

European cancer mortality predictions for the year 2014

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Background: From most recent available data, we projected cancer mortality statistics for 2014, for the European Union (EU) and its six more populous countries. Specific attention was given to pancreatic cancer, the only major neoplasm showing unfavorable trends in both sexes.

Patients and methods: Population and death certification data from stomach, colorectum, pancreas, lung, breast, uterus, prostate, leukemias and total cancers were obtained from the World Health Organisation database and Eurostat. Figures were derived for the EU, France, Germany, Italy, Poland, Spain and the UK. Projected 2014 numbers of deaths by age group were obtained by linear regression on estimated numbers of deaths over the most recent time period identified by a joinpoint regression model.

Results: In the EU in 2014, 1 323 600 deaths from cancer are predicted (742 500 men and 581 100 women), corresponding to standardized death rates of 138.1/100 000 men and 84.7/100 000 women, falling by 7% and 5%, respectively, since 2009. In men, predicted rates for the three major cancers (lung, colorectum and prostate cancer) are lower than in 2009, falling by 8%, 4% and 10%, respectively. In women, breast and colorectal cancers had favorable trends (−9% and −7%), but female lung cancer rates are predicted to rise 8%. Pancreatic cancer is the only neoplasm with a negative outlook in both sexes. Only in the young (25–49 years), EU trends become more favorable in men, while women keep registering slight predicted rises.

Conclusions: Cancer mortality predictions for 2014 confirm the overall favorable cancer mortality trend in the EU, translating to an overall 26% fall in men since its peak in 1988, and 20% in women, and the avoidance of over 250 000 deaths in 2014 compared with the peak rate. Notable exceptions are female lung cancer and pancreatic cancer in both sexes.

Key words: pancreatic cancer, cancer, Europe, mortality, projections, time trends

introduction

Estimates of cancer mortality statistics for the current year, extrapolated from officially available data from a few years earlier, have long been available for the United States, and have been published over the last few years for the European Union (EU) as a whole, as well as its six more populous countries, based on the World Health Organisation (WHO) mortality database [1–3].

Here, we provide corresponding figures for the year 2014 using the same methodology and WHO mortality database updated in May 2013. This report also focuses specifically on pancreatic cancer, the only major neoplasm not showing favorable mortality trends in both sexes over the last few decades in the EU as well as the USA [4–7].

materials and methods

This work is an update to the previous articles on predicted European cancer mortality, hence the methods are similar [3, 8, 9].

Official death certification data for stomach, colorectum, pancreas, lung, breast, uterus (cervix and corpus), prostate, leukemias and total cancer mortality were obtained from the WHO database (WHOSIS) [1]. Figures were derived for the EU in the period 1970–2009 and up to the most recent available year for six major European countries: France (2009), Germany (2011), Italy (2010), Poland (2011), Spain (2011) and the UK (2010). Details of the data sources and preparation can be found in the supplementary Appendix, available at *Annals of Oncology* online.

From the matrices of certified deaths and resident populations, we computed age-specific numbers of deaths and rates for each 5-year age group (from 0–4 to 80+ years) and calendar year. Age-standardized rates per 100 000 men and women, at all ages, were computed using the direct method, on the basis of the world standard population for all the studied cancers and countries [10].

We fit a logarithmic Poisson count data joinpoint regression model to each 5-year age-specific number of certified deaths in order to identify the most recent trend segment [11]. The joinpoint regression model was set to a maximum of six identifiable segments (five joinpoints) and to have at least five datapoints from the last available calendar year. Age-standardized rates for all countries and neoplasms were also analyzed with joinpoint regression models with up to four trend segments (three joinpoints). Joinpoint Regression Program, Version 4.0.4 from the National Cancer Institute was used.

