EDITOR'S CHOICE

Early influences on adult lung function in two national British cohorts

L Orfei,[1] D P Strachan,[1] A R Rudnicka,[1] M E J Wadsworth[2]

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[1] Division of Community Health Sciences, St George's, London, UK; [2] MRC National Survey of Health and Development, Department of Epidemiology and Public Health, University College London, London, UK

Correspondence to: D P Strachan, Division of Community Health Sciences, St George's, University of London, Cranmer Terrace, London, SW17 0RE, UK; d.strachan@sgul.ac.uk

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ABSTRACT

Objectives: To compare adult lung function in two national British cohorts, born in 1946 and 1958, in relation to birth weight, postnatal growth and early air-pollution exposure.

Design and setting: Persons born in England, Scotland and Wales during 1 week in March 1946 and in 1958 and followed from childhood into adult life.

Main outcome measures: Forced expiratory volume in 1 sec (FEV_1) and forced vital capacity (FVC), measured at age 43 years on subjects born in 1946 (n = 2167) and age 44–45 years on subjects born in 1958 (n = 5947). Spirometric indices were adjusted for gender, adult standing height, smoking history and socioeconomic position in childhood, and analysed in relation to birth weight, growth pattern and area of birth, classified into four groups of differing exposure to domestic coal smoke pollution.

Results: Within each cohort, FEV_1 and FVC were positively associated with birth weight and proportional sitting height independent of adult height. Pooling results for both cohorts, the mutually adjusted increment in FEV_1 per 1SD increment was 30 ml (95% CI 16 to 45) for birth weight and 19 ml (95% CI 5 to 33) for proportional sitting height. The proportion of adult height attained by age 7 years and early air-pollution exposure were unrelated to adult lung function.

Conclusions: A small but significant influence of birth weight and trunk size on lung function is confirmed, but neither differences in prenatal and postnatal growth nor differences in childhood air-pollution exposure are likely explanations of the differences in spirometric performance between British adults born in 1946 and 1958.

Although several individual cohort studies have related birth weight and weight gain in infancy to adult lung function with contradictory results,[1–4] a recently published meta-analysis of seven studies positively associated adult lung function with increasing birth weight.[5] Less attention has been given to the relationship between adult lung function and postnatal growth patterns.

Early exposure to air pollution from smoke and sulphur dioxide has been associated with lower birth weight[6 7] and reduced childhood height.[8] Many, but not all, studies from Europe and North America suggest that childhood lung function or lung-function growth is impaired by poor ambient air quality,[9] but little is known about long-term effects of childhood air-pollution exposure on the level of lung function attained in adult life.

In this paper we analyse data from two national British birth cohorts to explore the independent influence of birth weight, postnatal growth and early air-pollution exposure on adult lung function. We consider two measures of postnatal growth: adult sitting height, as a proportion of adult standing height and proportional growth up to the age of 7 years, in addition to birth weight.

METHODS

Populations

The MRC National Survey of Health and Development (NSHD), also known as the British 1946 national birth cohort[10] initially included all 16 500 singleton and legitimate children born in England, Wales and Scotland during 1 week of March 1946. At the first follow-up, a stratified sub-sample of this population was selected, taking into consideration the socio-economic distribution of British families at the time. Thus, a quarter of the children born whose fathers were in manual social class occupations were selected, while all the children whose fathers were in non-manual or agricultural occupations were retained, providing a sample for follow-up of 5362 individuals. Follow-up to age 43 (in 1989) years comprised 3839 individuals (excluding 365 deaths, 540 refusals, 618 residence abroad), and 3262 (85.0%) provided data at that age.

The National Child Development Study (NCDS), also known as the British 1958 national birth cohort,[11] is a prospective study of all persons born in England, Wales and Scotland during 1 week in March 1958, plus subsequent immigrants of the same date of birth up to the age 16 years (a total of 18 558 participants). At age 44–45 years (in 2002–2004), 12 069 cohort members who remained in active contact with the study team were invited to participate in a biomedical follow-up; 9377 (78%) provided data.

