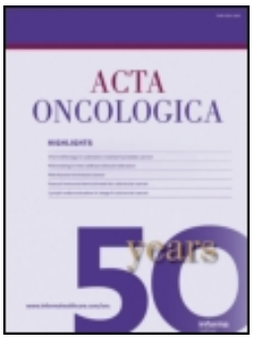

Acta Oncologica

ISSN: 0284-186X (Print) 1651-226X (Online) Journal homepage: informahealthcare.com/journals/ionc20

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To cite this article: Willi Oberaigner, Pamela Minicozzi, Magdalena Bielska-Lasota, Claudia Allemani, Roberta de Angelis, Lucia Mangone, Milena Sant & Eurocare Working Group (2012) Survival for Ovarian Cancer in Europe: The across-country variation did not shrink in the past decade, Acta Oncologica, 51:4, 441-453, DOI: 10.3109/0284186X.2011.653437

To link to this article: https://doi.org/10.3109/0284186X.2011.653437

Acta Oncologica, 2012; 51: 441–453

informa
healthcare

ORIGINAL ARTICLE

Survival for Ovarian Cancer in Europe: The across-country variation did not shrink in the past decade

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(Received 8 March 2011; accepted 22 December 2011)

ISSN 0284-186X print/ISSN 1651-226X online
DOI: 10.3109/0284186X.2011.653437

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Abstract

Background. Survival for ovarian cancer is the poorest of all gynaecological cancer sites. Our aim was to present the most up-to-date survival estimate for ovarian cancer by age and morphology and to answer the question whether survival for ovarian cancer improved in Europe during the 1990s. *Material and methods*. This analysis was performed with data from the EUROCARE database. We considered all adult women diagnosed with ovarian cancer between 1995 and 2002 and life status followed up until the end of 2003. A total of 97 691 cases were contributed by 72 European cancer registries in 24 countries. We estimated the most up-to-date relative survival for a mean of 23 661 patients followed up in 2000–2003 using the period hybrid approach and described the relative survival trends from the beginning of 1990s. *Results and conclusion.* Overall, the European age-standardised one-year, five-year and five-year conditional on surviving one-year relative survival were 67.2% (95% CI 66.6–67.8), 36.1% (95% CI 35.4–36.8) and 53.7% (95% CI 52.8–54.7), respectively. Five-year relative survival was 58.6% (95% CI 57.4–59.8), 37.1% (95% CI 36.1–38.1) and 20.5% (95% CI 19.1–21.9) in women aged 15–54, 55–74 and 75–99 years, respectively. The age-standardised five-year relative survival was 38.1% (95% CI 36.9–39.3) for serous tumours and 51.9% (95% CI 49.0–54.9) for mucinous cancers and the crude five-year relative survival was 85.6% (95% CI 81.2–90.0) for germ cell cancers. Overall, the age-standardised five-year relative survival increased from 32.4% (95% CI 31.7–33.2) in 1991–1993 to 36.3% (95% CI 35.5–37.0) in 2000–2003. There is a need to better understand the reasons for the wide variation in survival of ovarian cancer in Europe. Actions aiming to harmonise the protocols for therapy should contribute to narrowing the wide gap in survival and research on screening and early detection of ovarian cancer should be enforced.

Ovarian cancer is one of the four main gynaecological cancers accounting worldwide for about 4% of all female cancers and 10% of all gynaecological cancers (counting breast cancer as a gynaecological cancer) [1]. The incidence of ovarian cancer is relatively stable in Western countries, as reported for Norway [2], Ontario [3] and Finland [4]. However, the proportion of ovarian cancer among gynaecological cancers is increasing, bearing in mind the decrease in cervical cancer in European countries as a result of pap smear screening programmes [5]. Survival for ovarian cancer is the poorest of all gynaecological cancer sites [6]. EUROCARE-4 reported five-year relative survival of 36% [7]. The main reasons for this poor survival are the lack of early detection methods and an unfavourable anatomical situation. More than two-thirds of ovarian cancer cases are detected at an advanced stage, and therapy of ovarian cancer is very complex and presupposes expertise in both surgery and oncology [8–10]. There has been only one step towards progress in therapy of ovarian cancer, namely the introduction of intraperitoneal chemotherapy. However, the advantage of longer survival is accompanied by serious adverse events [11]. Thus, to date therapy of ovarian cancer is a challenge and prognosis is rather poor.

Given these facts, survival for ovarian cancer is being given special attention. As an extension of the overview figures presented in the EUROCARE-4 monograph [7], we aimed on the basis of the EUROCARE database with regard to ovarian cancer to: a) present the most up-to-date estimate of one-year and five-year survival and five-year relative survival conditional on surviving the first year after diagnosis (five-year conditional survival); b) analyse survival estimates by age group and morphology; c) answer the question whether relative survival in Europe improved from the beginning of the 1990s.

Material and methods

All analyses were performed with data from the EUROCARE database that collected incidence data on patients diagnosed from 1978 to 2002. All adult women (aged 15–99 years) diagnosed with malignant ovarian cancer between 1995 and 2002 were considered, regardless of the presence of tumours additional to the ovarian cancer under study. Thus, a total of 97 691 patients were contributed by 72 European cancer registries (CRs) in 24 countries participating in the EUROCARE-4 study (see Table I). One hundred seventy-four cases with invalid data or inconsistencies in date, sex, morphology or behaviour (major errors) were not included.

Whereas some countries were covered by nationwide registries (e.g. the Nordic countries and Austria), for others coverage was low (e.g. 1.3% in Germany); details are described in De Angelis et al. [12]. Compared to the first summary EUROCARE-4 publications [13,14], some modifications in the number of cases were reported [12].

For all cases, life status information (follow-up) is available up to the end of 2003, except for Austrian, German and West Bohemian patients, who had life status information updated up to the end of 2002.

Table I shows data quality indicators, such as the proportion of cases known by death certificate only (DCO) and incidentally discovered at autopsy (autopsy), the percentage of microscopically verified (MV) cases and of alive cases diagnosed in 1995–1998 and followed up for less than five years (censored). Since life status follow-up was closed at the end of 2003, the proportion of censored cases was computed only for women diagnosed from 1995 to 1998, who had a potential follow-up period of five years or more.

Anatomic site and tumour morphology were coded according to the third revision of the International Classification of Diseases for Oncology (ICDO-3) [15]. Ovarian cancers were selected on the basis of the following codes: C56.9 (ovary), C57.0–C57.4 and C57.7 (other and unspecified female genital organs, including uterine adnexa and fallopian tube). ICDO-3 morphological codes were grouped into five categories: serous (8251–8330, 8440–8461), mucinous (8470–8490), germ cell (9060–9101), other tumours (8011–8246, 8340, 8380–8430, 8503–9050, 9110–9581) and not otherwise specified (NOS, 8000–8010).

Analyses by morphological groups were performed by selecting MV cases only and excluding Denmark, UK Thames and Hérault CRs. Denmark and UK Thames were excluded from this analysis, because they did not provide consent to analyse morphological data and Hérault was excluded because morphology data were incomplete. Thus, 69 of the 72 CRs contributed to descriptive analyses by morphology in 1995–2002 (see Table II).

We used the direct method to estimate incidence per 100 000 person-years, age-standardised

to the European standard population, truncated to age group 15–99, for malignant ovarian cancers diagnosed in 1995–2002, by CR.

We estimated the most up-to-date five-year relative survival for ovarian cancer patients diagnosed up to 2002 with life status followed up to the end of 2003 using the period hybrid approach available in the SEER*Stat software [16,17] with three-year cohorts of diagnosis. This corresponds to consider the survival experience of patients diagnosed in 1996–2002 in the follow-up period 2000–2003. In the following, we will call this estimate period relative survival in 2000–2002.

Relative survival was defined as the ratio of the observed survival in the study group to the expected survival if the cases experienced the same mortality rates as did the general population from which they derive, for same age. Expected survival was estimated according to the Hakulinen method [18] using age, sex and calendar year-specific life tables for each CR population.

