

## Research Article

## International Variation in Lung Cancer Mortality Rates and Trends among Women

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## Abstract

**Background:** There is no recent comprehensive global analysis of lung cancer mortality in women. We describe contemporary mortality rates and trends among women globally.

**Methods:** We used the World Health Organization's Cancer Mortality Database covering 65 populations on six continents to calculate age-standardized (1960 Segi world standard) lung cancer death rates during 2006 to 2010 and annual percent change in rates for available years from 1985 to 2011 and for the most recent five data years by population and age group (30–49 and 50–74 years).

**Results:** Lung cancer mortality rates (per 100,000) among young women (30–49 years) during 2006 to 2010 ranged from 0.7 in Costa Rica to 14.8 in Hungary. Rates among young women were stable or declining in 47 of 52 populations examined. Rates among women 50 to 74 years ranged from 8.8 in Georgia and Egypt to 120.0 in Scotland. In both age groups, rates were highest in parts of Europe (Scotland, Hungary, Denmark) and North America and lowest in Africa, Asia, and Latin America. Rates in older women were increasing for more than half (36/64) of populations examined, including most countries in Southern, Eastern, and Western Europe and South America.

**Conclusions:** Although widespread reductions in lung cancer in young women provide evidence of tobacco control success, rates continue to increase among older women in many countries.

**Impact:** More concentrated efforts to initiate or expand tobacco control programs in these countries globally will be required to attenuate the future lung cancer burden. *Cancer Epidemiol Biomarkers Prev*; 23(6); 1025–36. ©2014 AACR.

## Introduction

Lung cancer is now the second leading cause of cancer death in women worldwide (1). An estimated 491,200 women died of lung cancer in 2012, 57% of whom resided in economically developing countries (1). Smoking is an important cause of lung cancer, accounting for 71% and 25% of female lung cancer deaths in industrialized and developing countries, respectively (2). Lung cancer deaths attributable to smoking begin to appear about 20 to 30 years after widespread smoking in the population and peak 30 to 40 years following peak smoking prevalence (3).

Differences in smoking patterns account for most of the variation in lung cancer rates across geography and time (4). Smoking in females became common in North America, Northern Europe, Australia, and New Zealand as

early as the 1940s, but remained rare throughout the 20th century in the developing world and in places with strong social norms against it, such as the Middle East (5). Only recently is female smoking becoming more common in many of these countries, because of increasing social acceptance, newly open markets, and/or targeted marketing by the tobacco industry (5, 6).

Lung cancer mortality among women has been studied little in low- and middle-income countries, especially in comparison with high-income countries. Furthermore, as the tobacco epidemic among women occurred later than it did among men, it requires ongoing documentation as it continues to unfold. Previous studies have shown increasing lung cancer mortality among women in Europe, North America, Australia, New Zealand, and parts of Asia through the first decade of the 2000s with plateauing or decreasing rates achieved more recently in a few countries, particularly among younger women (7–12). Increasing rates have also been reported in Latin America through 2000 (13). Because the tobacco epidemic among women has varied globally, updated research is needed to document and compare contemporary trends in lung cancer mortality and to identify opportunities for intervention. Examining trends among older women allows conclusions to be drawn about the trajectory of the tobacco epidemic, whereas trends among younger women reflect

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**Note:** Supplementary data for this article are available at Cancer Epidemiology, Biomarkers & Prevention Online (<http://cebp.aacrjournals.org/>).

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more recent changes in smoking prevalence and predict the future lung cancer burden (14). We analyzed available data for 61 countries and 4 subnational populations on 6 continents to describe trends in lung cancer mortality rates from 1985 to 2011 among women.

## Materials and Methods

We obtained lung cancer mortality rates (age-standardized to the 1960 Segi world standard population, modified by Doll and colleagues; ref. 15) from the World Health Organization's Cancer Mortality Database for available years from 1985 to 2011 and from 1950 for select countries (16). The database is a compilation of mortality statistics from national civil registration systems covering about one third of the world's population. Data are generally more complete and of higher quality for developed countries compared with developing countries (17). For Australia, mortality data for 2005 were obtained from the Australian Institute of Health and Welfare (18). Underlying cause of death was categorized according to the *International Classification of Diseases*, 9th revision (code 162) through 1991 and 10th revision (code C33-34) thereafter. The study population was restricted to women ages 30 to 74 years because lung cancer is rare in those younger than 30 and there is a higher likelihood of misclassification for underlying cause of death among the elderly (17, 19). Countries were excluded if there were no data beyond 2004 or if there was less than 70% mortality registration coverage at any point during 1990 to 2010 (the years for which coverage estimates are available). Although subpopulations of China had less than 70% coverage, China's sample registration system is representative of the population (17); the Hong Kong subpopulation was retained because of this fact and by meeting all other inclusion criteria.

We examined trends in lung cancer death rates between 1985 and 2011 using joinpoint regression analysis, which fits joined straight lines on a logarithmic scale to the observed annual age-standardized rates (20, 21). The joinpoint analysis yields the annual percent change (APC) for each line segment, which corresponds to a unique period of time, as well as the average annual percent change (AAPC) for the last 5 and 10 years of data. For this analysis, the joinpoint software default settings were applied: a maximum of 5 joinpoints were allowed for 27 or more years of data; 4 joinpoints for 22 to 26 years of data; 3 joinpoints for 17 to 21 years of data; 2 joinpoints for 12 to 16 years of data; and 1 joinpoint for 7 to 11 years of data. The minimum number of datapoints allowed between joinpoints was 4, and joinpoints were not allowed within 3 datapoints of the beginning or end of the series. We report 5-year AAPC to capture the most recent changes in the trends. Trends are described as "increasing" or "decreasing" when the APC or AAPC is statistically significantly different from zero and "stable" otherwise. Joinpoint analyses were conducted for younger (30–49 years) and older (50–74 years) age groups separately as well as combined (30–74 years). Additional

exclusion criteria were applied for the joinpoint analysis. Countries without 10 years of continuous data or with fewer than 10 deaths registered in any year were excluded from the joinpoint analysis, leaving a total of 61 countries and 4 subnational populations for the age group 30 to 74; 49 countries and 3 subnational populations for the age group 30 to 49; and 60 countries and 4 subnational populations for the age group 50 to 74. For a longer-term perspective, we also provide observed age-standardized lung cancer death rates for select populations from 1950 to 2011. In order to smooth the lines for visual inspection, 3-year moving averages were used for age groups 50 to 74 and 30 to 74, and 5-year moving averages were used for age group 30 to 49.

We also compared average annual lung cancer death rates during 2006 to 2010 expressed per 100,000 women. Countries were excluded from this comparison if there were fewer than 16 deaths registered or fewer than 4 years of data during 2006 to 2010, leaving 60 countries and 4 subnational populations for the age group 30 to 74; 56 countries and 4 subnational populations for the age group 30 to 49; and 60 countries and 4 subnational populations for the age group 50 to 74.

