

## Original Article

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# Early-life exposures and cardiovascular disease risk among Ghanaian migrant and home populations: the RODAM study

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## Abstract

Early-life environmental and nutritional exposures are considered to contribute to the differences in cardiovascular disease (CVD) burden. Among sub-Saharan African populations, the association between markers of early-life exposures such as leg length and sitting height and CVD risk is yet to be investigated. This study assessed the association between leg length, sitting height, and estimated 10-year atherosclerotic cardiovascular disease (ASCVD) risk among Ghanaian-born populations in Europe and Ghana. We constructed sex-specific quintiles for sitting height and leg length for 3250 participants aged 40–70 years (mean age 52 years; men 39.6%; women 60.4%) in the cross-sectional multicenter Research on Diabetes and Obesity among African Migrants study. Ten-year risk of ASCVD was estimated using the Pooled Cohort Equations; risk  $\geq 7.5\%$  was defined as “elevated” CVD risk. Prevalence ratios (PR) were estimated to determine the associations between sitting height, leg length, and estimated 10-year ASCVD risk. For both men and women, mean sitting height and leg length were highest in Europe and lowest in rural Ghana. Sitting height was inversely associated with 10-year ASCVD risk among all women (PR for 1 standard deviation increase of sitting height: 0.75; 95% confidence interval: 0.67, 0.85). Among men, an inverse association between sitting height and 10-year ASCVD risk was significant on adjustment for study site, adult, and parental education but attenuated when further adjusted for height. No association was found between leg length and estimated 10-year ASCVD risk. Early-life and childhood exposures that influence sitting height could be the important determinants of ASCVD risk in this adult population.

## Background

Cardiovascular diseases (CVDs) and their related deaths pose a major global health challenge, currently constituting about half of deaths from non-communicable diseases,<sup>1</sup> more than 80% of them in low- and middle-income countries (LMICs).<sup>2,3</sup> Recent findings from the multicentre Research on Obesity and Diabetes among African Migrants (RODAM) study showed a higher prevalence of diabetes and obesity<sup>4</sup> and estimated CVD risk<sup>5</sup> among Ghanaian populations residing in Europe as well as urban Ghana. The causes of the higher burden of CVD among sub-Saharan African migrant and home populations are not completely known. Dietary habits, lifestyle factors, and psychosocial stress have not fully explained these differences.<sup>5–7</sup>

The interplay between origin, epidemiologic, and socioeconomic transitions is considered to explain differences in disease risk and prevalence between and within populations.

The Developmental Origins of Health and Disease paradigm has shed light on the relationship between early-life development and susceptibility to chronic diseases in later life.<sup>8,9</sup> Impaired fetal development and poor birth outcomes such as low birth weight and preterm birth have been associated with an increased risk of obesity, CVD, and metabolic disorders in later life, including in LMICs.<sup>10,11</sup> Childhood socioeconomic disadvantages, malnutrition, and psychosocial stresses, for example, have been associated with inflammation and the clustering of metabolic risk markers in adulthood, resulting in age-related diseases such as CVDs.<sup>12–14</sup> It is suggested that the mismatch between the postnatal phenotype predicted by early-life conditions and subsequent reality in later life leads to health problems.<sup>15</sup> Populations born in LMICs might have had adverse early-life nutritional and environmental exposures than their counterparts born in high-income settings, making them more vulnerable to the negative effects of the obesogenic environment.

The proportion of height variation explained by shared environmental factors is shown to be greatest in early childhood,<sup>16</sup> and leg length and sitting height are widely used as objective markers of childhood nutrition and socioeconomic status. Recently, longer leg length has been shown to be associated with a lower risk of death from coronary heart disease,<sup>17,18</sup> the lower risk of diabetes,<sup>19</sup> lower blood pressure,<sup>20</sup> and a more favorable cardiovascular risk profile.<sup>21,22</sup> Sitting height or trunk length is also associated with reduced risk of circulatory diseases.<sup>18,23</sup> These specific associations suggest that skeletal growth may be a good indicator of early-life environmental exposures and is thus an important determinant for CVD risk in later life.<sup>18,23</sup> Greater absolute and relative leg length is an indicator of better living conditions, such as improved nutrition and fewer respiratory infections during infancy and prepubertal childhood, which might be influenced by childhood socioeconomic status.<sup>24,25</sup> Longer sitting height and trunk length reflect nutritional and lifestyle influences during infancy and childhood stages and their interactions with puberty onset.<sup>26</sup> The associations between early-life exposures, puberty, and health outcomes depend on the contextual environment and could differ among rural and urban populations particularly in LMICs.<sup>27,28</sup>

Exploring the role of early childhood exposures on CVD risk among sub-Saharan African populations could help understand the reasons for the differences and increased CVD burden observed among populations from this region. This study aims to assess whether anthropometric markers of early-life environmental conditions are associated with an estimated risk of atherosclerotic cardiovascular disease (ASCVD) in adulthood. Using an established risk algorithm,<sup>29</sup> we assessed the association between absolute and relative leg length and sitting height and 10-year ASCVD risk among Ghanaian-born adults residing in Ghana and Europe.

## Methods

### Study design and study population

Details of the RODAM study including the recruitment and sample size estimations have previously been described.<sup>30</sup> In summary, this multicenter cross-sectional study was conducted among Ghanaian adults in rural Ghana, urban Ghana, and Europe (Amsterdam, London, and Berlin) between July 2012 and September 2015 ( $n = 6,385$ ). For recruitment, in Ghana, census data of 2010 were used to draw rural and urban participants in the Ashanti Region. In Amsterdam, the Municipal Register was

