

## Technical Report

### Exploring ethnic differences in lung function: the Size and Lung function In Children (SLIC) study protocol and feasibility

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## Abstract

The Size and Lung function In Children (SLIC) study was designed as a prospective, cross-sectional and longitudinal study to investigate the factors contributing to ethnic differences in lung function. After adjusting for sex, age and height, the degree to which these differences can be reduced after further adjustment for body shape, size and composition was examined. The aim of this technical report is to describe the study design and protocol and to examine the feasibility of conducting complex physiological investigations in London primary schools.

**Methods:** Recruitment and assessments were undertaken in London primary schools. Children with parental consent were eligible and categorised into 4 broad ethnic groups: White; Black; South-Asian and other/mixed ethnicities. Assessments were performed in children aged 5-11y, on 2 occasions a year apart and included detailed anthropometry; 3D photonic scanning for regional body shape; body composition using bioelectrical impedance analysis and isotope dilution technique; spirometry and saliva samples (for cotinine & DNA analysis of genetic ancestry). Information on country of origin (child-parents-grandparents); self-reported ethnicity; the child's respiratory history, family socio-economic circumstances and tobacco smoking exposure were obtained, principally from parents via a questionnaire. Health status of the children was verified from medical records where feasible. Data linkages to pollution index and area deprivation scores were based on home postcodes.

**Results:** Fourteen London primary schools participated with 52% parental consent for children to take part in the study. Consent rate for each type of assessment was generally high and ranged from near 100% for spirometry and anthropometry to 88% for DNA sample collection. With the exception of 3D scanning for body shape, where acceptable data were only achieved in 68% children assessed, success rate for all assessments ranged from 88% to 99%. In total, 2171 (47% boys; 34% White; 29% Black; 25% South-Asian; 12% Other/mixed) children were assessed on 3302 test occasions over the two year period, with successful spirometry being achieved in 90% (2986/3302) of assessments. After excluding 20% of children with acute or chronic illness and 10% with failed spirometry, data was available from 1520 healthy children for final analysis.

**Summary:** This is the first study to demonstrate the feasibility (in terms of consent and success rate) of undertaking complex physiological assessments within the school environment in children as young as 5 years of age, including those for DNA. However, until software is refined and adapted for children, current technology for performing 3D scans for health related studies is not cost-effective. Approximately 30% of the children studied were preterm/LBW, had prior asthma or were symptomatic. Hence if the target population is healthy young children then the recruited sample size may need to be increased by 30% to ensure adequate power.

## Introduction

During recent years there has been increasing awareness of social and ethnic inequalities within some lung diseases and the need to reduce such disadvantage. Asthma prevalence and morbidity varies by ethnic group, being higher among Black and ethnic minority children compared with White children. While failure to access services and under-treatment might partly explain this differential, the Millennium Cohort(1) and 'DASH'(2) studies show that asthma is more prevalent in Black Caribbean than White adolescent boys in the UK. The UK government has recently redoubled efforts to tackle these health inequalities, including stronger incentives to diagnose problems earlier. There is also increasing awareness of childhood origins of chronic lung disease (3-5), the real burden of respiratory disease in young children(6-8), the need to identify and treat early changes in lung function (LF) in children with diseases such as cystic fibrosis(9), asthma (10), bronchopulmonary dysplasia (11) and sickle cell disease (12) before chronic, irreversible changes occur, and the limitations of parental reports of symptoms (13, 14). This has resulted in several major international initiatives i.e. development of sensitive LF tests for children as young as three years of age (15-17) and reference data with which to interpret results (18-20).

Accurate diagnosis and effective management of respiratory disease requires objective measures of LF. The availability of adequate reference values is critical to understand the effect of interventions and the nature of progression of lung disease such as asthma or sickle cell lung disease in children. Through international collaboration, we have developed LF growth charts from 3 through to 80 years for the White population, to provide a single reference with which to interpret spirometry results across all-ages and provided the foundation for continued collation of LF data from healthy subjects (19). While extensive reference data are available for White and older subjects, there is growing concern about the lack of appropriate reference equations for LF in Black and Minority Ethnic (BME) younger children. Recently, the Global Lung function Initiative (GLI), an European Respiratory Society Taskforce, published the first global, all age (3-95 years), multi-ethnic reference equations for spirometry (21). We have recently shown that these equations are appropriate for use in contemporary London primary school children (5-11 years), though equations for South Asians have yet to be developed (22). Furthermore, there is debate about the concepts of "race", "ethnicity" and "genetic ancestry" and their impact in medical research and treatment (23-25). Such data are no longer routinely recorded in some countries and, even when available, are complicated by the increase in multi-ethnic relationships (UK Census 2011).

Several attempts have been made to identify factors underlying ethnic differences in LF (26-32). While standing height, a major determinant of many LF outcome measures is a dependable anthropometric measurement, differences in body proportions may underpin much of the remaining observed differences between ethnic groups. A lower trunk:leg ratio, rather than psycho-social factors, was the predominant reason for the lower LF observed in Black adolescents in the recent DASH study (26), a finding that has also been described in younger children

(33, 34). By contrast, sitting height appears to be a less important determinant of LF in Asians (26, 28), suggesting that a more comprehensive approach to exploring variability in physique, including chest dimensions and body composition is required. Attempts to identify which linear measurements contribute to between-subject variability in LF have, however, been limited by the impracticality of undertaking a vast array of time-consuming anthropometric measurements, especially in children. Such limitations could potentially be overcome through the increasing availability of a new technology using whole body 3D photonic scanning, to provide rapid, detailed data on regional body shape and surface topography from digital anthropometric measurements (35). Body composition and growth have also been shown to be associated with subsequent health outcomes in both individuals and populations (20) and, if ignored, may lead to serious misinterpretation of LF results (36). The reliance of previous studies on derived rather than direct (37) measures of lean:fat mass may have contributed to conflicting results in the literature regarding the relationship between LF and height, chest circumference and fat free mass (FFM) in children (38-40).

Accurate, non-invasive measurements of body composition can now be readily obtained in the field using stable isotope technology (41) to enable assessment of the independent effects of somatic size (total lean mass) versus 'metabolic load' (total fat mass) (42) as predictors of LF. This 'whole-body' information could be further complemented by additional information regarding the distribution of body weight. Recent conceptual work to extend the applications of whole body 3D photonic scanning has identified key body girths that account for significant individual variability in adiposity versus muscle mass in adults (43). The same approach could be adapted for children.

The broad aim of this study is to improve normative reference ranges for LF that take differences in body physique into account. This would facilitate early diagnosis and treatment of lung disease in all children, irrespective of ethnic background. These reference ranges will be derived from a multi-ethnic community sample of primary school children in London.

We hypothesised that

- i) After adjusting for sex, age and standing height, inclusion of routine measures such as sitting height, chest width and fat-free mass or combinations thereof (as determined during the course of the study), would significantly reduce ethnic-specific variability of LF among children, thereby reducing the need for ethnic-specific equations when attempting to distinguish the effects of disease from those of growth and development;
- ii) Respiratory health is associated with the social patterning of key determinants of LF such as body size, shape and composition; socio-economic circumstances; air pollution; tobacco smoke exposure and physical activity;

The objectives of this paper are to:

- i. Provide a detailed description of the SLIC study protocol and
- ii. Examine the feasibility and challenges of undertaking physiological measurements in young children of varied ethnicity aged 5-11 years within the school environment.

## Materials and Methods

### SLIC Study design

The Size and Lung function In Children (SLIC) study was a prospective cross-sectional and longitudinal study designed to assess spirometric LF, body size, shape and composition in primary school children (5-10 years) within London schools where there is a high ethnic mix. Baseline measurements were undertaken over the course of 2 days for a subset of children, with selected tests being repeated a year later. The study was guided by a Steering Committee, and approved by the London-Hampstead research ethics committee (REC: **10/H0720/53**). Parental written consent and verbal assent from each child were obtained prior to assessments. A 12-month pilot study to assess feasibility of all aspects of the proposed study was undertaken prior to commencement of the definitive study.

### Study recruitment

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. The study was publicised using school newsletters and leaflets, local media and by inviting parents to attend presentations (evenings or end of school day). 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 in all techniques prior to study commencement, this training being supplemented by on-going quality assurance checks throughout the study.

**Subjects:** All children between 5-11 years with parental consent were eligible. Children were only excluded from assessments if they had overt signs of illness on test day. For final analysis, data were excluded from children with: current or chronic respiratory disease (current asthma, neonatal bronchopulmonary dysplasia, Cystic Fibrosis, Sickle cell disease) or significant congenital abnormalities (skeletal, neuromuscular, cardio-respiratory or developmental problems). A staged consent form was implemented to enable parents to opt in either for all assessments or just for selected subsets comprising:

- i) non-invasive assessments (e.g. anthropometry, spirometry, BIA, saliva sample for cotinine analysis)
- ii) Isotope dilution body composition
- iii) 3D body scans
- iv) DNA sample and

- v) Access to GP health records.

The SLIC study website ([www.ucl.ac.uk/slic](http://www.ucl.ac.uk/slic)) was set up to enable parents, children and teachers to follow the study progress.

**Questionnaires** (Appendix 1) were completed by parents to provide information regarding classification of their own and their child's ethnicity; country of origin of child, parents and grandparents for consistency checks on ethnic ancestry; socio-economic classification (based on parental education, standard of living items (e.g. family car, computer ownership) and Indices of multiple deprivation (IMD, see Appendix 5) score, based on home post codes (44)); child's history of respiratory disease and medication and, for children over 8 years of age, whether the child had entered puberty. To minimise data loss through non return of parental questionnaire, selected information such as country of origin, standard of living items, physical activity routinely undertaken were also obtained from the children at test day. Based on parental information received, children were broadly categorised into four main ethnic groups: White (European ancestry), Black (African or Caribbean ancestry); South Asian (ancestry from Indian sub-continent) and Other/mixed ethnicities.

**Assessment of pubertal status:** Initially, pubertal status was determined by self-report in children >8 years of age (45). The children were given some privacy to complete a pubertal questionnaire on the day of test and staff were available to assist or answer queries. Following concerns raised by one parent regarding collection of pubertal status via self-report, the child's pubertal questionnaire was withdrawn from the study protocol towards the end of Year 1 assessment and the following question was added to the parental questionnaire for the assessment of the child's pubertal status: "Has your child entered puberty (indicated by growth of arm-pit or pubic hair, and/or lowering of voice for boys or menstruation/periods for girls)? Yes/No". Puberty was deemed to have been reached if the child attained Tanner Stage III in their physical development (45).

### **School assessments**

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 3D scanner and all equipment) which was parked in the school grounds and children were escorted in small groups to and from the classroom by a researcher or teaching assistant. 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 1.

**Table 1. Schedule and description of assessments.**

| <b>Assessments</b>   | <b>Method and rationale</b>  | <b>Yr 1</b> | <b>Yr 2</b> |
|--|--|-------------|-------------|
| <b>Anthropometry</b>   |  |             |             |
| Standing height (Leicester stadiometer, Seca, Birmingham, UK)  | Assessment of growth and standard predictor for LF   | Y           | Y           |
| Weight (Seca digital scales, UK)   | Assessment of growth   | Y           | Y           |
| 3D scan for body shape ([TC] <sup>2</sup> , NX16 scanner, North Carolina)                            | Assessment of body shape & subsequent extraction of detailed body dimensions   | Y           | N           |
| Sitting height (Leicester stadiometer and a stool)   | Proposed as better predictor of LF compared to standing height (36)  | Y           | Y           |
| Chest circumference, width & depth# (~2-3 cm below axilla)   | Reported to account for some ethnic differences in LF(28)  | Y           | Y           |
| Waist circumference, width & depth# (narrowest girth)  | Marker for body size and shown to be associated with FVC (46)  | Y           | N           |
| Mid arm circumference#   | Marker of nutritional status (47)  | Y           | N           |
| Knee girth#  | Associated with frame size (48)  | Y           | N           |
| Calf Circumference#  | Marker of nutritional status (49)  | Y           | N           |
| Foot length#   | Correlates with standing height; used in clinical situations where standing and arm span are not practicable (50)  | Y           | N           |
| <b>Body composition:</b> Bioelectrical Impedance Analysis (BIA) (Tanita BC418 analyser, Netherlands) | BIA (cheaper method) was assessed in ALL children and calibrated against isotope dilution to improve calculation and prediction of lean mass.  | Y           | Y           |
| <b>Body composition:</b> Isotope dilution (Deuterium)  | To minimise project costs, isotope dilution was performed on a subset of 600 children, selected to represent a wide range of body compositions.  | Y           | Y           |
| <b>Spirometry</b> (Ultrasonic flowmeter, Easy-on-PC, ndd, Switzerland)                               | Factory calibrated, daily equipment calibration not required, although verification of zero flow was performed prior to every assessment; disposable spirettes used, thus suited to field studies                  | Y           | Y           |
| <b>Saliva sample:</b> Cotinine analysis  | Assessment of tobacco smoke exposure   | N           | Y           |
| <b>Saliva sample:</b> DNA analysis (Genotek Oragene DNA kit) for genetic ancestry                    | Assessment of genetic ancestry   | N           | Y           |
| <b>Parental questionnaire</b>  | To ascertain ethnicity, health status, socio-economic circumstances of child & family; Home and school post-codes used for data linkage to pollution index and English Indices of multiple deprivation 2010 (IMD). | Y           | Y           |
| <b>Pubertal questionnaire*</b>   | For pubertal staging; to examine associations of puberty with lung function  | Y           | Y           |
| <b>GP records</b>  | To verify child's health status  | N           | Y           |

Abbreviations: BIA: Bioelectrical Impedance Analysis; DNA: Deoxyribonucleic acid; FVC: Forced Vital Capacity; IMD:

Indices of multiple deprivation; #Circumferences assessed using Seca 201 tape measure; width & depth using Sliding calipers with deep jaws (Chasmors Ltd, London). \*Pubertal questionnaire was withdrawn at end of first year of data collection. Information was subsequently collected via a question added to parental questionnaire "Has your child entered puberty (indicated by growth of arm-pit or pubic hair, and/or lowering of voice for boys or menstruation/periods for girls)? Y/N "



**3D photonic scans** for regional body shape (using light technology) were undertaken to identify which linear measurements of body size contribute to between-subject variability in LF (see Appendix 2). Children were required to undress to their underclothes or change into form fitting undergarments within the 3D scanner ([TC]2 NX16 scanner, North Carolina)(35) and instructed to stand in a pre-specified stance for 8 seconds during quiet natural breathing while the scanner captures the body shape. Outcome measures include thoracic and waist circumference, width and depth, knee girth, calf circumference; shoulder height and waist height.

