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Chronic airflow obstruction and ambient particulate air pollution

Andre F S Amaral ¹, Peter G J Burney,¹ Jaymini Patel,¹ Cosetta Minelli ¹, Filip Mejza ², David M Mannino,³ Terence A R Seemungal,⁴ Padukudru Anand Mahesh ⁵, Li Cher Lo,⁶ Christer Janson ⁷, Sanjay Juvekar,⁸ Meriam Denguezli,⁹ Imed Harrabi,⁹ Emiel F M Wouters,¹⁰ Hamid Cherkaski,¹¹ Kevin Mortimer ^{12,13}, Rain Jogi,¹⁴ Eric D Bateman,¹⁵ Elaine Fuertes ¹, Mohammed Al Ghobain,¹⁶ Wan Tan,¹⁷ Daniel O Obaseki,¹⁸ Asma El Sony,¹⁹ Michael Studnicka,²⁰ Althea Aquart-Stewart,²¹ Parvaiz Koul,²² Herve Lawin,²³ Asaad Ahmed Nafees,²⁴ Olayemi Awopeju,¹⁸ Gregory E Erhabor,¹⁸ Thorarinn Gislason,^{25,26} Tobias Welte,²⁷ Amund Gulsvik,²⁸ Rune Nielsen,^{28,29} Louisa Gnatiuc,³⁰ Ali Kocabas,³¹ Guy B Marks ^{32,33}, Talant Sooronbaev,³⁴ Bertrand Hugo Mbatchou Ngahane,³⁵ Cristina Barbara,³⁶ A Sonia Buist,³⁷ The BOLD (Burden of Obstructive Lung Disease) Collaborative Research Group

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For numbered affiliations see end of article.

Correspondence to

Dr Andre F S Amaral, National Heart and Lung Institute, Imperial College London, London SW3 6LR, UK; a.amaral@imperial.ac.uk

AFSA and PGJB are joint first authors.

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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

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

Continued

Table 1 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) 10 km radius buffer (µg/m ³)
Portugal (Lisbon)	26/08/2008	13.9	9.5	61.6	22.1	25590	14	10.9	6.5
Saudi Arabia (Riyadh)	06/10/2012	3.5	2.8	48.3	2.2	51250	64	64.1	13.0
South Africa (Uitsig-Ravensmead)	05/04/2005	23.8	16.2	84.4	57.9	9610	8	7.5	4.5
Sri Lanka	28/09/2013	11.7	3.9	48.9	0.2	10370	15	14.2	10
Sudan (Gezeira)	25/04/2016	5.6	6.0	47.8	1.4	4260	40	40.2	5
Sudan (Khartoum)	25/03/2013	10.4	10.0	38.4	2.9	2690	39	38.4	6
Sweden (Uppsala)	20/03/2007	10.2	8.3	68.5	52.7	41850	8	6.7	7
Trinidad & Tobago	23/06/2015	6.6	6.7	51.3	12.0	33280	7	7.1	1
Tunisia (Sousse)	01/11/2010	8.4	2.0	79.9	9.1	9750	20	17.3	6
Turkey (Adana)	30/12/2003	19.8	9.1	81.0	30.5	9430	32	27.7	17
USA (Lexington, KY)	13/02/2006	13.6	16.2	78.6	54.3	47160	11	9.9	10

