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Survival trends in European cancer patients diagnosed from 1988 to 1999

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ABSTRACT

We analysed data from 49 cancer registries in 18 European countries over the period 1988–1999 to delineate time trends in cancer survival. Survival increased in Europe over the study period for all cancer sites that were considered. There were major survival increases in 5 year age-adjusted relative survival for prostate (from 58% to 79%), colon and rectum (from 48% to 54% men and women), and breast (from 74% to 83%). Improvements were also significant for stomach (from 22% to 24%), male larynx (from 62% to 64%), skin melanoma (from 78% to 83%), Hodgkin disease (from 77% to 83%), non-Hodgkin lymphoma (from 49% to 56%), leukaemias (from 37% to 42%), and for all cancers combined (from 34% to 39% in men, and from 52% to 59% in women). Survival did not change significantly for female larynx, lung, cervix or ovary. The largest increases in survival typically occurred in countries with the lowest survival, and contributed to the overall reduction of survival disparities across Europe over the study period.

Differences in the extent of PSA testing and mammographic screening, and increasing use of colonscopy and faecal blood testing together with improving cancer care are probably the major underlying reasons for the improvements in survival for cancers of prostate, breast, colon and rectum. The marked survival improvements in countries with poor survival may indicate that these countries have made efforts to adopt the new diagnostic procedures and the standardised therapeutic protocols in use in more affluent countries.

1. Introduction

EUROCARE has collected population-based data on European cancer patients since 1978, making it possible, in principle, to assess progress in cancer control in Europe over the years since then to about 2002 (latest year for which data are available). Trends in European cancer survival from 1978 to 1989 were analysed in a EUROCARE-2 paper[1] that considered data from 21 registries in 18 European countries. More recently the *period* approach[2] was applied to EUROCARE-4 data to identify survival improvements for major cancers diagnosed in Europe up to 2002; however, only

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60% of cancer registries had released data for the latest period.[3]

The aim of the present paper is to analyse survival time trends for European cancer patients for a wide range of cancer sites, over as much of the continent as possible, and over as long as time period as possible. Although a small number of European cancer registries data are available for the impressively long period of 1978 to 2002, we decided to restrict our scope to a 12-year period (1988–1999) so as to be able to include data from 49 of the 83 cancer registries participating in EUROCARE-4. These registries represent 18 countries, which are distributed widely over the continent, and most of them have been operating since at least the second half of the 1980s.

2. Materials and methods

Table 1 shows the numbers of adult (age 15 and over) cancer patients from each of the 18 countries, with contributing cancer registries, and percentages of national coverage. About 9 countries are represented by complete national data. Among those with partial registration coverage, 5 countries (Czech Republic, France, Germany, Poland and Spain) are represented by less than 10% of their populations. Survival time trends for all cancers combined and for 14 cancer sites (stomach, colon, rectum, larynx, lung, melanoma of the skin, breast, ovary, cervix, corpus uteri, prostate, Hodgkin's and non-Hodgkin's lymphomas and all leukaemias) were estimated for each country and for the European average (including all considered countries). The cancer sites were selected using topography and morphology, according to the International Classification of Diseases for Oncology, 3rd Revision (ICDO-3), as defined in.[3] These cancer sites are the same as those presented in the EUROCARE-2 analysis of European cancer survival trends.[1]

Only first primary malignant cancers were considered. Skin non-melanomas were excluded from survival estimates of all cancers combined. Cases known to registries by death certificate only or by autopsy were also excluded. The study period was divided into four 3-year intervals (diagnosis periods): 1988–1990, 1991–1993, 1994–1996 and 1997–1999.

2.1. *Statistical methods*

Time trends were derived from estimates (with 95% confidence intervals [CIs]) of age-specific and age-standardised 5 year cumulative relative survival for each country and each cancer site, by sex and diagnosis period, and also from estimates of average survival of the European pool of countries. The average survival in Europe was estimated, for each cancer site, sex and age class, by weighting region-specific survival estimates with weightings proportional to the population of the European region to which the country belonged. Five European regions were defined: Northern Europe (Denmark, Finland, Iceland, Norway and Sweden), United Kingdom (UK) and Ireland (here represented only by the English, Scottish and Welsh registries), Central Europe (Austria, Belgium, France, Germany, Netherlands and Switzerland), Eastern Europe (Czech Republic and Poland) and Southern Europe (Italy, Malta, Portugal, Slovenia and Spain). See De Angelis et al.[3] for further details of the weighting procedure. Survival

Table 1 – European adult (15–99 years) cancer patients, diagnosed from 1988 to 1999, included in the cancer survival time trend analysis by country. The second column shows the registries contributing the data, the other columns show the percentage of national registration coverage and the total number of patients analysed (all cancer sites).

Country	Cancer registry	Percentage of national coverage	Number of cases included in analysis
Austria	National	100	425,137
Czech Republic	West Bohemia	8	43,898
Denmark	National	100	315,442
Finland	National	100	232,231
France	Bas Rhin, Calvados, Cote d'Or digestive[a], Doubs, Haut Rhin, Isère, Somme, Tarn	9	173,378
Germany	Saarland	1	75,052
Iceland	National	100	11,469
Italy	Firenze, Genova, Modena, Parma, Ragusa, Romagna, Torino, Varese, Veneto	15	586,769
Netherlands	Amsterdam, Eindhoven	24	173,022
Norway	National	100	253,399
Poland	Cracow, Warsaw	6	97,585
Scotland	National	100	363,013
Slovenia	National	100	74,742
Spain	Basque country, Navarra, Tarragona	8	153,501
Sweden	National	100	472,031
Switzerland	Basel, Geneva, Grisons, St Gallen, Valais, Zurich[a]	43	85,910
England	East Anglia, Mersey, Northern and Yorkshire, Oxford, South Western, Thames, Trent, West Midlands	90	2,262,774
Wales	National	100	168,195
European pool	Pool of the 49 cancer registries listed above		5,967,548

a These registries provided data for digestive tract cancers only.

estimates were age-standardised using the method of the International Cancer Survival Standard (ICSS).[4]

For rare cancers and small cancer registry populations, data were missing for some periods. When data for 1 of the 4-diagnosis periods were missing for a given country, age-standardised relative survival was imputed using a linear regression model estimated on the 3-periods with data. If data from more than 1-period were missing, survival was not imputed, and the survival trend was not estimated for that country. Relative survival time trends were estimated, for each selected site and for all cancers combined, by sex (all ages), age (by sex), country and European average (by sex, all ages).

2.2. Testing the homogeneity of time trends

A statistical test of homogeneity was applied to the survival trends to elucidate any significant variation over time in relation to sex, age class and country. The test assumed a linear relation between the logarithm of minus, the logarithm of the relative survival and the period of diagnosis. The parameters of this linear model were estimated for both sexes, for each age group (sexes separate) and each country (sexes separate), by performing a weighted linear regression against time at diagnosis of the quantity U_i

$$U_i = \log(-\log(S_i)) = \beta_0 + \beta t_i, \qquad t_i = 0, 1, 2, 3 \tag{1}$$

where U_i is the double logarithmic transformation of S_i, S_i are the 5 year cumulative relative survival probabilities for periods i, and t_i are the categorical values representing each of the four 3-year intervals. The weights used for the regression were the inverse of the variances of U_i and are given by

$$\mathrm{var}(U_i) = \frac{\mathrm{var}[\log(S_i)]}{[\log(S_i)]^2}$$

The quantity $-\log(S_i)$ is the cumulative excess death rate at 5 years, and can be interpreted as the average *cancer* death rate over the 5 years of follow-up. This interpretation corresponds to assuming that the excess death risk observed in patients, compared to that expected in a comparable group of the general population, is totally attributable to cancer. In other words, relative survival is assumed to be a good estimator of cancer survival.

To compare improvements in survival, we used the regression Eq. (1) and tested for the homogeneity of the slopes β between sexes, age groups, and countries, by analysis of covariance. The results of the homogeneity tests are shown in Table 2.

