunk fat mass Z-score and leg fat mass Z-score were calculated for each sex, using the lambda-mu-sigma (LMS) method<sup>(17)</sup>.

All analyses were performed separately for boys and girls because of the significant differences in body composition between the sexes. Analyses were performed using SAS software, version 9.4 (SAS Institute) and R 4.1.2 (R Project for Statistical Computing, www.r-project.org). Statistical significance was defined as two-sided P < 0.05.

### Results

# Characteristics of participants

Characteristics of study participants are presented in Table 1. The median age of study participants was 13 years, with interquartile 10·5–15·4 years, and there were 6107 (44·85 %) girls. Girls showed significantly higher BMI (22·2 ± 5·7 v. 21·8 ± 5·6 kg/m<sup>2</sup>, P < 0.001), total fat mass (16·5 (11·7–22·9) v. 12·1 (8·8–19·4) kg, P < 0.001), trunk fat mass (6·2 (4·1–9·5) v. 4·3 (2·9–7·7) kg, P < 0.001) and leg fat mass (7·2 (5·2–9·6) v. 5·3 (3·7–8·2) kg, P < 0.001), but lower total fat-free mass (34·9 ± 9·7 v. 41·6 ± 14·8 kg, P < 0.001), height (152·9 ± 12·2 v. 158·4 ± 16·6 cm, P < 0.001), SBP (104·5 ± 9·4 v. 108·1 ± 10·6 mmHg, P < 0.001) and prevalence of obesity (19·45 v. 22·43 %, P < 0.001) than that of boys.

# Influence of total fat mass and total fat-free mass on systolic blood pressure

Multiple linear regression analyses were conducted to determine the association of SBP with total fat mass and total fat-free mass in boys and girls, respectively, as shown in Table 2. Unadjusted models showed that SBP was significantly determined by both total fat-free mass and total fat mass in both boys and girls. After further adjustment for age, sex, race/ethnicity and height, SBP was still significantly determined by total fat-free mass in both boys ( $\beta = 0.49$ , P < 0.001) and girls ( $\beta = 0.47$ , P < 0.001) and by total fat mass only in boys ( $\beta = 0.12$ , P < 0.001). Subgroup analyses stratified by obesity showed that, in obese boys and girls, total fat-free mass was also the major determinant of SBP, as displayed in Table 3. In all regression models, total fat-free mass had a markedly greater regression coefficient, in contrast to total fat mass. In addition, total muscle mass was also associated with SBP in boys and girls (see online Supplemental Table 55). Similar results were observed when Z-score values were used in the regression analyses, as seen in online supplementary files (see online Supplemental Tables S1 and S2).

# Influence of fat distribution on systolic blood pressure

Multiple linear regressions of SBP on total fat-free mass, trunk fat mass and leg fat mass were conducted to investigate the influence of body fat distribution on SBP in boys and girls, as shown in Table 4 for the entire population and in Table 5 for subgroups. In both boys and girls, SBP was significantly and positively associated with total fat-free mass (boys:  $\beta = 0.50$ , P < 0.001; girls:  $\beta = 0.40$ , P < 0.001) and trunk fat mass (boys:  $\beta = 0.26$ , P < 0.001; girls:  $\beta = 0.15$ , P < 0.001) but negatively associated with leg fat mass (boys:  $\beta = -0.16$ , P < 0.001; girls:  $\beta = -0.10, P < 0.001$ ). Similar associations were observed in both sexes after adjustment for covariates including age, sex, race/ ethnicity and height. Similar results also were observed while analysing the association of total muscle mass with SBP (see online Supplemental Table S6). Subgroup analyses in subjects with and without obesity also obtained consistent trends. Additional analyses using Z-score values showed similar results, as seen in online supplementary files (see online Supplemental Tables **S3** and **S4**).

# Proportionate contribution of each component of body composition to systolic blood pressure

Dominance analysis was performed to quantify the proportionate contribution of each component of body composition to SBP in both sexes. As shown in Fig. 1, among three components, in both boys and girls, total fat-free mass contributed the most to SBP (boys: 49 %; girls: 55·3 %), followed by trunk fat mass (boys:  $32\cdot1$  %; girls: 26·9 %); leg fat mass contributed the least to SBP in boys (18·9 %) and girls (17·8 %).

