

# European cancer mortality predictions for the year 2019 with focus on breast cancer

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**Background:** To overcome the lag with which cancer statistics become available, we predicted numbers of deaths and rates from all cancers and selected cancer sites for 2019 in the European Union (EU).

**Materials and methods:** We retrieved cancer death certifications and population data from the World Health Organization and Eurostat databases for 1970–2014. We obtained estimates for 2019 with a linear regression on number of deaths over the most recent trend period identified by a logarithmic Poisson joinpoint regression model. We calculated the number of avoided deaths over the period 1989–2019.

**Results:** We estimated about 1 410 000 cancer deaths in the EU for 2019, corresponding to age-standardized rates of 130.9/ 100 000 men (-5.9% since 2014) and 82.9 women (-3.6%). Lung cancer trends in women are predicted to increase 4.4% between 2014 and 2019, reaching a rate of 14.8. The projected rate for breast cancer was 13.4. Favourable trends for major neoplasms are predicted to continue, except for pancreatic cancer. Trends in breast cancer mortality were favourable in all six countries considered, except Poland. The falls were largest in women 50–69 (-16.4%), i.e. the age group covered by screening, but also seen at age 20–49 (-13.8%), while more modest at age 70–79 (-6.1%). As compared to the peak rate in 1988, over 5 million cancer deaths have been avoided in the EU over the 1989–2019 period. Of these, 440 000 were breast cancer deaths.

**Conclusion:** Between 2014 and 2019, cancer mortality will continue to fall in both sexes. Breast cancer rates will fall steadily, with about 35% decline in rates over the last three decades. This is likely due to reduced hormone replacement therapy use, improvements in screening, early diagnosis and treatment. Due to population ageing, however, the number of breast cancer deaths is not declining.

Key words: cancer, Europe, mortality rates, prediction models, breast cancer

#### Introduction

Current estimates of cancer mortality are crucial to evaluate disease management.

Since death certification figures are available with a few years lag, our group has been publishing cancer mortality predictions for the current year for the European Union (EU) since 2011 [1, 2], as has been long done for the United States [3]. In 2017 and 2018, we also published corresponding figures for a selection of other countries with good quality data [4, 5].

Here, we provide numbers and death rate estimates for the year 2019 from all cancers and selected major cancer sites in the EU as a whole and in its six major countries, and focus on breast cancer.

#### Materials and methods

We retrieved official death certification data from the World Health Organization (WHO) database [6] for cancers of the stomach, colorectum, pancreas, lung, breast, uterus, ovary, prostate, bladder, leukaemias and total cancer mortality. From the WHO and Eurostat databases [7], we obtained resident population estimates. Figures from 1970 to 2014 were derived for the EU (current 28 member states; Cyprus data were missing) and to the most recent available year for the six most populous countries: 2014 for France and 2015 for Germany, Italy, Poland, Spain and the United Kingdom.

Cancer deaths were recoded according to the 10th ICD Revision [8]: stomach (C16), colorectal (C17–C21, C26), pancreas (C25), lung (C33–C34), breast (C50), uterus (cervix and corpus) (C53–C55), ovary (C56), prostate (C61), bladder (C67), leukaemias (C91–C95), and total cancers (C00–D48).

We computed age-specific numbers of deaths and rates for 5-year age groups (0-4 to 85+ years) and calendar years or quinquennia. We calculated direct age-standardized (world standard population) rates (ASRs) for all ages and, for breast cancer, for ages 20–49, 50–69 and 70–79 years. We also applied joinpoint regression models with up to four trend segments to ASRs.

To identify the most recent trend segment, we fitted a logarithmic Poisson count data joinpoint regression model to each 5-year agespecific number of certified deaths [9], setting a maximum of six segments. We estimated predicted age-specific numbers of deaths and 95% prediction intervals (PIs) for 2019 by applying a linear regression to the mortality data from each age group over the most recent trend segment identified by the joinpoint model. We computed predicted age-specific and age-standardized death rates with 95% PIs using predicted agespecific numbers of deaths and predicted populations from Eurostat [7].

We estimated the number of averted cancer deaths over the 1989–2019 period by comparing observed deaths and expected ones on the basis of the 1988 age-specific peak rates.