A linear regression was carried out on mortality data from 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

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95% prediction intervals (PI) [12]. Predicted age-specific numbers of deaths and the predicted population data from Eurostat [13] were used to compute the predicted standardized death rates with 95% PI.

results

Table 1 shows the total numbers of predicted deaths (rounded to the nearest hundred) and the predicted age-standardized death rates for the analyzed neoplasms with 95% PI, in the EU as a whole in 2014, as well as corresponding figures for 2009. In the EU in 2014, 1 323 600 deaths from cancer are predicted (742 500 men and 581 100 women), compared with the 1 281 773 cancer deaths recorded in 2009 (718 355 men and 563 418 women). These numbers correspond to standardized death rates of 138.1/100 000 men and 84.7/100 000 women predicted for 2014, compared with 148.3 men and 89.1 women recorded in 2009, a 7% and 5% fall in men and women, respectively. The rise in certified deaths in spite of the fall in rates highlights the effect of population growth and ageing. Lung cancer is responsible for the largest number of predicted deaths in men with over 187 000 deaths (25% of total cancer deaths), followed by colorectal and prostatic cancer (92 900 and 70 100 deaths, respectively). Predicted death rates were 36.5/100 000 for lung, 16.5/100 000 for colorectum and 10.2/100 000 for prostate. These figures are lower than those recorded in 2009, falling by 8%, 4% and 10%, respectively. In women, breast cancer was responsible for the largest number of deaths with 89 300 predicted deaths (15%, 14.5/100 000), followed by lung cancer (84 500 deaths, 14.1/100 000) and colorectal cancer with 75 500 deaths

(9.5/100 000). Female breast and colorectal cancers had favorable rates (−9% and −7%, respectively), but differently from men, female lung cancer rates are predicted to rise 8%.

Figure 1A shows bar plots of standardized death rates per 100 000 population and certified deaths from all cancers for the year 2009, and the predicted rates and number of deaths for 2014, with the corresponding 95% PIs in men and women. Figure 1B shows bar plots of standardized death rates per 100 000 population for the year 2009, and the predicted rates for 2014 with 95% PIs for the specific sites considered for the EU (in men and women).

Figure 2 gives trends in all-age-standardized (world population) cancer mortality rates for men and women in quinquennia centered from 1972 to 2007, and the predicted rates for 2014 for all cancers.

Figure 3 gives corresponding trends and predictions for stomach, colorectum, pancreas, lung, breast, uterus, prostate and leukemias for EU men and women.

Overall cancer mortality trends are projected to continue their favorable trends into 2014 as they have in men since the late 1980s, and in women earlier still. Supplementary Appendix, with individual country data and analyses, is available at *Annals of Oncology* online.

Table 2 gives age-standardized pancreatic cancer death rates in 2000–2004 and 2005–2009, in the all ages, 25–49 and 50–64 age groups, and predictions for 2014 in men and women for the EU as a whole and its six largest countries. At all ages, the change between 2000–2004 and 2005–2009 is unfavorable for all countries in both men and women. Only Italian and Polish men predicted a modest fall for 2014. In the middle aged (50–64

Table 1. Number of predicted cancer deaths and mortality rates for the year 2014 and comparison figures for most recent data for the EU as a whole, with 95% prediction and confidence intervals

