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Review

Ambient Air Pollution and Cigarette Smoking: Co-drivers of Increased Burden of Lung Cancer in Europe

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Abstract: Background: Lung cancer is one of the leading causes of morbidity and mortality worldwide with 25% of deaths due to lung cancer occurring in Europe. This study therefore sought to assess the burden of lung cancer by country and to evaluate the magnitude of fine Particulate Matter (PM2.5) and cigarette smoking by country in Europe. **Methods:** An ecological study nested on the World Health Organization air pollution database 2016 was conducted. We sampled 30 European Countries, with a total of 1625 mean annual samples of Particulate Matter (PM2.5) collected from 1625 designated sites (n = 1625). We further used the 'World Health Disease Rankings' database to extract Lung Cancer Morbidity and Mortality Rate by country. We used SAS version 9.4 to indicate the distribution of PM2.5 and Lung Cancer Mortality Rate. **Results:** Lung cancer Relative Risk (*RR*) was 1.0 in all never- smokers. *RR* for Ex-smokers for Adeno carcinoma was 3.5 in males and 1.1 in females, small cell carcinoma was 16.2 in males and 3.8 in females. *RR* for current smokers for Adeno carcinoma was 8.0 in males and 4.1 in females, small cell carcinoma was 57.9 in males and 18.2 in females. Mean annual PM2.5 by country ranged from 6.01 to 37.28μg/m^3 whereas lung cancer mortality rate by country ranged from 19.67 to 54.26 deaths per 100,000 population. **Conclusion:** Cigarette smoking and exposure to both second hand smoke and high concentration of PM2.5 resulted into increased burden of lung cancer in Europe. Countries should re-strategize to reduce the burden of lung cancer in Europe.

Keywords: lung cancer; Fine Particulate Matter (PM2.5); secondhand smoking; cigarette smoking

1. Introduction

Europe's burden of cancer is significantly large on the global scale. In the year 2008, Europe reported 25% of the global burden of cancer [1,2]. The International Agency for Research on Cancer (IARC) in collaboration with population-based cancer registries in Europe and members of the European Network of Cancer Registries has been providing statistics of cancer burden in Europe for more than 25 years [3-8].

Lung cancer is the leading cause of cancer deaths in men and the second leading cause of cancer deaths in women in the world [9]. In 2015, lung cancer (along with trachea and bronchus cancers) caused 1.7 million deaths worldwide [9,10]. In men, the highest lung cancer mortality rates have been reported in the United States, Eastern European countries and South Central Asia while the lowest rates have been found in Africa, Central and South America [11-13]. In women, the highest lung

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cancer morbidity and mortality rates have been reported in North America and parts of Europe while the lowest rates have been reported in Africa, South Central Asia, and Latin America.

Research findings indicate that Asians who live in several countries in Asia have higher burden of lung cancer than Asians who live in the United States for both men and women. Lung cancer morbidity and mortality rates in Chinese men and women, Filipino men, and Thai women exceed the morbidity and mortality rates among women in many European countries [12,13].

The variations in the burden of lung cancer by country largely reflect differences in the stage and degree of the tobacco consumption [12,13] because smoking accounts for about 80% of global lung cancer deaths in men and 50% of the deaths in women [14,15]. Lung cancer mortality and morbidity rates have been decreasing in men and increasing in women in many western countries where tobacco use peaked by the middle of the last century [16,17]. On the other hand, the burden of lung cancer is increasing in countries undergoing industrialization due to high levels of ambient air pollution in addition to smoking [12,18].

Environmental exposures that may contribute to regional variations in lung cancer morbidity and mortality rates include radon and asbestos, certain metals (chromium, cadmium, arsenic), some organic chemicals, radiation, air pollution, coal smoke, and indoor emissions from burning other fuels [19]. For instance, despite the low smoking prevalence [20], the burden of lung cancer is higher among Chinese women than women in several European Countries because of their high exposure to indoor air pollution from unventilated coal-fueled stoves and from cooking fumes [18,21,22].

The burden of cancer is on an increase in Europe [1,2]. We therefore hypothesized that the increase in air pollution and secondhand smoking would result in the increase in the burden of lung cancer in Europe. This study sought to assess smoking rate, Particulate Matter (PM2.5) and Lung Cancer Mortality and Morbidity Rate in Europe.

