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Up-to-date estimates of breast cancer survival for the years 2000–2004 in 11 European countries: The role of screening and a comparison with data from the United States

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ABSTRACT

Introduction: We investigated survival in breast cancer patients by age group, focussing on those covered by screening programmes, using data from 12 European population-based cancer registries participating in the European Network for Indicators on Cancer Survival Working Group.

Methods: We calculated period estimates of 5-year relative survival for 2000–2004 and examined the change in survival estimates for four age groups between 1990–1994 and 2000–2004. Trends in age specific incidence, survival and mortality were additionally compared to those in the United States based on results from the Surveillance Epidemiology and End Results (SEER) programme.

Results: Breast cancer survival uniformly increased particularly in areas with lower breast cancer survival for patients diagnosed in 1990–1994. With the exception of Geneva, Scotland and Estonia, the rise in survival was always larger among the younger age groups than in the 70+ age group and the age-gradient widened over time. The 5-year relative survival of patients aged 70 and above in the European registries was at least 7 percentage points lower than the 5-year relative survival of patients in the same age group in the US in 2000–2004.

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During the study period, incidence increased in all age groups and populations with a few exceptions, an observation paralleled by declining mortality.

Conclusions: Results showed that some of the geographical differences in overall survival are even larger when considering age groups, in particular between Western and Eastern European countries. Furthermore, some of the differences in survival within the Northern and Western European areas could be due to variations in the implementation of screening programmes rather than economic inequalities.

1. Introduction

The increasing survival of patients diagnosed with breast cancer has been documented in a number of large population-based studies.[1–3] In Europe, the mean 5-year relative survival has reached almost 80% for women diagnosed with breast cancer in 1995–1999, an increase of about 4 percentage points compared to 1990–1994.[1] In the United States (US), 5-year relative survival reached over 90% in 2000,[4] while in Japan, a 5-year relative survival of about 85% was seen already in the period 1993–1996.[5] In the US, improvements in treatment and the diffusion of mammography screening were estimated to contribute almost equally to the increasing trends in survival and, more importantly, decreasing trends in breast cancer mortality.[6] Organised screening programmes, as well as most opportunistic early diagnosis practices, are usually offered within a precise age range, usually 50–69.[7] Opportunistic or, more rarely, organised screening is also offered to women within the 40–49 age group in several countries.

Previous population-based survival studies, such as those published in the consecutive rounds of the EUROCARE project (EUROpean CAncer REgistry-based study on survival and CARE of cancer patients),[1] did not take into account the age ranges for screening. Therefore, in this study we investigated trends in the survival of breast cancer patients, with a particular focus on age groups targeted by screening programmes in 11 different countries. Using data up to 2004 from long-standing population-based cancer registries taking part in the EUNICE (European Network for Indicators on Cancer) Survival Working Group,[3] we analyse trends in survival using period analysis techniques, compare these with trends in incidence and mortality and provide a transatlantic comparison by additionally comparing the time trends in breast cancer in the US.[4]

2. Materials and methods

2.1. Data sources

The EUNICE database includes relevant cancer information from 12 population-based registries in 11 countries representing major geographical regions of Europe (*Northern Europe*: Norway, Finland; *Western Europe*: Scotland (UK), Eindhoven (Netherlands); *Eastern Europe*: Estonia, Lithuania, Cracow (Poland); Central Europe: Saarland (Germany) and Geneva (Switzerland); *Southern Europe*: Tuscany (covering the Provinces of Florence and Prato, Italy), Turin (Italy) and Slovenia). Data preparation and general inclusion criteria have been described in detail elsewhere.[3] First primary invasive breast tumours diagnosed in women between 1990 and 2004 were included in this study. Although cancer registries also collected cases of in situ breast cancer, only invasive cases are considered in the analysis. We supplemented trends in registry-specific incidence with national level mortality in the same age groups using data from the World Health Organisation (WHO) mortality databank. To enable comparisons with the US, data from the SEER 9 registries were selected for the same years, using the same definitions, inclusion criteria and method of analysis as used in the above database. Information on screening programmes implemented in each area and country were extracted from relevant scientific and institutional publications.

