EUROCARE-5 on-line database

Data and methods

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

De Angelis R, Sant M, Coleman MP, Francisci S, Baili P, Pierannunzio D, Trama A, Visser O, Brenner H, Ardanaz E, Bielska-Lasota M, Engholm G, Nennecke A, Siesling S, Berrino F, Capocaccia R; EUROCARE-5 Working Group.

Lancet Oncol. 2014 Jan;15(1):23-34.

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), as in EUROCARE-4. Haematological neoplasms were defined in accordance with WHO classification. 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.

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.

Data quality checks

We applied standardised quality control procedures 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 99 cancer 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 **(table 1)**. 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.

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 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.

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%).

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 from lifetables of all-cause mortality by age, sex, cancer registry, and calendar year. Lifetables were smoothed 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. 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. 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, so that the lower bound of the CI was always positive. The analyses were done with SEER*Stat (version 8.0.4).

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. 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. 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. 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; 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 (**table 2**). Survival was unexpectedly high for Austria, Belgium, Croatia, 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. 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 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.

Table 1: Populations represented in the EUROCARE-5 study, with average proportions (%) of national population covered by cancer registration. Overall number and data quality indicators for adult malignant cancer cases included in the cohort 2000-2007 survival analysis.

Country/Area	National population covered by cancer registration, %	Number of cases diagnosed 2000–07	Excluded			Included in analyses	Quality indicators		
			Major errors %	DCO, % (1)	Autopsy, % (2)		MV, % (3)	Lost to follow-up % (4)	Unspecified morphology % (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
Northern Europe	**100**	**978,483**	**0·2**	**0·4**	**1·2**	**961,454**	**95·4**	**0·3**	**1·5**
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
Ireland and UK	**100**	**3,028,148**	**0·3**	**2·5**	**0·0**	**2,941,509**	**88·6**	**0·4**	**1·0**
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
The Netherlands	100	637,655	0·0	-	0·3	635,719	95·9	0·8	0·3
Central Europe	**35**	**2,348,989**	**0·1**	**4·4**	**0·1**	**2,229,993**	**96·1**	**2·0**	**0·6**
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
Southern Europe	**36**	**1,480,994**	**0·3**	**1·6**	**0·2**	**1,443,058**	**89·2**	**1·4**	**1·2**
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
Eastern Europe	**52**	**1,184,455**	**0·7**	**5·0**	**2·0**	**1,092,709**	**86·5**	**1·1**	**1·8**
European mean	**50**	**9,021,069**	**0·3**	**2·9**	**0·5**	**8,668,723**	**91·1**	**1·1**	**1·1**

(1) Proportion of cases known by death certificate only (DCO)

(2) Proportion of cases diagnosed incidentally at autopsy

(3) Proportion of microscopically verified cases

(4) Proportion of alive cases diagnosed in 2000-2003 censored with less than five years of follow-up. For the French registries this quality indicator was calculated on cases diagnosed in 2000-2002

(5) Proportion of cases with ICD-O-3 morphology codes 8000-8005 (morphology not specified)

* The Danish cancer registry provided specific ICD-O-3 morphology codes only for skin melanoma and haematological malignancies

'-' Not available because death certificate information is not used in the registration process

Table 2 : Age-standardised five-year relative survival (RS,%) for adult patients diagnosed in 2000-2007 with cancers of oesophagus, liver, pancreas, pleura and lung, by European country, with corresponding number of cases (N) and 95% confidence interval (95% CI). European average figures are population-weighted averages of the country-specific relative survival estimates. In bold values with lower limit of 95% confidence interval over the 3rd quartile.

