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RESEARCH PAPER

## Association between maternal education and blood pressure: mediation evidence through height components in the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil)

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### ABSTRACT

**Background:** Maternal education influences skeletal growth and offspring adult blood pressure (BP). Height components are negatively associated with BP in high-income countries.

**Aim:** To evaluate the association between maternal education and offspring adult systolic and diastolic BP (SBP/DBP), assessing whether different height components might mediate such an association.

**Subjects and methods:** Simple mediation modelling was used to evaluate the maternal education-offspring SBP/DBP association, estimating the contribution of offspring height components, in a cross-sectional sample of 13 571 Brazilians aged 34–75 from the ELSA-Brasil study.

**Results:** After full adjustment for confounders, and compared to participants whose mothers received low education, those whose mothers received high education had, on average, 0.2 mm Hg lower SBP (95% CI = -0.274, -0.132), as result of the link between maternal education and offspring adult height which, in turn, influenced SBP. Thus, 18–26% of the maternal education-SBP association occurred indirectly, through height, trunk and leg length, alternatively.

**Conclusions:** Better maternal education might influence higher leg and trunk lengths in offspring, which, in turn, might contribute to prevent higher BP in adults. The negative height-BP association reported in high-income countries is also present in a middle-income country with more recent economic development.

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### Introduction

Maternal education is a marker of early socio-economic status that has been shown to influence both offspring skeletal growth (Frost et al., 2005; Howe et al., 2012; Silva et al., 2013) and offspring blood pressure (BP) (Bouthoorn et al., 2014; van den Berg et al., 2013) in later life. Thus, maternal education may have an impact on both the early somatic growth of the descendants and the physiological development of their arterial structure and function (Bouthoorn et al., 2014). Therefore, understanding the relationship between early socio-economic conditions and offspring adult chronic non-communicable diseases is important, although the pathways through which maternal education influences offspring adult BP remain to be elucidated.

On the one hand, maternal education has been found to be associated with height components of the descendants, especially leg length (Gigante et al., 2009; Matijasevich et al., 2012). Leg length is a more sensitive marker of pre-pubertal growth (Davey Smith et al., 2001; Li et al., 2007), and it is likely to be more affected by socioeconomic status and nutrition in childhood than, for example, trunk length (Bogin &

Varela-Silva, 2010; Wadsworth et al., 2002). On the other hand, a broad body of evidence has described the associations between height components and adult BP at the individual level (Langenberg et al., 2003; Lawlor et al., 2004a), although the reasons and causal mechanisms for why shortness influences high BP remain largely unknown (Langenberg et al., 2003). In adults, while shorter leg length has been associated with higher BP (Davey Smith et al., 2001; Gunnell et al., 2003; Langenberg et al., 2005), there is a null or weak inverse association between trunk length and BP.

Most previous studies on the components of height-BP association were restricted to Western Europe and North America (Langenberg et al., 2003; Lawlor et al., 2004b). Longitudinal evidence from high-income countries indicates that better childhood conditions—mainly inferred from height and leg length—are usually protective against high BP (Hardy et al., 2004; Langenberg et al., 2003, 2005). However, this pattern has not been clearly observed in low- and middle-income countries or in locations where economic development is more recent. Short stature was associated with higher risk of hypertension in Brazilian adults (Sichieri et al., 2000), while other studies found little relation between height

components and adult BP in China (Schooling et al., 2007) and no association was observed between adult height and hypertension in Nigeria (Olatunbosun & Bella, 2000).

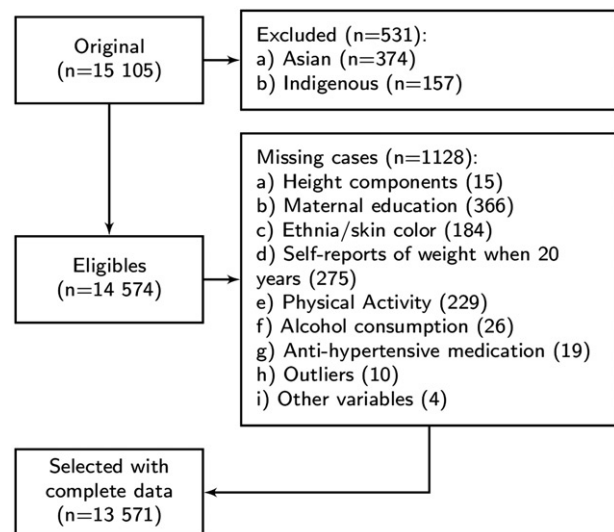
It is likely that individual early life—including pre-natal—exposures might also have been different in these transitioning countries. Evaluating their association with BP in adulthood is relevant, given that there is evidence of an early origin of the socioeconomic inequalities in BP being already present in childhood (Bouthoorn et al., 2014; Howe et al., 2012; van den Berg et al., 2013). Moreover, testing the negative associations between height components and BP within an individual level observed in Europe and North America is especially important in demographic transitioning populations (Schooling et al., 2007). Despite recent socioeconomic improvements, the greater exposure to adverse conditions during pregnancy and childhood of most Brazilians in the 20th century makes them quite different from populations of high-income countries (Araujo et al., 2014).

