

# Trends in net survival from 15 cancers in six European Latin countries: the SUDCAN population-based study material

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The aim of the SUDCAN collaborative study was to compare the net survival from 15 cancers diagnosed in 2000–2004 in six European Latin countries and provide trends in net survival and dynamics of excess mortality rates up to 5 years after diagnosis from 1992 to 2004 in France, Italy, Spain, and Switzerland, and from 2000 to 2004 in Belgium and Portugal. This paper presents a detailed description of the data analyzed and quality indicators. Incident cases from Belgium, France, Italy, Portugal, Spain, and Switzerland were retrieved from 56 general or specialized population-based cancer registries that participated in the EUROCORE-5 database. Fifteen cancer sites were analyzed. The data were checked according to the EUROCORE protocol. The percentages of excluded cases, cases based on death-certificate only, cases lost to follow-up at 5 years after diagnosis, and the proportions of microscopically verified cases were evaluated across countries and cancer sites. Data exclusions for major flaws were negligible. Cases based on death-certificate only were quite rare, except for some poor-prognosis cancers in some countries. The site-specific proportions of microscopically verified cases were generally high, but slightly lower in Italy than elsewhere. The percentage of cases lost to follow-up at 5 years after diagnosis was generally low. The net survival analyses in 2000–2004 included 873 314 tumors, whereas trend analyses included 1 426 004 tumors. The quality of the

data analyzed was generally good. In fact, the analyzed data have been already checked and accepted for EUROCORE-5. However, slight differences in quality indexes, for some cancers, should be kept in mind in the interpretation of survival comparisons across countries. *European Journal of Cancer Prevention* 26:S3–S8 Copyright © 2017 Wolters Kluwer Health, Inc. All rights reserved.

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## Introduction

The SUDCAN project aimed at providing detailed trend analyses of cancer net survival in six European Latin countries: Belgium, France, Italy, Portugal, Spain, and Switzerland. This study was carried out upon an initiative of the GRELL (<http://www.grell-network.org>), in collaboration with the EUROCORE network (<http://www.eurocare.it>).

Fifteen cancer sites were studied. The first aim of SUDCAN was to provide an overview of the net survival by country for cases diagnosed between 2000 and 2004. The second and main aim was to provide trends in net survival and dynamics of excess mortality rates up to

5 years after diagnosis on the longest possible period for each country. This paper presents the material used in the SUDCAN project. The method is presented in a dedicated paper (Uhry *et al.*, 2016) and the results for each cancer site are shown in specific papers of this monograph.

## Data sources

### Incident cases

Incident cases in the six European Latin countries were retrieved from the EUROCORE-5 database (Rossi *et al.*, 2015). Only solid tumors were considered. The study protocol required demographic characteristics (sex, date of birth, registry, country of residence, etc.) and clinical characteristics (date of cancer diagnosis, date of death or last known life status, cancer topography and morphology – according to ICD-0-3 – and basis of diagnosis). The end

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**Table 1 Cancer sites and topographies (ICD-O-3)**

Site	Topography <sup>a,b</sup>
Head and neck	C01–C06, C09–C14
Esophagus	C15
Stomach	C16
Colon	C18–C19
Rectum	C20
Liver	C22
Pancreas	C25
Lung	C33–C34
Skin melanoma <sup>b</sup>	C44, morphology: 8720–8790
Breast	C50
Cervix uteri	C53
Corpus uteri	C54
Ovary	C569–C574
Prostate	C61
Kidney	C64

<sup>a</sup>Only invasive tumors; malignant hemopathies are excluded.

<sup>b</sup>All morphologies included, except skin melanoma.

of follow-up was 1 January 2009, except for France (1 January 2008).

The EUROCORE standardized quality control procedures were applied to all the datasets (De Angelis *et al.*, 2009). The internal consistency checks identified all the values that lie outside the expected range. The inter-variable consistency checks involved groups date of birth, diagnosis, and follow-up; cancer site and morphology; age, sex and site; age, sex, and morphology; and morphology and behavior. Records with impossible combinations were classified as errors and sent back to the corresponding registries for corrections. Corrected data were checked again using the same procedures.