2. Materials and Methods

An ecological study was conducted on ambient air pollution, cigarette smoking, lung cancer incidence and lung cancer mortality rate in Europe. The study was nested on the World Health Organization air pollution database [23] available at: http://www.who.int/phe/health_topics/outdoorair/databases/cities/en/) and the World Health Disease Rankings database available at: http://www.worldlifeexpectancy.com/cause-of-death/lung-cancers/by-country/. Ambient air pollution (PM2.5) data were extracted from the World Health Organization Ambient Air Pollution database 2016. This database is made up of annual submissions of particulate matter (PM10 and PM2.5) data from designated air pollution monitoring sites by countries globally. Countries worldwide transmit data on various diseases morbidity and mortality rates to the World Health Organization and entered in the World Health Disease Rankings database [11].

We systematically sampled 30 European Countries, with a total of 1625 mean annual samples of Particulate Matter (PM2.5) collected from 1625 designated sites (n PM2.5) = 1625). All PM2.5 samples of this study were collected from the beginning of 2013 up to the end of 2014 from air monitoring stations located within the study area. The World Health Disease Rankings database [11] was used to extract Lung Cancer Mortality Rate (deaths per 100, 000 population) by country. World Health Rankings database contains various diseases mortality rates by country ranked from the highest to the lowest.

Multivariate computation was used for descriptive statistics while SAS version 9.4 (SAS Institute, Cary, NC, USA) displayed the distribution of PM2.5 and Lung Cancer Mortality Rate.

3. Results

3.1. Tobacco smoking: the main cause of lung cancer in Europe

Increasing body of knowledge has indicated that cigarette smoking is the main cause of lung cancer. There is an association between lung cancer risk and the number of cigarettes smoked per person per day. To a greater extent, the degree of inhalation and the age at initiation of smoking play

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a major role in contracting lung cancer. The risk of contracting lung cancer for a lifetime smoker is 20 – 30 times more than a non-smoker [24].

In this study, Turkey, Greece, Bulgaria, Cyprus and Croatia had a big proportion of smokers of 20 or more cigarettes per day thus presenting high risk of contracting lung cancer. On the other hand, Hungary, Slovakia, Latvia and France among other countries had high proportion of daily smokers of less than 20 cigarettes per day**. Figure 1** shows the details.

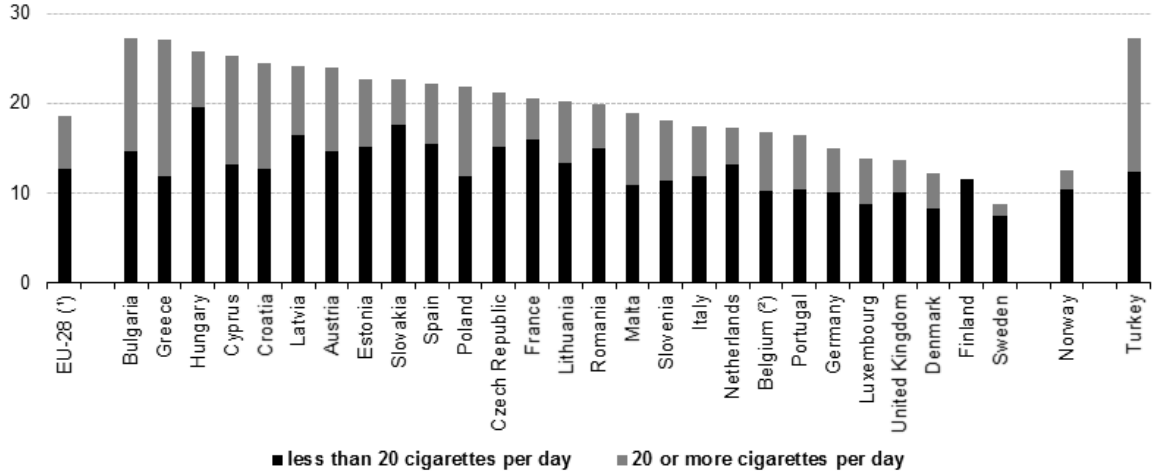

FIGURE 1: Proportion of daily cigarette smokers

As a matter of fact, smoking is a risk factor for all histological types of lung cancer, although the relative risk is greater for squamous cell and small cell carcinomas than for adenocarcinomas [24]. Relative risk of lung cancer for cigarette smoking by sex and histological type is shown in **Table 1**.

