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The cancer survival gap between elderly and middle-aged patients in Europe is widening

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ABSTRACT

The present study is aimed to compare survival and prognostic changes over time between elderly (70–84 years) and middle-aged cancer patients (55–69 years). We considered seven cancer sites (stomach, colon, breast, cervix and corpus uteri, ovary and prostate) and all cancers combined (but excluding prostate and non-melanoma skin cancers). Five-year relative survival was estimated for cohorts of patients diagnosed in 1988–1999 in a pool of 51 European populations covered by cancer registries. Furthermore, we applied the period-analysis method to more recent incidence data from 32 cancer registries to provide 1- and 5-year relative survival estimates for the period of follow-up 2000–2002.

A significant survival improvement was observed from 1988 to 1999 for all cancers combined and for every cancer site, except cervical cancer. However, survival increased at a slower rate in the elderly, so that the gap between younger and older patients widened, particularly for prostate cancer in men and for all considered cancers except cervical cancer in women. For breast and prostate cancers, the increasing gap was likely attributable to a larger use of, respectively, mammographic screening and PSA test in middle-aged with respect to the elderly. In the period analysis of the most recent data, relative survival was much higher in middle-aged patients than in the elderly. The differences were higher for breast and gynaecological cancers, and for prostate cancer. Most of this age gap was due to a very large difference in survival after the 1st year following the diagnosis. Differences were much smaller for conditional 5-year relative survival among patients who had already survived the first year.

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The increase of survival in elderly men is encouraging but the lesser improvement in women and, in particular, the widening gap for breast cancer suggest that many barriers still delay access to care and that enhanced prevention and clinical management remain major issues.

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1. Introduction

Populations of Western industrialised countries are quickly ageing and are dramatically changing their composition with the proportion of people aged more than 65 years increasing rapidly. The causes of this changing demographic pattern are the decrease in infant mortality, the increase in life expectancy, the reduction in mortality from infectious and cardiovascular diseases and the very high fertility rates after II World War.¹ For example, Italy and Sweden, which have some of the oldest populations in Europe, experienced an increase in life expectancy from 70 to 78 years in men and from 76 to 83 years in women over the period 1970–2000.²

Age is one of the main risk factors for cancer, with incidence and mortality rising exponentially above 50 years. In Europe during 2000, the incidence for all cancers combined ranged from 400 cases per 100,000 for age group 50–54 to 2280 for age group 70–74 in men and from 490 to 1210 in women. Over 65% of deaths from cancer occurred in elderly patients aged 65 years or more.³

As a consequence, the growing burden of social and health expenditure of cancer in the elderly is and will become a major challenge that health care systems of many countries will have to cope with. The mix composed of cancer, ageing and economic resource allocation is one of the major concerns for public health in this century.^{4–6}

Encouraging survival improvements occurred for several cancer sites in all age patients during the last two decades.^{7,8} During the same period, there was an increasing interest in geriatric oncology and a greater awareness by medical oncologists, which have led to better clinical management of the elderly.^{9,10} While there has been an increasing awareness of specific clinical needs of the elderly, very large differences in prognosis have been observed between the elderly and younger patients.¹¹ Elderly patients, especially women, experienced much higher relative excess risks (RERs) of dying, particularly 1-year after diagnosis.¹²

Quantifying and understanding the impact of improvements in specialist and geriatric treatment on health outcomes in the elderly are of the utmost interest, and will inform future policy. Time trends are routinely evaluated by epidemiologists, but little is known about the comparison of the survival trends between the elderly and younger adults. In particular, there has been a lack of data on the development of cancer survival in elderly patients in the recent years.

The present study is aimed at analysing differences in survival between elderly (70–84 years) and middle-aged cancer patients (55–69 years) and at evaluating changes over time. A question of particular interest is whether the prognostic gap has remained stable, widened or narrowed. We calculated cohort relative survival, over the period 1988–1999 to evaluate

the trends in time. The period methodology was used for the more recent years of 2000–2002 to provide more up-to-date estimates of survival in the elderly and to disclose the impact of recent improvements.

