Lung function in children in relation to ethnicity, physique and socio-economic factors

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Online data supplement

Introduction

This OLS contains supplementary tables, illustrations and other details for which there was no room in the Main manuscript.

1. Materials and Methods: additional information

1.1. Pilot study

A pilot study, funded by Asthma UK was undertaken between November 2010-October 2011 to assess feasibility and inform study design prior to undertaking the definitive study (subsequently awarded funding by the Wellcome Trust). Written parental consent was obtained from 201 (59%) of 340 children approached in two London schools. Acceptable spirometry data were available from 136 healthy children of Black-African origin and 21 non-Black children. The pilot study provided valuable experience and information regarding both practical issues, design of questionnaires and potential ways in which to improve consent rates for the definitive study.

1.2. Definitive study: School recruitment and assessments (October 2011 – July 2013)

London schools with a high ethnic mix were identified and sampled by education performance within boroughs to ensure a wide range of socio-economic circumstances, prior to seeking approval from Head teachers for recruitment. An all-inclusive strategy was adopted to ensure no child would feel excluded from a study that was being undertaken in the school. Thus children who obtained parental consent in the 2nd year but not the 1st year of study were still eligible to participate. To ensure adequate power for final analysis after exclusions, recruitment was extended to the whole school (rather than alternate year groups) during the 2nd year of data collection.

Parental awareness of the SLIC study was heightened by including lay summaries in school newsletters, inviting parents to attend presentations at school and publishing summaries in both Gujarat and English newspapers widely read by South-Asians in London. Interactive Science workshops were conducted in each class and recruitment packs (information sheets, consent forms and questionnaires) were given to all children to take home.

Researchers were fully trained prior to study commencement, this training being supplemented by on-going quality assurance checks throughout the study. Assessments were carried out by a single research team and were undertaken outside the classroom to minimise disruption. Baseline assessments (Year 1) were undertaken within a mobile laboratory (housing the 3-D scanner and all equipment). This was parked in the school grounds and children were escorted in small groups to and from the classroom by a researcher or teaching assistant. The assessments lasted ~45 minutes per child. Follow-up assessments 12 months later (Year 2) were performed in a room within the school. The schedule and description of assessments undertaken is shown in Table E1.To avoid bias due to seasonality (e.g. pollution, allergens and recent respiratory infections), follow-up assessments were timed to occur within 12m ±1m of the initial assessments. Despite potential language barriers due to the migrant population, consent to participate exceeded 50% and teachers, parents and pupils were enthusiastic in their feedback (www.ucl.ac.uk/slic).

Table E1. Schedule and description of assessments.

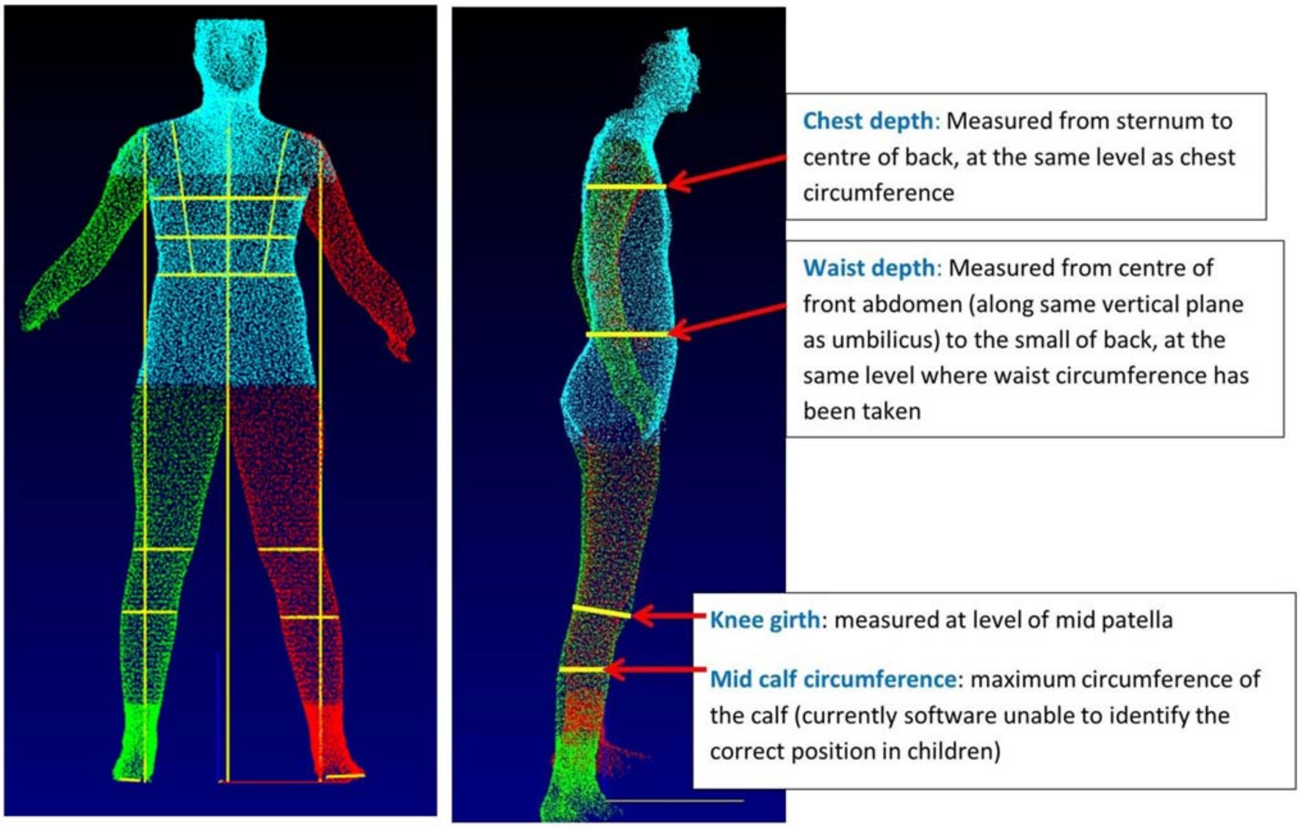
Assessments	**Yr 1**	**Yr 2**
Anthropometry		
Weight (Seca digital scales, UK)	Y	Y
Standing height (Leicester stadiometer, Seca, UK)	Y	Y
Sitting height (Leicester stadiometer and a stool)	Y	Y
Chest circumference, width & depth* (~2-3 cm below axilla)	Y	Y
Waist circumference, width & depth* (narrowest girth)	Y	N
Mid arm circumference*	Y	N
Knee girth*	Y	N
Calf Circumference*	Y	N
Foot length*	Y	N
3-D scan for body shape ([TC]^{E2}, NX16 scanner, North Carolina) Assessments include: all manual anthropometry mentioned above with exception of weight, standing and sitting height (Figure E1)	Y	N
Body composition: Bioelectrical Impedance Analysis (BIA) (Tanita BC418 analyser, Netherlands)	Y	Y
Body composition: Isotope dilution (Deuterium)	Y	Y
Spirometry†: Ultrasonic flowmeter, Easy-on-PC (ndd, Switzerland) used in ***definitive study*** Jaeger Masterscope (v4.67, CareFusion, San Diego, US) only used in ***pilot study***	Y	Y
Saliva sample: Cotinine analysis	N	Y
Parental questionnaire	Y	Y
GP records	N	Y

