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RESEARCH ARTICLE

Cancer survival in adult patients in Spain. Results from nine population-based cancer registries

M. D. Chirlaque[1,2] · D. Salmerón[1,2] · J. Galceran[3] · A. Ameijide[3] · A. Mateos[4] · A. Torrella[5] · R. Jiménez[6] · N. Larrañaga[2,7] · R. Marcos-Gragera[8] · E. Ardanaz[2,9] · M. Sant[10] · P. Minicozzi[10] · C. Navarro[1,2] · M. J. Sánchez[2,11] · the REDECAN Working Group

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Abstract

Introduction With the aim of providing cancer control indicators, this work presents cancer survival in adult (≥15 years) patients in Spain diagnosed during the period 2000–2007 from Spanish cancer registries participating in the EUROCARE project.

Methods Cancer cases from nine Spanish population-based cancer registries were included and analysed as a whole. All primary malignant neoplasms diagnosed in adult patients were eligible for the analysis. Cancer patients were followed until 31 December 2008. For each type of cancer, 1-, 3- and 5-year observed and relative survival were estimated by sex, age and years from diagnosis. Furthermore, age-standardized 5-year relative survival for the period 2000–2007 has been compared with that of the period 1995–1999.

Results Skin melanoma (84.6 95% CI 83.0–86.2), prostate (84.6% 95% CI 83.6–85.6) and thyroid (84.2% CI 95% 82.0–86.6) cancers showed the highest 5-year relative survival, whereas the worst prognosis was observed in pancreatic (6% 95% CI 5.1–7.0) and oesophageal (9.4% 95% CI 7.9–11.1) cancers. Overall, survival is higher in women (58.0%) than in men (48.9%). The absolute difference in relative survival between 2000–2007 and 1995–1999 was positive for all cancers as a whole (+4.8% in men, +1.6% in women) and for most types of tumours. Survival increased significantly for chronic myeloid leukaemia, non-Hodgkin's lymphoma and rectum cancer in both sexes, and for acute lymphoid leukaemia, prostate,

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✉ M. D. Chirlaque
mdolores.chirlaque@carm.es

1 Department of Epidemiology, Regional Health Authority, IMIB-Arrixaca, Murcia University, Ronda de Levante, 11, 30008 Murcia, Spain

2 CIBER in Epidemiology and Public Health (CIBERESP), Madrid, Spain

3 Tarragona Cancer Registry, Foundation Society for Cancer Research and Prevention, Pere Virgili Health Research Institute, Reus, Spain

4 Albacete Cancer Registry, Health and Social Welfare Authority, Castile-La Mancha, Spain

5 Castellón Cancer Registry, Public Health Directorate, Valencian Government, Castellón, Spain

6 Cuenca Cancer Registry, Health and Social Welfare Authority, Castile-La Mancha, Spain

7 Basque Country Cancer Registry, Basque Country Regional Authority, Vitoria-Gasteiz, Spain

8 Epidemiology Unit and Girona Cancer Registry (UERCG), Oncology Coordination Plan, Department of Health, Autonomous Government of Catalonia, Catalan Institute of Oncology (ICO), Girona Biomedical Institute (IDIBGI), University of Girona, Girona, Spain

9 Navarre Cancer Registry, Navarre Public Health Institute, Pamplona, Spain

10 Analytical Epidemiology and Health Impact Unit, Department of Preventive and Predictive Medicine, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

11 Granada Cancer Registry, Andalusian School of Public Health, Instituto de Investigación Biosanitaria ibs.GRANADA, Hospitales Universitarios de Granada/ Universidad de Granada, Granada, Spain

liver and colon cancers in men and Hodgkin's lymphoma and breast cancer in women. Survival patterns by age were similar in Europe and Spain. A decline in survival by age was observed in all tumours, being more pronounced for ovarian, corpus uteri, prostate and urinary bladder and less for head and neck and rectum cancers.
Conclusion High variability and differences have been observed in survival among adults in Spain according to the type of cancer diagnosed, from above 84% to below 10%, reflecting high heterogeneity. The differences in prognosis by age, sex and period of diagnosis reveal opportunities for improving cancer care in Spain.

Keywords Cancer · Survival · Cancer registries · Prognosis · Population-based · Spain

Introduction

Monitoring health outcomes by means of survival provides a valuable indicator for future actions in cancer control. Cancer prognosis is a major issue because, despite its aggressive spread, positive outcomes can progressively be achieved by means of cancer patient management in accordance with the recommended guidelines and more effective diagnoses and treatment [1]. Survival time after diagnosis is a quality indicator of cancer care and reflects the vital experience of patients with cancer. One-year survival is mainly related to tumour stage, 3-year survival partially indicates the aggressiveness and progression of the tumour and 5-year survival reflects the health care process as a whole. Cancer registries provide measures of survival at a population-based level, allowing comparisons among different regions and revealing the possibilities to improve prognosis.

The EUROCARE (EUROpean CAncer Registry-based project on Survival and CARE of cancer patients) collaborative research project has provided comparable estimates of cancer survival in Europe over 20 years. Recently, EUROCARE-5 has published 5-year survival estimates in Europe for patients diagnosed between 2000 and 2007 [2] and specific survival for several types of cancer [3–5]; however, few data have been published regarding specific indicators of cancer survival by country. Similarly, the CONCORD (global surveillance of cancer survival) programme measures worldwide survival, disseminating results on cancer prognosis around the world [6]. Both projects have included data from Spanish cancer registries, although adopting different scopes and methodology to fulfil their aims.

