Cancer Epidemiology 70 (2021) 101877

Contents lists available at ScienceDirect

Cancer Epidemiology

journal homepage: www.elsevier.com/locate/canep

Kaposi sarcoma incidence, survival and trends: Data from the information network on rare cancers in Europe (RARECAREnet)

Charles A Stiller [a], Laura Botta [b,*], Maria José Sánchez Perez [c,d,e,f], María Dolores Chirlaque López [g], Rafael Marcos-Gragera [h,i,j,k], Tiziana Scuderi [l], Dyfed Wyn Huws [m,n], Annalisa Trama [b], the RARECARENet WG[1]

[a] National Cancer Registration and Analysis Service, Public Health England, UK
[b] Research Department, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy
[c] Escuela Andaluza de Salud Pública (EASP), Granada, Spain
[d] Instituto de Investigación Biosanitaria ibs.GRANADA, Granada, Spain
[e] Centro de Investigación Biomédica en Red de Epidemiología y Salud Pública (CIBERESP), Madrid, Spain
[f] Department of Preventive Medicine and Public Health, University of Granada, Granada, Spain
[g] Department of Epidemiology, Murcia Regional Health Council, Universidad de Murcia, IMIB-Arrixaca. CIBERESP, Spain
[h] Epidemiology Unit and Girona Cancer Registry, Cancer Plan, Department of Health, Generalitat de Catalunya, Catalan Institute of Oncology, Girona, Spain
[i] Descriptive Epidemiology, Genetics and Cancer Prevention Group, Biomedical Research Institute (IDIBGI), Girona, Spain
[j] University of Girona (UdG), Girona, Spain
[k] Centro de Investigación Biomédica en Red: Epidemiología y Salud Pública (CIBERESP), Madrid, Spain
[l] UOS Registro Tumori Trapani-Agrigento, Dipartimento di Prevenzione, Asp Trapani, Trapani, Italy
[m] Welsh Cancer Intelligence and Surveillance Unit, Public Health Wales, Cardiff, Wales, UK
[n] Honorary Research Fellow, Swansea University, Swansea, Wales, UK

ARTICLE INFO

Keywords:
Rare cancers
Kaposi sarcoma
Incidence
Survival
Europe
Population-based study

ABSTRACT

Background: This study provides updated information on Kaposi sarcoma (KS) in Europe during 1995–2007 from the RARECARENet project.

Methods: Data comes from 59 population-based cancer registries in 22 countries. KS was defined as ICD-O-3 morphology code 9140 combined with any topography code. Crude and age-adjusted incidence rates and relative survival for years of diagnosis 2000–2007 and with trends during 1995–2007 were calculated overall, by age and by country.

Results: The crude annual incidence rate was 0.28 per 100,000 and age-adjusted incidence was 0.23 per 100,000; incidence increased with age, from 0.18/100,000 at age 0–44 to 0.25/100,000 at age 45–64 and 0.69/100,000 at age 65 and over. Age-adjusted incidence in males was more than four times that in females. Portugal, which had the highest incidence of AIDS in Europe, had by far the highest incidence of KS at age 0–44, 1.44/100,000, more than four times the rate in any other country. Incidence among males in Europe aged 0–44 fell significantly between 1995–1998 and 1999–2002, followed by a significant increase in 2003–2007. Younger patients, with predominantly AIDS-related KS, formerly had a worse prognosis, but since 1999–2001 5-year relative survival increased for patients aged under 65, and by 2005–2007 was 83–86 % for all three age groups 0–44, 45–64, and 65 and over.

Conclusion: Survival and quality of life for the increasing number of people in Europe affected by KS should improve further following the development of evidence-based guidelines for its management. Population-based cancer registries will continue to play a vital role in monitoring the burden of KS and improvements in its outcome.

Abbreviations: AIDS, acquired immune deficiency syndrome; CI, confidence interval; CR, cancer registry; DCO, death certificate only; HAART, highly active antiretroviral therapy; HIV, human immunodeficiency virus; KS, Kaposi sarcoma; KSHV, Kaposi sarcoma herpes virus; SE, standard error; RS, relative survival.

* Corresponding author at: Department of Research, Fondazione IRCCS Istituto Nazionale dei Tumori, Via Venezian 1, 20133, Milano, Italy.

E-mail addresses: charles.stiller@phe.gov.uk (C.A. Stiller), laura.botta@istitutotumori.mi.it (L. Botta), mariajose.sanchez.easp@juntadeandalucia.es (M.J. Sánchez Perez), mdolores.chirlaque@carm.es (M.D. Chirlaque López), rmarcos@iconcologia.net (R. Marcos-Gragera), registro.tumori@asptrapani.it (T. Scuderi), Dyfed.Huws@wales.nhs.uk (D.W. Huws), annalisa.trama@istitutotumori.mi.it (A. Trama).

