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Cancer mortality in the European Union, 1970–2003, with a joinpoint analysis

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Background: Cancer mortality peaked in the European Union (EU) in the late 1980s and declined thereafter.
Materials and methods: We analyzed EU cancer mortality data provided by the World Health Organization in 1970–2003, using joinpoint analysis.
Results: Overall, cancer mortality levelled off in men since 1988 and declined in 1993–2003 (annual percent change, APC = −1.3%). In women, a steady decline has been observed since the early 1970s. The decline in male cancer mortality has been driven by lung cancer, which levelled off since the late 1980s and declined thereafter (APC = 2.7% in 1997–2003). Recent decreases were also observed for other tobacco-related cancers, as oral cavity/pharynx, esophagus, larynx and bladder, as well as for colorectal (APC = −0.9% in 1992–2003) and prostate cancers (APC = −1.0% in 1994–2003). In women, breast cancer mortality levelled off since the early 1990s and declined thereafter (APC = −1.0% in 1998–2003). Female mortality declined through the period 1970–2003 for colorectal and uterine cancer, while it increased over the last three decades for lung cancer (APC = 4.6% in 2001–2003). In both sexes, mortality declined in 1970–2003 for stomach cancer and for a few cancers amenable to treatment.
Conclusion: This update analysis of the mortality from cancer in the EU shows favorable patterns over recent years in both sexes.
Key words: cancer, European Union, mortality, trends

introduction

Total cancer mortality has peaked in the European Union (EU) in the late 1980s and has declined from 1988 to 2002 by ∼15% in both sexes, corresponding to the avoidance of >150 000 deaths per year in the early 2000s as compared with the rates registered in the late 1980s [1–3]. These favorable trends were largely due to the decline in three major neoplasms, i.e. stomach with its long-term fall, intestines since the late 1990s and lung in men. For men, a relevant contribution to this fall was also given by other tobacco-related neoplasms, such as larynx, oral cavity, esophagus and bladder. Further, there were favorable trends for several neoplasms whose diagnosis and/or treatment has improved, including not only (cervix) uteri, testis, Hodgkin's lymphoma (HL) and leukemia, but also a few common neoplasms such as colorectum, breast and prostate [1–3].

On the basis of recent trends in cancer mortality in the EU, a projection was made of a further fall by 11% in age-standardized cancer mortality from 2000 to 2015, corresponding to additional 150 000 fewer deaths per year in 2015 as compared with the rates of 2000 [4].

To analyze and interpret recent patterns and monitor the progress in cancer mortality in the EU, we updated trends to 2003, using also joinpoint regression analysis.

materials and methods

Cancer death certification data for the 27 EU member states (defined as in January 2007) were derived from the World Health Organization (WHO) database as available on electronic support, for the period 1970–2003 [5]. Data for Cyprus were not available. For EU rates computation, when country data were missing for part of one or more calendar periods, data replication of the last available year was made up to the end of the last calendar period considered.

During the calendar period considered, four different revisions of the International Classification of Diseases (ICD) were used. Classification of cancer deaths was recoded, for all calendar periods, according to the ninth revision of the ICD [6]. All intestinal cancers (including rectum) were pooled together as all uterine cancers (cervix and endometrium).

Estimates of the resident population, on the basis of official censuses, were obtained from the same WHO database [5].

From the matrices of certified deaths and resident population, we computed age-specific rates for each 5-year age group and calendar year and age-standardized mortality rates per 100 000 men and women—at all

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ages and truncated 35–64 years —using the direct method and on the basis of the world standard population [7].

To identify significant changes in trend, we carried out joinpoint regression analysis using the software provided by the Surveillance Research Program of USA National Cancer Institute [8]. The aim of this analysis is to identify possible points where a significant change in the linear slope of the trend (in a log scale) is detected over the study period [9]. In joinpoint analysis, the best fitting points, called 'joinpoints', are chosen where the rate changes significantly. The analysis starts with the minimum number of joinpoints (e.g. zero joinpoints, which is straight line), and tests whether one or more joinpoints (up to three) are significant and must be added to the model. Each significant joinpoint that indicates a change in the slope (if any) is retained in the final model. To describe linear trends by period, the estimated annual percent change (APC) is then computed for each of those trends by fitting a regression line to the natural logarithm of the rates using calendar year as a regressor variable.

results

Table 1 shows the overall age-adjusted mortality rates from selected cancers per 100 000 men and women in the EU, ~1982, 1992 and 2002, and the corresponding percent changes in rates. In men, total cancer mortality was stable from 1982 to 1992 and declined by 13% from 1992 to 2002, from 185.5/100 000 to 162.3. In women, it declined by 2% from 1982 to 1992 (from 107.1/100 000 to 104.7) and by 8% from 1992 to 2002 (to 95.8/100 000). In men, most cancers showed declines in mortality, particularly from 1992 to 2002. These included cancers of the oral cavity and pharynx (−8%), esophagus (−7%), stomach (−30%), intestines (−7%), lung (−22%) and bladder (−17%), but also gall-bladder (−15%), larynx (−27%), testis (−28%), kidney (−13%), thyroid (−23%), HL (−44%) and non-Hodgkin's lymphoma (NHL) (−4%) and leukemias (−8%). Similarly, in women during the last decade there was a decline in the mortality from most cancers, including those of the stomach (−31%), intestines (−16%), breast (−13%), uterus (−20%), ovary (−3%) and leukamias (−10%), but also gall-bladder (−23%), bladder (−14%), kidney (−17%), thyroid (−28%), HL (−38%) and NHL (−5%).

Table 2 gives corresponding values for truncated rates at age 35–64 years. In middle-aged men, all cancer mortality was approximately stable ~240/100 000 from 1982 to 1992 and declined to 199.8 in 2002 (−17%). In middle-aged women, mortality declined from 159.1 to 152.5 from 1982 to 1992 (−4%) and to 137.4 in 2002 (−10%). In both sexes, mortality from most cancers showed declines similar to those observed for overall cancer mortality from 1992 to 2002.

