Cancer survival in Europe 1999–2007 by country and age: results of EUROCARE-5—a population-based study

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Summary

Background Cancer survival is a key measure of the effectiveness of health-care systems. EUROCARE—the largest cooperative study of population-based cancer survival in Europe—has shown persistent differences between countries for cancer survival, although in general, cancer survival is improving. Major changes in cancer diagnosis, treatment, and rehabilitation occurred in the early 2000s. EUROCARE-5 assesses their effect on cancer survival in 29 European countries.

Methods In this retrospective observational study, we analysed data from 107 cancer registries for more than 10 million patients with cancer diagnosed up to 2007 and followed up to 2008. Uniform quality control procedures were applied to all datasets. For patients diagnosed 2000–07, we calculated 5-year relative survival for 46 cancers weighted by age and country. We also calculated country-specific and age-specific survival for ten common cancers, together with survival differences between time periods (for 1999–2001, 2002–04, and 2005–07).

Findings 5-year relative survival generally increased steadily over time for all European regions. The largest increases from 1999–2001 to 2005–07 were for prostate cancer (73·4% [95% CI 72·9–73·9] *vs* 81·7% [81·3–82·1]), non-Hodgkin lymphoma (53·8% [53·3–54·4] *vs* 60·4% [60·0–60·9]), and rectal cancer (52·1% [51·6–52·6] *vs* 57·6% [57·1–58·1]). Survival in eastern Europe was generally low and below the European mean, particularly for cancers with good or intermediate prognosis. Survival was highest for northern, central, and southern Europe. Survival in the UK and Ireland was intermediate for rectal cancer, breast cancer, prostate cancer, skin melanoma, and non-Hodgkin lymphoma, but low for kidney, stomach, ovarian, colon, and lung cancers. Survival for lung cancer in the UK and Ireland was much lower than for other regions for all periods, although results for lung cancer in some regions (central and eastern Europe) might be affected by overestimation. Survival usually decreased with age, although to different degrees depending on region and cancer type.

Interpretation The major advances in cancer management that occurred up to 2007 seem to have resulted in improved survival in Europe. Likely explanations of differences in survival between countries include: differences in stage at diagnosis and accessibility to good care, different diagnostic intensity and screening approaches, and differences in cancer biology. Variations in socioeconomic, lifestyle, and general health between populations might also have a role. Further studies are needed to fully interpret these findings and how to remedy disparities.

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Introduction

Over the past 20 years, EUROCARE has provided systematic, quality-controlled, robustly comparable estimates of population-based cancer survival in Europe.[1–5] These studies have shown large and sometimes unexpected differences in survival between European populations; they have also shown that survival has improved, although the pace of improvement has varied. EUROCARE's findings have affected the organisation of cancer care in several European countries, contributing to the design of national cancer plans and the evaluation of their effectiveness.[6,7]

Cancer diagnosis and treatment have changed greatly in recent decades. Screening for breast cancer and cervical cancer, and to a lesser extent colorectal cancer, has been widely adopted.[8] Opportunistic screening for prostate cancer has become widespread, and early diagnosis initiatives have been introduced for melanoma, thyroid cancer, lung cancer, and other cancers.[9,10] Advances have also been made in diagnostic imaging, genetic profiling, and treatments,[11] including the introduction of targeted drugs, multidisciplinary care,[12] and a growing concentration of treatment in specialist centres.[13,14]

EUROCARE-5 provides updates of cancer survival for Europe. The EUROCARE-5 database contains about 22 million records of patients diagnosed from 1978 to 2007 and followed up to Dec 31, 2008. The participation of additional countries, especially from eastern Europe, has increased coverage. Here, we present survival estimates for adult patients (age ≥15 years) diagnosed in Europe during 2000–07. We also present survival trends by age and over time (1999–2007) by European region for ten common cancers.

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See Online for appendix

Methods

Study design and data collection

Data for adults with cancer were provided by 107 population-based cancer registries from 29 countries grouped into five regions: Denmark, Finland, Iceland, Norway, Sweden (northern Europe); England, Ireland, Northern Ireland, Scotland, Wales (UK and Ireland); Austria, Belgium, France, Germany, Netherlands, Switzerland (central Europe); Croatia, Italy, Malta, Portugal, Slovenia, Spain (southern Europe); and Bulgaria, Czech Republic, Estonia, Latvia, Lithuania, Poland, Slovakia (eastern Europe).

Cancers were defined by site (topography) and morphology according to the International Classification of Diseases for Oncology, 3rd edition (ICD-O-3),[15] as in EUROCARE-4.[16] Haematological neoplasms were defined in accordance with WHO classification (appendix).[17,18] All invasive, primary, malignant neoplasms except non-melanoma skin cancer were eligible for inclusion. Benign and in-situ urothelial cancers of the bladder were also included among urinary bladder cancers to ensure comparability between countries.

Anonymised cancer registration records were supplied. These records had to contain (according to study protocol) information for last known vital status (alive, dead, censored); dates of birth, diagnosis, and last known vital status; sex; topography and morphology of the cancer; and the basis for diagnosis. The protocol has been published online. Cases diagnosed at autopsy or registered only from a death certificate were excluded. Registries in which the proportion of death certificate only cases in 2000–07 exceeded 13% were excluded, which is consistent with previous EUROCARE studies.[16]

For the **EUROCARE-5 study protocol** see http://www.eurocare.it/Eurocare5/ProtocolsEU5/tabid/89/Default.aspx

All primary cancers were eligible, irrespective of whether other cancers of different type had been diagnosed previously in a patient. Patients who had more than one type of cancer were included in each of the counts, to reduce bias from survival comparisons between long-established and recently established registries.[19]

We applied standardised quality control procedures[16] to detect missing or invalid data items (major errors) and possible inconsistencies (eg, unlikely combinations of age, sex, site, and morphology). About 68 000 records with major or probable errors were returned to registries for correction or confirmation. We analysed data from 107 cancer registries, from which two datasets were extracted. The first had data from 99 registries to estimate survival for almost 9 million adults diagnosed in 2000–07, providing the widest geographic coverage. Of the 29 countries included, 21 had 100% national coverage. Countries which had only partial coverage included: Belgium, France, Germany, Switzerland, Italy, Portugal, Spain, and Poland. 12 specialised registries (eight in France, two in Spain, and two in Italy) provided data for some cancers, so that coverage for these countries varied with cancer site: 10–23% for France, 15–17% for Spain, and 34–35% for Italy.

The second dataset—consisting of data for more than 10 million cases from the 49 registries in 25 countries that provided data for cancer incidence from 1995 to 2007—was used to analyse survival over time for ten common cancers. Registries without complete data for 1995–2007 were excluded (Belgium, Croatia, Latvia, Portugal). The ten common cancers were: stomach cancer (ICD-O-3 topography: C16; morphology: 8000–9589), colon cancer (C18; 8000–9589), rectal cancer (C19–21; 8000–9589), lung cancer (C33–34; 8000–9049, 9060–9589), skin melanoma (C44; 8720–8790), breast cancer (C50; 8000–9589), ovarian cancer (C56–57; 8000–9589), prostate cancer (C619; 8000–9589), kidney cancer (C64–66, C68; 8000–9589), and non-Hodgkin lymphoma (appendix).[17,18]

Statistical analysis

We estimated 5-year relative survival, a standard indicator for comparison of cancer survival in population-based studies for which the underlying cause of death is unknown or unreliable. Relative survival is the ratio of the measured survival of patients to the expected survival in the general population for the same region (or country), age, sex, and calendar year. Relative survival accounts for mortality from causes other than the relevant cancer, which can vary widely between countries. We estimated expected survival by the Ederer II method[20] from lifetables of all-cause mortality by age, sex, cancer registry, and calendar year. Lifetables were smoothed[21] and checked against published official mortality data.