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

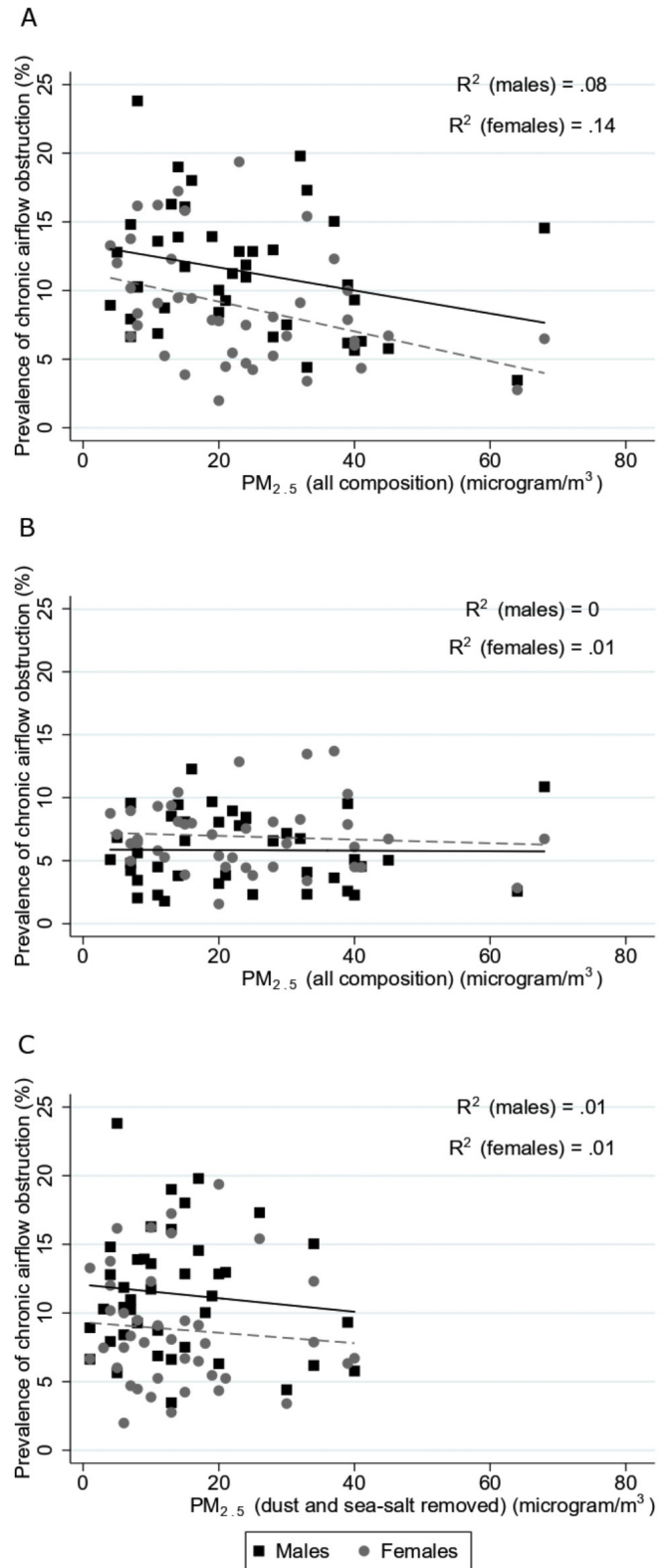


Figure 1 Relation between prevalence of chronic airflow obstruction and annual mean levels of (a) PM_{2.5} (all composition, µg/m³) for the whole sample, (b) PM_{2.5} (all composition, µg/m³) for never smokers and (c) PM_{2.5} (dust and sea-salt removed, µg/m³) for the whole sample.

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; ; PM2.5, 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.

Author affiliations

¹National Heart and Lung Institute, Imperial College London, London, UK

²Centre for Evidence Based Medicine, 2nd Department of Internal Medicine, Jagiellonian University Medical College, Krakow, Poland

³Preventive Medicine and Environmental Health, University of Kentucky, Lexington, Kentucky, USA

⁴Clinical Medical Sciences, The University of the West Indies at St Augustine, Saint Augustine, Tunapuna-Piarco, Trinidad and Tobago

⁵Respiratory Medicine, JSS Medical College and Hospital, Mysore, Karnataka, India

⁶Department of Medicine, RCSI & UCD Malaysia Campus, Georgetown, Pulau Pinang, Malaysia

⁷Respiratory, Allergy and Sleep Research, Department of Medical Sciences, Uppsala University, Uppsala, Sweden

⁸Vadu Rural Health Program, King Edward Memorial Hospital Pune, Pune, Maharashtra, India

⁹Laboratoire de Physiologie et des Explorations Fonctionnelles, Université de Sousse Faculté de Médecine de Sousse, Sousse, Tunisia

¹⁰Department of Respiratory Medicine, Maastricht University, Maastricht, The Netherlands

¹¹Service de Epidémiologie et Médecine Préventive, Université Badji Mokhtar Annaba Faculté de Médecine, Annaba, Algeria

¹²Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool, UK

¹³Respiratory Medicine, Aintree University Hospitals NHS Foundation Trust, Liverpool, UK

