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Chronic airflow obstruction and ambient particulate air pollution

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ABSTRACT

Smoking is the most well-established cause of chronic airflow obstruction (CAO) but particulate air pollution and poverty have also been implicated. We regressed sex-specific prevalence of CAO from 41 Burden of Obstructive Lung Disease study sites against smoking prevalence from the same study, the gross national income per capita and the local annual mean level of ambient particulate matter (PM_{2.5}) using negative binomial regression. The prevalence of CAO was not independently associated with PM_{2.5} but was strongly associated with smoking and was also associated with poverty. Strengthening tobacco control and improved understanding of the link between CAO and poverty should be prioritised.

INTRODUCTION

The most important cause of chronic airflow obstruction (CAO) is tobacco smoking. The Global Burden of Disease programme has suggested that air pollution is second only to smoking in determining loss of disability-adjusted life-years due to chronic respiratory disease.¹ Evidence for this was obtained by applying the risk of disease associated with air pollution exposure, as estimated from various studies, to the known distribution of fine particulate matter (PM_{2.5}) across the world.

In this analysis, we investigated the ecological association (ie, using aggregated data)² between the prevalence of CAO, as estimated from a large multisite study, and levels of ambient PM_{2.5}.

METHODS

The prevalence of CAO and the prevalence of smoking were estimated for 41 sites of the Burden of Obstructive Lung Disease (BOLD) study (online supplemental file for details).³ The level of poverty of each site was estimated from the gross national income (GNI) per capita at the time of the survey,

using data from the World Bank.⁴ Annual mean PM_{2.5} levels (all composition, and dust and sea-salt removed (DSSR)) for each site coordinates and a 10 km radius buffer (site as centre) were obtained from a public dataset.^{5,6}

The unit of our analysis was the site, and the analysis was stratified by sex (online supplemental file for details).

RESULTS

The prevalence of CAO across sites ranged from 3.5% to 23.2% in men, and from 2% to 19.4% in women (table 1). As expected, the prevalence of CAO was substantially lower among never smokers (online supplemental table S1).

The prevalence of smoking varied from 4.6% to 84.4% in men and from 0% to 61.3% in women. The levels of all composition PM_{2.5} ranged from 4 µg/m³ in Reykjavik (Iceland) to 68 µg/m³ in Karachi (Pakistan). The GNI varied from \$1120 in Malawi to \$51 250 in Saudi Arabia (table 1).

Lower PM_{2.5} levels were weakly correlated with a higher prevalence of CAO, in both sexes (figure 1A). Among never smokers (figure 1B) and when using DSSR PM_{2.5}, there was no correlation (figure 1C).

In both sexes, the prevalence of CAO was strongly positively associated with smoking and negatively associated with GNI. There was no association of prevalence of CAO with levels of PM_{2.5} (all composition) (table 2). The sensitivity analyses using all composition PM_{2.5} for a 10 km radius buffer and using DSSR PM_{2.5} showed no substantive difference from the main analysis (online supplemental tables S2–S4).

DISCUSSION

We were unable to show evidence of an ecological association between the prevalence of CAO and annual mean levels of PM_{2.5}, although we have shown clear independent associations with the



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Table 1 Survey date, prevalence of chronic airflow obstruction (CAO) and smoking in men and women, gross national income (GNI) per capita and annual mean PM_{2.5} levels for the 41 sites of the Burden of Obstructive Lung Disease study

