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Comparison of lung function in healthy Nigerian children living in Nigeria and in the UK

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To the Editor:

Early life determinants, such as passive smoking, indoor air pollution, childhood infections, nutritional status and socio-economic status (SES) affect lung development and the subsequent lung function trajectory throughout life.(1) However, the interaction between environmental exposures and genetics in determining lung function in healthy children is yet to be established, in part because of the paucity of comparative data in subjects with common genetic ancestry living in very different environments. *Sonnappa et al*, previously reported lower dynamic lung volumes in Indian semi-urban and rural children when compared to UK-Indian children, while spirometric outcomes between Indian urban children and UK-Indian children were virtually identical.(2)

We explored the hypothesis that Nigerian children would have lower lung function compared to UK-Nigerian children, due to socio-economic disadvantage.

This prospective cross-sectional study was conducted in Nigeria and the UK using the same equipment, techniques, and quality control criteria.(3) Healthy children were recruited in Nigeria in private and public urban schools in Kaduna city (north-central Nigeria) and in rural schools within 50 kilometers from Kaduna city in April 2017 (Barau Dikko Teaching Hospital Ethics Committee, Kaduna, HREC 16-0017).(4) Children of Nigerian origin in the UK (henceforth referred to as UK-Nigerians) were enrolled as part of the Size and Lung Function in Children (SLIC) study (London-Hampstead: REC 10/H0720/53)(3) between December 2010 and July 2013. Parental written consent and verbal assent from each participant were obtained.

Children aged 6-11 years were eligible. Exclusion criteria comprised children unwell on the test day, prematurity, current asthma or chronic disease/ congenital abnormalities likely to affect lung function.(3) The child's respiratory history, tribe group (only in Nigeria), family SES, tobacco and biomass smoke exposures were investigated via a questionnaire administered to the child by the researchers. Socio-economic status was evaluated using the Family Affluence Scale (FAS), based on collated score for number of computers, vehicle ownership, and whether the child had his/her own bedroom on a scale from 0 to 6.(3)

Spirometry was performed according to American Thoracic Society/European Respiratory Society standards adapted for children(5, 6) using a portable Easy-on-PC spirometer (ndd, Zurich, Switzerland). Multivariable regression analyses were performed in the Nigerian arm to investigate the relationship between potential determinants of lung function and FEV_1 & FVC z-scores. Validity of regression assumptions, the models' fit and multicollinearity (through the variance inflation factors (VIFs) for the independent variables) were verified.

Comparison of data from 97 children in the UK and 194 in Nigeria (ratio 1:2) would provide 80% power at the 5% significance level (2 tails) to detect a mean difference of at least 0.35 z scores (SD = 1) in spirometry outcomes between groups.(2) Power calculation was perfomed only before data collection in Nigeria.

After exclusions, data from 109 UK-Nigerian children (43% boys, mean(SD) age: 8.5(1.4) years) and 240 Nigerian peers (52% boys, mean(SD) age: 9.2(1.6) years) were analyzed. While all the UK-Nigerians lived in an urban environment (10% had low SES

[FAS 0-1]), the Nigerian arm comprised 135 (56% of total) urban children (23% low SES) and 105 (44% of total) rural children (81% low SES). Hausa was the most prevalent tribe group in both urban (48% of total) and rural cohorts (78% of total); Yoruba and Igbo (urban area), and Fula (rural area) were the other most represented tribe groups.

When data were analysed according to country of residence, dynamic lung volumes were comparable between UK-Nigerians and Nigeria-residents (mean difference FEV_1: -0.06 z-score, p= 0.6; FVC: 0.14 z-score, p= 0.1).

Twenty-seven percent (29/109) of UK-Nigerians were obese (BMI z-score >95th percentile). By contrast, 25% (29/116) of Nigeria-residents with low SES (FAS 0-1) were underweight (BMI z-score <5th percentile) and 34% (40/116) were stunted (height z-score <2nd percentile).

