Longitudinal study of the influence of lung function on vascular health from adolescence to early adulthood in a British multi-ethnic cohort

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Abstract

Background: Vascular and lung function develop and decline over the life course; both predict cardiovascular events and mortality but little is known of how they develop over time. We analysed their relationship in a multi-ethnic cohort study to test whether lung function (LF) from early adolescence to young adulthood affected vascular indices.

Methods: 'DASH' (http://dash.sphsu.mrc.ac.uk) included 6,643 children aged 11-13y in 2003; a representative 10% sample (n=665) participated in a pilot follow-up in 2013. Psychosocial, anthropometric, blood pressure (BP) and LF measures were collected in both surveys; aortic pulse wave velocity (PWV) and augmentation index (AIx) were measured at aged 21-23y. Relationships between Forced Expiratory Volume z-scores ($zFEV_1$), after Global Initiative-ethnic adjustments and blood pressure (BP), PWV and AIx were tested in linear regression and general estimating statistical models.

Results: 488 people with complete data were included. At 11-13y, systolic BP (SBP) was positively associated with $zFEV_1$ (coefficient=1.90, 95%CI 1.11-2.68, $p<0.001$); but not at 21-13y. The 10y increase in $zFEV_1$ was associated with rise in SBP (1.38, 0.25-1.51, $p<0.05$) in mixed effect models adjusted for age, sex, ethnicity, waist-height ratio, employment, reported racism, smoking and alcohol use but diastolic BP change was unrelated. In fully adjusted models, neither PWV nor central AIx (AIxao) were associated with $zFEV_1$ at 11-13y or 21-23y ($P>0.05$).

Conclusion: FEV_1 change is positively and independently associated with SBP change from adolescence to young adulthood, suggesting earlier lung function plays important roles in systolic BP development. Vascular indices were unrelated to lung function or its change.

Keywords: FEV_1, longitudinal studies, blood pressure, pulse wave velocity, augmentation index

Introduction

In adulthood, impaired lung function (LF) is inversely related to the incidence of stroke[1], myocardial infarction, and cardiovascular mortality[2], independently of (after adjustment for) traditional cardiovascular risk factors in middle-age populations. Given LF's significance for adult vascular health, surprisingly few studies have examined the interrelationships of their developmental trajectories from childhood. Lung development starts in utero and continues through adolescence and early adulthood[3, 4], which raises the question whether sub-optimal lung growth and development could affect later vascular function and blood pressure (BP).

Whether associations between low LF and incidence of vascular events could be related to or mediated by its link with blood pressure (BP) and vessel dysfunction remain unclear. The inverse association between LF and BP has been reported in several adult studies[5-7]. In middle-aged (45-59y) and elderly (>60y) population, LF parameters measured at age 40 were stronger predictors of arterial stiffness (aortic pulse wave velocity (PWV) and pressure or flow wave reflection measured as augmentation index (AIx)) than LF at age 60[8-10]. Furthermore, LF and vascular function may track each other through convergent inflammatory or metabolic pathways throughout life, or genetic susceptibility. Such low-grade systemic inflammation is indicated by higher levels of C-reactive protein, fibrinogen and other systemic inflammatory markers[11].

There is increasing evidence of ethnic differences in the development of both LF and BP. Lung function is lower among South Asians and Black African origin children compared with White European peers even after adjustment for age, gender and height, findings which led to the recent development of ethnic specific equations[12].

A faster rise of BP has been observed among African origin children in the US[13] and among all ethnic minority groups in the UK[14,15] than their White counterparts. These studies signal that ethnic differences in growth velocities in early life and postnatally are important determinants of cardio-respiratory development.

To date, information is lacking on the determinants of cardio-respiratory development from an ethnically diverse population in early adulthood, a time when physical health is at its peak and when early signs of disease begin to appear. Studies that tracked growth from childhood and collected biomarkers and vascular measures are mainly of White Europeans with few in Europe varying in ethnic make-up[16, 17]. The Determinants of Adolescent Social well-being and Health (DASH) study, established in 2002, has followed health and social exposures of over 6000 young Londoners (UK), including 80% ethnic minorities, over the last 12 years. A pilot follow-up study of the cohort, now in their early 20s, was recently completed. We used the DASH study to examine potential associations between LF and BP, PWV and AIx from early adolescence to early 20s, and whether any observed association is influenced by gender, health behaviours and socio-economic circumstances (SEC).

Method

Details of the DASH study can be found elsewhere[18].

In 2002-2003, a total of 6643 students, aged 11-13y, from 51 secondary schools in 10 London boroughs, were recruited. In 2005-06, 4785 (88% of children in 49 schools, 72% of the initial cohort), participated in the first follow-up aged 14-16y. A 10% subsample (N=665, 97% of those contacted) participated in the pilot follow-up, completed in March 2014. The subsample consisted of 107 White UK, 102 Black Caribbean, 132 Black African, 99 Indian, 111 Bangladeshi or Pakistani and 115 other (mainly mixed) ethnicities. We first located the sample and 81% (5414 of 6643) of the cohort was traced through friendship networks, social media, and community campaigns. We then randomly selected 100 (50 per gender) per ethnic group, and pragmatically attempted, by repeated random selection, to ensure representation across the London boroughs, schools and SEC at 11-13y.

The study was approved by the Multi-centre Research Ethics Committee and additionally at age 21-23y from NHS Local Research Ethics Committees. Written informed consent was obtained from all participants. Ethnicity was self-reported, checked against reported parental ethnicity and grandparents' country of birth. Bangladeshis and Pakistanis were combined due to small sample sizes.