Only CRs providing incidence data up to 2002 contributed to the survival estimates. Thus, 39 of the 72 CRs were included in period hybrid analyses with a mean number of 23 661 cases (see Table I, first column).

Relative survival estimates for all ages combined were age-standardised using the direct method and the International Cancer Survival Standards (ICSS) age distribution [19].

We also estimated the age-standardised relative survival at five years conditional on surviving the first year after diagnosis (conditional survival) as the ratio of the cumulative age-standardised relative survival at five years to the age-standardised cumulative relative survival at one year.

Standard errors in age-specific survival estimates were calculated with the Greenwood's formula. The method of propagation of errors (also called "Delta method", [20]) was applied to derive standard errors of age-specific conditional relative survival (see Appendix for algebraic details). The corresponding 95% confidence intervals (CIs) were estimated by applying the logarithmic transformation, thus the CIs of both age-standardised cumulative and conditional relative survival are not necessarily symmetric.

Five-year period relative survival in 2000–2002 by age group (15–54, 55–74, 75–99, see Table IV) and morphology (see Table V) was estimated.

Table I. Number of cases, years of diagnosis, quality indicators, cases eligible for survival analysis and age-standardised incidence rates for women with ovarian cancer in 1995–2002, by registry.

Area	Country	Registry	Years of diagnosis	Total malignant cases	Cases with multiple tumours (%)	DCO and autopsy[1] (%)	Cases eligible for survival analysis	Mean number of cases contributing to period analysis[2]	MV (%[3])	Censored[4] cases in 1995–1998 (%)	Incidence per 100 000 cases (95% CI)[5]	
North	Denmark	Denmark	1995–1999	2998	7.7	1.4	2956		94.6	0.5	24.4	(23.5–25.3)
	Finland	Finland	1995–2002*	3799	10.5	3.0	3686	1365	96.9	0.7	18.7	(18.1–19.3)
	Iceland	Iceland	1995–2002*	172	16.3	1.2	170	61	96.5	0.0	20.6	(17.6–24.1)
	Norway	Norway	1995–2002*	3867	10.3	1.0	3829	1453	94.9	0.0	24.0	(23.2–24.8)
	Sweden	Sweden	1995–2002*	6831	10.3	1.9	6700	2491	99.8	0.9	19.9	(19.4–20.4)
UK and	Ireland	Ireland	1995–2002	2453	3.8	3.2	2374	891	89.1	0.4	21.8	(20.9–22.7)
Ireland	England	UK East Anglia	1995–2002*	2536	6.1	1.9	2489	960	88.7	11.7	24.1	(23.2–25.1)
		UK Mersey	1995–1999	1320	5.0	5.4	1249		86.4	0.7	22.7	(21.4–24.0)
		UK North Western	1995–1999	2092	2.5	1.2	2067		84.4	0.0	21.0	(20.0–21.9)
		UK Northern and Yorkshire	1995–2002*	4583	5.9	1.8	4499	1729	88.6	0.0	20.9	(20.3–21.6)
		UK Oxford	1995–2002*	2035	2.9	0.9	2016	754	91.1	0.4	21.7	(20.7–22.7)
		UK South Western	1995–1999	3935	8.0	8.8	3587		77.1	0.4	22.4	(21.7–23.2)
		UK Thames	1995–1999	7300	5.6	14.8	6222		90.0	0.6	23.0	(22.4–23.5)
		UK Trent	1995–1999	2550	6.1	6.2	2391		83.1	0.0	22.0	(21.1–22.9)
		UK West Midlands	1995–2002*	4505	6.8	5.9	4238	1599	89.1	0.0	22.0	(21.3–22.7)
	Northern Ireland	UK Northern Ireland	1995–2002	1271	6.1	1.1	1257	474	85.6	0.3	22.6	(21.3–23.9)
	Scotland	UK Scotland	1995–2002*	4500	9.4	1.1	4451	1668	87.8	0.3	21.6	(20.9–22.3)
	Wales	UK Wales	1995–2002*	2977	9.2	11.9	2624	1005	59.5	0.0	24.5	(23.5–25.4)
Centre	Austria	Austria	1995–2002*	7163	4.9	10.3	6423	2396	92.4	12.9	18.8	(18.1–19.6)
	Belgium	Flemish	1997–2001	2790	1.7	0.2	2785		85.1	1.3	21.9	(21.3–22.4)
	France	Bas Rhin	1995–1997	257	4.7	0.0	257		96.9	1.6	19.9	(17.4–22.6)
		Calvados	1995–1997	146	2.1	0.0	146		98.6	1.4	16.9	(14.1–20.0)
		Doubs	1995–1999	118	1.7	0.0	118		94.9	0.0	18.8	(15.5–22.7)
		Haut Rhin	1995–1997	163	4.9	0.0	163		94.5	0.0	17.8	(15.0–20.8)
		Hérault	1995–1997	167	1.8	0.0	167		0.0	0.0	13.4	(11.4–15.8)
		Isère	1995–1997	209	3.8	0.0	209		91.9	1.0	15.5	(13.4–17.8)
		Manche	1995–1997	138	2.9	0.0	138		99.3	4.3	20.1	(16.6–24.0)
		Somme	1995–1997	127	4.7	0.0	127		92.1	2.4	17.4	(14.4–21.0)
		Tarn	1995–1997	93	7.5	0.0	93		90.3	0.0	16.7	(13.2–20.8)
	Germany	Saarland	1995–2002*	902	7.6	4.1	865	323	93.4	9.3	18.2	(17.0–19.5)
	Netherlands	Amsterdam	1995–2002*	1694	11.7	0.3	1689	621	97.0	0.7	16.9	(16.1–17.8)
		Eindhoven	1995–2001	535	7.9	0.0	535		98.1	0.0	18.2	(16.7–19.9)
		North Netherlands	1995–2001	1140	3.9	0.5	1134		96.3	0.0	17.4	(16.4–18.5)
		Twente	1995–2002	753	3.5	0.3	751	282	96.9	0.0	17.3	(16.1–18.7)

(*Continued*)

Table I. (*Continued*).

