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Survival of European adolescents and young adults diagnosed with cancer in 2010–2014

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ABSTRACT

Background: We used the comprehensive definition of AYA (age 15 to 39 years) to update 5-year relative survival (RS) estimates for AYAs in Europe and across countries and to evaluate improvements in survival over time.
Methods: We used data from EUROCARE-6. We analysed 700,000 AYAs with cancer diagnosed in 2000–2013 (follow-up to 2014). We focused the analyses on the 12 most common cancers in AYA. We used period analysis to estimate 5-year RS in Europe and 5-year RS differences in 29 countries (2010–2014 period estimate) and over time (2004–06 vs. 2010–14 period estimates).
Findings: 5-year RS for all AYA tumours was 84%, ranging from 70% to 90% for most of the 12 tumours analysed. The exceptions were acute lymphoblastic leukaemia, acute myeloid leukaemia, and central nervous system tumours, presenting survival of 59%, 61%, and 62%, respectively. Differences in survival were observed among European countries for all cancers, except thyroid cancers and ovarian germ-cell tumours. Survival improved over time for most cancers in the 15- to 39-year-old age group, but for fewer cancers in adolescents and 20- to 29-year-olds.
Interpretation: This is the most comprehensive study to report the survival of 12 cancers in AYAs in 29 European countries. We showed variability in survival among countries most likely due to differences in stage at diagnosis, access to treatment, and lack of referral to expert centres. Survival has improved especially for haematological cancers. Further efforts are needed to improve survival for other cancers as well, especially in adolescents.

1. Introduction

1.1. Background and rationale

In Europe, 112,000 people develop cancer between ages 15 and 39, corresponding to 5% of all new cancer diagnoses [1]. Although rare, cancer is the fourth leading cause of death in adolescents and young adults (AYAs) globally [2].

EUROCARE data on AYAs showed a 5-year relative survival (RS) of 79% in 1999–2002 for all cancers combined, improving significantly to 82% in 2005–07 [3]. However, the cancer types occurring in this age group have a unique distribution and survival varies by cancer type.

To ensure the best results, young people who develop malignant tumours should be referred to specialised centres. European cooperative studies have helped highlight the lack of equitable access to oncology services that provide expert cancer care [4]. However, initiatives to develop national policies for AYAs with cancer have been implemented in different forms and to different extents across Europe [4]. The last comparison of cancer survival among AYAs (aged 15–24 years) across European countries dates back to 1995 [5].

1.2. Objectives

To provide updated population-based analyses of 5-year RS for AYAs with cancer in Europe, across 29 European countries and present 5-year RS over time.

We have used the all-inclusive definition of the AYA age range, namely 15 to 39 years. To avoid masking the heterogeneity typical of AYA cancers, we also present results by sex and AYA age group for 12 major cancers typically occurring in AYAs.

2. Methods

We used the EUROCARE-6 adult database which includes data from 108 population-based cancer registries (CRs) from 29 countries. Registries provided information on the site and morphology of each diagnosed cancer, which were coded according to the International Classification of Disease for Oncology, Third Edition, first update (ICD-O-3.1). We included only malignant cancers. If two or more cancers were diagnosed in a patient within the study period, we included all of them. We excluded from the analyses cases ascertained solely through a death certificate or autopsy report, those alive at diagnosis with unknown survival time, and those with invalid data items.

The most common cancers in AYAs were grouped into 12 diagnostic categories adapted from Barr (Supplementary Material, Table S1) [6].

2.1. Overall survival

We calculated 5-year RS in the follow-up period 2010–2014 using the period approach based on cases diagnosed in 2006–2013, who were followed up for vital status to December 31, 2014 [7]. We estimated RS, the ratio of observed to expected survival in the general population of the same age, sex, and calendar year and calculate 95% confidence intervals (CIs). We estimated expected survival using the Ederer II method

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[8]. When comparing RS estimates, we considered differences to be significant if CIs did not overlap.

To provide valid estimates of European survival we applied population weightings to region-specific RS estimates to correct for differing numbers of AYAs in the five different regions of Europe (northern [Denmark, Finland, Iceland, and Norway], central [Austria, Belgium, France, Germany, Netherlands, and Switzerland], southern [Croatia, Cyprus, Italy, Malta, Portugal, Slovenia, and Spain], eastern [Bulgaria, Czechia, Estonia, Latvia, Lithuania, Poland, and Slovakia], and the UK and Ireland [England, Ireland, Northern Ireland, Scotland, and Wales]). The weightings applied to RS estimates for each European region consisted of the ratio of the population in the region to that of the European population as a whole.

5-year RS by sex was age standardised. Weightings for 15–19-, 20–29-, and 30–39-year-olds were based on the distribution of incident cases in the three age groups in the EUROCARE-6 database, corresponding to 6%, 27%, and 67%, respectively.

We used a funnel plot to identify relevant survival differences across European countries and the EUROCARE-6 pool as a proxy for Europe. We considered a difference to be relevant if it fell outside the ± 2 standard error band.

To identify differences in survival among countries, possibly due to differences in stage distribution at diagnosis, we calculated 5-year RS conditional to surviving one year as the ratio of 5-year to 1-year RS, for each AYA cancer across countries.

2.2. Survival time trends

We analysed survival trends from 2004 to 2014 using the period approach [9]. We defined two follow-up periods, namely 2010–2014 (cohort diagnosed in 2006–2013) and 2004–2006 (cohort diagnosed in 2000–2006). We presented changes over time in RS for AYA cancers using funnel plots for AYAs as a whole and by age groups (15–19, 20–29, 30–39 years-of-age). In both periods, 5-year RS was age standardised, using cancer-specific weights.

3. Results

Only 1% of cancers in AYAs were excluded. Most cancers (97%) were verified microscopically (Table 1). Morphology was unspecified in 4% of cancers eligible for analysis. Only 3% of cancers diagnosed in 2005–2008 were lost to follow-up (Table 1).

Table 2 shows 5-year RS for all cancers combined and for the 12 most frequently diagnosed tumours in AYAs. Five-year RS for all cancers combined was 84%. Haemopoietic malignancies were the most common cancers in the 15–19 and 20–29-year age groups. At all AYA ages, survival was 95% for Hodgkin lymphomas (HLs), 84% for Non-Hodgkin lymphomas (NHLs), 93% for Chronic myeloid leukaemia (CML), and 59% for Acute myeloid leukaemia (AML). Acute lymphoblastic leukaemia (ALL) survival was 61% overall but was higher in adolescents (73%) than in older adults (about 50%). Germ cell tumor (GCT) and skin melanoma were the second and third most common cancers in 15–19 and 19–29-year-olds; both had 5-year RS greater than 90% in all age groups. For all AYA ages, 5-year RS was 64% for osteosarcoma, 52% for Ewing family tumours, and 86% for chondrosarcoma. Among soft tissue sarcomas (STSs) for AYAs of all ages, good 5-year RS was observed for liposarcomas, leiomyosarcoma, synovial sarcoma, and fibromatous tumours, proving lowest for rhabdomyosarcomas.

Among the Central nervous system (CNS) tumours, survival from astrocytoma not otherwise spedified (NOS) differed between adolescents (83% and 30–39-year-olds (68%). Anaplastic astrocytoma was very low in adolescents, increasing in young adults but with no major differences in survival between age groups. For all AYA ages, survival was highest from ependymoma and lowest from glioblastoma. Carcinomas were rarely diagnosed in adolescents, but occurrence increased with advancing age. In adolescents, thyroid carcinoma was the most common carcinoma (5-year RS, 99%). In young adults, female genital tract and breast carcinomas were the most common malignancies, with 5-year RS of around 85% in all age groups. Other relatively common carcinomas in young adults were thyroid and colorectal carcinomas, showing excellent and intermediate 5-year RS (99% and 66%, respectively).

Table 3 shows 5-year RS by sex in AYAs and by AYA age groups. Survival was better for females than males for leukaemias, AML, lymphomas, NHLs, CNS tumours, STS, bone sarcomas, and skin melanoma. Differences were not observed in adolescents, with the exception of lymphomas, but increased from age 20–29 years onwards.

Table 4 shows 5-year RS by countries. Differences in survival were observed among European countries for all AYA cancers, except thyroid cancers and ovarian GCT. Testicular GCT, breast cancer, and HL were the cancers with the lowest intercountry differences in survival (ie, the difference between the countries with the best and worst survival): 12%, 13%, 15%, respectively. AML and bone sarcomas were the cancers with the highest intercountry difference in survival: 58% and 42%, respectively. For all the other cancers, the survival gap ranged from 20% to 40%.

Belgium, Germany, Norway, Denmark, and the Netherlands most often displayed survival above the European average (Table 4; Supplementary Material, Fig. S1). Poland and Bulgaria had lower survival than the EU average for most AYA cancers. We observed no differences from the European average for the remaining countries for most AYA cancers.

We observed lower conditional survival differences compared to differences in 5-year RS among countries for AML, NHL, CNS, and colorectal cancers but not for ALL, STS, bone sarcomas, and cervical cancers (Supplementary Material, Table S2).