Table 1. Overall age-adjusted (world population) mortality rates from selected cancers or groups of cancers per 100 000 men and women in the European Union, around 1982 (in 1980–1984), 1992 (in 1990–1994) and in 2002, and corresponding percent changes in rates[a]

	Men						Women					
	1982	1992	2002	Deaths[a]	% change 1992/1982	% change 2002/1992	1982	1992	2002	Deaths[a]	% change 1992/1982	% change 2002/1992
Oral cavity/pharynx	5.89	6.6	6.06	21 355	12.1	−8.2	0.99	1.08	1.15	5671	9.1	6.5
Esophagus	5.63	5.83	5.4	20 746	3.6	−7.4	1.17	1.16	1.14	6948	−0.85	−1.72
Stomach	18.91	13.99	9.75	40 759	−26.0	−30.3	8.78	6.36	4.41	27 980	−27.56	−30.66
Intestines	19.04	20.07	18.68	79 538	5.4	−6.9	13.91	13.32	11.23	73 303	−4.24	−15.69
Liver	3.69	4.29	5.8	23 231	16.3	35.2	1.86	1.5	2.06	12 386	−19.35	37.33
Gall-bladder/bile ducts	1.65	1.66	1.42	6009	0.6	−14.5	2.66	2.43	1.88	11 583	−8.65	−22.63
Pancreas	7.19	7.59	7.62	30 758	5.6	0.4	4.29	4.76	4.99	30 843	10.96	4.83
Larynx	5.09	4.52	3.28	12 371	−11.2	−27.4	0.3	0.29	0.28	1317	−3.33	−3.45
Lung	51.99	52.76	40.97	165 280	1.5	−22.3	8	9.66	11.34	58 574	20.75	17.39
Pleura	0.80	1.08	0.92	3560	35.0	−14.8	0.29	0.3	0.24	1324	3.45	−20.00
Bone	1.39	1	0.76	2443	−28.1	−24.0	0.75	0.53	0.42	1758	−29.33	−20.75
Connective/soft tissue	0.67	0.8	0.74	2476	19.4	−7.5	0.5	0.62	0.56	2321	24.00	−9.68
Skin including melanoma	1.93	2.23	2.31	8970	15.5	3.6	1.34	1.46	1.44	7833	8.96	−1.37
Breast	0.22	0.27	0.27	878	22.7	0.0	20.21	20.85	18.05	89 575	3.17	−13.43
Uterus (cervix/corpus)	–	–	–	–	–	–	8.44	7.03	5.63	27 806	−16.71	−19.91
Ovary	–	–	–	–	–	–	6.29	6.24	6.06	24 363	−0.79	−2.88
Prostate	13.43	14.92	13.97	66 960	11.1	−6.4	–	–	–	–	–	–
Testis	0.65	0.46	0.33	995	−29.2	−28.3	–	–	–	–	–	–
Bladder	7.09	7.18	5.97	26870	1.3	−16.9	1.51	1.5	1.29	9630	−0.66	−14.00
Kidney	4.07	4.75	4.15	16 061	16.7	−12.6	1.91	2.12	1.77	10 032	10.99	−16.51
Thyroid	0.43	0.4	0.31	1211	−7.0	−22.5	0.63	0.54	0.39	2341	−14.29	−27.78
Non-Hodgkin's lymphomas	3.1	4.17	3.99	15 395	34.5	−4.3	1.84	2.6	2.47	14 166	41.30	−5.00
Hodgkin's lymphoma	1.21	0.82	0.46	1614	−32.2	−43.9	0.66	0.48	0.3	1294	−27.27	−37.50
Multiple myeloma	1.7	2.04	2.2	9170	20.0	7.8	1.2	1.45	1.53	9279	20.83	5.52
Leukemias	6.07	5.7	5.23	20 419	−6.1	−8.2	4	3.58	3.22	17 405	−10.50	−10.06
All cancers, benign/malignant	183.45	185.42	162.3	666 300	1.1	−12.5	107.12	104.66	95.84	537 909	−2.30	−8.43

[a]Number of deaths in 2002.

Table 2. Age-adjusted (world population) mortality rates from selected cancers or groups of cancers per 100 000 men and women aged 35–64 in the European Union, in 1982 (in 1980–1984), 1992 (in 1990–1994) and in 2002, and corresponding percent changes in rates