2.3. Time trends by sex

Trends of age-standardised relative survival in Europe are presented separately for men and women. Differences between sex-specific trends were assessed by estimating the linear trend slopes by sex and testing for homogeneity as described above.

2.4. Time trends by age

Changes in survival for each age class in Europe were assessed as changes in relative rates of death, for 3 of the 3-

Table 2 – Results of between sex, age group and country tests for the homogeneity of linear regression slopes of the relative risk of death of European cancer cases diagnosed in 1988–1999. The null hypothesis corresponds to homogeneous time trends.

Cancer site	Homogeneity between sexes			Homogeneity between age classes						Homogeneity between countries					
				Men			Women			Male			Women		
	χ^2	*dof*	P value	χ^2	*dof*	P value	χ^2	*dof*	P value	χ^2	*dof*	P value	χ^2	*dof*	P value
Stomach	0.4	1	0.55	5.7	4	0.23	5.7	4	0.23	23.2	17	0.14	47.9	16	<0.01
Colon	0.2	1	0.65	2.4	4	0.66	10.5	4	0.03	41.0	17	<0.01	69.2	17	<0.01
Rectum	0.9	1	0.35	2.4	4	0.66	6.3	4	0.18	35.5	16	<0.01	27.5	16	0.04
Colon and rectum	1.5	1	0.23	3.4	4	0.49	10.6	4	0.03	64.4	17	<0.01	73.0	17	<0.01
Larynx	1.6	1	0.20	6.4	4	0.17	3.7	4	0.45	24.9	16	0.07	6.6	12	0.88
Lung	2.3	1	0.13	3.4	4	0.49	4.4	4	0.36	68.1	17	<0.01	51.8	16	<0.01
Melanoma of skin	0.1	1	0.80	10.5	4	0.03	2.2	4	0.69	63.9	16	<0.01	28.3	17	0.04
Breast (female)	–	–	–	–	–	–	204.1	4	<0.01	–	–	–	78.6	17	<0.01
Cervix	–	–	–	–	–	–	18.1	4	<0.01	–	–	–	46.7	17	<0.01
Corpus uteri	–	–	–	–	–	–	3.8	4	0.43	–	–	–	31.9	17	0.02
Ovary	–	–	–	–	–	–	19.5	4	<0.01	–	–	–	28.7	16	0.03
Prostate	–	–	–	265.3	4	<0.01	–	–	–	180.7	17	<0.01	–	–	–
Non-Hodgkin lymphoma	1.2	1	0.28	25.0	4	<0.01	2.2	4	0.69	43.0	17	<0.01	40.7	17	<0.01
Hodgkin disease	0.2	1	0.63	5.3	4	0.26	13.8	4	0.01	12.2	9	0.20	6.6	14	0.95
Leukaemia	0.7	1	0.39	11.6	4	0.02	17.1	4	<0.01	86.3	17	<0.01	47.5	17	<0.01
All cancers	42.9	1	<0.01	85.7	4	<0.01	340.0	4	<0.01	317.0	17	<0.01	330.8	17	<0.01

dof, degrees of freedom and –, not applicable.

year periods, compared to the first period (1988–1990). The relative excess risk of death RR_i for each period t_i was obtained from

$$RR_i = \frac{\log(S_i)}{\log(S_0)}, \qquad i = 1, 2, 3$$

2.5. Time trends by country

We used model-based estimates of relative survival time trends by country, in order to smooth their random variability. A measure of overall sex- and country-specific improvement in cancer death rate over the study period is obtained from the predicted value, T, of the logarithm of the relative excess risk of death of the last period relative to the first (RR_3). For each sex, country-specific estimates of T and their variances v were obtained from regression Eq. (1) of log(–log(S)) against period of diagnosis

$$T = \log(RR_3) = \log\left[\frac{\log(S_3)}{\log(S_0)}\right] = \beta t_3 = 3\beta \qquad (2)$$

Indicating with T_j the country-specific estimate of T for country j, a pooled trend estimate $\overline{T}$ was calculated as the weighted mean of the country-specific values

$$\overline{T} = \frac{\sum_{j=1}^{18} w_j T_j}{\sum_{j=1}^{18} w_j}$$

where $w_j = 1/v_j^2$ is the inverse of the variance of T_j.

An empirical Bayesian approach was then used to obtain a final estimate of the overall country-specific relative risk of death as the weighted average of the pooled ($\overline{T}$) and the country-specific (T_j) estimates of T

$$\hat{T}_j = \frac{v_j^2 \overline{T} + \Delta^2 T_j}{v_j^2 + \Delta^2} \qquad (3)$$

where Δ^2 is the between-country variance, estimated by a non-iterative method[5]

$$\Delta^2 = \frac{\left(\sum_{j=1}^{18} w_j (T_j - \overline{T})^2 - dof\right)}{\sum w_j - \left(\sum w_j^2 / \sum w_j\right)}$$

and *dof* is the degree of freedom, equal to the number of countries with complete data (generally 18, see Table 1) minus 1. The Bayesian estimate of change in survival provided by Eq. (3) is such that the weaker the statistical evidence for a given T_j (large country-specific variance v_j compared to estimated between-country variance Δ^2), the closer the overall country-specific estimate $\hat{T}_j$ is to the pooled estimate $\overline{T}$. If the quantity $\sum_{j=1}^{18} w_j (T_j - \overline{T})^2$ is less than *dof*, i.e. its expected value under the hypothesis of homogeneity, we considered a common estimate $(T_j = \overline{T})$ for all countries.

Relative survival for the first period (1988–1990) was estimated from the intercept β_0 of regression Eq. (1) for each sex and country. Country-specific Bayesian estimates (Eq. (3)) of the overall improvement in survival $\hat{T}_j$ were used to calculate the difference in survival between the first and the last diagnosis periods. Changes in area weighted European average survival were calculated from Eq. (3) in the same way as for each country, and are not constrained to remain within the range of estimated country-specific changes in survival.

3. Results

Table 2 shows the results of the between sex, age group, and country tests for the homogeneity of slopes of relative risk of death (β), for each considered cancer site. Time trends were usually homogeneous between the sexes, with the single exception of all cancers combined, attributable to the differing cancer case-mix between sexes. By contrast, time trends were usually significantly heterogeneous between countries, except for laryngeal and stomach sites in men, and Hodgkin's disease in both sexes. Non-homogeneity of time trends between age classes was more variable.

The main results of the time trend analyses are presented as a series of pages, 1 for each of the 14 selected cancer sites, and 1 for all cancers combined. Each page presents 5 graphs. The *top graph* shows trends in European average 5 year relative survival for the specific cancer site, for men and women separately, for each of the 4-diagnosis periods. The continuous line indicates the time trend for both sexes combined.

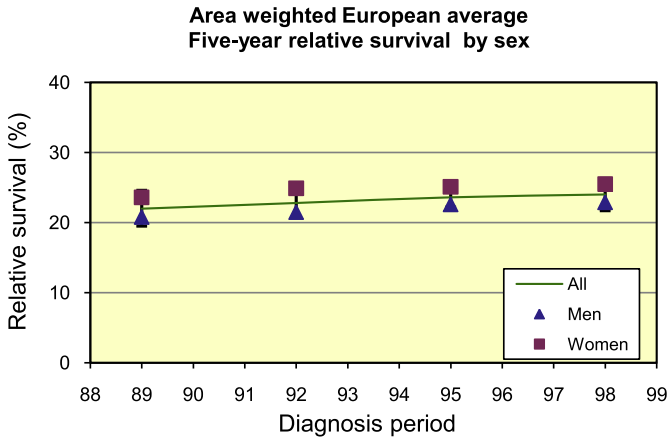
The *middle graphs* on each page show the estimated excess risk of death RR_i for men (left) and women (right) according to age at diagnosis. The excess risk of death for each age class (15–44, 45–54, 55–64, 65–74 and 75–99 years) is represented as an individual point. The continuous line represents the crude excess risk of death for all age groups, with the corresponding 95% CIs.