2. Materials and methods

Data analysed in this investigation were obtained from the database of EUROCARE project. The database includes information on patients diagnosed from 1978 to 2002.^{7,8} We carried out two different kinds of survival analysis. First, relative survival was computed by means of cohort analysis, using Hakulinen's method,¹³ for patients diagnosed from 1988 to 1999 and followed up for at least 5-years. The whole time period was categorised into four smaller intervals (1988–1990, 1991–1993, 1994–1996, 1997–1999), in order to describe survival trends. Second, a period analysis of relative survival was carried out based on cases diagnosed in the 1996–2002 period, exclusively considering the survival experience of cancer patients in 2000–2002, and thereby provides survival estimates that are expected to closely predict 5-year relative survival of patients diagnosed in this last period.¹⁴

Data used for the cohort and time trend analysis were restricted to 51 cancer registries (CRs), belonging to 16 European countries, with data available for the whole time period 1988–1999. The period analysis was applied to data collected by a still smaller group of 32 CRs from 14 European countries who were able to provide data on incident cases from 1996 to 2002 and the related follow-up required for the 2000–2002 period estimates. Malignant tumours of the stomach, colon, breast, cervix and corpus uteri, ovary, prostate and all cancers combined were included in the analyses. We based the choice of sites on their frequency and on the characteristics emerged in the previous studies on elderly patients. We selected stomach and colon for digestive tract, the first site with a rather poor survival, the second one with a quite good survival, and all gynaecological cancers owing to the relevant prognostic differences between elderly and younger patients. We excluded lung cancer because the previous analyses did not show any relevant prognostic difference by age.¹² Incidence and survival rates for prostate cancer are strongly affected by the use intensity of PSA test and by the variable times, when it was introduced into clinical practice in the different European areas. Therefore, we excluded prostate cancer (in addition to non-melanoma skin cancers) from all cancers combined to avoid wrong interpretations of time trends.

Patients were divided into two age groups: the elderly from 70 to 84 years, and the adults from 55 to 69 years. For the elderly, a lower limit at 70 years was preferred to that at 65 years, usually used in demography, because of its wider use in clinical publications. We excluded patients aged 85 and

older to avoid problems with small numbers and statistical instability in this age group. Data for the very old patients are often unreliable due to the lower completeness and poorer quality of data collection and registration.¹⁵ Analyses were done separately for men and women where applicable. Table 1 shows, by age class, the number of cases for all cancers combined and the related standard indicators of data quality (the proportion of cases with microscopically verified diagnosis and the proportion of cases recorded by CRs through death certificate only), for the pool of 51 CRs participating in the cohort-based trend analyses for 1988–1999 and the 32 CRs included in the period analysis for 2000–2002.

In order to accurately compare trends between sexes, which can have different age structures, the relative survival was adjusted by age using the direct method and the European standard cancer populations proposed by Corazziari and colleagues.¹⁶ All survival estimates are presented as pooled European estimates rather than by single registries. Pooled European estimates were obtained as weighted averages of pooled estimates for four major European regions as described by Verdecchia and co-authors.⁸ Survival trends for patients diagnosed in 1988–1999, and based on cohort analysis, are presented in terms of 5-year relative survival and of Estimated Annual Percent Changes (EAPCs), computed with their 95% confidence intervals by linear regression models. In order to highlight differences in prognosis by age, the Relative Excess Risks (RERs) of death were calculated as the ratio of the relative survival logarithm in 70–84 age group to that in 55–69. For the period analysis, results are presented as 1-year and 5-year relative survival. Furthermore, relative survival at 5-years from diagnosis conditional on being alive at 1-year

after diagnosis is also presented. Conditional survival calculated in this way reflects cumulative relative survival for years 2 to 5 following the diagnosis.

3. Results

3.1. Improvement in survival over time (1988–1999) according to tumour type, gender and age

Fig. 1 illustrates 5-year relative survival trends across four periods of diagnosis (1988–1990, 1991–1993, 1994–1996, 1997–1999) for the European pool and for some selected cancers: all cancers combined (except prostate and non-melanoma skin cancers), stomach, colon, prostate, female breast, cervix, corpus uteri and ovary. The EAPCs for the entire period are shown in Table 2 by sex and cancer site. There was a significant improvement in survival for all cancers combined in men for both the middle-aged and elderly, even without considering prostate cancers (EAPCs +2.2, statistically significant). Survival for women increased at a slower rate, albeit still significant rate, and was higher in the middle aged than in the elderly (EAPCs +1.7 and +1.2 in younger and older patients, respectively). The difference in survival between middle-aged and elderly women widened from 12% units in 1988–1990 to 16% unit in 1997–1999.

A statistically significant improvement of survival was observed in both the sexes also for stomach and colon cancers. Younger women showed more marked improvements than elderly women (EAPCs +1.7 versus +0.9 for stomach and +1.9 versus +1.2 for colon). As a result, the differences in survival between the two age groups increased from 6% units in 1988–1990 to 9% units in 1997–1999 for stomach cancer and from 4% units to 8% units for colon cancer. In men, survival rates increased in both the age groups with EAPCs being slightly higher in elderly than in younger patients (EAPCs +1.8 versus +1.4 for stomach cancer and +1.9 versus +1.4 for colon cancer).

