

Laryngeal cancer mortality trends in European countries

Liliane Chatenoud¹, Werner Garavello², Eleonora Pagan¹, Paola Bertuccio¹, Silvano Gallus¹, Carlo La Vecchia³, Eva Negri¹ and Cristina Bosetti¹

¹ Department of Epidemiology, IRCCS-Istituto Di Ricerche Farmacologiche "Mario Negri", Milan, Italy

² Clinica Otorinolaringoiatrica, Department of Surgery and Translational Medicine, Università Degli Studi Di Milano Bicocca, Milan, Italy

³ Department of Clinical Sciences and Community Health, Università Degli Studi Di Milano, Milan, Italy

After a steady increase between the 1950s and the 1970s, laryngeal cancer mortality has been levelling off since the early 1980s in men from most western and southern European countries and since the early 1990s in central and eastern Europe. To update trends in laryngeal cancer mortality, we analyzed data provided by the World Health Organization over the last two decades for 34 European countries and the European Union (EU) as a whole. For major European countries, we also identified significant changes in trends between 1980 and 2012 using joinpoint regression analysis. Male mortality in the EU was approximately constant between 1980 and 1991 (annual percent change, APC = -0.5%) and declined by 3.3% per year in 1991–2012. EU age-standardized (world population) rates were 4.7/100,000 in 1990–91 and 2.5/100,000 in 2010–2011. Rates declined in most European countries, particularly over the last two decades. In 2010–11, the highest male rates were in Hungary, the Republic of Moldova, and Romania (over 6/100,000), and the lowest ones in Finland, Norway, Sweden, and Switzerland (below 1/100,000). In EU women, mortality was stable around 0.29/100,000 between 1980 and 1994 and slightly decreased thereafter (APC = -1.3%; 0.23/100,000 in 2000–01). We also considered male incidence trends for nine European countries or cancer registration areas. In most of them, declines were observed over recent decades. Laryngeal cancer mortality thus showed favourable trends over the last few decades in most Europe, following favourable changes in tobacco and, mostly for Mediterranean countries, alcohol consumption.

After a steady increase between the 1950s and the 1970s, laryngeal cancer mortality has been levelling off since the early 1980s in men from most western and southern European countries, including France, Italy, and Spain which had exceedingly high rates in the past.^{1,2} Male laryngeal mortality rose up to the early 1990s and levelled off thereafter in several countries from central and eastern Europe, such as Hungary, Poland and the Russian Federation.^{1–3} In the European Union (EU) as a whole, male mortality declined from 5.1/100,000 in 1980–81 to 3.3/100,000 in 2000–01.² In the early 2000s, however, there was still a 10 to 15-fold variation in male laryngeal mortality between the highest rates (around 7–8/100,000) in central and eastern European countries, such as Croatia, Hungary, and the Russian Federation, and the

lowest ones (below 1/100,000) in Nordic countries, such as Finland, Norway, and Sweden. Laryngeal cancer mortality rates are much lower in women than in men,⁴ with rates around 0.3/100,000 in the EU between 1980 and 2012, in the absence of any appreciable trend over time.²

To update trends in mortality from laryngeal cancer in Europe, we analyzed data provided by the World Health Organization (WHO) over the last two decades. Moreover, for major European countries we used joinpoint regression analysis to identify significant changes in trends over the period 1980–2012. Incidence for a few countries providing long-term data were also considered in order to have a more complete picture of the patterns of laryngeal cancer.

Material and Methods

Official deaths certification data from laryngeal cancer for 34 European countries over the period 1980–2012 were derived from the WHO database available on electronic support.⁵ We considered European countries with: (i) at least 2 million inhabitants in the last year available; (ii) available data for 20 years or more; (iii) death certification coverage higher than 90%. Besides the UK as a whole, data were also presented for England and Wales, Scotland, and Northern Ireland separately. For Slovakia data were available since 1992. For Iceland and Ireland data were available up to 2009, for Belgium, Slovakia, Slovenia, Switzerland, the UK, and Northern Ireland up to 2010, and for Belarus, Bulgaria, France, the Russian Federation, and Scotland up to 2011.

Key words: laryngeal cancer, incidence, mortality, trends, Europe
Additional Supporting Information may be found in the online version of this article.

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Correspondence to: Cristina Bosetti, Department of Epidemiology, IRCCS-Istituto di Ricerche Farmacologiche "Mario Negri", Via Giuseppe La Masa 19 - 20156 Milan, Italy, Tel.: +39 0239014526, Fax: +39 0233200231, E-mail: cristina.bosetti@marionegri.it

What's new?

The study quantifies the favourable trends of laryngeal cancer mortality in most European countries over the last few decades, following reduction in tobacco and, for Mediterranean countries, alcohol consumption.

The EU was defined as the union of 28 member states as since July 2013, that is, Austria, Belgium, Bulgaria, Croatia, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and the UK. Data for Cyprus were not included, since they were available for the last few years only.

In the three decades considered, most countries used the Ninth revision of the International classification of diseases (ICD),⁶ but some still used the Eighth revision⁷ and some adopted the Tenth revision from 1995 onwards.⁸ Since there were no differences in the definition of laryngeal cancer across various revisions, in all countries laryngeal cancer deaths were recoded according to the 10th revision of the ICD (code: C32).⁸

Estimates of the resident population, based on official censuses, were obtained from the same WHO database⁵ or from the EUROSTAT database⁹ when data were not available in the WHO database. From the matrices of certified deaths

and resident populations, age-specific rates for each 5-year age group and calendar period were computed. Age-standardized rates per 100,000 at all ages and truncated at 35–64 years were computed using the direct method, and were based on the world standard population.¹⁰ In a few countries, data were missing for one or more calendar years. No extrapolation was made for missing data.