Site	Mid-date of survey	CAO in men (%)	CAO in women (%)	Ever smoking prevalence in men (%)	Ever smoking prevalence in women (%)	GNI per capita, PPP (current international \$)	PM _{2.5} (all composition) (µg/m ³)	PM _{2.5} (all composition) 10 km radius buffer (µg/m ³)	PM _{2.5} (dust and sea-salt removed) (µg/m ³)	PM _{2.5} (dust and sea-salt removed) 10 km radius buffer (µg/m ³)
Albania (Tirana)	17/02/2013	12.8	4.2	63.0	11.4	10750	25	16.7	15	10.0
Algeria (Annaba)	28/06/2012	9.3	4.5	76.5	0.7	13230	21	14.5	8	5.5
Australia (Sydney)	30/07/2006	7.9	13.8	60.8	47.5	32970	7	6.6	4	4.0
Austria (Salzburg)	11/01/2005	12.8	19.4	64.4	44.3	34940	23	18.1	20	16.0
Benin (Sèmè-Kpodji)	06/03/2014	6.6	8.1	4.6	0	2100	28	24.8	13	11.7
Cameroon (Limbe)	11/02/2015	6.3	4.3	35.9	2.9	3390	41	37.0	20	18.0
Canada (Vancouver)	30/12/2003	12.8	12.0	66.0	50.3	31540	5	5.9	4	5.2
China (Guangzhou)	26/11/2002	9.9	6.3	81.4	6.3	3520	40	38.7	39	37.2
England (London)	27/02/2007	16.1	15.8	71.8	57.1	35240	15	15.3	13	13.2
Estonia (Tartu)	25/02/2009	8.7	5.2	63.8	31.5	19880	12	10.7	11	9.4
Germany (Hannover)	16/07/2005	10.0	7.8	73.1	50	32350	20	20.0	18	18.2
Iceland (Reykjavik)	28/04/2005	8.9	13.3	70.7	61.3	35470	4	4.1	1	1.4
India (Kashmir)	11/03/2011	17.3	15.4	76.4	28.8	4580	33	33.6	26	26.7
India (Mumbai)	13/05/2007	6.2	7.9	15.6	0	3610	39	40.3	34	34.6
India (Mysore)	08/04/2012	11.2	5.5	22.1	1.4	4850	22	22.1	19	19.9
India (Pune)	24/09/2009	5.8	6.7	20.9	0.3	4000	45	44.9	40	39.3
Jamaica	01/03/2015	10.3	7.5	64.2	18.5	8280	8	6.5	3	2.3
Kyrgyzstan (Chui)	04/07/2013	13.9	7.9	77.9	7.5	3050	19	18.5	9	8.9
Kyrgyzstan (Naryn)	02/07/2013	11.0	4.7	60.4	2.4	3050	24	23.5	7	7.0
Malawi (Blantyre)	24/10/2013	6.9	9.1	30.6	2.5	1120	11	11.1	11	10.5
Malawi (Chikwawa)	15/04/2015	18.0	9.4	48.6	11.3	1190	16	15.5	15	14.5
Malaysia (Penang)	15/08/2013	4.4	3.4	49.7	0	23470	33	22.8	30	20.8
Morocco (Fes)	17/10/2010	11.9	7.5	59.3	1.0	6240	24	19.1	6	5.0
Netherlands (Maastricht)	30/06/2008	19.0	17.2	73.7	60.3	45110	14	14.1	13	12.6
Nigeria (Ile-Ife)	10/09/2011	7.5	6.7	23.4	3.7	4920	30	34.3	15	17.1
Norway (Bergen)	13/08/2005	14.8	10.2	71.0	57.8	48300	7	6.7	4	4.4
Pakistan (Karachi)	18/01/2015	14.6	6.5	48.6	8.0	5050	68	67.9	17	17.0
Philippines (Manila)	25/12/2005	13.0	5.2	83.9	31.1	5050	28	27.6	21	20.6
Philippines (Nampicuan-Talugtug)	21/08/2007	16.3	12.3	77.0	30.1	5710	13	12.6	10	10.2
Poland (Krakow)	10/05/2005	15.0	12.3	79.4	43.8	13650	37	35.8	34	33.5

