Online supplement

Poverty-attributable chronic airflow obstruction in the multinational Burden of Obstructive Lung Disease study

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Supplementary Methods

BOLD study details

The BOLD study protocol has been previously published.[1] In short, representative samples of the non-institutionalised population aged 40 years and above were recruited from a sample of sites from Africa, Asia, Australia, Caribbean, Europe and North America. All sites had approval from their local ethics committee, and participants gave informed consent. All study staff were trained, supervised and monitored during the survey. Spirometry was conducted using an EasyOne spirometer (ndd Medizintechnik AG, Zurich, Switzerland) to take a pre-bronchodilator reading. Post bronchodilator readings were also collected after inhaling Salbutamol (200 μg) via a spacer. All individual spirometry data were reviewed for quality control during the study. Information from participants on several risk factors was collected using a standardised questionnaire.

Calculation of the wealth score

It is difficult to measure wealth at an individual level, but Howe et al. have shown that household asset-based measures of wealth can be used to collect information about the wealth of an individual, that is stable over short-term economic fluctuations[2]. In the BOLD study, we have developed a wealth score using a Mokken scale approach applied to the data collected on household assets that could be used to compare individuals within and between countries[3]. We have shown that the mean number of assets owned in each site is highly correlated with the Gross National Income (GNI) per capita of the country[4], which is a strong indicator of the standard of living of an average citizen. We have also shown the high correlation of assets owned with educational level and other variables likely to be related to the socioeconomic position, which suggests that our Mokken scale is broadly indicative of an individual's wealth.

We calculated the wealth score based on questions which were part of the BOLD study core questionnaire[4]. This part of the questionnaire asked whether the participant or any person in the household owned any of the following 15 assets. Only 10 of these assets (highlighted in green below) were used to calculate the wealth score.

Please tell me whether this household, or any person who lives in the household, has/owns the following items [*Possible answers: Yes/No/Don't know*]:

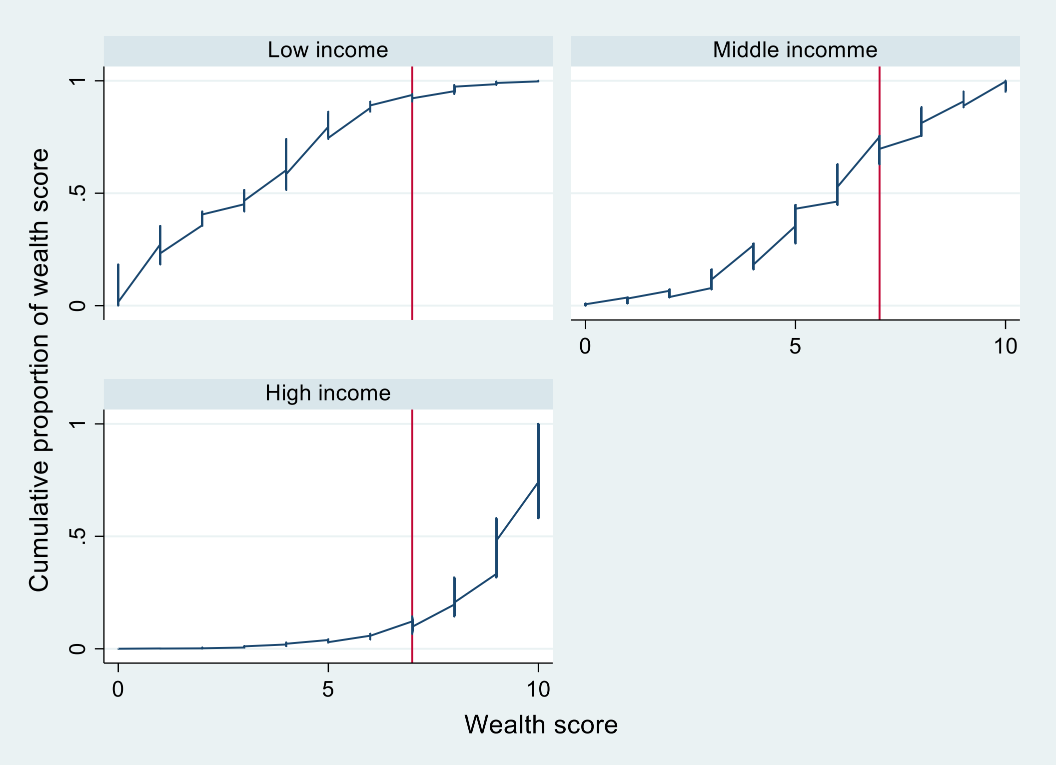
a. Electricity
b. Flush toilet
c. Fixed telephone
d. Cell telephone
e. Television
f. Radio
g. Refrigerator
h. Car
i. Moped/scooter/motorcycle
j. Washing machine
k. Own their own home
l. Indoor bath or shower
m. Indoor tap
n. Outdoor tap of their own

The response is then coded as 1 for "YES", 0 for "NO", and missing for "DON'T KNOW".

Definition of poverty

We used the World Bank data available at https://datahelpdesk.worldbank.org/knowledgebase/articles/906519, by the year of survey for each BOLD site, to classify countries as low-, middle- or high-income. In the sites in low- and middle-income countries, most participants had a wealth score of 7 or less, whereas in the sites in high-income countries it was the opposite, with most participants having a wealth score above 7 (Figure S2). Hence, we used a wealth score lower than or equal to 7 to define poverty.

Figure S1: Cumulative plot: Cumulative proportion of wealth score



Bayesian hierarchical model to estimate PAR

For each site, PAR of CAO for the exposure of interest (poverty or wealth score) can be calculated using the formula below:

$$PAR = \frac{Pe\ (RR - 1)}{RR}\ X\ Pd$$

where Pe is the proportion of cases exposed to poverty and Pd is the proportion of the disease in the population of interest, for each site.