For patients diagnosed in 2000–07 and followed up to 2008, we estimated 5-year relative survival by the classic cohort approach. To assess changes in survival over time, we estimated 5-year relative survival by the period approach[22] for patients under observation in 1999–2001 (diagnosed 1995–2001), 2002–04 (diagnosed 1998–2004), and 2005–07 (diagnosed 2001–07). The period approach provides reliable predictions of 5-year cohort survival when sufficient follow-up is not available for recently diagnosed patients.[23]

We calculated mean European survival after weighting country-specific survival by the country population. The age distribution of cancer patients varies between countries and over time. So, to improve comparability, we age-standardised survival estimates for all ages combined by the direct method using cancer-specific weightings obtained from the International Cancer Survival Standard.[24] We calculated 5-year relative survival for each country and for age groups. Age groups were 15–44 years, 45–54 years, 55–64 years, 65–74 years, and 75 years or older, except for prostate cancer, which was 15–54 years, 55–64 years, 65–74 years, 75–84 years, and 85 years or older, because the median age at presentation for prostate cancer is older than for other cancers. We calculated SEs by the Greenwood formula. To obtain two-sided 95% CIs, the data were logarithmically transformed,

	Proportion of population covered by cancer registration (%)	Number of cases diagnosed 2000–07	Excluded			Included in analyses	Quality indicators		
			Major errors (%)	Cases known by death certificate only (%)	Diagnosed incidentally at autopsy (%)		Microscopically verified (%)	Lost to follow-up (%)*	Unspecified morphology (%)†
European mean	50%	9 021 069	0·3%	2·9%	0·5%	8 668 723	91·1%	1·1%	1·1%
Northern Europe	100%	978 483	0·2%	0·4%	1·2%	961 454	95·4%	0·3%	1·5%
Denmark‡	100%	233 509	0·0%	0·0%	0·3%	232 657	93·1%	0·0%	..
Finland	100%	190 122	0·0%	1·0%	2·0%	184 488	93·5%	0·2%	3·9%
Iceland	100%	10 198	0·1%	0·1%	1·2%	10 047	96·4%	0·0%	0·1%
Norway	100%	178 071	0·7%	1·0%	0·5%	174 156	94·2%	0·5%	0·6%
Sweden	100%	366 583	0·2%	..	1·6%	360 106	98·6%	0·4%	0·7%
Ireland and UK	100%	3 028 148	0·3%	2·5%	0·0%	2 941 509	88·6%	0·4%	1·0%
Ireland	100%	174 386	0·7%	0·9%	0·3%	170 972	91·4%	0·0%	0·4%
UK (England)	100%	2 431 028	0·3%	2·7%	0·0%	2 356 447	89·4%	0·5%	1·0%
UK (Northern Ireland)	100%	75 156	0·6%	0·9%	0·1%	73 883	87·3%	0·0%	2·0%
UK (Scotland)	100%	216 685	0·3%	0·6%	0·1%	214 405	85·3%	0·1%	0·5%
UK (Wales)	100%	130 893	0·1%	3·8%	0·0%	125 802	77·1%	0·0%	1·0%
Central Europe	35%	2 348 989	0·1%	4·4%	0·1%	2 229 993	96·1%	2·0%	0·6%
Austria	100%	298 149	0·7%	7·3%	0·0%	274 230	97·8%	0·0%	1·3%
Belgium	58%	277 058	0·0%	..	0·0%	272 604	96·2%	0·0%	0·8%
France	23%	209 291	0·1%	..	0·0%	205 397	94·8%	4·6%	0·5%
Germany	23%	840 201	0·0%	9·6%	0·0%	758 134	96·2%	1·5%	0·7%
Switzerland	30%	86 635	0·2%	1·2%	1·1%	83 909	94·8%	8·2%	0·2%
Netherlands	100%	637 655	0·0%	..	0·3%	635 719	95·9%	0·8%	0·3%
Southern Europe	36%	1 480 994	0·3%	1·6%	0·2%	1 443 058	89·2%	1·4%	1·2%
Croatia	100%	163 187	0·2%	5·5%	0·0%	153 931	82·4%	0·0%	0·6%
Italy	35%	880 931	0·1%	1·0%	0·2%	868 167	88·3%	1·6%	1·5%
Malta	100%	10 997	1·0%	4·4%	0·2%	10 346	89·1%	0·0%	1·1%
Portugal	76%	185 352	1·8%	..	0·0%	178 194	96·1%	1·6%	1·2%
Slovenia	100%	83 378	0·0%	1·1%	1·0%	81 670	93·7%	0·0%	0·4%
Spain	17%	157 149	0·1%	2·9%	0·2%	150 750	90·7%	1·8%	0·6%
Eastern Europe	52%	1 184 455	0·7%	5·0%	2·0%	1 092 709	86·5%	1·1%	1·8%
Bulgaria	100%	248 732	0·0%	8·6%	0·0%	227 362	84·0%	1·0%	1·1%
Czech Republic	100%	399 463	0·2%	3·6%	4·9%	364 428	89·4%	0·7%	1·3%
Estonia	100%	44 264	0·1%	0·1%	1·4%	43 544	90·0%	0·4%	2·2%
Latvia	100%	69 479	0·9%	5·8%	2·0%	63 450	81·4%	0·0%	5·5%
Lithuania	100%	108 951	0·1%	3·2%	0·0%	105 026	88·2%	2·1%	5·1%
Poland	13%	149 132	4·1%	1·0%	0·1%	140 827	78·7%	3·6%	1·4%
Slovakia	100%	164 434	0·0%	8·7%	1·3%	148 072	90·8%	0·0%	0·4%

*Proportion of patients diagnosed while alive in 2000–03, censored with less than 5 years of follow-up. For the French registries this quality indicator was calculated for cases diagnosed in 2000–02. †Proportion of cases with ICD-O-3 morphology codes 8000–8005 (non-specific morphology). ‡The Danish cancer registry provided specific ICD-O-3 morphology codes only for skin melanoma and haematological cancers. Data unavailable for Sweden, Belgium, France, Netherlands, and Portugal because death certificate information is not used to initiate cancer registration.

Table 1: **Adult populations included 2000–07 survival analysis of the EUROCARE-5 study**

so that the lower bound of the CI was always positive. The analyses were done with SEER*Stat (version 8.0.4).