*Circumferences assessed using Seca 201 tape measure; width & depth using sliding calipers with deep jaws (Chasmors Ltd, London); See: http://discovery.ucl.ac.uk/1417500/ for further details of assessments; †Spirometry data assessed using the Jaeger Masterscope (pilot study) or the ndd Easy-on-PC system (definitive study) have been shown to produce very similar results[E1].

1.3. 3-D assessment for body shape and detailed manual anthropometric measurements

3-D photonic scanning for assessment of body shape is a relatively new technology primarily designed for use in adults, and its feasibility in children had not been demonstrated prior to commencing this study. Consequently, manual assessments (Table E1) were also undertaken during the first year of study to ensure detailed anthropometry would be available from all children. Both 3-D and manual measurements of chest dimensions were undertaken during quiet tidal breathing in this study. While others have performed assessments at end-tidal expiration[E2,3], we chose not to attempt such measurements during a breath-hold since this was unlikely to be reproducible in young children and impossible to monitor while they were inside the 3-D scanner.

Figure E1 Illustration of measurements from 3-D scan



1.4. Salivary cotinine cut-points

Saliva samples were collected for cotinine analysis to validate parental reports of tobacco smoke exposure (ABS Laboratory Ltd, UK). A saliva cotinine cut-point of 12ng/mL was used to discriminate self-reported non-smokers from smokers[E4] while a cut-point of 2.5ng/mL was used to reflect children's passive exposure from smoking households[E5].

2. Data management and statistical methods (additional information)

To ascertain which additional measures of body physique should be taken into account in order to minimise ethnic differences in spirometry, the semi-parametric Generalized Additive Models for Location, Scale and Shape (GAMLSS) regression models were used to summarise the distribution of absolute values of FEV_1 and FVC by age in boys and girls[E6]. These consist of two distinct regression models, one for the mean and one for the variance. Both models included log-transformed age as a cubic P-spline, allowing the mean and variance to vary smoothly by age. In addition, the mean model included ethnicity and detailed anthropometry (i.e. height, sitting height, chest circumference, chest width, chest depth, waist circumference, waist width, waist depth, mid-arm circumference, mid-calf circumference, knee girth and foot length) measured a) manually and b) with 3D scans. The anthropometry was log-transformed to allow for allometric scaling[E7]. Coefficients for ethnic differences were multiplied by 100 and treated as percentage differences[E8]. Nested models were compared using the Bayesian information criterion (BIC)[E9], where the smaller the BIC the better the model fit. Substantial difference between two models can be considered if the BIC difference is more than 6 units, with very strong evidence provided when BIC difference is more than 10 units[E10].The two-tailed significance level was set at 0.05 and R version 3.1.0 was used for the analyses[E11].

2.1. Interim analysis: Association between detailed anthropometric measurements & lung function

Of the 1632 children participating in the 1st year of the definitive study, one was excluded due to misreporting of sex and one was excluded as an outlier (z-FEV_1 ≥5 z-score), leaving 1630 children (870 girls; 760 boys). Of these 700 girls (80%) and 596 (78%) boys had complete data for all detailed manual anthropometry outcomes (Table E1). A summary of the association between detailed manual anthropometry and lung function (univariable analysis) is given in Table E2. A flow chart for modelling lung function outcomes as a function of manual anthropometry is given in Figure E2.