All data were anonymous, de-identified and for the study purposes were given without restrictions by the institutions hosting cancer registries.

2.2. Survival analysis

We calculated 5-year relative survival estimates, which quantify cancer-related excess mortality within a cancer patient population, as ratios of the observed survival of cancer patients and the expected survival of the underlying general population. The latter estimates were calculated according to the Ederer II method,[8] using registry, age, sex and calendar period specific life tables. All derived survival estimates were calculated with the period analysis method, which are exclusively based on the survival experience of patients during the specific calendar period for which they are derived, and which have been shown to closely predict the survival later observed for patients diagnosed in that period.[9] Survival estimates were calculated for the age groups 15–49, 50–59, 60–69 and 70+, for the calendar periods 1990–1994 and 2000–2004. For the period 2000–04, and for those registries with data on incident cases available only up until 2003 (Estonia, Slovenia and Tuscany), but followed-up until 2004, the analysis was slightly modified according to the principles of hybrid analysis.[10] This is a calculation strategy designed to allow for the estimation of up-to-date survival for situations where mortality data are more up-to-date than incidence. For each period and age group, a saturated model that is equivalent to period analysis was used to calculate strata-specific relative survival estimates. Tests for survival trends over the period were done by models including calendar period (1990–1994, 1995–1999 and 2000–2004) as a numerical variable. Standard errors of the modelled relative survival estimates were calculated using the delta method.

Table 1 – Age specific numbers and percentages of breast cancer cases in women in the 12 EUNICE registries and USA SEER 9 registries, 2000–2004.

Age group	Norway	Finland	Scotland	Eindhoven, Netherlands	Estonia[a]	Lithuania	Cracow, Poland	Saarland, Germany	Geneva, Switzerland	Tuscany[a], Italy	Turin, Italy	Slovenia[a]	Total	USA, SEER9
Registry (number of cases)														
15–49	2709	3822	3619	2070	493	1575	391	708	397	855	721	922	18 282	21 687
50–59	4088	5503	4809	2108	571	1402	525	775	514	946	789	908	22 938	22 633
60–69	3355	4271	4196	1800	597	1498	446	1035	536	1000	1056	946	20 736	19 533
70+	4499	5054	6130	2226	667	1821	583	1160	513	1281	1386	1227	26 547	30 078
Total	14 651	18 650	18 754	8204	2328	6296	1945	3678	1960	4082	3952	4003	88 503	93 931
Registry (percentage)														
15–49	18.5	20.5	19.3	25.2	21.2	25.0	20.1	19.2	20.3	20.9	18.2	23.0	20.7	23.1
50–59	27.9	29.5	25.6	25.7	24.5	22.3	27.0	21.1	26.2	23.2	20.0	22.7	25.9	24.1
60–69	22.9	22.9	22.4	21.9	25.6	23.8	22.9	28.1	27.3	24.5	26.7	23.6	23.4	20.8
70+	30.7	27.1	32.7	27.1	28.7	28.9	30.0	31.5	26.2	31.4	35.1	30.7	30.0	32.0
Total	100	100	100	100	100	100	100	100	100	100	100	100	100	100

[a] Numbers based on cases between 2000–2003 only.

3. Results

The total number of breast cancer cases in the period of 2000–04 was 88 503, ranging from 1945 in Cracow to 18 754 in Scotland, while from the SEER9 registries, 93 931 breast cancer cases were included (Table 1). The age distribution of incident cases was largely similar in all the areas, with approximately 20–25% of patients diagnosed in each of the age groups 15–49, 50–59 and 60–69, and about 30% of patients diagnosed at age 70 or older. The proportion of cases below 50 years of age was slightly higher in Eindhoven (25%) and Lithuania (25%), while the proportion aged above 70 years was slightly higher in Turin (35%), but lower in Geneva, Eindhoven and Finland (26–27%).