Role of the funding source

The sponsors of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. RDA, MS, and RC had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

For both datasets, only 0·3% of records were excluded for major errors that could not be corrected: this proportion was less than 1% in most registries but 2–4% in Poland and Portugal (table 1). Roughly 3–4% of cases were excluded because they were identified from death certificate only or were discovered at autopsy. Overall, 2·9% of cases were death certificate only, ranging from 0–9·6% (table 1). Overall, only 0·5% of valid cancer cases

For **SEER*Stat** see http://www.seer.cancer.gov/seerstat/

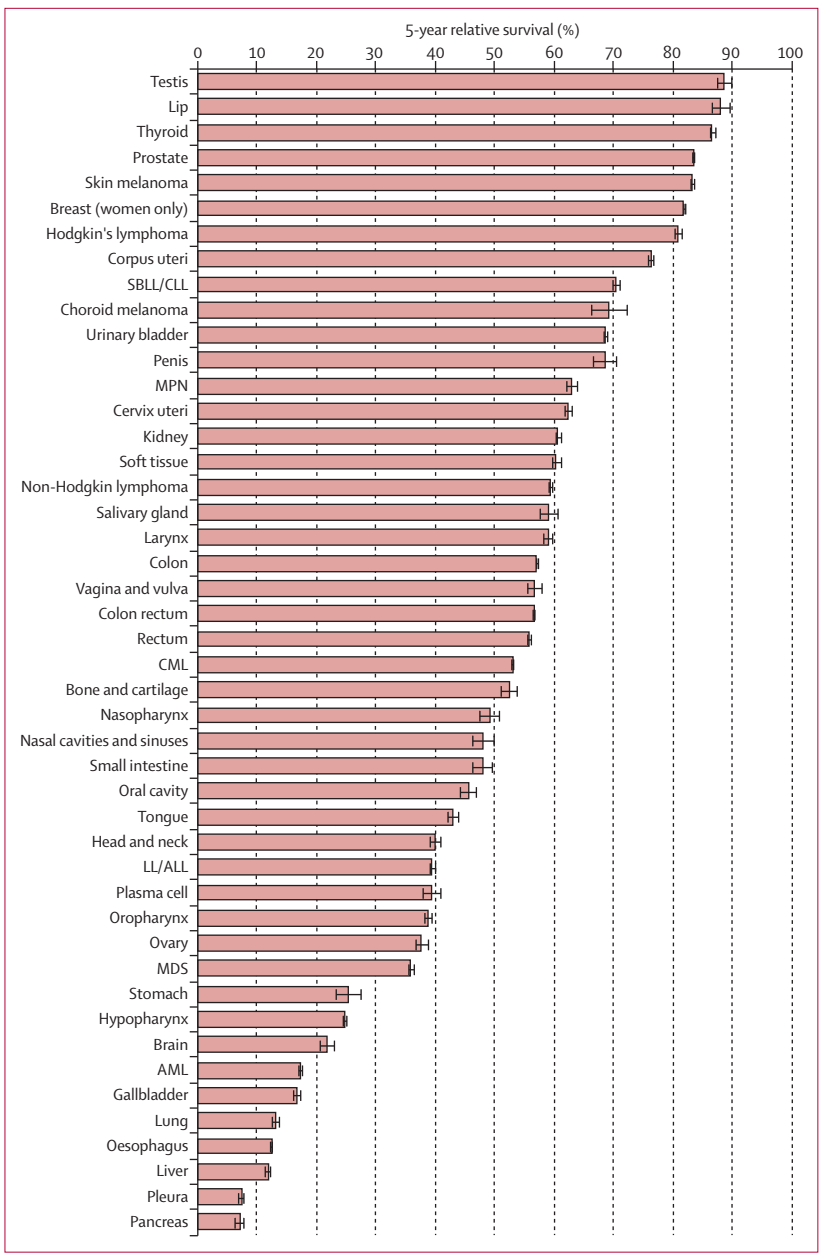

Figure 1: **European mean age-standardised 5-year relative survival for adult patients with cancer diagnosed in 2000–2007**

Error bars are 95% CIs. The European mean is the (population) weighted mean of country-specific relative survival estimates. See appendix for median data. SBLL/CLL=small B-cell lymphocytic lymphoma or B-cell chronic lymphocytic leukaemia. MPN=myeloproliferative neoplasm. CML=chronic myeloid leukaemia. LL/ALL=lymphoblastic lymphoma or acute (precursor cell) lymphatic leukaemia. MDS=myelodysplastic syndrome. AML=acute myeloid leukaemia.

were incidentally discovered at autopsy. Proportions were highest for Czech Republic, Latvia, and Finland (table 1). After exclusions, 8 668 723 records were included in the estimate of survival of patients diagnosed during 2000–07. From the second dataset examining patients diagnosed between 1995–2007, 10 219 439 records were included in the analysis of survival over different time periods.

For 24 countries, more than 85% of cancers were microscopically verified. Of cases diagnosed in 2000–03—with potential follow-up of least 5 years—the proportion censored while alive with less than 5 years of follow-up was mostly negligible (1%). Exceptions were France (4·6%) and Switzerland (8·2%). Only 1·1% of neoplasms were assigned a non-specific morphology code (8000–8005), with highest proportions in Latvia (5·5%) and Lithuania (5·1%).

Figure 1 shows the European mean age-standardised 5-year relative survival for 46 cancers. These cancers constituted 96% of all cancers recorded in 2000–07 by the participating registries. The cancers with the highest survival at 5 years were testicular cancer (88·6%, 95% CI 87·4–89·7) and lip cancer (88·1%, 86·6–89·4). Thyroid cancer (86·5%, 86·1–87·0), prostate cancer (83·4%, 83·1–83·6), skin melanoma (83·2%, 82·9–83·6), breast cancer (women only; 81·8%, 81·6–82·0) and Hodgkin's lymphoma (80·8%, 80·2–81·4) also had good survival. About a third of all cancer cases had survival greater than 80%, whereas about a quarter had survival below 30%. The appendix shows variation between countries for 5-year age-adjusted relative survival.

For stomach cancer, 5-year survival, as calculated from the first dataset, was poor (25·1%, 95% CI 24·8–25·4), with a significant difference between men and women (appendix). Geographical differences were large (table 2), with highest survival in southern and central Europe, particularly Italy, Portugal, Switzerland, Germany, Austria, and Belgium; intermediate survival in northern Europe; and lowest survival in eastern Europe and the UK and Ireland. In a post-hoc analysis of apparent outliers, Netherlands and Denmark had significantly lower survival ($p<0·0001$) than the mean for central and northern Europe, respectively. Survival decreased steeply with age in all regions (figure 2, appendix). In southern Europe, survival of patients aged 15–64 years was higher than in central Europe. When analysing the second database, we saw that 5-year survival increased from 23·3% (95% CI 22·9–23·8) in 1999–2001 to 25·1% (24·6–25·6) in 2005–07 (figure 3, appendix).

For colon cancer, the European mean age-standardised 5-year survival was 57·0% (95% CI 56·8–57·3), with negligible differences between the sexes (appendix). Northern, central, and southern Europe had similar survival, at around 60%. For eastern Europe, and the UK and Ireland, survival was lower (table 2). Several countries had significantly different survival compared with the mean of their respective regions, including Denmark, Croatia, Slovenia, and Ireland (table 2; $p<0·0001$). Survival age trends were similar for all European regions: survival was best for patients aged 15–44 years, roughly constant for those aged 45–64 years, and reduced thereafter (figure 2, appendix). European 5-year survival increased from 54·2% (53·9–54·6) in 1999–2001 to 58·1% (57·7–58·4) in 2005–07, with a similar change in each region (figure 3, appendix).