**Anthropometry:** Standing and sitting height and weight were undertaken using established protocols (11). Weight was measured in light clothing and no shoes, to the nearest 0.1kg using Seca digital scales (Seca, Birmingham, UK). Standing height was measured barefoot, with head in the Frankfort horizontal plane, to the nearest 0.1 cm using the portable Leicester stadiometer (Seca, Birmingham, UK). For sitting height, the child was instructed to sit on the stool (stool height: 60.2cm) placed on the stadiometer floor board, with his/her back and buttocks to the backboard of the stadiometer, knees directed straight ahead with arms resting on sides and hands on thighs. Sitting height measurement was performed with head in the Frankfort plane, to the nearest 0.1 cm. Corrected sitting height (i.e. sitting height minus stool height) was reported. In order to ensure that detailed anthropometric measures were available from children who did not have consent for 3D scans or those in whom acceptable 3D scans of body shape were not possible, additional detailed measures of chest, waist, mid-arm circumference, knee girth, calf circumference and foot length were also undertaken. Circumference measurements were performed using Seca 201 tape measure while width and depth measurements were undertaken using Sliding Calipers (Table 1; see Appendix 3 for detailed protocols).

**Body composition:** High accuracy isotope (Deuterium Oxide; CK Gas Products Ltd, Leicestershire, UK) measurements (expensive and thus not widely applicable) were used to calibrate the Tanita Bio-electrical Impedance Analysis (BIA, cheaper but less accurate) (51), which in turn was used to provide a mechanistic basis for the contribution of physique to variation in LF. To minimise project costs, isotope dilution for assessing total body water (TBW) was undertaken in a sub-sample of 600 children, distributed equally according to age, sex, ethnicity and body size, while the Tanita BIA was undertaken in ALL children on both occasions (baseline and 1 year later). For isotope assessments, TBW was assessed by deuterium ( $^2\text{H}$ , a stable isotope of hydrogen) labelled water dilution, using a dose equivalent to 0.05g  $^2\text{H}_2\text{O}$  per kg bodyweight. Saliva samples were collected pre-dose and at least 4 hours post-dose

using commercial salivettes (Sarstedt Ltd, UK) at least 30 minutes after ingestion of food or drink. Samples were stored at -20°C, and analysed in duplicate by Iso-Analytical Ltd (Crewe, UK) using an equilibration method (52). For calculating TBW, it was assumed that  $^2\text{H}_2\text{O}$  dilution space overestimated TBW by a factor of 1.044 (53). Correction was made for dilution of the dose by water intake during the 4 hour equilibration period. For BIA, whole body impedance was measured hand-foot and foot-foot using Tanita 418 segmental analyser (Tanita Corporation, Japan). The child wore light clothing and was instructed to stand on a footplate (without socks), ensuring the legs (thigh to foot) were not in skin contact at any point and that the arm grips of the analyser were held. Outcome measures: Fat mass (FM) and Fat-free mass (FFM).

**Spirometry** assessments were performed by experienced paediatric respiratory physiologists according to ATS/ERS standards adapted for children (15, 54) using the portable Easy-on-PC spirometer (ndd, Switzerland). All assessments were undertaken with the child seated, and nose clip in situ. Successful spirometry was defined as those with at least two technically acceptable forced expiratory manoeuvres according to ATS/ERS acceptability and repeatability criteria unless deemed acceptable by the senior respiratory physiologist (see Appendix 4). Outcome measures: FVC, forced expiratory volume in 1 second ( $\text{FEV}_{1s}$ ), forced expiratory flows across the mid-range of FVC ( $\text{FEF}_{25-75}$ ) and  $\text{FEV}_{1s}/\text{FVC}$ .

Parental consent to access medical health records was also sought to establish the health status of the child, particularly when such information was not provided or was missing from parental questionnaires.

**Tobacco smoke exposure:** Saliva samples of ~0.5 mL were collected from children on day of test. Children were requested to spit into a small container and the sample was pipette into a 1 mL plain bottle and stored in a freezer at -20°C as soon as possible following collection. The samples were later sent for cotinine assay using gas liquid chromatography at the ABS Laboratory Ltd, Hertfordshire, UK.

**Pollution index:** Air pollution values were linked to the children participating in the study by using their home and school postcodes at time of assessments. NOWCAST analysis will be undertaken to provide precise pollution level on a particular day (or series of days) before assessment. In addition to the main pollutants, a precise breakdown of particulate matter ( $\text{PM}_{10}$  and  $\text{PM}_{2.5}$ ) into exhaust and non-exhaust and total oxidant concentrations will also be performed using these new techniques. This will provide the opportunity to evaluate associations between both chronic and acute exposures to the various pollutants and the lung function and respiratory health of young children

(55). In addition, data from the SLIC study will be linked to the data collected from the London Emission Zone (LEZ) study to give enhanced power to refine estimates on the relationships between long term, acute and sub-acute pollution exposures and lung function.

Postcode level, air pollution data (modelled nitrogen dioxide (NO<sub>2</sub>), ozone (O<sub>3</sub>) and particulate matter, <10 and <2.5 microns diameter (PM<sub>10</sub> and PM<sub>2.5</sub> concentrations respectively) will be provided by the London Air Quality Network.

### Sample size and power of study

Recent findings from the GLI Task force indicated that ~300 subjects (50% male) per group are required to avoid sampling errors when attempting to detect differences in LF between groups of <0.4 z-scores (56). As children were broadly categorised into four main groups, namely White, Black, South-Asians and Other/mixed ethnicities, a sample size of 1200 children was therefore required. Based on previous experience and allowing for 25% attrition according to specified exclusion criteria on health grounds and technical failures (which may be highest in the youngest children), assessments were attempted in 1600 children on the first test occasion (comprising 140 5y-olds (School Year 1), 130 7y-olds (Year 3) and 130 9y-olds (Year 5) per ethnic group), with measurements repeated in these children one year later (at 6, 8 and 10 years of age). With technically satisfactory data from ~300 healthy children/ethnic group and two measurements/child there would be >95% power to detect differences in spirometric LF of 3-4% at the 5% significance between the main ethnic groups, with sufficient power to adjust for factors such as test site and undertake analysis of the disaggregated ethnic groups.

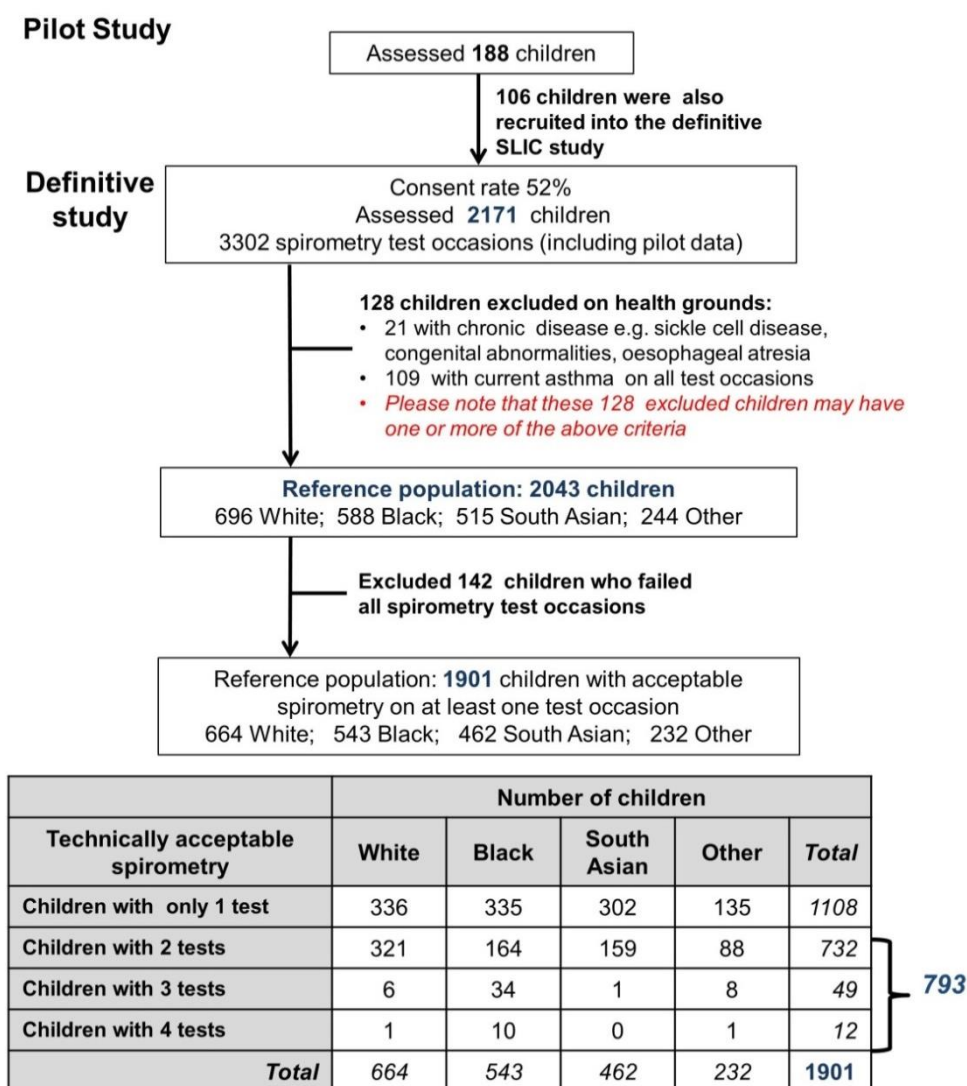
**Data management:** All data collected (questionnaire and anthropometry) were manually entered into a dedicated research database (Re-Base™ software, Re-Base Ltd, London, UK) and checked following completion of assessments in each school. To ensure data quality of all assessments was maintained throughout the study, inter-observer assessments of repeat anthropometric measurements within the same child were undertaken throughout the study. Following quality control of spirometry data, at least 10% of all analyses were over-read by a senior respiratory physiologist (RB/JK) before LF results were electronically exported to the research database to minimise transcription errors. Where available, data retrieved from GP health records were used to validate parental information to inform the categorisation of child's health status.

## Results

### Study recruitment

Of the 21 London primary schools contacted, 17 schools initially agreed to participate but three withdrew due to timing or space issues. Thus recruitment and assessments were undertaken in 14 schools during the first year of study. One school withdrew from the follow-up assessments due to space constraints. Over the two years of recruitment and assessments, 76 interactive Science workshops were performed prior to initial recruitment; with 19 presentations at school assemblies prior to recruitment at follow-up. 3166 parental consents were obtained over the two years of assessment (representing 52% of those approached). Assessments were performed in 2171 (46 % boys) children on 3302 test occasions (including data from pilot study; see Figure 1).

**Figure 1 Study recruitment and accrual (over both years of data collection)**



Repeat spirometry measures were available in 793 (39.1% boys) children (41.4% White, 26.2% Black, 20.2% South Asian, 12.2% Other) on 1659 test occasions. ( $732 \times 2 + 49 \times 3 + 12 \times 4 = 1659$ )

## Feasibility

Despite a complex study protocol which included assessments of 3D body shape, isotope dilution, collection of saliva samples for DNA analysis and access to GP records, among those participating in the study, the staged consents obtained for each of the more invasive assessments ranged from 84% to 99% and the proportions of consent were similar across the ethnic groups. A summary of consents and feasibility for all assessments is shown in Table 2.

**Table 2. Consent and feasibility of field assessments according to ethnicity**

|   | White      | Black     | South Asian | Other/mixed |
|---|------------|-----------|-------------|-------------|
| <b>3D scans consent</b>                 | 584 (94%)  | 436 (95%) | 304 (94%)   | 192 (94%)   |
| Acceptable data                         | 402 (69%)  | 261 (60%) | 200 (66%)   | 145 (76%)   |
| <b>Isotope body composition consent</b> | 584 (94%)  | 424 (92%) | 293 (90%)   | 187 (91%)   |
| Acceptable data                         | 158 (85%)  | 192 (95%) | 145 (87%)   | 106 (87%)   |
| Refusal by child                        | 5          | 0         | 5           | 1           |
| Failed test#                            | 24 (13%)   | 11 (5%)   | 16 (10%)    | 15 (12%)    |
| <b>BIA: Acceptable data</b>             | 1165 (99%) | 955 (99%) | 758 (99.6%) | 405 (100%)  |
| Refused to take socks/tights off        | 3          | 1         | 1           | 0           |
| <b>DNA consent</b>                      | 507 (89%)  | 263 (84%) | 380 (86%)   | 166 (92%)   |
| Acceptable sample                       | 466 (92%)  | 252 (96%) | 343 (90%)   | 161 (97%)   |
| Refusal                                 | 5 (1%)     | 3 (1%)    | 2 (0.5%)    | 0 (0%)      |
| Failed: insufficient saliva sample      | 32 (6%)    | 8 (3%)    | 34 (8%)     | 5 (3%)      |
| <b>Spirometry/anthropometry consent</b> | 1210       | 980       | 783         | 409         |
| Assessed*                               | 1173       | 962       | 761         | 406         |
| Acceptable spirometry results           | 1079 (92%) | 870 (90%) | 665 (87%)   | 372 (92%)   |
| Failure (% of assessed)                 | 94 (8%)    | 92 (10%)  | 96 (13%)    | 34 (8%)     |
| - < 7 years                             | 27 (11%)   | 36 (17%)  | 20 (11%)    | 10 (11%)    |
| - ≥ 7 years                             | 67 (7%)    | 56 (7%)   | 76 (13%)    | 24 (8%)     |
| <b>Parental Questionnaire completed</b> | 730 (99%)  | 570 (91%) | 536 (99%)   | 254 (96%)   |
| <b>GP health records access consent</b> | 717 (97%)  | 571 (94%) | 508 (94%)   | 256 (97%)   |
| Total records accessed                  | 523 (73%)  | 339 (59%) | 268 (53%)   | 157 (61%)   |
| Records unavailable <sup>§</sup>        | 12 (2%)    | 55 (16%)  | 0           | 18 (11%)    |
| Data retrieved                          | 511 (71%)  | 284 (50%) | 268 (53%)   | 139 (54%)   |

Data presented as n (%); \*Total assessed was slightly lower than total consent received as some children were absent from class or school during assessments. Percentage failure was calculated as a proportion of total assessments attempted. # Reasons for failure included insufficient saliva sample or that the post-dose sample

collected was less than 4 hours after dosing; § denoted records which were unavailable from GP surgeries as the child was no longer registered at the practice.