Survival rose from 2004–2006 to 2010–2014 for all AYA cancers except STS and thyroid tumours (Fig. 1a). In adolescents (Fig. 1b), there was no evidence of improvement in survival for AML, NHL, CNS tumours, bone sarcoma, ovarian GCT, skin melanoma, and cancers of the thyroid, colon, rectum, breast, and cervix. STS survival increased only in adolescents. In 20–29-year-olds (Fig. 1c), survival did not increase for bone sarcomas, STS, GCT of the ovary, and colorectal and thyroid cancers. In the older age group (Fig. 1d), STS and thyroid cancers were the only ones in which survival failed to improve. Detailed time trend survival data are shown in Supplementary Material, Table S3.

4. Discussion

Our two key findings were that AYAs have good 5-year RS (from 70% to 90%) for most cancers, with a slightly lower survival for AML, ALL, and CNS tumours, and that survival has improved over time for most cancers in the 15- to 39-year-old age group, but for fewer cancers in adolescents and 20- to 29-year-olds. Another important finding of our study was that differences in survival remained among European countries.

The observed survival for AML is in line with other studies [10]. Neither paediatric nor adult protocols are ideal for AYAs and the development of AYA-specific approaches is recommended [11]. We observed an increase in 5-year RS for AML, which reached the survival of ALL (nearly 60%). ALL survival is approximately 60%.

The application of paediatric protocols has improved ALL outcomes, but most AYA patients were still treated with an adult regimen [12]. We observed higher survival for ALL in adolescents compared to the older age groups, which likely reflects the increasing use of paediatric treatment protocols in adolescents.

The histological heterogeneity and low incidence of CNS tumours makes their management challenging in AYAs. We observed that adolescents have a higher proportion of embryonal tumours and a lower proportion of high-grade gliomas compared to young adults, which helps explain why survival from CNS tumours is higher in adolescents than in 30–39-year-olds. However, despite recent significant advances in neuro-oncology, CNS tumours among AYAs continued to contribute

Table 1
Cancer cases in adolescents and young adults (aged 15–39 years) diagnosed in 2000–13, in 29 European countries, with data quality indicators.

			Invalid cases excluded from survival analysis					Quality indicators		
Country	Percentage population covered by cancer registration (%)	Eligible cases diagnosed in 2000-13	Major errors	Death certificate only	Incidentally detected at autopsy	Alive cases at diagnosis with unknown survival time[#]	Valid cases for survival analysis	Microscopic confirmation	Morphology not otherwise specified[§]	2005-2008 Lost to follow-up*
AT_Austria National	100%	21 497	0 (0%)	200 (0.9%)	0 (0%)	0 (0%)	21 297	20 784 (97.6%)	621 (2.9%)	0/5382 (0%)
BE_Belgium National	100%	25 154	0 (0%)	0 (0%)	4 (0%)	330 (1.3%)	24 820	24 698 (99.5%)	228 (0.9%)	136/7789 (0%)
BG_Bulgaria National	100%	19 375	43 (0.2%)	627 (3.2%)	0 (0%)	0 (0%)	18 705	18 039 (96.4%)	864 (4.6%)	0/3435 (0%)
CR_Croatia National	100%	11 859	0 (0%)	72 (0.6%)	0 (0%)	69 (0.6%)	11 718	10 012 (85.4%)	2029 (17.3%)	0/2157 (0%)
CY_Cyprus National	100%	2099	0 (0%)	12 (0.6%)	0 (0%)	0 (0%)	2087	2071 (99.2%)	20 (1%)	0/637 (0%)
CZ_Czech Republic National	100%	29 773	4 (0%)	79 (0.3%)	191 (0.6%)	141 (0.5%)	29 361	28 616 (97.5%)	1065 (3.6%)	0/6666 (0%)
DK_Denmark National	100%	17 540	7 (0%)	0 (0%)	7 (0%)	2 (0%)	17 529	17 171 (98%)	616 (3.5%)	50/4091 (1.2%)
EE_Estonia National	100%	2973	0 (0%)	8 (0.3%)	23 (0.8%)	1 (0%)	2941	2871 (97.6%)	90 (3.1%)	11/636 (0%)
FI_Finland National	100%	12 467	86 (0.7%)	2 (0%)	44 (0.4%)	0 (0%)	12 378	12 296 (99.3%)	222 (1.8%)	0/2672 (0%)
FR_France (CRs Pool)	29%	34 079	0 (0%)	0 (0%)	0 (0%)	196 (0.6%)	33 883	33 663 (99.4%)	260 (0.8%)	85/7295 (0%)
GE_Germany (CRs Pool)	35%	57 383	39 (0.1%)	632 (1.1%)	19 (0%)	232 (0.4%)	56 493	53 963 (95.5%)	747 (1.3%)	217/13 575 (0%)
IC_Iceland National	100%	1015	0 (0%)	0 (0%)	4 (0.4%)	0 (0%)	1011	1006 (99.5%)	7 (0.7%)	0/220 (0%)
IR_Ireland National	100%	12 317	0 (0%)	8 (0.1%)	8 (0.1%)	0 (0%)	12 301	12 105 (98.4%)	304 (2.5%)	0/3097 (0%)
IT_Italy (CRs Pool)	49%	71 571	1 (0%)	68 (0.1%)	13 (0%)	221 (0.3%)	71 269	67 775 (95.1%)	4365 (6.1%)	702/20 720 (0%)
LT_Lithuania National	100%	7981	0 (0%)	108 (1.4%)	6 (0.1%)	19 (0.2%)	7848	7488 (95.4%)	572 (7.3%)	59/1696 (0%)
LV_Latvia National	100%	5026	6 (0.1%)	142 (2.8%)	36 (0.7%)	0 (0%)	4877	4582 (94%)	565 (11.6%)	0/826 (0%)
ML_Malta National	100%	1047	4 (0.4%)	2 (0.2%)	2 (0.2%)	0 (0%)	1042	1015 (97.4%)	23 (2.2%)	0/226 (0%)
NL_The Netherlands National	100%	50 942	3 (0%)	0 (0%)	31 (0.1%)	0 (0%)	50 910	49 043 (99.3%)	367 (0.7%)	0/11 249 (0%)
NO_Norway National	100%	15 101	237 (1.6%)	7 (0%)	13 (0.1%)	0 (0%)	14 847	14 713 (99.1%)	153 (1%)	0/3324 (0%)
PL_Poland National	100%	75 863	22 (0%)	332 (0.4%)	27 (0%)	486 (0.6%)	75 018	69 438 (92.6%)	9012 (12%)	0/16 650 (0%)
PT_Portugal (CRs Pool)	98%	23 188	91 (0.4%)	6 (0%)	0 (0%)	69 (0.3%)	23 023	22 575 (98.1%)	841 (3.7%)	56/5904 (0%)
SK_Slovakia National	100%	11 671	2 (0%)	194 (1.7%)	38 (0.3%)	0 (0%)	11 477	11 280 (98.3%)	281 (2.4%)	0/3153 (0%)
SL_Slovenia National	100%	5741	0 (0%)	0 (0%)	11 (0.2%)	0 (0%)	5730	5707 (99.6%)	45 (0.8%)	0/1436 (0%)
SP_Spain (CRs Pool)	21%	24 449	127 (0.5%)	71 (0.3%)	11 (0%)	11 (0%)	24 230	23 915 (98.7%)	439 (1.8%)	45/6482 (0%)
SW_Switzerland (CRs Pool)	24%	5419	33 (0.6%)	0 (0%)	1 (0%)	18 (0.3%)	5367	5342 (99.5%)	38 (0.7%)	131/1342 (0.1%)
UK_England National	100%	129 944	187 (0.1%)	409 (0.3%)	0 (0%)	0 (0%)	129 383	12 5100 (96.7%)	3078 (2.4%)	0/28 624 (0%)
UK_Northern Ireland National	100%	5190	0 (0%)	9 (0.2%)	2 (0%)	0 (0%)	5179	4873 (94.1%)	249 (4.8%)	0/1240 (0%)
UK_Scotland National	100%	14 850	1 (0%)	11 (0.1%)	12 (0.1%)	1 (0%)	14 826	14 621 (98.6%)	185 (1.2%)	15/3252 (0%)
UK_Wales National	100%	7201	1 (0%)	24 (0.3%)	0 (0%)	0 (0%)	7177	6301 (87.8%)	366 (5.1%)	0/1701 (0%)
European Pool (108 CRs)	**58%**	**702 715**	2417 (0%)	3023 (0.4%)	503 (0.1%)	1796 (0.3%)	**696 727**	67 1063 (96.3%)	27 652 (3.9%)	4949/170 799 (0%)

For "Invalid case excluded from survival analysis", the denominator for the percentages is the number of eligible cases diagnosed in 2000-2013 For data quality indicators, the denominator for the percentages is the number of valid cases for survival analysis, unless specified otherwise. [#]Patient alive at diagnosis but with no information on follow-up time [§]Morphology not otherwise specified (NOS) are: Unspecified leukaemias and related disorders (Morphologies=9800-9801,9805,9820,9860,9930, all sites), Unspecified lymphomas (Morphologies=9590,9596, all sites), Unspecified soft tissue sarcomas (Morphologies=8800-8802,8805, in all sites except C40.0-C41.9), Unspecified bone sarcomas (Morphologies=8000-8005,8800-8801,8805, in C40.0-C41.9), NOS morphologies of the Central Nervous system (Morphologies=8000-8005 in C700-C729,C751-C753) and NOS morphologies of all the all sites, except CNS (Morphologies=8000-8005, in C00-C399,C420-C699,C730-C750,C754-C809). *Proportion of patients diagnosed during 2005-2008, censored before Dec 31, 2013, with less than 5 years of follow-up; the proportion is calculated for cases diagnosed in 2005-07 in Croatia and Germany, where the follow-up closing date was Dec 31, 2012. In France, Germany, Italy, Portugal, Spain, and Switzerland registries are local rather than national and were pooled together; in Portugal the three registries participating in EUROCARE-6 cover the whole country (excluding the Azores), which is not the case in Spain and Italy.