Spirometry data management and exclusion criteria

Spirometric assessments were undertaken using a portable Micro-plus spirometer (Micro Medical Ltd., Kent, UK) at 11-13y and 21-23y in accordance with published guidelines[19]. Details of data quality and acceptability from 11-13y survey have been published[20]. Data collected at 21-23y were over-read by a senior respiratory physiologist (UCL Great Ormond Street Institute of Child Health) to ensure appropriate quality control.

As the cohort is a healthy community sample of young people, the forced expired volume in 1 second (FEV_1) provides the optimal survey measure of airway caliber, with lower values or rapid decline in FEV_1 being associated with higher morbidity or unfavorable prognosis[21]. Missing data, implausible values or extreme outliers (-3< or >3 z-scores) for height and FEV_1, (eg: when FEV1 between 11-13y and 21-23y differed by <100m/L), or those with current asthma were excluded (n=177; Figure S1).

After adjusting for gender, age and standing height, FEV_1 was expressed as z-scores using the Global Lung function Initiative (GLI-2012) ethnic-specific equations[22]. As reliable spirometric equations for South Asians are lacking, the GLI-Black equation, which provided a better approximation for interpreting South Asian data was used instead[23]. Within a healthy population, the mean (SD) FEV_1 z-scores would approximate 0(1). A z-score difference in FEV_1 is equivalent to 12% of predicted FEV_1 at these ages.

Anthropometry, blood pressure, Arterial Stiffness & wave reflection measurements

Field staff was trained for 1 week prior to the start of fieldwork, and were re-certified at 6 monthly intervals. Equipments were calibrated regularly by the field supervisors. During adolescence, assessments were conducted in schools and at 21-23y, in community locations (e.g. local general practitioner's surgeries, local community pharmacies, survey clinic rooms at Kings College London).

Height was measured using portable stadiometers (Leicester), to the nearest 0.1 cm and weight using Salter electronic scales, to the nearest 0.1 kg. Waist circumference (cm) was measured midway between the 10th rib and the top of the iliac crest, and 0.5 cm subtracted to correct for measurement over T-shirt or vest. The mean of two duplicate measures was derived for the waist to height ratio (WHtR). SBP and DBP were measured at both time-points using validated OMRON M5-I semi-automatic devices and appropriately-sized cuffs, after participant had sat quietly for a timed 5 min, with >1 min between three readings. The mean of second and third readings was analysed, as previously reported[14]. At 21- 23y, central SBP (cSBP), pulse, PWV, central AIx (AIxao) and brachial BP were also measured using the Arteriograph 24-h device, previously calibrated and standardized[24].

Social exposures

A self-administered questionnaire measured smoking, alcohol consumption, racism and SEC at 11-13y and 21-23y. Reported racism was assessed using validated questions on unfair treatment on grounds of race, skin color, country of birth, or religion in various locations (school, neighborhoods and work)[25]. In adolescence, SEC

was assessed using parental employment and the Family Affluence Scale[26] based on number of cars, computers, and holidays. In adulthood, SEC was measured using own education and employment.

Statistical analyses

Continuous variables (SBP, DBP, WHtR, FEV) did not require transformation as the Shapiro-Wilk test indicated normal distributions. For BP, we first examined the cross-sectional associations between FEV_1 z-score and BP at 11-13y and at 21-23y, using linear regression models. We then used linear mixed models to examine the association between the change in FEV_1 and the change in BP, between 11-13y and 21-23y. In these latter analyses $zFEV_1$, gender and ethnicity at 11-13y were added as fixed covariates, and change in $zFEV_1$ and remaining social exposures were added as time varying covariates. All variables were added stepwise and 2 models (model with age, gender, ethnicity, waist-height ratio, and the model with further adjustment for all social exposures) were presented. For outcomes that were measured only at 21-23y (cSBP, PWV, AIx and FEV1), linear regression models were used to examine associations between these outcomes and z-FEV_1 at 11-13y and at 21-23y. Two sets of models were run. The first set was with z-FEV1 at 11-13y to examine, whether at this critical period of adolescence, there was an association with these outcomes at 21-23y. The second repeated the analyses with z-FEV_1 at 21-23. All the analyses were performed STATA 13. P values <0.05 were considered to be statistically significant.

Results

Study population

After exclusions, 488 subjects (53.1% males) were included in the analyses. At age 11-13y, the longitudinal sample's profile for most anthropometric parameters, BP and FEV_1 did not vary significantly by gender (Table 1). At 21-23y, males were taller and had higher BP, brachial SBP, central SBP and PWV but a lower heart rate and AIxao. Mean $zFEV_1$ for all ethnic groups and at both ages were within ±0.5 z-scores.) (Table S1). The 10-year increase in height, SBP and DBP was greater for Whites than for other ethnic minority groups (Table S2). At 21-23y Whites also had a higher PWV and lower AIxao (Table S1).

$zFEV_1$ and BP

Analyses of the crossectional data at 11-13y showed that $zFEV_1$was positively and independently associated with SBP at 11-13y (Table 2). Unadjusted, an increase in 1 $zFEV_1$ score was associated with +2.1 (95% CI:1.3-2.9) mmHg rise in SBP. Adjusting for age, gender, ethnicity and WHtR reduced this effect a little (+1.90 (1.11-2.68) mmHg). There was no significant change on further adjustment of racism, parental employment, current smoking and alcohol use. zFEV1 was not associated with DBP at 11-13y. At 21-23y, zFEV1 was positively but not significantly associated with SBP (Table 2). Figure1 shows the predicted means by ethnicity, derived from the core model, adjusted for age, gender and waist:height ratio. A

similar pattern was observed across the ethnic groups, with a stronger association between zFEV1 and SBP at 11-13y than 21-23y. zFEV1 was not associated with DBP (Table S3).