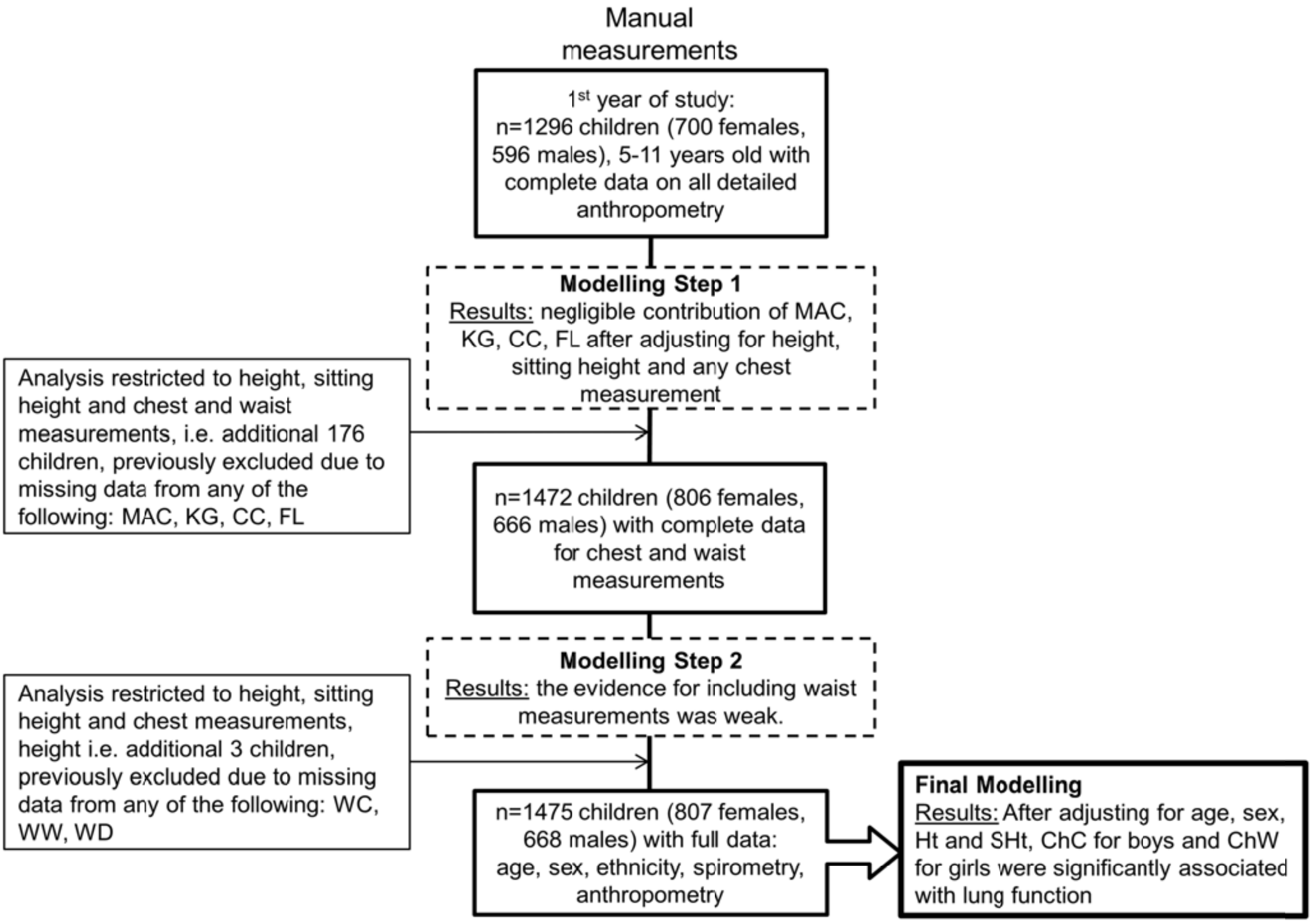
During interim analysis, results from 3-D scan measurements confirmed the findings from modelling lung function data using manual anthropometry measures (Figure E3), suggesting that sitting height and chest measurements additional to standing height contribute significantly to explain variability of lung function.

Table E2: Coefficients (95% confidence intervals) for the association between anthropometric measures (manually measured) and lung function outcomes in boys and girls.

	FEV_1		FVC	
	Boys	Girls	Boys	Girls
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Sitting height	**2.14 (1.70; 2.58)**	**2.29 (1.90; 2.67)**	**2.27 (1.86; 2.69)**	**2.44 (2.06; 2.81)**
Chest circumference	**0.29 (0.14; 0.44)**	**0.24 (0.11; 0.37)**	**0.44 (0.30; 0.59)**	**0.36 (0.23; 0.49)**
Chest width	**0.31 (0.16; 0.46)**	**0.35 (0.22; 0.49)**	**0.47 (0.32; 0.61)**	**0.47 (0.34; 0.59)**
Chest depth	**0.16 (0.03; 0.29)**	**0.21 (0.10; 0.32)**	**0.25 (0.13; 0.37)**	**0.27 (0.16; 0.38)**
Waist circumference	**0.16 (0.04; 0.28)**	**0.15 (0.05; 0.25)**	**0.29 (0.18; 0.4)**	**0.24 (0.14; 0.34)**
Waist width	**0.26 (0.14; 0.38)**	**0.24 (0.14; 0.34)**	**0.36 (0.25; 0.47)**	**0.31 (0.22; 0.41)**
Waist depth	0.03 (-0.07; 0.13)	0.08 (0.00; 0.17)	**0.16 (0.07; 0.26)**	**0.14 (0.06; 0.23)**
Mid-arm circumference	0.02 (-0.07; 0.12)	0.07 (-0.02; 0.16)	**0.12 (0.03; 0.21)**	**0.14 (0.06; 0.23)**
Calf circumference	**0.15 (0.01; 0.28)**	**0.22 (0.10; 0.35)**	**0.26 (0.13; 0.38)**	**0.34 (0.22; 0.46)**
Knee girth	0.07 (-0.10; 0.23)	**0.22 (0.08; 0.37)**	**0.17 (0.02; 0.33)**	**0.31 (0.17; 0.46)**
Foot length	0.06 (-0.24; 0.37)	-0.23 (-0.51; 0.05)	-0.1 (-0.39; 0.19)	-0.09 (-0.37; 0.18)