To identify significant changes in mortality trends over the period 1980–2012 for major European countries and the EU as a whole we used joinpoint regression models allowing for up to three joinpoints.^{11,12} We also computed the estimated annual percent changes (APC) for each of the identified trends and the average annual percent change (AAPC) over the whole period.¹³

Incidence data for laryngeal cancer were obtained from the Cancer Incidence in Five Continents database¹⁴ over the period 1980–2007 for a few countries providing long-term cancer registration data. For countries with more than one cancer registry, we aggregated data to ensure the highest geographic coverage and the analyses were restricted to the

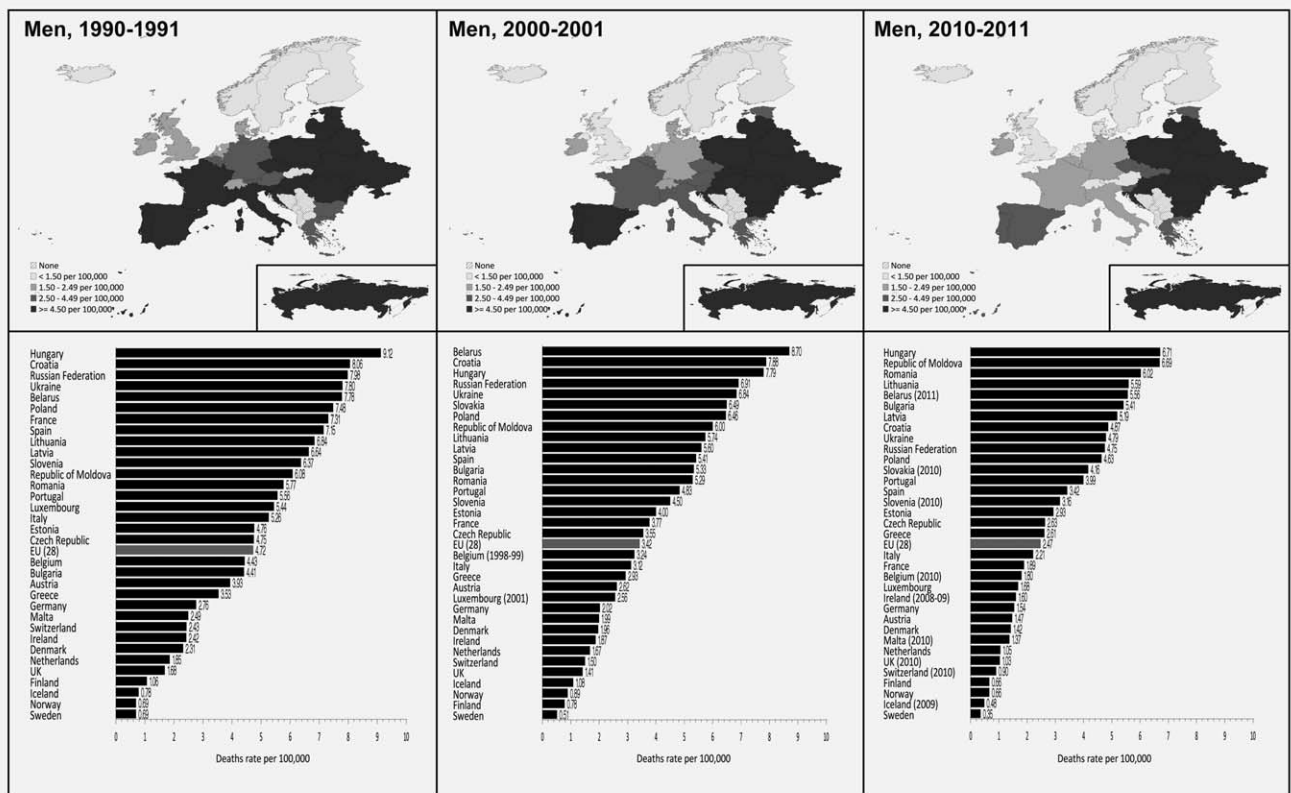


Figure 1. Geographic variation in age-standardized (world population) mortality rates from laryngeal cancer in men from 34 European countries and the European Union: a) 1990–91; b) 2000–01; c) 2010–11. Footnote: Russian Federation in the bottom frame.

Table 1. Joinpoint analysis for laryngeal cancer mortality in men (at all ages and truncated 35–64 years) in selected European countries and the European Union (EU), 1980–2012

Country, age group	Trend 1		Trend 2		Trend 3		Trend 4	
	Years	APC (95% CI)	Years	APC (95% CI)	Years	APC (95% CI)	Years	APC (95% CI)
Austria								
All ages	1980–1993	-0.6 (-1.8,0.6)	1993–2012	-4.5 (-5.3, -3.7)				-2.9 (-3.6, -2.3)
35–64 years	1980–1995	-0.7 (-2.0,0.6)	1995–2012	-5.6 (-6.8, -4.4)				-3.3 (-4.2, -2.)
Belgium								
All ages	1980–1989	1.7 (0.1,3.4)	1989–2010	-4.6 (-5.2, -4.1)				-2.8 (-3.3, -2.2)
35–64 years	1980–1991	2.4 (0.6,4.2)	1991–2010	-4.8 (-5.6, -4)				-2.2 (-3, -1.4)
Bulgaria								
All ages	1980–2008	1.8 (1.4,2.2)	2008–2011	-6 (-15.9,5.1)				1 (-0.1,2.1)
35–64 years	1980–2007	2 (1.5,2.5)	2007–2011	-6.2 (-13.6,1.8)				0.9 (-0.2,2)
Czech Republic								
All ages	1986–2012	-2.5 (-2.9, -2.1)						-2.5 (-2.9, -2.1)
35–64 years	1986–1994	0 (-2.3,2.2)	1994–2012	-3.4 (-4.1, -2.6)				-2.3 (-3.1, -1.6)
Denmark								
All ages	1980–1998	0 (-0.9,1)	1998–2012	-4.1 (-5.6, -2.6)				-1.8 (-2.6, -1)
35–64 years	1980–2003	-0.7 (-1.7,0.3)	2003–2012	-6.4 (-10.6, -1.9)				-2.3 (-3.7, -0.9)
Finland								
All ages	1980–2012	-4.1 (-4.8, -3.4)						-4.1 (-4.8, -3.4)
35–64 years	1980–2012	-4 (-5, -3)						-4 (-5, -3)
France								
All ages	1980–1990	-3.7 (-4.2, -3.1)	1990–2011	-6.7 (-6.9, -6.4)				-5.7 (-6, -5.5)
35–64 years	1980–1989	-3.6 (-4.3, -2.9)	1989–2011	-7.1 (-7.3, -6.8)				-6.1 (-6.3, -5.8)
Germany								
All ages	1980–1991	1.3 (0.7,2)	1991–2012	-3.1 (-3.4, -2.9)				-1.6 (-1.9, -1.4)
35–64 years	1980–1991	2.9 (1.9,3.9)	1991–2012	-3.9 (-4.2, -3.5)				-1.6 (-2, -1.2)
Greece								
All ages	1980–2012	-1.2 (-1.4, -1)						-1.2 (-1.4, -1)
35–64 years	1980–2012	-0.7 (-1.1, -0.3)						-0.7 (-1.1, -0.3)
Hungary								
All ages	1980–1992	4.2 (3.3,5.1)	1992–2012	-2.1 (-2.5, -1.7)				0.2 (-0.2,0.6)
35–64 years	1980–1991	6.3 (5.7,7)	1991–2012	-1.9 (-2.3, -1.5)				0.9 (0.3,1.4)