¹⁴Lung Clinic, Tartu University Hospital, Tartu, Estonia

¹⁵Division of Respiratory Medicine, University of Cape Town, Rondebosch, Western Cape, South Africa

¹⁶Department of Medicine, King Saud bin Abdulaziz University for Health Sciences & King Abdullah International Medical Research Centre, Riyadh, Saudi Arabia

¹⁷iCAPTURE Centre, The University of British Columbia, Vancouver, Ontario, Canada

¹⁸Medicine, Obafemi Awolowo University, Ile-Ife, Osun, Nigeria

¹⁹Director, Epi-Lab, Khartoum, Sudan

²⁰Department of Pulmonary Medicine, Paracelsus Medical University Salzburg, Salzburg, Austria

²¹Department of Internal Medicine, The University of the West Indies at Mona, Mona, Saint Andrew, Jamaica

²²Pulmonary Medicine, SKIMS, Srinagar, Jammu and Kashmir, India

²³Occupational and Environmental Health, University of Abomey-Calavi, Cotonou, Littoral, Benin

²⁴Community Health Sciences, Aga Khan University, Karachi, Pakistan

²⁵Department of Sleep, Landspítali University Hospital, Reykjavik, UK

²⁶Medicine, University of Iceland, Reykjavik, Iceland

²⁷Respiratory Medicine, Medizinische Hochschule Hannover, Hannover, Germany

²⁸Department of Thoracic Medicine, Haukeland University Hospital, Bergen, Norway

²⁹Department of Clinical Science, University of Bergen, Bergen, Norway

³⁰Nuffield Department of Population Health, Oxford University, Oxford, UK

³¹Department of Chest Disease, Cukurova University, School of Medicine, Adana, Turkey

³²Respiratory and Environmental Epidemiology, Woolcock Institute of Medical Research, Glebe, New South Wales, Australia

³³South Western Sydney Clinical School, University of New South Wales, Sydney, New South Wales, Australia

³⁴Department of Respiratory Medicine, National Center for Cardiology and Internal Medicine, Bishkek, Kyrgyzstan

³⁵Internal Medicine, Douala General Hospital, Douala, Cameroon

³⁶Institute of Environmental Health, Lisbon Medical School, Lisbon University, Lisboa, Portugal

³⁷Pulmonary and Critical Care Medicine, Oregon Health & Science University, Portland, Oregon, USA