In analysis of the longitudinal data, changes in zFEV1 between 11-13y to 21-23y were associated with SBP between 11-13y and 21-23y (Table 3). Adjusting for age, gender, ethnicity, changes in WHtR were positively associated with SBP, the pooled average being +1.38(0.3-1.6) mmHg, unaltered by lifestyle and social exposures. Changes in $zFEV_1$ were not associated with DBP between 11-13y and 21-23y (Table S4).

The associations between $zFEV_1$ and cSBP, PWV & AIxao

$zFEV_1$ at 11-13y or 21-23y was not significantly associated with cSBP, PWV or AIx at 21-23y (Table 4). PWV was significantly associated with gender (women lower), age, WHtR and heart rate, the latter 2 also reducing AIx, which was unaffected by age or social exposures.

Discussion

To the best of our knowledge, this is the first longitudinal study with a diverse ethnic composition, as yet from a pilot follow-up, to report an association between LF and SBP between adolescence and early adulthood. The longitudinal changes in LF are positively associated with SBP during this part of the life course when considerable

growth occurs. The mechanisms underlying these associations are not well understood but could illustrate how greater lung growth marginally, but likely reversibly, impairs venous return to the heart over this growth period, with a reflex rise in SBP.

Normal developmental trajectory for lung function shows that it increases in childhood, peaks in young adulthood and then gradually decreases with age[12, 27, 28]. A US based longitudinal study (N=508) showed that a decline in lung function from average peak age (29.4y) to 35 years significantly predicted incidence of hypertension between mean ages 35-45y. In correspondence with DASH findings, the cross-sectional WHeezing Illnesses Study LEidsche Rijn (WHISTLER) study of 5 year-olds (N=382) in the Netherlands showed a positive relationship between FEV_1 and SBP (+4.8mmHg/L, 95% CI: -0.3–10.0). WHISTLER also showed a positive relationship with DBP (+4.6mmHg/L, 95% CI:-0.2–9.4) adjusted for age, gender, weight and height[29]. The results of WHISTLER and DASH, though discrepant in relation to DBP, suggest that the positive relationship between blood pressure and LF is normal physiological development in childhood and in early adolescence. As the WHISTLER result suggests a litre change in FEV_1 was associated with ~5 mmHg in SBP change in a 5y old child, when mean (SD) FEV_1 would be only 1.3(0.2)L, a change of 200ml (1SD) in FEV_1 would be associated with a 1mmHg increase in SBP. Similar results were observed here in DASH.

As with LF, the association between PWV and lung function has not been studied before in healthy children. A cross-sectional study of asthmatic children (aged 6.1–

15.3y) in Switzerland showed that carotid-femoral pulse wave velocity (PWVcf) was inversely associated ($r^2 = 0.20$, $p = 0.004$) with FEV_1[30]. It is noteworthy that the effect size of about +2mmHg increase in SBP these studies with 1 Z score of FEV1 is comparable across these studies of 5y olds and of 11-13y in DASH. Perhaps in contrast to the DASH findings, a cross-sectional community-based study of 249-8-year old children in Australia showed FEV_1 was inversely associated with carotid (not brachial, as here) AIx75 (coef=-0.17, P=0.03) and FVC (coef=-0.29, P<0.001)[31].

Strengths and weaknesses of study

Social exposures, for example deprivation, influence growth[32], which in turn influences cardio-respiratory development. The studies cited above did not examine potential moderating influences from social exposures. DASH contains information on socio-economic disadvantage and behaviours, which enabled an examination of their association on the $zFEV_1$-CVD measure. DASH contains a diverse sample, has high retention rates and low item-non-response, mainly due to enormous community support. LF was not measured at the second follow-up of the cohort at 14-16y, which could have provided valuable insight into the pattern of changing associations with BP in adolescence. The lack of data before age 11y and the relatively small sample sizes for the ethnic groups in the pilot follow-up are limitations. Prior to DASH a large-scale study with an explicit focus on ethnicity had not been attempted. The use of the GLI-2012 ethnic-specific equations rather than absolute FEV also strengthened the analysis. These robust equations have been shown to be appropriate for London

school children[33] and the small offset (≤0.5 z-scores) in mean FEV_1 in all ethnic groups observed in this study suggest a sample size issue. Quanjer and colleagues suggested that a dataset of ≥300 (150 males and 150 females) would be required to validate reference values to avoid spurious differences due to sampling error[34]. Despite relatively small numbers, these findings in a tight age range provide strong justification for future studies on the degree and how childhood and adolescent LF influence vascular development to improve understanding of the developmental interaction of cardio-respiratory systems.

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Disclosures

None

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Table 1 Sample characteristics by gender. The Determinants of Adolescent Social well-being and Health study

