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## Lung cancer mortality in European women: Trends and predictions

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#### ABSTRACT

Female lung cancer mortality increased by 50% between the mid 1960s and the early 2000s in the European Union (EU). To monitor the current lung cancer epidemic in European women, we analyzed mortality trends in 33 European countries between 1970 and 2009 and estimated rates for the year 2015 using data from the World Health Organization. Female lung cancer mortality has been increasing up to recent calendar years in most European countries, with the exceptions of Belarus, Russia, and Ukraine, with relatively low rates, and the UK, Iceland and Ireland, where high rates were reached in mid/late 1990s to leveled off thereafter. In the EU, female lung cancer mortality rates rose over the last decade from 11.3 to 12.7/100,000 (+2.3% per year) at all ages and from 18.6 to 21.5/100,000 (+3.0% per year) in middleage. A further increase is predicted, to reach 14/100,000 women in 2015. Lung cancer mortality trends have been more favorable over the last decade in young women (20-44 years), particularly in the UK and other former high-risk countries from northern and central/eastern Europe, but also in France, Italy, and Spain where mortality in young women has been increasing up to the early 2000s. In the EU as a whole, mortality at age 20-44 years decreased from 1.6 to 1.4/100,000 (-2.2% per year). Although the female lung cancer epidemic in Europe is still expanding, the epidemic may be controlled through the implementation of effective anti-tobacco measures, and it will probably never reach the top US rates. © 2012 Elsevier Ireland Ltd. All rights reserved.

#### 1. Introduction

Lung cancer mortality in men has been declining since the late 1980s in most European countries, with a fall by 17% (from 55.4 to 44.0/100,000 men) in the European Union (EU) as a whole between the peak in 1988 and the rates in the early 2000s [1], and a predicted additional 15% fall to 37.2/100,000 in 2012 [2]. In women, lung cancer mortality in Europe has been appreciably lower than in men [3], but upward trends were observed up to the early 2000s, with an approximate 50% increase since the mid 1960s in the EU (from 5.5 to 11.2/100,000 women overall and from 9.2 to 17.9/100,000 in middle-aged women) [4,5]. Earlier and particularly sharp increases were observed in Denmark, Germany, Hungary, Poland, and the UK. In England and Wales a leveling off in overall rates was observed since the 1990s. Further, since the mid-late 1990s trends have been more favorable in young women from

To monitor the current and predict the future evolution of lung cancer epidemic in European women, we analyzed trends in mortality rates over the period 1970 and 2009 and provided estimates of lung cancer deaths and rates for the year 2015.

#### 2. Material and methods

We obtained official female death certification data for lung cancer from the World Health Organization (WHO) database [10] for 33 European countries in the period 1970–2009. The EU was defined as the 27 Member States in January 2007, with the exclusion of Cyprus for which data were available for a limited number of most recent years only. In a few countries, mortality data were missing for one or more calendar years. No interpolation was made for missing data except for the definition of the EU rates: when data were not available for one or more years within a country, the nearest available estimate (i.e., generally that of previous or subsequent year) was replicated.

many European countries, suggesting that female lung cancer epidemic in Europe may not reach the rates found in the USA in the 1990s, i.e. over 25/100,000 women [6–8]. However, steady upward trends were still observed even in the youngest age groups in some southern European countries such as France and Spain [9].

Abbreviations: APC, age-period-cohort; CI, confidence intervals; EAPC, estimated annual percent change; EU, European Union; ICD, International Classification of Diseases; OR, odds ratio; PI, prediction intervals; WHO, World Health Organization.

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**Table 1**World standardized death rates from lung cancer for 100,000 women (all-ages, and truncated 35–64 and 20–44 years) in selected European countries and in the European Union in the periods 2000–04 and 2005–09, and corresponding percent changes.