Table 1. Relative risk of lung cancer for cigarette smoking by sex and histological type in Europe.

	Males		Females	
	Adeno carcinoma	Squamous + small cell carcinoma	Adeno carcinoma	Squamous + small cell carcinoma
Non smoker	1.0	1.0	1.0	1.0
Ex-smoker	3.5*	16.2*	1.1	3.8*
Current smoker	8.0*	57.9*	4.1*	18.2*

*P < 0.05.

Passive exposure to tobacco smoke (ETS) is also a well-known risk factor for lung cancer. It is estimated that exposure to ETS increases risk by 15-20% [25]. Previous studies indicated that exposure to ETS increases the risk of squamous cell carcinoma more than adenocarcinoma and small-cell carcinoma [25].

3.2. Distribution of PM2.5 in Europe

PM2.5 results were obtained from 1625 designated sampling sites in 30 European Countries. The minimum, maximum, standard deviation and mean annual ambient fine Particulate Matter (PM2.5) for 30 European Countries are shown in **Table 2.** Turkey (37.28 µg/m^3) ranked the highest followed by Montenegro (25.6 µg/m^3) while Finland (7.05 µg/m^3) and Sweden (6.01 µg/m^3) reported the lowest Mean Annual concentration of PM2.5 during the study period. Mean annual PM2.5 by country ranged from 6.01 to 37.28µg/m^3.

Table 2. Particulate Matter (PM2.5) in 30 European Countries.

Country	No. of Sites	PM2.5			
		Minimum	Maximum	Mean	Std. Deviation
Austria	60	10	20	15.70	2.24
Belgium	43	9	21	15.88	3.01

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Croatia	5	11	23	19.00	4.74
Cyprus	5	13	17	16.00	1.73
Czech Republic	49	12	33	20.94	5.30
Denmark	5	7	11	10.00	1.73
Estonia	4	6	8	7.50	1.00
Finland	24	2.21	9	7.05	1.43
France	315	4	22	12.04	2.78
Germany	161	7	19	13.56	2.41
Greece	10	8	16	12.70	2.63
Hungary	17	14	29	20.53	4.35
Ireland	8	4	15	10.25	3.28
Italy	236	4	34	17.46	5.85
Lithuania	9	17	24	19.89	2.32
Malta	4	10	18	13.00	3.56
Montenegro	5	16	42	25.60	9.76
Netherlands	24	12	17	14.46	1.32
Norway	12	8	13	9.67	1.83
Poland	154	8	43	25.10	7.19
Portugal	12	6	15	10.33	2.54
Romania	42	8	29	17.52	4.36
Slovakia	21	15	25	19.48	2.84
Slovenia	13	15	23	19.62	2.47
Spain	225	4	18	9.52	2.97
Sweden	19	2.27	10	6.01	1.82
Switzerland	9	11	16	14.00	1.41
Turkey	81	7	67	37.28	12.80
United Kingdom	50	6	16	12.18	2.20
Serbia	3	19	23	20.67	2.08

*PM2.5 ($\mu g/m^3$).

SAS spatial map (Figure 2) shows details of the distribution of PM2.5 by Country in Europe. The trend displayed in the map indicate that the northern, western and south western Europe had low concentration of ambient fine particulate matter (PM2.5) as compared to central, eastern and southern Europe.