**3D scanning:** Assessments of 3D body shape, undertaken only in Year 1 of the definitive study, were performed in 1370 children of whom successful 3D data were obtained from 975 (71%) (Table 2). Calibration of the 3D scanner proved difficult on particularly cold winter mornings especially when the mobile lab was parked in an exposed location within the school grounds. Furthermore, it proved to be a challenge for the younger children to stand still even for 8 seconds during the data collection. Mean failure rate was higher in children <7 years of age (42%) compared with those ≥7 years (25%) and in Black children (38%) compared to their peers (White: 27%; South Asian: 30%; Other: 24%). The mean duration for the procedure to obtain at least one acceptable 3D scan (or 'bodymap') was approximately 10 minutes per child. Further details on these results will be reported separately.

Assessments of **anthropometry and body composition** (BIA) were well tolerated by all children with 99% success rate. The higher failure rate for isotope dilution assessments was primarily due to insufficient saliva sample from some children, food/liquid consumption within 30 minutes prior to post saliva sample collection, or insufficient time had been allowed (less than 4 hours) between pre and post saliva samples collection as a result of needing to fit in with school schedules.

**Lung function:** Spirometry was assessed in 2171 children on 3302 test occasions. Technically acceptable spirometry data were obtained on 2986 (90.4%) test occasions (Table 2). As expected, the mean failure rate for spirometry was higher in children <7 years compared to the older children (12.6% vs. 8.7% respectively). After excluding data from children with current and chronic respiratory disease (n=128) and those with failed spirometry (n=142), data were available from 1901 (87.6%) children on 2767 test occasions (Figure 1) for subsequent analysis.

Confirmation of **health status** from medical (GP) records

Consents for access to GP records were available in 95% of children participating in the study (Table 2). 115/273 (42%) GP practices across six National Health Service Trusts across London participated in the study and 1194 health records were retrieved (68% of total requested). The median (range) time taken to retrieve the records was 10 weeks (2 to 57 weeks).

## Agreement between parental and GP records

Information regarding gestational age (GA) and birth weight (BWt) was essential for categorising the child's health status. Birth weight data were provided by 78% (1695/2171) parents via the parental questionnaire (PQ), while details regarding gestational age at birth being provided for 89% (1927/2171) of the children. In contrast, health records could only be obtained from GPs for 1194 children (55% of total study population), with gestation and birth weight data only being available for 452 and 436 children respectively (representing 21% and 20% of the total population). Gestation and birth weight data from both parents and GP were available for 410 and 378 children respectively. Figure 2 and Figure 3 show that there was relatively good agreement between the two sources of information, despite wide limits of agreement due to a few outliers (Mean difference (PQ-GP) (95% limits of agreement) GA: 0.2 (-2.9; 3.3) weeks; BWt: -0.04 (-0.77; 0.69) kg). Given the very low return from GPs, a decision was therefore made to use data from parental questionnaire as the basis for categorising birth status, missing information being supplemented from GP records where available.

Figure 2. Gestational age: Agreement between data from Parental Questionnaire and GP records

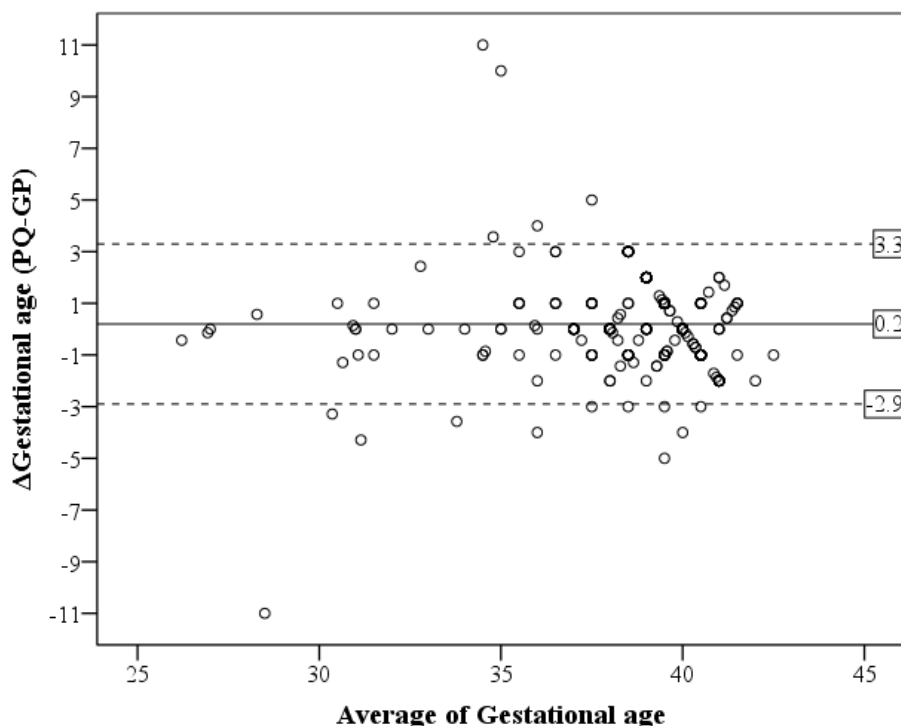
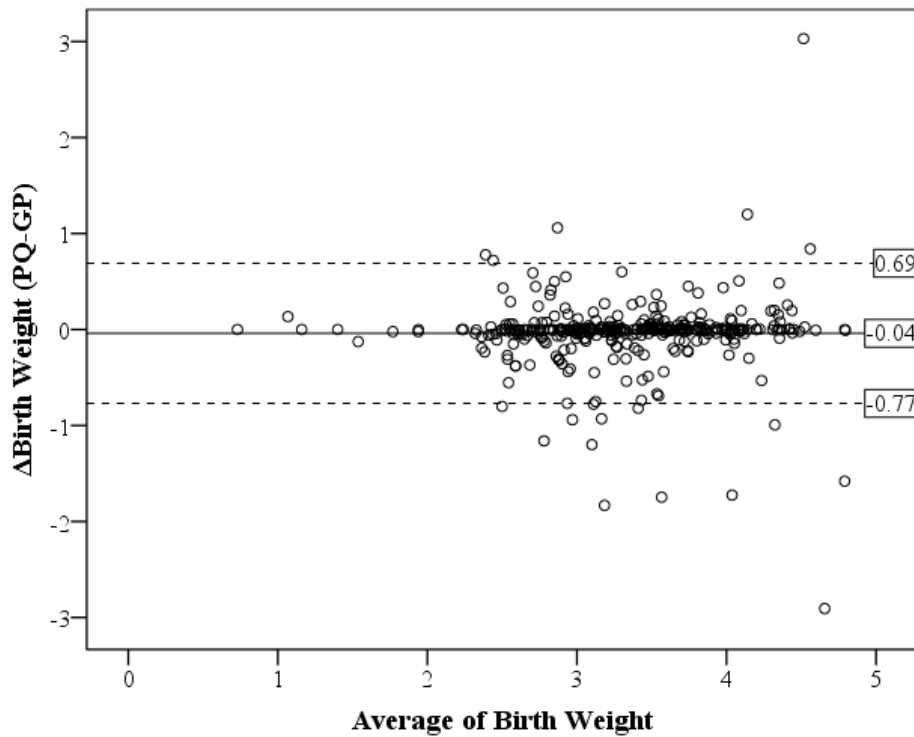


Figure 3. Birth weight: Agreement between data from Parental Questionnaire and GP records



### Assessment of pubertal status

Self-assessment of pubertal status was undertaken by 448 (88%) children over 8 years of age during the first year of study. Pubertal data were missing from 12.7% White, 25.3% Black, 13.1% South Asian and 19.7% Other/mixed ethnicity children. A similar proportion of boys and girls reported that they had attained puberty according to self-report (Table 3), with almost twice as many Black children reporting that they had entered puberty than children from other ethnic groups.



**Table 3. Background characteristics and self-reported (child) pubertal data in children >8 years of age**

|                        | <b>White: puberty n=71<br/>boys, 87 girls</b> |              | <b>Black: puberty<br/>n=66 boys, 120 girls</b> |             | <b>S Asian: puberty<br/>n=38 boys, 55 girls</b> |             | <b>Other: puberty<br/>n=25 boys, 51 girls</b> |              |
|------------------------|---|--------------|--|-------------|---|-------------|---|--------------|
|                        | <b>Yes</b>                                    | <b>No</b>    | <b>Yes</b>                                     | <b>No</b>   | <b>Yes</b>                                      | <b>No</b>   | <b>Yes</b>                                    | <b>No</b>    |
| <b>Boys,<br/>N(%)</b>  | 18 (25%)<br>***                               | 53 (75%)     | 38 (58%)                                       | 28 (42%)    | 10 (26%)<br>***                                 | 28 (74%)    | 5 (20%)<br>***                                | 20 (80%)     |
| Age (y)                | 10.1 (0.4)                                    | 9.9 (0.5)    | 10.0 (0.6)                                     | 9.8 (0.6)   | 10.0 (0.5)                                      | 10.0 (0.4)  | 10.1 (0.9)                                    | 10.0 (0.5)   |
| zHeight#               | 0.33 (1.15)                                   | 0.23 (1.07)  | 0.86 (1.24)                                    | 0.90 (1.14) | -0.53 (1.32)                                    | 0.12 (0.93) | 0.54 (0.88)                                   | 0.29 (1.26)  |
| zWeight#               | 0.74 (1.20)                                   | 0.41 (1.00)  | 1.16 (1.41)                                    | 0.94 (1.14) | -0.70 (1.74)                                    | 0.35 (1.37) | 1.27 (1.54)                                   | 0.44 (1.04)  |
| HtRatio                | 0.53 (0.01)                                   | 0.53 (0.01)  | 0.51 (0.01)                                    | 0.51 (0.01) | 0.52 (0.01)                                     | 0.52 (0.01) | 0.52 (0.01)                                   | 0.52 (0.02)  |
| zBMI#                  | 0.84 (1.24)                                   | 0.46 (1.00)  | 1.10 (1.51)                                    | 0.76 (1.19) | -0.54 (1.79)                                    | 0.41 (1.56) | 1.43 (1.69)                                   | 0.47 (0.96)  |
| <b>Girls,<br/>N(%)</b> | 35 (40%) *                                    | 52 (60%)     | 82 (68%)<br>***                                | 38 (32%)    | 20 (36%)<br>**                                  | 35 (64%)    | 25 (49%)                                      | 26 (51%)     |
| Age (y)                | 10.0 (0.4)                                    | 9.9 (0.4)    | 10.1 (0.6)<br>***                              | 9.6 (0.6)   | 10.2 (0.3)                                      | 10.0 (0.4)  | 10.1 (0.6)                                    | 9.8 (0.5)    |
| zHeight#               | 0.46 (0.79)<br>**                             | -0.15 (0.90) | 1.30(1.10)*                                    | 0.80 (1.01) | 0.31 (1.46)                                     | 0.02 (1.13) | 0.59 (0.82)<br>*                              | -0.04 (0.94) |
| zWeight#               | 0.74 (1.03)<br>**                             | -0.06 (1.08) | 1.43 (1.11)<br>**                              | 0.78 (1.26) | 0.52 (1.49)                                     | 0.07 (1.25) | 1.13 (0.94)<br>**                             | 0.22 (1.17)  |
| HtRatio                | 0.53 (0.01)                                   | 0.53 (0.01)  | 0.51 (0.01)                                    | 0.51 (0.01) | 0.52 (0.01)                                     | 0.51 (0.01) | 0.52 (0.01)                                   | 0.53 (0.01)  |
| zBMI#                  | 0.70 (1.21)<br>**                             | 0.01 (1.16)  | 1.19 (1.20)<br>*                               | 0.51 (1.53) | 0.59 (0.10)                                     | 0.10 (1.24) | 1.17 (1.02)<br>*                              | 0.33 (1.23)  |

Data presented as Mean (SD) unless otherwise indicated. #Adjusted for age and sex according to the British 1990 reference (57). Abbreviation: HtRatio: Sitting/Standing height. Independent t-test performed on pubertal status according to ethnic group. \*\*\* p < 0.001; \* p < 0.05.

Documented evidence of pubertal status were available from 829/902 (92%) parents of children >8 years of age during the 2nd year of study (Table 4). Overall, a much lower proportion of children had entered puberty according to these data than suggested by the children's self-report. In addition, when using parental report, as expected a higher proportion of girls than boys had entered puberty at time of test and children who attained pubertal status were significantly older, taller and heavier than their peers. A higher proportion of Black children had attained puberty at time of testing (18% boys; 50% girls) compared with other ethnic groups (6% boys; 27% girls).