Continued

Site	Mid-date of survey	CAO in men (%)	CAO in women (%)	Ever smoking prevalence in men (%)	Ever smoking prevalence in women (%)	GNI per capita, PPP (current international \$)	PM _{2.5} (all composition) (µg/m ³)	PM _{2.5} (all composition) 10 km radius buffer (µg/m ³)	PM _{2.5} (dust and sea-salt removed) (µg/m ³)	PM _{2.5} (dust and sea-salt removed) 10 km radius buffer (µg/m ³)
Portugal (Lisbon)	26/08/2008	13.9	9.5	61.6	22.1	25590	14	10.9	8	6.5
Saudi Arabia (Riyadh)	06/10/2012	3.5	2.8	48.3	2.2	51250	64	64.1	13	13.0
South Africa (Uitsig-Ravensmead)	05/04/2005	23.8	16.2	84.4	57.9	9610	8	7.5	5	4.5
Sri Lanka	28/09/2013	11.7	3.9	48.9	0.2	10370	15	14.2	10	9.3
Sudan (Gezeira)	25/04/2016	5.6	6.0	47.8	1.4	4260	40	40.2	5	5.0
Sudan (Khartoum)	25/03/2013	10.4	10.0	38.4	2.9	2690	39	38.4	6	5.7
Sweden (Uppsala)	20/03/2007	10.2	8.3	68.5	52.7	41850	8	6.7	7	5.7
Trinidad & Tobago	23/06/2015	6.6	6.7	51.3	12.0	33280	7	7.1	1	1.0
Tunisia (Sousse)	01/11/2010	8.4	2.0	79.9	9.1	9750	20	17.3	6	5.3
Turkey (Adana)	30/12/2003	19.8	9.1	81.0	30.5	9430	32	27.7	17	14.8
USA (Lexington, KY)	13/02/2006	13.6	16.2	78.6	54.3	47160	11	9.9	10	9.7

PM_{2.5}, particulate matter <2.5 µm aerodynamic diameter, PPP, Purchasing power parity.

prevalence of smoking and GNI.

Our findings suggest that PM_{2.5} is unlikely to have a substantial effect on the prevalence of CAO. We have previously shown that indoor burning of solid fuels, another source of PM_{2.5}, is