	Men						Women					
	1982	1992	2002	Deaths[a]	% change 1992/1982	% change 2002/1992	1982	1992	2002	Deaths[a]	% change 1992/1982	% change 2002/1992
Oral cavity/pharynx	11.92	14.32	13.36	12 839	20.1	−6.7	1.58	1.88	2.18	2179	19.0	16.0
Esophagus	9.29	10.05	9.15	8832	8.2	−9.0	1.36	1.45	1.54	1567	6.62	6.21
Stomach	22.53	16.91	11.55	11 126	−24.9	−31.7	9.5	7.24	5.19	5190	−23.79	−28.31
Intestines	20.62	22.15	20.32	19 649	7.4	−8.3	15.84	15.1	12.59	12 744	−4.67	−16.62
Liver	5.46	5.89	7.16	6793	7.9	21.6	2.5	1.88	2.3	2288	−24.80	22.34
Gall-bladder/bile ducts	1.74	1.73	1.44	1335	−0.6	−16.8	2.96	2.6	1.99	1950	−12.16	−23.46
Pancreas	9.99	10.51	10.68	10 305	5.2	1.6	5.07	5.52	5.86	5961	8.88	6.16
Larynx	9.51	8.41	6	5793	−11.6	−28.7	0.51	0.51	0.54	543	0.00	5.88
Lung	77.18	77.9	56.49	54 645	0.9	−27.5	12.82	14.83	18.59	18 704	15.68	25.35
Pleura	1.24	1.63	1.16	1059	31.5	−28.8	0.42	0.42	0.34	323	0.00	−19.05
Bone	1.88	1.34	0.89	852	−28.7	−33.6	0.9	0.6	0.41	413	−33.33	−31.67
Connective/soft tissue	0.91	1.11	0.97	890	22.0	−12.6	0.7	0.87	0.84	803	24.29	−3.45
Skin including melanoma	2.99	3.53	3.39	3245	18.1	−4.0	2.1	2.33	2.22	2189	10.95	−4.72
Breast	0.26	0.39	0.32	250	50.0	−17.9	40.35	40.58	33.8	33 693	0.57	−16.71
Uterus (cervix/corpus)	–	–	–	–	–	–	15.26	12.39	10.11	9982	−18.81	−18.40
Ovary	–	–	–	–	–	–	11.96	10.91	10.17	8275	−8.78	−6.78
Prostate	5.28	5.92	5.62	5451	12.1	−5.1	–	–	–	–	–	–
Testis	0.77	0.58	0.45	419	−24.7	−22.4	–	–	–	–	–	–
Bladder	6.43	5.92	4.55	4411	−7.9	−23.1	1.28	1.17	1.01	1028	−8.59	−13.68
Kidney	6.06	6.69	5.54	5165	10.4	−17.2	2.68	2.79	2.12	2065	4.10	−24.01
Thyroid	0.65	0.58	0.43	400	−10.8	−25.9	0.82	0.65	0.43	418	−20.73	−33.85
Non-Hodgkin's lymphomas	4.36	5.58	4.99	4700	28.0	−10.6	2.49	3.33	2.99	2955	33.73	−10.21
Hodgkin's lymphoma	1.97	1.31	0.67	636	−33.5	−48.9	0.95	0.65	0.37	367	−31.58	−43.08
Multiple myeloma	2.01	2.29	2.22	2068	13.9	−3.1	1.44	1.65	1.59	1563	14.58	−3.64
Leukemias	6.32	5.8	4.89	4701	−8.2	−15.7	4.57	4.02	3.36	3349	−12.04	−16.42
All cancers, benign/malignant	240.3	240.92	199.79	192 821	0.3	−17.1	159.09	152.53	137.4	137 814	−4.12	−9.92

[a]Number of deaths in 2002.

The findings from the joinpoint regression analysis over the period 1970–2003 for selected cancers (overall and truncated 35–64 years) in the EU as a whole are given in Table 3 and Figure 1 for men and Table 3 and Figure 2 for women. In men, mortality from all cancers started to decline since 1988, with a steeper decline in the last decade (APC = −1.3% from 1993 to 2003). Declines in mortality throughout the period considered were observed for stomach cancer, bone, testis, thyroid, HL and leukemias. More recent declines were observed for oral cavity and pharynx (APC = −4.1% from 2001 to 2003), intestines (APC = −0.9% from 1992 to 2003), gall-bladder (APC = −4.7% from 2000 to 2003), larynx (APC = −4.3% from 1997 to 2003), lung (APC = −2.7% from 1997 to 2003), pleura (APC = −1.8% from 1992 to 2003), connective and soft tissue sarcomas (APC = −1.2% from 1992 to 2003), prostate (APC = −1.0 from 1994 to 2003), bladder (APC = −2.1 from 1992 to 2001 and 0.06 from 2001 to 2003), kidney (APC = −1.8% from 1994 to 2003) and NHL (APC = −1.3 from 1996 to 2003). Mortality tended to increase throughout the period for liver, multiple myeloma and was approximately stable for cancer of the esophagus and pancreas. In women, all cancer mortality slightly declined throughout the period considered (APC = −0.4 only from 1999 to 2003). Continuous declines in trends were observed for stomach, intestines, gall-bladder, pleura, bone, uterus, thyroid, HL and leukemias. Declines in more recent years were observed for breast cancer (APC = −1.0% from 1998 to 2003), connective and soft tissue sarcomas (APC = −1.7 from 1993 to 2003), kidney (APC = −2.2% from 1994 to 2003) and NHL (APC = −2.1 from 1997 to 2003). Conversely, female mortality increased throughout the period for cancers of the pancreas, lung and multiple myeloma, and in the last two decades for liver cancer, while it was approximately stable for oral cavity and pharynx, esophagus, larynx, skin and bladder cancers. The results of the joinpoint analysis for middle-aged men and women were consistent with those for overall mortality.

discussion

This update analysis of the mortality from cancer in the EU shows a favorable pattern over recent years in both sexes. In terms of absolute number of deaths, this fall in age-adjusted rates correspond to a levelling to ∼1.2 million deaths per years over most recent calendar years [10, 11]. Total cancer mortality started to level off in men from the EU since 1988 and declined by 1.3% per year in the last 10 years, with larger reductions in middle age. In women, a steady decline has been observed since the early 1970s. The fall was of comparable

Table 3. Joinpoint analysis for selected cancer or groups of cancers, at all ages and truncated 35–64 years, in the European Union, 1970–2003[a]