[1] Supplementary material.

https://doi.org/10.1016/j.canep.2020.101877
Received 21 October 2020; Received in revised form 25 November 2020; Accepted 7 December 2020
Available online 29 December 2020

1. Introduction

Kaposi sarcoma (KS) is caused by infection with Kaposi sarcoma herpes virus (KSHV) and most often arises in skin, though mucosal sites, lymph nodes and viscera can also be involved [1,2]. It can occur at any age, and incidence is higher in males than females [2].

Classic KS is predominantly a disease of the elderly of Mediterranean or Middle Eastern origin without apparent immunosuppression. It also occurs among populations with very high levels of KSHV seroprevalence in sub-Saharan Africa. [3] Geographical variations in KSHV seroprevalence, and consequently in the incidence of classic KS, remain largely unexplained [4]. Most current cases of KS worldwide, however, are associated with immunosuppression [3], usually resulting from HIV infection (AIDS-related KS) or, less commonly, immunosuppressive therapy to combat rejection of a transplanted organ (iatrogenic KS) [5]. Consequently, geographical variation in KS incidence also reflects variation in HIV prevalence [6].

The RARECARE study of KS in Europe reported incidence and survival during 1995–2002. [7] Here, we provide updated information for the period 2000–2007, together with new analyses of time trends of incidence and survival for years of diagnosis 1995–2007, a period when uptake of highly active antiretroviral therapy (HAART) varied widely between countries. The analyses are based on data collected in the framework of the project 'Information Network on Rare Cancers' (RARECARENet www.rarecarenet.eu).

2. Methods

We extracted data from the EUROCARE-5 database, which includes incidence and follow-up data provided by 117 European population-based cancer registries (CRs) for patients with cancer diagnosed during the period 1978−2007. The RARECAREnet descriptive analysis database is a subset of the EUROCARE-5 database, containing data from 94 CRs after exclusion of specialised paediatric CRs, the Swedish and Turin CRs because they did not participate in the RARECAREnet study, the Danish CR as it did not provide the morphology detail needed to define most rare cancers, and a few other CRs due to geographical overlap with larger CRs, coverage of too short a calendar period, or more than 13 % of cases ascertained by death certificate only (DCO). We excluded 24 CRs because they did not provide complete data on non-melanoma skin cancers (e.g.French CRs) and 11 anatomical-site specific CRs because KS can occur in diverse anatomical sites; thus, 59 CRs were included in the analyses (Supplementary Table S1). Details of the RARECAREnet database can be found in the report on the project website (RARECARENet. Information Network on Rare Cancers. Indicators. http://www.rarecarenet.eu/rarecarenet/index.php/indicators, accessed 4 January 2020).

Sixteen countries were covered by national CRs (Austria, Bulgaria, Croatia, Czech Republic, Estonia, Iceland, Ireland, Latvia, Lithuania, Malta, The Netherlands, Slovakia, Slovenia, England, Northern Ireland and Wales) and six other countries (Belgium, Germany, Italy, Portugal, Spain and Switzerland) were represented by regional CRs, all population-based. The mean annual population covered by all CRs in the analyses over the period 2000–2007 was about 166,465,000, corresponding to 50 % of the total population of the participating countries.

KS was defined as ICD-O-3 morphology code 9140 combined with any topography code. Incidence rates were estimated as the number of new cases occurring in 2000–2007 divided by the total person-years in the general population in the registry areas considered, over the same period. The 1960 European standard population was used to derive age-adjusted rates, according to the RARECAREnet protocol. Age-adjusted KS incidence in Europe over time was calculated considering the pool of 30 RARECAREnet CRs, identified in italics in Supplementary Table S1, with available incidence data for all cancer types between 1995 and 2007. (Supplementary Table S2a). Incidence rates over time are provided for three period of diagnosis: 1995–1998, 1999–2002, and 2003–2007.Time trends in age-adjusted rates were also calculated using the 2011 European standard population (Supplementary Table S2b).

