

ORIGINAL ARTICLE

Cancer mortality in Europe in 2015 and an overview of trends since 1990

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Background: Cancer mortality in Europe has been decreasing since the late 1980s or 1990s in some countries with different patterns in many areas. In this study, we updated trends in cancer mortality in Europe.

Materials and methods: We extracted data from the World Health Organization mortality database for 24 cancer sites, 36 European countries and the European Union (EU) as a whole over the 1990–2017 period. We computed age-standardized death rates per 100 000 person-years, and we carried out a joinpoint regression analysis of mortality trends from all cancers and selected major neoplasms. The estimated annual percent change (APC) for each identified linear segment, and the weighted average APC (AAPC) over the entire study period were provided as summary measures of the changes in rates over the time period.

Results: In 2015, the age-standardized mortality rates from all cancers in the EU were 137.5 deaths per 100 000 in men and 85.7 in women. Eastern European countries showed the highest rates with values over 150 deaths per 100 000 in men and over 100 deaths per 100 000 in women. Mortality from all cancers in the EU declined annually by 1.5% in men since 2006 and by 0.8% in women since 2007. Most cancer sites showed decreasing trends, with steady declines over the whole period for cancers of stomach, intestines, lung in men, breast and prostate. Unfavourable mortality trends persisted for cancers of liver, lung in women, pancreas, besides skin and kidney in men.

Conclusions: The downward trends in total cancer mortality in Europe still continue over the last decade. However, the trends were less favourable in most eastern European countries. Tobacco control in men (but not in women), improvements in diagnosis and therapy were the main underlying factors of these trends.

Key words: cancer, mortality, Europe, trends

Introduction

Cancer mortality shows substantial variation across Europe. Steady declines were observed since the 1980s in most western European countries and a decade later in central and eastern Europe [1]. Such favourable trends have been attributed not only to the reduced prevalence of smoking in men [2, 3] and decreased alcohol consumption in Mediterranean countries [4], but also to the increased availability of screening, early diagnosis and treatment. However, suboptimal tobacco control, inadequate adoption of modern diagnostic techniques and effective treatment have produced remarkable disparities in cancer mortality across Europe [5] with systematically less favourable mortality trends in eastern European countries [1, 6].

In this study, we provide updated data on cancer mortality in Europe.

Materials and methods

We extracted official death certification data from the World Health Organization (WHO) database for 24 cancer sites and all neoplasms in 36 European countries, plus the European Union 28 Member States (EU-28) as a whole, for the 1990–2017 period [7]. All the countries considered had death certification coverage over 95%, except Serbia (84%). During the considered calendar years, we used three different Revisions of the International Classification of Diseases (ICD) and coded cancer deaths for all calendar years and countries, according to the 10th Revision of the ICD [8].

We obtained estimates of the resident population, based on official censuses, from the same WHO database [7]. Since population estimates for France and Ireland in 2015, Spain in 2016 and Switzerland in 2014 and 2015 were not available in the WHO database, these were obtained from the EUROSTAT database [9].

No interpolations were made for missing data in a few countries and calendar years, except for the calculation of the rates for the EU-28 as a whole.

Using the dataset with death counts and resident populations, we calculated age-specific rates for 18 age groups (from 0–4 to 80–84, and ≥ 85 years), sex and calendar year. We then computed age-standardized mortality rates per 100 000 person-years (at all ages and the 35–64 age-group), based on the world standard population [10].

For the EU-28 as a whole and a subset of 24 selected major countries (i.e. with populations over 5 million inhabitants), we carried out a joinpoint regression analysis on mortality data for all neoplasms, and selected major cancers (i.e. intestines, lung, breast and prostate), over the 1990–2017 period [11]. We thus identified the time point(s), called ‘joinpoints’, when a change in the linear slope (on a log scale) of the temporal trend occurred [12], by testing from a zero up to a maximum of four joinpoints. The estimated annual percent change (APC) for each identified linear segment, and the weighted average APC (AAPC) over the entire study period (1990–2017) as a summary measure, were computed for each joinpoint model [12, 13].

Results

Tables 1 and 2 provide the overall age-standardized mortality rates per 100 000 men and women, respectively, and the number of deaths from selected cancers registered in 2015 in 36 European countries and the EU-28 as a whole. [Supplementary Figures S1–S8](#), available at *Annals of Oncology* online, show rates (from largest to smallest) for the EU-28 by cancer site ([supplementary figure S1](#), available at *Annals of Oncology* online), and for all neoplasms ([supplementary figure S2](#), available at *Annals of Oncology* online) and selected major cancers ([supplementary figures S3–S8](#), available at *Annals of Oncology* online) by country ([supplementary material](#), available at *Annals of Oncology* online).

In men, all neoplasms mortality rate in the EU-28 was 137.5/100 000 corresponding to 760 123 deaths in 2015. Most eastern European countries and Russia showed the highest mortality rates, while northern European countries had the lowest ones. With regard to major cancers, in the EU-28, male mortality rates were 34.8/100 000 for lung cancer, 16.1 for intestinal cancer, 10.7 for prostate cancer, 7.9 for pancreatic cancer and 6.3 for stomach cancer. Mortality rates from lung cancer ranged between 15 and 23/100 000 in Scandinavian countries, 27 and 36 in the UK, France, Germany, Italy and Spain to 45–63 in eastern European countries and Russia. Mortality rates from intestinal cancer ranged from about 13 to 15/100 000 in major western countries to around 30/100 000 in Hungary, Slovakia and Croatia. The Russian rate was 18.7/100 000. Mortality from prostate cancer showed the highest rates (14–21/100 000) in Baltic and Scandinavian countries, while the lowest ones (7–9/100 000) were in Italy and other southern European countries. Mortality from pancreatic cancer ranged between 6.5 and 8.6/100 000 in the UK, Spain, Italy, France, and Germany to around 10–11/100 000 in several central and eastern European countries. Stomach cancer mortality rates ranged from 3–4 deaths/100 000 in northern and central European countries to 19.4/100,000 in Russia, followed by other eastern European countries. Portugal, Italy and Spain had relatively high rates, too.

In women, the total cancer mortality rate in the EU-28 was 85.7/100 000, corresponding to 603 984 deaths in 2015. The highest mortality rate was observed in Hungary, followed by other eastern and northern countries. In contrast, the lowest mortality rates were observed in southern and eastern countries, with the lowest one in Spain. With regard to major cancers, EU-28 female mortality rates were 14.5/100 000 for breast cancer, 14.3 for lung cancer, 9.4 for intestinal cancer, 5.5 for pancreatic cancer and 2.9 for stomach cancer. The highest breast cancer rates were in Serbia and other central European countries (around 15–18) and Russia (15.7), while the lowest ones were in Norway, other Scandinavian countries and Spain (about 10–11/100 000). The highest lung cancer rates were in Hungary (29.6/100 000), followed by some northern countries, while the lowest ones (3–6/100 000) were in eastern Europe. Mortality rates from intestinal cancer ranged between 7 and 8 deaths/100 000 in Austria, Greece, Switzerland and France to 15.1/100 000 in Hungary. Mortality from pancreatic cancer ranged from 3.6/100 000 in Ukraine, around 4 in Portugal and Spain to 7.3 deaths/100 000 in Hungary. Mortality from stomach cancer ranged from 1.5/100 000 in France, followed by most western and northern European countries (rates around 2) to 7.9/100 000 in Russia.

Corresponding figures for the 35–64 age group are displayed in the supplementary [tables S1 and S2](#) (available at *Annals of Oncology* online).