Within this context, we aim to evaluate the association between maternal education and offspring adult systolic/diastolic blood pressure (SBP/DBP), and to assess whether offspring height components might mediate such associations in ELSA-Brasil study participants. We hypothesise that higher maternal education is associated with higher height in offspring adults which, in turn, influences lower offspring BP. The Brazilian Longitudinal Study of Adult Health (ELSA-Brasil) is a unique opportunity to address these questions in a middle-income country like Brazil, within the largest Latin American cohort population.

## Methods

### Study recruitment and participants

ELSA-Brasil addresses the incidence of cardiovascular diseases and major associated risk factors; the design and preliminary findings of this study are available elsewhere (Aquino et al., 2012; Lotufo, 2013; Schmidt et al., 2015). Briefly, 15 105 civil servants aged 35–74 years from six cities in Brazil (Belo Horizonte, Porto Alegre, Rio de Janeiro, Salvador, São Paulo and Vitoria) were enrolled between August 2008 and December 2010 for baseline examination. Since then, all participants have reported potential health-adverse outcomes (e.g. occurrence of stroke, heart attack, diabetes, etc.) in standardised telephone interviews. The second wave of interviews began in September 2012 and ended in December 2014. All six participating centres approved the ELSA-Brasil protocol and all participants granted informed consent (Lotufo, 2013). From the original 15 105 participants and after excluding individuals with missing data for maternal education, components of adult height, and other variables such as physical activity, alcohol consumption, use of anti-hypertensive medication, among others (Figure 1), our study population finally included 13 571 subjects with complete data (mean (SD) age = 51.9 (9.0); 54.7% women). Non-selected participants ( $n = 1534$ ) tend to be older (54.3 vs 51.9 years), less educated, have higher SBP, and shorter trunks and legs (data not shown). Asian and individuals of indigenous origin were



**Figure 1.** Sample selection: The ELSA-Brasil cohort study, baseline data (2008–2010). Flow chart describing the final sample ( $n = 13\,571$ ), obtained after exclusion of participants.

not included in the sample due to the relatively small number of participants.