Relative survival was estimated as the ratio of observed survival to the expected survival in the general population of the same age and sex, using smoothed registry-specific life tables stratified by age, sex and calendar year. [8] We used the Ederer II method, multiplication of the annual relative survival ratios, because this tends to be less prone to over-estimation of relative survival than other methods [9]. Relative survival estimates are obtained by the cohort approach considering patients diagnosed with a rare cancer in the period 2000–2007 and followed up to 31 st December 2008. Since all patients are included (not only those followed up for 5 years) this method is also called 'complete' cohort analysis. We estimated differences in survival time with the period survival method [10] for three follow-up periods: 1999–2001 (cohorts diagnosed in 1 Jan 1995 to 31 Dec 2001), 2002–04 (cohorts diagnosed in 1 Jan 1998 to 31 Dec 2004), and 2005–07 (cohorts diagnosed in 1 Jan 2001 to 31 Dec 2007). Thirty CRs were included in the survival trends analyses (Supplementary Table S1). For survival analysis, cases with information from death certificate only (DCO) and cases incidentally discovered at autopsy were excluded because they do not report time of survival. Survival analyses included only the first case of KS in any patient. KS occurring before or after cancer of a different type was always included. Cases lost to follow-up were considered as censored at the date of last contact.

3. Results

The numbers of registrations and main data quality indicators for cases diagnosed in 2000–2007 are presented in Supplementary Table S1. Overall, 0.8 % of cases were DCO. Only 0.1 % of cases were diagnosed at autopsy. Microscopic verification was present in 93 % of cases. The proportion of cases diagnosed during 2000–2003 that were censored before five years was 1.4 %.

3.1. Incidence

Incidence analyses for the period 2000–2007 were carried out on 3660 cases. Crude annual incidence across the 59 contributing CRs was 0.28/100,000 (SE < 0.005) for all ages combined, and age-adjusted incidence was 0.23/100,000 (SE < 0.005). Incidence increased with age, from 0.18/100,000 (SE < 0.005) at age 0–44 to 0.25/100,000 (SE 0.009) at age 45–64 and 0.69/100,000 (SE 0.02) at age 65 and over. Age-adjusted incidence in males, 0.39/100,000 (SE 0.007), was more than four times that in females, 0.09/100,000 (SE < 0.005), data not shown. The peak in early adulthood was much more marked in males than in females, but the steep rise in incidence after age 65 was seen in both sexes (Fig. 1). Table 1 shows crude and age-adjusted incidence by European country. The highest rates, crude 1.36/100,000 and age-adjusted 1.12/100,000, were found in Iceland. The next highest rates, exceeding 0.5/100,000 crude and 0.45/100,000 age-adjusted, were in four countries of Southern Europe: Italy, Portugal, Malta and Spain. All other countries had crude and age-adjusted rates below 0.3/100,000. Fig. 2 shows age-specific incidence by country. In most countries incidence was highest at age 65 and over, but in the Netherlands and Wales incidence was highest at age 45–64, and in England at age 0–44. Portugal had by far the highest incidence at age 0–44, 1.44/100,000, more than four times the rate in any other country. At age 45–64, incidence was again highest in Portugal, 1.20/100,000, also exceeded 0.5/100,000 in Spain, Malta, Iceland and Italy, and was below 0.4/100,000 in all other countries. At age 65 and over, incidence was exceptionally high in Iceland, above 10/100,000, and exceeded 3/100,000 in Italy and Malta; moderately high rates, above 1/100,000, were observed in Spain and Portugal, and all other countries had incidence below 0.7/100,000.

Analyses of trends in incidence during 1995–2007 were carried out on 3979 cases from 30 contributing CRs. Fig. 3 shows age-adjusted

incidence in three successive calendar periods. Overall incidence in 1995–1998 was 0.26/100,000, decreasing to 0.18/100,000 in 1999–2002 and increasing again to 0.22/100,000 in 2003–2007. The decrease in age-adjusted rates from 1995 to 1998 to 1999–2002 and subsequent increase in 2003–2007 were only found in males; incidence in females was fairly constant across all three periods. Among males, incidence decreased significantly in the 0–44 and 45–64 age groups between 1995–1998 and 1999–2002, then increased again in 2003–2007, although not to the level observed in 1995–1998. There was no significant difference in incidence between 1995–1998 and 2003–2007 among males aged 65+ or among females in any age group.

More than 82 % of cases included in the analyses of trends in incidence were from just three countries, which exhibited contrasting patterns. In Italy, age-adjusted incidence in 1995–1998 was 1.09/100,000 (95 % CI 0.98–1.22) and decreased successively to 0.80 (95 % CI 0.71 to 0.90) in 1999–2002 and 0.69 (95 % CI 0.62 to 0.77) in 2003–2007. In England, incidence in 1995–1998 was 0.23/100,000 (95 % CI 0.21 to 0.26), decreased to 0.14 (95 % CI 0.13 to 0.16) in 1999–2002, and then increased to 0.24 (95 % CI 0.22 to 0.26) in 2003–2007. In the Netherlands, incidence in 1995–1998 was 0.41/100,000 (95 % CI 0.36 to 0.46), decreased to 0.24 (95 % CI 0.20 to 0.28) in 1999–2002, and increased only slightly to 0.26 (95 % CI 0.23 to 0.30) in 2003–2007. Results for all countries included in the analyses of incidence trends are shown in Supplementary Table S2. Age-adjusted rates in all three periods were nearly always higher when the 2011 European standard population, which gives greater weight to older age groups, was used, with especially large differences in Iceland and Malta. The patterns of trends over time, however, were similar whichever standard population was used.