The most notable results were seen for breast and prostate cancers which followed a parallel pattern with close survival in the two age groups during 1988–1990 and a large difference in 1997–1999. Prostate and breast cancers had higher EAPCs in middle-aged patients. The gap between younger and older patients widened at similar rates and, for both cancer sites during 1997–1999, 5-year relative survival reached values around 77% in elderly and 85% in middle-aged patients.

For cervical cancer, 5-year relative survival was stable throughout the whole period in both elderly and younger patients. By contrast, we registered a significant improvement for cancers of the corpus uteri and ovary, which was similar in both the age groups (EAPCs +0.7 for corpus uteri and +1.7 for ovary). The differences in age, among the largest found in the first period, did not largely change in the last one, remaining steady around 17% units for corpus and 14% units for cervix uteri and slightly widening for ovary from 11 to 14% units.

3.2. Trends in difference in survival between elderly and younger patients (1988–1999)

Table 3 illustrates the changes over time in survival gap between elderly and middle-aged patients through the RERs of

Table 1 – Summary of characteristics of cases for all cancers combined by age class and period, for the European pool of cancer registries (listed by geographical macro-region).

	Cases	DCO (%)	MV (%)
<i>Age class 55–69 years</i>			
1988–1999	951,731	1.5	86.8
1996–2002	258,121	1.7	93.7
<i>Age class 70–84 years</i>			
1988–1999	1,103,039	3.9	79.4
1996–2002	305,371	2.1	86.4

DCO%: proportion of cases recorded through death certificate only.
MV%: proportion of cases with microscopically verified diagnosis.

Northern Europe: Denmark*, Finland, Iceland, Norway, Sweden.

UK: East Anglia, Mersey*, Northern and Yorkshire, Oxford, Scotland, South Western*, Thames*, Trent*, Wales, West Midlands.

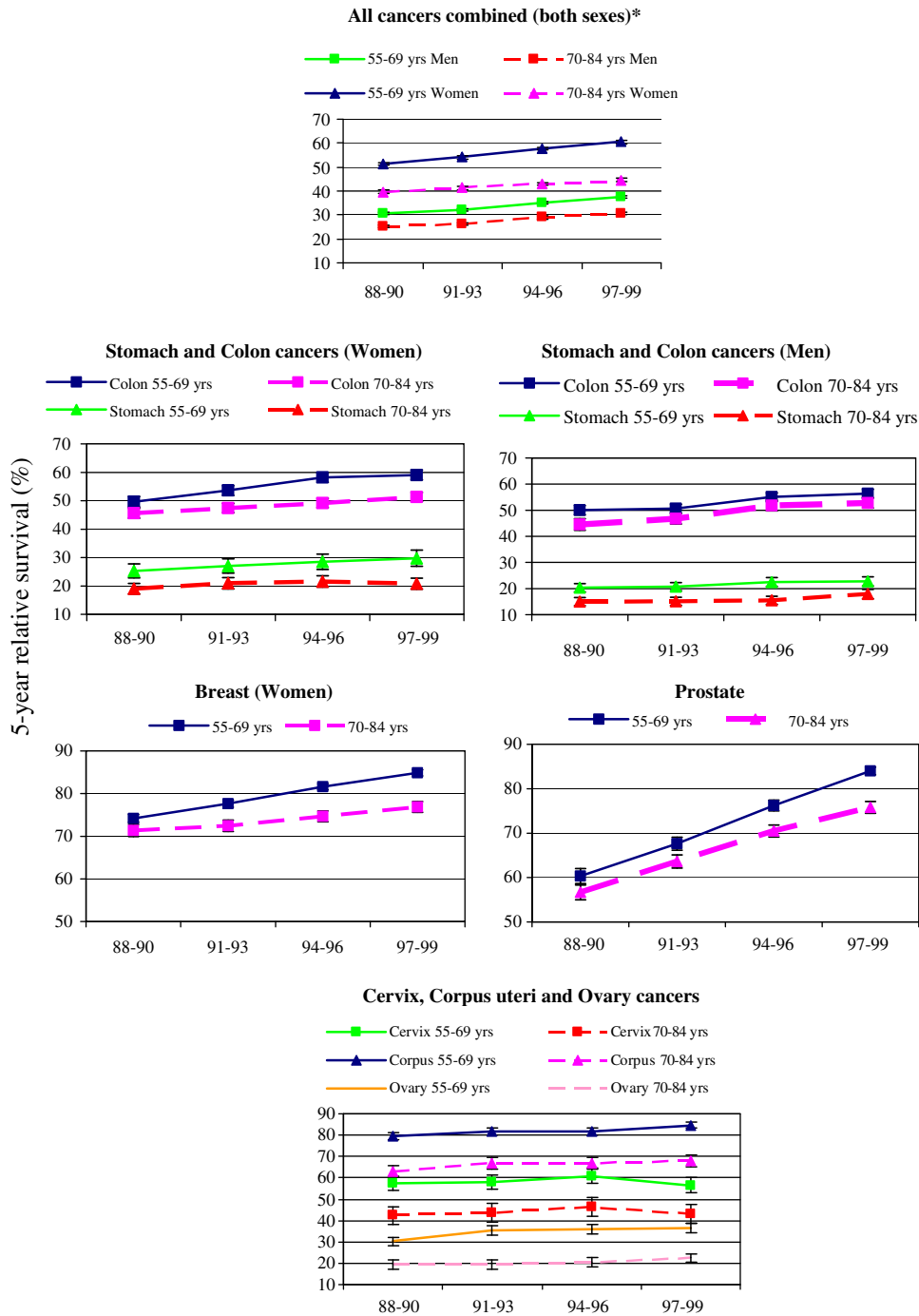
Central-Western Europe: Austria*, Bas-Rhin*, Calvados*, Calvados digestive*, Cote d'Or digestive, Cote d'Or haematological*, Doubs*, Haut-Rhin*, Isère*, Somme*, Tarn*, Saarland, Amsterdam, Eindhoven, Basel, Geneva, Grisons*, St. Gallen, Valais*, Zurich*.