Twitter Andre F S Amaral @andresamaral and Guy B Marks @Marks1Guy

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Collaborators The BOLD (Burden of Obstructive Lung Disease) Collaborative Research Group members: Albania: Hasan Hafizi (PI), Anila Aliko, Donika Bardhi, Holta Tafa, Natasha Thanasi, Arian Mezini, Alma Teferici, Dafina Todri, Jolanda Nikolla, and Rezarta Kazasi (Tirana University Hospital Shefqet Ndroqi, Albania); Algeria: Hamid Hacene Cherkaski (PI), Amira Bengraït, Tabarek Haddad, Ibtissem Zgaoula, Maamar Ghit, Abdelhamid Roubhia, Soumaya Boudra, Feryal Atoui, Randa Yakoubi, Rachid Benali, Abdelghani Bencheikh, and Nadia Ait-Khaled (Faculté de Médecine Annaba, Service de Epidémiologie et Médecine Préventive, El Hadjar, Algeria); Australia: Christine Jenkins (PI), Guy Marks (PI), Tessa Bird, Paola Espinel, Kate Hardaker, Brett Toelle (Woolcock Institute of Medical Research, Sidney, Australia); Austria: Michael Studnicka (PI), Torkil Dawes, Bernd Lamprecht, and Lea Schirhofer (Department of Pulmonary Medicine, Paracelsus Medical University, Salzburg, Austria); Bangladesh: Akramul Islam (PI), Syed Masud Ahmed (Co-PI), Shayla Islam, Qazi Shafayetul Islam, Mesbah-Ul-Haque, Tridib Roy Chowdhury, Sukantha Kumar Chatterjee, Dulal Mia, Shyamal Chandra Das, Mizanur Rahman, Nazrul Islam, Shahaz Uddin, Nurul Islam, Luiza Khatun, Monira Parvin, Abdul Awal Khan, and Maidul Islam (James P. Grant School of Public Health, BRAC [Building Resources Across Communities] University, Institute of Global Health, Dhaka, Bangladesh); Benin: Herve Lawin (PI), Arsene Kpangon, Karl Kpoussou, Gildas Agodokpessi, Paul Ayelo, Benjamin Fayomi (Unit of Teaching and Research in Occupational and Environmental Health, University of Abomey Calavi, Cotonou, Benin); Cameroon: Bertrand Mbatchou (PI), Atongno Humphrey Ashu (Douala General Hospital, Douala, Cameroon); Canada: Wan C. Tan (PI) and Christine Lo (Center for Heart Lung Innovation, University of British Columbia, Vancouver, BC, Canada); China: NanShan Zhong (Principal Investigator [PI]), Shengming Liu, Jiachun Lu, Pixian Ran, Dali Wang, Jingping Zheng, and Yumin Zhou (Guangzhou Institute of Respiratory Diseases, Guangzhou Medical College, Guangzhou, China); Estonia: Rain Jõgi (PI), Hendrik Laja, Katrin Ulst, Vappu Zobel, and Toomas-Julius Lill (Lung Clinic, Tartu University Hospital, Tartu, Estonia); Gabon: Ayola Akim Adegnika (PI) (Centre de Recherches Médicales de Lambarene, Lambarene, Gabon); Germany: Tobias Velte (PI), Isabelle Bodemann, Henning Geldmacher, and Alexandra Schweda-Linow (Hannover Medical School, Hannover, Germany); Iceland: Thorarinn Gislason (PI), Bryndis Benediktsdottir, Kristin Jörundsdottir, Lovisa Gudmundsdottir, Sigrun Gudmundsdottir, and Gunnar Gudmundsson, (Department of Allergy, Respiratory Medicine, and Sleep, Landspítali University Hospital, Reykjavik, Iceland); India: Mahesh Rao (PI) (JSS Medical College, Mysuru, India); Parvaiz A Koul (PI), Sajjad Malik, Nissar A Hakim, and Umar Hafiz Khan (Sher-i-Kashmir Institute of Medical Sciences, Srinagar, J&K, India); Rohini Chowgule (PI), Vasant Shetye, Jonelle Raphael, Rosel Almeda, Mahesh Tawde, Rafiq Tadvi, Sunil Katkar, Milind Kadam, Rupesh Dhanawade, and Umesh Ghurup (Indian Institute of Environmental Medicine, Mumbai, India); Sanjay Juvekar (PI), Siddhi Hirve, Somnath Sambhudas, Bharat Chaidhary, Meera Tambe, Savita Pingale, Arati Umap, Archana Umap, Nitin Shelar, Sampada Devchakke, Sharda Chaudhary, Suvarna Bondre, Savita Walke, Ashlesha Gawhane, Anil Sapkal, Rupali Argade, and Vijay Gaikwad (Vadu Health and Demographic Surveillance System, King Edward Memorial Hospital Research Centre Pune, Pune India); Sundeep Salvi (PI), Bill Brashier, Jyoti Londhe, and Sapna Madas (Chest Research Foundation, Pune India); Jamaica: Althea Aquart-Stewart (PI), Akosua Francia Aikman (University of the West Indies, Kingston, Jamaica); Kyrgyzstan: Talant M. Sooronbaev (PI), Bermet M. Estebeasova, Meerim Akmatalieva, Saadat Usenbaeva, Jypara Kydyrova, Eliza Bostonova, Ulan Sheraliev, Nuridin Marajapov, Nurgul Toktogulova, Berik Emilov, Toktogul Azilova, Gulnara Beishekeeva, Nasyikat Dononbaeva, and Aijamal Tabyshova (Pulmonology and Allergology Department, National Centre of Cardiology and Internal Medicine, Bishkek, Kyrgyzstan); Malawi: Kevin Mortimer (PI), Wezzie Nyapigoti, Ernest Mwangoka, Mayamiko Kambwili, Martha Chipeta, Gloria Banda, Suzgo Mkandawire, and Justice Banda (the Malawi Liverpool Wellcome Trust, Blantyre, Malawi); Malaysia: Li-Cher Loh (PI), Abdul Rashid, and Siti Sholehah (RCSI & UCD Malaysia Campus, Penang, Malaysia); Morocco: Mohamed C Benjelloun (PI), Chakib Nejari, Mohamed Elbiaze, and Karima El Rhazi (Laboratoire d'épidémiologie, Recherche Clinique et Santé Communautaire, Fès, Morocco); Netherlands: E.F.M. Wouters and Lowie Vanfleteren (Maastricht University Medical Centre, Maastricht, the Netherlands); Nigeria: Daniel Obaseki (PI), Gregory Erhabor, Olayemi Awopeju, and Olufemi Adewole (Obafemi Awolowo University, Ile-Ife, Nigeria); Norway: Amund Gulsvik (PI), Tina Endresen, and Lene Svendsen (Department of Thoracic Medicine, Institute of Medicine, University of Bergen, Bergen, Norway); Pakistan: Asaad A. Nafees (PI) Muhammad Irfan, Zafar Fatmi, Aysha Zahidie, Natasha Shaukat and Meesha Iqbal (Aga Khan University, Karachi, Pakistan); Philippines: Luisito F. Idolor (PI), Teresita S. de Guia, Norberto A. Francisco, Camilo C. Roa, Fernando G. Ayuyao, Cecil Z. Tady, Daniel T. Tan, Sylvia Banal-Yang, Vincent M. Balanag, Jr., Maria Teresita N. Reyes, and Renato B. Dantes (Lung Centre of the Philippines, Philippine General Hospital, Nampicuan and Talugtug, the Philippines); Renato B. Dantes (PI), Lourdes Amarillo, Lakan U. Berratio, Lenora C. Fernandez, Norberto A. Francisco, Gerard S. Garcia, Teresita S. de Guia, Luisito F. Idolor, Sullian S. Naval, Thessa Reyes, Camilo C. Roa, Jr., Ma. Flordeliza Sanchez, and Leander P. Simpao (Philippine College of Chest

