Global and regional trends in COPD mortality, 1990–2010

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ABSTRACT   Between 1990 and 2010, chronic obstructive pulmonary disease (COPD) moved from the fourth to third most common cause of death worldwide.

Using data from the Global Burden of Disease programme we quantified regional changes in the number of COPD deaths and COPD mortality rates between 1990 and 2010. We estimated the proportion of the change that was attributable to gross national income per capita and an index of cumulative smoking exposure, and quantified the difference in mortality rates attributable to demographic changes.

Despite a substantial decrease in COPD mortality rates, COPD deaths fell only slightly, from three million in 1990 to 2.8 million in 2010, because the mean age of the population increased. The number of COPD deaths in 2010 would have risen to 5.2 million if the age- and sex-specific mortality rates had remained constant. Changes in smoking led to only a small increase in age- and sex-specific mortality rates, which were strongly associated with changes in gross national income.

The increased burden of COPD mortality was mainly driven by changes in age distribution, but age- and sex-specific rates fell as incomes rose. The rapid response to increasing affluence suggests that changes in COPD mortality are not entirely explained by changes in early life.

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COPD age-standardised mortality rates decrease as incomes increase, but COPD deaths increase as population ages http://ow.ly/I66ND

Introduction

Global patterns of mortality are changing, mainly due to three related transformations: 1) an epidemiological transition driven by change in global risks, with falling death rates in childhood associated with infectious disease; 2) a demographic transition with more people surviving into later life, and 3) a healthcare transition with improved effectiveness of both preventive and curative or palliative treatments. The reassessment of the Global Burden of Disease programme in 2010 identified chronic obstructive pulmonary disease (COPD) as the third most common cause of death worldwide [1], up from fourth in 1990 [2]. Understanding the reasons for this is important in order to identify potential public health interventions. In particular, we need to know whether this change has been caused by an increase in the mortality rate or by an increase in the absolute number of deaths due to increased prevalence, for example associated with ageing in the population. Alternatively, the change may be a relative one, with COPD mortality having declined less than mortality from other causes.

Cigarette smoking is regarded as the most important cause of COPD, with other inhaled hazards from occupational, domestic or outdoor sources thought to play an important role [3]. However, in a study of mortality in local authorities in England and Wales, BARKER and OSMOND [4] noted that there was a strong association between childhood deaths from pneumonia and bronchitis in the 1920s and deaths from "COPD" in the 1970s, with high death rates from both conditions being strongly associated with poverty. As this association was not noted for lung cancer, this relationship was unlikely to be strongly confounded by cigarette smoking. Subsequently, by following up a cohort of men born in the 1920s, with very complete health records from the first year of life, the authors showed associations between early life factors and death from COPD and adult lung function, again associations that were not explained by smoking habits [5]. More recently, the Burden of Obstructive Lung Disease (BOLD) study has shown a strong ecological association between national levels of poverty and the prevalence of both a low forced vital capacity (FVC) and national COPD mortality rates [6].

Many descriptions of national and regional mortality trends over time have been published previously [7–14]. These have reported variable trends, mostly at a local level, and have rarely analysed the drivers of change. In this study we have examined trends in COPD mortality rates for all 21 Global Burden of Disease regions. We have assessed the impact of population changes on the number of COPD deaths, the associations between changes in age- and sex-specific mortality rates from COPD, and changes in both national income and smoking. By analysing trends within regions over time, we have avoided much of the confounding between national income and other factors that vary across regions, which is inevitable in purely cross-sectional analyses.

Methods

Between 1990 and 1999, mortality data were collected by country and year in countries allocated to 21 Global Burden of Disease regions from 566 vital registration sources, 27 surveillance reports and one verbal autopsy report. Between 2000 and 2010, mortality data were collected by country and year in the same regions from 894 vital registration sources, 24 surveillance reports and eight verbal autopsy reports. Our definition of COPD is based on in International Classification of Diseases-9 codes 490–492, 494 and 496, and International Classification of Diseases-10 codes J40–J44, J47. We used previously developed algorithms [15] to improve the quality of the information on mortality by redistributing vague and unsatisfactory causes of death (garbage codes) to more likely causes of death using similar methods in all countries and years. The selection of the model used to assign deaths to specific causes was based on its out-of-sample predictive validity [15]. Our model of COPD mortality assigns each death to a single cause.