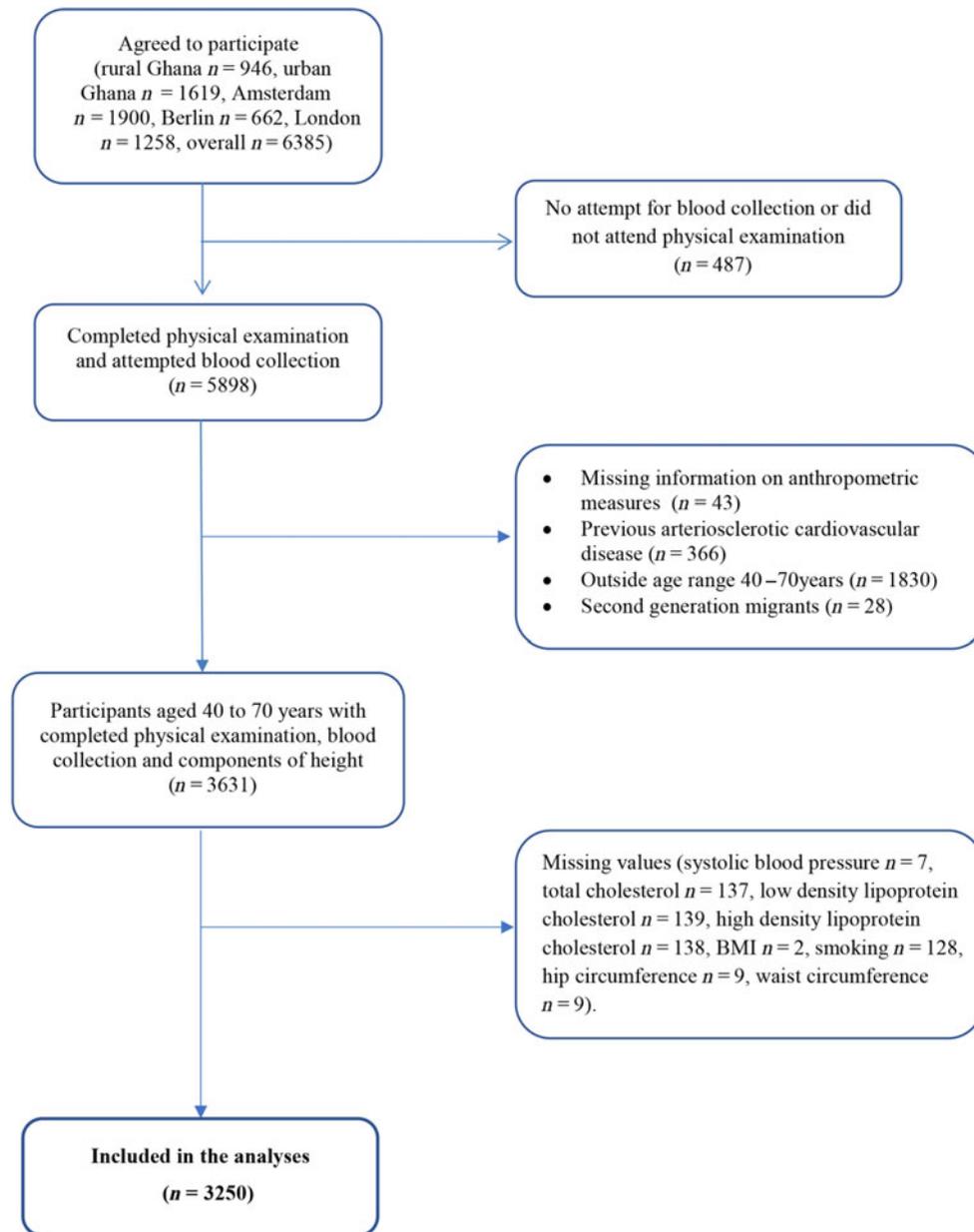
used to randomly select Ghanaian migrants who have been invited to be part of the study by postal mail and home visits. In London and Berlin, Ghanaian organizations, church communities, and social unions served as the sampling frame for recruitment. The response rates were 76% in rural Ghana and 74% in urban Ghana. In Amsterdam, 67% replied by response card or after a home visit. Of these, 53% agreed and participated in the study. In London, of those individuals who were invited based on their registration in Ghanaian organizations, 75% agreed and participated in the study. In Berlin, this figure was 68%.

All Ghanaian-born RODAM study participants aged 40 to 70 years, without a history of clinical ASCVD and complete information on leg length and sitting height, were included in the current analysis. Study participants with missing data (systolic blood pressure  $n = 7$ ; total cholesterol  $n = 137$ ; low-density lipoprotein [LDL] cholesterol  $n = 139$ ; high-density lipoprotein [HDL] cholesterol  $n = 138$ ; body mass index [BMI]  $n = 2$ ; smoking  $n = 128$ ; hip circumference  $n = 9$ ; and waist circumference  $n = 9$ ) were excluded. This resulted in a final sample size of 3250 (Fig. 1).

### Measurements

Trained study personnel performed all measurements with validated devices according to standardized operating procedures across all study sites. Fasting venous blood samples were collected, manually processed, and immediately aliquoted, and then temporarily stored at the local research location at  $-20^{\circ}\text{C}$ . The samples were then transported to the respective local laboratories for registration and storage at  $-80^{\circ}\text{C}$  and were subsequently transported according to standardized procedures, to Berlin (Germany) for biochemical analysis to avoid intralaboratory variability. Total cholesterol, HDL cholesterol, and LDL cholesterol were determined using the ABX Pentra 400 chemistry analyzer (HORIBA ABX, Montpellier, France). Type 2 diabetes was defined as fasting glucose  $\geq 7.0$  mmol/l or reported current use of medication prescribed to treat diabetes or self-reported diabetes.<sup>31</sup> Blood pressure (BP) was measured three times using a validated semiautomated device (The Microlife WatchBP home) with appropriate cuffs in a sitting position after at least 5-min rest. The mean of the last two measurements was used in the analyses. All anthropometric measurements were performed twice by the same examiner and the mean of the two measurements was used for analyses. Weight was measured twice in light clothing and without shoes with SECA 877 scales to the nearest 0.1 kg. Height was also measured twice without shoes with a portable stadiometer (SECA 217) to the nearest 0.1 cm. Waist circumference (cm) was measured at the midpoint between the lower rib and the upper margin of the iliac crest using a measuring tape. Hip circumference was taken around the widest portion of the buttocks using a measuring tape.<sup>32</sup> BMI was calculated as weight in kilograms divided by height in meters squared. Overweight and obesity were defined as BMI  $\geq 25$  to  $< 30$  kg/m<sup>2</sup> and  $\geq 30$  kg/m<sup>2</sup>, respectively.<sup>32</sup> For sitting height, measurement was taken from the floor to the top of the participant's head, with the participant sitting upright on the base plate on a flat seat, and with the head in the Frankfort plane position, feet on the floor, and with the thighs unsupported. Sitting height was calculated as the measurement – seat height. Leg length (cm) was calculated as standing height – sitting height.<sup>24</sup> Relative leg length was estimated as (leg length/height) \* 100.

**Questionnaire-based interviews** were conducted by a trained research assistant or self-administration of a paper questionnaire



**Fig. 1.** Selection of study participants.

or digital online version depending on the preference of the participant.<sup>30</sup> Sociodemographic information included age, sex, and educational level. The educational level of the participants and their parents was recorded according to the following categories: never been to school or elementary school, lower vocational schooling or lower secondary schooling, intermediate vocational schooling or intermediate/higher secondary schooling, and higher vocational schooling or university. The use of antihypertensive medication was assessed based on a “Yes” or “No” response to the question “Do you use any antihypertensive medication, including combinations?”. Smoking status was assessed based on either a “Yes,” “No, but I used to smoke” or “No, I’ve never smoked” response to the question “Do you smoke at all?”. Age of migration was categorized as according to <13 years (representing the mean age at menarche among Ghanaian adolescents<sup>33</sup>), 13–22 years (the maximum age at which most people achieve full growth<sup>34</sup>) and  $\geq 22$  years.

### Estimated 10-year CVD risk

The outcome variable was predicted 10-year ASCVD risk, estimated from the Pooled Cohort Equations (PCE) for African-American men and women.<sup>29</sup> The equations are derived, using pooled data from ethnically and geographically diverse community-based cohorts, permitting the creation of sex- and ethnic-specific equations for non-Hispanic White American and Black women and men.<sup>29</sup> The model combines age, sex, total cholesterol, HDL cholesterol, systolic blood pressure, use of antihypertensive medication, diagnosed with diabetes, and smoking to estimate the 10-year absolute risk of ASCVD in people without pre-existing ASCVD.<sup>29</sup> In their updated clinical practice guidelines for the treatment of blood cholesterol to reduce aASCVD, the American College of Cardiology and American Heart Association recommended the PCE as a novel tool to estimate 10-year ASCVD risk.<sup>35</sup> The guidelines provide a strong recommendation (Class I, Level of Evidence: A)

for consideration of statin treatment in individuals with a 10-year ASCVD risk  $\geq 7.5\%$  and a moderate recommendation (Class IIa, Level of Evidence: B) in individuals with a 10-year ASCVD risk of 5% to  $<7.5\%$ . CVD risk  $\geq 7.5\%$  was considered as an “elevated” risk of CVD based on the prior work by Goff et al.<sup>29</sup> The distribution of estimated 10-year ASCVD risk between Ghanaian migrant and home populations has been shown in previous analyses.<sup>5,36</sup>

