European Journal of Cancer (2015) 51, 2120–2129

Available at www.sciencedirect.com

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journal homepage: www.ejcancer.com

Age and case mix-standardised survival for all cancer patients in Europe 1999–2007: Results of EUROCARE-5, a population-based study

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Received 13 March 2015; received in revised form 8 July 2015; accepted 17 July 2015

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http://dx.doi.org/10.1016/j.ejca.2015.07.025

KEYWORDS
Cancer survival
Population-based cancer registries
EUROCARE
All cancer
Case-mix by cancer site

Abstract ***Background:*** Overall survival after cancer is frequently used when assessing a health care service's performance as a whole. It is mainly used by the public, politicians and the media, and is often dismissed by clinicians because of the heterogeneous mix of different cancers, risk factors and treatment modalities. Here we give survival details for all cancers combined in Europe, correlating it with economic variables to suggest reasons for differences.

Methods: We computed age and cancer site case-mix standardised relative survival for all cancers combined (ACRS) for 29 countries participating in the EUROCARE-5 project with data on more than 7.5 million cancer cases from 87 population-based cancer registries, using complete and period approach.

Results: Denmark, United Kingdom (UK) and Eastern European countries had lower survival than neighbouring countries. Five-year ACRS has been increasing throughout Europe, and substantial increases, between 1999–2001 and 2005–2007, have been achieved in countries where survival was lower in the past. Five-year ACRS for men and women are positively correlated with macro-economic variables like the Gross Domestic Product (GDP) and Total National Expenditure on Health (TNEH) (R^2 about 70%). Countries with recent larger increases in GDP and TNEH had greater increases in cancer survival.

Conclusions: ACRS serves to compare all cancer survival in Europe taking account of the geographical variability in case-mixes. The EUROCARE-5 data on ACRS confirm previous EUROCARE findings. Survival appears to correlate with macro-economic determinants, particularly with investments in the health care system.

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1. Introduction

Population-based cancer registries (CRs) began to operate in Europe from the 1940s onwards, mainly providing indicators of risk, prognosis and burden of cancer [1]. Over the years increasing numbers of CRs have run studies on survival, in evaluation service of clinical practice and of mass screening programmes, aetiological research [1] and survivorship studies [2–4]. The role of cancer registration is strongly recognised, and CRs are considered a pillar of cancer control by the World Cancer Declaration of the Union for International Cancer Control (UICC) [5] and European Commission [6,7].

In general, clinicians tend to underuse the findings of population-based survival studies and rely more on studies of selected patient groups in randomised clinical trials or outcome studies from hospitals (or groups of hospitals) [8]. However, population-based survival data can provide essential information for administrators and policy makers. For instance, in 2000, cancer action plans were implemented in Denmark and the United Kingdom (UK) with the aim of improving cancer treatment and outcomes, following the discovery of unexpectedly poor cancer survival in these countries by the EUROCARE [8]. Cancer registry data have also been widely used for evaluations and monitoring the impact of action plans [9]. Although some countries have used cancer survival statistics to set priorities for the provision of cancer care, the economic and social implications of changes in cancer survival are not widely appreciated [8].

These considerations are especially appropriate if we consider the measure of survival for all cancers combined. Epidemiologists and clinicians acknowledge that the complex mixture of different cancer types and subtypes with different risk factors, diagnostic methods, therapies and prognosis makes it problematic to base conclusions on overall measures (incidence, survival and mortality) [10]. However, the general public, journalists, politicians and administrators often prefer summary measures (such as survival for all cancers combined) as they offer a broad picture of cancer burden and serve to evaluate the impact of cancer control plans [10]. Population-based relative survival for all cancers has been proposed as a useful indicator for monitoring cancer control across countries [11].

The present paper illustrates the results of survival analyses for all cancers combined for each country participating in EUROCARE-5 [12]. Survival data must be comparable, in order to deliver a correct benchmark across administrative borders (e.g. among countries). Cancer survival statistics are usually considered comparable if the original data are: (a) collected in a standardised way (EUROCARE-5 data originate from CRs working to standardised data collection and coding rules), (b) estimated by the same methods (the EUROCARE-5 methods are described elsewhere [12]) and (c) if the results presented are age-standardised [13]. In presenting data for all cancers combined, it is also essential to consider the differing case-mixes of cancers in different countries, and to eliminate the confounding effect if, for example, the incidence of highly lethal cancers is higher in one country than in another. Here, therefore, we present the population-based age-standardised and cancer site-standardised relative survival for all cancers combined correlating it with economic variables so to interpret any differences [11].

2. Materials and methods

EUROCARE-5 materials and methods are fully described elsewhere [12]. We shall just summarise the features used in estimating survival for all cancers combined.

Ninety-nine CRs, collecting data for adult (⩾15 years) cancer patients, contributed to the EUROCARE-5 study. For analyses of all cancers combined, 12 registries were excluded as they only gathered data for specific cancer sites [12].

