

1 **Prevalence and population attributable risk for chronic airflow obstruction in a large**
2 **multinational study**

3 Peter Burney¹, Jaymini Patel¹, Cosetta Minelli¹, Louisa Gnatiuc², André F.S. Amaral¹, Ali
4 Kocabaş³, Hamid Hacene Cherkaski⁴, Amund Gulsvik⁵, Rune Nielsen⁵, Eric Bateman⁶,
5 Anamika Jithoo⁶, Kevin Mortimer⁷, Talant M. Sooronbaev⁸, Hervé Lawin⁹, Chakib Nejjari¹⁰,
6 Mohammed Elbiaze¹¹, Karima El Rhazi¹⁰, Jin-Ping Zheng¹², Pixin Ran¹², Tobias Welte¹³, Daniel
7 Obaseki¹⁴, Gregory Erhabor¹⁴, Asma Elsony¹⁵, Nada Bakri Osman¹⁵, Rana Ahmed¹⁵, Ewa
8 Nizankowska-Mogilnicka¹⁶, Filip Mejza¹⁷, David M. Mannino¹⁸, Cristina Bárbara¹⁹, Wouters
9 E.F.M.²⁰, Luisito F. Idolor²¹, Li-Cher Loh²², Abdul Rashid²², Sanjay Juvekar²³, Thorarinn
10 Gislason^{24,25}, Mohamed Al Ghobain²⁶, Michael Studnicka²⁷, Imed Harrabi²⁸, Meriam
11 Denguezli²⁸, Parvaiz A Koul²⁹, Christine Jenkins^{30,31,32}, Guy Marks^{30,31,32}, Rain Jögi³³, Hasan
12 Hafizi³⁴, Christer Janson³⁵, Wan C. Tan³⁶, Althea Aquart-Stewart³⁷, Bertrand Mbatchou³⁸,
13 Asaad Nafees³⁹, Kirithi Gunasekera⁴⁰, Terry Seemungal⁴¹, Mahesh PA⁴², Paul Enright⁴³,
14 William M. Vollmer⁴⁴, Marta Blangiardo⁴⁵, Fadlalla G. Elfadaly⁴⁶, A Sonia Buist⁴⁷

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

16 **²Nuffield Department of Population Health, University of Oxford, Oxford, UK**

17 **³Cukurova University School of Medicine, Department of Chest Diseases, Adana, Turkey**

18 **⁴Department of Pneumology, Faculty of Medecine and CHU Annaba, Algeria**

19 **⁵Department of Thoracic Medicine, Institute of Medicine, University of Bergen, Bergen,**
20 **Norway**

21 **⁶University of Cape Town Lung Institute, Cape Town, South Africa**

22 **⁷The Malawi Liverpool Wellcome Trust, Blantyre, Malawi**

23 **⁸Pulmonology and Allergology Department, National Centre of Cardiology and Internal**
24 **Medicine, Bishkek, Kyrgyzstan**

25 ⁹Unit of Teaching and Research in Occupational and Environmental Health, Cotonou,
26 Benin

27 ¹⁰Laboratoire d'épidémiologie, Recherche Clinique et Santé Communautaire, Fès, Morocco

28 ¹¹Department of Respiratory Medicine, Faculté de Médecine, University Hospital, Fès,
29 Morocco

30 ¹²State Key Laboratory of Respiratory Disease, National Clinical Research Center For
31 Respiratory Diseases, Guangzhou Institute of Respiratory Health, First Affiliated Hospital
32 of Guangzhou Medical College, Guangzhou, China

33 ¹³Department of Pneumology, Hannover Medical School and German Center of Lung
34 Research, Hannover, Germany

35 ¹⁴Obafemi Awolowo University, Ile-Ife, Nigeria

36 ¹⁵The Epidemiological Laboratory, Khartoum, Sudan

37 ¹⁶Division of Pulmonary Diseases, Department of Medicine, Jagiellonian University School
38 of Medicine, Krakow, Poland

39 ¹⁷Center for Evidence Based Medicine, 2nd Department of Internal Medicine, Jagiellonian
40 University Medical College, Kraków, Poland

41 ¹⁸University of Kentucky, Lexington, Kentucky, USA

42 ¹⁹Institute of Environmental Health, Lisbon Medical School, Lisbon University, Lisbon
43 Portugal

44 ²⁰Maastricht University Medical Center, Maastricht, the Netherlands

45 ²¹ Philippine College of Chest Physicians, Manila, Philippines

46 ²²Royal College of Surgeons in Ireland and University College Dublin Malaysia Campus
47 (RUMC),
48 Penang, Malaysia

- 49 ²³Vadu HDSS, KEM Hospital Research Centre Pune, Pune, India
- 50 ²⁴Landspítali University Hospital, Dept.Sleep, Reykjavik, Iceland
- 51 ²⁵University of Iceland, Faculty of Medicine, Reykjavik, Iceland
- 52 ²⁶Saudi Thoracic Society, Riyadh, Saudi Arabia
- 53 ²⁷Paracelsus Medical University, Department of Pulmonary Medicine, Salzburg, Austria
- 54 ²⁸Faculté de Médecine, Sousse, Tunisia
- 55 ²⁹Sher-i-Kashmir Institute of Medical Sciences, Srinagar, J&K, India
- 56 ³⁰Woolcock Institute of Medical Research, Sydney, Australia
- 57 ³¹University of Sydney, Sydney, New South Wales, Australia
- 58 ³²University of New South Wales, Sydney, New South Wales, Australia
- 59 ³³Lung Clinic, Tartu University Hospital, Tartu, Estonia
- 60 ³⁴Tirana University Hospital "Shefqet Ndroqi", Albania
- 61 ³⁵Department of Medical Sciences, Respiratory, Allergy and Sleep Research, Uppsala
62 University, Sweden
- 63 ³⁶Centre for Heart Lung Innovation, University of British Columbia, Vancouver, BC, Canada
- 64 ³⁷University of the West Indies, Kingston, Jamaica
- 65 ³⁸Douala General Hospital, Douala, Cameroon
- 66 ³⁹Aga Khan Univeristy, Karachi, Pakistan
- 67 ⁴⁰Medical Research Institute, Central Chest Clinic, Colombo, Sri Lanka
- 68 ⁴¹University of the West Indies, St. Augustine, Trinidad and Tobago
- 69 ⁴²JSS University, Mysore, India
- 70 ⁴³University of Arizona, Tucson, AZ
- 71 ⁴⁴Kaiser-Permanente Center for Health Research, Portland OR, USA
- 72 ⁴⁵School of Public Health, Imperial College, London, UK

73 ⁴⁶**School of Mathematics and Statistics, STEM, The Open University, Milton Keynes, UK**

74 ⁴⁷**Oregon Health & Science University, Portland, OR, USA**

75

76 **Funding:** Supported by Wellcome Trust grant 085790/Z/08/Z for the Burden of Obstructive

77 Lung Disease (BOLD) study. The initial BOLD program was funded in part by unrestricted

78 educational grants to the Operations Center in Portland, Oregon from Altana, Aventis,

79 AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Merck, Novartis, Pfizer,

80 Schering-Plough, Sepracor, and the University of Kentucky (Lexington, KY). A full list of local

81 funders can be found at <https://www.boldstudy.org>.

82

83 **Running head:** Population attributable risk for chronic airflow obstruction

84

85 **Descriptor:** 9.6 COPD: Epidemiology

86

87 Main text word count: 3490

88 Abstract word count: 250

89

90 This article has an online data supplement, which is accessible from this issue's table of

91 content online at www.atsjournals.org.

92 **Abstract**

93 **Rationale:** The Global Burden of Disease programme identified smoking, and ambient and
94 household air pollution as the main drivers of death and disability from Chronic Obstructive
95 Pulmonary Disease (COPD).

96 **Objective:** To estimate the attributable risk of chronic airflow obstruction (CAO), a
97 quantifiable characteristic of COPD, due to several risk factors.

98 **Methods:** The Burden of Obstructive Lung Disease study is a cross-sectional study of adults,
99 aged ≥ 40 , in a globally distributed sample of 41 urban and rural sites. Based on data from
100 28,459 participants, we estimated the prevalence of CAO, defined as a post-bronchodilator
101 one-second forced expiratory volume to forced vital capacity ratio $<$ lower limit of normal,
102 and the relative risks associated with different risk factors. Local RR were estimated using a
103 Bayesian hierarchical model borrowing information from across sites. From these RR and
104 the prevalence of risk factors, we estimated local Population Attributable Risks (PAR).

105 **Measurements and Main Results:** Mean prevalence of CAO was 11.2% in men and 8.6% in
106 women. Mean PAR for smoking was 5.1% in men and 2.2% in women. The next most
107 influential risk factors were poor education levels, working in a dusty job for ≥ 10 years, low
108 body mass index (BMI), and a history of tuberculosis. The risk of CAO attributable to the
109 different risk factors varied across sites.

110 **Conclusions:** While smoking remains the most important risk factor for CAO, in some areas
111 poor education, low BMI and passive smoking are of greater importance. Dusty occupations
112 and tuberculosis are important risk factors at some sites.

113 **Introduction**

114 Chronic lung disease is one of the four chronic diseases prioritised by the United Nations.¹

115 The Global Burden of Disease (GBD) programme concluded that in 2010 it was the third
116 most common cause of death, responsible for the 9th highest years of life lost globally,² and
117 the 9th most influential disease in reducing disability-adjusted life-years.³

118 The importance of smoking is well recognised both as a risk factor for chronic airflow
119 obstruction (CAO), an essential component of chronic obstructive pulmonary disease
120 (COPD), and as a risk factor for mortality attributed to COPD.⁴ However, estimates of the
121 proportion of disease caused by smoking have varied widely,⁵ and recognition that many
122 people with CAO have no history of smoking has led to the search for other causes.⁶

123 Genetics, second-hand smoke, outdoor air pollution, indoor air pollution from biomass
124 burning, diet, occupation, tuberculosis and longstanding asthma have all been suggested as
125 additional causes.⁶ The GBD programme has provided comprehensive estimates of the
126 burden of COPD, measured as disability-adjusted life-years lost, attributable to different risk
127 factors, concluding that the most important ones, in order, were smoking, outdoor
128 particulate pollution, household pollution, occupational exposure to particles, exposure to
129 ozone and second-hand tobacco smoke.⁷ However, for most low- and middle-income
130 countries these are based on indirect evidence.

131 We have previously identified the main modifiable risk factors for CAO in the Burden of
132 Obstructive Lung Disease (BOLD) study,⁸ and here we have quantified the local prevalence
133 of CAO that can be attributed to each of these main risk factors in each of 41 sites in 35
134 countries.

135

136

137 **Methods**

138 Study population

139 The BOLD protocol has been published elsewhere.⁹ Representative samples of adults, aged
140 ≥ 40 , were identified from centres with populations of at least 150,000 people. Standardised
141 questionnaires were translated into the local language, back-translated and checked before
142 being administered by trained fieldworkers. Questions were taken from standardised
143 questionnaires, where these were available, and covered respiratory symptoms, smoking
144 and other risk factors, including age, sex, educational attainment, a history of tuberculosis,
145 and a history of working in a dusty job. Height and weight were measured and spirometry
146 was performed using an EasyOne spirometer (ndd Medizintechnik AG, Zurich, Switzerland),
147 before and after the administration of 200 μ g salbutamol via a spacer (Clement Clarke
148 International, Harlow, UK). All spirometry was checked centrally by one of the two
149 pulmonary function reading centres. Tests used had to include at least three acceptable
150 curves (no hesitation, complete blow, no artefact affecting the FEV₁ or FVC), with the two
151 best blows being within 200mL of each other.

152

153

154 Outcome and Exposures

155 We defined CAO as a post-bronchodilator FEV₁/FVC ratio < lower limit of normal using the
156 equations for European Americans in the NHANESIII study.¹⁰ As potential exposures, we
157 analysed the modifiable risk factors for CAO identified in a preliminary analysis of only 14 of
158 the BOLD sites,⁸ omitting self-reported medical conditions and reports of hospitalisation
159 with respiratory disease below the age of 10 as all these can be viewed as the consequences
160 rather than the fundamental causes of CAO.

161 Statistical analysis

162 By population attributable risk (PAR) we mean the excess prevalence of CAO in the
163 population that is attributable to a risk factor. We estimated the PAR for each of the
164 following: body mass index (BMI) (underweight, normal weight, overweight, obese), doctor-
165 diagnosed tuberculosis (ever/never), working in a dusty job (>10 years, ≤ 10 years),
166 education (none to primary, secondary, more than secondary school), passive smoking
167 (presence of somebody else smoking in the subject's home in the last two weeks), and pack-
168 years of any smoking (never smoker, 1-5 pack-years, 6-15 pack-years, 16-25 pack-years, >25
169 pack-years). We defined a pack-year as consumption of 20 cigarettes/day for a year.
170 Equivalent values for other types of smoking products were taken from the Smoking Pack-
171 Years Calculator.¹¹

172 PAR depends on the strength of the association between risk factor and outcome (relative
173 risk), as well as the prevalence of the exposure to the risk factor and the prevalence of the
174 outcome in the population of interest. For each of the 41 sites, we obtained a site-specific
175 PAR ("local PAR") by first estimating the population attributable fraction (PAF) using the
176 model-based approach described by Miettinen,¹² and then multiplying PAF by the
177 prevalence of CAO to obtain PAR:

$$178 \quad PAF = \frac{Pe(RR-1)}{RR} \quad \text{[equation 1.1]}$$

$$179 \quad PAR = PAF * Pd \quad \text{[equation 1.2]}$$

180 where Pe is the proportion of cases exposed to the risk factor in the population under
181 study, RR is the relative risk of CAO for the risk factor, and Pd is the prevalence of CAO in
182 the population. Where there was no exposed individual to a given risk factor in the sample,
183 we have not calculated a value for PAR and it is effectively estimated to be zero.

184 For smoking and education, we estimated the PAR for each category, and we also estimated
185 the overall PAR for the variable by combining PAR values across categories “c”, using the
186 following formula:¹³

$$187 \quad PAR = \left(\sum_{i=1}^c Pe_i \left(\frac{RR_i - 1}{RR_i} \right) \right) * Pd \quad \text{[equation 1.3]}$$

188 where Pe_i is the proportion of cases exposed to the i^{th} level of the risk factor and RR_i is the
189 RR for CAO for the i^{th} category.

190 The RR of each risk factor was estimated by regressing the presence of CAO against age and
191 all risk factors within each site using a log-binomial model, fitted separately for men and
192 women. We investigated the heterogeneity of the RR estimates across sites using the I^2
193 statistic.¹⁴ To increase the precision of the estimates of the site-specific RRs, and hence of
194 site-specific PARs, we used a Bayesian hierarchical model where information on mean and
195 variance of the RRs was borrowed across sites.¹⁵ This leads to more robust point and
196 interval estimates, particularly for sites with smaller sample sizes, lower prevalence of CAO
197 or lower prevalence of exposure. The model assumes that the RRs vary across sites, but that
198 all site-specific RRs come from the same underlying distribution. In this model, we
199 accounted for non-response, by adjusting for variables that affect the probability of
200 selection in the survey (see Supplement),¹⁶ and for a cluster and/or stratified sampling
201 framework in some sites, by including an additional level of hierarchy in the model.
202 The uncertainty around the PAR estimate, which reflects not only the uncertainty in RR but
203 also the uncertainty in Pd and Pe (see Supplement), is expressed by 95% credible intervals
204 (95%CrI), which represent the Bayesian equivalent to the frequentist 95% confidence
205 intervals.

206 For each site, a *total* local PAR, representing the proportion of CAO at a single site explained
207 by all risk factors considered, was derived by first estimating the *total* PAF using the formula
208 proposed by Miettinen,¹² and then multiplying the total PAF by the prevalence of CAO:

$$209 \quad Total\ PAF = 1 - \prod_{k=1}^K (1 - PAF_k) \quad [equation\ 2.1]$$

$$210 \quad Total\ PAR = Total\ PAF * Pd \quad [equation\ 2.2]$$

211 where k represents the risk factor and K the total number of risk factors for which PAR is
212 estimated.

213

214

215 **Results**

216 Of the 56,961 individuals invited to participate, 6.4% were ineligible and 7.9% could not be
217 reached. A further 21.4% refused to take part and 4.1% did not complete the interviews. A
218 further 10% had unacceptable spirometry. The 28,459 individuals included in the analyses
219 thus represent 58.2% of the 48,830 people whom we were able to find and who were
220 eligible for the study (Figure 1). The sampling strategy and response rates for each site are
221 reported in table S1.

222 Just over half of the sample (52.6%) was female. The mean age was 55 years in men and 54
223 years in women, the youngest population being in Mysore (India) (48 in men; 46 in women)
224 and the oldest being in Lisbon (Portugal) (64 in men; 63 in women) (Table 1). On average
225 59% of men and 22% of women had ever smoked, and 25% of men and 7% of women had
226 smoked more than 20 pack-years; 31% of men and 14% of women had worked in dusty jobs
227 for >10 years; 29% of men and 36% of women had had no more than primary school; and
228 3% of men and 2% of women reported a history of tuberculosis.