Eastern Europe: West Bohemia, Cracow, Warsaw.

Southern Europe: Ferrara°, Genoa, Modena, Parma, Ragusa, Romagna, Sassari°, Torino, Tuscany, Varese*, Veneto, Malta°, Slovenia, Basque Country*, Navarra*, Tarragona*.

* = Cancer registries which provided data only for the period 1988–1999 (cohort analysis).

° = Cancer registries which provided data only for the period 1996–2002 (period analysis).



* = All cancers sites except prostate and non-melanoma skin cancers.

Fig. 1 – Five-year relative survival trend (1988–1999) for elderly (70–84 years) and middle-aged (55–69 years) cancer patients by sex and cancer site (weighted European pool; cohort analysis method).

death at 5-years since diagnosis of the 70–84 with respect to the 55–69 age group, by sex and cancer site. In men, the RERs were essentially stable over time for all cancers combined and the specific cancer sites. Prostate cancer was the only big exception, showing a striking RER increase from 1.1 in 1988–1990 to 1.6. For women, the RERs were stable or not changed significantly for stomach and cervical cancers. They increased for colon cancer (from 1.1 in 1988–1990 to

about 1.3 in the third and fourth periods), for corpus uteri cancer (from 2.0 to 2.3 in the last period), and for all cancers combined (from 1.4 to 1.6). Breast cancer presented the largest RER increase: from 1.1 in 1988–1990 to 1.6 in 1997–1999. For cancer of the ovary, RERs increased, even though not significantly, from 1.4 in 1988–1990 to 1.6 in 1991–1993 and remained almost constant thereafter.

Table 2 – Estimated annual percent change (EAPC) in 5-year relative survival over the period 1988–1999, for elderly (70–84 years) and middle-aged (55–69 years) cancer patients by sex and cancer site (weighted European pool; cohort analysis method).

		Women		Men	
		55–69 yrs	70–84 yrs	55–69 yrs	70–84 yrs
All cancers ^a	EAPC	+1.74	+1.23	+2.15	+2.19
	95% CI	+1.42/+2.06	+1.01/+1.44	+1.72/+2.59	+1.75/+2.63
Stomach	EAPC	+1.70	+0.93	+1.35	+1.81
	95% CI	+1.38/+2.02	+0.22/+1.64	+0.95/+1.75	+1.02/+2.60
Colon	EAPC	+1.86	+1.23	+1.41	+1.90
	95% CI	+1.34/+2.37	+1.02/+1.45	+1.00/+1.82	+1.39/+2.41
Prostate	EAPC			+3.46	+3.00
	95% CI			+2.76/+4.16	+2.38/+3.61
Breast	EAPC	+1.42	+0.82		
	95% CI	+1.16/+1.69	+0.65/+0.98		
Cervix uteri	EAPC	+0.09	+0.38		
	95% CI	–0.47/+0.66	–0.33/+1.11		
Corpus uteri	EAPC	+0.61	+0.70		
	95% CI	+0.43/+0.79	+0.37/+1.03		
Ovary	EAPC	+1.72	+1.73		
	95% CI	+0.88/+2.58	+1.14/+2.31		

95% CI = confidence intervals at 95%.
a All cancers sites except prostate and non-melanoma skin cancers.