However, when analysed according to SES, compared with UK-Nigerian children, deprived (FAS 0-1) children in Nigeria, had significantly reduced FVC (mean difference(95%CI) -0.26 z-scores (-0.52 to -0.01, p = 0.04)) (table 1 & figure 1).

On multivariable linear regression analysis in data from Nigerian children, low SES (FAS 0-1) was significantly associated with lower FEV_1 (-0.43 z-score, p = 0.006) and FVC (-0.37 z-score, p = 0.009) while decrement per BMI z-score was associated with statistically significant reduction in FEV_1 (-0.19 z-scores) and FVC (-0.23 z-scores). The VIFs for the covariates included (sex, age, height z-zscore, BMI z-score, urban residency (vs rural), low SES (FAS 0-1) vs intermediate-high SES (FAS 2-6), biomass smoke exposure) were all below 2.5, ruling out multicollinearity.(7)

Our data showed comparable FEV_1 and FVC in affluent Nigerian children living in the UK and Nigeria after adjusting for age, height and sex. Similarly, *Sonnappa et al* reported comparable spirometry results in wealthy urban Indian children living in the UK and India,(2) whereas *Kuehni et al* did not find differences in spirometry outcomes between south-Asian children of UK-born mothers *versus* immigrant mothers.(8)

In children with low SES (FAS 0-1) resident in Nigeria, however, we found that FEV_1 and FVC were significantly reduced, despite adjustment for a number of confounders. Similar findings were also reported from Bangalore, India, where children living in rural areas with low SES (FAS 0-1), had FEV_1 and FVC reduced by approximately 0.75 z-scores (adjusted) compared with more affluent urban peers.(2) Socio-economic deprivation from childhood to adulthood is associated with a lower lung function trajectory both in western countries(9) and in sub-Saharan Africa(10). Possible mediators of this relationship could be stunted growth and lower BMI observed in Nigerian children from low SES, thus affecting chest size and lower dynamic lung function as observed in this study.(11) Hausa was the most represented tribe within the SES groups; hence differences in genetic background (between different tribes) would not be able to explain the significantly lower lung function observed in children from low SES. No association was found between exposure to indoor air pollution from biomass fuels and spirometry outcomes.

The main strength of this study is that identical and extensive methodology was used to collect data in children with similar ancestry living in different continents. However, the absence of longitudinal data to evaluate the prognostic meaning, if any, of a lower lung function in deprived Nigerian children was a limitation. Moreover, genetic data, prenatal and trans-generational determinants of lung function(12) were not investigated.

In conclusion this study showed comparable lung function in affluent Nigerian children living in Nigeria and in the UK, whereas among Nigeria-residents, socio-economic deprivation was associated with lower (but not necessarily pathological) dynamic lung volumes, probably through an impact on body size.

Competing interests. There are no competing interests for any author.

Funding. The SLIC study was funded by the Wellcome Trust [WT094129MA]. For data collection in Nigeria: "Sickle Cell Cohort Research Foundation" (www.scorecharity.com) and "A.L.P.I." associazione allergie pneumopatie infantile' (https://alpiassociazione.it/) offered financial support to refund travel expenses to Nigeria for two investigators (MA and CZ).

Contributors. MA conceived the study, performed data collection, performed analyses, interpreted data and wrote the manuscript; SL, PC & BI conceived the study, interpreted data and contributed to the manuscript; CZ, LGD, RZ, ER, ADS performed data collection and revised the manuscript; LC performed statistical analysis, interpreted data and revised the manuscript. All the authors approved the final draft of the manuscript.