**Table 4. Background characteristics and pubertal data from parental information**

|                   | White: puberty<br>n=162 boys, 181 girls |             | Black: puberty<br>n=61 boys, 92 girls |             | S Asian: puberty<br>n=96 boys, 137 girls |             | Other: puberty<br>n=44 boys, 56 girls |             |
|-------------------|---|-------------|---------------------------------------|-------------|--|-------------|---------------------------------------|-------------|
|                   | Yes                                     | No          | Yes                                   | No          | Yes                                      | No          | Yes                                   | No          |
| <b>Boys N (%)</b> | 9 (6%)                                  | 153 (94%)   | 11 (18%)                              | 50 (82%)    | 6 (6%)                                   | 90 (94%)    | 3 (5%)                                | 54 (95%)    |
| Age (y)           | 10.4 (1.0) *                            | 9.8 (1.0)   | 10.8 (0.3) ***                        | 9.7 (0.8)   | 11.0 (0.3) **                            | 9.8 (1.0)   | 10.1 (1.6)                            | 9.2 (1.3)   |
| zHeight#          | 0.79 (0.74)                             | 0.38 (1.03) | 1.10 (1.02)                           | 0.68 (1.07) | 1.01 (1.43)                              | 0.18 (1.15) | 0.89 (1.15)                           | 0.20 (1.11) |
| zWeight#          | 1.35 (0.76) **                          | 0.38 (1.04) | 1.30 (1.02)                           | 0.84 (1.17) | 1.40 (1.62)                              | 0.23 (1.39) | 1.16 (1.52)                           | 0.46 (1.19) |
| HtRatio           | 0.53 (0.01)                             | 0.53 (0.01) | 0.51 (0.01)                           | 0.51 (0.01) | 0.51 (0.01)                              | 0.52 (0.01) | 0.52 (0.01)                           | 0.53 (0.02) |
| zBMI              | 1.40 (0.75) **                          | 0.27 (1.14) | 1.15 (1.11)                           | 0.75 (1.22) | 1.33 (1.93)                              | 0.19 (1.54) | 1.05 (1.62)                           | 0.53 (1.19) |
| <b>Girls N(%)</b> | 32 (18%)                                | 149 (82%)   | 46 (50%)                              | 46 (50%)    | 39 (28%)                                 | 98 (72%)    | 20 (36%)                              | 36 (64%)    |
| Age (y)           | 10.6 (0.9) ***                          | 9.8 (1.0)   | 10.3 (0.9) ***                        | 9.6 (0.9)   | 10.4 (0.9) ***                           | 9.8 (0.8)   | 10.7 (0.8) **                         | 9.8 (1.0)   |
| zHeight#          | 0.68 (0.75) **                          | 0.05 (0.99) | 1.38 (1.01) **                        | 0.74 (0.90) | 0.69 (0.78) ***                          | 0.02 (1.06) | 0.83 (0.68) *                         | 0.29 (0.94) |
| zWeight#          | 0.84 (0.91) ***                         | 0.06 (1.13) | 1.32 (1.23)                           | 0.98 (1.11) | 0.61 (1.07) **                           | 0.02(1.16)  | 1.22 (0.86) **                        | 0.34 (1.22) |
| HtRatio           | 0.53 (0.02)                             | 0.53 (0.01) | 0.51 (0.01) ***                       | 0.52 (0.02) | 0.52 (0.01)                              | 0.52 (0.01) | 0.52 (0.01) *                         | 0.53 (0.01) |
| zBMI#             | 0.68 (1.07) **                          | 0.03 (1.18) | 0.92 (1.40)                           | 0.84 (1.45) | 0.33 (1.35)                              | -0.00(1.24) | 1.12 (1.01) *                         | 0.22 (1.46) |

Data presented as Mean (SD) unless otherwise indicated; # according to British 1990 reference (57); HtRatio:

Sitting/Standing height. Independent t-test performed on pubertal status within each ethnic group. \*\*\* p < 0.001;

\*\* p < 0.01; \* p < 0.05.

Paired data on pubertal status were available from 246 children (i.e. via self-report in Y1 and parental questionnaire in Y2) and the agreement between parental and child data were examined (Table 5). While there was agreement between parental assessments and self-report of pubertal status in at least 68% of children, the proportion of children having attained puberty based on self-report (Table 3 and Table 5) appeared to be overestimated by 17%, suggesting that pubertal data from self-report were unreliable. Thus, use of pubertal status for subsequent analysis was limited to data obtained from parents. To minimise missing data, it was agreed that for those children who had

not attained puberty by Year 2, that it could be inferred that this status also applied to Year 1. However, the reverse could not be assumed to be true.

**Table 5. Pubertal assessment: Agreement between child and parental report**

| Pubertal status                         | N (%)     |
|---|-----------|
| Agreement (child and parent data agree) | 167 (68%) |
| Underestimation (Child=No; Parent=Yes)* | 37 (15%)  |
| Overestimation (Child=Yes; Parent=No)   | 42 (17%)  |

\*Information from both sources may be correct in that the child may not have reached puberty in year 1 but had done so by year 2. Thus the true proportion of underestimation is less than 15%.

### Population characteristics

Table 6 summarises the group characteristics of all children assessed on the first test occasion according to ethnicity. Sex and age distribution was similar across the ethnic groups as were the proportions of children born preterm. Fewer White children had a birth weight <2.5kg, but the proportion with birth weight < 2kg was similar across all groups. Black children were on average taller and heavier than those from other ethnic groups, while South Asian children were significantly lighter. A significantly higher proportion of Black children received free school meals compared to the other groups. When socio-economic circumstances were further assessed using IMD scores (see Appendix 5) and an adapted family affluent scale (FAS), a significant higher proportion of Black children were from the most deprived areas in London, had families on the lowest quintile for income and were twice as likely to score 1 out of 5 for FAS (

**Table 6).** Significantly more White children and those from Other/mixed ethnicities had mothers who smoked during pregnancy and were exposed to household smoking at time of test; though cotinine analysis demonstrated the mean exposure for the groups was low.

**Table 6. Group characteristics of ALL children assessed at first test occasion**

|                      | White         | Black         | South-Asian   | Other/mixed   | Total           |
|----------------------|---------------|---------------|---------------|---------------|-----------------|
| % boys (n)           | 50% (367/739) | 44% (273/628) | 49% (263/540) | 47% (123/264) | 47%(1020/2171)  |
| Gestational age <37w | 5.1% (38/739) | 6.5% (41/628) | 6.3% (34/540) | 4.9% (13/264) | 5.8% (126/2171) |

|  |                 |                 |                 |                 |                  |
|--|-----------------|-----------------|-----------------|-----------------|------------------|
| Birthweight <2.5kg,                                  | 5.1% (38/739)   | 7.0% (44/628)   | 10% (56/540)    | 8.3% (22/264)   | 7.4% (160/2171)  |
| Birthweight <2.0 kg                                  | 2.0% (15/739)   | 3.0% (19/628)   | 2.6% (14/540)   | 1.1% (3/264)    | 2.3% (51/2171)   |
| Born in the UK                                       | 86% (630/729)   | 86% (497/581)   | 79% (416/528)   | 91% (234/258)   | 85% (1777/2096)  |
| Age (y) <sup>†</sup>                                 | 8.2 (1.6)       | 8.2 (1.6)       | 8.3 (1.6)       | 8.3 (1.7)       | 8.2 (1.6)        |
| Weight (z-score) <sup>†#</sup>                       | 0.38 (1.06)     | 1.01 (1.15)     | 0.01 (1.28)     | 0.49 (1.26)     | 0.48 (1.23)      |
| Height (z-score) <sup>†#</sup>                       | 0.27 (0.98)     | 0.95 (1.06)     | 0.13 (1.08)     | 0.31 (1.08)     | 0.44 (1.09)      |
| Sit/Stand height ratio <sup>†</sup>                  | 0.54 (0.01)     | 0.52 (0.02)     | 0.53 (0.01)     | 0.53 (0.02)     | 0.53 (0.02)      |
| BMI (z-score) <sup>†#</sup>                          | 0.33 (1.12)     | 0.75 (1.27)     | -0.10 (1.36)    | 0.45 (1.31)     | 0.36 (1.29)      |
| <b>Respiratory history</b>                           |                 |                 |                 |                 |                  |
| Prior wheeze   | 10% (67/672)    | 13% (62/493)    | 12% (58/467)    | 13% (29/225)    | 12% (216/1857)   |
| Prior asthma   | 7.0% (52/739)   | 8.0% (50/628)   | 4.8% (26/540)   | 12% (31/264)    | 7.3% (159/2171)  |
| Current asthma                                       | 6.0% (44/739)   | 6.4% (40/628)   | 5.6% (30/540)   | 8.3% (22/264)   | 6.3% (136/2171)  |
| Symptomatic on test day                              | 8.9% (66/739)   | 7.5% (47/628)   | 8.9% (48/540)   | 6.1% (16/264)   | 8.2% (177/2171)  |
| Sickle cell disease                                  | 0.30% (2/739)   | 1.6% (10/628)   | -               | -               | 0.60% (12/2171)  |
| Other health problems                                | 0.68% (5/739)   | 0.48% (3/628)   | 0.38% (1/264)   | -               | 0.40% (9/2171)   |
| <b>Socio-economic circumstances</b>                  |                 |                 |                 |                 |                  |
| Maternal routine/manual occupation <sup>‡</sup>      | 20% (120/600)   | 38% (166/435)   | 34% (134/391)   | 21% (47/228)    | 28% (467/1654)   |
| Total number of computers                            |                 |                 |                 |                 |                  |
| None   | 2.6% (15/567)   | 3.0% (13/429)   | 1.9% (10/524)   | 1.9% (4/207)    | 2.4% (42/1727)   |
| One  | 38% (213/567)   | 46% (195/429)   | 40% (208/524)   | 35% (73/207)    | 40% (689/1727)   |
| Two  | 37% (211/567)   | 35% (149/429)   | 34% (178/524)   | 32% (67/207)    | 35% (605/1727)   |
| More than two  | 23% (128/567)   | 17% (72/429)    | 24% (128/524)   | 30% (63/207)    | 23% (391/1727)   |
| Total number of vehicles                             |                 |                 |                 |                 |                  |
| None   | 22% (126/570)   | 43% (190/443)   | 20% (104/522)   | 23% (47/208)    | 27% (467/1743)   |
| One  | 51% (292/570)   | 47% (206/443)   | 54% (282/522)   | 52% (109/208)   | 51% (889/1743)   |
| Two or more  | 27% (152/570)   | 11% (47/443)    | 26% (136/522)   | 25% (52/208)    | 22% (387/1743)   |
| Shared bedroom, child                                | 42% (242/574)   | 56% (269/478)   | 54% (281/522)   | 41% (87/214)    | 49% (879/1788)   |
| Persons sharing bedroom, n                           | 2% (0-4)        | 2% (0-8)        | 2% (0-5)        | 2% (0-5)        | 2% (0-8)         |
| People in house, n                                   | 4 (1-14)        | 4 (1-23)        | 5 (1-12)        | 4 (1-8)         | 4 (1-23)         |
| Bedrooms in home, n                                  | 3 (1-6)         | 3 (1-8)         | 3 (1-8)         | 3 (1-6)         | 3 (1-8)          |
| English first language                               | 76% (406/534)   | 75% (214/286)   | 45% (187/415)   | 84% (152/181)   | 68% (959/1416)   |
| Family affluent scale <sup>β</sup> (score:1/5)       | 6.7% (49/732)   | 14% (79/576)    | 7.8% (42/539)   | 7.4% (19/258)   | 9.0% (189/2105)  |
| Free school meals                                    | 19% (133/700)   | 54% (236/440)   | 13% (66/517)    | 33% (75/229)    | 27% (510/1886)   |
| IMD score <sup>γ</sup> : 1 <sup>st</sup> quintile    | 11% (78/731)    | 0.7% (4/608)    | 0% (0/535)      | 6.3% (16/255)   | 4.6% (98/2129)   |
| IMD score <sup>γ</sup> : 5 <sup>th</sup> quintile    | 28% (206/731)   | 65% (397/608)   | 22% (115/535)   | 45% (115/255)   | 39% (833/2129)   |
| Income score <sup>γ</sup> : 1 <sup>st</sup> quintile | 10% (75/731)    | 0.3% (2/608)    | 0% (0/535)      | 4.3% (11/255)   | 4.1% (88/2129)   |
| Income score <sup>γ</sup> : 5 <sup>th</sup> quintile | 37% (268/731)   | 76% (461/608)   | 25% (135/535)   | 47% (119/255)   | 46% (983/2129)   |
| <b>Smoking exposure</b>                              |                 |                 |                 |                 |                  |
| Smoking in pregnancy                                 | 8.2% (59/720)   | 1.9 (11/572)    | 7.5 (19/252)    | 1.5 (8/526)     | 4.7 (97/2070)    |
| Exposure to household smoking                        | 31% (194/630)   | 14% (61/432)    | 18% (79/430)    | 37% (81/221)    | 24% (415/1713)   |
| Cotinine (ng/mL) <sup>§</sup>                        | 0.00(0.00-0.20) | 0.00(0.00-0.00) | 0.00(0.00-0.00) | 0.00(0.00-0.10) | 0.00 (0.00-0.00) |

Data presented as % (n/N) unless otherwise indicated. Abbreviations: SEC: Socio-economic circumstances; IMD:

Index of Multiple Deprivation. † Mean (SD); # According to British 1990 reference(57); Asthma classification was

based on parental report of doctor diagnosis of asthma. Current asthma defined as those having symptoms, asthma

medication with or without a diagnosis of asthma over the past 12 month even if no prior diagnosis of asthma; ‡ according to the National Statistics Socio-economic classification (NS SeC) – rebased on SOC2010 user manual (58); ¥: according to the English indices of multiple deprivation (IMD) 2010 (44); <sup>β</sup>Family affluent scale based on collated score for numbers of computers, vehicle ownership and whether the child had own bedroom (59); <sup>§</sup>median (Inter-quartile range).

