OPEN ACCESS

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

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/thoraxjnl-2020-216223).

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.

Received 17 September 2020
Revised 4 March 2021
Accepted 8 April 2021
Published Online First 11 May 2021

To cite: Amaral AFS, Burney PGJ, Patel J, *et al*. *Thorax* 2021;**76**:1236–1241.

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/m^3 in Reykjavik (Iceland) to 68 µg/m^3 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

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	10 750	25	16.7	15	10.0
Algeria (Annaba)	28/06/2012	9.3	4.5	76.5	0.7	13 230	21	14.5	8	5.5
Australia (Sydney)	30/07/2006	7.9	13.8	60.8	47.5	32 970	7	6.6	4	4.0
Austria (Salzburg)	11/01/2005	12.8	19.4	64.4	44.3	34 940	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	31 540	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	35 240	15	15.3	13	13.2
Estonia (Tartu)	25/02/2009	8.7	5.2	63.8	31.5	19 880	12	10.7	11	9.4
Germany (Hannover)	16/07/2005	10.0	7.8	73.1	50	32 350	20	20.0	18	18.2
Iceland (Reykjavik)	28/04/2005	8.9	13.3	70.7	61.3	35 470	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	23 470	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	45 110	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	48 300	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	13 650	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/m³)	$PM_{2.5}$ (all composition) 10 km radius buffer (µg/m³)	$PM_{2.5}$ (dust and sea-salt removed) (µg/m³)	$PM_{2.5}$ (dust and sea-salt removed) 10 km radius buffer (µg/m³)
Portugal (Lisbon)	26/08/2008	13.9	9.5	61.6	22.1	25 590	14	10.9	8	6.5
Saudi Arabia (Riyadh)	06/10/2012	3.5	2.8	48.3	2.2	51 250	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	10 370	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	41 850	8	6.7	7	5.7
Trinidad & Tobago	23/06/2015	6.6	6.7	51.3	12.0	33 280	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	47 160	11	9.9	10	9.7

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

shown clear independent associations with the 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