[Figure 1](#) and [supplementary table S3](#), available at *Annals of Oncology* online show the joinpoint regression analysis of mortality trends for 23 cancer sites plus all neoplasms in the EU-28 from 1990 to 2015 at all ages and for the 35–64 age group, in men and women. The downward trends in total cancer mortality started in the early 1990s and the mortality rate at all ages declined annually by 1.5% in men since 2006 and by 0.8% in women since 2007. Downward trends were observed for most major cancer sites, with steady declines for cancers of stomach, intestines, lung in men, breast and prostate. In contrast, unfavourable trends were observed for lung cancer in women and increasing or stable rates were observed for pancreatic cancer. Favourable trends were also observed for most other cancer sites, except liver over the recent calendar years, skin and kidney in men.

[Figure 2A–E](#) ([supplementary table S4a–e](#), available at *Annals of Oncology* online) give the results from the joinpoint analysis of mortality trends (1990–2017) for all neoplasms and major cancer sites in 24 selected countries. Mortality from all neoplasms declined in most countries for both sexes, with the exceptions of Bulgaria, Greece and Romania. The favourable trends started after the mid-1990s in most eastern countries, Norway and Spain. Upward trends were observed in mortality rates from intestinal cancer in East Europe. Lung cancer mortality decreased in most countries in men, except in Bulgaria, Portugal and Romania. Lung cancer mortality in women increased in most countries, while breast cancer decreased by 2%–4% per year over the most recent period in most northern European countries, and around 1.5% in most western and southern countries. In Russia, breast cancer mortality started to decline over the last few years. Greater declines in breast cancer were observed among middle-aged women. After the increasing trends observed over the 1990s, mortality from prostate cancer declined in most countries, with a few exceptions in East Europe.

Table 1. Age-standardized (world population) mortality rates (first row) and number of deaths (second row) from selected cancers per 100 000 men in 36 European countries plus the European Union as a whole (EU-28) in 2015^a

ICD-10	Oral cavity, pharynx		Oesophagus		Stomach		Intestines		Primary liver		Gallbladder and biliary tract		Pancreas		Larynx		Lung		Bone and soft tissue		Skin		Prostate		Testis		Bladder		Kidney		Thyroid		HL		NHL		MM		Leukemias		All neoplasms	
	C00-C14	C15	C16	C17-C21	C22.0-C22.7	C23-C24	C25	C32	C33-C34	C40-C41	C42-C49	C43-C44	C61	C62	C67	C64-C66, C68	C73	C81	C82-C85, C96	C88, C90	C89, C95	C91-C95	C00-D48																			
Austria	4.71	3.21	4.94	12.76	6.17	0.88	9.29	1.26	27.60	0.46	0.99	3.08	9.77	0.24	3.87	4.23	0.30	0.11	3.31	2.01	3.72	121.36																				
Belarus	372	267	462	1238	556	83	866	112	2396	27	78	306	1128	14	381	405	28	13	315	195	358	11246																				
Belgium	11.18	5.50	17.55	16.73	3.36	-	8.06	4.43	39.97	-	-	1.81	12.10	-	4.01	-	-	-	3.04	1.26	4.88	160.46																				
Bulgaria	706	351	1124	1089	213	-	510	282	2550	-	-	110	799	-	261	-	-	-	179	79	288	10156																				
Croatia	4.13	5.09	3.92	13.91	4.36	0.56	6.93	1.40	36.76	0.62	0.83	1.97	9.74	0.13	4.71	3.96	0.24	0.26	3.26	1.89	4.00	128.60																				
Denmark	424	554	472	1790	482	71	815	155	4338	54	88	238	1532	11	673	513	29	33	418	269	511	15873																				
Estonia	5.31	2.23	9.88	20.18	3.28	0.81	8.70	5.68	40.81	1.35	0.53	2.47	10.71	0.89	5.79	4.18	0.31	0.50	2.73	0.88	4.05	151.20																				
Finland	327	146	718	1542	226	60	624	378	2746	61	24	172	949	44	453	283	21	29	166	60	255	10581																				
France	7.40	3.56	10.81	28.13	4.61	2.19	8.44	4.54	51.03	1.34	0.43	4.39	16.12	0.68	7.18	5.74	0.29	0.36	4.33	2.19	5.74	191.52																				
Germany	274	140	478	1247	195	102	363	185	2101	39	17	175	824	16	344	239	11	13	174	101	231	8184																				
Greece	6.12	4.64	5.74	20.70	2.96	2.55	10.33	2.35	34.67	0.46	1.19	3.12	11.55	0.36	5.07	7.81	0.17	0.35	2.62	1.62	4.47	147.68																				
Hungary	553	443	590	2200	300	276	1038	225	3568	34	66	321	1327	27	571	794	18	31	270	2.28	4.00	129.99																				
Iceland	4.45	5.04	4.08	15.62	4.09	1.06	7.95	1.22	29.51	0.39	0.83	3.24	15.34	0.33	4.98	4.08	0.13	0.26	2.90	2.28	4.00	151.25																				
Ireland	241	299	246	1015	235	64	481	73	1894	17	39	194	1170	11	346	242	9	17	176	152	273	8289																				
Italy	7.71	5.99	13.65	19.90	5.93	1.85	10.16	2.55	44.16	1.66	2.06	2.55	21.63	0.39	6.00	7.89	0.22	0.44	5.68	2.12	5.20	183.77																				
Latvia	77	60	149	235	66	21	110	27	506	8	14	33	292	3	74	92	3	4	59	26	60	2083																				
Lithuania	2.63	3.27	4.00	12.10	4.86	1.43	8.83	0.64	22.55	0.26	0.92	2.81	11.88	0.52	2.47	3.83	0.36	0.23	3.82	2.17	3.23	105.43																				
Luxembourg	143	185	244	748	303	92	535	36	1381	11	43	171	859	15	168	236	21	13	253	140	198	6481																				
Macedonia	5.07	4.62	4.05	13.51	7.46	0.55	7.98	1.43	35.99	0.56	0.89	2.09	9.08	0.25	4.78	4.87	0.24	0.27	3.33	2.02	4.28	135.70																				
Malta	2944	2961	2816	10291	4934	452	5417	916	22728	281	513	1486	8665	102	3980	3497	170	151	2511	1646	3215	95086																				
Poland	5.03	4.82	5.43	13.86	4.59	1.54	8.57	1.43	30.84	0.39	0.96	2.21	11.21	0.27	3.36	5.59	0.31	0.22	3.35	1.43	4.44	126.55																				
Portugal	4086	4269	5429	14491	4491	1611	8497	1291	29378	255	734	2231	13900	145	3963	5954	300	180	3532	1519	4290	126546																				
Romania	2.24	1.34	6.48	12.01	3.32	0.71	8.03	2.45	46.98	0.63	1.04	1.77	9.03	0.39	6.92	3.53	0.23	0.38	2.97	1.62	4.72	138.87																				
Slovakia	250	158	842	1798	407	96	1011	322	5745	68	90	231	1763	23	1078	474	28	45	323	240	624	18493																				
Slovenia	15.25	5.74	9.70	31.84	2.03	2.46	10.76	4.82	62.83	0.47	1.74	3.70	12.54	0.67	7.23	5.57	0.27	0.32	3.81	1.45	6.56	208.73																				
Spain	1167	464	853	2890	177	219	946	389	5356	27	99	319	1258	40	679	481	24	24	321	130	489	17935																				
Sweden	1.79	2.98	3.36	12.85	3.36	0.18	7.47	-	15.74	-	-	2.20	14.21	-	3.38	6.26	0.79	0.40	3.25	1.60	5.48	95.66																				
Switzerland	5	9	11	41	1	1	25	-	48	-	-	5	56	-	12	19	3	1	11	7	15	311																				
Turkey	3.83	7.23	5.00	17.37	4.42	0.46	7.67	1.29	27.03	0.47	0.83	3.47	11.84	0.10	3.87	4.01	0.39	0.43	3.95	2.25	3.66	124.36																				
Ukraine	140	274	193	683	167	18	297	48	1043	17	27	133	527	3	170	156	13	14	159	93	141	4848																				
United Kingdom	2.92	1.93	6.92	14.02	5.85	1.80	7.46	1.75	31.38	0.63	0.82	2.23	6.98	0.26	4.77	3.76	0.29	0.48	3.52	2.11	4.83	126.24																				
United States	1899	1359	5491	11599	4270	1518	5555	1319	24405	273	486	1637	7214	99	4440	2968	219	254	2674	1757	3406	99591																				
Yemen	9.62	6.83	16.64	17.09	2.40	1.00	10.66	4.38	40.57	0.80	1.00	3.30	20.32	0.65	8.67	7.10	0.35	0.38	3.21	1.95	4.52	183.47																				
Other EU-28	148	106	278	315	38	20	170	67	674	12	13	59	392	8	158	124	7	5	55	33	78	3094																				
EU-28	11.15	7.65	16.21	19.55	3.82	1.39	9.46	5.48	45.90	0.60	1.34	2.95	18.32	0.42	6.28	8.16	0.44	0.37	3.08	1.76	5.66	192.23																				
World	236	172	414	527	89	35	227	122	1098	11	20	71	544	6	180	197	11	9	75	47	134	4721																				
World (95% CI)	1.89	2.43	2.78	12.69	4.49	0.92	5.22	1.88	28.94	0.21	1.32	2.49	9.71	0.21	3.90	2.12	0.39	0.27	2.34	2.35	6.07	108.12																				
World (95% CI)	10	12	15	63	25	5	27	8	145	1	6	13	55	1	22	14	3	1	12	12	29	561																				
World (95% CI)	2.97	1.50	12.54	15.86	7.03	0.82	7.99	5.08	44.44	0.97	0.36	3.62	11.78	0.59	5.40	1.46	0.16	0.57	1.26	1.16	2.83	141.59																				
World (95% CI)	44	23	198	249	108	12	122	81	689	13	4	54	203	7	84	23	3	8	18	19	42	2198																				
World (95% CI)	4.11	2.74	3.06	14.51	3.55	1.01	11.82	1.09	31.42	0.87	1.01	1.00	7.88	0.54	4.00	3.32	0.13	0.36	4.01	1.51	2.26	111.58																				
World (95% CI)	17	12	17	70	15	5	50	5	148	2	3	4	39	2	19	15	1	1	20	7	10	512																				