### Reference or healthy population?

After excluding children with current and chronic lung disease (e.g. sickle cell disease; cystic fibrosis; current asthma) and those with congenital abnormalities (n=128), data were available for 1901 children (46% boys; 35% White; 29% Black; 24% South-Asian; 12% other/mixed ethnicity; mean(range) age 8.3 (5.2-11.9) years) on 2767 test occasions. Within this group, “healthy” children were defined as those with no prior asthma or hospitalisation for a respiratory problem, born full term (gestational age  $\geq$  37 weeks) with birth weight  $>$  2.5 kg and asymptomatic at test. After adjusting for sex, age and height, mean (SD) zFEV<sub>1</sub> and zFVC approximated 0(1) showing the GLI-2012 multi-ethnic reference equations (21) are broadly appropriate for this “healthy” population (Table 7). However, if data for children born preterm and/or low birthweight (LBW) were also included, group mean LF results were similar to those from the “healthy” group (Table 7). Furthermore, if data for those with prior asthma or who were symptomatic at test were added, the mean and SD for each outcome also remained very similar (Table 7).

**Table 7. Impact of health status on lung function**

|                        | <b>Healthy</b> | <b>+ Preterm/ LBW</b> | <b>+ Prior asthma</b> | <b>+ Symptomatic<br/>(Total Reference population)</b> |
|------------------------|----------------|-----------------------|-----------------------|---|
| Subjects, n            | 1520           | 1676                  | 1825                  | 1901  |
| Boys, %                | 44%            | 45%                   | 45%                   | 45%   |
| Tests, n               | 2199           | 2431                  | 2626                  | 2767  |
| zFEV <sub>1</sub>      | 0.04 (0.90)    | 0.03 (0.90)           | 0.01 (0.92)           | 0.00 (0.94)   |
| zFVC                   | 0.17 (0.92)    | 0.17 (0.93)           | 0.16 (0.93)           | 0.15 (0.95)   |
| zFEV <sub>1</sub> /FVC | -0.24 (0.98)   | -0.25 (0.98)          | -0.28 (0.99)          | -0.29 (0.99)  |

Data expressed as mean (SD) except where indicated.

Group characteristics of the reference population (i.e. after excluding children with current or chronic respiratory disease and those with failed spirometry; Table 8) were similar to that from the entire study population (Table 6). Additional details and group characteristics of Black and South Asian children according to their respective sub-groups are given in Table 9 and Table 10 respectively.

Among the South Asian children, with the exception of Pakistani children who were taller and heavier, anthropometric measurements were very similar across all other subgroups, while Bangladeshi children were from more deprived circumstances i.e. significantly more receiving free school meals and more families with IMD and Income score below the 5th quintile (most deprived)

Table 10).

**Table 8. Group characteristics of reference population**

|  | <b>White</b>      | <b>Black</b>     | <b>South-Asian</b> | <b>Other/mixed</b> | <b>Total</b>     |
|--|-------------------|------------------|--------------------|--------------------|------------------|
| % boys (n/N)                                     | 49% (322/664)     | 42% (226/543)    | 48% (220/462)      | 45% (105/232)      | 46% (873/1901)   |
| Gestational age <37w                             | 5.0% (33/664)     | 7.0% (38/543)    | 5.8% (27/462)      | 5.6% (13/232)      | 5.8% (111/1901)  |
| Birthweight <2.5kg,                              | 4.4% (29/664)     | 6.6% (36/543)    | 11% (50/462)       | 9.5% (22/232)      | 7.2% (137/1901)  |
| Birthweight <2.0 kg,                             | 2.0% (13/664)     | 2.8% (15/543)    | 2.6% (12/462)      | 1.3% (3/232)       | 2.3% (43/1901)   |
| Born in the UK                                   | 87% (566/654)     | 86% (430/502)    | 79% (357/452)      | 90% (203/226)      | 85% (1556/1834)  |
| Age (y) <sup>†</sup>                             | 8.2 (1.6)         | 8.3 (1.6)        | 8.3 (1.7)          | 8.3 (1.7)          | 8.3 (1.6)        |
| Weight (z-score) <sup>†#</sup>                   | 0.38 (1.0)        | 1.0 (1.1)        | 0.01 (1.3)         | 0.47 (1.2)         | 0.49 (1.2)       |
| Height (z-score) <sup>†#</sup>                   | 0.28 (0.97)       | 0.95 (1.0)       | 0.11 (1.1)         | 0.32 (1.1)         | 0.44 (1.1)       |
| Sit/Stand height ratio <sup>†</sup>              | 0.54 (0.01)       | 0.52 (0.02)      | 0.53 (0.01)        | 0.53 (0.02)        | 0.53 (0.02)      |
| BMI (z-score) <sup>†#</sup>                      | 0.32 (1.1)        | 0.79 (1.2)       | -0.08 (1.4)        | 0.42 (1.3)         | 0.37 (1.3)       |
| <b>Respiratory history</b>                       |                   |                  |                    |                    |                  |
| Prior Wheeze                                     | 5.8% (35/602)     | 8.7% (37/424)    | 7.7% (31/401)      | 8.1% (16/197)      | 7.3% (119/1624)  |
| Prior asthma                                     | 7.8% (52/664)     | 9.6% (52/543)    | 5.2% (24/462)      | 13% (30/232)       | 8.3% (158/1901)  |
| Symptomatic on test day                          | 6.3% (42/664)     | 5.9% (32/543)    | 6.3% (29/462)      | 3.4% (8/232)       | 5.8% (111/1901)  |
| <b>Socio-economic circumstances</b>              |                   |                  |                    |                    |                  |
| Maternal routine/manual occupation <sup>‡</sup>  | 20% (109/536)     | 39% (146/377)    | 33% (112/343)      | 21% (41/199)       | 28% (408/1455)   |
| Total number of computers                        |                   |                  |                    |                    |                  |
| None   | 2.2% (14/628)     | 2.7% (12/451)    | 2.0% (9/452)       | 1.8% (4/217)       | 2.2%(39/1748)    |
| One  | 35% (219/628)     | 44% (199/451)    | 39% (174/452)      | 32% (70/217)       | 38%(662/1748)    |
| Two  | 36% (226/628)     | 34% (153/451)    | 35% (160/452)      | 34% (74/217)       | 35%(613/1748)    |
| More than two                                    | 27% (169/628)     | 19% (87/451)     | 24% (109/452)      | 32% (69/217)       | 25%(434/1748)    |
| Total number of vehicles                         |                   |                  |                    |                    |                  |
| None   | 18% (116/629)     | 40% (185/458)    | 20% (91/450)       | 21% (46/217)       | 25%(438/1754)    |
| One  | 50% (314/629)     | 50% (227/458)    | 54% (241/450)      | 54% (118/217)      | 51%(900/1754)    |
| Two or more                                      | 32% (199/629)     | 10% (46/458)     | 26% (118/450)      | 24% (53/217)       | 24%(416/1754)    |
| Shared bedroom, child                            | 39% (244/630)     | 57% (267/469)    | 54% (241/450)      | 39% (84/215)       | 47%(836/1764)    |
| Persons sharing bedroom, n                       | 2 (1-4)           | 2 (1-8)          | 2 (1-5)            | 2 (1-5)            | 2 (1-8)          |
| People in house, n                               | 4 (2-14)          | 5 (2-23)         | 5 (3-12)           | 4 (2-7)            | 4 (2-23)         |
| Bedrooms in home, n                              | 3 (1-6)           | 2 (1-8)          | 3 (1-7)            | 3 (1-5)            | 3 (1-8)          |
| English first language                           | 77% (370/482)     | 76% (183/242)    | 47% (164/353)      | 84% (134/159)      | 69% (851/1236)   |
| Family affluent scale <sup>B</sup> (score:0-1/6) | 7.2% (45/625)     | 15% (67/444)     | 8.0% (36/449)      | 7.4% (16/215)      | 9.5%(164/1733)   |
| Family affluent scale <sup>B</sup> (score:5-6/6) | 30% (190/625)     | 11% (49/444)     | 21% (95/449)       | 27% (57/215)       | 23% (391/1733)   |
| Free school meals                                | 19% (115/608)     | 53% (198/373)    | 12% (52/430)       | 32% (63/198)       | 27% (428/1609)   |
| IMD score¥: 1 <sup>st</sup> quintile             | 11% (73/657)      | 0.8% (4/524)     | 0% (0/458)         | 6.3% (14/224)      | 4.9% (91/1863)   |
| IMD score¥: 5 <sup>th</sup> quintile             | 28% (186/657)     | 66% (343/524)    | 22% (99/458)       | 43% (97/224)       | 39% (725/1863)   |
| IMD Income: 1 <sup>st</sup> quintile             | 11% (71/657)      | 0.4% (2/524)     | 0% (0/458)         | 4.0% (9/224)       | 4.4% (82/1863)   |
| IMD Income:5 <sup>th</sup> quintile,             | 36% (239/657)     | 77% (402/524)    | 26% (117/458)      | 45% (100/224)      | 46% (858/1863)   |
| <b>Smoking exposure, n (%)</b>                   |                   |                  |                    |                    |                  |
| Smoking in pregnancy                             | 7.5% (49/650)     | 1.6% (8/494)     | 1.8% (8/451)       | 7.2% (16/221)      | 4.5% (81/1816)   |
| Exposure to household smoking                    | 31% (175/573)     | 13% (49/365)     | 19% (68/366)       | 34% (67/196)       | 24% (359/1500)   |
| Cotinine (ng/mL) §                               | 0.00 (0.00-0.2.0) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00)   | 0.00 (0.00-0.03)   | 0.00 (0.00-0.00) |

Data presented as % (n/N) unless otherwise indicated. Abbreviation: IMD: Index of Multiple Deprivation. <sup>†</sup>Mean (SD);

<sup>#</sup>According to British 1990 reference(57); Asthma classification was based on parental report of doctor diagnosis of asthma;



‡according to the National Statistics Socio-economic classification (NS SeC) – rebased on SOC2010 user manual (58); ¥: according to the English indices of multiple deprivation (IMD) 2010 (44); §median (IQR); <sup>§</sup>Family affluent scale based on collated score for numbers of computers, vehicle ownership and whether the child had own bedroom (59).

**Table 9. Background characteristics of Black reference children according to subgroups**

|   | African       | Caribbean     | Black Other   | Black (Total) |
|---|---------------|---------------|---------------|---------------|
| Subjects, n   | 388 (71%)     | 113 (21%)     | 42 (8%)       | 543 (100%)    |
| Boys  | 44% (169/388) | 34% (38/113)  | 45% (19/42)   | 42% (226/543) |
| UK born*  | 82% (300/365) | 94% (100/106) | 97% (30/35)   | 86%           |
| Total assessments (n)                               | 581           | 165           | 59            | 805           |
| Birthweight (kg)                                    | 3.26 (0.78)   | 3.29 (0.58)   | 3.16 (0.50)   | 3.26 (0.71)   |
| zWeight   | 1.1 (1.1)     | 0.8 (1.2)     | 0.9 (1.1)     | 1.0 (1.1)     |
| zHeight   | 1.0 (1.1)     | 0.9 (1.1)     | 1.3 (1.1)     | 0.95 (1.0)    |
| zBMI  | 0.9 (1.1)     | 0.5 (1.3)     | 0.3 (1.3)     | 0.79 (1.2)    |
| Sit/Stand Height                                    | 0.519 (0.016) | 0.518 (0.015) | 0.522 (0.188) | 0.52 (0.02)   |
| Maternal: Routine/manual occupation                 | 39% (102/260) | 39% (35/89)   | 32% (9/27)    | 39% (146/376) |
| Family affluent scale <sup>§</sup> (score:0-1 of 6) | 17% (54/322)  | 9.8% (9/92)   | 13% (4/30)    | 15% (67/444)  |
| Free School Meals                                   | 56% (151/270) | 44% (36/81)   | 50% (11/22)   | 53% (198/373) |
| IMD score <5th quintile                             | 67% (252/374) | 53% (57/108)  | 81% (34/42)   | 66% (343/524) |
| Income score <5th quintile                          | 79% (295/374) | 69% (74/108)  | 79% (33/42)   | 77% (402/524) |

Data presented as % (n/N) or Mean (SD) or as indicated. Black other: defined as “Black other” from self-report or from mixed ethnicities (African/Caribbean). <sup>§</sup>Family affluent scale based on collated score for numbers of computers, vehicle ownership and whether the child had own bedroom (59)

**Table 10. Background characteristics of South Asian reference children according to subgroups**

|  | Indian        | Bangladeshi   | Pakistani     | Sri Lankan    | SA Other      | South Asian<br>(Total) |
|--|---------------|---------------|---------------|---------------|---------------|------------------------|
| Subjects, n                                      | 318 (69%)     | 48 (10%)      | 39 (8%)       | 47 (10%)      | 10 (2%)       | 462                    |
| Boys   | 49% (156/318) | 48% (23/48)   | 51% (20/39)   | 34% (16/47)   | 50% (5/10)    | 48%(220/462)           |
| UK born*   | 78% (241/311) | 90% (43/48)   | 87% (33/38)   | 78% (35/45)   | 50% (5/10)    | 79%(357/452)           |
| Total assessments                                | 429           | 54            | 54            | 69            | 17            | 623                    |
| Birthweight (kg)                                 | 2.99 (0.54)   | 3.05 (0.58)   | 3.30 (0.59)   | 3.06 (0.52)   | 3.00 (0.33)   | 3.03 (0.55)            |
| zWeight  | -0.1 (1.3)    | 0.3 (1.2)     | 0.7 (1.2)     | 0.3 (1.2)     | 0.0 (1.3)     | 0.01 (1.3)             |
| zHeight  | 0.1 (1.1)     | 0.0 (1.1)     | 0.7 (0.9)     | 0.1 (0.9)     | 0.3 (0.7)     | 0.11 (1.1)             |
| zBMI   | -0.2 (1.4)    | 0.4 (1.2)     | 0.5 (1.4)     | 0.2 (1.2)     | -0.3 (1.6)    | -0.08 (1.4)            |
| Sit/Stand Height                                 | 0.527 (0.014) | 0.525 (0.013) | 0.525 (0.013) | 0.523 (0.014) | 0.526 (0.015) | 0.53 (0.01)            |
| Maternal: Routine/manual occupation              | 30% (80/265)  | 42% (11/26)   | 18% (3/17)    | 55% (16/29)   | 33% (2/6)     | 33%(112/343)           |
| Family affluent scale <sup>β</sup> (score:0-1/6) | 7.7% (24/309) | 10% (5/48)    | 5.4% (2/37)   | 6.6% (3/45)   | 20% (2/10)    | 8% (36/449)            |
| Free School Meals                                | 4% (11/299)   | 58% (26/45)   | 24% (8/34)    | 14% (6/44)    | 13% (1/8)     | 12% (52/430)           |
| IMD score <5th quintile                          | 13% (42/315)  | 79% (37/47)   | 28% (11/39)   | 8.5% (4/47)   | 50% (5/10)    | 22% (99/458)           |
| Income score <5th quintile                       | 19% (59/315)  | 77% (36/47)   | 26% (10/39)   | 17% (8/47)    | 40% (4/10)    | 26%(117/458)           |

Data presented as % (n/N) or Mean (SD) or as indicated. SA Other: defined as “South-Asian Other” from self-report or from mixed South-Asian ethnicities; <sup>β</sup>Family affluent scale based on collated score for numbers of computers, vehicle ownership and whether the child had own bedroom (59).