The RR for CAO of poverty, adjusted for age and sex (and additional covariates in the secondary analyses), was estimated for each site using a Bayesian log-binomial hierarchical model. The hierarchical model allowed us to address the issue of difficult RR estimation (and hence difficult estimation of PAR) in sites with very low numbers. By assuming that all local estimates of RR come from a single distribution of values with a common mean and variance, we could "borrow" information from the other sites to increase the precision of the estimate in each single site. More detail about the model can be found at https://spiral.imperial.ac.uk/handle/10044/1/89220 (Chapter 2, page 63).

The specification of the Bayesian log-binomial hierarchical model to estimate the RR is as follows.

Let CAO_{ij} be the observed binary outcome (yes/no) for j^{th} subject i^{th} site,

CAO_{ij}= 1 if subject has a disease
= 0 otherwise,

The model is specified as:

$CAO_{ij} \sim Bernoulli(p_{ij})$, i=1,2,………,21 & j=1,2,…..n_i

$log\left(P_{ij}\right) = \alpha_i + \sum_s \beta_{is} * X_{ijs}$

where p_{ij} is the probability of the outcome CAO_{ij}, α_i is the intercept for site i, $X_{ij}s$=1 if j^{th} subject in the site i^{th} is exposed to s^{th} exposure of interest and 0 otherwise, and n_i is the sample size for i^{th} site . The RR of the exposure of interest or confounder "s" is given by exp (β_{is}).

For the hierarchical specification of the model, we assign the following priors for the intercept α_i and β_{is} :

For (i in 1: 21) {

$\alpha_i \sim Normal(\mu.alpha, \sigma^2.alpha)$

$\beta_{is} \sim Normal\ (\mu.betas, \sigma^2.betas)$

}

with hyper priors:

$\mu.alpha \sim Normal(0, 10^4)$

$\sigma^2.alpha \sim Gamma(1{,}0.005)$

$\mu.betas \sim Normal(0, 10^2)$

$\sigma^2.beta \sim Gamma(1{,}0.005)$

The β_{is} and α_i are assumed to come from a normal distribution, but there is a distinct normal distribution for each β_{is} and α_i.

All Bayesian analyses were conducted in Stata 14 with the use of user-written program to call Open Bugs[5,6]. We used two MCMC chains, where 50,000 samples were drawn from the posterior distribution of each parameter, after discarding 50,000 burn-in iterations. For the point estimate of the PAR we used the posterior mean, together with the 95% credibility interval (95%CrI) corresponding to the 2.5% and 97.5% percentiles.

Investigation of heterogeneity in the RR estimates across sites

We investigated the heterogeneity of RR estimates across sites using the I^2 statistic of their meta-analysis[7]. For conveniency, the meta-analysis was performed in a frequentist framework using the 'metan' command in the Stata package[8].

Directed acyclic graphs (DAGs)

To help us decide which possible confounders we should adjust the analyses for, we drew directed acyclic graphs (DAGs) based on available knowledge. In particular, we used DAGitty[9], implemented through the *dagitty* command in R (www.rdocumentation.org/packages/dagitty/versions/0.3-1/topics/dagitty), with poverty as the exposure (and similar reasoning for wealth score as a continuous variable) and CAO as the outcome (and again similar reasoning for FEV_1/FVC).

We considered the following factors: age, sex, education, smoking pack-years, exposure to a dusty job, passive smoking, body mass index, childhood hospitalisation due to respiratory infection, family history of respiratory disease, and history of tuberculosis.

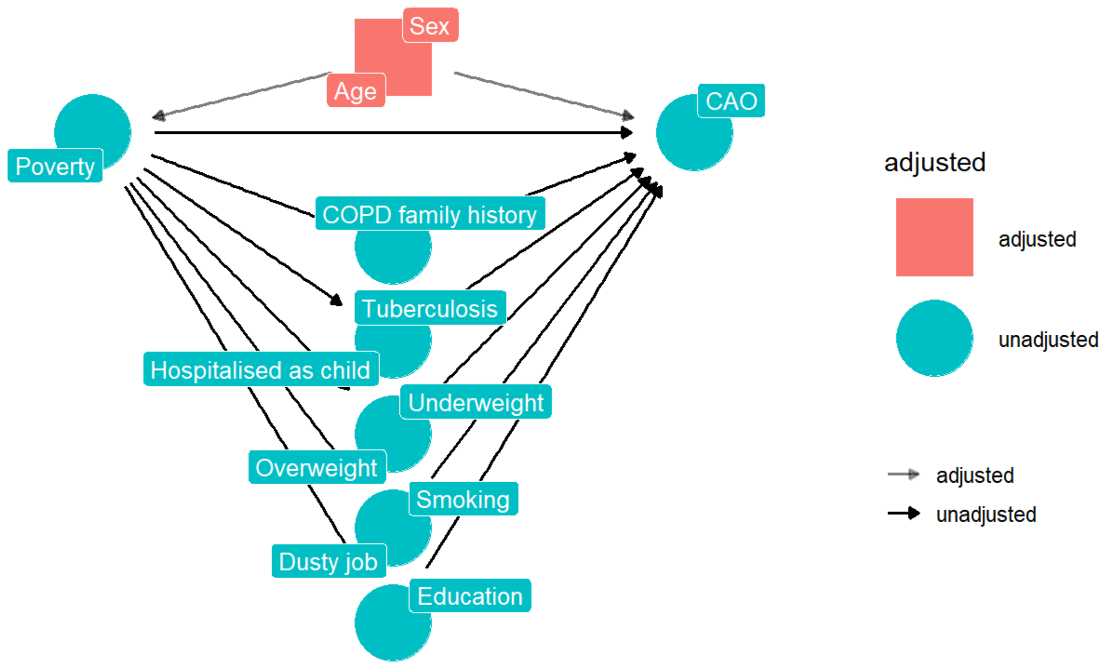
The three DAGs in Figure S1 (a to c) illustrate three different scenarios defining possible confounders (for which we should adjust the model) versus possible mediators of the effect of poverty on CAO (for which we should not adjust).

