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Survival from common and rare cancers in Germany in the early 21st century

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Background: Until recently, population-based data of cancer survival in Germany mostly relied on one registry covering \sim 1 million people (1.3% of the German population). Here, we provide up-to-date cancer survival estimates for Germany based on data from 11 population-based cancer registries, covering 33 million people and compare them to survival estimates from the United States.

Patients and methods: Cancer patients diagnosed in 1997–2006 were included. Period analysis was employed to calculate 5-year relative survival for 38 cancers for 2002–2006. German and USA survival rates were compared utilizing the Surveillance, Epidemiology and End Results 13 database.

Results: Five-year relative survival >80% was observed for testicular cancer (93.5%), skin melanoma (89.4%), cancers of the prostate (89.1%) and thyroid (87.8%), Hodgkin's lymphoma (84.5%) and cancers of the breast (83.7%) and endometrium (81.0%), which together account for almost 40% of cases. For the majority of cancers, German survival estimates were close to or below those in the United States. Exceptions with higher survival in Germany were cancers of the stomach, pancreas and kidney and Hodgkin's lymphoma.

Conclusions: German cancer survival estimates are mostly higher than the 2000–2002 pan-European estimates. Further research is needed to investigate causes responsible for differences between German and USA cancer survival rates.

Key words: cancer survival, Germany, period analysis

introduction

Three of the 10 leading causes of death in Germany are cancers of the lung, colorectum and breast [1], which emphasize the importance of monitoring survival of cancer patients. Population-based cancer survival data provide important prognostic information for clinicians, patients and public health decision makers.

Until recently, population-based data on cancer survival in Germany mostly relied on the Saarland Cancer Registry, which covers only ~1 million people (1.3% of the German population) [2]. In particular, Germany was represented in international comparative studies (EUROCARE, EUNICE) so far by the Saarland and occasionally by the Munich Cancer

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Registry only [3–6]. By now, population-based cancer registries have been built up in all federal states of Germany and a collaborative project funded by the German Cancer Aid was set up between 13 population-based German cancer registries and the Division of Clinical Epidemiology and Aging Research at the German Cancer Research Center (DKFZ) in order to provide comprehensive monitoring of cancer survival in Germany.

This article gives an overview of the data collection and provides the most comprehensive report available to date on overall and age-specific 5-year relative cancer survival in Germany for the period of 2002–2006 for the 25 most common forms of cancer representing >95% of the cancer cases in the pooled dataset. In addition, 5-year relative survival is provided for 13 rare cancers for which population-based survival estimates are generally sparse. Furthermore, comparisons of cancer survival in Germany and the United States are provided. In order to achieve up-to-date monitoring of cancer survival, period analysis was used allowing the exclusive use of the most recent available follow-up information [7].

materials and methods

data sources

Data were submitted for the present project from cancer registries covering 12 out of the 16 German federal states and the Münster administrative district of North Rhine-Westphalia. According to the estimations from the Robert Koch Institute (Germany's central public health institute), the completeness of cancer registration was >80% in all states and >90% in most states in 2004-2006 [8]. Degree of completeness was calculated using incidence/mortality ratio. Expected incidence data were initially retrieved from the Saarland Cancer registry, the only population-based cancer registry in Germany working continuously for >40 years. The development of the age-specific quotients over time is modeled in a log-linear approach with polynomial trends. Further registries successively contribute to the data pool of reference registry, once the completeness of these registries has been confirmed in a comparison with the Saarland [8].

In two federal states of Germany (Baden-Württemberg and Hesse), cancer registration is still in an early phase of build-up; data from Berlin were not delivered due to known major deficiencies in the completeness of registration. After detailed additional datachecks, data from two registries (Saxony-Anhalt and Thuringia) were excluded from further survival analysis because they did not meet the following criteria: percentage of death certificate only (DCO) cases <20% throughout the study period or decrease by at least two percentage points per year to levels <20% by the end of the study period. The latter criterion was chosen as high DCO rates in initial years of registration of young registries occur even in cases of high completeness of registration. For the states of Bavaria, Schleswig-Holstein and Rhineland-Palatinate, data were used from those administrative regions where these criteria were met. Finally, data from 11 cancer registries, covering a population of 33 million people, were retained (Table 1).

Patients with primary malignant tumors diagnosed in 1997-2006 who were at least 15 years old at the time of diagnosis with follow-up date until the end of December 2006 were included in the analysis. Cancer topography, morphology and behavior were originally coded in accordance with the International Classification of Diseases for Oncology (ICD-O)-3 guidelines and later converted into ICD-10 using 'IARC crgTools' [9].

The registries were recording cancer cases according to rules set up by the International Agency for Research on Cancer (IARC). Cancer patient follow-up was carried out via linkage to death certificates of the respective state and in some registries, additional linkage to population registries in order to get information about deaths or migration to another state. Two of the cancer registries (Hamburg and Bremen) registered out-migrations by record linkage with population registries. Out-migration rates leading to the loss of follow-up were 1.7% in Hamburg and 2.8% in Bremen.