## Results

### Contemporary rates

During 2006 to 2010, age-standardized lung cancer mortality rates per 100,000 women ages 30–49 years ranged from 0.7 in Costa Rica to 14.8 in Hungary (Fig. 1A). The rate in Hungary is about 50% higher than the next highest rate of 9.0 in the Netherlands, followed by France (7.6), Serbia (7.1), Denmark (6.8), and Canada (6.7). Among women ages 50 to 74 years, rates varied from 8.8 in Georgia and Egypt to 120.0 in Scotland (Fig. 1B). In addition to Scotland, rates were >90 in Denmark, Hungary, Canada, Iceland, the United States, and the Netherlands. Among both younger and older women, the lowest rates occurred primarily in the former Soviet states, Latin America, and Africa, while the highest rates were in Northern and Western Europe and Hungary.

### Trends in younger women

Among younger women, mortality rates in the most recent 5-year data are decreasing or stable in almost all countries (Table 1 and Supplementary Fig. S1). Exceptions include Egypt (increasing 3.2% annually), Bulgaria (1.7%), Portugal (2.3%), Belgium (1.6%), and Venezuela (1.2%). However, visual examination of trends in Portugal indicates a peak or impending peak which is not yet detectable by joinpoint analysis (Fig. 2). In many countries, rates increased quickly within the past few decades, but have since declined equally rapidly. The largest average declines in the past 5 years include Argentina (7.1%), Canada (4.9%), and the United States (4.7%). The 2 countries with the highest rates in 2006 to 2010, Hungary and the Netherlands, also experienced declines in the last 5 years.

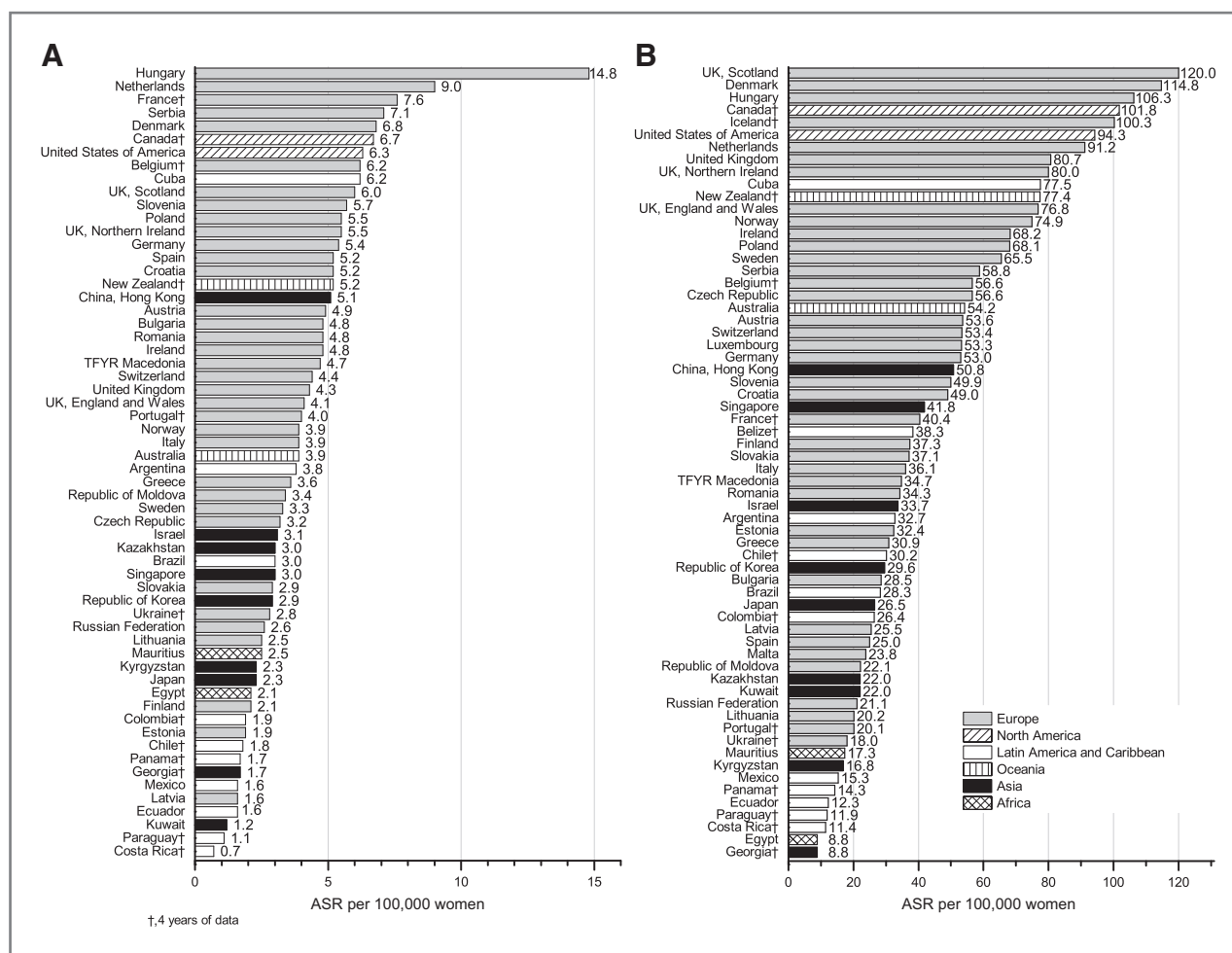


Figure 1. Lung cancer mortality rates among women by age group, 2006 to 2010. A, younger women ages 30 to 49 years; B, older women ages 50 to 74 years. ASR indicates age-standardized rate. Rates standardized to the 1960 Segi world standard.

### Trends in older women

Among older women, mortality rates in the most recent 5-year data are stable or decreasing in Northern Europe (except Finland, Norway, England and Wales, and Northern Ireland), North America, Oceania, and Asia (except the Philippines and Japan) and select countries in Central and South America (Costa Rica, Mexico, Panama, and Colombia; Table 2 and Supplementary Fig. S2). In the 2 populations with the highest rates in 2006 to 2010 (Fig. 1B), average rates during the last 5 years were stable in Scotland, whereas they had an average annual decrease of 0.7% in Denmark. The largest average declines among older women over the past 5 years include Colombia (4.8%), Uzbekistan (4.0%), and Kazakhstan (3.3%). Mortality rates are still increasing among older women in Southern and Western Europe (except the Netherlands), South America (except Colombia), and Egypt (Fig. 3). The largest average increases over the past 5 years include the Former Yugoslav Republic of Macedonia (6.9%), Spain (6.4%), and Greece (6.3%). Rates also are rapidly increasing in Eastern

European countries, with the exception of the post-Soviet states (Belarus, Moldova, Russia, and Ukraine), where they are stable or decreasing. For example, rates are increasing by more than 3% annually in Hungary, Poland, and Slovakia. Of the total 64 populations considered in this analysis, rates among older women in the most recent 5 data years increased for 56% of populations, decreased for 27%, and were stable for 17%.

The lung cancer rates and trends in the age group 30 to 74 closely mirror those in the age group 50 to 74 and are available in the online supplement (Supplementary Figs. S3, S4, S5, and Table S1).