#### **Expected mortality rates in the general population**

To estimate net survival, the expected mortality rates from causes other than the cancer studied are required. Actually, it is common to use all-cause mortality rates from the general population assuming that, for each cancer site, the cancer-specific mortality is negligible in all-cause mortality. These rates were derived by sex, age (up to 99), year of diagnosis, and registry from the life-tables available in the EUROCORE database (Baili *et al.*, 2005). In addition, national mortality rates were extracted from the Human Mortality Database (HMD) for Spain and Portugal (Human Mortality Database, 2014) because of their higher reliability in the elderly population.

**Table 2 Study periods, number of participating registries, and population coverage**

Country	Net survival analyses			Trend analyses		
	Study period	Number of registries <sup>a</sup>	Population coverage <sup>a</sup> (%)	Study period	Number of registries <sup>a</sup>	Population coverage <sup>a</sup> (%)
Belgium	2000–2004	1	58	1999–2007	1	58
France	2000–2004	9–11	11–15	1989–2004	6–7	7–9
Italy	2000–2004	24–25	30–31	1988–2004	9	14
Portugal	2000–2004	2	76	2000–2005	2	76
Spain <sup>b</sup>	2000–2004	7–9	11–13	1990–2004	4	11
Switzerland	2000–2004	6	29	1989–2007	5	25

<sup>a</sup>Ranges over the cancer sites (number of registries depends on the cancer site).

<sup>b</sup>Incident cases in 2004 were not available for Murcia.

**Table 3 Exclusions table (all site and countries combined)**

Reasons for exclusion	2000–2004 analyses [n (%)]	Trend analyses [n (%)]
DCO/autopsy case	9182 (1.04)	23 638 (1.63)
Major data quality errors	3050 (0.34)	4109 (0.28)
Missing date of follow-up	175 (0.02)	364 (0.03)
Sex or age missing	77 (0.01)	138 (0.01)
Date of follow-up < date of diagnosis	148 (0.02)	414 (0.03)
Other EUROCORE control error	2650 (0.30)	3193 (0.22)
Overall	12 232 (1.39)	27 747 (1.92)
Total number of cases before exclusions	885 546	1 453 751

Indeed, population data sources in Spain and Portugal are sometimes aggregated for individuals older than 85 years and HMD uses a particularly robust method to estimate the annual-age rates from aggregated data.

#### **Site definition, included registries, study period, and excluded cases**

The cancer sites included in the present study are shown in Table 1. A few ICD-O-3 topography codes used here differ from those used in the EUROCORE-5 study. Here, the codes for some cancers were as follows: C18–C19 for colon cancer, C20 for rectum cancer, ovary (C569–C574) for ovarian cancer, and C64 for kidney cancer.

A cancer registry was excluded whenever the average percentage of cases on the basis of death-certificate only (DCO) was greater than 13% (this case did not occur) or the average percentage of lost to follow-up cases at 5 years was higher than 10% (only one registry excluded). The registries included are listed in Supplementary Tables S1 and S2 (Supplemental digital content 1, <http://links.lww.com/EJCP/A104>).

Table 2 shows for each country and each objective (net survival analysis 2000–2004 and trend analysis) the number of registries included and the range of the national population coverage according to the cancer sites (some registries in France, Italy, and Spain are cancer specific). For trend analyses, the study periods were specific for each country and chosen by making a