Cases were excluded if they were identified only by death certificate or the diagnosis was issued on the day when the patient died (Table 1). Cases whose cancer diagnosis could not be converted from ICD-O-3 to ICD-10 were not included in survival analysis. Very few cases were removed because of additional problems (e.g. inconsistency of date of diagnosis or date of last follow-up). The percentage of diagnoses that were microscopically confirmed was >90% in all registries (Table 1).

Primary malignant tumors diagnosed in 1997-2006 were selected from the Surveillance, Epidemiology and End Results (SEER) 13 database for comparative analysis. Patients identified by DCO were excluded.

statistical methods

Five-year relative survival estimates for the time period of 2002–2006 were calculated. Relative survival, which quantifies cancer-related excess mortality in the cancer patient population, was calculated as the ratio of the observed survival in the patient group divided by the expected survival of a comparable group in the general population [10]. Expected survival was estimated according to the Ederer II method using life tables stratified by age, sex, calendar period and region as obtained from the participating cancer registries and the German Federal Statistical Office [11]. All relative survival estimates are period estimates, considering only the survival experience in 2002-2006, the most recent 5-year interval for which data were available. Period analysis has been shown to provide more up-to-date estimates of cancer survival than traditional cohort-based analysis [7, 12].

Table 1. Overview of participating cancer registries in the present analysis

Registry	Underlying population in	Diagnosis period	Date of last follow-up	Cases diagnosed (1997–2006)	Microscopically confirmed	Exclusions base	Other ^b	Available cases (1997–2006)
	2006 (million)			(N)	cases (%)	cases ^a (%)	(N)	(N)
Brandenburg	2.55	1961-2006	2006	130 080	96.3	16.0	99	109 207
Mecklenburg- Vorpommern	1.69	1961–2006	2006	87 647	96.2	14.3	46	75 095
Saxony	4.25	1961-2006	2006	232 993	95.8	14.0	50	200 230
Bremen	0.66	1998-2006	2006	34 196	96.7	15.3	9	28 958
Hamburg	1.75	1991-2007	2007	87 146	95.2	14.8	12	74 264
Bavaria ^c	8.13	2002-2006	2006	209 624	99.3	19.0	7	169 729
Saarland	1.04	1970-2006	2006	60 723	97.3	6.8	13	56 554
Lower Saxony	7.98	2001-2006	2008	249 975	90.5	19.3	55	201 716
North Rhine- Westphalia ^c	2.62	1988–2004	2004	99 214	97.1	9.5	30	89 770
Schleswig- Holstein ^c	1.85	1999–2006	2006	95 228	98.4	21.8	16	74 488
Rhineland- Palatinate ^c	0.52	1998–2006	2006	26 200	94.4	18.5	8	21 347
Total	33.04							1 101 358

^aIncluding also cases that were not registered as death certificate only case, but cancer diagnosis was made on the day of death.

bOther: conversion problem from International Classification of Diseases for Oncology (ICD-O)-3 to ICD-10 or inconsistent incidence/death date or missing sex. ^cSelected administrative districts only.

The differences between the survival estimates of the German and American cancer populations were tested for statistical significance by model-based period analysis [13].

For the 25 most common forms of cancer, 5-year overall relative survival estimates were calculated with age adjustment according to the International Cancer Survival Standards using the following age groups: 15–44, 45–54, 55–64, 65–74 and 75+ years [14]. In addition, 5-year survival was estimated for two major age groups: <75 years (age-adjusted estimate using four age groups: 15–44, 45–54, 55–64, 65–74 years) and 75+ years (age-specific estimate). For additional 13 less common cancers, only overall age-adjusted 5-year relative survival is shown.

All calculations were carried out with SAS software (version 9.2; SAS Institute, Cary, NC), using macros developed for period analysis [15].

results

Table 2 shows the number of cases of the 25 most common cancers jointly representing >95% of the total cases of the pooled- German dataset. The most frequent cancer sites (each contributing at least 10% and >100 000 cases to the pooled dataset) were the colorectum, lung, breast and prostate. Another 13 cancer sites that are not among the 25 most frequent ones but contributed at least 500 cases to the pooled dataset are shown in Table 3.

Age-adjusted 5-year relative survival estimates for the 25 most common types of cancer in Germany for the time period of 2002-2006 are shown in Table 4. Survival of cancer patients in Germany ranged from 9.0% (for pancreatic cancer) to 93.5% (testicular cancer). Cases with good prognosis (5-year relative survival >80%) made up almost 37% of the pooled dataset, including women diagnosed with cancers of the breast or endometrium, men with testicular or prostate cancer and patients diagnosed with melanoma, Hodgkin's disease and thyroid cancer. Survival for patients with non-Hodgkin's lymphoma and cancers of the connective tissue, colorectum, larynx, cervix, kidney and bladder was between 80% and 60%. These cases contributed almost 30% of the pooled dataset. Survival between 59% and 20% were observed for patients with seven cancers (leukemia, multiple myeloma and cancers of the stomach, gallbladder, ovary, brain and the oral cavity), accounting for \sim 15% of the cases. The prognosis was worst (5-year relative survival <20%) for patients with cancers of the esophagus, liver, pancreas and lung, representing ~15% of the pooled dataset.