	Stomach cancer	Colon cancer	Rectal cancer	Lung cancer	Skin melanoma	Breast cancer (women only)	Ovarian cancer	Prostate cancer	Kidney cancer	Non-Hodgkin lymphoma
European mean	25·1 (24·8–25·4)	57·0 (56·8–57·3)	55·8 (55·5–56·1)	13·0 (12·9–13·1)	83·2 (82·9–83·6)	81·8 (81·6–82·0)	37·6 (37·1–38·0)	83·4 (83·1–83·6)	60·6 (60·2–61·0)	59·4 (59·0–59·7)
Northern Europe	21·9 (21·2–22·6)	59·0 (58·5–59·4)	59·5 (58·9–60·2)	12·2 (11·9–12·5)	87·7 (87·2–88·2)	84·7 (84·4–85·1)	41·1 (40·3–42·0)	85·0 (84·6–85·3)	55·8 (55·0–56·6)	63·3 (62·7–63·9)
Denmark	16·0 (14·7–17·4)	53·6 (52·6–54·6)	54·6 (53·3–55·8)	10·3 (9·8–10·8)	87·8 (86·7–88·8)	81·5 (80·7–82·3)	35·5 (33·8–37·2)	69·3 (68·0–70·6)	44·8 (43·1–46·6)	63·6 (62·2–64·9)
Finland	25·3 (23·9–26·7)	61·2 (59·9–62·4)	60·1 (58·6–61·6)	11·5 (10·8–12·2)	85·3 (84·0–86·5)	85·7 (84·9–86·5)	43·1 (41·3–45·0)	90·1 (89·3–90·8)	59·3 (57·7–60·9)	59·7 (58·4–61·0)
Iceland	34·5 (27·8–41·3)	62·0 (56·8–66·8)	73·2 (65·2–79·6)	13·9 (11·5–16·7)	85·0 (77·8–90·0)	87·2 (83·1–90·4)	39·1 (30·6–47·4)	82·5 (78·2–86·0)	60·7 (54·3–66·5)	74·1 (67·2–79·8)
Norway	22·7 (21·1–24·3)	59·2 (58·1–60·2)	62·5 (61·1–63·8)	12·9 (12·3–13·6)	86·4 (85·3–87·5)	84·7 (83·8–85·6)	41·4 (39·5–43·3)	83·5 (82·6–84·3)	56·4 (54·6–58·2)	63·7 (62·3–65·1)
Sweden	21·7 (20·5–22·9)	61·1 (60·3–62·0)	60·8 (59·7–61·8)	14·7 (14·1–15·3)	89·2 (88·5–90·0)	86·0 (85·4–86·5)	44·1 (42·5–45·6)	87·5 (87·0–88·0)	59·6 (58·2–61·0)	64·5 (63·5–65·5)
UK and Ireland	17·2 (16·8–17·5)	51·8 (51·5–52·1)	53·7 (53·3–54·1)	9·0 (8·8–9·1)	85·6 (85·2–86·0)	79·2 (79·0–79·4)	31·0 (30·6–31·5)	80·6 (80·3–80·9)	47·6 (47·1–48·1)	57·4 (57·0–57·8)
Ireland	20·3 (18·7–22·0)	55·0 (53·6–56·3)	53·0 (51·3–54·7)	11·8 (11·1–12·6)	86·4 (84·8–87·9)	79·0 (77·8–80·1)	30·3 (28·3–32·4)	85·6 (84·5–86·6)	51·8 (49·4–54·1)	63·0 (61·3–64·7)
UK (England)	17·0 (16·6–17·4)	51·3 (51·0–51·7)	53·7 (53·3–54·2)	8·8 (8·6–9·0)	85·3 (84·9–85·8)	79·3 (79·0–79·5)	30·6 (30·0–31·1)	80·4 (80·1–80·7)	47·3 (46·7–47·9)	56·7 (56·3–57·2)
UK (Northern Ireland)	18·1 (15·8–20·4)	54·2 (52·3–56·2)	54·3 (51·8–56·8)	11·0 (10·0–12·1)	90·7 (88·1–92·8)	81·9 (80·3–83·5)	32·3 (29·3–35·3)	83·4 (81·4–85·2)	48·6 (45·1–51·9)	59·0 (56·4–61·5)
UK (Scotland)	16·1 (14·9–17·3)	53·9 (52·8–54·9)	54·2 (52·8–55·5)	8·7 (8·2–9·1)	88·8 (87·5–90·0)	78·5 (77·7–79·3)	34·0 (32·5–35·6)	78·9 (77·8–80·0)	46·1 (44·4–47·8)	60·3 (59·0–61·7)
UK (Wales)	17·8 (16·2–19·5)	49·9 (48·6–51·3)	52·6 (50·9–54·3)	8·6 (7·9–9·2)	80·0 (78·1–81·8)	78·2 (77·2–79·2)	31·7 (29·7–33·7)	78·2 (76·9–79·3)	49·8 (47·6–52·0)	56·6 (54·9–58·3)
Central Europe	28·1 (27·6–28·5)	60·5 (60·2–60·8)	60·1 (59·7–60·4)	14·8 (14·6–14·9)	87·6 (87·2–88·0)	83·9 (83·6–84·1)	40·5 (39·9–41·1)	88·1 (87·9–88·4)	64·6 (64·1–65·1)	62·5 (62·1–62·9)
Austria	31·0 (29·9–32·2)	61·2 (60·3–62·0)	61·1 (60·0–62·2)	16·7 (16·1–17·2)	83·1 (82·0–84·2)	82·1 (81·4–82·7)	41·4 (40·0–42·9)	90·4 (89·7–91·0)	71·4 (70·1–72·6)	61·0 (59·8–62·1)
Belgium*	30·5 (29·1–32·0)	61·7 (60·8–62·6)	62·9 (61·8–64·1)	15·4 (14·9–16·0)	83·4 (82·0–84·7)	82·7 (82·0–83·3)	42·4 (40·7–44·1)	89·6 (89·0–90·2)	62·8 (61·3–64·2)	65·1 (63·8–66·3)
France*	26·3 (24·9–27·6)	59·7 (58·7–60·5)	57·9 (56·8–59·0)	13·8 (13·2–14·4)	87·2 (85·8–88·4)	86·1 (85·4–86·8)	40·1 (38·2–42·1)	88·9 (88·2–89·6)	64·1 (62·5–65·7)	65·9 (64·8–66·9)
Germany*	31·3 (30·6–32·0)	62·2 (61·7–62·8)	60·2 (59·5–60·9)	15·6 (15·3–16·0)	89·4 (88·7–90·0)	83·6 (83·2–84·0)	40·3 (39·3–41·3)	89·4 (88·8–89·9)	70·2 (69·4–71·0)	63·5 (62·7–64·3)
Switzerland*	31·6 (29·2–34·1)	61·4 (59·8–63·1)	62·5 (60·2–64·6)	15·3 (14·4–16·3)	90·4 (88·9–91·7)	84·6 (83·4–85·7)	38·9 (36·0–41·8)	86·8 (85·5–87·9)	61·9 (59·1–64·6)	65·8 (63·8–67·7)
Netherlands	20·4 (19·7–21·2)	58·1 (57·6–58·7)	59·0 (58·2–59·7)	13·4 (13·1–13·7)	88·4 (87·7–89·1)	84·5 (84·0–84·9)	39·9 (38·7–41·1)	83·4 (82·8–83·9)	52·7 (51·7–53·7)	59·3 (58·4–60·1)
Southern Europe	29·6 (29·2–30·0)	58·5 (58·1–58·8)	55·4 (54·9–55·9)	13·2 (13·0–13·4)	82·6 (82·1–83·2)	83·6 (83·3–83·9)	38·0 (37·3–38·7)	86·3 (86·0–86·7)	64·4 (63·8–65·0)	58·7 (58·2–59·2)
Croatia	21·3 (20·2–22·5)	49·6 (48·3–50·8)	48·5 (47·1–49·8)	14·8 (14·2–15·5)	70·6 (68·5–72·6)	76·3 (75·1–77·5)	38·6 (36·6–40·6)	71·3 (69·4–73·1)	60·7 (58·5–62·8)	47·6 (45·7–49·5)
Italy*	32·4 (31·7–33·0)	60·8 (60·4–61·3)	58·3 (57·6–59·0)	14·3 (14·0–14·6)	85·4 (84·7–86·1)	85·5 (85·1–85·8)	38·1 (37·2–39·1)	88·6 (88·1–89·0)	67·1 (66·4–67·9)	61·6 (61·0–62·3)
Malta	18·7 (14·2–23·6)	58·1 (53·4–62·4)	52·8 (46·5–58·7)	10·3 (7·9–13·0)	87·7 (78·7–93·1)	80·8 (77·0–84·0)	39·3 (32·2–46·2)	84·9 (79·0–89·2)	48·4 (39·3–56·9)	47·8 (41·8–53·6)
Portugal*	31·8 (30·9–32·7)	58·3 (57·3–59·2)	56·0 (54·8–57·3)	11·2 (10·6–11·9)	80·3 (78·4–82·1)	83·3 (82·4–84·2)	41·0 (38·6–43·3)	89·2 (88·1–90·2)	66·7 (64·4–69·0)	54·2 (52·7–55·6)
Slovenia	26·6 (24·9–28·4)	54·0 (52·2–55·8)	49·7 (47·7–51·6)	10·7 (9·9–11·6)	80·4 (78·0–82·5)	78·7 (77·2–80·2)	37·9 (34·9–40·9)	74·4 (72·2–76·4)	57·1 (54·0–60·0)	55·3 (52·7–57·7)
Spain*	25·6 (24·3–26·8)	57·1 (56·1–58·1)	56·4 (55·0–57·7)	10·7 (10·2–11·2)	84·6 (82·9–86·1)	82·8 (81·9–83·6)	36·8 (34·7–38·9)	84·7 (83·8–85·6)	57·8 (56·0–59·6)	60·4 (58·9–61·9)
Eastern Europe	18·8 (18·4–19·2)	49·4 (48·9–49·8)	44·6 (44·1–45·1)	10·6 (10·4–10·9)	74·3 (73·6–75·1)	73·7 (73·2–74·1)	34·4 (33·7–35·1)	72·0 (71·3–72·6)	57·5 (56·8–58·2)	49·7 (48·9–50·5)
Bulgaria	11·9 (11·1–12·7)	45·2 (44·1–46·3)	38·4 (37·1–39·6)	6·2 (5·8–6·7)	49·6 (47·0–52·1)	71·7 (70·6–72·7)	33·4 (31·7–35·1)	50·5 (48·4–52·5)	44·2 (41·9–46·5)	37·8 (35·7–39·8)