### Discussion

The accumulation of risk factors for hypertension is far less in childhood and adolescence than that in adulthood, which makes children and adolescents a suitable population for investigating the relationship between body composition and the SBP level. In the present study, based on a large cohort with relatively healthy boys and girls, we showed that fat-free mass was not only significantly associated with SBP but also the most dominant contributor to SBP in American children and adolescents. Additionally, we found a significantly negative relationship between fat mass in the legs and SBP in boys and girls, which is similar to that observed in adults. These findings provide a comprehensive insight in understanding the impact of body composition on SBP variation in childhood and adolescence.

Hypertension is closely related to obesity defined by excess fat mass<sup>(18)</sup>. Thus, previous investigations have been focused on the impact of fat mass on BP, whereas fat-free mass/muscle mass to some extent is neglected, in particular in adults. Indeed, our previous study<sup>(11)</sup> and other researchers' studies<sup>(19-22)</sup> have demonstrated the dominant role of fat mass in determining BP in adults. However, this may not be exactly the case in children and adolescents. The development of the muscular and skeletal systems is a remarkable characteristic of the childhood to adolescence period<sup>(23)</sup>, which may drive an increased metabolic need and lead to an elevation in BP in a dominant manner. Daniels et al. measured the body composition of 201 boys and girls aged 6 to 17 years using a DXA scan and found that only fatfree mass was associated with SBP<sup>(7)</sup>. Similar results were reported by several other studies<sup>(24-26)</sup>, although body composition in these studies was assessed by methodologies based on bioimpedance analysis which was thought less accurate than the gold standardised method (DXA scan)<sup>(27)</sup>. All these studies suggest that fatfree mass may play a dominant role in determining SBP in children and adolescents. In our present study, we investigated a total of 13 618 boys and girls aged from 8 to 17 years with body composition measured by whole-body DXA and quantified the proportionate contributions of components of body composition to SBP. We confirmed that fat-free mass contributed the most to the SBP variation. Inconsistently, Brion et al. indicated that both fat-free mass and fat mass were significantly associated with SBP, but fat mass showed a relatively higher regression coefficient<sup>(10)</sup>. It should be noted that only 9-year-old children were included in Brion et al.'s study, and the comparison on regression coefficients of two mutually related variables derived from the sample