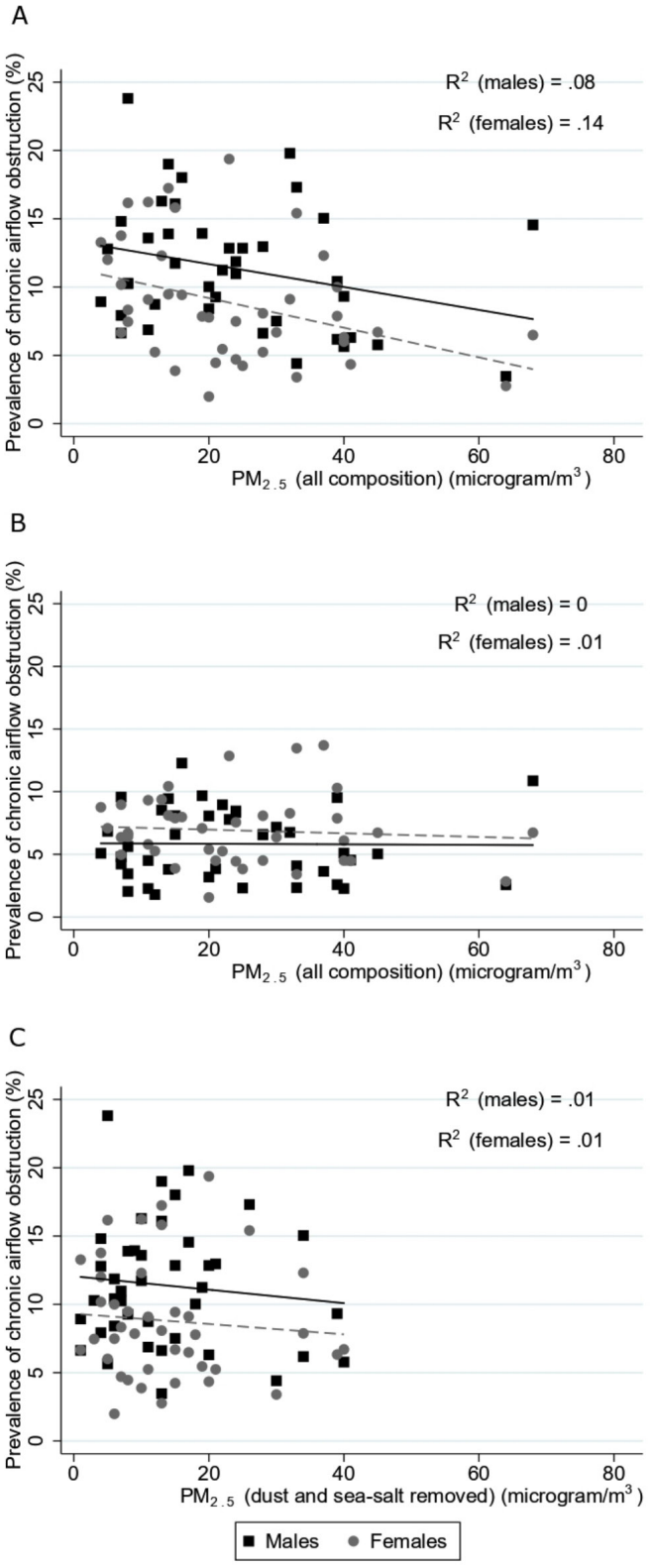

Figure 1 Relation between prevalence of chronic airflow obstruction and annual mean levels of (a) $PM_{2.5}$ (all composition, µg/m³) for the whole sample, (B) $PM_{2.5}$ (all composition, µg/m³) for never smokers and (C) $PM_{2.5}$ (dust and sea-salt removed, µg/m³) for the whole sample.

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

	men			women		
Variable	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.

that indoor burning of solid fuels, another source of $PM_{2.5}$, is 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 FEV_1/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 spirograms 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 smoking[12] and poverty[13] 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/m^3 in Reykjavik (Iceland) to 68 µg/m^3 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 properties[15] or sources[16] 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
[1]National Heart and Lung Institute, Imperial College London, London, UK
[2]Centre for Evidence Based Medicine, 2nd Department of Internal Medicine, Jagiellonian University Medical College, Krakow, Poland
[3]Preventive Medicine and Environmental Health, University of Kentucky, Lexington, Kentucky, USA
[4]Clinical Medical Sciences, The University of the West Indies at St Augustine, Saint Augustine, Tunapuna-Piarco, Trinidad and Tobago
[5]Respiratory Medicine, JSS Medical College and Hospital, Mysore, Karnataka, India
[6]Department of Medicine, RCSI & UCD Malaysia Campus, Georgetown, Pulau Pinang, Malaysia
[7]Respiratory, Allergy and Sleep Research, Department of Medical Sciences, Uppsala University, Uppsala, Sweden
[8]Vadu Rural Health Program, King Edward Memorial Hospital Pune, Pune, Maharashtra, India
[9]Laboratoire de Physiologie et des Explorations Fonctionnelles, Universite de Sousse Faculte de Medecine de Sousse, Sousse, Tunisia
[10]Department of Respiratory Medicine, Maastricht University, Maastricht, The Netherlands
[11]Service de Epidemiologie et Medecine Preventive, Universite Badji Mokhtar Annaba Faculte de Medecine, Annaba, Algeria
[12]Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool, UK
[13]Respiratory Medicine, Aintree University Hospitals NHS Foundation Trust, Liverpool, UK
[14]Lung Clinic, Tartu University Hospital, Tartu, Estonia
[15]Division of Respiratory Medicine, University of Cape Town, Rondebosch, Western Cape, South Africa
[16]Department of Medicine, King Saud bin Abdulaziz University for Health Sciences & King Abdullah International Medical Research Centre, Riyadh, Saudi Arabia
[17]iCAPTURE Centre, The University of British Columbia, Vancouver, Ontario, Canada
[18]Medicine, Obafemi Awolowo University, Ile-Ife, Osun, Nigeria
[19]Director, Epi-Lab, Khartoum, Sudan
[20]Department of Pulmonary Medicine, Paracelsus Medical University Salzburg, Salzburg, Austria
[21]Department of Internal Medicine, The University of the West Indies at Mona, Mona, Saint Andrew, Jamaica
[22]Pulmonary Medicine, SKIMS, Srinagar, Jammu and Kashmir, India
[23]Occupational and Environmental Health, University of Abomey-Calavi, Cotonou, Littoral, Benin
[24]Community Health Sciences, Aga Khan University, Karachi, Pakistan
[25]Department of Sleep, Landspitali University Hospital, Reykjavik, UK
[26]Medicine, University of Iceland, Reykjavik, Iceland
[27]Respiratory Medicine, Medizinische Hochschule Hannover, Hannover, Germany
[28]Department of Thoracic Medicine, Haukeland University Hospital, Bergen, Norway
[29]Department of Clinical Science, University of Bergen, Bergen, Norway
[30]Nuffield Department of Population Health, Oxford University, Oxford, UK
[31]Department of Chest Disease, Cukurova University, School of Medicine, Adana, Turkey
[32]Respiratory and Environmental Epidemiology, Woolcock Institute of Medical Research, Glebe, New South Wales, Australia
[33]South Western Sydney Clinical School, University of New South Wales, Sydney, New South Wales, Australia
[34]Department of Respiratory Medicine, National Center for Cardiology and Internal Medicine, Bishkek, Kyrgyzstan
[35]Internal Medicine, Douala General Hospital, Douala, Cameroon
[36]Institute of Environmental Health, Lisbon Medical School, Lisbon University, Lisboa, Portugal
[37]Pulmonary and Critical Care Medicine, Oregon Health & Science University, Portland, Oregon, USA