Current guidelines for CVD risk reduction have emphasized the need to assess all risk factors as a more effective basis to deliver CVD prevention interventions.<sup>37</sup> Absolute CVD risk estimates, using established risk algorithms, help to determine the probability of a cardiovascular event occurring within a specified time horizon. Most established CVD risk algorithms do not, however, address appropriately the ethnic and socioeconomic differences relating to CVDs.<sup>38,39</sup> Contextual differences in risk factors among various ethnic groups contribute significantly to differences in CVD,<sup>40</sup> making ethnicity an important parameter when estimating CVD risk. The PCE, developed and validated among African American and European and Asian men and women, has been shown to be comparatively accurate in estimating CVD risk among ethnic and minority populations.<sup>41</sup>

### Statistical analysis

General characteristics, CVD risk factors, and anthropometric characteristics of the study sample are summarized as percentages for categorical variables, mean  $\pm$  standard deviation (SD) for normally distributed continuous variables, and as median (interquartile range) for non-normally distributed variables. We estimated the mean or prevalence of sociodemographic characteristics and CVD risk factors by sex-specific quintiles of absolute and relative leg lengths and sitting height. Respective *P*-values for trend were assessed using Pearson  $\chi^2$  for proportions and Pearson correlations for continuous variables. Prevalence ratios (PR) and 95% confidence intervals (95% CI) were calculated by Poisson regression with robust variance<sup>42</sup> to assess the associations between the anthropometric markers of early-life exposures (per quintile) and estimated high 10-year risk of ASCVD. In addition, the associations with estimated high 10-year ASCVD risk were calculated per 1 SD increase of the sitting height and leg length. Adjusted regression models were constructed by sex. Early-life exposures might have different effects in male and female biology, and the influence of possible confounders such as age at menarche might also be different for men and women.<sup>43,44</sup> Male and female puberty might differ in terms of behavior, hormonal factors, and changes in body composition. Both men and women put in fat mass. But while women tend to gain more in adiposity, men tend to gain more in muscles and fat free mass. These might create differentials in risks for CVDs.<sup>45–47</sup> Model 1 was adjusted for study site (categorical, reference=rural Ghana) and adult and parental education (categorical, reference=no education). For women, model 2 adjusted further for age at menarche (continuous) and model 3 (which is model 2 for men) additionally adjusted for BMI (continuous) and waist and hip circumference (continuous). For leg length and sitting height, a final model (models 3 and 4 for men and women, respectively) was constructed to account for total height (continuous). Variables included in the CVD risk score (age, smoking, total cholesterol, HDL cholesterol, and use of antihypertensives) were not adjusted for to avoid overadjusting. The analyses were further stratified by current residence or study site to explore the contextual differences in early-life exposures and their association with CVD risk. For all statistical tests, a *P*-value of  $<0.05$  was

considered statistically significant. Data were analyzed with STATA 13 (StataCorp LLC).<sup>48</sup>

### Results

Table 1 presents the results of the distribution of sociodemographic, anthropometric measures, and CVD risk factors by study site. Adult and parental level of education was highest in Europe and lowest in rural Ghana for both men and women. BMI, waist circumference, hip circumference, and sitting height were highest in Europe and lowest in rural Ghana in both men and women. Among the migrant population, none of the men migrated to Europe before the age of 13 years and only 5.7% migrated before the age of 22 years. Among women, 0.5% and 11.6% migrated before ages of 13 and 22 years, respectively.

CVD risk factors and demographic data are presented according to quintiles of the relative and absolute leg lengths and sitting height in Table 2. Age was inversely related to sitting height in both men and women. Among women, mean BMI and proportion of parental education had positive gradient, whereas mean LDL and total cholesterol, age at menarche, and 10-year risk of ASCVD had negative gradient across quintiles of sitting height. Systolic BP, BMI, and parental education had positive gradient, whereas age had negative gradient across quintiles of sitting height among men. Systolic BP and age at menarche had positive gradient, whereas BMI had negative gradient across quintiles of leg length in women. BMI, waist, and hip circumference were inversely related to relative leg length in both men and women.

The associations between sitting height and leg length and estimated 10-year risk of ASCVD are presented in Table 3. Among the total Ghanaian men, there was an inverse association between sitting height and 10-year ASCVD risk, which was significant on adjustment for study site and adult and parental education in model 1 (PR for 1 SD of sitting height 0.94, 95% CI: 0.89, 0.99) and other possible confounders in subsequent models. The effect attenuated after adjusted for adult height in model 3. Absolute and relative leg lengths were not associated with 10-year ASCVD risk.

Among women, sitting height was inversely associated with 10-year ASCVD risk. A 48% lower PR for elevated 10-year ASCVD risk was observed in the highest quintile, as compared with the lowest quintile of sitting height (PR 0.52, 95% CI: 0.41, 0.68  $p_{\text{trend}} \leq 0.001$ ). The association remained consistent after further adjustment for possible confounders (PR for Q1 vs. Q5 0.51, 95% CI: 0.36, 0.73,  $P_{\text{trend}} \leq 0.001$ , fully adjusted model). One SD increase in sitting height was associated with a 25% (PR 0.75; 95% CI: 0.67, 0.85) lower PR of elevated 10-year ASCVD risk. Relative leg length was positively associated with 10-year ASCVD, but the effect was no longer significant after adjusting for age at menarche and anthropometric characteristics. In the analyses stratified for current residence (Supplementary Tables S1–S3), sitting height was inversely associated with 10-year risk of ASCVD among Ghanaian women in Europe, rural and urban Ghana and men in urban Ghana.

### Discussion

This study was conducted to investigate the association of markers of early-life nutritional and environmental exposures with CVD risk among Ghanaian-born populations resident in Europe and Ghana. We found an inverse association between sitting height and 10-year estimated risk of ASCVD among Ghanaian women

**Table 1.** Mean or prevalence of anthropometric characteristics and parental education

Variables	Europe	Urban Ghana	Rural Ghana
	N = 847	N = 224	N = 217
<b>Men</b>			
Age, mean $\pm$ SD	52 $\pm$ 6.7	53 $\pm$ 8.1	54 $\pm$ 8.8
<b>Education</b>			
Never/elementary	15.2	25.4	46.5
Lower	41.7	44.2	36.4
Intermediate	23.7	19.2	12.4
Tertiary	18.4	11.2	4.6
<b>Maternal education</b>			
Never/elementary	83.3	90.6	93.1
Lower	6.1	6.3	3.7
Intermediate	5.4	1.8	1.8
Tertiary	4.7	0.9	0.9
<b>Father education</b>			
Never/elementary	66.6	72.8	89.9
Lower	8.4	16.1	5.5
Intermediate	15.3	7.1	2.3
Tertiary	9.6	4.0	1.4
Systolic BP (mean $\pm$ SD)	139 $\pm$ 17.5	134 $\pm$ 21.3	126 $\pm$ 19.7
Antihypertensives	32.1	8.5	6.0
LDL cholesterol (mean $\pm$ SD)	3.3 $\pm$ 0.9	3.5 $\pm$ 1.1	2.5 $\pm$ 0.8
HDL cholesterol (mean $\pm$ SD)	1.3 $\pm$ 0.3	1.2 $\pm$ 0.3	1.2 $\pm$ 0.4
Total cholesterol (mean $\pm$ SD)	5.1 $\pm$ 1.0	5.2 $\pm$ 1.2	4.2 $\pm$ 1.0
Type 2 diabetes	16.3	16.1	3.7
BMI (mean $\pm$ SD)	27.2 $\pm$ 3.9	24.5 $\pm$ 3.7	20.6 $\pm$ 2.9
Overweight	52.8	36.2	6.9
Obese	18.6	7.6	0.5
Smoking	7.5	2.2	6.9
Waist circumference (mean $\pm$ SD)	94.2 $\pm$ 10.6	86.8 $\pm$ 10.3	77.3 $\pm$ 8.1
Hip circumference (mean $\pm$ SD)	99.7 $\pm$ 7.7	94.6 $\pm$ 8.8	86.2 $\pm$ 7.1
Length of stay in Europe <sup>#</sup>	20.9 (12.6, 25.0)		
Age at migration (mean $\pm$ SD)	32 $\pm$ 7.7		
<13	0.0		
13–21	5.7		
>21	94.3		
Sitting height (mean $\pm$ SD)	85.1 $\pm$ 3.6	83.5 $\pm$ 3.7	82.6 $\pm$ 3.8
Leg length (mean $\pm$ SD)	86.3 $\pm$ 4.7	85.8 $\pm$ 4.8	85.0 $\pm$ 4.8
Relative leg length (mean $\pm$ SD)	50.3 $\pm$ 1.6	50.7 $\pm$ 1.5	50.7 $\pm$ 1.4