Variables	11-13y		21-23y	
	Male	Female	Male	Female
Age (year)	12.6(12.5,12.7)	12.5(12.4,12.6)	22.9(22.8,23.0)	22.7(22.6,22.8)
Height (cm)	155.0(153.7,156.3)	155.7(154.7,156.7)	176.1(175.2,176.8)	163.7(162.8,164.5)
Waist: height ratio	0.40(0.41,0.44)	0.43(0.42,0.44)	0.48(0.47,0.49)	0.49(0.08,0.50)
SBP(mmHg)	109.2(107.94,110.50)	107.2(106.0,108.3)	120.2(118.9,121.4)	107.1(105.8,108.4)
DBP(mmHg)	66.5(65.5,67.5)	66.7(65.8,67.6)	73.5(72.5,74.5)	71.4(70.4,72.4)
FEV_1 (L)	2.4(2.3,2.5)	2.3(2.3,2.4)	3.9(3.7,4.1)	2.9(2.8,2.9)
$zFEV_1$ (Forced Expiratory Volume in 1 second)	-0.22(1.08)	-0.32(1.09)	-0.43(0.98)	-0.43(1.01)
Pulse (beats/minute)			66.4(65.0,67.7)	71.3(69.8,72.7)
$zFEV_1$ (%)				
-1 to +1 z score	62.1(56.3,68.1)	61.6(55.2,68.1)	62.5(56.6,68.3)	65.8(59.4,72.1)
<-1 z score	24.5(19.4,29.7)	28.8(22.7,34.8)	28.6(23.2,34.1)	26.5(20.6,32.4)
>1 z score	13.4(9.3,17.5)	9.6(5.7,13.5)	8.9(5.5,12.3)	7.8(4.2,11.3)
Brachial SBP(mmHg)			121.8(120.3,123.3)	112.7(111.0,114.4)
†cSBP(mmHg)			109.6(108.2,111.0)	103.6(102.2,105.0)
PWV(m/s)*			7.4(7.19,7.6)	6.8(6.6,6.9)
Aixao(%)			12.1(11.0,13.3)	15.6(14.1,17.0)
Currently smoking				
Yes(%)	0.01(-0.001,0.2)	0.02(0.001,0.03)	32.7(27.1,38.3)	37.4(31.0,43.9)
Alcohol use				
Yes(%)	25.7(20.4,30.9)	24.7(18.9,30.4)	53.2(47.2,59.2)	61.2(54.7,67.7)
Reported racism				
Yes(%)	20.4(15.6,25.3)	20.1(14.8,25.4)	43.9(37.9,49.8)	43.4(36.8,50.0)
Parental/own employment				

Yes(%)	75.8(70.7,81.0)	77.6(72.1,83.2)	48.3(42.3,54.3)	52.5(45.9,59.2)
Family Affluence Scale ϕ				
≥3	53.5(47.5,59.5)	53.0(46.3,59.6)		
1--2	27.5(22.4,32.9)	29.7(23.6,35.8)		
Education				
Completed a university degree (%)			40.9(35.0,46.8)	57.5(51.0,64.1)

Values are mean (95%CI) or percentage (95%CI). Z score of FEV1 are mean(SD).

CI: confidence Interval.

†cSBP, central SBP. *PWV, pulse wave velocity.

ϕ Family affluence scale comprises of number of holidays last year, computers, cars or vans.

Table 2 Cross-sectional associations between Forced Expiratory Volume in 1second ($zFEV_1$) and SBP at 11-13y and at 21-23y. The Determinants of Adolescent Social well-being and Health (DASH) study

Anthropometry, lifestyle, social factors	11-13y		21-23y	
	Core modelϕ	+lifestyle and social variable‡	Core modelϕ	+lifestyle and social variable‡
$zFEV_1$	1.9(1.1,2.7) ξ	2.1(1.3,2.9) ξ	0.5(-0.3,1.4)	0.5(-0.3,1.4)
Ethnicity (White UK:ref)				
Black Caribbean	-0.02(-2.9,2.9)	-0.3(-3.2,2.5)	-1.9(-4.8,1.1)	-1.7(-4.8,1.4)
Black African	0.4(-2.3,3.1)	-0.1(-2.9,2.7)	-2.0(-4.8,0.8)	-2.0(-5.1,1.1)
India	-0.7(-3.6,2.2)	-1.4(-4.4,1.6)	-4.0(-7.0,-1.0)#	-4.0(-7.2,-0.8)*
Pakisitani/Bangladeshi	-4.6(-7.4,-1.8)	-5.4(-8.5,-2.5) ξ	-7.1(-10.0,-4.2) ξ	-6.8(-10.2,-3.4) ξ
Others	-1.2(-3.9,1.6)	-1.0(-3.7,1.7)	-4.0(-6.9,-1.2)#	-3.8(-6.8,-0.8)*
Female	-1.8(-3.4,-0.1)*	-1.6(-3.2,0.1)	-13.6(-15.3,-11.9) ξ	-13.9(-15.6,-12.1) ξ
Age	2.4(1.0,3.7) ξ	2.9(1.2,4.3) ξ	0.5(-0.7,1.6)	0.3(-0.9,1.5)
Waist:Height ratio	31.4(16.8,46.1) ξ	26.9(12.4,41.4) ξ	31.2(19.4,42.9) ξ	31.9(20.0,43.9)
Reported racism (no:ref)				
Yes		-1.3(-3.4,0.8)		0.2(-2.0,1.6)
Parental/own employment (yes:ref)				
NO		-0.6(-2.9,1.7)		-1.0(-3.1,1.1)
Current smoking (Yes: ref)				
No		-6.3(-13.3,0.6)		0.2(-2.1,2.5)
Alcohol use (Yes:ref)				
NO		-1.3(-3.4,0.9)		0.3(-1.9,2.5)

*Data were statistically significant at P<0.05; #Data were statistically significant at P<0.01; ξData were statistically significant at P<0.001.

ϕCore model: linear models adjusted for age, gender, ethnicity and waist:height ratio at 11-13y and 21-23y separately (11-13y R^2=0.14, 21-23y R^2=0.37)

‡Final model: core model +reported racism + employment +lifestyle factors (smoking and alcohol use) (11-13y R^2=0.17, 21-23y R^2=0.36).