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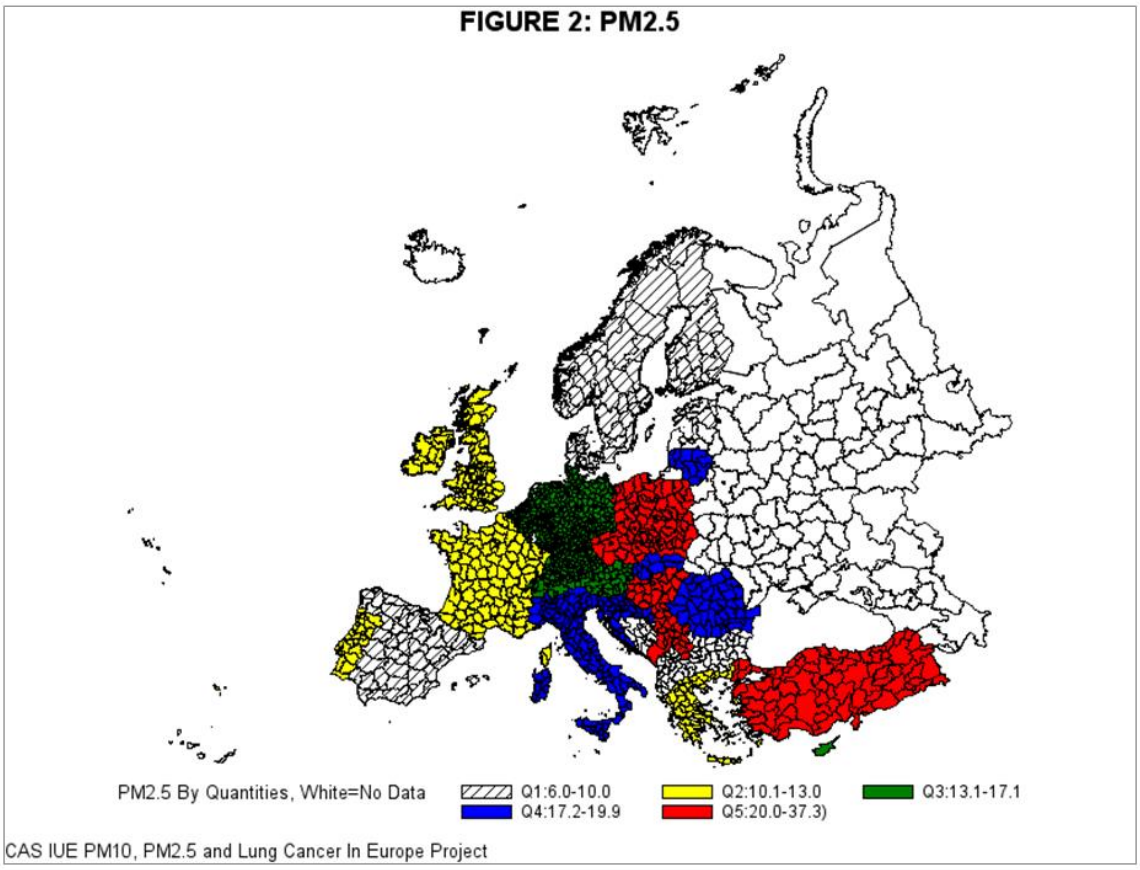

Figure 2. Distribution of PM2.5 in Europe.

3.3. Cigarette smoking, PM2.5, lung cancer incidence and mortality rate

Turkey and Greece had the highest percentage of daily cigarette smokers followed by Hungary, Cyprus and Croatia. On the other hand, Sweden, Finland, Norway and Denmark had the lowest percentage of daily cigarette smokers in Europe during the study period. Mean concentration of PM2.5 was highest in Turkey followed by Poland, Czech Republic and Hungary in that order while Finland, Estonia, Sweden and Norway had the lowest Mean concentration of PM2.5 in that order.

In terms of lung cancer incidence, Hungary ranked highest in Europe followed by Croatia and Poland in that order while Finland and Portugal had the lowest lung cancer incidence rates. In all European countries, Lung cancer incidence is much higher in males than in females. Results of ranked Lung Cancer Mortality Rate by country in Europe obtained from the World Health Rankings database ranged from 19.7 to 54.3 deaths per 100,000 population. Hungary (54.3), Serbia (45.8), Montenegro (41.6), Poland and Denmark reported the five highest lung cancer death rates while Sweden (19.87) and Cyprus (19.7) reported lowest lung cancer death rates in that order. Details are shown in **Table 3**.

Table 3. Smoking, PM2.5 and Lung Cancer Incidence Rate in Europe.