### Inter-observer repeatability of anthropometry assessments

Seven researchers performed anthropometric assessments during the study period. Repeat measures were successfully carried out in 54 children for height; 49 for sitting height and 40 for chest dimensions (Table 11). Inter-observer repeatability for all assessments was high with a mean difference for each measure being 0.1cm and there was no systematic bias between the researchers (data not shown). However the limits of agreement for chest circumference were wider compared to assessments of chest width and depth (Table 11).

**Table 11. Anthropometric assessments: Inter-observer repeatability**

| Measurement         | n  | Age (range) y    | Mean (SD)<br>difference (cm) | 95% Limits of<br>agreement (cm) |
|---------------------|----|------------------|------------------------------|---------------------------------|
| Height              | 54 | 9.2 (6.7 – 11.4) | 0.1 (0.3)                    | -0.5; 0.7                       |
| Sitting height      | 49 | 9.1 (6.7 – 11.6) | 0.1 (0.5)                    | -0.9; 1.2                       |
| Chest circumference | 40 | 9.1 (6.1 -11.3)  | 0.1 (1.7)                    | -3.2; 3.4                       |
| Chest width         | 40 | 9.1 (6.1 -11.3)  | -0.1 (0.8)                   | -1.7; -1.5                      |
| Chest depth         | 40 | 9.1 (6.1 -11.3)  | 0.1 (1.0)                    | -1.8; 2.0                       |

## Discussion points

### Summary of Key Findings:

- This study represents the largest study of lung function and detailed anthropometry undertaken in a multi-ethnic population of London primary school children (age 5-11y) to date, and shows that it is feasible to undertake a wide range of complex physiological assessments in young children under field conditions within the school environment.
- Despite potential language barriers, consent to participate was high (>50%) across all groups and teachers, parents and pupils provided enthusiastic and positive feedback with respect to participation ([www.ucl.ac.uk/slic](http://www.ucl.ac.uk/slic)).
- Amongst the 52% of London primary school children recruited to the study, the proportions of children with low birthweight, born prematurely and with a history of wheeze or asthma ever were similar across the ethnic groups, and similar to that currently reported across England (60). The children recruited to the SLIC study appear to be representative of an inner city population of multi-ethnic school children (2011 Census; (61)).
- The higher proportion of South Asian children with birthweight <2.5 kg was not surprising given that 69% of South Asian children recruited to this study were of Indian origin (Table 10) and average birth weight of South Asian infants (especially Indians) born in the UK are ~300g lighter than those in White infants (62).
- A higher proportion of Black children were from families with poorer SEC compared to White or South Asian children. When analysed according to the South Asian sub-groups, >70% of the Bangladeshi children were from families living in the most deprived areas in London and had income score <5th quintile nationally. These figures are consistent with recent reports results that, within the UK, “income poverty rate varies substantially between ethnic groups: Bangladeshis (65%), Pakistanis (55%) and Black Africans (45%) have the highest rates; Black Caribbeans (30%), Indians (25%), White Other (25%) and White British (20%) have the lowest rates and that 70% of those in income poverty in inner London are from minority ethnic groups” (63).
- In addition to obtaining a unique set of lung function and anthropometric data using identical equipment and techniques in a multi-ethnic population of primary school children, we undertook essential studies to validate the widely available Tanita Bio-electrical Impedance Analysis (BIA) method of assessing body

composition (51) against the highly accurate but expensive isotope (Deuterium) measurements in this multi-ethnic population of children.

- Since recent studies have used genetic markers to describe the variability among ethnic groups (64, 65), saliva samples were collected in this study and have been stored for future DNA analysis once funding becomes available.
- In contrast to the high success rate for most of the physiological assessments, the ability of 3D photonic scanning to provide reliable, consistent anthropometric data was disappointing, as was the difficulty experienced in extracting data from GP records, and the sparsity of key information such as birth data, even when records could be accessed.
- Relaxing the exclusion criteria increased the sample size by 25%. As the aim of the SLIC study was to derive lung function equations that were unbiased and generalisable for use in clinics and hospitals for management of lung disease, it was agreed the reference sample can be all-inclusive. However, should a “healthy” population be required for final analysis, the target sample size should be increased by 30% to ensure adequate power when designing studies.

### Strengths of the study

- All assessments were undertaken using identical equipment and standardised protocols by a core team of respiratory physiologists trained in every aspects of the study protocol, such that assessments proceeded smoothly, maximising time available to complete the procedures within the school day.
- The high inter-observer repeatability of anthropometric measurements (Table 11) and the over-read of spirometry data by the senior respiratory physiologist ensured appropriate quality control, thereby increasing the reliability of data reported.
- Use of identical equipment, techniques and quality control, together with the diverse nature of assessments and documentation of relevant past history, socio-economic circumstances and exposures to environmental pollution will allow the true impact of ethnicity on LF to be clarified once other major determinants of LF have been taken into account, in a way that is impossible when comparing data between different studies.
- By assessing all children with parental consent, while attempting to document relevant past and current medical history, analysis of the dataset can either be limited to ‘healthy’ children with no evidence of any

prior or current acute or chronic illness, or can be extended to a more representative 'reference population whereby only those children with clear evidence of diseases known to impact on lung function, such as current asthma, CF or sickle cell disease are excluded. Results derived from this reference population would also be widely applicable for use in clinics for the management of children with lung disease.

### **Limitations of the study**

- The major potential limitation of this study, as with all such studies, relates to the difficulties in defining ethnicity. Broad ethnic categorisation into four main groups for this study was a pragmatic approach based on local population characteristics and therefore did not include sufficient children of South East Asian (e.g. Chinese) origin to constitute a separate ethnic group. While there is increasing debate about the concepts of "race" and "ethnicity", the accepted standard for defining "race" is by self-identification. There are, however, practical problems with respect to how the "admixed" population should be categorised. Furthermore, even when categorised according to broad subgroups is feasible, such categories fail to take into consideration the genetic diversity (and associated differences in body size and shape) that can occur across continents. Not only would attempts to analyse according to smaller sub-categories as illustrated in Table 9 and Table 10, require huge numbers of children to achieve sufficient power of study, making such a study both unaffordable and impractical, but this still would not tackle the issue of interpreting LF in children who do not fit neatly into any of the designated groups
- The other major weakness in this study is the proportion of missing data on background information for these children. Since this was a field study, we were dependent on the parents to complete the questionnaire for the background information including ethnicity, socio-economic circumstances and respiratory health of the child. Overall 96% of parents returned completed questionnaires, this being slightly lower (91%) from parents of Black children (Table 2). Having anticipated there would be some degree of missing information, the study was designed to supplement such information from GP records as well as using these to validate the information extracted from parental questionnaire. Some studies have suggested that retrospectively collected information such as birthweight and gestational age may be biased (62), whereas others have found no evidence of systematic bias (66, 67) and have reported that parental recall of birth data was reliable across the social classes up to 16 years after delivery (67). In this study, we

found good agreement between GP data and parental information (Figure 2 and Figure 3). We also adopted the approach that parents with children born preterm or low birthweight were more likely to recall and report such data. Thus missing information on GA (11%) and BWt (22%) were considered most likely to be from children who were born full term and with normal birthweight.

- Prior to this study, most of the data collected using 3D photonic scanning for body shape had been for clothes sizing surveys conducted in adults (68-70), with limited data available in children. While the data collection process for these large adult sizing surveys could be streamlined for effective processing of the 3D scans, the process was not so easily streamlined for younger children, who needed more time and assistance to dress and undress for the procedure. In addition, the adult hand grip which had been designed to facilitate maintaining the correct stance for the 3D scans was not easily adapted for children. Such factors contributed to the relatively poor success rate for 3D scans in children. The failure rate in children was compounded by analysis issues which demonstrated that the current hardware and software for data collection and analysis would need to be further refined and adapted for children before this technology can become cost-effective.

### Challenges of field study in young children

- Recruitment:
  - An all-inclusive strategy was adopted to ensure no child would feel excluded from a study that was being undertaken in the school. However, depending on final outcomes, this does require appropriate increase in the initial recruitment targets to ensure adequate power for final analysis after exclusions.
  - Every effort was made to ensure parents were aware that the school had agreed to participate in our research study by inclusion of study summary in the school's newsletters to parents and the interactive Science Workshops for the children.
  - In one school, where over half the parents did not speak English – a summary of the study was published in the Gujarat Samachar (weekly newspaper in Gujarati) and the Asian Voice (English paper widely read by South Asians in London).
- Assessment of pubertal status: In children with paired data, we found a 20% over-estimation of pubertal status especially in boys. These observations were similar to that previously reported by others when comparing between self-report and physical examination by doctors (71-73) and Rabbini et al concluded that self-assessments should not be used as a substitute method for pubertal assessments for early or mid-

pubertal groups(72). Parental assessment may provide a better assessment of pubertal status for children in early or mid-puberty groups especially in large epidemiology studies.

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Dear Parent/Guardian



**We have invited your child to be a part of the SLIC study  
(Size and Lung Function in Children)**



In this study we will investigate the relationship between lung growth and body size and composition in healthy children of all ethnicities.

We hope this will allow us to understand how the lungs change as children grow and will help us to help all children with lung disease. For more information about the study please visit: <http://www.ucl.ac.uk/slic>

**THE INFORMATION ON THE FIRST PAGE WILL NEVER BE SEEN BY ANYONE OUTSIDE THE SURVEY TEAM.**

What is today's date? \_\_\_\_\_

1. The person who has completed this questionnaire is (please tick as appropriate):

Mum  Dad  Stepmum/Stepdad  Grandparent  Other  (please specify) \_\_\_\_\_

2. What is your child's name? \_\_\_\_\_  
(First name) \_\_\_\_\_ (Last name) \_\_\_\_\_

3. What is your child's date of birth? \_\_\_\_\_  
DAY DAY / MONTH MONTH / YEAR YEAR YEAR YEAR

4. Your child is a... (please tick) Boy  Girl

5. What is your child's home address? (please write) \_\_\_\_\_  
Post code \_\_\_\_\_

6. Home Telephone Number: (please write) \_\_\_\_\_

7. GP's Name: (please write) \_\_\_\_\_

8. GP's address (including postal code): (please write) \_\_\_\_\_

9. GP's Telephone Number: (please write) \_\_\_\_\_

10. Some general information about both parents (please write)

MOTHER'S name? (First name) \_\_\_\_\_ (Last name) \_\_\_\_\_ (Date of Birth) \_\_\_\_\_

FATHER'S name? (First name) \_\_\_\_\_ (last name) \_\_\_\_\_ (Date of Birth) \_\_\_\_\_

How can we contact you?: Phone Number \_\_\_\_\_

EMAIL: \_\_\_\_\_

**PART ONE: QUESTIONS ABOUT RACE or ETHNIC GROUP**

**1. Which country was your child born in?** (please write).....

**2. In which country were the following born?**

(please write in the space provided and if you don't know tick the box)

**Don't know**

|   |  |  |
|---|--|--|
| Mum   |  |  |
| Mum's mother<br>(grandmother on mum's side) |  |  |
| Mum's father<br>(grandfather on mum's side) |  |  |
| Dad   |  |  |
| Dad's mother<br>(grandmother on dad's side) |  |  |
| Dad's father<br>(grandfather on dad's side) |  |  |

**3. How long has your child lived in the UK? Tick ONE box only**

- |  |  |
|--|--|
| <input type="checkbox"/> All of their life | <input type="checkbox"/> Over 10 years |
| <input type="checkbox"/> 6 – 10 years      | <input type="checkbox"/> 1 – 5 years   |
| <input type="checkbox"/> Less than 1 year  |  |