#### Table 1. Characteristics of the study participants

	Тс	otal ( <i>n</i> 13 618)	В	loys ( <i>n</i> 7511)	C	Girls ( <i>n</i> 6107)		
Variables	Median	Interquartile range	Median	Interquartile range	Median	Interquartile range	Р	
Age (year)	13.0	10·5, 15·4	13.0	10.7, 15.5	13.0	10.3, 15.2	0.003	
	п	%	п	%	п	%		
Race/ethnicity							0.039	
Mexican American	3817	28.03	2132	28.39	1685	27.59		
Other Hispanic	895	6.57	489	6.51	406	6.65		
Non-Hispanic White	3669	26.94	1990	26.49	1679	27.49		
Non-Hispanic Black	3954	29.04	2233	29.73	1721	28.18		
Other ethnic groups	1283	9.42	667	8.88	616	10.09		
Obesity	2873	21.10	1685	22.43	1188	19.45	<0.001	
	Mean	SD	Mean	SD	Mean	SD		
BMI (kg/m²)	21.9	5.6	21.8	5.6	22.2	5.7	<0.001	
BMI Z-score	0.60	1.13	0.58	1.18	0.64	1.08	0.008	
Height (cm)	155.9	15.0	158.4	16.6	152.9	12.2	<0.001	
Height Z-score	0.15	1.06	0.20	1.05	0.09	1.07	<0.001	
	Median	Interguartile range	Median	Interquartile range	Median	Interguartile range		
Waist-to-height ratio	0.46	0.43, 0.53	0.45	0.42, 0.52	0.48	0.44, 0.54	<0.001	
	Mean	SD	Mean	SD	Mean	SD		
Total fat-free mass (kg)	38.6	13:2	41.6	14.8	34.9	9.7	<0.001	
Total fat-free mass Z-score	0.004	0.960	0.007	0.968	0.0004	0.951	0.131	
	Median	Interguartile range	Median	Interquartile range	Median	Interguartile range	0.01	
Total fat mass (kg)	14.2	9.7, 21.2	12.1	8.8, 19.4	16.5	11.7, 22.9	<0.001	
rotariat mass (kg)	Mean	SD	Mean	SD	Mean	SD	<0.001	
Total fat mass <i>Z</i> -score	0.049	0.084	0.068	0.806	0.027	0.889	0.005	
	Median	Interguartile range	Median	Interguartile range	Median	Interguartile range	0 000	
Trunk fat mass (kg)	5.2	3.3, 8.6	4.3	2.9, 7.7	6.2	4·1, 9·5	<0.001	
frank lat mass (kg)	Mean	SD	Mean	SD	Mean	SD	<0.001	
Trunk fat mass Z-score	0.070	0.821	0.093	0.761	0.042	0.889	0.001	
	Median	Interguartile range	Median	Interguartile range	Median	Interquartile range	0.001	
Leg fat mass (kg)	6.2	4·2, 8·9	5.3	3·7, 8·2	7.2	5·2, 9·6	<0.001	
Leg lat mass (kg)	Mean	4-2, 8-9 SD	Mean	SD	Mean	5.2, 9.0 SD	<0.001	
Leg fat mass Z-score	0.041	0.912	0.024	0.900	0.062	0.926	0.018	
SBP (mmHq)	106.5	10.2	108.1	10.6	104.5	9.4	<0.018	
SBP Z-score	-0.03	1.02	-0.04	1.01	-0.03	9:4 1:03	<0.001 0.546	
DBP (mmHg)	-0.03 57.8	11.1	-0·04 57·4	11.5	-0.03 58.3	10.5	0·546 <0·001	
( 0)	57·8 0·63	1.34	57·4 0·60	1.28	-0.65	1.38	<0.001 0.020	
DBP, Z-score							0.020	
L hun automations	n	%	n	%	n	%	0.404	
Hypertension	641	4.71	362	4.82	279	4.57	0.491	

SBP, systolic blood pressure; DBP, diastolic blood pressure.

Continuous variables are represented as means ± SD or median (interquartile range), and qualitative parameters are presented as numbers with the percentage in parentheses.

For continuous variables, the differences in characteristics between the sexes were detected using two-sample Student's t test or Mann–Whitney U test when appropriate, and the x<sup>2</sup> test was used for categorical variables.

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### Table 2. The association of SBP with total fat-free mass and total fat mass in boys and girls

		Boys			Girls				
Models	β	Р	R <sup>2</sup>	β	Р	R <sup>2</sup>			
Model 1									
Total fat-free mass (kg)	0.36	<0.001	0.322	0.37	<0.001	0.186			
Total fat mass (kg)	0.11	<0.001		0.06	0.002				
Model 2									
Total fat-free mass (kg)	0.49	<0.001	0.327	0.47	<0.001	0.190			
Total fat mass (kg)	0.12	<0.001		0.03	0.186				

SBP, systolic blood pressure.

Linear regression models were used. Model 1 included total fat-free mass and total fat mass. Model 2 further adjusted for potential covariates including age, race/ethnicity and height.

Table 3. The association of SBP with total fat-free mass and total fat mass stratified by sex and obesity

			Bo	bys			Girls					
	Witho	out obesity (	n 5826)	Obesity ( <i>n</i> 1685)			Without obesity (n 4919)			With obesity (n 1188)		
Independent variables	β	Р	R <sup>2</sup>	β	Р	R <sup>2</sup>	β	Р	R <sup>2</sup>	β	Р	R²
Total fat-free mass (kg) Total fat mass (kg)	0·49 0·07	<0·001 <0·001	0.286	0·48 0·05	<0·001 0·069	0.290	0·41 0·05	<0·001 0·009	0.154	0·57 −0·08	<0·001 0·145	0.173

SBP, systolic blood pressure. Linear regression models were used.