229 The mean prevalence of CAO was 11.2% in men and 8.6% in women, but ranged from 3.5%
230 in Riyadh (Saudi Arabia) to 23.2% in Uitsig and Ravensmead (South Africa) in men, and from
231 2% in Sousse (Tunisia) to 19.4% in Salzburg (Austria) in women (Table 2).

232 After mutual adjustment, the RRs for the several risk factors were mostly consistent across
233 sites, as shown by the I^2 values in Figure 2. Smoking more than 25 pack-years, compared to
234 never smoking, was associated with a RR of 3.1 (95%CrI: 2.6, 3.8) in women and 3.4 (95%CrI:
235 2.8, 4.1) in men, with significant variation across the sites only for men. Other risk factors
236 with statistically significant results were passive smoking, having secondary school or less,
237 being underweight compared with normal weight, having a history of tuberculosis, and
238 having worked >10 years in a dusty job.

239 The mean and range of the local PARs are given in Table 3. The local values of PAR for each
240 risk factor associated with CAO are shown in Figures 3A (men) and 3B (women), with
241 detailed results in Tables S2A (men) and S2B (women). On average, 5.2% of men and 2.2% of
242 women aged ≥ 40 have CAO attributable to smoking, but in Uitsig and Ravensmead (South
243 Africa) this figure is 11.7% for men and in Lexington, KY (USA) 9.5% for women. On average,
244 2.3% of men and 1.4% of women in the same age group have CAO attributable to poor
245 education (defined as having secondary school or less), rising to 6.2% for men in Uitsig and
246 Ravensmead (South Africa) and 4.3% for women in Kashmir (India). Lesser amounts of
247 disease are attributable to long-term occupation in dusty jobs (men: 0.65%; women: 0.29%),
248 being underweight (men: 0.43%; women: 0.30%), and having a history of tuberculosis (men:
249 0.36%; women: 0.26%), though in Uitsig and Ravensmead (South Africa) 3.8% of men and
250 2.1% of women had CAO attributable to tuberculosis.

251 All variables together explained on average 64.6% of CAO in men and 48.1% in women; over
252 75% of CAO was explained for men in Tirana (Albania), Guangzhou (China), Adana (Turkey),

253 Kashmir (India) and Uitsig and Ravensmead (South Africa), while for women over 75% of
254 CAO was explained only in Limbe (Cameroon) (Table 3; Figures 3A and 3B).

255

256

257 **Discussion**

258 In this large study, the mean prevalence of CAO in adults aged ≥ 40 years was 11.2% in men
259 and 8.6 % in women. The mean prevalence of CAO attributable to smoking was 5.2% in men
260 and 2.2% in women. The next most influential risk factor was poor education, followed by
261 low BMI, passive smoking, working in a dusty job for >10 years, and a history of tuberculosis,
262 but the contributions of different risk factors varied markedly from place to place. This is the
263 first attempt to provide estimates of local attributable risks for CAO from direct observation
264 of post-bronchodilator lung function on a multinational scale within a standardised
265 framework.

266 Because the RRs associated with each of the risk factors are similar in all sites, variation in
267 PAR across sites is mostly determined by the prevalence of the risk factor. Tobacco
268 consumption was the most influential risk factor, though there are many sites where it was
269 not, particularly among women. The high prevalence of CAO attributable to tobacco in
270 Kashmir is due to the high prevalence of hookah smoking in older people of both sexes in
271 this area. As in a previous analysis,⁸ we confirm a smaller, but still significant, RR associated
272 with passive smoking, and $>1\%$ of women estimated to have CAO attributable to second-
273 hand smoke in Adana (Turkey), Salzburg (Austria), Kashmir (India) Lexington, KY (USA) and
274 Uitsig and Ravensmead (South Africa).

275 The risk factor with the highest PAR after tobacco was poor education. This is one of several
276 markers of social position associated with COPD. In an earlier analysis involving a subset of

277 BOLD sites, a lower prevalence of CAO was associated with a higher asset score based on
278 household assets. This effect was largely independent of education and other variables,
279 suggesting that education accounts for only part of the effects of deprivation.^{17,18} Because
280 the asset score was measured only in some sites, we could not include it in this analysis.
281 CAO was associated with being underweight, as previously shown in a subset of the BOLD
282 sites.¹⁹ We have presented the risk here in comparison to the normal weight group
283 (18.5<BMI<25), though in fact the risk continues to decline in the overweight and obese
284 groups. The association is consistent, independent of other risk factors, such as smoking,
285 and has been shown in non-smokers.²⁰ Although a low BMI could be the result of the illness
286 causing CAO (reverse causation), prospective analysis of FEV₁ decline in clinical trials has
287 shown a slower decline in those with a higher BMI²¹ and obstruction has been shown to
288 develop in people with a low body mass for reasons unconnected to airway disease, such as
289 anorexia nervosa.²² We suggest that this association is at least partly causal, possibly linked
290 to an inadequate diet, including, potentially a poor diet in early life or during gestation and
291 other factors affecting BMI from childhood. We estimate that >1% of men have CAO
292 attributable to being underweight in Sri Lanka, Nampicuan-Talugtug (Philippines), Chikwawa
293 (Malawi) and Uitsig and Ravensmead (South Africa).
294 We confirmed that there is a consistent association between working in a dusty job for >10
295 years and CAO. However, we have found the PAR to be much lower than would be implied
296 by some earlier estimates,²³ the highest prevalence of CAO attributable to >10 years in a
297 dusty job being 1.6% (95%CrI: 0.4, 3.6) in men from Karachi (Pakistan) and 0.9% (95%CrI:
298 0.25, 1.76) in women from Salzburg (Austria). Our questionnaire uses a very simple question
299 and the definition of a dusty job could be expected to vary considerably both from person to
300 person and from place to place, and any random error in the answers to this question would

301 reduce the estimated RR. However, this question is the same as that used in other studies,
302 including some reporting the much higher estimates that are often quoted.^{24,25} In addition,
303 there is very little heterogeneity between places in the association (RR) between a positive
304 answer to this question and the probability of CAO, but there are wide variations in the PAR
305 ranging up to 0.9% of women in Salzburg (Austria) with CAO attributable to working in a
306 dusty job and to 1.6% among men in Karachi (Pakistan). Where previous studies have been
307 undertaken preferentially in populations where the exposure is more prevalent, as might be
308 expected in studies focused on occupational risks, this will have given an inflated estimate
309 of the average contribution of occupation. Our figures might also be lower because we have
310 not included exposure to gases and fumes and because we asked about dust exposure
311 lasting at least 10 years, so excluding short term effects. Nevertheless, we are not the first
312 to suggest that the effects of occupation on airflow obstruction reported in the literature
313 may have been exaggerated.²⁶

314 An association between tuberculosis and CAO has been known for many years in addition to
315 any association with reduced lung volumes,²⁷ and in our study the RR was very consistent
316 across sites. Our definition of tuberculosis is based on a self-reported history. It seems
317 unlikely that people would not know if they had been treated for tuberculosis, though there
318 might be reluctance in some communities to admit to the diagnosis. In many sites there was
319 no mention of tuberculosis by any of the participants, but in sites with a high burden of
320 tuberculosis, CAO attributable to tuberculosis was a substantial problem. In Uitsig and
321 Ravensmead (South Africa) 4% of men and 2.05% of women aged ≥ 40 have CAO attributable
322 to tuberculosis.

323 The GBD programme is the most comprehensive attempt to estimate attributable risks for
324 COPD as they relate to mortality and disability-adjusted life-years lost.⁷ Both the GBD

325 analysis and the current analysis agree that the most important risk factor is tobacco
326 smoking, but the GBD analysis places particulate air pollution and indoor pollution as the
327 next most important factors. We were not able to find any association between CAO and
328 burning solid fuels in previous BOLD analyses.²⁸ Three large Chinese cohorts that have
329 recorded both lung function and cooking fuel use have also failed to show any such
330 association.²⁹⁻³¹ The main evidence for the contrary view comes from small studies which
331 are more prone to the play of chance and which demonstrate a strong publication bias.³²
332 The evidence from BOLD does not support the view that indoor air pollution causes a
333 substantial amount of CAO. We do not have individual data on personal exposure to
334 outdoor air pollution in this study and did not investigate this further in this analysis.
335 In order to present findings that are intuitively accessible, we have reported results with
336 reference to the prevalence of CAO. We have defined this by the lower limit of normal
337 using NHANES III equations for European Americans.¹⁰ The use of a single standard for all
338 population groups is reasonable for the FEV₁/FVC ratio, while this is not true for the FEV₁
339 and the FVC on their own. Kiefer et al. showed that whereas >10% of the variance in the
340 FEV₁ or FVC was explained by ethnicity in the NHANES III study,³³ this was <1% for the
341 FEV₁/FVC ratio. We have selected the 5th centile as the definition of “normal”. This is an
342 arbitrary cut-off to define CAO and, although it does determine the nominal prevalence of
343 “CAO”, it does not affect the estimate of PAR.³⁴
344 The sites in BOLD were selected to represent all the regions defined by the GBD except for
345 Latin America and the high-income countries of Asia Pacific. We also failed to find a site in
346 Oceania. Within this plan, the sites were self-selecting as they had to have local teams able
347 and willing to take on the project. The stipulation that the sampled population had to have a
348 size of at least 150,000 individuals prevented very small and unrepresentative populations

349 from being selected, but the sites themselves are not strictly representative of the regions.
350 The very consistent RRs estimates across sites suggest that these could be used to estimate
351 local PAR for other areas, if local estimates of the prevalence of risk factors and CAO are
352 known.

353 Exposure to all the risk factors were assessed by self-report, as in most other similar studies.
354 Differences in reporting across sites do not appear to have affected the RRs, which appear
355 to be very consistent across sites. Differences in reporting will, however, have had more
356 influence on the estimated prevalence of the risk factors, which could have affected the
357 estimates of attributable risk.

358 Attributable risks can sum to more than 1.³⁵ All estimates of attributable risk make a strong
359 assumption that the estimated associations are entirely causal. Some parts of these
360 associations, however, are either confounded or the product of reverse causation. Mutual
361 adjustment of the RRs used in the current analysis reduces the problem of confounding, but
362 does not eliminate it, and does not address the issue of reverse causation. We estimated
363 risk from cross-sectional rather than longitudinal data. In a chronic irreversible condition
364 this is likely to lead to less bias than with some other conditions, but differences in mortality
365 in different risk groups may still bias the RR estimates. Other risks of bias include the
366 “healthy worker”³⁶ and even a “healthy smoker”³⁷ effect that can lead people with poorer
367 health to avoid certain risky exposures possibly including, in this case, dusty jobs and
368 smoking. We are unable to address this limitation further in a cross-sectional study. With all
369 these limitations, the risk factors considered in this analysis account for, on average, 64.6%
370 of CAO in men and 48.1% in women. The measurement of some of the risk factors was very
371 crude and with better measurements we would expect to explain more of the condition,

372 and addition of other unmeasured risks such as a more specific estimate of wealth might
373 also have accounted for more.

374

375

376 **Conclusions**

377 There is substantial variation in the prevalence of CAO and the single most important risk
378 factor globally remains tobacco smoking, followed by measures that we interpret as
379 indicators of deprivation, such as poor education and low BMI. Passive smoking is also an
380 important risk factor. Of the more specific risk factors, >10 years in a dusty job is associated
381 with CAO, but the risk attributable to this exposure in the BOLD sites is less than some
382 previous reports have suggested. Dusty jobs need further investigation to identify the main
383 contributing occupations and exposures and how these can be remediated. Tuberculosis is
384 also an important risk factor in areas where this disease is still common. More needs to be
385 done to understand the link between poor education and the prevalence of CAO. Local
386 estimates of PARs are important for prioritising public health programmes, and these results
387 should contribute to this process.

388

389

390

391 **Acknowledgements**

392 The BOLD (Burden of Obstructive Lung Disease) Collaborative Research Group members:
393 Albania: Hasan Hafizi (PI), Anila Aliko, Donika Bardhi, Holta Tafa, Natasha Thanasi, Arian
394 Mezini, Alma Teferici, Dafina Todri, Jolanda Nikolla, and Rezarta Kazasi (Tirana University
395 Hospital Shefqet Ndroqi, Albania); Algeria: Hamid Hacene Cherkaski (PI), Amira Bengrait,
396 Tabarek Haddad, Ibtissem Zgaoula, Maamar Ghit, Abdelhamid Roubhia, Soumaya Boudra,
397 Feryal Atoui, Randa Yakoubi, Rachid Benali, Abdelghani Bencheikh, and Nadia Ait-Khaled
398 (Faculté de Médecine Annaba, Service de Epidémiologie et Médecine Préventive, El Hadjar,
399 Algeria); Australia: Christine Jenkins (PI), Guy Marks (PI), Tessa Bird, Paola Espinel, Kate
400 Hardaker, Brett Toelle (Woolcock Institute of Medical Research, Sidney, Australia); Austria:
401 Michael Studnicka (PI), Torkil Dawes, Bernd Lamprecht, and Lea Schirhofer (Department of
402 Pulmonary Medicine, Paracelsus Medical University, Salzburg, Austria); Bangladesh: Akramul
403 Islam (PI), Syed Masud Ahmed (Co-PI), Shayla Islam, Qazi Shafayetul Islam, Mesbah-UI-
404 Haque, Tridib Roy Chowdhury, Sukantha Kumar Chatterjee, Dulal Mia, Shyamal Chandra
405 Das, Mizanur Rahman, Nazrul Islam, Shahaz Uddin, Nurul Islam, Luiza Khatun, Monira
406 Parvin, Abdul Awal Khan, and Maidul Islam (James P. Grant School of Public Health, BRAC
407 [Building Resources Across Communities] University, Institute of Global Health, Dhaka,
408 Bangladesh); Benin: Herve Lawin (PI), Arsene Kpangon, Karl Kpossou, Gildas Agodokpessi,
409 Paul Ayelo, Benjamin Fayomi (Unit of Teaching and Research in Occupational and
410 Environmental Health, University of Abomey Calavi, Cotonou, Benin); Cameroon: Bertrand
411 Mbatchou (PI), Atongno Humphrey Ashu (Douala General Hospital, Douala, Cameroon);
412 Canada: Wan C. Tan (PI) and Wen Wang (iCapture Center for Cardiovascular and Pulmonary
413 Research, University of British Columbia, Vancouver, BC, Canada); China: NanShan Zhong
414 (Principal Investigator [PI]), Shengming Liu, Jiachun Lu, Pixin Ran, Dali Wang, Jin-ping Zheng,

415 and Yumin Zhou (Guangzhou Institute of Respiratory Health, First Affiliated Hospital of
416 Guangzhou Medical College, Guangzhou, China); Estonia: Rain Jõgi (PI), Hendrik Laja, Katrin
417 Ulst, Vappu Zobel, and Toomas-Julius Lill (Lung Clinic, Tartu University Hospital, Tartu,
418 Estonia); Gabon: Ayola Akim Adegnika (PI) (Centre de Recherches Medicales de Lambarene,
419 Lambarene, Gabon); Germany: Tobias Welte (PI), Isabelle Bodemann, Henning Geldmacher,
420 and Alexandra Schweda-Linow (Dept. of Pneumology, Hannover Medical School and
421 German Center of Lung Research, Hannover, Germany.); Iceland: Thorarinn Gislason (PI),
422 Bryndis Benediktsdottir, Kristin Jörundsdottir, Lovisa Gudmundsdottir, Sigrun
423 Gudmundsdottir, and Gunnar Gudmundsson, (Department of Allergy, Respiratory Medicine,
424 and Sleep, Landspítali University Hospital, Reykjavik, Iceland); India: Mahesh Rao (PI) (JSS
425 Medical College, Mysuru, India); Parvaiz A Koul (PI), Sajjad Malik, Nissar A Hakim, and Umar
426 Hafiz Khan (Sher-i-Kashmir Institute of Medical Sciences, Srinagar, J&K, India); Rohini
427 Chowgule (PI), Vasant Shetye, Jonelle Raphael, Rosel Almeda, Mahesh Tawde, Rafiq Tadvii,
428 Sunil Katkar, Milind Kadam, Rupesh Dhanawade, and Umesh Ghurup (Indian Institute of
429 Environmental Medicine, Mumbai, India); Sanjay Juvekar (PI), Siddhi Hirve, Somnath
430 Sambhudas, Bharat Chaidhary, Meera Tambe, Savita Pingale, Arati Umap, Archana Umap,
431 Nitin Shelar, Sampada Devchakke, Sharda Chaudhary, Suvarna Bondre, Savita Walke,
432 Ashleshsa Gawhane, Anil Sapkal, Rupali Argade, and Vijay Gaikwad (Vadu Health and
433 Demographic Surveillance System, King Edward Memorial Hospital Research Centre Pune,
434 Pune India); Sundeep Salvi (PI), Bill Brashier, Jyoti Londhe, and Sapna Madas (Chest
435 Research Foundation, Pune India); Jamaica: Althea Aquart-Stewart (PI), Akosua Francia
436 Aikman (University of the West Indies, Kingston, Jamaica); Kyrgyzstan: Talant M.
437 Sooronbaev (PI), Bermet M. Estebesova, Meerim Akmatalieva, Saadat Usenbaeva, Jypara
438 Kydyrova, Eliza Bostonova, Ulan Sheraliev, Nuridin Marajapov, Nurgul Toktogulova, Berik