We present analyses of three different datasets: (a) analysis on cancer patients diagnosed in 2000–2007 in 87 CRs in 29 countries and followed up to the end of 2008 [12]; (b) time trend survival analysis by country from 58 CRs in 25 countries (data for the last period were not available in France and Spain [12]); (c) time trend survival analysis by five EUROCARE-5 European regions (Ireland and UK, and Northern, Central, Southern and Eastern Europe) from 44 CRs in 24 countries [12]. The following periods were considered in the time trends: 1999–2001 (based on cases diagnosed in 1995–2001), 2002–2004 (based on cases diagnosed in 1998–2004) and 2005–2007 (based on cases diagnosed in 2001–2007).

2.1. Statistical analysis: Complete and period approach

For patients diagnosed in 2000–2007, we estimated 1- and 5-year relative survival (RS) [14,15] and 5-year relative survival conditional to surviving the first year after diagnosis (conditional RS [16]), using the *complete approach*. To assess changes in survival over time, we estimated 5-year RS by country and European region, using the *period approach* [17,18]. The Ederer II method was used to estimate the expected survival [19]. Analyses were done with SEER*Stat (version 8.0.4) [20].

2.2. Statistical analysis: Standardisation

We age-standardised RS (ARS) figures for all ages combined using the direct method of age-specific weightings from the International Cancer Survival Standards [13]. To take account of the geographical variability in the distribution of all cancers by site, ARS was standardised using the direct method with weights proportional to the cancer site distribution of cases diagnosed in 2000–2007 from the 87 CRs entered in the cohort analysis. For weighting, we considered malignancies with more than 1.4% of the total 2000–2007 cancer cases by sex using the EUROCARE-5 classification for the definition of malignancies [12]. Therefore: (a) malignancies with fewer cases were grouped in the residual category 'Other cancers'; (b) ACRS was estimated using different weights for men, women and both sexes combined. For simplicity's sake in tables and figures we generally refer to ACRS but to be exact we should refer to ACRS-M for men, ACRS-F for women and ACRS-MF for both sexes.

The same methods were applied to obtain case-mix weights for the sensitivity analysis which was done to estimate ACRS, excluding cancer sites with over-diagnosis problems [10] (i.e. breast cancer in women and prostate cancer in men).

European survival estimates were obtained as weighted averages of country- or region-specific ARS and ACRS figures [12].

2.3. Ecologic study: Correlation with economic variables

In the European Partnership for Action Against Cancer (EPAAC) framework [21], data on socio-economic variables in the CR areas participating in EUROCARE-5 were collected from EUROSTAT [22] and various National Statistics Offices. National data of Gross Domestic Product (GDP) and Total National Expenditure on Health (TNEH) in $PPP (purchasing power parity) per capita were available from 1995 to 2009 and for each country involved in EUROCARE-5. To give an interpretation to ACRS values, we performed univariate log-linear regression analysis to study the effect of GDP and TNEH on 5-year ACRS for all cases, as in ecological studies.

3. Results

Table 1 shows the case-mix weights applied for ACRS estimates by sex, and the range of different weights across Europe (weights are associated with the frequency with which each cancer appears in a given country cancer site distribution). Several sites showed a four-fold ratio between max and minimum. Large ranges were for male lung cancer (8% points in Sweden to 26% points in Poland), female lung cancer (3% in Malta to 15% in Scotland), female breast cancer (21% in Lithuania to 37% in Belgium), cervical cancer (1% in Finland to 9% in Bulgaria) and prostate cancer (10% in Bulgaria to 39% in Sweden). This variable case-mix distribution among countries is reflected in the difference between ARS and ACRS (Table 2). For example, ACRS was lower than ARS, in countries with a low percentage of lethal cancers (e.g. lung cancer) or high percentage of cancers with a good prognosis (e.g. prostate cancer). In Sweden (where lung cancer shows the lowest frequency and prostate cancer the highest) ARS for men was 65%, while ACRS was 52%. In contrast, in Poland (where the frequency of lung cancer cases was the highest) ARS for men was 35% while ACRS was 39%. Case-mix adjustment reduced differences among countries: for men, 5 years after diagnosis, the absolute difference between best and worst ARS was 35 percentage points, while it was 21 percentage points for ACRS. For women, these figures were 17 and 14.

Five-year ACRS was lowest in Bulgaria, for men (32%) and women (47%), and highest in Austria, for men (53%), and in Iceland, for women (61%) and men and women combined (58%). In various countries five-year ACRS for men and women separately, was 8–12 percentage points lower, when we excluded female breast and prostate cancers in a separate analysis, but the minimum and maximum remained the same in Bulgaria and Iceland (data not shown).