Outcome measures

In the NSHD, lung function was measured using a Micro Medical Micro Plus turbine spirometer (Micro Medical Chatham, UK) at 43 years. Three blows were recorded, and the variation in FEV_1 across the best two of these trials was within 5% for 77.5% of the sample.[12] Spirometry in the NCDS was performed using the Vitalograph Micro pneumotachograph spirometer (Vitalo graph, Buckingham, UK) on those aged 44–45 years. At least three blows were recorded, and up to five were performed if the best-test variation (assessed by the sum of FEV_1 and FVC) was greater than 5%.

In both cohorts, FEV in 1 sec (FEV_1) and forced vital capacity (FVC) were measured in the standing position, without noseclips, after instruction and under the supervision of a trained research nurse. In both cohorts subjects were excluded from

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subsequent analyses if the best two lung function readings differed by more than 10% from each other and if readings were outside the normal range after adjusting for gender and height (standardised residuals greater than 3 SD units from the mean).

Measures of growth

Birth-weight measures were taken from hospital or midwife records for both cohorts. Measurements of height at age 7 and 11 years and in adulthood were available for both cohorts, and ages 15 in NSHD and 16 years in NCDS. As a measure of early growth, we used height at age 7 and divided it by adult height in middle age (measured at 43 years in the 1946 cohort and 44–45 years in the 1958 cohort) to obtain the proportion of height reached by age 7. As a measure more closely related to chest size, we considered adult sitting height and divided it by standing height to obtain the proportion of height represented by the trunk and head.

Measures of height at ages 2 and 4 years were available for the 1946 cohort only. These were analysed in both absolute terms and as a proportion of adult height, in relation to the height measures available for both cohorts.

Measures of environmental exposure and lifestyle

Outdoor air-pollution exposure in childhood was estimated using the index developed by Douglas and Waller for the 1946 cohort.[12] This classified areas of residence into four groups according to domestic coal consumption during the postwar rationing period, and was subsequently validated by direct measures of smoke and sulphur-dioxide pollution. These four categories were used to rank the birth areas in each cohort.

Other confounders considered here were social class in childhood and smoking status in adulthood. For the NSHD, social class was derived from the occupation of the head of household at the birth of the cohort child. In NCDS, socio-economic position in childhood was based on the father's occupation recorded in 1958 (or age 7 if data were unavailable at birth; n = 422). Social class was categorized into manual and non-manual. Smoking habit at the time of the adult lung function measurements was defined as current smoker, ex-smoker or never smoker.

Statistical analysis

All analyses were performed using Stata version 8.0 (StataCorp, Texas). The Stata procedure "regress" with probability weights was used to compensate for the stratified sample selection in the NSHD to ensure appropriate estimates for standard errors. It included only those in each study for whom data was available for all variables (NSHD n = 2167; NCDS n = 5947).

Multiple linear regression models were fitted, where the outcome variables were measurements of FEV_1 and FVC in turn. To compare our analyses with a recent published meta-analysis,[5] we examined the relationship between lung function and birth weight, adjusting for gender, height, adult smoking status and social class in childhood. We also included a dummy variable to estimate the difference between the cohorts. Models were expanded to adjust for air-pollution exposure in childhood, proportion of adult height represented by the trunk and proportion of adult height reached by age 7. All regression coefficients were modelled as fixed effects and represent the absolute change of FEV_1 and FVC in ml.

Comparison of spirometers in a validation sample

As an evaluation of the technical performance of the two types of spirometer used, 35 members of staff at St George's, University of London, were tested using both a MicroMedical turbine spirometer (as used in the 1946 cohort) and a Vitalograph Micro pneumotachograph spirometer (as used in the 1958 cohort). The order of tests was randomly allocated and subjects rested for at least 5 min between the two sets of blows. The calibration of each spirometer was checked at the start and after every four subjects using a 1l syringe. The best FEV1 and FVC were selected using the same criteria as in the main studies and paired differences were analysed.

FINDINGS

Measures of height, growth and adult lung function in the two cohorts are summarised (table 1) within strata of paternal social class. The 1958 cohort had significantly greater adult standing height, percentage of standing height reached by age 7 and both FEV_1 and FVC, while the percentage of standing height represented by the trunk was significantly larger in the 1946 cohort, that is, the 1946 cohort had shorter adult leg length. Within each social class, the two cohorts did not differ substantially in birth weight and adult sitting height.