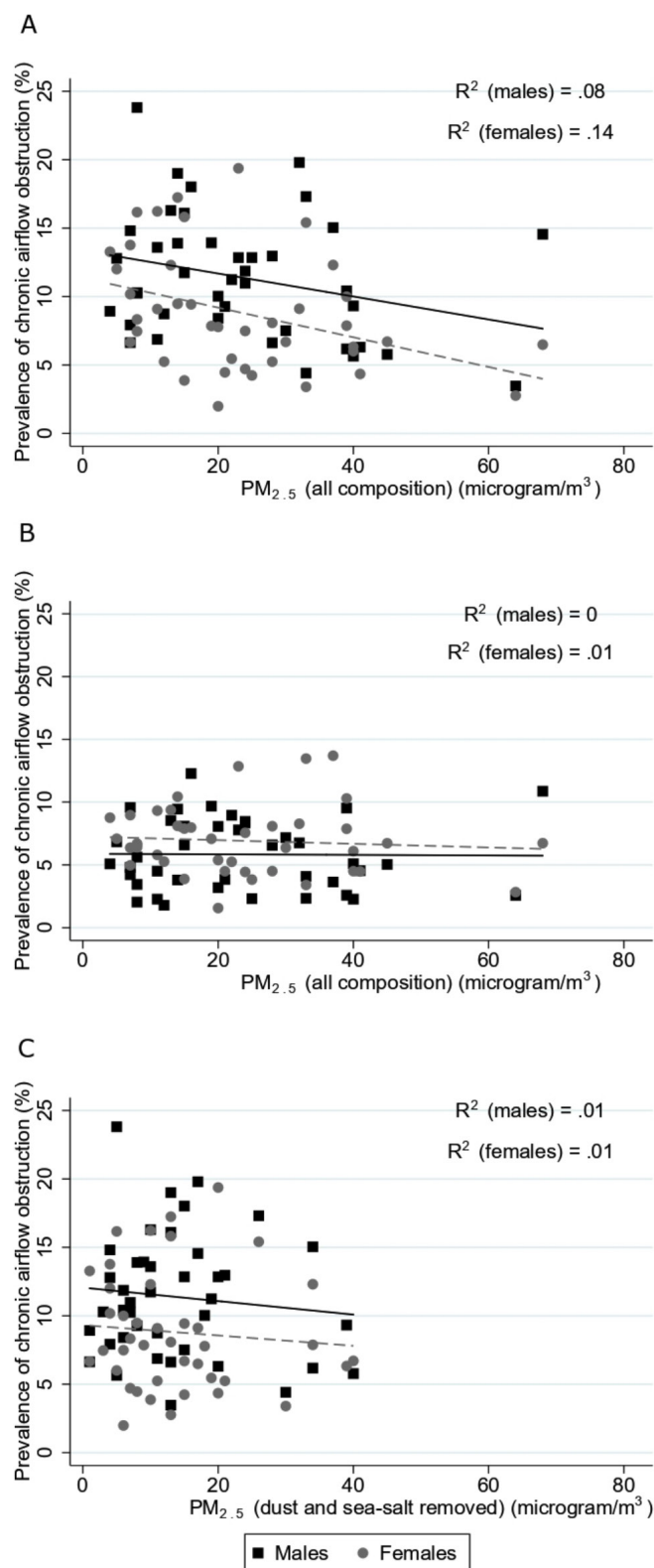


Figure 1 Relation between prevalence of chronic airflow obstruction and annual mean levels of (a) PM_{2.5} (all composition, µg/m³) for the whole sample, (b) PM_{2.5} (all composition, µg/m³) for never smokers and (c) PM_{2.5} (dust and sea-salt removed, µg/m³) for the whole sample.

Table 2 Ecological negative binomial regression of chronic airflow obstruction against log(GNI), smoking and log(PM_{2.5}), by sex

Variable	men			women		
	Rate ratio	95% CI	P value	Rate ratio	95% CI	P value
Smoking	4.17	2.40 to 7.26	<0.001	11.3	5.64 to 22.6	<0.001
Log(GNI)	0.90	0.81 to 0.99	0.04	0.83	0.73 to 0.94	0.003
Log(PM _{2.5})	0.92	0.78 to 1.07	0.28	1.05	0.89 to 1.25	0.55

GNI, gross national income; ; PM_{2.5}, particulate matter <2.5µm aerodynamic diameter.

also unlikely to be substantially associated with CAO,⁷ a conclusion supported by the findings of three large Chinese studies.^{8–10} Our findings are compatible with the large European ESCAPE project, which showed little evidence of an effect of any pollutant on the FEV₁/FVC or its change over time.¹¹

This analysis has several strengths. The aggregate data on prevalence of CAO and smoking were taken directly from the BOLD study. Spirometry was post-bronchodilator, and its quality was assured with a strong training programme and regular review of all spirometers in a quality control centre.

All ecological analyses have potential weaknesses. One is the temptation to ascribe the associations observed at the site level to similar associations at an individual level. In this instance, there is independent analysis showing the association of CAO with smoking¹² and poverty¹³ at the individual level within the BOLD study.

Ecological analyses are also prone to confounding. There are strong ecological associations between the prevalence of smoking, GNI and PM_{2.5}. The poorer countries have fewer smokers, less CAO and greater pollution levels. This probably explains the negative association of CAO with PM_{2.5} in the population as a whole, which was not seen for never smokers (figure 1B), or with DSSR PM_{2.5}, or in the regression analysis adjusted for smoking prevalence and GNI.

Ecological analyses can be misleading if the average exposure in a site does not represent the exposure of those with the disease.¹⁴ Although there may be differences in pollution exposure within each site, these are likely to be small compared with the larger variation between sites, which ranged from 4 µg/m³ in Reykjavik (Iceland) to 68 µg/m³ in Karachi (Pakistan). It is unlikely that anyone living in Karachi will have exposure to ambient PM_{2.5} lower than any of those living in Reykjavik. The wide variation in income across sites is probably less well represented by GNI. Using the same estimate of GNI for rural and urban areas is likely to lead to more substantial errors than the approximations made for PM_{2.5}. Nevertheless, we have found an association between poverty and CAO both at the ecological and individual levels in the BOLD study,¹³ and it is likely that the imprecision introduced here by using GNI to represent the site income has reduced the strength of association with CAO.

These results do not imply that air pollution is not harmful to lung growth in utero and during childhood, lung health or general health, and we clearly do not address in this study the potential of PM_{2.5} to cause other pathologies or to trigger acute exacerbations of disease. We cannot exclude the possibility that the toxicology of PM_{2.5} varies geographically, that a component of PM_{2.5} causes CAO but it is not always present, or that there is another pollutant that is highly correlated with PM_{2.5} in some sites that causes CAO. Several researchers have suggested that the properties¹⁵ or sources¹⁶ of particles may also be important in determining their effects.