Continued

Table 2. Age-standardized (world population) mortality rates (first row) and number of deaths (second row) from selected cancers per 100 000 women in 36 European countries plus the European Union as a whole (EU-28) in 2015^a

IC-D10	Oral cavity, pharynx		Oesophagus		Stomach		Intestines		Primary liver		Gallbladder and biliary tract		Pancreas		Larynx		Lung		Bone and soft tissue		Connective tissue		Skin		Breast		Uterus		Ovary		Bladder		Kidney		Thyroid		HL		NHL		MM		Leukemias		All neoplasms	
	C00-C14	C15	C16	C17-C21	C22.0-C22.7	C23-C24	C25	C32	C33-C34	C40-C41	C43-C44	C47, C49	C53-C55	C56-C57.4	C64-C66, C68	C73	C81	C82-C85, C96	C88, C90	C91-C95	C00-D48																									
Austria	1.40	0.66	2.74	6.78	2.08	1.02	6.18	0.21	15.04	0.26	0.83	1.62	13.81	3.83	4.18	0.90	1.69	0.23	0.15	1.92	1.31	2.52	81.76																							
Belarus	1.53	0.38	3.63	9.73	2.42	1.48	8.05	2.1	14.93	1.4	61	2.01	15.68	4.13	4.65	152	246	36	15	273	1.75	332	9755																							
Belgium	0.96	0.38	6.60	9.38	1.15	-	3.73	0.04	3.11	-	-	1.37	11.87	7.30	4.74	0.33	-	-	-	1.39	1.19	2.40	71.34																							
Bulgaria	88	40	719	1107	1.14	-	4.09	5	339	-	-	1.22	11.06	6.47	4.22	49	-	-	-	152	1.23	253	7171																							
Croatia	1.29	1.38	1.59	8.56	1.75	0.46	5.42	0.18	15.68	0.35	0.67	1.48	15.25	3.59	4.62	1.20	1.53	0.30	0.13	1.94	1.22	2.91	83.45																							
Denmark	1.62	2.01	2.68	1.541	2.70	95	8.95	26	1936	41	87	2.19	21.67	5.24	6.69	252	253	46	18	374	2.29	507	12750																							
Estonia	1.22	0.36	4.46	10.08	1.24	0.90	5.16	0.38	8.86	0.63	0.09	1.15	16.11	9.78	5.27	1.40	1.05	0.26	0.62	1.54	0.62	1.93	87.02																							
Finland	92	28	441	1095	1.24	94	5.20	32	739	43	11	1.19	13.43	7.26	4.16	1.43	93	28	29	118	58	175	7575																							
France	1.45	0.72	4.98	13.31	1.74	1.98	6.54	0.21	14.01	0.68	0.81	2.29	18.14	6.34	5.88	1.66	1.91	0.22	0.23	2.57	1.56	3.42	103.10																							
Germany	68	40	323	889	96	142	3.99	12	720	32	17	1.52	10.38	3.46	3.22	1.31	1.35	16	9	173	98	183	6122																							
Greece	1.63	0.65	3.29	10.69	1.02	2.70	6.70	0.21	13.25	0.40	0.75	1.67	12.35	6.13	6.28	1.39	2.93	0.28	0.22	1.81	1.41	2.53	90.36																							
Hungary	1.90	1.26	1.88	11.60	1.44	0.93	6.36	0.24	25.63	0.21	0.65	2.45	16.09	7.53	7.26	2.42	4.19	43	29	272	2.03	370	12311																							
Iceland	0.99	0.97	1.31	9.35	1.30	6.2	4.80	0.10	9.02	0.77	2.14	1.83	13.74	7.19	5.58	0.97	2.87	0.91	0.15	2.16	1.23	2.76	100.65																							
Ireland	0.94	0.52	6.24	11.20	1.69	1.57	5.46	0.06	10.27	0.17	0.80	1.18	11.86	3.23	5.64	0.69	1.87	0.34	0.10	2.84	1.57	2.02	72.54																							
Italy	16	10	127	261	36	37	1.28	2	166	5	5	55	240	1.15	106	26	82	20	2	54	42	70	1826																							
Latvia	0.95	1.10	2.10	7.58	2.04	1.40	6.53	0.06	10.27	0.17	0.80	1.18	11.86	3.23	5.64	0.69	1.87	0.34	0.10	2.84	1.57	2.02	72.54																							
Lithuania	1.18	0.95	1.54	7.97	1.84	0.51	5.26	0.23	12.34	0.33	0.60	1.19	14.54	3.96	4.00	0.93	1.60	0.20	0.12	1.80	1.25	2.44	76.03																							
Luxembourg	909	865	1536	9074	1.793	6.25	5339	156	9055	226	461	1.130	12.233	3.995	3.458	1.202	1.683	232	95	2072	1.494	2625	71313																							
Macedonia	1.29	1.00	2.77	8.33	1.74	1.39	6.26	0.25	15.18	0.23	0.74	1.32	15.45	3.71	4.69	1.08	2.28	0.28	0.12	1.91	0.93	2.65	85.01																							
Malta	1378	1238	3829	12572	2.126	2.090	8659	205	15881	168	690	1.637	18.136	4.143	5.573	1.872	3.362	4.16	132	2915	1.280	3579	107396																							
Poland	0.70	0.21	2.94	7.02	1.15	0.42	4.91	0.18	10.35	0.37	0.69	1.08	13.60	3.55	4.21	0.97	1.08	0.29	0.29	1.32	1.25	2.99	72.63																							
Portugal	1.21	0.90	4.55	15.08	0.67	2.39	7.28	0.74	29.42	0.25	1.20	1.55	17.88	8.02	6.13	1.88	2.04	0.35	0.26	2.20	1.24	4.21	122.80																							
Romania	305	113	647	2229	82	365	1032	74	3397	12	79	2.25	22.20	8.83	7.28	2.80	2.94	55	22	285	1.67	470	15443																							
Slovakia	2	5	12	32	9	5	28	-	22.08	-	1.04	0.51	18.07	2.69	4.41	0.73	1.05	0.29	0.15	2.21	0.53	1.30	89.16																							
Slovenia	0.97	2.62	2.66	9.59	2.07	0.79	5.25	0.21	17.80	0.25	0.39	1.60	16.67	5.94	6.49	1.35	1.74	0.39	0.24	2.61	1.62	2.21	94.23																							
Spain	46	132	135	471	90	43	250	9	785	8	18	90	6.78	2.31	2.67	71	89	19	11	127	82	105	4241																							
Sweden	1.03	0.48	3.52	8.97	1.88	1.49	5.49	0.17	10.71	0.36	0.60	1.24	14.12	3.55	3.94	0.88	1.37	0.29	0.25	2.11	1.46	2.73	80.02																							
Switzerland	990	485	3933	10450	2.043	1.777	5945	161	9570	200	407	1.197	12.312	2.969	3.659	1.214	1.470	331	170	2234	1.688	2629	79500																							
Turkey	1.39	0.88	6.43	11.22	1.15	0.84	5.69	0.04	7.68	0.50	0.78	2.54	17.02	11.39	8.35	1.44	2.85	0.62	0.25	1.96	1.57	3.96	100.51																							
Ukraine	36	21	194	405	36	31	202	3	217	8	17	70	4.45	2.61	2.12	6.1	102	21	5	63	41	97	2901																							
United Kingdom	1.80	0.78	6.51	10.08	1.28	1.43	5.10	0.37	5.79	0.62	0.66	1.57	15.92	10.46	7.57	0.79	2.57	0.35	0.33	1.73	1.30	3.10	92.64																							
Yugoslavia	60	31	269	494	59	61	243	10	246	16	23	77	5.71	3.59	2.82	5.3	123	22	8	94	61	115	3784																							