439 Emilov, Toktogul Azilova, Gulnara Beishekeeva, Nasyikat Dononbaeva, and
440 AijamalTabyshova (Pulmunology and Allergology Department, National Centre of Cardiology
441 and Internal Medicine, Bishkek, Kyrgyzstan); Malawi: Kevin Mortimer (PI), Wezzie Nyapigoti,
442 Ernest Mwangoka, Mayamiko Kambwili, Martha Chipeta, Gloria Banda, Suzgo Mkandawire,
443 and Justice Banda (the Malawi Liverpool Wellcome Trust, Blantyre, Malawi); Malaysia: Li-
444 Cher Loh (PI), Abdul Rashid, and Siti Sholehah (Royal College of Surgeons in Ireland and
445 University College Dublin Malaysia Campus (RUMC)); Morocco: Mohamed C Benjelloun (PI),
446 Chakib Nejjari, Mohamed Elbiaze, and Karima El Rhazi (Laboratoire d'épidémiologie,
447 Recherche Clinique et Santé Communautaire, Fès, Morocco); Netherlands: E. F. M. Wouters
448 and G. J. Wesseling (Maastricht University Medical Center, Maastricht, the Netherlands);
449 Nigeria: Daniel Obaseki (PI), Gregory Erhabor, Olayemi Awopeju, and Olufemi Adewole
450 (Obafemi Awolowo University, Ile-Ife, Nigeria); Norway: Amund Gulsvik (PI), Tina Endresen,
451 and Lene Svendsen (Department of Thoracic Medicine, Institute of Medicine, University of
452 Bergen, Bergen, Norway); Pakistan: Asaad A. Nafees (PI) (Aga Khan Univeristy, Karachi,
453 Pakistan); Philippines: Luisito F. Idolor (PI), Teresita S. de Guia, Norberto A. Francisco, Camilo
454 C. Roa, Fernando G. Ayuyao, Cecil Z. Tady, Daniel T. Tan, Sylvia Banal-Yang, Vincent M.
455 Balanag, Jr., Maria Teresita N. Reyes, and Renato. B. Dantes (Lung Centre of the Philippines,
456 Philippine General Hospital, Nampicuan and Talugtug, the Philippines); Renato B. Dantes
457 (PI), Lourdes Amarillo, Lakan U. Berratio, Lenora C. Fernandez, Norberto A. Francisco,
458 Gerard S. Garcia, Teresita S. de Guia, Luisito F. Idolor, Sullian S. Naval, Thessa Reyes, Camilo
459 C. Roa, Jr., Ma. Flordeliza Sanchez, and Leander P. Simpao (Philippine College of Chest
460 Physicians, Manila, the Philippines); Poland: Ewa Nizankowska-Mogilnicka (PI), Jakub Frey,
461 Rafal Harat, Filip Mejza, Pawel Nastalek, Andrzej Pajak, Wojciech Skucha, Andrzej Szczeklik,
462 and Magda Twardowska, (Division of Pulmonary Diseases, Department of Medicine,

463 Jagiellonian University School of Medicine, Krakow, Poland); Portugal: Cristina Bárbara (PI),
464 Fátima Rodrigues, Hermínia Dias, João Cardoso, João Almeida, Maria João Matos, Paula
465 Simão, Moutinho Santos, and Reis Ferreira (the Portuguese Society of Pneumology, Lisbon,
466 Portugal); Saudi Arabia: M. Al Ghobain (PI), H. Alorainy (PI), E. El-Hamad, M. Al Hajjaj, A.
467 Hashi, R. Dela, R. Fanuncio, E. Doloriel, I. Marciano, and L. Safia (Saudi Thoracic Society,
468 Riyadh, Saudi Arabia); South Africa: Eric Bateman (PI), Anamika Jithoo (PI), Desiree Adams,
469 Edward Barnes, Jasper Freeman, Anton Hayes, Siphon Hlengwa, Christine Johannisen,
470 Mariana Koopman, Innocentia Louw, Ina Ludick, Alta Olckers, Johanna Ryck, and Janita
471 Storbeck, (University of Cape Town Lung Institute, Cape Town, South Africa); Sri Lanka: Kirthi
472 Gunasekera (PI), Rajitha Wickremasinghe (Medical Research Institute, Central Chest Clinic,
473 Colombo, Sri Lanka); Sudan: Asma Elsony (PI), Hana A. Elsadig, Nada Bakery Osman, Bandar
474 Salah Noory, Monjda Awad Mohamed, Hasab Alrasoul Akasha Ahmed Osman, Namarig
475 Moham ed Elhassan, Abdel Mu'is El Zain, Marwa Mohamed Mohamaden, Suhaiba Khalifa,
476 Mahmoud Elhadi, Mohand Hassan, and Dalia Abdelmonam (the Epidemiological Laboratory,
477 Khartoum, Sudan); Sweden: Christer Janson (PI), Inga Sif Olafsdottir, Katarina Nisser, Ulrike
478 Spetz-Nyström, Gunilla Hägg, and Gun-Marie Lund (Department of Medical Sciences:
479 Respiratory Medicine and Allergology, Uppsala University, Uppsala, Sweden); Trinidad and
480 Tobago: Terence Seemungal (PI), Fallon Lutchmarsingh, Liane Conyette (University of the
481 West Indies, St. Augustine, Trinidad and Tobago); Tunisia: Imed Harrabi (PI), Myriam
482 Denguezli, Zouhair Tabka, Hager Daldoul, Zaki Boukheroufa, Firas Chouikha, and Wahbi
483 Belhaj Khalifa (University Hospital Farhat Hached, Faculté de Médecine, Sousse, Tunisia);
484 Turkey: Ali Kocabaş (PI), Attila Hancioglu, Ismail Hanta, Sedat Kuleci, Ahmet Sinan
485 Turkyilmaz, Sema Umut, and Turgay Unalan (Department of Chest Diseases, Cukurova
486 University School of Medicine, Adana, Turkey); United Kingdom: Peter GJ Burney (PI),

487 Anamika Jithoo, Louisa Gnatiuc, Hadia Azar, Jaymini Patel, Caron Amor, James Potts,
488 Michael Tumilty, and Fiona McLean, Risha Dudhaiya (National Heart and Lung Institute,
489 Imperial College London, London, UK); United States of America: A Sonia Buist (PI),(Oregon
490 Health & Science University, Portland, OR) Mary Ann McBurnie, William M Vollmer, Suzanne
491 Gillespie (Kaiser Permanente Center for Health Research, Portland, OR); Sean Sullivan
492 (University of Washington, Seattle, WA); Todd A Lee, Kevin B Weiss, (Northwestern
493 University, Chicago, IL); Robert L Jensen, Robert Crapo (Latter Day Saints Hospital, Salt Lake
494 City, Utah); Paul Enright (University of Arizona, Tucson, AZ); David M. Mannino (PI), John
495 Cain, Rebecca Copeland, Dana Hazen, and Jennifer Methvin, (University of Kentucky,
496 Lexington, KY).

497

498 **Additional local support for BOLD clinical sites was provided by:** Boehringer Ingelheim
499 China. (**GuangZhou, China**); Turkish Thoracic Society, Boehringer-Ingelheim, and Pfizer
500 (**Adana, Turkey**); Altana, Astra-Zeneca, Boehringer-Ingelheim, GlaxoSmithKline, Merck
501 Sharpe & Dohme, Novartis, Salzburger Gebietskrankenkasse and Salzburg Local
502 Government (**Salzburg, Austria**); Research for International Tobacco Control, the
503 International Development Research Centre, the South African Medical Research Council,
504 the South African Thoracic Society GlaxoSmithKline Pulmonary Research Fellowship, and the
505 University of Cape Town Lung Institute (**Cape Town, South Africa**); and Landspítali-
506 University Hospital-Scientific Fund, GlaxoSmithKline Iceland, and AstraZeneca Iceland
507 (**Reykjavik, Iceland**); GlaxoSmithKline Pharmaceuticals, Polpharma, Ivax Pharma Poland,
508 AstraZeneca Pharma Poland, ZF Altana Pharma, Pliva Kraków, Adamed, Novartis Poland,
509 Linde Gaz Polska, Lek Polska, Tarchomińskie Zakłady Farmaceutyczne Polfa, Starostwo
510 Proszowice, Skanska, Zasada, Agencja Mienia Wojskowego w Krakowie, Telekomunikacja

511 Polska, Biernacki, Biogran, Amplus Bucki, Skrzydlewski, Sotwin, and Agroplon (**Cracow,**
512 **Poland**); Boehringer-Ingelheim, and Pfizer Germany (**Hannover, Germany**); the Norwegian
513 Ministry of Health's Foundation for Clinical Research, and Haukeland University Hospital's
514 Medical Research Foundation for Thoracic Medicine (**Bergen, Norway**); AstraZeneca,
515 Boehringer-Ingelheim, Pfizer, and GlaxoSmithKline (**Vancouver, Canada**); Marty Driesler
516 Cancer Project (**Lexington, Kentucky, USA**); Altana, Boehringer Ingelheim (Phil),
517 GlaxoSmithKline, Pfizer, Philippine College of Chest Physicians, Philippine College of
518 Physicians, and United Laboratories (Phil) (**Manila, Philippines**); Air Liquide Healthcare P/L,
519 AstraZeneca P/L, Boehringer Ingelheim P/L, GlaxoSmithKline Australia P/L, Pfizer Australia
520 P/L (**Sydney, Australia**), Department of Health Policy Research Programme, Clement Clarke
521 International (**London, United Kingdom**); Boehringer Ingelheim and Pfizer (**Lisbon,**
522 **Portugal**), Swedish Heart and Lung Foundation, The Swedish Association against Heart and
523 Lung Diseases, Glaxo Smith Kline (**Uppsala, Sweden**)

524 **References**

- 525 1. United Nations General Assembly. Resolution adopted by the General Assembly on 19
526 September 2011 66/2. Political Declaration of the High-level Meeting of the General Assembly on
527 the Prevention and Control of Non-communicable Diseases 2012.
- 528 2. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, et al. Global and regional mortality from
529 235 causes of death for 20 age groups in 1990 and 2010: a systematic. *Lancet* 2013; **380**(9859):
530 2095-128.
- 531 3. Murray CJL, Vos T, Lozano R, et al. Disability-adjusted life years (DALYs) for 291 diseases and
532 injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010.
533 *Lancet (North American ed)* 2012; **380**(9859): 2197-223.
- 534 4. Doll R, Peto R. Mortality in relation to smoking: 20 years' observations on male British
535 doctors. *British medical journal* 1976; **2**(6051): 1525.
- 536 5. Wilson D, Adams R, Appleton S, Ruffin R. Difficulties identifying and targeting COPD and
537 population-attributable risk of smoking for COPD: A population study. *Chest* 2005; **128**(4): 2035-42.
- 538 6. Eisner M, Anthonisen N, Coultas D, et al. An official American Thoracic Society public policy
539 statement: Novel risk factors and the global burden of chronic obstructive pulmonary disease. *Amer*
540 *J Respir Crit Care Med* 2010; **182**(5): 693-718.
- 541 7. GBD 2015 Chronic Respiratory Disease Collaborators. Global, regional, and national deaths,
542 prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive
543 pulmonary disease and asthma, 1990–2015: a systematic analysis for the Global Burden of Disease
544 Study 2015. *Lancet Respir Med* 2017; **5**(9): 691-706.
- 545 8. Hooper R, Burney P, Vollmer W, et al. Risk factors for COPD spirometrically defined from the
546 lower limit of normal in the BOLD project. *The European respiratory journal : official journal of the*
547 *European Society for Clinical Respiratory Physiology* 2012; **39**(6): 1343-53.
- 548 9. Buist AS, Vollmer WM, Sullivan SD, et al. The Burden of Obstructive Lung Disease Initiative
549 (BOLD): rationale and design. *COPD: Journal of Chronic Obstructive Pulmonary Disease* 2005; **2**(2):
550 277-83.
- 551 10. Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the
552 general U.S. population. *American journal of respiratory and critical care medicine* 1999; **159**(1): 179-
553 87.
- 554 11. Masters N, Tutt C. Smoking pack year calculator. 2007. <http://smokingpackyears.com/>
555 (accessed 18/9/2015 2015).
- 556 12. Miettinen. Proportion of disease caused or prevented by a given exposure, trait, or
557 intervention. *American journal of epidemiology* 1974; **99**: 325-32.
- 558 13. Rockhill B, Newman B, Weinberg C. Use and misuse of population attributable fractions.
559 *American journal of public health* 1998; **88**(1): 15-9.
- 560 14. Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses.
561 *Bmj* 2003; **327**(7414): 557-60.
- 562 15. Gelman A, Hill J. Multilevel linear models: varying slopes, non-nested models, and other
563 complexities. Data analysis using regression and multilevel/hierarchical models. Cambridge:
564 Cambridge University Press; 2006.
- 565 16. Gelman A. Struggles with Survey Weighting and Regression Modeling. *Stat Sci* 2007; **22**(2):
566 153-64.
- 567 17. Townend J, Minelli C, Mortimer K, et al. The association between chronic airflow obstruction
568 and poverty in 12 sites of the multinational BOLD study. *Eur Respir J* 1601880 2017; **49**: 1601880.
- 569 18. Mariam Atassi M, Kava A, .C.F. , Nejjari C, et al. Association between chronic airflow
570 obstruction and socio-economic position in Morocco: BOLD results. *Int J Tuberc Lung Dis* 2020; [in
571 press].
- 572 19. Vanfleteren LEGW, Lamprecht B, Studnicka M, et al. Body mass index and chronic airflow
573 limitation in a worldwide population-based study. *Chronic Respiratory Disease* 2016; **13**(2): 90-101.

- 574 20. Lamprecht B, McBurnie M, Vollmer W, et al. COPD in Never-Smokers: Results from the
575 population-based BOLD Study. *Chest* 2010.
- 576 21. Sun Y, Milne S, Erh J, et al. BMI is associated with FEV1 decline in chronic obstructive
577 pulmonary disease: a meta-analysis of clinical trials. *Respiratory Research volume 20, Article number:*
578 *236 (2019) Cite this article* 2019; **20**: 236.
- 579 22. Coxson HO, Chan IH, Mayo JR, Hlynsky J, Nakano Y, Birmingham CL. Early emphysema in
580 patients with anorexia nervosa. *Am J Respir Crit Care Med* 2004; **170**(7): 748–52.
- 581 23. Blanc PD. Occupation and COPD: A brief review. *Journal of Asthma* 2012; **49**(1): 2-4.
- 582 24. Blanc PD, Eisner MD, Balmes JR, Trupin L, Yelin EH, Katz PP. Exposure to Vapors, Gas, Dust,
583 or Fumes: Assessment by a Single Survey Item Compared to a Detailed Exposure Battery and a Job
584 Exposure Matrix. *American journal of industrial medicine* 2005; **48**(2): 110-7.
- 585 25. Blanc PD, Annesi-Maesano I, Balmes JR, et al. The Occupational Burden of Nonmalignant
586 Respiratory Diseases: An Official American Thoracic Society and European Respiratory Society
587 Statement. *Amer J Resp Crit Care Med* 2019; **199**(11): 1312-34.
- 588 26. Cullinan P. Occupation and chronic obstructive pulmonary disease (COPD). *British Medical*
589 *Bulletin* 2012; **104**: 143-61.
- 590 27. Allwood BW, Myer L, Bateman ED. A Systematic Review of the Association between
591 Pulmonary Tuberculosis and the Development of Chronic Airflow Obstruction in Adults. *Respiration*
592 2013; **86**(1): 76-85.
- 593 28. Amaral AFS, Patel J, Kato BS, et al. Airflow Obstruction and Use of Solid Fuels for Cooking or
594 Heating: BOLD Results. *American journal of respiratory and critical care medicine* 2018; **197**(5): 595-
595 610.
- 596 29. Smith M, Li L, Augustyn M, et al. Prevalence and correlates of airflow obstruction in 317,000
597 never-smokers in China. *Eur Respir J* 2014; **44**(1): 66-77.
- 598 30. Fang L, Gao P, Bao H, et al. Chronic obstructive pulmonary disease in China: a nationwide
599 prevalence study. *Lancet Respir Med* 2018; **6**: 421–30.
- 600 31. Wang C, Xu J, Yang L, et al. Prevalence and risk factors of chronic obstructive pulmonary
601 disease in China (the China Pulmonary Health [CPH] study): a national cross-sectional study. *Lancet*
602 2018; **391**: 1706–17.
- 603 32. Smith KR, Bruce N, Balakrishnan K, et al. Millions Dead: How Do We Know and What Does It
604 Mean? Methods Used in the Comparative Risk Assessment of Household Air Pollution. *Annu Rev*
605 *Public Health* 2014; **35**: 185–206.
- 606 33. Kiefer E, Hankinson J, Barr RG. Similar Relation of Age and Height to Lung Function Among
607 Whites, African Americans, and Hispanics. *American journal of epidemiology* 2011; **173**(4): 376-87.
- 608 34. Burney P, Minelli C. Using reference values to define disease based on the lower limit of
609 normal biased the population attributable fraction, but not the population excess risk: the example
610 of chronic airflow obstruction. *J Clin Epidemiol* 2018; **93**: 76-8.
- 611 35. Rowe AK, Powell KE, Flanders WD. Why Population Attributable Fractions Can Sum to More
612 Than One. *Am J Prev Med* 2004; **26**(3): 243-9.
- 613 36. Fox AJ, Collier PF. Low mortality rates in industrial cohort studies due to selection for worker
614 and survival in the industry. *Br J Prev Soc Med* 1976; **30**: 225-30.
- 615 37. Becklake MR, Laloo U. The 'Healthy Smoker': A Phenomenon of Health Selection? .
616 *Respiration* 1990; **57**: 137-44.