Area	Country	Registry	Years of diagnosis	Total malignant cases	Cases with multiple tumours (%)	DCO and autopsy[1] (%)	Cases eligible for survival analysis	Mean number of cases contributing to period analysis[2]	MV (%[3])	Censored[4] cases in 1995–1998 (%)	Incidence per 100 000 cases (95% CI)[5]	
	Switzerland	Basel	1995–2001	242	6.6	0.8	240		99.6	7.6	14.6	(12.7–16.7)
		Geneva	1995–2002*	293	5.5	1.7	288	109	94.8	0.0	17.7	(15.6–19.9)
		St. Gallen	1995–2002*	408	16.7	0.5	406	157	94.3	31.1	21.0	(18.9–23.3)
		Ticino	1995–2002	201	4.0	2.0	197	84	98.0	0.0	17.4	(15.0–20.2)
		Valais	1995–1998	97	5.2	1.0	96		97.9	28.1	20.9	(16.9–25.6)
East	Czech Republic	West Bohemia	1995–2002*	759	6.6	7.4	703	276	92.7	11.4	24.0	(22.2–25.7)
	Poland	Cracow	1995–2002*	806	14.3	0.7	800	307	84.3	4.7	28.9	(26.9–31.0)
		Kielce	1995–2002	781	0.4	0.0	781	305	87.6	0.0	18.6	(17.3–20.0)
		Warsaw	1995–2002*	1345	7.1	1.4	1326	473	88.9	0.7	19.3	(18.3–20.4)
	Slovakia	Slovakia	1995–2002*	3035	4.9	11.2	2695	1003	95.6	0.4	17.3	(16.7–17.9)
South	Italy	Alto Adige	1995–2002	344	3.8	0.6	342	128	91.5	0.6	18.7	(16.7–20.9)
		Biella	1995–2002	148	3.4	2.7	144	55	93.8	0.0	15.6	(12.9–18.6)
		Ferrara	1995–2002*	272	5.9	1.5	268	106	82.8	0.0	14.9	(13.0–17.0)
		Firenze	1995–2002*	993	5.5	0.5	988	364	80.1	1.2	18.4	(17.2–19.6)
		Friuli V.G.	1995–2002	1033	3.2	3.2	1000	378	89.4	0.2	17.7	(16.6–19.0)
		Genova	1995–2000	652	6.6	1.8	640		86.6	0.5	18.3	(16.8–20.0)
		Macerata	1995–1999	154	6.5	0.6	153		86.9	0.0	18.3	(15.3–21.7)
		Modena	1995–2002*	513	6.0	0.8	509	188	84.3	0.0	17.5	(15.9–19.2)
		Napoli	1996–2000	136	0.0	2.2	133		79.7	0.0	13.9	(11.7–16.5)
		Parma	1995–2002*	415	7.2	2.2	406	161	86.7	0.0	20.6	(18.4–22.9)
		Ragusa	1995–2002*	192	8.3	0.5	191	68	81.2	0.0	17.1	(14.7–19.8)
		Reggio Emilia	1995–2002	310	2.3	0.3	309	132	81.6	0.0	17.4	(15.3–19.6)
		Romagna	1995–2002*	821	6.6	2.2	803	300	86.2	0.5	17.6	(16.3–19.0)
		Salerno	1996–2001	470	0.6	1.7	462		78.4	0.0	15.5	(14.1–17.0)
		Sassari	1995–2002	260	3.8	4.2	249	94	86.3	0.0	14.2	(12.5–16.1)
		Torino	1995–2001	726	5.5	2.3	709		89.1	0.0	18.9	(17.5–20.4)
		Trento	1995–2000	292	2.4	2.1	286		81.8	0.0	20.4	(18.0–23.1)
		Umbria	1995–2002	697	5.7	1.1	689	255	79.5	0.0	18.0	(16.6–19.5)
		Varese	1995–1999	400	9.0	1.3	395		89.6	11.3	17.5	(15.7–19.4)
		Veneto	1995–2000	1100	6.3	2.1	1077		86.4	0.0	16.1	(15.1–17.2)
	Malta	Malta	1995–2002	252	1.6	1.6	248	93	92.3	0.9	19.7	(17.3–22.3)
	Portugal	South Portugal	1998–1999	576	4.2	0.0	576		92.2	2.1	12.8	(11.7–13.9)
	Slovenia	Slovenia	1995–2002*	1247	3.2	1.6	1227	459	96.3	0.0	16.8	(15.8–17.7)

(*Continued*)

Table I. (*Continued*).

Area	Country	Registry	Years of diagnosis	Total malignant cases	Cases with multiple tumours (%)	DCO and autopsy[1] (%)	Cases eligible for survival analysis	Mean number of cases contributing to period analysis[2]	MV (%[3])	Censored[4] cases in 1995–1998 (%)	Incidence per 100 000 cases (95% CI)[5]
	Spain	Basque Country	1995–1999	665	5.9	3.5	642		91.0	0.0	13.2 (12.2–14.3)
		Girona	1995–2002	307	1.6	4.2	294	106	90.8	0.0	14.2 (12.6–16.1)
		Murcia	1995–1998	244	2.5	2.5	238		92.0	2.1	14.1 (12.3–16.1)
		Navarra	1995–1999	194	8.2	1.5	191		91.1	1.4	14.9 (12.7–17.3)
		Tarragona	1995–1999	192	4.7	3.1	186		90.9	0.0	13.8 (11.8–16.0)
Total cases				**97 691**	**6.6**	**4.5**	**93 292**	**23 661**	**89.4**	**1.9**	**20.2 (20.1–20.3)**

[1]Women diagnosed from the death certificate only (DCO) and incidentally discovered at autopsy (autopsy).
[2]Mean number of cases contributing to period estimates of five-year relative survival in 2000–2002.
[3]Proportions were calculated with respect to the number of cases eligible for survival analysis in 1995–2002, MV: microscopically verified cases.
[4]Alive cases with follow-up less than five years.
[5]Incidence is age-standardised with weights of the European standard population truncated to age group 15–99, CI: confidence interval;
*CRs included in time trend survival analyses from the beginning of 1990s.

Because of the low number of cases in Iceland and Malta, we did not show results of five-year relative survival for these countries separately, however they were included in the overall estimates. The same approach was adopted for Spain in the morphology analysis.

In addition, because of the lack of cases in one or more age classes, age-standardisation was performed only for the three largest morphological groups (serous, mucinous and other tumours).

For the analysis of survival time trend, the whole time period was categorised in four intervals: 1991–1993, 1994–1996, 1997–1999 and 2000–2003. The five-year age-standardised relative survival was estimated with the standard cohort approach for cases diagnosed in 1991–1999 and with the period hybrid approach for women followed up in 2000–2003. Since the period hybrid approach has been proven to produce reliable predictions of the cohort survival estimates [17], we were confident in using this method even though complete follow-up was not available.

We included in time trend analyses the 26 CRs belonging to 16 countries that provided data for every year of diagnosis from 1991 to 2002. These CRs are indicated with an asterisk in the first column of Table I.

All analyses excluded DCO and autopsy cases and were performed using SEER*Stat software [21].

Results

Table I shows the total number of malignant ovarian cancer cases, the available years of diagnosis for each CR, the percentages of multiple tumours, of DCO and autopsy cases, the patients eligible for survival analysis and the mean number of cases contributing to the five-year period relative survival in 2000–2002. In addition, Table I also shows two other quality indicators, namely the proportion of MV cases and of those lost or censored before five years from diagnosis. The overall percentage of DCO and autopsy cases was 4.5% with fairly small variability among the registries; only four CRs showed a DCO proportion equal to 10.0% or higher (UK Thames, UK Wales, Austria, Slovakia). The overall proportion of MV cases was 89.4%; only one registry had a MV proportion of less than 75% (UK Wales).

The last two columns of Table I show the incidence rates age-standardised to the European standard population and the corresponding 95% CIs. The overall incidence of malignant ovarian tumours diagnosed in 1995–2002 was 20 per 100 000 person-years.

Table II. Number of cases and distribution (%) of morphological groups for microscopically verified cases diagnosed in 1995–2002 (and 2000–2002) provided by 69[1] CRs, by country.