Table 3 – Time trend (1988–1999) of 5-year relative excess risks of death (RER) for the elderly (70–84 years) compared with middle-aged adults (55–69 years) by sex and cancer site (weighted European pool; cohort analysis method).

		Women				Men			
		88–90	91–93	94–96	97–99	88–90	91–93	94–96	97–99
All cancers ^a	RER	1.39	1.44	1.54	1.60	1.17	1.17	1.19	1.20
	95% CI	1.37–1.41	1.42–1.46	1.53–1.56	1.58–1.62	1.15–1.19	1.16–1.18	1.17–1.20	1.19–1.21
Stomach	RER	1.21	1.19	1.22	1.30	1.19	1.20	1.25	1.16
	95% CI	0.95–1.46	0.97–1.42	0.99–1.46	1.03–1.57	0.96–1.42	0.98–1.43	1.01–1.48	0.97–1.36
Colon	RER	1.12	1.20	1.31	1.27	1.17	1.12	1.10	1.11
	95% CI	1.08–1.16	1.16–1.23	1.27–1.35	1.24–1.30	1.13–1.21	1.08–1.15	1.08–1.13	1.09–1.14
Prostate	RER					1.12	1.16	1.29	1.61
	95% CI					1.10–1.14	1.14–1.17	1.28–1.30	1.60–1.61
Breast	RER	1.13	1.27	1.44	1.60				
	95% CI	1.13–1.14	1.27–1.28	1.43–1.44	1.60–1.61				
Cervix uteri	RER	1.55	1.52	1.54	1.48				
	95% CI	1.44–1.66	1.41–1.63	1.43–1.65	1.36–1.60				
Corpus uteri	RER	2.03	1.96	1.99	2.32				
	95% CI	1.99–2.07	1.93–1.99	1.96–2.02	2.29–2.36				
Ovary	RER	1.37	1.58	1.54	1.48				
	95% CI	1.16–1.59	1.33–1.84	1.30–1.78	1.27–1.69				

95% CI = confidence intervals at 95%.
a All cancers sites except prostate and non-melanoma skin cancers.

3.3. Up-to-date 1- and 5-year survival rates and RERs for elderly compared to younger patients in the period 2000–2002

Survival data presented in this paragraph refer to the calendar period 2000–2002 and derived from the European pool of 32 CRs. Table 4 shows the 1- and 5-year relative survival for 55–69 and 70–84 age groups, by sex and cancer site. Conditional 5-year relative survival for those who have survived for 1-year is shown in the last three columns.

Relative survival was much higher in the middle-aged patients than in the elderly for every cancer site in both sexes; however, in men the differences were smaller. Differences in relative survival between the two age groups are described in Table 4 by means of RERs of death in the elderly compared to middle-aged patients by sex and cancer site. Elderly women had RERs higher than elderly men at both 1- and 5-years from diagnosis: for all cancers combined (excluding non-melanoma skin and prostate cancers) the 1-year RERs were 2.0

Table 4 – One-year and 5-year relative survival (RS) from diagnosis by sex and cancer site for elderly (70–84 years) and middle-aged (55–69 years) cancer patients in 2000–2002, and 5-year relative survival conditional on surviving 1-year. Relative excess risks of death (RER) for the elderly (70–84 years) compared with middle-aged adults (55–69 years) (weighted European pool; period analysis method).