In Table 2, five-year relative survival estimates by age group for women diagnosed in the years 2000–2004 along with changes since 1990–94 are shown. Geographical areas were ranked according to the starting year of organised screening programmes implemented in areas covered by the population-based cancer registries. Women aged 50–59 exhibited the highest survival in five populations (Finland, Scotland, Turin, Estonia and Cracow), whereas women aged 15–49 had the highest survival estimates in Tuscany, Saarland, Lithuania, Slovenia and Geneva had the highest 5-year survival (90.5%) in both age groups 15–49 and 50–59. In the three remaining populations, the highest survival was seen in women aged 60–69 (Eindhoven, Norway and the US). Differences between the three age groups (15–49, 50–59 and 60–69) were less than 2 percentage points in Tuscany, Turin, Geneva and Estonia, between 2% and 4% points in the US, Finland, Scotland and Norway, between 4% and 5% points in Cracow, Saarland, Slovenia and Eindhoven and were at 7.4% points in Lithuania. Among the populations with no established screening programme in the study period, survival estimates, with the exception of Lithuania, were very similar in age groups 15–49 and 50–59 but somewhat lower among patients aged 60–69.

In each European Registry, survival among women aged 70 or older was lower than in all the other age groups. In 8 out of 12 Registries, survival was more than 9 percentage points higher in the age group 60–69 in comparison with survival in the oldest age group. In contrast, the relative survival of patients aged 70 or older in the US was essentially similar to the survival observed among younger patients.

Increases in survival since the period 1990–94 were particularly striking in Cracow and Lithuania, for which estimates have been historically low. In all Registries with the exception of Geneva, Scotland and Estonia, the rise in survival since 1990–94 was, always larger among the younger age groups than in the 70+ age group, and thereby the difference in survival between the youngest and the oldest age group has widened over time in the majority of European Registries.

By 2000–2004, there was a slightly higher survival in Finland, Tuscany, Turin and Geneva than seen in the US across the age groups 15–49 and 50–59. In contrast, the 5-year relative survival of patients aged 70 and above in the European registries was at least 7 percentage points lower than the 5-year relative survival of patients in the same age group in the US in 2000–2004.

In Table 3, we compared age-specific incidence and mortality rates in the European countries and the US, between

Table 2 – Period estimates of 5-year relative survival in 2000–2004, standard errors (SE) and differences (Diff) with 1990–1994 estimates, by age-group and screening programmes.

Registry and screening programmes	15–49	SE[a]	Diff [b]	50–59	SE[a]	Diff [b]	60–69	SE[a]	Diff [b]	70+	SE[a]	Diff [b]	Starting year of screening
Established screening programmes													
Finland	89	0.5	8	92	0.4	7	89	0.6	8	79	1.0	5	1987[20]
Scotland	83	0.7	10	86	0.6	13	83	0.7	11	69	1.0	11	1989[7]
Tuscany, Italy	91	0.9	7	90	1.0	7	90	1.1	8	79	1.6	4	1990[23]
Eindhoven, Netherlands	83	0.9	5	86	0.9	10	88	1.0	17	81	1.5	8	1991[21]
Turin, Italy	88	1.3	9	90	1.1	12	89	1.1	13	79	1.7	3	1992[24]
Norway	85	0.7	9	87	0.6	13	89	0.7	13	78	1.0	4	1995[22]
Geneva, Switzerland	91	1.7	6	91	1.5	9	90	1.6	10	82	2.7	13	1999[28]
None or partial screening program or opportunistic screening													
Estonia	71	1.8	6	71	1.9	7	70	2.0	9	64	2.6	10	2005[25]
Saarland, Germany	86	1.3	9	86	1.4	16	81	1.5	3	78	2.0	6	2006[7]
Lithuania	72	1.2	18	65	1.4	18	66	1.4	18	59	1.7	12	2006[26]
Cracow, Poland	79	2.2	19	80	2.2	22	75	2.5	19	66	3.1	16	2007[7]
Slovenia	83	1.2	13	82	1.3	17	78	1.4	12	68	1.8	5	2008[27]
US SEER 9	87	0.2	5	89	0.2	6	90	0.3	5	89	0.4	4	