Continued

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European Union

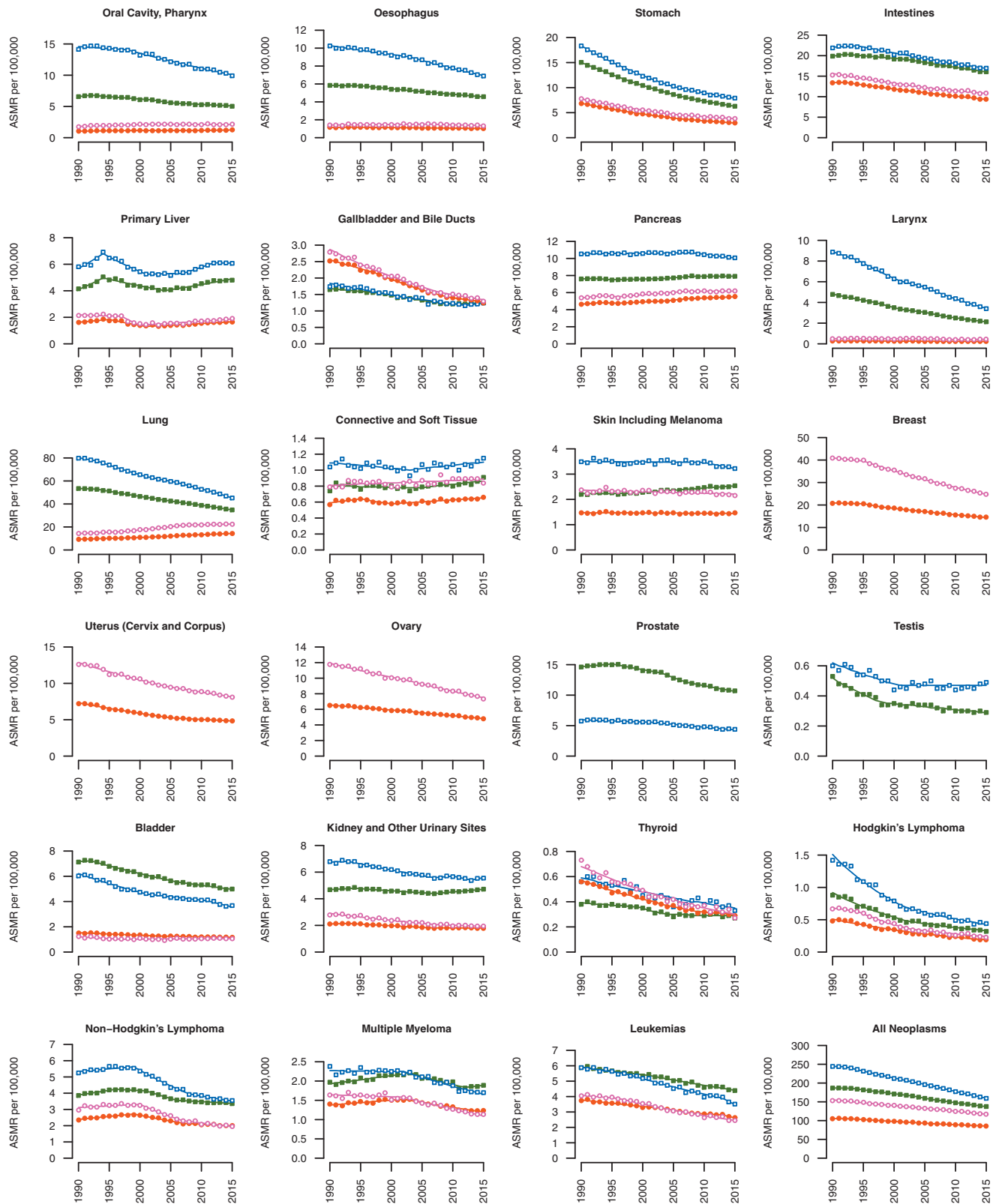


Figure 1. Joinpoint analysis of trends in age-standardized (world population) mortality rates from 23 cancer sites and all neoplasms in the European Union, from 1990 to 2015. Filled boxes represent men, all ages; empty boxes men, 35–64 age group; filled circles women, all ages; empty circles women, 35–64 age group.