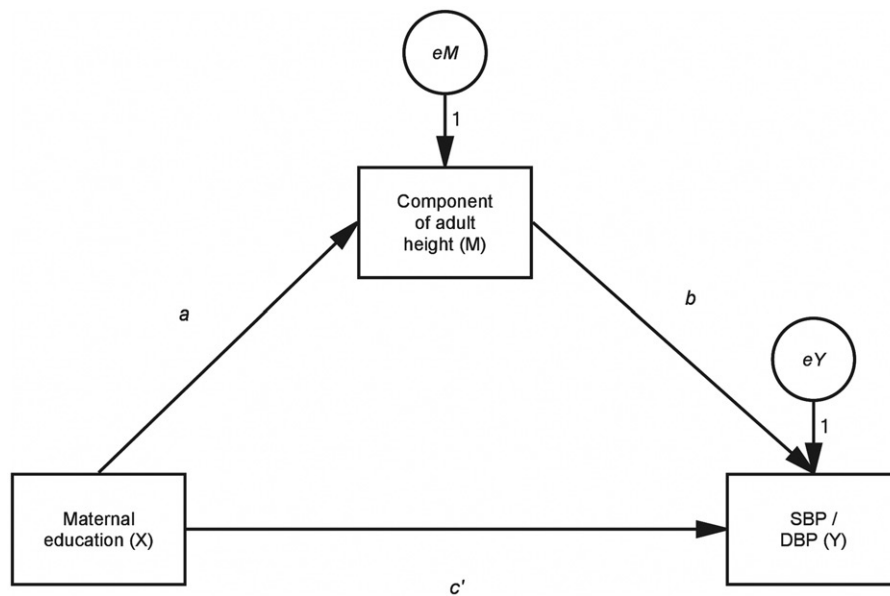
## Variables

### Early life exposure

Maternal education was used as a proxy of socioeconomic circumstances early in life. Maternal education is considered an indicator of early life exposures, affecting post-natal growth (Silva et al., 2013; Wadsworth et al., 2002) and BP (Bouthoorn et al., 2014). Maternal education was originally defined as superior complete, high school complete, primary complete and primary incomplete or less. However, only a small proportion (6.5%) of participants have mothers with a university degree and about half of them never attended or did not complete elementary school (Aquino et al., 2012). Therefore, and in order to avoid problems related to unbalanced categories, we decided to use a broader indicator of maternal education. Despite dichotomisation often indicating a lack of information, we used maternal education as a binary variable with 1 = high (superior and high school complete) and 0 = low (primary complete/incomplete or less) maternal education.

### Height components

Total height and its components have been shown to be indicators of early life conditions (Wadsworth et al., 2002) and determinants of adult BP (Hardy et al., 2004; Lawlor et al., 2004a). Adult height (cm) and trunk length (sitting height) (cm) were assessed directly. Leg length (cm) was obtained by subtracting trunk length from height. All anthropometric parameters—including waist circumference and weight—were measured using standard equipment and techniques (NHANES, 2007) by trained personnel, who were also in charge of the standardisation and certification of the measures (Lohman et al., 1988).



**Figure 2.** Conceptual simple mediation model for estimating the direct association between maternal education and adult blood pressure and the indirect mediating association through height components (total height/trunk length/leg length), alternatively. ELSA-Brasil, 2008–2010. SBP: systolic blood pressure; DBP: diastolic blood pressure; X: independent variable/exposure; Y: dependent variable; M: mediators;  $c'$ : direct association;  $axb$ : indirect association; total association = direct + indirect.

### Outcomes

We evaluated two outcomes: SBP and DBP (mm Hg). Resting BP was taken using a validated certified oscillometric device (Omron HEM 705CPINT) after a 5-minute rest with the subject in a sitting position in a quiet, temperature controlled room (20–24 °C) (O'Brien et al., 1996). Three measurements were taken at 1-minute intervals and the average of the second and third measurements were used in the analyses (Aquino et al., 2012). Reliability coefficient estimated by bootstrap techniques taken during the same visit for SBP was 0.883; 95% confidence interval (CI) = 0.823, 0.907.

### Confounders

We included a variety of confounding factors in the analysis, in order to account for the correlation existing among adult socioeconomic status, health risk behaviours and other cardiovascular disease risk factors, with both the exposure and outcome. Own education, self-reported ethnic group/skin colour, waist circumference (cm) (reliability coefficients = 0.995; 95% CI = 0.991, 0.996) and weight change (kg) since age 20—based on self-reports of the weight when 20 years-old and measured current weight, were included. Weight and all other anthropometric measurements were taken following standard techniques (Lohman et al., 1988). We decided not to consider body mass index, since it has been suggested that the strong correlation between standard waist circumference and body mass index does not allow assessment of their relative contributions to health in the same model without a risk of making erroneous estimations (Ngueta et al., 2014). Moreover, smoking status and alcohol consumption were both defined as (1) never or (2) ex- or current-consumer/smoker. Physical activity was measured using the long version of the International Physical Activity Questionnaire (IPAQ, 2005), an instrument for cross-national monitoring of physical activity and inactivity (Craig et al., 2003). All interviews were done by trained nurses

under strict quality control. Physical activity was grouped by (1) low and (2) moderate or vigorous. Finally, we included the use of anti-hypertensive medication (when treated with medication during the past 2 weeks).

Blood pressure and all anthropometric indicators were assessed by trained nurses in the six research centres under strict quality control. All training processes were centralised in the research centre of São Paulo. All staff were certificated before the beginning of data collection and regularly re-certificated twice a year. Each research centre also had a supervisor responsible for the quality and control of all BP and anthropometric proceedings. The quality control Committee made unexpected visits to all centres to check proceedings *in loco*. All study routines were published in 2013 (Bensenor et al., 2013; Mill et al., 2013; Schmidt et al., 2013).