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Model included total fat-free mass, total fat mass, age, race/ethnicity and height.

# Table 4. The association of SBP with fat distribution in boys and girls

		Boys		Girls				
Models	β	$\beta$ P $R^2$		β	Р	R <sup>2</sup>		
Model 1								
Total fat-free mass (kg)	0.50	<0.001		0.40	<0.001			
Trunk fat mass (kg)	0.26	<0.001	0.328	0.15	<0.001	0.189		
Leg fat mass (kg)	-0.16	<0.001		-0.10	<0.001			
Model 2								
Total fat-free mass (kg)	0.44	<0.001		0.44	<0.001			
Trunk fat mass (kg)	0.28	<0.001	0.332	0.15	<0.001	0.192		
Leg fat mass (kg)	-0.14	<0.001		-0.11	<0.001			

SBP, systolic blood pressure.

Linear regression models were used. Model 1 included total fat-free mass, trunk fat mass and leg fat mass.

Model 2 further adjusted for potential covariates including age, race/ethnicity and height.

Table 5. The association of SBP with fat distribution stratified by sex and obesity

			Bo	bys			Girls					
	Withou	ut obesity (n	5826)	With obesity (n 1685)			Without obesity (n 4919)			With obesity (n 1188)		
Independent variables	β	Р	R <sup>2</sup>	β	Р	R <sup>2</sup>	β	Р	R <sup>2</sup>	β	Р	R²
Total fat-free mass (kg) Trunk fat mass (kg) Leg fat mass (kg)	0·45 0·20 −0·11	<0·001 <0·001 <0·001	0.291	0·40 0·30 −0·24	<0·001 <0·001 <0·001	0.306	0·40 0·08 –0·02	<0·001 0·008 0·415	0.155	0·51 0·16 –0·22	<0.001 0.012 <0.001	0.183

SBP, systolic blood pressure.

Linear regression models were used.

Model included total fat-free mass, trunk fat mass, leg fat mass, age, race/ethnicity and height.

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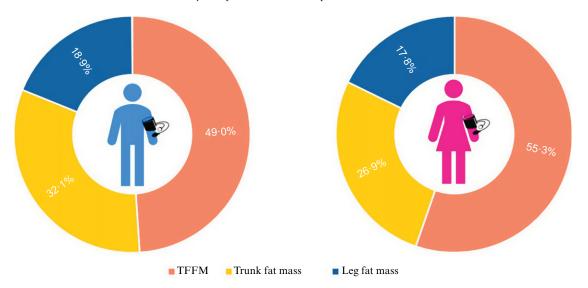


Fig. 1. Proportionate contribution of various components of body composition to SBP in children and adolescents. SBP, systolic blood pressure; TFFM, total fat-free mass.

regression model may not appropriately imply dominance<sup>(28)</sup>. Taken together, incorporating physiological theory and findings from our present study, fat-free mass may dominate the relationship between body composition and SBP in children and adolescents.

In our study, we used the absolute values (rather than the corresponding percentages) of components of body composition in all primary analyses. As well known, the addition of the percentages of total fat mass and fat-free mass is exactly equal to 100%, which means a higher percentage of fat mass (FM %) companied by a relatively lower percentage of fat-free mass (FFM %). Under this circumstance, by simultaneously including both FM % and FFM % into the same regression model, we will observe the opposite impacts of fat mass and fat-free mass on BP, as seen in previous studies (FM % positively and FFM % negatively associated with BP)<sup>(29)</sup>. However, the real situation may be that both fat mass and fatfree mass positively relate to BP, as observed in our study and other previous studies<sup>(7,10)</sup>. Hence, in terms of investigating the impact of the fat mass and fat-free mass on cardiometabolism, we suggest using the absolute values of components of body composition as well as the corresponding Z-score values which were also reported in our study (in supplementary files) and showed consistent results.