A greater proportion of the 1946 cohort within each social class was born in areas of high air pollution ($p<0.001$), and members of that cohort were more likely to be current smokers ($p<0.001$, table 2). The inter-cohort difference in both FEV1 and FVC was consistently found within categories of air-pollution exposure, gender and smoking (table 2).

Table 3 shows the correlation between different measures of growth within the 1946 cohort only. The proportion of adult height attained by age 7 years was strongly correlated with proportional growth earlier in childhood, but the proportion of adult height represented by sitting height was not associated with the proportion of adult height achieved by age 2 or 4 years in either sex. Indeed, both males and females with longer legs in adulthood (ie, sitting height as a lower proportion of adult height) tended to have slightly less proportional growth in early childhood, although in absolute terms they were taller throughout childhood and in adult life.

The proportional of adult height attained by age 7 was not a statistically significant predictor of adult lung function in either of the two cohorts (table 4). However, a relatively larger trunk in adulthood had a small but statistically significant effect on both FEV_1 and FVC, independent of standing height, in the 1958 cohort and in the combined population (tables 4 and 5).

When results from the two cohorts were pooled and mutually adjusted, a 1 SD increase in birth weight was associated with a 30.4 ml increase in FEV_1 (95% CI 16.1 to 44.8). Analogously, 1 SD increase in proportional sitting height and proportional height at age 7 resulted in turn in an increase of 19.0 (95% CI 5.3 to 32.6) and 4.0 ml (95% CI −12.9 to 20.9) in FEV_1. Moreover, the increase in FVC associated with 1 SD increase in the anthropometric measures was 26.9 ml for birth weight (95% CI 8.0 to 46.0), 31.5 for proportional sitting height (95% CI 13.9 to 49.1) and 13.0 for proportional height at 7 years (95% CI −10.4 to 36.4).

After adjustment for a range of factors shown in table 5, there was a difference between the two cohorts of 0.24 l in FEV1 and 0.48 l in FVC. However, in the direct comparison of the two spirometers in the validation sample, similar differences were observed: FEV1 measured by the Vitalograph Micro was on average 0.24 l (95% CI 0.20 to 0.27) higher than the readings obtained by the MicroMedical turbine spirometer, and the corresponding difference for FVC was 0.34 l (95% CI 0.28 to 0.40).

Table 1 Mean biometrical measures and lung function by social class at birth in both cohorts, restricted to subjects with data on all measures included in subsequent regression models

	1946 cohort mean (SD)	1958 cohort mean (SD)	p Value
Children of non manual workers	1181	1796	
Birth weight (g)	3384 (500)	3408 (494)	ns
Adult standing height (cm)	169.2 (9.1)	170.7 (9.2)	***
Adult sitting height (cm)	89.6 (4.6)	89.8 (4.5)	ns
% Sitting height	53.0 (1.7)	52.7 (1.6)	***
% Growth 0–7	71.4 (3.4)	72.7 (3.6)	***
FEV (ml)	3068 (687)	3412 (755)	***
FVC (ml)	3755 (890)	4328 (970)	***
Children of manual workers	986	4,151	
Birth weight (g)	3392 (518)	3359 (502)	ns
Adult standing height (cm)	167.8 (8.9)	168.9 (9.2)	***
Adult sitting height (cm)	89.1 (4.6)	89.1 (4.6)	ns
% Sitting height	53.1 (1.9)	52.8 (1.6)	***
% Growth 0–7	71.1 (3.4)	72.5 (3.6)	***
FEV (ml)	2980 (680)	3271 (751)	***
FVC (ml)	3599 (874)	4151 (977)	***

Measures were compared using independent sample Student's t tests assuming equal variances. Significance levels are reported as: ns: $p \geqslant 0.05$, *$p<0.05$, **$p<0.01$, ***$p<0.001$

INTERPRETATION

This is the first formal comparison of spirometric data from two postwar national cohorts born and brought up under different social and environmental conditions.