#### **Results**

Table 1 shows EU-predicted cancer deaths and ASRs with the corresponding 95% PIs for 2019 for selected cancers, in comparison with observed data for 2014. We predict an increase of about 4.8% in total cancer deaths: in 2019, we estimate 1 409 700 cancer deaths (787 800 men, 621 900 women), compared with 1 345 680 in 2014, while the all neoplasms ASR is predicted to decline from 139.1/100 000 men to 130.9 in 2019 (5.9% fall) and, in women, from 86.0 to 82.9 (3.6% fall).

Figure 1 shows observed and predicted EU ASRs per 100 000 person years with 95% PIs for all neoplasms and 10 cancer sites. Lung cancer has the highest predicted rates for both sexes:  $32.3/100\ 000\ men\ (35.6\ in\ 2014,\ -9.2\%)$ , and 14.8 women (14.2 in

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2014, +4.4%). Female lung cancer deaths in 2019 exceed breast cancer ones (96 800 versus 92 800). In women, the second highest rate is 13.4 for breast cancer, declining 8.7% since 2014. Colorectal cancer rates are predicted to decline by 5.5% in men, to reach 15.2/100 000, and by 6.4% in women, to reach 8.8. Prostate cancer accounts for 77 600 predicted deaths, giving the third highest rate in 2019, 10.0/100 000 (7.3% fall since 2014). Pancreatic cancer shows stable trends for men (around 8.0/ 100 000 in 2019) and unfavourable for women (5.6, +1.6%). Stomach cancer shows the most favourable declines, with a 17.1% decrease in men and a 13.7% in women since 2014. Uterine and ovarian cancers showed declines of 2% and 9.4%, respectively. Bladder cancer and leukaemias account for about 45 000 deaths each, with declines in both sexes.

Figure 2 displays cancer mortality trends in guinguennia (from 1970-1974 to 2010-2014) and predicted rates for 2019, with 95% PIs, for all neoplasms in EU men and women (left), and for specific cancer sites for men (centre) and women (right). In men, the favourable all neoplasms trend since the late 1980s was strongly influenced by lung and stomach cancer. Colorectum, prostate and bladder cancers rose up to the early 1990s, to then have favourable trends. In women, major declines were for breast cancer since the 1990, and for colorectal and stomach cancer over the whole period. Uterine cancer also showed a strong decline to then flatten over the last decade. Lung cancer in women rises up to 2019, overetaking breast cancer around 2016. Ovarian cancer rates rose up to the late 1980s and steadily decreased thereafter. Pancreatic cancer rates remain unfavourable for both sexes. Since the 1990s, bladder cancer rates declined in men, and leukaemia ASRs fall in both sexes up to 2019, particularly in women. Additional country-specific data and analyses are available in the supplementary Tables S1-S9 and Figures S1-S3, available at Annals of Oncology online.

		Observed number of deaths 2014	Predicted number of deaths 2019 (95% PI)	Observed ASR <sup>a</sup> 2014	Predicted ASR <sup>a</sup> 2019 (95% PI)	% difference 2019/2014
Men	Stomach	35 290	32 700 (32 003–33 406)	6.48	5.37 (5.24–5.5)	-17.1
	Colorectum	91 452	96 300 (94 721–97 871)	16.09	15.2 (14.93–15.47)	-5.5
	Pancreas	41 571	45 600 (45 043–46 236)	7.91	7.92 (7.81–8.03)	0.1
	Lung	184 095	183 200 (180 170–186 284)	35.59	32.3 (31.67–32.93)	-9.2
	Prostate	73 544	77 600 (76 344–78 910)	10.82	10.04 (9.84–10.23)	-7.3
	Bladder	31 080	33 500 (32 697–34 283)	4.96	4.67 (4.53-4.8)	-5.9
	Leukaemias	23 574	25 400 (24 770–26 032)	4.44	4.05 (3.9-4.2)	-8.8
	All cancers (malignant and benign)	751 228	787 800 (779 182–796 336)	139.11	130.85 (129.14–132.57)	-5.9
Women	Stomach	22 777	20 700 (20 089–21 386)	3.01	2.6 (2.49–2.7)	-13.7
	Colorectum	76 335	76 700 (74 898–78 597)	9.42	8.82 (8.6–9.03)	-6.4
	Pancreas	41 330	45 100 (44 560–45 688)	5.48	5.57 (5.48–5.66)	1.6
	Lung	86 746	96 800 (95 334–98 189)	14.19	14.81 (14.56–15.06)	4.4
	Breast	92 001	92 800 (91 666–94 006)	14.64	13.36 (13.12–13.6)	-8.7
	Uterus (cervix and corpus)	29 202	30 800 (30 060–31 590)	4.87	4.77 (4.65–4.9)	-2
	Ovary	30 018	29 600 (28 882–30 310)	4.88	4.42 (4.28-4.56)	-9.4
	Bladder	10 833	11 400 (11 075–11 645)	1.18	1.16 (1.13–1.19)	-1.5
	Leukaemias	18 986	19 600 (19 229–20 031)	2.69	2.32 (2.22–2.42)	-13.7
	All cancers (malignant and benign)	594 452	621 900 (615 440–628 340)	86.00	82.88 (81.76-84)	-3.6