Table 1. Joinpoint analysis for laryngeal cancer mortality in men (at all ages and truncated 35–64 years) in selected European countries and the European Union (EU), 1980–2012 (Continued)

Country, age group	Trend 1		Trend 2		Trend 3		Trend 4	
	Years	APC (95% CI)	Years	APC (95% CI)	Years	APC (95% CI)	Years	APC (95% CI)
Ireland								
All ages	1980–2009	-1.1 (-1.7, -0.4)						-1.1 (-1.7, -0.4)
35–64 years	1980–2009	-1.5 (-2.6, -0.5)						-1.5 (-2.6, -0.5)
Italy								
All ages	1980–1985	-0.3 (-2.2, 1.6)	1985–2011	-4.2 (-4.4, -4.1)				-3.6 (-3.9, -3.3)
35–64 years	1980–1984	0.1 (-3.4, 3.8)	1984–2000	-5.7 (-6.2, -5.2)	2000–2011	-4 (-5.3, -2.8)		-4.4 (-5, -3.7)
The Netherlands								
All ages	1980–1998	0 (-0.8, 0.7)	1998–2012	-4.3 (-5.4, -3.2)				-1.9 (-2.5, -1.3)
35–64 years	1980–2001	0.2 (-0.6, 1.1)	2001–2012	-6.3 (-8.5, -4)				-2.1 (-3, -1.1)
Poland								
All ages	1980–1990	2.6 (1.7, 3.5)	1990–2007	-1.7 (-2.1, -1.3)	2007–2012	-5.9 (-8.2, -3.6)		-1.1 (-1.5, -0.6)
35–64 years	1980–1984	5.7 (0.9, 10.8)	1984–1992	1.1 (-0.6, 2.8)	1992–2007	-2.5 (-3.1, -1.9)	2007–2012	-1.3 (-2.2, -0.5)
Portugal								
All ages	1980–2007	-0.9 (-1.3, -0.5)	2007–2012	-5.3 (-9.5, -1)				-1.6 (-2.3, -0.8)
35–64 years	1980–2012	-0.9 (-1.3, -0.6)						-0.9 (-1.3, -0.6)
Romania								
All ages	1980–1996	2.3 (1.7, 2.9)	1996–2001	-4.5 (-8.6, -0.1)	2001–2005	5.2 (-2.1, 13.1)	2005–2012	-1.1 (-2.9, 0.7)
35–64 years	1980–1995	3 (2.3, 3.8)	1995–2001	-3.6 (-7, -0.1)	2001–2005	4.3 (-4, 13.3)	2005–2012	0.8 (-0.5, 2.1)
Russian Federation								
All ages	1980–1994	2.5 (2.1, 2.8)	1994–2011	-3.8 (-4, -3.5)				-1 (-1.2, -0.8)
35–64 years	1980–1994	2.4 (2, 2.8)	1994–2011	-4.5 (-4.8, -4.2)				-1.5 (-1.7, -1.2)
Spain								
All ages	1980–1991	-0.6 (-1.1, -0.1)	1991–1999	-2.6 (-3.6, -1.6)	1999–2012	-4.6 (-5, -4.2)		-2.7 (-3.1, -2.4)
35–64 years	1980–1997	-1.3 (-1.7, -0.9)	1997–2012	-5.6 (-6.2, -5)				-3.4 (-3.7, -3)
Sweden								
All ages	1980–2012	-2.2 (-2.8, -1.7)						-2.2 (-2.8, -1.7)
35–64 years	1980–2012	-2.4 (-3.3, -1.6)						-2.4 (-3.3, -1.6)
Switzerland								
All ages	1980–2010	-3.8 (-4.2, -3.4)						-3.8 (-4.2, -3.4)
35–64 years	1980–2010	-4.3 (-5, -3.5)						-4.3 (-5, -3.5)

Table 1. Joinpoint analysis for laryngeal cancer mortality in men (at all ages and truncated 35–64 years) in selected European countries and the European Union (EU), 1980–2012 (Continued)

Country, age group	Trend 1		Trend 2		Trend 3		Trend 4		
	Years	APC (95% CI)	Years	APC (95% CI)	Years	APC (95% CI)	Years	AAPC (95% CI)	
UK									
All ages	1980–1992	0.2 (–0.5, –0.9)	1992–2010	–2.6 (–3, –2.2)				–1.5 (–1.8, –1.2)	
35–64 years	1980–1989	0.8 (–0.4, –2.1)	1989–2002	–1.6 (–2.4, –0.9)	2002–2010	–4.4 (–5.9, –2.8)		–1.7 (–2.3, –1)	
Ukraine									
All ages	1981–1993	4.5 (3.8, –5.1)	1993–2012	–3.3 (–3.6, –3.1)				–0.4 (–0.6, –0.1)	
35–64 years	1981–1993	4.8 (4.1, –5.5)	1993–2012	–4 (–4.3, –3.7)				–0.7 (–1, –0.4)	
EU (28)									
All ages	1980–1991	–0.5 (–0.7, –0.3)	1991–2012	–3.3 (–3.4, –3.2)				–2.3 (–2.4, –2.3)	
35–64 years	1980–1983	1.3 (–1.3, 6)	1983–1991	–0.9 (–1.5, –0.3)	1991–2006	–3.5 (–3.7, –3.2)	2006–2012	–4.4 (–5.3, –3.5)	–2.6 (–2.9, –2.3)

APC: annual percent change; AAPC: average annual percent change over the period 1980–2012; CI: confidence interval.

longest common calendar period between registries. We computed sex-specific age-standardized (direct method, world standard population¹⁰) incidence rates.