### Discussion

Consistent with findings from previous studies, we found that lung cancer mortality rates continue to increase among women in many countries. Rates remain elevated in many high-income populations, including Scotland, Hungary, Denmark, Canada, Iceland, the Netherlands, and the United States. Among older women, rates are generally

**Table 1.** Trends in lung cancer mortality rates among women ages 30 to 49 years, 1985 to 2011

	Trend 1		Trend 2		Trend 3		Trend 4		AAPC	
	Years	APC	Years	APC	Years	APC	Years	APC	Last five years	
Africa										
Eastern Africa										
Mauritius <sup>e</sup>										
Northern Africa										
Egypt	2000–2011	3.2 <sup>a</sup>							2007–2011	3.2 <sup>a</sup>
Asia										
Eastern Asia										
China, Hong Kong	1985–2011	–1.2 <sup>a</sup>							2007–2011	–1.2 <sup>a</sup>
Japan	1985–1998	1.7 <sup>a</sup>	1998–2003	–6.3 <sup>a</sup>	2003–2011	–2.0 <sup>a</sup>			2007–2011	–2.0 <sup>a</sup>
Republic of Korea	1985–1997	1.3	1997–2011	–2.2 <sup>a</sup>					2007–2011	–2.2 <sup>a</sup>
Central Asia										
Kazakhstan	1985–2010	–1.6 <sup>a</sup>							2006–2010	–1.6 <sup>a</sup>
Kyrgyzstan	1985–2010	–1.7							2006–2010	–1.7
Uzbekistan	1985–2005	–1.6 <sup>a</sup>							2001–2005	–1.6 <sup>a</sup>
South-Eastern Asia										
Philippines <sup>c</sup>	1992–2008	–0.5							2000–2008	–0.5
Singapore	1985–2011	–1.9 <sup>a</sup>							2007–2011	–1.9 <sup>a</sup>
Western Asia										
Israel <sup>e</sup>										
Europe										
Eastern Europe										
Belarus <sup>c</sup>	1985–2009	–1.7 <sup>a</sup>							2002–2009	–1.7 <sup>a</sup>
Bulgaria	1985–2011	1.7 <sup>a</sup>							2007–2011	1.7 <sup>a</sup>
Czech Republic	1986–1996	1.1	1996–2011	–3.5 <sup>a</sup>					2007–2011	–3.5 <sup>a</sup>
Hungary	1985–1996	7.0 <sup>a</sup>	1996–2002	1.3	2002–2011	–3.4 <sup>a</sup>			2007–2011	–3.4 <sup>a</sup>
Poland <sup>b</sup>	1985–1996	6.0 <sup>a</sup>	1996–2009	–2.1 <sup>a</sup>	2009–2011	–14.9			2007–2011	–8.7
Republic of Moldova	1985–2011	–0.9							2007–2011	–0.9
Romania	1985–2006	1.6 <sup>a</sup>	2006–2011	–4.4 <sup>a</sup>					2007–2011	–4.4 <sup>a</sup>
Russian Federation	1985–1997	–0.3	1997–2006	–2.4 <sup>a</sup>	2006–2010	1.7			2006–2010	1.7
Slovakia	1992–2010	–2.2 <sup>a</sup>							2006–2010	–2.2 <sup>a</sup>
Ukraine <sup>b</sup>	1985–2011	–1.2 <sup>a</sup>							2006–2011	–1.2 <sup>a</sup>
Northern Europe										
Denmark	1985–1994	3.0	1994–2011	–2.8 <sup>a</sup>					2007–2011	–2.8 <sup>a</sup>
Estonia <sup>e</sup>										
Finland	1985–2011	–0.6							2007–2011	–0.6
Iceland <sup>e</sup>										
Ireland	1985–2010	0.4							2006–2010	0.4
Latvia	1985–2003	3.0 <sup>a</sup>	2003–2010	–10.0					2006–2010	–10.0
Lithuania	1985–2010	0.6							2006–2010	0.6
Norway	1985–1996	4.7 <sup>a</sup>	1996–2011	–3.8 <sup>a</sup>					2007–2011	–3.8 <sup>a</sup>
Sweden	1985–1992	2.6	1992–2010	–3.5 <sup>a</sup>					2006–2010	–3.5 <sup>a</sup>
United Kingdom	1985–1999	–0.8 <sup>a</sup>	1999–2010	–2.6 <sup>a</sup>					2006–2010	–2.6 <sup>a</sup>
UK, England and Wales	1985–1999	–0.9 <sup>a</sup>	1999–2010	–2.7 <sup>a</sup>					2006–2010	–2.7 <sup>a</sup>
UK, Northern Ireland <sup>e</sup>										
UK, Scotland	1985–2010	–1.2 <sup>a</sup>							2006–2010	–1.2 <sup>a</sup>
Southern Europe										
Croatia	1985–2003	2.9 <sup>a</sup>	2003–2011	–3.0					2007–2011	–3.0
Greece	1985–2010	0.3							2006–2010	0.3
Italy <sup>b</sup>	1985–2002	1.7 <sup>a</sup>	2002–2010	–0.9					2006–2010	–0.9
Portugal <sup>c</sup>	1985–2011	2.3 <sup>a</sup>							2007–2011	2.3 <sup>a</sup>

*(Continued on the following page)*

**Table 1.** Trends in lung cancer mortality rates among women ages 30 to 49 years, 1985 to 2011 (Cont'd)

	Trend 1		Trend 2		Trend 3		Trend 4		AAPC	
	Years	APC	Years	APC	Years	APC	Years	APC	Last five years	
Serbia	1998–2011	0.3							2007–2011	0.3
Slovenia <sup>e</sup>										
Spain	1985–2004	6.6 <sup>a</sup>	2004–2011	–1.9 <sup>a</sup>					2007–2011	–1.9 <sup>a</sup>
TFYR Macedonia <sup>e</sup>										
Western Europe										
Austria	1985–2011	0.0							2007–2011	0.0
Belgium <sup>c</sup>	1985–2009	1.6 <sup>a</sup>							2005–2009	1.6 <sup>a</sup>
France	1985–2003	7.9 <sup>a</sup>	2003–2009	–0.9					2005–2009	–0.9
Germany	1985–1997	5.3 <sup>a</sup>	1997–2005	0.7	2005–2011	–3.9 <sup>a</sup>			2007–2011	–3.9 <sup>a</sup>
Luxembourg <sup>e</sup>										
Netherlands	1985–2003	4.2 <sup>a</sup>	2003–2011	–4.3 <sup>a</sup>					2007–2011	–4.3 <sup>a</sup>
Switzerland	1985–1999	2.4 <sup>a</sup>	1999–2010	–2.7 <sup>a</sup>					2006–2010	–2.7 <sup>a</sup>
Latin America and the Caribbean										
Caribbean										
Cuba	1985–1997	3.0 <sup>a</sup>	1997–2010	–2.3 <sup>a</sup>					2006–2010	–2.3 <sup>a</sup>
Central America										
Costa Rica <sup>e</sup>										
Guatemala <sup>e</sup>										
Mexico	1985–2010	–2.1 <sup>a</sup>							2006–2010	–2.1 <sup>a</sup>
Panama <sup>d,e</sup>										
South America										
Argentina	1985–2004	2.3 <sup>a</sup>	2004–2010	–7.1 <sup>a</sup>					2006–2010	–7.1 <sup>a</sup>
Brazil	1985–1987	12.5	1987–1990	–4.5	1990–2008	2.0 <sup>a</sup>	2008–2010	–6.4	2006–2010	–2.3
Chile	1985–2009	–1.1 <sup>a</sup>							2005–2009	–1.1 <sup>a</sup>
Colombia	1985–2009	–1.7 <sup>a</sup>							2005–2009	–1.7 <sup>a</sup>
Ecuador <sup>e</sup>										
Paraguay <sup>e</sup>										
Venezuela <sup>b</sup>	1985–2007	1.2 <sup>a</sup>							2003–2007	1.2 <sup>a</sup>
Northern America										
Canada	1985–2002	0.0	2002–2009	–4.9 <sup>a</sup>					2005–2009	–4.9 <sup>a</sup>
United States of America	1985–1998	–2.2 <sup>a</sup>	1998–2005	0.6	2005–2010	–4.7 <sup>a</sup>			2006–2010	–4.7 <sup>a</sup>
Oceania										
Australia	1985–2011	–0.8 <sup>a</sup>							2007–2011	–0.8 <sup>a</sup>
New Zealand	1985–2009	–1.1							2005–2009	–1.1