Sex	Cancer	Observed number of deaths 2009	Predicted number of deaths 2014	Lower prediction limit (95%)	Upper prediction limit (95%)	Observed ASR ^a 2009	Predicted ASR ^a 2014	Lower prediction limit (95%)	Upper prediction limit (95%)
Men	Stomach	36 562	34 300	33 741	34 950	7.45	6.38	6.27	6.49
	Colorectum	87 864	92 900	91 648	94 091	17.31	16.54	16.27	16.82
	Pancreas	36 714	41 300	40 693	41 969	7.85	8.13	8.00	8.27
	Lung	183 480	187 300	184 450	190 152	39.49	36.46	35.86	37.06
	Prostate	69 036	70 100	68 945	71 350	11.36	10.19	10.03	10.36
	Leukemias	22 048	23 100	22 494	23 621	4.64	4.18	4.03	4.33
	All cancers	718 355	742 500	734 307	750 601	148.26	138.08	136.35	139.82
	(malignant and benign)								
Women	Stomach	23 977	20 800	20 117	21 429	3.43	2.78	2.67	2.89
	Colorectum	75 063	75 500	74 549	76 503	10.13	9.46	9.31	9.62
	Pancreas	36 725	41 000	40 296	41 755	5.33	5.56	5.47	5.66
	Lung	73 727	84 500	83 192	85 739	13.06	14.07	13.82	14.32
	Breast	89 514	89 300	87 786	90 867	15.81	14.45	14.12	14.79
	Uterus (cervix and corpus)	27 590	27 800	27 291	28 340	5.01	4.71	4.60	4.82
	Leukemias	17 995	18 600	18 193	18 986	2.82	2.53	2.43	2.63
	All cancers	563 418	581 100	576 440	585 805	89.05	84.65	83.81	85.49
(malignant and benign)									

^aASR, age-standardized mortality rate, standardized using the world standard population.

years), only German men and Italian women registered a fall in rates between 2000–2004 and 2005–2009. In the young (25–49 years), the outlook is favorable for men, with all the projected rates being lower than those recorded for 2005–2009. Conversely, in women rates are projected to continue rising, with the exceptions of Poland, Spain and Italy.

Figure 4 shows joinpoint analysis of EU pancreatic cancer age-standardized mortality rates in the three age groups considered for men and women, with projections to 2014 and corresponding PIs. Pancreatic cancer in the all ages and middle aged has had a steady rise in women since the 1970s and is projected to continue while, in men, it seemed to have reached a slowly rising plateau in the late 1980s, but rises are projected until 2014. In the young, there is a stable trend in women that is

projected to rise, but the PIs show the projection is in the range of stability while, in young men, the falls recorded from the early 1980s onward are projected to continue up to 2014.

discussion

Due to their short-term nature and the large numbers involved in their computation, the EU cancer mortality predictions should not be affected by major unexpected events or oscillations. However, if a change or even a trend reversal were to have occurred within the last few years, it is unlikely that this model would totally account for it. Even though a more recent world standard population that better reflects the global aging