Results

Geographic variation in age-standardized mortality rates from laryngeal cancer in men from Europe in 1990–91, 2000–01, and 2010–11 are shown in Figure 1. In the EU, mortality rates were 4.7/100,000 in 1990–91, 3.4/100,000 in 2000–01, and 2.5/100,000 in 2010–2011. In 1990–1991, the highest male rates were in Hungary (9.1/100,000), followed by Croatia, the Russian Federation, Ukraine, and Belarus (about 8/100,000) and the lowest ones were in Sweden, Iceland, and Norway (below 1/100,000) (Table 1 and Fig. 1). In 2010–11, the highest male rates were in Hungary, the Republic of Moldova, and Romania (over 6/100,000), and the lowest ones in Finland, Iceland, Norway, Sweden, and Switzerland (below 1/100,000). Among women from the EU, mortality rates were 0.28, 0.26 and 0.23/100,000 respectively in 1990–91, 2000–01, and 2010–11 (Supporting Information Fig. 1). In 1990–91, the highest female rates were in Denmark and Hungary (over 0.5/100,000) and the lowest ones in Iceland and Sweden (below 0.1/100,000). In 2010–11, the highest female rates were in Hungary (0.75/100,000) and the lowest ones in Belarus, Finland, Sweden, and Ukraine (below 0.1/100,000). With the exception of major European countries, however, these rates were based on a very limited number of deaths and hence largely affected by random variation.

Truncated (age 35–64 years) age-standardized mortality rates from laryngeal cancer in men and women from various European countries and from the EU as a whole in 1990–91, 2000–01, and 2010–11 are given in Supporting Information Table 1. In the EU, male laryngeal cancer mortality rates were 8.8/100,000 in 1990–91, 6.1/100,000 in 2000–01, and 4.3/100,000 in 2010–11. In middle-aged women, EU mortality rates were 0.49, 0.46 and 0.42/100,000 in 1990–91, 2000–01, and 2010–11, respectively.

Figure 2 shows the trends in laryngeal cancer mortality, at all ages and truncated 35–64 years, in men from selected European countries and the EU as a whole between 1980 and 2012. Different scales were adopted for each country in order to provide more readable and interpretable trends. Table 1 gives the corresponding results from the joinpoint regression analysis. Mortality in the EU men was approximately constant between the early 1980s and early 1990s (APC = –0.5%) and declined by 3.3% per year thereafter. Steady decreases over the last three decades were observed in southern European countries, such as Italy (AAPC = –3.6%), Spain (AAPC = –2.7%), and particularly France (AAPC = –5.7%), which had exceedingly high rates in the past. Male laryngeal mortality rose up to the early/mid 1990s in countries from central and eastern Europe, such as Germany, Hungary, Poland, the Russian Federation and Ukraine (APC between 1.3% in Germany and 4.5% in Ukraine), to

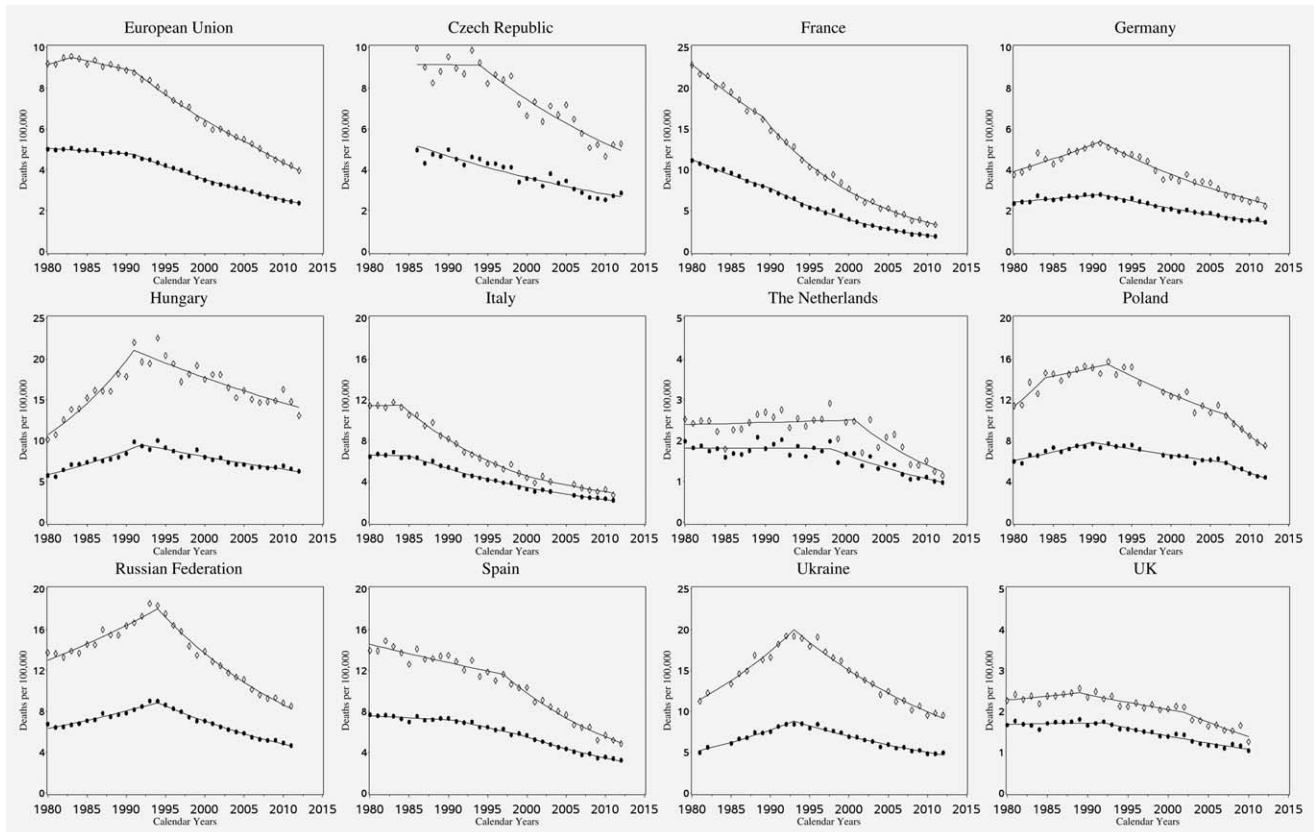


Figure 2. Trends in age-standardized (world population) mortality rates from laryngeal cancer in men (all ages, and truncated 35–64 years) from selected European countries and the European Union, 1980–2012. Footnote: Men, all ages ●—●. Men, 35–64 years ◇—◇.

decrease only thereafter (APC between -2.1% in Hungary and -5.9% in Poland). In the EU, truncated rates were approximately stable up to the early 1990s to decline by about 3% per year thereafter. In most European countries,

trends in middle-aged men over the period 1980–2012 were consistent with the overall ones.