(Continued)

**Table 1.** (Continued)

Variables	Europe	Urban Ghana	Rural Ghana
	N = 847	N = 224	N = 217
Women	N = 1102	N = 521	N = 339
Age (mean $\pm$ SD)	50 $\pm$ 6.7	51 $\pm$ 7.6	52 $\pm$ 8.8
<b>Education</b>			
Never/elementary	30.3	57.4	72.3
Lower	35.2	34.0	23.9
Intermediate	23.9	6.7	2.3
Tertiary	8.5	1.9	1.5
<b>Mother's education</b>			
Never/elementary	81.0	90.4	96.5
Lower	7.4	7.8	2.7
Intermediate	5.6	1.3	0.6
Tertiary	6.0	0.2	0.3
<b>Father's education</b>			
Never/elementary	57.0	70.4	90.9
Lower	10.7	19.5	6.2
Intermediate	18.7	7.1	2.4
Tertiary	13.3	2.7	0.6
Systolic BP (mean $\pm$ SD)	136 $\pm$ 16.9	128.2 $\pm$ 17.7	127.0 $\pm$ 22.4
Antihypertensives	37.2	16.4	12.1
LDL cholesterol (mean $\pm$ SD)	3.3 $\pm$ 0.8	3.6 $\pm$ 0.9	3.1 $\pm$ 1.0
HDL cholesterol (mean $\pm$ SD)	1.5 $\pm$ 0.3	1.3 $\pm$ 0.3	1.2 $\pm$ 0.3
Total cholesterol (mean $\pm$ SD)	5.1 $\pm$ 0.9	5.5 $\pm$ 1.1	4.8 $\pm$ 1.1
Type 2 diabetes	11.3	10.3	7.7
BMI (mean $\pm$ SD)	30.8 $\pm$ 5.0	28.5 $\pm$ 5.4	23.4 $\pm$ 4.8
Overweight	37.8	36.3	24.2
Obese	52.6	36.3	8.8
Smoking	1.3	0.0	0.0
Waist circumference (mean $\pm$ SD)	97.4 $\pm$ 11.6	92.9 $\pm$ 11.5	84.4 $\pm$ 11.6
Hip circumference (mean $\pm$ SD)	109.0 $\pm$ 10.5	101.7 $\pm$ 10.1	92.9 $\pm$ 10.4
Length of stay in Europe <sup>#</sup>	20.4 (12.7, 25.9)		
Age at migration (mean $\pm$ SD)	30.8 $\pm$ 8.5		
<13	0.5		
13–21	11.6		
>21	87.9		
Sitting height (mean $\pm$ SD)	81.04 $\pm$ 3.3	78.5 $\pm$ 3.6	77.2 $\pm$ 3.9
Leg length (mean $\pm$ SD)	80.0 $\pm$ 4.3	79.8 $\pm$ 4.6	79.6 $\pm$ 5.0
Relative leg length (mean $\pm$ SD)	49.7 $\pm$ 1.6	50.4.0 $\pm$ 1.8	50.7 $\pm$ 2.1
Age at menarche (mean $\pm$ SD)	14.0 $\pm$ 3.9	15.0 $\pm$ 1.6	14.6 $\pm$ 2.3

BP, blood pressure; SD, standard deviation median (25th, 75th percentile).

**Table 2.** Mean or prevalence of sociodemographic characteristics and CVD risk factors by leg length, relative leg length and sitting height

Variables	Men					P for trend	Women					P for trend
	Quintiles						Quintiles					
Sitting height (cm)	1 (67.2–81.2) N = 264	2 (81.3–83.5) N = 253	3 (83.5–85.3) N = 258	4 (85.3–87.7) N = 256	5 (87.7–95.7) N = 257		1 (63.3–76.7) N = 398	2 (76.7–78.8) N = 404	3 (78.8–80.6) N = 383	4 (80.6–82.2) N = 388	5 (82.8–123.8) N = 389	
Site						<0.001						<0.001
Europe	16.6	17.8	18.4	23.7	23.4		13.6	15.6	19.1	23.7	27.9	
Urban Ghana	24.1	21.4	25.4	13.8	15.2		24.1	26.9	21.5	18.2	9.2	
Rural Ghana	29.5	27.6	18.4	12.9	11.5		36.0	23.6	20.4	11.8	8.3	
Age (mean ± SD)	55 ± 8.4	53 ± 7.8	53 ± 7.3	50 ± 6.2	50 ± 6.4	<0.001	55 ± 8.3	52 ± 7.5	50 ± 6.8	50 ± 6.7	48 ± 5.9	<0.001
Education						0.664						0.096
Never/elementary	22.1	24.5	19.8	23.5	20.1		48.8	46.4	40.3	42.1	45.8	
Lower	39.3	40.6	38.1	43.1	45.2		32.5	33.8	36.8	30.1	31.6	
Intermediate	20.6	21.8	24.9	20.0	17.8		12.3	14.7	15.9	19.0	16.5	
Tertiary	16.4	12.3	16.7	13.1	15.8		6.0	4.6	5.3	7.5	4.4	
Systolic BP (mean ± SD)	134 ± 20.7	135 ± 20.0	137 ± 20.3	136 ± 16.1	139 ± 18.2	0.009	132 ± 20.5	131 ± 18.2	131 ± 18.6	134 ± 17.7	134 ± 17.6	0.010
Antihypertensives	18.3	22.2	26.7	24.2	27.0	0.173	25.3	23.9	27.5	30.6	30.1	0.1456
LDL cholesterol (mean ± SD)	3.2 ± 0.9	3.1 ± 1.0	3.1 ± 0.9	3.3 ± 1.0	3.3 ± 0.9	0.079	3.4 ± 0.9	3.3 ± 0.9	3.3 ± 0.9	3.3 ± 0.9	3.2 ± 0.9	0.026
HDL cholesterol (mean ± SD)	1.3 ± 0.3	1.3 ± 0.3	1.2 ± 0.3	1.3 ± 0.3	1.3 ± 0.3	0.810	1.4 ± 0.3	1.4 ± 0.3	1.4 ± 0.4	1.4 ± 0.3	1.4 ± 0.3	0.043
Total cholesterol (mean ± SD)	4.9 ± 1.1	4.9 ± 1.2	4.9 ± 1.1	5.0 ± 1.1	5.0 ± 1.1	0.068	5.3 ± 1.1	5.2 ± 1.1	5.1 ± 1.0	5.2 ± 1.1	5.1 ± 1.0	0.006
Type 2 diabetes	12.6	11.9	14.8	13.8	17.8	0.341	10.8	11.4	7.3	13.0	9.5	0.097
BMI (mean ± SD)	24.7 ± 4.5	24.9 ± 4.4	25.5 ± 4.3	26.4 ± 4.1	26.7 ± 4.6	<0.001	26.8 ± 5.7	28.2 ± 5.3	29.0 ± 5.7	29.9 ± 5.3	31.0 ± 5.7	<0.001
Overweight	41.6	37.5	41.6	47.3	43.2	<0.001	35.3	37.8	33.0	35.3	33.9	<0.001
Obese	9.2	10.7	12.8	16.5	19.3		27.5	35.3	40.6	46.9	54.0	
Smoking	4.2	5.0	7.8	8.8	6.6	0.475	0.2	0.4	0.9	0.7	1.5	0.115
Waist circumference (mean ± SD)	86.7 ± 11.8	87.8 ± 11.6	87.8 ± 11.6	92.0 ± 11.9	94.2 ± 11.9	<0.001	89.9 ± 13.1	92.6 ± 11.5	93.8 ± 12.1	96.3 ± 11.5	98.5 ± 12.8	<0.001
Hip circumference (mean ± SD)	93.3 ± 9.7	94.4 ± 8.8	96.3 ± 8.5	98.4 ± 8.8	100.4 ± 8.6	<0.001	98.1 ± 12.1	102.1 ± 10.8	104.4 ± 11.9	107.1 ± 10.6	110.0 ± 11.4	<0.001
Length of stay in Europe <sup>†</sup>	18 (11, 25)	20 (12, 25)	21 (12, 25)	20 (13, 24)	22 (14, 26)	0.131	22 (11, 28)	22 (12, 28)	20 (12, 26)	21(14, 26)	20 (14, 24)	0.010
Age at migration (mean ± SD)	35 ± 8.9	33 ± 8.0	32 ± 8.2	32 ± 6.4	31 ± 7.0	<0.001	34 ± 10.1	31 ± 8.7	31 ± 8.2	30 ± 7.9	30 ± 7.7	<0.001
Father educated	15.2	25.7	26.1	31.9	32.0	0.001	26.8	29.7	32.7	40.9	37.1	<0.001
Mother educated	13.7	8.8	14.4	14.6	14.7	0.001	9.8	11.9	13.4	16.0	18.4	<0.001
10-year CVD risk ≥7.5	51.1	49.0	55.3	47.7	48.6	0.441	32.8	22.1	17.4	22.1	17.2	<0.001
Age at menarche							14.5 ± 3.0	14.5 ± 3.1	14.4 ± 2.9	14.2 ± 3.3	14.0 ± 3.7	0.044