Footnote: each anthropometry measure was log-transformed. FEV_1 and FVC were regressed on each anthropometric measure, adjusted for standing height and age, separately for boys and girls. Results shown in bold were significant (p at least<0.05) on univariable analysis.

Figure E2 Flow chart for modelling lung function outcomes as a function of manual anthropometry, during interim analysis.



1st year of study: n=1296 children (700 females, 596 males), 5-11 years old with complete data on all detailed anthropometry

Modelling Step 1
Results: negligible contribution of MAC, KG, CC, FL after adjusting for height, sitting height and any chest measurement

Analysis restricted to height, sitting height and chest and waist measurements, i.e. additional 176 children, previously excluded due to missing data from any of the following: MAC, KG, CC, FL

n=1472 children (806 females, 666 males) with complete data for chest and waist measurements

Modelling Step 2
Results: the evidence for including waist measurements was weak.

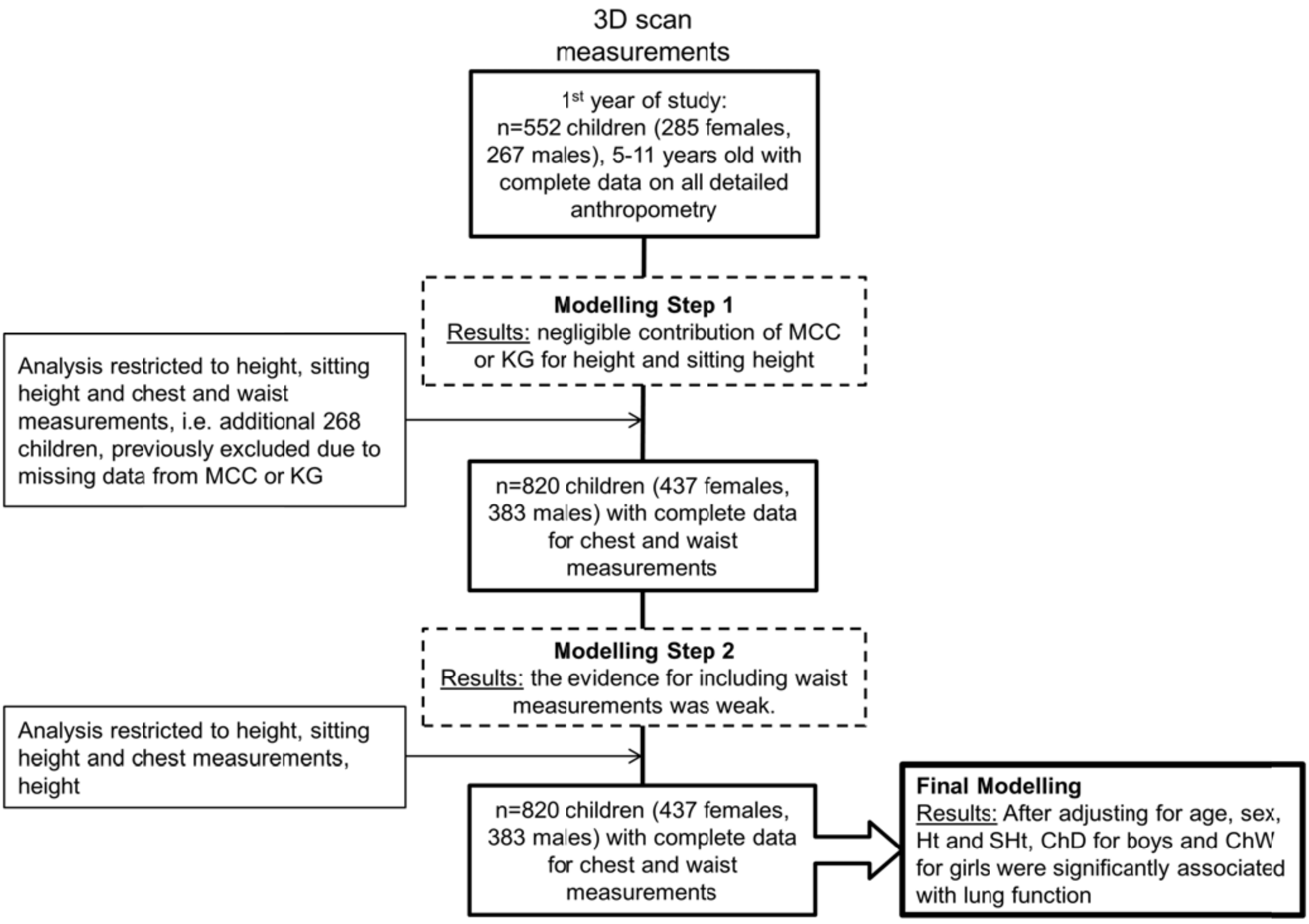
Analysis restricted to height, sitting height and chest measurements, height i.e. additional 3 children, previously excluded due to missing data from any of the following: WC, WW, WD

n=1475 children (807 females, 668 males) with full data: age, sex, ethnicity, spirometry, anthropometry