Laryngeal cancer mortality trends in women from major European countries and the EU as a whole in 1980–2012 are

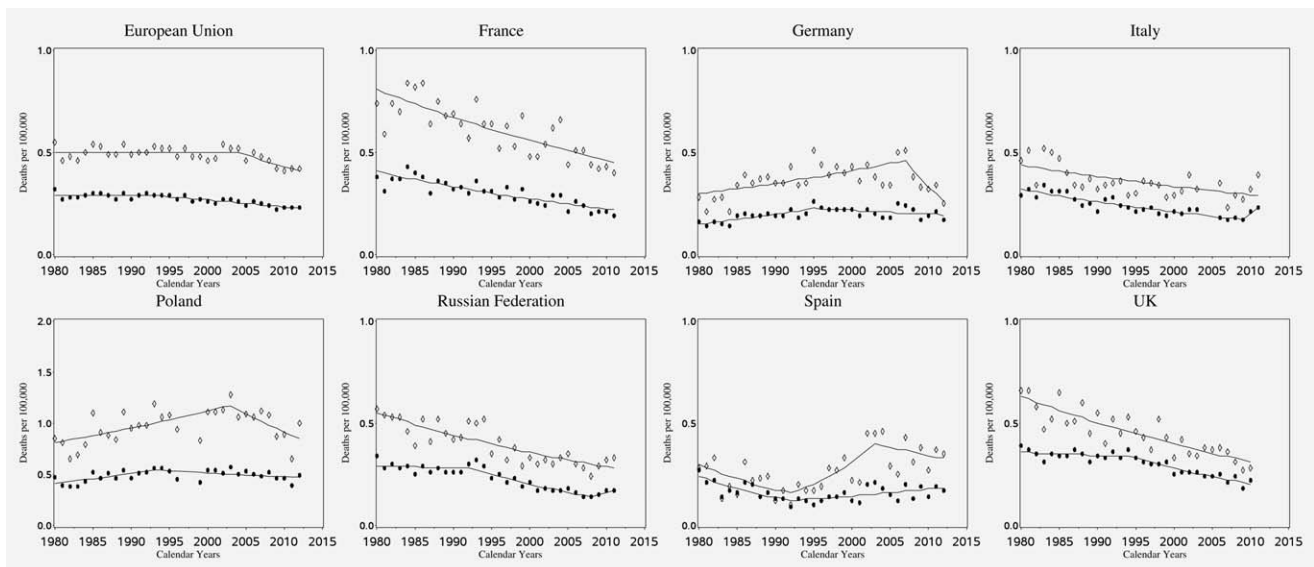


Figure 3. Trends in age-standardized (world population) mortality rates from laryngeal cancer in women (all ages, and truncated 35–64 years) from selected European countries and the European Union, 1980–2012. Footnote: Women, all ages ●—●. Women, 35–64 years ◇—◇.

Table 2. Jointpoint analysis for laryngeal cancer mortality in women (at all ages and truncated 35–64 years), in major European countries and the European Union (EU), 1980–2012

Country, age group	Trend 1		Trend 2		Trend 3	
	Years	APC (95% CI)	Years	APC (95% CI)	Years	APC (95% CI)
France						
All ages	1980–2011	-2 (-2.4, -1.6)				-2 (-2.4, -1.6)
35–64 years	1980–2011	-1.8 (-2.3, -1.4)				-1.8 (-2.3, -1.4)
Germany						
All ages	1980–1995	2.8 (1.4,4.2)	1995–2012	-0.9 (-1.9,0.1)		0.8 (0,1.6)
35–64 years	1980–2007	1.6 (0.8,2.5)	2007–2012	-10.5 (-19.2, -1)		-0.4 (-2.1,3)
Italy						
All ages	1980–2009	-2.1 (-2.5, -1.7)	2009–2011	16.7 (-9.2,49.8)		-1 (-2.5,0.6)
35–64 years	1980–2011	-1.3 (-1.9, -0.7)				-1.3 (-1.9, -0.7)
Poland						
All ages	1980–1993	2.2 (0.6,3.8)	1993–2012	-0.8 (-1.6,0.1)		0.4 (-0.3,1.2)
35–64 years	1980–2003	1.6 (0.7,2.6)	2003–2012	-3.5 (-6.5, -0.4)		0.2 (-0.9,1.2)
Russian Federation						
All ages	1980–1993	-0.5 (-1.6,0.6)	1993–2008	-4.4 (-5.5, -3.3)	2008–2011	7.7 (-5.8,23.2)
35–64 years	1980–2011	-2.2 (-2.6, -1.7)				-2.2 (-2.6, -1.7)
Spain						
All ages	1980–1992	-5.5 (-8.3, -2.5)	1992–2012	2.1 (0.6,3.7)		-0.8 (-2.2,0.6)
35–64 years	1980–1992	-5.1 (-9.7, -0.4)	1992–2003	8.9 (2.4,15.7)	2003–2012	-2.2 (-7.2,3.1)
UK						
All ages	1980–1994	-0.4 (-1.3,0.4)	1994–2010	-3 (-3.8, -2.3)		-1.8 (-2.4, -1.3)
35–64 years	1980–2010	-2.3 (-2.8, -1.8)				-2.3 (-2.8, -1.8)
EU (28)						
All ages	1980–1994	-0.1 (-0.7,0.6)	1994–2012	-1.3 (-1.7, -0.9)		-0.8 (-1.1, -0.4)
35–64 years	1980–2004	0 (-0.3,0.3)	2004–2012	-2.6 (-4.3, -1)		-0.7 (-1.1, -0.2)

APC: annual percent change; AAPC: average annual percent change over the period 1980–2012; CI: confidence interval.

