

## ORIGINAL ARTICLE

# European cancer mortality predictions for the year 2018 with focus on colorectal cancer

M. Malvezzi<sup>1</sup>, G. Carioli<sup>1</sup>, P. Bertuccio<sup>1</sup>, P. Boffetta<sup>2</sup>, F. Levi<sup>3</sup>, C. La Vecchia<sup>1\*</sup> & E. Negri<sup>4</sup>

<sup>1</sup>Department of Clinical Sciences and Community Health, Università degli Studi di Milano, Milan, Italy; <sup>2</sup>Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, USA; <sup>3</sup>Institute of Social and Preventive Medicine (IUMSP), Lausanne University Hospital, Lausanne, Switzerland; <sup>4</sup>Department of Biomedical and Clinical Sciences, Università degli Studi di Milano, Milan, Italy

\*Correspondence to: Prof. Carlo La Vecchia, Department of Clinical Sciences and Community Health, Università degli Studi di Milano, Via Vanzetti 5, 20122 Milan, Italy. Tel: +39-02-503-20-863; Fax: +39-02-503-20-866; E-mail: carlo.lavecchia@unimi.it

**Background:** We projected cancer mortality statistics for 2018 for the European Union (EU) and its six more populous countries, using the most recent available data. We focused on colorectal cancer.

**Materials and methods:** We obtained cancer death certification data from stomach, colorectum, pancreas, lung, breast, uterus, ovary, prostate, bladder, leukaemia, and total cancers from the World Health Organisation database and projected population data from Eurostat. We derived figures for France, Germany, Italy, Poland, Spain, the UK, and the EU in 1970–2012. We predicted death numbers by age group and age-standardized (world population) rates for 2018 through joinpoint regression models.

**Results:** EU total cancer mortality rates are predicted to decline by 10.3% in men between 2012 and 2018, reaching a predicted rate of 128.9/100 000, and by 5.0% in women with a rate of 83.6. The predicted total number of cancer deaths is 1 382 000 when compared with 1 333 362 in 2012 (+3.6%). We confirmed a further fall in male lung cancer, but an unfavourable trend in females, with a rate of 14.7/100 000 for 2018 (13.9 in 2012, +5.8%) and 94 500 expected deaths, higher than the rate of 13.7 and 92 700 deaths from breast cancer. Colorectal cancer predicted rates are 15.8/100 000 men (−6.7%) and 9.2 in women (−7.5%); declines are expected in all age groups. Pancreatic cancer is stable in men, but in women it rose +2.8% since 2012. Ovarian, uterine and bladder cancer rates are predicted to decline further. In 2018 alone, about 392 300 cancer deaths were avoided compared with peak rates in the late 1980s.

**Conclusion:** We predicted continuing falls in mortality rates from major cancer sites in the EU and its major countries to 2018. Exceptions are pancreatic cancer and lung cancer in women. Improved treatment and—above age 50 years—organized screening may account for recent favourable colorectal cancer trends.

**Key words:** cancer, Europe, mortality rates, prediction models, colorectal cancer

## Introduction

Since 2011, we have published current year estimates for cancer mortality statistics based on recent data [1–3]. In this work, we present statistics for 2018 for the European Union (EU) and its six most populous countries, for the most common sites of cancer death plus all cancers combined. We also added bladder and ovarian cancer due to the high number of deaths in the EU [4, 5]. Since reports from outside the EU found increasing trends of colorectal cancer incidence/mortality below age 50 years, in contrast to the favourable trends at older ages [6], a specific focus was devoted to analysing colorectal cancer mortality by age group.

## Materials and methods

We obtained official death certification data from the WHO databases (WHOSIS) [7] for cancers of the stomach, colorectum, pancreas, lung, breast, uterus, ovary, prostate, bladder, leukaemia, and total cancer mortality. We retrieved resident population estimates from the same WHO database, and the Eurostat database [8]. We obtained figures from 1970 to 2012 for the EU (28 member states; data for Cyprus were missing) and up to the most recent available year for the six largest European countries: France (2013), Germany (2014), Italy (2012), Poland (2014), Spain (2014), and the UK (2013).

Cancer deaths were recoded according to the tenth ICD Revision [9]: stomach (C16), colorectal (C17–C21, C26), pancreas (C25), lung

**Table 1. Number of predicted deaths and mortality rate for the year 2018 and comparison figures for 2012, for the EU, with 95% prediction intervals**

