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Original Paper

Variation in Survival of Patients with Prostate Cancer in Europe Since 1978

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Since the incidence of prostate cancer has increased considerably over the past two decades in most European countries, knowledge of the variation in survival is pertinent. The collaboration across Europe in the EUROCARE study has now been extended to 45 registries in 17 countries. We report on variation in relative survival according to age of 65 728 patients diagnosed with prostate cancer between 1985 and 1989 and also explore time trends since 1978 for most countries. Considerable variation in survival was found within and between countries, with the highest survival in Switzerland (5-year relative survival 72%), followed by Germany (67%) and the Nordic countries (except Denmark). The lowest survival was found in Estonia (39%), preceded by Slovenia (40%), Denmark (41%) and England (45%). Between 1978 and 1986, relative survival barely changed over time, but it improved from 55% (95% confidence interval [CI] 53–57) during 1984–1986 to 59% (CI 56–61) during 1987–1989. A small but unexpected deterioration of survival for patients aged between 45 and 54 years from 61% to 56% was observed in the early 1980s. It is likely that variation in both detection methods and treatment plays a role in the observed variation in survival, but more information is needed to assess each contribution. © 1998 Elsevier Science Ltd. All rights reserved.

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INTRODUCTION

In Most European countries, the incidence of prostate cancer has increased more than any other cancer over the past two decades [1]. Prostate cancer is mainly a cancer of old age. Being very uncommon in the young, the annual incidence increases steeply after the age of 50 years to 1 per 100 men aged 80 years and over. A very high prevalence of so-called 'latent' prostate cancer (of up to 40% at the age of 70 years) was found in various autopsy studies of men who had no clinical diagnosis or suspicion of prostate cancer before death [2]. An increasing proportion of these latent cancers has been detected due to the increased use of transurethral resection of the prostate (TURP). Application of this surgical procedure for the treatment of symptoms of benign prostatic hyperplasia

results in the unexpected diagnosis of prostate cancer in approximately 10% of cases [3]. Since increased detection of subclinical cases not only results in an increase in the incidence [4], but also in improved survival [5], access to this surgical procedure in a region is an important determinant of the prognosis. Increased detection of insignificant tumours may be accelerated by the introduction of improved diagnostic techniques, such as transrectal ultrasound, ultrasound guided biopsy and prostate-specific antigen (PSA) testing (length time bias). Moreover, the diagnosis of prostate cancer following a positive PSA test appears to advance the diagnosis by up to 5-10 years [6], resulting in improved survival as well (lead-time bias). Stage at diagnosis is an important determinant of prognosis. Once the disease has metastasised, cure is no longer possible and treatment is directed primarily at relief of symptoms. If prostate cancer is detected at an early stage, curative treatment by radical prostatectomy [7] or radiotherapy [8] is possible. However, surveillance appears to provide similar results for patients with low-grade

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^{*}The EUROCARE Working Group for this study is listed in the Appendix.

Table 1. Data quality by country for patients with prostate cancer (EUROCARE II)

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	% DCO	% HV	% Lost to follow-up
Northern Europe			
Iceland	0.2	93	0
Finland	0.5	97	0.02
Sweden*	0	99	0
Denmark	0	92	0
U.K.			
Scotland	2.3	84	0
England	7.1	73	0.1
Western and Central Eu	rope		
The Netherlands*	0	98	1.8
Germany*	2.4	91	0
Austria*	1.5	83	0
Switzerland*	0.3	99	11
France*	0	97	0.4
Southern Europe			
Spain*	15	89	0
Italy*	3.6	79	0.6
Eastern Europe			
Slovenia	6.7	84	0.1
Slovakia	8.1	81	0
Poland*	0.9	60	7.1
Estonia	0.1	66	0.7
Europe	4.6	83	0.1

^{*&}lt;20% of the national population covered. DCO, death certificate only; HV, histologically verified.

tumours [9, 10]. There is no consensus about the usefulness of screening for prostate cancer. Large trials that address this issue are currently under way in the U.S.A. and Europe [11].

Meanwhile, the incidence, mainly of low-grade cancer, has increased in several European countries following the introduction of opportunistic PSA testing [12, 13]. Since there was no report on prostate cancer in the first part of the EUROCARE study [14], this is the first report on survival of prostate cancer across Europe. The collaboration across Europe in the EUROCARE study has now been extended to 45 registries in 17 countries that have accumulated data on 3.5 million new patients, most of them diagnosed between 1978 and 1992. We now report on variation in relative survival of patients with prostate cancer according to age from 1985 to 1989 and we also explore time trends since 1978 for most countries.