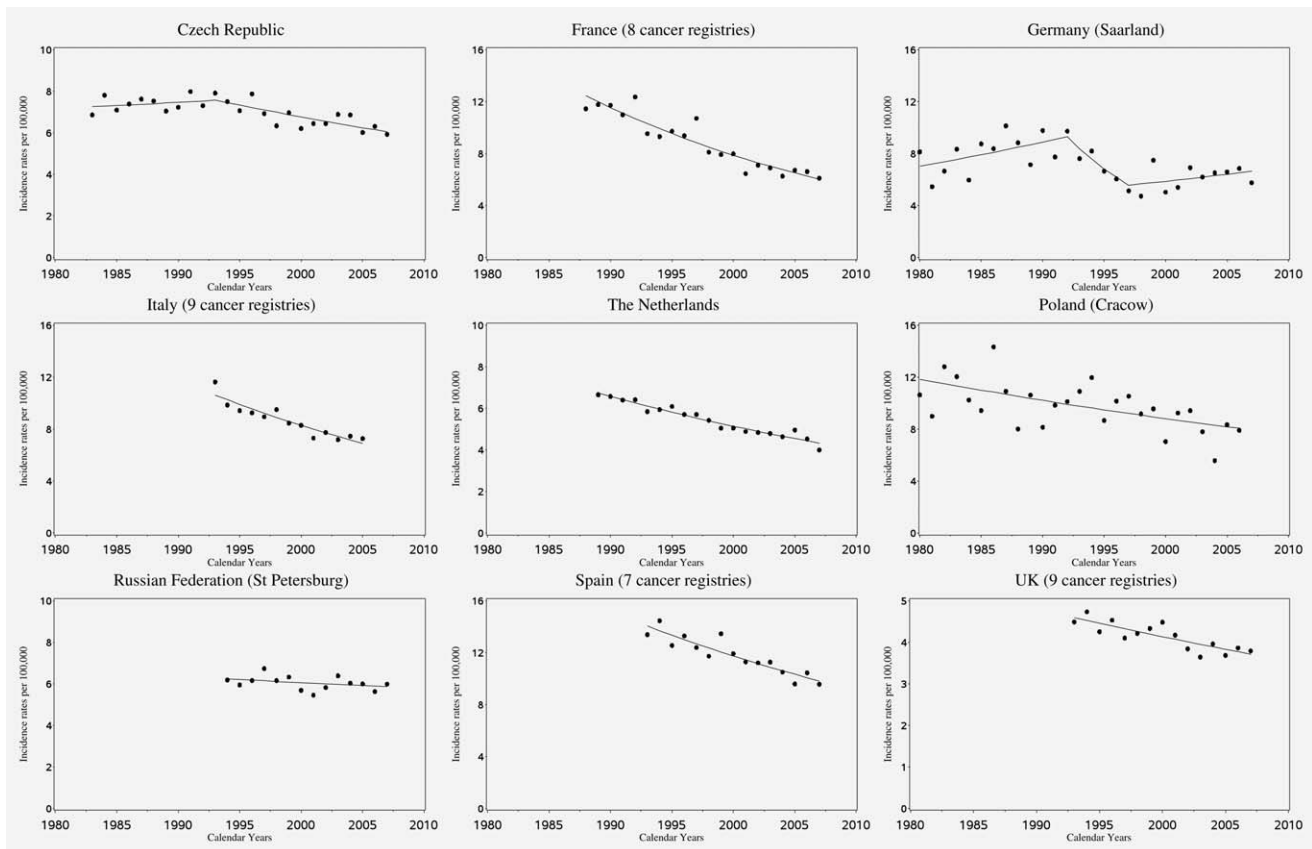


Figure 4. Trends in age-standardized (world population) incidence rates per 100,000 men for laryngeal cancer in selected European countries, 1980–2007. Footnote: The registries include: the Czech Republic (1983–2007); France (1988–2007); Bas-Rhin, Calvados, Doubs, Haut-Rhin, Herault, Isere, Somme, Tarn; Germany (1980–2007): Saarland; Italy (1993–2005): Ferrara Province, Florence, Modena, Parma, Ragusa Province, Romagna, Torino, Lombardy, Varese province, Sassari Province; the Netherlands (1989–2007); Poland (1980–2006): Cracow; the Russian Federation (1994–2007): St Petersburg; Spain (1993–2007): Albacete, Granada, Murcia, Navarra, Tarragona, Girona, Cuenca; and UK (1993–2007): England, Merseyside and Cheshire, England, North Western, England, Oxford, England, South and Western Regions, England, Birmingham and West Midlands Region, England, Yorkshire, East of England Region, Scotland, Northern Ireland.

shown in Figure 3, and corresponding findings from the joint-point regression analysis in Table 2. In the EU, female mortality was approximately stable between the early 1980s and the mid 1990s, while it slightly decreased thereafter (APC = -1.3% in 1994–2012). Over the period 1980–2012, trends were declining in France (AAPC = -2%), Italy (AAPC = -1%), UK (AAPC = -1.8%), and the Russian Federation (AAPC = -1.7%). In Germany and Poland rates rose up to the mid-late 1990s (APC = 2.8% in 1980–1995 and 2.2% in 1980–1993, respectively) and levelled off thereafter (APC = -0.9% in 1995–2012 and -0.8% in 1993–2012, respectively). Only in Spain rates declined between 1980 and 1992 (APC = -5.5%) to rise again over the last decade (APC = 2.1% in 1992–2012).

Trends in laryngeal cancer incidence in men from nine European countries or registration areas over the period 1980–2007 are given in Figure 4. In most countries considered, incidence rates were declining over the last two/three decades. No clear trends were observed in Germany and the Russian Federation, although incidence data in these countries were based on a single cancer registry.