Although different instruments were used to assess adult lung function, early comparisons of turbine spirometers and pneumotachograph flow integration meters with bellows spirometry suggested that FEV_1 measurements with all devices are similar,[13 14] but turbine spirometers tend to underestimate forced vital capacity. However, our small cross-validation study observed a systematic difference in both FEV1 and FVC between the MicroMedical turbine spirometer used in the 1946 cohort fieldwork and the Vitalograph Micro pneumotachograph used in the 1958 cohort study. This difference was of

Table 2 Mean lung function measures (standard deviation in parenthesis) by level of exposure to air pollution and smoking stratified by social class at birth in both cohorts, restricted to subjects with data on all measures included in subsequent regression models

	1946 cohort			1958 cohort		
	N (%)	Mean FEV in ml (SD)	Mean FVC in ml (SD)	N (%)	Mean FEV in ml (SD)	Mean FVC in ml (SD)
Children of non manual workers	1181			1796		
Air pollution:						
Very low	270 (23)	2982 (709)	3672 (916)	665 (37)	3452 (757)	4351 (952)
Low	367 (31)	3087 (680)	3770 (851)	306 (17)	3394 (717)	4298 (934)
Moderate	313 (26)	3124 (668)	3819 (905)	622 (35)	3416 (791)	4353 (1022)
High	231 (20)	3064 (693)	3742 (900)	203 (11)	3302 (685)	4222 (921)
Males:						
Never smoked	204 (36)	3610 (539)	4422 (755)	436 (48)	3960 (605)	4972 (803)
Ex-smoker	198 (35)	3608 (585)	4462 (749)	314 (35)	4029 (590)	5119 (746)
Current smoker	169 (30)	3384 (589)	4143 (788)	154 (17)	3700 (596)	4843 (714)
Females:						
Never smoked	289 (47)	2666 (434)	3244 (582)	480 (54)	2899 (449)	3638 (593)
Ex-smoker	165 (27)	2698 (389)	3217 (544)	277 (31)	2907 (434)	3686 (600)
Current smoker	156 (26)	2469 (465)	3079 (564)	135 (15)	2753 (506)	3595 (604)
Children of manual workers	986			4151		
Air pollution:						
Very low	145 (15)	2984 (695)	3621 (898)	1436 (35)	3302 (745)	4162 (977)
Low	339 (34)	2995 (687)	3591 (867)	873 (21)	3226 (742)	4091 (956)
Moderate	276 (28)	2969 (698)	3613 (899)	1319 (32)	3298 (752)	4185 (985)
High	226 (23)	2972 (647)	3581 (845)	523 (13)	3195 (777)	4089 (988)
Males:						
Never smoked	145 (29)	3588 (556)	4233 (726)	904 (44)	3879 (605)	4878 (793)
Ex-smoker	175 (36)	3557 (521)	4320 (745)	603 (30)	3818 (600)	4850 (803)
Current smoker	173 (35)	3226 (514)	3973 (728)	531 (26)	3622 (621)	4700 (819)
Females:						
Never smoked	200 (41)	2582 (364)	3089 (519)	944 (45)	2822 (455)	3516 (619)
Ex-smoker	129 (26)	2589 (422)	3097 (541)	614 (29)	2828 (463)	3552 (601)
Current smoker	164 (33)	2364 (463)	2894 (602)	555 (26)	2604 (481)	3381 (612)

Table 3 Correlations of absolute and proportional height measurements at different ages in the 1946 cohort only (males in upper triangle, females in lower triangle, numbers of subjects in parentheses)