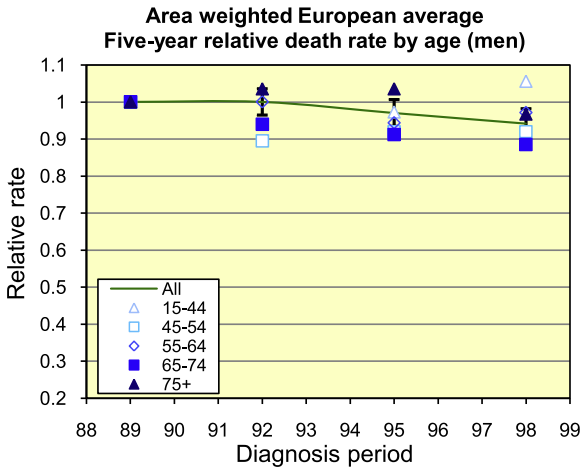
The *bottom graphs* on the page present 5 year age-adjusted estimated relative survival changes by country for men (left) and women (right) separately. The countries, plus the European average labelled as Europe, are ordered by relative survival in 1988–1990, with lowest at the top and highest at the bottom. The complete bar for each country indicates survival in the last period (1997–1999), and the coloured portion indicates survival in the first period (1988–1990); the number by the bar indicates the absolute difference in percentage points between survival in the first and in the last period, obtained by linear modelling and empirical Bayesian smoothing.

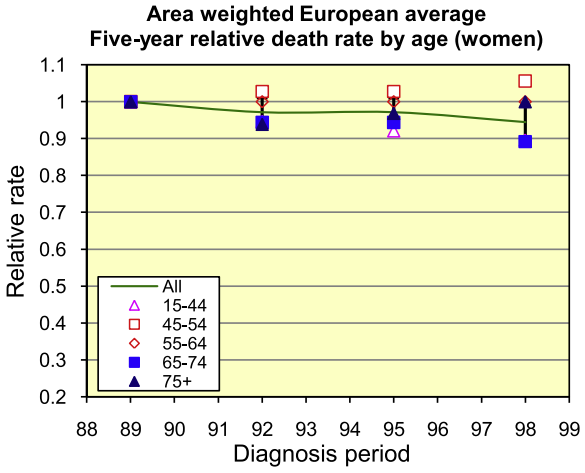
3.1. Digestive tract

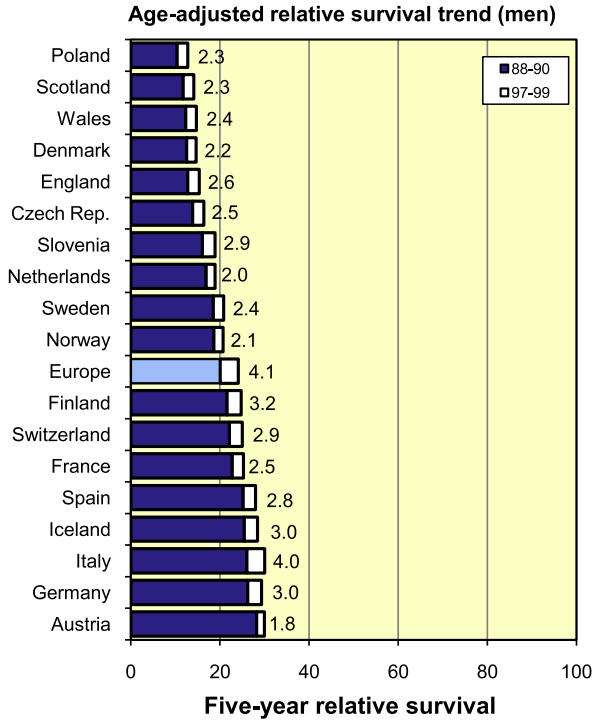
Average European survival for stomach cancer increased uniformly in both sexes over the study period, but remained poor, at around 25%. The relative risk of death for stomach cancer declined with age, although the test for homogeneity was not significant (Table 2). Both survival (in the latest period) and the survival increase varied with country for men (ranges 12–30% for survival and 1.8–4.1% for survival increase)

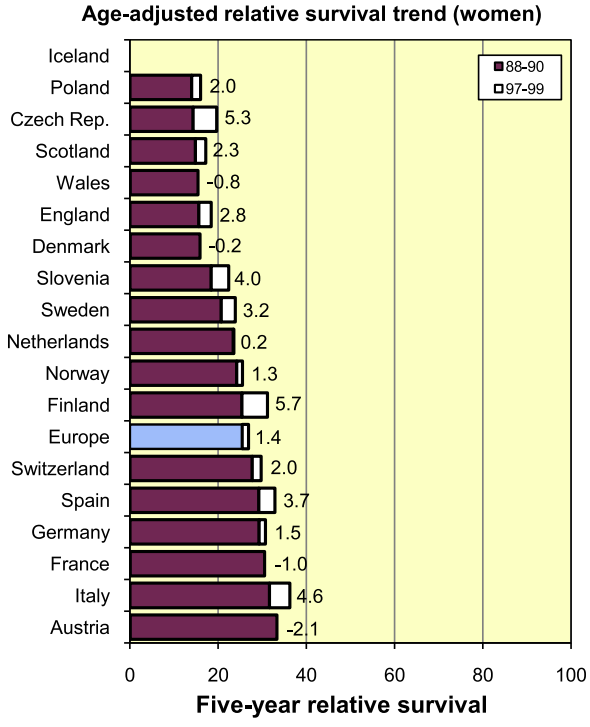
STOMACH


Area weighted European average
Five-year relative survival by sex
Relative survival (%)
Diagnosis period
All
Men
Women

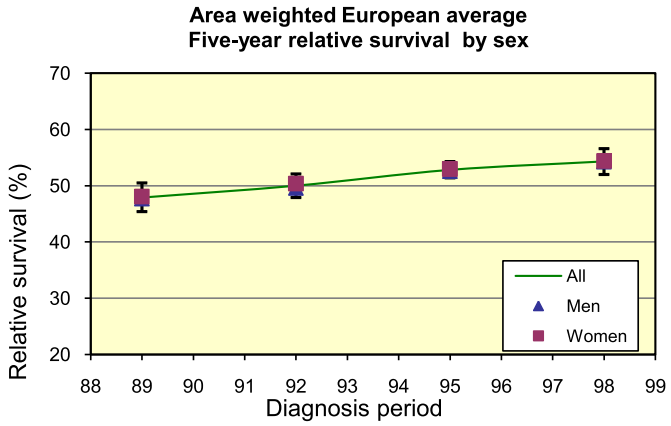

Area weighted European average
Five-year relative death rate by age (men)
Relative rate
Diagnosis period
All
15-44
45-54
55-64
65-74
75+

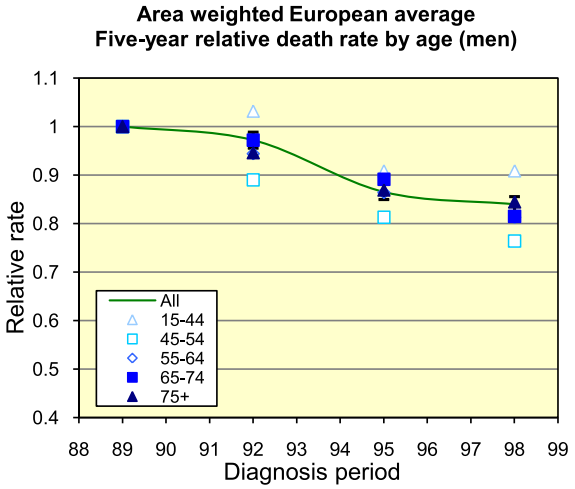

Area weighted European average
Five-year relative death rate by age (women)
Relative rate
Diagnosis period
All
15-44
45-54
55-64
65-74
75+