Additionally, Table 4 shows comparisons of survival of cancer patients in Germany and in the United States. Five-year relative survival was lower in Germany than in the United States for several cancers, including the most common ones such as colorectal, breast, prostate and lung cancers; as well as melanoma and cancers of the bladder, thyroid, oral cavity and connective tissue. Five-year relative survival was higher in Germany for some of the common cancers, such as Hodgkin's lymphoma, multiple myeloma and cancers of the stomach, pancreas and kidney.

Five-year relative survival for younger (aged 15–74 years) and older (aged 75 years and older) cancer patients in Germany and in the United States are shown in Table 5. For several cancer sites (cervical, ovarian, thyroid and brain cancer as well as to all hematological malignancies), survival was much worse among older patients than among younger patients in both countries.

Table 2. Number of cases for the 25 most common cancers in 1997–2006 in the pooled-German dataset

Cancer site	ICD-10 code	Number of cases	% of the pooled dataset
Oral cavity	0-14	32 868	3.0
Esophagus	15	14 532	1.3
Stomach	16	44 867	4.1
Colorectum	18-21	168 409	15.3
Liver	22	13 254	1.2
Gallbladder	23-24	11 632	1.1
Pancreas	25	26 191	2.4
Larynx	32	10 307	0.9
Trachea, lung, bronchus	33-34	113 936	10.4
Skin melanoma	43	37 129	3.4
Connective and soft tissue	49	6083	0.6
Breast (female)	50	165 615	15.0
Cervix	53	15 685	1.4
Corpus uteri	54	30 906	2.8
Ovary	56	21 651	2.0
Prostate	61	141 412	12.8
Testis	62	11 504	1.0
Kidney	64	37 520	3.4
Bladder	67	45 208	4.1
Brain and nervous system	71–72	14 051	1.3
Thyroid	73	12 419	1.1
Hodgkin's lymphoma	81	5 283	0.5
Non-Hodgkin's lymphoma	82-85	33 009	3.0
Multiple myeloma ^a	90	11 922	1.1
Leukemia	91–96	23 064	2.1
Total		1 048 457	95.3

^aIncludes malignant plasma cell neoplasms as well.

Table 3. Number of cases for 13 rare cancers in 1997–2006 in the pooled-German dataset

Cancer site	ICD-10 code	Number of cases	% of the pooled dataset
Small intestine	17	3248	0.3
Nasal cavity, middle ear and accessory sinuses	30–31	1726	0.2
Heart	38	750	0.1
Bone	40-41	1970	0.2
Mesothelioma	45	3465	0.3
Peritoneum	48	1310	0.1
Breast cancer in males	50	1261	0.1
Vulva	51	5281	0.5
Vagina	52	1162	0.1
Penis	60	1516	0.1
Renal pelvis	65	3325	0.3
Ureter	66	1865	0.2
Eye	69	1769	0.2
Total		28 648	2.7

Table 4. Estimates of age-adjusted 5-year relative survival (%) for the period of 2002-2006 utilizing the pooled-German dataset and compared with SEER

Cancer site	1				2		
	Germany		Difference	P value ^a	SEER	SEER	
	RS (%)	SE	between (2) and (1)		RS (%)	SE	
Oral cavity	48.7	0.6	7.1	< 0.001	55.8	0.5	
Esophagus	18.3	0.6	-1.0	0.080	17.3	0.5	
Stomach	31.8	0.4	-4.8	< 0.001	27.0	0.4	
Colorectum	63.0	0.2	2.5	< 0.001	65.5	0.2	
Liver	13.1	0.5	-0.1	0.866	13.0	0.4	
Gallbladder and biliary tract	20.1	0.7	-3.0	0.002	17.1	1.0	
Pancreas	9.0	0.3	-2.7	< 0.001	6.3	0.2	
Larynx	63.4	1.1	-1.9	0.017	61.5	0.8	
Trachea, lung, bronchus	16.5	0.2	0.9	< 0.001	17.4	0.1	
Skin melanoma	89.4	0.3	1.6	< 0.001	91.0	0.2	
Connective and soft tissue	60.4	1.0	5.7	< 0.001	66.1	0.8	
Breast (female)	83.7	0.2	6.1	< 0.001	89.8	0.2	
Cervix	64.7	0.6	0.1	0.186	64.8	0.7	
Corpus uteri	81.0	0.4	-0.6	0.006	80.4	0.4	
Ovary	40.7	0.5	-0.7	0.692	40.0	0.5	
Prostate	89.1	0.4	9.9	< 0.001	99.0	0.2	
Testis	93.5	1.4	0.3	0.003	93.8	1.6	
Kidney	73.7	0.5	-6.4	< 0.001	67.3	0.4	
Bladder	66.3	0.4	12.7	< 0.001	79.0	0.3	
Brain and nervous system	25.0	0.5	1.7	0.838	26.7	0.4	
Thyroid	87.8	0.6	5.1	< 0.001	92.9	0.4	
Hodgkin's lymphoma	84.5	0.7	-3.9	< 0.001	80.6	0.6	
Non-Hodgkin's lymphoma	62.8	0.5	2.0	0.378	64.8	0.3	
Multiple myeloma	41.1	0.7	-4.4	< 0.001	36.7	0.5	
Leukemia	50.5	0.5	-2.3	< 0.001	48.2	0.4	