PATIENTS AND METHODS

Survival analysis was carried out on prostate cancer cases diagnosed between 1985 and 1989 in 17 countries recorded in 40 population-based registries. Some of these (in Finland, Denmark, Estonia, Slovenia, Iceland, Scotland, Slovakia) cover the whole country, some a large proportion (England) and the rest up to 20% (Sweden, The Netherlands, Germany, Austria, Switzerland, France, Italy, Spain, Poland). Cases discovered at autopsy (1.5%), patients known on the basis of a death certificate only (DCO) (4.6%) or patients first diagnosed with another tumour were not included (Table 1). The protocol specified a minimum follow-up of 5 years. With respect to time trends, the following 3-year periods were used: 1978-1980, 1981-1983, 1984-1986, and 1987-1989. Age-specific survival was calculated for the following age groups: 55-64, 65-74 and 75-84 years of age. Relative survival was computed as the ratio between the observed (crude) survival and the expected survival, derived from general mortality data [15]. Age-standardised survival could not be

Table 2. Number of patients with prostate cancer diagnosed between 1985 and 1989 in Europe by age group and country (EUROCAREII)

	Age (years)					T '1 105	
	15–54	55-64	65–74	75–84	85–99	Total	Incidence per 10 ⁵ in 1983–1987†
Northern Europe							
Iceland	6	73	147	165	47	438	52
Finland	94	853	2101	2138	380	5566	36
Sweden*	41	436	1338	1473	292	3580	50
Denmark	102	817	2597	2773	650	6939	30
U.K.							
Scotland	85	638	2137	2159	457	5476	28
England	375	3213	10 202	11 423	2398	27 611	23
Western and Central Europe							
The Netherlands*	22	130	312	285	70	819	29
Germany*	32	190	373	386	54	1035	29
Austria*	3	49	130	163	19	364	52‡
Switzerland*	16	129	391	433	103	1072	51
France*	34	332	755	869	163	2153	32
Southern Europe							
Spain*	31	234	670	738	133	1806	27
Italy*	72	531	1496	1619	274	3992	26
Eastern Europe							
Slovenia	23	142	359	446	42	1012	19
Slovakia	70	508	1004	1031	112	2725	20
Poland*	13	105	167	127	25	437	12
Estonia	23	121	295	243	21	703	19
Europe	1042	8501	24 474	26 471	5240	65 728	_

^{*&}lt;20% of the national population covered. †World Standardised Rate, adapted from Parkin and associates [26]. ‡Incidence in 1988–1992.

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calculated for Iceland, The Netherlands and Poland because, in the data of these registries, one of the age strata contained no cases. General European estimates of survival were weighted according to the national incidence (reflecting the size of the population). Survival trends were also computed as weighted rates. Changes in relative survival over time were calculated for the following age groups: 15–44, 45–54, 65–74 and 75–99 years of age. Only data from registries that could provide data for the entire period 1978–1989 were used for these calculations. Standard errors of survival, used for calculation of 95% confidence intervals, were calculated according to Greenwood's method [16].

RESULTS

Survival rates (age-standardised) within each country (including overall EU data)

The number of patients with prostate cancer in the EUROCARE database was 65 728, of which 15% was below 65 years of age and 48% was aged 75 years or older (Table 2). Considerable variation in survival was observed between countries, which was apparent by 1 year (Figure 1). Patients diagnosed in Switzerland had the highest survival (5-year relative survival 72%) followed by Germany and the Nordic countries, except Denmark. The lowest survival was observed in Estonia (39%), preceded by Slovenia and Denmark. Within Spain, Italy and France a geographical variation between different registries of up to 20% emerged, whilst hardly any variation in survival was found within England (data not shown; see EUROCARE II monograph [17]).

Table 3. Age-specific relative survival of patients with prostate cancer in Europe, 1985–1989 (EUROCARE II)

	% Relative survival						
	55–64 years		65–74	years	75-84 years		
	1-year	5-year	1-year	5-year	1-year	5-year	
Northern Europe							
Iceland	98	77	93	70	90	60	
Finland	92	58	93	64	89	63	
Sweden*	95	66	94	68	91	64	
Denmark	87	40	87	45	80	39	
U.K.							
Scotland	88	54	83	50	77	45	
England	86	48	83	46	76	44	
Western and Central Eu	ırope						
The Netherlands*	86	58	93	66	86	46	
Germany*	94	71	91	73	87	58	
Austria*	89	72	95	64	78	48	
Switzerland*	95	64	94	73	92	77	
France*	90	58	92	68	85	56	
Southern Europe							
Spain*	86	54	87	50	81	45	
Italy*	88	55	87	53	78	43	
Eastern Europe							
Slovenia	81	43	75	41	74	41	
Slovakia	84	52	80	55	75	64	
Poland*	74	43	71	42	60	25	
Estonia	75	33	74	40	68	41	
Europe	89	58	88	60	82	51	

^{*&}lt;20% of the national population covered.