Table 2
Five-year relative survival (RS) estimates for the most common cancers affecting European adolescents and young adults (aged 15–39 years) in 2010–2014, reported with number of cases (N) and 95% confidence intervals (95%CI).

	15-39 years			15-19 years			20-29 years			30-39 years		
	N	RS (95% CI)	SE	N	RS (95% CI)	SE	N	RS (95% CI)	SE	N	RS (95% CI)	SE
Leukaemias and related disorders	9971	73·5% (72·5% - 74·4%)	0·5%	1678	71·8% (69.2–74.2%)	1.2%	3158	71.0% (69.2–72.8%)	0.9%	5136	75.4% (74.1–76.6%)	0.6%
-Acute lymphoblastic leukaemia	2311	60.9% (58.6–63.2%)	1.1%	872	73.2% (69.7–76.4%)	1.7%	817	55.1% (51.0–58.9%)	2.0%	641	52.0% (47.6–56.2%)	2.1%
-Acute myeloid leukaemia	3323	59.3% (57.4–61.2%)	0.9%	470	61.1% (55.6–66.2%)	2.7%	1154	61.6% (58.2–64.7%)	1.6%	1700	57.4% (54.7–60.0%)	1.3%
-Chronic myeloid leukaemia	1451	93.1% (91.4–94.5%)	0.8%	108	89.0% (79.6–94.2%)	3.5%	454	93.9% (90.6–96.1%)	1.3%	893	92.9% (90.7–94.6%)	1.0%
Lymphomas	25 071	89.8% (89.4–90.2%)	0.2%	3357	92.1% (91.0–93.1%)	0.5%	9 654	91.1% (90.4–91.7%)	0.3%	12 061	88.1% (87.4–88.8%)	0.3%
-Non-Hodgkin lymphomas	9907	84.0% (83.2–84.8%)	0.4%	875	83.6% (80.6–86.2%)	1.4%	3 037	83.2% (81.6–84.6%)	0.7%	6018	84.4% (83.4–85.4%)	0.5%
- Lymphoblastic	343	60.8% (55.0–66.1%)	2.8%	92	68.3% (56.6–77.4%)	5.2%	143	56.7% (47.7–64.7%)	4.3%	112	59.7% (48.5–69.2%)	5.2%
- Burkitt	622	75.0% (70.8–78.6%)	2.0%	127	75.0% (64.0–83.0%)	4.7%	214	79.5% (72.4–84.9%)	3.1%	286	70.8% (64.2–76.4%)	3.0%
- Diffuse large B-cell (DLBCL)	3418	82.1% (80.6–83.5%)	0.7%	257	88.1% (83–91.7%)	2.1%	1123	83.2% (80.5–85.5%)	1.3%	2 049	81.1% (79.1–83.0%)	1.0%
- Primary mediastinal large B-cell excluded from DLBCL	421	90.4% (85.7–93.6%)	1.9%	49	91.7%* (79.3%* −96.8%*)	4%	174	87.5% (77.9–93.1%)	3.6%	196	91.8% (87.0–94.9%)	1.9%
- Anaplastic T- and null-cell, excluding NK/T-cell	375	81.9% (76.6–86.0%)	2.3%	70	81.0% (66.8–89.6%)	5.6%	149	84.0% (75.5–89.8%)	3.5%	159	78.8% (70.5–85.0%)	3.6%
- Follicular	1543	94.6% (93.2–95.8%)	0.6%	46	95.4% (85.2–98.6%)	2.7%	296	93.1% (88.5–95.9%)	1.8%	1212	94.9% (93.2–96.2%)	0.7%
- NK/T-cell (excluded from anaplastic T-cell)	515	58.1% (52.8–63.0%)	2.6%	46	67.4%* (50.8%* - 79.5%*)	7.3%	166	61.8% (52.1–70.2%)	4.5%	304	55.0% (48.2–61.4%)	3.3%
- MALT (mucosa-associated lymphoid tissue)	659	95.1% (93.0–96.6%)	0.9%	30	100% (100–100%)	0.0%	176	96.8% (93.1–98.5%)	1.2%	450	93.8% (91.0–95.8%)	1.2%
- Other non-Hodgkin lymphoma NOS	1548	85.3% (83.0–87.3%)	1.1%	127	84.6%* (76.6%* - 90.0%*)	3.4%	484	87.6% (83.6–90.7%)	1.8%	943	84.1% (81.0–86.8%)	1.5%
-Hodgkin lymphoma	13 604	95.0% (94.6–95.3%)	0.2%	2379	95.5% (94.5–96.3%)	0.4%	6256	95.3% (94.7–95.8%)	0.3%	4970	94.2% (93.5–94.9%)	0.4%
Central nervous system and other intracranial and intraspinal neoplasms	9722	61.6% (60.5–62.8%)	0.6%	1004	64.3% (60.6–67.8%)	1.8%	3271	66.0% (64.0–67.9%)	1.0%	5448	58.5% (57.0–60.0%)	0.8%
-Oligodendroglioma	1180	77.5% (74.7–80.0%)	1.3%	63	65.1% (51.1–76.0%)	6.3%	377	77.9% (72.8–82.3%)	2.4%	744	78.6% (75.1–81.7%)	1.6%
- Oligodendroglioma, low grade/ NOS	837	84.8% (82.0–87.3%)	1.3%	42	82.5% (67.2–91.1%)	5.7%	272	84.7% (79.2–88.8%)	2.4%	525	85.0% (81.3–88.0%)	1.7%
- Oligodendroglioma, anaplastic	348	59.2% (53.0–64.8%)	3.0%	22	29.4%* (12.3%* - 49.0%)	9.9%	106	57.2% (44.4–68.1%)	6.0%	222	62.9% (55.3–69.6%)	3.6%
-Ependymoma	657	88.1% (85.0–90.5%)	1.4%	96	86.7% (77.3–92.4%)	3.6%	227	87.7% (81.5–91.9%)	2.5%	333	88.6% (84.3–91.9%)	1.9%
-Medulloblastoma	372	72.6% (67.5–77.1%)	2.4%	107	70.8% (59.8–79.3%)	4.9%	162	72.1% (64.0–78.7%)	3.7%	106	74.2% (64.7–81.4%)	4.2%
-Astrocytoma, low grade/NOS	1415	74.0% (71.2–76.6%)	1.3%	137	82.8% (73.1–89.3%)	4.0%	508	81.8% (77.3–85.5%)	2.0%	775	68.1% (64.2–71.7%)	1.9%
-Astrocytoma, anaplastic	885	49.1% (45.0–53.1%)	2.0%	57	37.0%* (24.5%*−49.6%*)	6.5%	329	52.1% (45.2–58.5%)	3.3%	507	49.6% (44.1–54.8%)	2.7%
-Glioblastoma	1748	22.2% (19.9–24.5%)	1.2%	128	23.5% (14.7–33.5%)	4.8%	465	27.9% (22.6–33.4%)	2.7%	1167	20.4% (17.7–23.1%)	1.4%
Bone sarcomas	2860	69.6% (67.6–71.5%)	1.0%	910	65.2% (61.6–68.6%)	1.7%	1028	68.5% (65.1–71.7%)	1.6%	935	74.9% (71.6–78.0%)	1.6%
-Osteosarcoma	995	64.7% (61.2–67.9%)	1.7%	452	67.0% (61.8–71.6%)	2.4%	319	62.0% (55.6–67.7%)	3.0%	228	64.9% (57.6–71.3%)	3.4%
-Chondrosarcoma	694	85.8% (82.3–88.7%)	1.6%	69	84.0% (72.4–91.0%)	4.5%	233	91.1% (86.2–94.3%)	2.0%	396	84.1% (79.3–87.9%)	2.1%
-Ewing family of tumours of bone	718	51.9% (47.6–56.0%)	2.1%	310	54.0% (47.7–60.0%)	3.1%	293	49.1% (42.2–55.6%)	3.3%	122	51.8% (40.9–61.6%)	5.2%
Soft tissue sarcomas (excluding skin sarcomas)	4710	69.0% (67.5–70.5%)	0.7%	653	67.0% (62.8–70.9%)	2.0%	1471	65.2% (62.3–68.0%)	1.4%	2599	71.5% (69.4–73.4%)	1.0%
-Liposarcoma	743	86.5% (83.6–89.0%)	1.4%	37	100%* (100%* - 100%*)	0.0%	163	89.0% (81.5–93.5%)	2.9%	542	84.8% (81.2–87.8%)	1.6%
-Leiomyosarcoma	585	74.7% (70.1–78.6%)	2.1%	27	91.7%* (70.0%* - 97.9%*)	5.7%	124	80.3% (69.4–87.6%)	4.5%	435	70.9% (65.3–75.8%)	2.6%
-Synovial sarcoma	586	64.9% (60.4–69.0%)	2.1%	104	72.1% (61–80.6%)	4.9%	223	67.2% (59.8–73.6%)	3.4%	260	59.9% (53.1–66.1%)	3.3%
-Fibromatous neoplasms	577	85.4% (81.7–88.5%)	1.7%	50	87.2% (77–93.1%)	3.9%	199	87.6% (81.6–91.7%)	2.5%	332	83.4% (77.7–87.7%)	2.5%
-Rhabdomyosarcoma	408	41.7% (36.2–47.1%)	2.7%	183	46.6% (38.3–54.5%)	4.1%	138	35.5% (26.7–44.5%)	4.5%	97	37.1%* (27.0%* −47.2%*)	5.2%
- Paediatric rhabdomyosarcoma	239	37.5% (30.9–44.2%)	3.3%	127	42.1% (32.6–51.2%)	4.7%	80	33.2% (22.5–44.2%)	5.5%	39	29.7%* (15.8%* - 45.0%*	7.7%
- Embryonal rhabdomyosarcoma, NOS	101	54.8% (43.7–64.6%)	5.3%	52	60.6% (43.9–73.7%)	7.5%	35	55.5%* (36.9%* - 70.7%*)	5.1%	17	36.9%* (15.1%* −59.1%*)	12.0%
- Alveolar rhabdomyosarcoma	138	20.3% (13.2–28.6%)	3.9%	75	23.4%* (14.1%* - 34.1%*)	5.2%	45	14.7% (6.0–27.0%)	5.4%	22	22.0%* (7.0%* - 42.1%*)	9.5%
- Rhabdomyosarcoma, NOS	132	45.5% (33.2–57.0%)	6.0%	46	47.7% (29.9–63.5%)	8.6%	45	47.1% (24.9–66.5%)	10.9%	41	37.6%* (20.3%* - 54.9%*)	9.2%
Germ cell and trophoblastic of testis	24 184	96.9% (96.6–97.2%)	0.1%	1157	97.0% (95.7–98.0%)	0.5%	10 197	96.6% (96.1–97.0%)	0.2%	12 844	97.1% (96.7–97.5%)	0.2%