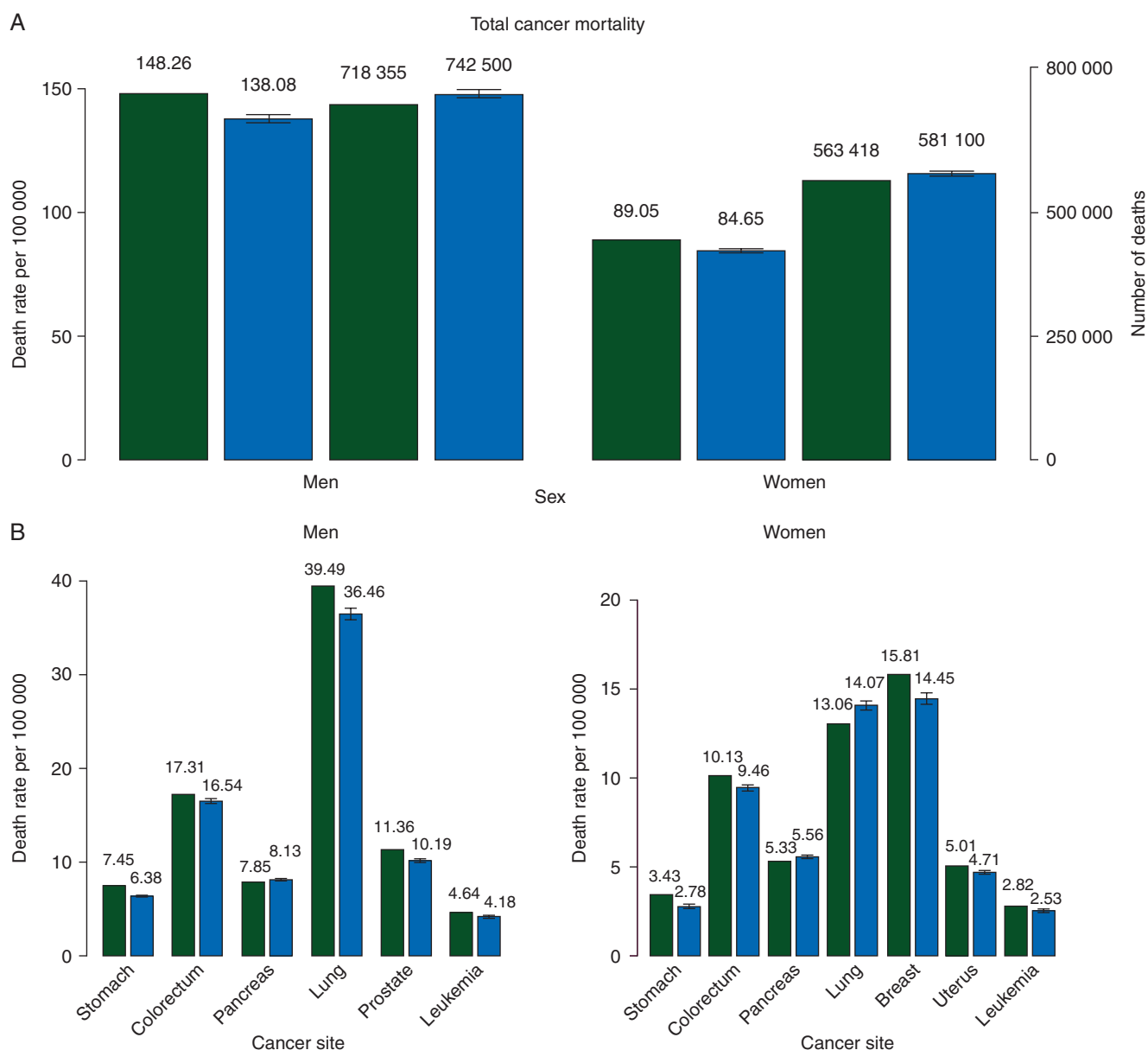


Figure 1. (A) Bar plots of age-standardized (world population) death rates per 100 000 and certified deaths for the year 2009 (green) and predicted rates and number of deaths (predicted numbers of deaths are rounded to the nearest hundred) for 2014 (blue) with 95% prediction intervals (PIs) for total cancer mortality in the EU in men and women. (B) Bar plots of age-standardized death rates per 100 000 population for year 2009 (green) and predicted rates for 2014 with 95% PIs (blue) in the EU in men and women for selected cancer sites.