	No. of cases		serous		mucinous		germ-cell		other tumours		NOS[2]	
Finland	3571	*(1338)*	50.5	*(52.5)*	12.5	*(11.4)*	2.4	*(2.5)*	25.4	*(24.1)*	9.2	*(9.5)*
Iceland	164	*(65)*	60.4	*(64.6)*	7.3	*(4.6)*	1.8	*(1.5)*	26.2	*(24.6)*	4.3	*(4.6)*
Norway	3635	*(1407)*	55.5	*(54.9)*	7.3	*(8.2)*	1.5	*(1.7)*	32.4	*(32.1)*	3.2	*(3.1)*
Sweden	6685	*(2467)*	47.9	*(48.8)*	9.4	*(8.1)*	1.3	*(1.5)*	39.7	*(40.3)*	1.6	*(1.3)*
Ireland	2116	*(812)*	45.9	*(44.8)*	12.2	*(11.1)*	1.4	*(1.1)*	34.2	*(36.5)*	6.2	*(6.5)*
UK England	19 384	*(4756)*	42.0	*(43.6)*	10.4	*(8.8)*	1.2	*(1.2)*	39.7	*(39.2)*	6.7	*(7.2)*
UK Northern Ireland	1076	*(407)*	41.3	*(47.2)*	9.7	*(8.4)*	1.6	*(1.7)*	37.5	*(32.9)*	9.9	*(9.8)*
UK Scotland	3906	*(1415)*	41.3	*(42.9)*	12.1	*(8.6)*	1.1	*(1.0)*	40.1	*(40.8)*	5.4	*(6.7)*
UK Wales	1562	*(700)*	38.5	*(41.4)*	9.3	*(9.3)*	1.3	*(1.3)*	37.7	*(35.0)*	13.2	*(13.0)*
Austria	5937	*(2077)*	45.1	*(45.1)*	7.2	*(6.6)*	2.0	*(1.4)*	33.2	*(32.4)*	12.4	*(14.5)*
Belgium	2371	*(1018)*	45.5	*(48.7)*	9.2	*(9.5)*	1.5	*(1.3)*	33.9	*(32.7)*	9.9	*(7.8)*
France	1189	*(-)*	51.3	*(-)*	13.2	*(-)*	2.4	*(-)*	29.8	*(-)*	3.3	*(-)*
Germany	808	*(318)*	53.7	*(55.3)*	10.4	*(10.4)*	1.4	*(1.6)*	23.8	*(22.6)*	10.8	*(10.1)*
Netherlands	3984	*(1277)*	50.5	*(50.3)*	11.4	*(10.1)*	1.7	*(2.0)*	35.8	*(37.2)*	0.6	*(0.5)*
Switzerland	1182	*(382)*	57.4	*(57.6)*	9.6	*(7.3)*	1.3	*(0.8)*	30.4	*(33.5)*	1.4	*(0.8)*
Czech Republic	652	*(249)*	39.3	*(34.9)*	10.9	*(8.8)*	1.2	*(2.0)*	42.0	*(48.6)*	6.6	*(5.6)*
Poland	2537	*(936)*	40.2	*(40.7)*	7.5	*(5.8)*	1.7	*(1.5)*	39.1	*(41.5)*	11.4	*(10.6)*
Slovakia	2576	*(917)*	53.1	*(50.5)*	13.3	*(14.7)*	1.9	*(1.3)*	28.3	*(30.8)*	3.4	*(2.7)*
Italy	8303	*(2441)*	44.2	*(44.8)*	9.6	*(9.5)*	1.2	*(1.1)*	34.9	*(34.0)*	10.2	*(10.5)*
Malta	229	*(102)*	36.7	*(42.2)*	17.9	*(15.7)*	3.1	*(2.0)*	38.4	*(38.2)*	3.9	*(2.0)*
Portugal	531	*(-)*	42.7	*(-)*	10.9	*(-)*	4.0	*(-)*	32.8	*(-)*	9.6	*(-)*
Slovenia	1182	*(470)*	55.6	*(59.1)*	6.2	*(5.7)*	1.9	*(2.1)*	32.7	*(29.6)*	3.6	*(3.4)*
Spain	1413	*(102)*	47.5	*(56.9)*	13.3	*(5.9)*	2.1	*(2.9)*	33.3	*(31.4)*	3.8	*(2.9)*
Total cases	**74 993**	***(23 656)***	**45.8**	***(47.0)***	**10.1**	***(8.9)***	**1.5**	***(1.4)***	**35.9**	***(35.6)***	**6.8**	***(7.0)***

[1]Data for 69 CRs only are shown, as data for three cancer registries were not available (see text for further details).
[2]Not otherwise specified (NOS) morphology.

Distribution by morphology was calculated for serous, mucinous, germ cell cancer, other tumours and NOS. In 1995–2002 for all 69 CRs without Denmark, UK Thames and Hérault CRs, the overall proportions for the morphological groups were 45.8%, 10.1%, 1.5%, 35.9% and 6.8%, respectively, see Table II. The proportion of NOS tumours in elderly patients was 34.1%, and 82.3% of germ cell tumours were in age group 15–54 (data not shown). Similar proportions were found for patients diagnosed in 2000–2002 only.

Table III shows the age-standardised period estimates in 2000–2002 of one-year, five-year and five-year

Table III. Age-standardised period relative survival estimates for patients followed up in 2000–2003. One-year, five-year relative survival and five-year conditional on surviving one-year relative survival and 95% confidence interval (CI), by country.

Country	1-year survival	95% CI	5-year survival	95% CI	5-year conditional survival	95% CI
Finland	74.6	(72.2–77.0)	43.4	(40.4–46.5)	58.2	(54.7–61.9)
Norway	75.6	(73.4–77.8)	41.7	(38.9–44.5)	55.2	(52.0–58.5)
Sweden	79.3	(77.6–81.0)	42.1	(39.9–44.3)	53.1	(50.6–55.6)
Ireland	60.7	(57.5–64.0)	29.1	(25.8–32.4)	47.9	(43.5–52.7)
UK England	60.7	(59.4–62.0)	30.0	(28.6–31.4)	49.5	(47.5–51.5)
UK Northern Ireland	62.9	(58.7–67.2)	35.5	(30.7–40.2)	56.4	(50.3–63.1)
UK Scotland	60.8	(58.5–63.2)	31.5	(29.1–34.0)	51.8	(48.5–55.4)
UK Wales	62.9	(59.8–66.0)	32.3	(29.1–35.5)	51.4	(47.2–55.8)
Austria	70.9	(68.9–72.9)	45.1	(42.7–47.5)	63.6	(60.8–66.5)
Germany	69.7	(64.4–74.9)	39.0	(31.7–46.4)	56.0	(47.3–66.4)
Netherlands	69.5	(66.3–72.7)	39.5	(35.8–43.2)	56.8	(52.5–61.5)
Switzerland	78.5	(74.3–82.7)	42.1	(36.4–47.7)	53.6	(47.5–60.5)
Czech Republic	64.9	(58.4–71.4)	38.6	(30.0–47.3)	59.6	(49.0–72.4)
Poland	66.4	(63.2–69.6)	37.8	(34.1–41.5)	56.9	(52.3–62.0)
Slovakia	56.1	(52.4–59.8)	25.3	(22.4–28.2)	45.1	(41.1–49.5)
Italy	69.6	(67.7–71.5)	37.1	(35.0–39.3)	53.3	(50.7–56.0)
Slovenia	68.8	(64.4–73.2)	36.7	(31.8–41.7)	53.4	(47.5–60.0)
Spain	63.6	(55.1–72.2)	37.2	(27.4–47.0)	58.5	(46.8–73.0)
European average	**67.2**	**(66.6–67.8)**	**36.1**	**(35.4–36.8)**	**53.7**	**(52.8–54.6)**

Table IV. Period relative survival estimates for patients followed up in 2000–2003 and 95% confidence interval (CI), by country and age.

Country	15–54	55–74	75–99
Finland	66.8	46.0	25.2
	(61.8–71.8)	(41.8–50.2)	(18.6–31.8)
Norway	64.8	46.0	20.8
	(60.0–69.6)	(41.6–50.4)	(15.6–26)
Sweden	57.5	42.8	30.0
	(53.7–61.3)	(39.8–45.8)	(25.2–34.8)
Ireland	50.8	31.4	13.0
	(44.6–57.0)	(26.4–36.4)	(7.0–19.0)
UK England	48.5	30.3	18.0
	(45.5–51.5)	(28.3–32.3)	(15.2–20.8)
UK Northern Ireland	51.6	40.7	15.5
	(43.0–60.2)	(33.5–47.9)	(7.3–23.7)
UK Scotland	53.0	30.9	17.4
	(47.6–58.4)	(27.5–34.3)	(13–21.8)
UK Wales	54.8	31.0	20.5
	(48.2–61.4)	(26.6–35.4)	(13.9–27.1)
Austria	73.5	47.8	23.7
	(69.7–77.3)	(44.4–51.2)	(18.9–28.5)
Germany	60.1	38.3	30.6
	(47.5–72.7)	(28.9–47.7)	(13.6–47.6)
Netherlands	61.9	40.6	23.3
	(55.5–68.3)	(35.4–45.8)	(15.7–30.9)
Switzerland	58.5	51.4	15.4
	(47.5–69.5)	(42.6–60.2)	(6.6–24.2)
Czech Republic	53.7	31.8	41.4
	(42.9–64.5)	(21.8–41.8)	(18.6–64.2)
Poland	54.4	40.8	21.8
	(49.2–59.6)	(36.0–45.6)	(12.8–30.8)
Slovakia	55.8	23.3	10.8
	(50.8–60.8)	(19.3–27.3)	(4.6–17.0)
Italy	68.1	36.4	19.0
	(64.1–72.1)	(33.2–39.6)	(15.0–23.0)
Slovenia	67.0	36.3	17.6
	(58.8–75.2)	(29.5–43.1)	(6.6–28.6)
Spain	69.9	31.6	23.6
	(52.9–86.9)	(18.2–45.0)	(4.8–42.4)
European average	**58.6**	**37.1**	**20.5**
	(57.4–59.8)	**(36.1–38.1)**	**(19.1–21.9)**