	Observed number of deaths 2012	Predicted number of deaths 2018 (95% PI)	Observed ASR 2012	Predicted ASR 2018 (95% PI)
<b>Men</b>				
Stomach	36 256	33 200 (32 498–33 905)	6.91	5.60 (5.48–5.72)
Colorectum	92 483	98 000 (96 808–99 198)	16.95	15.82 (15.6–16.03)
Pancreas	39 822	44 500 (43 773–45 135)	7.90	7.89 (7.76–8.01)
Lung	185 591	183 100 (180 585–185 531)	37.26	32.43 (31.95–32.9)
Prostate	71 840	77 000 (75 698–78 284)	11.08	10.14 (9.93–10.35)
Bladder	31 388	34 700 (33 963–35 367)	5.26	5.05 (4.94–5.15)
Leukaemias	23 599	24 700 (24 025–25 417)	4.66	4.01 (3.82–4.19)
All cancers (malignant and benign)	745 296	765 000 (758 579–771 415)	143.81	128.94 (127.74–130.15)
<b>Women</b>				
Stomach	23 501	21 100 (20 461–21 728)	3.21	2.66 (2.56–2.75)
Colorectum	78 021	79 400 (78 315–80 483)	9.98	9.23 (9.09–9.38)
Pancreas	39 669	44 400 (43 819–45 080)	5.43	5.58 (5.48–5.69)
Lung	82 107	94 500 (92 964–95 984)	13.85	14.65 (14.38–14.93)
Breast	91 821	92 700 (91 400–93 998)	15.18	13.74 (13.49–13.99)
Uterus (cervix and corpus)	28 971	29 600 (28 955–30 216)	4.98	4.64 (4.53–4.75)
Ovary	30 068	31 200 (30 420–31 954)	5.02	4.70 (4.56–4.84)
Bladder	10 684	11 100 (10 732–11 398)	1.20	1.14 (1.10–1.17)
Leukaemias	18 849	19 800 (19 305–20 196)	2.82	2.41 (2.32–2.51)
All cancers (malignant and benign)	588 066	617 000 (612 136–621 817)	88.01	83.61 (82.79–84.42)

ASR, age-standardized mortality rates per 100 000 persons using the world standard population.

(C33–C34), breast (C50), uterus (cervix and corpus) (C53–C55), ovary (C56), prostate (C61), bladder (C67), leukaemia (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 year or quinquennia. We used the direct method (world standard population) to calculate age-standardized rates.

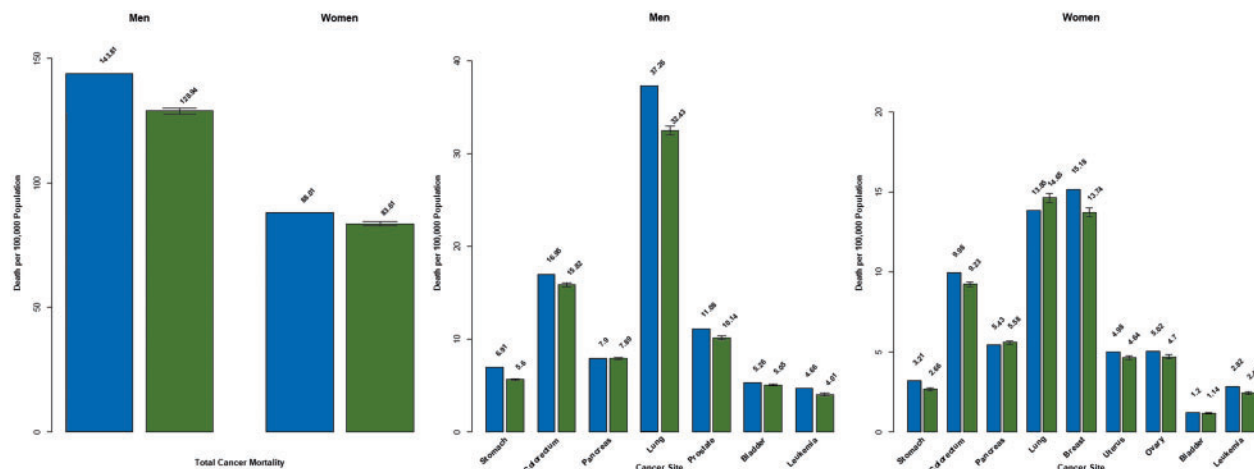
We fitted a Poisson count data joinpoint regression model to the logarithm of each 5-year age-specific death number to identify the most recent trend segment [10]. The model was set to a maximum of six segments (five joinpoints) and to include at least five data points in the last segment. Age-standardized rates were also analysed with joinpoint regression models with up to four trend segments. We estimated predicted age-specific numbers of deaths and 95% prediction intervals (PIs) for 2018 by applying a linear model to the mortality data from each age group over the most recent trend segment identified by the joinpoint model. We used predicted age-specific numbers of deaths and the predicted population from Eurostat [8] to compute the predicted age-specific and age-standardized death rates (world population) with 95% PIs.