Table 3 The influence of Forced Expiratory Volume in 1second ($zFEV_1$) on systolic blood pressure from early childhood to young adulthood. The Determinants of Adolescent Social well-being and Health (DASH) study

Anthropometry, lifestyle, social factors	Difference from baseline mean systolic blood pressure		
	Core model	+Lifestyle variables†	+Social variables‡
Change in zFEVs between baseline (11-13y) and follow up (21-23y)			
$\Delta zFEV_1$	1.4(0.3,1.5)*	1.4(0.3,2.6)*	1.4(0.3,2.5)*
$zFEV_1$ at baseline	-0.1(-1.2,1.0)	-0.1(-1.2,1.1)	0.02(-1.2,1.1)
Female	-7.8(-9.2,-6.5)ξ	-7.7(-9.1,-6.3)ξ	-7.7(-9.1,-6.3)
Ethnicity (White UK:ref)			
Black Caribbean	-0.9(-3.3,1.5)	-0.9(-3.4,1.5)	-0.8(-3.3,1.6)
Black African	-0.8(-3.1,1.5)	-1.0(-3.4,1.4)	-0.8(-3.2,1.6)
India	-2.4(-4.8,0.0)*	-2.6(-5.1,-0.1)*	-2.5(-5.0,0.0)
Pakisitani/Bangladeshi	-6.0(-8.3,-3.6)#	-6.6(-9.1,-4.0) ξ	-6.4 (-9.0,-3.8) ξ
Others	-2.6(-4.9,-0.3)*	-2.6(-4.9,-0.3) ξ	-2.4(-4.8,-0.1)*
Time-dependent variables			
ΔAge	0.5(0.4,0.6)ξ	0.4(0.3,0.6) ξ	0.4(0.3,0.6) ξ
Δwasit:height ratio	27.1(17.1,37.0)ξ	26.5(16.5,36.4) ξ	26.4(16.4,36.3) ξ
Current smoking (No: ref)			
Δyes		2.5(0.4,4.6)*	2.5(0.4,4.6)*
Acohol use (No:ref)			
ΔYes		0.8(-2.4,0.7)	0.8(-2.4,0.8)
Employment (Yes:ref)			
NO			-0.2(-1.8,1.3)
Racism (no:ref)			
Yes			-0.9(-4.6,2.8)

*Data were statistically significant at P<0.05; #Data were statistically significant at P<0.01; ξData were statistically significant at P<0.001.

Core model: mixed effect models adjusted for age, gender, ethnicity, waist:height ratio and baseline $zFEV_1$.

† Core model + lifestyle factors (alcohol and smoking).

‡Core model +lifestyle factors+ employment +reported racism.

Table 4 The influence of Forced Expiratory Volume in 1second ($zFEV_1$) from early childhood to young adults on Central Blood Pressure, Pulse Wave Velocity & AIxao at 21-23y. The Determinants of Adolescent Social well-being and Health (DASH) study

Anthropometry, lifestyle, social factors	cSBP		PWV		AIxao	
	Core modelϕ	+lifestyle and social variableǂ	Core modelϕ	+lifestyle and social variableǂ	Core modelϕ	+lifestyle and social variableǂ
$zFEV_1$ at 21-23y	0.7(-0.9,2.2)	0.4(-2.1,3.0)	-0.05(-0.2,0.1)	0.03(-0.2,0.1)	0.03(-1.2,1.3)	0.2(-1.1,1.5)
$zFEV_1$ at 11-13y	-0.7(-2.2,0.7)	-0.7(-3.3,1.8)	0.02(-0.1,0.2)	0.005(-0.2,0.2)	-0.4(-1.6,0.7)	-0.5(-1.7,0.7)
Age	-0.1(-1.5,1.4)	-2.6(-6.6,1.5)	0.4(0.2,0.5) ξ	0.7(0.2,0.7) ξ	-0.2(-1.4,1.0)	-1.6(-3.5,0.4)
Female	-7.0((-9.2,-4.8) ξ	-5.5(-9.5,-1.5) ξ	-0.8(-1.0,-0.5) ξ	-0.7(-1.0,-0.4) ξ	2.2(-0.3,4.6)	2.3(-0.3,4.9)
Ethnicity (White UK:ref)						
Black Caribbean	-0.7(-4.4,3.0)	-2.4(-8.5,3.6)	-0.1(-0.5,0.3)	-0.1(-0.6,0.3)	0.8(-2.2,3.8)	0.1(-3.1,3.3)
Black African	-0.9(-4.4,2.6)	1.4(-5.2,8.0)	-0.2(-0.6,0.2)	-0.3(-0.7,0.2)	2.3(-0.5,5.2)	3.0(-0.3,6.3)
India	-6.0(-9.6,-2.4) ξ	-5.0(-11.5,1.5)	-0.2(-0.6,0.2)	-0.2(-0.7,0.2)	0.4(-2.7,3.4)	1.5(-2.0,4.9)
Pakisitani/Bangladeshi	-6.8(-10.4,-3.2) ξ	-3.4(-11.4,4.6)	-0.3(-0.7,0.1)	-0.5(-1.0,0.1)	2.9(-0.2,5.9)	3.3(-0.5,7.1)
Others	-3.9(-7.3,-0,5)*	-1.2(-7.1,4.8)	-0.2(-0.6,0.1)	-0.3(-0.8,0.1)	0.5(-2.3,3.4)	0.9(-2.1,4.0)
Waist:Height ratio	60.4(44.2,76.5) ξ	65.8(27.6,104.0) ξ	2.6(0.7,4.6) #	2.9(0.4,5.4)*	-0.3(-0.5,-0.2) ξ	-0.3(-0.5,-0.2) ξ
Pulse	-0.01((-0.1,0.1)	-0.03(-0.2,0.1)	0.05(0.034,0.06) ξ	0.04(0.03,0.05) ξ	-0.3(-0.4,-0.2) ξ	-0.3(-0.4,-0.2) ξ
brSBP			0.007(-0.00,0.02)	0.01(-0.00,0.02)	-0.1(0.05,0.2)	0.1(0.04,0.2)#

*Data were statistically significant at P<0.05; #Data were statistically significant at P<0.01; ξData were statistically significant at P<0.001.