Specific studies on cancer survival at the population level are scarce in Spain. Marcos-Gragera et al. [7] published trends in prostate cancer survival, showing a significant increase from 1999 to 2003. Salmerón et al. [8] analysed lung cancer prognosis in Spain, evidencing low survival with slightly better prognosis in women. Survival rates for nine cancers [9] were presented in Spain for tumours diagnosed from 1995 to 1999. Detailed and updated information on cancer prognosis in Spain is, therefore, relevant, useful and needed. In accordance with one of the main goals of REDECAN [10] (Spanish Network of Cancer Registries) and in collaboration with EUROCARE [11], the present work provides data from Spanish cancer registries for cancer survival in adult patients in Spain diagnosed between 2000 and 2007 using information from EUROCARE-5. Survival has also been included for 1995–1999 (EUROCARE-4) to compare with the later period.

Methods

Study population

Spanish data on primary malignant tumours were gathered and analysed within the context of the EUROCARE-5 [2] study, covering cases diagnosed from 2000 to 2007. Moreover, to allow comparisons with previous years, data from the EUROCARE-4 [12] study (1995–1999) were also analysed. The number of malignant cancers in $\geq$15 year-olds diagnosed in Spain from 2000 to 2007 and 1995–1999 were, respectively, 157,149 and 103,231. The nine participating population-based cancer registries in EUROCARE-5 are in the north (Euskadi and Navarra), central (Cuenca), east (Girona, Tarragona, Castellón) and south (Albacete, Murcia and Granada) of Spain. With the exception of Cuenca, all participated in EUROCARE-4. These cancer registries are included in the REDECAN network, which covers more than 7 million inhabitants and represents almost 20% of the total Spanish population.

The participant cancer registries regularly publish their data on incidence in CI5 (cancer incidence on five continents) [13] and their results on survival in EUROCARE and CONCORD, with good global quality indicators and high population coverage. Most of the registries have been operating for over 20 years [1].

Cancer patients

Spanish cancer registries collected and registered all new malignant tumours diagnosed in their covered areas. The study design and database have been described in Rossi et al. [14]. Briefly, cases included in the analysis were defined by topography and morphology following the International Classification of Disease for Oncology, 3rd edition (ICDO-3) [15]. Haematological tumours were

grouped using the WHO classification [16]. All primary tumours and invasive malignant neoplasms were eligible for analysis. Non-melanoma skin cancers were excluded and urothelial cancer of the bladder, benign, in situ or uncertain, were included to ensure comparability among regions. Only adult patients (15 years old or over at cancer diagnosis) were selected for analysis. All primary cancers according to IARC–ENCR (International Agency for Research in Cancer/European Network of Cancer Registries) rules for multiple primary cancers have been included in EUROCARE-5, regardless of whether first, second and following multiple primary cancers have occurred [17]. In EUROCARE-4, applying the same criteria for primary cancer, only first primary cancers were included in the analysis. Cases whose only source of information were the death certificate (DCO) or cases diagnosed at autopsy were excluded from the survival analysis.

Cancer registries contributed to the EUROCARE database and jointly carried out the quality control procedures to correct missing or invalid data and inconsistencies. Finally, the information was analysed by EUROCARE for all participating European countries. Here, we present a sub-analysis of the EUROCARE-4 and -5 projects using data from Spain.

Follow-up

Follow-up of cancer patients diagnosed between 2000 and 2007 was done using common criteria for the collection of variables in all cancer registries. Cases were followed from the date of diagnosis to the end of follow-up (31 December 2008) ascertaining vital status. Multiple sources of information like the National Death Index, the social security database, municipal census and hospital and primary care records were used when necessary and available. Patients' life status was categorized as follows: alive at the end of follow-up, dead at the end of follow-up—including date of *exitus*—or censored by loss or incomplete follow-up. For the incident cases in the period 1995–1999, the follow-up was carried out until 31 December 2003.

The datasets of the nine cancer registries are registered as stipulated by law with the Spanish data protection authority [18]. All data collected in the database for survival analysis were anonymous, and therefore, no ethical approval was required [19].

Statistical methods

Statistical analysis has been described elsewhere [14]. Briefly, for the period 2000–2007, 5-year observed survival, 5-year relative survival (5y-RS), and age-standardized relative survival at 1, 3 and 5 years since diagnosis, with 95% confidence interval (95% CI) were computed using the Ederer II method [20]. We present results by all malignant neoplasms by specific cancer types. Relative survival estimate is the ratio of observed patient survival to the survival that would have been expected if cancer patients had the same all-cause mortality as the general population of the same age, sex, region and period. Thus, it reflects the excess mortality in cancer patients and is an indicator for the comparison of population-based cancer survival when the cause of death is unknown.

Age specific survival was estimated by age group (15–44, 45–54, 55–64, 65–74 and 75+ years) for all tumours, except prostate cancer (15–54, 55–64, 65–74, 75–84 and 85+ years) because of its higher median age at diagnosis. Figures comparing mean European survival with the Spanish survival by age group were performed for all specific tumours. To take into account differences in the age distribution of the population and to warrant comparability between sexes, regions and periods, we estimated age-standardized 5y-RS using international standards [21].

For the period 1995–1999 (EUROCARE-4), the Hakulinen method [22] was used to estimate the age-standardized 5y-RS, which was extracted from published results and compared with the most recent 2000–2007 results. The methods used in EUROCARE-4, slightly different from those used in EUROCARE-5, have also been previously described [12]. The cohort approach was used in both EUROCARE 4 and 5 to estimate the relative survival as a prognosis indicator of cancer. The Z test [23] was used to compare survival between periods, and the differences were considered to be significant when p value <0.05.

Results

The Spanish cancer cases included in the survival analysis, after applying the exclusion criteria detailed below, comprised 227,006 incident cases diagnosed in the participating cancer registries for the period 1995–2007. Cases excluded from the analyses were DCO (3.5%) and diagnosed incidentally at autopsy (0.1%). A total of 9% of cases were censored after fewer than 5 years of follow-up in EUROCARE-4 and 2.5% of cases were lost to follow-up in EUROCARE-5. Over 90% were diagnosed by microscopic verification.