	Men								Women							
	Trend 1		Trend 2		Trend 3		Trend 4		Trend 1		Trend 2		Trend 3		Trend 4	
	Years	APC	Years	APC	Years	APC	Years	APC	Years	APC	Years	APC	Years	APC	Years	APC
All ages																
Oral cavity/pharynx	1970–1984	2.07[a]	1984–1992	1.15[a]	1992–2001	−0.97[a]	2001–2003	−4.13[a]	1970–2000	0.91[a]	2000–2003	−0.45				
Esophagus	1970–1993	0.42[a]	1993–2001	−1.22[a]	2001–2003	2.92			1970–2001	−0.34[a]	2001–2003	7.46[a]				
Stomach	1970–1993	−3.03[a]	1993–2003	−3.75[a]					1970–1984	−3.68[a]	1984–1991	−2.99[a]	1991–2003	−3.76[a]		
Intestines	1970–1992	0.63[a]	1992–2003	−0.89[a]					1970–1991	−0.13[a]	1991–2003	−1.78[a]				
Liver	1970–1982	2.15[a]	1982–1985	−2.50	1985–2003	2.94[a]			1970–1982	−0.64	1982–1986	−8.17	1986–2003	2.40[a]		
Gall-bladder/bile ducts	1970–1974	−1.65	1974–1988	0.78[a]	1988–2000	−1.12[a]	2000–2003	−4.74[a]	1970–1972	−5.13	1972–1987	−0.14	1987–2001	−2.00[a]	2001–2003	−8.17
Pancreas	1970–1979	1.39[a]	1979–1982	−0.21	1982–1987	1.35[a]	1987–2003	−0.05	1970–1989	1.14[a]	1989–2003	0.39[a]				
Larynx	1970–1976	1.75[a]	1976–1988	−0.39[a]	1988–1997	−2.26[a]	1997–2003	−4.34[a]	1970–2003	−0.48[a]						
Lung	1970–1987	1.23[a]	1987–1997	−0.95[a]	1997–2003	−2.67[a]			1970–1987	2.46[a]	1987–2001	1.41[a]	2001–2003	4.60[a]		
Pleura	1970–1976	1.26	1976–1987	4.66[a]	1987–1992	1.96	1992–2003	−1.83[a]	1970–1975	−3.19[a]	1975–1994	0.60[a]	1994–2003	−2.76[a]		
Bone	1970–1974	−0.27	1974–2003	−2.98[a]					1970–1975	−1.64[a]	1975–1989	−3.66[a]	1989–2003	−2.34[a]		
Connective/soft tissue	1970–1975	0.70	1975–1981	6.40[a]	1981–1992	1.89[a]	1992–2003	−1.20[a]	1970–1977	1.49	1977–1980	9.80	1980–1993	2.25[a]	1993–2003	−1.67[a]
Skin including melanoma	1970–1980	0.70[a]	1980–1987	2.53[a]	1987–2003	0.34[a]			1970–1993	0.70[a]	1993–2003	−0.14				
Breast									1970–1988	0.78[a]	1988–1995	−0.46[a]	1995–1998	−2.71[a]	1998–2003	−1.03[a]
Uterus (cervix/corpus)									1970–1980	−2.76[a]	1980–2003	−2.01[a]				
Ovary									1970–1994	0.03	1994–1999	−1.50[a]	1999–2003	1.35		
Prostate	1970–1982	0.51[a]	1982–1988	1.44[a]	1988–1994	0.41	1994–2003	−1.01[a]								
Testis	1970–1977	−0.24	1977–1984	−5.30[a]	1984–2003	−3.07[a]										
Bladder	1970–1979	1.25[a]	1979–1992	0.18[a]	1992–2001	−2.13[a]	2001–2003	0.06	1970–1976	1.29[a]	1976–1993	−0.23[a]	1993–1998	−2.30[a]	1998–2003	−0.18
Kidney	1970–1987	2.03[a]	1987–1994	1.17[a]	1994–2003	−1.84[a]			1970–1994	0.94[a]	1994–2003	−2.20[a]				
Thyroid	1970–1977	0.13	1977–2000	−1.03[a]	2000–2003	−5.57[a]			1970–1977	−0.04	1977–1987	−2.39[a]	1987–1991	−0.29	1991–2003	−3.05[a]
Non-Hodgkin's lymphoma	1970–1981	0.22	1981–1989	4.07[a]	1989–1996	0.92[a]	1996–2003	−1.33[a]	1970–1981	0.20	1981–1988	5.15[a]	1988–1997	1.28[a]	1997–2003	−2.08[a]
Hodgkin's lymphoma	1970–1992	−3.46[a]	1992–2003	−5.29[a]					1970–1981	−2.85[a]	1981–1985	−5.68[a]	1985–1993	−2.09[a]	1993–2003	−4.82[a]
Multiple Myeloma	1970–1978	4.00[a]	1978–1981	−2.93	1981–1987	3.97[a]	1987–2003	0.55[a]	1970–1977	4.06[a]	1977–1980	−3.13	1980–1988	3.01[a]	1988–2003	0.42[a]
Leukemias	1970–1978	0.24	1978–1988	−0.43[a]	1988–1996	−1.05[a]	1996–2003	−0.61[a]	1970–1982	−0.44[a]	1982–2003	−1.11[a]				
All cancers, benign/malignant	1970–1988	0.37[a]	1988–1993	−0.30	1993–2003	−1.28[a]			1970–1981	−0.50[a]	1981–1992	−0.15[a]	1992–1999	−1.14[a]	1999–2003	−0.42[a]
35–64 years old																
Oral cavity/pharynx	1970–1983	4.09[a]	1983–1992	1.81[a]	1992–2001	−0.90[a]	2001–2003	−4.86[a]	1970–1978	0.67	1978–1981	4.21	1981–2003	1.62[a]		
Esophagus	1970–1985	1.88[a]	1985–1994	0.25	1994–2001	−1.56[a]	2001–2003	1.58	1970–1987	−0.24	1987–1993	1.57	1993–2001	−0.40	2001–2003	7.74
Stomach	1970–1984	−3.23[a]	1984–1988	−2.13[a]	1988–1997	−3.46[a]	1997–2003	−4.44[a]	1970–1984	−3.48[a]	1984–1991	−2.40[a]	1991–2003	−3.46[a]		
Intestines	1970–1993	0.65[a]	1993–2003	−1.24[a]					1970–1993	−0.42[a]	1993–2003	−2.08[a]				
Liver	1970–1982	2.26[a]	1982–1985	−2.68	1985–2003	1.90[a]			1970–1992	−2.15[a]	1992–2003	1.72[a]				
Gall-bladder/bile ducts	1970–1973	−2.66	1973–1988	0.46[a]	1988–2000	−1.21[a]	2000–2003	−6.24[a]	1970–1989	−0.68[a]	1989–2003	−2.78[a]				
Pancreas	1970–1987	0.95[a]	1987–2003	0.08					1970–2003	0.73[a]						
Larynx	1970–1978	2.22[a]	1978–1988	−0.25	1988–1997	−2.54[a]	1997–2003	−4.70[a]	1970–2003	0.00						
Lung	1970–1988	1.15[a]	1988–1997	−1.52[a]	1997–2003	−3.38[a]			1970–1979	2.25[a]	1979–1998	1.52[a]	1998–2003	3.31[a]		
Pleura	1970–1975	0.13	1975–1987	4.78[a]	1987–1992	1.24	1992–2003	−3.38[a]	1970–2003	−0.77[a]						
Bone	1970–1975	0.11	1975–1997	−3.19[a]	1997–2003	−4.89[a]			1970–1975	−0.32	1975–1979	−6.69[a]	1979–2003	−3.52[a]		
Connective/soft tissue	1970–1976	0.67	1976–1979	11.41	1979–1992	2.27[a]	1992–2003	−1.73[a]	1970–1993	3.25[a]	1993–2003	−1.64[a]				