Table 2. (Continued)

Variables	Men					P for trend	Women					P for trend
	Quintiles						Quintiles					
	1 (67.2–81.2) N = 264	2 (81.3–83.5) N = 253	3 (83.5–85.3) N = 258	4 (85.3–87.7) N = 256	5 (87.7–95.7) N = 257		1 (63.3–76.7) N = 398	2 (76.7–78.8) N = 404	3 (78.8–80.6) N = 383	4 (80.6–82.2) N = 388	5 (82.8–123.8) N = 389	
Leg length (cm)						0.013						0.554
Site												
Europe	17.7	19.2	21.3	20.8	21.0		19.9	20.1	18.9	21.4	19.8	
Urban Ghana	22.3	19.2	19.6	20.1	18.8		20.5	18.6	21.7	19.2	20.0	
Rural Ghana	28.1	23.5	18.0	14.3	16.1		20.6	22.1	21.5	16.8	18.9	
Age	53 ± 7.6	53 ± 7.4	52 ± 7.5	51 ± 7.5	51 ± 6.8	<0.001	52 ± 7.6	51 ± 7.2	51 ± 7.3	51 ± 7.5	51 ± 7.3	0.195
Education						0.026						0.467
Never/elementary	30.0	21.6	19.5	17.1	21.9		49.0	44.9	45.7	42.9	40.7	
Lower	40.2	43.2	43.2	40.9	38.7		29.4	34.6	32.8	33.7	32.3	
Intermediate	17.6	20.8	24.4	22.2	19.9		14.1	13.9	16.2	17.1	17.1	
Tertiary	12.0	13.1	11.3	19.1	19.1		6.0	5.1	3.8	5.8	7.2	
Systolic BP (mean ± SD)	135 ± 20.1	137 ± 19.0	137 ± 19.2	135 ± 20.1	136 ± 19.1	0.910	133 ± 19.1	133 ± 19.3	130 ± 17.5	132 ± 18.1	133 ± 18.9	0.900
Antihypertensives	24.9	24.7	21.1	23.0	24.6	0.712	28.4	26.8	24.2	30.9	26.9	0.312
LDL cholesterol (mean ± SD)	3.2 ± 1.0	3.2 ± 1.0	3.2 ± 0.9	3.3 ± 1.0	3.1 ± 1.0	0.436	3.4 ± 0.9	3.3 ± 0.9	3.3 ± 0.9	3.3 ± 0.9	3.3 ± 0.9	0.122
HDL cholesterol (mean ± SD)	1.3 ± 0.3	1.3 ± 0.3	1.3 ± 0.4	1.3 ± 0.3	1.3 ± 0.3	0.367	1.4 ± 0.3	1.4 ± 0.3	1.4 ± 0.3	1.4 ± 0.3	1.4 ± 0.3	0.335
Total cholesterol (mean ± SD)	5.0 ± 1.2	5.0 ± 1.1	4.9 ± 1.1	5.1 ± 1.1	4.9 ± 1.1	0.758	5.2 ± 1.0	5.2 ± 1.1	5.1 ± 1.1	5.1 ± 1.0	5.1 ± 1.0	0.151
Type 2 diabetes	14.9	17.0	9.0	14.8	15.2	0.094	10.8	8.6	10.4	10.8	11.5	0.726
BMI (mean ± SD)	25.6 ± 4.8	25.8 ± 4.5	25.5 ± 4.1	25.8 ± 4.6	25.3 ± 4.1	0.528	30.0 ± 6.1	29.3 ± 5.7	28.3 ± 5.8	28.5 ± 5.4	28.2 ± 5.4	<0.001
Overweight	38.7	41.3	46.2	42.4	42.6	0.657	32.9	36.4	33.1	37.4	35.5	<0.001
Obese	15.3	15.8	11.3	14.8	11.3		48.5	43.9	38.1	38.4	34.8	
Smoking	3.1	6.6	5.6	6.6	10.5	0.018	0.3	0.3	1.3	0.7	1.0	0.439
Waist circumference (mean ± SD)	88.0 ± 12.7	89.6 ± 11.8	90.2 ± 11.6	91.1 ± 12.1	91.7 ± 11.5	<0.001	93.3 ± 12.6	93.9 ± 11.9	92.9 ± 13.7	94.6 ± 12.0	95.3 ± 12.1	0.018
Hip circumference (mean ± SD)	93.6 ± 9.6	95.7 ± 9.0	96.8 ± 9.3	97.7 ± 8.7	99.1 ± 8.9	<0.001	103.7 ± 13.1	104.2 ± 11.4	103.0 ± 12.0	104.6 ± 11.2	106.0 ± 11.9	0.007
Age at migration (mean ± SD)	33 ± 6.5	33 ± 8.0	33 ± 8.3	32 ± 8.0	32 ± 7.7	0.129	31.6 ± 8.9	30.5 ± 7.9	30.0 ± 8.1	31.3 ± 8.1	30.4 ± 9.6	0.443
Length of stay in Europe <sup>#</sup>	21 (15, 25)	22 (13, 25)	19 (12, 25)	21 (12, 25)	21 (13, 26)	0.565	20 (13, 25)	21 (13, 26)	21 (12, 26)	20 (13, 26)	20 (12, 27)	0.532
Father educated	19.1	29.3	29.3	31.5	31.2	0.042	31.2	33.1	28.8	34.4	39.6	0.064
Mother educated	8.4	13.1	16.2	15.6	12.9	0.078	11.1	15.7	12.1	13.3	17.1	0.140
10-year CVD risk ≥7.5	51.7	52.9	48.9	46.7	51.6	0.622	25.1	22.0	21.5	21.4	21.7	0.683
Age at menarche							14.2 ± 3.2	14.2 ± 3.5	14.3 ± 3.3	14.4 ± 3.3	14.8 ± 2.6	0.010