**4. Which ethnic origin best describes you and your family? Tick only ONE box for EACH person.**

| WHITE |                                     | MUM | DAD | CHILD |
|-------|-------------------------------------|-----|-----|-------|
| 01    | White: UK                           |     |     |       |
| 02    | White: Irish                        |     |     |       |
| 03    | White: Greek                        |     |     |       |
| 04    | White: Turkish                      |     |     |       |
| 05    | White: Jewish                       |     |     |       |
| 06    | White: Kurdish                      |     |     |       |
|       | White: Other (please write)         |     |     |       |
| BLACK |                                     | MUM | DAD | CHILD |
| 07    | Black: Somali                       |     |     |       |
| 08    | Black: Ugandan                      |     |     |       |
| 09    | Black: Nigerian                     |     |     |       |
| 10    | Black: Ghanaian                     |     |     |       |
|       | Black: Other African (please write) |     |     |       |
| 11    | Black: Caribbean                    |     |     |       |
| 12    | Black: British                      |     |     |       |
|       | Black: Black Other (please write)   |     |     |       |
| ASIAN |                                     | MUM | DAD | CHILD |
| 13    | Asian: Indian                       |     |     |       |
| 14    | Asian: Pakistani                    |     |     |       |
| 15    | Asian: Bangladeshi                  |     |     |       |
|       | Asian: Other (please write)         |     |     |       |
| 16    | Asian: Chinese                      |     |     |       |
| 17    | Asian: Vietnamese                   |     |     |       |
| MIXED |                                     | MUM | DAD | CHILD |
| 18    | Mixed: White and Black Caribbean    |     |     |       |
| 19    | Mixed: White and Black African      |     |     |       |
| 20    | Mixed: White and Asian              |     |     |       |
| 21    | Mixed: Asian and Black              |     |     |       |
|       | Mixed: Other (please write)         |     |     |       |
|       | Other (please write)                |     |     |       |

**5. What is the main language spoken at home?** \_\_\_\_\_

**PART TWO: QUESTIONS ABOUT THE CHILD AND FAMILY HEALTH**

6. Was your child born on time?  Yes  No



7. If the child was born early please state how many weeks early? \_\_\_\_\_

8. What was your child's **BIRTH** weight?  pounds  ounces **OR**  .  Kilograms

9. Was your child born as a twin or triplet?  No  Yes (Twin)  Yes (Triplet)  
If YES, what was their birth order: 1 /2 /3 (delete as appropriate)

10. Was he/she admitted to a special care baby unit?  Yes  No

11. Did he/she need a machine to help with breathing?  Yes  No

12. Has your child EVER had any of the conditions listed below (i.e. from birth to now)?

|   |  | Age, in years when first diagnosed |                             | Any problems in last 3 months? |  |
|---|--|------------------------------------|-----------------------------|--------------------------------|--|
| 1 | Asthma   | Yes <input type="checkbox"/>       | No <input type="checkbox"/> |                                | Yes <input type="checkbox"/> No <input type="checkbox"/> |
| 2 | Wheeze (whistling sound heard when breathing out)                    | Yes <input type="checkbox"/>       | No <input type="checkbox"/> |                                | Yes <input type="checkbox"/> No <input type="checkbox"/> |
| 3 | Bronchiolitis  | Yes <input type="checkbox"/>       | No <input type="checkbox"/> |                                |  |
| 4 | Pneumonia  | Yes <input type="checkbox"/>       | No <input type="checkbox"/> |                                | Yes <input type="checkbox"/> No <input type="checkbox"/> |
| 5 | Persistent cough (more than 3 weeks)                                 | Yes <input type="checkbox"/>       | No <input type="checkbox"/> |                                | Yes <input type="checkbox"/> No <input type="checkbox"/> |
| 6 | Cystic Fibrosis  | Yes <input type="checkbox"/>       | No <input type="checkbox"/> |                                | Yes <input type="checkbox"/> No <input type="checkbox"/> |
| 7 | Sickle Cell  | Yes <input type="checkbox"/>       | No <input type="checkbox"/> |                                | Yes <input type="checkbox"/> No <input type="checkbox"/> |
| 8 | Any other health conditions/allergies not listed (please state)..... |                                    |                             |                                |  |

13. Has the child ever been prescribed a bronchodilator? (e.g. Puffer, Reliever, Inhaler, Nebuliser)

Tick **ONE** box only:  Yes  No  I don't know

If yes, what colour was it: (please write) ..... and

has your child used the bronchodilator in the past 3 months?  Yes  No

14. Have any of the family ever been diagnosed with the following by a doctor? (please tick)

|          | Child's Mum  | Child's Dad  | Sibling (if applicable)  | Half Sibling (if applicable)   |
|----------|--|--|--|--|
| Asthma   | Yes <input type="checkbox"/> No <input type="checkbox"/> Don't know <input type="checkbox"/> | Yes <input type="checkbox"/> No <input type="checkbox"/> Don't know <input type="checkbox"/> | Yes <input type="checkbox"/> No <input type="checkbox"/> Don't know <input type="checkbox"/> | Yes <input type="checkbox"/> No <input type="checkbox"/> Don't know <input type="checkbox"/> |
| Wheeze   | Yes <input type="checkbox"/> No <input type="checkbox"/> Don't know <input type="checkbox"/> | Yes <input type="checkbox"/> No <input type="checkbox"/> Don't know <input type="checkbox"/> | Yes <input type="checkbox"/> No <input type="checkbox"/> Don't know <input type="checkbox"/> | Yes <input type="checkbox"/> No <input type="checkbox"/> Don't know <input type="checkbox"/> |
| Eczema   | Yes <input type="checkbox"/> No <input type="checkbox"/> Don't know <input type="checkbox"/> | Yes <input type="checkbox"/> No <input type="checkbox"/> Don't know <input type="checkbox"/> | Yes <input type="checkbox"/> No <input type="checkbox"/> Don't know <input type="checkbox"/> | Yes <input type="checkbox"/> No <input type="checkbox"/> Don't know <input type="checkbox"/> |
| Hayfever | Yes <input type="checkbox"/> No <input type="checkbox"/> Don't know <input type="checkbox"/> | Yes <input type="checkbox"/> No <input type="checkbox"/> Don't know <input type="checkbox"/> | Yes <input type="checkbox"/> No <input type="checkbox"/> Don't know <input type="checkbox"/> | Yes <input type="checkbox"/> No <input type="checkbox"/> Don't know <input type="checkbox"/> |

**15. Have any relatives (e.g. parents, siblings, grandparents, aunt, uncle, cousins) been diagnosed with**

**Cystic Fibrosis?** (Please tick one)  Yes  No

State which relative(s): \_\_\_\_\_

**with Sickle Cell?** (Please tick one)  Yes  No

State which relative(s): \_\_\_\_\_

**16. If your child is 8 years or older, please answer the following question.**

Changes in growth and development (puberty) occur in a wide range of ages in children. These changes are linked with growth spurts and answering this question will help us to understand how growth spurts may influence lung growth.

**Has your child entered puberty (indicated by growth of arm-pit or pubic hair, and/or lowering of voice for boys or menstruation/ periods for girls)?**  Yes  No

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**PART THREE: QUESTIONS ABOUT SMOKING AND AIR POLLUTION**

---

**17. Did mum smoke during pregnancy?**  Yes  No

**18. Please state the number of people who smoke tobacco who have regular contact with the child?** (please write) \_\_\_\_\_

**19. How does your child usually get to school?** Tick **ONE** main mode of transport only

- Walk  Bus  Train  Car  
 Cycle  Tube  Other (please write).....

The following sections contain questions on your family's socioeconomic background. The information provided will help us to understand if lung function differs in children with different backgrounds. All the information will be anonymised and treated confidentially.

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**PART FOUR: QUESTIONS ABOUT FAMILY AND HOME**

---

**20. Does your child regularly live in more than 1 home, during the school year (excluding holidays)?**

**21. How**  Yes  No **many people live in the main residence?** \_\_\_\_\_

**22. If Yes to Q20, how many people live in the alternative residence?** \_\_\_\_\_

**23. Does your child receive free school lunches?**  Yes  No

**24. How many bedrooms are there in your house?**  .....

**25a. Does the child have their own bedroom?**  Yes  No

**b. If No → How many people share the room (including your child)?**  .....

**26. Does your family own a car, van or truck?**  No  Yes, one  Yes, two or more

**27. How many computers (laptop or desktop) does your family own?**

- None  One  Two  More than two



**PART FIVE: QUESTIONS ABOUT MUM'S (or STEP-MUM'S) EDUCATION AND EMPLOYMENT HISTORY**

**28. How many years did MUM (or STEP-MUM) spend in FULL TIME education after the age of 16?**

Approximately   years

**29. What best describes MUM's (or STEP-MUM's) occupation?** Tick **ONE** box only

- |  |  |
|--|--|
| <input type="checkbox"/> Works full time                         | <input type="checkbox"/> Sick/disabled                             |
| <input type="checkbox"/> Works part-time                         | <input type="checkbox"/> Mum or Step-Mum has never worked          |
| <input type="checkbox"/> Full time mother/Home maker             | <input type="checkbox"/> Neither Mum or Step -Mum lives with child |
| <input type="checkbox"/> Full-time student (area of study _____) |  |
| <input type="checkbox"/> Unemployed                              |  |

**30. What is MUM'S (or STEP-MUM) current job title?** (e.g. assistant chef)

 .....

**Description of the job:** (e.g. make meals)

 .....

**31. Type of employer:** (e.g. school)

 .....

**32a. Which one of these best describes her current work?** Tick **ONE** box only

- |                                     |   |
|-------------------------------------|---|
| <input type="checkbox"/> Employee   | <input type="checkbox"/> Self-employed with NO paid employees |
| <input type="checkbox"/> Manager    | <input type="checkbox"/> Self-employed with paid employees    |
| <input type="checkbox"/> Supervisor |   |

**32b. How many people are employed where she works?** Tick **ONE** box only

- |   |   |
|---|---|
| <input type="checkbox"/> Under 25 staff | <input type="checkbox"/> Between 25 and 499 staff |
| <input type="checkbox"/> Over 500 staff | <input type="checkbox"/> Don't Know               |

**When you have completed this section, go to Part Six.**

**33. If MUM (or STEP-MUM) is not currently employed, what was her previous job title:** (e.g. assistant chef)

 .....

**Description of the job:** (e.g. make meals)

 .....

**34. Type of employer:** (e.g. school)

 .....

**35a. Which one of these best describes her PREVIOUS work?** Tick **ONE** box only

- |                                     |   |
|-------------------------------------|---|
| <input type="checkbox"/> Employee   | <input type="checkbox"/> Self-employed with NO paid employees |
| <input type="checkbox"/> Manager    | <input type="checkbox"/> Self-employed with paid employees    |
| <input type="checkbox"/> Supervisor |   |

**35b. How many people are employed where she USED to work?** Tick **ONE** box only

- |   |   |
|---|---|
| <input type="checkbox"/> Under 25 staff | <input type="checkbox"/> Between 25 and 499 staff |
| <input type="checkbox"/> Over 500 staff | <input type="checkbox"/> Don't know               |

**PART SIX: Questions about DAD's (or STEP-DAD's) education and employment history**

**36. How many years did DAD (or STEP-DAD) spend in FULL TIME education after the age of 16?**

Approximately   years

**37. What best describes DAD'S (or STEP-DAD'S) occupation?** Tick **ONE** box only

- |   |  |
|---|--|
| <input type="checkbox"/> Works full time                              | <input type="checkbox"/> Sick/disabled                             |
| <input type="checkbox"/> Works part-time                              | <input type="checkbox"/> Dad or Step-Dad has never worked          |
| <input type="checkbox"/> Full time father/Home maker                  | <input type="checkbox"/> Neither Dad or Step -Dad lives with child |
| <input type="checkbox"/> Full-time student (area of study<br>✍ _____) |  |
| <input type="checkbox"/> Unemployed                                   |  |

**38. What is DAD'S (or STEP-DAD'S) current job title?** (e.g. assistant chef)

✍ .....

**Description of the job:** (e.g. make meals)

✍ .....

**39. Type of employer:** (e.g. school)

✍ .....

**40a. Which one of these best describes his current work?** Tick **ONE** box only

- |                                     |   |
|-------------------------------------|---|
| <input type="checkbox"/> Employee   | <input type="checkbox"/> Self-employed with NO paid employees |
| <input type="checkbox"/> Manager    | <input type="checkbox"/> Self-employed with paid employees    |
| <input type="checkbox"/> Supervisor |   |

**41b. How many people are employed where he works?** Tick **ONE** box only

- |   |   |
|---|---|
| <input type="checkbox"/> Under 25 staff | <input type="checkbox"/> Between 25 and 499 staff |
| <input type="checkbox"/> Over 500 staff | <input type="checkbox"/> Don't know               |

*Thank you, you have now completed the questionnaire.*

**42. If DAD (or STEP-DAD) is not currently employed, what was his previous job title:** (e.g. assistant chef)

✍ .....

**Description of the job:** (e.g. make meals)

✍ .....

**43. Type of employer:** (e.g. school)

✍ .....