Physicians, Manila, the Philippines); Poland: Ewa Nizankowska Mogilnicka (PI), Jakub Frey, Rafal Harat, Filip Mejza, Pawel Nastalek, Andrzej Pajak, Wojciech Skucha, Andrzej Szczeklik, and Magda Twardowska, (Division of Pulmonary Diseases, Department of Medicine, Jagiellonian University School of Medicine, Krakow, Poland); Portugal: Cristina Bárbara (PI), Fátima Rodrigues, Hermínia Dias, João Cardoso, João Almeida, Maria João Matos, Paula Simão, Moutinho Santos, and Reis Ferreira (the Portuguese Society of Pneumology, Lisbon, Portugal); Saudi Arabia: M. Al Ghobain (PI), H. Alorainy (PI), E. El-Hamad, M. Al Hajjaj, A. Hashi, R. Dela, R. Fanuncio, E. Doloriel, I. Marciano, and L. Safia (Saudi Thoracic Society, Riyadh, Saudi Arabia); South Africa: Eric Bateman (PI), Anamika Jithoo (PI), Desiree Adams, Edward Barnes, Jasper Freeman, Anton Hayes, Siphohle Hengwa, Christine Johannisen, Mariana Koopman, Innocentia Louw, Ina Ludick, Alta Olckers, Johanna Ryck, and Janita Storbeck, (University of Cape Town Lung Institute, Cape Town, South Africa); Sri Lanka: Kirithi Gunasekera (PI), Rajitha Wickremasinghe (Medical Research Institute, Central Chest Clinic, Colombo, Sri Lanka); Sudan: Asma Elsony (PI), Hana A. Elsadig, Nada Bakery Osman, Bandar Salah Noory, Monjda Awad Mohamed, Hasab Alrasoul Akasha Ahmed Osman, Namarig Moham ed Elhassan, Abdel Mu'is El Zain, Marwa Mohamed Mohamaden, Suhaiba Khalifa, Mahmoud Elhadi, Mohand Hassan, and Dalia Abdelmonam (the Epidemiological Laboratory, Khartoum, Sudan); Sweden: Christer Janson (PI), Inga Sif Olafsdottir, Katarina Nisser, Ulrike Spetz Nyström, Gunilla Hägg, and Gun-Marie Lund (Department of Medical Sciences: Respiratory Medicine and Allergology, Uppsala University, Uppsala, Sweden); Trinidad and Tobago: Terence Seemungal (PI), Fallon Lutchmansingh, Liane Conyette (University of the West Indies, St. Augustine, Trinidad and Tobago); Tunisia: Imed Harrabi (PI), Myriam Denguezli, Zouhair Tabka, Hager Daldoul, Zaki Boukheroufa, Firas Chouikha, and Wahbi Belhaj Khalifa (University Hospital Farhat Hached, Faculté de Médecine, Sousse, Tunisia); Turkey: Ali Kocabaş (PI), Atilla Hancocklu, Ismail Hanta, Sedat Kuleci, Ahmet Sinan Turkyilmaz, Sema Umut, and Turgay Unalan (Department of Chest Diseases, Cukurova University School of Medicine, Adana, Turkey); United Kingdom: Peter GJ Burney (PI), Anamika Jithoo, Louisa Gnatiuc, Hadia Azar, Jaymini Patel, Caron Amor, James Potts, Michael Tumilty, and Fiona McLean, Risha Dudhaiya (National Heart and Lung Institute, Imperial College London, London, UK); United States of America: A Sonia Buist (PI), (Oregon University of Health Sciences, Portland, OR) Mary Ann McBurnie, William M Vollmer, Suzanne Gillespie (Kaiser Permanente Center for Health Research, Portland, OR); Sean Sullivan (University of Washington, Seattle, WA); Todd A Lee, Kevin B Weiss, (Northwestern University, Chicago, IL); Robert L Jensen, Robert Crapo (Latter Day Saints Hospital, Salt Lake City, Utah); Paul Enright (University of Arizona, Tucson, AZ); David M. Mannino (PI), John Cain, Rebecca Copeland, Dana Hazen, and Jennifer Methvin, (University of Kentucky, Lexington, KY).