## Results

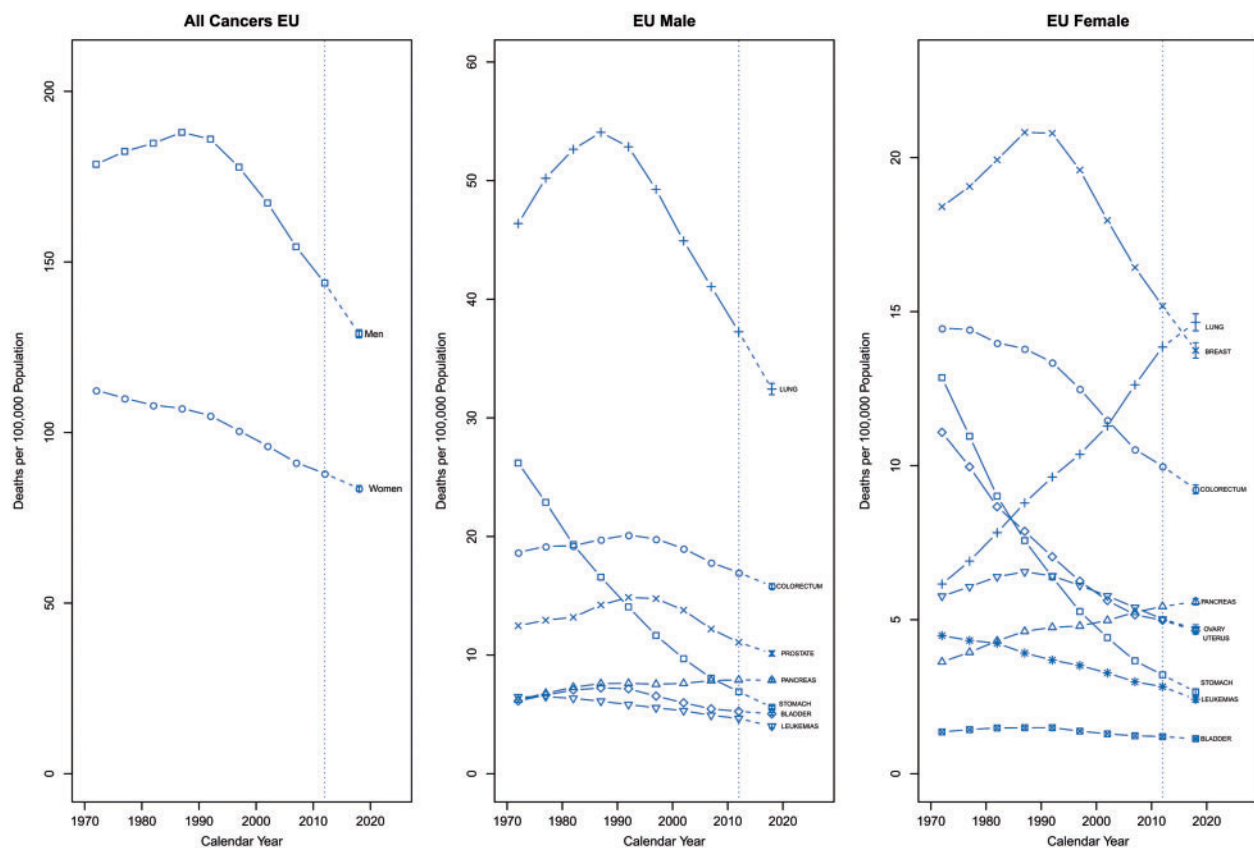
Table 1 shows predicted cancer deaths and age-standardized rates with 95% PIs for 2018 for the studied neoplasms in the whole EU, and comparison data for 2012. In men, we predict 765 000 cancer deaths in 2018, and 617 000 in women, for a total of 1 382 000 deaths, compared with 1 333 362 in 2012, thus increasing by 3.6%. The predicted age-standardized rates for 2018 are 128.9/100 000 men and 83.6/100 000 women, compared with 143.8/100 000 men and 88.0/100 000 women in 2012, with falls of 10.3% in men and 5.0% in women.

Figure 1 shows bar plots of age-standardized death rates per 100 000 population for all neoplasms and the 10 considered sites in 2012, and expected rates for 2018 in EU men and women, with 95% PIs. Lung cancer has the highest predicted rates in both sexes, 32.4/100 000 in men and 14.7 in women; however, we registered a 13.0% fall in men since 2012, and a 5.8% rise in women. Expected deaths in 2018 were 183 100 men and 94 500 women (~20% of total cancer deaths). Colorectal cancer accounts for the second highest number of deaths for 2018 with 177 400 deaths, with rates of 15.8/100 000 men and 9.2/100 000 women, declining since 2012 by 6.7% in men and 7.5% in women. Breast cancer has the second highest predicted rate in women, 13.7/100 000 (92 700 deaths), with a 9.5% decline since 2012. Prostate cancer has the third highest rate in men, 10.1/100 000, and declines by 8.5%. Pancreatic cancer shows stable rates in men, 7.9/100 000, but is unfavourable in women (5.6/100 000 in 2018, +2.8%). Stomach cancer falls 19.0% in men and 17.1% in women. Uterine and ovarian cancers display similar behaviour, with predicted rates around 4.7/100 000, falls over 6%, and about 30 000 deaths. Bladder cancer rates are 5.1/100 000 in men (–4.0%; 34 700 deaths) and 1.1/100 000 in women (–5.0%; 11 100 deaths). Leukaemia represents 3% of total cancer deaths (14% fall since 2012).

Figure 2 shows cancer mortality rates for EU men and women in quinquennia from 1970 to 2012, and predicted rates for 2018 with 95% PIs, for all neoplasms (left) and each cancer site for men (centre) and women (right). In men, the falling rates are mainly influenced by lung cancer, since the late 1980s, and stomach cancer, which declined over the whole period. In women the greatest falls were for breast, colorectal and stomach cancer, while lung cancer steadily increased. Pancreatic cancer shows a steady