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

Acknowledgements The authors thank the participants and field workers of this study for their time and cooperation, and the BOLD (Burden of Obstructive Lung Disease) Coordinating Centre members for their technical and scientific support.

Collaborators The BOLD (Burden of Obstructive Lung Disease) Collaborative Research Group membersAlbania: 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 Bengrait, 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 Kpossou, 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, Pixin 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 Medicale de Lambarene, Lambarene, Gabon); Germany: Tobias Welte (PI), Isabelle Bodemann, Henning Geldmacher, and Alexandra Schweda-Linow (Hannover Medical School, Hannover, Germany); Iceland: Thorarinn Gislason (PI), Bryndis Benedikdtsdottir, Kristin Jörundsdottir, Lovisa Gudmundsdottir, Sigrun Gudmundsdottir, and Gunnar Gundmundsson, (Department of Allergy, Respiratory Medicine, and Sleep, Landspitali 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, Ashleshsa 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. Estebesova, Meerim Akmatalieva, Saadat Usenbaeva, Jypara Kydyrova, Eliza Bostonova, Ulan Sheraliev, Nuridin Marajapov, Nurgul Toktogulova, Berik Emilov, Toktogul Azilova, Gulnara Beishekeeva, Nasyikat Dononbaeva, and AijamalTabyshova (Pulmunology 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 Nejjari, 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 Center, 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, Sipho Hlengwa, 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: Kirthi 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), Attila Hancioglu, 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.

Funding Supported by Wellcome Trust grant 085790/Z/08/Z for the BOLD (Burden of Obstructive Lung Disease) Study. The initial BOLD programprogramme was funded in part by unrestricted educational grants to the Operations CenterCentre in Portland, Oregon from Altana, Aventis, AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Merck, Novartis, Pfizer, Schering-Plough, Sepracor, and the University of Kentucky (Lexington, KY). A full list of local funders can be found at https://www.boldstudy.org.

Competing interests RN reports grants and personal fees from Boehringer Ingelheim, AstraZeneca and Novartis outside the submitted work. EDB reports personal fees from Novartis, AstraZeneca, Orion, Menarirni, Boehringer Ingelheim and ALK outside the submitted work. KM reports grants from GlaxoSmithKline during the conduct of the study. TW reports grants from Boehringer Ingelheim and Pfizer during the conduct of the study. FM reports fees from Medycyba Praktyczna, Sandoz and Chiesi outside the submitted work. DM reports salary and shares from GlaxoSmithKline outside the submitted work. IH reports grants from Boehringer Ingelheim during the conduct of the study.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