(*continued on next page*)

Table 2 (*continued*)

	15-39 years			15-19 years			20-29 years			30-39 years		
	N	RS (95% CI)	SE	N	RS (95% CI)	SE	N	RS (95% CI)	SE	N	RS (95% CI)	SE
Germ cell and trophoblastic of ovary	861	95.5% (93.4–96.9%)	0.9%	213	96.3% (91.8–98.4%)	1.5%	420	96.2% (93.6–97.8%)	1.0%	236	92.8% (86.8–96.1%)	2.2%
Melanoma - malignant	25 402	92.9% (92.5–93.2%)	0.2%	801	94.6% (92.5–96.1%)	0.9%	7448	94.0% (93.3–94.7%)	0.3%	17 160	92.3% (91.8–92.7%)	0.2%
Thyroid carcinoma	19 290	99.5% (99.4–99.6%)	0.1%	1 024	99.5% (98.6–99.8%)	0.3%	5927	99.7% (99.4–99.8%)	0.1%	12 326	99.4% (99.2–99.6%)	0.1%
Carcinoma of colon and rectum (excluding appendix)	7872	65.9% (64.7–67.1%)	0.6%	85	54.1% (41.9–64.8%)	5.8%	1409	64.4% (61.3–67.3%)	1.5%	6385	66.4% (65.1–67.7%)	0.6%
Carcinoma of breast	34 002	86.4% (86.0–86.8%)	0.2%	29	88.4% (71.3–95.6%)	5.5%	3402	84.1% (82.7–85.4%)	0.7%	30 637	86.7% (86.3–87.1%)	0.2%
Carcinoma of uterine cervix	14 091	85.9% (85.1–86.6%)	0.4%	18	86.3%* (54.6%* - 96.5%)	9.2%	3254	88.3% (86.4–89.9%)	0.9%	10 912	85.2% (84.4–86.0%)	0.4%
All cancers	**212 135**	**84.1% (83.9–84.3%)**	**0.1%**	**12 441**	**84.2% (83.5–84.9%)**	**0.4%**	**57 994**	**87.1% (86.8–87.4%)**	**0.2%**	**141 727**	**82.9% (82.7–83.1%)**	**0.1%**

*=Not area-weighted
NOS= Not otherwise specified

significantly to mortality [13].

HL, NHL, CML, testicular GCT, skin melanoma, STS, bone sarcomas, thyroid, breast, cervical, and colorectal cancers displayed 5-year RS between 70% and 90%. Survival was highest among 30–39-year-olds for bone sarcomas, STS, and colorectal cancers. The tumour case mix helps explain the differences for bone sarcomas and STS. Chondrosarcoma had a high RS ($>$ 80%), representing 40% of bone sarcomas in the 30–39 age group compared to only 8% in adolescents. Liposarcoma and leiomyosarcomas also had a high RS and were more common in 30–39-year-olds than among adolescents, who had a high rate of rhabdomyosarcomas with an RS of approximately 50%. Finally, lower survival for colorectal cancer in adolescents has been attributed to the higher proportion of advanced stage lesions and a worse histological subtype compared to older AYAs [14].

Survival rose over the study period for almost all tumours (Fig. 1). The tumours with the greatest increase in survival were ALL and CML (11%) followed by AML and NHL (8% and 6%, respectively). Paediatric protocols have been reported to contribute to improved ALL survival; allogeneic haematopoietic stem-cell transplantation and tyrosine kinase inhibitors (TKI) have helped increase survival in CML [15]; whereas advances in diagnostics, and better use of classic chemotherapy have contributed to better AML survival [16]. Risk-adapted therapy and better assessment and prognostication in AYA with NHL can contribute to explain improvements in survival [17]. For the other cancers we observed an increase in survival between 2% and 4% but they were all tumours which already had a survival between 80% and 90%, in 2004–2006.

In adolescents, we found no evidence of survival improvement for AML, CNS tumours, and bone sarcomas whereas survival for STS rose. These results are consistent with data from earlier periods and have been attributed both to failure to treat adolescents with cancer at optimal settings and to their lower enrolment in clinical trials [3,18]. Rhabdomyosarcoma (RMS) is the most common sarcoma in adolescents. The number of adolescents with RMS enroled in European paediatric Soft Tissue Sarcoma Study Group protocols (period 2008–2015) compared to the expected number of adolescent cases was 0.64. This was similar to the ratio in children, which stood at 0.77 [19].

Our study confirmed that differences in survival remained among European countries. STS, bone sarcomas, and CNS cancers are rare and complex to treat, and treatment should be centralised in expert centres [20], meaning that different levels of centralisation can help explain differences in survival among countries. In Poland, for example, at the time of the study, most CNS cancers and STS were centralised at the cancer centres in Warsaw and survival was in line with the other countries for these tumours only. For cervical cancers, various availability of and access to screening or human papilloma virus vaccination may explain some of the differences in survival among countries. Cervical cancer survival was lower than the European average in most countries where screening was opportunistic or unavailable, or roll out was incomplete [21]. However, differences in survival may also be due to the quality of and access to care. Countries with low survival for cervical cancer (eg, Bulgaria and Poland) also had low survival for many other cancers that lack screening programmes. In the case of ALL, TKI availability remains a significant issue owing to its financial burden on patients [22]. Furthermore, treatment adherence and the expertise of the multidisciplinary team are underestimated prognostic factor for ALL [23].

For AML, NHL, CNS, and colorectal cancers, we observed lower differences among countries in conditional survival than in 5-year RS, supporting the importance of healthcare organisation in providing earlier detection. Finally, cancers in AYA have distinctive clinical features which make treatment more complex than similar cancers in adults or children. For example, breast cancer in AYA is biologically more aggressive than in older women [24]; young-onset skin melanoma has a distinct biology [25]. Thus, differing access to clinical expertise may be particularly relevant for AYAs with cancers.

Table 3
Age-standardised and age-stratified 5-year relative survival (RS) in European adolescents and young adults (aged 15–39 years) in 2010–2014 for the most common cancers, by sex, reported by number of cases (N) and 95% confidence intervals (95%CI).