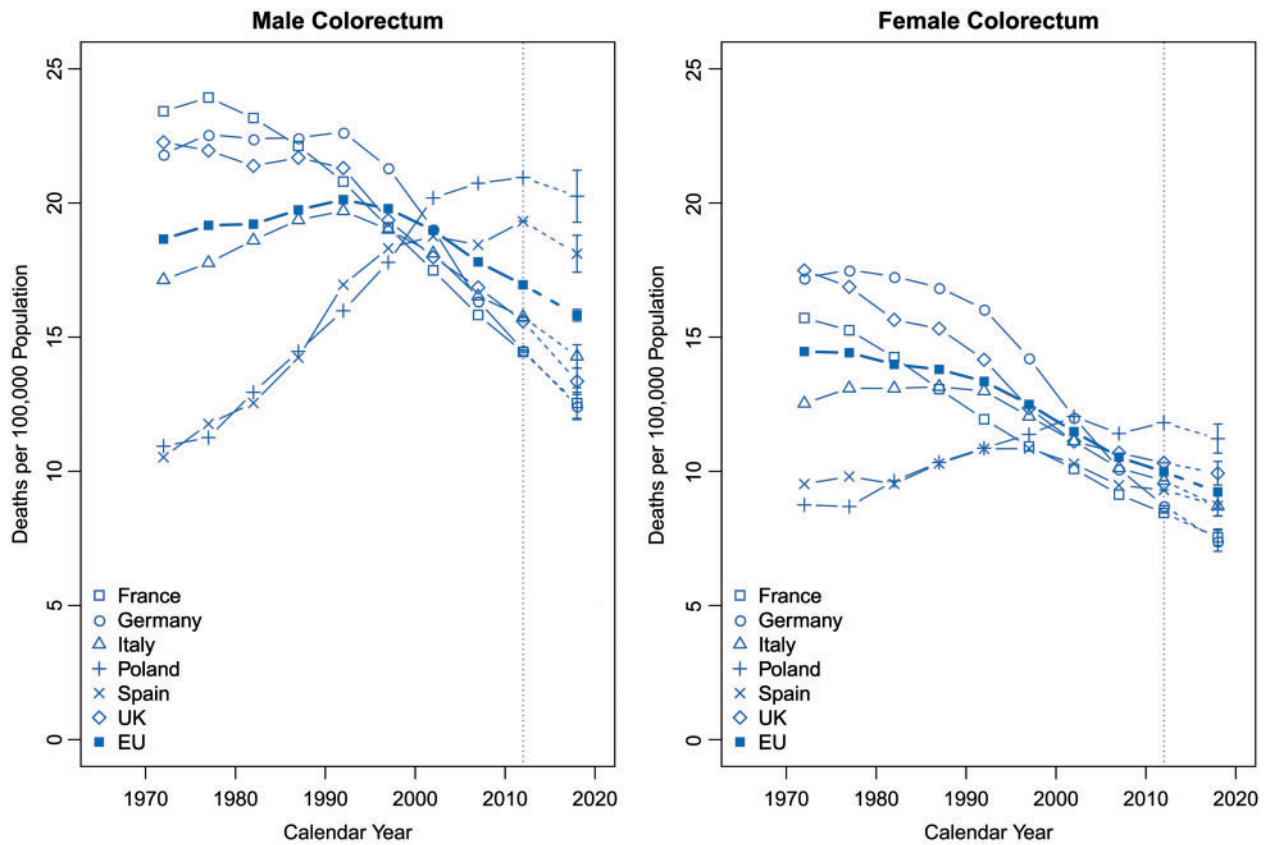
**Figure 1.** Bar-plots of age-standardized (world population) death rates per 100 000 persons for the year 2012 (dark grey, blue online) and predicted rates for 2018 (light grey, green online) with 95% prediction intervals (PIs) for total cancer and the ten major cancer sites in EU men and women.



**Figure 2.** Age-standardized (world population) cancer mortality rate trends (per 100 000 persons) in quinquennia from 1970–1974 to 2005–2009 plus the year 2012 and predicted rates for 2018 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.

rise for women, while in men rates are predicted to remain stable, after earlier rises. Male bladder cancer showed unfavourable trends up to the early 1990s, to then fall and reach a plateau. In women, rates were stable. Uterine cancer displays strong declining trends since the 1970s, which recently slowed down. Ovarian cancer declined since the early 1990s. Further details on

country-specific data and analyses can be found in the [supplementary Appendix](#), available at *Annals of Oncology* online ([supplementary Tables S1–S9](#) and [Figures S1](#) and [S2](#), available at *Annals of Oncology* online). In general, they show earlier and larger declines in Western Europe, and a tendency towards a levelling of rates across the EU.



**Figure 3.** Age-standardized (world population) cancer mortality rate trends for men and women in quinquennia from 1970–1974 to 2005–2009 plus the year 2012 and predicted rates for 2018 with 95% PIs for colorectal cancer in studied countries and the EU as a whole.