<sup>a</sup>The APC or AAPC is statistically different from zero.

<sup>b</sup>Time series missing 1 to 2 years of data (Poland, 1997–1998; Ukraine, 2007; Italy, 2004–2005; Venezuela, 1991, 1995).

<sup>c</sup>Time series missing 3 to 4 years of data (Philippines, 2004–2007; Belarus, 1996, 2004–2006; Portugal, 2004–2006; Belgium, 2000–2002).

<sup>d</sup>Time series missing 5+ years of data (Panama, 1990–1995).

<sup>e</sup>Trend could not be assessed because at least 1 year during the time interval had fewer than 10 deaths.

stable or decreasing in regions where the tobacco epidemic began earlier, such as Northern Europe, North America, and Oceania, whereas they continue to increase in several regions where smoking uptake occurred later, such as parts of Eastern Europe, Southern and Western Europe, and South America. Notably, rates among older women in Hungary are increasing by 5.4% annually and have already exceeded the peak rates in U.S. women. Also consistent with other studies, we found that rates among younger

women in countries where smoking uptake began earliest have been decreasing for 10 years or more. In addition, we found stable or decreasing rates over the last 5 years among younger women in most countries examined, including those in South America and Asia.

Trends among young women reflect recent changes in risk factors and predict the future direction of overall trends. For example, in countries where the tobacco epidemic began earlier, such as the United Kingdom and the United States,

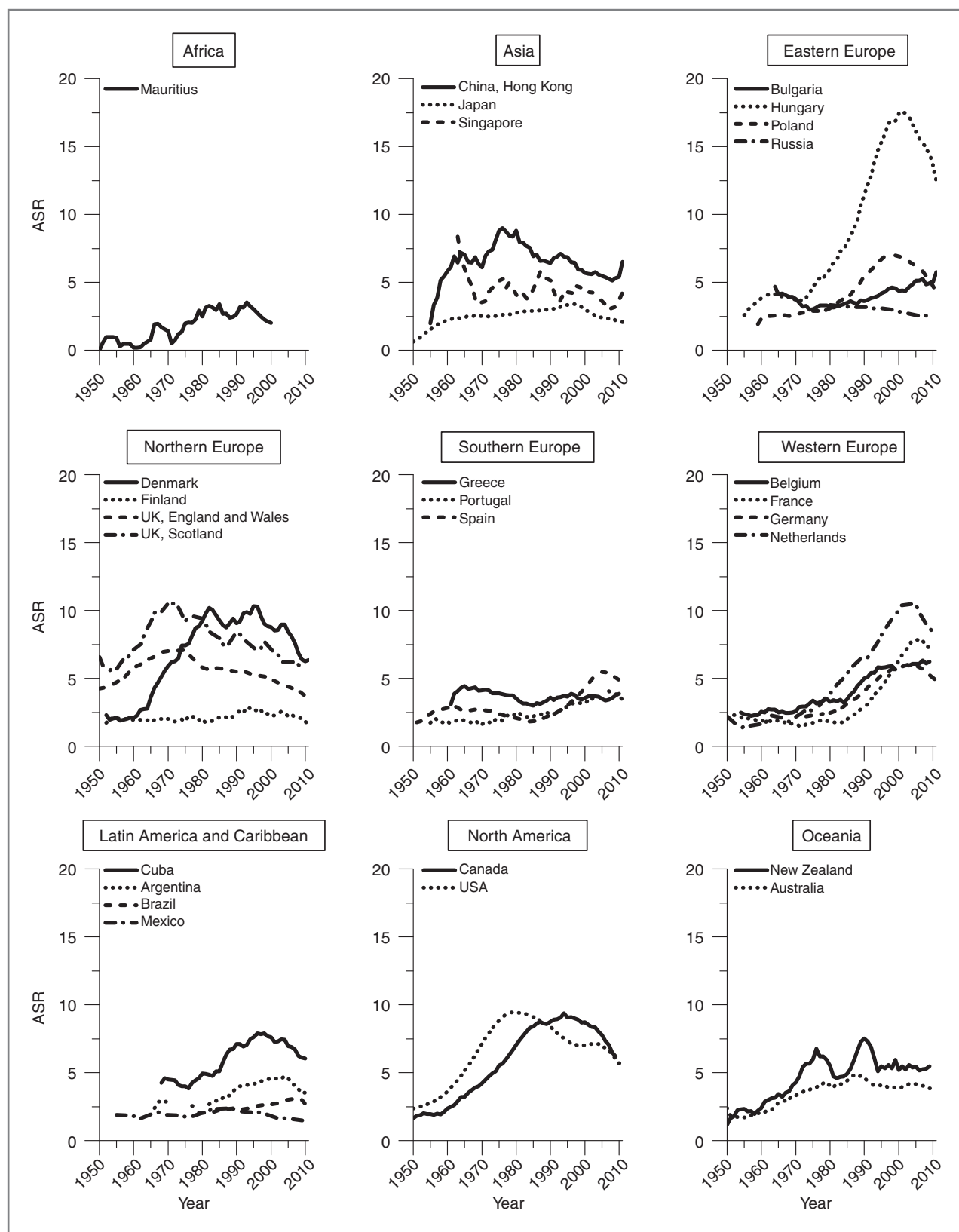


Figure 2. Trends in lung cancer mortality rates among women ages 30 to 49 years for select areas, 1950 to 2011. ASR indicates age-standardized rate (world), 5-year moving averages.