Country	Daily Cigarette smokers (%)	PM2.5	Lung Cancer Incidence Rate		Lung Cancer Mortality Rate
			Male	Female	
Austria	24	15.7	42.1	12	25.9
Belgium	18	15.9	76.4	11.1	35.7
Croatia	25	19.0	82.5	11.8	37.2
Cyprus	26	16.0	41	8.4	19.7
Czech Republic	21.5	20.9	68.9	12.7	29.8

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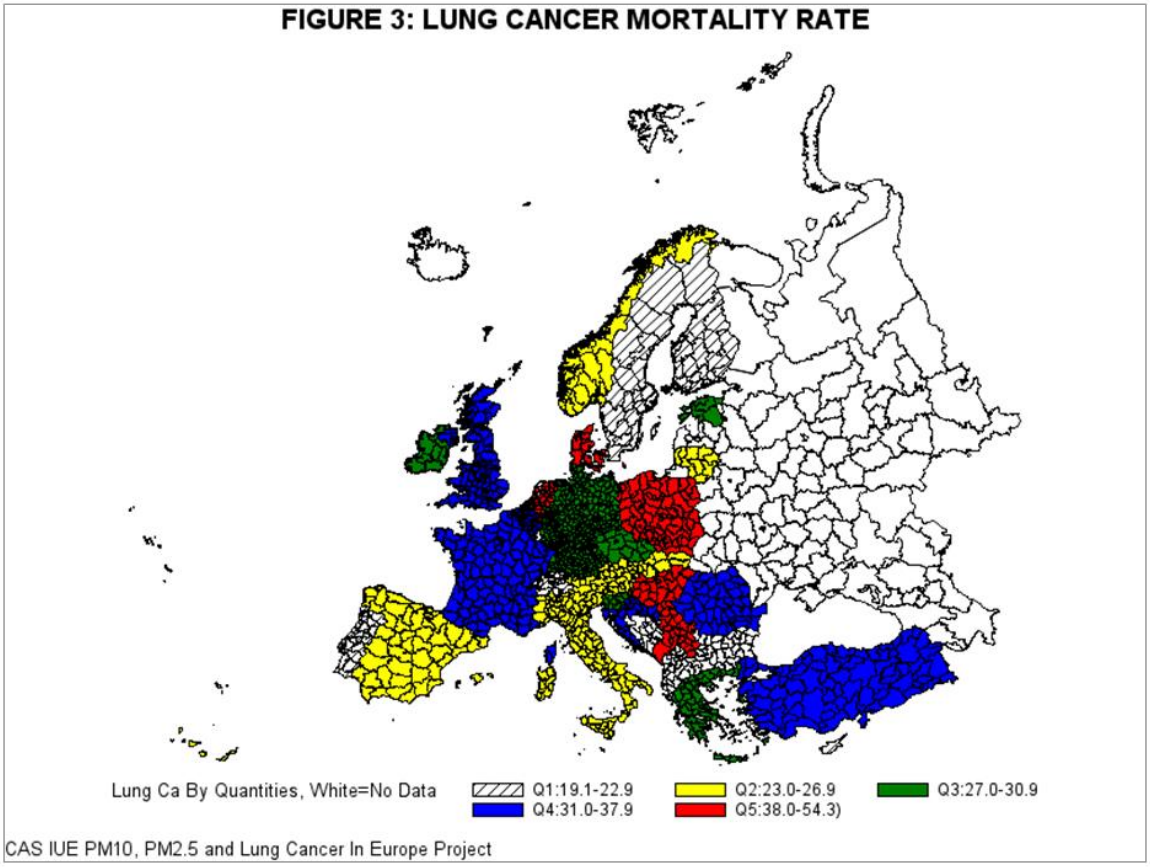
Denmark	13	10.0	46.8	27.7	39.0
Estonia	23	7.5	69.9	9.5	28.9
Finland	12	7.1	36.8	8.9	20.2
France	21	12.0	53.5	7.4	31.5
Germany	15	13.6	50.2	11.4	27.8
Greece	27.5	12.7	55.8	8.3	29.7
Hungary	26.5	20.5	95.5	22.6	54.3
Italy	18	17.5	59.4	9	25.2
Lithuania	20	19.9	57.7	5.8	23.9
Malta	19	13.0	44.5	5.3	23.6
Netherlands	18	14.5	62	17.5	38.8
Norway	13	9.7	35.1	16.6	26.9
Poland	22	25.1	78.2	12.8	39.5
Portugal	17	10.3	33.9	5.5	21.5
Romania	20	17.5	50.7	8.3	31.4
Slovakia	23	19.5	68.5	9	25.1
Slovenia	18	19.6	64.4	11.1	29.9
Spain	22	9.5	53.2	4	27.2
Sweden	9	6.0	21.4	21.8	19.9
Turkey	27.5	37.3	70.6	9.8	31.4
United Kingdom	14	12.2	47.6	21.8	31.4

SAS spatial map (**Figure 3**) shows details of the distribution of lung cancer mortality rate by Country in Europe. The trend in lung cancer mortality rate is closely related to concentration of fine particulate matter as seen from the spatial map where northern Europe reported low death rates of lung cancer while Central and Eastern Europe reported highest lung cancer death rates.