In both sexes, for the nine Spanish regions combined in the period 2000–2007 (Table 1), the 5y-RS was lower than 10% for pancreatic (5.0% 95% CI 4.2–5.9) and oesophagus cancer (9.6% 95% CI 8.2–11.3). Thyroid cancer showed a 5y-RS of 90.4% (95% CI 88.8–92.1) followed by Hodgkin's lymphoma (85.0% 95% CI 82.4–87.6) and skin melanoma (84.3% 95% CI 82.6–86.0). In men, testicular cancer presented a survival of 95.0% (95% CI 93.2–96.8), followed by prostate cancer with 84.5% (95% CI

Table 1 5-year observed survival (OS) and relative survival (RS) with 95% confidence interval (95% CI) for adult patients (≥15 years) diagnosed with cancer in Spain in 2000–2007 by sex

	Male			Female			All		
	OS	RS	95% CI	OS	RS	95% CI	OS	RS	95% CI
Head and neck	32.7	35.7	33.9–37.6	48.6	53.6	49.5–57.9	35.5	38.9	37.2–40.6
Oesophagus	8.2	9.3	7.8–11.0	11.0	12.2	8.2–18.0	8.6	9.6	8.2–11.3
Stomach	19.3	23.1	21.6–24.6	21.9	25.4	23.5–27.5	20.2	23.9	22.7–25.1
Colon	45.1	55.1	53.7–56.4	47.9	55.5	54.0–57.1	46.3	55.3	54.3–56.3
Rectum	46.7	55.9	54.2–57.6	47.3	54.2	52.1–56.5	46.9	55.3	54.0–56.7
Liver	11.9	13.8	12.3–15.4	9.5	10.6	8.7–13.0	11.3	12.9	11.7–14.3
Gallbladder	15.1	18.5	15.6–21.9	9.7	11.7	9.8–14.0	11.9	14.5	12.8–16.5
Pancreas	4.0	4.6	3.7–5.8	4.7	5.4	4.3–6.8	4.3	5.0	4.2–5.9
Larynx	54.8	61.5	59.5–63.6	69.3	71.8	63.8–80.8	55.4	61.9	60.0–63.9
Lung	8.6	10.0	9.4–10.5	14.2	15.3	13.7–17.1	9.3	10.6	10.1–11.2
Skin melanoma	68.6	78.2	75.3–81.2	82.7	88.7	86.7–90.7	76.6	84.3	82.6–86.0
Breast				78.9	85.2	84.5–85.8			
Cervix uteri				63.4	66.1	63.4–68.9			
Corpus uteri				70.2	76.1	74.4–77.7			
Ovary				40.2	42.6	40.4–44.9			
Prostate	68.6	84.5	83.6–85.4						
Testis	94.0	95.0	93.2–96.8						
Kidney	50.9	58.7	56.5–60.9	52.1	57.8	54.7–61.1	51.3	58.4	56.6–60.2
Urinary bladder	56.5	68.5	67.3–69.8	55.9	66.8	63.9–69.9	56.4	68.3	67.1–69.4
Central nervous system	12.0	12.7	10.9–14.8	11.3	11.7	9.9–13.9	11.7	12.2	10.9–13.7
Thyroid	78.3	82.5	78.0–87.2	89.9	92.5	90.9–94.2	87.4	90.4	88.8–92.1
Hodgkin's lymphoma	80.5	82.9	79.4–86.5	86.2	88.1	84.4–92.0	82.7	85.0	82.4–87.6
Non Hodgkin lymphoma	52.0	59.9	57.9–62.0	56.2	62.4	60.3–64.6	53.9	61.0	59.6–62.5
Myeloma	26.6	31.7	28.3–34.5	28.7	32.7	29.3–36.6	27.6	32.2	29.7–34.8
Chronic lymphoid leukaemia	59.4	72.0	68.0–76.3	61.7	72.9	68.2–78.0	60.3	72.4	69.3–75.6
Acute lymphoid leukaemia	31.8	33.6	26.2–43.2	24.3	25.3	18.1–35.4	28.4	29.8	24.4–36.5
Acute myeloid leukaemia	17.1	19.0	15.8–22.8	23.2	24.6	20.7–29.2	19.8	21.4	18.9–24.3
Chronic myeloid leukaemia	54.5	61.0	53.1–70.1	61.5	65.2	56.9–74.6	57.6	62.9	57.1–69.4
All malignant neoplasms	41.2	49.0	48.6–49.4	54.0	59.4	59.0–59.9	46.3	53.2	52.9–53.5

83.6–85.4). 5y-RS for breast cancer in women was 85.2% (95% CI 84.5–85.8). The largest differences between relative and observed survival were found in cancers of the prostate, urinary bladder, colorectal and chronic lymphoid leukaemia.

The age-standardized 5y-RS increased from 1995–1999 to 2000–2007 for most of the analysed tumours, and for both sexes overall. In particular, there was a 4.8 percentage point (+4.8%) increase in age-standardized 5y-RS in men and a +1.6% rise in women (Table 2), both statistically significant. In men, the age-standardized 5y-RS increased for chronic myeloid leukaemia, acute lymphoid leukaemia, prostate, non-Hodgkin's lymphoma, rectum, liver and colon cancers, whilst urinary bladder and larynx cancer showed a decrease in survival. In women, the improvement was observed for chronic myeloid leukaemia, non-Hodgkin's lymphoma, acute myeloid leukaemia, Hodgkin's lymphoma, rectum and breast cancer. A decrease in survival was observed for urinary bladder cancer. All these differences were statistically significant.