	All AYA patients (age-standardised)						15-19 years					
	Male			Female			Male			Female		
	N	RS (95% CI)	SE	N	RS (95% CI)	SE	N	RS (95% CI)	SE	N	RS (95% CI)	SE
Leukaemias and related disorders	5575	71.6% (70.2% - 73.0%)	0.7%	4412	75.6% (74.2% - 77.0%)	0.7%	1003	72.3% (69.3% - 75.0%)	1.5%	675	70.7% (67.0% - 74.1%)	1.8%
-Acute lymphoblastic leukaemia	1491	51.9% (48.0% - 55.6%)	1.9%	842	57.0% (52.1% - 61.5%)	2.4%	579	75.5% (71.6% - 78.9%)	1.9%	296	69.1% (63.4% - 74.1%)	2.7%
-Acute myeloid leukaemia	1704	54.9% (52.1% - 57.5%)	1.3%	1635	60.6% (57.9% - 63.3%)	1.3%	239	57.3% (50.3% - 63.6%)	3.4%	231	62.4% (55.5% - 68.5%)	3.3%
-Chronic myeloid leukaemia	884	92.3% (90.2% - 93.9%)	0.9%	573	93.8% (91.2% - 95.6%)	1.1%	66	89.4% (78.6% - 94.9%)	3.9%	43	93.3% (80.6% - 97.8%)	3.7%
Lymphomas	13 710	87.5% (86.9% - 88.1%)	0.3%	11 389	90.3% (89.7% - 90.9%)	0.3%	1784	90.8% (89.3% - 92.1%)	0.7%	1600	93.4% (92% - 94.6%)	0.6%
-Non-Hodgkin lymphomas	5858	82.5% (81.4% - 83.6%)	0.6%	4076	86.0% (84.9% - 87.1%)	0.6%	559	82.0% (78.4% - 85.1%)	1.7%	321	87.3% (82.8% - 90.6%)	2.0%
-Hodgkin lymphoma	6940	93.5% (92.7% - 94.2%)	0.4%	6687	94.8% (94.0% - 95.4%)	0.4%	1152	95.4% (94.0% - 96.5%)	0.6%	1243	95.3% (93.9% - 96.4%)	0.6%
Central Nervous System and other intracranial and intraspinal neoplasms	5582	58.2% (56.8% - 59.5%)	0.7%	4151	62.9% (61.4% - 64.4%)	0.8%	580	65.0% (60.8% - 68.8%)	2.0%	431	64.3% (59.3% - 68.8%)	2.4%
Bone sarcomas	1696	68.6% (65.5% - 71.5%)	1.5%	1182	77.7% (74.6% - 80.5%)	1.5%	582	61.6% (57.4% - 65.5%)	2.1%	328	70.5% (65.1% - 75.2%)	2.6%
Soft tissue sarcomas (excluding skin sarcomas)	2460	65.0% (62.9% - 66.9%)	1.0%	2269	72.7% (70.6% - 74.6%)	1.0%	388	62.6% (57.4% - 67.3%)	2.5%	272	71.4% (65.4% - 76.6%)	2.9%
Melanoma - malignant	9165	89.8% (89.1% - 90.4%)	0.3%	16 255	95.2% (94.8% - 95.5%)	0.2%	313	93.9% (90.4% - 96.1%)	1.4%	492	94.8% (92.3% - 96.5%)	1.0%
Thyroid carcinoma	3881	98.8% (98.2% - 99.1%)	0.2%	15 387	99.7% (99.5% - 99.8%)	0.1%	224	98.3% (95.1% - 99.4%)	0.9%	801	99.7% (98.6% - 99.9%)	0.2%
Carcinoma of colon and rectum (excluding appendix)	4063	64.2% (62.4% - 66.0%)	0.9%	3833	62.8% (60.9% - 64.7%)	1.0%	56	58.1% (43.2% - 70.3%)	7.0%	33	47.4% (29.6% - 63.3%)	8.8%
Carcinoma of breast	113	82.2% (70.4% - 89.6%)	4.7%	33 957	85.3% (84.4% - 86.2%)	0.5%	NE	NE	NE	28	86.1% (67.0% - 94.6%)	6.5%

	20-29 years						30-39 years					
	Male			Female			Male			Female		
	N	RS (95% CI)	SE	N	RS (95% CI)	SE	N	RS (95% CI)	SE	N	RS (95% CI)	SE
Leukaemias and related disorders	1770	67.8% (65.4% - 70.0%)	1.2%	1389	74.2% (71.7% - 76.4%)	1.2%	2 802	73.1% (71.4% - 74.8%)	0.9%	2349	76.6% (74.7% - 78.3%)	0.9%
-Acute lymphoblastic leukaemia	527	55.6% (51.1% - 59.8%)	2.2%	291	57.9% (51.7% - 63.7%)	3.1%	385	48.3% (43.0% - 53.4%)	2.7%	256	55.5% (48.8% - 61.7%)	3.3%
-Acute myeloid leukaemia	605	57.0% (52.7% - 61.0%)	2.1%	553	64.8% (60.5% - 68.7%)	2.1%	860	53.8% (50.3% - 57.2%)	1.8%	852	58.8% (55.2% - 62.2%)	1.8%
-Chronic myeloid leukaemia	276	93.8% (90.1% - 96.2%)	1.5%	178	94.7% (89.9% - 97.3%)	1.8%	542	91.9% (89.1% - 94.0%)	1.2%	353	93.5% (90.1% - 95.7%)	1.4%
Lymphomas	5004	89.6% (88.7% - 90.5%)	0.4%	4650	91.9% (91.1% - 92.7%)	0.4%	6922	86.4% (85.5% - 87.2%)	0.4%	5140	89.4% (88.5% - 90.3%)	0.4%
-Non-Hodgkin lymphomas	1719	81.9% (79.9% - 83.7%)	1.0%	1319	84.6% (82.5% - 86.5%)	1.0%	3581	82.8% (81.4% - 84.0%)	0.7%	2437	86.5% (85% - 87.8%)	0.7%
-Hodgkin lymphoma	3082	94.3% (93.4% - 95.1%)	0.4%	3180	95.3% (94.5% - 96.0%)	0.4%	2706	93% (91.9% - 93.9%)	0.5%	2264	94.5% (93.4% - 95.4%)	0.5%
Central Nervous System and other intracranial and intraspinal neoplasms	1857	64.2% (61.9% - 66.4%)	1.1%	1417	67.4% (64.8% - 69.8%)	1.3%	3146	55.1% (53.3% - 56.9%)	0.9%	2303	61.0% (59% - 63.1%)	1.0%
Bone sarcomas	609	61.8% (57.8% - 65.6%)	2.0%	425	75.5% (71.0% - 79.5%)	2.2%	505	72.0% (67.8% - 75.8%)	2.1%	430	79.2% (74.9% - 82.9%)	2.0%
Soft tissue sarcomas (excluding skin sarcomas)	764	58.4% (54.7% - 62.0%)	1.8%	708	71.5% (67.9% - 74.7%)	1.7%	1309	67.8% (65.1% - 70.3%)	1.3%	1290	73.3% (70.8% - 75.7%)	1.3%
Melanoma - malignant	2442	90.3% (89.0% - 91.5%)	0.6%	5015	96.5% (95.9% - 97.0%)	0.3%	6411	89.2% (88.4% - 90.0%)	0.4%	10749	94.7% (94.3% - 95.1%)	0.2%
Thyroid carcinoma	1132	99.3% (98.4% - 99.7%)	0.3%	4787	99.8% (99.6% - 99.9%)	0.1%	2526	98.6% (97.9% - 99.0%)	0.3%	9800	99.6% (99.4% - 99.7%)	0.1%
Carcinoma of colon and rectum (excluding appendix)	741	62.7% (58.9% - 66.1%)	1.8%	683	61.6% (57.7% - 65.1%)	1.9%	3267	65.4% (63.7% - 67.1%)	0.9%	3118	64.7% (63.0% - 66.4%)	0.9%
Carcinoma of breast	15	74.6% (39.7% - 91.1%)	12.8%	3389	83.2% (81.9% - 84.5%)	0.7%	99	85.4% (76.1% - 91.3%)	3.8%	30 540	86.1% (85.7% - 86.5%)	0.2%

NE=Not Estimable.

We confirmed the female sex to be an indicator of better survival compared to the male sex. Our results are coherent with previous reports of a minimal female advantage at birth, which then grows from puberty until menopause [26]. Our data supports also a similar level of tumour aggressiveness in both sexes, although the underlying reasons are not well understood. Some hypotheses include behavioural factors and health care access [27], biological differences [28], and psychological factors [29].

Our study has several strengths. We evaluated the results in a large, unbiased population-based database. We used the updated classification of tumours occurring in AYA [6]. This is the most comprehensive study to include most AYA cancers and countries. Although follow-up did not extend beyond 2014, we estimated 5-year RS using the period approach to provide reliable predictions of 5-year RS for patients diagnosed up to the end of the study period.

Limitations include the relatively old diagnostic period and the end of follow-up used for the analyses. Our data also lack grade, stage, and treatment data, limiting interpretations of the results.

Tumours of AYAs can be treated effectively resulting in excellent survival in most cases, but they are mostly rare. Accordingly, AYAs developing malignancies should be referred to expert centres [4]. Collaboration among the European reference networks (PaedCAN, EURACAN, EuroBloodNet) is recommended to ensure the definition of a trans-age treatment protocol. International cooperative groups also play an important role in organising clinical research for these young people. Cancer registries remain an important source of information for monitoring cancer survival in AYAs.

CRediT authorship contribution statement

Guevara Marcela: Writing – review & editing. **Bernasconi Alice:** Data curation, Formal analysis, Methodology, Writing – original draft. **Demuru Elena:** Writing – review & editing. **Mousavi Seyed Mohsen:** Writing – review & editing. **Blum Marcel:** Writing – review & editing. **Eberle Andrea:** Writing – review & editing. **Ferrari Andrea:** Writing – review & editing. **Stiller Charles:** Writing – review & editing. **Visser Otto:** Writing – review & editing. **Cañete-Nieto Adela:** Writing – review & editing. **Spycher Ben:** Writing – review & editing. **Bielska-Lasota Magdalena:** Writing – review & editing. **Katalinic Alexander:** Writing – review & editing. **Working Group EUROCARE-6:** Writing – review & editing, Data curation. **Lasalvia Paolo:** Data curation, Formal analysis, Methodology, Writing – original draft. **Marcos-Gragera Rafael:** Writing – review & editing. **Vener Claudia:** Writing – review & editing. **Paapsi Keiu:** Writing – review & editing. **Innos Kaire:** Writing – review & editing. **Trama Annalisa:** Conceptualization, Funding acquisition, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing. **Botta Laura:** Methodology, Supervision, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

We analysed pseudonymised data collected from 108 population-based cancer registries, after approval by the Ethics Committee of the National Cancer Institute of Milan (INT73/16; April 21, 2016). We hold these data in trust from each participating registry for the statistical analyses agreed in the EUROCARE-6 protocol, available at http://www.eurocare.it. We are not allowed to share individual data. Aggregated level data, in the form of counts, rates, or survival proportions, can be only shared after express permission from the participating registries. These data should be requested by contacting the corresponding author or the Eurocare Secretariat (eurocare.secretariat@istitutotumori.mi.it).