		1-year relative survival (%) from diagnosis			5-year relative survival (%) from diagnosis			5-year relative survival (%), conditional on surviving one year		
		55–69 yrs	70–84 yrs	RER	55–69 yrs	70–84 yrs	RER	55–69 yrs	70–84 yrs	RER
<i>Women</i>										
All cancers ^a	RS	80.4	64.4	2.02	62.0	45.6	1.64	77.0	70.8	1.32
	95% CI	80.0–80.8	63.9–64.9	2.01–2.03	61.5–62.5	45.0–46.2	1.62–1.66	76.9–77.2	70.6–71.0	1.32–1.33
Stomach	RS	55.0	42.9	1.42	30.4	22.1	1.30	55.3	51.5	1.12
	95% CI	51.6–58.5	40.4–45.5	1.31–1.52	27.4–33.7	19.9–24.5	1.02–1.52	54.2–56.4	50.3–52.6	1.10–1.14
Colon	RS	83.1	72.2	1.76	61.5	53.3	1.30	74.0	73.7	1.01
	95% CI	81.9–84.4	71.0–73.5	1.74–1.77	59.8–63.3	51.6–54.9	1.27–1.33	73.5–74.5	73.2–74.2	1.01–1.02
Breast	RS	97.3	93.1	2.65	85.7	77.6	1.65	88.1	83.3	1.43
	95% CI	97.0–97.7	92.5–93.7	2.65–2.65	85.0–86.4	76.4–78.8	1.64–1.65	87.8–88.3	82.9–83.7	1.43–1.43
Cervix uteri	RS	82.8	71.2	1.80	58.1	44.1	1.51	70.2	61.9	1.35
	95% CI	79.6–86.1	67.4–75.2	1.75–1.84	54.3–62.1	39.8–48.9	1.38–1.63	69.2–71.2	60.5–63.5	1.34–1.37
Corpus uteri	RS	95.0	89.3	2.22	84.1	71.2	1.97	88.5	79.7	1.86
	95% CI	94.2–95.9	87.8–90.9	2.22–2.23	82.6–85.7	68.5–74.0	1.95–1.99	88.1–88.9	78.8–80.6	1.86–1.87
Ovary	RS	78.5	55.5	2.43	39.8	25.0	1.51	50.7	45.0	1.18
	95% CI	76.6–80.4	53.1–58.1	2.35–2.51	37.5–42.2	22.6–27.6	1.32–1.69	49.8–51.6	43.8–46.2	1.15–1.20
<i>Men</i>										
All cancers ^a	RS	62.4	51.6	1.41	38.7	31.3	1.23	62.0	60.7	1.04
	95% CI	62.0–62.9	51.0–52.1	1.40–1.41	38.2–39.2	30.7–31.9	1.21–1.24	61.7–62.3	60.1–61.3	1.04–1.05
Stomach	RS	51.6	39.3	1.41	24.5	19.2	1.17	47.5	48.8	0.96
	95% CI	49.3–53.9	37.3–41.4	1.33–1.49	22.6–26.5	17.3–21.3	0.98–1.36	46.6–48.3	47.5–50.1	0.94–0.99
Colon	RS	80.2	72.2	1.47	58.1	54.7	1.11	72.4	75.8	0.86
	95% CI	79.0–81.4	70.9–73.6	1.46–1.48	56.5–59.8	52.8–56.8	1.09–1.13	72.0–72.9	75.1–76.5	0.86–0.86
Prostate	RS	97.9	93.9	3.01	86.6	77.0	1.82	88.4	82.0	1.62
	95% CI	97.6–98.3	93.3–94.5	3.01–3.01	85.7–87.6	75.7–78.3	1.81–1.83	88.1–88.8	81.6–82.4	1.61–1.62

95% CI = confidence intervals at 95%.

^a All cancers sites except prostate and non-melanoma skin cancers.

versus 1.4 and the 5-year RERs were 1.6 versus 1.2, in women and men respectively. In women the highest RERs were registered for breast (2.7 and 1.7 at 1- and 5-years, respectively) and gynaecological cancers (5-year RERs ranging from 1.5 to 2.0); in men the highest RERs were those of prostate cancer (3.0 and 1.8 at 1- and 5-years, respectively).

Most of this age gap was due to a very large difference in the survival during the 1st year following the diagnosis. Differences were much smaller among patients, who had already survived the first year. Elderly men had a conditional survival very similar to that of younger men for all considered cancers, except for prostate cancer (RER 1.6). Middle-aged women had better conditional survival than elderly women with differences higher than 4% units for all cancer sites, except colon, and RERs which remained particularly high for corpus uteri and breast cancers (1.9 and 1.4, respectively). Conditional survival for all cancers combined was 77% in younger and 71% in older women, while men had very similar values in both age groups (slightly above 60%).

4. Discussion

The present report describes the characteristics of cancer survival in European elderly patients. We have compared the prognosis of middle-aged adults (55–69 years old) with that of older patients (70–84 years old) by two different points of view. First, a longitudinal investigation on time trends from 1988 to 1999 was carried out; second, a transversal analysis with the available data updated to the period 2000–2002 was performed.

4.1. Period analysis of relative survival for the period 2000–2002

The results obtained for the period 2000–2002 confirmed three main findings for survival in elderly patients, identified in previous EUROCARE studies.^{12,17} First, the difference in survival between elderly and middle-aged patients was much greater at 1-year after diagnosis than that at 5-years for all cancer sites studied. Conditional survival analysis showed that elderly patients who survived the first year experienced a prognosis very similar to that of younger adults in the subsequent years and that differential mortality near the diagnosis accounted for most of the age gap in survival. Second, women showed larger differences in survival between elderly and middle-aged than men. Lastly, gynaecological cancers showed a larger difference in survival than gastro-intestinal tumours, which may partially explain the larger gap in overall survival for women.