3.2. Survival

Survival for the period 2000–2007 was estimated from 3601 cases. Five-year relative survival was 80 % overall (Fig. 4). Five-year relative survival increased slightly with age, being 75 % (95 % CI 73–78) for age 0–44, 79 % for age 45–64 (95 % CI 76–83) and 84 % (95 % CI 80–88) for age 65 + . There was no statistical significant difference in survival between the sexes (Fig. 4). Fig. 4 shows 5-year relative survival by European country. Among countries with more than 300 cases for analysis, five-year relative survival from KS ranged from 54 % (95 % CI 48–59) in Portugal to 86 % (95 % CI 83–89) in Italy.

Fig. 5 shows 5-year relative survival by age group for the periods 1999–2001, 2002–2004 and 2005–2007. In 1999–2001 the age groups 0–44 and 45–64 years had lower survival than the 65+ age group. Survival increased between 1999–2001 and 2005–2007 for the two younger age groups, but there was no sign of a trend in the 65+ group, so that by 2005–2007 relative survival was very similar across all three age groups. In each of the three countries contributing the largest numbers of cases, survival for the 0–44 age group increased markedly between 1999–2001 and 2005–2007, from 74 % (95 % CI 60–84) to 85 % (95 % CI 66–94) in Italy, from 73 % (95 % CI 61–82) to 90 % (95 % CI 80–95) in the Netherlands, and from 70 % (95 % CI 62–76) to 85 % (95 % CI 80–89) in England. Broadly similar increases were observed for age 45–64 in the Netherlands, from 68 % (95 % CI 48–81) to 89 % (95 % CI 72–96), and in England, from 69 % (95 % CI 54–80) to 81 % (95 % CI 70–88), but in Italy survival increased only slightly from 83 % (95 % CI 66–92) to 90 % (95 % CI 72–96). For age 65+ in Italy, the only country with reasonably large numbers available for analysis, there was little indication of substantial increase in survival between 1999–2001 (85 %, 95 % CI 69–93) and 2005–2007 (95 %, 95 % CI 61–99).Relative survival increased steadily through the three periods for males but no consistent trend was observed for females (data available from the corresponding author)

Table 1
Kaposi sarcoma crude and age adjusted incidence rate by country. RARECAR-Enet cancer registries (2000-2007).

	Observed	Crude Rate x 100,000	SE	Age adjusted Rate x 100,000	SE
Portugal	406	1.42	0.07	1.27	0.06
Iceland	32	1.36	0.24	1.12	0.20
Italy	1,352	1.14	0.03	0.76	0.02
Malta	19	0.60	0.14	0.52	0.12
Spain	88	0.52	0.06	0.43	0.05
Netherlands	361	0.28	0.01	0.26	0.01
Switzerland	18	0.27	0.06	0.22	0.05
England	883	0.22	0.01	0.21	0.01
Croatia	47	0.13	0.02	0.10	0.01
Lithuania	27	0.11	0.02	0.09	0.02
Ireland	36	0.11	0.02	0.11	0.02
Latvia	20	0.11	0.02	0.09	0.02
Bulgaria	62	0.10	0.01	0.07	0.01
Czech Republic	75	0.09	0.01	0.07	0.01
Germany	104	0.08	0.01	0.06	0.01
Belgium	36	0.07	0.01	0.06	0.01
Wales	17	0.07	0.02	0.07	0.02
Northern Ireland	9	0.07	0.02	0.07	0.02
Estonia	7	0.06	0.02	0.04	0.02
Slovenia	9	0.06	0.02	0.05	0.02
Austria	33	0.05	0.01	0.04	0.01
Slovakia	19	0.05	0.01	0.05	0.01
All participating countries	3,660	0.28	0.00	0.23	0.00

4. Discussion

In the first decade of the new millennium, Kaposi sarcoma in Europe had a crude incidence rate of 0.28/100,000, but incidence varied more than 20-fold between countries. The incidence rate increased with age, from 0.18/100,000 below the age of 45 years to 0.69/100,000 above the age of 65 years.