ϕCore Models: linear models adjusted for age, gender, ethnicity and wait:height ratio, pulse and (brachial blood pressure for PWV and AIXao) at 21-23 years years (R^2=0.19, 0.27& 0.19).

ǂFinal Model: core model+ reported racism, employment, education, smoking and alcohol using at 21-23y+ adolescent adjustment (R^2=0.17, 0.29 & 0.23).

Table S1 Sample characteristics by gender. The Determinants of Adolescent Social well-being and Health study

Variables	White UK N=86	Black Caribbean N=73	Black African N=88	India N=71	Pakistani/Bangladeshi N=82	Other N=88
Boys	45	35	46	41	42	50
Age						
11-13y	12.6(12.5,12.7)	12.6(12.5,12.8)	12.6(12.5,12.7)	12.5(12.3,12.6)	12.4(12.3,12.6)	12.6(12.5,12.7)
21-23y	22.7(22.6,22.8)	22.8(22.6,23.0)	22.7(22.5,22.9)	22.9(22.7,23.1)	22.7(22.6,22.9)	22.9(22.8,23.1)
Height(cm)						
11-13y	155.6(153.6,157.5)	157.3(155.2,159.5)	159.4(157.6,161.2)	151.6(149.7,153.5)	151.9(149.7,154.1)	155.6(153.7,157.5)
21-23y	173.1(171.1,175.0)	170.6(168.4,172.9)	172.3(170.4,174.3)	168.5(166.2,170.7)	168.1(166.1,170.0)	170.0(168.2,171.9)
Waist-Height Ratio						
11-13y	0.43(0.42,0.44)	0.426(0.41,0.44)	0.43(0.41,0.44)	0.43(0.42,0.45)	0.42(0.41,0.43)	0.432(0.42,0.44)
21-23y	0.47(0.46,0.49)	0.48(0.46,0.50)	0.48(0.47,0.50)	0.49(0.47,0.51)	0.49(0.48,0.50)	0.48(0.46,0.49)
SBP(mmHg)						
11-13y	109.1(107.14,111.0)	109.4(106.8,111.9)	109.6(107.6,111.6)	108.8(106.7,111.0)	105.1(102.9,107.3)	107.9(105.8,110.0)
21-23y	116.7(113.8,119.6)	114.6(112.0,117.2)	114.9(112.5,117.3)	114.1(111.2,117.0)	111.9(109.3,114.4)	113.5(111.2,115.9)
DBP(mmHg)						
11-13y	66.6(65.0,68.1)	67.9(65.8,69.9)	66.6(65.2,68.0)	68.0(66.2,69.7)	65.7(64.1,67.3)	65.2(63.7,66.8)
21-23y	73.4(71.6,75.3)	73.5(71.7,75.2)	72.9(71.2,74.6)	72.8(70.9,74.7)	71.4(69.7,73.1)	71.4(69.7,73.0)
FEV_1(L)						
11-13y	2.6(2.5,2.7)	2.4(2.2,2.5)	2.4(2.3,2.5)	2.1(2.0,2.3)	2.3(2.2,2.4)	2.4(2.3,2.5)
21-23y	3.9(3.7,4.1)	3.3(3.1,3.4)	3.3(3.1,3.4)	3.2(3.0,3.3)	3.3(3.2,3.5)	3.5(3.3,3.6)
$zFEV_1$						
11-13y	-0.43(1.12)	-0.21(1.07)	-0.28(1.04)	-0.25(0.98)	0.13(1.05)	-0.51(1.16)
21-23y	-0.52(1.00)	-0.35(0.90)	-0.49(0.95)	-0.46(0.75)	-0.15(1.02)	-0.58(1.21)
†cSBP(mmHg)						
21-23y	108.9(106.4,11.4)	109.1(106.1,112.1)	107.6(105.2,110.0)	104.8(102.2,107.3)	105.2(102.9,107.5)	104.5(102.3,106.6)
Brachial SBP(mmHg)						
21-23y	120.6(117.1,124.0)	119.8(116.9,122.8)	118.7(115.5,121.9)	116.6(113.8,119.4)	114.4(111.8,117.0)	116.2(113.7,118.7)

Pulse						
21-23y	71.0(68.5,73.6)	66.6(64.2,69.0)	65.2(62.7,67.6)	69.0(66.2,71.8)	70.6(68.3,72.9)	68.7(66.4,71.1)
PWV(m/s)						
21-23y	7.4(7.0,7.8)	7.1(6.8,7.4)	6.87(6.59,7.2)	7.2(6.9,7.5)	7.1(6.8,7.5)	7.1(6.8,7.4)
AIXao (%)						
21-23y	11.5(9.6,13.5)	14.3(12.1,16.5)	15.4(12.3,18.5)	12.9(10.7,15.0)	14.6(12.4,16.9)	13.2(11.5,15.0)
Reported racism (%)						
11-13y	14.0(6.6,21.3)	20.5(11.2,29.9)	20.5(12.0,29.0)	15.5(7.0,24.0)	26.8(17.2,36.5)	23.9(14.9,32.8)
21-23y	22.1(13.3,30.9)	50.7(39.1,62.3)	51.1(40.6,61.7)	40.8(29.30,52.4)	46.3(35.5,57.2)	51.1(40.6,61.7)
Employment (%)						
Parental	87.2(80.1,94.3)	78.1(68.5,87.7)	78.4 (69.7,87.1)	77.5(67.7,87.3)	52.4(41.5,63.3)	85.2(77.8,92.7)
Own	53.5(42.9,64.1)	50.7(39.1,62.3)	52.3(41.8,62.8)	50.7(39.0,62.4)	41.5(30.7,52.2)	52.3(41.8,62.8)
Current smoking (yes) (%)						
11-13y	0.02(-0.001,0.05)	0.05(0.002,0.1)	0	0	0.01(-0.01,0.04)	0
21-23y	29.1(19.4,38.7)	39.7(28.4,51.1)	39.8(29.5,50.1)	33.8(22.7,44.9)	26.8(17.2,36.5)	39.8(29.5,50.1)
Alcohol Using (yes) (%)						
11-13y	48.8(38.2,59.5)	38.4(27.1,59.16	18.2(10.1,26.3)	4.2(-0.5,9.00)	1.2(-1.2,3.6)	37.5(27.3,47.7)
21-23y	89.5(83.0,96.1)	74.0(63.8,84.1)	52.3(41.8,62.8)	49.3(37.6,61.0)	8.3(2.43,14.6)	65.91(55.9,75.9)
Family Affluence Scaleϕ (%)						
>=3	57.0(46.4,67.5)	53.4(41.9,65.0)	54.5(44.1,65.0)	47.9(36.2,59.6)	43.9(33.1,54.7)	61.4(51.1,71.6)
1--2	30.2(20.5,40.0)	28.8(18.3,39.3)	22.7(13.9,31.6)	31.0(20.1,41.8)	31.7(21.6,41.9)	27.3(17.9,36.7)
Education (%)						
Has degree	40.7(30.2,51.2)	35.6(24.5,46.7)	62.5(52.3,72.7)	63.4(52.1,74.7)	45.1(34.3,56.0)	43.2(32.7,53.6)