Contributors AFSA, CM and PGJB analysed the data. AFSA and PGJB drafted the manuscript. AFSA, PGJB, JP, CM, FM, DM, TARS, MPA, LCL, CJ, SJ, MD, IH, EFMW, HC, KM, RJ, EDB, EF, MAG, WT, DO, AES, MS, AAS, PK, HL, AAN, OA, GE, TG, TW, AG, RN, LG, AK, GM, TS, BMN, CB and ASB discussed the results, read and approved the final manuscript.

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ORCID iDs

Andre F S Amaral <http://orcid.org/0000-0002-0369-9449>

Cosetta Minelli <http://orcid.org/0000-0001-9166-3958>

Filip Mejza <http://orcid.org/0000-0002-5615-5867>

Padukudru Anand Mahesh <http://orcid.org/0000-0003-1632-5945>

Christer Janson <http://orcid.org/0000-0001-5093-6980>

Kevin Mortimer <http://orcid.org/0000-0002-8118-8871>

Elaine Fuertes <http://orcid.org/0000-0003-0205-9025>

Guy B Marks <http://orcid.org/0000-0002-8976-8053>

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1 [Online supplement](#)

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

3

4 André F.S. Amaral^{1*}, Peter Burney^{1*}, Jaymini Patel¹, Cosetta Minelli¹, Filip Mejza², David Mannino³,
5 Terence Seemungal⁴, Mahesh PA⁵, Li Cher Loh⁶, Christer Janson⁷, Sanjay Juvekar⁸, Meriam
6 Denguezli⁹, Imed Harrabi¹⁰, Emiel F.M. Wouters¹¹, Hamid Chersaki¹², Kevin Mortimer¹³, Rain Jögi¹⁴,
7 Eric Bateman¹⁵, Elaine Fuertes¹, Mohamed Al Ghobain¹⁶, Wan Tan¹⁷, Daniel Obaseki¹⁸, Asma El
8 Sony¹⁹, Michael Studnicka²⁰, Althea Aquart-Stewart²¹, Parvaiz Koul²², Hervé Lawin²³, Asaad Ahmed
9 Nafees²⁴, Olayemi Awopeju¹⁸, Gregory Erhabor¹⁸, Thorarinn Gislason^{25,26}, Tobias Welte²⁷, Amund
10 Gulsvik²⁸, Rune Nielsen^{28,29}, Louisa Gnatiuc³⁰, Ali Koçabas³¹, Guy Marks^{32,33}, Talant Sooronbaev³⁴,
11 Bertrand Hugo Mbatchou Ngahane³⁵, Cristina Bárbara³⁶, A Sonia Buist³⁷