[a] SE: standard error.
[b] Diff: difference between the 5-year relative survival estimate in 2000–2004 and 1990–1994.

the years 1990–1992 and 2002–2004 (1998–2002 for incidence). In most populations we observed a general reduction of mortality rates which was particularly pronounced for women aged 15–49. The most consistent reduction of mortality across all ages was observed in Geneva (Switzerland). In almost all European areas and across all age groups breast cancer incidence is still rising. However, we observed a decrease of incidence among women aged 15–49 in the US (–2%), Norway (–4%) and Saarland (–6%), and among women aged 70 and over in Norway (–6%).

4. Discussion

The results presented in this paper provide insights into the increases in breast cancer survival in different age groups across diverse regions in Europe. The highest survival was recorded in western European areas and in those where screening programmes were established from the beginning of the 1990s or earlier. Although the increases in survival were higher for areas with lower survival in the baseline period of diagnosis (as seen in Lithuania and Cracow), the increase between 1990–1994 and 2000–2004 in breast cancer survival was observed in each of the Registry populations studied. Age-specific survival estimates and trends in the US up to age of 70 were comparable to those European areas where screening programmes are established longest, although more striking differences were apparent in the oldest age group.

Previous comparative studies such as EUROCARE in its consecutive rounds[1] have reported values of 5-year relative survival estimates (based on the cohort approach) between 62% (Czech Republic) and 87.6% (Iceland) for patients diagnosed in 1995–1999. Large variations in the survival increase over the previous period (1990–1994) were also observed, ranging from a 12 percentage point increase in Poland to a 1.6 percentage point increase in Sweden.[1] A period analysis of EUROCARE data extending the survival estimates up to 2000–2002 showed that the estimates were higher than those for the 1995–1999 cohort,[2] but estimates were still lower than those from our recent EUNICE analysis for the year 2004.[3] Evidence of continuous increases in survival is observed when comparing results from consecutive periods in different studies. For example, 5-year relative survival in Finland was 83.6% in the cohort analysis for 1995–1999[1], 85.7% in the period analysis for 2000–2004[2] and 86.8% in the period analysis for 2004.[3] Respectively, Norway showed values of 82.5%, 84.1%, 84.7%; Scotland 75.0%, 77.3%, 78.5% and finally, Slovenia 71.9%, 75.3% and 75.6%.

The validity of international comparisons of survival estimates have been challenged on the ground of the impact of incomplete registration,[11] the effects of the different clinical criteria for case definition, or the definition of specific life tables used for calculating relative survival.[12] Nevertheless, artefacts are likely to explain only a small part of the observed geographical differences and time trends. The main criticism arises from the use of survival data for comparing the quality of health care in different populations in the presence of screening where incidence is likely to have been inflated by prevalence rounds that occur at different times in different populations.[13] Additional analyses of incidence and mortality data for the same age-groups in each area, during approximately the same period, indicated that incidence consistently increased in all ages in our study, with the exception of Norway, Saarland and SEER areas where decreases in incidence were observed in the age group 15–49.

In general, a concurrent decline in mortality was present in all European populations and in the US in all patient groups up to the age of 70 years and confirmed by other studies.[6,14] Exceptions were Lithuania and Estonia, where breast cancer mortality increased in the examined periods in both the age groups 50–59 and 60–69. The decline in mortality was less striking in the oldest age group, with two countries (Estonia and Lithuania) showing a major increase of breast cancer

Table 3 – Age standardised incidence and corresponding national mortality rates per 100 000 population and changes in the rates (in %), by registry.