Values are mean (95%CI) or percentage (95%CI). zscore of FEV1 are mean(SD).

CI: confidence Interval.

†cSBP, central SBP. *PWV, pulse wave velocity.

ϕ Family Affluence Scale comprises of number of holidays last year

Table S2 The difference in anthropometric measures between 21-23y and 11-13y, by ethnicity

Variables	White UK	Black Caribbean	Black African	India	Pakistani/Bangladeshi	Other
Height (cm)	17.5(15.3,19.7)	13.3(11.3,15.3)	13.0(11.0,14.9)	16.9(14.4,19.3)	16.2(13.9,18.4)	14.5(12.6,16.3)
Waist-Height Ratio	0.04(0.03,0.06)	0.06(0.04,0.07)	0.06(0.04,0.07)	0.05(0.03,0.07)	0.07(0.05,0.08)	0.05(0.04,0.06)
SBP(mmHg)	7.6(5.0,10.2)	5.21(1.9,8.5)	5.3(3.0,7.7)	5.3(2.6,8.02)	6.7(3.9,9.6)	5.5(3.2,8.0)
DBP(mmHg)	6.8(5.0,8.7)	5.62(3.5,7.8)	6.3(4.5,8.1)	4.8(2.6,7.1)	5.7(3.76,7.7)	6.1(4.2,8.0)
FEV_1(L)	1.3(1.1,1.4)	0.9(0.8,1.1)	0.9(0.8,1.0)	1.0(0.9,1.2)	1.0(0.9,1.2)	1.1(0.9,1.2)
$zFEV_1$	-0.09(-0.24,0.07)	-0.14(-0.32,0.05)	-0.21(-0.37,-0.05)	-0.21(-0.39,-0.03)	-0.28(-0.47,-0.09)	-0.07(-0.23,0.09)

Table S3 The cross-sectional associations between Forced Expiratory Volume in 1second ($zFEV_1$) and DBP at 11-13y and 21-23y separately. Sample characteristics by gender. The Determinants of Adolescent Social well-being and Health study

Anthropometry, lifestyle, social factors	11-13y		21-23y	
	Core modelϕ	+lifestyle and social variableǂ	Core modelϕ	+lifestyle and social variableǂ
$zFEV_1$	0.5(-0.1,1.1)	0.6(-0.02,1.2)	-0.4(-1.0,0.3)	-0.4(-1.0,0.3)
Ethnicity (White UK:ref)				
Black Caribbean	1.2(-1.02,3.5)	1.0(-1.3,3.2)	-0.04(-2.4,2.3)	0.3(-2.2,2.7)
Black African	0.1(-2.,2.2)	-0.3(-2.5,1.9)	-0.7(-3.0,1.5)	-0.1(-2.6,2.3)
India	1.1(-1.2,3.4)	0.7(-1.7,3.1)	-1.3(-3.7,1.1)	-0.7(-3.2,1.8)
Pakisitani/Bangladeshi	-0.8(-3.0,1.5)	-1.5(-3.9,1.0)	-2.6(-5.0,-0.3)*	-1.5(-4.2,1.2)
Others	-1.3(-3.5,0.8)	-1.3(-3.5,0.8)	-2.4(-4.7,-0.2)*	-2.0(-4.3,0.4)
Female	0.4(-1.0,1.7)	0.5(-0.8,1.8)	-2.5(-3.9,-1.1) ξ	-2.6(-4.0,-1.2) ξ
Age	0.9(-0.2,2.0)	1.2(0.1,2.3)*	0.3(-0.6,1.2)	0.1(-0.8,1.1)
Waist:Height ratio	32.0(20.4,43.6) ξ	28.7(17.1,40.2) ξ	31.3(21.9,40.7) ξ	30.9(21.4,40.4) ξ
Reported racism (no:ref)				
Yes		-1.0(-2.6,0.7)		-0.1(-1.6,1.3)
Parental/own employment (yes:ref)				
NO		0.6(-1.2,2.4)		-1.0(-2.7,0.7)
Current smoking (Yes: ref)				
No		-3.5(-9.0,2.1)		1.5(-0.3,3.4)
Alcohol use (Yes:ref)				
NO		-0.5(-2.3,1.2)		1.4(-0.3,3.2)

*Data were statistically significant at P<0.05; #Data were statistically significant at P<0.01; ξData were statistically significant at P<0.001.