617

Table 1A. Characteristics of study population and prevalence of risk factors in 41 sites (men).

Site	Sample size	Age (Mean)	BMI (Mean)	Underweight (%)	Smoking (Pack-years)					Passive smoking (%)	Education			History of TB (%)	Dusty job, >10y(%)
					Never-smokers (%)	(1-5) (%)	(6-15) (%)	(16-25) (%)	(25+) (%)		None to primary school (%)	Secondary school (%)	More than secondary school (%)		
Albania (Tirana)	467	56.40	27.81	0.21	37.04	0.86	7.92	8.57	45.61	22.91	13.06	46.68	40.26	1.07	55.89
Algeria (Annaba)	442	53.34	25.74	3.85	23.53	7.01	16.29	16.52	36.65	5.88	32.13	36.88	31	3.39	42.08
Australia (Sydney)	251	58.33	28.02	0.40	39.44	15.94	12.35	11.55	20.72	10.76	2.39	31.47	66.14	1.20	26.69
Austria (Salzburg)	685	57.87	26.68	0.58	35.62	10.80	12.99	13.72	26.86	19.27	8.47	65.26	26.28	2.48	23.36
Benin (Sèmè-Kpodji)	237	53.22	24.61	4.22	95.78	1.27	1.69	0.84	0.42	0	68.78	25.32	5.91	0.84	31.65
Cameroon (Limbe)	171	52.42	25.20	1.75	63.16	9.94	15.20	5.85	5.85	2.92	53.22	34.50	12.28	0.58	50.29
Canada (Vancouver)	343	54.43	27.07	0.58	34.11	19.83	12.83	9.91	23.32	6.71	2.04	18.08	79.88	3.21	16.33
China (Guangzhou)	236	54.03	23.30	5.08	18.64	6.36	14.83	21.61	38.56	18.64	20.76	63.14	16.10	4.66	30.93
England (London)	323	57.92	27.55	0.31	28.17	12.38	16.72	11.76	30.96	15.17	5.88	40.25	53.87	2.17	21.05
Estonia (Tartu)	307	59.97	28.32	0.98	36.16	11.07	15.64	12.70	24.43	10.42	2.93	44.95	52.12	7.82	23.78
Germany (Hannover)	349	58.56	27.71	0.57	26.93	12.89	16.05	14.04	30.09	15.19	1.43	63.32	35.24	3.15	20.06
Iceland (Reykjavik)	403	55.90	28.30	0.50	29.28	19.60	11.17	16.87	23.08	16.38	7.20	14.64	78.16	3.97	24.32
India (Kashmir)	411	51.62	21.80	10.22	23.60	2.19	7.06	1.70	65.45	61.80	73.24	22.87	3.89	0.24	0.73
India (Mumbai)	275	51.44	23.45	8.36	84.36	2.91	6.18	4	2.55	0.36	11.27	51.27	37.45	0.36	8.36
India (Mysore)	256	47.96	24.61	2.73	77.73	3.13	11.33	4.30	3.52	0	12.89	42.58	44.53	0	3.52
India (Pune)	501	53.38	22.20	16.37	79.04	14.37	4.39	1.60	0.60	10.58	42.51	47.31	10.18	1.20	10.58
Jamaica	243	56.94	24.04	9.05	35.80	8.23	11.93	12.76	31.28	12.76	27.57	61.32	11.11	0.41	54.32
Kyrgyztan (Chui)	270	52.95	26.22	1.11	22.59	12.96	13.33	14.44	36.67	1.85	1.11	52.59	46.30	1.48	32.96
Kyrgyztan (Naryn)	315	52.83	25.19	2.22	39.37	12.70	17.14	10.79	20	0.32	4.76	40	55.24	0.32	6.67
Malawi (Blantyre)	160	53.73	22.98	10.63	69.38	15	10	3.13	2.50	3.13	47.50	46.88	5.63	4.38	18.75
Malawi (Chikwawa)	221	54.91	20.89	19.46	51.58	20.81	20.81	3.62	3.17	1.36	88.24	11.31	0.45	4.07	20.36
Malaysia (Penang)	340	54.98	25.78	2.94	50.29	5.88	13.53	8.53	21.76	16.47	32.06	61.47	6.47	0	35.88
Morocco (Fes)	354	56.51	25.85	1.98	40.68	10.73	12.99	9.89	25.71	7.91	65.25	23.16	11.58	1.13	53.67
Netherlands (Maastricht)	297	57.54	27.43	0	25.93	15.49	15.15	14.81	28.62	21.89	12.12	27.61	60.27	0.67	18.86
Nigeria (Ile-Ife)	345	56.17	23.83	5.22	76.52	15.36	5.22	1.45	1.45	1.74	34.78	39.13	26.09	0.87	25.80
Norway (Bergen)	323	58.94	26.86	0.62	29.10	9.91	20.43	18.89	21.67	24.46	5.57	54.18	40.25	0.62	35.91
Pakistan (Karachi)	268	54.29	25.09	8.58	51.49	10.07	11.94	7.46	19.03	9.33	44.40	38.06	17.54	0.37	34.70
Philippines (Manila)	378	52.16	24.37	8.73	16.14	15.87	21.69	16.14	30.16	39.68	7.67	71.43	20.90	10.58	40.21
Philippines (Nampicuan-Talugtug)	356	53.79	21.35	20.51	23.03	5.90	13.76	20.51	36.80	36.52	16.29	69.94	13.76	5.06	25.28
Poland (Krakow)	265	55.26	27.43	0	20.75	6.04	15.09	16.98	41.13	40.75	34.72	52.08	13.21	3.77	57.36
Portugal (Lisbon)	331	63.98	27.97	0	38.37	10.27	6.65	8.76	35.95	11.18	44.41	31.12	24.47	5.74	45.62
Saudi Arabia (Riyadh)	371	50.66	29.59	0.81	51.75	5.12	9.97	9.70	23.45	3.23	20.75	44.47	34.77	2.70	19.41
South Africa (Uitsig & Ravensmead)	311	53.56	24.64	11.25	15.76	14.47	30.87	19.61	19.29	47.59	40.51	50.80	8.68	19.61	38.26
Sri Lanka	457	54.15	23.17	13.35	51.42	18.16	17.29	6.56	6.56	5.03	30.85	66.74	2.41	1.09	43.54
Sudan (Gezeira)	298	55.44	23.94	8.72	52.68	16.44	15.44	7.38	8.05	6.71	64.43	27.52	8.05	0.34	27.18
Sudan (Khartoum)	306	55.74	25.17	5.88	61.44	8.82	14.05	6.86	8.82	4.25	55.56	29.74	14.71	0.65	21.90
Sweden (Uppsala)	283	58.45	27.22	0	31.45	18.73	19.08	12.37	18.37	6.71	13.78	37.81	48.41	0.71	27.56
Trinidad & Tobago	435	55.46	26.98	2.30	48.97	7.36	11.03	10.80	21.84	17.47	37.47	39.77	22.76	0	40.23
Tunisia (Sousse)	309	53.33	26.94	1.62	20.06	1.29	8.41	18.12	52.10	20.39	35.92	47.25	16.83	0	51.78
Turkey (Adana)	389	53.80	27.66	0.77	19.02	7.97	11.05	14.14	47.81	44.99	72.75	22.11	5.14	2.83	49.10
USA (Lexington, KY)	205	57.20	30.29	0	20.98	13.17	6.83	4.88	54.15	28.78	2.44	50.73	46.83	1.46	51.71

Table 1B. Characteristics of study population and prevalence of risk factors in 41 sites (women).

Site	Sample size	Age (Mean)	BMI (Mean)	Underweight (%)	Smoking (Pack-years)					Passive smoking (%)	Education			History of TB (%)	Dusty job, >10y (%)
					Never-smokers (%)	(1-5) (%)	(6-15) (%)	(16-25) (%)	(25+) (%)		None to primary school (%)	Secondary school (%)	More than secondary school (%)		
Albania (Tirana)	472	52.79	28.28	0.64	88.56	1.69	4.24	3.60	1.91	45.55	12.08	48.73	39.19	0.42	48.09
Algeria (Annaba)	448	51.65	30.84	0.22	99.33	0.22	0.22	0	0.22	17.19	50	38.62	11.38	1.12	5.36
Australia (Sydney)	265	58.93	27.92	0.38	52.08	13.21	11.70	8.30	14.72	11.70	3.77	39.25	56.98	0.38	12.08
Austria (Salzburg)	573	57.41	26.12	1.57	55.67	8.55	13.96	8.73	13.09	25.48	13.96	63.53	22.51	2.97	13.61
Benin (Sèmè-Kpodji)	308	50.50	28.07	3.25	100	0	0	0	0	0.32	84.09	14.61	1.30	0.32	13.96
Cameroon (Limbe)	116	51.95	28.75	2.59	99.14	0.86	0	0	0	1.72	63.79	30.17	6.03	1.72	62.07
Canada (Vancouver)	483	57.20	26.45	1.04	49.69	13.46	12.42	8.70	15.73	5.38	2.48	24.22	73.29	3.11	9.73
China (Guangzhou)	236	54.22	23.38	5.51	93.64	1.69	1.69	0.42	2.54	28.81	37.71	53.81	8.47	2.12	27.54
England (London)	354	58.39	26.69	1.13	42.94	12.15	14.41	9.89	20.62	17.51	5.37	38.98	55.65	2.82	6.78
Estonia (Tartu)	305	61.72	28.62	1.31	68.52	11.15	10.49	6.89	2.95	18.36	3.28	43.61	53.11	7.21	15.74
Germany (Hannover)	334	57.64	26.84	0.90	50	9.28	11.98	10.48	18.26	22.16	1.80	73.65	24.55	4.19	8.08
Iceland (Reykjavik)	354	57.03	27.53	0.28	38.70	16.38	16.95	11.86	16.10	17.51	10.45	43.79	45.76	5.65	5.93
India (Kashmir)	341	51.13	23.18	10.26	70.97	1.76	1.76	0.29	25.22	68.62	91.79	6.74	1.47	0.59	0
India (Mumbai)	165	50.41	24.43	7.27	100	0	0	0	0	2.42	37.58	47.27	15.15	1.82	1.21
India (Mysore)	345	45.91	24.77	5.51	98.55	0.58	0.29	0.58	0	0	25.22	51.01	23.77	0	1.16
India (Pune)	341	51.06	21.82	22.29	99.71	0	0	0	0.29	12.02	78.89	19.35	1.76	0.29	2.64
Jamaica	335	55.13	30.05	2.99	81.49	6.87	5.37	3.28	2.99	17.91	19.70	65.37	14.93	0.90	17.91
Kyrgyzstan (Chui)	588	52.96	29.55	1.02	92.35	3.40	1.70	1.87	0.68	9.69	3.57	57.48	38.95	1.19	16.33
Kyrgyzstan (Naryn)	505	53.66	28.11	1.58	97.43	2.18	0	0	0.40	4.75	5.74	37.62	56.63	0.99	1.19
Malawi (Blantyre)	241	51.27	26.42	3.73	97.51	1.24	0.83	0.41	0	2.90	66.80	29.88	3.32	6.22	11.62
Malawi (Chikwawa)	211	52.69	22.68	12.32	88.63	5.21	3.79	0.47	1.90	5.21	93.84	5.69	0.4	3.79	2.84
Malaysia (Penang)	323	54.06	26.34	2.17	100	0	0	0	0	35.29	38.70	53.56	7.74	0	12.38
Morocco (Fes)	414	53.93	29.62	1.21	99.03	0	0.24	0.24	0.48	18.84	84.30	12.56	3.14	2.17	13.04
Netherlands (Maastricht)	289	57.54	27.46	1.04	39.79	10.73	14.88	11.76	22.84	17.99	13.84	36.33	49.83	2.08	4.84
Nigeria (Ile-Ife)	538	54.84	26.32	5.02	96.28	2.97	0.56	0.19	0	1.67	56.69	27.14	16.17	0.19	12.08
Norway (Bergen)	334	60.56	26.25	1.20	42.22	8.38	22.46	13.17	13.77	18.56	9.28	57.19	33.53	0	18.56
Pakistan (Karachi)	339	49.38	27.55	3.83	92.04	2.06	0.88	1.18	3.83	15.34	67.55	20.06	12.39	0.59	9.14
Philippines (Manila)	515	52.48	25.30	5.24	68.93	16.12	8.54	3.11	3.30	55.15	12.23	63.50	24.27	5.24	19.03
Philippines (Nampicuan-Talugtug)	366	54.33	21.74	21.58	69.95	9.56	11.75	5.74	3.01	55.74	15.30	71.04	13.66	2.19	13.66
Poland (Krakow)	257	55.92	28.03	1.56	55.64	10.12	14.40	10.51	9.34	38.91	41.25	44.36	14.40	1.56	22.96
Portugal (Lisbon)	379	62.80	28.44	0.26	78.10	5.80	5.54	1.58	8.97	19.79	49.87	33.25	16.89	3.69	39.31
Saudi Arabia (Riyadh)	325	49.95	33.14	0.31	97.85	0	0.62	0.31	1.23	7.69	54.77	30.77	14.46	0.92	1.23
South Africa (Uitsig & Ravensmead)	529	54.47	29.79	5.48	42.16	11.91	25.14	9.64	11.15	50.85	47.26	46.69	6.05	12.48	22.87
Sri Lanka	566	53.41	25.05	7.07	99.82	0	0	0.18	0	11.31	24.56	72.44	3	0.53	12.01
Sudan (Gezeira)	277	52.27	28.86	0.72	98.56	1.08	0.36	0	0	17.69	66.79	27.08	6.14	0.72	7.58
Sudan (Khartoum)	210	51.51	28.32	7.62	97.14	1.43	0.95	0.48	0	11.90	57.62	30.95	11.43	1.43	5.71
Sweden (Uppsala)	264	58.35	26.79	0	47.35	13.26	15.53	10.98	12.88	5.30	12.12	37.12	50.76	1.52	9.47
Trinidad & Tobago	656	53.26	30.20	2.44	87.96	3.20	3.51	2.44	2.90	26.22	39.18	41.01	19.82	0	10.52
Tunisia (Sousse)	352	52.71	31.26	0.85	90.91	1.70	3.98	1.14	2.27	51.14	65.06	29.55	5.40	0	25.57
Turkey (Adana)	417	53.47	31.45	0.48	69.54	9.59	8.63	5.76	6.47	63.07	84.41	13.67	1.92	2.16	29.26
USA (Lexington, KY)	302	56.18	31.11	0.33	45.70	7.95	7.28	8.28	30.79	32.12	2.98	48.68	48.34	1.99	16.23

Table 2. Prevalence of chronic airflow obstruction (CAO) by site and sex.

Site	Men			Women		
	Sample size	CAO N	CAO %	Sample size	CAO N	CAO %
Albania (Tirana)	467	60	12.85	472	20	4.24
Algeria (Annaba)	442	41	9.28	448	20	4.46
Australia (Sydney)	251	19	7.57	265	35	13.21
Austria (Salzburg)	685	88	12.85	573	111	19.37
Benin (Sèmè-Kpodji)	237	18	7.59	308	24	7.79
Cameroon (Limbe)	171	9	5.26	116	4	3.45
Canada (Vancouver)	343	44	12.83	483	58	12.01
China (Guangzhou)	236	22	9.32	236	15	6.36
England (London)	323	52	16.10	354	56	15.82
Estonia (Tartu)	307	27	8.79	305	16	5.25
Germany (Hannover)	349	35	10.03	334	26	7.78
Iceland (Reykjavik)	403	36	8.93	354	47	13.28
India (Kashmir)	411	71	17.27	341	53	15.54
India (Mumbai)	275	17	6.18	165	13	7.88
India (Mysore)	256	29	11.33	345	19	5.51
India (Pune)	501	29	5.79	341	23	6.74
Jamaica	243	25	10.29	335	25	7.46
Kyrgyzstan (Chui)	270	39	14.44	588	47	7.99
Kyrgyzstan (Naryn)	315	36	11.43	505	25	4.95
Malawi (Blantyre)	160	11	6.88	241	22	9.13
Malawi (Chikwawa)	221	40	18.10	211	20	9.48
Malaysia (Penang)	340	15	4.41	323	11	3.41
Morocco (Fes)	354	42	11.86	414	31	7.49
Netherlands (Maastricht)	297	57	19.19	289	50	17.30
Nigeria (Ile-Ife)	345	26	7.54	538	36	6.69
Norway (Bergen)	323	48	14.86	334	34	10.18
Pakistan (Karachi)	268	39	14.55	339	22	6.49
Philippines (Manila)	378	49	12.96	515	27	5.24
Philippines (Nampicuan-Talugtug)	356	58	16.29	366	45	12.30
Poland (Krakow)	265	40	15.09	257	31	12.06
Portugal (Lisbon)	331	46	13.90	379	36	9.50
Saudi Arabia (Riyadh)	371	13	3.50	325	9	2.77
South Africa (Uitsig & Ravensmead)	311	73	23.47	529	86	16.26
Sri Lanka	457	54	11.82	566	22	3.89
Sudan (Gezeira)	298	17	5.70	277	15	5.42
Sudan (Khartoum)	306	32	10.46	210	21	10.00
Sweden (Uppsala)	283	29	10.25	264	22	8.33
Trinidad & Tobago	435	28	6.44	656	44	6.71
Tunisia (Sousse)	309	26	8.41	352	7	1.99
Turkey (Adana)	389	77	19.79	417	38	9.11
USA (Lexington, KY)	205	28	13.66	302	49	16.23

Table 3. Mean and range of population attributable risks (PAR)* for chronic airflow obstruction across study sites by risk factor and sex.