Table 4. Change in 5-year relative survival of patients with prostate cancer in Europe over time by age group (years), 1978–1989 (EUROCARE II)

	15–44 %	45–54 %	55–64 %	65–74 %	75–99 %	All* % (95% CI)
1978–1980	56	61	57	52	61	56 (53–59)
1981-1983	47	56	61	53	43	55 (53–58)
1984–1986	49	58	60	50	48	55 (53–57)
1987–1989	57	60	61	55	59	59 (56–61)

^{*}Age-standardised; CI, confidence interval.

Survival rates according to age distribution for each country

Taking all participating countries together, relative 5-year survival of patients aged between 55 and 64 years was slightly lower than those aged between 65 and 74 years (58% versus 60%), whereas survival of patients aged between 75 and 84 years was substantially lower (51%) (Table 3). The lower survival for the ages 55–64 years, generally apparent within 1 year, was observed in most countries, except Iceland, the U.K., Italy and Slovenia. Five-year relative survival for patients aged between 75 and 84 years was, by far, the lowest in Poland (25%), and the highest in Switzerland (77%), followed by Sweden and Slovakia (both 64%).

Change in survival over time 1978–1989 for each country

Overall, survival barely changed before 1986. Only between 1984–1986 and 1987–1989 a modest but significant improvement was observed from 55% (95% confidence interval (CI) 53–57) to 59% (CI 56–61) and was mainly due to an improvement for patients aged 65 years or older (Table 4). This improvement occurred predominantly in France, Italy and Estonia and to a lesser extent in Sweden,

Table 5. Change in age-standardised 5-year relative survival of patients with prostate cancer for each country† in Europe, 1978–1989 (EUROCARE II)

	% Survival						
	1978–1980	1981–1983	1984–1986	1987–1989			
Northern Europe							
Iceland	55	61	65	66			
Finland	55	56	60	63			
Sweden*	60	60	62	67			
Denmark	40	38	41	40			
U.K.							
Scotland	44	43	44	49			
England	44	44	46	43			
Western and Central	Europe						
The Netherlands*	52	60	55	56			
Germany*	72	70	64	68			
Switzerland*	55	49	60	60			
France*	56	50	54	69			
Italy*	39	46	46	53			
Eastern Europe							
Poland*	29	_	44	33			
Estonia	35	31	32	43			
Europe	56	55	55	59			

^{*&}lt;20% of the national population covered. †Excludes Austria, Spain, Slovenia and Slovakia, where registries did not contribute data for the whole period 1978–1989.

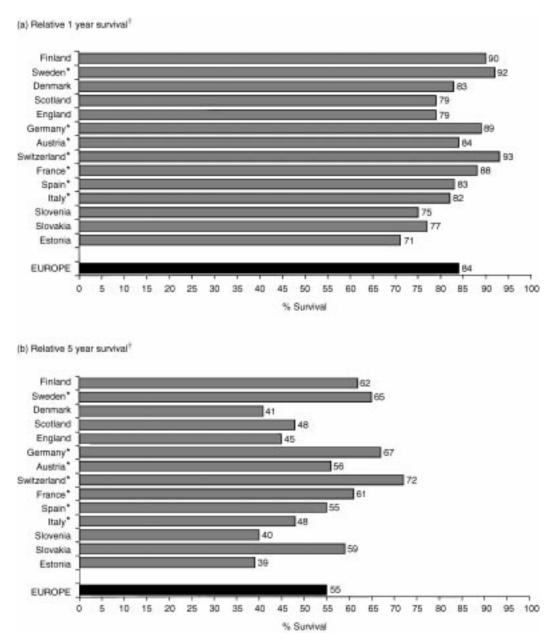


Figure 1. Relative 1-year (a) and 5-year (b) survival rates (age-standardised) for prostate cancer patients, 1985-1989. *<20% of the national population covered. †Age-standardised survival could not be calculated for Iceland, The Netherlands and Poland because one of the age strata contained no cases (EUROCARE II).

Scotland and Germany (Table 5). Between 1978 and 1983, survival had already improved in Iceland, Finland and Italy. Relative survival of patients under the age of 55 years deteriorated unexpectedly in the early 1980s (Table 4), followed by a return to the initial value during 1987–1989.