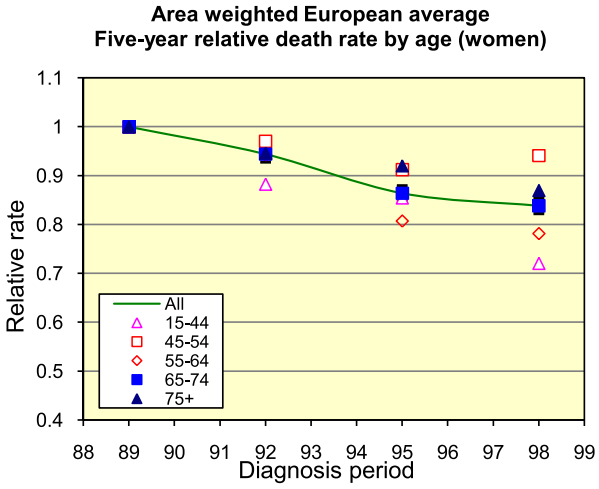

Age-adjusted relative survival trend (men)
88-90
97-99
Poland 2.3
Scotland 2.3
Wales 2.4
Denmark 2.2
England 2.6
Czech Rep. 2.5
Slovenia 2.9
Netherlands 2.0
Sweden 2.4
Norway 2.1
Europe 4.1
Finland 3.2
Switzerland 2.9
France 2.5
Spain 2.8
Iceland 3.0
Italy 4.0
Germany 3.0
Austria 1.8
Five-year relative survival

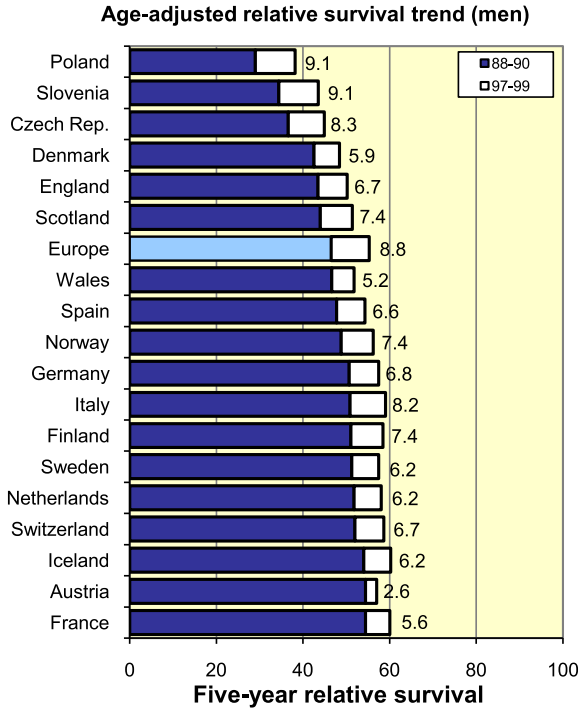

Age-adjusted relative survival trend (women)
88-90
97-99
Iceland
Poland 2.0
Czech Rep. 5.3
Scotland 2.3
Wales -0.8
England 2.8
Denmark -0.2
Slovenia 4.0
Sweden 3.2
Netherlands 0.2
Norway 1.3
Finland 5.7
Europe 1.4
Switzerland 2.0
Spain 3.7
Germany 1.5
France -1.0
Italy 4.6
Austria -2.1
Five-year relative survival

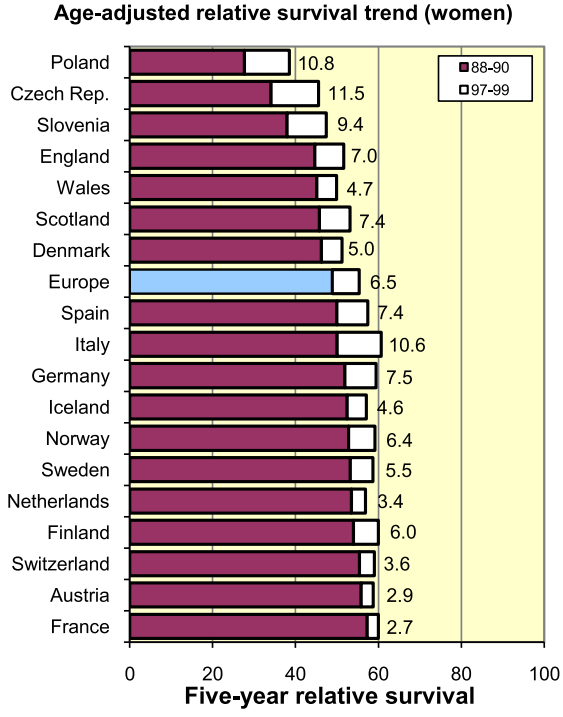
COLON


Area weighted European average
Five-year relative survival by sex
Relative survival (%)
70
60
50
40
30
20
88 89 90 91 92 93 94 95 96 97 98 99
Diagnosis period
All
Men
Women

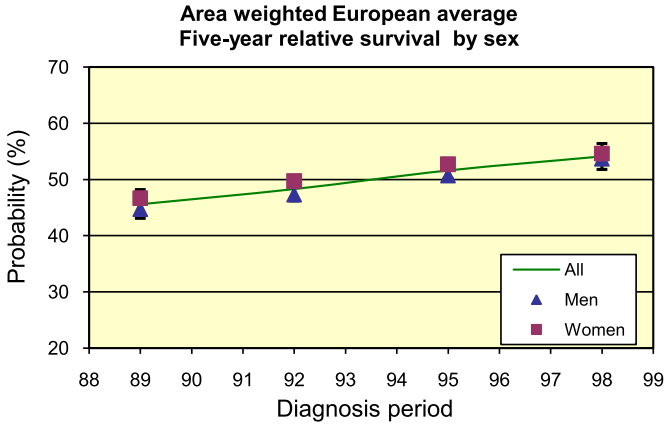

Area weighted European average
Five-year relative death rate by age (men)
Relative rate
1.1
1
0.9
0.8
0.7
0.6
0.5
0.4
88 89 90 91 92 93 94 95 96 97 98 99
Diagnosis period
All
15-44
45-54
55-64
65-74
75+

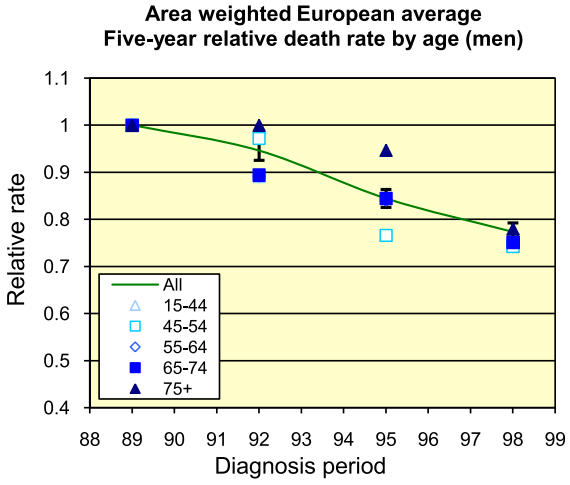

Area weighted European average
Five-year relative death rate by age (women)
Relative rate
1.1
1
0.9
0.8
0.7
0.6
0.5
0.4
88 89 90 91 92 93 94 95 96 97 98 99
Diagnosis period
All
15-44
45-54
55-64
65-74
75+