(Continues on next page)

	Stomach cancer	Colon cancer	Rectal cancer	Lung cancer	Skin melanoma	Breast cancer (women only)	Ovarian cancer	Prostate cancer	Kidney cancer	Non-Hodgkin lymphoma
(Continued from previous page)										
Czech Republic	22·0 (21·1–23·0)	52·5 (51·8–53·2)	48·7 (47·9–49·6)	11·5 (11·0–11·9)	83·4 (82·4–84·3)	78·0 (77·3–78·7)	36·3 (35·0–37·6)	78·2 (77·1–79·2)	59·9 (58·9–60·9)	57·3 (56·0–58·5)
Estonia	22·8 (21·0–24·7)	51·7 (49·2–54·2)	47·9 (45·0–50·8)	11·7 (10·5–13·0)	71·7 (67·7–75·2)	72·1 (69·8–74·3)	34·1 (30·8–37·5)	72·9 (69·7–75·8)	61·1 (57·6–64·4)	51·6 (48·2–54·9)
Latvia	20·2 (18·7–21·7)	42·9 (40·8–45·0)	36·1 (33·7–38·4)	12·2 (11·2–13·2)	65·1 (61·3–68·6)	69·3 (67·4–71·1)	33·7 (31·2–36·2)	65·7 (62·8–68·4)	59·3 (56·5–61·9)	47·0 (43·5–50·4)
Lithuania	23·1 (21·9–24·4)	47·1 (45·3–48·9)	43·0 (41·1–44·9)	9·1 (8·4–9·9)	69·2 (66·1–72·1)	66·7 (65·1–68·2)	31·7 (29·7–33·8)	82·8 (80·9–84·5)	59·4 (57·2–61·6)	49·3 (47·0–51·6)
Poland*	15·6 (14·4–16·7)	46·7 (45·3–48·1)	44·3 (42·6–45·9)	14·4 (13·8–15·0)	61·5 (58·9–64·0)	71·6 (70·3–72·9)	34·5 (32·5–36·5)	66·6 (64·6–68·5)	55·1 (53·0–57·1)	44·3 (42·2–46·3)
Slovakia	20·9 (19·6–22·1)	51·4 (50·2–52·7)	44·7 (43·3–46·1)	10·3 (9·6–11·0)	74·7 (72·8–76·6)	73·9 (72·6–75·2)	34·5 (32·2–36·8)	65·3 (63·2–67·4)	57·3 (55·1–59·5)	48·5 (46·5–50·5)

Data are % relative survival (95% CI). European mean data are population-weighted means of the country-specific relative survival estimates. *Countries with only part of national population covered by cancer registration.

Table 2: **5-year age-standardised relative survival for adult patients with cancer, diagnosed 2000–07**

For patients with rectal cancer, the European mean age-standardised 5-year survival was 55·8% (95% CI 55·5–56·1), and was better for women than for men (appendix). Central and northern Europe had highest survival, with several countries above 60%. Southern Europe and the UK and Ireland had intermediate survival, and eastern Europe had much lower survival (table 2). Survival age trends were similar for all regions: little difference up to age 74 years, with a substantial drop thereafter (figure 2, appendix). European survival increased from 52·1% (51·6–52·6) in 1999–2001 to 57·6% (57·1–58·1) in 2005–07, with the steepest increase in eastern Europe (figure 3, appendix).

The European mean age-standardised 5-year survival for lung cancer was the poorest of the ten index cancers (13·0%, 95% CI 12·9–13·1), and better for women than for men (appendix). Geographical differences were small, varying from 9·0% (8·8–9·1) in the UK and Ireland to 14·8% (14·6–14·9) in central Europe. Age was a strong determinant of survival, ranging from 24·3% (23·4–25·1) for patients aged 15–44 years, to 7·9% (7·7–8·1) for patients aged older than 75 years (figure 2, appendix). European 5-year survival increased significantly from 11·6% (11·4–11·8) in 1999–2001 to 13·4% (13·2–13·6) in 2005–07 (appendix), with similar trends in each region (figure 3, appendix).

European mean age-standardised survival for skin melanoma was good (83·2%, 95% CI 82·9–83·6), but women had much better survival than men (appendix). For most regions, survival was 80–90%, but for eastern Europe it was generally 50–75%. Exceptions were Croatia—with similar survival to eastern Europe—and Czech Republic (which had above regional mean survival; table 2). Survival decreased steadily with age in all regions (figure 2, appendix). Survival increased from 82·4% (81·9–83·0) in 1999–2001 to 85·2% (84·7–85·6) in 2005–07, with the largest increase in eastern Europe (figure 3, appendix).

For most countries, 5-year survival for breast cancer (women only) was fairly close to the European mean (81·8%, 95% CI 81·6–82·0). In all regions except eastern Europe, survival was 76–86% (table 2). In all northern and central European countries, and also Italy, Spain, and Portugal, survival was greater than 80% (table 2). In most eastern European countries—except Czech Republic—survival was 10–15% lower than in the rest of Europe. For all regions, survival peaked at 45–54 years, and fell with age thereafter (figure 2, appendix). Survival of women aged 75 years and older was particularly low in the UK and Ireland, accounting for most of the survival difference between these countries and the European mean (figure 2, appendix). Survival for the whole of Europe increased over time: from 78·4% (78·1–78·8) in 1999–2001 to 82·4 (82·2–82·7) in 2005–07 (figure 3, appendix); this increase was steepest in eastern Europe and the UK and Ireland, so the survival gap between these regions and Europe decreased.