Discussion

The present updated analysis of laryngeal cancer mortality in Europe confirms the steady decline in men from the EU. This reflects the long-term declines in western and southern European countries, such as France, Italy, and Spain which had the highest male rates in the past, but also the more recent falls in countries from central, eastern and northern Europe, such as Hungary, Russia, and Ukraine, where mortality has been increasing up to the late 1990s/early 2000s. Mortality in women is extremely low and showed stable or slightly decreasing trends in most countries over recent decades. Similar trends in mortality from male laryngeal cancer were observed in the USA, where rates declined since the early 1990s, although over the last years the trends were levelling off (APC = 2.3% in 2009–11).¹⁵

Death certification for laryngeal cancer is sufficiently reliable to permit meaningful inference on trends for most European countries.^{16,17} No major changes in the classification and coding of laryngeal cancer occurred across subsequent Revisions of the ICD, thus it is unlikely that mortality trends have been materially influenced by changes in diagnosis and

certification of the disease. In particular, data in middle-age are more reliable and valid than the overall ones.

Improvements in disease managements, including earlier diagnosis and better adoption of integrated therapeutic schemes, may have had some influence on mortality trends, although only slight improvements laryngeal cancer survival have been reported over the last decades in some, though not all, European countries.^{18–21} Indeed, over the past two decades, treatment of advanced-stage laryngeal cancer has undergone a shift from primary surgical therapy to an organ-preserving approach,²² this improving more patients' quality of life rather than survival. Five-year survival from laryngeal cancer is lower in eastern European countries (about 40%) than in other countries particularly of northern Europe (over 60%),^{23–25} this partly explaining the differences in laryngeal cancer mortality across Europe.

The variable geographical distribution and temporal trends in mortality from laryngeal cancer in Europe likely reflect differences in the pattern of exposure to tobacco and alcohol consumption—that is, the two major recognized risk factors for this neoplasm²⁶—across Europe and their variation over time. The importance of tobacco and alcohol on laryngeal cancer mortality is also reflected by the similarity of trends to those for lung cancer^{27,28} and other tobacco- and alcohol-related neoplasms.²⁹ Moreover, as reported in a few other studies,^{20,30–32} over the last few decades declines were also observed in laryngeal cancer incidence, influenced by changes in risk factors exposures only, in the absence of populations programs of screening for the disease. Thus, the steady decrease and the changes in tobacco use in subsequent generations of European men largely explains the fall in male laryngeal cancer mortality in several countries, particularly in middle-age.^{33,34} The delays in the implementation of tobacco preventive measures in countries from central and eastern Europe as compared to western European ones³⁵ account for the differences in mortality trends between these areas.

Alcohol consumption in men from western and southern European countries (such as France, Italy, and Spain) has been steadily declining since the early 1970s. This likely explains the long-term favourable trends in male laryngeal

cancer mortality in these countries, which had exceedingly high rates in the past. In contrast, alcohol drinking prevalence has been increasing at least up to more recent years in countries of central and eastern Europe.^{33,36} Such countries have now the highest laryngeal mortality rates on a European scale, and the control of laryngeal cancer—as well as of other tobacco and alcohol-related cancers²⁹—remains a major public health problem in these areas.

Dietary habits may have also had an impact on laryngeal cancer mortality. In particular, a more varied and widespread consumption of vegetables and fruit—which have been inversely associated to laryngeal cancer risk^{37–39}—may have contributed to the declines in western Europe, but only more recently in former nonmarket economies of eastern Europe.⁴⁰

Laryngeal cancer mortality in women remained substantially lower than in men and has slightly declined over the last decades in the EU and in most European countries. Indeed, larynx is the non sex-related site with the largest male to female ratio.²⁹ As for men, the trends in women reflect the patterns of tobacco and alcohol consumption in European women,⁴¹ and there are similarities with other tobacco and alcohol-related cancers.^{27,29} Thus, for example, the absence of favourable trends in Spain reflects the rise in tobacco consumption in subsequent generations of Spanish women since the 1970s⁴²; while for Ukraine the key reason of the low female rates (in contrast to male ones) is that Ukrainian (as well as Russian) women have had traditionally low tobacco and alcohol consumption.^{43,44}

In conclusion, laryngeal cancer mortality showed favourable trends over the last few decades in most countries not only of western and southern Europe, but also of central and eastern Europe, following favourable changes in exposure patterns to tobacco and, mostly in Mediterranean countries, alcohol consumption. However, a wide variation in male laryngeal cancer mortality persists, indicating that there is still large scope for the improvement in laryngeal cancer prevention and treatment in Europe.

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References

- Levi F, Lucchini F, Negri E, et al. Cancer mortality in Europe, 1995–1999, and an overview of trends since 1960. *Int J Cancer* 2004;110:155–69.
- Bosetti C, Garavello W, Levi F, et al. Trends in laryngeal cancer mortality in Europe. *Int J Cancer* 2006;119:673–81.
- Levi F, Lucchini F, Negri E, et al. Trends in cancer mortality in the European Union and accession countries, 1980–2000. *Ann Oncol* 2004;15:1425–31.
- Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0. Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. Available at: <http://globocan.iarc.fr>. (Accessed on October 6, 2014).
- World Health Organization Statistical Information System. WHO mortality database. Geneva: World Health Organization. Available at: http://www.who.int/healthinfo/statistics/mortality_rawdata/en/index.html. (Accessed on November 3, 2014).
- World Health Organization, eds. International Classification of Disease: 9th revision. Geneva: World Health Organization, 1977.
- World Health Organization, eds. International Classification of Disease: 8th revision. Geneva: World Health Organization, 1967.
- World Health Organization, eds. International Classification of Disease and related Health Problems: 10th revision. Geneva: World Health Organization, 1992.
- European Commission. EUROSTAT population database. Available at: http://appsso.eurostat.ec.europa.eu/nui/show.do?dataset=demo_pjan&lang=en. (Accessed on November, 3 2014).
- Doll R, Smith PG. Comparison between registries: age-standardized rates. Vol. IV. IARC Sci Publ No. 42. In: Waterhouse JAH, Muir CS, Shanmugaratnam K, Powell J, Peacham D, Whelan S, eds. Cancer Incidence in Five Continents. Lyon: IARC, 1982:671–5.
- Kim HJ, Fay MP, Feuer EJ, et al. Permutation tests for jointpoint regression with applications to cancer rates. (Erratum in: *Stat Med* 2001;20: 655). *Stat Med* 2000;19:335–51.