The differences in age-standardized relative survival at 1, 3 and 5 years from diagnosis (Table 3) for all malignant neoplasms were larger between 1- and 3-year survival (decrease of 13.5%) than between 3- and 5-year survival (5.2%). There was a higher reduction among men than women in the first period (14.8% vs. 11.8%), but percentages were the same in the second period (Suppl Table 1). Pancreatic cancer presented the worst prognosis at 1-year with 23.3% (95% CI 21.8–24.8), and skin melanoma the highest (96.1% 95% CI 95.3–96.9). The fastest decline from 1- to 3-year survival was observed in oesophagus cancer (age-standardized 5y-RS: from 38.2 to

Table 2 Number of cancer cases and age-standardised 5-year relative survival (RS) with 95% confidence interval (95% CI) for adult patients (≥15 years) diagnosed with cancer in Spain in 1995–99 (EUROCARE-4) and 2000–2007 (EUROCARE-5) by sex and period

	Male						Diff	Female						Diff
	EUROCARE-4 (1995–1999)			EUROCARE-5 (2000–2007)				EUROCARE-4 (1995–1999)			EUROCARE-5 (2000–2007)			
	N	RS	95% CI	N	RS	95% CI		N	RS	95% CI	N	RS	95% CI	
Head and neck	2532	37.5	36.0–39.0	3201	34.6	32.3–37.1	−2.8	435	51.9	49.3–54.7	701	53.1	48.9–57.7	1.2
Oesophagus	1168	9.8	8.8–11.0	1505	9.0	7.4–11.0	−0.8	138	na	na–na	225	na	na–na	
Stomach	3164	26.2	25.3–27.1	4038	24.2	22.7–25.8	−2.0	1798	30.4	29.2–31.7	2266	28.3	26.2–30.6	−2.1
Colon	4569	53.9	53.0–54.8	8295	56.6	55.2–57.9	2.7*	3696	56.3	55.4–57.3	5934	58.1	56.7–59.6	1.8
Rectum	3103	51.3	50.2–52.4	5047	56.1	54.4–57.8	4.8*	1974	52.3	51.0–53.6	2852	56.9	54.8–59.0	4.6*
Liver	1517	11.1	10.2–12.1	2493	14.5	12.9–16.2	3.4*	611	13.9	12.1–16.0	923	15.0	12.2–18.3	1.0
Gallbladder	504	16.6	14.7–18.8	815	20.2	16.9–24.3	3.6	945	15.5	14.0–17.2	1148	na	na–na	
Pancreas	1058	5.3	4.6–6.1	1870	5.2	4.2–6.5	−0.1	881	5.3	4.5–6.3	1623	7.0	5.5–8.8	1.6
Larynx	2496	63.5	62.0–65.1	3085	59.5	57.1–61.9	−4.0*	99	70.4	64.3–77.1	127	69.2	58.2–82.3	−1.2
Lung	10,215	10.2	9.8–10.5	14,759	10.1	9.5–10.6	−0.1	1119	13.4	12.4–14.5	1997	14.7	13.1–16.6	1.3
Skin melanoma	794	78.3	76.5–80.1	1344	79.1	76.4–81.8	0.8	1105	87.7	86.5–89.0	1766	88.9	87.1–90.8	1.2
Breast								13,171	80.3	79.8–80.9	18,474	82.8	81.9–83.6	2.4*
Cervix uteri								1172	62.7	61.2–64.3	1347	63.9	61.2–66.7	1.2
Corpus uteri								2479	73.1	72.0–74.3	3733	74.4	72.7–76.2	1.3
Ovary								1359	36.9	35.5–38.4	2211	36.8	34.7–39.0	−0.1
Prostate	7345	75.4	74.5–76.4	18,418	84.6	83.6–85.6	9.1*							
Testis	400	94.9	90.4–99.7	694	na	na–na								
Kidney	1518	59.8	58.2–61.5	2788	57.5	55.3–59.8	−2.3	678	58.2	56.1–60.3	1232	59.4	56.5–62.5	1.3
Urinary bladder	5929	73.7	72.9–74.5	9735	70.3	69.1–71.5	−3.4*	1016	75.2	73.6–76.8	1618	70.8	68.1–73.6	−4.4*
Central nervous system	902	14.9	13.8–16.2	1278	17.2	15.1–19.7	2.3	719	na	na–na	1110	17.8	15.4–20.7	
Thyroid	222	71.9	68.3–75.6	365	75.6	70.3–81.4	3.7	716	85.5	83.7–87.4	1369	86.8	84.4–89.3	1.3
Hodgkin's lymphoma	418	80.1	77.7–82.5	528	78.7	75.0–82.5	−1.4	302	80.2	77.8–82.6	348	86.1	82.0–90.5	5.9*
Non Hodgkin lymphoma	1745	50.2	48.6–51.8	3257	58.2	56.1–60.4	8.0*	1453	54.2	52.8–55.7	2663	63.3	61.2–65.4	9.0*
Myeloma	532	31.3	29.1–33.7	902	34.2	30.9–37.9	2.9	486	37.2	34.8–39.7	839	38.7	34.9–42.9	1.5
Chronic lymphoid leukaemia	415	75.3	72.4–78.4	837	73.1	69.4–77.1	−2.2	317	81.2	78.4–84.1	560	75.6	71.2–80.2	−5.6
Acute lymphoid leukaemia	85	25.3	21.1–30.5	138	40.3	32.6–49.7	14.9*	63	na	na–na	111	27.6	19.8–38.4	
Chronic myeloid leukaemia	231	37.6	34.2–41.2	177	54.4	46.4–63.7	16.8*	140	43.3	39.1–48.0	140	59.6	51.7–68.8	16.3*
Acute myeloid leukaemia	256	15.2	13.2–17.5	583	17.5	14.4–21.3	2.3	239	14.4	12.2–17.1	445	21.4	17.7–25.8	6.9*
All malignant neoplasms	50,550	44.1	43.8–44.4	85,099	48.9	48.5–49.3	4.8*	35,061	56.3	56.0–56.6	56,296	58.0	57.5–58.4	1.6*

na these values could not be calculated due to the low number of cases or negligible mortality

Diff absolute difference in percentage points

* p value <0.05 from Z test for trend

12.8%), and the slowest in thyroid cancer (age-standardized 5y-RS: from 90.8 to 87.5%). In the second period, the fastest decrease was found in myeloma and the slowest in acute myeloid leukaemia.