Final Modelling
Results: After adjusting for age, sex, Ht and SHt, ChC for boys and ChW for girls were significantly associated with lung function

Detailed anthropometry: Ht: standing height, SHt: sitting height, ChC: chest circumference, ChW: chest width, ChD: chest depth, WC: waist circumference, WW: waist width, WD: waist depth, MAC: mid-arm circumference, KG: knee girth, CC: calf circumference, FL: foot length
Modelling: performed using the GAMLSS method (Rigby and Stasinopoulos. Appl Statist 2005)

Figure E3 Flow chart for modelling lung function outcomes as a function of anthropometry, measured using 3D scans measurements, during interim analysis.



Detailed anthropometry: Ht: standing height, SHt: sitting height, ChC: chest circumference, ChW: chest width, ChD: chest depth, WC: waist circumference, WW: waist width, WD: waist depth, MCC: mid-calf circumference, KG: knee girth
Modelling: performed using the GAMLSS method (Rigby and Stasinopoulos. Appl Statist 2005)

2.2. Proportion of missing data for categorising health status

Since assessments were undertaken during school hours and without parental attendance, the study questionnaire was sent home with the children for the parents to complete, which inevitably resulted in some missing data. Among the returned questionnaires, information on birthweight and gestational age were missing on average on 19% and 9.3% of occasions respectively, higher proportions of missing data being observed for Black-African origin children than other ethnic groups (Table E3).

Table E3: Proportion of missing birth data from parental questionnaires

	White	Black	South Asian	Other	Total
Birthweight	59 (8.0%)	243 (39%)	81 (15%)	37 (14%)	420 (19%)
Gestational Age	53 (7.2%)	97 (15%)	26 (4.8%)	25 (9.5%)	201 (9.3%)

Attempts were also made to collect birth data via health records from General Practitioners (GP) in primary care clinics. As recently reported, there were no significant difference in birthweight or gestational age between parental questionnaires and GP data[E12]. However, given the low retrieval of data from GPs compared to parents (22% vs. 95%), analysis using birth data for this study has been primarily based on parental questionnaires. Since it was assumed that parents would generally recall details had their child had been born preterm or with low birthweight, for the purposes of subsequent analyses children with missing birth information were assumed to have been "full term" with appropriate birthweight.

3. Categorisation of ethnicity

Parents were requested to provide information regarding the child's ethnicity, including information regarding country of birth for child, parents and grandparents to aid the categorisation of ethnicity. Based on parental reports, children were categorised into four broad ethnic groups, "White" which included European, Hispanic or Latino and Middle Eastern; "Black-African origin" which included Black African; Black Caribbean or Black Other; "South-Asian" which included Indian, Pakistani, Bangladeshi and Sri Lankan; and "Other" which included any other ethnicities such as Chinese, Filipino or any children of mixed ethnic origins (e.g. South-Asian / White).

3.1. Detailed characteristics of children from Black and South-Asian sub-groups

- Characteristics of Black-African origin reference children according to subgroups
    - 71% African; 21% Caribbean; 8% Other (total=543)
    - After adjusting for age and sex, anthropometry was similar across the sub groups
- Characteristics of South-Asian reference children according to subgroups
    - 69% Indian; 10% Bangladeshi; 8% Pakistani; 10% Sri Lankan; 2% Other (total=462)
    - After adjusting for age and sex, Pakistani children were significantly taller and heavier than children from other South-Asian subgroups.
    - Significantly more Bangladeshi children were from families below the 5th quintile for IMD score (area level) though there was no significant difference when assessed according to family affluent score (individual level)
- Other/mixed ethnicities (6% Chinese; 9% Filipino; 4% Other; 81% mixed ethnicities)

4. Socio-economic classification and ethnicity

The pattern of socio-economic circumstances (SEC) observed between ethnic groups was similar irrespective of whether SEC was assessed on an individual level (FAS) or area level (IMD scores) (Table E4).

Table E4: Distribution of measures of socio-economic circumstances by ethnicity.

	White	Black	South Asian	Other	Total
Family affluence scale, % (n)					
High (5-6)	30% (190)	11% (49)	21% (95)	27% (57)	23% (391)
Moderate (2-4)	62% (390)	74% (328)	71% (318)	66% (142)	68% (1178)
Low (0-1)	7.2% (45)	15% (67)	8.0% (36)	7.4% (16)	9.5% (164)
Index of multiple deprivation score, % (n)					
1st quintile (least deprived)	11% (73)	0.8% (4)	0% (0)	6.3% (14)	4.9% (91)
2nd quintile	20% (130)	3.2% (17)	17% (80)	13% (28)	14% (255)
3rd quintile	21% (137)	4.0% (21)	14% (65)	17% (37)	14% (260)
4th quintile	20% (131)	27% (139)	47% (214)	21% (48)	29% (532)
5th quintile (most deprived)	28% (186)	65% (343)	22% (99)	43% (97)	39% (725)
Index of multiple deprivation income score, % (n)					
1st quintile (least deprived)	11% (71)	0.4% (2)	0% (0)	4.0% (9)	4.4% (82)
2nd quintile	11% (74)	1.7% (9)	14% (65)	8.5% (19)	9.0% (167)
3rd quintile	18% (119)	3.2% (17)	9.6% (44)	13% (29)	11% (209)
4th quintile	23% (154)	18% (94)	51% (232)	30% (67)	29% (547)
5th quintile (most deprived)	36% (239)	77% (402)	26% (117)	45% (100)	46% (858)

Table E5: Anthropometry and body composition by sex and ethnicity.