In our main analysis (Figure S1a), we only adjusted for age and sex as, as we hypothesised that all other factors could well act as mediators. In the analysis of FEV_1/FVC, age and sex were added to the model, while in the analysis of CAO, age and sex are already accounted for as they are used to calculate the LLN (CAO defined as FEV_1/FVC < Lower Limit of Normal).

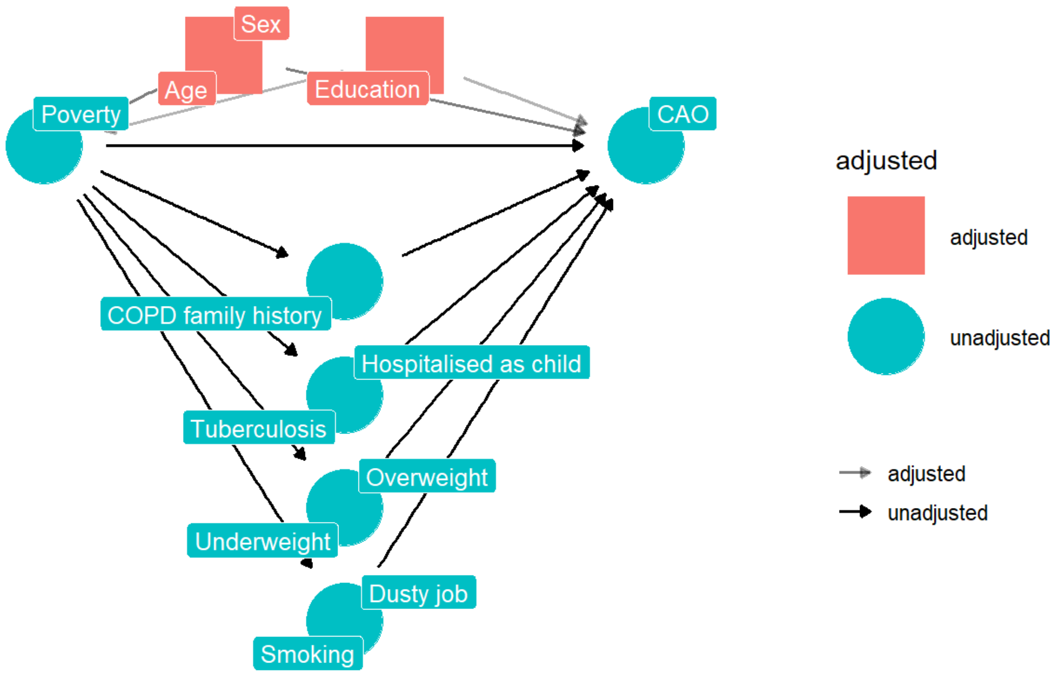
However, to assess the impact on the estimate of the association between poverty and CAO when further adjusting for the other factors, we performed two secondary analyses: a) further adjusting for education (Figure S1b); and b) adjusting for all factors considered (Figure S1c).

Figure S2

a) Model 1 (main model) - Adjusted only for age and sex



b) Model 2 - Adjusted for age, sex and education



c) Model 3 – Adjusted for all variables

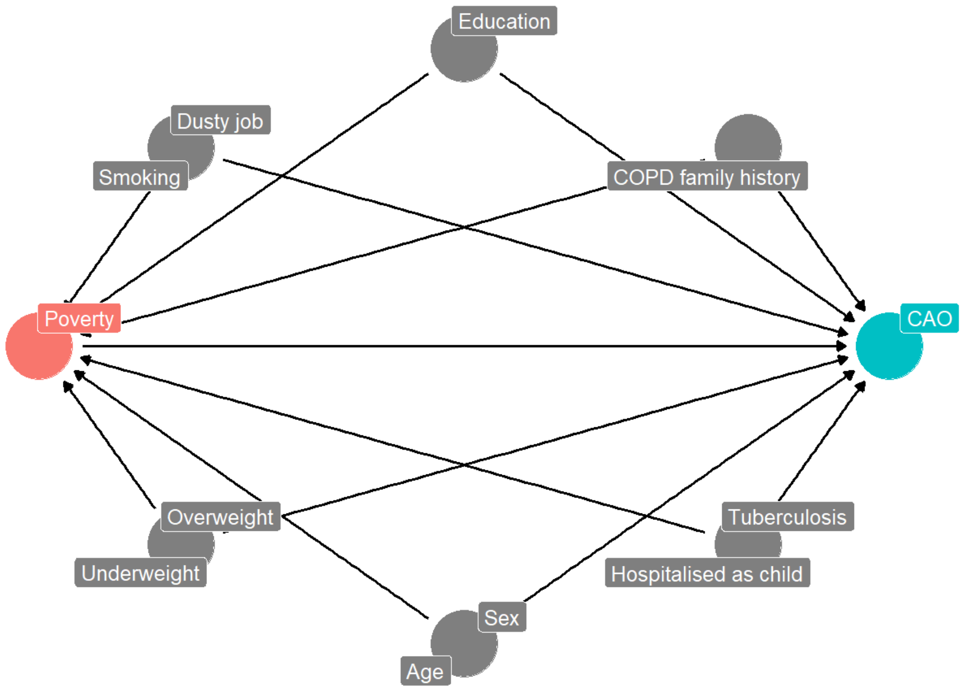


Figure S3: Association between wealth score and FEV_1/FVC (%) across the 21 sites