<sup>a</sup>ASR, age-standardized mortality rates using the world standard population.

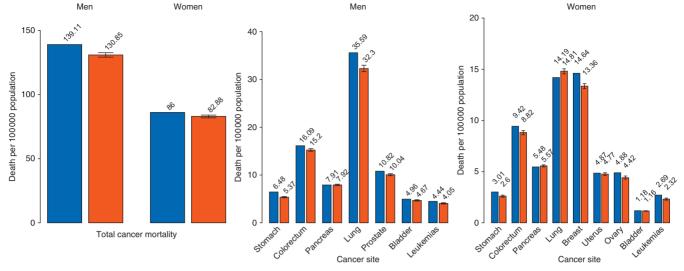
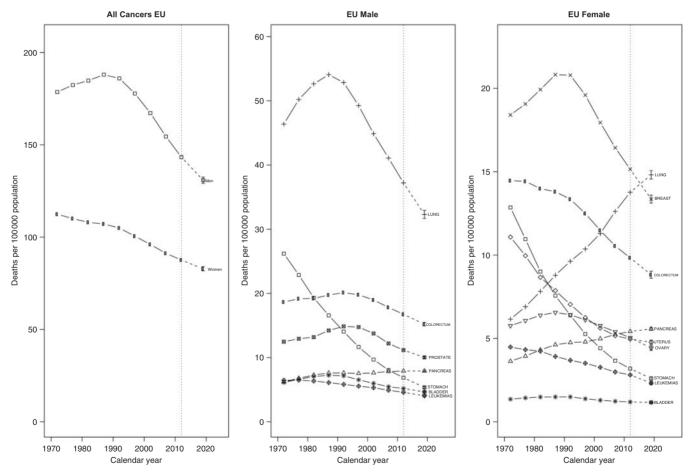


Figure 1. Bar plots of age-standardized (world population) death rates per 100 000 persons for the year 2014 (blue, dark grey) and predicted rates for 2019 (orange, light grey) with 95% prediction intervals (PIs) for total cancer and the 10 major cancer sites in EU men and women.



**Figure 2.** Age-standardized (world population) cancer mortality rate trends in quinquennia from 1970–1974 to 2010–2014 and predicted rates for 2019 with 95% prediction intervals (PIs), for all neoplasms and both sexes (left) and each cancer site under study for men (centre) and women (right), in the EU.

Figure 3 shows trends in breast cancer ASRs in quinquennia from 1970 to 2014, along with the estimates for 2019, for the EU and the six countries considered. Except for Poland,

rates have been declining since the early 1990s; the UK trend was the most favourable one, starting from the highest rates.

Table 2 shows breast cancer ASRs by country in 2005–2009, 2010–2014 and 2019, and rates for the 20–49, 50–69 and 70–79 years age groups for the EU only. Except for Spain, which maintains the lowest rate at 10.4/100 000, rates in other countries converged between 13.3 and 15.2. Only for Poland the rate is expected to rise, becoming the highest value. With reference to age-specific rates in the EU, women aged 50–69 years show the greatest fall, 16.4% since 2010–2014. The fall was 13.8% at age 20–49 and only 6.1% at age 70–79.

Figure 4 displays joinpoint analysis of the EU breast cancer ASRs by age group, and predictions for 2019. All age groups showed rising trends up to the late 1980s or early 1990s and declines thereafter.

Figure 5 shows the estimated number of averted cancer deaths for the EU from 1989 to 2019. We predict a total of 5 290 000 avoided deaths (3 517 000 men and 1 773 000 women) over the whole period and, in 2019 alone 359 000 avoided deaths (237 000 men and 122 000 women).