FIGURE 3: LUNG CANCER MORTALITY RATE



Ambient air pollution and secondhand smoking are the two major contributors of increasing rate of lung cancer among never-smokers. 1 in every 5 female lung cancer patients are nonsmokers and 1 in every 10 male lung cancer patients are never-smokers [25].

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4. Discussion

Although cigarette smoking continues to be the major cause of lung cancer in Europe, this timely ecological study has revealed that ambient air pollution and second hand smoking are the contributors of lung cancer among the never-smokers hence the observed increase in the burden of lung cancer in Europe. Lung cancer incidence is generally high in countries with large percentage of smokers although some countries such as Norway, United Kingdom and Finland with low percentage of smokers have high lung cancer incidence rate. Denmark, Hungary, United Kingdom and Sweden also have high lung cancer incidence among females compared to other European countries. The observed gap between low percentages of smokers with high incidence rate of lung cancers among certain countries points to the existence of other etiological factors of lung cancer such as PM2.5. This study has shown that the concentration of fine particulate matter (PM2.5) varies widely by country or region across the European Continent. Countries such as Sweden and Finland have relatively low concentration of fine particulate matter while countries like Turkey and Montenegro have high concentration of fine particulate matter.

Variations in lung cancer mortality rate have also been observed by country or region across Europe. Countries such as Hungary, Serbia and Montenegro have high lung cancer mortality rates as compared to countries like Sweden, Finland and Portugal. Studies conducted on cancer incidence patterns indicated that the observed variations in ambient air pollution as well as cancer mortality are attributed to the fact that different countries have different national health system policies and administrations which are implemented differently [26].

Many epidemiological studies have demonstrated an association between long-term exposure to ambient air pollution and mortality from respiratory diseases [27-42]. A good number of these studies were cohort studies tand clearly demonstrated an association between fine particulate matter and mortality from cardiovascular diseases (CVDs), and respiratory diseases.

In a study conducted by the American Cancer Society (ACS) which was controlled for active and passive smoking levels reported stronger association between air pollution and lung cancer in active and former smokers [41]. In another study conducted in Japan where potential confounding factors for respiratory diseases were controlled, significant increases in risk due to particulate and gaseous air pollution were observed [43]. This study has confirmed at ecological level that high exposure to ambient air pollution results into increased burden of lung cancer as observed from increasing incidence of lung cancer in the never- smokers. Therefore, ambient air pollution and cigarette smoking are the main confounding factors of lung cancer causation in Europe.

In this study however, we have strongly emphasized the need to strengthen and implement appropriate measures because lung cancer trends are worrying in Europe especially Central and Eastern Europe [44]. Since some countries within the same European Community are reporting low concentration of ambient air pollution and low levels of cigarette smoking as well as low burden of lung cancer, our study hereby emphasize the need for those countries reporting high concentration of ambient air pollution and high lung cancer burden to make adjustments to their health policies and implementation programs to be in line with the well-performing countries.

Our study had some limitations; we could not assess point incidence and mortality rate in line with designated particulate matter sampling sites as World Health Rankings database only indicate mortality rates at country level. Secondly, not all countries are contained in the World Health Organization 'who-aap-database-may2016.'

In conclusion, exposure to high risk cigarette smoking, second hand smoking and exposure to high concentration of ambient air pollution resulted into increased lung cancer burden in Europe. This study therefore emphasize the need for those countries reporting high level of cigarette smoking and high concentration of ambient air pollution as well as high lung cancer burden to make adjustments to their health policies and implementation programs so as to lower the incidence and mortality rate of lung cancer in Europe.

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Authors contributions: MK designed the study; MK and HS conducted the study; LL provided technical advice, model selection and analysis; MK wrote the paper. All authors read and approved the final manuscript. The results reported here and the conclusions based on them are the sole responsibility of the authors.
Competing interests: Authors declare that they have no competing interests.

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