We analysed COPD mortality rates for 1990 and 2010 for each region and each age- and sex-specific group, limiting the analyses to people aged ⩾40 years (18 groups per region, nine groups for age and two groups for sex). We used information on regional mortality rates from lung cancer for the same age and sex groups to create a proxy for smoking exposure, based on a modification of the method proposed by PETO et al. [16]. This uses the strong association between smoking and lung cancer mortality to estimate the cumulative lifetime exposure to tobacco. Briefly, a common baseline mortality rate from lung cancer was assumed in the absence of smoking and estimated from the age- and sex-specific lung cancer mortality rates among nonsmokers in the American Cancer Society's Cancer Prevention Study II. Subtracting these figures from the age- and sex-specific lung cancer mortality rates recorded in the Global Burden of Disease data, we derived an index of cumulative smoking exposure for each group. This index, referred to as the smoking index, is expressed as a rate per 100000. Gross national income (GNI) per capita was estimated in US dollars and adjusted for purchasing power parity using data from the World Bank [17]. The average GNI for each country in the region was weighted by the total population of each country to provide a regional value for 1990 and 2010. To compare COPD mortality rates across regions, we estimated age-standardised mortality rates by applying the regional age-specific rates to a standard

world population covering the same age span (⩾40 years). For each region, the number of deaths that would have been expected in 2010 if the population had been the same as in 1990 was calculated, by taking the age- and sex-specific COPD mortality rates for 2010 and applying them to the age and sex population distribution of 1990. The difference between this figure and the actual number of deaths in 2010 gave the change in deaths due to changes in the age and sex structure and size of the population.

To analyse the effects of GNI and smoking on COPD mortality rates in 1990 and 2010, and their impact on the change in COPD mortality between the two time-points, we used multilevel regression analysis accounting for the clustering of the data within regions. We first analysed the COPD mortality rate against GNI and smoking index separately for 1990 and 2010, adjusting for age and sex, with log transformation of the mortality rate, GNI and smoking index. In order to log transform the smoking index we added a small constant (180 per 100 000) to ensure that all values were positive. We then analysed the change in COPD mortality rates using a multilevel linear regression model with the log of the 2010:1990 mortality rate ratio as the outcome and the corresponding 2010:1990 log ratios for GNI and smoking index as linear predictors, and adjusting for age and sex as categorical predictors with additive effects. As a sensitivity analysis, we reran the analysis after dropping the regions where the change in GNI had been highest, namely East Asia, South-East Asia, Andean Latin America, and southern Latin America.

We estimated the population attributable fraction of the change in COPD mortality for GNI and smoking, *i.e.* the percentage of change in COPD mortality between 1990 and 2010 that was attributable to changes in GNI and smoking, using the programme margins in Stata (StataCorp., College Station, TX, USA) [18]; all analyses were undertaken in Stata 12.2.

Results

Most deaths from COPD occur in low-income regions including East, South and South-East Asia and central Africa, where age-standardised rates are also higher (fig. 1). Globally, the total number of COPD deaths fell from three million in 1990 to 2.8 million in 2010, a fall of 5.5%, whereas the expected number of age- and sex-specific rates were maintained at the 1990 levels, which was very much higher at 5.2 million (table 1). There was a clear fall in age- and sex-specific rates for all groups between 1990 and 2010 (fig. 2a), and COPD mortality fell in all age groups, with the greatest relative declines in younger people (fig. 2b). There was substantial variation in the 2010:1990 mortality rate ratio but clear reductions in all regions, except the North America high-income region where the mortality rate remained stable (fig. 3).