conditional survival, by country. The overall age-standardised five-year period relative survival was 36.1% (95% CI 35.4–36.8%) with a wide variation from 45.1% in Austria to 25.3% in Slovakia. The highest estimates were observed in Austria and Finland (43.4%); also in Norway, Sweden and Switzerland survival was above 40%, Netherlands being close to this group with 39.5%. The next group of countries, namely Germany, Czech Republic, Poland, Italy, Slovenia and Spain, showed estimates below 40%, but still above the overall estimate. All the UK countries, Ireland and Slovakia had estimates below the European average. The overall one-year period relative survival estimate was 67.2% (95% CI 66.6–67.8%), with a wide variation from 79.3% in Sweden to 56.1% in Slovakia. All the UK countries and Ireland, together with Czech Republic, Poland, Slovakia and Spain, were below the European average. The overall five-year conditional survival estimate was 53.7% (95% CI 52.8–54.7%) with a wide variation from 63.6% in Austria to 45.1% in Slovakia. For Sweden and Switzerland showing high one-year and five-year period relative survival we observed a five-year conditional survival below the European average.

Table IV shows the estimates of five-year period relative survival in 2000–2002, by country and age. Overall, the estimates for age groups 15–54, 55–74 and 75–99 were 58.6% (95% CI 57.4–59.8%), 37.1% (95% CI 36.1–38.1%) and 20.5% (95% CI 19.1–21.9%) respectively. For patients aged 15–54, estimates by country ranged from 73.5% in Austria to 48.5% in UK England, for age group 55–74 from 51.4% in Switzerland to 23.3% in Slovakia and for age group 75–99 from 41.4% in Czech Republic to 10.8% in Slovakia. The range of across-country variation in age-specific estimates was as wide as that for the age-standardised estimates. However, for some countries CIs were wide.

Table V shows the crude and age-standardised five-year period relative survival in 2000–2002, by morphological group. Overall, the highest crude survival estimates were seen for germ cell cancers, namely 85.6% (95% CI 81.2–90.9%), ranging from 100% in UK Northern Ireland, Switzerland and Slovakia to 52.3% in UK Wales. In Czech Republic survival for germ cell tumours was 0.0%, but the number of cases was very small. Age-standardised five-year period relative estimate for serous cancers was 38.1% (95% CI 36.9–39.3%), ranging from 48.0% in Austria to 23.9% in Slovakia; for municous cancer it was 51.9% (95% CI 49.0–54.9%), ranging from 60.6% in Norway to 35.4% in Slovakia.

Tables VI and VII show the five-year survival time trend by country and age, respectively. Looking at the differences in survival between the age-standardised estimates for patients diagnosed in 1991–1993 and patients followed up in 2000–2003, we observed an overall increase from 32.4% (95% CI 31.7–33.2%) to 36.3% (95% CI 35.5–37.0%). This is an absolute increase of 3.9% points. By country, a wide variation in increase from 14.2% in Czech Republic to -3.1% in Slovakia was seen. We can divide countries into three groups: the first group (Czech Republic, Finland, Poland, Switzerland and Slovenia) showed an increase of 10% points and more; Norway, Austria, Italy, Netherlands and Sweden improved above the European average. In Scotland, Wales, Germany, England and Slovakia we observed no variation in time trend or a slight decrease in five-year relative survival.

Split by age group, from the beginning of 1990s we observed an overall increase in survival estimates in both the 15–54 and 55–74 age groups: from 55.1%

Table V. Period estimates for patients followed up in 2000–2003 of crude and age-standardised[1] five-year relative survival and 95% confidence interval (CI), by country and morphological groups.

	Crude					Age-standardised		
Country	serous	mucinous	germ cell	other tumours	NOS[2]	serous	mucinous	other tumours
Finland	47.6	64.8	83.4	52.4	26.4	43.1	55.0	48.5
	(43.2–52.0)	*(56.4–73.2)*	*(67.0–99.8)*	*(46.0–58.8)*	*(17.2–35.6)*	(38.6–47.7)	(44.2–65.9)	(41.6–55.3)
Norway	43.0	65.0	80.2	52.4	35.2	37.8	60.6	47.8
	(39.0–47.0)	*(54.4–75.6)*	*(62.4–98.0)*	*(46.8–58.0)*	*(18.8–51.6)*	(34.0–41.6)	(47.5–73.8)	(42.7–53.0)
Sweden	40.7	62.7	88.0	44.1	31.2	39.5	58.1	41.8
	(37.7–43.7)	*(55.3–70.1)*	*(77.0–99.0)*	*(40.7–47.5)*	*(14.8–47.6)*	(36.4–42.7)	(49.8–66.3)	(38.3–45.2)
Ireland	32.1	68.3	79.1	34.7	32.2	25.5	57.8	28.8
	(26.9–37.3)	*(57.5–79.1)*	*(50.9–100.0)*	*(28.1–41.3)*	*(18.2–46.2)*	(20.8–30.1)	(43.2–72.3)	(21.7–35.9)
UK England	36.4	54.8	84.6	31.4	11.5	34.7	51.9	29.1
	(34.0–38.8)	*(49.4–60.2)*	*(74.2–95.0)*	*(29.0–33.8)*	*(7.3–15.7)*	(31.9–37.4)	(45.5–58.3)	(26.8–31.5)
UK Northern Ireland	47.3	56.6	100.0	34.9	21.3	46.0	37.8	31.9
	(39.1–55.5)	*(36.4–76.8)*	*(–)*	*(26.5–43.3)*	*(6.1–36.5)*	(36.7–55.3)	(21.3–54.3)	(23.9–39.9)
UK Scotland	34.0	57.8	87.3	33.6	16.0	33.6	52.1	32.7
	(29.6–38.4)	*(48.0–67.6)*	*(68.3–100.0)*	*(29.4–37.8)*	*(6.4–25.6)*	(28.9–38.3)	(40.4–63.8)	(28.7–36.7)
UK Wales	35.4	55.4	52.3	28.5	22.3	33.8	56.1	27.0
	(28.2–42.6)	*(40.6–70.2)*	*(0.0–100.0)*	*(22.3–34.7)*	*(12.5–32.1)*	(26.1–41.5)	(39.2–73.0)	(20.9–33.2)
Austria	54.1	67.7	84.4	50.4	44.9	48.0	56.4	46.8
	(50.3–57.9)	*(58.5–76.9)*	*(70.8–98.0)*	*(45.8–55.0)*	*(37.3–52.5)*	(44.1–51.9)	(44.4–68.4)	(42.3–51.3)
Germany	40.4	65.9	[3]	48.0	17.6	39.8	[3]	40.7
	(31.0–49.8)	*(35.3–96.5)*		*(32.2–63.8)*	*(0.6–34.6)*	(30.2–49.5)		(24.8–56.5)
Netherlands	43.9	51.6	88.4	42.3	62.0	40.8	41.5	37.1
	(38.5–49.3)	*(40.0–63.2)*	*(69.2–100.0)*	*(35.7–48.9)*	*(11.4–100.0)*	(35.1–46.4)	(29.5–53.5)	(31.1–43.1)
Switzerland	49.8	45.0	100.0	42.1	[3]	46.4	[3]	38.8
	(41.6–58.0)	*(22.8–67.2)*	*(–)*	*(30.9–53.3)*		(38.6–54.3)		(28.1–49.5)
Czech Republic	48.1	45.3	0.0	40.8	[3]	33.6	[3]	[3]
	(36.3–59.9)	*(21.5–69.1)*	*(0–0)*	*(29.6–52.0)*		(24.1–43.2)		
Poland	44.6	47.4	73.6	44.9	29.8	42.9	46.8	37.5
	(39.0–50.2)	*(34.2–60.6)*	*(50.4–96.8)*	*(39.1–50.7)*	*(20.2–39.4)*	(34.8–51.0)	(34.6–59.0)	(31.7–43.3)
Slovakia	33.9	51.4	100.0	33.7	30.9	23.9	35.4	25.7
	(29.7–38.1)	*(41.8–61.0)*	*(–)*	*(27.5–39.9)*	*(9.1–52.7)*	(19.8–28.0)	(25.1–45.7)	(20.2–31.2)
Italy	47.5	56.4	87.7	41.5	23.6	42.5	49.5	37.1
	(43.7–51.3)	*(48.4–64.4)*	*(69.1–100.0)*	*(37.3–45.7)*	*(16.6–30.6)*	(38.6–46.3)	(41.1–57.9)	(33.1–41.1)
Slovenia	44.5	44.1	90.3	42.8	33.6	37.6	[3]	36.0
	(37.5–51.5)	*(22.9–65.3)*	*(69.1–100.0)*	*(33.6–52.0)*	*(4.4–62.8)*	(29.8–45.4)		(28.0–44.0)
European average	**41.8**	**58.5**	**85.6**	**39.8**	**26.1**	**38.1**	**51.9**	**36.3**
	(40.8–42.8)	***(56.1–60.9)***	***(81.2–90.0)***	***(38.6–41.0)***	***(23.5–28.7)***	**(36.9–39.3)**	**(49.0–54.9)**	**(35.1–37.6)**