Differences between Central and Eastern Europe (i.e. comparison of the areas with the highest and the lowest survival) were higher for 1- and 5-year ACRS (around 9 percentage points) than for conditional ACRS (4 percentage points) (Fig. 1). Differences between conditional and unconditional ACRS were higher in Eastern Europe (24 percentage points) and Ireland and UK (23 percentage points) than other regions (19–20 percentage points). Five-year ACRS decreased with age (Fig. 1).

Focusing on ACRS trends over the period 1999–2007 (Fig. 2, Supplementary Fig. 1), ACRS increased in all regions and countries. The main absolute increases for all cases five-year ACRS were in Lithuania (9 percentage points between 1999–2001 and 2005–2007) and Denmark (7 percentage points). In all the regions (and in the majority of countries), changes in survival trends were primarily due to changes in prostate cancer survival for men and breast cancer survival for women (data not shown).

We divided the ACRS shown in Fig. 1 into tertiles, and calculated the average GDP and TNEH of the countries in each tertile (Table 3). Survival increased by tertile with mean GDP and TNEH. Coefficients of linear determination (R^2 from univariate log-linear regressions) between GDP and ACRS and between TNEH and ACRS of about 70% suggest that differences in survival could be explained by macro-economic indicators. R^2 were similar after excluding female breast and prostate cancers (data not shown). Fig. 3 compares 5-year ACRS for countries ranked by TNEH and ACRS as estimated by the regression including TNEH as explanatory variable (the superimposed curve, i.e. the curve estimates ACRS only in relation to TNEH). Countries like Austria, Iceland, Germany, Belgium, Sweden, Finland, Italy, Spain, Portugal, Malta, Czech Republic, Croatia, Lithuania, Estonia (for which the

Table 1
Weights (with minimum and maximum among countries) used in case-mix standardisation of relative survival for men and women.

Cancer site	Men			Women			Men and women		
	Weight	Min	Max	Weight	Min	Max	Weight	Min	Max
Head & Neck	2.8%	1.3% (IS)	7.3% (SK)	–	–	–	2.0%	1.2% (IS)	4.2% (SK)
Oesophagus	2.2%	0.9% (BG)	3.9% (SC)	–	–	–	1.6%	0.6% (BG)	3.1% (SC)
Stomach	4.2%	2.4% (DK)	8.8% (PT)	3.0%	1.3% (DK)	7.1% (PT)	3.6%	1.9% (DK)	8.0% (PT)
Colon	8.3%	4.8% (LT)	10.2% (PT)	8.5%	6.2% (LT)	11.7% (NO)	8.4%	5.5% (LT)	10.5% (NO)
Rectum	5.8%	3.1% (IS)	8.7% (SK)	4.5%	3.1% (IS)	6.0% (SK)	5.2%	3.1% (IS)	7.4% (SK)
Liver, primary	1.7%	0.6% (NL)	4.2% (IT)	–	–	–	–	–	–
Pancreas	2.5%	1.5% (PT)	3.8% (BG)	2.7%	1.8% (PT)	3.9% (FI)	2.6%	1.6% (PT)	3.7% (LV)
Larynx	1.8%	0.7% (IS)	4.1% (BG)	–	–	–	–	–	–
Lung	15.6%	7.6% (SE)	25.9% (PL)	7.9%	3.0% (MT)	15.5% (SC)	12.0%	7.3% (SE)	17.6% (PL)
Melanoma of the Skin	2.8%	1.1% (LT)	4.5% (NO)	3.5%	1.3% (BG)	5.6% (CH)	3.1%	1.3% (BG)	5.0% (NO)
Female Breast	–	–	–	30.2%	20.9% (LT)	37.2% (BE)	14.5%	9.9% (LT)	17.7% (MT)
Cervix Uteri	–	–	–	2.9%	1.4% (FI)	8.8% (BG)	–	–	–
Corpus Uteri	–	–	–	5.4%	3.5% (SC)	9.3% (LV)	2.6%	1.7% (IE)	4.7% (LV)
Ovary and uterine adnexa	–	–	–	4.3%	3.0% (PT)	6.9% (LV)	2.0%	1.4% (PT)	3.5% (LV)
Prostate	23.6%	10.4% (BG)	39.2% (SE)	–	–	–	12.4%	5.3% (BG)	20.6% (SE)
Testis	1.4%	0.5% (LT)	2.4% (SK)	–	–	–	–	–	–
Urinary Bladder	5.8%	3.4% (NO)	9.0% (ES)	2.1%	1.3% (FR)	3.2% (WL)	4.1%	2.5% (NO)	6.3% (ES)
Kidney, Ureter, Other Urinary Organs	3.6%	2.1% (PT)	6.6% (CZ)	2.4%	1.5% (PT)	4.4% (CZ)	3.0%	1.8% (PT)	5.5% (CZ)
Thyroid	–	–	–	1.8%	0.7% (WA)	4.7% (PT)	–	–	–
Non Hodgkin lymphomas	4.4%	2.6% (LV)	5.3% (MT)	4.1%	2.3% (BG)	4.9% (CH)	4.3%	2.5% (BG)	4.9% (IE)
Other cancers[a]	13.5%	10.2% (AT)	17.6% (MT)	16.7%	13.5% (LV)	19.3% (ES)	18.6%	15.6% (BE)	23.7% (BG)