Major age-related survival differences, as those registered in Europe, were not observed in the United States. A large population-based study, which compared cancer survival in the US and Europe, found that the decrease of survival rates with increasing age at diagnosis was more marked in Europe and that elderly American patients had better prognosis than their European counterparts. The authors affirmed that the differences were unlikely to be due to artefacts but, more probably, to earlier disease stage at diagnosis and more aggressive treatments in the US.¹⁸

The underlying reasons for such prognostic gaps are multiple, and may be attributed to variations in tumour factors, clinical/prognostic characteristics and/or treatment. The elderly are more likely to delay seeking medical advice due to socio-economic, psychological and cognitive factors, which may lead to diagnosis at a later stage, particularly for gynaecological cancers.^{19,20} Comorbid conditions influence treatment options, most notably surgical eligibility,²¹ and are probably responsible for the higher risk of dying within the first year. However, the good outcomes observed for stomach and colon cancers in elderly men confirm that surgery may be performed safely in old patients, as long as it is not an emergency surgery.²² The impairment of one or more organ systems with an associated comorbidity and poor general health are the main factors used to identify patients, who may need additional attention during the first month after diagnosis.²³

4.2. Relative survival time trend from 1988 to 1999

Geriatricians and oncologists have increasingly been collaborating, due to the overlap of the specialities, in the treatment of cancer patients and research. As a result, advances in the treatment of cancer in the elderly have been made over the last 15 years, accompanied by an increase in the studies on malignancies and old age.^{10,24} Despite these efforts, survival trends here presented seem to confirm that the optimal clinical management of cancer in the elderly is slow in coming days. Prognosis for elderly patients improved for almost each cancer studied, but the difference in survival between younger adults and the elderly did not seem to diminish in any cancer site. The survival for all cancers combined improved in both the sexes and age groups but with differing intensity. Survival in men increased at the same pace in older and middle-aged adults, while survival in middle-aged women improved more than in elderly women. This resulted in a prognostic gap that widened in women and essentially remained stable in men. The most notable results were seen for breast cancer in women and prostate cancer in men; the relative risks were largely increasing over time, and the prognostic disadvantage of elderly patients was rapidly rising throughout the study period.

During the 1990s, mammographic breast cancer screening was introduced in several European countries, with a subsequent decline in mortality and increase in survival, which was most pronounced in middle-aged women, the primary target group in most screening programmes. Most likely, increases in survival are partially attributable to earlier detection by screening, but also due to improvement in clinical care and treatment, most notably in adjuvant therapies.^{25,26} However, screening programmes rarely include elderly, even if there is little evidence to support limiting breast cancer screening solely on the basis of old age and resource availability and allocation. The choice of an upper limit of screening should be based on life expectancy and a multidimensional evaluation.^{27,28} Therefore we can affirm that mammographic screening had a clear effect on the survival of middle-aged breast cancer patients and not on that of the oldest group.

Many barriers still delay access to care of elderly women, who receive an optimal medical treatment with definitive

and curative intent less often than younger patients.^{29,30} Older women with breast cancer are more likely to have large tumours and positive metastatic axillary nodes, but are less likely to receive adjuvant therapy than younger women with a similar stage. After adjusting for comorbid conditions, pathological and biological factors, older women are less likely to receive radio- and chemotherapy than younger women.^{29,31,32} In particular, variations in adjuvant therapy may explain the differences in survival by age observed for colon cancer, as elderly patients less frequently receive adjuvant chemotherapy and more often discontinue treatment before completion.³³ A population-based study of Lemmens et al. found that elderly women and patients with a low socio-economic status were less likely to be treated with adjuvant therapy.³⁴ Likewise, elderly women presenting with early-stage tumours are less likely to receive curative treatment.³⁵

Prostate cancer survival increased rapidly: improvements were greater for middle-aged patients, probably due to the more frequent use of the Prostate Specific Antigen (PSA) Test in men under 70.³⁶ The PSA test became widely available in the mid-1990's as an opportunistic screening, causing a striking rise of incidence followed by only a slight decline in mortality, owing to the high probability to identify prostate tumours that otherwise would likely have remained undiagnosed during the life span.³⁷ Therefore, unlike breast and colon cancers, the age variation for prostate is likely to be due to the impact of PSA testing and a greater effect of the lead time bias on middle-aged adults rather than a difference in treatment. As prostate cancer represents about one-fifth of all cancers in males, it is not clear whether survival rates for all cancers combined reflect a real tendency or are inflated by this phenomenon. As a consequence, we excluded this tumour from all cancer sites. However, such exclusion did not affect substantially our results: there was an absolute decrease in survival rates, the EAPCs declined from +3.0 (data not shown) to +2.2 (Table 3) in both the age groups and the RERs did not change.