^aThe differences between relative survival rates were tested using model-based period analysis.

For Hodgkin's lymphoma, survival was higher among younger patients in Germany than in the United States, whereas an opposite pattern was seen among the older patients. There was a major age gradient in 5-year breast cancer survival in Germany but not in the United States.

Age-adjusted 5-year relative survival for patients in Germany and in the United States diagnosed with rare cancers are displayed in Table 6. In Germany, survival for rare cancers ranged from 11.9% (mesothelioma) to 74.7% (male breast cancer). USA survival estimates were higher than those in Germany for cancer sites, such as the heart, eye, vulva and male breast. Mesothelioma patients in Germany had better survival than in the United States.

discussion

The present study provides up-to-date estimates of cancer survival for the time period of 2002-2006 using data from 11 population-based cancer registries covering 33 million people (\sim 40% of the German population). Five-year survival of cancer patients in Germany varied from 9.0% to 93.5% for the 38 most common cancers. Five-year relative survival >80% were observed for testicular cancer, skin melanoma, cancers of the prostate and thyroid, Hodgkin's lymphoma and cancers of the breast and endometrium, which together account for almost 40% of cases. Survival estimates in Germany were below those in the United States for several of the more common cancers, including cancers of the colorectum, breast, lung and prostate. On the other hand, 5 years after the diagnosis, German patients diagnosed with Hodgkin's lymphoma, multiple myeloma and cancers of the stomach, pancreas and kidney had higher relative survival than American patients.

In our analysis, estimates for Saarland were very close to the pooled- German estimates in most cases. For example, 5-year relative survival for colorectal, lung, breast and prostate cancers were 64.6%, 17.9%, 83.8% and 91.7% in Saarland compared with 63.0%, 16.5%, 83.7% and 89.1%, respectively, in the pooled dataset. However, the pooled database covering an ~30-fold larger population allowed derivation of survival estimates at a much higher precision.

A recent study used data from 47 European cancer registries in order to calculate region weighted pan-European 5-year relative survival estimates for 2000–2002 by period analysis [5]. Comparing these estimates to the results of the present study reveals that 5-year survival estimates for the most common cancers for 2002-2006 in Germany were higher than the pan-European ones for 2000-2002. However, there is strong and persistent variation in cancer survival between European

RS, 5-year relative survival; SE, standard error; SEER, Surveillance, Epidemiology and End Results.

Table 5. Estimates of five-year relative survival of German and USA cancer patients for the period of 2002–2006 by two major age groups