### Statistical analysis

Simple mediation modelling was conducted to estimate the total, direct and indirect associations (total = direct + indirect) between maternal education and adult BP. While the direct association involved the maternal education–BP relationship, the indirect path included such an association via the proposed mediators, height components—total height, trunk length and leg length, alternatively. Therefore, the indirect associations were obtained by multiplying two regression coefficients: the coefficient when maternal education was the exposure and a height component, the outcome; and the coefficient when a height component was the exposure and SBP/DBP the outcomes. Figure 2 describes the conceptual simple mediation model for the mentioned associations.

Rather than hypothesising only a direct causal relationship between maternal education and BP, the use of a simple mediational model allowed us to test the hypothesis that

maternal education was associated to offspring adult height and its components (mediators), which in turn influenced BP (Hayes, 2013). The mediator variable then serves to clarify the nature of the relationship between maternal education and BP (MacKinnon, 2008; Valeri & VanderWeele, 2013). Thus, the mediation analysis proposed by Hayes (2013) is an adequate alternative to test mediation and our associational hypothesis. The modern path modelling approach that we applied here (Hayes, 2013) has three major advantages over the traditional approach to testing mediation (Baron & Kenny, 1986). First, the capacity to determine whether there is a significant indirect 'effect' (association) and quantify it; second, the application of a non-parametric bootstrapping mediation method to determine the significance of direct and indirect associations between variables (this is beneficial because it better respects the irregularity of the sampling distribution of the indirect association); and, third, the application of a more powerful approach to conducting inferential statistics (see Hayes, 2013).

Mediation modelling involved ordinary least squares path analysis using the 'PROCESS' tool for SPSS (version 21) (Hayes, 2013). Results were derived from 1000 bootstrapped samples, obtaining unstandardised regression coefficients, heteroscedastic-consistent standard errors and bias-corrected 95% CI. We found non-significant interactions for sex in the maternal education–BP association mediated by height components. Therefore, we assumed that the potential benefit 'effect' of high maternal education on lower BP is similar for men and women and, consequently, we present sex-adjusted rather than sex-stratified analysis. Two models were presented in which SBP and DBP were the outcomes and height components, entered alternatively as continuous sex-specific SD scaled variables, were the potential mediators. Each model has three different versions, depending on the proposed mediator considered (total height, trunk length and leg length). Unadjusted associations were not included for simplification. Model 1 summarised the maternal education–SBP/DBP associations, mediated by height components, and adjusted by age, sex, ethnicity and use of anti-hypertensive medication. Model 2 added control for own education, waist circumference, weight change since aged 20, smoking status, alcohol consumption and physical activity to Model 1. Comparing Models 1 and 2 allowed the estimation of the contribution of adult socioeconomic status, health risk behaviours and other cardiovascular disease risk factors to the described associations.

Additionally, the ratio of indirect to total associations for each height component—a measure of effect size (MacKinnon et al., 1995)—was calculated in order to estimate how much of the maternal education–SBP occurred indirectly. The closer this ratio is to one, the more of the maternal education–BP association can be said to operate through height components; the closer the ratio is to zero, the less the maternal education–BP relationship is due to an indirect process through height components (Hayes, 2013).

Finally, we performed a sensitivity analysis excluding participants above 60 years-old, in order to reduce the bias of older individuals who are shorter and have higher levels of SBP.

**Table 1.** Characteristics of the study population by height components. ELSA-Brasil, 2008–2010 ( $n = 13\ 571$ ).

	%/mean (SD)	Height component, mean (cm)		
		Height	Trunk length	Leg length
<i>Maternal education</i>				
Superior complete	6.6	168.3	89.6	78.7
High school complete	17.6	167.2	88.8	78.4
Primary complete	19.3	165.4	87.8	77.6
Primary incomplete or less	56.4	164.0	86.9	77.0
<i>Age groups (years)</i>				
35–44	22.6	167.3	89.0	78.4
45–54	39.9	165.6	88.0	77.5
55–64	27.7	163.5	86.6	76.9
65–74	9.8	162.8	85.7	77.1
<i>Ethnic group/skin colour</i>				
White	54.8	165.8	88.3	77.5
Brown ('Pardos')	28.9	164.5	87.3	77.2
Black	16.4	164.0	86.0	78.0
<i>Own education</i>				
Superior complete	53.7	166.1	88.3	77.8
High school complete	34.8	164.1	87.0	77.0
Primary complete	6.4	163.9	86.5	77.4
Primary incomplete or less	5.1	163.0	85.8	77.2
<i>Waist circumference (cm)</i>	91.2 (12.8)	–	–	–
<i>Weight change (Kg)*</i>	15.7 (12.2)	–	–	–
<i>Smoking status</i>				
Never	57.2	164.6	87.4	77.2
Ex-smoker	29.9	165.8	88.0	77.8
Current	12.9	165.6	87.8	77.8
<i>Alcohol consumption</i>				
Never	10.3	160.3	85.2	75.2
Ex-consumer	19.9	164.1	87.0	77.0
Current	69.8	166.1	88.1	78.0
<i>Physical activity†</i>				
Low	54.9	164.4	87.2	77.1
Moderate	35.2	165.6	87.9	77.7
Vigorous	9.9	167.6	88.9	78.7
<i>Anti-hypertensive medication</i>				
No	71.2	165.4	87.8	77.6
Yes	28.9	164.4	87.1	77.2