	White	Black	South Asian	Other
Boys (*n, test occasions*)	459	316	286	145
Age (years)	8.4 (1.6)	8.4 (1.6)	8.2 (1.7)	8.2 (1.6)
Height (cm)	131.8 (10.7)	134.8 (11.5)	129.4 (11)	130.4 (11.5)
Sitting height (cm)	70.6 (4.6)	69.9 (4.8)	68.1 (4.8)	69.5 (4.8)
Leg length (cm)	61.2 (6.4)	64.9 (7.2)	61.4 (6.5)	60.9 (7.2)
Chest circumference (cm)	65.3 (6.9)	67.5 (7.9)	63.5 (8.3)	64.4 (7)
Chest width (cm)	22.2 (2.4)	22.6 (2.8)	21.5 (2.8)	21.8 (2.4)
Chest depth (cm)	15.7 (1.6)	16.2 (1.7)	15.3 (2)	15.4 (1.7)
Chest depth/width	0.709 (0.05)	0.717 (0.05)	0.715 (0.05)	0.708 (0.05)
Chest area (cm^2)	276 (57)	291 (66)	262 (71)	267 (55)
Fat free mass (kg)[*]	22.1 (4.8)	24.3 (5.7)	19.7 (5)	21.3 (4.9)
Girls (*n, test occasions*)	541	489	337	194
Age (years)	8.5 (1.7)	8.7 (1.6)	8.7 (1.7)	8.8 (1.7)
Height (cm)	131.6 (11.1)	136.6 (12.2)	131.8 (12.1)	133.9 (11.6)
Sitting height (cm)	70.3 (4.9)	70.7 (5.3)	69 (5.3)	70.8 (5.3)
Leg Length (cm)	61.3 (6.5)	65.9 (7.4)	62.7 (7.1)	63.1 (6.8)
Chest circumference (cm)	64.6 (7.3)	68.3 (9.2)	65 (8.8)	66.6 (9.4)
Chest width (cm)	21.9 (2.5)	22.8 (3)	21.9 (2.8)	22.5 (3.2)
Chest depth (cm)	15.4 (1.7)	16.2 (2)	15.2 (1.9)	15.6 (2)
Chest depth/width	0.704 (0.05)	0.711 (0.05)	0.698 (0.05)	0.699 (0.06)
Chest area (cm^2)	268 (58)	293 (74)	265 (68)	280 (75)
Fat free mass (kg)[*]	21.3 (4.8)	24.5 (6.3)	20 (5.4)	22.7 (6.2)

Results are presented as mean (SD) unadjusted for sex and age; [*]Fat free mass (FFM) was calculated from BIA data using a calibration factor derived from a subset of the population in whom both deuterium and BIA were assessed[E13]. See Table 2, main manuscript for age adjusted height z-scores. Chest area calculated assuming chest is an elliptical shape.