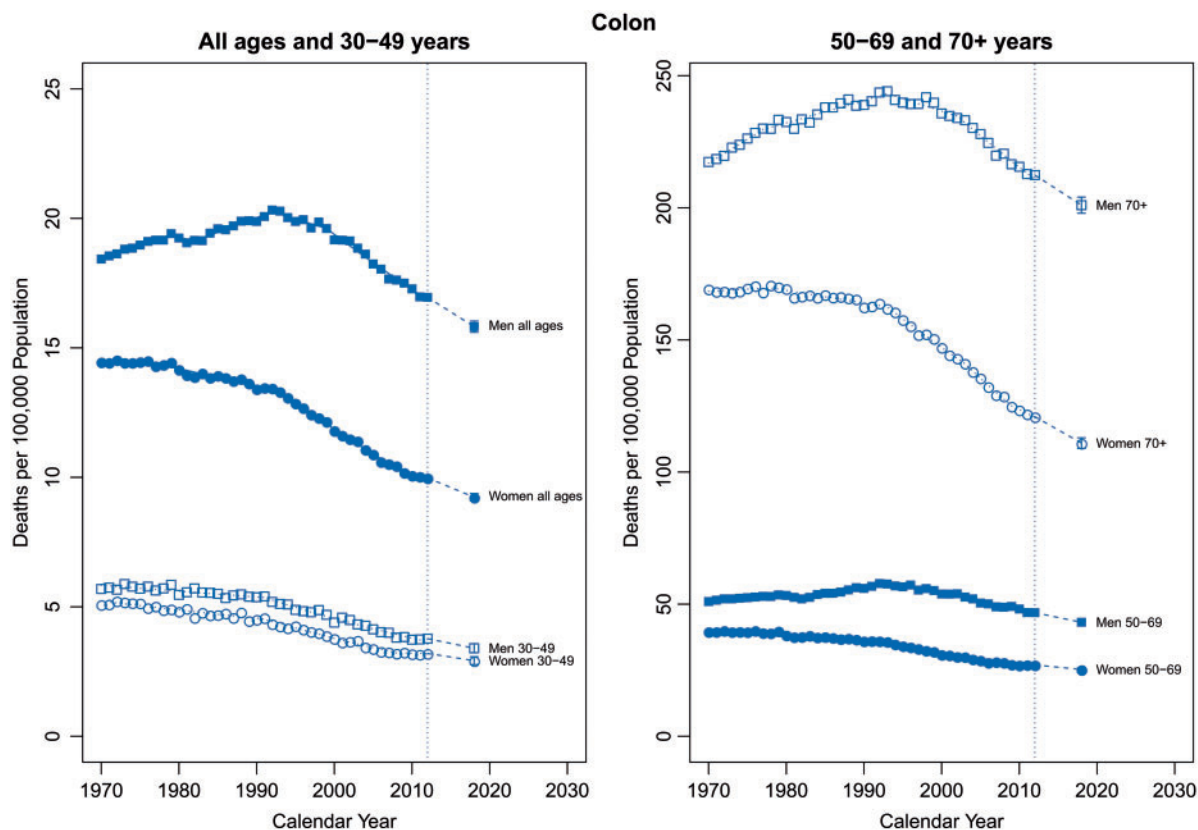
**Table 2.** Age-standardized colorectal cancer mortality rates for all ages in selected European countries, in men and women, and for the EU as a whole for all ages, 30–49, 50–69, and 70+ years in the 2005–2009 quinquennium, in 2012 and predicted for 2018, with percentage differences between 2012 and 2018

	Men				Women			
	ASR 2005–2009	ASR 2012	Predicted ASR 2018 (95% PI)	% difference (2018/2012)	ASR 2005–2009	ASR 2012	Predicted ASR 2018 (95% PI)	% difference (2018/2012)
France	15.83	14.45	12.54 (11.97–13.12)	–13.2	9.13	8.45	7.54 (7.23–7.85)	–10.8
Germany	16.35	14.52	12.44 (11.93–12.94)	–14.4	10.09	8.72	7.41 (7.02–7.8)	–15.1
Italy	16.53	15.75	14.29 (13.85–14.72)	–9.3	10.12	9.65	8.70 (8.33–9.08)	–9.8
Poland	20.74	20.95	20.25 (19.28–21.22)	–3.3	11.41	11.81	11.22 (10.68–11.76)	–5.0
Spain	18.44	19.32	18.11 (17.42–18.8)	–6.3	9.48	9.30	8.72 (8.34–9.09)	–6.3
UK	16.85	15.59	13.35 (12.86–13.85)	–14.3	10.69	10.31	9.93 (9.49–10.37)	–3.7
EU								
All ages	17.81	16.95	15.82 (15.6–16.03)	–6.7	10.53	9.98	9.23 (9.09–9.38)	–7.5
Truncated 30–49 years	3.96	3.77	3.40 (3.23–3.58)	–9.8	3.28	3.20	2.92 (2.77–3.07)	–8.8
Truncated 50–69 years	49.69	46.98	43.14 (42.06–44.21)	–8.2	28.16	27.11	25.27 (24.56–25.98)	–6.8
Truncated 70+ years	221.71	212.37	200.99 (197.94–204.03)	–5.4	130.10	120.96	110.94 (108.94–112.93)	–8.3

ASR, age-standardized mortality rates using the world standard population.

Figure 3 shows colorectal cancer quinquennial age-standardized rates from 1970 to 2012 for men and women for the six studied countries and the EU, and predicted rates for 2018 with 95% PIs. In men, trends were favourable for the last two decades, except for

Poland and Spain. Poland had an increasing trend up to 2002, to then reach a plateau. In 2018 Poland (20/100 000 men) and Spain (18.1/100 000) display the highest rates. The pattern of trends was similar in women, with, however, lower rates.



**Figure 4.** Annual colorectal cancer age-standardized (world population) death rates in the EU per 100 000 for all-ages, 30–49, 50–69, and 70+ years age groups from 1970 to 2012, the resulting joinpoint regression models, and predicted rates for the year 2018 with 95% PIs. On the left, men and women at all-ages (full squares and full circles, respectively) and at 30–49 years (empty squares and empty circles), on the right, men and women at 50–69 years (full squares and full circles), and at 70+ years (empty squares and empty circles).