[1]Age-standardisation was only applied for the three largest morphological groups.
[2]Not otherwise specified (NOS) morphology.
[3]Not enough cases in study to estimate survival.

(95% CI 53.7–56.5%) to 58.6% (95% CI 57.2–60.0%) for 15–54 years and from 31.8% (95% CI 30.8–32.8%) to 37.1% (95% CI 36.1–38.1%) for 55–74 years. A stable situation is seen for patients aged 75–99 (see Table VII).

Discussion

This study provides population-based survival estimates in Europe for adult women with diagnosis of malignant ovarian cancer in the 1990s. We observed a wide across-country variation in survival estimates for ovarian cancer in the European countries.

It is known that age of ovarian cancer cases correlates strongly with survival, as for most cancer sites [22]. The influence of age has been highlighted in our analysis by presenting both age-standardised estimates and estimates by age group. For all countries, except for Czech Republic, five-year period relative survival in 2000–2002 decreased with advancing age. The age-specific figures we found in our study for the CRs in Northern Europe were in line with those reported by a Nordic population-based study [23], although definition of age groups was different.

Overall, the most up-to-date age-standardised five-year relative survival estimate was 36.1% and varied between 45.1% in Austria and 25.3% in Slovakia. The range of variation is of the same size for one-year and five-year conditional survival and also for five-year

Table VI. Time trend in age-standardised five-year relative survival and 95% confidence intervals (CIs), including 26[1] CRs, by country.

Country	1991–1993[2]	1994–1996[2]	1997–1999[2]	2000–2003[3]	Change[4]
Finland	30.9	35.8	40.1	43.4	12.5
	(28.2–33.7)	*(33.0–38.7)*	*(37.1–43.0)*	*(40.4–46.5)*	
Norway	34.4	34.9	38.9	41.7	7.3
	(31.5–37.2)	*(32.2–37.7)*	*(36.1–41.7)*	*(38.9–44.5)*	
Sweden	37.9	40.8	43.3	42.1	4.2
	(35.8–40.1)	*(38.7–43)*	*(40.9–45.6)*	*(39.9–44.3)*	
UK England	29.4	27.2	29.1	30.0	0.6
	(27.9–31)	*(25.6–28.7)*	*(27.6–30.5)*	*(28.6–31.4)*	
UK Scotland	28.2	30.3	31.2	31.5	3.3
	(25.9–30.6)	*(27.9–32.6)*	*(28.6–33.8)*	*(29.1–34.0)*	
UK Wales	29.8	30.6	31.3	32.3	2.5
	(26.3–33.3)	*(27.2–34.0)*	*(28.2–34.5)*	*(29.1–35.5)*	
Austria	39.7	43.4	44.4	45.1	5.4
	(37.3–42.1)	*(41.0–45.7)*	*(42.0–46.7)*	*(42.7–47.5)*	
Germany	37.4	35.2	33.9	39.0	1.6
	(31–43.8)	*(29.1–41.2)*	*(27.8–39.9)*	*(31.7–46.4)*	
Netherlands	33.5	33.7	34.8	38.0	4.5
	(29.6–37.5)	*(29.8–37.7)*	*(30.7–38.9)*	*(33.4–42.5)*	
Switzerland	30.4	38.0	42.7	40.9	10.5
	(25–35.8)	*(31.7–44.4)*	*(36.6–48.8)*	*(34.5–47.3)*	
Czech Republic	24.4	27.1	[5]	38.6	14.2
	(18.3–30.5)	*(20.0–34.2)*		*(30.0–47.3)*	
Poland	26.7	28.0	33.8	38.1	11.4
	(22.4–31)	*(24.6–31.4)*	*(29.6–37.9)*	*(33.6–42.6)*	
Slovakia	28.4	28.3	29.0	25.3	–3.1
	(24.2–32.5)	*(24.3–32.2)*	*(25.5–32.6)*	*(22.4–28.2)*	
Italy	31.9	35.1	34.3	37.2	5.3
	(28.8–35.1)	*(32.1–38.1)*	*(31.3–37.3)*	*(34.2–40.1)*	
Slovenia	26.7	33.1	35.4	36.7	10
	(22–31.5)	*(26.6–39.6)*	*(30.3–40.5)*	*(31.8–41.7)*	
European average	**32.4**	**33.8**	**35.4**	**36.3**	**3.9**
	(31.7–33.2)	***(33.0–34.6)***	***(34.6–36.2)***	***(35.5–37.0)***	

[1]26 CRs provided continuous incident data in 1991–2002 for trend analyses (see text for further details).
[2]Survival estimated using the cohort approach.
[3]Survival estimated for patients followed up in 2000–2003 using the period hybrid approach.
[4]Absolute difference in percent points between the estimates for 2000–2003 and 1991–1993.
[5]Not enough cases to estimate survival.

survival split by age group. High survival estimates were found in Northern Europe and are comparable with results reported in Klint et al. [23] (Finland: 43% vs. 44%; Norway: 42% vs. 41%; Sweden: 42% vs. 43%), while low estimates were observed in UK and Ireland. The five-year period relative survival estimates for most other countries were on the average.

Higher survival estimates in Norway than in UK were also reported by Coleman et al. [24], with the same figures for UK Wales (33%) and similar for Norway (41% in our study vs. 40%), whereas some differences in survival were found in UK England (30% in our study vs. 34%) and UK Northern Ireland (35% in our study vs. 38%). These discrepancies might be explained by taking into account the different follow-up closure time (2003 vs. 2007), the different approach (period hybrid vs. cohort) used to analyse survival and the different methods to estimate relative survival (Hakulinen [18] vs. Estève [25]).

Our survival estimates by morphology fit to some estimates in the literature, see for example an analysis from the large SEER database [26]. However, the question whether mucinous cases have better or worse survival than do serous cases is the subject of controversy, because mucinous cancers share a more favourable staging distribution, however, they show poorer response to chemotherapy [27].

Besides the factors discussed in the previous paragraphs, which other factors can help explain the wide across-country variation in survival observed by us?

Stage at diagnosis largely influences survival, however stage-adjusted or -specific comparisons depend on the diagnostic examinations performed for disease staging. Our study, however, does not have adequate data on such analyses. Therapy is known to have a very great influence: aggressive primary surgery and optimal tumour debulking are two of the key factors in achieving good survival [8,28,29], as well as adherence to guidelines [30] and proportion

Table VII. Time trend in five-year relative survival *and* 95% confidence intervals (CIs) including 26[1] CRs, by age.