SD: standard deviation.

\*Based on self-reports of weight when 20 years old and actual measured weight.

†Derived from the International Physical Activity Questionnaire (IPAQ).

## Results

### Descriptive analysis

Table 1 shows the sample characteristics by height components. More than half of the participants have mothers with primary incomplete or lower education; they have shorter trunks and legs compared to those with a higher educational maternal background. Younger individuals are taller and have longer trunks. Moreover, white individuals have longer trunks but shorter legs than black participants. More than half of the participants have superior studies (they are taller and have longer trunks than those with lower educational attainment), revealing an educational gradient in the anthropometric indicators.

Table 2 shows the Pearson correlations among height components and SBP/DBP. All height components were significantly and negatively correlated to SBP and DBP, except for trunk length–DBP in men (Table 2).



**Table 2.** Correlation matrix between blood pressure and total height, trunk and leg lengths ELSA-Brasil, 2008–2010 ( $n = 13\ 571$ ).

Blood pressure (mm Hg)	Height		Trunk length		Leg length	
	Men	Women	Men	Women	Men	Women
SBP	−0.126	−0.157	−0.147	−0.174	−0.072	−0.096
<i>p</i> -value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
DBP	−0.043	−0.074	−0.013	−0.039	−0.055	−0.082
<i>p</i> -value	<0.01	<0.001	0.312	<0.001	<0.001	<0.001

SBP: systolic blood pressure; DBP: diastolic blood pressure; *p*-value for Pearson correlations.

**Table 3.** Simple mediation models on the total, direct, and indirect associations between maternal education and systolic blood pressure. Unstandardised regression coefficients for systolic blood pressure are shown. Indirect associations include the mediation through height, trunk, and leg length, alternatively; ELSA-Brasil, 2008–2010 ( $n = 13\ 571$ ).

Model	Direct association		Indirect association		Total association	
	Coef.	95% CI	Coef.	95% CI	Coef.	95% CI
<i>Height</i>						
Model 1	−1.669	−2.289, −1.049	−0.277	−0.379, −0.191	−1.946	−2.561, −1.332
Model 2	−0.556	−1.183, 0.072	−0.196	−0.274, −0.132	−0.752	−1.377, −0.126
<i>Trunk length</i>						
Model 1	−1.792	−2.412, −1.171	−0.154	−0.251, −0.062	−1.946	−2.561, −1.332
Model 2	−0.618	−1.246, 0.010	−0.134	−0.198, −0.079	−0.752	−1.377, −0.126
<i>Leg length</i>						
Model 1	−1.730	−2.348, −1.113	−0.216	−0.294, −0.147	−1.946	−2.561, −1.332
Model 2	−0.614	−1.240, 0.012	−0.138	−0.199, −0.088	−0.752	−1.377, −0.126

Exposure: 1 = high maternal education vs 0 = low maternal education; Outcome: Systolic blood pressure; Model 1 included adjustment for age, sex, ethnicity and use of anti-hypertensive medication; Model 2 additionally included own education, smoking and alcohol status, physical activity, waist circumference and change of weight since when 20 years old to Model 1; indirect association = association between maternal education and systolic blood pressure through height components, alternatively; total association = direct + indirect;  $\beta$ : estimated regression coefficient; CI: confidence interval.