This ecological study shows that, after adjustment for smoking and GNI, ambient PM_{2.5} is unlikely to explain a substantial amount of the prevalence of CAO, while the ecological

association of smoking with CAO is strong and the association of poverty with CAO indicates that this is also likely to play an important role in its origins.

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1 [Online supplement](#)

2 **Chronic airflow obstruction and ambient particulate air pollution**

3

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74 BOLD study details

75 The BOLD study has been described in detail elsewhere¹. Briefly, representative samples of the
76 general population over the age of 40 were drawn from a sample of sites taken from around the
77 world. These were drawn so as to represent most of the regions defined by the Global Burden of
78 Disease (the exceptions were Latin America which had a separate study, the high-income countries
79 of Asia, and Oceania) with a bias towards larger regions such as South Asia. All sites received
80 approval from their local ethics committee, and participants provided informed consent. Spirometry
81 was conducted before and after a bronchodilator (200 µg Salbutamol inhaled via a spacer) using a
82 forced manoeuvre and an EasyOne spirometer (ndd Medizintechnik AG, Zurich, Switzerland). All
83 spirometry data were reviewed for quality control during the study in either Salt Lake City or
84 London. CAO was defined as a post-bronchodilator ratio of the forced expiratory volume in the first
85 second (FEV₁) to the forced vital capacity (FVC), less than the lower limit of normal, which was
86 determined using the equations for white Americans in the NHANES III study². Information from
87 participants on several risk factors, including whether they had ever smoked, was collected using a
88 standardised questionnaire.

89

90 PM_{2.5} concentrations

91 The concentrations of annual mean PM_{2.5} were downloaded from a freely available resource on the
92 Atmospheric Composition Analysis Group website.³ Briefly, global ground-level PM_{2.5} concentrations
93 were estimated by combining aerosol optical depth data from satellites with simulation-based data
94 from a chemical transport model. These were then calibrated to ground-based observations of PM_{2.5}
95 using a geographically weighted regression, which allows the estimation of local levels.⁴ We used
96 data at a spatial resolution of 0.01° latitude by 0.01° longitude.

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Statistical analysis

The unit of our ecological analysis was the site, and the analysis was performed separately for males and females. The counts of the male and female cases of CAO in each site were regressed separately in negative binomial models, with the local sample size as an offset. The analyses included the prevalence of male, or female, smoking in the site as measured from the BOLD sample, the GNI and the level of PM_{2.5} (all composition) for the site. Both GNI and PM_{2.5} were log transformed as there is evidence in each case of a non-linear relationship with chronic lung disease^{5,6}. We conducted a series of sensitivity analyses in which we re-run the main analysis: 1) using PM_{2.5} (all composition) estimates for a 10-km radius buffer; and 2) using dust and sea-salt removed PM_{2.5} instead of all composition PM_{2.5}.

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125 burden of disease attributable to ambient fine particulate matter exposure. *Environmental health*
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127

128 **Table S1.** Sample size and prevalence of chronic airflow obstruction (CAO) in the population and in
 129 never smokers by site and sex.