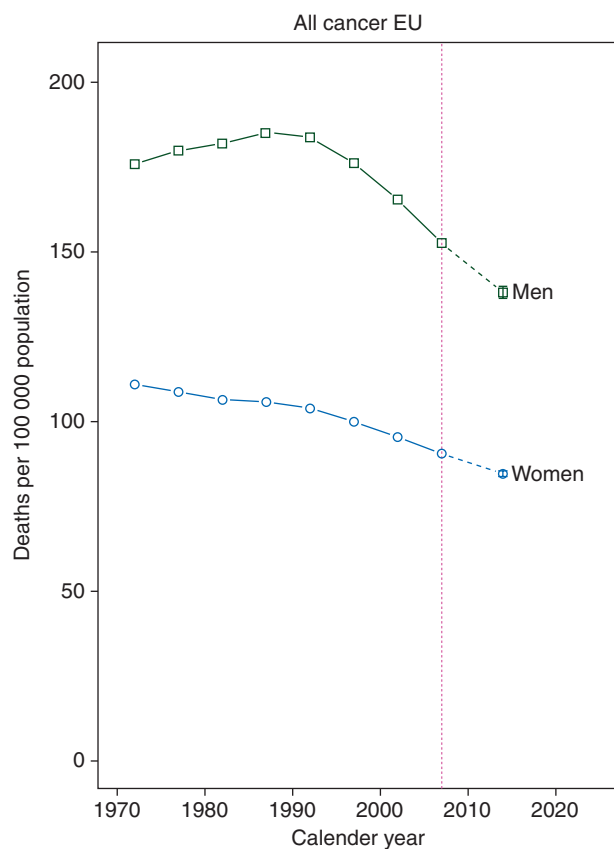


Figure 2. Age-standardized (world population) total cancer mortality trends in quinquennia from 1970–1974 to 2005–2009 and predicted rates for 2014, for men (squares) and women (circles) in the EU.

population has been published [14], we chose to keep using the 1982 version to maintain comparability with previous work [10].

Total male cancer mortality rate is 63% higher than the female rate, but is falling faster. This difference is mainly attributable to the different smoking pattern history in the two sexes. In fact, incidence of lung- and other tobacco-related cancer sites have been growing over the last two decades in EU women [15–17]. Lung cancer in men peaked in the late 1980s, with a rate over 50 and has since fallen by about a third to about 36/100 000 men. This is still higher than the US rate, now about 30/100 000 [2, 16]. Conversely, in women, rates have been rising throughout the studied period reaching a predicted rate of 14.1/100 000 women. Meanwhile, EU overall female breast cancer mortality rates fell over 8% in 5 years to 14.5/100 000, confirming that lung cancer will become the first cause of cancer death in women over the next few years [3, 15]. Similarity, the US breast cancer mortality rate was 14.0/100 000 in 2010 [1]. All the countries that have a lung cancer mortality rate higher than that of the EU as a whole also have a higher total cancer rate. This indicates that smoking habits remain the single strongest determinant of cancer mortality in the EU.

Stomach cancer has been one of the main drivers for the favorable overall cancer trends in both sexes. An age-period cohort analysis of stomach cancer showed a tendency to reach

an asymptote in the effects of the most recent cohorts in countries with low mortality rates [18–20].

In the EU, cancer of the colorectum was the second cause of cancer mortality in men and overall, after lung cancer. Examining the major EU countries, the situation remains heterogeneous, with an over 70% difference in men between France and Poland. In spite of these differences, compared with the 1970s, rates have been converging, particularly for women, across Europe. The earlier favorable trend in women may be attributable to better lifestyle habits and the use of oral contraceptives and other exogenous female hormone preparations [21].

Steady falls in mortality rates are also predicted for major cancers amenable to treatment, including leukemias in both sexes, breast and uterine cancers and prostate cancer. Early diagnosis and screening, in addition to improved therapies and disease management are the key contributors to the falling trends predicted for these cancers [22, 23]. In breast cancer, in particular, falls in mortality have reached 30%–50% in several countries over the last three decades [24].

2011 Mortality data for Germany, Poland and Spain have now been published in the WHOSIS; hence, we can compare our previous predictions. The predictions for Poland were over a short (2008–2011) period and carried out within the 95% PIs, with the exceptions of male lung cancer and total female cancer mortality that were slightly overestimated, but still within a 5% margin. However, German and Spanish mortality projections were over longer periods (2006–2011 and 2005–2011, respectively) and overestimated falls in mortality for most cancers; nonetheless, it should be noted that, in many cancers, changes in trends occurred within the projected period and were therefore unpredictable by this model.