Table 2. Trends in lung cancer mortality rates among women ages 50 to 74 years, 1985 to 2011

	Trend 1		Trend 2		Trend 3		Trend 4		Trend 5		AAPC	
	Years	APC	Years	APC	Years	APC	Years	APC	Years	APC	Years	APC
Africa												
Eastern Africa												
Mauritius <sup>e</sup>	2000–2011	4.6 <sup>a</sup>										
Northern Africa												
Egypt												4.6 <sup>a</sup>
Asia												
Eastern Asia												
China, Hong Kong	1985–1999	-4.0 <sup>a</sup>	1999–2011	-1.5 <sup>a</sup>								
Japan	1985–2000	0.1	2000–2003	-2.6	2003–2011	0.5 <sup>a</sup>						
Republic of Korea	1985–1995	7.9 <sup>a</sup>	1995–2011	-1.3 <sup>a</sup>								
Central Asia												
Kazakhstan	1985–1990	4.3 <sup>a</sup>	1990–2010	-3.3 <sup>a</sup>								
Kyrgyzstan	1985–2010	-0.8 <sup>a</sup>										
Uzbekistan	1985–2005	-4.0 <sup>a</sup>										
South-Eastern Asia												
Philippines <sup>c</sup>	1992–2008	1.3 <sup>a</sup>										
Singapore	1985–2011	-2.5 <sup>a</sup>										
Western Asia												
Israel	1985–2010	0.3										
Europe												
Eastern Europe												
Belarus <sup>c</sup>	1985–2009	-1.5 <sup>a</sup>										
Bulgaria	1985–2001	-0.3	2001–2011	2.3 <sup>a</sup>								
Czech Republic	1986–1999	2.9 <sup>a</sup>	1999–2011	1.3 <sup>a</sup>								
Hungary	1985–1993	4.6 <sup>a</sup>	1993–2005	2.8 <sup>a</sup>	2005–2011	5.4 <sup>a</sup>						
Poland <sup>b</sup>	1985–1999	2.5 <sup>a</sup>	1999–2011	3.7 <sup>a</sup>								
Republic of Moldova	1985–2011	-1.0 <sup>a</sup>										
Romania	1985–2011	1.5 <sup>a</sup>										
Russian Federation	1985–1993	0.2	1993–2000	-4.0 <sup>a</sup>	2000–2010	-0.8 <sup>a</sup>						
Slovakia	1992–1995	-8.8	1995–2010	3.3 <sup>a</sup>								
Ukraine <sup>b</sup>	1985–1989	3.4 <sup>a</sup>	1989–2006	-2.9 <sup>a</sup>	2006–2011	-0.1						
Northern Europe												
Denmark	1985–1995	3.5 <sup>a</sup>	1995–2011	-0.7 <sup>a</sup>								
Estonia	1985–2011	0.1										
Finland	1985–1996	0.1	1996–2011	2.7 <sup>a</sup>								
Iceland	1985–2009	0.4										
Ireland	1985–2010	-0.5 <sup>a</sup>										

(Continued on the following page)

Table 2. Trends in lung cancer mortality rates among women ages 50 to 74 years, 1985 to 2011 (Cont'd)

	Trend 1		Trend 2		Trend 3		Trend 4		Trend 5		AAPC	
	Years	APC	Years	APC	Years	APC	Years	APC	Years	APC	Years	APC
Latvia	1985-2010	-0.9 <sup>a</sup>									2006-2010	-0.9 <sup>a</sup>
Lithuania	1985-2010	-0.8 <sup>a</sup>									2006-2010	-0.8 <sup>a</sup>
Norway	1985-1997	5.5 <sup>a</sup>	1997-2011	1.2 <sup>a</sup>							2007-2011	1.2 <sup>a</sup>
Sweden	1985-2005	3.4 <sup>a</sup>	2005-2010	-1.1							2006-2010	-1.1
United Kingdom	1985-1989	1.7 <sup>a</sup>	1989-2003	-1.3 <sup>a</sup>	2003-2010	0.8 <sup>a</sup>					2006-2010	0.8 <sup>a</sup>
UK, England and Wales	1985-1989	1.7 <sup>a</sup>	1989-2003	-1.4 <sup>a</sup>	2003-2010	0.9 <sup>a</sup>					2006-2010	0.9 <sup>a</sup>
UK, Northern Ireland	1985-2010	0.5 <sup>a</sup>									2006-2010	0.5 <sup>a</sup>
UK, Scotland	1985-1994	0.8 <sup>a</sup>	1994-2001	-1.4 <sup>a</sup>	2001-2010	0.5					2006-2010	0.5
Southern Europe												
Croatia	1985-1997	0.7	1997-2011	3.6 <sup>a</sup>							2007-2011	3.6 <sup>a</sup>
Greece	1985-2005	0.1	2005-2010	6.3 <sup>a</sup>							2006-2010	6.3 <sup>a</sup>
Italy <sup>b</sup>	1985-1999	0.6 <sup>a</sup>	1999-2010	2.0 <sup>a</sup>							2006-2010	2.0 <sup>a</sup>
Portugal <sup>c</sup>	1985-2011	1.5 <sup>a</sup>									2007-2011	1.5 <sup>a</sup>
Serbia	1998-2011	5.3 <sup>a</sup>									2007-2011	5.3 <sup>a</sup>
Slovenia	1985-2010	2.4 <sup>a</sup>									2006-2010	2.4 <sup>a</sup>
Spain	1985-1998	0.9 <sup>a</sup>	1998-2011	6.4 <sup>a</sup>							2007-2011	6.4 <sup>a</sup>
TFYR Macedonia	1991-1999	4.8 <sup>a</sup>	1999-2002	-7.8	2002-2010	6.9 <sup>a</sup>					2006-2010	6.9 <sup>a</sup>
Western Europe												
Austria	1985-2011	2.5 <sup>a</sup>									2007-2011	2.5 <sup>a</sup>
Belgium <sup>c</sup>	1985-2009	3.1 <sup>a</sup>									2005-2009	3.1 <sup>a</sup>
France	1985-2000	3.0 <sup>a</sup>	2000-2009	5.8 <sup>a</sup>							2005-2009	5.8 <sup>a</sup>
Germany	1985-1991	4.1 <sup>a</sup>	1991-1997	1.9 <sup>a</sup>	1997-2011	3.4 <sup>a</sup>					2007-2011	3.4 <sup>a</sup>
Luxembourg	1985-2011	1.9 <sup>a</sup>									2007-2011	1.9 <sup>a</sup>
Netherlands	1985-1993	6.2 <sup>a</sup>	1993-2007	4.1 <sup>a</sup>	2007-2011	1.2					2007-2011	1.2
Switzerland	1985-1991	2.3	1991-1994	10.1	1994-1997	-4.9	1997-2000	8.4	2000-2010	2.5 <sup>a</sup>	2006-2010	2.5 <sup>a</sup>
Latin America and the Caribbean												
Caribbean												
Cuba	1985-1994	-0.1	1994-2010	3.3 <sup>a</sup>							2006-2010	3.3 <sup>a</sup>
Central America												
Costa Rica	1985-2009	-2.2 <sup>a</sup>									2005-2009	-2.2 <sup>a</sup>
Guatemala	1986-2008	2.1 <sup>a</sup>									2004-2008	2.1 <sup>a</sup>
Mexico	1985-1999	0.1	1999-2010	-2.5 <sup>a</sup>							2006-2010	-2.5 <sup>a</sup>
Panama <sup>d</sup>	1985-2009	-0.2									2005-2009	-0.2
South America												
Argentina	1985-2000	1.9 <sup>a</sup>	2000-2010	3.6 <sup>a</sup>							2006-2010	3.6 <sup>a</sup>
Brazil	1985-2010	2.5 <sup>a</sup>									2006-2010	2.5 <sup>a</sup>
Chile	1985-2009	1.3 <sup>a</sup>									2005-2009	1.3 <sup>a</sup>
Colombia	1985-2005	1.1 <sup>a</sup>	2005-2009	-4.8 <sup>a</sup>							2005-2009	-4.8 <sup>a</sup>