Cancer site	Age 15–74 years						Age 75+ years					
	1		2	2			1		2			
	Germa	Germany			Difference	P value ^b	Germany		SEER		Difference	P value ^b
	RS ^a	SE	RS ^a	SE	between		RS	SE	RS	SE	between	
	(%)		(%)		(2) and (1)		(%)		(%)		(2) and (1)	
Oral cavity	47.9	0.5	59.6	0.5	11.7	< 0.001	50.6	1.8	46.3	1.1	-4.3	0.491
Esophagus	19.9	0.6	19.3	0.6	-0.6	0.140	14.5	1.4	12.6	0.9	-1.9	0.348
Stomach	34.0	0.4	28.5	0.5	-5.5	< 0.001	26.6	0.7	23.4	0.7	-3.2	0.002
Colorectum	65.4	0.2	67.8	0.2	2.4	< 0.001	57.2	0.4	59.8	0.4	2.6	< 0.001
Liver	14.7	0.6	15.3	0.5	0.6	0.311	9.1	0.9	7.4	0.7	-1.7	0.187
Gallbladder and	21.8	0.9	19.1	1.3	-2.7	0.013	15.7	1.0	12.3	1.4	-3.4	0.080
biliary tract												
Pancreas	10.2	0.4	7.9	0.3	-2.3	< 0.001	6.2	0.5	2.6	0.2	-3.6	< 0.001
Larynx	63.1	0.8	62.5	0.8	-0.6	0.044	64.1	3.1	58.9	2.1	-5.2	0.183
Trachea, lung, bronchus	18.5	0.2	19.4	0.2	0.9	< 0.001	11.7	0.4	12.5	0.2	0.8	< 0.001
Skin melanoma	90.2	0.3	92.4	0.2	2.2	< 0.001	84.2	1.5	82.2	1.0	-2.0	0.301
Connective and soft tissue	61.6	1.1	67.7	0.8	6.1	< 0.001	53.2	3.0	56.3	2.1	3.1	0.235
Breast (female)	85.7	0.2	89.9	0.1	4.2	< 0.001	78.8	0.6	89.5	0.4	10.7	< 0.001
Cervix	68.6	0.6	68.7	0.7	0.1	0.179	40.7	2.0	41.1	2.3	0.4	0.677
Corpus uteri	84.7	0.4	84.1	0.3	-0.6	0.058	72.0	1.1	71.4	1.0	-0.6	0.011
Ovary	47.5	0.6	46.7	0.6	-0.8	0.665	24.2	1.0	23.7	0.9	-0.5	0.588
Prostate	90.6	0.5	99.9	0.1	9.3	< 0.001	85.3	0.7	97.1	0.4	11.8	< 0.001
Testis	95.5	0.6	94.6	0.9	-0.9	0.001	75.1	12.8	86.5	13.5	11.4	0.327
Kidney	75.6	0.4	71.4	0.4	-4.2	< 0.001	69.1	1.3	57.1	1.1	-12.0	< 0.001
Bladder	71.0	0.4	82.7	0.3	11.7	< 0.001	55.0	0.8	69.9	0.6	14.9	< 0.001
Brain and nervous system	28.0	0.6	30.6	0.5	2.6	0.161	6.9	1.0	2.8	0.5	-4.1	0.010
Thyroid	92.4	0.5	95.1	0.3	2.7	< 0.001	59.6	2.8	79.5	2.1	19.9	< 0.001
Hodgkin's lymphoma	89.6	0.6	84.9	0.6	-4.7	< 0.001	38.9	4.4	42.1	3.3	3.2	0.406
Non-Hodgkin's lymphoma	69.5	0.5	70.2	0.4	0.7	0.004	46.5	1.1	51.7	0.7	5.2	0.036
Multiple myeloma	47.1	0.9	43.3	0.7	-3.8	< 0.001	26.5	1.4	20.5	0.9	-6.0	< 0.001
Leukemia	57.6	0.6	54.0	0.5	-3.6	< 0.001	33.1	1.2	33.8	0.8	0.7	0.062

^aAge adjusted using four age groups (15-44, 45-54, 55-64, 65-74 years).

Table 6. Estimates of age-adjusted 5-year relative survival and SEs for the period of 2002–2006 utilizing the pooled-German dataset and compared with SEER results

Cancer site	1				2	
	Germany				SEER	
	RS (%)	SE	Difference	P value ^a	RS (%)	SE
			between (2) and (1)			
Small intestine	57.4	1.6	-0.8	0.128	56.6	1.1
Nasal cavity and middle ear	50.3	2.1	1.1	0.822	51.4	1.8
Heart	17.5	2.2	10.3	0.008	27.8	4.3
Bone	53.7	1.7	8.4	0.001	62.1	1.5
Mesothelioma	11.9	1.0	-1.5	< 0.001	10.4	0.9
Peritoneum	38.9	2.3	-4.7	0.735	34.2	1.2
Breast (males)	74.7	2.7	12.5	< 0.001	87.2	2.1
Vulva	68.6	1.1	7.7	< 0.001	76.3	1.2
Vagina	47.0	2.4	2.2	0.998	49.2	2.2
Penis	65.5	2.5	-2.7	0.388	62.8	2.6
Renal pelvis	53.1	1.5	-0.9	0.586	52.2	1.6
Ureter	58.4	2.1	-3.3	0.152	55.1	2.2
Eye	66.0	2.3	12.5	<0.001	78.5	1.8

^aThe differences between relative survival rates were tested using model-based period analysis.

^bThe differences between relative survival rates were tested using model-based period analysis.

RS, 5-year relative survival; SE, standard error; SEER, Surveillance, Epidemiology and End Results.

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countries, which was shown to be associated with the total national expenditure on health and our survival estimates for Germany are mostly comparable to those of countries with higher expenditure, such as France and Switzerland [5, 16–18].

When examining differences between German and USA survival estimates, it has to be kept in mind that for some cancer sites, the SEER coverage population may not be representative of the USA population [19–21]. There are indications that SEER covers the more affluent areas of the USA [20]. Strong evidence for socioeconomic differences in cancer survival was revealed for many cancers in many populations [22-24]. There are additional complexities involved in interpreting comparisons of survival estimates such as differences in health care systems. In 2002, Germany spent \sim 11% of the gross domestic product on health care compared with 14.6% in the United States [25, 26]. German health care secures a universal coverage of the population. In the United States, however, 18% of the non-elderly population was without health insurance in 2006 [27]. Additionally, different multiple primary coding rules were followed by the SEER program and the German cancer registries, which applied the IARC suggestions. Application of the IARC multiple primary coding rules could result in fewer cancer cases [28]. Furthermore, given the number of tests carried out, chance may have operated in some of the findings in the study.