For ovarian cancer, European mean age-standardised 5-year survival was low (37·6%, 95% CI 37·1–38·0) and decreased steeply with advancing age (70·9%, 69·6–72·1 at 15–44 years; 20·1%, 19·2–21·1 at ≥75 years). Geographical variation was substantial, with survival ranging from 31·0% (30·6–31·5) in the UK and Ireland, to 41·1% (40·3-42·0) in northern Europe (table 2). Survival did not change significantly over time Europe overall. Significant ($p<0·05$), although not substantial, changes occurred in all regions except southern Europe; the largest gains were in eastern Europe (figure 3, appendix).

For prostate cancer, European mean age-standardised 5-year survival was high (83·4%, 95% CI 83·1–83·6). In most European countries except those in eastern Europe, survival was roughly 80–90% (exceptions were Croatia, Denmark, and Slovenia; table 2). Survival was lower in eastern Europe, except for Czech Republic and Lithuania. European 5-year relative survival was highest

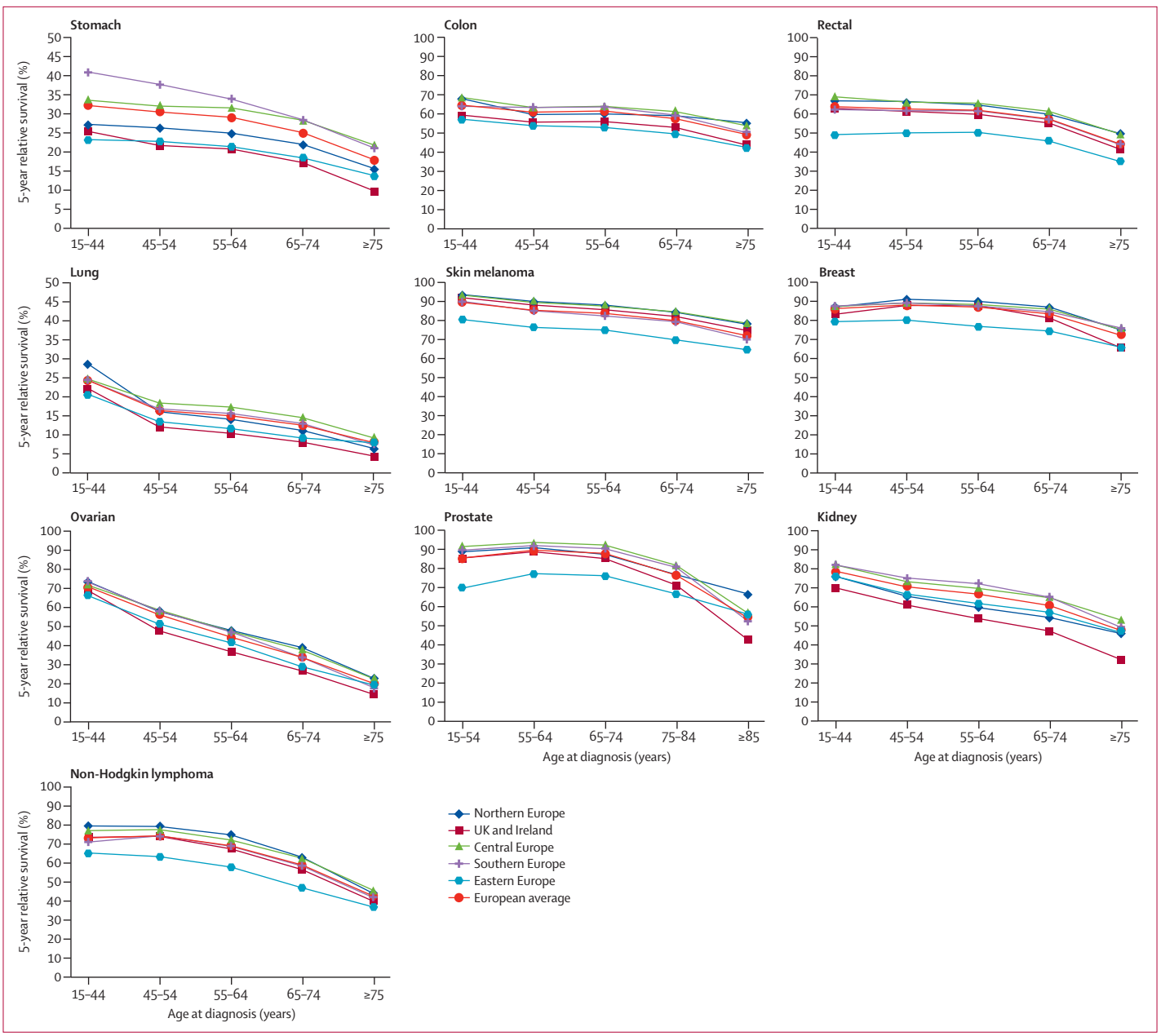

Figure 2: **Age-specific 5-year relative survival for adults with cancer diagnosed in 2000–07**
The European mean is the (population) weighted mean of country-specific relative survival estimates.

at age 55–64 years and lowest for patients aged 85 years and older (figure 2). The fall with age was steeper for the UK and Ireland, central Europe, and southern Europe than for eastern and northern Europe (figure 2). Survival increased over time throughout Europe (from 73·4% [72·9–73·9] to 81·7% [81·3–82·1]) and especially in eastern Europe (figure 3, appendix), so the gap between eastern Europe and the overall European mean decreased from 15·2% in 1999–2001 to 5·7% in 2005–07.

For kidney cancer, the European mean age-standardised 5-year survival was 60·6% (95% CI 60·2–61·0); with better survival for women than for men. Survival differences within European regions were large. Survival was best (above 60%) in southern and central Europe, particularly Austria, Belgium, France, Germany, Italy, and Portugal (table 2). Survival was intermediate (50–60%) in most other countries, but was below 50% in Bulgaria, Denmark, and UK (table 2). Survival fell steeply with age (figure 2). Survival was lowest for the oldest patients in the UK and Ireland. Survival improved over time in all regions (figure 3, appendix). 5-year survival overall for Europe increased significantly from 56·4%