**Table 4 Percentage of excluded cases by cancer site and country**

Cancer site	2000–2004 net survival analyses						Trend analyses					
	BE	FR	IT	PT	ES	CH	BE	FR	IT	PT	ES	CH
Head and neck	0.0	0.0	0.7	1.9	1.5	0.9	0.0	0.0	1.0	1.8	1.2	0.7
Esophagus	0.0	0.1	2.0	2.1	2.8	2.4	0.0	0.2	3.0	1.9	3.4	2.6
Stomach	0.0	0.0	1.9	2.8	3.8	3.3	0.0	0.2	3.4	2.5	5.6	3.4
Colon	0.0	0.0	1.2	2.3	3.0	2.4	0.0	0.1	1.9	2.1	3.9	3.3
Rectum	0.0	0.0	1.1	2.6	1.7	1.6	0.0	0.1	1.4	2.4	2.3	2.2
Liver	0.0	0.2	3.5	1.9	9.3	8.3	0.0	0.4	6.3	1.8	14.0	9.8
Pancreas	0.0	0.2	3.0	0.9	8.2	8.0	0.1	0.3	4.9	0.8	12.0	6.9
Lung	0.1	0.0	2.3	1.5	3.9	3.1	0.0	0.0	3.3	1.4	5.4	3.6
Skin melanoma	0.0	0.1	0.3	2.4	1.0	0.2	0.0	0.0	0.5	2.1	0.9	0.1
Breast	0.0	0.0	0.8	1.3	1.5	0.9	0.0	0.0	1.3	1.2	2.3	0.9
Cervix uteri	0.0	0.1	0.4	1.4	1.2	1.2	0.0	0.1	0.6	1.4	1.3	0.8
Corpus uteri	0.0	1.4	0.8	3.6	1.1	1.8	0.8	0.8	0.9	3.3	1.1	1.4
Ovary	0.0	0.2	2.1	2.1	3.3	1.9	0.0	0.1	2.6	1.9	3.4	1.8
Prostate	0.0	0.0	1.3	2.9	3.3	3.0	0.0	0.0	1.8	2.6	5.3	4.3
Kidney	0.2	0.1	2.0	2.3	3.3	6.5	0.1	0.1	2.1	2.0	4.4	7.9

BE, Belgium; CH, Switzerland; ES, Spain; FR, France; IT, Italy; PT, Portugal.

**Table 5 Percentage of microscopically confirmed cases by cancer site and country**

Cancer site	2000–2004 net survival analyses						Trend analyses					
	BE	FR	IT	PT	ES	CH	BE	FR	IT	PT	ES	CH
Head and neck	98.8	99.1	96.6	98.9	98.9	98.9	98.9	99.0	96.3	99.0	98.8	98.6
Esophagus	97.6	97.5	90.4	96.9	96.4	97.4	97.5	97.2	87.2	96.9	95.7	97.7
Stomach	97.1	98.1	92.1	97.7	94.7	96.9	97.0	97.4	89.9	97.7	94.7	96.7
Colon	96.6	97.5	94.1	97.6	95.0	96.8	96.9	97.0	92.3	97.6	94.2	97.0
Rectum	97.9	98.7	95.5	98.5	97.2	98.9	98.1	98.3	94.0	98.5	96.5	98.3
Liver	77.0	52.7	45.2	90.5	46.0	57.3	77.3	59.5	45.3	91.0	52.9	65.9
Pancreas	69.8	62.8	48.8	69.5	56.3	69.4	74.0	62.5	44.9	70.3	55.7	72.8
Lung	90.8	95.2	75.5	94.3	87.2	92.3	91.1	95.4	74.8	94.0	89.1	93.5
Skin melanoma	99.1	99.8	98.4	98.9	99.6	99.8	99.3	99.8	97.9	98.9	99.6	99.9
Breast	98.1	99.1	96.9	98.8	98.6	98.8	98.2	93.9	95.9	98.9	98.2	98.3
Cervix uteri	97.4	99.2	96.8	99.2	99.2	99.5	97.7	99.2	97.2	99.3	99.1	99.4
Corpus uteri	98.5	98.9	97.2	98.7	98.2	99.7	98.4	99.1	97.4	98.9	98.5	99.4
Ovary	94.0	94.0	86.6	93.9	91.0	94.2	94.1	93.1	86.5	94.0	92.6	94.9
Prostate	97.4	98.2	92.3	96.2	91.4	95.1	97.2	97.5	88.1	96.3	90.6	95.0
Kidney	92.3	91.4	83.8	93.2	83.4	91.2	92.7	91.7	82.3	93.5	83.6	91.2

BE, Belgium; CH, Switzerland; ES, Spain; FR, France; IT, Italy; PT, Portugal.

compromise between the length of the period and the maximum number of registries that could be included. Registries were included only if they covered the entire study period.