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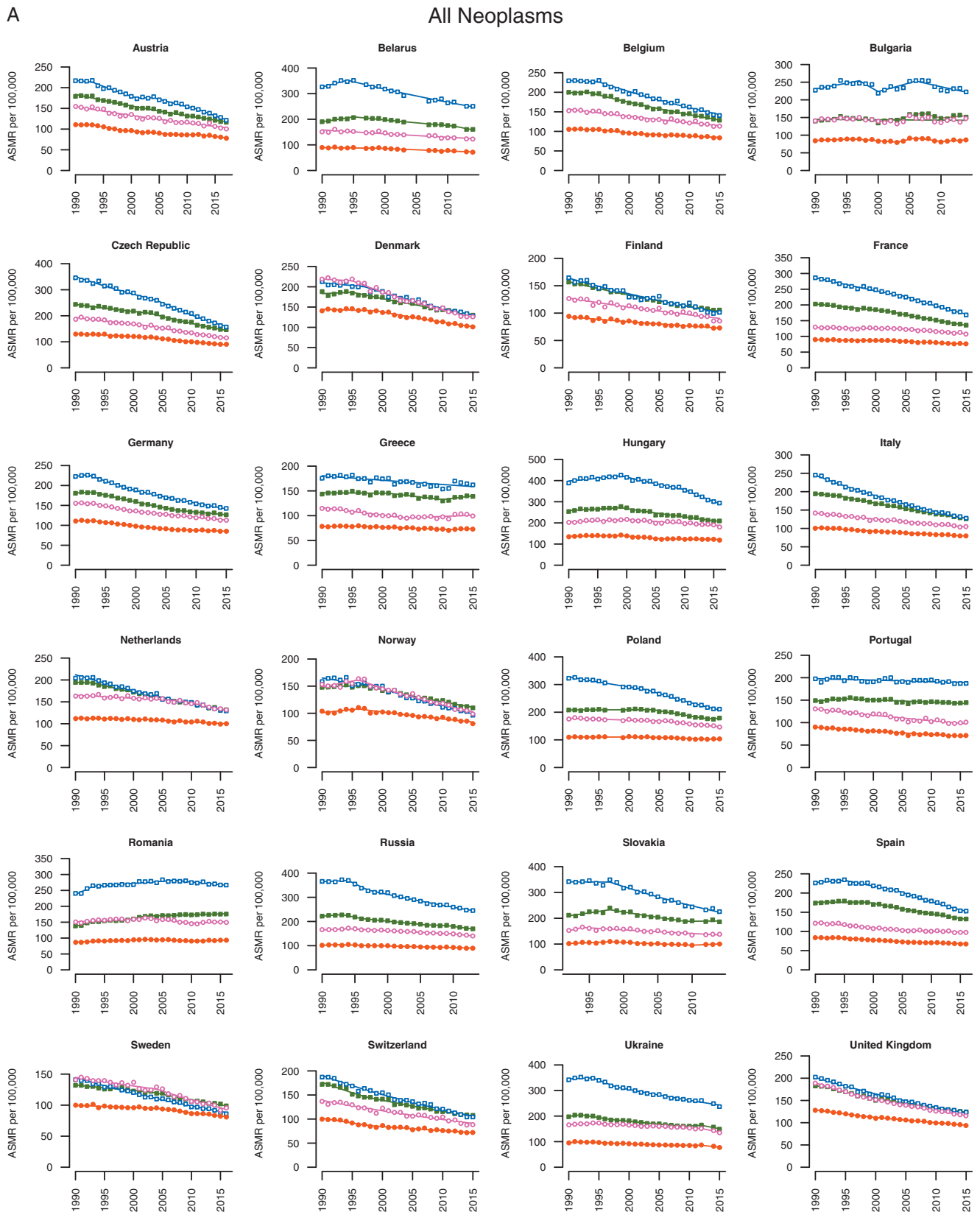


Figure 2. Joinpoint analysis of trends in age-standardized (world population) mortality rates from all neoplasms (A), cancers of intestines (B), lung (C), breast (D) and prostate (E), in 24 selected European countries, from 1990 to 2017 (according to data availability). Filled boxes represent men, all ages; empty boxes men, 35–64 age group; filled circles women, all ages; empty circles women, 35–64 age group.

B

Intestinal cancer

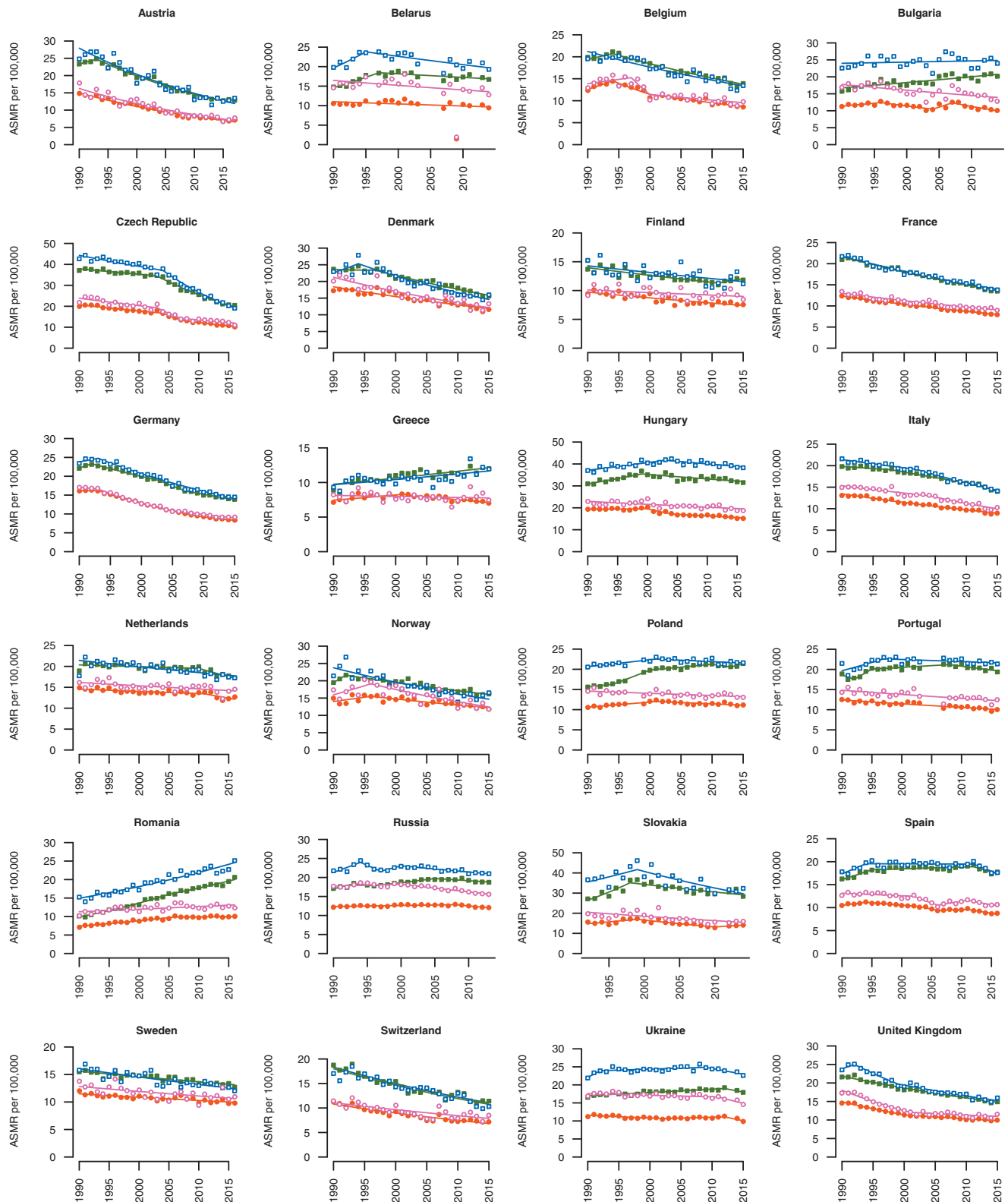


Figure 2. Continued.