	1991–1993[2]	1994–1996[2]	1997–1999[2]	2000–2003[3]	Change[4]
15–54	55.1	57.0	58.3	58.6	3.5
	(53.7–56.5)	*(55.6–58.4)*	*(56.9–59.7)*	*(57.2–60.0)*	
55–74	31.8	33.2	35.3	37.1	5.3
	(30.8–32.8)	*(32.2–34.2)*	*(34.3–36.3)*	*(36.1–38.1)*	
75–99	19.8	20.4	21.3	21.0	1.2
	(18.2–21.4)	*(18.8–22.0)*	*(19.7–22.9)*	*(19.4–22.6)*	
15–99	**37.3**	**38.7**	**39.9**	**40.3**	**3.0**
	(36.5–38.1)	***(37.9–39.5)***	***(39.1–40.7)***	***(39.5–41.1)***	

[1]26 CRs provided continuous incident data in 1991–2002 for trend analyses (see text for further details).
[2]Survival estimated using the cohort approach.
[3]Survival estimated for patients followed up in 2000–2003 using the period hybrid approach.
[4]Absolute difference in percent points between the estimates for 2000–2003 and 1991–1993.

of patients treated in the framework of studies [31]. Moreover, hospital volume, surgeon's training and expertise and treatment by specialists in gynaecologic oncology were also shown to have an influence on survival [32,33]. Because EUROCARE-4 collects no data on therapy, we cannot analyse the influence of therapy on survival.

Coding problems could also play a role in survival estimates, bearing in mind that up to one quarter of ovarian cancer cases are borderline tumours, see for example [34]. If registration or coding problems caused some of the registries to miscode part of the borderline tumours as malignancies, the survival estimates would change because borderline tumours have rather good survival [35,36].

Although some residual bias could exist, it is unlikely that miscoded borderline cancer cases can explain a larger part of the across-country variation.

Concerning time trend in survival estimates, the increase in survival is moderate in patients aged 55–74, while no improvements were seen in women aged 75–99 at the time of diagnosis. The literature reports inconsistent findings on this question. For example, in Norway and Ontario, five-year survival was stable over a period of 10 years [2,37], and Engel showed a similar trend for Bavaria with improvement in long-term survival only in stages I/II [38]. Brenner et al. showed a large increase in survival in Saarland up to 1995 [39], Laurvick reported an increase in Western Australia that correlated with a trend towards more surgery [40]. Barnholtz-Sloan et al. [41] and Coleman et al. [24] also reported improved survival in the US and in Australia, Canada and in Nordic European countries, respectively. The result for age group 75–99 is plausible from a clinical point of view bearing in mind that this group correlates strongly with advanced stage and also with co-morbidity, thus leaving only small potential for improved survival because neither factor is modifiable [9,42,43]. It is also known that in elderly women there is a danger of unspecific symptoms being overlooked [42], and Janda et al. [44] stress the importance of standard therapy also for elderly patients. The observation that there is a small improvement in survival for cases in age group 55–74 and no improvement in elderly women is consistent with an analysis showing that, in general, the gap in survival between younger and elderly cancer patients is widening [6]. Both the poor survival for ovarian cancer in the UK and the fact that no substantial increase in survival could be observed in the decade from 1991 to 2002 have heightened concern in the UK, and actions aimed at understanding the reasons for this poor survival have meanwhile been commenced [45].

A major strength of our study is the large study size, thus providing reliable results for most European countries. Furthermore, the analysis is based on the fourth edition of the EUROCARE studies, data collection is based on common protocols and DCO proportions are low. The analysis is based on well accepted methods, and relative survival estimates were calculated with the period approach [12]. Nevertheless, we are faced with a number of limitations: estimates are compared at the country level, but country coverage by the participating registries varies largely, namely from nationwide registries, e.g. all Nordic countries, to 1.3% coverage of Germany by the Saarland registry. Consequently, it is at least questionable how representative the survival estimates are for those countries with only low coverage. Also, population size differs widely. For some of the smaller countries, the number of cases is small and consequently the confidence intervals very wide, e.g. in Iceland and Malta.

Therefore, it is strongly recommended that CIs be looked at when interpreting estimates for specific countries. The greatest limitation is most likely the lack of information on confounding factors like co-morbidity, stage, therapy, therapy guidelines, waiting times, etc, which could contribute to understanding some of the variation observed between countries.

Collection of data on the extent of disease was not compulsory in EUROCARE-4. The analysis on extent of disease evidenced that this information was available and of sufficiently good quality for only a small number of CRs. However, ovarian cancer staging is more complex than is staging for most other solid tumours. For this reason, we decided not to include an analysis of extent of disease in this paper. An analysis focusing on a subset of CRs with available data will be performed in future.

Although organised screening has thus far not proven to be effective for ovarian cancer, several European countries routinely perform CA 125 tests and ultrasound for early diagnosis.

Despite all the possible limitations discussed above, we observed a wide across-country variation in five-year period relative survival estimates that did not shrink in the last decade and can only in small part be explained by age or morphology. We can conclude that a large part of the variation in survival between European countries is likely to reflect real differences in survival.

However, we have very limited data to explain these differences, and there is a need for research to better understand the wide across-country variation in survival of ovarian cancer in Europe. Actions aiming to harmonise the protocols for therapy should contribute to narrowing the wide gap in survival. In addition, research on screening and early detection of ovarian cancer should be enforced.

Acknowledgements

We thank Mary Margreiter for editing the English, and Patricia Gscheidlinger, Chiara Margutti and Samba Sowe for the secretarial support. The EUROCARE-4 Project was supported by the Foundation Compagnia di San Paolo, Turino, Italy.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

[1] Ferlay J, Bray F, Pisani P, Parkin DM. GLOBOCAN 2002. Cancer incidence, mortality and prevalence worldwide. IARC CancerBase No. 5, version 2.0 Lyon: IARC Press; 2004.

[2] Tingulstad S, Skjeldestad FE, Halvorsen TB, Hagen B. Survival and prognostic factors in patients with ovarian cancer. Obstet Gynecol 2003;101(5 Pt 1):885–91.

[3] Elit L, Bondy SJ, Chen Z, Paszat L. A tale of two time periods: Ovarian cancer trends in Ontario. Curr Oncol 2007;14:57–60.

[4] Curado MP, Edwards B, Shin HR, Storm H, Ferlay J, Heanue J, et al. Cancer incidence in five continents. Volume IX (IARC Scientific Publications No. 160). Lyon: IARC; 2007.

[5] Anttila A, Ronco G, Clifford G, Bray F, Hakama M, Arbyn M, et al. Cervical cancer screening programmes and policies in 18 European countries. Br J Cancer 2004;91:935–41.

[6] Quaglia A, Tavilla A, Shack L, Brenner H, Janssen-Heijnen M, Allemani C, et al. The cancer survival gap between elderly and middle-aged patients in Europe is widening. Eur J Cancer 2009;45:1006–16.

[7] Capocaccia R, Gavin A, Hakulinen T, Lutz JM, Sant M. Survival of cancer patients in Europe, 1995–2002: The EUROCARE 4 Study. Eur J Cancer 2009;45:901–1094.

[8] Marth C, Hiebl S, Oberaigner W, Winter R, Leodolter S, Sevelda P. Influence of department volume on survival for ovarian cancer: Results from a prospective quality assurance program of the Austrian Association for Gynecologic Oncology. Int J Gynecol Cancer 2009;19:94–102.

[9] Chan JK, Urban R, Cheung MK, Osann K, Shin JY, Husain A, et al. Ovarian cancer in younger vs older women: A population-based analysis. Br J Cancer 2006;95:1314–20.

[10] Nagle CM, Bain CJ, Green AC, Webb PM. The influence of reproductive and hormonal factors on ovarian cancer survival. Int J Gynecol Cancer 2008;18:407–13.

[11] Jaaback K, Johnson N. Intraperitoneal chemotherapy for the initial management of primary epithelial ovarian cancer. Cochrane Database Syst Rev 2006:CD005340.