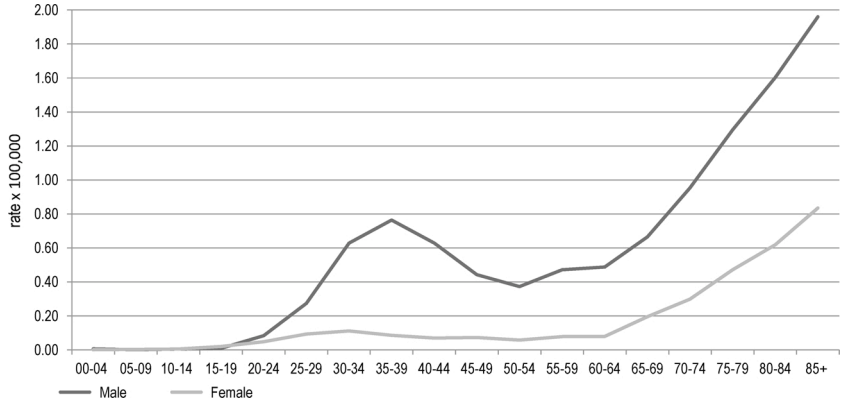


Fig. 1. Kaposi sarcoma incidence in Europe by age at diagnosis for males and females. RARECAREnet cancer registries (2000-2007).

Epidemiological subtype of KS is not generally recorded by CRs and was not included in the data analysed here, but age at diagnosis is widely used as a proxy. In an Italian study, between 1985 and 1998, 92 % of cases of AIDS-related KS occurred before the age of 55, while classic KS accounted for 97 % of all KS in people aged 65 years and above. [11] The RARECARE study showed that non-skin sites, which are more typical of AIDS-related KS, were more common at younger ages, supporting the idea that AIDS-related KS is typical of younger age groups [7]. In the present study 38 % of registered cases were diagnosed at age 0–44 years, 23 % at age 45–64 years and 39 % at age 65 and over. These data suggest that around 40 % of KS cases in Europe were of the classic subtype and over 50 % were AIDS-related.

Total incidence, and the pattern of incidence by age, varied markedly between countries. The highest age-adjusted rates were found in Iceland and four countries of Southern Europe, namely Italy, Portugal, Spain and Malta. The broad pattern of high incidence in the youngest and oldest age groups in some southern European countries that was found in the previous RARECARE study covering the period 1995–2002 [7] continued during 2000–2007. The high rates in Iceland and Malta were largely due to high incidence in the elderly, and both of these countries are known to have high incidence of classic KS [12,13]. Classic KS is also relatively frequent in Italy, especially in the south [11], and incidence at age 65 and over was correspondingly high. The especially high incidence observed at age 0–44 in Portugal and the moderately high rates in the same age group in Spain and Italy were presumably due to AIDS-related KS. In two provinces of Catalonia, in Spain, during 1997–1999, the standardised incidence ratio for KS in men with AIDS was 458 (95 % CI 195–906) [14]. Portugal, which had the highest national incidence of AIDS in Europe in the early 2000s [15], still had the highest AIDS incidence outside countries of the former Soviet Union in 2015 [16]. The relative contributions of classic KS and AIDS-related KS to the fairly high incidence in Portugal and Spain at age 45–64 and at age 65 and over are unknown. However, the number of persons aged 50 and over who were living with HIV more than doubled between 2000 and 2007 in all world regions including Europe, [17] by 2016–2017 Portugal had the highest median age for new HIV diagnoses of any European country [18,19], and people with AIDS who were aged 50 and over in Italy were less likely to receive antiretroviral therapy than younger patients [20].

Between 1995–1998 and 1999–2002, age-adjusted incidence of KS in Europe decreased by 43 % at age 0–44 and by 39 % at age 45–64, the age groups where AIDS-related KS predominates. These striking decreases roughly coincide with the early- HAART period. [21,22] Broadly similar decreases occurred among males, but incidence among females remained fairly constant. The absence of further decrease in 2003–2007, at the start of the late-HAART period, probably reflects underlying increases in AIDS prevalence in some countries, rather than decreasing coverage or efficacy of HAART, although HAART coverage has tended to be lower in that region [16]. It seems likely, however, that incidence will have further decreased since then in countries with higher HAART coverage. A linkage study between the Spanish AIDS Research Network cohort and the Spanish Cancer Registry Network found that the standardised incidence ratio for AIDS-defining cancers among HIV-infected people declined from 435 (95 % CI 308–561) in 2004–2009 to 164 (95 % CI 114–214) in 2010–2015, although data were not shown specifically for KS [23]. In the United States SEER cancer registries between 2000 and 2013, incidence trends for KS varied with age, with a significant increase of 2.4 % per year for the 20–29 age group, significant decreases of 6.1 % per year for age 30–39 and 2.5 % per year for age 40–54, and no significant change for age 55 and over, but also with marked differences between geographical regions and racial groups [24]. The marked decreasing trends in age-adjusted incidence in Iceland and Malta are unexplained, though presumably reflect decreases in incidence of classic KS, but the results for these two small countries are based on correspondingly small numbers of cases.