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Table 1. Population characteristics and lung function in children aged 6-11 years of Nigerian origin living in the UK (UK-Nigerian) and in Nigeria (Nigerian) according to socio-economic status (SES)

	UK-Nigerian	**Nigerian high & intermediate SES#**	**Nigerian low SES#**
Subjects, N (%boys)	109 (43%)	124 (54%)	116 (49%)
Age, yr	8.5 (1.4)	9.3 (1.5)**	9.3 (1.6)**
Weight z-score	1.28 (1.13)	0.18 (1.59)**	-1.57 (1.05)**
Height z-score	1.10 (0.92)	0.28 (1.46)**	-1.56 (1.0)**
BMI z-score	0.97 (1.24)	0.08 (1.51)**	-0.91 (0.98)**
Household smoking	8 (10%)§	6 (5%)	22 (19%)
Solid fuels for cooking at home	0	46 (37%)	80 (76%)
Prior asthma	10 (9%)	7 (6%)	2 (2%)*
FEV_1 z-score	-0.20 (1.03)	-0.03 (0.87)	-0.25 (1.00)
FVC z-score	0.06 (1.01)	-0.01 (0.79)	-0.20 (0.91)*

Definition of abbreviations: SES, socio-economic status; BMI, body mass index;
Results are presented as mean (SD), unless otherwise specified.
BMI and height z-scores based on World Health Organization growth reference.
Spirometry z-scores based on Global Lung Function Initiative 2012 equations for African Americans.
#High & intermediate SES" = Family Affluence Score 2-6; "Low SES" = Family Affluence Score 0-1
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Figure 1. Spirometry data from UK Nigerian (n. 109) and Nigeria resident children (n. 240) according to socio-economic status (SES). Spirometry z-scores obtained using the Global Lung Function Initiative–2012 “black” equations. Solid black lines indicate mean and SD. Dashed lines depict ± 2 z scores, within which 95% of the reference population children would fall.

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To the Editor:

Early life determinants, such as passive smoking, indoor air pollution, childhood infections, nutritional status and socio-economic status (SES) affect lung development and the subsequent lung function trajectory throughout life.(1) However, the ~~importance of~~interaction between environmental exposures ~~over~~ and genetics in determining lung function in healthy children is yet to be established, ~~mainly~~ in part because of the paucity of comparative data in subjects with common genetic ancestry living in very different environments. *Sonnappa et al*, previously reported lower dynamic lung volumes in Indian semi-urban and rural children when compared to UK-Indian children, while spirometric outcomes between Indian urban children and UK-Indian children were virtually identical.(2) We explored the hypothesis that Nigerian children would have lower lung function compared to UK-Nigerian children, due to socio-economic disadvantage.

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Spirometry was performed according to American Thoracic Society/European Respiratory Society standards adapted for children(5, 6) using a portable Easy-on-PC spirometer (ndd, Zurich, Switzerland). Multivariable regression analyses were performed in the Nigerian arm to investigate the relationship between potential determinants of lung function and FEV_1 & FVC z-scores. Validity of regression assumptions, the models' fit and multicollinearity (through the variance inflation factors (VIFs) for the independent variables) were verified.

Comparison of data from ~~113~~ 97 children in the UK and ~~226~~ 194 in Nigeria (ratio 1:2) would provide 8~~7~~0% power at the 5% significance level (2 ~~1~~ tails) to detect a mean difference of at least 0.3~~2~~5 z scores (SD = 1) in spirometry outcomes between groups.(2) Power calculation was perfomed only before data collection in Nigeria.

After exclusions, data from 109 UK-Nigerian children (43% boys, mean(SD) age: 8.5(1.4) years) and 240 Nigerian peers (52% boys, mean(SD) age: 9.2(1.6) years) were analyzed. While all the UK-Nigerians lived in an urban environment (10% had low SES [FAS 0-1]), the Nigerian arm comprised 135 (56% of total) urban children (23% low SES) and 105 (44% of total) rural children (81% low SES). Hausa was the most prevalent tribe group in both urban (48% of total) and rural cohorts (78% of total); Yoruba and Igbo (urban area), and Fula (rural area) were the other most represented tribe groups.

When data were analysed according to country of residence, dynamic lung volumes were comparable between UK-Nigerians and Nigeria-residents (mean difference FEV_1: -0.06 z-score, p= 0.6; FVC: 0.14 z-score, p= 0.1).

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However, when analysed according to SES, compared with UK-Nigerian children, deprived (FAS 0-1) children in Nigeria, had significantly reduced FVC (mean difference(95%CI) -0.26 z-scores (-0.52 to -0.01, p = 0.04)) (table 1 & figure 1).