Cases were excluded whenever there were major flaws in data quality checks (e.g. missing sex, age, or date; inconsistency between topography and morphology) or cases were based on DCO or autopsy. Overall, the percentage of excluded cases for major data quality flaws was low (<0.5% all sites and countries combined, Table 3 – see Table 4 for percentages of excluded cases by cancer site and country). The proportion of excluded DCO cases was overall small (<2%, Table 3). It should be noted that registries included for France, Belgium, and Portugal do not have DCO cases. Percentages of DCO excluded cases by cancer site and country are presented in Supplementary Table S3 (Supplemental digital content 1, <http://links.lww.com/EJCP/A104>). The latter were globally low, but varied according to cancer site and country. They were not negligible for liver and pancreas cancers

in Spain and Switzerland (range 6.5–14%). Proportions of DCO per cancer site and for three 5-year period in Italy, Spain, and Switzerland are presented in Supplementary Table S4 (Supplemental digital content 1, <http://links.lww.com/EJCP/A104>). These proportions were higher for most lethal cancers and tended to decrease over time. Primary and further multiple independent primary cancers were included. Multiple primary cancers were defined according to the IARC-ENCR rules (Curado *et al.*, 2004). The finally analyzed datasets included 873 314 tumors for 2000–2004 net survival analyses and 1 426 004 tumors for trend analyses.

#### Data comparability

The percentage of microscopically verified (%MV) cases varied by cancer site (Table 5); it was generally the lowest in Italy whatever the site. For liver and pancreas cancers, there were significant differences between countries. In fact, the %MV cases ranged between 45 and 90% for liver cancer and between 45 and 74% for

**Table 6 Number of cases, number of deaths within 5 years, and percentage of loss to follow-up at 5 years in 2000–2004 net survival analyses**

Cancer site	Number of cases						Number of deaths within 5 years						Loss to follow-up at 5 years (%)					
	BE	FR	IT	PT	ES	CH	BE	FR	IT	PT	ES	CH	BE	FR	IT	PT	ES	CH
Head and neck	3234	6759	8632	3619	3600	1294	1954	4345	5089	2454	2303	754	2.0	1.8	0.9	2.0	1.3	3.9
Esophagus	2327	3966	3986	1987	1536	740	1868	3424	3579	1754	1403	621	1.3	1.1	0.5	3.2	0.7	1.9
Stomach	4243	5456	25232	11001	5693	1372	3265	4199	19079	7844	4468	1014	1.5	2.4	0.5	4.0	1.5	2.1
Colon	15521	18981	53085	14792	14441	4230	7915	9236	27015	7705	7646	2086	1.8	3.8	0.7	2.5	1.6	3.5
Rectum	6556	6780	14193	6574	4969	1509	3159	3335	7409	3461	2591	707	1.1	3.3	0.6	2.3	1.6	4.0
Liver	1008	4835	16670	1397	3066	1012	845	4215	14584	1209	2693	886	2.6	1.0	0.6	2.6	1.0	1.0
Pancreas	2913	4526	15073	2034	3114	1423	2671	4204	14348	1879	2966	1357	0.9	1.4	0.3	0.7	0.6	0.6
Lung	18840	16295	58584	10664	14830	5378	16298	13903	51750	9459	13366	4606	1.1	1.1	0.5	1.6	0.8	1.8
Skin melanoma	3631	4109	12088	2360	2757	2558	830	756	2667	698	632	466	3.9	8.4	1.2	1.7	2.5	7.3
Breast	27340	27857	73276	18368	16392	7970	5715	4384	14839	4074	3392	1608	1.6	4.3	0.9	2.0	2.4	5.5
Cervix uteri	1892	1707	4033	2788	1182	429	617	619	1452	1093	426	148	2.6	6.1	1.7	2.2	2.6	5.6
Corpus uteri	3977	3226	10891	2839	3341	1234	1121	971	3072	943	995	333	2.0	5.4	0.8	1.4	1.8	5.5
Ovary	2904	2758	8243	1847	1966	942	1709	1553	5130	1011	1165	580	1.0	3.2	0.8	1.9	1.7	3.7
Prostate	26829	29387	55598	17094	16377	7563	7074	6644	15389	4783	5066	2043	2.3	4.2	0.6	2.7	2.5	5.9
Kidney	3853	4194	13558	2121	2814	1051	1598	1589	5349	795	1295	428	2.2	2.7	0.6	1.5	1.8	4.5

BE, Belgium; CH, Switzerland; ES, Spain; FR, France; IT, Italy; PT, Portugal.