Changes in smoking index varied widely between regions, from a reduction of 15.3% in South Sub-Saharan Africa to an increase of 14.5% in East Asia (table 2). GNI increased in all regions over this

Standardised mortality per 100 000

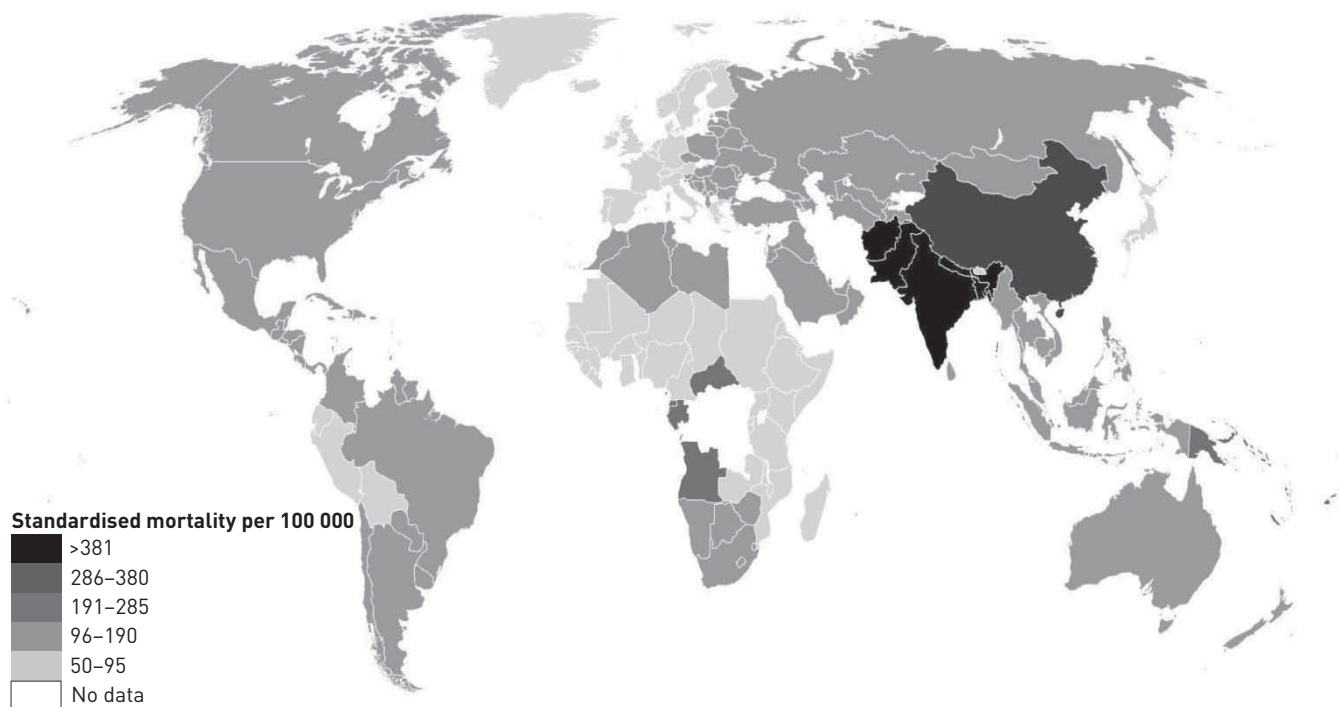|	
■	>381
■	286–380
■	191–285
■	96–190
■	50–95
□	No data

FIGURE 1 Age- and sex-adjusted chronic obstructive pulmonary disease mortality in 2010.

TABLE 1 Chronic obstructive pulmonary disease (COPD) deaths, total population and age-standardised COPD mortality rates by region and year