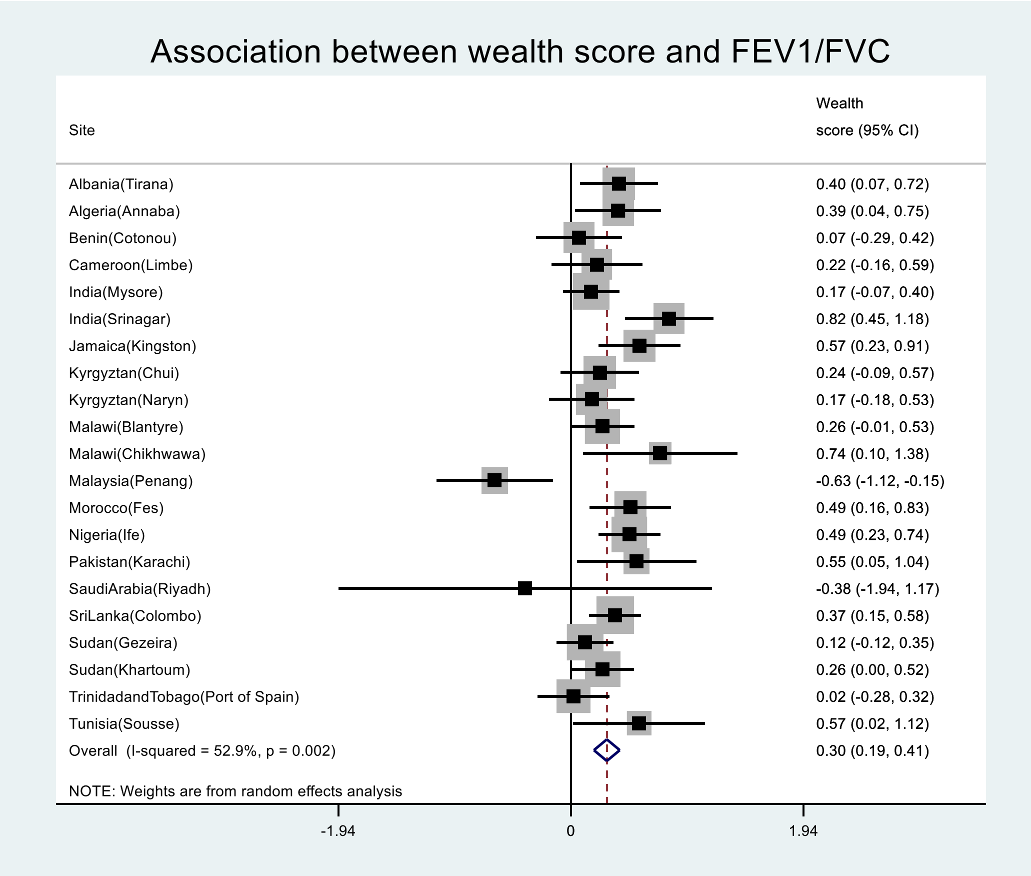


Figure S4: Association between wealth score and FEV_1/FVC<LLN across the 21 sites