12. National Cancer Institute. Joinpoint Regression Program, version 3.5. Available at: <http://srab.cancer.gov/joinpoint/2011>.
13. Clegg LX, Hankey BF, Tiwari R, et al. Estimating average annual per cent change in trend analysis. *Stat Med* 2009;28:3670–82.
14. Ferlay J, Bray F, Steliarova-Foucher E, eds. Cancer Incidence in Five Continents, CI5plus: IARC CancerBase No. 9 [Internet]. Lyon, France: International Agency for Research on Cancer, 2014. Available at: <http://ci5.iarc.fr>. (Accessed on July 15, 2015).
15. Kohler BA, Sherman RL, Howlander N, et al. Annual report to the nation on the status of cancer, 1975–2011, featuring incidence of breast cancer subtypes by race/ethnicity, poverty, and state. *J Natl Cancer Inst* 2015;107.
16. Percy C, Stanek E III, Gloeckler L. Accuracy of cancer death certificates and its effect on cancer mortality statistics. *Am J Public Health* 1981;71:242–50.
17. Boyle P. Relative value of incidence and mortality data in cancer research. *Recent Results Cancer Res* 1989;114:41–63.
18. Verdecchia A, Guzzinati S, Francisci S, et al. Survival trends in European cancer patients diagnosed from 1988 to 1999. *Eur J Cancer* 2009;45:1042–66.
19. Hakulinen T, Engholm G, Gislum M, et al. Trends in the survival of patients diagnosed with cancers in the respiratory system in the Nordic countries 1964–2003 followed up to the end of 2006. *Acta Oncol* 2010;49:608–23.
20. van Dijk BA, Karim-Kos HE, Coebergh JW, et al. Progress against laryngeal cancer in The Netherlands between 1989 and 2010. *Int J Cancer* 2014;134:674–81.
21. La Vecchia C, Rota M, Malvezzi M, et al. Potential for improvement in cancer management: reducing mortality in the European union. *Oncologist* 2015;20:495–8.
22. Forastiere AA, Goepfert H, Maor M, et al. Concurrent chemotherapy and radiotherapy for organ preservation in advanced laryngeal cancer. *N Engl J Med* 2003;349:2091–8.
23. Zigon G, Berrino F, Gatta G, et al. Prognoses for head and neck cancers in Europe diagnosed in 1995–1999: a population-based study. *Ann Oncol* 2011;22:165–74.
24. Engholm G, Ferlay J, Christensen N, et al. NORDCAN: Cancer Incidence, Mortality, Prevalence and Survival in the Nordic Countries, Version 7.1 (09.07.2015). Association of the Nordic Cancer Registries. Danish Cancer Society. Available at: <http://www.ncr.nu>. (Accessed on July 16, 2015).
25. De Angelis R, Sant M, Coleman MP, et al. Cancer survival in Europe 1999–2007 by country and age: results of EURO-CARE–5—a population-based study. *Lancet Oncol* 2014;15:23–34.
26. Boffetta P, La Vecchia C. Neoplasms. In: Detels R, Beaglehole R, Lansang MA, Martin Gulliford M. Oxford Textbook of Public Health. 5th Edition. New York: Oxford University Press, 2009:997–1020.
27. Bosetti C, Malvezzi M, Rosso T, et al. Lung cancer mortality in European women: trends and predictions. *Lung Cancer* 2012;78:171–8.
28. Malvezzi M, Bosetti C, Rosso T, et al. Lung cancer mortality in European men: trends and predictions. *Lung Cancer* 2013;80:138–45.
29. Bosetti C, Bertuccio P, Malvezzi M, et al. Cancer mortality in Europe, 2005–2009, and an overview of trends since 1980. *Ann Oncol* 2013;24:2657–71.
30. Ligier K, Belot A, Launoy G, et al. Descriptive epidemiology of upper aerodigestive tract cancers in France: incidence over 1980–2005 and projection to 2010. *Oral Oncol* 2011;17:302–7.
31. Izarzugaza MI, Ardanaz E, Chirlaque MD, et al. Tobacco-related tumours of the lung, bladder and larynx: changes in Spain. *Ann Oncol* 2010;21 Suppl 3:iii52–60.
32. Znaor T, Vucemilo L, Kulis T, et al. Incidence and mortality trends of head and neck cancer in Croatia in the period 1988–2008. *Acta Otolaryngol* 2013;133:305–12.
33. La Vecchia C, Bosetti C, Bertuccio P, et al. Trends in alcohol consumption in Europe and their impact on major alcohol-related cancers. *Eur J Cancer Prev* 2014;23:319–22.
34. World Health Organization Regional Office for Europe. Health for all database (HFA-DB). Available at: <http://data.euro.who.int/hfad/>. (Accessed on May 2015).
35. Martinez-Sanchez JM, Fernandez E, Fu M, et al. Smoking behaviour, involuntary smoking, attitudes towards smoke-free legislations, and tobacco control activities in the European Union. *PLoS One* 2010;5:e13881.
36. World Health Organization. World Health Organization Statistical Information System. Global Information System on Alcohol and Health (GISAH). Available at: <http://apps.who.int/gho/data/node.main.GISAH/>. (Accessed on July 2013).
37. Bosetti C, La Vecchia C, Talamini R, et al. Food groups and laryngeal cancer risk: a case-control study from Italy and Switzerland. *Int J Cancer* 2002;100:355–60.
38. World Cancer Research Fund/American Institute for Cancer Research, eds. Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective. Washington, DC: American Institute for Cancer Research, 2007.
39. Chuang SC, Jenab M, Heck JE, et al. Diet and the risk of head and neck cancer: a pooled analysis in the INHANCE consortium. *Cancer Causes Control* 2012;23:69–88.
40. Zatonski W, Didkowska J. Closing the gap: cancer in Central and Eastern Europe (CEE). *Eur J Cancer* 2008;44:1425–37.
41. World Health Organization Regional Office for Europe. Health for all database (HFA-DB). Available at: <http://data.euro.who.int/hfad/>. (Accessed on 2012).
42. Levi F, Bosetti C, Fernandez E, et al. Trends in lung cancer among young European women: the rising epidemic in France and Spain. *Int J Cancer* 2007;121:462–5.
43. Giovino GA, Mirza SA, Samet JM, et al. Tobacco use in 3 billion individuals from 16 countries: an analysis of nationally representative cross-sectional household surveys. *Lancet* 2012;380:668–79.
44. Zaridze D, Lewington S, Boroda A, et al. Alcohol and mortality in Russia: prospective observational study of 151,000 adults. *Lancet* 2014;383:1465–73.