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

REFERENCES

1 GBD 2015 Chronic Respiratory Disease Collaborators. Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990-2015: a systematic analysis for the global burden of disease study 2015. *Lancet Respir Med* 2017;5:691–706.
2 Morgenstern H. Ecologic studies in epidemiology: concepts, principles, and methods. *Annu Rev Public Health* 1995;16:61–81.
3 Buist AS, Vollmer WM, Sullivan SD, *et al*. The burden of obstructive lung disease initiative (BOLD): rationale and design. *COPD* 2005;2:277–83.
4 World Bank. Gni per capita, ppp (current international $). Available: https://databank.worldbank.org/indicator/NY.GNP.PCAP.CD/1ff4a498/Popular-Indicators [Accessed 19 Oct 2019].
5 Atmospheric Composition Analysis Group. Surface PM2.5. Available: http://fizz.phys.dal.ca/~atmos/martin/?page_id=140 [Accessed 18 Feb 2020].
6 van Donkelaar A, Martin RV, Brauer M, *et al*. Global estimates of fine particulate matter using a combined Geophysical-Statistical method with information from satellites, models, and monitors. *Environ Sci Technol* 2016;50:3762–72.
7 Amaral AFS, Patel J, Kato BS, *et al*. Airflow obstruction and use of solid fuels for cooking or heating: BOLD results. *Am J Respir Crit Care Med* 2018;197:595–610.
8 Smith M, Li L, Augustyn M, *et al*. Prevalence and correlates of airflow obstruction in ~317,000 never-smokers in China. *Eur Respir J* 2014;44:66–77.
9 Fang L, Gao P, Bao H, *et al*. Chronic obstructive pulmonary disease in China: a nationwide prevalence study. *Lancet Respir Med* 2018;6:421–30.
10 Wang C, Xu J, Yang L, *et al*. Prevalence and risk factors of chronic obstructive pulmonary disease in China (the China Pulmonary Health [CPH] study): a national cross-sectional study. *Lancet* 2018;391:1706–17.
11 Schikowski T, Adam M, Marcon A, *et al*. Association of ambient air pollution with the prevalence and incidence of COPD. *Eur Respir J* 2014;44:614–26.
12 Buist AS, McBurnie MA, Vollmer WM, *et al*. International variation in the prevalence of COPD (the BOLD study): a population-based prevalence study. *Lancet* 2007;370:741–50.
13 Townend J, Minelli C, Mortimer K, *et al*. The association between chronic airflow obstruction and poverty in 12 sites of the multinational BOLD study. *Eur Respir J* 2017;49:1601880.
14 Greenland S, Morgenstern H. Ecological bias, confounding, and effect modification. *Int J Epidemiol* 1989;18:269–74.
15 Künzli N, Mudway IS, Götschi T, *et al*. Comparison of oxidative properties, light absorbance, total and elemental mass concentration of ambient $_{PM2.5}$ collected at 20 European sites. *Environ Health Perspect* 2006;114:684–90.
16 Muala A, Rankin G, Sehlstedt M, *et al*. Acute exposure to wood smoke from incomplete combustion--indications of cytotoxicity. *Part Fibre Toxicol* 2015;12:33.

Online supplement

Chronic airflow obstruction and ambient particulate air pollution

André F.S. Amaral[1*], Peter Burney[1*], Jaymini Patel[1], Cosetta Minelli[1], Filip Mejza[2], David Mannino[3], Terence Seemungal[4], Mahesh PA[5], Li Cher Loh[6], Christer Janson[7], Sanjay Juvekar[8], Meriam Denguezli[9], Imed Harrabi[10], Emiel F.M. Wouters[11], Hamid Chersaki[12], Kevin Mortimer[13], Rain Jögi[14], Eric Bateman[15], Elaine Fuertes[1], Mohamed Al Ghobain[16], Wan Tan[17], Daniel Obaseki[18], Asma El Sony[19], Michael Studnicka[20], Althea Aquart-Stewart[21], Parvaiz Koul[22], Hervé Lawin[23], Asaad Ahmed Nafees[24], Olayemi Awopeju[18], Gregory Erhabor[18], Thorarinn Gislason[25,26], Tobias Welte[27], Amund Gulsvik[28], Rune Nielsen[28,29], Louisa Gnatiuc[30], Ali Koçabas[31], Guy Marks[32,33], Talant Sooronbaev[34], Bertrand Hugo Mbatchou Ngahane[35], Cristina Bárbara[36], A Sonia Buist[37]