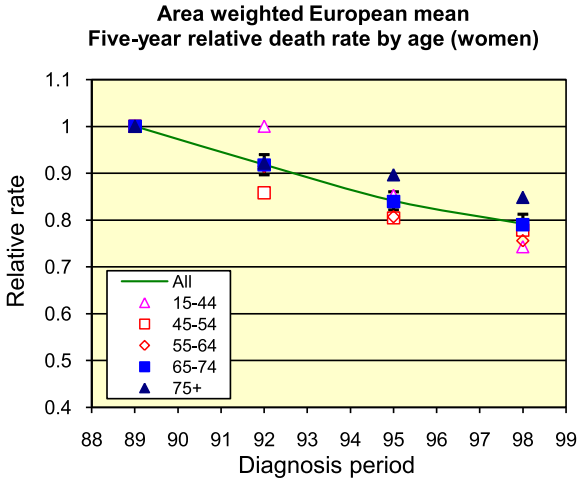

Age-adjusted relative survival trend (men)
88-90
97-99
Poland 9.1
Slovenia 9.1
Czech Rep. 8.3
Denmark 5.9
England 6.7
Scotland 7.4
Europe 8.8
Wales 5.2
Spain 6.6
Norway 7.4
Germany 6.8
Italy 8.2
Finland 7.4
Sweden 6.2
Netherlands 6.2
Switzerland 6.7
Iceland 6.2
Austria 2.6
France 5.6
0 20 40 60 80 100
Five-year relative survival

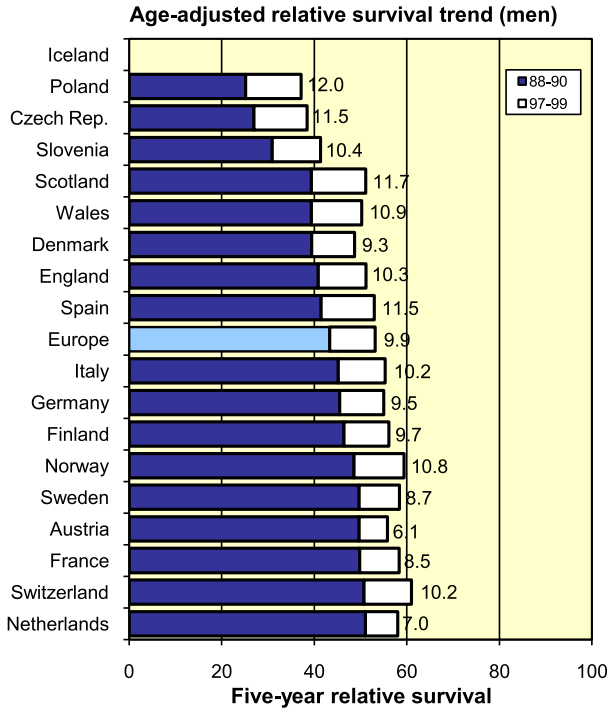

Age-adjusted relative survival trend (women)
88-90
97-99
Poland 10.8
Czech Rep. 11.5
Slovenia 9.4
England 7.0
Wales 4.7
Scotland 7.4
Denmark 5.0
Europe 6.5
Spain 7.4
Italy 10.6
Germany 7.5
Iceland 4.6
Norway 6.4
Sweden 5.5
Netherlands 3.4
Finland 6.0
Switzerland 3.6
Austria 2.9
France 2.7
0 20 40 60 80 100
Five-year relative survival

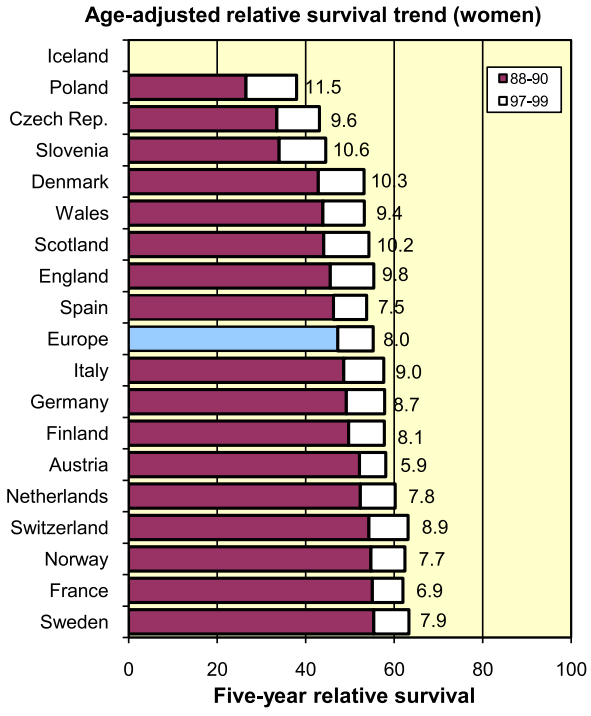
RECTUM


Area weighted European average
Five-year relative survival by sex
Probability (%)
70
60
50
40
30
20
88 89 90 91 92 93 94 95 96 97 98 99
Diagnosis period
All
Men
Women

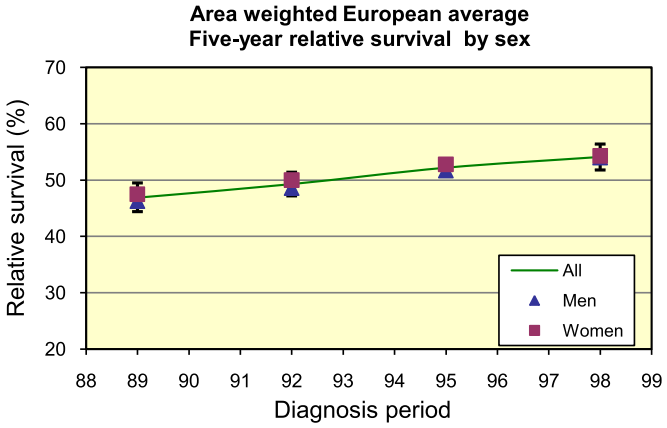

Area weighted European average
Five-year relative death rate by age (men)
Relative rate
1.1
1
0.9
0.8
0.7
0.6
0.5
0.4
88 89 90 91 92 93 94 95 96 97 98 99
Diagnosis period
All
15-44
45-54
55-64
65-74
75+

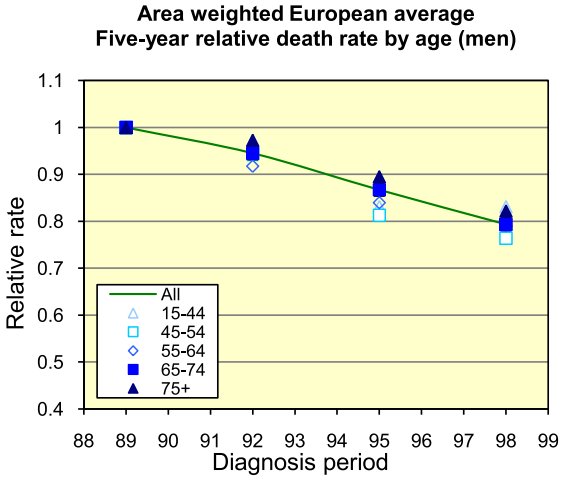

Area weighted European mean
Five-year relative death rate by age (women)
Relative rate
1.1
1
0.9
0.8
0.7
0.6
0.5
0.4
88 89 90 91 92 93 94 95 96 97 98 99
Diagnosis period
All
15-44
45-54
55-64
65-74
75+

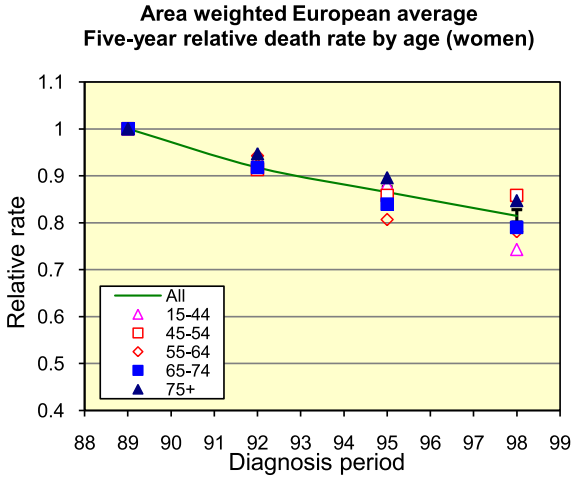

Age-adjusted relative survival trend (men)
Iceland
Poland 12.0
Czech Rep. 11.5
Slovenia 10.4
Scotland 11.7
Wales 10.9
Denmark 9.3
England 10.3
Spain 11.5
Europe 9.9
Italy 10.2
Germany 9.5
Finland 9.7
Norway 10.8
Sweden 8.7
Austria 6.1
France 8.5
Switzerland 10.2
Netherlands 7.0
88-90
97-99
0 20 40 60 80 100
Five-year relative survival