**Table 7 Number of cases, number of deaths within 5 years, and percentage of loss to follow-up at 5 years in trend analyses**

Cancer site	Number of cases						Number of deaths within 5 years						Lost to follow-up at 5 years (%)					
	BE	FR	IT	PT	ES	CH	BE	FR	IT	PT	ES	CH	BE	FR	IT	PT	ES	CH
Head and neck	5926	13964	14063	4417	8360	4145	3240	9485	8913	2950	5518	2369	1.5	0.9	0.2	1.9	1.7	2.8
Esophagus	4352	7343	6489	2363	3628	2091	3295	6549	5940	2093	3327	1759	1.1	0.5	0.2	2.8	0.9	1.2
Stomach	7541	10472	47215	13203	13222	4571	5477	8281	36574	9297	10360	3489	1.2	1.6	0.1	3.7	1.4	1.8
Colon	28193	33676	77706	18176	25301	13050	12864	17895	41959	9170	14082	6453	1.4	2.0	0.2	2.4	1.8	2.2
Rectum	12069	11980	22921	8046	9119	4497	5025	6419	12890	4084	5117	2095	1.1	1.7	0.1	2.2	1.9	2.4
Liver	1999	7650	22567	1777	5618	2499	1569	6950	20542	1534	5047	2230	1.9	0.7	0.3	2.3	1.1	0.6
Pancreas	5410	7896	22000	2574	5851	4102	4813	7448	21160	2374	5578	3882	0.9	0.7	0.1	0.8	0.8	0.8
Lung	34796	29385	97484	13239	27981	16100	28761	25492	87701	11639	25290	13767	0.9	0.8	0.1	1.5	0.8	1.3
Skin melanoma	7023	6490	16491	2941	5008	6796	1321	1363	4047	821	1238	1213	2.7	4.2	0.3	1.4	3.8	5.0
Breast	49718	46074	103455	22233	29030	23040	8797	9344	24227	4689	7017	5284	1.2	2.6	0.3	1.7	2.4	3.6
Cervix uteri	3400	3722	7286	3317	2705	1450	975	1331	2860	1258	1027	521	2.2	3.6	0.5	1.9	2.3	4.5
Corpus uteri	7100	6080	16674	3461	6350	3885	1784	1980	4932	1137	1958	1116	1.6	2.8	0.2	1.3	2.5	3.5
Ovary	5179	5587	13110	2227	3986	3089	2748	3388	8469	1192	2378	1870	0.8	2.0	0.2	1.8	2.1	2.4
Prostate	49340	36425	65114	21096	23135	20643	10731	11767	24361	5558	9043	6460	1.8	1.9	0.2	2.6	2.3	3.5
Kidney	7095	7097	20944	2617	5360	3204	2597	2994	8931	952	2578	1395	1.6	1.5	0.2	1.5	1.9	2.7

BE, Belgium; CH, Switzerland; ES, Spain; FR, France; IT, Italy; PT, Portugal.

pancreas cancer. For lung cancer, %MV was lower in Italy than in the other countries (75 vs. 87–95%).

The percentage of cases lost to follow-up at 5 years after diagnosis (Tables 6 and 7) was generally low ( $\leq 3\%$  in 69 and 81 out of 90 site-registry combinations, for 2000–2004 net survival and trend analyses, respectively) and was lower in trends than in net survival analyses, except in Spain. In Switzerland (in both analyses) and France (especially in 2000–2004 net survival analyses), this percentage was slightly higher than that in the other countries for several cancer sites. The highest percentages of lost-to-follow-up cases were observed in skin melanoma (up to 7.3 and 8.4% in 2000–2004 net survival analyses in Switzerland and France, respectively).