[12] De Angelis R, Francisci S, Baili P, Marchesi F, Roazzi P, Belot A, et al. The EUROCARE-4 database on cancer survival in Europe: Data standardisation, quality control and methods of statistical analysis. Eur J Cancer 2009;45:909–30.

[13] Berrino F, De Angelis R, Sant M, Rosso S, Bielska-Lasota M, Coebergh JW, et al. Survival for eight major cancers and all cancers combined for European adults diagnosed in 1995–99: Results of the EUROCARE-4 study. Lancet Oncol 2007;8:773–83.

[14] Sant M, Allemanni C, Santaquilani M, Knijn A, Marchesi F, Capocaccia F, et al. EUROCARE-4. Survival of cancer patients diagnosed in 1995–1999. Results and commentary. Eur J Cancer 2009;45:931–91.

[15] Percy C, Fritz A, Jack A, Shanmugarathan S, Sobin L, Parkin D, et al., editors. International classification of diseases for oncology (ICD-O) 3rd ed. Geneva: WHO; 2000.

[16] Verdecchia A, Francisci S, Brenner H, Gatta G, Micheli A, Mangone L, et al. Recent cancer survival in Europe: A 2000–02 period analysis of EUROCARE-4 data. Lancet Oncol 2007;8:784–96.

[17] Cronin K, Mariotto A, Scoppa S, Green D, Clegg L. Differences between Brenner et al. and NCI methods for calculating period survival. Statistical Research and Applications Branch, National Cancer Institute. Technical Report #2003-02-A [cited 2011 Nov 30]. Available from: http://surveillance.cancer.gov/reports/

[18] Hakulinen T. Cancer survival corrected for heterogeneity in patient withdrawal. Biometrics 1982;38:933–42.

[19] Corazziari I, Quinn M, Capocaccia R. Standard cancer patient population for age standardising survival ratios. Eur J Cancer 2004;40:2307–16.

[20] Oehlert GW. A note on the delta method. Am Stat 1992;46:27–9.

[21] Surveillance Research Program, SEER*Stat software 6.4.4 ed. Bethesda, MD: National Cancer Institute; 2008 [cited 2007 May 28]. Available from: http://www.seer.cancer.gov/seerstat.

[22] Berrino F, Capocaccia R, Coleman MP, Esteve J, Gatta G, Hakulinen T, et al. Survival of cancer patients in Europe: The EUROCARE-3 Study. Ann Oncol 2003;14(Suppl 5):9–155.

[23] Klint A, Tryggvadottir L, Bray F, Gislum M, Hakulinen T, Storm HH, et al. Trends in the survival of patients diagnosed

with cancer in female genital organs in the Nordic countries 1964–2003 followed up to the end of 2006. Acta Oncol 2010;49:632–43.
[24] Coleman MP, Forman D, Bryant H, Butler J, Rachet B, Maringe C, et al. Cancer survival in Australia, Canada, Denmark, Norway, Sweden, and the UK, 1995–2007 (the International Cancer Benchmarking Partnership): An analysis of population-based cancer registry data. Lancet 2011;377:127–38.
[25] Estève J, Benhamou E, Croasdale M, Raymond L. Relative survival and the estimation of net survival: Elements for further discussion. Stat Med 1990;9:529–38.
[26] Choi M, Fuller CD, Thomas CR, Jr., Wang SJ. Conditional survival in ovarian cancer: Results from the SEER dataset 1988–2001. Gynecol Oncol 2008;109:203–9.
[27] Mackay HJ, Brady MF, Oza AM, Reuss A, Pujade-Lauraine E, Swart AM, et al. Prognostic relevance of uncommon ovarian histology in women with stage III/IV epithelial ovarian cancer. Int J Gynecol Cancer 2010;20:945–52.
[28] Aletti GD, Dowdy SC, Podratz KC, Cliby WA. Surgical treatment of diaphragm disease correlates with improved survival in optimally debulked advanced stage ovarian cancer. Gynecol Oncol 2006;100:283–7.
[29] Rose PG, Nerenstone S, Brady MF, Clarke-Pearson D, Olt G, Rubin SC, et al. Secondary surgical cytoreduction for advanced ovarian carcinoma. N Engl J Med 2004;351:2489–97.
[30] Akeson M, Zetterqvist BM, Holmberg E, Horvath G. Improved survival with clinical guidelines? Evaluation of a quality register linked to clinical guidelines for ovarian cancer in the western health care region in Sweden between 1 September 1993 and 1 June 1998. Acta Obstet Gynecol Scand 2005;84:1113–8.
[31] Du Bois A, Rochon J, Lamparter C, Pfisterer J. Pattern of care and impact of participation in clinical studies on the outcome in ovarian cancer. Int J Gynecol Cancer 2005;15:183–91.
[32] Kumpulainen S, Grenman S, Kyyronen P, Pukkala E, Sankila R. Evidence of benefit from centralised treatment of ovarian cancer: A nationwide population-based survival analysis in Finland. Int J Cancer 2002;102:541–4.
[33] Oberaigner W, Stuhlinger W. Influence of department volume on cancer survival for gynaecological cancers – a population-based study in Tyrol, Austria. Gynecol Oncol 2006;103:527–34.
[34] Skirnisdottir I, Garmo H, Wilander E, Holmberg L. Borderline ovarian tumors in Sweden 1960–2005: Trends in incidence and age at diagnosis compared to ovarian cancer. Int J Cancer 2008;123:1897–901.
[35] Rettenmaier MA, Lopez K, Abaid LN, Brown JV, 3rd, Micha JP, Goldstein BH. Borderline ovarian tumors and extended patient follow-up: An individual institution's experience. J Surg Oncol 2010;101:18–21.
[36] Sherman ME, Mink PJ, Curtis R, Cote TR, Brooks S, Hartge P, et al. Survival among women with borderline ovarian tumors and ovarian carcinoma: A population-based analysis. Cancer 2004;100:1045–52.
[37] Elit L, Bondy SJ, Paszat L, Przybysz R, Levine M. Outcomes in surgery for ovarian cancer. Gynecol Oncol 2002;87:260–7.
[38] Engel J, Eckel R, Schubert-Fritschle G, Kerr J, Kuhn W, Diebold J, et al. Moderate progress for ovarian cancer in the last 20 years: Prolongation of survival, but no improvement in the cure rate. Eur J Cancer 2002;38:2435–45.
[39] Brenner H, Stegmaier C, Ziegler H. Trends in survival of patients with ovarian cancer in Saarland, Germany, 1976–1995. J Cancer Res Clin Oncol 1999;125:109–13.
[40] Laurvick CL, Semmens JB, Leung YC, Holman CD. Ovarian cancer in Western Australia (1982–1998): Trends in surgical intervention and relative survival. Gynecol Oncol 2003;88:141–8.
[41] Barnholtz-Sloan JS, Schwartz AG, Qureshi F, Jacques S, Malone J, Munkarah AR. Ovarian cancer: Changes in patterns at diagnosis and relative survival over the last three decades. Am J Obstet Gynecol 2003;189:1120–7.
[42] Fotopoulou C, Savvatis K, Steinhagen-Thiessen E, Bahra M, Lichtenegger W, Sehouli J. Primary radical surgery in elderly patients with epithelial ovarian cancer: Analysis of surgical outcome and long-term survival. Int J Gynecol Cancer 2010;20:34–40.
[43] Steer CB. Chemotherapy for ovarian cancer in the older adult. Curr Treat Options Oncol 2009;10:159–70.
[44] Janda M, Youlden DR, Baade PD, Jackson D, Obermair A. Elderly patients with stage III or IV ovarian cancer: Should they receive standard care? Int J Gynecol Cancer 2008;18:896–907.
[45] Van Lent WAM, de Beer RD, van Harten WH. International benchmarking of specialty hospitals. A series of case studies on comprehensive cancer centres. Bethesda, MD: National Center for Biotechnology Information; 2010 [cited 2010 Nov 15]. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20807408.

Supplementary material available online

Supplementary Appendix material available online at http://www.informahealthcare.com/doi/abs/10.3109/0284186X.2011.653437.