Figure 1 shows that, in general, patterns of 5y-RS by age group and sex in Europe and Spain were similar, with the exception of stomach cancer, liver cancer and chronic myeloid leukaemia, which had a slightly better prognosis in Spain, and pancreatic cancer and lung cancer, which had a worse prognosis than in Europe. Prognosis falls with advancing age, and was as good in women as in men or better than in men for most cancers. For all cancers

Table 3 Age-standardised relative survival (RS) with 95% confidence interval (95% CI) for adult patients (≥15 years) diagnosed with cancer in Spain in 2000–2007 at 1, 3, 5 years from diagnoses

	1 year RS (95% CI)	3 year RS (95% CI)	5 year RS (95% CI)
Head and neck	70.2 (68.5–72.0)	45.4 (43.5–47.3)	38.2 (36.1–40.2)
Oesophagus	38.2 (35.9–40.7)	12.8 (11.2–14.7)	9.4 (7.9–11.1)
Stomach	49.4 (48.1–50.7)	30.2 (29.0–31.5)	25.6 (24.4–26.9)
Colon	77.5 (76.7–78.2)	63.5 (62.6–64.4)	57.1 (56.1–58.1)
Rectum	81.2 (80.3–82.1)	64.5 (63.3–65.7)	56.4 (55.1–57.7)
Liver	39.4 (37.7–41.1)	21.0 (19.5–22.5)	14.3 (13.0–15.8)
Gallbladder	39.5 (36.9–42.4)	22.1 (19.8–24.7)	17.6 (15.4–20.2)
Pancreas	23.3 (21.8–24.8)	8.4 (7.4–9.5)	6.0 (5.1–7.0)
Larynx	84.1 (82.6–85.7)	66.8 (64.8–68.9)	59.8 (57.5–62.2)
Lung	37.7 (36.9–38.4)	14.9 (14.4–15.5)	10.7 (10.2–11.2)
Skin melanoma	96.1 (95.3–96.9)	89.1 (87.9–90.4)	84.6 (83.0–86,2)
Kidney	74.7 (73.4–76.1)	63.2 (61.6–64.9)	57.8 (56.1–59.6)
Urinary bladder	86.8 (86.1–87.4)	75.7 (74.8–76.6)	70.4 (69.3–71.4)
Central nervous system	40.2 (38.4–42.2)	22.7 (21.0–24.5)	17.5 (15.8–19.3)
Thyroid	90.8 (89.1–92.5)	87.5 (85.5–89.6)	84.2 (82.0–86.6)
Hodgkin's lymphoma	90.9 (88.8–93.0)	84.6 (82.0–87.2)	81.5 (78.7–84.5)
Non Hodgkin lymphoma	77.1 (76.0–78.2)	66.1 (64.8–67.5)	60.4 (59.0–-61.0)
Myeloma	72.7 (70.5–74.9)	49.2 (46.7–51.8)	36.4 (33.8–39.1)
Chronic lymphoid leukaemia	92.0 (90.4–93.5)	82.1 (79.7–84.5)	74.3 (71.3–77.3)
Acute lymphoid leukaemia	53.8 (47.8–60.5)	38.8 (33.0–45.8)	35.1 (29–3-42.2)
Acute myeloid leukaemia	35.9 (33.1–38.9)	20.8 (18.3–23.5)	19.3 (16.9–22.0)
Chronic myeloid leukaemia	78.9 (74.3–83.8)	62.1 (56.7–68.0)	56.7 (50.9–63.2)
All malignant neoplasms	71.5 (71.2–71.7)	58.0 (57.8–58.3)	52.8 (52.5–53.1)

combined, 5y-RS figures across age groups ranged from 80 to 40% in women and 70–40% in men, overlapping with the European mean.

Discussion

The present study provides useful information for monitoring cancer prognosis in the Spanish population as a whole, showing differences in survival within cancer types by sex, age group and time from diagnosis. We analysed more than 260,000 patients diagnosed in nine population cancer registries (representing 20% of the total Spanish population) between 1995 and 2007, with a follow-up at least 5 years from diagnosis. Melanoma displayed the highest survival in both study periods and sexes, with higher values among women than men at 5 years from diagnosis. These differences by gender were the largest observed by cancer type and have also been found in several other studies [24–26]. Although explanations for these findings are scarce, those that have been postulated include more self-detection among women, more melanoma on non-easily visible locations in men than women, and differences in hormonal regulation [27, 28].

Thyroid cancer was the tumour with the second most favourable prognosis, also much better among females than males. An increase in thyroid examination by benign lesion leads to early detection of thyroid cancer, greatly increasing the incidence of papillary thyroid microcarcinoma [29] (less than 1 cm) in high-income countries [30].