On multivariable linear regression analysis in data from Nigerian children, low SES (FAS 0-1) was significantly associated with lower FEV_1 (-0.43 z-score, p = 0.006) and FVC (-0.37 z-score, p = 0.009) while decrement per BMI z-score was associated with statistically significant reduction in FEV_1 (-0.19 z-scores) and FVC (-0.23 z-scores). The VIFs There was no multicollinearity among for the covariates included (sex, age, height z-zscore, BMI z-score, urban residency (vs rural), low SES (FAS 0-1) vs intermediate-high SES (FAS 2-6), biomass smoke exposure) were all below 2.5, ruling out multicollinearity.(7)

Our data showed comparable FEV_1 and FVC in healthy affluent Nigerian children living in the UK and Nigeria after adjusting for age, height and sex. Similarly, *Sonnappa et al* reported comparable spirometry results in wealthy urban Indian children living in the UK and India,(2) whereas *Kuehni et al* did not find differences in spirometry outcomes between south-Asian children of UK-born mothers *versus* immigrant mothers.(8) The present study offers additional evidence supporting the importance of genetic ancestry over environment in determining lung function in children without socio-economic deprivation.

In children with low SES (FAS 0-1) resident in Nigeria, however, we found that FEV_1 and FVC were significantly reduced, despite adjustment for a number of confounders. Similar findings were also reported from Bangalore, India, where children living in rural areas with low SES (FAS 0-1), had FEV_1 and FVC reduced by approximately 0.75 z-scores (adjusted) compared with more affluent urban peers.(2) Socio-economic deprivation in from childhood to adulthood is associated with a lower lung function trajectory both in western countries(9) and in sub-Saharan Africa(10). Possible mediators of this relationship could be stunted growth and lower BMI observed in Nigerian children from low SES, thus affecting chest size and lower dynamic lung function as observed in this study.(11) Hausa was the most represented tribe within the SES groups; hence differences in genetic background (between different tribes) would not be able to explain the significantly lower lung function observed in children from low SESexplain the . No association was found between exposure to indoor air pollution from biomass fuels and spirometry outcomes.

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In conclusion this study showed ~~that FEV$_1$ and FVC were~~ comparable lung function was found in~~in~~ affluent Nigerian children living in Nigeria and in the UK~~, despite significant differences in environmental exposures between the two populations~~, whereas ~~.~~ a~~A~~mong Nigeria-residents, socio-economic deprivation was associated with lower (but not necessarily pathological) dynamic lung volumes, probably through an impact on body size.

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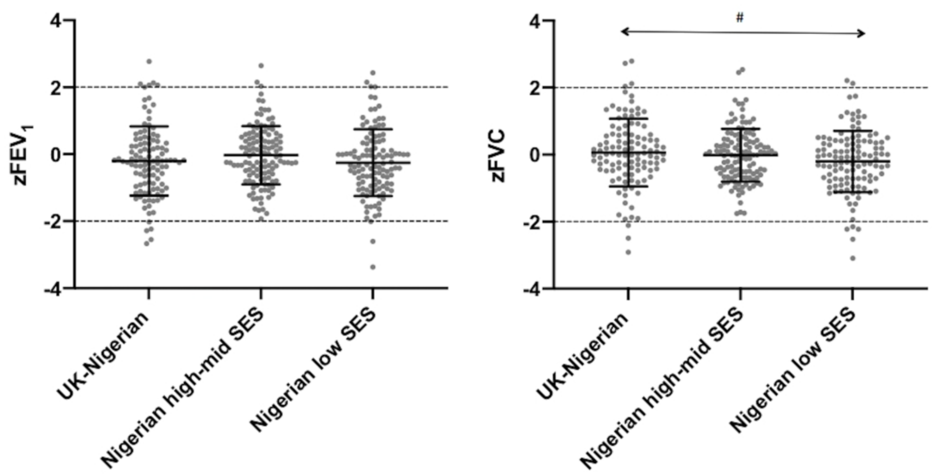

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