Table 4
Five-year relative survival (RS) estimates for the most common cancers affecting European adolescents and young adults (aged 15–39 years) in 2010–2014, by country, reported by number of cases (N) and 95% confidence intervals (95%CI).

	Acute lymphoblastic leukaemia			Acute myeloid leukaemia			Non-Hodgkin lymphomas			Hodgkin lymphoma			CNS and other intracranial and intraspinal neoplasms			Bone sarcomas		
	N	RS (95% CI)	SE	N	RS (95% CI)	SE	N	RS (95% CI)	SE	N	RS (95% CI)	SE	N	RS (95% CI)	SE	N	RS (95% CI)	SE
AT_Austria National	69	67.3% (54.6% - 77.2%)	5.8%	100	56.8% (46.0% - 66.2%)	5.2%	243	83.5% (78.2% - 87.6%)	2.4%	293	95.0% (91.8% - 97.0%)	1.3%	283	70.0% (64.4% - 74.9%)[#]	2.7%	86	69.6% (58.5% - 78.3%)	5.1%
BE_Belgium National	117	63.7% (54.1% - 71.9%)	4.6%	162	63.3% (55.0% - 70.6%)	4.0%	487	85.4% (81.8% - 88.3%)	1.7%	576	97.0% (95.1% - 98.2%)[#]	0.7%	404	63.3% (58.3% - 67.8%)	2.4%	137	74.1% (65.5% - 80.9%)	3.9%
BG_Bulgaria National	57	50.5% (35.6% - 63.7%)	7.3%	74	21.2% (12.9% - 30.8%)[$]	4.6%	195	71.1% (64.1% - 77.0%)[$]	3.3%	280	83.1% (78.1% - 87.1%)[$]	2.3%	256	48.8% (42.5% - 54.8%)[$]	3.2%	77	48.6% (37.2% - 59.0%)[$]	5.6%
CR_Croatia National	31	54.3% (31.5% - 72.3%)	10.7%	40	37.5% (19.9% - 55.0%)[$]	9.3%	151	76.9% (66.7% - 84.3%)	4.4%	186	88.7% (81.7% - 93.2%)[$]	2.9%	187	67.1% (58.4% - 74.4%)	4.1%	60	79.3% (63.2% - 89.0%)	6.4%
CY_Cyprus National	13	57.7% (31.4% - 77.0%)	12.1%	17	79.1% (53.2% - 91.7%)[#]	9.4%	50	87.6% (74.3% - 94.3%)	4.8%	85	96.7% (89.6% - 99.0%)	2.0%	18	64.5% (37.2% - 82.3%)	11.8%	12	79.2% (47.9% - 92.9%)	10.8%
CZ_Czech Republic National	62	58.0% (43.1% - 70.3%)	7.0%	93	51.1% (39.6% - 61.6%)	5.7%	336	86.5% (82.0% - 90.0%)	2.0%	505	94.9% (92.3% - 96.6%)	1.1%	369	57.7% (52.2% - 62.9%)	2.7%	90	58.6% (46.9% - 68.5%)	5.5%
DK_Denmark National	60	80.4% (67.9% - 88.4%)[#]	5.1%	57	59.3% (43.8% - 71.8%)	7.2%	183	88.3% (82.8% - 92.1%)	2.3%	230	95.3% (91.4% - 97.4%)	1.5%	166	58.8% (50.9% - 66.0%)	3.9%	62	69.4% (56.2% - 79.3%)	5.9%
EE_Estonia National	19	50.6% (26.1% - 70.8%)	11.9%	16	56.8% (30.2% - 76.6%)	12.3%	57	71.4% (59.2% - 80.6%)[$]	5.5%	75	90.8% (80.8% - 95.8%)	3.6%	45	72.1% (56.6% - 82.9%)	6.7%	10	90.3% (46.1% - 98.7%)[#]	9.5%
FI_Finland National	47	69.7% (54.1% - 80.9%)	6.8%	53	68.5% (53.7% - 79.4%)	6.6%	213	82.0% (76.2% - 86.5%)[#]	2.6%	302	98.3% (95.8% - 99.3%)[#]	0.8%	210	61.8% (54.8% - 68.1%)	3.4%	43	78.3% (63.3% - 87.8%)	6.1%
FR_France (CRs Pool)	123	67.7% (58.8% - 75.0%)	4.1%	185	67.3% (58.2% - 73.7%)[#]	3.5%	551	87.6% (84.5% - 90.1%)[#]	1.4%	790	94.9% (92.2% - 96.0%)	0.8%	443	60.1% (54.7% - 64.4%)	2.3%	162	71.3% (63.3% - 77.9%)	3.4%
GE_Germany (CRs Pool)	220	62.9% (55.3% - 69.5%)	3.6%	319	60.2% (54.1% - 65.8%)	3.0%	837	85.9% (83.0% - 88.3%)	1.3%	1,095	97.1% (95.7% - 98.0%)[#]	0.6%	775	64.3% (60.5% - 67.8%)	1.9%	234	66.5% (59.1% - 72.8%)	3.5%
IC_Iceland National	3	50.0% (5.8% - 84.5%)	25.0%	+	+	+	10	91.0% (50.4% - 98.7%)	8.7%	21	100% (100% - 100%)	0.0%	11	56.6% (24.4% - 79.4%)	14.9%	3	100% (100% - 100%)	0.0%
IR_Ireland National	41	64.1% (47.5% - 76.7%)	7.5%	59	64.4% (50.4% - 75.4%)	6.4%	177	90.0% (84.0% - 93.9%)[#]	2.4%	249	96.6% (93.1% - 98.3%)	1.2%	190	71.1% (63.5% - 77.4%)[#]	3.5%	44	59.5% (42.3% - 73.1%)	8.0%
IT_Italy (CRs Pool)	220	53.6% (46.7% - 60.0%)[$]	3.4%	325	65.5% (59.6% - 70.8%)[#]	2.9%	1,177	85.3% (83.0% - 87.4%)	1.1%	1,519	95.9% (94.8% - 96.8%)	0.5%	691	61.6% (57.8% - 65.2%)	1.9%	236	74.9% (68.7% - 80.1%)	2.9%
LV_Latvia National	13	58.6% (32.1% - 77.7%)	12.1%	17	54.2% (30.1% - 73.2%)	11.4%	56	67.3% (54.0% - 77.6%)[$]	6.0%	114	92.1% (84.9% - 96.0%)	2.7%	108	65.2% (55.0% - 73.7%)	4.8%	28	57.7% (37.5% - 73.5%)	9.4%
LT_Lithuania National	34	58.1% (38.7% - 73.2%)	9.0%	35	45.9% (28.9% - 61.4%)	8.5%	109	80.4% (71.0% - 87.0%)	4.0%	144	97.2% (91.9% - 99.1%)	1.5%	123	59.1% (50.0% - 67.1%)	4.4%	32	59.2% (40.0% - 74.1%)	8.8%
ML_Malta National	4	28.6% (1.4% - 69.1%)	22.3%	2	66.7% (5.4% - 94.5%)	27.2%	32	71.0% (51.7% - 83.8%)	8.2%	24	92.4% (72.3% - 98.1%)	5.3%	12	84.0% (49.3% - 95.8%)[#]	10.5%	3	50.0% (0.6% - 91.1%)	35.4%
NO_Norway National	58	59.1% (45.1% - 70.6%)	6.6%	63	72.7% (59.4% - 82.2%)[#]	5.8%	181	91.7% (86.5% - 94.9%)[#]	2.1%	253	97.8% (94.9% - 99.1%)[#]	1.0%	213	64.2% (57.4% - 70.2%)	3.3%	59	74.5% (61.7% - 83.6%)	5.5%
PL_Poland National	299	53.2% (47.1% - 59.0%)[$]	3.0%	378	46.3% (40.9% - 51.6%)[$]	2.7%	787	74.7% (71.3% - 77.8%)[$]	1.7%	1,720	91.3% (89.8% - 92.7%)[$]	0.7%	1,746	63.8% (61.3% - 66.2%)	1.2%	412	63.7% (58.5% - 68.4%)[$]	2.5%
PT_Portugal (CRs Pool)	48	55.1% (39.3% - 68.3%)	7.5%	87	52.6% (40.9% - 63.0%)	5.7%	384	80.8% (75.9% - 84.8%)	2.2%	495	94.4% (91.9% - 96.2%)	1.1%	266	59.3% (52.9% - 65.2%)	3.1%	79	56.9% (44.4% - 67.6%)[$]	6.0%
SK_Slovakia National	44	45.7% (26.8% - 62.8%)	9.5%	50	59.7% (39.5% - 75.0%)	9.2%	125	84.7% (73.9% - 91.3%)	4.3%	199	89.5% (84.2% - 93.2%)[$]	2.3%	164	58.3% (49.4% - 66.2%)	4.3%	47	58.0% (38.9% - 73.0%)	8.9%
SL_Slovenia National	15	75.1% (40.8% - 91.2%)	12.5%	21	49.5% (26.6% - 68.8%)	11.2%	71	90.4% (80.7% - 95.4%)	3.5%	86	97.2% (90.6% - 99.2%)	1.8%	57	68.6% (54.7% - 79.1%)	6.2%	21	63.3% (39.9% - 79.6%)	10.3%
SP_Spain (CRs Pool)	82	49.8% (37.6% - 60.9%)	6.0%	130	60.4% (50.8% - 68.7%)	4.6%	418	81.9% (77.5% - 85.6%)	2.0%	476	92.1% (89.2% - 94.2%)[$]	1.3%	266	58.8% (52.6% - 64.5%)	3.0%	84	61.0% (49.5% - 70.6%)	5.4%
SW_Switzerland (CRs Pool)	13	52.0% (22.5% - 75.1%)	14.3%	28	61.6% (40.4% - 77.1%)	9.5%	79	87.7% (77.5% - 93.4%)	3.9%	133	98.3% (93.0% - 99.6%)[#]	1.2%	64	63.3% (49.7% - 74.1%)	6.3%	18	74.3% (44.6% - 89.6%)	11.2%
NL_The Netherlands National	148	70.3% (62% - 77.0%)[#]	3.8%	209	63.3% (56.0% - 69.6%)	3.5%	660	86.1% (83.2% - 88.5%)	1.4%	789	97.1% (95.5% - 98.1%)[#]	0.6%	601	59.2% (55.0% - 63.1%)	2.1%	197	75.8% (68.9% - 81.3%)	3.2%
UK_England National	417	67.5% (62.5% - 72.0%)[#]	2.4%	704	58.0% (54.1% - 61.6%)	1.9%	1,970	85.2% (83.5% - 86.7%)	0.8%	2,532	94.3% (93.3% - 95.1%)	0.5%	1,774	57.7% (55.3% - 59.9%)[$]	1.2%	554	73.5% (69.5% - 77.0%)	1.9%
UK_Northern Ireland National	11	72.8% (37.1% - 90.3%)	13.4%	22	55.2% (34.6% - 71.7%)	9.7%	44	74.7% (58.9% - 85.2%)	6.6%	82	94.2% (85.9% - 97.7%)	2.7%	74	60.0% (47.2% - 70.6%)	6.0%	20	59.9% (33.5% - 78.6%)	11.8%
UK_Scotland National	51	65.9% (50.9% - 77.2%)	6.7%	62	64.7% (50.6% - 75.7%)	6.5%	194	82.6% (76.3% - 87.4%)	2.8%	266	94.8% (91.2% - 97.0%)	1.4%	155	48.0% (39.9% - 55.6%)[$]	4.0%	58	71.0% (57.3% - 81.0%)	6.0%
UK_Wales National	23	49.3% (27.2% - 68.1%)	10.9%	35	69.1% (48.9% - 82.6%)	8.6%	77	84.9% (73.4% - 91.6%)	4.5%	107	86.3% (78.0% - 91.7%)[$]	3.4%	102	66.2% (55.3% - 75.1%)	5.1%	34	71.9% (52.6% - 84.5%)	8.1%
Eurocare-6 Pool (Area weighted)	**2,311**	**60.9% (58.6% - 63.2%)**	**1.1%**	**3,323**	**59.3% (57.4% - 61.2%)**	**0.9%**	**9,907**	**84.0% (83.2% - 84.8%)**	**0.4%**	**13,604**	**95.0% (94.6% - 95.3%)**	**0.2%**	**9,722**	**61.6% (60.5% - 62.8%)**	**0.6%**	**2,860**	**69.6% (67.6% - 71.5%)**	**1.0%**