*Co-first authors

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

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

3 University of Kentucky, Lexington, KY, USA

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

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

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

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

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

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

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

Amaral AFS, *et al. Thorax* 2021;0:1–6. doi: 10.1136/thoraxjnl-2020-216223

11 Maastricht University Medical Center, Maastricht, The Netherlands

12 Faculté de Médecine de Annaba, Service de Epidémiologie et Médecine Préventive, El Hadjar, Algeria

13 Liverpool School of Tropical Medicine, Liverpool, UK

14 Lung Clinic, Tartu University Hospital, Tartu, Estonia

15 University of Cape Town Lung Institute, Cape Town, South Africa

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

17 Centre for Heart Lung Innovation, University of British Columbia, Vancouver, BC, Canada

18 Obafemi Awolowo University, Ile-Ife, Nigeria

19 The Epidemiological Laboratory, Khartoum, Sudan

20 Department of Pneumology, Paracelsus Medical University, Salzburg, Austria

21 University of the West Indies, Kingston, Jamaica

22 Sher-i-Kashmir Institute of Medical Sciences, Srinagar, J&K, India

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

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

25 Department of Sleep, Landspítali - The National University Hospital of Iceland, Reykjavik, Iceland

26 University of Iceland, Faculty of Medicine, Reykjavik, Iceland

27 Hannover Medical School, Hannover, Germany

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

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

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

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

32 Woolcock Institute of Medical Research, Sydney, NSW, Australia

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

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

35 Douala General Hospital, Douala, Cameroon

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

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

Corresponding author:

Andre F.S. Amaral

National Heart and Lung Institute, Imperial College London

London SW3 6LR, UK

a.amaral@imperial.ac.uk

Table of content

BOLD study details

The BOLD study has been described in detail elsewhere[1]. Briefly, representative samples of the general population over the age of 40 were drawn from a sample of sites taken from around the world. These were drawn so as to represent most of the regions defined by the Global Burden of Disease (the exceptions were Latin America which had a separate study, the high-income countries of Asia, and Oceania) with a bias towards larger regions such as South Asia. All sites received approval from their local ethics committee, and participants provided informed consent. Spirometry was conducted before and after a bronchodilator (200 μg Salbutamol inhaled via a spacer) using a forced manoeuvre and an EasyOne spirometer (ndd Medizintechnik AG, Zurich, Switzerland). All spirometry data were reviewed for quality control during the study in either Salt Lake City or London. CAO was defined as a post-bronchodilator ratio of the forced expiratory volume in the first second (FEV_1) to the forced vital capacity (FVC), less than the lower limit of normal, which was determined using the equations for white Americans in the NHANES III study[2]. Information from participants on several risk factors, including whether they had ever smoked, was collected using a standardised questionnaire.

$PM_{2.5}$ concentrations

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

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 $PM_{2.5}$.

References

1. Buist AS, Vollmer WM, Sullivan SD, et al. The Burden of Obstructive Lung Disease Initiative (BOLD): rationale and design. *Copd* 2005; **2**(2): 277-83.

2. Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general U.S. population. *American journal of respiratory and critical care medicine* 1999; **159**(1): 179-87.

3. Atmospheric Composition Analysis Group. Surface PM2.5. http://fizz.phys.dal.ca/~atmos/martin/?page_id=140 (accessed 18 February 2020).

4. van Donkelaar A, Martin RV, Brauer M, et al. Global Estimates of Fine Particulate Matter using a Combined Geophysical-Statistical Method with Information from Satellites, Models, and Monitors. *Environ Sci Technol* 2016; **50**(7): 3762-72.

5. Burney P, Jithoo A, Kato B, et al. Chronic obstructive pulmonary disease mortality and prevalence: the associations with smoking and poverty--a BOLD analysis. *Thorax* 2014; **69**(5): 465-73.

124 6. Burnett RT, Pope CA, Ezzati M, et al. An integrated risk function for estimating the global
125 burden of disease attributable to ambient fine particulate matter exposure. *Environmental health*
126 *perspectives* 2014; **122**(4): 397-403.
127

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

	Males			Females		
Site	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

N, sample size.

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

	Males			Females		
Variable	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.

	Males			Females		
Variable	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.

	Males			Females		
Variable	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.