Age group, measure	Registry												
	Norway	Finland	Scotland, UK	Eindhoven, Netherlands	Estonia	Lithuania	Cracow, Poland	Saarland	Geneva, Switzerland	Tuscany, Italy[a]	Turin, Italy[a]	Slovenia	US, SEER9 white[1]
15–49													
Incidence													
1990–1992	39	42	44	49	27	26	27	47	48	51	41	34	51
1998–2002	38	46	45	58	33	31	31	44	53	61	53	37	50
Change (%)	**–4**	**7**	**4**	**19**	**20**	**17**	**14**	**–6**	**12**	**19**	**30**	**10**	–2
Mortality													
1990–1992	9	8	11	11	9	10	8	10	9	9	9	10	10
2002–2004	6	6	8	9	6	9	6	7	6	7	7	7	7
Change (%)	**–27**	**–27**	**–31**	**–17**	**–35**	**–13**	**–25**	**–34**	**–33**	**–23**	**–23**	**–33**	**–29**
50–59													
Incidence													
1990–1992	150	225	250	182	103	96	134	172	262	203	202	123	254
1998–2002	248	291	280	263	150	135	176	248	346	276	259	176	288
Change (%)	**65**	**29**	**12**	**44**	**45**	**40**	**31**	**44**	**32**	**35**	**28**	**44**	**13**
Mortality													
1990–1992	47	47	80	75	55	52	47	61	62	59	59	65	60
2002–2004	45	41	55	61	59	56	45	50	42	49	49	55	45
Change (%)	**–4**	**–13**	**–32**	**–18**	**7**	**7**	**–3**	**–18**	**–33**	**–18**	**–18**	**–14**	**–25**
60–69													
Incidence													
1990–1992	193	197	277	278	118	115	166	234	317	260	262	162	370
1998–2002	287	294	275	319	157	146	218	284	457	301	353	209	410
Change (%)	**49**	**49**	**–1**	**15**	**34**	**27**	**32**	**21**	**44**	**16**	**35**	**29**	**11**
Mortality													
1990–1992	73	65	106	108	68	64	63	89	96	82	82	77	93
2002–2004	60	58	79	84	71	71	60	79	78	72	72	76	70
Change (%)	**–18**	**–11**	**–26**	**–23**	**4**	**12**	**–5**	**–11**	**–18**	**–11**	**–11**	**–1**	**–25**
70+													
Incidence													
1990–1992	270	236	281	313	132	103	160	305	346	258	258	198	449
1998–2002	254	288	313	395	164	159	264	325	345	281	320	254	451
Change (%)	**–6**	**22**	**11**	**26**	**24**	**55**	**66**	**6**	**–0.5**	**9**	**24**	**28**	**0.4**
Mortality													
1990–1992	127	99	158	175	77	72	84	140	189	126	126	136	137
2002–2004	110	102	152	150	97	96	90	132	131	120	120	143	119
Change (%)	**–14**	**4**	**–4**	**–14**	**26**	**33**	**6**	**–6**	**–31**	**–5**	**–5**	**4**	**–13**

[a] Mortality data for the years 2000–2002.

mortality, while many areas recorded only minor decreases.. However, mortality, as an indicator is also associated with potential artefacts, and it can be affected by a lack of accuracy in the cause of death certification and subsequent coding, so limiting international comparisons.[15]

Our results confirm that, in Europe but not in the US, there are some disparities in case-fatality in older patients diagnosed with breast cancer, as compared to the younger age groups. Although the underlying reasons for such gaps are not easily revealed in population-based studies, investigations aimed at assessing the impact of factors – such as delays in seeking medical advice that may lead to more advanced tumours and co-morbidity[16] – are warranted. Previous studies, based on resident populations of Geneva and Manchester have shown that older women with breast cancer were less likely to receive radiotherapy and chemotherapy leading to substantial under-treatment, even after adjusting for co-morbidity and staging.[17,18] Elderly women were less likely to receive adjuvant therapy, but even at early stages of breast cancer they have been shown to receive less curative treatment.[19]