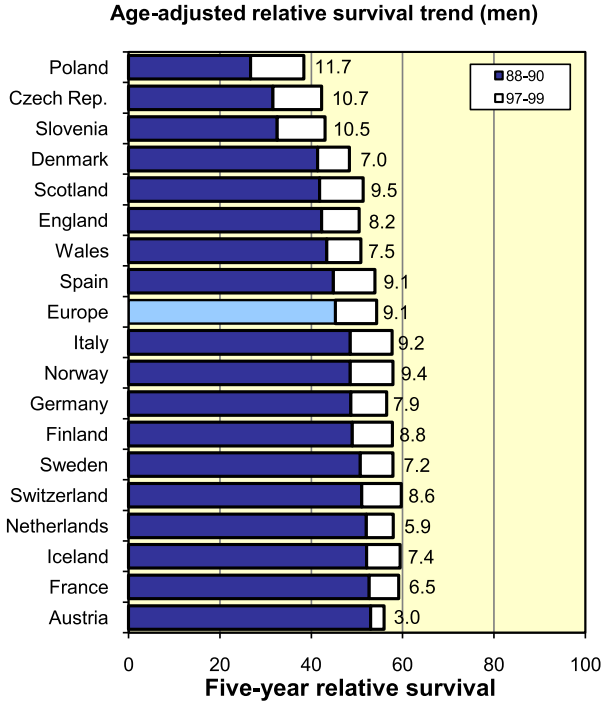

Age-adjusted relative survival trend (women)
Iceland
Poland 11.5
Czech Rep. 9.6
Slovenia 10.6
Denmark 10.3
Wales 9.4
Scotland 10.2
England 9.8
Spain 7.5
Europe 8.0
Italy 9.0
Germany 8.7
Finland 8.1
Austria 5.9
Netherlands 7.8
Switzerland 8.9
Norway 7.7
France 6.9
Sweden 7.9
88-90
97-99
0 20 40 60 80 100
Five-year relative survival