#### Discussion

The present work confirms the continuing fall in total cancer mortality in the EU [1, 2], showing a 6% decline in men and a 4% in women since 2014. In contrast, the number of deaths rises moderately, due to the European population ageing and increasing in size [10].

The more marked favourable trend in men likely reflects the different changes in smoking patterns over generations of the two sexes [11]. In most European countries (except the UK and Denmark) smoking became frequent in women in the 1970s, i.e. for generations born in the 1950s and 1960s, for whom an epidemic of lung cancer is developing now [12]. The epidemic developed much earlier in men, and is now declining. Still, tobacco remains a priority for prevention, since lung cancer in 2019 is predicted to cause about a fifth of the total cancer deaths in the EU.

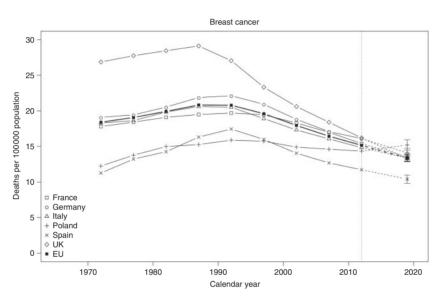
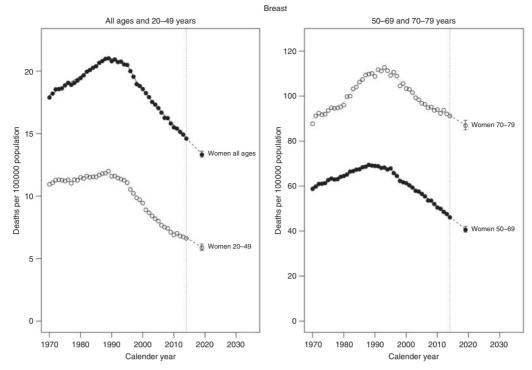


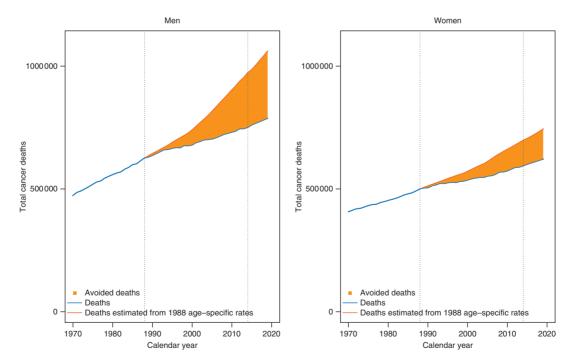
Figure 3. Age-standardized (world population) cancer mortality rate trends for women in quinquennia from 1970–1974 to 2010–2014 and predicted rates for 2019 with 95% PIs for breast cancer in studied countries and in the EU as a whole.

Table 2. Age-standardized breast cancer mortality rates for all ages in selected European countries, and for the EU as a whole for all ages, 20–49, 50–69 and 70-79 years in the 2005-2009, 2010-2014 quinquennia and predicted for 2019, with percentage differences between 2010-2014 and 2019 ASR<sup>a</sup> 2005-2009 ASR<sup>a</sup> 2010-2014 Predicted ASR<sup>a</sup> % difference 2019/2010-2014 2019 (95% PI) France 16.98 15 39 13.52 (12.98-14.06) -121 Germany 17.08 16.1 14.09 (13.44-14.73) -12.5 14.82 -9.7 Italy 16.06 13.38 (12.89-13.88) Poland 14.61 14 34 15.21 (14.49-15.93) 6.1 Spain 12.68 11.73 10.4 (9.82-10.99) -11.3 UK 18.39 16.19 13.33 (12.85-13.81) -17.7 FU All ages 16.44 1515 13.36 (13.12-13.6) -11.8 Truncated 20–49 years 7.59 6.86 5.91 (5.66-6.17) -13.8 Truncated 50–69 years 54 52 48 82 40.81 (39.54-42.08) -164 Truncated 70-79 years 95 5 92.81 87.12 (85.01-89.22) -6.1

<sup>a</sup>ASR, age-standardized mortality rates using the world standard population.



**Figure 4.** Annual breast cancer age-standardized (world population) death rates in the EU per 100 000 for all ages, 20–49, 50–69 and 70–79 age groups from 1970 to 2014, the resulting joinpoint regression models and predicted rates for the year 2019 with 95% Pls. On the left, all ages (full circles) and 20–49 (empty circles) age groups; on the right, 50–69 (full circles) and 70–79 (empty circles) age groups.