It is worthy to note that fat-free mass remained to be the dominant determinant of SBP in the subgroup of obese children and adolescents in our study, which is distinct from that in adults<sup>(11)</sup>. One of the reasons underlying this phenomenon could be the different trends of body composition change between children/adolescents and adults. Lean mass increases dramatically in childhood and adolescence<sup>(6,9)</sup>; however, in adults (especially overweight and obese), lean mass increases slightly or even decreases with ageing, whereas fat mass accumulates significantly<sup>(30,31)</sup>. Additionally, on the basis of this phenomenon, we speculate that the accumulation of adipose tissue dysfunction in children and adolescents may be less than that in adults. Future investigations are warranted to verify this speculation.

In most studies examining the association between fat mass and BP, total fat mass was often included in the analysing models and considered as a whole. However, recent investigations have demonstrated that adipose tissue in various depots possesses different effects on body metabolisms<sup>(11,12,32,33)</sup>. For instance, fat mass in the trunk and legs had the opposite impact on the BP level in adults<sup>(11-14)</sup>. Under this circumstance, the association between SBP and total fat mass could be attenuated by the counteraction between trunk fat mass and leg fat mass in relation to SBP. In our study, when both fat-free mass and total fat mass were included in regression models, total fat mass was not significantly associated with SBP in girls after adjustment for other covariates. However, when total fat mass was broken down into fat mass in the trunk and legs, both trunk fat mass and leg fat mass were significantly associated with SBP in all models. Thus, in future studies, in particular longitudinal cohort studies focusing on the association between fat accumulation and cardiometabolic profile, total fat mass should be broken down into various parts according to their distinct clinical and biological effects.

Many studies have reported the negative association between fat mass in the legs (also referred to as peripheral fat tissue) and BP in adults<sup>(11-14)</sup>. In the present study with a focus on children and adolescents, we found similar results, indicating that the protective effect of peripheral adipose tissue is across ages. However, the biological mechanisms underlying the beneficial role of adipose tissue distribution in the legs are not fully understood. It was reported that adipocytes located in peripheral regions are less sensitive to factors stimulating lipolysis and have a lower lipolysis rate than adipose tissue in central regions<sup>(34,35)</sup>. Compared with abdominal subcutaneous fat, leg subcutaneous adipose tissue has shown less sensitivity to lipotoxicity due to dysregulated release of free fatty acids<sup>(36)</sup>. Adipose tissue in the lower body is also capable of recruiting additional adipocytes in response to weight gain and displays fewer signs of inflammation<sup>(37)</sup>. More biological studies (e.g. lipidome profiling of adipose

tissues in various parts) are needed to reveal the underlying mechanisms of the protective effect of peripheral adipose tissue in human cardiometabolism.

The results presented in the current study should be interpreted under their limitations. First, we were not able to infer causality between components of body composition and the SBP variation due to the cross-sectional nature of our study. Second, diet and exercise have an important impact on BP; however, these factors were not included in our analysis due to a lack of corresponding data. Third, in our study, we did not break down trunk fat mass into subcutaneous fat and visceral fat mass, whereas subcutaneous fat in the trunk was reported not associated with incident hypertension<sup>(19)</sup>. Lastly, the data collection was from 1999 to 2018 and the Z-scores for BMI, height and weight were based on CDC 2000 reference, and this may cause some bias in the *Z*-scores we calculated. Future studies overcoming these drawbacks are needed to further confirm our findings.

To conclude, our study demonstrated that fat-free mass was the dominant factor among the components of body composition in determining SBP in children and adolescents, although both fat-free mass and total fat mass were significantly associated with SBP. Also, we found a negative association between SBP and leg fat mass, which suggested that fat tissue in the legs may play a protective role in the cardiometabolism of children and adolescents. These findings imply that the impact of fat-free mass should not be neglected in understanding the mechanisms of BP elevation and in preventing hypertension in children and adolescents.

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S. Y. and S. Z. conceived the idea, curated the data, formulated and performed the data analysis, interpreted the results, and drafted and revised the manuscript. J. T., Y. Z., C. X. and M. L. interpreted the data and reviewed the manuscript. Y. X. and Y. Z. reviewed and revised the manuscript.

The authors declare that there is no potential conflict of interest.

#### Supplementary material

For supplementary material/s referred to in this article, please visit https://doi.org/10.1017/S0007114523002131

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