AT, Austria; BE, Belgium; BG, Bulgaria; CH, Switzerland; CZ, Czech Republic; DK, Denmark; ES, Spain; FI, Finland; FR, France; IE, Ireland; IS, Iceland; IT, Italy; LT, Lithuania; LV, Latvia; MT, Malta; NL, The Netherlands; NO, Norway; PL, Poland; PT, Portugal; SC, UK, Scotland; SE, Sweden; SK, Slovakia; WA, UK, Wales.

[a] Malignancies with less than 1.4% of the total 2000–2007 cancer cases.

Table 2
Age-standardised relative survival (ARS,%) and age and case mix-standardised relative survival (ACRS,%) for all cancers combined at 5 years after diagnosis. Patients aged 15 years or over and diagnosed in 2000–2007.

	Men		Women		Men and women	
	ARS (%)	ACRS (%)	ARS (%)	ACRS (%)	ARS (%)	ACRS (%)
Northern Europe	*58.2*	*49.3*	*60.3*	*59.3*	*59.6*	*54.5*
Denmark	47.3	43.6	53.8	55.4	50.9	48.9
Finland	59.7	50.8	62.2	60.2	61.4	55.7
Iceland	60.4	52.1	60.9	61.5	61.2	57.6
Norway	56.7	48.3	59.9	59.5	58.6	54.1
Sweden	64.8	51.6	63.9	61.0	64.7	56.4
Ireland and UK	*46.9*	*44.7*	*52.4*	*53.3*	*50.1*	*49.1*
Ireland	53.1	47.6	54.0	55.1	53.9	51.8
UK, England	46.9	44.5	52.7	53.2	50.2	48.9
UK, Northern Ireland	47.7	46.8	53.7	55.1	51.0	50.9
UK, Scotland	43.0	43.7	49.6	53.0	46.6	48.4
UK, Wales	47.3	44.1	51.9	52.6	49.9	48.7
Central Europe	*54.7*	*50.9*	*61.3*	*59.3*	*58.0*	*55.3*
Austria	59.4	53.3	60.8	59.5	60.1	56.7
Belgium	56.7	51.8	64.0	60.3	60.4	56.3
France	54.5	49.9	63.3	59.2	58.6	54.5
Germany	56.2	52.3	62.1	60.2	59.1	56.4
Switzerland	56.3	50.9	61.9	60.1	59.1	55.7
The Netherlands	49.8	47.8	59.0	57.4	54.6	52.6
Southern Europe	*49.9*	*50.1*	*58.9*	*58.8*	*54.3*	*54.5*
Croatia	40.0	44.2	53.4	55.0	46.2	49.8
Italy	52.9	52.3	60.7	60.5	56.8	56.3
Malta	47.5	46.4	58.0	54.7	52.9	51.3
Portugal	52.1	49.7	60.7	58.9	56.4	54.8
Slovenia	42.0	43.0	54.1	54.6	47.8	48.3
Spain	48.9	48.3	58.0	57.1	52.8	52.9
Eastern Europe	*39.3*	*41.1*	*50.9*	*51.2*	*45.0*	*46.3*
Bulgaria	29.8	31.8	47.8	47.2	38.7	39.2
Czech Republic	46.4	45.3	55.2	54.2	50.7	50.0
Estonia	39.9	40.4	51.6	52.4	46.0	46.9
Latvia	35.4	37.7	47.8	48.6	41.7	43.3
Lithuania	43.0	42.2	49.0	49.1	46.1	46.7
Poland	34.7	38.8	46.5	49.4	40.6	44.5
Slovakia	38.2	40.4	51.9	51.6	44.8	45.5
Europe[a]	*50.3*	*48.7*	*58.0*	*57.1*	*54.2*	*52.5*
Max–Min[b]	35.0	21.5	17.5	14.3	26.0	18.4

[a] Country-weighted estimates.
[b] Absolute difference in percentage points between the best and the worst survival figures.

curve exceeds the bars) have better survival than would be expected when TNEH alone is considered as the explanatory variable of survival. Finally, we related the increase from the five-year ACRS time trend analyses of 1999–2007 to the GDP and TNEH increases, between 1996–2000 and 2002–2006 (Table 4). Countries with a larger relative increase in GDP also had a greater absolute increase in cancer survival.