### Simple mediation modelling

Table 3 shows the results for the simple mediation models, estimating the association between maternal education and adult SBP directly, as well as indirectly, through different height components, alternatively. Model 1 shows such associations adjusted for age, sex, ethnicity, and use of hypertensive medication. In the direct association participants whose mothers had high maternal education show significantly lower SBP than those whose mothers had low education (when height is the mediator:  $\beta = -1.669$ , 95% CI =  $-2.289, -1.049$ ; when trunk length is included:  $\beta = -1.792$ , 95% CI =  $-2.412, -1.171$ ; when leg length is included:  $\beta = -1.730$ , 95% CI =  $-2.348, -1.113$ ). However, there is a significant indirect relationship between maternal education and SBP through total height ( $\beta = -0.277$ , 95% CI =  $-0.379, -0.191$ ), trunk length ( $\beta = -0.154$ , 95% CI =  $-0.251, -0.062$ ) and leg length ( $\beta = -0.216$ , 95% CI =  $-0.294, -0.147$ ) respectively; i.e. high maternal education is associated with higher height and longer trunks and legs, which are associated with lower SBP.

After controlling for all confounders in the fully adjusted models (Models 2, Table 3)—including own education, waist circumference, weight change since aged 20, smoking status, alcohol consumption and physical activity—the direct associations between maternal education and SBP are no longer significant. However, the single mediating paths through the different height components of the maternal education–SBP association remain significant to the control for confounding factors: the indirect associations are somehow attenuated but remain statistically significant (for total height,  $\beta = -0.196$ , 95% CI =  $-0.274, -0.132$ ; for trunk length,  $\beta = -0.134$ , 95% CI =  $-0.198, -0.079$ ; for leg length,  $\beta = -0.138$ , 95%

CI =  $-0.199, -0.088$ , alternatively). So, after full adjustment and relative to those with low educated mothers, those participants whose mothers had high level of education have, on average, 0.2 mm Hg lower SBP (95% CI =  $-0.274, -0.132$ ), as as a result of link between maternal education and height, which, in turn, influences SBP. Moreover, the ratio of indirect to total associations for different height components (Table 4) ranges between 0.178 for trunk length and 0.261 for total height, indicating that, after full adjustment, 18–26% of the association between maternal education and SBP occurs indirectly. Furthermore, higher height and longer trunks and legs are associated with lower SBP.

Similar results are found for DBP (data not shown). In the fully adjusted model, while the direct associations are no longer significant, the indirect maternal education–DBP relationships through height and leg length, alternatively, remain significant. Moreover, when excluding participants above 60 years-old, we found small attenuations of the indirect maternal education–BP associations (i.e. lower mediation by height components), although the associations remain significant, except for trunk length in DBP (see S-Table 1 in ‘Supplementary information’).

### Discussion

We found evidence of single indirect mediating paths—through total height, leg and trunk lengths, alternatively—for the association between maternal education and SBP/DBP. Relative to those participants whose mothers received low education, those whose mothers had a high educational level have, on average, 0.2 mm Hg lower SBP, as a result of a link between high maternal education and higher offspring adult

**Table 4.** Ratio of the indirect to total associations between maternal education and systolic blood pressure in the fully adjusted model (Model 2). Indirect associations represent the mediation through height, trunk and leg length, alternatively; ELSA-Brasil, 2008–2010 ( $n = 13\,571$ ).

Height component	Indirect association, Coef (95% CI)	Total association, Coef (95% CI)	Ratio (indirect/total)
Height	−0.196 (−0.274, −0.132)	−0.752 (−1.377, −0.126)	0.260
Trunk length	−0.134 (−0.198, −0.079)	−0.752 (−1.377, −0.126)	0.178
Leg length	−0.138 (−0.199, −0.088)	−0.752 (−1.377, −0.126)	0.184

Total association = direct + indirect association; Coef.: estimated regression coefficient; CI: confidence interval; Model 2: adjustments included age, sex, ethnicity, use of anti-hypertensive medication, own education, smoking and alcohol status, physical activity, waist circumference and change of weight since when 20 years old; Exposure: 1 = high maternal education vs 0 = low maternal education; Outcome: systolic blood pressure.

height/longer trunk and legs, which in turn, might influence lower offspring SBP. After full adjustment, 18–26% of the maternal education–SBP association occurs indirectly through different height components (~18% through trunk and leg lengths and 26% through total height), independent of own education and current health risk health behaviours.