(Continued on the following page)



Table 2. Trends in lung cancer mortality rates among women ages 50 to 74 years, 1985 to 2011 (Cont'd)

	Trend 1		Trend 2		Trend 3		Trend 4		Trend 5		AAPC	
	Years	APC	Years	APC	Years	APC	Years	APC	Years	APC	Years	APC
Ecuador	1985–2010	1.5 <sup>a</sup>									2006–2010	1.5 <sup>a</sup>
Paraguay	1995–2009	2.7 <sup>a</sup>									2005–2009	2.7 <sup>a</sup>
Venezuela <sup>b</sup>	1985–2007	0.8 <sup>a</sup>									2003–2007	0.8 <sup>a</sup>
Northern America												
Canada	1985–1994	3.0 <sup>a</sup>	1994–2009	0.2							2005–2009	0.2
United States of America	1985–1990	3.2 <sup>a</sup>	1990–1994	1.4	1994–2004	-0.9 <sup>a</sup>	2004–2010	-2.3 <sup>a</sup>			2006–2010	-2.3 <sup>a</sup>
Oceania												
Australia	1985–1991	2.4 <sup>a</sup>	1991–2011	-0.1							2007–2011	-0.1
New Zealand	1985–2009	0.4									2005–2009	0.4

<sup>a</sup>The APC or AAPC is statistically different from zero.

<sup>b</sup>Time series missing 1 to 2 years of data (Poland, 1997–1998; Ukraine, 2007; Italy, 2004–2005; Venezuela, 1991, 1995).

<sup>c</sup>Time series missing 3 to 4 years of data (Philippines, 2004–2007; Belarus, 1996, 2004–2006; Portugal, 2004–2006; Belgium, 2000–2002).

<sup>d</sup>Time series missing 5+ years of data (Panama, 1990–1995).

<sup>e</sup>Trend could not be assessed because at least 1 year during the time interval had fewer than 10 deaths.

lung cancer mortality rates among younger women began to decrease around the 1970s, whereas overall declines did not begin for 2 to 3 more decades. The decreasing rates among younger women seen in almost all countries examined, including those where the tobacco epidemic began later, such as Latin America and Southern and Western Europe, represent early evidence of a potentially reversing tide in the lung cancer epidemic for many regions. These declines are likely the result of the implementation of tobacco control measures and heightened awareness of the health hazards of smoking, which decrease initiation of smoking and increase smoking cessation (22). Smoking cessation among younger women has a large impact on risk; women who quit by middle age (around 40 years) will avoid about 90% or more of the risk of lung cancer death compared with that of those who continue to smoke (23, 24). Should the progress in tobacco control be maintained or strengthened in these countries, a downturn in overall lung cancer mortality rates among women is likely in the coming decades as these low-risk cohorts age.

Decreasing lung cancer mortality rates among older women have been achieved in some countries and will likely occur in the coming decades in many others. In countries where the tobacco epidemic began earliest, such as the United Kingdom, United States, and Denmark, lung cancer mortality rates among women 50 to 74 began to decrease between the late 1980s and mid-1990s. These downturns have been attributed to public health campaigns and policies against tobacco use over the past 5 decades, including educating the public on the health hazard of smoking, smoke-free air laws, and increases in excise taxes on tobacco products (22). Declines in lung cancer mortality rates among older women likely reflect a combination of smoking cessation in that age group and the aging of a lower-risk cohort. Reductions in mortality among older women could potentially be accelerated through intensive smoking cessation efforts aimed at older women. Women who quit by their 50s, 60s, or 70s can reduce their risk of dying of lung cancer by 63%, 38%, or 21%, respectively (23, 24). Widespread cessation among older women could slow the rapidly increasing rates we observed in some countries, such as the Former Yugoslav Republic of Macedonia, Spain, and Greece.

Lung cancer death rates have been stable or decreasing in Russia and other former Soviet states of Eastern Europe and Central Asia, where tobacco control has only recently begun to be implemented. Although the reasons for these declines are unclear, in Russia they may reflect the low risk in the cohort of women who were teenagers during and after World War II, when cigarettes are said to have been scarce (25). These trends may also be a product of incomplete mortality data. Importantly, smoking prevalence among women has been increasing in Russia and other former Soviet states since the 1990s with the entry of transnational tobacco companies and their marketing campaigns targeting women (6, 26). In Russia, smoking prevalence among women doubled from 7% in 1992 to 15% in 2003 (6, 26); more recent rates in 2009 are reported