C

Lung cancer

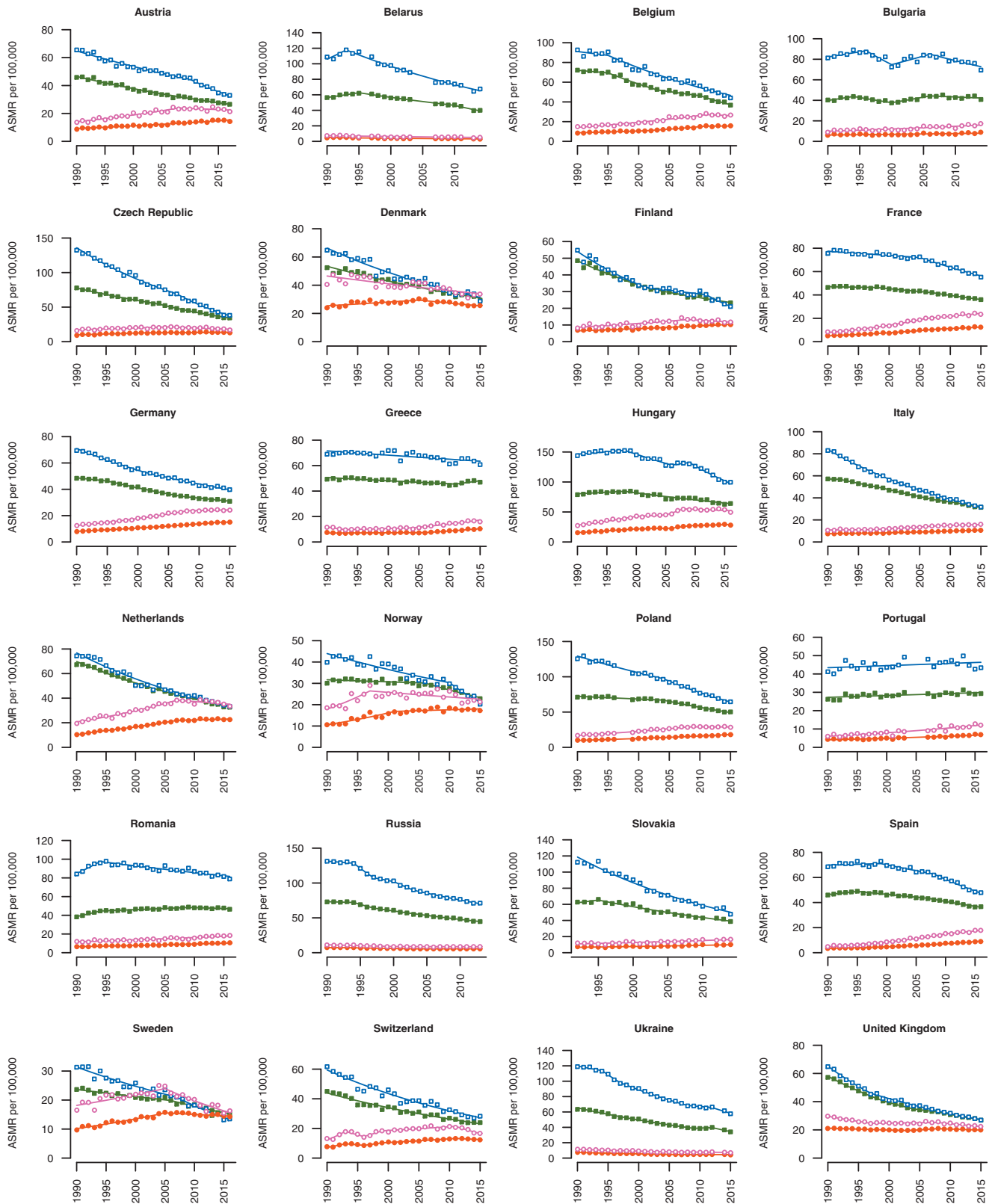


Figure 2. Continued.

D

Breast cancer

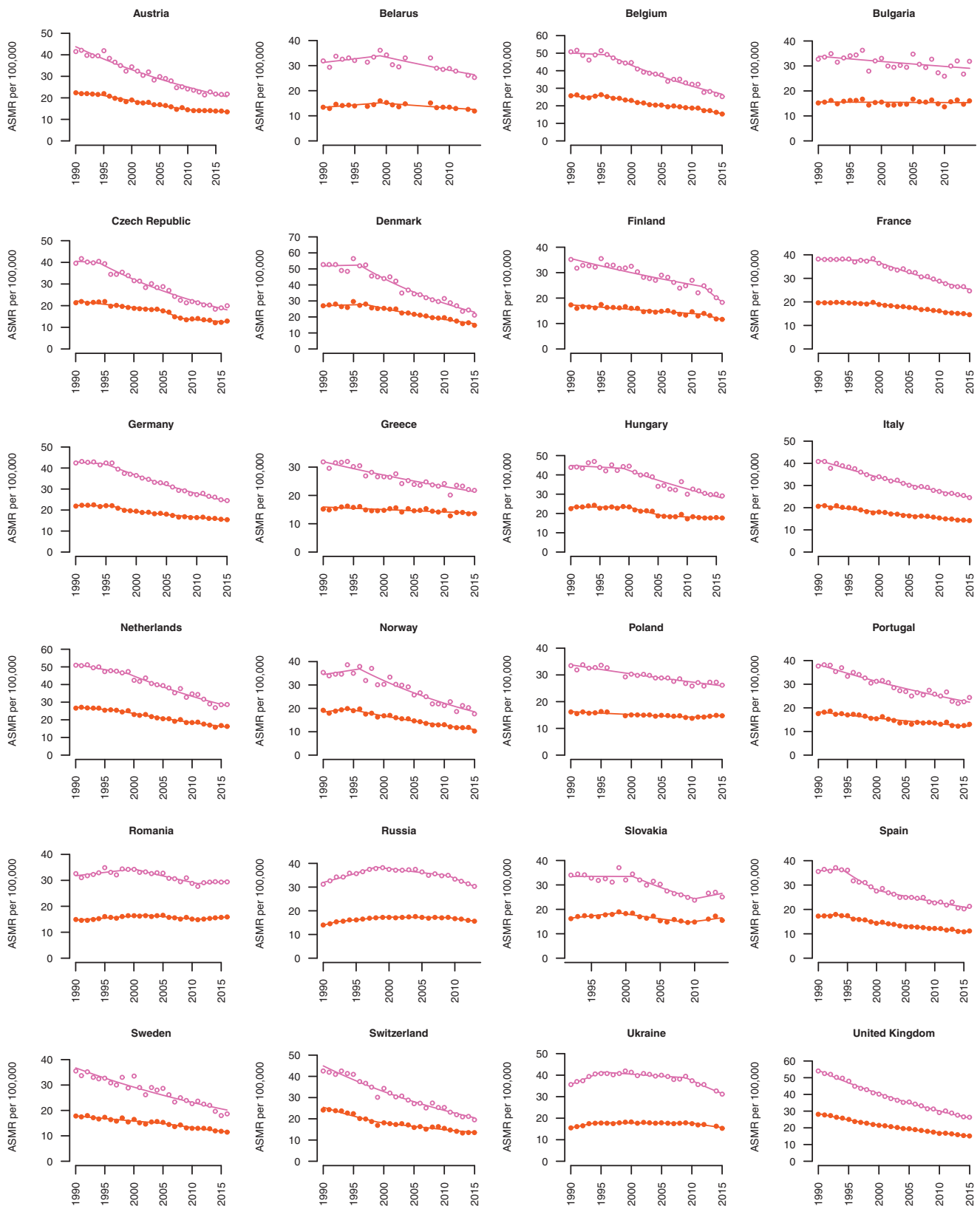


Figure 2. Continued.