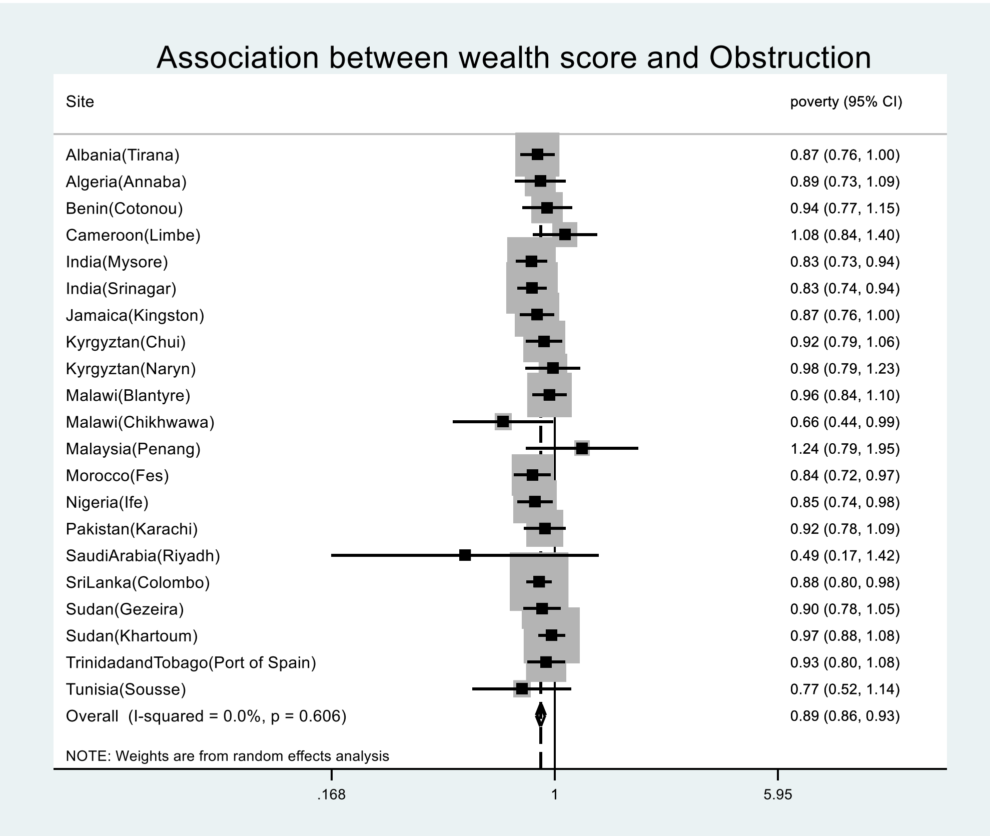


Figure S5: Association between poverty and FEV_1/FVC (%) across the 21 sites

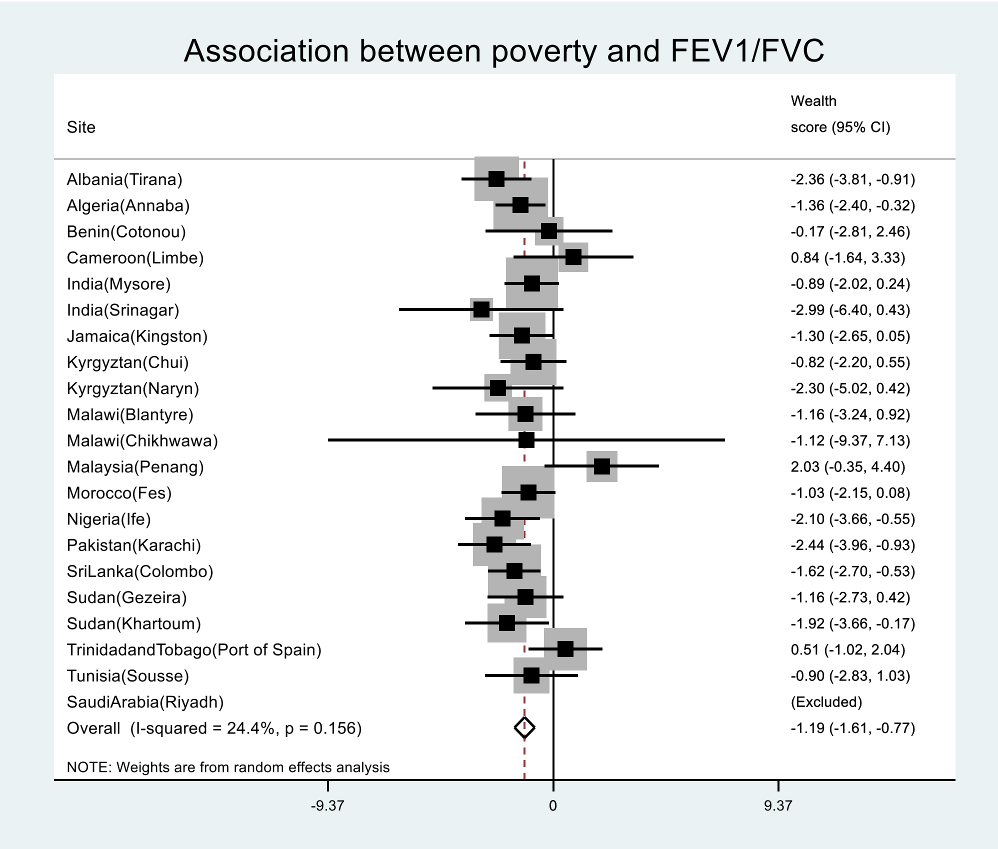


Figure S6: Association between poverty and FEV_1/FVC<LLN across the 21 sites

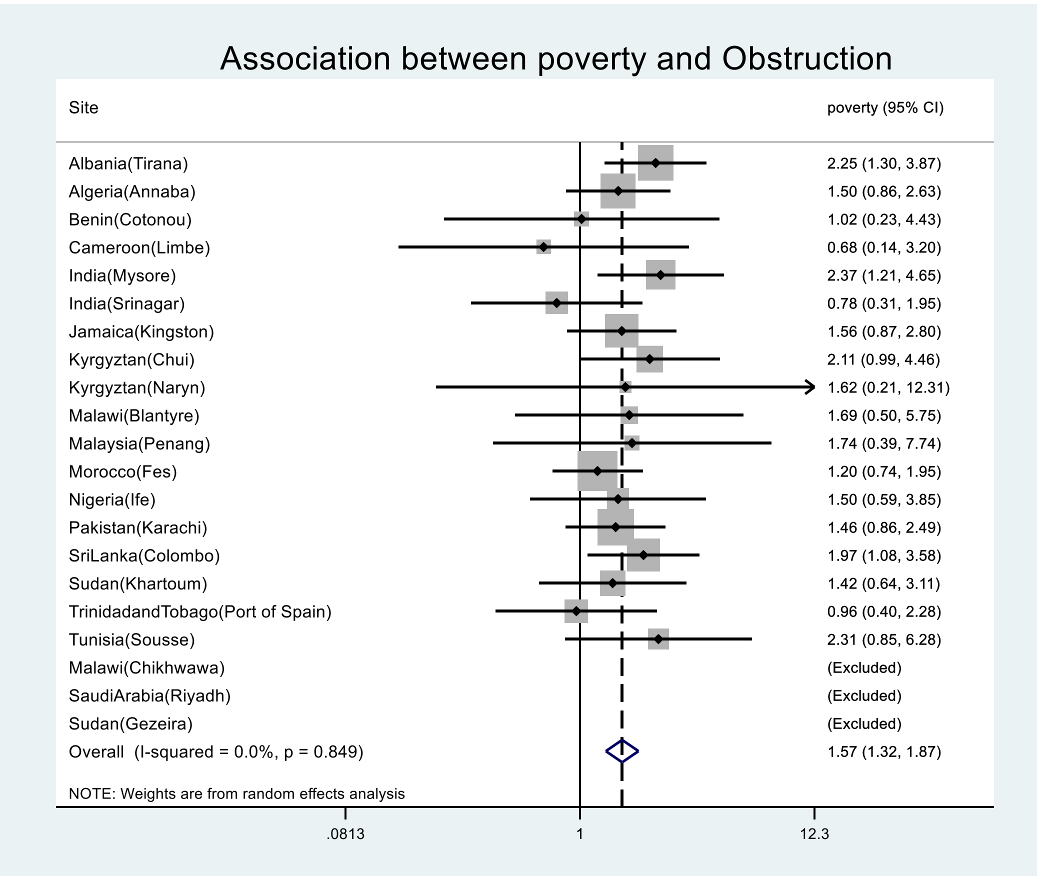


Figure S7: Comparison of site-specific estimates of PAR for CAO due to poverty from three different models: (1) main analysis - model adjusted only for age and sex; (2) secondary analysis - model adjusted for age, sex and education; (3) secondary analysis - model adjusted for age, sex, education, BMI, smoking pack years, passive smoking, exposure to dusty job, family history of respiratory infection, hospitalisation before the age of 10, and history of tuberculosis