Table 3. (*Continued*)

	Men							
	Trend 1		Trend 2		Trend 3		Trend 4	
	Years	APC	Years	APC	Years	APC	Years	APC
Skin including melanoma	1970–1988	2.52[a]	1988–2003	−0.04				
Breast								
Uterus (cervix/corpus)								
Ovary								
Prostate	1970–1978	1.03[a]	1978–1981	−1.39	1981–1991	1.49[a]	1991–2003	−0.76[a]
Testis	1970–2003	−2.59[a]						
Bladder	1970–1984	0.27[a]	1984–1992	−1.10[a]	1992–2003	−2.62[a]		
Kidney	1970–1986	1.76[a]	1986–1994	0.45	1994–2003	−2.11[a]		
Thyroid	1970–1992	−0.80[a]	1992–2003	−2.96[a]				
Non-Hodgkin's lymphoma	1970–1981	−0.23	1981–1988	3.98[a]	1988–1996	0.96[a]	1996–2003	−2.22[a]
Hodgkin's lymphoma	1970–1993	−3.63[a]	1993–2003	−6.50[a]				
Multiple myeloma	1970–1977	3.03[a]	1977–1980	−5.55	1980–1988	2.74[a]	1988–2003	−0.29
Leukemias	1970–1985	−0.44[a]	1985–1999	−1.08[a]	1999–2003	−2.62[a]		
All tumors, benign/malignant	1970–1987	0.53[a]	1987–1993	−0.44[a]	1993–2003	−1.86[a]		

	Women							
	Trend 1		Trend 2		Trend 3		Trend 4	
	Years	APC	Years	APC	Years	APC	Years	APC
Skin including melanoma	1970–1990	1.64[a]	1990–2003	−0.17				
Breast	1970–1988	0.59[a]	1988–1994	−0.64[a]	1994–2003	−2.08[a]		
Uterus (cervix/corpus)	1970–1983	−3.72[a]	1983–2003	−1.93[a]				
Ovary	1970–1972	−2.81	1972–1978	0.28	1978–2001	−0.97[a]	2001–2003	1.92
Prostate								
Testis								
Bladder	1970–1979	0.89	1979–1982	−4.70	1982–2003	−1.06[a]		
Kidney	1970–1992	0.77[a]	1992–2003	−2.72[a]				
Thyroid	1970–1978	−0.44	1978–2003	−2.96[a]				
Non-Hodgkin's lymphoma	1970–1981	−0.13	1981–1988	4.52[a]	1988–1997	1.02[a]	1997–2003	−3.06[a]
Hodgkin's lymphoma	1970–1997	−3.62[a]	1997–2003	−7.41[a]				
Multiple myeloma	1970–1977	2.60[a]	1977–1982	−2.68	1982–1989	2.67[a]	1989–2003	−0.50
Leukemias	1970–1981	−0.46[a]	1981–1999	−1.25[a]	1999–2003	−2.99[a]		
All tumors, benign/malignant	1970–1982	−0.69[a]	1982–1991	−0.31[a]	1991–2003	−1.07[a]		

[a]Significantly different from 0 ($P < 0.05$).
APC, estimated annual percent of change.

magnitude to that observed in the United States of America since 1992 [12, 13], although somewhat larger in women from the EU. The use of the joinpoint method of analysis has allowed a detailed and accurate description of the pattern of cancer mortality in recent years, since it identifies the calendar years in which statistically significant changes in trends occurred. This offers a clearer picture of actual trends in mortality over long periods of time rather than using only one trend statistic. The joinpoint regression and other similar methods have been applied to age-adjusted cancer mortality and incidence rates for different cancer sites by sex and race and for truncated rates [12].

The role of major cancer sites in these trends, starting from major tobacco-related ones, is described below.

In men, the decline in cancer mortality has been driven by lung cancer mortality, which levelled off in the late 1980s and declined thereafter, following the persistent reduction in tobacco consumption in men from most European countries [14]. Occupational, environmental as well as dietary factors may also have exerted some favorable influence on these favorable trends [15, 16]. Conversely, lung cancer mortality in women from the EU has been steadily increasing, with even stronger increase in the last years. This reflects the different pattern in tobacco consumption in European women as compared with men, with an increase in later calendar years, and a persistent increment in recent years, particularly in some European countries such as France and Spain [17, 18].

A contribution to the decline in male cancer mortality has been given by the recent reduction in the mortality from other tobacco-related cancers, including those of oral cavity/pharynx, esophagus, larynx and bladder [19]. Male mortality from oral and pharyngeal cancer peaked in the early 1990s and levelled off thereafter, starting to decline—particularly in middle-aged men—in most recent years [20]. For esophageal cancer, the decrease in male mortality was less evident, probably reflecting the greater importance of alcohol consumption in this neoplasm, and the increase in adenocarcinoma of the esophagus observed in various countries mainly of northern Europe in recent years [21–23]. Trends were somewhat more favorable for male laryngeal cancer, with an earlier (since the late 1980s) and larger decline, likely reflecting the predominant role of tobacco in laryngeal carcinogenesis [19, 24]. Bladder cancer mortality started to level off in the early 1990s in men and even earlier in women and declined thereafter. Mortality rates for male bladder cancer well reflect the patterns of tobacco smoking for subsequent generations of European men [19, 23]. Moreover, a role in the fall has been played by reduced occupational exposure to carcinogens, mainly aromatic amines. The decreases in women are more difficult to explain. Better control of urinary tract infections has probably played a role, while the role of dietary and other potential urinary tract carcinogens remains unquantified [23].