Table 2. (Continued)

Variables	Men					P for trend	Women					P for trend
	Quintiles						Quintiles					
	1 (67.2–81.2) N = 264	2 (81.3–83.5) N = 253	3 (83.5–85.3) N = 258	4 (85.3–87.7) N = 256	5 (87.7–95.7) N = 257		1 (63.3–76.7) N = 398	2 (76.7–78.8) N = 404	3 (78.8–80.6) N = 383	4 (80.6–82.2) N = 388	5 (82.8–123.8) N = 389	
Relative leg length (%)												
Site						0.001						<0.001
Europe	23.5	20.8	18.2	19.0	18.5		28.4	21.7	18.1	17.3	14.4	
Urban Ghana	15.6	17.0	21.9	20.5	25.0		10.4	17.1	23.8	24.6	23.2	
Rural Ghana	11.1	20.3	24.9	23.5	20.3		7.7	18.9	19.7	22.1	31.6	
Age	52 ± 6.2	53 ± 7.3	52 ± 7.7	52 ± 7.9	53 ± 7.8	0.011	49 ± 6.5	50 ± 6.5	51 ± 7.4	52 ± 7.4	53 ± 8.3	<0.001
Education						0.177						0.185
Never/elementary	20.0	26.2	27.0	23.4	19.7		46.6	45.8	45.9	42.6	48.1	
Lower	44.6	46.2	37.3	36.5	41.7		29.7	33.4	31.3	37.1	33.2	
Intermediate	20.4	18.1	21.2	21.9	23.6		17.1	14.9	17.4	15.7	13.2	
Tertiary	15.0	9.6	16.5	18.1	15.1		6.5	5.8	5.3	4.5	5.6	
Systolic BP (mean ± SD)	140 ± 18.1	135 ± 19.0	133 ± 17.2	138 ± 20.6	135 ± 20.2	0.066	135 ± 18.4	132 ± 18.7	132 ± 18.6	131 ± 17.6	132 ± 19.7	0.062
Antihypertensives	28.8	23.1	21.9	22.7	21.6	0.278	28.9	30.4	25.3	28.5	24.1	0.227
LDL cholesterol (mean ± SD)	3.4 ± 1.0	3.3 ± 1.0	3.1 ± 0.9	3.1 ± 1.0	3.2 ± 1.0	0.006	3.4 ± 0.9	3.3 ± 0.9	3.3 ± 0.9	3.4 ± 0.9	3.4 ± 0.9	0.381
HDL cholesterol (mean ± SD)	1.3 ± 0.3	1.3 ± 0.3	1.3 ± 0.4	1.3 ± 0.3	1.3 ± 0.4	0.428	1.4 ± 0.3	1.4 ± 0.3	1.3 ± 0.3	1.4 ± 0.3	1.4 ± 0.3	0.119
Total cholesterol (mean ± SD)	5.1 ± 1.1	5.0 ± 1.1	4.8 ± 1.1	4.9 ± 1.1	5.0 ± 1.1	0.038	5.2 ± 1.0	5.1 ± 1.0	5.1 ± 1.1	5.2 ± 1.0	5.2 ± 1.1	0.243
Type 2 diabetes	16.2	15.0	12.3	13.0	14.7	0.690	10.3	9.9	10.4	9.6	11.9	0.853
BMI (mean ± SD)	27.0 ± 4.5	26.1 ± 4.5	25.2 ± 4.1	25.3 ± 4.4	24.5 ± 4.2	<0.001	31.5 ± 5.6	30.0 ± 5.6	28.6 ± 5.4	28.0 ± 5.5	26.4 ± 5.6	<0.001
Overweight	46.9	43.5	39.6	42.3	39.0	<0.001	29.7	38.7	37.1	36.6	33.1	<0.001
Obese	20.0	16.5	11.5	12.7	7.7		59.2	46.8	39.1	34.6	24.1	
Smoking	5.4	3.8	6.5	5.8	10.8	0.015	0.8	0.8	0.5	0.8	0.8	0.926
Waist circumference (mean ± SD)	92.6 ± 11.9	90.9 ± 12.2	88.6 ± 12.2	89.5 ± 11.8	88.9 ± 11.5	<0.001	97.2 ± 12.9	95.1 ± 12.1	93.5 ± 12.1	92.7 ± 13.1	91.6 ± 12.0	<0.001
Hip circumference (mean ± SD)	98.0 ± 8.5	96.9 ± 9.8	95.9 ± 9.4	96.6 ± 9.2	95.6 ± 9.1	0.005	109.0 ± 12.5	106.1 ± 11.7	103.3 ± 11.4	102.5 ± 11.9	100.5 ± 11.9	<0.001
Age at migration (mean ± SD)	32 ± 6.5	32 ± 8.0	33 ± 8.3	33 ± 8.7	32 ± 8.4	0.258	30 ± 8.3	31 ± 7.6	31 ± 7.9	32 ± 8.5	32 ± 10.0	0.007
Length of stay in Europe <sup>‡</sup>	22 (14, 25)	22 (14, 25)	20 (11, 24)	19 (11, 25)	20 (13, 27)	0.399	20 (14, 26)	20 (13, 25)	22 (12, 26)	20 (12, 27)	20 (12, 27)	0.542
Father educated	29.6	29.5	29.6	28.1	28.2	0.019	37.0	35.9	32.6	30.6	30.9	<0.001
Mother educated	11.9	13.1	16.5	12.7	12.0	0.105	17.1	14.9	12.9	11.1	13.2	<0.001
10-year CVD risk ≥7.5	51.2	49.6	45.4	51.5	54.1	0.372	19.4	20.3	23.0	22.2	26.8	0.104
Age at menarche							14.0 ± 3.8	14.0 ± 3.5	14.6 ± 2.9	14.5 ± 3.3	14.8 ± 2.4	<0.001

BP, blood pressure; SD, standard deviation.

Responses are in percentages, unless otherwise stated; #median (25th, 75th percentiles).