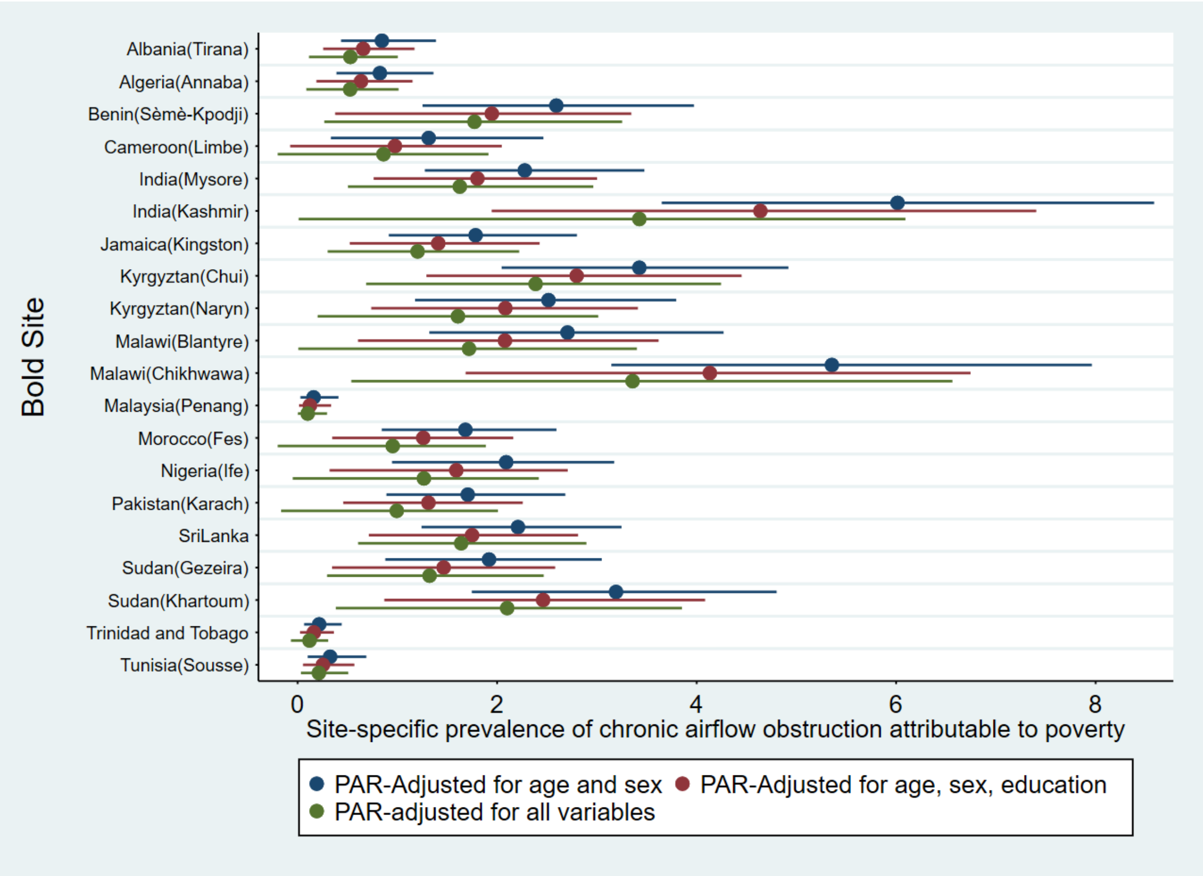


Table S1: **Data collection period of BOLD sites**

BOLD site	Start date	End date
India (Mysore)	27-Mar-10	21-Apr-14
Morocco (Fes)	11-May-10	26-Mar-11
Tunisia (Sousse)	14-Jun-10	21-Mar-11
India (Kashmir)	24-Oct-10	28-Jul-11
Nigeria (Ife)	23-May-11	30-Dec-11
Riyadh (Saudi Arabia)	05-Oct-11	09-Oct-13
Algeria (Annaba)	04-Mar-12	22-Oct-12
Sudan (Khartoum)	27-Jun-12	21-Dec-13
Albania (Tirana)	02-Oct-12	05-Jul-13
Malawi (Blantyre)	04-Feb-13	13-Jul-14
Kyrgyzstan (Chui)	05-Jun-13	03-Aug-13
Kyrgyzstan (Naryn)	06-Jun-13	29-Jul-13
Sri Lanka	15-Jun-13	12-Jan-14
Malaysia (Penang)	08-Jul-13	23-Sep-13
Benin (Sèmè-Kpodji)	23-Dec-13	19-May-14
Pakistan (Karachi)	02-Jun-14	06-Sep-15
Cameroon (Limbe)	19-Oct-14	07-Jun-15
Jamaica (Kingston)	06-Nov-14	24-Jun-15
Malawi (Chikhwawa)	06-Nov-14	22-Sep-15
Trinidad and Tobago (Port of Spain)	07-Mar-15	09-Oct-15
Sudan (Gezeira)	25-Aug-15	26-Dec-16