| Country               | All ages |         |          | 35-64 years |         |          | 20-44 years |         |          |
|-----------------------|----------|---------|----------|-------------|---------|----------|-------------|---------|----------|
|                       | 2000-04  | 2005-09 | % Change | 2000-04     | 2005-09 | % Change | 2000-04     | 2005-09 | % Change |
| Austria               | 11.53    | 12.57   | 9.1      | 20.44       | 22.65   | 10.8     | 1.57        | 1.19    | -24.4    |
| Belarus               | 3.69     | 3.51    | -5.0     | 5.62        | 5.74    | 2.2      | 0.75        | 0.59    | -20.5    |
| Belgium               | 11.69    | 12.86   | 10.0     | 20.99       | 25.05   | 19.3     | 1.55        | 1.96    | 27.1     |
| Bulgaria              | 6.39     | 7.49    | 17.3     | 11.58       | 14.30   | 23.4     | 1.52        | 2.13    | 39.8     |
| Croatia               | 10.72    | 11.74   | 9.6      | 17.88       | 20.20   | 13.0     | 2.07        | 1.25    | -39.6    |
| Czech Republic        | 12.66    | 13.00   | 2.7      | 20.31       | 20.75   | 2.2      | 1.14        | 0.92    | -19.4    |
| Denmark               | 28.01    | 29.73   | 6.1      | 39.57       | 41.52   | 4.9      | 2.06        | 2.17    | 5.4      |
| Estonia               | 7.79     | 8.09    | 3.9      | 11.90       | 12.96   | 8.9      | 0.99        | 0.61    | -38.5    |
| Finland               | 8.05     | 8.86    | 10.1     | 11.46       | 13.03   | 13.7     | 0.65        | 0.45    | -30.9    |
| France                | 8.24     | 10.18   | 23.5     | 15.72       | 20.07   | 27.7     | 2.18        | 2.11    | -3.2     |
| Germany               | 11.12    | 12.76   | 14.7     | 19.19       | 22.76   | 18.7     | 1.62        | 1.52    | -6.4     |
| Greece                | 7.34     | 7.72    | 5.1      | 10.77       | 12.69   | 17.8     | 1.14        | 0.90    | -21.2    |
| Hungary               | 22.27    | 24.41   | 9.6      | 43.93       | 50.63   | 15.2     | 4.82        | 3.52    | -27.0    |
| Iceland               | 25.14    | 25.34   | 0.8      | 36.03       | 30.72   | -14.8    | 1.67        | 1.67    | -0.0     |
| Ireland               | 17.79    | 18.58   | 4.5      | 20.22       | 23.43   | 15.9     | 1.28        | 1.30    | 1.6      |
| Italy                 | 8.61     | 9.35    | 8.6      | 12.62       | 14.41   | 14.1     | 1.31        | 1.15    | -12.0    |
| Latvia                | 6.06     | 6.47    | 6.7      | 8.61        | 9.40    | 9.2      | 0.66        | 0.57    | -13.6    |
| Lithuania             | 5.40     | 5.62    | 4.1      | 7.48        | 8.82    | 17.9     | 0.84        | 0.76    | -9.3     |
| Luxembourg            | 10.93    | 13.23   | 21.0     | 17.94       | 21.77   | 21.4     | 1.68        | 1.11    | -33.9    |
| Malta                 | 5.57     | 5.37    | -3.5     | 8.88        | 10.23   | 15.1     | 0.55        | 1.09    | 96.6     |
| Netherlands           | 18.11    | 21.38   | 18.1     | 32.38       | 37.02   | 14.3     | 2.67        | 2.39    | -10.3    |
| Norway                | 16.42    | 17.66   | 7.6      | 24.92       | 25.35   | 1.7      | 1.49        | 0.95    | -35.9    |
| Poland                | 13.28    | 15.21   | 14.5     | 24.31       | 28.23   | 16.1     | 1.66        | 1.32    | -20.7    |
| Portugal              | 4.99     | 5.74    | 15.1     | 8.11        | 10.04   | 23.7     | 1.25        | 1.39    | 11.4     |
| Romania               | 7.93     | 8.66    | 9.2      | 13.81       | 15.05   | 8.9      | 1.69        | 1.54    | -9.0     |
| Russian Federation    | 5.80     | 5.55    | -4.2     | 8.88        | 8.62    | -3.0     | 1.09        | 0.91    | -17.0    |
| Slovakia              | 7.67     | 8.43    | 9.9      | 12.32       | 14.28   | 15.9     | 1.41        | 0.71    | -49.4    |
| Slovenia              | 11.39    | 12.76   | 12.1     | 19.18       | 21.92   | 14.3     | 1.78        | 1.91    | 7.5      |
| Spain                 | 5.14     | 6.17    | 20.1     | 9.82        | 12.42   | 26.5     | 1.71        | 1.47    | -14.2    |
| Sweden                | 14.19    | 15.59   | 9.9      | 22.69       | 22.21   | -2.1     | 1.07        | 0.91    | -14.7    |
| Switzerland           | 10.96    | 12.58   | 14.7     | 18.97       | 21.76   | 14.7     | 1.31        | 0.82    | -37.5    |
| Ukraine               | 5.17     | 4.66    | -9.9     | 8.55        | 7.96    | -6.9     | 1.21        | 1.18    | -2.6     |
| United Kingdom (UK)   | 19.69    | 20.53   | 4.3      | 24.71       | 25.09   | 1.5      | 1.16        | 1.09    | -6.6     |
| UK, England and Wales | 18.76    | 19.58   | 4.4      | 23.62       | 24.01   | 1.7      | 1.11        | 1.03    | -7.0     |
| UK, Northern Ireland  | 19.34    | 19.55   | 1.1      | 24.60       | 25.14   | 2.2      | 0.90        | 1.19    | 31.9     |
| UK Scotland           | 28.86    | 30.13   | 4.4      | 35.49       | 35.81   | 0.9      | 1.78        | 1.61    | -9.5     |
| European Union (27)   | 11.30    | 12.67   | 12.1     | 18.55       | 21.45   | 15.7     | 1.64        | 1.44    | -12.6    |