German cancer survival estimates were close to or below those in the United States for the majority of the cancer sites, such as melanoma and cancers of the breast, colorectum, oral cavity, lung and prostate. Higher USA survival estimates compared with Saarland/Germany have previously been documented for cancers of the breast, colorectum and prostate and might be mostly ascribed to earlier detection [2]. For example, in the United States, the percentage of women aged ≥40 years who reported that they have had a mammogram in the previous 2 years reached 70% by 2000 and showed a small decline to 66% by 2005 [29]. Organized breast cancer screening started in Germany in 2005 only [30]. Lower breast cancer survival among women in Germany might therefore reflect differences in the implementation of screening. Similarly, more widespread utilization of prostate-specific antigen (PSA) testing in the United States leading to overdiagnosis might be responsible for the differences in prostate cancer survival [31]. In Germany, ∼1.5 million PSA test were purchased in 2002 (corresponding to \sim 12% of the German male population >50 years of age), while in 2001, 57% of the United States male population aged ≥50 years had a PSA test within the previous year [32, 33]. Likewise, earlier detection of colorectal cancer may have improved survival chances of patients in the United States. In 2004–2005, the proportion of the German population aged ≥50 years who had colorectal endoscopy within the previous 10 years was \sim 25% compared with almost 50% in the United States as of 2004 [34, 35]. Stage of cancer was reported to be an important factor in explaining differences in of colorectal cancer survival between the Unites States and Europe [36].

Survival estimates in Germany were higher than the USA rates for some of the more common cancers, including stomach cancer and Hodgkin's lymphoma. For stomach cancer, differences might be explained by differences in the subsite distribution of cancers (considerably worse prognosis for cardia cancers), which is related to the prevalence of Helicobacter pylori infection [37-39]. For Hodgkin's lymphoma, a large proportion of patients in Germany have been included in randomized trials with substantially advanced care for this malignancy [40–42].

Although age at the time of diagnosis can also influence cancer survival, age standardization and the usage of relative survival methodology through the analysis of the survival data minimized its impact. Worse survival of the older cancer patients compared with the younger ones in Europe has been addressed before [43]. There are several indications that some of the gaps in survival between older and younger patients might be due to the fact that older patients are less likely to get the best available care for their disease [44, 45]. In addition, comorbidity in older cancer patients can have a negative influence on survival due to a higher rate of treatment-related complications [46].

Cancer survival can be influenced by factors such as quality of registration or completeness of follow-up [47, 48]. Completeness of cancer registration is a major concern especially in the build-up phase of new registries. For this study, only cancer registries were selected whose estimated completeness in 2004-2006 exceeded 80% (for most registries, estimated completeness reached 90%) [8]. However, in some of the recently established German registries, the percentage of cases identified through only death certificate was still high. In the initial years of a newly established cancer registry, high proportions of DCO cases can be due to the fact that many dying cancer patients may have had their diagnosis before the establishment of the registry. A high percentage of DCO cases even in the longer run can indicate that the registry did not have access to a number of cancer diagnoses, such as cancer diagnoses at advanced stages among older patients.

Misclassification of cancer cases could be a source of inconsistency in the data. As an example, higher estimates of bladder cancer survival in the United States than in Germany might be partially explained by differences in cancer registration such as separation of in situ/non-invasive and superficially invasive carcinomas as well as papillary and nonpapillary lesions [49].

In the absence of a national death index, most of the cancer registries that have submitted data for the project rely on record linkage with vital statistics from the state they cover, thereby potentially missing deaths among patients who migrated out of the state. Two cancer registries (Hamburg and Bremen, essentially covering the cities of Hamburg and Bremen, respectively) registered such out-migration and censored patients at the date of out-migration. When patients in these two registries were recoded as alive at the end of the study period (December 2006) in order to mimic follow-up procedures in the other federal states, the estimates of 5-year age-adjusted relative survival were only slightly elevated. As an example, 5-year age-adjusted relative survival of lung cancer changed from 13.8% to 13.9% in Hamburg and from 17.5% to 18.3% in Bremen. Potential bias from missed deaths due to out-migration is likely to be of even less concern for the other registries, covering much larger states with both urban and rural areas. Nevertheless, some bias due to incomplete ascertainment of deaths cannot be ruled out and may account

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for some of the apparent variation between registries in 5-year relative survival for cancer with poor prognosis, such as lung cancer (11.5%–20.9%) or pancreatic cancer (5.2%–11.6%).