In the EUROCARE study, geographical differences in survival have been examined in relation to national expenditure on health,[1] showing that a low level of health expenditure was associated to lower survival in Eastern European countries. However, this indicator, did not explain survival differences within Northern and Western European countries. For these countries some of the differences in survival could be due to variations in the implementation of screening programmes rather than economic inequalities. For example, in Saarland in Germany, an organised screening programme was implemented in 2006, and the survival proportion was only slightly lower compared to other affluent countries in the 50–59 age group.

Among the areas included in the present study, six populations had long-established screening programmes running since the end of the 1980s (Finland[20], Scotland[7]) and since the beginning of the 1990s (Eindhoven,[21] Norway,[22] Tuscany,[23] Turin,[24]) with complete coverage of populations at screening age. However, the build up of screening programmes and age group covered were not homogenous across these areas. For example, Scotland did not extend mammography to women up to the age of 70 years until 2003–2004 and in Norway the screening programme reached nationwide coverage only in 2004.[22] In four other areas screening programmes started only recently: Saarland in 2006,[7] Estonia in 2005,[25] Lithuania in 2006,[26] Cracow in 2007[7] and Slovenia in 2008, where, however, opportunistic screening has been offered to women since the early 1990s.[27] In contrast, in Geneva, there is a long established spontaneous practice of early diagnosis and diffusion of mammography among the population with the screening programme starting in 1999.[28]

Screening may introduce lead time and length biases,[13] as well as over-diagnosis,[29] and the survival differences and their relation to screening programmes must be considered with due caution: national and local health policies greatly affect the outcome of screening programmes in terms of completeness, efficiency and subsequent patient care.[7] Nevertheless, the presence of a population-based screening programme with sufficient coverage will likely have a ‘genuine’ beneficial effect on survival given that screening increases the number of patients with earlier stage cancers for which therapy is more effective. Furthermore, beneficial effects of screening on survival, comparing patients at the same stage and receiving the same treatment have been recently reported by Wishart and colleagues.[30] Unfortunately, it is beyond the possibilities of our descriptive study to detect whether increased survival of women diagnosed within the screening programmes resulted from genuine improvements in prognosis, through the detection of less malignant breast cancers, or because of longer sojourn times. Other than earlier detection, the introduction of new therapies, at the beginning of this century could have influenced recent survival trends.

In summary, the calculation of up-to-date survival estimates is important for monitoring the impact of new therapies and the effects of public health interventions, such as screening programmes, that develop over many years. This study has shown that some of the persisting geographical differences in breast cancer survival are particularly large when considering the age groups served by efficient population based screening programmes. In particular, a deficit in survival in certain Eastern European populations has been observed, notably among older patients, stressing the need for the Europe-wide implementation of efficient and accessible care systems that fully integrate early diagnosis, effective therapy and clinical follow-up.

Conflict of interest statement

None declared.

Authors’ contributions

S.R. and A.G. designed the study; A.G. carried out the statistical analysis; S.R. drafted the manuscript; R.Z. and A.P. contributed to the study design and in writing the manuscript; F.B. revised the statistical analysis and edited the draft; M.Z., T.Z. and G.S. contributed to the writing of the manuscript particularly on the situation of organised and sporadic screening programmes in Eastern Europe; D.H.B., E.C. and A.C.V. contributed to the discussion and to the manuscript’s revision, H.B. coordinated the EUNICE Survival Working Group, planned the research and developed the statistical models; the members of the EUNICE Survival Working Group provided the data and contributed to the critical revision of the paper.

All authors read and approved the final manuscript.

The corresponding author has the final responsibility to submit the manuscript for publication.

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