Pancreatic cancer is the only examined neoplasm with a negative outlook in both sexes at all-ages in the EU as a whole. In the young, the situation in the EU becomes more favorable in men, while women keep registering slight predicted rises, likely reflecting trends in smoking in recent generations of European men and women [25]. Tobacco is in fact the main recognized risk factor for pancreatic cancer and is the probable factor behind the fall in male pancreatic cancer rates in the UK between the late 1970s and late 1990s [26]. Obesity and diabetes are other recognized risk factors, together with high alcohol intake, and a family history of pancreatic cancer [27–31]. However, tobacco accounts for less than a third of all cases of pancreatic cancer, and all the known causes together account for <40% [32]. Some of the unfavorable trends in pancreatic cancer mortality are likely due to improved diagnosis and certification following widespread imaging utilization over recent calendar years. In the United States, trends in pancreatic cancer mortality were inconsistent across sexes and races over the last two decades, however, in the absence of any clear downward trend in either sex, despite the major fall in tobacco consumption in men [5, 6]. This may be partly related to the rise in obesity in the United States. The prognosis from this tumor is bleak with 5-year survival being <5%, making mortality from this cancer a close proxy of its incidence [4]. This makes pancreatic cancer a priority in research and control.

Cancer mortality predictions for the year 2014 confirm the overall favorable trend in total cancer mortality in the EU, as reported in the United States [2, 33]. The fall in cancer mortality rates since their peak in 1988 corresponds to more than 250 000