The most aggressive tumour was pancreatic cancer, a rapidly progressive illness that presented 23% standardized RS at 1 year from diagnosis, decreasing to 6% at 5 years. Compared with the European mean, 1st year survival was lower in Spain, while 5th year was similar; both were very low [2, 5]. It is also worth pointing out that no improvement in survival has been detected in Spain and Europe for pancreatic cancer, coinciding with the findings of a study in Canada, where there had been little or no improvement in long-term survival in patients diagnosed with this cancer [31]. Despite advances in new selective molecules against specific cellular targets becoming available for pancreatic cancer therapy in recent years, prognosis of this cancer remains poor. Early detection is not effective, although molecular biomarkers and imaging techniques are now being developed [32, 33].

Head and neck cancers displayed better prognosis among women than men, and the decline with age was not

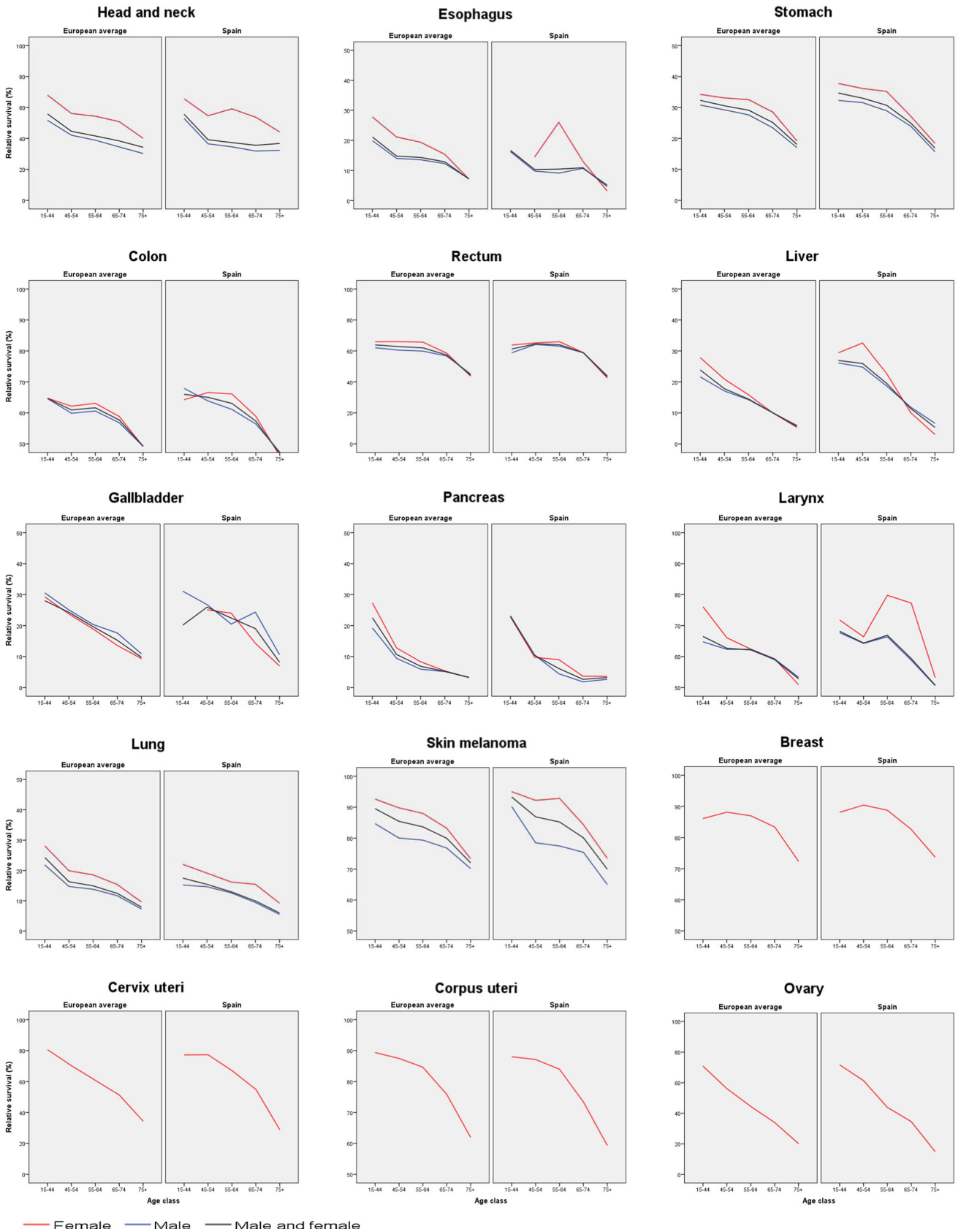

Fig. 1 Relative survival at 5 years for adult patients (≥15) diagnosed in 2000–2007 with cancer. Spain and Europe by age class and sex

