International trends in COPD mortality, 1995–2017

To the Editor:

Since 2016, chronic obstructive pulmonary disease (COPD) has been the third-leading cause of death worldwide, with an estimated 3 million deaths (5.3% of all deaths), but with large regional variations [1]. Observed data from high-income countries (HICs) [2–5] and modelled data in two global studies [6, 7] have reported declines in COPD mortality rates since the 1990s. Globally, since 2006, modelled COPD mortality rates decreased by 21% [8]. Yet, little is known about observed trends in COPD mortality in Latin America, and more recently in Oceania and Europe.

Mortality data can be expressed in many ways, for different purposes. Absolute death counts are useful to clinicians and for local use; crude mortality rates allow comparisons with other conditions, and regional healthcare planning. Finally, standardised mortality rates are valuable for comparison between countries and/or period by adjusting for differences in the demographic composition. For our study, COPD death counts were extracted from the World Health Organization (WHO) mortality database [9] between 1995 and 2017, using International Classification of Disease-10 codes of chronic bronchitis (J40–J42), emphysema (J43) and other COPD (J44) [5]. No redistribution of ill-defined codes was performed. Countries with ⩾2 million inhabitants in 2010 and vital statistics covering >90% of their national population, a proportion of ill-defined causes of death <10% since 2000, data until at least 2013, for >10 continuous years by sex and <5% of unknown age at COPD death were selected. Corresponding population data were obtained from the United Nations population 2017 revision estimates [10].

COPD age-standardised mortality rates were computed for ages 50–84 years using the world standard population, corrected for unknown age at death. The Joinpoint regression programme (version 4.7.0.0; https://surveillance.cancer.gov/joinpoint/) was used to model temporal changes in mortality rates. It performs a linear regression of the observed rates *versus* years and then iteratively tests (with a Monte Carlo Permutation) whether break points (so-called joinpoints) would improve the fitness of the model. The selected model is the most parsimonious one and provides an estimation of the annual percentage change in rates based on the slope of the linear trend between two joinpoints (or the first/last observation).

24 countries (six in Latin America and the Caribbean; two in each of North America, Asia and Oceania; and 12 in Europe), covering 12% of the world's population, were included in this study. In total, close to 3.36 million COPD deaths (56% male) were analysed. Throughout 1995–2017, in Latin America and the Caribbean, Asia and Oceania, COPD mortality rates, in both sexes, declined or remained stable (figure 1a). For instance, rates declined by −5.2% and −5.6% per year in Costa Rica, in males and females, respectively. The exceptions were the increasing rates observed among Cuban (+1.5% per year) and Australian (+2.4% per year since 2009) females. In Europe, mortality rates have also been declining among males in most countries, but remained stable in Hungary (since 2005) and increased in the Czech Republic and Croatia. Meanwhile, among females, COPD mortality rates have been increasing in half of the studied countries, from +2% per year in Austria to +4.2% or +4.8% per year in the Czech Republic and Hungary, respectively.

During the latest 2 years available (circa 2016), COPD mortality rates were highest in Hungary and Kyrgyzstan among males (141 and 135 deaths per 100 000 person-years, respectively) and in the USA and Hungary among females (75 and 71 deaths per 100 000 person-years, respectively). COPD mortality rates were lowest among males in Italy, Costa Rica and Israel (32, 39 and 39 deaths per 100 000 person-years, respectively) and among females in Latvia, Spain, and Lithuania (6, 9 and 10 deaths per 100 000

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In our international study over 1995–2017, COPD mortality rates declined in most countries. Yet, in females, they remained stable in North America and increased in six countries in Europe. The number of deaths increased or remained stable in most countries. http://bit.ly/2niUQ8d