During the calendar period considered, three different Revisions of the International Classification of Diseases (ICD) were used. Since differences in lung cancer mortality classification between various Revisions were minor, data were re-coded for all countries according to the Tenth Revision of the ICD (code = C34) [11].

Estimates of the resident population, based on official censuses, were obtained from the same WHO database [10]. Population projection estimates for the year 2015 were obtained from the EUROSTAT database [12].

From the matrices of certified deaths and resident populations, we computed age-specific rates and number of deaths for each 5-year age group  $(0, 1-4, 5-9, ..., 80-84, \ge 85 \text{ years})$  and calendar year. Age-standardized rates, per 100,000 women, at all ages and truncated at age 35-64 and 20-44 years, were computed by the direct method using the world standard population [13].

To identify changes in trends for seven major European countries and for the EU as a whole, we used joinpoint analysis, which allows to identify the points, called "joinpoints", where a significant change in the linear slope of the trend (on a log-scale) occurs [14,15]. For each of the identified trends, we also computed the estimated annual percent change (EAPC) by fitting a regression line to the natural logarithm of the rates using calendar year as a regression variable.

Moreover, for the seven major European countries and the EU we provided estimates of lung cancer deaths and rates for the year 2015. These were derived by fitting a joinpoint model to the number of certified deaths in each 5-year age group, in order to identify the most recent trend slope, and by applying a linear regression

on mortality data in each age group over the time period identified by the joinpoint model, in order to compute the predicted age-specific certified number of deaths, and the corresponding 95% confidence intervals (CI) and prediction intervals (PI) [16]. Predicted standardized death rates (and corresponding 95% CIs and PIs) were computed using the predicted population data from EURO-STAT [12].

The age-specific mortality rates per 100,000 women for 5-year age groups (from 20–24 to 75–79 years) and for 5-year periods considered (from 1970–74 to 2005–09) were used for the age-period-cohort (APC) analysis. Cohorts were defined according to their central year of birth. Thus, the earliest possible cohort, centered in 1895, relates to individuals aged 75–79, who died in the quinquennium 1970–74 and hence were born in the 10 years from 1890 to 1899. We evaluated the effects of age, cohort of birth and period of death with a log-linear Poisson model using a likelihood penalizing function method to solve the identifiability problem [17,18]. The age values are interpretable in terms of mean age-specific death rates in the period considered, cohort and period of death values are expressed in relative terms against their weighted averaged set to unity. A parametric bootstrap simulation technique was used to compute 95% CIs [19,20].

#### 3. Results

Table 1 gives the age-standardized mortality rates from lung cancer in women (at all ages and truncated at 35–64 and 20–44 years) in 33 European countries and in the EU as a whole, in

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