PAR by risk factor	Men		Women	
	Mean	(Min, Max)	Mean	(Min, Max)
Smoking	5.07	(0.53, 11.7)	2.11	(0, 9.46)
Poor education#	2.33	(0.65, 6.25)	1.37	(0.34, 4.32)
Passive smoking	0.31	(0, 1.64)	0.48	(0, 2.18)
History of tuberculosis	0.36	(0, 3.77)	0.26	(0, 2.05)
Working in a dusty job, (>10 years)	0.65	(0.02, 1.6)	0.29	(0, 0.9)
Underweight	0.43	(0, 3)	0.30	(0, 1.52)
Total PAR (unadjusted)†	9.15	(2.6, 27.79)	4.81	(0.92, 15.77)
Total PAR (adjusted)‡	7.24	(2.21, 18.17)	4.14	(0.94, 11.21)
Total prevalence	11.2		8.6	
% Prevalence explained	64.6		48.1	

*PAR represents the percentage of the total population (aged ≥ 40 years) with chronic airflow obstruction attributable to the specified risk factor. #Poor education, defined as having secondary school or less. †The total unadjusted PAR is the sum of all estimates across all causes. It is slightly different from the sum of the figures reported above because it is computed from the individual sites and there is some rounding effect. ‡The total adjusted PAR is obtained using equations 2.1 and 2.2 in the methods section and is slightly less than the unadjusted PAR.

Table S1. Sampling strategy and response rate for each site.

Site	Sampling design	N	N*	N**	Response rate (%)	Cooperation rate (%)
Albania (Tirana)	Cluster sample	997	941	939	82	84
Algeria (Annaba)	Stratified random sample	917	892	890	95	95
Australia (Sydney)	Stratified random sample	585	541	516	25	33
Austria (Salzburg)	Stratified random sample	1349	1258	1,258	65	67
Benin (Sèmè-Kpodji)	Stratified cluster sample	848	694	545	97	97
Cameroon (Limbe)	Stratified random sampling	433	321	287	71	71
Canada (Vancouver)	Random digit dialling	856	827	826	26	51
China (Guangzhou)	Stratified random sample	602	473	472	87	87
England (London)	Stratified random sample	697	677	677	17	37
Estonia (Tartu)	Stratified random sample	658	615	612	49	70
Germany (Hannover)	Stratified random sample	713	683	683	59	61
Iceland (Reykjavik)	Simple random sample	758	757	757	81	84
India (Kashmir)	Stratified cluster sample	953	763	752	87	88
India (Mumbai)	Stratified cluster sample	515	440	440	55	66
India (Mysore)	Cluster sample	725	601	601	98	99
India (Pune)	Simple random sample	1388	849	842	97	97
Jamaica	Cluster sampling	796	578	578	89	90
Kyrgyzstan (Chui)	Cluster sample	1070	891	858	98	100
Kyrgyzstan (Naryn)	Cluster sample	1105	859	820	98	100
Malawi (Blantyre)	Stratified random sample	586	403	401	85	85
Malawi (Chikwawa)	Stratified random sampling	828	448	432	100	100
Malaysia (Penang)	Stratified random sample	713	670	663	59	88
Morocco (Fes)	Cluster sample	966	769	768	98	98
Netherlands (Maastricht)	Stratified random sample	634	590	586	48	55
Nigeria (Ile-Ife)	Stratified cluster sample	1148	904	883	76	98
Norway (Bergen)	Stratified random sample	707	658	657	68	71
Pakistan (Karachi)	Cluster sampling	1052	610	607	63	100
Philippines (Manila)	Stratified cluster sample	918	893	893	58	58
Philippines (Nampicuan-Talugtug)	Stratified cluster sample	991	722	722	86	86
Poland (Krakow)	Stratified random sample	603	526	522	78	79
Portugal (Lisbon)	Stratified cluster sample	745	714	710	10	27
Saudi Arabia (Riyadh)	Stratified random sample	784	700	696	98	98
South Africa (Uitsig & Ravensmead)	Cluster sample	896	847	840	63	68
Sri Lanka	Stratified cluster sample	1184	1036	1,023	85	85
Sudan (Gezeira)	Cluster sampling	834	590	575	79	79
Sudan (Khartoum)	Simple random sampling	595	516	516	93	93
Sweden (Uppsala)	Stratified random sample	588	547	547	61	63
Trinidad & Tobago	Stratified random sampling	1387	1097	1,091	100	100
Tunisia (Sousse)	Stratified cluster sample	717	661	661	90	92
Turkey (Adana)	Stratified cluster sample	875	806	806	82	85
USA (Lexington, KY)	Random digit dialling	563	508	507	14	27

The response rate is the number with complete information for this analysis divided by the total number of people contacted. The cooperation rate is the number of responders divided by the total number of responders plus active refusers. N, total number of responders: defined as participants who completed the core questionnaire and have post-bronchodilator spirometry; N*, participants with post-bronchodilator FEV₁/FVC; N**, Non-missing data for this analysis.

Table S2A. Population attributable risks for chronic airflow obstruction, expressed as percent of total population aged ≥ 40 years, with 95% credible intervals, by risk factors and site (men).

Site	Smoking	Poor education	Passive smoking	History of tuberculosis	Dusty job, >10 years	Underweight	Total PAR
Albania (Tirana)	7.78 (5.76 - 10.10)	2.23 (1.12 - 3.67)	0.40 (-0.85 - 1.11)	0.30 (0.08 - 0.77)	1.35 (-0.07 - 2.77)	0.04 (0.00 - 0.24)	9.36 (7.16 - 11.95)
Algeria (Annaba)	5.17 (3.46 - 7.40)	1.92 (1.00 - 3.26)	0.11 (-0.07 - 0.40)	0.46 (0.15 - 1.04)	0.58 (-0.23 - 1.39)	0.41 (0.08 - 1.03)	6.65 (4.72 - 9.05)
Australia (Sydney)	3.91 (2.15 - 6.37)	0.79 (0.13 - 1.85)	0.20 (-0.09 - 0.71)	0.38 (0.08 - 1.13)	0.28 (-0.10 - 0.91)	0.20 (0.00 - 0.77)	4.84 (2.92 - 7.60)
Austria (Salzburg)	5.71 (4.19 - 7.49)	2.37 (0.89 - 4.08)	0.42 (-0.03 - 1.08)	0.30 (0.10 - 0.66)	0.48 (-0.06 - 1.07)	0.05 (-0.04 - 0.23)	7.62 (5.89 - 9.68)
Benin (Sèmè-Kpodji)	0.53 (0.05 - 1.59)	2.35 (1.17 - 4.12)	/	0.10 (0.00 - 0.58)	0.58 (-0.12 - 1.49)	0.33 (0.01 - 1.11)	3.53 (1.99 - 5.69)
Cameroon (Limbe)	2.09 (0.71 - 4.82)	1.33 (0.50 - 2.84)	0.09 (-0.07 - 0.52)	0.34 (0.05 - 1.25)	0.43 (-0.19 - 1.33)	0.12 (-0.00 - 0.76)	3.58 (1.69 - 6.57)
Canada (Vancouver)	6.15 (4.05 - 9.05)	0.65 (0.05 - 1.44)	0.04 (-0.06 - 0.22)	0.27 (0.05 - 0.77)	0.24 (-0.10 - 0.69)	0.14 (0.00 - 0.60)	6.93 (4.72 - 9.80)
China (Guangzhou)	5.70 (3.34 - 8.94)	1.81 (0.57 - 3.52)	0.47 (-0.08 - 1.42)	0.39 (0.07 - 1.17)	0.60 (-0.09 - 1.61)	0.50 (0.09 - 1.40)	7.18 (4.59 - 10.65)
England (London)	7.75 (5.20 - 10.78)	1.90 (-0.01 - 3.64)	0.29 (-0.37 - 0.90)	0.36 (0.09 - 0.97)	0.95 (0.04 - 2.10)	0.10 (-0.14 - 0.50)	9.58 (6.65 - 12.88)
Estonia (Tartu)	4.75 (2.79 - 7.60)	0.95 (-0.11 - 2.02)	0.20 (-0.16 - 0.65)	0.40 (0.07 - 1.02)	0.16 (-0.20 - 0.56)	0.05 (-0.03 - 0.38)	5.61 (3.46 - 8.42)
Germany (Hannover)	5.63 (3.66 - 8.25)	1.79 (0.35 - 3.60)	0.29 (-0.10 - 0.89)	0.27 (0.05 - 0.78)	0.50 (0.01 - 1.21)	0.05 (-0.00 - 0.36)	6.91 (4.71 - 9.77)
Iceland (Reykjavik)	4.07 (2.51 - 6.09)	0.94 (0.38 - 1.83)	0.19 (-0.17 - 0.58)	0.23 (0.04 - 0.69)	0.29 (-0.16 - 0.83)	0.12 (0.00 - 0.49)	5.07 (3.33 - 7.19)
India (Kashmir)	10.58 (8.06 - 13.53)	5.00 (2.59 - 7.51)	1.05 (-0.95 - 2.64)	0.06 (0.00 - 0.34)	0.02 (-0.02 - 0.15)	0.47 (-0.32 - 1.20)	13.02 (10.18 - 16.24)
India (Mumbai)	2.40 (1.10 - 4.69)	1.05 (0.17 - 2.20)	0.02 (-0.02 - 0.18)	0.22 (0.02 - 0.79)	0.24 (-0.04 - 0.78)	0.40 (0.03 - 1.16)	3.64 (1.99 - 6.05)
India (Mysore)	2.52 (1.01 - 4.60)	2.00 (0.90 - 3.60)	/	/	0.08 (-0.02 - 0.39)	0.18 (-0.00 - 0.70)	4.83 (2.82 - 7.43)
India (Pune)	0.65 (0.11 - 1.48)	1.38 (0.64 - 2.38)	0.10 (-0.06 - 0.33)	0.19 (0.04 - 0.57)	0.12 (-0.04 - 0.39)	0.87 (0.29 - 1.77)	2.78 (1.68 - 4.19)
Jamaica	4.99 (2.88 - 8.07)	2.46 (1.12 - 4.53)	0.23 (-0.12 - 0.80)	0.10 (0.00 - 0.55)	0.64 (-0.32 - 1.69)	0.90 (0.22 - 2.16)	7.16 (4.65 - 10.60)
Kyrgyzstan (Chui)	6.60 (4.15 - 9.91)	1.38 (0.09 - 2.87)	0.06 (-0.05 - 0.32)	0.21 (0.03 - 0.76)	0.95 (0.01 - 2.18)	0.18 (0.02 - 0.74)	8.17 (5.50 - 11.57)
Kyrgyzstan (Naryn)	3.69 (1.98 - 6.00)	1.48 (0.38 - 2.93)	0.02 (-0.03 - 0.16)	0.07 (0.00 - 0.43)	0.16 (-0.04 - 0.53)	0.06 (-0.01 - 0.36)	4.98 (3.01 - 7.46)
Malawi (Blantyre)	1.94 (0.58 - 4.44)	2.05 (0.86 - 4.09)	0.04 (-0.04 - 0.33)	0.15 (0.00 - 0.86)	0.20 (-0.15 - 0.80)	0.91 (0.14 - 2.45)	4.30 (2.16 - 7.42)
Malawi (Chikwawa)	4.09 (1.66 - 7.60)	6.25 (3.52 - 9.57)	0.03 (-0.04 - 0.23)	0.72 (0.20 - 1.74)	1.23 (0.07 - 2.89)	2.44 (0.86 - 4.75)	11.21 (7.83 - 15.38)

Site	Smoking	Poor education	Passive smoking	History of tuberculosis	Dusty job, >10 years	Underweight	Total PAR
Malaysia (Penang)	2.30 (1.18 - 4.04)	0.84 (0.29 - 1.77)	0.07 (-0.08 - 0.32)	/	0.51 (-0.01 - 1.29)	0.05 (-0.04 - 0.33)	3.09 (1.82 - 5.07)
Morocco (Fes)	4.73 (3.01 - 7.02)	3.12 (1.57 - 4.97)	0.17 (-0.08 - 0.58)	0.27 (0.06 - 0.77)	1.00 (-0.64 - 2.22)	0.12 (-0.04 - 0.50)	7.38 (5.14 - 10.05)
Netherlands (Maastricht)	10.11 (7.12 - 13.85)	2.70 (1.25 - 4.61)	0.49 (-0.49 - 1.40)	0.08 (0.00 - 0.45)	0.59 (-0.22 - 1.48)	/	11.95 (8.73 - 15.79)
Nigeria (Ile-Ife)	0.69 (0.03 - 1.68)	1.66 (0.79 - 2.92)	0.02 (-0.03 - 0.15)	0.28 (0.06 - 0.83)	0.27 (-0.20 - 0.75)	0.11 (-0.05 - 0.48)	2.77 (1.57 - 4.39)
Norway (Bergen)	6.39 (4.14 - 9.64)	2.66 (1.03 - 4.67)	0.56 (-0.17 - 1.43)	0.07 (0.00 - 0.42)	0.92 (-0.18 - 2.06)	0.15 (0.01 - 0.61)	8.83 (6.23 - 12.18)
Pakistan (Karachi)	4.74 (2.75 - 7.34)	3.74 (2.00 - 6.05)	0.34 (-0.10 - 1.06)	0.09 (0.00 - 0.52)	1.60 (0.29 - 3.45)	0.45 (-0.08 - 1.27)	8.64 (5.93 - 11.87)
Philippines (Manila)	6.46 (4.25 - 9.09)	2.63 (0.79 - 4.60)	0.72 (-0.32 - 1.76)	1.27 (0.54 - 2.26)	1.25 (-0.02 - 2.73)	0.49 (-0.43 - 1.25)	9.21 (6.61 - 12.14)
Philippines (Nampicuan-Talugtug)	8.48 (6.08 - 11.48)	3.11 (1.22 - 5.17)	0.83 (-0.23 - 1.94)	1.00 (0.44 - 1.92)	0.72 (-0.21 - 1.61)	2.12 (0.61 - 3.85)	11.72 (8.92 - 14.96)
Poland (Krakow)	8.75 (5.85 - 12.36)	3.50 (1.74 - 5.69)	1.10 (-0.17 - 2.72)	0.08 (0.00 - 0.47)	1.44 (-0.30 - 3.17)	/	11.21 (8.06 - 14.93)
Portugal (Lisbon)	6.31 (4.30 - 8.98)	3.30 (1.81 - 5.25)	0.14 (-0.12 - 0.51)	0.95 (0.40 - 1.90)	1.50 (0.22 - 3.21)	/	9.29 (6.76 - 12.42)
Saudi Arabia (Riyadh)	1.59 (0.69 - 3.02)	0.65 (0.17 - 1.48)	0.04 (-0.04 - 0.23)	0.06 (0.00 - 0.37)	0.13 (-0.04 - 0.44)	0.13 (0.00 - 0.55)	2.21 (1.14 - 3.84)
South Africa (Uitsig & Ravensmead)	11.70 (8.32 - 16.13)	6.22 (3.79 - 9.25)	1.64 (-0.12 - 3.49)	3.77 (2.21 - 5.77)	1.46 (0.08 - 3.04)	3.00 (1.64 - 5.01)	18.17 (14.30 - 22.49)
Sri Lanka	3.09 (1.68 - 4.90)	2.80 (1.32 - 4.49)	0.05 (-0.06 - 0.23)	0.13 (0.02 - 0.47)	0.51 (-0.43 - 1.27)	1.37 (0.60 - 2.63)	6.36 (4.40 - 8.60)
Sudan (Gezeira)	1.32 (0.42 - 2.83)	1.60 (0.75 - 2.91)	0.05 (-0.04 - 0.28)	0.08 (0.00 - 0.47)	0.35 (-0.13 - 0.94)	0.63 (0.14 - 1.57)	3.30 (1.86 - 5.26)
Sudan (Khartoum)	1.93 (0.78 - 3.66)	2.65 (1.35 - 4.43)	0.05 (-0.05 - 0.27)	0.19 (0.02 - 0.71)	0.30 (-0.13 - 0.89)	0.13 (-0.05 - 0.57)	4.61 (2.85 - 6.90)
Sweden (Uppsala)	4.76 (2.76 - 7.61)	1.64 (0.72 - 3.02)	0.13 (-0.10 - 0.52)	0.20 (0.02 - 0.74)	0.37 (-0.24 - 1.00)	/	6.11 (3.93 - 9.01)
Trinidad & Tobago	2.51 (1.40 - 4.13)	1.56 (0.74 - 2.76)	0.16 (-0.12 - 0.51)	/	0.70 (0.06 - 1.66)	0.18 (0.01 - 0.59)	4.06 (2.60 - 5.97)
Tunisia (Sousse)	4.40 (2.61 - 6.88)	1.96 (0.92 - 3.47)	0.10 (-0.18 - 0.42)	/	0.84 (-0.15 - 1.95)	0.06 (-0.01 - 0.40)	5.87 (3.80 - 8.61)
Turkey (Adana)	11.54 (8.83 - 14.85)	5.36 (2.86 - 7.90)	1.16 (-0.39 - 2.67)	0.41 (0.12 - 0.98)	1.39 (-0.39 - 2.96)	0.04 (-0.02 - 0.29)	14.72 (11.73 - 18.22)
USA (Lexington, KY)	9.34 (6.28 - 13.19)	1.59 (0.22 - 3.31)	0.56 (-0.26 - 1.63)	0.12 (0.00 - 0.63)	0.92 (-0.26 - 2.24)	/	10.45 (7.13 - 14.51)

The Total PAR is adjusted using equations 2.1. and 2.2 in the Methods section of the paper. The Total PAR is less than the sum of the individual estimates.