Region	1990			2010			Expected COPD deaths in 2010[#]
	COPD deaths	Population	Age-standardised COPD mortality per 100000	COPD deaths	Population	Age-standardised COPD mortality per 100000	
Asia-Pacific[¶]	30075	69100 000	91	45041	95700000	55	72297
Asia							
Central	17210	16000000	249	15934	23600000	166	23696
East	1430132	314000000	1044	967505	563000000	419	2500856
South	874239	233000000	980	1009473	418000000	639	1591997
Southeast	77567	95800000	213	121999	183000000	185	148331
Australasia	7357	7660514	175	8773	12000000	104	13669
Caribbean	4178	7459902	110	6525	12500000	105	6873
Europe							
Central	43513	47600000	180	38076	57000000	110	61533
Eastern	97358	88300000	246	60063	98700000	125	121998
Western	152394	168000000	142	169312	218000000	98	229961
Latin America							
Andean	2974	7878512	99	5294	14400000	82	6358
Central	24604	32500000	180	47789	65500000	165	47131
Southern	10340	15400000	138	15756	22400000	121	17562
Tropical	34090	34500000	256	54320	65800000	184	75753
North Africa/ Middle East	29997	56100000	137	46593	114000000	108	60998
North America[¶]	105704	106000000	163	167299	158000000	159	157969
Oceania	1067	1010723	324	1483	1881734	248	2004
Sub-Saharan Africa							
Central	7592	9093840	237	9992	15300000	192	12900
East	18259	34800000	143	21014	60400000	94	33310
Southern	8170	9741673	251	9625	16500000	167	15178
West	18238	36000000	144	16011	59000000	75	31543
Total	2995058	1390000000	544	2837877	2280000000	291	5231916

Data are presented as n. [#]: calculated as the number of deaths expected in 2010 if the population had been the same as in 1990 in terms of age and sex; [¶]: high income.

period of time, except in West Sub-Saharan Africa. In most regions this increase was substantial and in East Asia it was >700%. Plotting age-standardised COPD mortality rates by GNI showed a negative association. Because this appeared nonlinear we transformed GNI to a log scale.

Multilevel regression analysis, adjusting for age and sex, showed a highly statistically significant association of smoking index and GNI with COPD mortality rate for both years (table 3). Since the model is a log–log
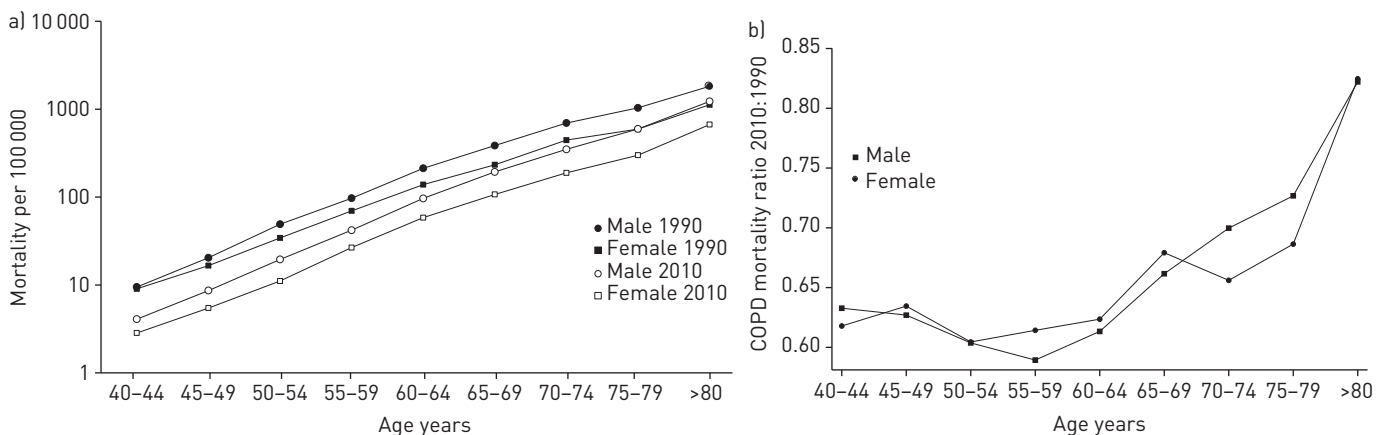