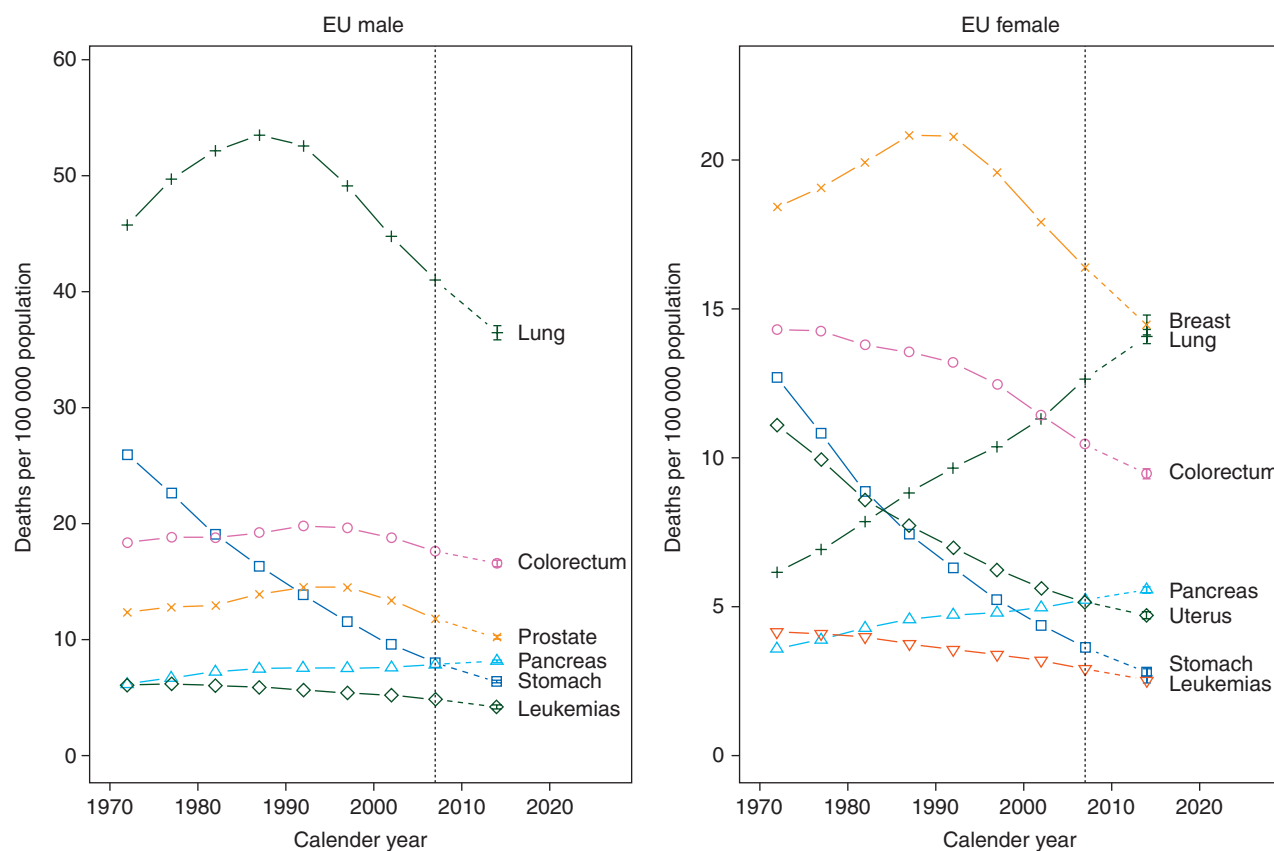


Figure 3. Age-standardized (world population) EU male and female cancer mortality in quinquennia from 1970–1974 to 2005–2009 and predicted rates for 2014. Men: stomach (squares), colorectum (circles), pancreas (triangles), lung (crosses), prostate (x’s) and leukemias (diamonds). Women: stomach (squares), colorectum (circles), pancreas (triangles), lung (crosses), breast (x’s), uterus (diamonds) and leukemias (inverted triangles).

Table 2. Age-standardized pancreatic cancer mortality death rates for all ages, 25–49 and 50–64 years in the quinquennia 2000–2004 and 2005–2009 with predicted rate for the year 2014 in the EU and selected countries

	All ages			25–49 years			50–64 years		
	ASR ^a 2000–2004	ASR ^a 2005–2009	Predicted ASR ^a 2014	ASR ^a 2000–2004	ASR ^a 2005–2009	Predicted ASR ^a 2014	ASR ^a 2000–2004	ASR ^a 2005–2009	Predicted ASR ^a 2014
Men									
France	7.57	7.96	8.76	1.88	1.80	1.64	20.59	21.68	26.85
Germany	8.20	8.35	8.55	1.73	1.65	1.64	22.20	22.08	20.95
Italy	7.39	7.60	7.47	1.55	1.57	1.39	19.72	19.88	19.54
Poland	8.03	8.16	8.11	2.61	2.21	1.42	23.94	24.74	25.99
Spain	6.43	6.59	6.64	1.82	1.70	1.61	18.16	18.65	18.64
The UK	6.35	6.47	6.56	1.36	1.17	1.15	16.06	16.19	17.26
European Union (27)	7.60	7.83	8.13	1.92	1.76	1.57	20.78	21.36	22.77
Women									
France	4.44	4.80	5.35	0.91	0.96	1.12	10.00	11.14	13.40
Germany	5.56	5.88	6.13	0.99	0.96	1.07	12.85	13.65	12.31
Italy	5.06	5.15	5.33	0.89	0.94	0.89	11.52	11.31	11.49
Poland	5.01	5.16	5.20	1.14	1.09	1.09	13.09	13.33	15.10
Spain	3.74	3.99	4.08	0.86	1.00	0.99	8.65	9.13	9.92
The UK	4.75	5.02	5.22	0.81	0.81	0.93	11.13	11.31	10.99
European Union (27)	4.97	5.23	5.56	0.98	0.99	1.05	11.72	12.29	12.47

^aASR, age-standardized mortality rate, standardized using the world standard population.