**Table 3.** Association between sitting height, leg length, relative leg length, and 10-year cardiovascular disease risk among Ghanaian populations

Model	PRs (95% confident intervals)					P-value for trend	PR per 1 standard deviation increase	P-value
	Q1 (ref.)	Q2	Q3	Q4	Q5			
<b>Men</b>								
Sitting height		PR (95% CI)	PR (95% CI)	PR (95% CI)	PR (95% CI)			
“Elevated CVD risk”/total	132/264	135/253	135/258	122/256	125/257			
Crude	1.00	0.96 [0.81, 1.14]	1.08 [0.92, 1.27]	0.93 [0.78, 1.11]	0.95 [0.80, 1.13]	0.519	0.97 [0.92, 1.03]	0.304
Model 1	1.00	0.94 [0.80, 1.12]	1.03 [0.88, 1.22]	0.86 [0.72, 1.02]	0.88 [0.74, 1.04]	0.062	<b>0.94 [0.89, 0.99]</b>	<b>0.033</b>
Model 2	1.00	0.91 [0.78, 1.08]	1.00 [0.85, 1.16]	<b>0.82 [0.69, 0.98]</b>	<b>0.80 [0.67, 0.95]</b>	0.058	<b>0.91 [0.86, 0.97]</b>	<b>0.002</b>
Model 3	1.00	0.94 [0.79, 1.10]	1.04 [0.88, 1.23]	0.87 [0.73, 1.04]	0.88 [0.72, 1.08]	0.163	0.93 [0.87, 1.00]	0.057
<b>Leg length</b>								
“Elevated CVD risk”/total	135/261	136/257	130/263	116/252	132/255			
Crude	1.00	1.02 [0.87, 1.21]	0.94 [0.80, 1.12]	0.90 [0.76, 1.08]	1.00 [0.84, 1.18]	0.505	0.98 [0.93, 1.04]	0.474
Model 1	1.00	1.02 [0.87, 1.20]	0.92 [0.78, 1.09]	0.87 [0.73, 1.03]	0.97 [0.82, 1.14]	0.257	0.97 [0.92, 1.02]	0.278
Model 2	1.00	1.01 [0.86, 1.18]	0.89 [0.75, 1.06]	<b>0.84 [0.71, 0.99]</b>	0.91 [0.77, 1.08]	0.062	0.95 [0.90, 1.01]	0.080
Model 3	1.00	1.06 [0.90, 1.24]	0.99 [0.82, 1.20]	0.98 [0.79, 1.21]	1.12 [0.88, 1.42]	0.641	1.07 [0.98, 1.17]	0.150
<b>Relative leg length</b>								
“Elevated CVD risk”/total	132/258	129/258	117/257	132/258	139/257			
Crude	1.00	0.97 [0.82, 1.15]	0.89 [0.74, 1.06]	1.01 [0.85, 1.19]	1.06 [0.90, 1.24]	0.432	1.00 [0.95, 1.06]	0.980
Model 1	1.00	1.00 [0.85, 1.19]	0.94 [0.79, 1.12]	1.07 [0.90, 1.26]	1.11 [0.94, 1.31]	0.150	1.02 [0.97, 1.07]	0.493
Model 2	1.00	1.00 [0.85, 1.19]	0.97 [0.82, 1.15]	1.09 [0.93, 1.29]	1.09 [0.93, 1.28]	0.144	1.02 [0.97, 1.07]	0.447
<b>Women</b>								
<b>Sitting height</b>								
“Elevated CVD risk”/total	126/398	86/404	74/383	80/388	71/389			
Crude	1.00	<b>0.67 [0.53, 0.85]</b>	<b>0.54 [0.42, 0.70]</b>	<b>0.67 [0.53, 0.85]</b>	<b>0.52 [0.41, 0.68]</b>	<b>&lt;0.001</b>	<b>0.80 [0.74, 0.87]</b>	<b>&lt;0.001</b>
Model 1	1.00	<b>0.67 [0.53, 0.85]</b>	<b>0.52 [0.40, 0.68]</b>	<b>0.65 [0.51, 0.82]</b>	<b>0.50 [0.38, 0.65]</b>	<b>&lt;0.001</b>	<b>0.77 [0.71, 0.85]</b>	<b>&lt;0.001</b>
Model 2	1.00	<b>0.67 [0.53, 0.85]</b>	<b>0.59 [0.46, 0.77]</b>	<b>0.63 [0.48, 0.81]</b>	<b>0.55 [0.42, 0.73]</b>	<b>&lt;0.001</b>	<b>0.77 [0.71, 0.85]</b>	<b>&lt;0.001</b>
Model 3	1.00	<b>0.67 [0.52, 0.86]</b>	<b>0.62 [0.47, 0.81]</b>	<b>0.66 [0.51, 0.87]</b>	<b>0.60 [0.44, 0.80]</b>	<b>&lt;0.001</b>	<b>0.79 [0.71, 0.87]</b>	<b>&lt;0.001</b>
Model 4	1.00	<b>0.67 [0.52, 0.86]</b>	<b>0.62 [0.47, 0.83]</b>	<b>0.67 [0.48, 0.92]</b>	<b>0.60 [0.41, 0.87]</b>	<b>&lt;0.001</b>	<b>0.75 [0.67, 0.85]</b>	<b>&lt;0.001</b>
<b>Leg length</b>								
“Elevated CVD risk”/total	99/396	86/393	84/394	84/393	84/386			
Crude	1.00	0.87 [0.68, 1.12]	0.85 [0.66, 1.10]	0.85 [0.66, 1.10]	0.87 [0.67, 1.11]	0.268	0.96 [0.88, 1.05]	0.358
Model 1	1.00	0.89 [0.69, 1.14]	0.86 [0.67, 1.09]	0.86 [0.67, 1.11]	0.89 [0.69, 1.14]	0.362	0.97 [0.89, 1.05]	0.469
Model 2	1.00	0.89 [0.69, 1.14]	0.84 [0.65, 1.09]	0.85 [0.66, 1.10]	0.86 [0.66, 1.11]	0.237	0.97 [0.89, 1.05]	0.433

Model 3	1.00	0.88 [0.68, 1.12]	0.81 [0.63, 1.06]	0.84 [0.64, 1.10]	0.88 [0.66, 1.16]	0.356	0.97 [0.88, 1.06]	0.480
Model 4	1.00	0.97 [0.76, 1.26]	1.01 [0.75, 1.36]	1.16 [0.84, 1.62]	1.37 [0.92, 2.03]	0.114	<b>1.28 [1.05, 1.56]</b>	<b>0.012</b>
Relative leg length								
"Elevated CVD risk"/total	76/393	80/392	89/391	87/394	105/392			
Crude	1.00	1.04 [0.80, 1.38]	1.18 [0.90, 1.55]	1.15 [0.87, 1.50]	1.38 [1.07, 1.79]	<b>0.013</b>	<b>1.12 [1.02, 1.25]</b>	<b>0.022</b>
Model 1	1.00	1.04 [0.78, 1.38]	1.14 [0.87, 1.51]	1.10 [0.83, 1.46]	1.34 [1.02, 1.76]	<b>0.036</b>	1.11 [0.99, 1.24]	0.063
Model 2	1.00	1.05 [0.79, 1.40]	1.16 [0.88, 1.53]	1.11 [0.84, 1.48]	1.34 [1.02, 1.76]	0.058	1.11 [0.99, 1.24]	0.070
Model 3	1.00	1.05 [0.79, 1.38]	1.11 [0.84, 1.46]	1.06 [0.80, 1.42]	1.29 [0.97, 1.72]	0.106	1.09 [0.97, 1.23]	0.127

PR, prevalence ratio; Ref, reference category.

Men: model 1: adjusted for study site and adult and parental education; model 2: model 1 + body mass index, waist circumference, hip circumference; model 3: model 2 + adult height.

Women: model 1: adjusted for study site and adult and parental education; model 2: model 1 + age at menarche; model 3: model 2 + body mass index, waist circumference, hip circumference; model 4: model 3 + adult height.

at all study sites and among Ghanaian men in urban Ghana. Leg length was not associated with 10-year estimated ASCVD risk in this population.