FIGURE 2 a) Chronic obstructive pulmonary disease (COPD) mortality rates for 1990 and 2010, and b) COPD mortality ratios for 2010:1990 according to sex and age.
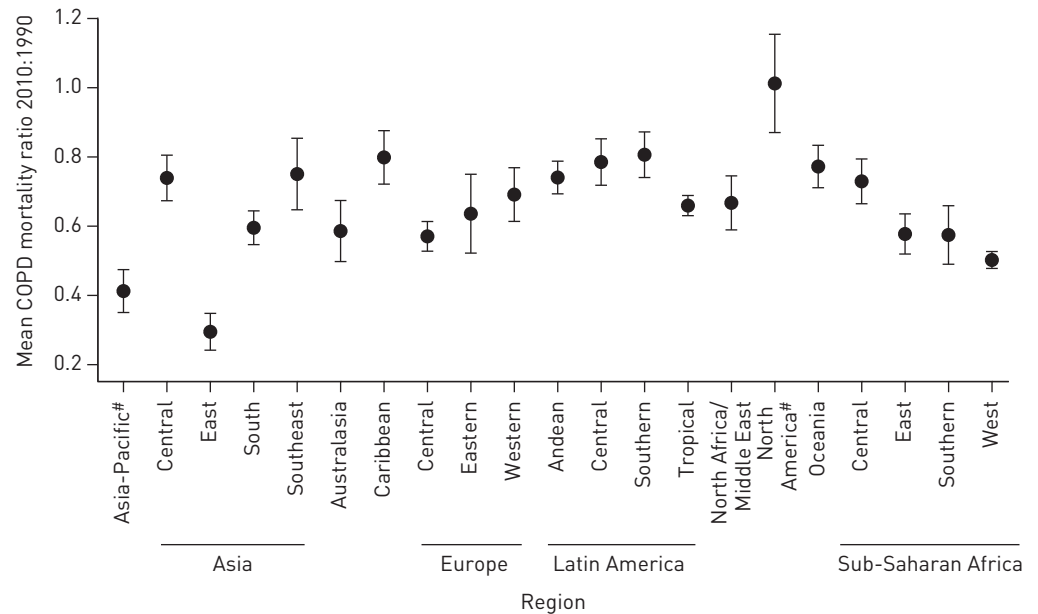
FIGURE 3 Mean age- and sex-specific chronic obstructive pulmonary disease (COPD) mortality ratios for 2010:1990 for each of the 21 regions. [#]: high income.

regression (exposure and outcome both log transformed), the coefficients for GNI and smoking represent the percentage change in COPD mortality rate given a certain percentage change in GNI or smoking, while keeping all other variables constant. For example, in the 1990 analysis, if we consider the effect of a 50% increase in exposure (1.5 times), the GNI coefficient of −0.47 means a decrease in mortality rate of 17% ($1.5^{-0.47}$=0.83, *i.e.* 17% reduction); similarly, the smoking coefficient of 0.43 means a 19% increase in mortality rate. Corresponding figures for 2010 were a 12% (95% CI 3–19%) decrease for a 50% increase in GNI and a 17% (95% CI 12–21%) increase for a 50% increase in smoking index. As expected, for both 1990 and 2010 the model showed COPD mortality rates were higher in older age groups and in men, independent of smoking.

The multilevel regression analysis of the ratio of COPD mortality rates between 2010 and 1990, also analysed as a log–log model, showed a 13% decrease in mortality rate for a 50% increase in GNI from 1990 to 2010 (p=0.02). The effect of change in smoking index (2010:1990 mortality rate ratio) on change in COPD mortality was also statistically significant, although its magnitude was much smaller; a 0.16% (95% CI 0.08–0.17%) increase in COPD mortality rate for a 50% increase in smoking index (table 3). In agreement with figure 2, the multilevel regression model showed large between-region variation in COPD mortality, with an intraclass correlation coefficient of 0.69. When we dropped the four regions with the highest change in GNI from the analysis we obtained the same coefficient for the smoking index and only a small change in the coefficient for GNI, with a 16% (95% CI 4–25%) decrease in COPD mortality rate for a 50% increase in GNI from 1990 to 2010. This remained statistically significant.

Finally, we estimated the percentage change in COPD mortality that was attributable to the change in GNI and smoking exposure. Changes in GNI and smoking exposure accounted for a 26.2% (95% CI 4.7–47.7%) and for 3.9% (95% CI 3.2–4.6%) change in COPD mortality.