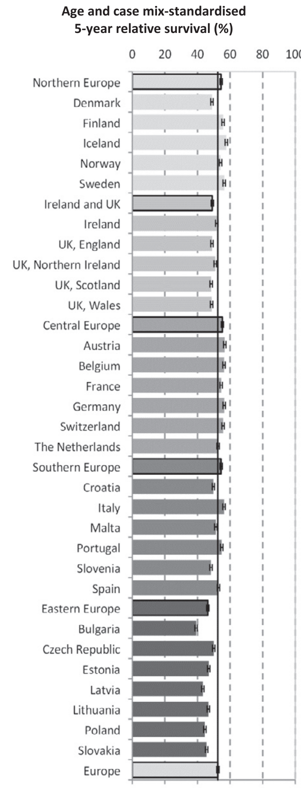
4. Discussion

We analysed over 7.5 million cancer cases from the European CRs participating in the EUROCARE-5 project, and conducted a comprehensive survival analysis on all cancer cases, in 29 European countries. Most of the CRs had participated in the European Network of Cancer Registries survey in 2010–2012 [1]. We focused on survival for all cancers combined and in this general indicator we did not analyse the role of different cancer sites, as survival for specific cancer sites is dealt with in other EUROCARE-5 companion articles [23–33]. However ‘all cancers combined’ is still the sum of ‘all single cancer sites’ so all caveats in the comparison of survival for single cancer sites must be considered: (a) incomplete registration and presence of DCO cases [34], (b) role of multiple tumours [35], (c) comparison of data from national and not national CRs [36], (d) incomplete follow-up [37]. EUROCARE-5 analysed the original datasets from all CRs using a common method. Particular attention was paid to analyse and evaluate

All cases

Age and case-mix-standardised 1-year, 5-year relative survival, and 5-year relative survival conditional to surviving 1 year, with 95% confidence intervals in parentheses

	Number of cases	1-year		5-year		Conditional	
Northern Europe	**928,937**	**73.0**	**(72.9-73.1)**	**54.5**	**(54.4-54.6)**	**74.7**	**(74.6-74.8)**
Denmark	223,627	69.2	(69.0-69.4)	48.9	(48.6-49.2)	70.7	(70.5-70.8)
Finland	183,986	73.2	(73.0-73.4)	55.7	(55.4-56.0)	76.1	(75.9-76.3)
Iceland	9,520	76.1	(75.3-77.0)	57.6	(56.3-59.0)	75.7	(74.8-76.6)
Norway	171,326	73.2	(72.9-73.4)	54.1	(53.8-54.5)	74.0	(73.8-74.2)
Sweden	340,478	75.1	(75.0-75.3)	56.4	(56.2-56.6)	75.1	(74.9-75.2)
Ireland and UK	**2,383,394**	**67.6**	**(67.6-67.7)**	**49.1**	**(49.0-49.2)**	**72.6**	**(72.5-72.6)**
Ireland	121,671	69.1	(68.9-69.4)	51.8	(51.5-52.2)	75.0	(74.7-75.2)
UK, England	1,869,405	67.6	(67.5-67.7)	48.9	(48.8-49.0)	72.4	(72.3-72.4)
UK, Northern Ireland	54,887	67.9	(67.6-68.3)	50.9	(50.1-51.7)	74.9	(74.1-75.7)
UK, Scotland	212,282	67.5	(67.3-67.7)	48.4	(48.1-48.7)	71.7	(71.4-72.0)
UK, Wales	125,149	66.3	(66.0-66.6)	48.7	(48.3-49.0)	73.4	(73.1-73.7)
Central Europe	**2,062,220**	**74.2**	**(74.2-74.3)**	**55.3**	**(55.2-55.4)**	**74.5**	**(74.4-74.6)**
Austria	273,848	73.7	(73.5-73.8)	56.7	(56.5-56.9)	77.0	(76.8-77.1)
Belgium	261,270	76.4	(76.3-76.6)	56.3	(56.0-56.5)	73.6	(73.5-73.8)
France	180,651	75.1	(74.9-75.4)	54.5	(54.2-54.8)	72.6	(72.4-72.7)
Germany	670,685	75.0	(74.9-75.1)	56.4	(56.3-56.6)	75.3	(75.2-75.4)
Switzerland	83,008	76.4	(76.1-76.7)	55.7	(55.3-56.1)	72.9	(72.6-73.2)
The Netherlands	592,758	71.9	(71.8-72.0)	52.6	(52.5-52.8)	73.2	(73.1-73.4)
Southern Europe	**1,295,447**	**72.9**	**(72.8-73.0)**	**54.5**	**(54.4-54.6)**	**74.8**	**(74.7-74.9)**
Croatia	153,799	65.2	(64.9-65.5)	49.8	(49.4-50.2)	76.4	(76.1-76.6)
Italy	739,981	75.2	(75.1-75.3)	56.3	(56.1-56.5)	74.9	(74.7-75.0)
Malta	10,322	68.5	(67.6-69.3)	51.3	(50.0-52.5)	74.9	(74.0-75.8)
Portugal	176,173	72.7	(72.5-72.9)	54.8	(54.5-55.1)	75.4	(75.2-75.6)
Slovenia	69,293	69.0	(68.5-69.5)	48.3	(47.8-48.8)	70.0	(69.8-70.2)
Spain	145,879	71.8	(71.6-72.0)	52.9	(52.5-53.2)	73.6	(73.4-73.9)
Eastern Europe	**1,016,620**	**65.6**	**(65.5-65.7)**	**46.3**	**(46.2-46.5)**	**70.6**	**(70.5-70.8)**
Bulgaria	202,915	60.0	(59.7-60.3)	39.2	(38.8-39.5)	65.3	(65.0-65.5)
Czech Republic	360,828	67.8	(67.6-68.0)	50.0	(49.6-50.3)	73.7	(73.4-73.9)
Estonia	43,335	67.9	(67.4-68.3)	46.9	(46.2-47.6)	69.1	(68.6-69.7)
Latvia	63,191	63.2	(62.7-63.7)	43.3	(42.7-43.9)	68.5	(68.0-68.9)
Lithuania	92,193	64.8	(64.4-65.1)	46.7	(46.2-47.2)	72.1	(71.7-72.5)
Poland	132,722	65.8	(65.5-66.2)	44.5	(44.0-45.0)	67.6	(67.2-68.0)
Slovakia	121,436	66.7	(66.4-67.1)	45.5	(45.1-46.0)	68.2	(68.0-68.5)
Europe	**7,686,618**	**71.9**	**(71.9-71.9)**	**52.5**	**(52.4-52.5)**	**74.0**	**(74.0-74.0)**