Site	Males			Females		
	N	CAO %	CAO % in never smokers	N	CAO %	CAO % in never smokers
Albania (Tirana)	467	12.8	2.3	472	4.2	3.8
Algeria (Annaba)	442	9.3	3.8	448	4.5	4.5
Australia (Sydney)	265	7.9	4.8	276	13.8	9.0
Austria (Salzburg)	685	12.8	7.8	573	19.4	12.9
Benin (Sèmè-Kpodji)	302	6.6	6.6	396	8.1	8.1
Cameroon (Limbe)	206	6.3	4.5	138	4.3	4.5
Canada (Vancouver)	344	12.8	6.8	483	12.0	7.1
China (Guangzhou)	236	9.9	2.3	237	6.3	4.5
England (London)	323	16.1	6.6	354	15.8	7.9
Estonia (Tartu)	309	8.7	1.8	305	5.2	5.3
Germany (Hannover)	349	10.0	3.2	334	7.8	5.4
Iceland (Reykjavik)	403	8.9	5.1	354	13.3	8.8
India (Kashmir)	416	17.3	4.1	344	15.4	13.5
India (Mumbai)	275	6.2	2.6	165	7.9	7.9
India (Mysore)	258	11.2	9.0	348	5.5	5.2
India (Pune)	502	5.8	5.0	343	6.7	6.7
Jamaica	243	10.3	3.4	335	7.5	6.6
Kyrgyzstan (Chui)	280	13.9	9.7	611	7.9	7.1
Kyrgyzstan (Naryn)	328	11.0	8.5	531	4.7	4.4
Malawi (Blantyre)	160	6.9	4.5	242	9.1	9.3
Malawi (Chikwawa)	222	18.0	12.3	212	9.4	8.0
Malaysia (Penang)	340	4.4	2.3	323	3.4	3.4
Morocco (Fes)	354	11.9	8.3	414	7.5	7.6
Netherlands (Maastricht)	300	19.0	3.8	290	17.2	10.4
Nigeria (Ile-Ife)	346	7.5	7.2	538	6.7	6.4
Norway (Bergen)	324	14.8	9.6	334	10.2	5.0
Pakistan (Karachi)	268	14.6	10.0	339	6.5	6.7
Philippines (Manila)	378	13.0	6.6	515	5.2	4.5
Philippines (Nampicuan-Talugtug)	356	16.3	8.5	366	12.3	9.4
Poland (Krakow)	266	15.0	3.6	260	12.3	13.7
Portugal (Lisbon)	331	13.9	9.4	380	9.5	8.1
Saudi Arabia (Riyadh)	375	3.5	2.6	325	2.8	2.8
South Africa (Uitsig-Ravensmead)	315	23.8	2.0	532	16.2	6.7
Sri Lanka	460	11.7	8.1	568	3.9	3.9
Sudan (Gezeira)	301	5.6	5.1	283	6.0	6.1
Sudan (Khartoum)	307	10.4	9.5	210	10.0	10.3
Sweden (Uppsala)	283	10.2	5.6	264	8.3	6.4
Trinidad & Tobago	437	6.6	4.2	660	6.7	6.4
Tunisia (Sousse)	309	8.4	8.1	352	2.0	1.6
Turkey (Adana)	389	19.8	6.8	417	9.1	8.3
USA (Lexington, KY)	206	13.6	2.3	302	16.2	5.8

130 N, sample size.

Table S2. Sensitivity analysis – as for table 3, with estimates of PM_{2.5} for a 10-km radius buffer.

Variable	Males			Females		
	Rate ratio	95%CI	P	Rate ratio	95%CI	P
Smoking	4.17	2.39-7.29	< 0.001	11.1	5.66-21.8	< 0.001
Log(GNI)	0.90	0.81-0.99	0.048	0.83	0.73-0.94	0.003
Log(PM _{2.5})	0.93	0.79-1.09	0.37	1.05	0.89-1.25	0.55

GNI, gross national income per capita; PM_{2.5}, particulate matter <2.5µm aerodynamic diameter.

Table S3. Sensitivity analysis – as for table 3, with estimates of PM_{2.5} with dust and sea-salt removed.

Variable	Males			Females		
	Rate ratio	95%CI	P	Rate ratio	95%CI	P
Smoking	4.38	2.51-7.62	< 0.001	10.4	5.52-19.6	< 0.001
Log(GNI)	0.92	0.83-1.02	0.1	0.83	0.73-0.94	0.003
Log(PM _{2.5})	1.04	0.92-1.18	0.48	1.03	0.92-1.16	0.59

GNI, gross national income per capita; PM_{2.5}, particulate matter <2.5µm aerodynamic diameter.

Table S4. Sensitivity analysis – as for table 3, with estimates of PM_{2.5} with dust and sea-salt removed for a 10-km radius buffer.

Variable	Males			Females		
	Rate ratio	95%CI	P	Rate ratio	95%CI	P
Smoking	4.41	2.53-7.68	< 0.001	10.3	5.47-19.4	< 0.001
Log(GNI)	0.92	0.84-1.02	0.11	0.83	0.73-0.94	0.004
Log(PM _{2.5})	1.06	0.93-1.19	0.39	1.03	0.92-1.16	0.60

GNI, gross national income per capita; PM_{2.5}, particulate matter <2.5µm aerodynamic diameter.