Discussion

The relative increased burden from COPD mortality compared with mortality from other causes is largely due to changes in population structure. The apparent paradox that COPD has risen to be the third most common cause of death at a time when age-standardised mortality rates from COPD have been falling is explained by the relatively faster decline in all-cause mortality. Between 1990 and 2010 the total number of COPD deaths fell from 3 to 2.8 million, a fall of 5.5%, while during the same period deaths due to all causes fell by 17%. The increase in COPD mortality due to population ageing explains why the absolute number of COPD deaths has decreased only slightly although age- and sex-specific mortality rates have been decreasing in almost all regions. Much of this decline is associated with changes in GNI, with countries with the greatest improvement in GNI having the greatest relative improvement in COPD mortality rates. Changes over time in the cumulative exposure to cigarette smoking have had relatively little impact.

TABLE 2 Gross national income (GNI) per capita and smoking index by region and year

Region	GNI per capita $			Smoking index								
	1990	2010	% change[#]	Overall			Male			Female		
				1990	2010	% change[#]	1990	2010	% change[#]	1990	2010	% change[#]
Asia-Pacific[¶]	16 237	33 840	108.4	279.0	277.7	−0.5	342.1	339.3	−0.8	215.9	216.0	0.1
Asia												
Central	2444	3329	36.2	251.6	223.2	−11.3	311.0	261.6	−15.9	192.1	184.9	−3.8
East	884	7733	774.7	279.1	319.7	14.5	316.7	382.1	20.7	241.6	257.2	6.5
South	864	3084	256.9	187.2	195.1	4.2	197.7	208.1	5.3	176.7	182.2	3.1
Southeast	1689	5042	198.6	230.3	247.0	7.2	250.3	277.7	10.9	210.3	216.2	2.8
Australasia	16 259	35 200	116.5	305.2	266.2	−12.8	379.2	300.4	−20.8	231.3	232.0	0.3
Caribbean	3595	6692	86.1	265.5	259.5	−2.2	307.0	293.9	−4.3	223.9	225.1	0.5
Europe												
Central	6173	15 569	152.2	308.0	294.9	−4.2	406.1	376.2	−7.4	209.9	213.7	1.8
Eastern	7466	15 907	113.1	316.9	275.2	−13.2	436.3	360.3	−17.4	197.5	190.0	-3.8
Western	15 216	35 460	133.0	313.8	278.3	−11.3	41.2	338.4	−18.5	212.5	218.1	2.7
Latin America												
Andean	3033	7754	155.7	202.7	193.0	−4.8	210.3	192.1	−8.6	195.1	193.9	−0.6
Central	6330	11 458	81.0	208.7	203.2	−2.6	223.4	213.1	−4.6	194.0	193.4	−0.3
Southern	4893	15 242	211.5	267.9	243.3	−9.2	338.8	287.4	−15.2	197.0	199.1	1.1
Tropical	4975	10 789	116.9	221.2	218.5	−1.3	247.5	237.5	−4.1	194.9	199.5	2.3
North Africa/Middle East	4108	9743	137.2	225.3	218.3	−3.1	258.6	248.7	−3.8	192.0	187.8	−2.2
North America[¶]	22 450	46 337	106.4	353.5	315.2	−10.8	427.9	348.1	−18.7	279.1	282.3	1.1
Oceania	1383	2711	96.0	197.0	195.5	−0.8	197.9	193.1	−2.4	196.1	197.9	0.9
Sub-Saharan Africa												
Central	927	949	2.5	181.3	182.1	0.4	183.2	185.0	1.0	179.5	179.3	−0.1
East	561	1294	130.8	166.9	167.1	0.1	159.6	161.1	1.0	174.2	173.1	−0.7
Southern	5193	9854	89.7	256.3	217.2	−15.3	300.9	238.4	−20.8	211.7	195.9	−7.4
West	854	769	−9.9	168.1	166.4	−1.0	166.7	164.4	−1.4	169.6	168.5	−0.6

Data are presented as n, unless otherwise stated. [#]: calculated as $(value_{2010} - value_{1990}/value_{1990}) \times 100$; [¶]: high income.