**44a. Which one of these best describes his PREVIOUS work?** Tick **ONE** box only

- |                                     |   |
|-------------------------------------|---|
| <input type="checkbox"/> Employee   | <input type="checkbox"/> Self-employed with NO paid employees |
| <input type="checkbox"/> Manager    | <input type="checkbox"/> Self-employed with paid employees    |
| <input type="checkbox"/> Supervisor |   |

**44b. How many people are employed where he USED to work?** Tick **ONE** box only

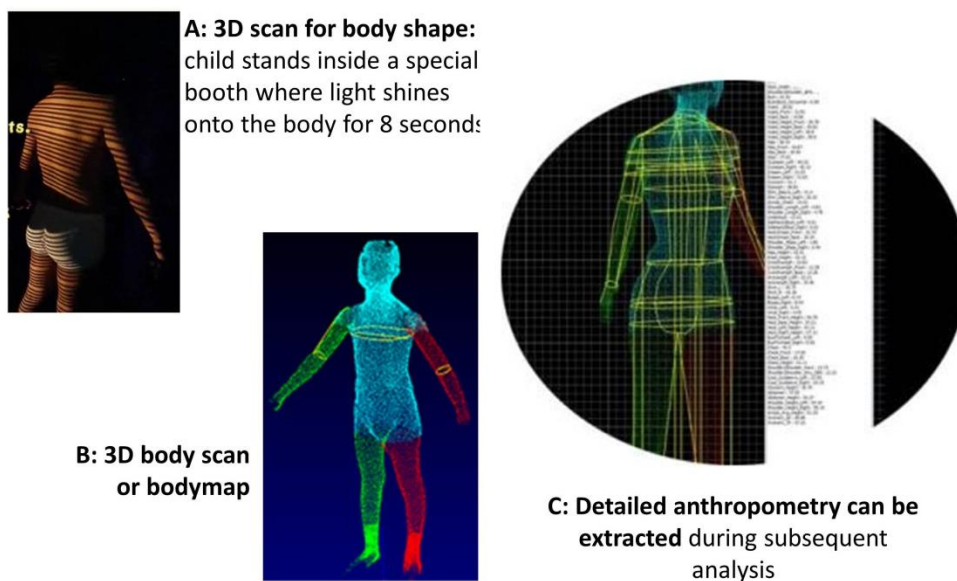
- |   |   |
|---|---|
| <input type="checkbox"/> Under 25 staff | <input type="checkbox"/> Between 25 and 499 staff |
| <input type="checkbox"/> Over 500 staff | <input type="checkbox"/> Don't Know               |

**Thank you for completing the questionnaire**

## Appendix 2. Whole body 3-Dimensional photonic scanning

Over the past decade, whole-body photonic scanners based on photogrammetric and laser technology have been developed by clothing industry including the [TC]<sup>2</sup> light stripe scanner used in several national sizing surveys.(refs) Such apparatus captures highly accurate and detailed information in the form of raw point cloud data, and then uses computerised algorithms to reconstruct surface topography. While this technology has revolutionised the categorisation of clothing sizes and preparation of made-to-measure garments, the potential contribution of 3D photonic scanning to medical research and clinical practice was unknown prior to this study.

Figure A1: 3D photonic scanning to provide detailed data on regional body shape



### Appendix 3. Detailed anthropometry

#### *Chest Circumference (using a Seca 201 measuring tape)*

1. Any bulky outer clothes (e.g. jumper, shirt) should be removed. A light vest may be left on if child prefers.
2. Ensure the subject is standing straight with shoulders relaxed, arms hanging at the side and feet together.
3. Measure and record the chest circumference during quiet tidal breathing.
4. Place tape measure ~2.5cm below the axilla and ensure measurement is taken on a horizontal plane. For pubescent girls, assessment will need to be adjusted and measured above the breasts. The tape measure should be in contact with the skin without compressing it.
5. Measurement is recorded to the nearest 0.1cm and is repeated at least twice. The difference between the measurements should not exceed 0.3cm and the mean result is reported



Figure A2: Chest width measurement using callipers and tape measure.

#### *Chest Width (same level as circumference measurement using a sliding caliper, Figure A2)*

1. Ensure the tape measure is at the same position/level as the chest circumference measurement.
2. Ensure subject is standing straight with shoulders relaxed, with their hands on their hips and facing away from the researcher.
3. Place the caliper arms at the level/position to encompass both sides of the chest as marked by the tape. The calliper must be read at eye level.
4. The measurement is recorded to the nearest 0.1cm and is repeated at least twice. The difference between the measurements should not exceed 0.3cm and the mean result is reported.

#### *Chest Depth (measured at same level as the circumference measurement using a sliding caliper)*

1. Instructions as for chest width but for chest depth, assessments are performed from the side.
2. Ensure subject is standing straight with shoulders relaxed, their arms hanging at the side & feet together.
3. Place the caliper arms at the level/position to encompass the front and back of the chest to measure its depth. The calliper must be read at eye level.
4. The measurement is recorded to the nearest 0.1cm and is repeated at least twice. The difference between the measurements should not exceed 0.3cm and the mean result is reported.

#### *Waist Circumference (WHO/Lohman method, Figure A3)*

1. Ensure any clothing is removed or lifted up to ensure it does not interfere with the measurement.
2. Ensure the subject is standing straight with abdomen relaxed, arms hanging at the side and feet together.
3. Measurement should be done during quiet tidal breathing.
4. Operator faces the subject and finds the narrowest girth. If this proves to be difficult, instruct the subject to bend to the side so that the point at which the trunk folds can be identified (Figure below). For obese subjects the smallest horizontal circumference between the lowest rib and top of the iliac crest is measured.

5. Measure the waist circumference with the tape measure ensuring the tape is in contact with the skin without compressing the waist.
6. The measurement is recorded to the nearest 0.1cm and is repeated at least twice. The difference between the measurements should not exceed 0.3cm and the mean result is reported.

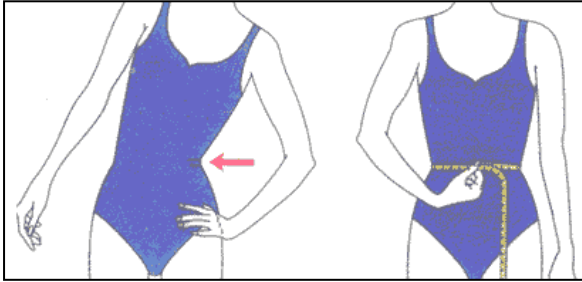


Figure A3 Waist circumference measurement

### *Waist Width and waist depth*

1. Ensure the tape measure is at the same position/level as the waist circumference measurement.
2. For **waist width** measurement, ensure the subject is standing straight and relaxed, with their hands on their hips and facing away from the researcher.
3. Place the caliper arms at the level/position to encompass both sides of the waist as marked by the tape. The calliper must be read at eye level.
4. For **waist depth**, instruct the subject to stand with their side facing the researcher.
5. Ensure subject is standing straight and remains relaxed, with arms down and feet together.
6. Place the caliper arms at the level/position to encompass the front and back of the waist to measure its depth. The calliper must be read at eye level.
7. Both width and depth measurements are recorded to the nearest 0.1cm and repeated at least twice. The difference between each set of measurements should not exceed 0.3cm and the mean result is reported.

### *Knee Girth (Figure A4)*

1. Ensure the subject is standing straight with feet slightly apart and body relaxed.
2. The subject is instructed to bend their non-dominant leg and then straighten and the girth is measured at the point where the knee bends. The tape must be perpendicular to the long axis of the calf and tight enough to be in contact with the skin without compression.
3. The measurement is recorded to the nearest 0.1cm and is repeated at least twice. The difference between the measurements should not exceed 0.3cm and the mean result is reported. Position of non-dominant leg is also recorded.



Figure A4 Knee girth measurement

### *Calf Circumference (Figure A5)*

1. Ensure the subject is standing with feet slightly apart, body relaxed and weight evenly distributed over both legs.
2. Identify the non-dominant leg and calf circumference is measured at its widest point with the Seca tape, perpendicular to the long axis of the calf and tight enough to be in contact with the skin without compression.
3. The measurement is recorded to the nearest 0.1cm and is repeated at least twice. The difference between the measurements should not exceed 0.3cm, the mean result is reported.



Figure A5  
Calf circumference  
measurement

### *Foot Length (Figure A6)*

1. Ensure the subject is standing with feet slightly apart, body relaxed and weight evenly distributed over both legs and feet must be flat on the floor, i.e. no arched toes.
2. The operator lays the calliper on a level floor and the subject is instructed to place the non-dominant foot within the calliper arms.
3. Ensure the calliper is positioned with the ruler aligned with the length of the foot and the calliper arms are adjusted to the length of the foot.
4. The measurement is recorded to the nearest 0.1cm and is repeated at least twice. The difference between the measurements should not exceed 0.3cm and the mean result is reported.

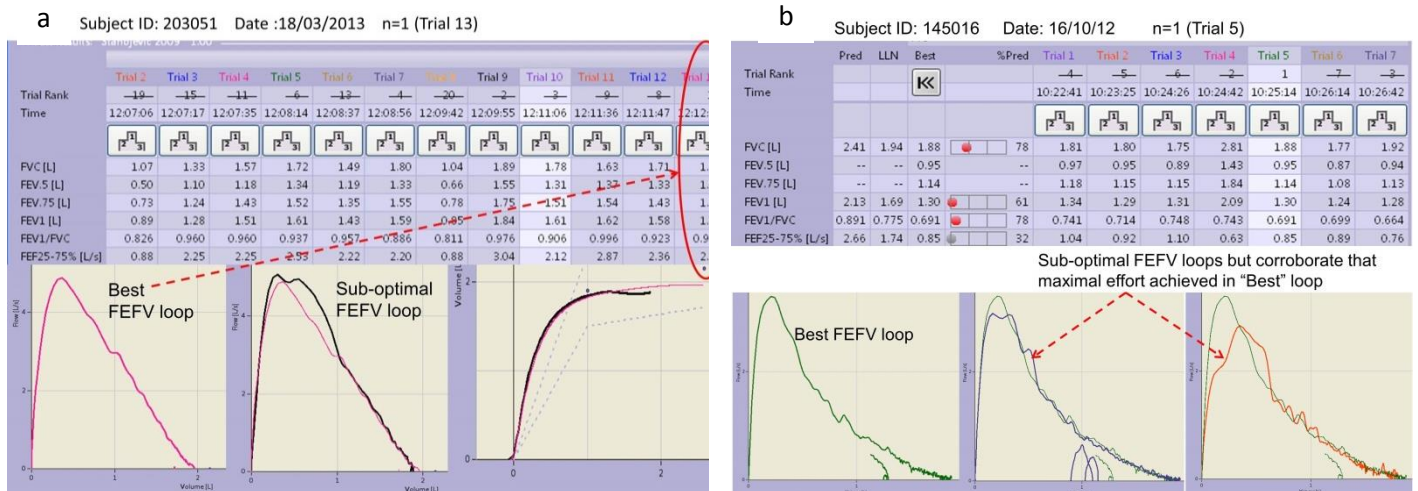


Figure A6 Measurement of  
foot length

## Appendix 4. Acceptability criteria for spirometry

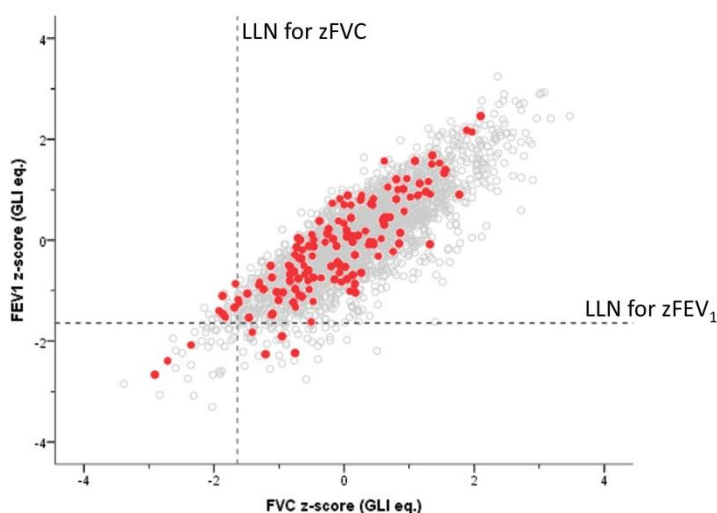
Successful spirometry was defined as those tests with at least two technically acceptable forced expiratory manoeuvres according to ATS/ERS acceptability and repeatability criteria. However, on occasions where only one technically acceptable FEV<sub>1</sub> loop was available but with evidence from other “imperfect” trials which corroborated the fact that maximal FEV<sub>1</sub> and FVC had been achieved (Figures A7a & b), this may be deemed acceptable by the senior respiratory physiologist.

Figure A7a-b: Examples where FEV<sub>1</sub> (n=1) was deemed as acceptable data



Technically acceptable and repeatable data (n≥2) were available from 2627 test occasions while a further 140 test occasions from 138 children were deemed to have 1 acceptable test, with other non-acceptable trials validating the data. Mean (SD) FEV<sub>1</sub> z-scores from tests with n=1 and n≥2 were -0.18 (0.99) and 0.01 (0.92) respectively. Data for both groups were evenly distributed across the range of lung function obtained (Figure A8) with only 5% of children with FEV<sub>1</sub> data <-1.64 z-scores while 6% had FVC <-1.64 z-scores.

Figure A8: Overlay of data with n=1 vs. all data with n≥2



Red symbols denote data with n=1 while those in grey denote those where acceptable data were available from at least 2 FEV<sub>1</sub> loops (n≥2)

## Appendix 5. Deprivation scores as a measure of small area socio-economic circumstances (SEC).

The indices of multiple deprivation 2010 (IMD 2010), derived from the English Indices of Deprivation 2010 are widely used as measures of SEC in epidemiological studies(67, 74) and provide an overall measure of multiple deprivation experienced by people living in an area. The IMD 2010 is a composite deprivation score for small areas (average 1400 people) in the UK and based on the seven distinct deprivation domains (i.e. Income; employment; health and disability; education and training; barriers to housing and services; living environment and crime) (44), thus allowing the most, and least deprived areas of the country to be identified. These small areas were ranked on the basis of the continuous IMD score and then divided into normative deprivation quintiles: <8.49; 8.50 to 13.78; 13.79 to 21.34; 21.34 to 34.16; >34.16 (44).

**Income deprivation domain:** measures the proportion of the population in an area experiencing deprivation related to low income and is calculated by summing the following indicators: adults and children in i) Income support families ii) income-based jobseeker's allowance families iii) Pension credit families iv) Child tax credit families whose equivalised income (combined income adjusted for household size) is below 60% of the median before housing costs v) asylum seekers in England in receipt of subsistence support, accommodation support or both.