For most types of cancer, survival decreases with increasing age. [25] By contrast, younger KS patients, with predominantly AIDS-related disease, had a worse prognosis than older patients during the pre-HAART period [7]. Since 1999–2001, however, 5-year relative survival increased markedly for patients aged under 65, whereas there was little sign of increased survival at age 65 years and over, when KS is mostly of the classic form. By 2005–2007, survival was 82–86 % for all three age groups 0–44, 45–64, and 65 and over, and age as a prognostic factor had largely disappeared.

Survival of patients with KS in 2000–2007 varied considerably between countries with sufficient cases to give reasonably precise estimates. Five-year relative survival was above 80 % in England, Italy and the Netherlands, compared with 54 % in Portugal. Some of this variation was likely due to differences in the age-incidence distribution and consequently in the relative frequencies of patients in different age groups. In a comparative study of rare cancers in Europe and the United States during 2000–2007, KS was the only one of 196 entities to have significantly lower incidence and significantly higher survival in Europe than in the United States. [26]

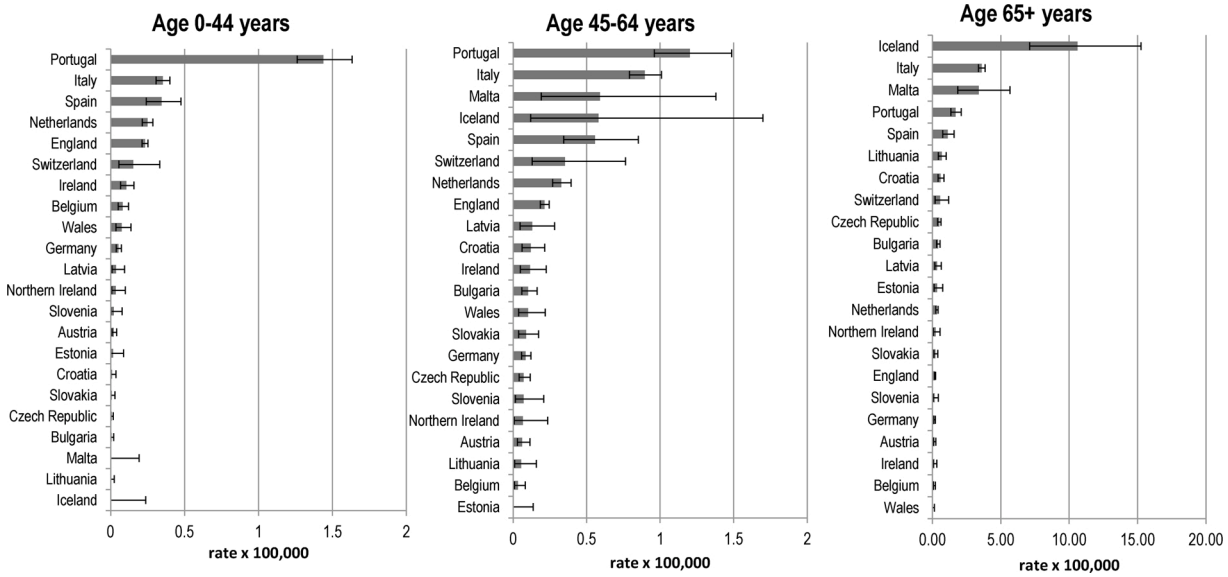


Fig. 2. Kaposi sarcoma (KS) incidence rate by age groups and country. RARECAREnet cancer registries (2000-2007).