The ecological design of this study limits conclusions to inferences about populations rather than individuals but, unlike most ecological studies, the longitudinal design and analysis of within-region changes over time largely overcomes the usual problem of confounding with other large between-region differences, which is typical of many ecological studies.

Since the middle of the 19th century, the analysis of cause of death data has provided important insights into disease burden and the causes of ill health [19]. The data are nevertheless limited by incomplete records and inaccuracies in disease coding. Our definition of COPD mortality is deliberately broad, including all chronic lower respiratory tract causes whether bronchitic or obstructive, with the sole exception of asthma. Narrower definitions are more prone to misclassification and to local variation in the practice of both medicine and cause of death coding. With chronic diseases in particular, the assumption of a single underlying cause of death is often unrealistic, and those certifying the cause of death generally have limited information on which to determine the underlying cause of death and limited options on what cause to code it to. Poor practice often exacerbates these limitations. The protocols of the Global Burden of Disease programme have been developed to minimise these disadvantages, and the algorithms used to improve the reliability of these data, taking account of changes in the quality of cause of death coding and changes in the International Classification of Disease over time [15], have been extensively tested by out-of-sample tests of their predictive power.

The smoking index used provides a summary of smoking experience during a lifetime for each age group and has been extensively used, with the original paper being widely cited [16]. However, the estimates of cigarette smoking are indirect and depend on a high and consistent proportion of lung cancer deaths being attributable to smoking. This is an approximation. The population attributable fraction of lung cancer in men associated with smoking has been estimated as 92% in industrialised regions but as only 67% in developing regions [20]. Although the method would be improved by using local estimates of "nonsmoking" lung cancer, these are not universally available thus we have kept to a single estimate. Any

TABLE 3 Results of the multilevel regression models for chronic obstructive pulmonary disease (COPD) mortality rate and the COPD mortality rate ratio

Variable	log COPD mortality rate				log COPD mortality rate ratio for 2010:1990	
	1990		2010		Coefficient (95% CI)	p-value
	Coefficient (95% CI)	p-value	Coefficient (95% CI)	p-value		
log smoking index	0.43 (0.33–0.52)	<0.001	0.38 (0.28–0.48)	<0.001		
log GNI	−0.47 (−0.68−−0.26)	<0.001	−0.31 (−0.53−−0.08)	0.01		
log smoking index ratio for 2010:1990					0.004 (0.002–0.004)	<0.001
log GNI ratio for 2010:1990					−0.34 (−0.60−−0.06)	0.02
Age years						
40–44	Ref.		Ref.		Ref.	
45–49	0.69 (0.56–0.81)	<0.001	0.72 (0.58–0.86)	<0.001	0·04 (−0·04–0.11)	0.38
50–54	1.47 (1.35–1.59)	<0.001	1.47 (1.34–1.61)	<0.001	0·01 (−0·07–0.09)	0.76
55–59	2.16 (2.03–2.28)	<0.001	2.19 (2.05–2.32)	<0.001	0·05 (−0·03–0.13)	0.24
60–64	2.81 (2.68–2.94)	<0.001	2.88 (2.74–3.01)	<0.001	0·10 (0.02–0.18)	0.02
65–69	3.60 (3.47–3.72)	<0.001	3.76 (3.62–3.89)	<0.001	0·19 (0.11–0.27)	<0.001
70–74	3.91 (3.78–4.04)	<0.001	4.08 (3.94–4.22)	<0.001	0·20 (0.12–0.28)	<0.001
75–79	4.42 (4.29–4.55)	<0.001	4.62 (4.48–4.77)	<0.001	0·21 (0.13–0.29)	<0.001
>80	5.11 (4.98–5.24)	<0.001	5.43 (5.28–5.57)	<0.001	0·26 (0.18–0.34)	<0.001
Sex						
Male	Ref.		Ref.		Ref.	
Female	−0.56 (−0.62−−0.50)	<0.001	−0.64 (−0.70−−0.57)	<0.001	−0.12 (−0.16−−0.07)	<0.001

GNI: gross national income; Ref.: reference.

bias introduced by this simplification would have only small effects on within-region comparisons between 1990 and 2010. Using this index is better than attempting to reconstruct smoking exposure over a lifetime from alternative sources such as surveys and tobacco sales, providing a relatively consistent source of information on the cumulative lifetime exposure to tobacco.