The present study with >1 million cancer diagnoses from 11 population-based German cancer registries and with an underlying population of 33 million people is the most comprehensive report on cancer survival in Germany available to date. Furthermore, the study provides estimates of relative survival for rare cancers, which were available previously only for Saarland. Period methodology was used through this project to incorporate the most recent follow-up information into the analysis. Estimates of cancer survival in Germany for 2002-2006 were somewhat lower than in the United States for the same time period for several cancer sites but were higher than most of the pan-European ones estimated for the time period of 2000–2002. German patients diagnosed with Hodgkin's lymphoma, multiple myeloma and cancers of the stomach, pancreas and kidney had higher relative survival than American patients. Further research is needed to investigate factors that might be responsible for the different cancer survival rates in Germany and in the United States.

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references

- World Health Organisation. Mortality Country Fact Sheet 2006. Germany http://www.who.int/whosis/mort/profiles/mort_euro_deu_germany.pdf (16 February 2011, date last accessed).
- Gondos A, Arndt V, Holleczek B et al. Cancer survival in Germany and the United States at the beginning of the 21st century: an up-to-date comparison by period analysis. Int J Cancer 2007; 121: 395–400.
- De Angelis R, Francisci S, Baili P et al. The EUROCARE-4 database on cancer survival in Europe: data standardisation, quality control and methods of statistical analysis. Eur J Cancer 2009; 45: 909–930.
- Gondos A, Bray F, Hakulinen T, Brenner H. Trends in cancer survival in 11 European populations from 1990 to 2009: a model-based analysis. Ann Oncol 2009; 20: 564–573.

- Brenner H, Francisci S, de Angelis R et al. Long-term survival expectations of cancer patients in Europe in 2000-2002. Eur J Cancer 2009; 45: 1028–1041.
- Capocaccia R, Gatta G, Roazzi P et al. The EUROCARE-3 database: methodology of data collection, standardisation, quality control and statistical analysis. Ann Oncol 2003; 14 (Suppl 5): v14–v27.
- Brenner H, Gefeller O, Hakulinen T. Period analysis for 'up-to-date' cancer survival data: theory, empirical evaluation, computational realisation and applications. Eur J Cancer 2004; 40: 326–335.
- Robert Koch-Institut und die Gesellschaft der epidemiologischen Krebsregister in Deutschland e.V. (Hrsg.). Cancer in Germany 2005/2006. Incidence and Trends. Berlin, Germany: Robert Koch Institute 2010.
- Ferlay J, Burkhard C, Whelan S, Parkin DM. Check and conversion programs for cancer registries. (IARC/IACR tools for cancer registries). Lyon, France: IARC Technical Report No. 42 2005.
- 10. Henson DE, Ries LA. The relative survival rate. Cancer 1995; 76: 1687-1688.
- Ederer F, Heise H. Instructions to IBM 650 Programmers in Processing Survival Computations. Bethesda, MD: National Cancer Institute 1959.
- Brenner H, Hakulinen T. Advanced detection of time trends in long-term cancer patient survival: experience from 50 years of cancer registration in Finland. Am J Epidemiol 2002; 156: 566–577.
- Brenner H, Hakulinen T. Up-to-date and precise estimates of cancer patient survival: model-based period analysis. Am J Epidemiol 2006; 164: 689–696.
- Corazziari I, Quinn M, Capocaccia R. Standard cancer patient population for age standardising survival ratios. Eur J Cancer 2004; 40: 2307–2316.
- Brenner H, Gefeller O, Hakulinen T. A computer program for period analysis of cancer patient survival. Eur J Cancer 2002; 38: 690–695.
- Berrino F, Verdecchia A, Lutz JM et al. Comparative cancer survival information in Europe. Eur J Cancer 2009; 45: 901–908.
- Berrino F, De Angelis R, Sant M et al. Survival for eight major cancers and all cancers combined for European adults diagnosed in 1995-99: results of the EUROCARE-4 study. Lancet Oncol 2007; 8: 773-783.
- OECD Health Data 2006. How Does Germany Compare? http://www.oecd.org/ dataoecd/31/5/36957221.pdf (16 February 2011, date last accessed).
- Frey CM, McMillen MM, Cowan CD et al. Representativeness of the surveillance, epidemiology, and end results program data: recent trends in cancer mortality rates. J Natl Cancer Inst 1992; 84: 872–877.
- Mariotto A, Capocaccia R, Verdecchia A et al. Projecting SEER cancer survival rates to the US: an ecological regression approach. Cancer Causes Control 2002; 13: 101–111.
- Merrill RM, Dearden KA. How representative are the surveillance, epidemiology, and end results (SEER) program cancer data of the United States? Cancer Causes Control 2004: 15: 1027–1034.
- 22. Woods LM, Rachet B, Coleman MP. Origins of socio-economic inequalities in cancer survival: a review. Ann Oncol 2006; 17: 5–19.
- Coleman MP, Rachet B, Woods LM et al. Trends and socioeconomic inequalities in cancer survival in England and Wales up to 2001. Br J Cancer 2004 90: 1367–1373.
- Dejardin O, Remontet L, Bouvier AM et al. Socioeconomic and geographic determinants of survival of patients with digestive cancer in France. Br J Cancer 2006: 95: 944–949.
- European Observatory on Health Systems and Policies. Fact Sheet on Germany http://www.euro.who.int/__data/assets/pdf_file/0008/98846/E85472sum.pdf (10 January 2010 date last accessed).
- OECD Communication. Health Spending in Most OECD Countries Rises, with the U.S. far Outstripping all Others http://www.oecd.org/document/36/0,2340, en_2649_201185_31938380_1_1_1_1_1,00.html (10 January 2010 date last accessed).
- Hoffman C, Paradise J. Health insurance and access to health care in the United States. Ann N Y Acad Sci 2008; 1136: 149–160.
- Hotes JL, Ellison LF, Howe HL et al. Variation in breast cancer counts using SEER and IARC multiple primary coding rules. Cancer Causes Control 2004; 15: 185–191.
- Breen N, A Cronin K, Meissner HI et al. Reported drop in mammography: is this cause for concern? Cancer 2007; 109: 2405–2409.