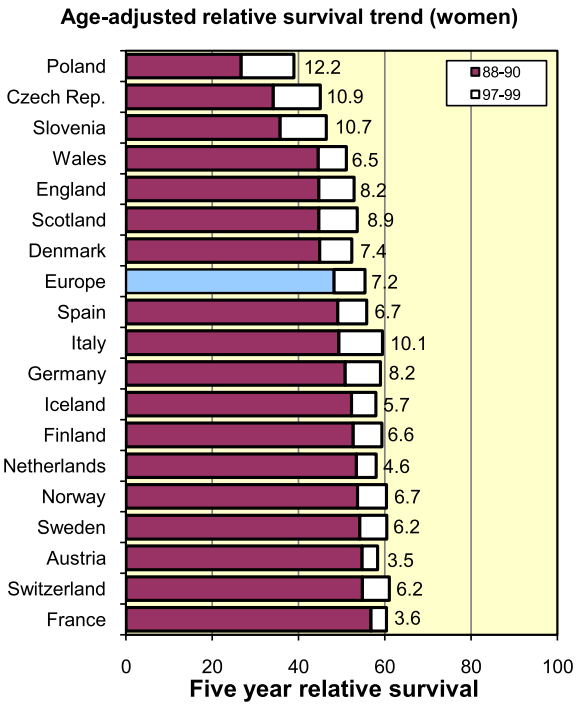
COLON AND RECTUM



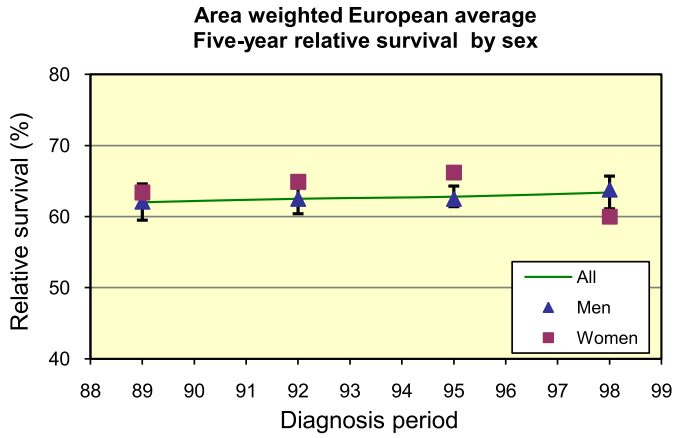


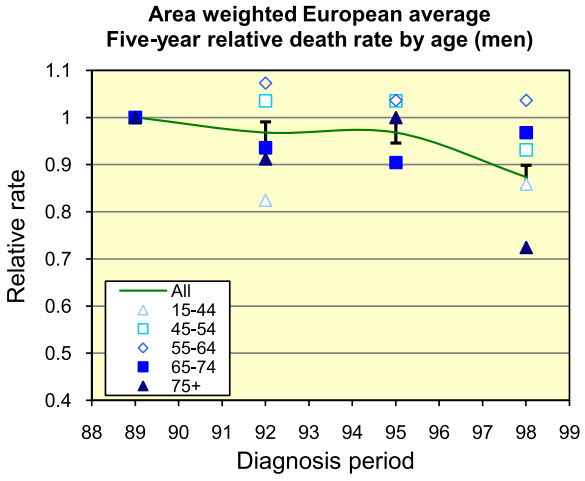


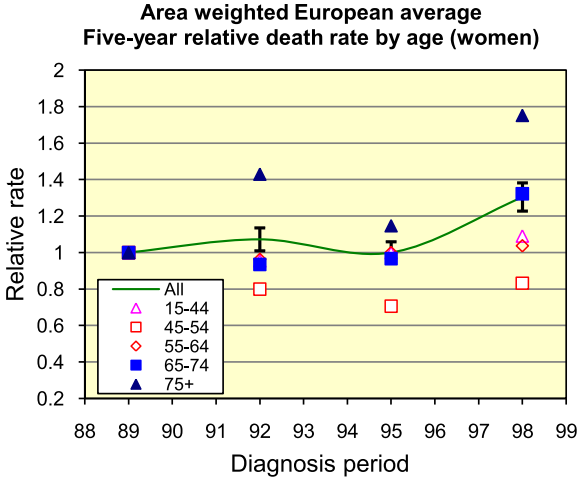


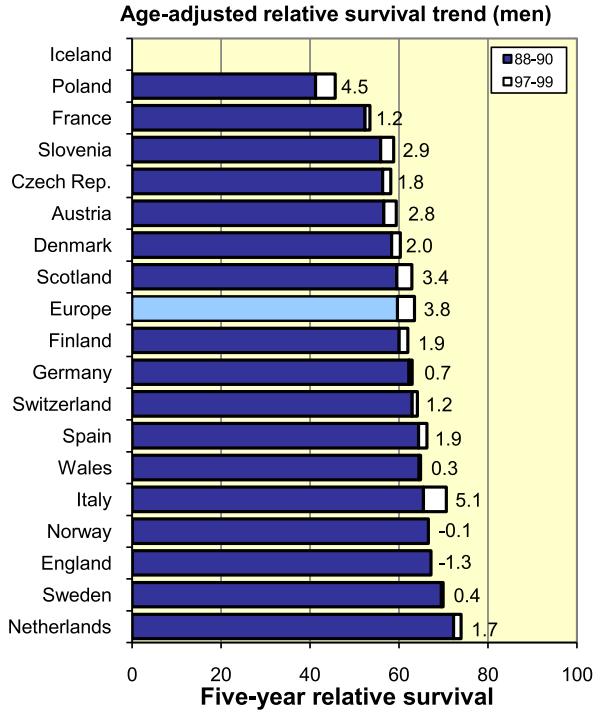


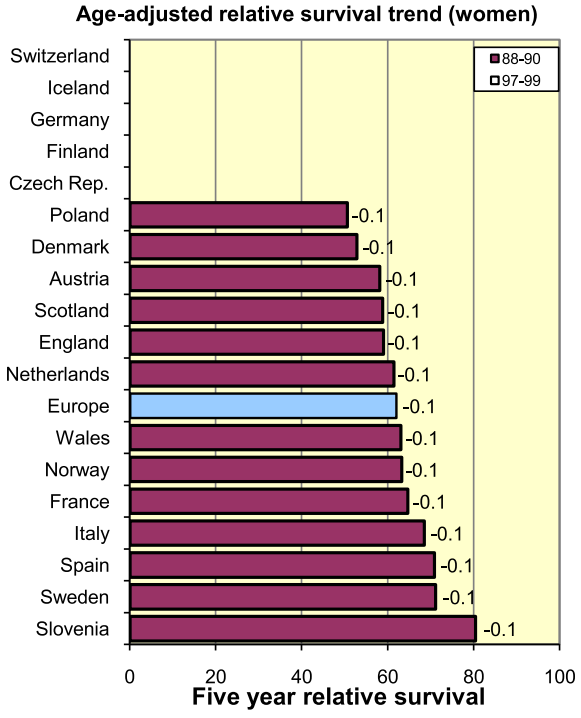
LARYNX


Area weighted European average
Five-year relative survival by sex
Relative survival (%)
80
70
60
50
40
88 89 90 91 92 93 94 95 96 97 98 99
Diagnosis period
All
Men
Women

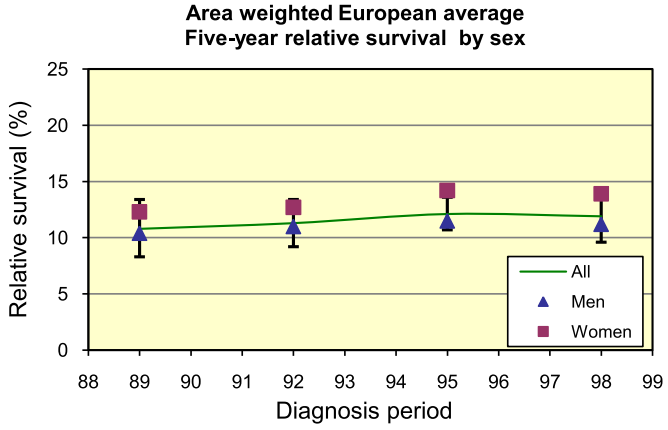

Area weighted European average
Five-year relative death rate by age (men)
Relative rate
1.1
1
0.9
0.8
0.7
0.6
0.5
0.4
88 89 90 91 92 93 94 95 96 97 98 99
Diagnosis period
All
15-44
45-54
55-64
65-74
75+

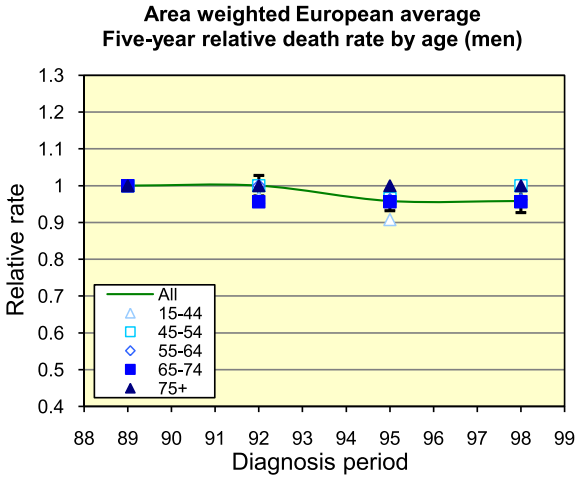

Area weighted European average
Five-year relative death rate by age (women)
Relative rate
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
88 89 90 91 92 93 94 95 96 97 98 99
Diagnosis period
All
15-44
45-54
55-64
65-74
75+

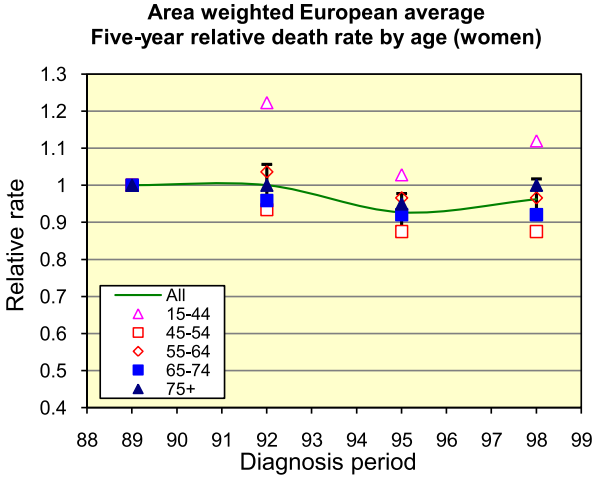

Age-adjusted relative survival trend (men)
88-90
97-99
Iceland
Poland 4.5
France 1.2
Slovenia 2.9
Czech Rep. 1.8
Austria 2.8
Denmark 2.0
Scotland 3.4
Europe 3.8
Finland 1.9
Germany 0.7
Switzerland 1.2
Spain 1.9
Wales 0.3
Italy 5.1
Norway -0.1
England -1.3
Sweden 0.4
Netherlands 1.7
0 20 40 60 80 100
Five-year relative survival

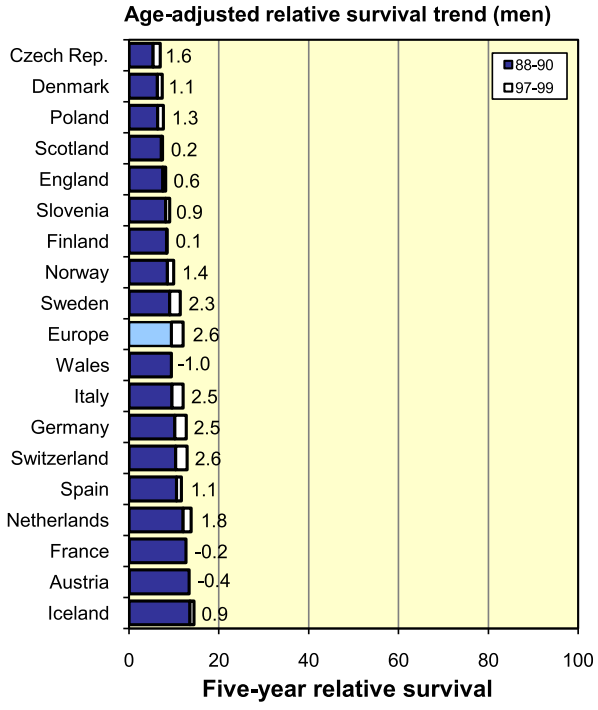

Age-adjusted relative survival trend (women)
88-90
97-99
Switzerland
Iceland
Germany
Finland
Czech Rep.
Poland -0.1
Denmark -0.1
Austria -0.1
Scotland -0.1
England -0.1
Netherlands -0.1
Europe -0.1
Wales -0.1
Norway -0.1
France -0.1
Italy -0.1
Spain -0.1
Sweden -0.1
Slovenia -0.1
0 20 40 60 80 100
Five year relative survival