ϕ Core model: adjusted for age, gender, ethnicity and waist:height ratio at 11-13y and 21-23y separately (11-13y R^2=0.09, 21-23y R^2=0.12)

ǂFinal model: core model +reported racism + employment +lifestyle factors (alcohol and smoking) (11-13y R^2=0.13, 21-23y R^2=0.14).

Table S4 The influence of Forced Expiratory Volume in 1second ($zFEV_1$) from early childhood to young adults on DBP. Sample characteristics by gender. The Determinants of Adolescent Social well-being and Health study

Anthropometry, lifestyle, social factors	Difference from baseline mean diastolic blood pressure		
	Core model	+Lifestyle variables†	+Social variables‡
Change in zFEVs between baseline (11-13y) and follow up (21-23y)			
$\Delta zFEV_1$	-0.2(-1.0,0.7)	-0.2(-1.0,0.7)	-0.2(-1.0,0.7)
$zFEV_1$ at baseline	0.4(-0.5,1.2)	0.4(-0.5,1.2)	0.4(-0.5,1.3)
Female	-1.1(-2.2,-0.004)*	-1.0(-2.1,0.03)	-1.0(-2.1,0.05)
Ethnicity (White UK:ref)			
Black Caribbean	0.6(-1.3,2.5)	0.7(-1.2,2.5)	0.7(-1.2,2.6)
Black African	-0.3(-2.1,1.4)	-0.2(-2.1,1.6)	-0.2(-2.0,1.7)
India	-0.2(-2.1,1.7)	-0.06(-2.0,1.9)	-0.02(-2.0,1.9)
Pakisitani/Bangladeshi	-1.8(-3.6,0.1)	-1.8(-3.7,0.2)	-1.7(-3.7,0.3)
Others	-1.9(-3.7,-0.1)*	-1.7(-3.5,0.06)	-1.7(-3.5,0.2)
Time-dependent variables			
ΔAge	0.4(0.3,0.5) ξ	0.3(0.2,0.4) ξ	0.3(0.2,0.4) ξ
Δwasit:height ratio	29.9(22.3,37.5) ξ	29.5(22.0,37.1) ξ	29.5(22.0,37.1) ξ
Current smoking (No: ref)			
Δyes		2.3(0.75,3.85)#	2.3(0.74,3.9)#
Acohol use (No:ref)			
ΔYes		0.3(-0.9,1.4)	0.3(-0.9,1.4)
Employment (Yes:ref)			
NO			0.1 (-1.0,1.3)
Racism (no:ref)			
Yes			-0.4(-1.4,0.7)

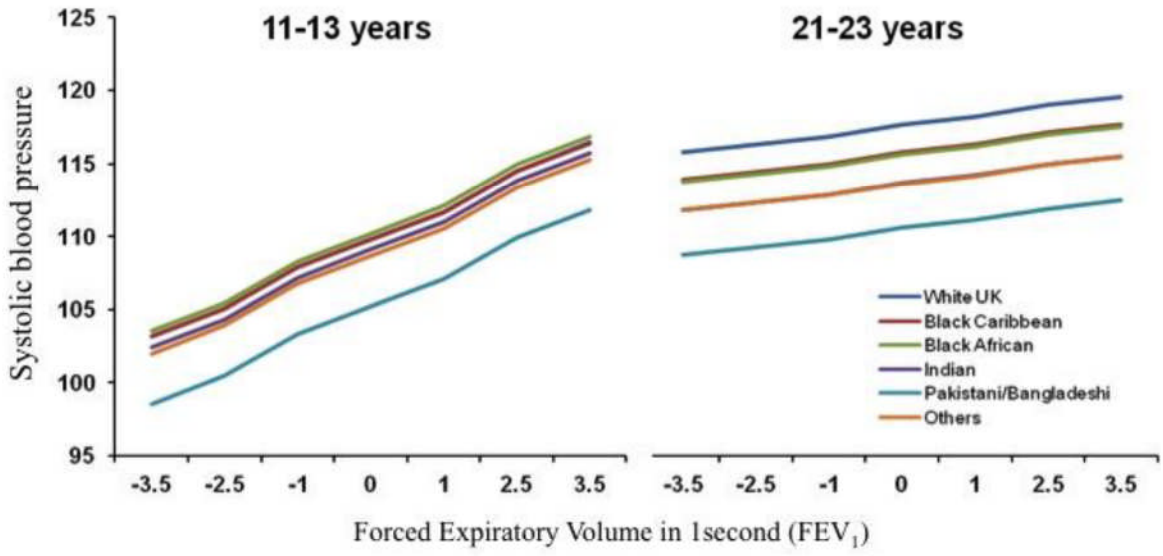
*Data were statistically significant at P<0.05; #Data were statistically significant at P<0.01; ξData were statistically significant at P<0.001.

Core model: adjusted for age, gender, ethnicity, waist:height ratio and baseline $zFEV_1$.

† Core model + lifestyle factors (smoking and alcohol use)

‡Core model +lifestyle factors+ employment +reported racism.

Figure 1 Predicted mean systolic blood pressure by z-FEV1 (Forced Expiratory Volume in 1second, superscript for footnote) at 11-13 years and at 21-23 years, derived from linear regression models adjusted for age, gender, ethnicity and waist to height ratio. The Determinants of Adolescent Social Well-being and Health (DASH) study



zFEV$_1$ was derived with reference[22] FEV$_1$, adjusted for gender, age and standing height, expressed as z-scores using the Global Lung function Initiative (GLI-2012) ethnic-specific equations.

Figure 1S A flow diagram of participant enrollment.