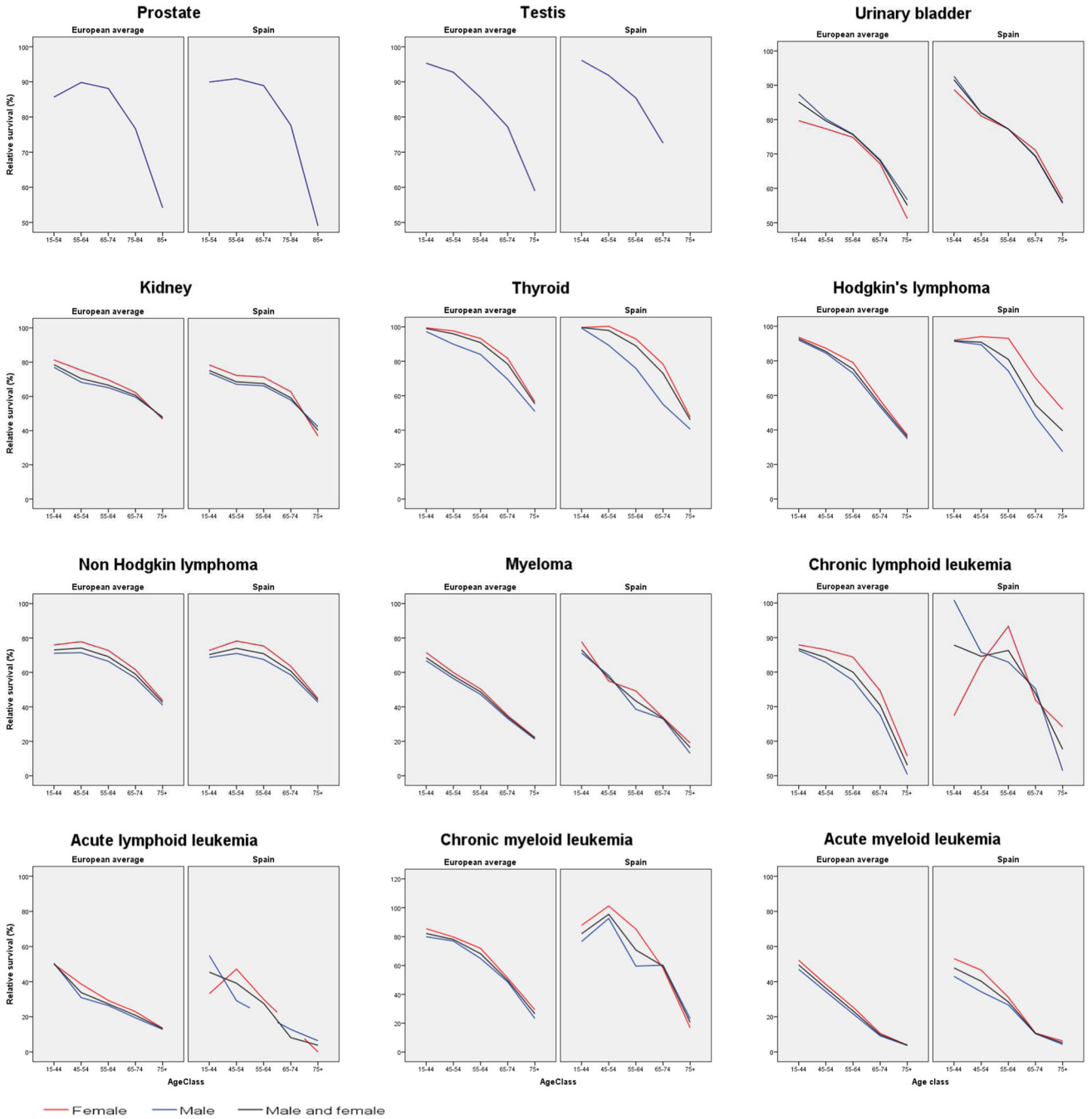

Fig. 1 continued

as pronounced as with other tumours. Survival during the two analysed periods did not show improvements in Spain, whereas in Europe a slight overall increase was observed between the periods 1999–2001 and 2005–2007 [34]. With a Spanish mean near to 40%, similar to Europe, prognosis remained poor. Survival of larynx cancer slightly decreased in Spain, although the average is also close to the European mean. Anatomical subsites are important for interpreting these results because case-mix could partly explain the differences. Thus, cancers arising in the hypopharynx displayed lower survival than those located in the larynx. Other factors like tobacco exposure, papillomavirus infection or differences in stage at diagnosis could influence disparities in survival [35].

The gastrointestinal tumour that presented the worst prognosis was oesophagus cancer (9.4% 5y-RS), which was lower than the European mean (12.4%) [36]. The most favourable prognosis was found in colon and rectal cancer

(60%), which was equal to the European figures [37] and within the range 50–59% described for many countries worldwide [6]. Stomach cancer, with a survival rate of <30%, and liver and gallbladder cancer, with <20%, showed a bad prognosis, although 1–2% above the European mean. Data published in CONCORD showed that in most countries survival from stomach cancer remained within the narrow range of 25–30% [6]. However, international comparisons are more limited for liver cancer than for other malignant tumours due to a high proportion of cancer registered with death certificate only. The increase in 5y-RS from 1995–1999 to 2000–2007 in Spain was from 1 to 5 percentage points for all gastrointestinal tumours, except oesophagus and stomach cancer, where no improvement was seen.

Lung cancer, which is very common in men and emerging in women, is a very aggressive disease. Some histology groups, such as squamous cell carcinoma and adenocarcinoma, presented better prognosis than others, like small-cell carcinoma [8]. This heterogeneity should be considered when interpreting results. No changes in prognosis were detected for the two study periods and survival was two points lower than the European mean [33]. For most geographical areas, worldwide survival was typically low (10–20%) [6].

Kidney cancer continued to have a moderate prognosis. Bladder cancer survival worsened during the two periods. Urinary bladder tumours are a heterogeneous malignancy difficult to compare due to problems following international recommendations, with several different grading classifications and non-standardized pathological reports. Differences in coding and registration practices need to be considered when comparing results over time [38]. For this reason, there was a large variation among regions within the same country or between different countries, as observed in EUROCARE-5, where 5y-RS age-standardized ranged from 50 to 80% [39].

Poor prognosis was detected for malignancies of the central nervous system. In this group of tumours, a specific analysis by sub-type would be necessary due to its heterogeneous composition causing marked differences in survival, ranging from 58% in ependymoma to only 6% in glioblastoma [40].

Females presented very different cancer survival patterns when measured by site of malignancy diagnosed, the highest values being for breast cancer, with 95% survival at 1 year from diagnosis, and the lowest for ovarian cancer with 70% at 1 year, but decreasing to 37% at 5 years. The prognosis was similar for both periods analysed and close to the European average [2, 4]. Ovarian cancer is a tumour with an unfavourable prognosis and no clear increase in survival rate has been detected in recent decades. Survival rates for cervix and corpus uteri cancer were stable when comparing the two periods studied. The global range for cervical cancer survival was very wide in different parts of the world, the majority of countries falling within the range 60–69% [6].