	Absolute standing height at ages:				As a proportion of adult height:			
	2 years	4 years	7 years	43 years	2 years	4 years	7 years	Sitting height
Absolute standing height at ages:								
2 years		0.51 (884)	0.49 (919)	0.44 (919)	0.81 (919)	0.20 (884)	0.19 (919)	−0.15 (919)
4 years	0.49 (883)		0.71 (983)	0.61 (983)	0.16 (884)	0.63 (983)	0.32 (983)	−0.18 (983)
7 years	0.49 (915)	0.75 (1007)		0.73 (1064)	0.06 (919)	0.15 (983)	0.60 (1064)	−0.18 (1064)
43 years	0.43 (915)	0.63 (1007)	0.73 (1103)		−0.17 (919)	−0.24 (983)	−0.11 (1064)	−0.25 (1064)
As a proportion of adult standing height:								
2 years	0.74 (915)	0.05 (883)	−0.02 (915)	−0.28 (915)		0.37 (884)	0.28 (919)	0.01 (919)
4 years	0.20 (883)	0.66 (1007)	0.24 (1007)	−0.17 (1007)	0.33 (883)		0.50 (983)	0.03 (983)
7 years	0.23 (919)	0.37 (1007)	0.63 (1103)	−0.08 (1103)	0.29 (915)	0.55 (1007)		0.03 (1064)
Sitting height	−0.07 (915)	−0.17 (1007)	−0.21 (1103)	−0.25 (1103)	0.10 (915)	0.03 (1007)	−0.02 (1103)	

Table 4 Mutually adjusted effects of birth weight, proportional sitting height and childhood growth on adult FEV_1 and FVC within each cohort

Outcome	Explanatory variables	Units	1946 Cohort increment (95% CI)	1958 Cohort increment (95% CI)
FEV_1 (ml)	Birth weight	Per 1 kg	41.3 (−4.7 to 87.5)	66.6 (41.3 to 92.0)***
	Adult sitting height	% Standing	10.2 (−3.5 to 24.0)	11.1 (3.1 to 19.1)**
	Height at 7 years	% Standing	4.8 (−3.8 to 13.4)	−0.6 (−5.5 to 4.3)
FVC (ml)	Birth weight	Per 1 kg	47.9 (−13.0 to 108.9)	47.6 (14.8 to 80.4)**
	Adult sitting height	% Standing	10.9 (−6.5 to 28.3)	25.2 (14.6 to 35.7)***
	Height at 7 years	% Standing	7.9 (−4.4 to 20.2)	1.9 (−4.5 to 8.3)

Adjusted for gender, adult height, smoking status, childhood social class and air pollution exposure.
*p<0.05, **p<0.01, ***p<0.001.

similar magnitude to the adjusted mean difference between the two cohorts, suggesting that technical factors may explain a large part of the inter-cohort difference. Since this discrepancy occurred despite prior and subsequent calibration by a 1l syringe, it is presumably due to device-dependent characteristics in the integration of flow to volume at flow rates typical of forced expiratory manoeuvres obtained in epidemiological fieldwork.

Differences in the methods of measurements are less of a concern for comparisons within each cohort. We confirmed that there is a positive linear association between adult lung function and birth weight and compared two measures of postnatal growth: trunk size versus total body size, and early growth versus later growth. Using proportional instead of absolute measures for postnatal growth greatly reduces the correlation between these measures and adult height. Sitting height (or its converse, leg length) has been proposed as a marker of growth in early childhood.[15] However, we found that proportional growth by age 7 and proportional sitting height are very weakly inter-correlated, implying that these two measures represent different aspects of growth, and can be included in the analysis together with adult height without the risk of collinearity. Furthermore, within the 1946 cohort, adult leg length was only weakly correlated with the proportion of adult height achieved by ages 2 and 4, and this association was in the opposite direction to that expected. In contrast, proportional growth by age 7 was strongly correlated with the proportion of adult height achieved by ages 2 and 4 years.

The magnitude of birth-weight effects on FEV_1 in each cohort and in the combined data set were consistent with the meta-analysis recently published by Lawlor *et al*.[5] However, there was no substantial difference between the cohorts in terms of birth weight, so prenatal growth is unlikely to explain inter-cohort differences in lung function. Of the two measures of postnatal

Table 5 Mutually adjusted effects on adult FEV_1 and FVC of gender, adult height, smoking status, childhood social class, air pollution, birth weight, proportional sitting height, proportional childhood growth and cohort; both cohorts combined