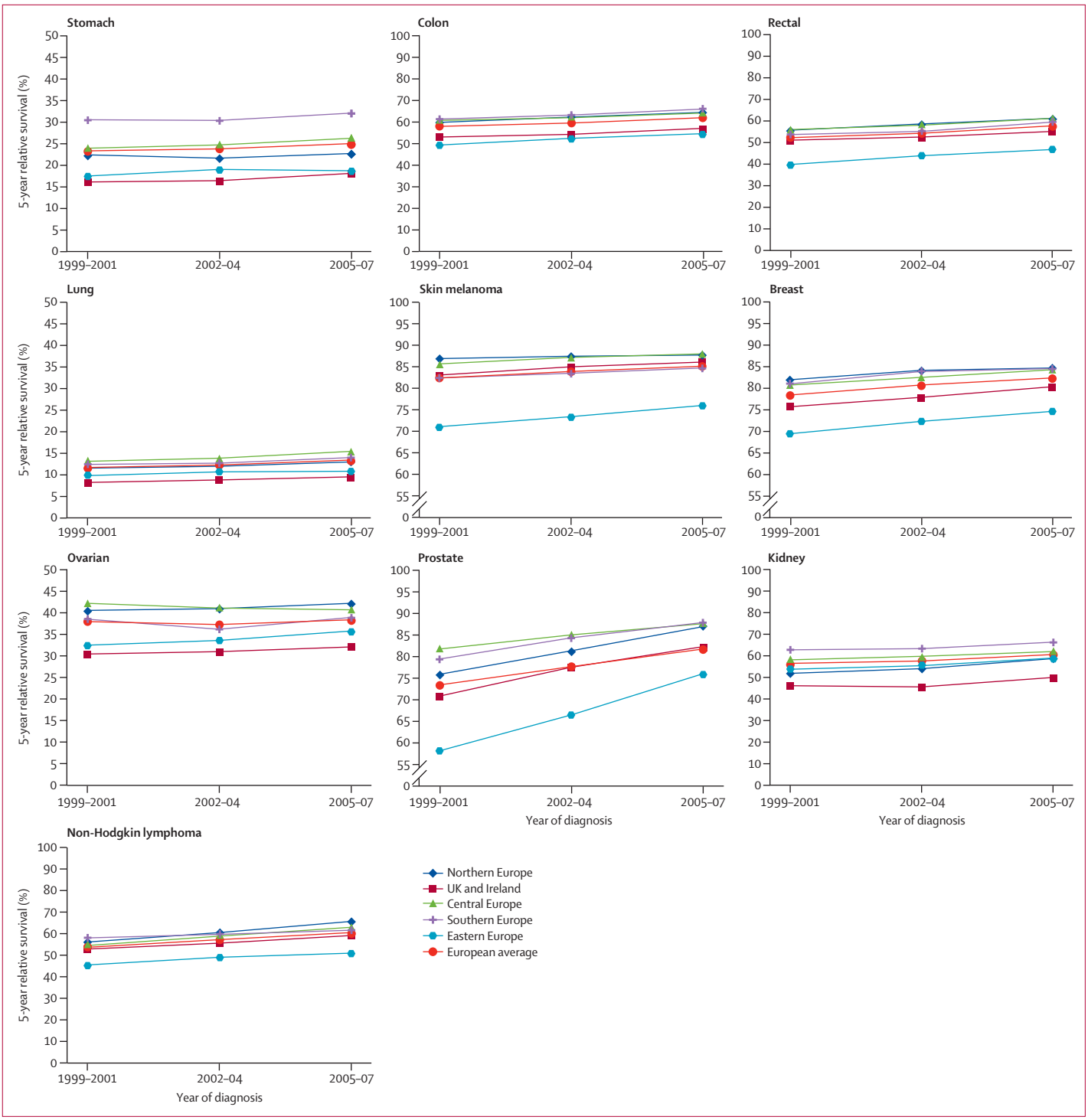

Figure 3: **Age-standardised 5-year relative survival for adult cancer patients followed up in 1999–2001, 2002–04, and 2005–07**
The European mean is the (population) weighted mean of country-specific relative survival estimates.

(55·7–57·0) in 1999–2001 to 60·5% (59·9–61·0) in 2005–07 (p<0·0001).

For non-Hodgkin lymphoma, European mean age-standardised 5-year survival was 59·4% (95% CI 59·0–59·7); and higher for women then men (appendix). Survival ranged from 49·7% (48·9–50·5) in eastern Europe to 63·3% (62·7–63·9) in northern Europe (table 2). Significant outliers were Czech Republic,

Iceland, and Ireland (above region means), and Bulgaria, Croatia, and Malta (below region means). Regional differences were greater for young patients than for old patients; survival fell after age 55 years (figure 2). Survival improved with time, from 53·8% (53·3–54·4) in 1999–2001, to 60·4% (60·0–60·9) in 2005–07 (p<0·0001), especially for northern Europe and central Europe, so that geographical differences have widened over time (figure 3, appendix).

Survival for rapidly fatal cancers (oesophagus, liver, pancreas, and pleura) varied by country (appendix). Incidence rates and 5-year survival by country were highly correlated for breast cancer (Pearson's correlation coefficient 0·78), prostate cancer (0·73), and skin melanoma (0·73; appendix).

Discussion

The EUROCARE project provides the largest European population-based dataset for comparison of cancer survival with a unique standardised protocol for data collection, checking, and analysis. The survival differences by region and time period were not systematic but varied both by cancer type and by age group, and were consistent with the range of variation reported previously.[3,25] The proportion of the European population monitored was larger in this study than in previous EUROCARE studies. The most important additions were for eastern Europe, with the national registries of Bulgaria, Estonia, Latvia, Lithuania, and Slovakia now included. Population coverage also increased for other countries: from 1% to 23% for Germany, 34% to 100% for Netherlands, 8% to 100% for Czech Republic, 43% to 76% for Portugal, and 27% to 35% for Italy. Increased coverage for Czech Republic resulted in higher survival than in EUROCARE-4, in which only West Bohemia was represented, whereas for the other countries with increased coverage, survival rankings relative to previous EUROCARE studies were similar.[25] The large study size, wider population coverage in eastern, central, and southern regions, and increased number of countries covered by national registries, all contributed to improving the robustness of the survival estimates, rendering them more representative of the cancer survival range in Europe as a whole (panel).

International variation in the quality of cancer registration has often been invoked to explain international survival differences, but results of a simulation study show that even implausibly high proportions of errors—eg, routine registration of recurrences as new diagnoses or failure to capture long-term survivors—could not explain the survival differences between the UK and other European countries.[26] Nevertheless, incomplete follow-up (some deaths not recorded) and failure to capture all incident cases can bias survival comparisons, particularly for cancers that have a poor prognosis;[27] thus, we excluded registries with high proportions of cases discovered by death certificate-only. Very low proportions of death certificate only cases also raise concern, because some rapidly fatal cases might not be registered. Incomplete ascertainment of fatal cases is also possible for registries that do not use death certificates as a routine source of notification. A high proportion of patients who were alive and censored before the end of follow-up, because of difficulties with updating vital status information or because of emigration, can—although not necessarily—imply selective censoring and survival biases.

Survival for rapidly fatal cancers (ie, oesophagus, lung, pancreas, pleura, and liver cancer) was analysed partly to investigate such shortcomings (appendix). Survival was unexpectedly high for Austria, Belgium, Croatia,[28] Germany, and Poland, suggesting difficulties with ascertainment of vital status. Findings for Estonia and Lithuania do not suggest substantial overestimation, although privacy regulations limited access to mortality data for the study period.[29] Such hindrances can severely bias long-term survival estimates, and also suggest that caution is needed for interpretation of 5-year survival differences for cancers with poor prognosis, since survival estimates for these cancers are particularly sensitive to poor quality of follow-up data.

Eight of the 29 participating countries did not have national registration. This shortcoming is not an issue of data quality but is a result of the variation in implementation of cancer registration across Europe. The extent to which a regional registry population is

Panel: Research in context

Systematic review

The survival of patients with cancer increased steadily in Europe from 1980 to 2002,[1–4] but international differences were still large for patients diagnosed up to 2002, with high survival in northern and central Europe and low survival in the UK and eastern Europe.[4,5] Major changes in cancer diagnosis and treatment occurred in 2000s.[9,11,12,14] The EUROCARE-5 study assessed the effect of these changes on population-level survival in 29 European countries, and to provide some of the evidence needed to formulate more effective policies to control cancer.