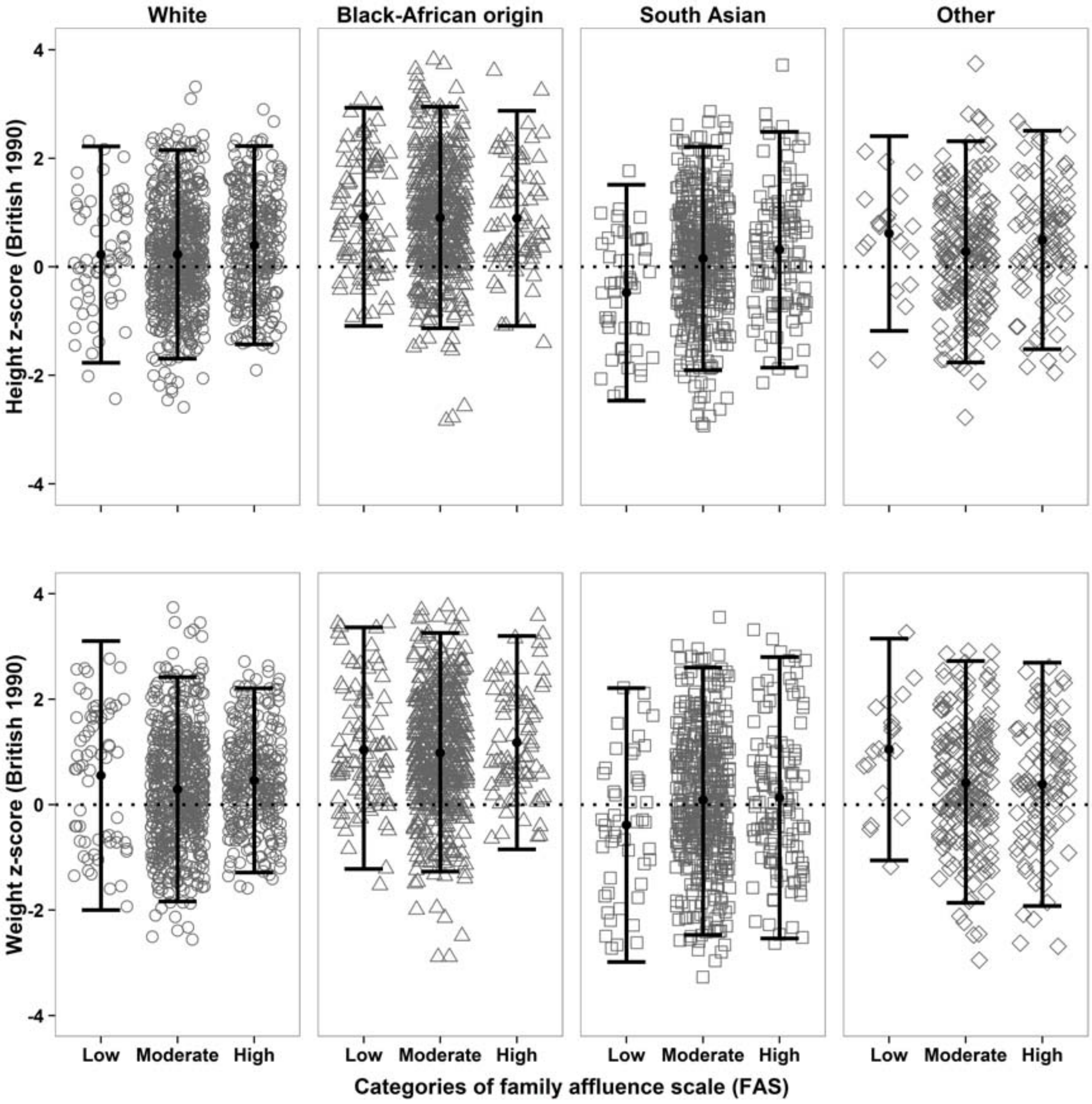
Table E6: Variables included in the final regression models for z-FEV$_1$ and z-FVC (n=2751).

Age	Sex	Height	Ethnicity	Sitting height	Chest dimensions			BIC*
					Circumference	Width	Depth	
z-FEV$_1$ (GLI 2012-based on White equation)								
X	X	X	-	-	-	-	-	6892
-	-	-	X	-	-	-	-	6303
X	X	X	X	-	-	-	-	6277
X	X	X	X	-	-	-	X	6258
X	X	X	X	-	X	-	X	6245
X	X	X	X	-	X	X	X	6240
X	X	X	X	-	X	-	-	6238
X	X	X	X	-	X	X	-	6234
X	X	X	X	-	-	X	X	6233
X	X	X	X	-	-	X	-	6228
X	X	X	X	X	-	-	-	6218
X	X	X	X	X	-	-	X	6207
X	X	X	X	X	-	X	X	6201
X	X	X	X	X	X	X	X	6197
X	X	X	X	X	X	-	-	6195
X	X	X	X	X	X	X	-	6191
X	X	X	X	X	-	X	X	6189
X	**X**	**X**	**X**	**X**	**-**	**X**	**-**	**6183**
z-FVC (GLI 2012 based on White equation)								
X	X	X	-	-	-	-	-	6803
-	-	-	X	-	-	-	-	6234
X	X	X	X	-	-	-	-	6188
X	X	X	X	-	-	-	X	6149
X	X	X	X	X	-	-	-	6101
X	X	X	X	-	X	-	X	6087
X	X	X	X	-	X	-	-	6079
X	X	X	X	X	-	-	X	6074
X	X	X	X	-	X	X	X	6065
X	X	X	X	-	-	X	X	6060
X	X	X	X	-	X	X	-	6057
X	X	X	X	-	-	X	-	6054
X	X	X	X	X	X	-	X	6028
X	X	X	X	X	X	-	-	6020
X	X	X	X	X	X	X	X	6007
X	X	X	X	X	-	X	X	6000
X	X	X	X	X	X	X	-	5999
X	**X**	**X**	**X**	**X**	**-**	**X**	**-**	**5993**

Footnote: the models examined were not nested models in total thus the Bayesian information criterion (BIC) was used when selecting the best model. Substantial difference between two models can be considered if the BIC difference is more than 6 units, with very strong evidence provided when BIC difference is more than 10 units[E10];