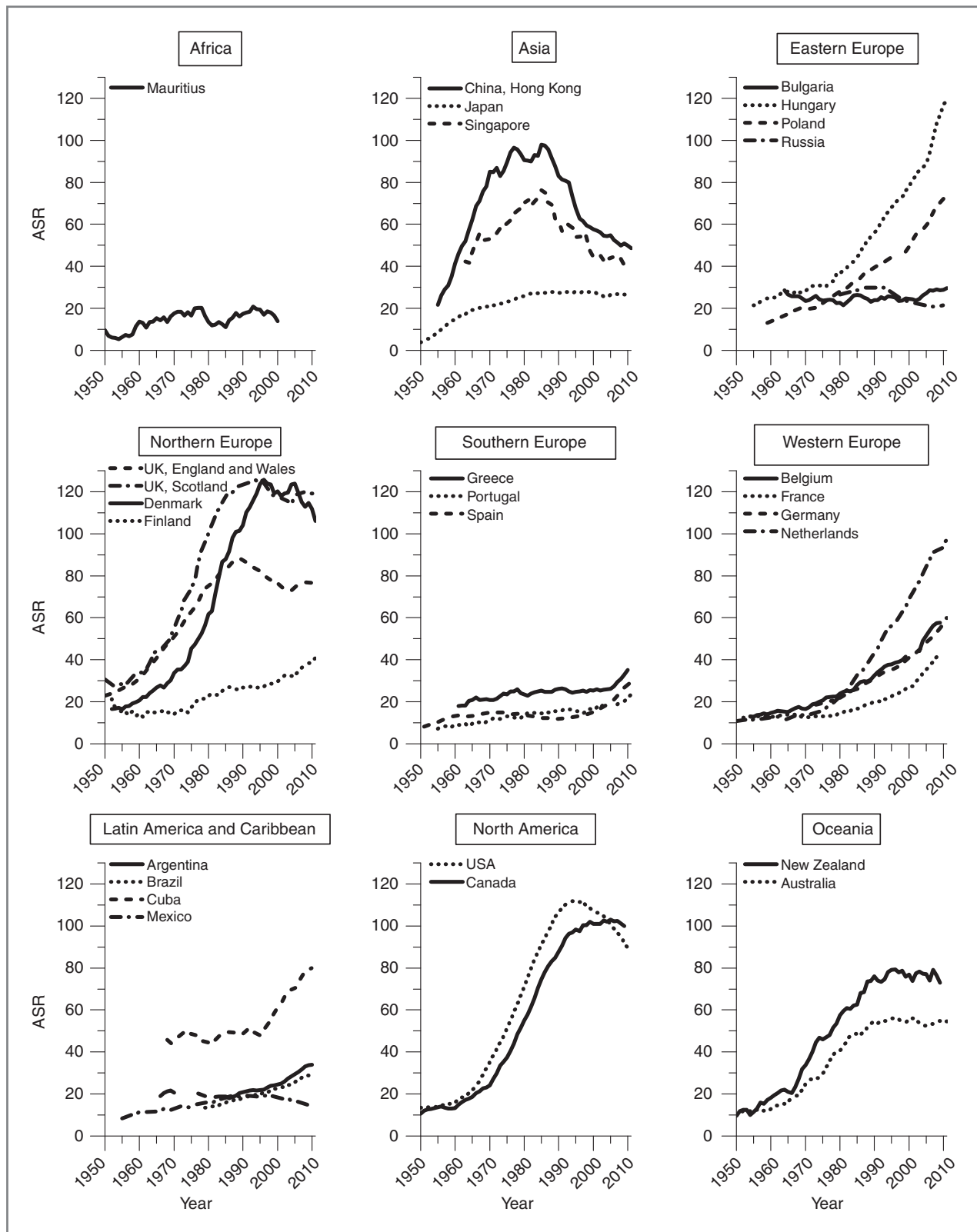


Figure 3. Trends in lung cancer mortality rates among women ages 50 to 74 years for select areas, 1950 to 2011. ASR indicates age-standardized rate (world), 3-year moving averages.

to be even higher, at 22% among women 15 years and older and 33% among young women ages 15 to 24 years (26). Russia recently enacted new comprehensive tobacco control legislation and is in the process of implementing tobacco control policies, which will potentially reduce smoking prevalence in the near term and limit the future lung cancer burden (27).

The greatest opportunity for thwarting the cigarette epidemic is in countries where smoking among women remains rare, such as Africa and most of Asia. Female smoking in Africa remains below 10% in all countries and less than 2% in most (28). In Western Asia, smoking among women is uncommon (except in Lebanon and Yemen), with a prevalence of 3% or less (28). Smoking prevalence has remained less than 10% among women in Eastern, Southern, and Southeastern Asia, except for more developed urban populations (Singapore, Hong Kong, Japan) and Nepal (28). Although smoking prevalence among women 15 years and older in China is low at 2.4% in 2010, it has one of the largest populations of female smokers in the world (estimated at 12.6 million; ref. 26) and limited evidence suggests that it may be increasing among young women (26, 29). In these and other countries where the tobacco epidemic has not yet advanced, tobacco control measures are imperative to prevent uptake among the young and promote cessation among those who have already begun to smoke.

In addition to tobacco control, there may also be future opportunities to reduce lung cancer mortality through improvements in early detection and treatment. Screening using low-dose helical computed tomography has been shown to be effective in reducing mortality by 20% compared with chest x-ray among current and former heavy smokers in the United States, although this finding has yet to be confirmed in other countries (30, 31); however, because of the technical infrastructure and expertise required, this type of screening is unlikely to benefit those in the developing world in the near term. Survival has improved slightly in developed countries in recent decades (32, 33), although it generally remains poor.

A strength of this study is its comprehensive nature resulting from the use of all available lung cancer mortality data in the WHO Mortality Database. Also, the use of recent data through 2011 adds to and updates the existing literature on the lung cancer burden in women. Unfortunately, many regions, especially in Africa and Asia, still lack adequate death registration and were not included in this analysis. The lack of data for mainland China is particularly unfortunate given its considerable population size and indications that lung cancer mortality rates are increasing among women in rural China (9). In many developing countries underrepresented in this study, especially in Asia and Africa, other risk factors in addition to tobacco, such as indoor air pollution, also contribute to the lung cancer burden (34, 35). We were not, however, able to explore mortality in most of these areas because of a lack of data.

Another limitation of our study is the unknown effect of variations in the quality of mortality registration between

countries and over time because of changes or errors in data recording. Although data were censored in the case of too few deaths recorded in order to improve reliability, results may still be less reliable because of small numbers in certain populations and especially in the younger age group. Cancer mortality data are available for more countries and for a longer time period compared with incidence data, and thus was the focus of this analysis. Ideally, mortality would be examined together with incidence and survival data; however, restricting the analysis to those countries with available mortality, incidence, and survival data would significantly limit the scope of the study, especially for developing countries. Furthermore, survival for lung cancer has remained low for several decades with only marginal improvements witnessed in developed countries (7, 8, 32, 36, 37) and country-specific lung cancer incidence and mortality trends are generally similar, even in economically developed countries (38).

Decreasing trends among younger women show promising evidence of tobacco control successes and future lung cancer deaths averted. Although these trends are encouraging, many countries still lack adequate tobacco control, and most have yet to implement the full array of available tobacco control options (39). This constitutes a missed opportunity to reduce smoking further and avert deaths through known evidence-based measures. If comprehensive tobacco control measures (including a doubling of cigarette prices) were implemented worldwide, there would be an estimated 271 million fewer smokers by 2030 (40). As it stands, lung cancer rates among women remain extremely high in many countries. Continued and improved tobacco control measures are urgently needed to accelerate this progress and curtail lung cancer deaths in countries where the tobacco epidemic has not yet taken hold.

#### Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

#### Disclaimer

No staff at the American Cancer Society, other than the study investigators, reviewed or approved the article.