## Discussion

The data included in the present study have already been checked and approved for publication in the EURO CARE-5 study (Rossi *et al.*, 2015).

The EURO CARE checks identified only a negligible proportion of data to be excluded for major flaws ( $< 0.5\%$ ). The majority of the other exclusions were DCO cases, which, in accordance with standard procedure, were excluded from survival analyses because their survival time is 0 (De Angelis *et al.*, 2009). Although the percentage of DCO was generally low, some variability across countries in certain cancer sites (liver, pancreas, lung, stomach, and kidney) should be considered in the interpretation of the results. However, the interpretation of DCO percentages is not straightforward because not all participant registries have access to or use death certificates in their routine activity. This is the case in France, Belgium, and Portugal. The absence of DCO or a near-zero percentage of DCO – which means possible incomplete registration of poor-prognosis cancers – may lead to overestimate survival. Also, the exclusion of a high percentage of DCO (e.g. for liver or pancreas cancers) inflates artificial survival by excluding the cases with the worst prognosis. However, low percentages of DCO may result from very good trackback of clinical information of cases initially extracted from death certificates. This leads to inclusion in the analyses cases with rather short periods of observation, and thus to survival underestimation. Finally, when the percentage of DCO is low, survival might generally be underestimated (Silcocks, 2006), although the actual effect is unpredictable.

In this study, the examination of overall data on DCO suggested that incidence data collected by cancer registries were almost complete. Slight overestimations in Spain and Switzerland should be considered when comparing survivals from some of the most lethal cancers (e.g. liver, pancreas, and lung). In any case, for more reliable survival comparisons, the DCO percentages should be age adjusted (Brenner *et al.*, 2016).

For MV cases, the overall proportion was very high, with slight differences between countries and lower values in

some countries versus others for liver and pancreas cancers. These results are expected on the basis of the average data from other European cancer registries or other continents (Forman *et al.*, 2013). What may be worrying is the variability between countries in some cancer sites. In fact, %MV ranged from 45 to 90% for liver cancer and from 45 to 74% for pancreas cancer. Assuming similar clinical and diagnostic patterns across countries, the highest %MV in Portugal and Belgium could be because of a possible case selection (e.g. surgically treated cases) or a certain amount of under-reporting that may explain differences in survival with other countries. Moreover, the %MV has lost its relevance over time because of the development of imaging techniques or the use of biomarkers (e.g.  $\alpha$ -feto-protein testing) that provide as accurate diagnoses as MV.

In the present study, some cancer sites were excluded because their inclusion could not lead to reliable comparisons between countries. This was the case for bladder cancer; the heterogeneity in the definition of invasive cancer and, therefore, the heterogeneity in the inclusion of in situ and borderline tumors may have an important impact on survival indicators (Marcos-Gragera *et al.*, 2015). Similarly, we decided not to include leukemia and lymphomas because of time-varying changes in the definition of these types of cancers. Moreover, we did not consider gallbladder and biliary tract tumors because the data available did not allow distinguishing gallbladder, common bile duct, and Vater ampulla cancers, which have very different prognoses (Lepage *et al.*, 2015).

It would have been very useful to analyze the stage at diagnosis and the treatment to disentangle the roles of early diagnosis and treatment in evaluating survival differences and their change over time (Allemani *et al.*, 2010). Unfortunately, stage and treatment data were not available in the dataset analyzed; however, the amount of information and the quality of clinical data collected by cancer registries are increasing, which will soon allow high-resolution studies (Allemani *et al.*, 2010).

Some of the differences in survival may be explained by uncontrolled methodological differences in cancer registration and follow-up procedures. However, the results of the checks of data quality performed by EURO CARE suggest that such methodological differences would cause only minor biases (De Angelis *et al.*, 2014).

## Conclusion

The quality of the data analyzed in this SUDCAN project was generally satisfactory. Some caution should nevertheless be exercised when comparing estimates of survival from cancers with very poor prognoses between countries with very different percentages of DCO or MV cases.

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### Conflicts of interest

There are no conflicts of interest.

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