The central questions of whether elderly patients are (i) under treated because emphasis is placed on chronological age, with the assumption this makes them unfit for treatment or (ii) treatment is appropriate and is limited by physiological impairment or comorbidity at diagnosis, remain to be clearly disentangled. Both the situations would be an ideal target to improve outcomes in the elderly. However, currently, the elderly are under-represented in randomised clinical trials, thereby limiting the ability to produce evidence-based guidelines for elderly cancer patients.^{38,39}

Since elderly patients surviving the first year experience a prognosis similar to middle-aged patients, distinguishing the frail elderly from those with a good health status, through multidimensional evaluation tools, such as the comprehensive geriatric assessment, would identify those that could benefit from intensive treatment.⁴⁰ This strategy would focus the attention on patients, who would benefit from the same standard protocols applied to younger people, avoiding over-treatment in the frail elderly. Nevertheless clearly identifying patients with moderate levels of comorbidity (between frail and healthy) would remain a challenge.

Treatment of the elderly can be highly complex with social conditions and family concerns, all influencing management.

Socio-economic conditions having disadvantages often go along with a limited social support, decreased access to health care and physical or perceived ability to undertake treatments. In particular, socio-economic status may partially explain differences between elderly women and elderly men compared to their younger counterparts.^{4,5,34} Elderly women are more likely to be older than elderly males due to a longer life expectancy, to be widows, living alone with an overall lower income and educational level, resulting in a low degree of social independence.

By its nature, survival analysis is less timely than incidence and mortality data, and many health policies and initiatives started after the end of our study period could not be evaluated. Nevertheless, the results obtained for the period 2000–2002, even if not included in the trend evaluation, can be useful to extend our observation to a more recent period.

Data completeness and accuracy could represent a major source of artefact in the analyses of older populations,¹⁵ particularly owing to an incomplete ascertainment of incident cases and other patient details.^{41,42} Elderly patients diagnosed at a late stage and receiving only palliative care in the community, with little hospital care, may be less likely to have a diagnosis recorded in cancer registry database. The selective loss of poor prognosis patients may lead to survival overestimation, particularly over 85 years,⁴³ and for this reason we excluded patients over this age from the analysis. The 51 CRs selected for computing the time trend and the 32 used to estimate the survival for the period 2000–2002 may not be representative of all the 83 CRs participating in EURO-CARE-4; however, no variation in relative survival by age was found between both the groups of registries.

Differences in the case mix, i.e. in the frequency of each cancer site included in the broad category of all cancers combined, both across geographical areas and over time, can influence the interpretation of survival comparisons. In the present study, it is relevant to assess if the results reported for whole the European pool of CRs correspond to a similar survival pattern in the included European countries, or is just the average of different patterns in the different regions. For this reason, survival rates were separately analysed also for five European macro-regions (North, UK, Centre-West, South and East) and no relevant variation emerged in the survival ratios between younger and older patients. These results are not presented in the paper for the sake of brevity. However, for example, breast cancer, which had the most marked RER increase, showed trends very similar in every macro-region: in Southern Europe the RERs ranged from 1.0 to 1.65, in Central-Western Europe from 1.16 to 1.60 and in the UK from 1.27 to 1.67. There was a large increase also in Eastern and Northern Europe, but with different absolute values (from 1.09 to 1.40 and from 1.40 to 1.99, respectively).

The interpretation of time trends could be made difficult also by the variations of case mix over time. From this point of view, the largest possible bias could come from the dramatic increase of prostate cancer incidence, whose contribution of all cancers increased by 4% units from 1988 to 1999 (data not shown), while that of stomach and lung decreased by 1.7 and 1.9% units respectively. The proportion of no other single cancer changed by more than 1% of the total number of observed cancer patients. It was, therefore, decided to

exclude prostate cancer from the analysis of all cancer combined. However, as discussed above, even the inclusion or exclusion of prostate cancer did not substantially affect the results. We are, therefore, confident that no other major confounding effect can be due to the changes in case mix during the considered period.

5. Conclusions

The number of elderly people diagnosed with cancer and living with cancer will grow over the next decades due to longer life expectancy and increased survival, further highlighting the importance of research in the elderly in order to provide a culturally competent and rational management. Despite an increasing proportion of the cancer population being elderly, increases in survival continue to be more pronounced in middle-aged than elderly patients, particularly among women. Further research needs to be done to ensure elderly patients who would benefit from active treatment are identified, whereas treatment decisions based mainly on age are avoided. New high resolution studies, focusing on the elderly and taking into account possible geographical differences, may be useful to better understand the reasons for the survival disadvantage of elderly patients and to suggest ways to overcome it.

Conflict of interest statement

None declared.

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