**Figure 5.** Total avoided cancer deaths for EU men and women between the top rate in 1988 and 2019 (gold, light grey area); observed numbers of cancer deaths from 1970 to 2014 and predicted cancer deaths from 2015 to 2019 (blue, dark grey line); estimated numbers of total cancer deaths by applying 1988 age-specific peak mortality rate (orange, light grey line). During the 31 years period, 5 290 000 cancer deaths have been avoided (3 517 000 in men and 1 773 000 in women). In 2019 alone are predicted to be avoided 237 000 in men and 1 22 000 in women, for a total of 359 000.

In the EU, breast cancer is the second cause of cancer death in women, despite favourable mortality trends since the 1990s [13]. Due to the ageing of the population, however, there was no fall in the absolute number of deaths (92 000 in 2014, 92 800 predicted in 2019). Thus, the medical and public health burden of breast cancer in Europe is not due to decrease.

Reproductive and hormonal factors, and obesity in postmenopausal women, are the main recognized determinants of breast cancer [14, 15]. No favourable changes in parity and breast-feeding patterns, nor in age at menarche or menopause, have been registered over the last decades [16], and obesity prevalence is increasing [17].

Breast cancer incidence has been rising in some Northern and Eastern European countries, has remained stable in several others, and some declines were only registered in southern European countries [18]. Thus, the downward mortality trends are due to screening (organized, but also spontaneous), early diagnosis and therapy [13, 19, 20]. These also reflect improvements in breast cancer management [21]. The more favourable trends were in EU women aged 50-69, which is the age group generally targeted by organized screening. A Swedish observational study estimated the impact of modern mammography in reducing breast cancer mortality between 47% and 60% at age 40–69 [22], though quantification is still under discussion [23]. In the EU, rates were only slightly decreasing in women aged 70-79, although in some countries like the UK the patterns were more favourable. The implementation of population-based organized breast cancer screening in the EU has greatly improved between 2007 and 2016 [24], and the estimated target population has risen considerably. It may thus be too early to observe an effect in the 70-79 age group; also this age group may benefit less from improvements in therapies, as comorbidities and other problems may prevent their use in older women.

Poland and other Eastern European countries do not have favourable predicted breast cancer mortality patterns [13], indicating the importance to improve breast cancer diagnosis and management in these countries.

The decline in menopausal hormone use may also partly explain the falls in mortality trends [25].

Favourable breast cancer trends were also observed in highincome countries in North America and Oceania, but less consistent patterns were observed in Latin America and several other middle-income countries [26].

Pancreatic cancer is the major site not showing favourable trends in recent years; in men the predicted trend reaches a plateau, in women it has still been rising; only in young men some declines were registered [27]. This probably reflects the different trends in smoking, the main recognized risk factor for this neoplasm, in the two sexes. Tobacco control is partly counterbalanced by the increase in obesity and diabetes registered in several European countries over the last decade [17], as well as in the United States [28]. However, this cannot fully explain the difference in pancreatic cancer trends compared to other tobaccorelated cancers.

The persisting and substantial downward trends in ovarian cancer over the last three decades are mainly due to the long-term protective effects of oral contraceptive (OC) use [29]. Declines in menopausal hormonal therapy use also favourably affected trends [30]. These improvements are less marked in Eastern Europe, where OCs were introduced later and used less frequently. Exposure to occupational carcinogens and tobacco influenced trends in bladder cancer [31], explaining the fourfold higher rates and larger decline in men.

The lower prevalence in *Helicobacter pylori* infection over subsequent decades and the decline in tobacco use in men, along with better dietary habits caused marked declines in stomach cancer [32]; advancement in screening and treatments reduced mortality for colorectal cancer [33]. Improvements in diagnosis and screening positively impact cervix uteri incidence [34], and better therapeutic procedures caused declines in leukaemia mortality trends [35]. Prevention and early detection, together with modern medical, surgical and radiological therapies favourably affect prostate cancer mortality, too [36].

#### Conclusion

Any prediction should always be considered with caution. Our predictions are based on numbers of deaths. If we had used rates, the projected numbers of deaths (in quinquennia of age) would have had to be derived from population projections, which are subjected to additional uncertainties. In any case, the actual data confirmed our previous mortality predictions for 2014 [1] and predicted figures from this work are consistent with other model-ling projections [37].

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#### Disclosure

The authors have declared no conflicts of interest.

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