A significant influence on cancer mortality trends in EU is given by the persistent fall of gastric cancer. Gastric cancer mortality has been declining in the EU since several decades, with no evidence of levelling off over recent years. A steady reduction in gastric cancer mortality was observed in middle age too, suggesting that the decline will continue in the near

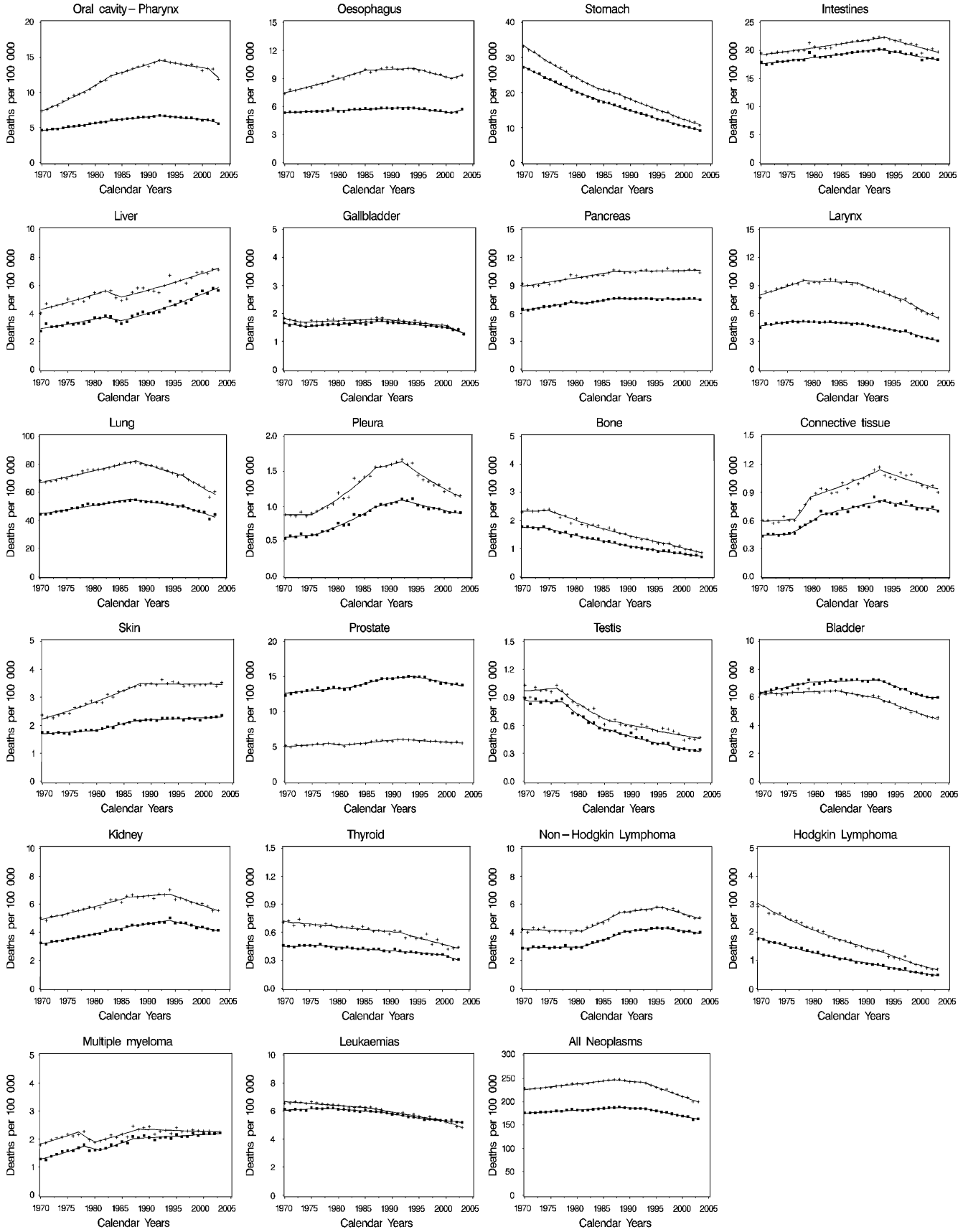

Figure 1. Joinpoint analysis for selected cancer mortality in men (all ages and aged 35–64 years) from the European Union, 1970–2002. Men, all ages ●——●; Men, 35–64 years. +——+.