(*continued on next page*)

Table 4 (*continued*)

	Soft tissue sarcomas (excluding skin)			Germ cell and trophoblastic of testis			Melanoma - malignant			Carcinoma of colon and rectum (excluding appendix)			Carcinoma of breast			Carcinoma of uterine cervix		
	N	RS (95% CI)	SE	N	RS (95% CI)	SE	N	RS (95% CI)	SE	N	RS (95% CI)	SE	N	RS (95% CI)	SE	N	RS (95% CI)	SE
AT_Austria National	150	71.4% (63.4% - 77.9%)	3.7%	684	96.6% (94.8% - 97.7%)	0.7%	784	95.7% (94.0% - 97.0%)#	0.7%	188	70.8% (63.8% - 76.8%)	3.3%	837	86.6% (84.2% - 88.6%)	1.1%	262	86.6% (81.8% - 90.2%)	2.1%
BE_Belgium National	219	79.2% (72.9% - 84.3%)#	2.9%	890	96.8% (95.3% - 97.9%)	0.6%	1,435	95.5% (94.2% - 96.5%)#	0.6%	340	73.6% (68.4% - 78.1%)#	2.5%	1,928	88.9% (87.3% - 90.2%)#	0.7%	481	89.2% (86.0% - 91.7%)#	1.5%
BG_Bulgaria National	170	65.2% (57.2% - 72.1%)	3.8%	519	87.4% (84.1% - 90.1%)$	1.5%	217	67.9% (61.2% - 73.7%)$	3.2%	217	49.8% (43.0% - 56.2%)$	3.4%	906	80.4% (77.6% - 82.9%)$	1.3%	776	69.2% (65.7% - 72.5%)$	1.7%
CR_Croatia National	51	61.9% (44.2% - 75.4%)	8.1%	312	93.8% (89.5% - 96.4%)	1.7%	211	87.9% (81.7% - 92.1%)	2.6%	132	57.5% (47.3% - 66.5%)	4.9%	354	83.9% (78.5% - 88.0%)	2.4%	197	83.0% (75.5% - 88.3%)	3.2%
CY_Cyprus National	24	80.0% (57.7% - 91.3%)	8.2%	86	99.0% (91.9% - 99.9%)	1.1%	35	73.1% (54.5% - 85.1%)$	7.7%	28	66.9% (46.5% - 81.0%)	8.9%	135	92.7% (86.7% - 96.0%)#	2.3%	30	87.5% (69.6% - 95.2%)	6.0%
CZ_Czech Republic National	190	63.4% (55.8% - 70.1%)	3.7%	1,218	94.8% (93.2% - 96.0%)$	0.7%	946	93.6% (91.6% - 95.1%)	0.9%	350	61.8% (56.2% - 66.9%)	2.7%	1,161	85.2% (82.8% - 87.3%)	1.1%	955	87.3% (84.8% - 89.3%)	1.1%
DK_Denmark National	111	66.9% (56.9% - 75.1%)	4.7%	697	99.4% (98.1% - 99.8%)#	0.4%	1,347	97.4% (96.3% - 98.1%)#	0.5%	145	63.5% (55.1% - 70.8%)	4.0%	685	87.4% (84.6% - 89.7%)	1.3%	480	91.8% (89.0% - 94.0%)#	1.3%
EE_Estonia National	23	60.7% (37.6% - 77.5%)	10.4%	56	96.9% (84.1% - 99.4%)	2.7%	105	94.2% (86.5% - 97.6%)	2.5%	25	60.6% (37.6% - 77.3%)	10.3%	110	90.1% (82.4% - 94.5%)	3.0%	99	90.4% (82.6% - 94.8%)	3.0%
FI_Finland National	90	68.2% (57.4% - 76.8%)	5.0%	403	96.2% (93.7% - 97.8%)	1.0%	430	95.9% (93.4% - 97.5%)#	1.0%	119	74.0% (64.8% - 81.1%)	4.1%	482	84.7% (81.1% - 87.7%)	1.7%	177	88.8% (83.1% - 92.6%)	2.4%
FR_France (CRs Pool)	235	72.3% (66.0% - 77.7%)	3.0%	1,103	96.8% (95.2% - 97.7%)	0.6%	1,241	93.4% (92.1% - 95.0%)	0.7%	390	69.5% (64.7% - 73.8%)	2.3%	2,103	88.6% (86.8% - 89.8%)#	0.7%	405	87.0% (82.7% - 89.9%)	1.7%
GE_Germany (CRs Pool)	377	67.4% (61.8% - 72.4%)	2.7%	2,888	97.8% (97.1% - 98.4%)#	0.3%	2,786	95.8% (94.9% - 96.6%)#	0.4%	710	71.0% (67.1% - 74.6%)#	1.9%	3,183	88.2% (86.9% - 89.4%)#	0.6%	1,239	87.1% (84.9% - 89.1%)	1.1%
IC_Iceland National	8	83.4% (27.1% - 97.5%)	15.2%	27	100% (100% - 100%)	0.0%	45	100% (100% - 100%)	0.0%	10	85.8% (33.1% - 97.9%)	13.2%	37	87.6% (72.4% - 94.7%)	5.3%	33	92.1% (77.3% - 97.4%)	4.4%
IR_Ireland National	76	67.9% (55.7% - 77.4%)	5.6%	457	98.0% (95.9% - 99.1%)	0.7%	463	90.3% (87.0% - 92.7%)	1.4%	141	70.3% (61.5% - 77.4%)	4.1%	598	83.7% (80.4% - 86.5%)	1.5%	392	85.9% (81.9% - 89.1%)	1.8%
IT_Italy (CRs Pool)	447	71.8% (67.2% - 75.9%)	2.2%	1,937	97.2% (96.3% - 97.9%)	0.4%	2,465	93.9% (92.8% - 94.8%)	0.5%	622	66.6% (62.6% - 70.3%)	2.0%	3,293	88.3% (87.2% - 89.3%)#	0.5%	566	84.8% (81.5% - 87.6%)	1.6%
LV_Latvia National	36	64.1% (45.0% - 78.0%)	8.5%	81	90.3% (81.0% - 95.2%)	3.4%	66	84.0% (72.1% - 91.2%)	4.7%	47	66.6% (50.1% - 78.7%)	7.3%	165	80.8% (73.5% - 86.3%)	3.2%	182	71.4% (64.2% - 77.4%)$	3.3%
LT_Lithuania National	53	67.3% (52.0% - 78.8%)	6.8%	94	93.5% (84.7% - 97.3%)	2.9%	110	86.6% (78.5% - 91.8%)	3.3%	58	67.4% (53.2% - 78.1%)	6.4%	254	79.2% (73.7% - 83.7%)$	2.5%	276	82.7% (77.5% - 86.8%)	2.4%