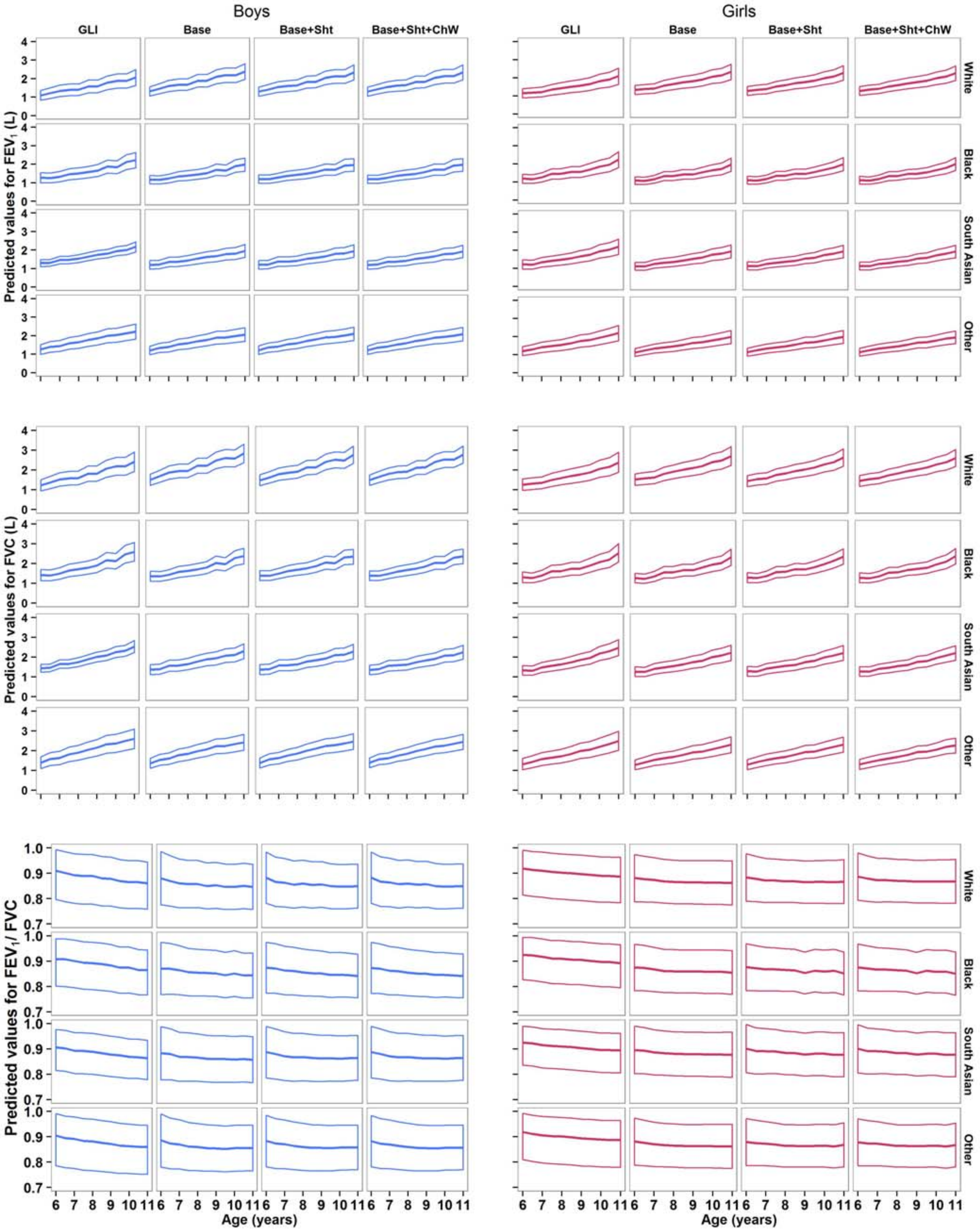
Models are ranked in descending order by BIC (the lower BIC value indicates a better model). The inclusion of ethnicity in any model improved its fit, as shown from the decreased BIC values, but this was further improved by the inclusion of additional anthropometric measures especially with respect to sitting height and chest width. The models in **bold** fonts are the best models. Effect of SEC and body composition were also assessed but as these models ranked lower than the models presented above, these data are not shown.

Figure E4: Associations between socio-economic circumstances with growth according to ethnicity



No differences in anthropometry were evident between categories of FAS within any ethnic group. Dots represent mean values; error bars represent ±2SD from the mean. For South-Asians, there was a trend between growth and FAS, but the magnitude of the association was small.

Figure E5 Predicted values of FEV$_1$, FVC and FEV$_1$/FVC according to GLI all-age multi-ethnic equations and the various SLIC prediction models



Predicted values for spirometry are presented as the median (**BOLD** lines) and the 5th and 95th percentiles (thinner lines) for age with average height, sitting height (SHt) and Chest width (ChW) according to sex based on the SLIC data, The Base model derived from the SLIC data is equivalent to the GLI equations. With regards to the predictive value for FEV$_1$/FVC, chest width rather than sitting height contributed significantly. Sitting height was then included in the final model to assess its importance.

As can be seen from the graphs above, despite their contribution to model fit, inclusion of sitting height and/or chest width made minimal impact to predicted median values, i.e. predicted values were similar whether or not sitting height and chest width were included. For example, when based on an ‘age and height’ adjusted model as used for the GLI equations[E14], the predicted median (95% CI) FEV_1 for boys of White European origin and average height-for-age ranged from 1.25L (0.99; 1.52) in a 6 year-old to 2.22L (1.81; 2.63) in an 11-year old. The corresponding values using the Base (SLIC) models were 1.32L (1.07; 1.56) and 2.39L (1.97; 2.81) respectively. These values remained similar when sitting height and chest width were included in the model, being 1.3L (1.06; 1.55) for a 6-year old and 2.34L (1.94; 2.74) for an 11-year old). For those of Black African origin, predicted FEV_1 ranged from 1.18L (0.95; 1.4) in a 6-year old to 1.99L (1.63; 2.34) in an 11-year old when using the Base model and from 1.2L (0.97; 1.42) in a 6-year old to 1.97L (1.63; 2.31) in an 11-year old when also adjusting for sitting height and chest width.

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