European country	Oesophagus			Liver			Pancreas			Pleura			Lung		
	N	RS	95% CI	N	RS	95% CI	N	RS	95% CI	N	RS	95% CI	N	RS	95% CI
Denmark	3,165	8·9	(7·6-10·2)	2,159	5·1	(3·9-6·5)	6,502	4·2	(3·5-5·0)	735	4·6	(2·8-7·2)	30,964	10·3	(9·8-10·8)
Finland	1,798	12·0	(10·0-14·1)	2,292	7·8	(6·3-9·5)	6,604	4·6	(3·8-5·5)	605	6·3	(4·3-8·9)	16,467	11·5	(10·8-12·2)
Iceland	120	-	-	56	-	-	230	4·5	(1·7-9·5)	16	-	-	1,112	13·9	(11·5-16·7)
Norway	1,442	10·0	(7·8-12·5)	943	8·1	(6·0-10·6)	4,933	5·0	(4·1-6·0)	577	-	-	18,034	12·9	(12·3-13·6)
Sweden	3,128	11·7	(10·2-13·2)	2,549	10·4	(8·9-12·0)	6,814	5·5	(4·7-6·3)	937	-	-	24,845	14·7	(14.1-15.3)
Ireland	2,673	**15·6**	(13·8-17·4)	940	13·0	(10·4-15·9)	3,029	6·9	(5·7-8·2)	230	-	-	13,721	11·8	(11·1-12·6)
UK, England	49,286	12·4	(12·0-12·8)	17,580	8·2	(7·7-8·8)	46,571	4·7	(4·4-5·0)	13,166	4·5	(3·8-5·3)	239,688	8·8	(8·6-9·0)
UK, Northern Ireland	1,283	**16·1**	(13·6-18·8)	461	8·9	(5·7-12·9)	1,321	3·0	(1·8-4·8)	255	-	-	7,204	11·0	(10·0-12·1)
UK, Scotland	6,492	11·0	(9·9-12·1)	2,443	7·4	(6·0-8·9)	4,946	3·4	(2·7-4·3)	1,736	-	-	37,120	8·7	(8·2-9·1)
UK, Wales	3,444	13·1	(11·6-14·7)	1,199	8·7	(6·6-11·1)	3,149	5·4	(4·3-6·6)	592	4·8	(2·5-8·2)	16,274	8·6	(7·9-9·2)
Austria	2,567	**16·3**	(14·5-18·2)	5,327	11·8	(10·7-12·9)	8,295	7·9	(7·1-8·7)	540	**9·3**	(6·4-12·9)	27,197	**16·7**	(16·1-17·2)
Belgium	3,936	**21·8**	(20·2-23·4)	1,748	**17·7**	(15·5-20·0)	4,826	**10·5**	(9·4-11·6)	1,102	4·3	(2·7-6·6)	30,925	**15·4**	(14·9-16·0)
France	4,499	13·9	(12·7-15·1)	5,706	13·1	(12·1-14·2)	5,347	7·4	(6·5-8·3)	610	6·6	(3·8-10·4)	17,709	13·8	(13·2-14·4)
Germany	9,037	**16·2**	(15·1-17·3)	8,515	**13·4**	(12·4-14·3)	17,630	**8·7**	(8·2-9·3)	2,275	**9·6**	(7·8-11·5)	72,177	**15·6**	(15·3-16·0)
Switzerland	1,190	**18·4**	(15·6-21·5)	1,656	13·2	(11·2-15·3)	2,277	6·6	(5·2-8·3)	304	7·0	(3·6-12·0)	8,800	**15·3**	(14·4-16·3)
The Netherlands	11,629	13·0	(12·2-13·8)	2,616	10·3	(8·9-11·8)	13,019	4·0	(3·6-4·5)	3,390	4·0	(2·8-5·4)	77,854	13·4	(13·1-13·7)
Croatia	1,676	10·2	(8·2-12·5)	2,745	12·1	(10·6-13·7)	4,441	**10·9**	(9·8-12·1)	442	**13·5**	(9·4-18·4)	22,777	**14·8**	(14·2-15·5)
Italy	5,488	11·7	(10·7-12·8)	24,443	**16·1**	(15·5-16·8)	22,138	7·2	(6·7-7·7)	4,462	7·2	(6·0-8·4)	83,934	14·3	(14·0-14·6)
Malta	86	-	-	63	-	-	307	-	-	42	-	-	956	10·3	(7·9-13·0)
Portugal	2,530	10·0	(8·6-11·5)	1,944	12·1	(10·5-13·9)	2,881	**8·7**	(7·6-10·0)	255	-	-	14,642	11·2	(10·6-11·9)
Slovenia	712	8·3	(6·1-11·0)	1,009	3·9	(2·6-5·7)	2,016	5·0	(3·9-6·3)	329	3·8	(1·9-6·6)	8,926	10·7	(9·9-11·6)
Spain	1,730	9·3	(7·8-11·1)	3,416	**14·3**	(13·0-15·7)	3,493	6·0	(5·1-7·0)	285	3·3	(1·5-6·4)	16,756	10·7	(10·2-11·2)
Bulgaria	1,145	6·1	(4·2-8·5)	2,911	4·2	(3·3-5·4)	6,690	5·1	(4·4-5·8)	282	-	-	25,693	6·2	(5·8-6·7)
Czech Republic	3,282	10·6	(9·2-12·1)	4,327	5·8	(4·9-6·8)	11,279	5·6	(5·0-6·2)	444	6·2	(3·4-10·0)	42,502	11·5	(11·0-11·9)
Estonia	426	7·0	(4·2-10·8)	459	5·5	(3·3-8·6)	1,431	5·5	(4·1-7·3)	30	-	-	5,392	11·7	(10·5-13·0)
Latvia	809	-	-	429	-	-	2,367	5·5	(4·4-6·9)	85	-	-	8,379	12·2	(11·2-13·2)
Lithuania	1,121	5·7	(3·8-8·1)	844	8·8	(6·6-11·3)	2,918	6·1	(5·1-7·2)	75	-	-	10,522	9·1	(8·4-9·9)
Poland	1,328	6·5	(4·7-8·6)	840	7·1	(5·1-9·5)	3,680	7·9	(6·9-9·0)	223	**14·1**	(9·3-20·0)	23,387	**14·4**	(13·8-15·0)
Slovakia	1,658	6·9	(5·1-9·1)	1,297	6·5	(5·0-8·3)	3,449	5·9	(5·0-6·9)	122	-	-	13,284	10·3	(9·6-11·0)
European mean	127,680	12·4	(12·2-12·6)	100,917	11·7	(11·5-11·8)	202,583	6·9	(6·8-7·0)	34,146	7·2	(6·9-7·5)	917,241	13·0	(12·9-13·1)