Table S2B. Population attributable risks for chronic airflow obstruction, expressed as percent of total population aged ≥ 40 years, with 95% credible intervals, by risk factors and site (women).

Site	Smoking	Poor education	Passive smoking	History of tuberculosis	Dusty job, >10 years	Underweight	Total PAR
Albania (Tirana)	0.64 (0.14 - 1.43)	0.52 (-0.26 - 1.23)	0.49 (-0.02 - 1.15)	0.06 (0.00 - 0.31)	0.66 (0.14 - 1.50)	0.05 (0.00 - 0.29)	2.01 (1.01 - 3.37)
Algeria (Annaba)	0.27 (-0.06 - 0.86)	0.76 (0.04 - 1.65)	0.19 (-0.01 - 0.53)	0.06 (0.00 - 0.34)	0.06 (-0.03 - 0.27)	0.05 (0.00 - 0.30)	1.36 (0.53 - 2.43)
Australia (Sydney)	5.05 (2.84 - 8.02)	1.12 (-0.86 - 2.89)	0.38 (-0.06 - 1.04)	0.10 (0.00 - 0.59)	0.14 (-0.13 - 0.54)	0.22 (0.03 - 0.79)	6.31 (3.84 - 9.38)
Austria (Salzburg)	5.98 (4.09 - 8.26)	2.65 (0.31 - 4.94)	1.06 (0.17 - 1.93)	0.38 (0.13 - 0.87)	0.90 (0.25 - 1.76)	0.16 (0.02 - 0.47)	9.31 (6.85 - 11.93)
Benin (Sèmè-Kpodji)	/	1.78 (0.10 - 3.58)	0.04 (-0.00 - 0.26)	0.09 (0.00 - 0.47)	0.20 (-0.04 - 0.64)	0.18 (0.02 - 0.66)	2.57 (0.84 - 4.51)
Cameroon (Limbe)	1.00 (-0.17 - 3.38)	1.03 (0.18 - 2.85)	0.09 (-0.01 - 0.65)	0.23 (0.01 - 1.27)	0.37 (-0.10 - 1.37)	0.50 (0.07 - 1.75)	2.68 (0.93 - 5.85)
Canada (Vancouver)	4.46 (2.69 - 6.55)	0.81 (-0.21 - 2.07)	0.25 (0.02 - 0.67)	0.39 (0.12 - 0.93)	0.23 (-0.04 - 0.62)	0.05 (0.00 - 0.29)	5.58 (3.69 - 7.74)
China (Guangzhou)	1.60 (0.51 - 3.52)	1.35 (0.05 - 2.96)	0.41 (-0.04 - 1.17)	0.12 (0.00 - 0.63)	0.22 (-0.19 - 0.77)	0.39 (0.07 - 1.18)	3.43 (1.73 - 5.91)
England (London)	7.45 (5.13 - 10.43)	1.19 (-0.63 - 3.06)	0.88 (0.21 - 1.84)	0.54 (0.16 - 1.26)	0.37 (-0.03 - 0.94)	0.25 (0.05 - 0.75)	9.13 (6.53 - 12.33)
Estonia (Tartu)	0.95 (0.10 - 2.23)	0.34 (-0.51 - 1.10)	0.20 (-0.04 - 0.63)	0.33 (0.07 - 0.99)	0.07 (-0.10 - 0.38)	0.07 (0.00 - 0.43)	1.83 (0.67 - 3.45)
Germany (Hannover)	2.81 (1.31 - 4.85)	0.79 (-0.66 - 2.28)	0.46 (-0.00 - 1.14)	0.20 (0.02 - 0.68)	0.18 (-0.06 - 0.63)	0.07 (0.00 - 0.41)	3.93 (2.18 - 6.24)
Iceland (Reykjavik)	5.72 (3.64 - 8.38)	0.95 (-0.62 - 2.31)	0.58 (0.03 - 1.34)	0.41 (0.11 - 1.04)	0.35 (-0.01 - 0.89)	0.06 (0.00 - 0.37)	7.06 (4.76 - 9.85)
India (Kashmir)	3.30 (1.50 - 5.42)	4.32 (1.19 - 7.65)	1.72 (-1.11 - 3.60)	0.20 (0.03 - 0.69)	/	0.95 (0.34 - 1.89)	8.38 (4.97 - 11.68)
India (Mumbai)	/	1.51 (0.20 - 3.42)	0.18 (0.01 - 0.76)	0.65 (0.15 - 1.79)	0.16 (-0.03 - 0.71)	0.33 (0.04 - 1.22)	3.28 (1.45 - 5.90)
India (Mysore)	0.49 (0.04 - 1.29)	1.01 (-0.03 - 2.42)	/	/	0.03 (-0.01 - 0.22)	0.27 (0.05 - 0.81)	1.83 (0.67 - 3.39)
India (Pune)	0.35 (-0.08 - 1.08)	1.51 (0.23 - 3.04)	0.07 (-0.05 - 0.33)	0.08 (0.00 - 0.46)	0.14 (0.00 - 0.51)	0.87 (0.30 - 1.77)	2.72 (1.35 - 4.53)
Jamaica	1.22 (0.35 - 2.58)	0.90 (-0.57 - 2.16)	0.17 (-0.06 - 0.57)	0.08 (0.00 - 0.44)	0.58 (0.08 - 1.39)	0.51 (0.15 - 1.24)	3.02 (1.50 - 4.93)
Kyrgyzstan (Chui)	0.76 (0.21 - 1.53)	0.60 (-0.67 - 1.73)	0.20 (0.00 - 0.54)	0.18 (0.04 - 0.54)	0.32 (-0.06 - 0.77)	0.04 (0.00 - 0.22)	1.98 (0.71 - 3.29)
Kyrgyzstan (Naryn)	0.32 (-0.11 - 0.92)	0.47 (-0.12 - 1.12)	0.02 (-0.01 - 0.15)	0.05 (0.00 - 0.30)	0.02 (-0.01 - 0.16)	0.04 (0.00 - 0.26)	0.94 (0.24 - 1.83)
Malawi (Blantyre)	0.49 (-0.19 - 1.50)	1.88 (0.44 - 3.91)	0.05 (-0.00 - 0.32)	0.43 (0.09 - 1.23)	0.55 (0.07 - 1.50)	0.09 (0.00 - 0.53)	3.26 (1.58 - 5.60)
Malawi (Chikwawa)	1.26 (0.00 - 2.91)	2.65 (0.73 - 5.11)	0.22 (-0.00 - 0.79)	0.69 (0.17 - 1.75)	0.05 (-0.02 - 0.37)	0.56 (0.11 - 1.45)	4.63 (2.45 - 7.56)

Site	Smoking	Poor education	Passive smoking	History of tuberculosis	Dusty job, >10 years	Underweight	Total PAR
Malaysia (Penang)	/	0.62 (-0.13 - 1.51)	0.24 (-0.10 - 0.72)	/	0.33 (0.03 - 0.92)	0.07 (0.00 - 0.42)	1.53 (0.62 - 2.87)
Morocco (Fes)	0.29 (-0.08 - 0.88)	1.86 (0.59 - 3.43)	0.50 (0.08 - 1.14)	0.25 (0.05 - 0.72)	0.19 (-0.04 - 0.55)	0.22 (0.05 - 0.67)	2.98 (1.60 - 4.71)
Netherlands (Maastricht)	6.75 (3.98 - 10.04)	1.09 (-1.43 - 2.58)	0.54 (-0.18 - 1.30)	0.52 (0.15 - 1.29)	0.28 (-0.02 - 0.81)	0.20 (0.03 - 0.71)	8.31 (5.31 - 11.74)
Nigeria (Ile-Ife)	0.33 (-0.36 - 0.87)	1.23 (0.24 - 2.37)	0.02 (-0.00 - 0.14)	0.05 (0.00 - 0.29)	0.21 (-0.04 - 0.57)	0.30 (0.08 - 0.74)	2.00 (0.91 - 3.28)
Norway (Bergen)	4.66 (2.70 - 7.32)	1.28 (-0.44 - 3.28)	0.92 (0.19 - 2.03)	0.08 (0.00 - 0.46)	0.36 (-0.15 - 0.97)	0.17 (0.02 - 0.62)	6.17 (3.96 - 9.13)
Pakistan (Karachi)	0.47 (-0.06 - 1.26)	1.16 (0.12 - 2.49)	0.07 (-0.04 - 0.33)	0.08 (0.00 - 0.45)	0.32 (0.02 - 0.90)	0.17 (0.02 - 0.61)	2.14 (0.92 - 3.77)
Philippines (Manila)	0.80 (0.06 - 1.74)	0.67 (-0.32 - 1.71)	0.64 (0.00 - 1.37)	0.37 (0.12 - 0.88)	0.04 (-0.06 - 0.20)	0.39 (0.13 - 0.91)	2.42 (1.27 - 3.87)
Philippines (Nampicuan-Talugtug)	2.22 (0.86 - 3.95)	1.47 (-1.11 - 3.37)	1.20 (-0.16 - 2.52)	0.29 (0.06 - 0.84)	0.48 (-0.16 - 1.15)	1.43 (0.55 - 2.61)	5.72 (3.31 - 8.26)
Poland (Krakow)	2.04 (0.53 - 3.89)	2.29 (0.18 - 4.56)	0.64 (-0.42 - 1.65)	0.10 (0.00 - 0.59)	0.67 (-0.04 - 1.62)	0.22 (0.02 - 0.82)	5.13 (2.78 - 7.93)
Portugal (Lisbon)	1.93 (0.94 - 3.45)	1.89 (0.19 - 3.62)	0.44 (0.01 - 1.08)	0.39 (0.11 - 0.99)	0.76 (-0.08 - 1.63)	0.06 (0.00 - 0.36)	4.52 (2.75 - 6.71)
Saudi Arabia (Riyadh)	0.38 (-0.06 - 1.21)	0.58 (0.08 - 1.48)	0.09 (0.00 - 0.39)	0.20 (0.03 - 0.71)	0.03 (-0.02 - 0.23)	0.07 (0.00 - 0.41)	1.26 (0.52 - 2.52)
South Africa (Uitsig & Ravensmead)	6.04 (4.01 - 8.60)	3.41 (1.24 - 5.89)	2.18 (0.68 - 3.76)	2.05 (1.24 - 3.18)	0.57 (-0.28 - 1.23)	1.52 (0.83 - 2.55)	11.03 (8.51 - 13.88)
Sri Lanka	0.22 (-0.05 - 0.67)	0.71 (-0.29 - 1.54)	0.12 (0.01 - 0.37)	0.05 (0.00 - 0.27)	0.23 (-0.00 - 0.62)	0.36 (0.12 - 0.83)	1.50 (0.60 - 2.54)
Sudan (Gezeira)	0.43 (-0.10 - 1.35)	1.11 (0.09 - 2.40)	0.09 (-0.04 - 0.41)	0.10 (0.00 - 0.55)	0.09 (-0.02 - 0.42)	0.08 (0.00 - 0.47)	1.85 (0.69 - 3.46)
Sudan (Khartoum)	0.57 (-0.20 - 1.78)	2.13 (0.47 - 4.38)	0.65 (0.13 - 1.64)	0.31 (0.04 - 1.13)	0.12 (-0.03 - 0.54)	0.96 (0.32 - 2.22)	4.21 (2.18 - 6.97)
Sweden (Uppsala)	2.67 (1.06 - 4.95)	1.13 (-0.19 - 2.71)	0.25 (0.01 - 0.78)	0.25 (0.03 - 0.90)	0.31 (0.01 - 0.92)	/	4.10 (2.21 - 6.64)
Trinidad & Tobago	0.62 (0.17 - 1.28)	0.97 (0.00 - 1.94)	0.38 (0.01 - 0.84)	/	0.14 (-0.04 - 0.40)	0.03 (0.00 - 0.20)	2.02 (1.03 - 3.16)
Tunisia (Sousse)	0.60 (0.08 - 1.65)	0.47 (0.07 - 1.17)	0.23 (-0.01 - 0.70)	/	0.18 (-0.02 - 0.60)	0.17 (0.02 - 0.61)	1.38 (0.59 - 2.75)
Turkey (Adana)	1.81 (0.48 - 3.19)	2.39 (0.67 - 4.30)	1.10 (0.03 - 2.25)	0.16 (0.02 - 0.55)	0.52 (-0.07 - 1.22)	0.14 (0.02 - 0.53)	4.86 (3.05 - 7.07)
USA (Lexington, KY)	9.46 (6.62 - 12.97)	1.68 (-0.48 - 4.15)	1.52 (0.45 - 2.97)	0.21 (0.02 - 0.74)	0.64 (-0.06 - 1.47)	0.19 (0.02 - 0.67)	11.21 (8.15 - 14.86)

The Total PAR is adjusted using equations 2.1. and 2.2 in the Methods section of the paper. The Total PAR is less than the sum of the individual estimates.

Figure 1. Flow diagram showing recruitment to the study.