The downward trend for age- and sex-specific mortality rates from COPD have been demonstrated for the UK. MARKS AND BURNEY [7] reviewed mortality rates for respiratory causes of death from the beginning of the 20th century and showed that mortality rates began to decline around the start of the First World War. The effect of the smoking epidemic was to slow, or halt, this decline rather than lead to an absolute increase in rates. ADAIR et al. [11] and ERBAS et al. [12] showed similar results in Australia, with much lower and declining rates in the first half of the 20th century, followed by increasing rates up to 1970–1990 among men and 1990–2000 among women. PRIDE and SORIANO [8] also noted falling rates for bronchitis between 1931 and 1965 among 45–64 year olds in the UK, at a time when death rates from lung cancer were increasing. The strong association between COPD mortality and poverty is not new. In the UK this association was demonstrated at an ecological level by BARKER et al. [5] and was shown to be far stronger than the association between poverty and lung cancer. At an individual level, the social class gradient of the mortality rate for COPD has been steeper than those for lung cancer, or even for tuberculosis [21].

The strong association we observed between changes in COPD mortality and GNI and the relatively weak association with changes in smoking index depend on the rate of change in GNI and smoking index, as well as on the strength of their association with COPD mortality. The positive association of COPD mortality with the smoking index in both 2010 and 1990, and the positive association between changes in the smoking index and changes in COPD mortality, confirm the relevance of cigarette smoking to COPD mortality rates. The relatively small impact of smoking changes is largely due to the small change in global smoking rates, with improvements in some regions being offset by major increases in smoking in the populous regions of South, East and South-East Asia. Nevertheless the far greater impact of GNI requires some further explanation.

The BOLD study has shown a strong ecological association between the prevalence of airway obstruction and the prevalence of smoking, but has shown no such association with poverty. However, it did show a strong association between the prevalence of poverty and the prevalence of a low FVC, and the prevalence of a low FVC increases sharply in countries with a per capita GNI <$15 000 per annum [6]. Data from the USA have also shown that survival is much more strongly linked to FVC than to forced expiratory volume in 1 s/FVC, with the latter showing very little association with mortality once smoking had been adjusted

for [22]. Although some discount the low FVC in poor countries as being confounded by race, evidence from the USA shows that the outcome from a low FVC is no different in African–Americans and White Americans after adjusting for age, sex and height [23]. These studies suggest that the high mortality from COPD in low-income countries is associated with a low FVC and not obstruction, as has generally been assumed, and raises an important question over the origins of this low FVC. There is good evidence that low ventilatory function in later life is associated with low birthweight [5, 24–27] and possibly with early infections [4, 5, 28], and these conditions are associated with poverty [4, 29, 30]. However, COPD mortality appears to respond immediately to improvements in GNI, and it is therefore unlikely that the changes noted here are solely related to effects from poverty in early life. The mechanism of this more immediate effect and whether it is mediated through general changes in lifestyle, including environmental changes, or through access to healthcare is unclear. It is unlikely that it is due to specific changes in care for COPD, but general access to support could be part of an explanation.

These findings have important implications for both policy and research. The association between COPD mortality and smoking emphasise the need to reduce smoking rates in all regions, particularly those with increasing smoking rates, but our results show that this will not be enough. The strong association with poverty, particularly in the poorest regions of the world, demonstrate that poverty reduction will be critical in reversing the growing importance of COPD mortality. In the meantime, further research is required to understand what mediates the effects of poverty on COPD mortality.

In conclusion, the increase in the global burden of COPD mortality between 1990 and 2010 has been due to changes in the age distribution, while improved economic conditions, particularly in the poorest countries, have been associated with a fall in age- and sex-specific COPD mortality rates. The change in global smoking rates has been relatively small over the past 20 years, with decreases in some areas offset by increases in others. This accounts for the relatively small influence of changes in smoking habits on global COPD mortality changes.

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