European case-mix, age-specific and age-standardised observed (obs, %) and relative (rel, %) survival

Age group	Number of cases		1-year	3-year	5-year
15-44	557,606	obs	83.8	70.9	65.8
		rel	83.9	71.2	66.3
45-54	877,395	obs	79.9	65.5	60.0
		rel	80.2	66.4	61.4
55-64	1,652,498	obs	76.6	61.4	55.0
		rel	77.3	63.2	57.9
65-74	2,236,315	obs	70.4	54.0	46.1
		rel	72.0	57.9	52.3
75+	2,362,804	obs	56.8	37.5	27.9
		rel	61.3	47.4	42.1
All cases	7,686,618	obs	70.0	53.5	45.7
		rel	71.9	58.0	52.5
Men (52%)					
15-44	212,639	obs	78.6	63.4	57.6
		rel	78.7	63.8	58.3
45-54	362,152	obs	75.4	59.5	53.9
		rel	75.8	60.6	55.6
55-64	891,331	obs	72.9	56.8	50.3
		rel	73.8	59.0	53.9
65-74	1,337,700	obs	67.7	50.3	42.3
		rel	69.6	55.1	49.8
75+	1,215,888	obs	55.0	35.0	25.2
		rel	60.0	45.6	40.3
All cases	4,019,710	obs	66.9	49.3	41.2
		rel	69.2	54.4	48.7
Women (48%)					
15-44	344,967	obs	87.7	76.4	71.6
		rel	87.8	76.6	71.9
45-54	515,243	obs	84.2	71.2	65.7
		rel	84.4	71.8	66.6
55-64	761,167	obs	81.2	67.3	61.0
		rel	81.6	68.5	62.9
65-74	898,615	obs	74.8	59.8	52.0
		rel	75.9	62.6	56.6
75+	1,146,916	obs	59.9	41.3	31.5
		rel	64.1	50.9	45.4
All cases	3,666,908	obs	74.0	58.7	51.1
		rel	75.6	62.6	57.1

Fig. 1. Age-specific and age-standardised, case mix-standardised relative survival for all adult cancers diagnosed in 2000–2007, by European region, country, gender and overall.

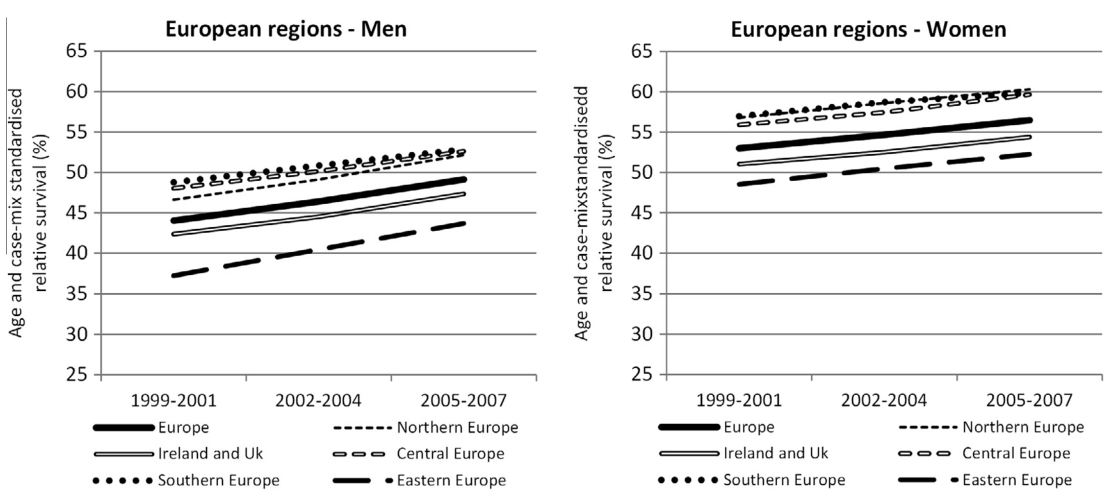


Fig. 2. Time trend in age and case-mix standardised 5-year relative survival by European region and gender.