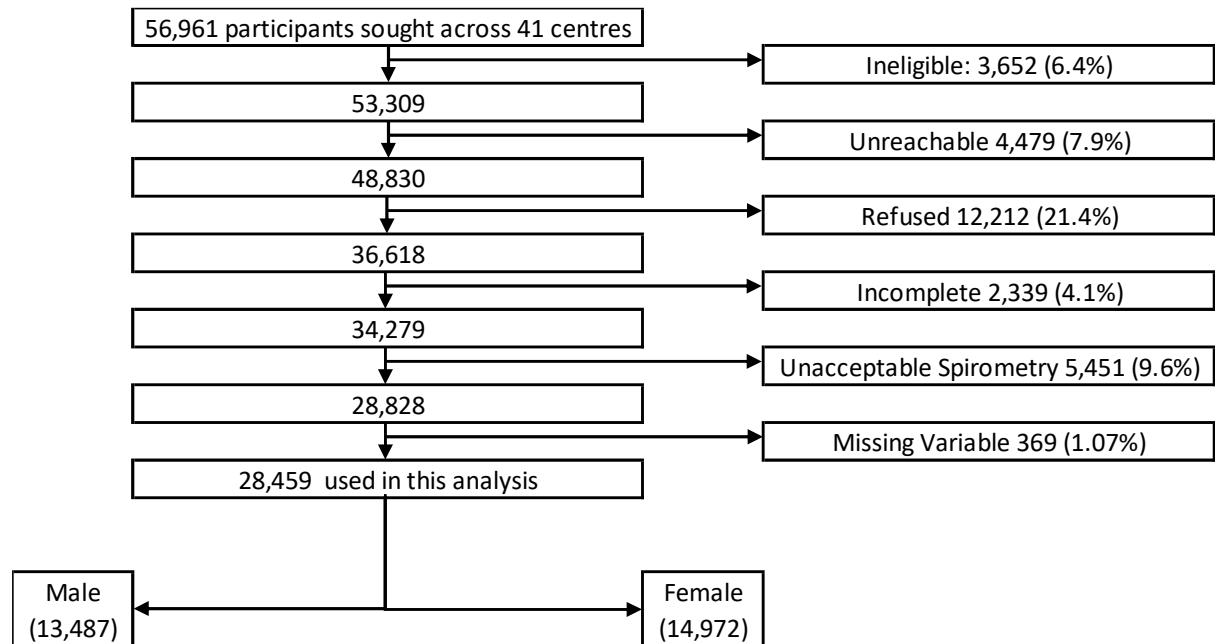
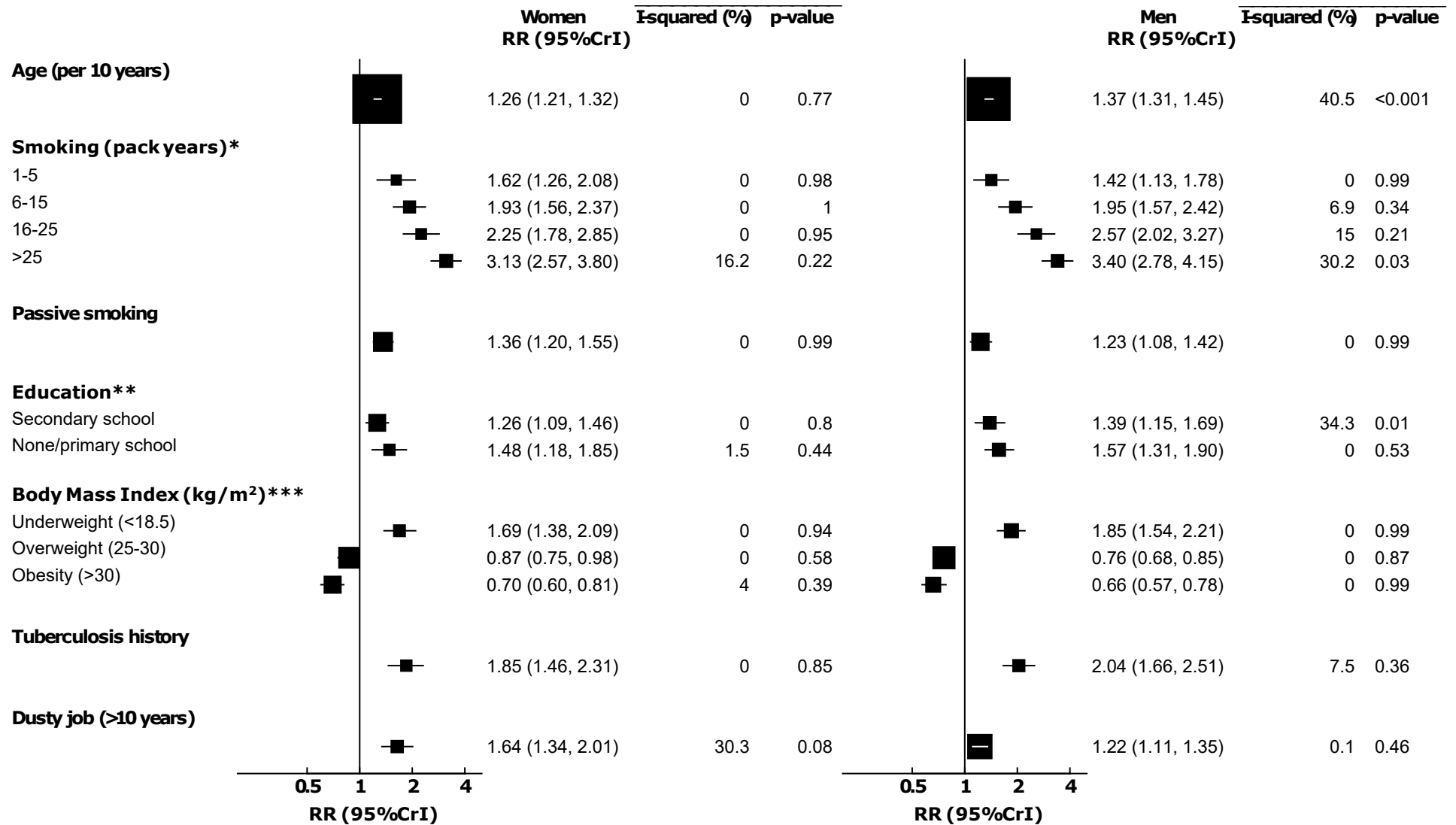
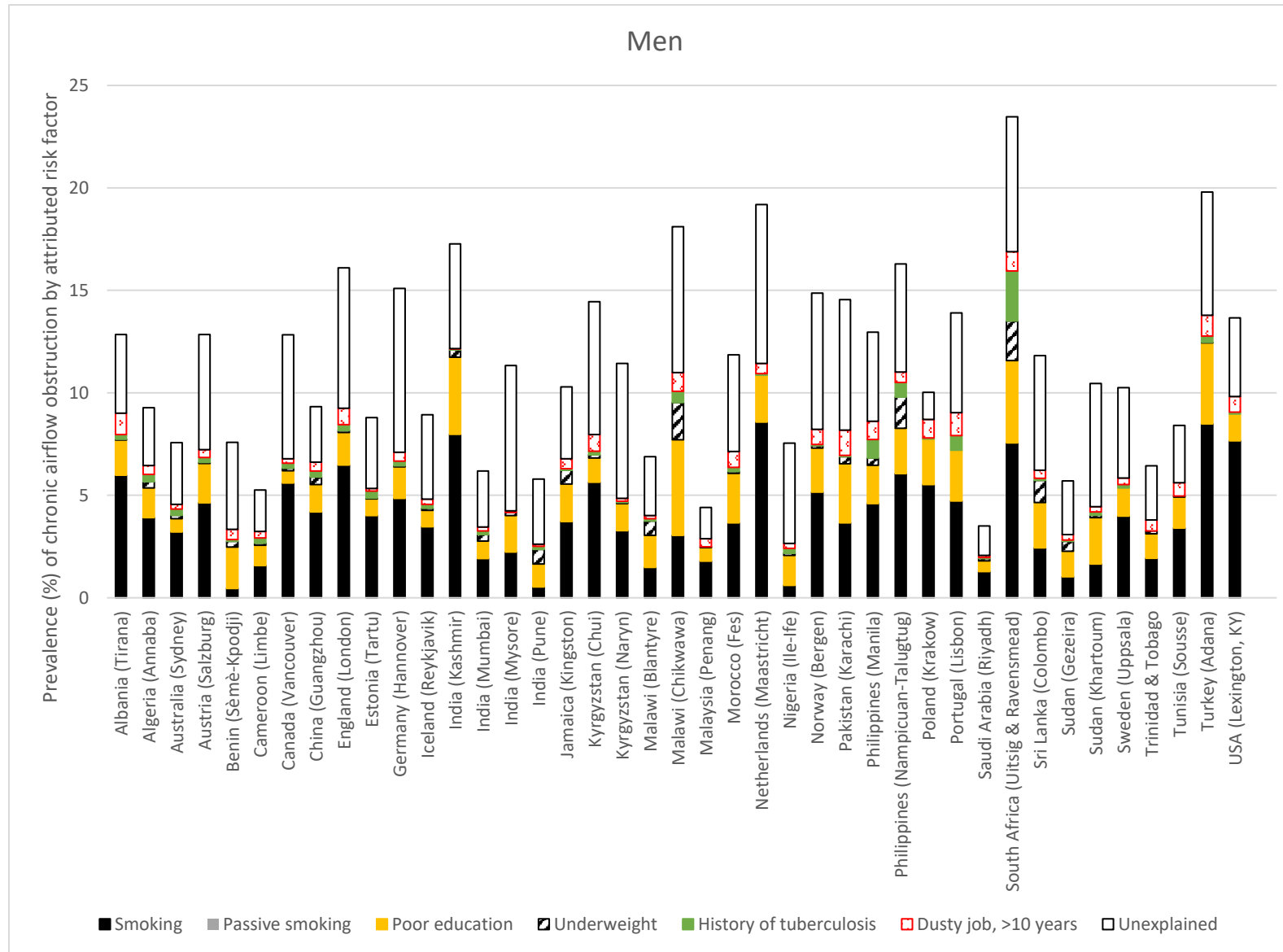


Figure 2. Sex-specific relative risk for chronic airflow obstruction among 28,459 adults age 40-89 years, and their variation across sites.



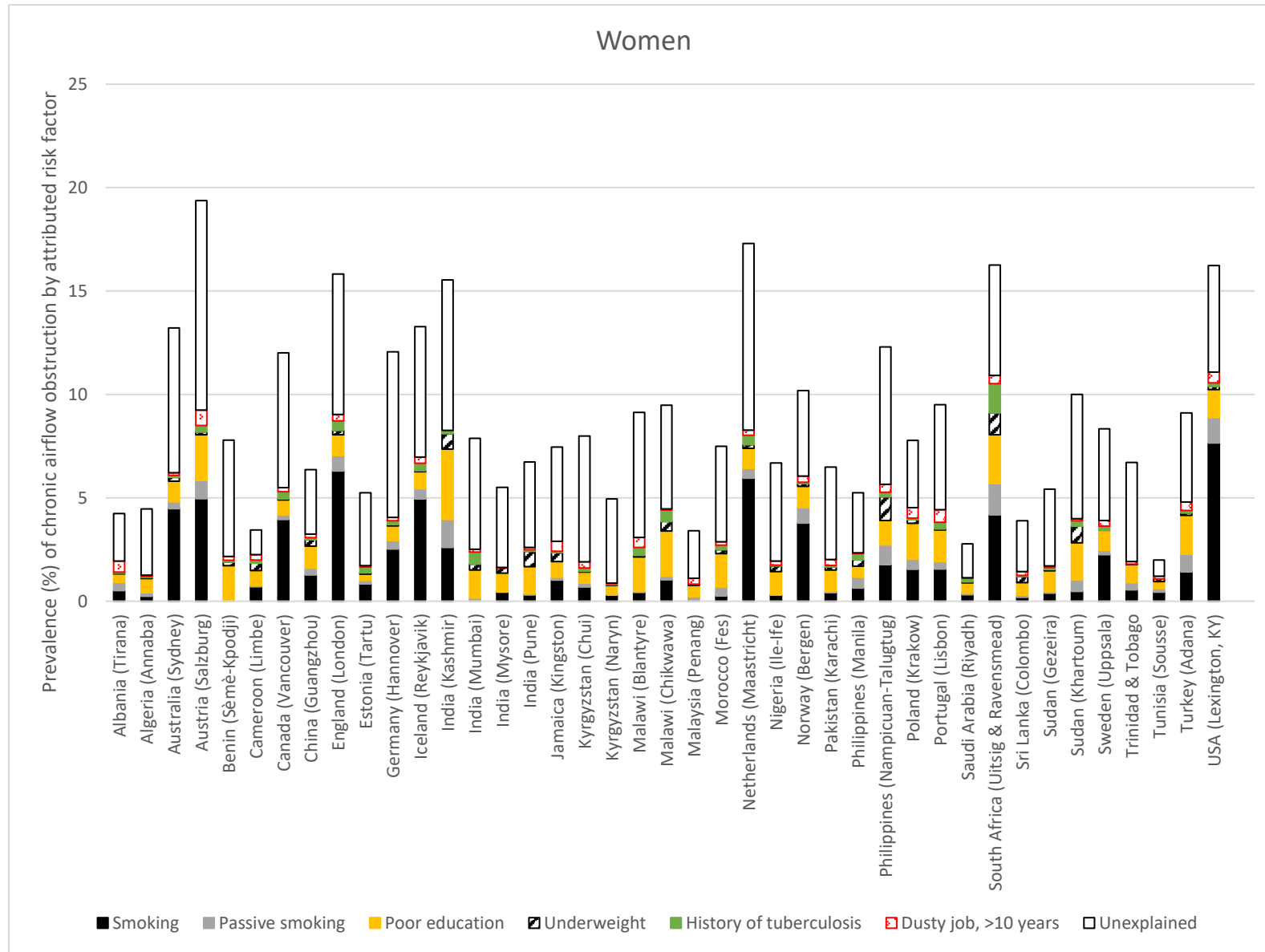
The I-squared statistic indicates the percent variability across sites. The p-value relates to the significance of the I-squared value. Square sizes reflect the amount of statistical information (ie, inversely proportional to the variance of the log RR), together with the 95% credible intervals (horizontal lines) representing the Bayesian equivalent to the frequentist 95% confidence intervals. RR, relative risk mutually adjusted for all risk factors shown here. *Reference: Never smoker; **Reference: More than secondary school; ***Reference: Normal weight (18.5-24.9 kg/m²).

Figure 3A. Population Attributable Risk (PAR) (i.e. prevalence of chronic airflow obstruction (CAO) attributable to different risk factors) by site for men.



The heights of the bars represent the prevalence of CAO. Values have been scaled back so that the total PAR explained in the figure is equal to the total PAR adjusted using equations 2.1. and 2.2.

Figure 3B. Population Attributable Risk (PAR) (i.e. prevalence of chronic airflow obstruction attributable to different risk factors) by site for women.



The heights of the bars represent the prevalence of CAO. Values have been scaled back so that the total PAR explained in the figure is equal to the total PAR adjusted using equations 2.1. and 2.2.

Supplement

Prevalence and population attributable risk for chronic airflow obstruction in a large multinational study

Peter Burney¹, Jaymini Patel¹, Cosetta Minelli¹, Louisa Gnatiuc², André F.S. Amaral¹, Ali Kocabaş³, Hamid Hacene Cherkaski⁴, Amund Gulsvik⁵, Rune Nielsen⁵, Eric Bateman⁶, Anamika Jithoo⁶, Kevin Mortimer⁷, Talant M. Sooronbaev⁸, Hervé Lawin⁹, Chakib Nejjari¹⁰, Mohammed Elbiaze¹¹, Karima El Rhazi¹⁰, Jin-Ping Zheng¹², Pixin Ran¹², Tobias Welte¹³, Daniel Obaseki¹⁴, Gregory Erhabor¹⁴, Asma Elsony¹⁵, Nada Bakri Osman¹⁵, Rana Ahmed¹⁵, Ewa Nizankowska-Mogilnicka¹⁶, Filip Mejza¹⁷, David M. Mannino¹⁸, Cristina Bárbara¹⁹, Wouters E.F.M.²⁰, Luisito F. Idolor²¹, Li-Cher Loh²², Abdul Rashid²², Sanjay Juvekar²³, Thorarinn Gislason^{24,25}, Mohamed Al Ghobain²⁶, Michael Studnicka²⁷, Imed Harrabi²⁸, Meriam Denguezli²⁸, Parvaiz A Koul²⁹, Christine Jenkins^{30,31,32}, Guy Marks^{30,31,32}, Rain Jõgi³³, Hasan Hafizi³⁴, Christer Janson³⁵, Wan C. Tan³⁶, Althea Aquart-Stewart³⁷, Bertrand Mbatchou³⁸, Asaad Nafees³⁹, Kirthi Gunasekera⁴⁰, Terry Seemungal⁴¹, Mahesh PA⁴², Paul Enright⁴³, William M. Vollmer⁴⁴, Marta Blangiardo⁴⁵, Fadlalla G. Elfadaly⁴⁶, A Sonia Buist⁴⁷

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

²Nuffield Department of Population Health, University of Oxford, Oxford, UK

³Cukurova University School of Medicine, Department of Chest Diseases, Adana, Turkey

⁴Department of Pneumology, Faculty of Medicine and CHU Annaba, Algeria

⁵Department of Thoracic Medicine, Institute of Medicine, University of Bergen, Bergen,

Norway

⁶University of Cape Town Lung Institute, Cape Town, South Africa

⁷The Malawi Liverpool Wellcome Trust, Blantyre, Malawi

24 ⁸Pulmonology and Allergology Department, National Centre of Cardiology and Internal
25 Medicine, Bishkek, Kyrgyzstan

26 ⁹Unit of Teaching and Research in Occupational and Environmental Health, Cotonou,
27 Benin

28 ¹⁰Laboratoire d'épidémiologie, Recherche Clinique et Santé Communautaire, Fès, Morocco
29 ¹¹Department of Respiratory Medicine, Faculté de Médecine, University Hospital, Fès,
30 Morocco

31 ¹²State Key Laboratory of Respiratory Disease, National Clinical Research Center For
32 Respiratory Diseases, Guangzhou Institute of Respiratory Health, First Affiliated Hospital
33 of Guangzhou Medical College, Guangzhou, China

34 ¹³Department of Pneumology, Hannover Medical School and German Center of Lung
35 Research, Hannover, Germany

36 ¹⁴Obafemi Awolowo University, Ile-Ife, Nigeria

37 ¹⁵The Epidemiological Laboratory, Khartoum, Sudan

38 ¹⁶Division of Pulmonary Diseases, Department of Medicine, Jagiellonian University School
39 of Medicine, Krakow, Poland

40 ¹⁷Center for Evidence Based Medicine, 2nd Department of Internal Medicine, Jagiellonian
41 University Medical College, Kraków, Poland

42 ¹⁸University of Kentucky, Lexington, Kentucky, USA

43 ¹⁹Institute of Environmental Health, Lisbon Medical School, Lisbon University, Lisbon
44 Portugal