Interpretation

Estimates of population-based 5-year relative survival from EUROCARE-5 include data for more than 10 million patients diagnosed from 1995 to 2007: an unprecedented 50% of the population of the 29 participating countries, with wider coverage (particularly in eastern Europe) than any previous study. Survival increased steadily in all countries, particularly for non-Hodgkin lymphoma and rectal cancer, possibly because of improved treatment and—for prostate cancer—probably in relation to earlier diagnosis. Differences between countries remained large within Europe, but the survival gap between eastern Europe and the rest of Europe fell (except for non-Hodgkin lymphoma). Now with national coverage, survival in the Czech Republic was shown to be closer to the European mean than in previous studies. Survival in the UK and Ireland was close to the European mean for rectal cancer, breast cancer, prostate cancer, and skin melanoma, but remained low for other cancers. Possible explanations for persistent international differences in survival include differences in cancer biology, use of diagnostic tests and screening, stage at diagnosis, and access to high-quality care. Further studies and more detailed data are needed to disentangle all the factors affecting cancer outcome.

representative of the whole nation depends on variation in socioeconomic status within a country. In Italy and Belgium registries were mainly located in affluent regions (northern Italy and Flanders), which might have had better than average survival, whereas little evidence exists of similar patterns in France, Germany, or Spain. The increased coverage for Germany, Netherlands, and Portugal compared with previous EUROCARE studies did not modify the survival ranking of these countries. On the contrary, the survival ranking of Czech Republic was higher than that formerly estimated for the single region of West Bohemia.

The differences in survival partly represent differences in resources allocated to health care, so that countries with high total national expenditure on health generally had better survival than did countries that spent less.[4,30] Nevertheless, differences in survival between countries with similar medium-to-high total national expenditure on health suggest that health spending is not the only factor affecting cancer outcome.

Differences in cancer survival can be affected by factors other than the provision and organisation of health care, such as socioeconomic status, lifestyle, and general health status differences between populations. In turn, these factors are likely to lead to differences in health-care-seeking behaviours, patient management decisions, and treatment effectiveness that can directly or indirectly affect cancer outcomes. In particular, a poor performance status because of comorbidities can limit the treatment options and their efficacy, and thus reduce cancer survival.

Variation in casemix between countries, by histology or subsite, with concomitant differences in prognosis (eg, small cell *vs* non-small cell lung cancers), could also contribute to survival differences. For example, the proportion of gastric cardia cancers, which have poorer prognosis than gastric cancers at distal subsites,[31] ranged from 5% to 40% and exceeded 25% in some countries with poor survival and low stomach cancer incidence (Denmark, Netherlands, and UK).

Mass screening and intense diagnostic activity—increasing both incidence and survival—can also contribute to variations in survival. Early diagnosis increases detection of early-stage cancers, which might respond well to treatment, but can also result in overdiagnosis and lead-time bias, which prolong survival without significantly reducing mortality. These effects are well documented for prostate cancer, for which international differences for survival and incidence closely relate to differences of testing for prostate-specific antigen.[32] We report strong correlations between incidence and survival by country for breast cancer, prostate cancer, and skin melanoma (appendix): all cancers that are targeted for early diagnosis.

However, the main limitation to the interpretation of differences of cancer survival is the absence of information about major prognostic factors such as stage at diagnosis and treatment. Detailed information for these factors is needed to fully assess survival differences. At present, such data are usually only obtained by ad-hoc studies of samples of cases—systematic collection of clinical data by European cancer registries would be useful. Furthermore, staging practices vary over time and region, and although staging changes as scientific understanding improves, it would be an advantage if practices were uniform across the continent.[33]

The survival gap of eastern Europe was larger at young and intermediate ages than in elderly patients for non-Hodgkin lymphoma, rectal cancer, prostate cancer, and breast cancer. The major socioeconomic upheavals that convulsed some eastern European countries from the 1990s did not spare their health-care systems. Shortage of public funding,[30] absence of national cancer plans, late or incomplete implementation of screening programmes,[8,34,35] decentralisation of cancer care, and poor access to standard care[30] might all be related to poorer survival in eastern Europe.

The low survival of UK and Danish cancer patients has been extensively analysed; the main cause seems to be delayed diagnosis.[36–38] Underuse of potentially successful treatments (possibly related to advanced stage at presentation) and poor or unequal access to treatment also seem to play a part, particularly for colorectal,[36,39] lung,[36] and ovarian cancers.[40] Older English women with breast cancer have been reported to be more likely than young patients to receive non-standard treatments, including under-utilisation of surgery, failure to perform standard assessments, and failure to give radiotherapy after conservative surgery.[41,42] A study comparing prostate cancer survival in England, Norway, and Sweden showed poorer survival for elderly prostate cancer patients in England than in the other countries, with a higher proportion of men in England diagnosed at a very advanced stage.[43] Survival disparities by age are an important public health issue and will be analysed in further EUROCARE studies.

The substantial improvements in 5-year relative survival for non-Hodgkin lymphoma are probably related to major treatment advances since the 1990s. High-dose chemotherapy, autologous stem-cell reconstitution, and anti-CD20 monoclonal antibody (rituximab), in combination with chemotherapy and radiotherapy, became established treatments for patients with indolent and aggressive non-Hodgkin lymphoma.[44] Lack of access to modern treatment protocols might be one reason why survival for non-Hodgkin lymphoma was worse for eastern Europe than the other regions.

The improvement in mean European survival for rectal cancer is probably related to an increase in the proportion of patients receiving curative surgery, widespread adoption of total mesorectal excision,[45] the development of effective neoadjuvant radiotherapy,[46] and improved early postoperative care.[47]

The increases in survival over time and disparities in cancer survival across Europe suggests that further

improvements could be made by application of proven treatment protocols and ensuring that all cancer patients have access to early diagnosis and high quality treatment. The aim of monitoring international differences of cancer survival is to identify regions where survival can be improved, and to stimulate research into the clinical reasons for survival differences. Survival is a complex indicator. Longer survival might be a result of better treatments or improved efficacy of existing treatments applied to patients diagnosed earlier. However, other factors—eg, amount of diagnostic testing, cancer biology, comorbidities, and socioeconomic status—can directly or indirectly affect trends of survival. Analytical studies are needed to assess the effect of stage, staging practices, and treatment protocols on survival differences. The prerequisite for such studies is routine collection of detailed clinical information by cancer registries.

Population-based survival is a measure of the survival of practically all cancer patients, not simply those enrolled in clinical trials, and is thus an indicator of the effectiveness of cancer control in health-care systems. Survival—as well as incidence—can be inflated by overdiagnosis and lead time bias, which arise from early diagnosis initiatives, so changes in survival over time need to be investigated alongside trends in incidence and mortality to interpret progress and to formulate effective cancer control policies; mortality on its own—a consequence of past incidence and survival trends—is insufficient.[48–50]

Contributors

MS, RC, FB, MPC, and RDA drafted the study protocol. RDA, RC, and MS designed the study and drafted the report. The EUROCARE-5 Working Group revised the study protocol, collected, prepared, and transmitted raw data for the study database, corrected data after quality controls, and checked the results of the analyses. RDA, RC, SF, DP, PB, AT, and MS prepared data and did quality controls. RDA, SF, RC, and DP did the statistical analyses. MPC, FB, AT, OV, HB, EA, MB-L, GE, AN, and SS revised the report. All authors interpreted data, wrote the report, and reviewed and approved the final version.

Conflicts of interest

We declare that we have no conflicts of interest.

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