In this study, we found that greater sitting height was associated with a lower 10-year estimated ASCVD risk, especially among women. This was independent of adult and parental education as well as anthropometric characteristics and age at menarche. To our knowledge, this is the first study to report on sitting height and risk of estimated ASCVD among a sub-Saharan African population exposed to different environmental contexts. Our findings are in line with results of sitting height in relation to circulatory disease in both men and women among 409,748 adults from the European Prospective Investigation in Cancer and Nutrition,<sup>49</sup> and to CVD mortality among 135,000 Chinese men and women.<sup>50</sup> However, some studies reported no association between sitting height and CVD.<sup>51,52</sup>

Adult anthropometric characteristics offer an alternative avenue to study the relationship between early-life exposures and CVD risk in adulthood when data on early-life growth and environments are not available.<sup>26</sup> Favorable childhood exposures have been associated with long-term physiological changes that decrease CVD risk, such as larger coronary vessel diameters, slower heart rate, and a greater lung capacity among people with higher sitting height.<sup>22,25,53</sup> Increase in height due to sitting height reflects accelerated growth mainly during the pubertal stage. In women, the growth of the trunk or torso continues even after puberty when estrogen surges to cause the cessation of leg growth.<sup>26</sup>

It is postulated that a lower relative leg length reflects the consequences of negative environmental conditions leading to delay in linear growth.<sup>54</sup> We observed a positive association between relative leg length and 10-year ASCVD risk among women in this study. The association between relative leg length and 10-year ASCVD risk was, however, partly explained by the proxies of adiposity (BMI, waist, and hip circumference) and age at menarche. Differences in relative leg length and growth in general are found to be related to body fat.<sup>54,55</sup> In this study, BMI, waist, and hip circumference had negative gradient, whereas age at menarche had positive gradient across quintiles of the relative leg length. An inverse association between BMI, waist circumference, and relative leg length is also reported in previous anthropometric studies.<sup>54,56</sup> Among growth delayed individuals or populations, inter-related compensatory physiological adjustments such as improved energetic efficiency and the low oxidation of fat are suggested to work together to promote fat storage.<sup>54</sup>

The differences in early-life environmental exposures could influence pubertal maturation and age at menarche among women and affect growth and CVD risk in adulthood.<sup>57</sup> Among urban and rural South African women, age at menarche has been shown to be positively associated with relative leg length.<sup>27</sup> Observations from other populations also showed an association between leg length and age at menarche.<sup>28,58,59</sup> A study based on the third National Health And Nutrition Survey found that earlier menarche was associated with shorter stature, mainly due to shorter leg length.<sup>28</sup> The association between age at menarche and leg length, however, depends on the contextual environment; earlier menarche predicts taller stature among developing countries, whereas it predicts shorter stature in developed countries.<sup>28</sup> Earlier pubertal timing is also predictive of greater risk of obesity<sup>60</sup> and type 2 diabetes<sup>61</sup> and with CVD in women.<sup>62</sup>

We found no association between absolute leg length and estimated 10-year CVD risk among Ghanaian populations. Previous analysis in this study also found no association between absolute

and relative leg lengths and type 2 diabetes among Ghanaian women.<sup>63</sup> The majority of subjects involved in this study were aged 40–50 years, possibly sharing similar early-life nutritional exposures, such as drought and hunger in Ghana especially from 1981 to 1983<sup>64</sup> and a period of economic and political instability between 1964 and 1992. None of the men and only 0.5% of the women in this study migrated before the age of 13 years. Adverse experience across all socioeconomic groups and in both rural and urban areas in the prepubertal years might have resulted in lower relative leg length. Similar observation and little variation in leg length was reported from a study of Mozambicans exposed to Civil unrest and warfare that characterized the late Colonial period.<sup>65</sup> Early nutritional exposures that influence leg length would, therefore, have been experienced in Ghana, resulting in little variation in leg length for RODAM study participants.

The associations between sitting height and predicted CVD risk in this study were generally independent of adult and parental educational status. However, the association between sitting height and ASCVD risk among men became significant, whereas the association for rural Ghana was attenuated after adjustment for adult and parental education. Educational attainment is found as an important pathway for the prediction of adult CVD risk by childhood or adolescent adversity.<sup>66</sup> However, although parental education could indicate childhood socioeconomic status, the general health status and access to healthcare depend on the physical environment, behavioral, and psychosocial stressors. Other factors such as maternal relationships, health behaviors, financial stress, and lack of medical care might also define parental socioeconomic background and influence the pathway between childhood malnutrition and risk CVD risk.<sup>66</sup>

Despite having higher sitting height among the migrant population, previous analysis in this population showed a less beneficial CVD risk factor profile and estimated CVD risk especially among men in the migrants compared to the home population.<sup>4,5</sup> Most chronic diseases including CVDs are seen as an interaction between environmental factors, such as diet and one's genetic susceptibility. Although a homogeneous African population may have similar early-life exposures, upon moving to an urbanized setting, there is an exposure to a larger variation in lifestyle, diet, and the entire societal context,<sup>67</sup> which determines gene–environment interactions and subsequent CVD developments in adulthood. The mismatch between the early-life conditions and subsequent reality in later life leads to health problems.<sup>15</sup> We suggest further investigation into the different socioeconomic exposures and origins of migration and their relation with CVD risk to get more insight into how physiological adaptations to early-life environment may have long-term consequences in a different environment.

### Strength and limitations

The RODAM study, conducted among a sub-Saharan African population of Ghanaians, provides a unique opportunity to assess the association between early-life exposures and the development of CVD in adulthood. This study provides important evidence on the association between markers of early-life growth (tailored by environmental exposure such as nutrition and socioeconomic status) and CVD risk among sub-Saharan African populations living in industrialized cities in Europe and their home country counterparts. Given its cross-sectional nature, the correlation of predicted ASCVD risk with incident CVD events requires confirmation from prospective studies as the PCE risk algorithms used in

predicting ASCVD in this study have not been yet validated for sub-Saharan African populations.

Although well-standardized approaches for measurement procedures were applied across all sites during recruitment of subjects, the strategies had to be adapted to local circumstances due to different civil registration systems in the various study sites. Study participants might therefore be a biased subset of the target population as they tend to overrepresent those with risk factors but without the disease, referred to as the “worried well.” This represents independent bias in both risk factor and disease distribution and could produce minor to moderate errors in CVD risk calculated in this study.<sup>68</sup> However, a nonrespondent analysis undertaken demonstrated a fairly similar distribution of respondents and nonrespondents. Evidence also suggests that most Ghanaians in Europe are affiliated with Ghanaian organizations.<sup>69</sup> This indicates that the members of these organizations may be representative of the Ghanaian population residing in various cities in Europe cities, thereby rendering unlikely, the bias of CVD risk factor differences between European sites caused by the variation in sampling strategy.

Lastly, although these analyses took into consideration the possibility of multiple testing based on the Bonferroni<sup>70</sup> and Holm<sup>71</sup> methods, the effects of multiple outcome measurements cannot be fully precluded since we might not have exhausted all possible methods to check for this.

### Conclusions

This study contributes to the understanding of childhood influences on CVD risk. We found an association between sitting height and CVD risk among Ghanaian men and women. Adjustment for lifestyle factors and length of stay in Europe did not alter the association. The association in men was, however, seen for urban but not rural Ghana. These findings suggest that childhood nutritional exposures that influence sitting height may be important factors involved in adult CVD risk among Ghanaian populations. Further research in the differences in origin of migration and early-life exposures of SSA migrants and how this influences CVD risk in later life is recommended.

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**Conflict of interest.** None.

**Ethical standards.** The RODAM study was conducted according to the guidelines laid down in the Declaration of Helsinki. All procedures involving human subjects were reviewed and approved by the respective ethics committees in

Ghana, the Netherlands, the UK, and Germany. Written informed consent was obtained from all participants.

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