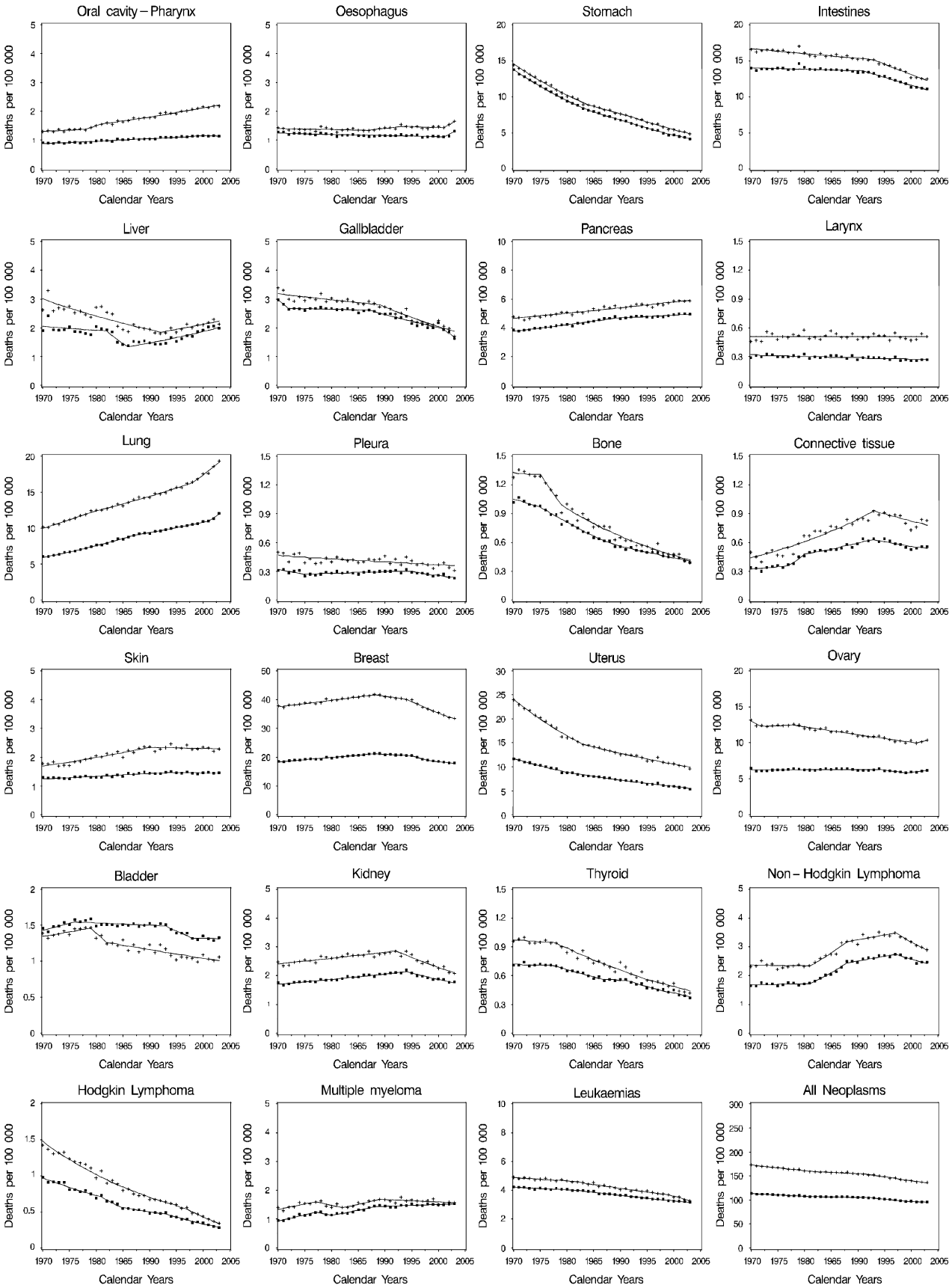

Figure 2. Joinpoint analysis for selected cancer mortality in women (all ages and aged 35–64 years) from the European Union, 1970–2002. Women, all ages ●——●; Women, 45–59 years +——+.

future. The reasons for this persistent decline are complex, but almost certainly include a more varied and affluent diet, better food conservation—including refrigeration—in addition to the control of *Helicobacter pylori* infection and reduced tobacco smoking [25, 26]. Whether improvements in diagnosis and treatment have also played a role on the favorable trends in gastric cancer throughout Europe, particularly over most recent calendar periods, remain open to evaluation [26].

A levelling off in mortality from intestinal cancer in men from the EU—particularly in middle-aged ones—was observed since the early 1990s, following the earlier favorable pattern observed in women. The trends in colorectal cancer mortality over recent years likely reflect favorable modifications in (dietary) risk factors, although early diagnosis and treatment of the disease may have had some effect on these trends [27–29]. Hormone replacement therapy and other female hormones may also have played a role in the fall of colorectal cancer mortality in women and explain the earlier and more favorable patterns observed in women as compared with men [30].

A levelling and subsequent decline in breast cancer mortality in the EU was first observed in the early 1990s, and has continued in recent years, with a more evident reduction in middle-aged women. The fall in breast cancer mortality is largely attributable to advancements in therapy, but some role of (mammographic) screening is also possible [28, 31].

Mortality from prostate cancer has been rising up to the late 1980s and declining since the mid-1990s. Improved treatment is likely to have played a role, including earlier adoption of transurethral resection of the prostate, as well as hormone (androgen blockage) and radiotherapy for patients with locally advanced disease [32]. It remains unclear whether—and to which extent—the earlier rises in prostate cancer rates were due to improved diagnosis and certification of prostate cancer, and whether the recent falls have been influenced by earlier diagnosis of the disease, including introduction of prostate-specific antigen in Europe since the late 1980s.

With reference to other cancer sites, trends in liver cancer mortality are extremely difficult to understand and interpret, since the liver is one of the most common sites of secondaries, and the distinction between primary and metastatic liver cancer is variable across countries and calendar periods. Moreover, mortality patterns differ widely across European countries. Still, on a EU scale, the consistent trends in all-age and truncated 35–64 years rates, but the different trends in the two sexes (steady upwards in men, downwards first with subsequent rise in women) probably reflect some real underlying trend, which has to be related to the main recognized causes of liver cancer, i.e. hepatitis B and C viruses and alcohol [33, 34]. Tobacco is another recognized risk factor for liver cancer, but its potential impact on national mortality rates remains difficult to evaluate [19].

Mortality from cancers of the gall-bladder and bile ducts is higher in women than in men, but rates have been declining in EU women since the 1970s, the fall being larger over most recent calendar years. Overall, male rates in the EU have remained stable up to the early 2000s, but have started to decline in the last years. The recent favorable trends in gall-bladder cancer mortality essentially reflect the increase in cholecystectomy, due to improvements in surgical techniques (including laparoscopic cholecystectomy), since gallstones are the major risk factor for the disease [35]. The trends may have been also influenced by changes in diagnosis and certification, nutrition and diet, antibiotic use, alcohol and perhaps tobacco consumption [36].

Mortality from cancer of the pancreas rose for both sexes in the EU up to the late 1980s, but has tended to level off thereafter, particularly in men. At least part of the earlier trends may be due to improved diagnosis and certification of the disease, following the introduction of ultrasound, computed tomography, endoscopic retrograde cholangiopancreatography and fine-needle aspiration [37]. It is unlikely, however, that these diagnostic improvements have played a major role over more recent calendar periods, in consideration also of the similar pattern of rates in middle age, i.e. when diagnosis and certification is known to be more accurate. The favorable trends recently observed mainly in men reflect the pattern of cigarette smoking, confirming the relevant role of tobacco in pancreatic carcinogenesis [19].