E

Prostate cancer

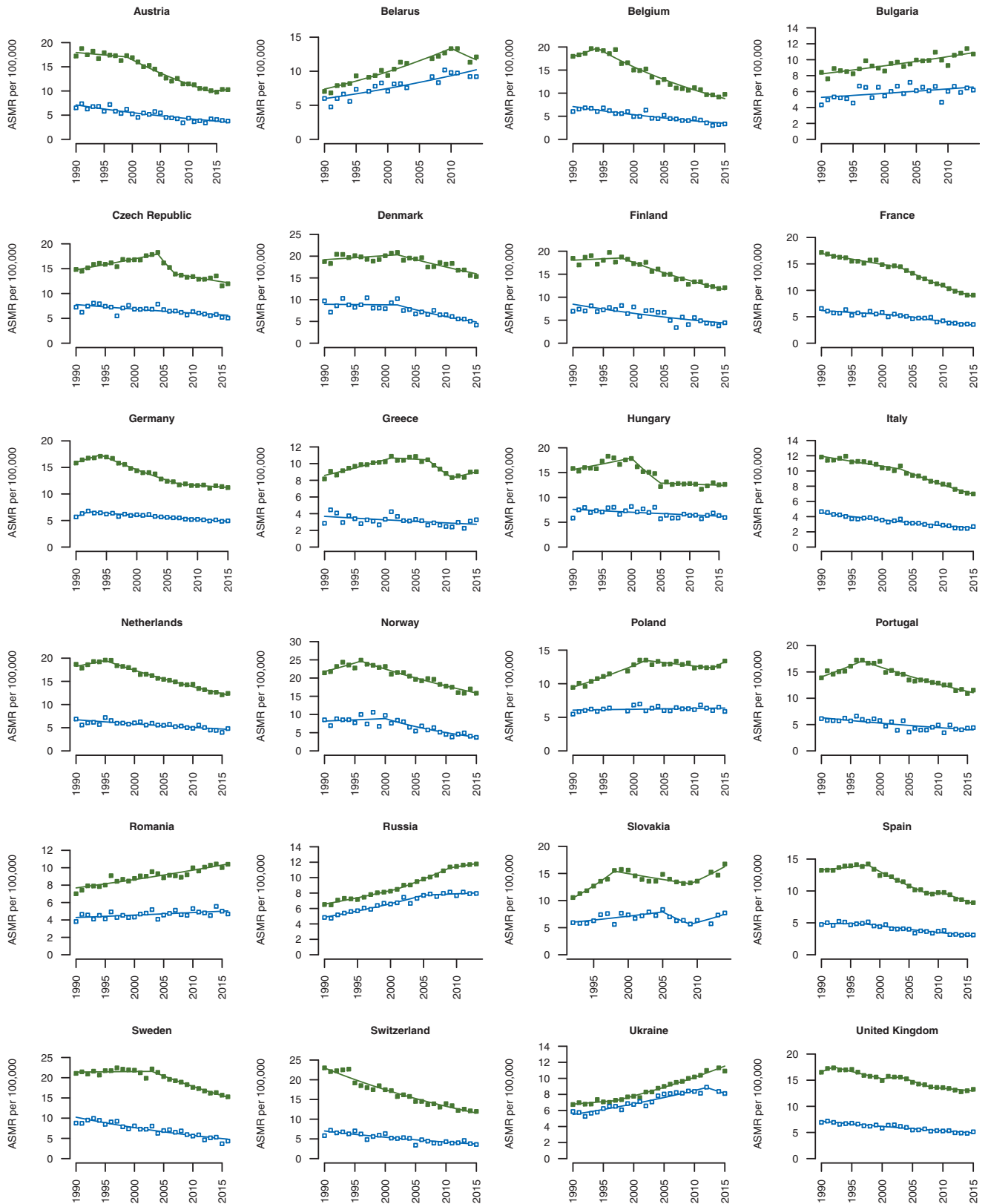


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Discussion

Mortality rates from major cancer sites continued to decline in the EU-28 over the 2000s, with the only exception of pancreatic, skin and kidney (only in men) cancers and of some increase in mortality from liver cancer in both sexes and lung cancer in women. However, there are substantial differences among EU countries, with less favourable trends taking place in some eastern European countries.

The downward trends in overall cancer mortality are mainly driven by the declines in mortality from most tobacco-related cancers in men consequent to the reduction in male smoking prevalence across Europe [2, 3]. The opposite trend in female lung cancer mortality reflects the different stage in the smoking epidemic between sexes and the lagged decline in smoking prevalence in women compared with men [2, 14, 15].

The potential impact of tobacco reduction in men on mortality from pancreatic cancer was partly counterbalanced by the rising prevalence of obesity and diabetes over the last three decades [16]. Moreover, improved diagnosis and certifications may have played some role on the unfavorable mortality trend from pancreatic cancer.

Apart from the smoking prevalence reduction in men, the steady decline in stomach cancer mortality could also be attributed to improved water sanitation, lifestyle and environmental conditions that resulted in reduced prevalence of *Helicobacter pylori* infection [17]. The reduced consumption of food preserved by salting, pickling and smoking may have also contributed to the downward trend [18].

Improved working conditions and less exposure to occupational carcinogens [19, 20] have also contributed to the downward trends in mortality from lung and bladder cancer.

Reductions in alcohol consumption, especially in southern Europe, partly explain the decline in cancer of oral cavity, pharynx and esophagus [4]. On the other hand, increased alcohol consumption in northern Europe and increased prevalence of HCV in northern and eastern Europe [4] have driven the increment in primary liver cancer mortality all over Europe [21, 22].

Screening and early diagnosis have contributed to the reduction in mortality from colorectal cancer [23, 24]. However, the screening uptake differs among countries due to resource availability that may explain some of the between-country variability in mortality patterns and trends [25, 26].

Mammography screening programs, early diagnosis and mostly availability of effective therapy, including progress in radiotherapy and surgery are the key factors for the substantial downward trends in breast cancer mortality in Europe [27, 28], as in other (high-income) areas of the world [29]. Some eastern countries, including Romania, Russia and Ukraine showed less favorable trends. Breast cancer rates in those areas of the continent were particularly low in the past [30], and this may reflect some levelling of rates across Europe. In addition, delays in the adoption of effective screening programs and treatments are possible in those countries [6].

Wider adoption of radical prostatectomy in combination with adjuvant hormonal therapy for localized cancers may partly explain the downward trend in prostate cancer mortality observed since the late 1990s in Europe, though a favourable role of PSA testing is likely, but still unquantified [31].

The decline in mortality from cancer of the testis observed since 1970s continued over the 1990s but levelled off during the 2000s. This pattern has been mainly attributed to the adoption of effective treatments, mainly platinum-derived chemotherapy and its analogues [32].

Subsequent advancements in therapies were the key underlying factors of the downward trend in mortality from leukaemias, targeted therapy has improved the prognosis of patients with chronic myelogenous leukemia and allogeneic hematopoietic cell transplantation improved survival in all malignant hematologic diseases [33–36].