the caveats in the data: in fact, some CRs were not included in the project since we were not confident about the plausibility of their data. The EUROCARE-5 methods and caveats of cancer survival comparison are described elsewhere in a dedicated paper [12].

Big differences in survival persist across Europe for all cancers combined. Five years after diagnosis a cancer patient living in Central or Northern Europe has a better probability of surviving than a patient in Bulgaria or Latvia (with a difference of 15–20 percentage points). As in previous EUROCARE projects [8] patients in Denmark, UK and Eastern European countries have lower survival than patients in other neighbouring countries. ACRS differences among regions are higher for one- and five-year ACRS than for survival conditional of survival at one year. A large amount of

Table 3
Average Gross Domestic Product (GDP) and Total National Expenditure on Health (TNEH) according to tertiles of 5-year age- and case-mix-standardised relative survival (ACRS[a]) for all cancer cases diagnosed in 2000–2007.

Tertiles of ACRS	No. countries	Countries	Average per tertile (per capita $PPP), 2000–2007	
			GDP[b]	TNEH[c]
[39–49%)	9	BG, LV, PL, SK, LT, EE, SL, UK, DK	$17,896	$1,334
[49–55%)	9	CR, CZ, MT, IE, NL, ES, NO, FR, PT	$26,888	$2,311
[55–58%)	8	CH, FI, BE, IT, SE, DE, AT, IS	$31,433	$3,035

PPP, Purchasing Power Parity.Source of GDP and TNEH: EUROSTAT [19].
AT, Austria; BE, Belgium; BG, Bulgaria; CH, Switzerland; CR, Croatia; CZ, Czech Republic; DE, Germany; DK, Denmark; EE, Estonia; ES, Spain; FI, Finland; FR, France; IE, Ireland; IS, Iceland; IT, Italy; LT, Lithuania; LV, Latvia; MT, Malta; NL, The Netherlands; NO, Norway; PL, Poland; PT, Portugal; SE, Sweden; SK, Slovakia; SL, Slovenia; UK, the United Kingdom.
[a] ACRS estimated using the weights for men and women indicated in Table 1.
[b] R^2 from univariate log-linear regressions between GDP and ACRS = 69%.
[c] R^2 from univariate log-linear regressions between TNEH and ACRS = 73%.

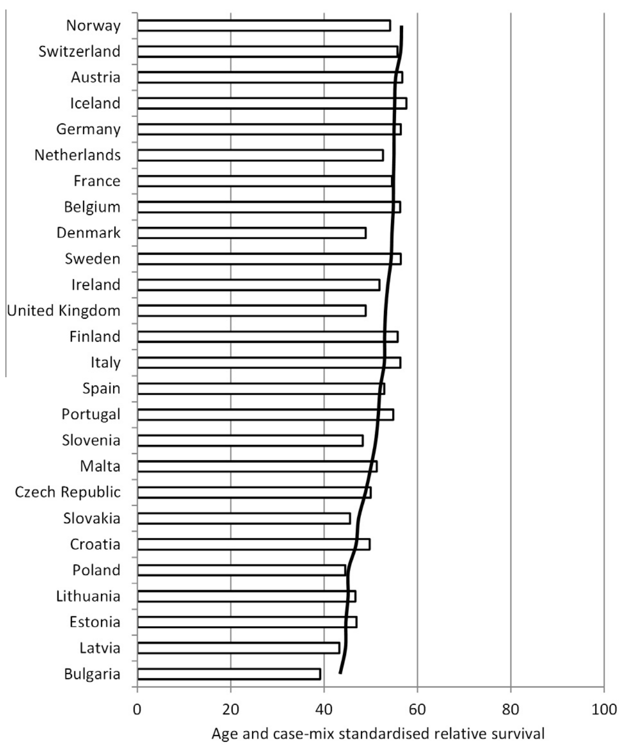


Fig. 3. Five-year age- and case-mix-standardised relative survival (ACRS) for all cases diagnosed in 2000–2007 ranked by Total National Expenditure on Health (TNEH[a]). The superimposed curve is formed by the ACRS figures expected when TNEH alone is considered the explanatory variable of survival[b].
[a]Average TNEH (per capita $PPP) between 2000 and 2007 (Source: EUROSTAT [19]). [b]ACRS estimated by univariate log-linear regression including TNEH as explanatory variable.

the survival differences relates to the first year after diagnosis, probably reflecting the higher proportion of cases diagnosed at an advanced stage in areas with lower ACRS. Survival felt with higher age at diagnosis.