12 *Co-first authors

13

14 1 National Heart and Lung Institute, Imperial College London, London, UK

15 2 Centre for Evidence Based Medicine, 2nd Department of Internal Medicine, Jagiellonian University
16 Medical College, Kraków, Poland

17 3 University of Kentucky, Lexington, KY, USA

18 4 Faculty of Medical Sciences, University of West Indies, St Augustine, Trinidad and Tobago

19 5 Department of Respiratory Medicine, JSS Medical College, Mysore, India

20 6 Department of Medicine, RCSI & UCD Malaysia Campus, Penang, Malaysia

21 7 Department of Medical Sciences: Respiratory, Allergy and Sleep Research, Uppsala University,
22 Uppsala, Sweden

23 8 Vadu Rural Health Program (VRHP), KEM Hospital Research Centre, Pune, India

24 9 Laboratoire de Physiologie et des Explorations Fonctionnelles, Faculté de Médecine de Sousse,
25 Université de Sousse, Sousse, Tunisia

26 10 Faculté de Médecine, Université de Sousse, Sousse, Tunisia

- 27 11 Maastricht University Medical Center, Maastricht, The Netherlands
- 28 12 Faculté de Médecine de Annaba, Service de Epidémiologie et Médecine Préventive, El Hadjar,
- 29 Algeria
- 30 13 Liverpool School of Tropical Medicine, Liverpool, UK
- 31 14 Lung Clinic, Tartu University Hospital, Tartu, Estonia
- 32 15 University of Cape Town Lung Institute, Cape Town, South Africa
- 33 16 Department of Medicine, King Saud bin Abdulaziz University for Health Sciences & King Abdullah
- 34 International Medical Research Centre, Riyadh, Saudi Arabia
- 35 17 Centre for Heart Lung Innovation, University of British Columbia, Vancouver, BC, Canada
- 36 18 Obafemi Awolowo University, Ile-Ife, Nigeria
- 37 19 The Epidemiological Laboratory, Khartoum, Sudan
- 38 20 Department of Pneumology, Paracelsus Medical University, Salzburg, Austria
- 39 21 University of the West Indies, Kingston, Jamaica
- 40 22 Sher-i-Kashmir Institute of Medical Sciences, Srinagar, J&K, India
- 41 23 Occupational and Environmental Health, University of Abomey Calavi, Cotonou, Benin
- 42 24 Department of Community Health Sciences, Aga Khan University, Karachi, Pakistan
- 43 25 Department of Sleep, Landspítali - The National University Hospital of Iceland, Reykjavik, Iceland
- 44 26 University of Iceland, Faculty of Medicine, Reykjavik, Iceland
- 45 27 Hannover Medical School, Hannover, Germany
- 46 28 Department of Thoracic Medicine, Haukeland University Hospital, Bergen, Norway
- 47 29 Department of Clinical Science, University of Bergen, Bergen, Norway
- 48 30 Nuffield Department of Population Health, Oxford University, Oxford, UK
- 49 31 Department of Chest Disease. Cukurova University School of Medicine. Adana, Turkey
- 50 32 Woolcock Institute of Medical Research, Sydney, NSW, Australia
- 51 33 South Western Sydney Clinical School, University of New South Wales, Sydney, Australia

52 34 Department of Respiratory Medicine, National Center for Cardiology and Internal Medicine,

53 Bishkek, Kyrgyzstan

54 35 Douala General Hospital, Douala, Cameroon

55 36 Institute of Environmental Health, Lisbon Medical School, Lisbon University, Lisbon, Portugal

56 37 Oregon Health & Science University, Portland, OR, USA

57

58 **Corresponding author:**

59 Andre F.S. Amaral

60 National Heart and Lung Institute, Imperial College London

61 London SW3 6LR, UK

62 a.amaral@imperial.ac.uk

63

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65 **Table of content**

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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.

97

98

99

100 **Statistical analysis**

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

110

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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.

131

132 **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	<i>P</i>	Rate ratio	95%CI	<i>P</i>
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

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

134

135

136 **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	<i>P</i>	Rate ratio	95%CI	<i>P</i>
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

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

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139

140 **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	<i>P</i>	Rate ratio	95%CI	<i>P</i>
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

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

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