ML_Malta National	9	29.0% (5.6% - 58.8%)	15.5%	33	97.0% (76.7% - 99.6%)	3.3%	36	97.4% (80.7% - 99.7%)	2.7%	15	84.0% (56.7% - 94.8%)#	8.8%	48	81.3% (66.9% - 89.9%)	5.7%	13	89.0% (43.1% - 98.4%)	10.5%
NO_Norway National	76	73.1% (61.3% - 81.8%)	5.2%	770	99.0% (97.7% - 99.6%)#	0.4%	601	93.3% (90.9% - 95.1%)	1.1%	193	69.3% (62.1% - 75.4%)	3.4%	552	86.0% (82.6% - 88.7%)	1.6%	393	92.2% (89.1% - 94.5%)#	1.4%
PL_Poland National	535	66.7% (62.2% - 70.8%)	2.2%	2,995	92.9% (91.8% - 93.8%)$	0.5%	1,485	82.7% (80.5% - 84.7%)$	1.1%	896	57.1% (53.5% - 60.6%)$	1.8%	3,198	81.3% (79.8% - 82.8%)$	0.8%	1,242	75.1% (72.4% - 77.6%)$	1.3%
PT_Portugal (CRs Pool)	167	68.1% (60.2% - 74.8%)	3.7%	399	97.0% (94.5% - 98.4%)	0.9%	370	94.1% (91.1% - 96.2%)	1.3%	313	63.5% (57.8% - 68.6%)$	2.7%	1,291	88.4% (86.6% - 90.0%)	0.9%	420	85.9% (81.8% - 89.1%)	1.9%
SK_Slovakia National	85	62.5% (49.8% - 72.8%)	5.9%	456	95.2% (91.7% - 97.3%)	1.4%	201	84.7% (77.3% - 89.8%)$	3.1%	119	55.4% (45.8% - 63.9%)$	4.7%	287	81.6% (76.9% - 85.4%)	2.2%	289	83.6% (77.3% - 88.3%)	2.8%
SL_Slovenia National	27	45.5% (25.3% - 63.7%)$	10.2%	252	98.0% (94.8% - 99.3%)	1.0%	242	90.2% (85.8% - 93.3%)	1.9%	64	57.1% (44.4% - 67.9%)	6.0%	216	90.0% (85.4% - 93.3%)	2.0%	106	96.3% (89.9% - 98.6%)#	1.9%
SP_Spain (CRs Pool)	175	64.2% (56.2% - 71.2%)	3.8%	652	97.5% (95.7% - 98.5%)	0.7%	543	92.4% (89.7% - 94.5%)	1.2%	254	71.5% (65.5% - 76.7%)	2.9%	1,180	87.2% (85.2% - 88.9%)	1.0%	264	80.8% (75.3% - 85.2%)$	2.5%
SW_Switzerland (CRs Pool)	33	64.0% (41.5% - 79.7%)	9.9%	210	97.4% (93.8% - 99.0%)	1.2%	276	96.6% (93.3% - 98.3%)#	1.2%	45	72.2% (55.3% - 83.6%)	7.2%	245	88.1% (83.0% - 91.7%)	2.2%	50	98.0% (86.2% - 99.7%)#	2.0%
NL_The Netherlands National	275	70.6% (64.6% - 75.7%)	2.8%	1,842	98.4% (97.6% - 98.9%)#	0.3%	2,572	94.0% (93.0% - 94.9%)#	0.5%	535	67.9% (63.8% - 71.7%)	2.0%	2,716	87.2% (85.9% - 88.4%)	0.6%	766	89.5% (87.1% - 91.5%)#	1.1%
UK_England National	944	67.5% (64.4% - 70.4%)	1.5%	4,207	98.1% (97.6% - 98.5%)#	0.2%	5,160	93.7% (93.0% - 94.4%)#	0.3%	1,642	61.3% (58.9% - 63.6%)$	1.2%	6,768	84.1% (83.2% - 85.0%)$	0.4%	3,247	86.8% (85.6% - 87.9%)	0.6%
UK_Northern Ireland National	35	47.3% (30.6% - 62.2%)$	8.3%	159	99.0% (94.8% - 99.8%)#	0.8%	212	95.0% (90.9% - 97.3%)	1.6%	57	71.9% (58.0% - 81.9%)	6.1%	220	83.8% (78.2% - 88.1%)	2.5%	207	92.1% (87.5% - 95.1%)#	1.9%
UK_Scotland National	90	58.6% (47.2% - 68.4%)	5.4%	455	98.2% (96.2% - 99.2%)	0.7%	614	95.4% (93.3% - 96.9%)#	0.9%	146	59.2% (50.8% - 66.6%)	4.1%	660	79.9% (76.6% - 82.8%)$	1.6%	451	88.8% (85.5% - 91.4%)	1.5%
UK_Wales National	54	59.9% (44.9% - 72.0%)	7.0%	240	96.7% (92.9% - 98.5%)	1.3%	263	87.7% (82.8% - 91.2%)$	2.1%	77	60.1% (47.4% - 70.6%)	6.0%	295	86.0% (81.4% - 89.5%)	2.1%	196	82.6% (76.4% - 87.4%)	2.8%
Eurocare-6 Pool (Area weighted)	**4,710**	**69% (67.5% - 70.5%)**	**0.7%**	**24,184**	**96.9% (96.6% - 97.2%)**	**0.1%**	**25,402**	**92.9% (92.5% - 93.2%)**	**0.2%**	**7,872**	**65.9% (64.7% - 67.1%)**	**0.6%**	**34,002**	**86.4% (86.0% - 86.8%)**	**0.2%**	**14,091**	**85.9% (85.1% - 86.6%)**	**0.4%**

NE=Not Estimable; #=Survival above the European average; $=Survival below the European average.

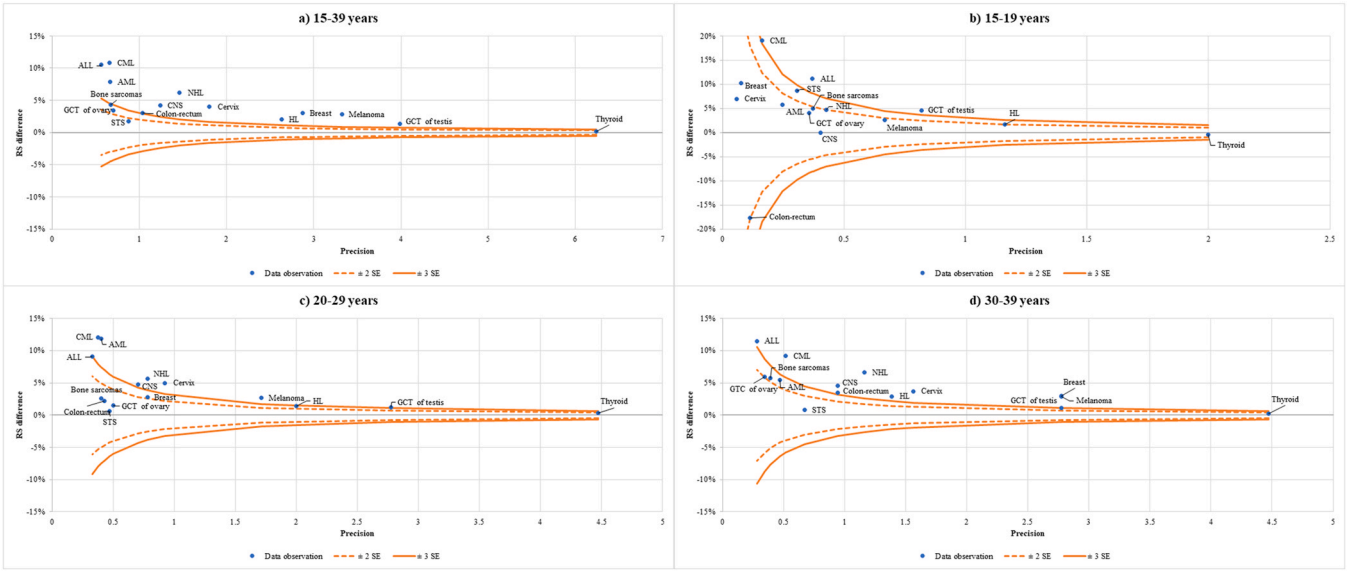

Fig. 1. Funnel plot of the difference in 5-year relative survival (RS) between the periods 2004–2006 and 2010–2014, by cancer type and age groups: (a) 15–39 years; (b) 15–19 years; (c) 20–29 years; (d) 30–39 years.

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Data access

Annalisa Trama had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ejca.2024.113558.

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