Trends for (mesothelioma) of the pleura are difficult to interpret, since death certification data for this neoplasm are subject to substantial uncertainties, given the difficulties in diagnosis and certification validity [38]. These cautions notwithstanding, it is nonetheless clear that the asbestos-related pleural cancer epidemic is not anymore expanding in the EU, some fall in rates being observed in the last decades, mostly in middle-aged men. This pattern likely reflects the control of asbestos use in Europe since the early 1970s and the changes in the type of asbestos used in different European countries over time [38, 39]. The apparent fall in pleural cancer mortality over recent calendar years is largely spurious, and due to the recent inclusion in the EU of Poland, Romania and other Eastern European countries with low rates.

After the steady rise up to the late 1980s and early 1990s, skin cancer rates tended to level off in EU men and women, particularly in middle age. It appears therefore that control of excessive sunshine exposure and sunburns has led to a levelling in previous rises in mortality from skin cancers—mainly melanomas—most clearly in young and middle-aged population [40]. Better access to health care, earlier detection of the disease, with consequent improved survival, could also explain the improvement of mortality trends for skin cancer [41].

Mortality from uterine cancer has been steadily declining over the last few decades in the EU, mostly in young and middle-aged women. Although it is not possible on the basis of mortality data to distinguish between cervical and endometrial cancer, this steady fall is likely due mainly to a decline in cervical cancer mortality, following the adoption of cervical screening [1, 28]. Mortality from cervical cancer remains, however, high in several Central and Eastern European countries [42].

After earlier rises, overall ovarian cancer mortality has stabilized in the EU over the last three decades, while truncated (35–64 years) mortality rates have tended to decline. The appreciable declines in ovarian cancer mortality for middle-aged women can be related to the changing prevalence of oral

contraceptive use, which has a long-term favorable effect on ovarian cancer risk [43]. The role of other risk factors for ovarian cancer, as well as of improvements in diagnosis and treatment (particularly for germ-cell neoplasms), and consequently in survival, remains unquantified [44].

Mortality from testicular cancer has long been falling. These favorable trends are mainly attributable to the adoption of platinum-based therapy in the 1970s, which made testicular cancer one of the neoplasms most amenable to treatment. Substantial differences in mortality from this neoplasm were found between Western and Eastern European countries, due to different availability of the expensive drugs required to treat testicular cancer [45]. There is therefore urgency for further advancements in this largely avoidable cause of cancer death.

After earlier rises, mostly in men, kidney cancer mortality rates have started to decline since the early 1990s in both sexes, particular in middle-aged population. Kidney cancer is related to tobacco smoking, though less strongly than respiratory or bladder cancers [19]. It is also related to overweight and hypertension [46]. Thus, the recent favorable pattern, particularly in men, may be related to an earlier control of tobacco (at least in men) and hypertension in several countries of the EU [47].

Mortality from thyroid cancer—which is more common in women than in men—tended to decline over the last three decades, the falls being larger in women. Since thyroid cancer incidence has been increasing, it is unclear how much of the decline in mortality is due to better diagnosis of benign thyroid nodules—which are the best recognized risk factor for thyroid cancer—rather than to improved treatment of thyroid neoplasms [48].

Mortality from HL has been declining in both men and women from the EU, since this is a neoplasm highly amenable to treatment [49]. The persistence of favorable trends over the most recent calendar years indicates that continuing progress in integrated treatment is still in course in several countries of the EU. As for testicular cancer, there is still scope for advancements in HL trends, particularly in several Central and Eastern European countries.

In contrast with rates for HL, mortality from NHL has been increasing in the EU up to the late 1990s, with a tendency to decline only in more recent years. NHL is much less amenable to treatment than HL. The earlier rises registered almost certainly reflect real increases in disease incidence, although the causes of these neoplasms remain largely undefined [50]. The subsequent phases of the AIDS epidemic, the spread of hepatitis C virus and the increased number of transplantations can, in fact, explain only a limited proportion of the earlier rises.

Mortality from multiple myeloma has tended to rise until the late 1980s in the EU, although in the more recent years rates tended to levell off. Earlier upward trends were at least in part attributed to advancements in the diagnosis of the disease [51]. Whether and to which extent the unfavorable trends in mortality also reflect real rises in the incidence remains unclear. Also the reasons for the recent decline remain largely undefined, though improved treatment may have some role.

Mortality rates from leukemias steadily declined in both men and women from the EU in the last decades. Leukemias include a heterogeneous group of neoplasms, some of which—as acute lymphoblastic leukemias of children and the young—are largely amenable to treatment and consequently contribute to the overall favorable trends observed [52].

In conclusion, mortality from most common cancers in the EU showed a persistent favorable trend over more recent years. The inclusion of data from former nonmarket economy countries has led to some increases in absolute EU cancer mortality rates and to some quantitatively less favorable trends because the rates in Central and Eastern European countries which entered the EU in 2004 and 2007 were higher than in the preexisting EU member countries [2, 53]. In particular, Central and Eastern European accession countries had the highest rates not only for lung cancer and other tobacco-related cancers but also for gastric, cervical cancer and leukemias [2, 11, 53]. Moreover, for all cancer sites, trends were more favorable in the former 15 EU countries than in accession countries.

The maintenance—and potential improvement—of favorable trends in cancer mortality in the EU in the near future would therefore require a strategy focusing on the control of tobacco and alcohol consumption, nutrition and diet and avoiding excessive sun exposure [28]. Early diagnosis for selected neoplasms—including cervix, breast, colorectum and perhaps prostate—can also have a relevant impact. Universal adoption of therapeutic advancements in various European countries—mainly form Central and Eastern Europe—may contribute to reduce the cancer mortality burden in the EU [2, 53].

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