DISCUSSION

Considerable variation was observed in survival of patients with prostate cancer in Europe. The lowest rates were found in East European countries (except Slovakia) and the U.K., the highest in Switzerland and the Nordic countries (except Denmark). The very high survival in Switzerland may be biased due to the high proportion that was lost to follow-up (11%) and due to emigration of patients [17]. Barriers to specialised care, resulting in delayed diagnosis, probably played a role in the lower survival in Eastern countries.

Delayed diagnosis may also be caused by hesitance to consult a physician due to limited awareness of prostate cancer among the general public. However, international differences in how and when to treat prostate cancer may also result in variation in survival. Increased inclusion of insignificant cases (e.g. detected unexpectedly by TURP) results in spuriously improved survival rates [5]). Similar mortality rates for prostate cancer in the Nordic countries, but strikingly lower survival in Denmark could be explained by the rather reserved attitude of Danish physicians, which appears to result in limited diagnosis of asymptomatic prostate cancer cases [18]. In Table 6, variation in survival is shown in relation to agestandardised incidence for most participating countries. Countries at high incidence also exhibit relatively high survival, suggesting more intensive diagnostic activity, leading to earlier stages. The low incidence and survival

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Table 6. Incidence (world standardised rate), adapted from three volumes of Cancer Incidence in Five Continents [25–27] in relation to survival (H > 50%; L < 50%; M = 50%)

	Incidenc	Relative survival			
	1978–1982	1983–1987	1988–1992	1981–1983	1987–1989
Northern Europe					
Iceland	36.2	52.4	61.0	H	H
Finland	34.2	36.1	41.3	H	H
Sweden	45.9	50.2	55.3	H	H
Denmark	27.7	29.9	31.0	L	L
U.K.					
Scotland	23.3	27.8	31.2	L	L
England	20.9	23.1	28.0	L	L
Western and Central Europe					
The Netherlands (Eindhoven)	28.3	29.9	35.6	H	H
Germany (Saarland)	28.7	28.9	35.9	H	H
Austria	_	_	51.6	_	H
Switzerland	50	51	50	M	H
France (Calvados)	26.8	31.8	50.5	M	H
Southern Europe					
Spain (Navarra)	20.5	26.8	27.2	_	H
Italy (Varese)	20.3	25.5	28.2	L	Н
Eastern Europe					
Slovenia	18.7	18.6	20.7	_	L
Slovakia	15.8	19.9	22.0	_	L
Poland (Warsaw)	11.5	11.9	15.7	L	L
Estonia	_	18.8	21.6	L	L

rates in the Eastern countries may also indicate that the incidence only represented symptomatic cases. Although variation in the occurrence of co-morbidity influences survival [19], using relative survival (so correcting for expected survival) should have removed most of this variation [15]. Differences in treatment may explain part of the variation in survival. Along with the reserved attitude of Danish physicians with respect to diagnosis, only a minority of patients receive curative treatment in Denmark [20]. In the U.K., radical prostatectomy has been advocated only for a small minority of patients [21]. Although early diagnosis makes curative treatment (radical prostatectomy or radiotherapy) accessible, the benefit of treatment, especially for low-grade tumours, is not undisputed [10]. Interpretation of the international variation in survival is difficult without proper information on the differences in the proportion of insignificant tumours, stage at diagnosis and treatment. Standardised monitoring of staging procedures, tumour characteristics and treatment by registries participating in the EUROCARE study should provide a better understanding of the observed differences in survival.

Overall, survival of prostate cancer patients barely changed in Europe. In Sweden, a marked improvement in survival was observed between 1960 and 1980, which was attributed largely to increased diagnosis of insignificant ('non-lethal') cases [5]. A similar improvement might have occurred in other European countries between 1960 and 1980, but this time period was not included in the EUROCARE study. We observed only a modest improvement between 1978 and 1989, in contrast to the U.S.A., where 5-year relative survival improved from 71% in 1978 to 83% in 1987 [22]. Therefore, increased diagnosis of insignificant tumours seems to play a limited role only in Europe in the time period studied. Relative survival did not improve in the age band 45–54 years, as

might have been expected, but even deteriorated (transiently) in the early 1980s. A large increase in incidence under the age of 60 years was reported for Southeastern Netherlands and East Anglia (U.K.) without an improvement in prognosis [23]. Multivariate analyses of mortality between 1955 and 1992 revealed an increasing risk for consecutive birth cohorts for men born around 1930 in most European countries (except France and Italy) [24]. However, the assumption of an increased risk of fatal prostate cancer has not yet been supported by evidence of a specific risk factor.

In conclusion, a large variation in survival was observed within Europe, for which the role of early diagnosis, diagnosis of insignificant tumours and the variation in treatment is difficult to disentangle. In spite of increased awareness of prostate cancer, survival improved only modestly since 1978.

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APPENDIX

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