Pancreas EU

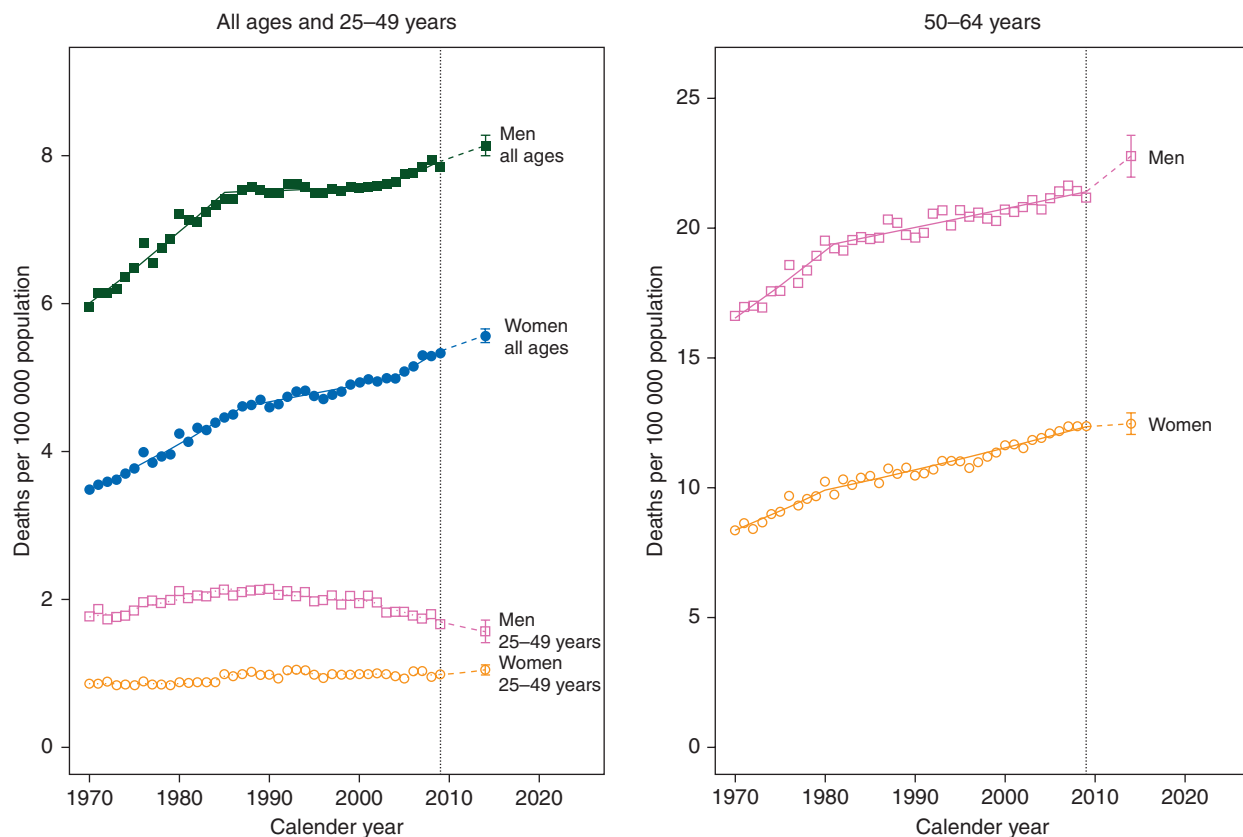


Figure 4. Annual pancreatic cancer age-standardized (world population) death rates in the EU per 100 000 for all ages, 25–49 and 50–64 years age groups from 1970 to 2009, the resulting joinpoint regression models, and predicted rates for the year 2014 with 95% prediction intervals. On the left, men all ages (full squares), men 25–49 (squares), women all ages (full circles) and women 25–49 (circles). On the right men 50–64 (squares) and women 50–64.

avoided deaths in 2014. A substantial differential in cancer mortality between western countries and the former nonmarket economy ones of Central and Eastern Europe remains. This is at least partly due to inadequate cancer management and therapy in those areas of the continent [23, 34], which require urgent attention.

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disclosure

The authors have declared no conflicts of interest.

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Phase I trial of olaparib in combination with cisplatin for the treatment of patients with advanced breast, ovarian and other solid tumors

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Background: To establish the maximum tolerated dose, determine safety/tolerability and evaluate the pharmacokinetics and preliminary efficacy of olaparib in combination with cisplatin in patients with advanced solid tumors.

Patients and methods: Patients aged ≥ 18 years with advanced solid tumors, who had progressed on standard treatment, were assigned to a treatment cohort and received oral olaparib [50–200 mg twice daily (bid); 21-day cycle] continuously or intermittently (days 1–5 or 1–10) in combination with cisplatin (60–75 mg/m² intravenously) on day 1 of each cycle.

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