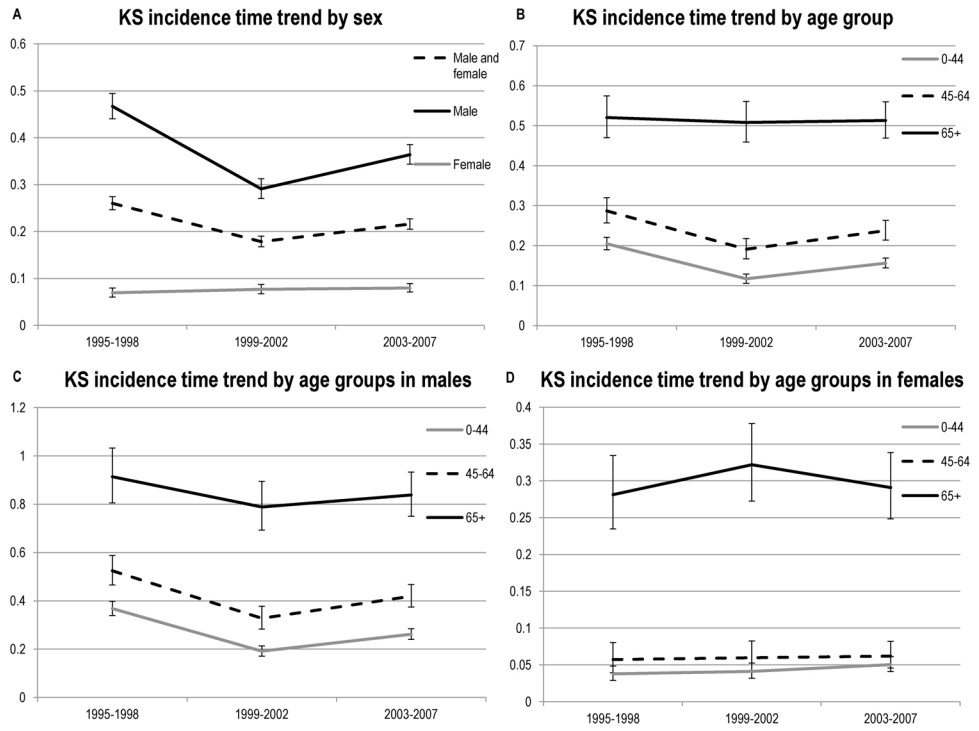
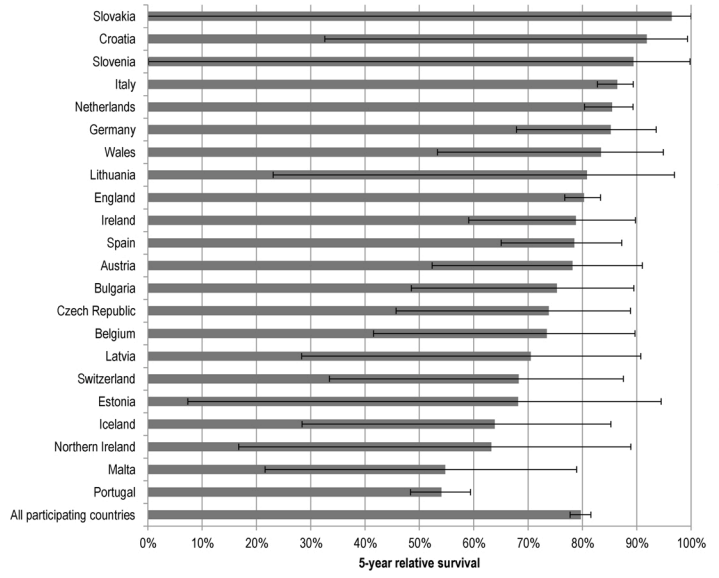


Fig. 3. Kaposi sarcoma (KS) incidence trends by sex (A); by age group (B); by age groups in males (C) and females (D). RARECAREnet cancer registries (1995-2007).



	N	RS	SE
0-44 years	1,355	75.37%	1.26%
Male	1,156	75.77%	1.36%
Female	199	73.05%	3.35%
45-64 years	814	79.48%	1.62%
Male	696	80.87%	1.72%
Female	118	71.86%	4.52%
65+ years	1,432	84.33%	2.05%
Male	915	83.79%	2.63%
Female	517	85.16%	3.26%

Fig. 4. Kaposi sarcoma (KS) 5-year relative survival (RS) by country and Europe overall together with relative survival by age group and sex. RARECAREnet cancer registries (2000-2007). Bars are 95 % confidence intervals; SE is the standard error.

This study has important strengths. The data are from population-based CRs and have been subjected to uniform, stringent validation procedures. It contains information from more CRs than the previous RARECARE study, and the number of cases available for analysis was considerably increased. Six additional countries are represented, all from Eastern Europe. Coverage in the Netherlands and England has been extended from regional (34 % and 58 % respectively) to national. Population coverage in Germany has been increased from 1.3%–20%. The study does still, however, have some limitations. Epidemiological subtype of KS is not generally recorded by CRs; age group was used as a proxy for AIDS-related and classic KS, and it was not possible to make inferences concerning iatrogenic KS. Data were available only on patients diagnosed up to 2007. However, these are the most recent population-based data on KS across Europe until the EUROCARE-6 database becomes available for analyses. Population coverage in Eastern Europe has been substantially improved but, with the exception of the Baltic states, there are still no data from countries of the former Soviet Union, where AIDS incidence is high. There are also still no data from Greece, which has high incidence of classic KS [27] and where, more recently, AIDS incidence has been moderately high [16].