#### Authors' Contributions

**Conception and design:** E.M. Ward, A. Jemal

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**Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.):** L.A. Torre

**Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis):** L.A. Torre, R.L. Siegel

**Writing, review, and/or revision of the manuscript:** L.A. Torre, R.L. Siegel, E.M. Ward, A. Jemal

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## References

1. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. 2013 [cited 2013 December 12]; Available from: <http://globocan.iarc.fr>.
2. Ezzati M, Henley SJ, Lopez AD, Thun MJ. Role of smoking in global and regional cancer epidemiology: current patterns and data needs. *Int J Cancer* 2005;116:963–71.
3. Lopez AD, Collishaw N, Piha T. A descriptive model of the cigarette epidemic in developed countries. *Tob Control* 1994;3:242–7.
4. Thun M, Peto R, Boreham J, Lopez AD. Stages of the cigarette epidemic on entering its second century. *Tob Control* 2012;21:96–101.
5. Centers for Disease Control and Prevention. Women and smoking: a report of the surgeon general. Rockville, MD: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2001.
6. Perlman F, Bobak M, Gilmore A, McKee M. Trends in the prevalence of smoking in Russia during the transition to a market economy. *Tob Control* 2007;16:299–305.
7. Bosetti C, Malvezzi M, Rosso T, Bertuccio P, Gallus S, Chatenoud L, et al. Lung cancer mortality in European women: trends and predictions. *Lung Cancer* 2012;78:171–8.
8. Bray FI, Weiderpass E. Lung cancer mortality trends in 36 European countries: secular trends and birth cohort patterns by sex and region 1970–2007. *Int J Cancer* 2010;126:1454–66.
9. Guo P, Huang ZL, Yu P, Li K. Trends in cancer mortality in China: an update. *Ann Oncol* 2012;23:2755–62.
10. Jemal A, Simard EP, Dorell C, Noone AM, Markowitz LE, Kohler B, et al. Annual report to the nation on the status of cancer, 1975–2009, featuring the burden and trends in human papillomavirus (HPV)-associated cancers and HPV vaccination coverage levels. *J Natl Cancer Inst* 2013;105:175–201.
11. Tyczynski JE, Bray F, Aareleid T, Dalmas M, Kurtinaitis J, Plesko I, et al. Lung cancer mortality patterns in selected Central, Eastern and Southern European countries. *Int J Cancer* 2004;109:598–610.
12. Youlden DR, Cramb SM, Baade PD. The International Epidemiology of Lung Cancer: geographical distribution and secular trends. *J Thorac Oncol* 2008;3:819–31.
13. Bosetti C, Malvezzi M, Chatenoud L, Negri E, Levi F, La Vecchia C. Trends in cancer mortality in the Americas, 1970–2000. *Ann Oncol* 2005;16:489–511.
14. Doll R. Progress against cancer: an epidemiologic assessment. The 1991 John C. Cassel Memorial Lecture. *Am J Epidemiol* 1991;134:675–88.
15. Doll R, Cook P. Summarizing indices for comparison of cancer incidence data. *Int J Cancer* 1967;2:269–79.
16. World Health Organization International Agency for Research on Cancer. Cancer mortality database; 2013 June 2013 [cited 2013 December 13]; Available from: <http://www-dep.iarc.fr/WHOdb/WHOdb.htm>.
17. Mathers CD, Fat DM, Inoue M, Rao C, Lopez AD. Counting the dead and what they died from: an assessment of the global status of cause of death data. *Bull World Health Organ* 2005;83:171–7.
18. Australian Institute of Health and Welfare (AIHW). Australian cancer incidence and mortality books; 2011 [cited 2012 September 13]; Available from: <http://www.aihw.gov.au/acim-books/>.
19. Spitz MR, Wu X, Wilkinson A, Wei Q. Cancer of the lung. In: Schottenfeld D, Fraumeni J Jr., editors. *Cancer epidemiology and prevention*. 3rd ed. New York: Oxford University Press; 2006. p. 638–58.
20. Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Institute. Jointpoint regression program, version 4.0.4. - May 2013.
21. Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for jointpoint regression with applications to cancer rates. *Stat Med* 2000;19:335–51.(correction: 2001;20:655).
22. Jha P. Avoidable global cancer deaths and total deaths from smoking. *Nat Rev Cancer* 2009;9:655–64.
23. Pirie K, Peto R, Reeves GK, Green J, Beral V. The 21st century hazards of smoking and benefits of stopping: a prospective study of one million women in the UK. *Lancet* 2013;381:133–41.
24. Thun MJ, Carter BD, Feskanich D, Freedman ND, Prentice R, Lopez AD, et al. 50-year trends in smoking-related mortality in the United States. *N Engl J Med* 2013;368:351–64.
25. Shkolnikov V, McKee M, Leon D, Chenet L. Why is the death rate from lung cancer falling in the Russian Federation? *Eur J Epidemiol* 1999;19:203–6.
26. Giovino GA, Mirza SA, Samet JM, Gupta PC, Jarvis MJ, Bhala N, 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.
27. World Health Organization. WHO FCTC: Russian Federation- President signs comprehensive tobacco control law; 2013 [cited 2013 April 25]; Available from: [http://www.who.int/fctc/implementation/news/news\\_russia/en/index.html](http://www.who.int/fctc/implementation/news/news_russia/en/index.html).
28. Eriksen M, Mackay J, Ross H. The tobacco atlas. 4th ed. Atlanta, GA: American Cancer Society; 2012.
29. Ho MG, Ma S, Chai W, Xia W, Yang G, Novotny TE. Smoking among rural and urban young women in China. *Tob Control* 2010;19:13–8.
30. Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, Fagerstrom RM, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. *N Engl J Med* 2011;365:395–409.
31. Smith RA, Brooks D, Cokkinides V, Saslow D, Brawley OW. Cancer screening in the United States, 2013: a review of current American cancer society guidelines, current issues in cancer screening, and new guidance on cervical cancer screening and lung cancer screening. *CA Cancer J Clin* 2013;63:88–105.
32. Karim-Kos HE, de Vries E, Soerjomataram I, Lemmens V, Siesling S, Coebergh JW. Recent trends of cancer in Europe: a combined approach of incidence, survival and mortality for 17 cancer sites since the 1990s. *Eur J Cancer* 2008;44:1345–89.
33. Coleman MP, Quaresma M, Berrino F, Lutz JM, De Angelis R, Capocaccia R, et al. Cancer survival in five continents: a worldwide population-based study (CONCORD). *Lancet Oncol* 2008;9:730–56.
34. Danaei G, Vander Hoorn S, Lopez AD, Murray CJ, Ezzati M. Causes of cancer in the world: comparative risk assessment of nine behavioural and environmental risk factors. *Lancet* 2005;366:1784–93.
35. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Vol. 100E Personal Habits and Indoor Combustions. 2012.
36. Coleman MP, Forman D, Bryant H, Butler J, Rachet B, Maringe C, et al. Cancer survival in Australia, Canada, Denmark, Norway, Sweden, and the UK, 1995–2007 (the International Cancer Benchmarking Partnership): an analysis of population-based cancer registry data. *Lancet* 2011;377:127–38.
37. Malvezzi M, Bosetti C, Rosso T, Bertuccio P, Chatenoud L, Levi F, et al. Lung cancer mortality in European men: trends and predictions. *Lung Cancer* 2013;80:138–45.
38. Jemal A, Thun MJ, Ries LA, Howe HL, Weir HK, Center MM, et al. Annual report to the nation on the status of cancer, 1975–2005, featuring trends in lung cancer, tobacco use, and tobacco control. *J Natl Cancer Inst* 2008;100:1672–94.
39. World Health Organization. WHO report on the global tobacco epidemic; 2013. Geneva. 2013.
40. Mendez D, Alshaqeety O, Warner KE. The potential impact of smoking control policies on future global smoking trends. *Tob Control* 2012;22:46–51.

# Cancer Epidemiology, Biomarkers & Prevention

## International Variation in Lung Cancer Mortality Rates and Trends among Women

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