Table S2: Characteristics of the population by site

Site	N	FEV1/FVC<LLN	FEV1/FVC (%) (SD)	Prevalence of poverty (%)	Wealth score (SD)	Male (%)	Age (SD)	BMI (SD)	Smoking pack-years (SD)	Post-primary education (%)	Passive smoking (%)	Family history of COPD (%)	Childhood hospitalisation (%)	History of tuberculosis (%)
Albania (Tirana)	939	8.5	78.44 (8.96)	14.0	8.76 (1.56)	50	54.6 (10.8)	28.04 (4.7)	12.28 (20.46)	87.4	34.3	7.9	0.3	0.7
Algeria (Annaba)	890	6.9	78.57 (7.27)	25.1	8.26 (1.26)	50	52.5 (9.9)	28.31 (5.65)	10.78 (19.17)	58.9	11.6	5.8	1.9	2.2
Benin (Seme Copadi)	628	7.5	79.29 (7.13)	95.9	4.36 (1.48)	43	51.6 (9.8)	26.41 (5.56)	0.22 (2.00)	24.5	0.1	0.0	0.3	0.4
Cameroon (Limbe)	287	4.5	80.57 (6.94)	88.9	4.56 (2.10)	60	52.2 (9.4)	26.63 (5.35)	2.94 (8.39)	42.5	2.4	3.8	4.9	1.0
India (Mysore)	601	8.0	79.51 (7.39)	57.4	6.94 (2.38)	43	46.8 (7.2)	24.70 (3.78)	1.45 (5.97)	80.0	0.0	0.0	0.2	0.0
India (Kashmir)	754	16.4	76.42 (10.6)	96.0	4.18 (1.79)	55	51.4 (10.4)	22.43 (3.60)	136.03 (207.9)	18.3	64.9	2.4	0.1	0.4
Jamaica (Kingston)	578	8.7	78.42 (9.19)	45.8	7.29 (1.96)	42	55.9 (11.6)	27.52 (6.57)	12.01 (29.96)	77.0	15.7	1.6	0.7	0.7
Kyrgyzstan (Chui)	857	10.0	77.2 (8.17)	83.1	6.05 (1.58)	31	53.0 (8.8)	28.50 (5.64)	7.04 (16.37)	97.2	7.2	7.5	4.0	1.3
Kyrgyzstan (Naryn)	820	7.4	77.83 (7.31)	97.4	5.15 (1.22)	38	53.3 (10.0)	26.99 (4.98)	4.48 (11.17)	94.6	3.0	2.2	1.5	0.7
Malawi (Blantyre)	399	8.2	78.23 (7.81)	86.0	3.62 (2.70)	40	52.2 (9.8)	25.05 (5.36)	2.17 (25.06)	40.9	3.0	21.7	0.7	5.5
Malawi (Chikhwawa)	425	13.9	76.29 (9.09)	99.1	0.75 (1.24)	51	53.8 (10.5)	21.77 (3.88)	2.51 (6.50)	9.0	3.2	4.9	0.5	3.9
Malaysia (Penang)	662	3.9	81.03 (6.79)	4.7	9.43 (1.03)	51	54.5 (9.5)	26.05 (4.52)	6.60 (15.85)	64.7	25.6	5.1	3.0	0.0
Morocco (Fes)	768	9.5	78.12 (8.3)	46.5	7.54 (1.64)	46	55.1 (10.3)	27.88 (5.26)	7.79 (20.23)	24.5	13.8	10.0	0.7	1.7
Nigeria (Ife)	864	7.0	78.54 (8.36)	87.8	4.90 (2.00)	39	55.4 (12.0)	25.35 (5.36)	0.72 (4.59)	51.9	1.7	0.5	0.8	0.5
Pakistan (Karachi)	606	10.0	80.02 (9.72)	37.6	7.36 (1.49)	44	51.6 (9.6)	26.46 (5.54)	7.25 (22.08)	42.7	12.7	13.8	1.2	0.5
Saudi Arabia (Riyadh)	700	3.1	82.63 (6.03)	0.0	9.94 (0.28)	54	50.3 (7.7)	31.22 (5.95)	9.53 (23.57)	63.4	5.3	3.4	0.9	2.0
Sri Lanka	1,006	7.4	79.74 (8.69)	69.8	6.08 (2.31)	45	53.7 (9.5)	24.21 (4.60)	2.67 (8.58)	72.6	8.5	2.8	2.9	0.8
Sudan (Gezeira)	570	5.4	80.15 (7.19)	84.8	5.03 (2.42)	52	53.9 (10.1)	26.31 (5.94)	7.40 (71.72)	34.4	12.0	9.6	2.4	0.5
Sudan (Khartoum)	506	10.3	77.90 (8.45)	80.0	5.18 (2.69)	59	54.0 (10.4)	26.45 (6.42)	6.53 (51.88)	43.6	7.4	1.7	1.4	1.0
Trinidad and Tobago (Port of Spain)	1,090	6.6	79.62 (7.55)	8.6	8.96 (1.44)	40	54.1 (10.8)	28.91 (7.61)	7.92 (30.19)	61.5	22.7	3.8	1.5	0.0
Tunisia (Sousse)	661	5.0	80 (7.52)	7.6	8.84 (0.93)	47	53.0 (9.1)	29.24 (5.62)	14.99 (24.81)	48.6	36.8	6.4	2.7	0.0

N: Number of people with usable post-bronchodilator spirometry and questionnaire data; FEV_1: forced expiratory volume in one second; FVC: forced vital capacity; LLN: lower limit of normal; Poverty: defined as a wealth score lower than or equal to 7; BMI: body mass index; smoking pack-years: 1 pack-year equals an average of 20 cigarettes per day for 1 year or the equivalent amount of other types of tobacco smoking; passive smoking: somebody else in the household smoked during the past 2 weeks; post-primary education: the highest level of education completed was above primary school; family history of COPD: a close sibling or parent had been diagnosed as having emphysema, chronic bronchitis or COPD by a health professional; childhood hospitalisation: hospitalised for breathing problems before the age of 10 years; History of tuberculosis: ever diagnosed with tuberculosis

Table S3: Association of wealth score and poverty with FEV_1/FVC (%) and CAO, adjusted for possible confounding factors (Model 3)