Table 2 shows age-standardized mortality rates for colorectal cancer for the six countries in 2005–2009 and 2012, and the predicted rates for 2018 with 95% PIs. Rates for all ages and truncated for 30–49, 50–69, and 70+ years age groups for the EU are also presented. All trends were favourable. In men, France, Germany and the UK showed the greatest declines between 2012 and 2018 (14%), while Poland the lowest one. In women the greatest decline is registered for Germany and the lowest one in the UK.

Figure 4 displays joinpoint analysis of colorectal cancer age-standardized mortality rates for the EU, in both sexes and different age groups, along with predictions for 2018 and 95% PIs. Except for age 30–49 years, male rates rose up to the mid-1990s, thereafter trends decrease appreciably. Women in all age groups and men aged 30–49 display steady downward patterns, with favourable predicted trends.

Figure 5 shows the estimated number of avoided cancer deaths for the EU from 1989 (light grey area, green online) due to the declines in rates since 1990. We predict 392 000 avoided deaths in 2018 alone (275 000 men and 117 000 women) and a total of 4 930 000 (3 288 000 in men and 1 642 000 in women) over the whole period.

## Discussion

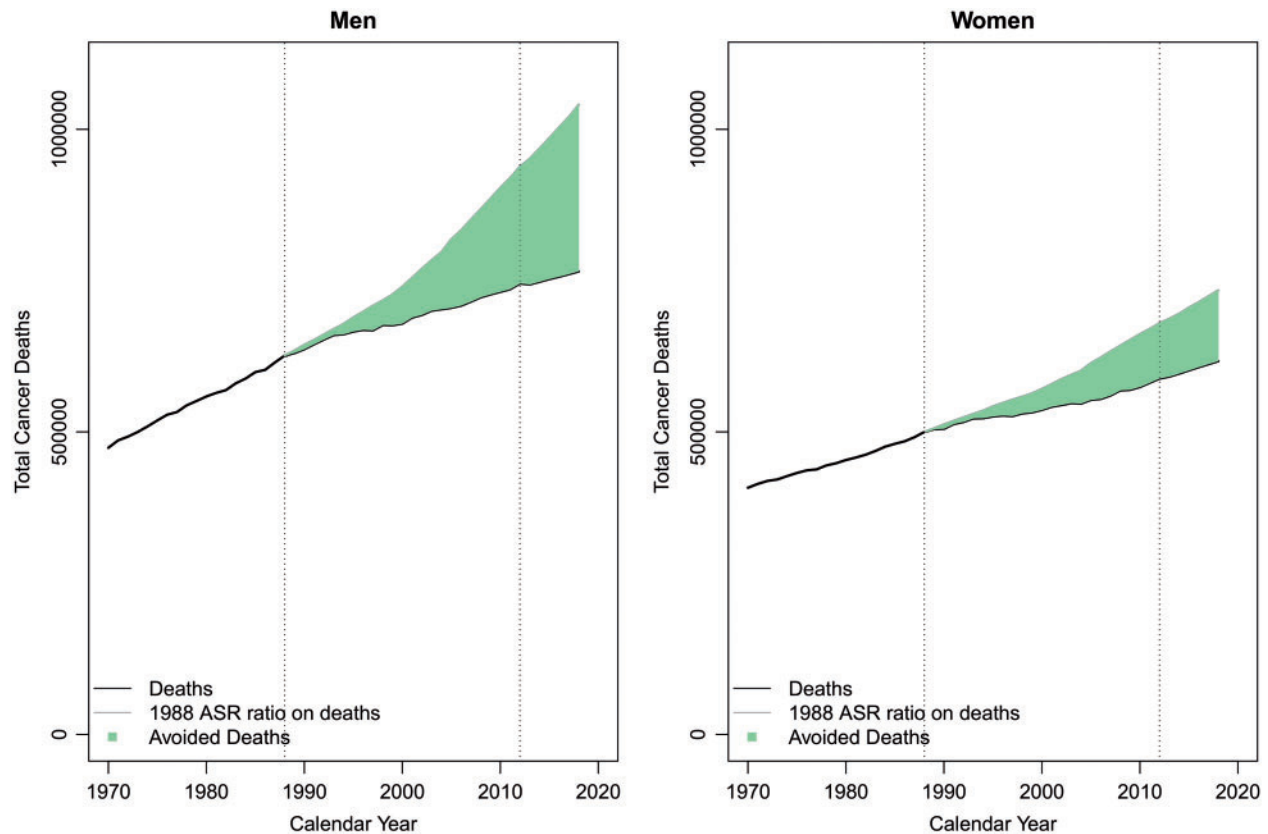
The steady declines in overall cancer mortality rates in the EU in both sexes are predicted to continue up to 2018, with male rates falling 10.3% and 5.0% in women since 2012. Unlike the United

States [11], cancer death numbers are increasing slightly, mainly due to population aging. Mortality from major cancer sites is decreasing, including stomach, colorectum, bladder and leukaemia in both sexes, prostate and lung in men; and breast, uterus (cervix and corpus), and ovary in women. Conversely, lung cancer rates in women are increasing, and pancreas mortality rates are predicted to level off.

Interpretation of the prediction models' results needs caution. We updated aggregate mortality data for the EU, and minor inconsistencies with previous reports are likely. The temporal length of the projection is also relatively large at 6 years (2012–2018) and at the limit for short term model reliability. The large populations under analysis should protect from random variation, but very recent changes in trends, as well as cohort-like effects are difficult to detect for this model. In addition, predictions are less valid for rarer cancers, such as stomach [12].