Between 2005 and 2015, incidence and prevalence of AIDS were decreasing through most of Western Europe. [16] Therefore, incidence of KS would be expected to continue to decline, although the high survival rate would still lead to increasing prevalence. A recent analysis of

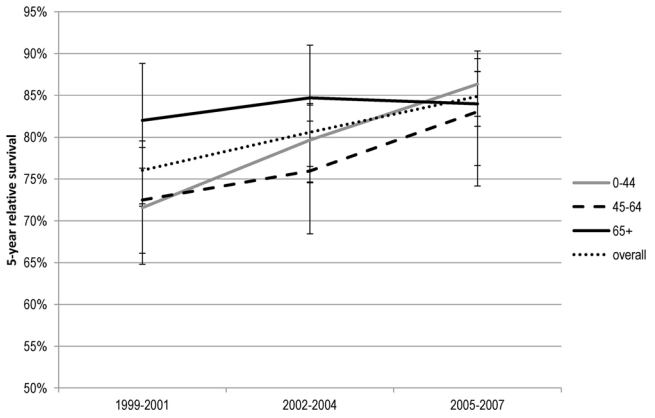


Fig. 5. Kaposi sarcoma 5-year relative survival trends by age group in Europe. RARECAREnet cancer registries (1999-2007).

data from 11 population-based cancer registries of the FRANCIM network in France found that age-adjusted incidence decrease significantly at a rate of 4.1 % per year between 2000 and 2013. [28] In countries of the former Soviet Union, however, incidence and prevalence of AIDS increased between 2005 and 2015 [16] and this, together with generally lower rates of ART coverage than in Western Europe, would be expected to lead to continuing increases in KS incidence. Also, the proportion of people with AIDS who are at least 50 years of age has been increasing [29], which could result in increasing numbers of older patients with AIDS-related KS. Thus, KS will likely continue to require a substantial amount of health care resource throughout Europe for the foreseeable future. Evidence-based guidelines for the management of KS developed by a group from 15 European countries [30], together with improved access to treatment, may lead to further improvements in survival and quality of life for the increasing number of people in Europe affected by this disease. Clinical trials of local and systemic therapies for KS, whether local or systemic, have generally included small numbers of patients [30]. Population-based cancer registries will continue to play a vital role in monitoring the burden of KS and improvements in its outcome.

Authorship contribution statement

- Conception or design of the work Charles Stiller, Annalisa Trama
- Data analysis and interpretation Charles Stiller, Laura Botta, Annalisa Trama,
- Data collection Dyfed Wyn Huws, Tiziana Scuderi, Rafael Marcos Gragera, María Dolores Chirlaque López, Maria José Sánchez Perez, and all the RARECARENet WG
- Drafting the article Charles Stiller, Annalisa Trama
- Critical revision of the article Dyfed Wyn Huws, Tiziana Scuderi, Rafael Marcos Gragera, María Dolores Chirlaque López, Maria José Sánchez Perez, Laura Botta
- Final approval of the version to be published All authors including the RARECARENet WG

Data statement

All aggregated data generated for this study are included in the manuscript and/or the supplementary files. The row data that support the findings of this study are available from the corresponding author but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available.

Funding

This work was supported by the European Commission through the Consumers, Health, Agriculture, and Food Executive Agency (Chafea) [grant number 2000111201]–Information network on rare cancers—RARECARENet. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Ethics statement

The study was approved by the Ethics Committee of the IRCCS National Cancer Institute. Being a retrospective study on a rare cancer, the written consent was not necessary.

CRediT authorship contribution statement

Charles A Stiller: Supervision, Visualization, Writing - review & editing, Writing - original draft, Methodology, Conceptualization. **Laura Botta:** Visualization, Writing - review & editing, Data curation, Investigation, Formal analysis, Validation, Methodology. **Maria José Sánchez Perez:** Writing - review & editing, Investigation. **María Dolores Chirlaque López:** Writing - review & editing, Investigation. **Rafael Marcos-Gragera:** Writing - review & editing, Investigation. **Tiziana Scuderi:** Writing - review & editing, Investigation. **Dyfed Wyn Huws:** Writing - review & editing, Investigation. **Annalisa Trama:** Project administration, Supervision, Visualization, Writing - review & editing, Writing - original draft, Data curation, Investigation, Formal analysis, Validation, Methodology.

Declaration of Competing Interest

The authors report no declarations of interest.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.canep.2020.101877.

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