Outcome variable	FEV_1/FVC (%)		CAO (FEV_1/FVC<LLN)	
Variable	Model with poverty Coeff (95% Crl)	Model with wealth score Coeff (95% Crl)	Model with poverty RR (95% Crl)	Model with wealth score RR (95% Crl)
Wealth score		0.20 (0.11, 0.29)		0.96 (0.93, 0.99)
Poverty	-0.81 (-1.16, -0.45)		1.36 (1.16, 1.59)	
Age (years)	-2.48 (-2.73, -2.22)	-2.48 (-2.74, -2.22)		
Females	0.97 (0.40, 1.54)	0.97 (0.40, 1.54)		
BMI ($kg.m^{-2}$)				
<18.5	-1.70 (-2.70, -0.69)	-1.68 (-2.70, -0.67)	1.67 (1.38, 2.03)	1.63 (1.35, 1.98)
>=18.5-<25				
>=25-<=30	1.02 (0.70, 1.34)	0.97 (0.65, 1.28)	0.80 (0.70, 0.92)	0.82 (0.72, 0.94)
>30	1.58 (1.11, 2.06)	1.55 (1.05, 2.04)	0.63 (0.52, 0.76)	0.64 (0.53, 0.77)
Education level completed	0.15 (-0.03, 0.32)	0.09 (-0.07, 0.26)	0.88 (0.82, 0.93)	0.88 (0.82, 0.93)
Smoking pack-years	-0.56 (-0.71, -0.40)	-0.55 (-0.71, -0.40)	1.10 (1.07, 1.14)	1.10 (1.07, 1.13)
Passive smoking	-0.11 (-0.61, 0.39)	-0.10 (-0.59, 0.39)	1.07 (0.91, 1.26)	1.07 (0.92, 1.25)
Worked in a dusty job (years)	-0.03 (-0.04, -0.01)	-0.03 (-0.04, -0.01)	1.01 (1.01, 1.02)	1.01 (1.01, 1.02)
Family history of COPD	-1.04 (-1.75, -0.32)	-1.09 (-1.82, -0.36)	1.41 (1.13, 1.75)	1.44 (1.15, 1.79)
Hospitalised as a child	-2.55 (-4.01, -1.09)	-2.52 (-3.99, -1.04)	2.78 (1.94, 3.99)	2.73 (1.92, 3.90)
History of tuberculosis	-3.39 (-5.25, -1.53)	-3.40 (-5.27, -1.53)	2.51 (1.83, 3.45)	2.51 (1.84, 3.42)

FEV_1: forced expiratory volume in one second; FVC: forced vital capacity; LLN: lower limit of normal; Poverty: defined as a wealth score lower than or equal to 7; BMI: body mass index; smoking pack-years: 1 pack-year equals an average of 20 cigarettes per day for 1 year or the equivalent amount of other types of tobacco smoking; passive smoking: somebody else in the household smoked during the past 2 weeks; Education: the highest level of education completed; family history of COPD: a close sibling or parent had been diagnosed as having emphysema, chronic bronchitis or COPD by a health professional; childhood hospitalisation: hospitalised for breathing problems before the age of 10 years; history of tuberculosis: ever diagnosed with tuberculosis

Table S4: PAR for CAO due to poverty, expressed as percent of total population aged ≥40 years, with 95% credible intervals

Site	Model 1		Model 2		Model 3	
Albania (Tirana)	0.85	(0.43, 1.39)	0.66	(0.26, 1.17)	0.53	(0.11, 1.00)
Algeria (Annaba)	0.83	(0.39, 1.36)	0.64	(0.19, 1.15)	0.53	(0.09, 1.01)
Benin (Sèmè-Kpodji)	2.59	(1.25, 3.97)	1.95	(0.38, 3.34)	1.77	(0.27, 3.25)
Cameroon (Limbe)	1.31	(0.33, 2.46)	0.98	(-0.08, 2.05)	0.86	(-0.20, 1.91)
India (Mysore)	2.28	(1.28, 3.48)	1.80	(0.76, 3.00)	1.63	(0.50, 2.96)
India (Kashmir)	6.01	(3.65, 8.59)	4.64	(1.94, 7.40)	3.43	(0.01, 6.09)
Jamaica (Kingston)	1.78	(0.91, 2.80)	1.41	(0.52, 2.44)	1.20	(0.30, 2.22)
Kyrgyztan (Chui)	3.43	(2.04, 4.92)	2.80	(1.29, 4.45)	2.39	(0.69, 4.24)
Kyrgyztan (Naryn)	2.52	(1.18, 3.80)	2.08	(0.74, 3.41)	1.61	(0.20, 3.01)
Malawi (Blantyre)	2.71	(1.32, 4.27)	2.08	(0.60, 3.62)	1.72	(0.01, 3.40)
Malawi (Chikhwawa)	5.36	(3.14, 7.96)	4.13	(1.68, 6.75)	3.36	(0.54, 6.56)
Malaysia (Penang)	0.16	(0.03, 0.41)	0.12	(0.01, 0.34)	0.10	(0.002, 0.30)
Morocco (Fes)	1.68	(0.84, 2.60)	1.26	(0.35, 2.16)	0.95	(-0.20, 1.89)
Nigeria (Ife)	2.09	(0.95, 3.17)	1.59	(0.32, 2.71)	1.27	(-0.05, 2.42)
Pakistan (Karachi)	1.71	(0.89, 2.68)	1.31	(0.46, 2.26)	0.99	(-0.17, 2.01)
Sri Lanka	2.21	(1.24, 3.25)	1.75	(0.71, 2.81)	1.64	(0.61, 2.90)
Sudan (Gezeira)	1.92	(0.88, 3.05)	1.46	(0.34, 2.58)	1.32	(0.30, 2.47)
Sudan (Khartoum)	3.19	(1.75, 4.80)	2.46	(0.87, 4.09)	2.10	(0.38, 3.85)
Trinidad and Tobago (Port of Spain)	0.22	(0.07, 0.44)	0.16	(0.02, 0.36)	0.12	(-0.07, 0.31)
Tunisia (Sousse)	0.33	(0.10, 0.69)	0.25	(0.05, 0.57)	0.21	(0.03, 0.51)

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