Tumours diagnosed only in males showed high survival figures, testicular cancer being the tumour with the best prognosis (95% of patients alive 5 years from diagnosis), which remained stable during the periods studied. Improvements in prostate cancer prognosis have been observed in the present study, in accordance with the findings of other studies [7], but survival dropped rapidly among older age groups for advanced stage at diagnosis and high-risk category on the Gleason scale [41, 42]. The elevated survival observed can be partially attributable to over diagnosis through PSA testing [6]. Low survival (<40% at 5th year) was observed in other regions around the world.

Comparisons of haematological malignancies over time are difficult due to changes in disease classification between the EUROCARE-4 [43] and EUROCARE-5 [14] study periods. Hodgkin's lymphoma showed the best prognosis, with values of 82% for 5 years overall survival and maintained until 54 years of age, similar to the European mean (81%) [44]; this value also increased significantly between 1995–1999 and 2000–2007 in women but not men. Contrarily, acute myeloid leukaemia showed the worst prognosis with 19%, higher than the European mean of 17%. Chronic myeloid leukaemia experienced the highest increase in survival when comparing the two periods of study, followed by non-Hodgkin's lymphoma; this reflects the benefits of therapeutic advances in specific haematological malignancies [45]. In all haematological malignancies, we observed a better prognosis among women than men, with the exception of acute lymphoid leukaemia. The largest difference between relative and observed survival was in prostate cancer, a tumour that mainly affects old people.

The gap in survival by gender for all malignant tumours was close to the absolute value of 10%, and higher among women. This difference has been widely described in many regions of the world [46]. Between-sex differences could be influenced by cancer case-mix because cancers with low survival rates (e.g. lung cancer) are more frequent in men and cancers with high survival rates are more common in women (e.g. breast cancer). That said, differences in prognosis between men and women still remain after adjusting for case-mix [47, 48]. Of the diverse causes hypothesized, the most commonly described is the role of sex hormone patterns giving women an advantage over men with regard to survival [46, 49].

Among the strengths of the study, we should mention that all available survival data from cancer registries have been included and that this is the most accurate information

available on survival for the Spanish population. Although variations across Spain cannot be ruled out, a previous study did not show a clear pattern by regions in Spain [9]. One limitation of the study is the lack of results for some regions where cancer registries do not operate and it was not possible to collect information for survival or incidence. A common methodology used for population-based cancer registries (mainly European rules) was applied to collect and follow cancer cases, and a common procedure was carried out to ensure good quality indicators by means of checking data in the European context. Nevertheless, some slight differences in case registration and follow-up procedures cannot be ruled out across registries. It is worth noting the high number of cancer patients included in the study when all cases are considered, whether hospitalized or not, in private or public facilities, and involved in clinical trials or not. Thus, the results will be applicable to the general population.

Some limitations have to be taken into account in the comparison between EUROCARE-4 and 5. In EUROCARE-5, all primary tumours diagnosed in patients were included in the analysis so as to reduce possible differences in survival when comparing long- and recently established cancer registries. However, in EUROCARE-4 only first primary cancers were considered in the analysis. Rosso et al. [50] have shown that the overall effect of selecting all primary tumours is to reduce survival. Thus, although a direct comparison could be misleading, the increasing survival for some cancer types indicates not only a slight improvement in prognosis over time, but also an additional step forward in survival. This excess increase cannot be evaluated due to the different methodologies applied in the two periods of comparison. A further aspect to consider is the slight differences in follow-up. EUROCARE-5 followed all cancer patients until the end of 2008 and EUROCARE-4 did so until the end of 2003. This difference could underestimate survival in EUROCARE-5 because it has more accurate information on vital status for patients with short survival. Different methods were used to estimate relative survival (Ederer II in EUROCARE-5 and Hakulinen in EUROCARE-4). However, 5y-RS was adjusted for age using the same international standard and significant differences between these two approached are therefore, not expected [51]. Additionally, as shown in Rosso et al. [50], the Ederer II estimator provided lower RS than the Hakulinen estimator and the differences in survival estimates are larger for non age-standardized values.

In summary, high variability and large differences have been observed in Spain depending on the cancer type diagnosed in adults. Skin melanoma was the tumour that presented the best prognosis, followed by thyroid cancer. The most aggressive tumour was pancreatic cancer, a rapidly progressive disease, followed by oesophagus and lung cancer. Women presented both the highest survival, for breast cancer, and the lowest, for ovarian cancer. Men diagnosed with testis and prostate cancer presented good prognosis. Among the haematological malignancies, Hodgkin's lymphoma showed the best prognosis and acute myeloid leukaemia the worst. Although a decline in survival by age was observed for all tumours, this was more pronounced for ovarian and prostate cancer and less for head and neck cancer. Most cancers showed improvement in survival between the two periods studied (colorectal, thyroid, prostate, breast, chronic myeloid leukaemia, non Hodgkin's lymphoma), while some displayed a stable (lung, ovary, testis) or slightly lower (larynx, urinary bladder) rate. However, these changes must be interpreted with care. A gap in survival was found by gender for all malignant tumours combined, it being ten points higher among women than men. Many years of registering incident cancer cases and determining vital status have made it possible to monitor the prognosis of all types of tumours at the population level in Spain, highlighting the important role played by population-based cancer registries. This information is of great use for professionals involved in the management of cancer patients, for cancer prevention and for the patients themselves, improving information on cancer prognosis in Spain.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This work does not contain clinical studies or patient data.

Informed consent For this type of study formal consent is not required.

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