Previous research has shown that children who grow up under adverse socioeconomic circumstances are also at higher risk of hypertension and this effect may be independent of their adult socioeconomic position (Langenberg et al., 2003). Similarly, the low maternal education–high offspring BP association was recently described in Brazilian adolescents (Silva et al., 2013). However, we found that the maternal education–offspring BP direct association observed in the partially adjusted model is attenuated to non-significant values after full adjustment, which included own education and health risk behaviours. There is a large body of evidence of education affecting health-related behaviours such as smoking decisions (Jürges et al., 2011), obesity (Webbink et al., 2010) and exercise (Park & Kang, 2008). This might lead to the suggestion that the particularly high educational level in our study population (more than 50% of our participants have superior education) may have contributed to overcome the negative influence of low maternal education on offspring adult BP; i.e. in addition to the 18–26% of the maternal education–SBP association explained by height components, other factors such as the development of health-related behaviours, socioeconomic status and psycho-social skills when coping with stress might explain the maternal education–SBP association.

Although indirectly, the mediation process through height components could be partially explained by physiological mechanisms related to adult height and high BP, as described in other studies (Langenberg et al., 2003; Smulyan et al., 1998). Furthermore, Langenberg et al. (2005) have shown that short people may be more susceptible to the effects of ageing on the arterial tree: compared to taller participants, a 10-year increment in SBP was greater in those individuals whose legs were shorter; the effects of both height and leg length on high SBP became significantly stronger with age (Langenberg et al., 2005). We found a similar influence of age on SBP (see S-Table 1 in 'Supplementary information'). One of the main reasons for distinguishing between the associations of each height component with BP is that the former are supposed to be differently affected by early life conditions (Bogin & Varela-Silva, 2010). Studies have reported that leg length is a more sensitive marker of pre-pubertal growth—mainly in high income countries (Li et al., 2007)—and one that would

be expected to be more affected by nutrition and socioeconomic status in childhood than, for example, trunk length, which changes mainly during post-puberty. However, and as previously reported in a Brazilian cohort of young males (Gigante et al., 2009), we did not find clear distinctive effects of maternal education on leg and trunk lengths, since all height components were significantly and negatively associated with maternal education.

The little or no relation between height and BP risk reported in low-income (Olatunbosun & Bella, 2000) and recent economically developed populations (Schooling et al., 2007, 2008) is not observed in our study. In contrast, we found a significant inverse association between components of height and adult BP, which is consistent with most findings from the US and European populations (Langenberg et al., 2003, 2005) and with previously reported results for Brazil (Sichieri et al., 2000). Previous studies in Brazilian children living in metropolitan areas showed that the height deficit in Brazil was corrected in recent years (Figueiroa et al., 2012), as well as the prevalence of malnutrition in adults that is now very low (Batista Filho & Rissin, 2003). Both data give support to the similarity of our results with the data of high-income countries. Additionally, similarities with high-income countries might be due to the ELSA-Brasil sample selection strategy, which somehow limits the investigation into the domains of the extremely poor and unemployed individuals (Schmidt et al., 2015). Indeed, ELSA-Brasil participants have higher monthly income than the general population in Brazil. These features may moderate the effect of the relatively recent demographic and epidemiological transitions in Brazil. Consequently, the height-BP association may be 'under-estimated' and might not be fully extrapolated to the middle-age and older Brazilian population. In other words, the sample might have under-estimated the results because the height difference would be larger for the population as a whole. In this sense, the excluded participants—who are older, less educated, have higher SBP, shorter trunks and legs—might characterise part of the social strata not represented in our study, and would have probably stronger associations with cardiovascular health disease and associated risk factors.

The maternal education–offspring BP association described in the present study occurred within the context of adiposity and health transition in Brazil. As expected, we found a positive relationship between offspring adult waist circumference and weight gain since age 20 with offspring SBP (see S-Table 2 in 'Supplementary information'). One SD in waist circumference (11.9 cm in men and 12.6 cm in women)

and one SD in weight gain (increments of 12.5 kg in men and 12.0 kg in women) were associated with 1.8 and 0.8 mm Hg higher SBP, respectively. This highlighted the relevance of understanding our findings within the existing health situation and that our results are not independent of the current epidemiological situation in Brazil.