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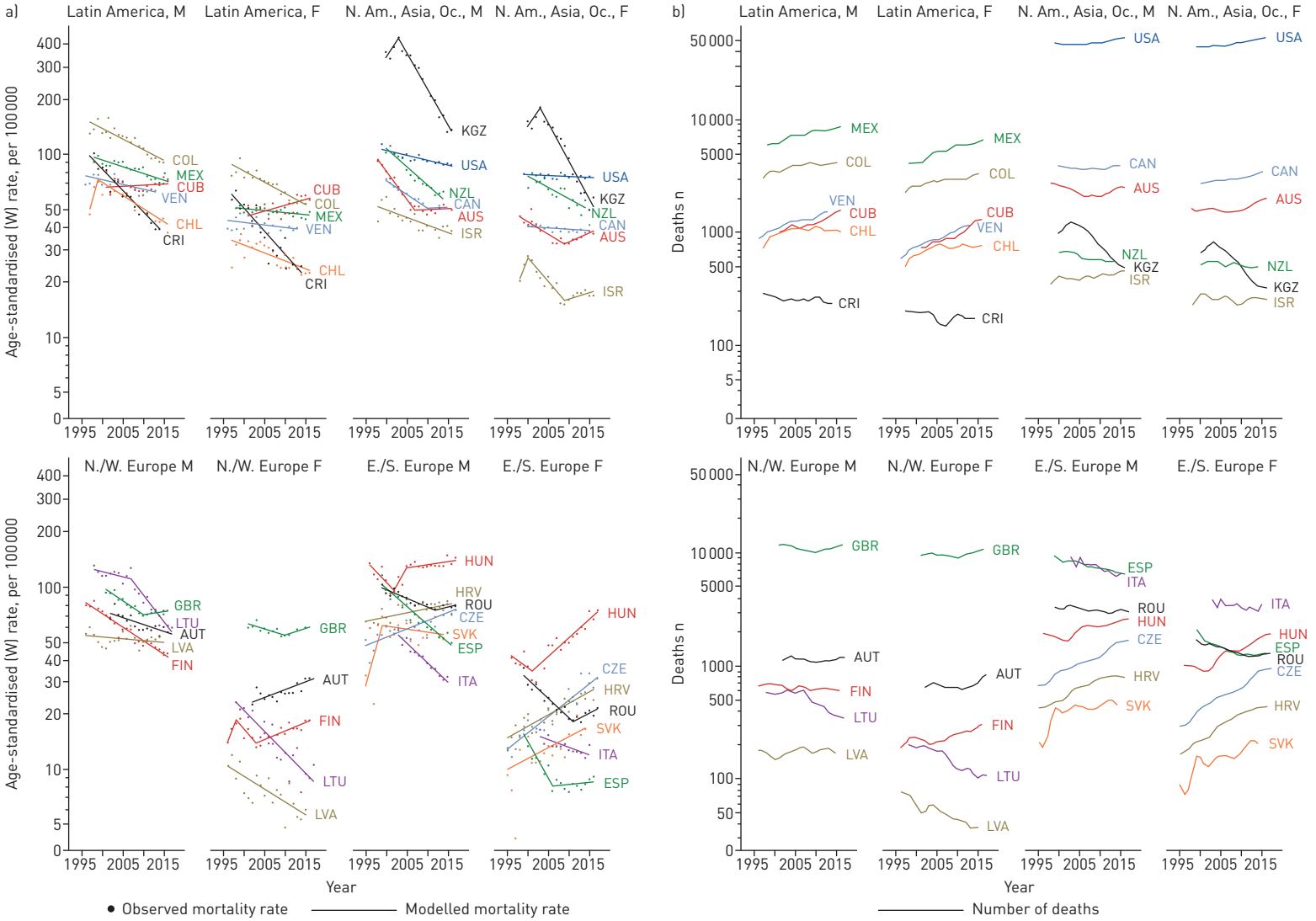

FIGURE 1 Trends in chronic obstructive pulmonary disease (COPD) mortality by region and sex, ages 50–84 years. a) Age-standardised mortality rates; b) number of deaths. Death counts were smoothed with a moving average of 30% of the values. W: world; AUS: Australia; AUT: Austria; CAN: Canada; CHL: Chile; COL: Colombia; CRI: Costa Rica; CUB: Cuba; CZE: Czech Republic; ESP: Spain; FIN: Finland; GBR: United Kingdom; HRV: Croatia; HUN: Hungary; ISR: Israel; ITA: Italy; KGZ: Kyrgyzstan; LTU: Lithuania; LVA: Latvia; MEX: Mexico; NZL: New Zealand; ROU: Romania; SVK: Slovakia; USA: United States of America; VEN: (Bolivarian Republic of) Venezuela; N. Am.: North America; Oc.: Oceania; N./W. Europe: Northern and Western Europe; E./S. Europe: Eastern and Southern Europe.

person-years, respectively). Despite the observed convergence between males and females in 18 out of 24 countries over the whole study period, COPD mortality rates remained twice as high in males as in females in each country, except in the USA, New Zealand and the UK, where rates almost matched.

Finally, assessing changes in absolute number of deaths between 2000 and 2015, the number of COPD deaths increased by >10% in 11 countries, particularly in Latin America, North America, Eastern and Southern Europe (almost doubling in the Czech Republic and Croatia), and decreased by >10% in six countries (40% and 50% in Lithuania and Kyrgyzstan, respectively). In the other seven countries COPD deaths were more or less stable (figure 1b).

In this international study, with few exceptions (mainly among European females), COPD mortality rates have been declining (markedly, for some countries). For instance, mortality rates were halved in 15 years in both sexes in Costa Rica, Kyrgyzstan and Lithuania. Nevertheless, COPD death counts increased in almost half and remained stable in a quarter of the countries studied.