The less favorable trend in mortality from skin cancer may reflect the increased recreational exposure to sunlight ultraviolet radiation and use of tanning beds [37], while the growing obesity [16] and hypertension rates are possible explanation of the increased mortality due to kidney cancer [38].

Despite possible problems in data quality, death certification is reasonably valid in all the European countries considered and allows therefore to obtain a meaningful time trends analysis for most countries considered [39, 40].

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Disclosure

The authors have declared no conflicts of interest.

References

1. Bosetti C, Bertuccio P, Malvezzi M et al. Cancer mortality in Europe, 2005-2009, and an overview of trends since 1980. *Ann Oncol* 2013; 24(10): 2657–2671.
2. GBD 2015 Tobacco Collaborators. Smoking prevalence and attributable disease burden in 195 countries and territories, 1990-2015: a systematic analysis from the Global Burden of Disease Study 2015. *Lancet* 2017; 389: 1885–1906.
3. Gallus S, Lugo A, La Vecchia C et al. Pricing Policies and Control of Tobacco in Europe (PPACTE) project: cross-national comparison of smoking prevalence in 18 European countries. *Eur J Cancer Prev* 2014; 23(3): 177–185.
4. La Vecchia C, Bosetti C, Bertuccio P et al. Trends in alcohol consumption in Europe and their impact on major alcohol-related cancers. *Eur J Cancer Prev* 2014; 23(4): 319–322.
5. Hojgaard L, Lowenberg B, Selby P et al. The European Cancer Patient's Bill of Rights, update and implementation 2016. *ESMO Open* 2016; 1(6): e000127.
6. Levi F, Lucchini F, Negri E, La Vecchia C. Trends in mortality from major cancers in the European Union, including acceding countries, in 2004. *Cancer* 2004; 101(12): 2843–2850.
7. World Health Organization Statistical Information System. WHO mortality database; http://www.who.int/healthinfo/statistics/mortality_raw_data/en/index.html (10 December 2018, date last accessed).

8. World Health Organization. International Statistical Classification of Disease and Related Health Problems: 10th Revision. Geneva: World Health Organization 1992.
9. European Commission. Eurostat population database; <http://epp.eurostat.ec.europa.eu/portal/page/portal/population/data/database> (1 September 2018, date last accessed).
10. Esteve J, Benhamou E, Raymond L, Techniques for the analysis of cancer risk. In: Statistical methods in cancer research. Volume IV. Descriptive epidemiology. Oxford: Oxford University Press 1994.
11. National Cancer Institute. Joinpoint Regression Program, version 4.1. <http://srab.cancer.gov/joinpoint/> (23 March 2018, date last accessed).
12. Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates [erratum appears in Stat Med 2001; 20: 655]. Stat Med 2000; 19: 335–351.
13. Clegg LX, Hankey BF, Tiwari R et al. Estimating average annual per cent change in trend analysis. Stat Med 2009; 28(29): 3670–3682.
14. Bosetti C, Malvezzi M, Rosso T et al. Lung cancer mortality in European women: trends and predictions. Lung Cancer 2012; 78(3): 171–178.
15. Islami F, Torre LA, Jemal A. Global trends of lung cancer mortality and smoking prevalence. Transl Lung Cancer Res 2015; 4(4): 327–338.
16. Gallus S, Lugo A, Murisic B et al. Overweight and obesity in 16 European countries. Eur J Nutr 2015; 54(5): 679–689.
17. Roberts SE, Morrison-Rees S, Samuel DG et al. Review article: the prevalence of *Helicobacter pylori* and the incidence of gastric cancer across Europe. Aliment Pharmacol Ther 2016; 43(3): 334–345.
18. Boccia S, La Vecchia C. Dissecting causal components in gastric carcinogenesis. Eur J Cancer Prev 2013; 22(6): 489–491.
19. Antoni S, Ferlay J, Soerjomataram I et al. Bladder cancer incidence and mortality: a global overview and recent trends. Eur Urol 2017; 71(1): 96–108.
20. Negri E, La Vecchia C. Epidemiology and prevention of bladder cancer. Eur J Cancer Prev 2001; 10(1): 7–14.
21. Pimpin L, Cortez-Pinto H, Negro F et al. Burden of liver disease in Europe: epidemiology and analysis of risk factors to identify prevention policies. J Hepatol 2018; 69(3): 718–735.
22. Bosetti C, Turati F, La Vecchia C. Hepatocellular carcinoma epidemiology. Best Pract Res Clin Gastroenterol 2014; 28(5): 753–770.
23. Manser CN, Bachmann LM, Brunner J et al. Colonoscopy screening markedly reduces the occurrence of colon carcinomas and carcinoma-related death: a closed cohort study. Gastrointest Endosc 2012; 76(1): 110–117.
24. Lieberman D. Colon cancer screening and surveillance controversies. Curr Opin Gastroenterol 2009; 25(5): 422–427.
25. Benard F, Barkun AN, Martel M, von Renteln D. Systematic review of colorectal cancer screening guidelines for average-risk adults: summarizing the current global recommendations. World J Gastroenterol 2018; 24: 124–138.
26. Ait Ouakrim D, Pizot C, Boniol M et al. Trends in colorectal cancer mortality in Europe: retrospective analysis of the WHO mortality database. BMJ 2015; 351: h4970.
27. Giordano SB, Gradishar W. Breast cancer: updates and advances in 2016. Curr Opin Obstet Gynecol 2017; 29(1): 12–17.
28. Autier P, Boniol M, La Vecchia C et al. Disparities in breast cancer mortality trends between 30 European countries: retrospective trend analysis of WHO mortality database. BMJ 2010; 341(aug11 1): c3620.
29. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. CA A Cancer J Clin 2019; 69(1): 7–34.
30. La Vecchia C, Lucchini F, Negri E et al. Trends of cancer mortality in Europe, 1955–1989: III, breast and genital sites. Eur J Cancer 1992; 28A(4–5): 927–998.
31. Etzioni R, Gulati R, Tsodikov A et al. The prostate cancer conundrum revisited: treatment changes and prostate cancer mortality declines. Cancer 2012; 118(23): 5955–5963.
32. Hellerstedt BA, Pienta KJ. Testicular cancer. Curr Opin Oncol 2002; 14(3): 260–264.
33. Hunter AM, Zhang L, Padron E. Current management and recent advances in the treatment of chronic myelomonocytic leukemia. Curr Treat Options Oncol 2018; 19(12): 67.
34. Sharma S, Rai KR. Chronic lymphocytic leukemia (CLL) treatment: so many choices, such great options. Cancer 2019; 125(9):1432–1440.
35. Wingard JR, Majhail NS, Brazauskas R et al. Long-term survival and late deaths after allogeneic hematopoietic cell transplantation. J Clin Oncol 2011; 29(16): 2230–2239.
36. Raj RV, Abedin SM, Atallah E. Incorporating newer agents in the treatment of acute myeloid leukemia. Leuk Res 2018; 74: 113–120.
37. Apalla Z, Lallas A, Sotiriou E et al. Epidemiological trends in skin cancer. Dermatol Pract Concept 2017; 7(2): 1–6.
38. De P, Otterstatter MC, Semenciw R et al. Trends in incidence, mortality, and survival for kidney cancer in Canada, 1986–2007. Cancer Causes Control 2014; 25(10): 1271–1281.
39. Mathers CD, Fat DM, Inoue M et al. 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(3): 171–177.
40. World Health Organization Statistical Information System. Health statistics and health information systems. WHO mortality database: Tables. Estimated coverage of mortality data; <https://www.who.int/healthinfo/statistics/morttables/en/> (10 December 2018, date last accessed).