45 ²⁰Maastricht University Medical Center, Maastricht, the Netherlands

46 ²¹ Philippine College of Chest Physicians, Manila, Philippines

47 ²²Royal College of Surgeons in Ireland and University College Dublin Malaysia Campus
48 (RUMC),
49 Penang, Malaysia
50 ²³Vadu HDSS, KEM Hospital Research Centre Pune, Pune, India
51 ²⁴Landspítali University Hospital, Dept.Sleep, Reykjavik, Iceland
52 ²⁵University of Iceland, Faculty of Medicine, Reykjavik, Iceland
53 ²⁶Saudi Thoracic Society, Riyadh, Saudi Arabia
54 ²⁷Paracelsus Medical University, Department of Pulmonary Medicine, Salzburg, Austria
55 ²⁸Faculté de Médecine, Sousse, Tunisia
56 ²⁹Sher-i-Kashmir Institute of Medical Sciences, Srinagar, J&K, India
57 ³⁰Woolcock Institute of Medical Research, Sydney, Australia
58 ³¹University of Sydney, Sydney, New South Wales, Australia
59 ³²University of New South Wales, Sydney, New South Wales, Australia
60 ³³Lung Clinic, Tartu University Hospital, Tartu, Estonia
61 ³⁴Tirana University Hospital "Shefqet Ndroqi", Albania
62 ³⁵Department of Medical Sciences, Respiratory, Allergy and Sleep Research, Uppsala
63 University, Sweden
64 ³⁶Centre for Heart Lung Innovation, University of British Columbia, Vancouver, BC, Canada
65 ³⁷University of the West Indies, Kingston, Jamaica
66 ³⁸Douala General Hospital, Douala, Cameroon
67 ³⁹Aga Khan Univeristy, Karachi, Pakistan
68 ⁴⁰Medical Research Institute, Central Chest Clinic, Colombo, Sri Lanka
69 ⁴¹University of the West Indies, St. Augustine, Trinidad and Tobago
70 ⁴²JSS University, Mysore, India

71 ⁴³University of Arizona, Tucson, AZ

72 ⁴⁴Kaiser-Permanente Center for Health Research, Portland OR, USA

73 ⁴⁵School of Public Health, Imperial College, London, UK

74 ⁴⁶School of Mathematics and Statistics, STEM, The Open University, Milton Keynes, UK

75 ⁴⁷Oregon Health & Science University, Portland, OR, USA

76

77

78

79

80 The population attributable risk (PAR) is the prevalence of disease in the total population
81 (P_d) minus the prevalence of disease in the unexposed population (P_u).¹

$$82 \quad PAR = P_d - P_u \quad [1]$$

83 The population attributable fraction (PAF) is the population attributable disease divided by
84 the total prevalence of disease in the population.²

$$85 \quad PAF = (P_d - P_u) / P_d \quad [2]$$

86 Based on [1] and [2], the formula for PAR can be rewritten as:

$$87 \quad PAR = PAF * P_d \quad [3]$$

88 PAF can also be estimated from the relative risk (RR) of the disease and the prevalence of
89 exposure (P_e) using the formula given by Miettinen:³

$$90 \quad PAF = \frac{P_e (RR - 1)}{RR} \quad [4]$$

91 So that PAR becomes:

$$92 \quad PAR = \frac{P_e (RR - 1)}{RR} * P_d \quad [5]$$

93 Using formula [5], a PAR ("local PAR") for a given risk factor was calculated from the RR, P_d
94 and P_e for each study site. A RR adjusted for confounders and for the other risk factors was
95 estimated by multivariable regression analysis using a log-binomial model.

96 For smoking and education, we estimated the PAR for each category, and we also estimated
97 the overall PAR for the variable by combining PAR values across categories "c", using the
98 following formula:⁴

$$99 \quad PAR = \left(\sum_{i=1}^c P_{e_i} \left(\frac{RR_i - 1}{RR_i} \right) \right) * P_d \quad [6]$$

100 where P_{e_i} is the proportion of cases exposed to the i^{th} level of the risk factor and RR_i is the
101 RR for CAO for the i^{th} category.

102 A difficulty arises when the numbers in any one site are too low to get a precise estimate of
103 the RR and of PAR. For this reason, we used a Bayesian hierarchical log-binomial model to
104 estimate the RR for each site, assuming that all local estimates of RR come from a common
105 distribution. This allows us to “borrow” information from the other sites to increase the
106 precision of the RR estimate in each single site.⁵ By adjusting the log-binomial model for age
107 (confounder) and level of education as a proxy measure for socio-economic status (risk
108 factor of interest), we accounted for non-response as these are the main factors affecting
109 the probability of selection in the survey.⁶ Additionally, we accounted for a cluster and/or
110 stratified sampling framework in some sites by including an additional level of hierarchy in
111 the model.⁷ We used separate models for men and women.

112 For Pe and Pd , we assumed that under the cross-sectional design, when the total sample
113 size of the site is fixed, the observed number of subjects in each cross-classification of the
114 disease by exposure contingency table follows the multinomial distribution.⁸ Both models,
115 hierarchical log-binomial and multinomial model, were implemented simultaneously to
116 estimate PAF and PAR.

117 The parameters of interest were estimated by an iterative Monte Carlo Markov Chain
118 (MCMC) process using the Gibbs sampling, implemented in the freely available OpenBUGS
119 package.⁹ Our model was run with two chains, using a burn-in of 50,000 iterations and
120 50,000 iterations to estimate the posterior distribution of each parameter. In order to
121 reduce the autocorrelation in the chains, we retained only 1 in every 10 iterations in the
122 posterior sample. To check the convergence of the model, we calculated the Gelman-Rubin
123 statistic ($R\text{-hat}$)¹⁰ and inspected the trace plots, as well as the density plots of all estimated
124 PARs. We calculated the posterior mean, 95% credible interval limit (CrI) using 2.5% and
125 97.5% percentiles of the PAR for all modifiable variables in the model.

126 The analysis was conducted in the statistical package Stata, version 14, with a user-written
 127 program to call OpenBUGS into Stata.¹¹ Across all analyses, the R-hat statistic for all
 128 parameters was between 0.99 to 1.01, suggesting that convergence was reached. The trace
 129 plots showed that the two chains were mixing well for all parameters in all models. The
 130 density plots for the PAR estimate for all risk factors of interest showed good convergence
 131 of the model, except for sites with a low prevalence of the risk factor of interest.

132 Details of our model, as applied to the specific example of PAR of chronic airflow
 133 obstruction (CAO) for passive smoking is given in the OpenBUGS code below.

134 Covariates used in the model are: pack-years (five categories: never-smoker (reference), 1-5
 135 pack-years, 6-15 pack-years, 16-25 pack-years, >25 pack-years), education (three categories:
 136 none to primary, secondary, more than secondary school (reference)), passive smoking
 137 (yes/no), doctor-diagnosed tuberculosis (ever/never), working in a dusty job (>10 years vs. ≤
 138 10 years), body mass index (BMI) (four categories: underweight, normal weight (reference),
 139 overweight, obese), age.

140

141 **# OpenBUGS code:**

```
142 model {
143   for (j in 1:N) {           # j stands for number of observations
144     # Defining log-binomial hierarchical model
145     CAO[j]~dbern(p[j])
146     log(p[j]) <- (alpha[centre[j]] + b.pack_5cat[pack_5cat[j],centre[j]] + b.age[centre[j]]*age10[j]
147     + b.bmi[bmicat4[j],centre[j]] + b.educ[educ3[j],centre[j]] + b.passive[passive[j],centre[j]] +
148     b.tb[tuberc[j],centre[j]] + b.dusty[dusty10cat[j],centre[j]] + b.cluster[cluster[j]] +
149     b.strata[strata[j]])
```

```

150 # Restricting probabilities between 0 and 1.
151 ones[j] <- 1
152 ones[j] ~ dbern(C1[j])
153 C1[j] <- step(1-p[j])
154 }
155 # cluster = 1 which represents those centres which do not use cluster sampling
156 b.cluster[1]<-0
157 #strata = 1 which represents those centres which did not use stratified sampling
158 b.strata[1]<-0
159
160 # Priors
161 for ( r in 1:R) {      # r represents the centre number
162   alpha[r] ~ dnorm(alpha_mu, alpha_prec)
163   b.pack_5cat[1,r] <-0
164   b.pack_5cat[2,r] ~ dnorm(mu_pack3, prec_pack2)
165   b.pack_5cat[3,r] ~ dnorm(mu_pack3, prec_pack3)
166   b.pack_5cat[4,r] ~ dnorm(mu_pack4, prec_pack4)
167   b.pack_5cat[5,r] ~ dnorm(mu_pack5, prec_pack5)
168   b.age[r] ~ dnorm(mu_age, prec_age)
169   b.bmi[1,r] <-0
170   b.bmi[2,r] ~ dnorm(mu_bmi2, prec_bmi2)
171   b.bmi[3,r] ~ dnorm(mu_bmi3, prec_bmi3)
172   b.bmi[4,r] ~ dnorm(mu_bmi4, prec_bmi4)
173   b.educ[3,r] <- 0

```

```

174   b.educ[1,r] ~ dnorm(mu_educ1, prec_educ1)
175   b.educ[2,r] ~ dnorm(mu_educ2, prec_educ2)
176   b.passive[2,r] <-0
177   b.passive[1,r] ~ dnorm(mu_passive,prec_passive)
178   b.tb[2,r] <-0
179   b.tb[1,r] ~ dnorm(mu_tb, prec_tb)
180   b.dusty[2,r] <- 0
181   b.dusty[1,r] ~ dnorm(mu_dusty10, prec_dusty10)
182
183   # Calculation of RRs
184   RR_pack2[r] <- exp(b.pack_5cat[2,r])
185   RR_pack3[r] <- exp(b.pack_5cat[3,r])
186   RR_pack4[r] <- exp(b.pack_5cat[4,r])
187   RR_pack5[r] <- exp(b.pack_5cat[5,r])
188   RR_age[r] <- exp(b.age[r])
189   RR_bmi2[r] <- exp(b.bmi[2,r])
190   RR_bmi3[r] <- exp(b.bmi[3,r])
191   RR_bmi4[r] <- exp(b.bmi[4,r])
192   RR_educ1[r] <- exp(b.educ[1,r])
193   RR_educ2[r] <- exp(b.educ[2,r])
194   RR_passive[r] <- exp(b.passive[1,r])
195   RR_tb[r] <- exp(b.tb[1,r])
196   RR_dusty[r] <- exp(b.dusty[1,r])
197

```

```

198 for ( k in 2:C) {           # k stands for number of clusters
199   b.cluster[k] ~
200   dnorm(mu_cluster[in.which.centre.cluster[k]],tau_cluster[in.which.centre.cluster[k]]) #
201   in.which.centre tells the programme to include only centres with cluster exist
202   RR_cluster[k] <- exp(b.cluster[k])
203 }
204 for ( s in 2:S) {           # s stands for number of strata
205   # in.which.strata tells the programme to include only centres with strata
206   b.strata[s] ~
207   dnorm(mu_strata[in.which.centre.strata[s]],tau_strata[in.which.centre.strata[s]])
208 }
209 # Introducing a Hierarchy on cluster, c- indicates cluster number
210 mu_c [r] ~ dnorm(0.0, 0.01)
211 tau_c[r] ~ dgamma(1, 0.005)
212 mu_cluster[r] <- step(cluster.start[r]-2)*mu_c [r]
213 tau_cluster[r] <- step(cluster.start[r]-2)*tau_c[r]
214
215 # Introducing a Hierarchy on strata, s - indicates strata number
216 mu_s [r] ~ dnorm(0.0, 0.01)
217 tau_s[r] ~ dgamma(1, 0.005)
218 mu_strata [r] <- step(strata.start[r]-2)*mu_s [r]
219 tau_strata[r] <- step(strata.start[r]-2)*tau_s[r]
220
221

```



```

222 #Calculation of multinomial probabilities
223 # a, b, c ,d are the cells of 4x4 table for outcome X exposure
224 eta[r,1]<-a[r]+beta[r,1]
225 eta[r,2]<-b[r]+beta[r,2]
226 eta[r,3]<-c[r]+beta[r,3]
227 eta[r,4]<-d[r]+beta[r,4]
228 f[r,1:4] ~ ddirich(eta[r,1:4])
229 Pa[r] <-f[r,1]
230 Pb[r] <-f[r,2]
231 Pc[r] <-f[r,3]
232 Pd[r] <-f[r,4]
233
234 # Calculating proportion of the cases exposed to passive smoking (Pe_passive) and
235 proportion of CAO in the population (Pd_passive)
236 Pe_passive[r] <- Pc[r] /(Pa[r] + Pc[r])
237 Pd_passive[r] <- (Pc[r] + Pa[r]) /( Pb[r] + Pa[r] + Pc[r] + Pd[r] )
238
239 # Estimating centre-specific PAF and PAR for passive smoking
240 PAF_passive[r] <- (Pe_passive[r]* ((RR_passive[r]-1) / RR_passive[r]))
241 PAR_passive[r] <- ((Pe_passive[r]* ((RR_passive[r]-1) / RR_passive[r]))) * Pd_passive[r]
242 }
243 # Hyper Prior distributions for all coefficients and intercept (alpha)
244 alpha_mu ~ dnorm(0.0, 0.0001)
245 alpha_prec ~ dgamma(1, 0.005)

```

246 $\mu_{\text{age}} \sim \text{dnorm}(0.0, 0.01)$
247 $\text{prec}_{\text{age}} \sim \text{dgamma}(1, 0.005)$
248 $\mu_{\text{bmi2}} \sim \text{dnorm}(0.0, 0.01)$
249 $\text{prec}_{\text{bmi2}} \sim \text{dgamma}(1, 0.005)$
250 $\mu_{\text{bmi3}} \sim \text{dnorm}(0.0, 0.01)$
251 $\text{prec}_{\text{bmi3}} \sim \text{dgamma}(1, 0.005)$
252 $\mu_{\text{bmi4}} \sim \text{dnorm}(0.0, 0.01)$
253 $\text{prec}_{\text{bmi4}} \sim \text{dgamma}(1, 0.005)$
254 $\mu_{\text{pack2}} \sim \text{dnorm}(0.0, 0.01)$
255 $\text{prec}_{\text{pack2}} \sim \text{dgamma}(1, 0.005)$
256 $\mu_{\text{pack3}} \sim \text{dnorm}(0.0, 0.01)$
257 $\text{prec}_{\text{pack3}} \sim \text{dgamma}(1, 0.005)$
258 $\mu_{\text{pack4}} \sim \text{dnorm}(0.0, 0.01)$
259 $\text{prec}_{\text{pack4}} \sim \text{dgamma}(1, 0.005)$
260 $\mu_{\text{pack5}} \sim \text{dnorm}(0.0, 0.01)$
261 $\text{prec}_{\text{pack5}} \sim \text{dgamma}(1, 0.005)$
262 $\mu_{\text{passive}} \sim \text{dnorm}(0.0, 0.01)$
263 $\text{prec}_{\text{passive}} \sim \text{dgamma}(1, 0.005)$
264 $\mu_{\text{tb}} \sim \text{dnorm}(0.0, 0.01)$
265 $\text{prec}_{\text{tb}} \sim \text{dgamma}(1, 0.005)$
266 $\mu_{\text{educ1}} \sim \text{dnorm}(0.0, 0.01)$
267 $\text{prec}_{\text{educ1}} \sim \text{dgamma}(1, 0.005)$
268 $\mu_{\text{educ2}} \sim \text{dnorm}(0.0, 0.01)$
269 $\text{prec}_{\text{educ2}} \sim \text{dgamma}(1, 0.005)$

270 `mu_dusty10 ~ dnorm(0.0, 0.01)`

271 `prec_dusty10 ~ dgamma(1, 0.005)`

272 `}`

273

274

275 **References**

276 1. Levin ML. The occurrence of lung cancer in man. *Acta Unio Int Contra Cancrum* 1953;
277 **9**(3): 531-41.

278 2. Rothman K, Greenland S. *Modern Epidemiology*: Lippincott Williams and Wilkins;
279 1998.

280 3. Miettinen OS. Proportion of Disease Caused or Prevented by a Given Exposure, Trait
281 or Intervention. *American journal of epidemiology* 1974; **99**(5): 325-32.

282 4. Rockhill B, Newman B, Weinberg C. Use and misuse of population attributable
283 fractions. *American journal of public health* 1998; **88**(1): 15-9.

284 5. Gelman A, Hill J. *Multilevel linear models: varying slopes, non-nested models, and*
285 *other complexities. Data analysis using regression and multilevel/hierarchical models.*
286 Cambridge: Cambridge University Press; 2006.

287 6. Gelman A. Struggles with Survey Weighting and Regression Modeling. *Stat Sci* 2007;
288 **22**(2): 153-64.

289 7. Raudenbush S, Bryk A. *Hierarchical Linear Models. Applications and Data Analysis*
290 *Methods*: Sage Publications; 2002.

291 8. Walter SD. The estimation and interpretation of attributable risk in health research.
292 *Biometrics* 1976; **32**(4): 829-49.

- 293 9. Lunn D, Spiegelhalter D, Thomas A, Best N. The BUGS project: Evolution, critique and
294 future directions. *Statistics in medicine* 2009; **28**(25): 3049-67.
- 295 10. Brooks S, Roberts G. Assessing Convergence of Markov Chain Monte Carlo
296 Algorithms. *Statistics and Computing* 1997; **8**: 319-35.
- 297 11. Palmer T, Thompson J, Moreno S. Performing Bayesian analysis in Stata using
298 WinBUGS. *Stata Journal* 2007; **6**(4): 530-49.
- 299