- Malek A, Rabe P et al. Evaluationsbericht 2005–2007 Ergebnisse des Mammographie-Screening Programms in Deutschland. Kooperationsgemeinschaft Mammographie. 2009.
- Telesca D, Etzioni R, Gulati R. Estimating lead time and overdiagnosis associated with PSA screening from prostate cancer incidence trends. Biometrics 2008; 64: 10–19.
- Becker N. Epidemiological aspects of cancer screening in Germany.
 J Cancer Res Clin Oncol 2003; 129: 691–702.
- Sirovich BE, Schwartz LM, Woloshin S. Screening men for prostate and colorectal cancer in the United States: does practice reflect the evidence? JAMA 2003; 289: 1414–1420.
- Stock C, Brenner H. Utilization of lower gastrointestinal endoscopy and fecal occult blood test in 11 European countries: evidence from the Survey of Health, Aging and Retirement in Europe (SHARE). Endoscopy 2010; 42 (7): 545–556.
- Stock C, Haug U, Brenner H. Population-based prevalence estimates of history of colonoscopy or sigmoidoscopy: review and analysis of recent trends. Gastrointest Endosc 2010; 71: 366–381. e362.
- Ciccolallo L, Capocaccia R, Coleman MP et al. Survival differences between European and US patients with colorectal cancer: role of stage at diagnosis and surgery. Gut 2005; 54: 268–273.
- Brenner H, Arndt V, Stegmaier C et al. Is Helicobacter pylori infection a necessary condition for noncardia gastric cancer? Am J Epidemiol 2004; 159: 252–258.
- 38. Perez-Perez Gl, Rothenbacher D, Brenner H. Epidemiology of Helicobacter pylori infection. Helicobacter 2004; 9 (Suppl 1): 1–6.
- Pinheiro PS, van der Heijden LH, Coebergh JW. Unchanged survival of gastric cancer in the southeastern Netherlands since 1982: result of differential trends in incidence according to Lauren type and subsite. Int J Cancer 1999; 84: 28–32.

- Draube A, Behringer K, Diehl V. German Hodgkin's Lymphoma Study Group trials: lessons from the past and current strategies. Clin Lymphoma Myeloma 2006; 6: 458–468.
- Behringer K, Diehl V. Twenty-five years clinical trials of the German Hodgkin Study Group (GHSG). Eur J Haematol Suppl 2005; 66: 21–25.
- 42. Pfreundschuh M, Trumper L, Osterborg A et al. CHOP-like chemotherapy plus rituximab versus CHOP-like chemotherapy alone in young patients with goodprognosis diffuse large-B-cell lymphoma: a randomised controlled trial by the MabThera International Trial (MInT) Group. Lancet Oncol 2006; 7: 379–391.
- Quaglia A, Tavilla A, Shack L et al. The cancer survival gap between elderly and middle-aged patients in Europe is widening. Eur J Cancer 2009; 45: 1006–1016.
- Crivellari D, Aapro M, Leonard R et al. Breast cancer in the elderly. J Clin Oncol 2007; 25: 1882–1890.
- Sanoff HK, Bleiberg H, Goldberg RM. Managing older patients with colorectal cancer. J Clin Oncol 2007; 25: 1891–1897.
- Janssen-Heijnen ML, Houterman S, Lemmens VE et al. Age and co-morbidity in cancer patients: a population-based approach. Cancer Treat Res 2005; 124: 89–107.
- 47. Berrino F, Micheli A, Sant M, Capocaccia R. Interpreting survival differences and trends. Tumori 1997; 83: 9–16.
- Brenner H, Hakulinen T. Population-based monitoring of cancer patient survival in situations with imperfect completeness of cancer registration. Br J Cancer 2005; 92: 576–579.
- Ries LAG, Young YL, Keel GE et al. Patient and Tumor Characteristics. In SEER Survival Monograph: Cancer Survival Among Adults: U.S. SEER Program, 1988-2001. Bethesda, MD: National Cancer Institute 2007; SEER Program, NIH Pub. No. 07-6215.