COPD may result from longstanding exposure to tobacco smoking, occupational chemical substances, indoor and outdoor air pollution, with a role played by genetic susceptibility, poverty, stunting and bronchial infections such as tuberculosis [2, 5, 11–13]. The contribution of these factors depends on the socioeconomic level of the countries. Tobacco smoking and second-hand smoking are leading risk factors in HICs, while poverty, environmental exposures and early-life events predominate in low- and middle-income countries [14]. As evidence, in 2012, in Kyrgyzstan, where 3% of females smoked, the female COPD mortality rate was ~70 per 100 000, similar to that in the UK which had a decreasing yet very high female smoking prevalence of 20% [15]. The declines in the COPD mortality rates in the highest-income nations probably reflect previous declines in smoking prevalence in addition to recent progress in the diagnosis and management [16]. In fast-growing economies, such as in Latin America, reductions in poverty probably also contribute [6, 17]. The narrowing of the gender gap in COPD mortality rates in three-quarters of the countries (mostly HICs) was previously reported in Europe [4]. The same phenomenon was observed in tobacco-related cancer mortality [18], supporting the strong association between tobacco smoking and COPD mortality in HICs. In countries where females have been smoking as much and as long as males (*e.g.* USA, New Zealand and the UK) [15] female mortality from COPD became very similar to that of males.

In spite of declining COPD mortality rates in the majority of the countries studied, the number of COPD deaths has actually been increasing, or at the minimum stabilising, due to population growth and ageing (*e.g.* in Colombia, Mexico, Venezuela and the USA). The number of COPD deaths will probably grow further due to greater exposure to risk factors such as outdoor air pollution in the growing urban populations [19, 20], and the benefits of additional declines in mortality from cardiovascular disease and acute infection [16].

The strengths of this study include the extensive international coverage of COPD mortality, with up-to-date high-quality observed data. Nevertheless, several limitations are worth mentioning. Firstly, underdiagnosis and under-reporting of COPD are universal [16], probably more so in older people, especially in middle-income countries. However, restricting the analysis to ages 50–69 years led to similar conclusions (data not shown), supporting the robustness of our analysis on ages 50–84 years. Secondly, expanding the analysis to the contributing causes of death mentioned on the death certificates would give a better picture of the mortality attributable to COPD and should be pursued [16]. Therefore, our study probably underestimates the true mortality burden of COPD. In addition, we acknowledge the reduced global reach of our study due to the scarcity of high-quality mortality registration in most low- and middle-income countries such as China and India (population coverages of 4% and 8%, respectively) and some HICs including Germany and Japan (proportions of ill-defined causes of death of 11% and 16%, respectively). Another populous country, the Russian Federation, combines COPD and asthma deaths in reporting to the WHO mortality database, and was therefore excluded. Increasing high-quality and availability of mortality data in low- and middle-income countries, with escalating issues related to urbanisation and higher exposure to air pollution than in HICs, would offer valuable insight. Finally, comprehensive information on differences in diagnostic practices and access to treatment for COPD could elucidate disparities between countries with otherwise similar profiles of risk factor exposure.

In most of the countries studied, declines in COPD mortality rates were observed, but were not mirrored by reductions in the number of COPD deaths. Necessary steps to curtail the future burden are to regionally tailor primary prevention measures to decrease exposure to the main COPD risk factors, to cope with multi-morbidity [21], and to expand access to diagnosis and treatment [14, 22].

Joannie Lortet-Tieulent[1], Isabelle Soerjomataram[1], José Luis López-Campos[2,3], Julio Ancochea[4], Jan Willem Coebergh[5] and Joan B. Soriano[2,4]
[1]Section of Cancer Surveillance, International Agency for Research on Cancer, Lyon, France. [2]Centro de Investigación Biomédica en Red de Enfermedades Respiratorias (CIBERES), Instituto de Salud Carlos III, Madrid, Spain. [3]Unidad

Médico-Quirúrgica de Enfermedades Respiratorias, Instituto de Biomedicina de Sevilla (IBiS), Hospital Universitario Virgen del Rocío/Universidad de Sevilla, Seville, Spain. [4]Instituto de Investigación, Hospital Universitario de la Princesa, Universidad Autónoma de Madrid, Madrid, Spain. [5]Dept of Public Health, Erasmus MC University Medical Center, Rotterdam, The Netherlands.

Correspondence: Joannie Lortet-Tieulent, Section of Cancer Surveillance, International Agency for Research on Cancer, Lyon, France. E-mail: tieulentj@fellows.iarc.fr

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