Risk factors	FEV_1 (ml) Difference (95% CI)	FVC (ml) Difference (95% CI)
Females vs males	−526.3 (−566.6 to −486.0)***	−606.7 (−660.0 to −553.4)***
Adult height (cm)	35.8 (33.6 to 38.1)***	50.8 (47.9 to 53.8)***
Ex-smoker vs non smoker	−35.5 (−63.2 to −7.7)*	−6.5 (−43.6 to 30.6)
Current smoker vs non smoker	−234.3 (−265.1 to −203.5)***	−160.6 (−201.8 to −119.5)***
Manual vs non manual	−41.7 (−64.4 to −19.1)***	−76.7 (−106.5 to −47.0)***
Low vs very low air pollution	−12.4 (−46.0 to 21.2)	−16.7 (−61.5 to 28.2)
Moderate vs very low pollution	−4.5 (−34.9 to 25.9)	22.9 (−17.9 to 63.7)
High vs very low air pollution	−33.3 (−70.6 to 3.9)	−20.3 (−71.1 to 30.5)
Birth weight (1 kg)	54.4 (28.8 to 80.1)***	48.2 (14.2 to 82.1)**
Adult sitting height (% standing)	11.4 (3.2 to 19.6)**	18.9 (8.4 to 29.4)***
Height at 7 (% adult standing)	1.1 (−3.6 to 5.8)	3.6 (−2.9 to 10.1)
Cohort (1958 vs 1946)	240.2 (213.6 to 266.7)***	476.0 (440.0 to 512.0)***

*p<0.05, **p<0.01, ***p<0.001

What is already known on this topic

- Birth weight has a weak positive association with adult lung function, independent of adult height.
- Children brought up in areas of high air pollution in the 1946 cohort had lower birth weight and shorter stature in childhood.

What this study adds

- The proportion of adult height represented by sitting height is a weak determinant of adult lung function, while proportion of adult height reached by 7 years is not.
- Differences in lung function in middle age, between adults born in 1946 and 1958, are not explained by birth weight, adult height, proportional growth measures, smoking status or early air-pollution exposure.
- Technical differences between turbine and pneumotachograph spirometers, despite similar calibration results, may substantially confound comparisons between epidemiological surveys.

growth, sitting height (as a proportion of standing height) was the more strongly correlated with lung function. We believe this is the first population-based study to address this association, independent of adult height and growth during childhood. It is plausible that a relatively larger trunk size is associated with larger lungs. We were unable to detect an independent effect of height at 7 years on adult lung function.

A difference in FEV_1 between the cohorts, of a similar magnitude to the effect of current smoking, persisted after adjustment for gender, height, prenatal and postnatal growth, social class, smoking history and air-pollution exposure in childhood. We included estimated air-pollution exposure as a confounder in our analyses because it has previously been associated with low birth weight and shorter stature in childhood in the 1946 cohort. Although childhood chest illnesses were more common in highly polluted urban areas,[12] air-pollution exposure from age 2 to 11 years was not associated with respiratory symptoms or reduced peak expiratory flow at age 36 years, after adjustment for current smoking, socio-economic status, parental history of bronchitis and history of asthma or chest illness before age 2 years.[16] Extending this analysis to the larger 1958 birth cohort confirms the lack of association between urban upbringing and adult lung function.

Although we confirm a small but significant influence of birth weight and trunk size on adult lung function, we conclude that neither differences in prenatal and postnatal growth, nor differences in childhood air pollution exposure, are likely explanations of the differences in spirometric performance between British adults born in 1946 and 1958. However, the true difference in lung function between the two cohorts is likely to have been overestimated owing to technical differences in the spirometers used in each study.

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DPS and MEJW conceived the idea for the current paper. LO carried out the statistical analyses. LO, DPS and ARR wrote the paper and all authors contributed to revising the manuscript. All authors approved the final version. DPS and MEJW are the guarantors for the conduct of the spirometric studies, had access to the data and controlled the decision to publish.

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Competing interests: None.

Ethics approval: Ethics approval for the medical examination of the British 1958 birth cohort was obtained from the South East MREC (ref: 01/1/44), and ethics approval for the data collection in 1989 in the 1946 national birth cohort was given by the Joint UCH/UCL Committee on the Ethics of Clinical Investigations.

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