## Colorectal cancer

In the EU, colorectal cancer mortality has been declining since 1993 in men, and over the whole period in women. However, individual countries followed different trajectories. In the early 1970s there was an over twofold variation between high and low rates. Rates progressively converged up to the early 2000s (12% variation in men and 16% in women). Thereafter trends diverged, particularly in men, with a reversal in country rankings



**Figure 5.** Total avoided cancer deaths for EU men and women between the top rate in 1988 and 2018 (light grey area, green online); observed numbers of cancer deaths from 1970 to 2012 and predicted cancer deaths from 2013 to 2018 (black line); estimated numbers of total cancer deaths by applying 1988 age-specific peak mortality rate (dark grey line). During the 31 years period 4 930 000 cancer deaths have been avoided (3 288 000 in men and 1 642 000 in women). In 2018 alone are predicted to be avoided 275 000 in men and 117 000 in women, for a total of 392 000. ASR, age specific rate.

compared with the 1970s. The convergence of rates has been attributed to homogenization of diet and lifestyles across the EU [4, 13]. Migrant studies showed that colorectal cancer mortality tends to change faster than for other cancers following lifestyle and diet modification [14]. The subsequent divergence is difficult to explain. Identified risk factors for colorectal cancer include alcohol and tobacco, obesity and diabetes, sedentariness, and unhealthy dietary patterns [15]. Oral contraceptive (OC) and hormone replacement therapy (HRT) use may have decreased risk in women, partly explaining sex differences. The increased use of aspirin, mainly for cardiovascular disease prevention, likely reduces colorectal cancer incidence [16]. Substantial progresses in management and treatment of colorectal cancer have taken place. Screening is very effective in reducing colorectal cancer mortality and incidence [17].

Trends in risk factor exposure differed within Europe, with declines in tobacco and alcohol consumption in men and increased prevalence of obesity, diabetes and sedentariness in several countries. OC and, until the early 2000s, HRT use increased. Differential access to effective treatment across Europe can also play a role [18, 19]. Since the early 2000s several European countries have introduced organized screening above 50 years of age [20], and differential implementation and uptake may influence recent trends.

Since the early 2000s, incidence and/or mortality trends in the United States, Canada, Australia and Norway have been

decreasing above 50 years of age, but increasing below [6]. Increases in obesity, sedentariness and other unfavourable lifestyle habits, not counterbalanced by screening, may explain rises in early onset colorectal cancer. In the EU, mortality below age 50 years is not increasing, but rates levelled off since 2008 in both sexes.

### Bladder cancer

There is an over fourfold difference between male and female bladder cancer mortality rates. More frequent exposure in men to the two major established risk factors [21, 22], i.e. tobacco and occupational exposure to aromatic amines and other bladder carcinogens, can partly explain the wide gender gap. Bladder cancer incidence rates are highly influenced by changes in classification, coding, and registration, but these are unlikely to affect mortality rates and criteria for death certification did not change appreciably over the considered period [4]. Temporal trends in exposure to tobacco and occupational carcinogens can largely account for bladder cancer mortality trends in EU men. The role of other risk factors remains undefined [22]. There are similarities in mortality trends from lung and bladder cancers, confirming the important role played by tobacco in bladder cancer burden. Since 2008, however, trends have become less favourable in men, contrary to lung cancer.

## Ovarian cancer

Since the late 1980s, ovarian cancer mortality has been falling in the EU, after earlier increases, and a further 6% fall is predicted between 2012 and 2018. Falls started earlier in the UK and Germany, who once had the highest rates, and only later into the 2000s in Poland. OC use decreases the risk of ovarian cancer, and its spread throughout Europe largely accounts for the favourable trends and the different timing of onset [5]. A detailed analysis [5] showed that falls were larger in young women, although in some countries, including the UK and Germany, earlier spread of OC use resulted in substantial declines in women aged 70–79 years. Reductions in HRT use, a risk factor for ovarian cancer, after unfavourable results [23], may also have contributed. The role of other risk factors is difficult to evaluate, while improvements in management and therapy may have played a minor role, since European mean 5-year survival was low and no substantial gains were observed over time [24].

## Other cancer sites

Lung cancer mortality mainly reflects different past smoking patterns in the two sexes. Lung cancer is now the leading cause of cancer deaths in both sexes in the EU. In spite of decreases in men, the tobacco death toll remains huge, and abating tobacco consumption remains a priority.

The marked decreases in breast cancer and leukaemia mortality are largely due to progress in management and treatment [25, 26].

Stomach cancer steadily declined since the 1970s, mostly because of reduced *Helicobacter pylori* infection and tobacco smoking, and improvements in food preservation and diet [27].

The decrease in uterine cancer mortality is largely due to the decreased incidence of cancer of the cervix uteri, due to the spreading across Europe of effective screening [20].

## Funding

This work was conducted with the contribution of the Italian Association for Cancer Research (AIRC, Project No. 18440), MIUR (Ministero dell'Istruzione, dell'Università e della Ricerca), with an SIR (Scientific Independence of Young Researchers) 2014 grant (project RBSI1465UH).

## Disclosure

The authors have declared no conflicts of interest.