Cancer mortality in the EU has steadily declined since the late 1980s [38], and cancer survival is increasing all over Europe, with major increases in countries with lower survival before: Czech Republic, Estonia, Denmark and Lithuania had a more than 5.5 percentage point increase in five-year ACRS between 1999–2001 and 2005–2007. ACRS differences among countries still persisted when excluding those cancers more likely influenced by over-diagnosis (breast cancer for women and prostate cancer for men [10]).

Survival for all cancers combined (an aggregated group of very different diseases) has been considered with scepticism by clinicians. In fact, comparison of survival rates for all cancers combined would require in-depth knowledge of (a) diagnostic methods, (b) the potential for effective treatment regimens [9], (c) different early diagnosis strategies (which can imply over-diagnosis [39]) and (d) registration practices (e.g. which could affect urinary bladder cancer survival comparisons [30]).

Nevertheless, the measure is of political interest and has been accepted as an indicator for health care systems performance, which has been correlated at an aggregate level with macro-economic indicators using the ecologic regression approach [8,11,36,40]. There are clear limits to this ecologic regression analysis that studies relationships between properties (i.e. variables) of groups, organizations or places: ecologic analysis poses major problems of interpretation as it cannot control for biologic and contextual effects. Although it is important not to interpret the ecologic associations as the effect at the individual level, they can still give a picture of the effects of social processes or population interventions such as new programmes, policies or legislation [41].

In previous EUROCARE studies the correlation between survival and macro-economic variables, that describes a country's welfare and health system, suggested that cancer survival increases with wealth and health funding (using GDP and TNEH as proxy) [8,11,40,42–47]. The present analysis confirmed these findings for both ACRS for all cancers and ACRS for all cancers, excluding female breast and prostate cancers: countries such as Denmark and UK continue to perform worse than expected for their level of TNEH (under the ecological hypothesis that differences in survival are explained by differences in TNEH).

Table 4
Average Gross Domestic Product (GDP) and Total National Expenditure on Health (TNEH) increases between 1996–2000 and 2002–2006 in relation to tertiles of 5-year age- and case-mix-standardised relative survival (ACRS[a]) increase between 1999–2001 and 2005–2007.

Tertiles of absolute ACRS increase 2005–2007 versus 1999–2001	No. of countries	Countries	Average per tertile, 2002–2006 versus 1996–2000	
			GDP relative increase	TNEH relative increase
<3.7%	6	SK, MT, DE, UK, FI, SE	33%	53%
[3.7–4.5%)	7	IT, PL, CH, BG, SL, IS, NL	35%	55%
≥4.5%	7	AT, NO, EE, CZ, IE, DK, LT	48%	55%

Source of GDP and TNEH: EUROSTAT [19].
AT, Austria; BG, Bulgaria; CH, Switzerland; CZ, Czech Republic; DE, Germany; DK, Denmark; EE, Estonia; FI, Finland; IE, Ireland; IS, Iceland; IT, Italy; LT, Lithuania; MT, Malta; NL, The Netherlands; NO, Norway; PL, Poland; SE, Sweden; SK, Slovakia; SL, Slovenia; UK, the United Kingdom.
[a] ACRS estimated using the weights for men and women indicated in Table 1.

5. Conclusion

The EUROCARE-5 data suggest that on a clinical level cancer survival depends on the widespread application of effective diagnosis and treatment modalities, and can be correlated with macro-economic determinants, in particular investment in the health care system. Our data, together with those of clinical registries [48], could be used by clinicians too, to engage local governments in discussions on the relevance of ACRS differences across Europe and to seek long-term effects of treatments and survivorship issues [2–4]. In conclusion, the findings presented here are the result of the important data collection work of the CRs across Europe, confirming their fundamental role in cancer control. Health planners and clinicians should consider that data collectable by CRs might be useful to study the reasons for survival differences at population level, for instance investigating different levels of multidisciplinary approach, accessibility and waiting times, skilled medical specialists in different countries etc.

Role of funding sources

The study was funded by the Compagnia di San Paolo, Fondazione Cariplo Italy, Italian Ministry of Health (Ricerca Finalizzata 2009, RF-2009-1529710) and the European Commission (European Action Against Cancer, EPAAC, Joint Action No. 20102202). The funding sources had no role in study design, data collection, analysis or interpretation, the writing of the report or the decision to submit the article for publication.

Conflict of interest statement

None declared.

Acknowledgements

Thanks to Chiara Margutti, Simone Bonfarnuzzo and Camilla Amati for their assistance.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.ejca.2015.07.025.

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