In our study, the differences in height components between younger and older participants might be mainly due to secular trends (Castilho & Lahr, 2001). A cohort effect on stature—cohort improvement in early nutrition, with a reduction of stunting in recent cohorts (Schooling et al., 2008)—might be observed through an age-gradient in components of height. In this sense, an inter-generational increase in stature has been reported in Brazil (Sichieri et al., 2000) as in other populations with a recent history of economic development (Leung et al., 1996). It, thus, appears that a significant portion of the secular increase in standing height is accounted for by leg length (Malina et al., 2004). Thus, the increase in height from one generation to the next occurs mainly in the first 2 years of life, due to increases in leg length (Cole, 2003). Although less important due to our relatively young cohort, there may be an age-related osteoporosis decline (MacLaughlin et al., 2006). Evidence for Brazil suggests that the shrinkage with age by loss of bone by osteoporosis, which mainly affects trunk length, is similar to other Latin American countries and some regions of Europe (Clark et al., 2009). Finally, we cannot forget the potential impact of selective mortality, which is higher at older ages.

Older people in ELSA-Brasil are shorter and have higher levels of SBP. In order to eliminate the potential bias of older participants to be more exposed than younger individuals, we performed a sensitivity analysis excluding participants above 60 years-old (S-Table 1; 'Supplementary information'). Compared to our main findings, we observed lower mediation by height components in the maternal education–BP associations. This suggests that our findings are replicable at younger ages, although for men above 60 years-old the observed associations may be somehow over-estimated. This must be taken into account in further studies comprising older people.

### **Limitations and potential bias**

This study has some limitations that must be taken into account when interpreting our findings. The use of indirect estimations of leg length by subtracting trunk length to total height is a drawback in our study. This practice, although widely accepted due to the difficulty of measuring anatomical leg length in living human beings, can lead to bias, especially in high body fat populations (Bogin & Varela-Silva, 2010). Thus, it is likely that, in our sample—where 40% of participants are overweight and 23% obese—the accumulation of buttock fat (gluteo-femoral fat) may under-estimate and obscure accurate estimations of leg length by increasing sitting height (Bogin & Varela-Silva, 2008). This implies the existence of measurement errors in trunk length due to variability in buttock fat in our sample. Consequently, this somehow limits the scope of analysis for the relative importance of

maternal education on the growth of different height components and on BP. Moreover, maternal education might not be fully representative of the socioeconomic conditions in Brazil during the period in which participants grew-up. Although parental education has been largely shown to be an important predictor of later life health (Myrskylä et al., 2014), the use of a family income indicator would have probably been more indicative, since it has been suggested that income is the main correlate of Brazilian population heights in the second half of the 20th century (de Oliveira & Quintana-Domeque, 2014). An additional indicator of pre-natal exposures such as self-reports of birth weight was originally considered. However, its subjective nature, the high number of non-responses—15% of the sample—and that the birth weight–BP associations were weaker than those for maternal education, prevented us from including it in the analysis. Furthermore, the use of anti-hypertensive medication was associated with both maternal education and BP, but not with height components, and this might be an issue when estimating the height component–BP association. We performed a sensitivity analysis (data not shown) without adjusting for anti-hypertensive medication and, while we got similar results for the indirect association, the total 'effect' of maternal education on SBP was stronger, and the direct 'effect' of maternal education on SBP remained significant—for all height components—after full adjustment. The differences observed for the direct associations suggest that adjusting for the use of anti-hypertensive medication is appropriate. We consider this a better option rather than under-estimating or not detecting high BP levels in those participants who use medication.

As previously highlighted, findings from ELSA-Brasil are not fully extrapolated to the middle-age and older Brazilian population due to their higher socioeconomic background. The difference in SBP in low vs high maternal education is relatively small (0.2 mm Hg) and, therefore, vulnerable to even small degrees of residual confounding. This association is somehow attenuated in our study and might be stronger when considering individuals from a lower socioeconomic background. However, and given the described limitations, the use of simple mediation analysis to test our hypothesis has been shown to be a proper approach to estimate cross-sectional associations and make our findings stronger.

In summary, we found single indirect mediating paths including, alternatively, total height, leg, and trunk lengths for the association between maternal education and SBP (high maternal education associated to higher height/longer trunks and lengths in offspring, related to lower offspring BP). Furthermore, 18–26% of the maternal education–SBP association occurs indirectly, through different height components, and such associations are independent of adult socioeconomic status, health risk behaviours, and other cardiovascular disease risk factors. Additionally, and despite the described limitations, our data suggest that the relatively strong and negative height–BP association reported in high-income countries is also present in a middle-income country with more recent economic development, probably due to the relatively advanced epidemiologic transition in Brazil. Our findings add considerations to previous evidence



suggesting that better maternal education might influence higher height in offspring which in turn contributes to preventing higher BP in adults.

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## Disclosure statement

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