## References

- Malvezzi M, Arfe A, Bertuccio P et al. European cancer mortality predictions for the year 2011. *Ann Oncol* 2011; 22(4): 947–956.
- Malvezzi M, Bertuccio P, Levi F et al. European cancer mortality predictions for the year 2013. *Ann Oncol* 2013; 24(3): 792–800.
- Malvezzi M, Carioli G, Bertuccio P et al. European cancer mortality predictions for the year 2017, with focus on lung cancer. *Ann Oncol* 2017; 28(5): 1117–1123.
- Bosetti C, Bertuccio P, Chatenoud L et al. Trends in mortality from urologic cancers in Europe, 1970–2008. *Eur Urol* 2011; 60(1): 1–15.
- Malvezzi M, Carioli G, Rodriguez T et al. Global trends and predictions in ovarian cancer mortality. *Ann Oncol* 2016; 27(11): 2017–2025.
- Siegel RL, Miller KD, Fedewa SA et al. Colorectal cancer statistics, 2017. *CA Cancer J Clin* 2017; 67(3): 177–193.
- World Health Organization Statistical Information System. WHO mortality database; [http://www.who.int/healthinfo/statistics/mortality\\_raw\\_data/en/index.html](http://www.who.int/healthinfo/statistics/mortality_raw_data/en/index.html) (1 September 2017, date last accessed).
- European Commission. Eurostat population database; <http://epp.eurostat.ec.europa.eu/portal/page/portal/population/data/database> (1 September 2017, date last accessed).
- World Health Organization. International Classification of Disease and Related Health Problems: 10th Revision. Geneva: World Health Organization 1992.
- Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joint-point regression with applications to cancer rates. (Erratum in: *Stat Med* 2001; 20: 655.) *Stat Med* 2000; 19(3): 335–351.
- Jemal A, Ward EM, Johnson CJ et al. Annual report to the nation on the status of cancer, 1975–2014, featuring survival. *J Natl Cancer Inst* 2017; 109(9). doi: 10.1093/jnci/djx030.
- Malvezzi M, Bertuccio P, Rosso T et al. European cancer mortality predictions for the year 2015: does lung cancer have the highest death rate in EU women? *Ann Oncol* 2015; 26(4): 779–786.
- Fernandez E, La Vecchia C, Gonzalez JR et al. Converging patterns of colorectal cancer mortality in Europe. *Eur J Cancer* 2005; 41(3): 430–437.
- Kolonel LN, Wilkens LR. Migrant studies. In D Schottenfeld, JF Fraumeni (eds) *Cancer Epidemiology and Prevention*, 3rd edition. New York, NY: Oxford University Press 2006; 189–201.
- Turati F, Bravi F, Di Maso M et al. Adherence to the World Cancer Research Fund/American Institute for Cancer Research recommendations and colorectal cancer risk. *Eur J Cancer* 2017; 85: 86–94.
- Cuzick J, Thorat MA, Bosetti C et al. Estimates of benefits and harms of prophylactic use of aspirin in the general population. *Ann Oncol* 2015; 26(1): 47–57.
- Issa IA, Noureddine M. Colorectal cancer screening: an updated review of the available options. *WJG* 2017; 23(28): 5086–5096.
- Ait Ouakrim D, Pizot C, M B et al. Trends in colorectal cancer mortality in Europe: retrospective analysis of the WHO mortality database. *BMJ* 2015; 351: h4970.
- Bosetti C, Levi F, Rosato V et al. Recent trends in colorectal cancer mortality in Europe. *Int J Cancer* 2011; 129(1): 180–191.
- Ponti A, Anttila A, Ronco G et al. Cancer screening in the European Union (2017). Report on the implementation of the Council Recommendation on cancer screening (second report). European Commission; [https://ec.europa.eu/health/sites/health/files/major\\_chronic\\_diseases/docs/2017\\_cancerscreening\\_2ndreportimplementation\\_en.pdf](https://ec.europa.eu/health/sites/health/files/major_chronic_diseases/docs/2017_cancerscreening_2ndreportimplementation_en.pdf) (15 November 2017, date last accessed).
- Cumberbatch MG, Rota M, Catto JW, La Vecchia C. The role of tobacco smoke in bladder and kidney carcinogenesis: a comparison of exposures and meta-analysis of incidence and mortality risks. *Eur Urol* 2016; 70(3): 458–466.
- Pelucchi C, Bosetti C, Negri E et al. Mechanisms of disease: the epidemiology of bladder cancer. *Nat Clin Pract Urol* 2006; 3(6): 327–340.
- Rossouw JE, Anderson GL, Prentice RL et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial. *JAMA* 2002; 288: 321–333.
- De Angelis R, Sant M, Coleman MP et al. Cancer survival in Europe 1999–2007 by country and age: results of EUROCORE-5—a population-based study. *Lancet Oncol* 2014; 15(1): 23–34.
- Carioli G, Malvezzi M, Rodriguez T et al. Trends and predictions to 2020 in breast cancer mortality in Europe. *Breast* 2017; 36: 89–95.
- Malvezzi M, Carioli G, Bertuccio P et al. European cancer mortality predictions for the year 2016 with focus on leukaemias. *Ann Oncol* 2016; 27(4): 725–731.
- Peleteiro B, La Vecchia C, Lunet N. The role of *Helicobacter pylori* infection in the web of gastric cancer causation. *Eur J Cancer Prev* 2012; 21(2): 118–125.