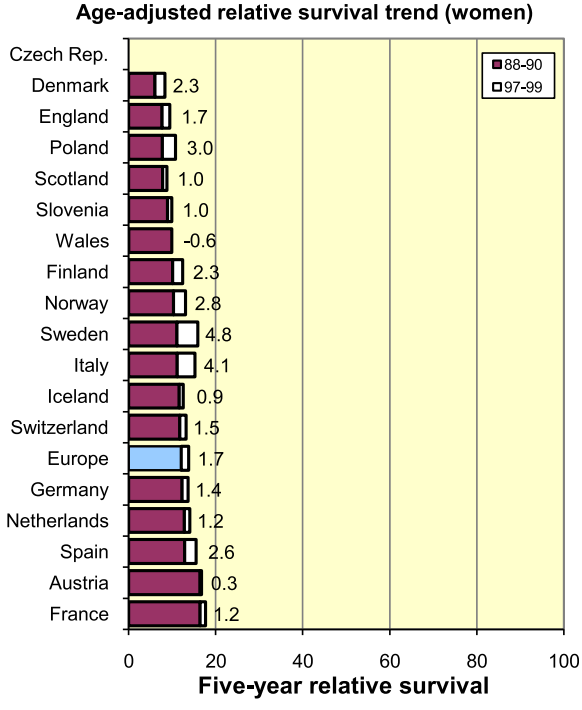
LUNG


Area weighted European average
Five-year relative survival by sex
Relative survival (%)
Diagnosis period
All
Men
Women

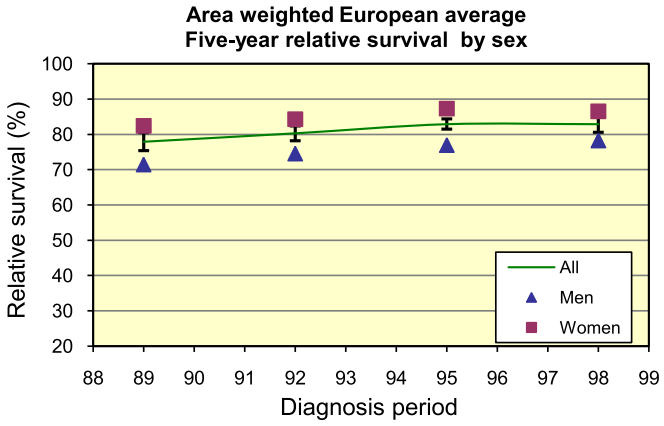

Area weighted European average
Five-year relative death rate by age (men)
Relative rate
Diagnosis period
All
15-44
45-54
55-64
65-74
75+

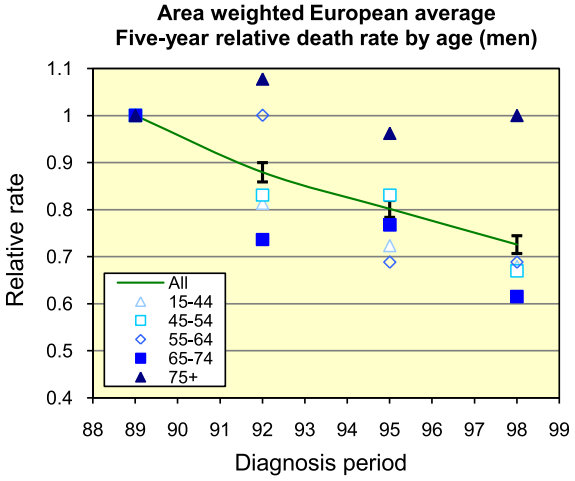

Area weighted European average
Five-year relative death rate by age (women)
Relative rate
Diagnosis period
All
15-44
45-54
55-64
65-74
75+

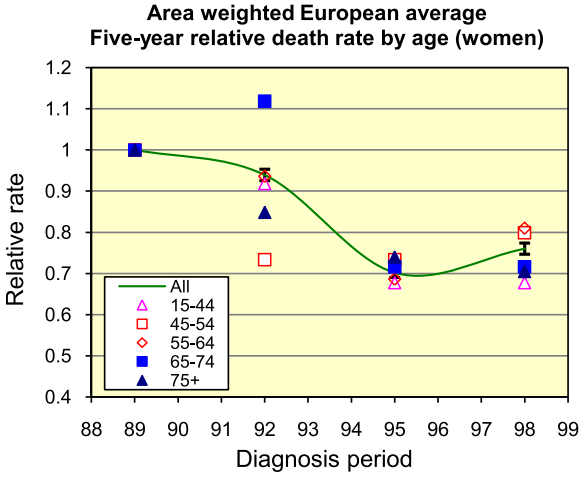

Age-adjusted relative survival trend (men)
88-90
97-99
Czech Rep. 1.6
Denmark 1.1
Poland 1.3
Scotland 0.2
England 0.6
Slovenia 0.9
Finland 0.1
Norway 1.4
Sweden 2.3
Europe 2.6
Wales -1.0
Italy 2.5
Germany 2.5
Switzerland 2.6
Spain 1.1
Netherlands 1.8
France -0.2
Austria -0.4
Iceland 0.9
Five-year relative survival

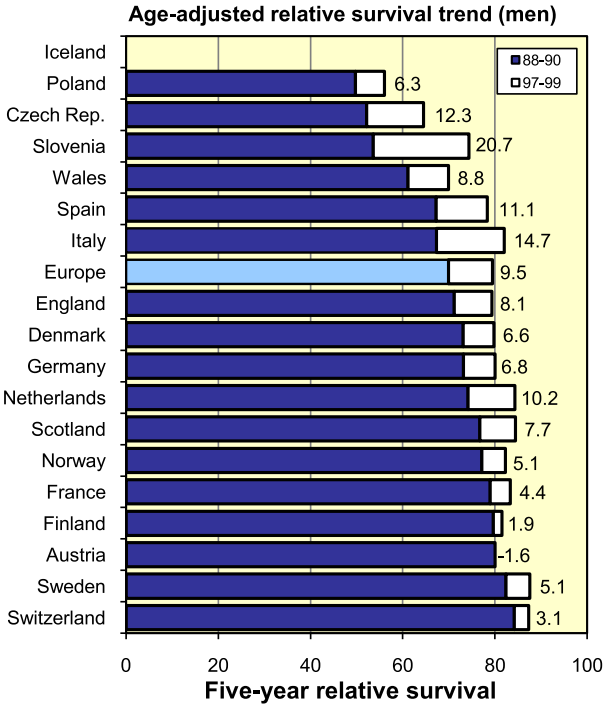

Age-adjusted relative survival trend (women)
88-90
97-99
Czech Rep.
Denmark 2.3
England 1.7
Poland 3.0
Scotland 1.0
Slovenia 1.0
Wales -0.6
Finland 2.3
Norway 2.8
Sweden 4.8
Italy 4.1
Iceland 0.9
Switzerland 1.5
Europe 1.7
Germany 1.4
Netherlands 1.2
Spain 2.6
Austria 0.3
France 1.2
Five-year relative survival

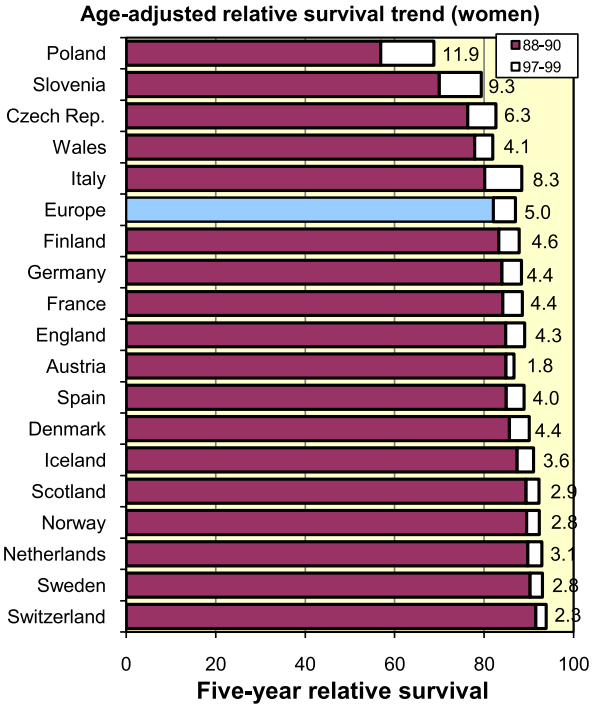
MELANOMA OF THE SKIN



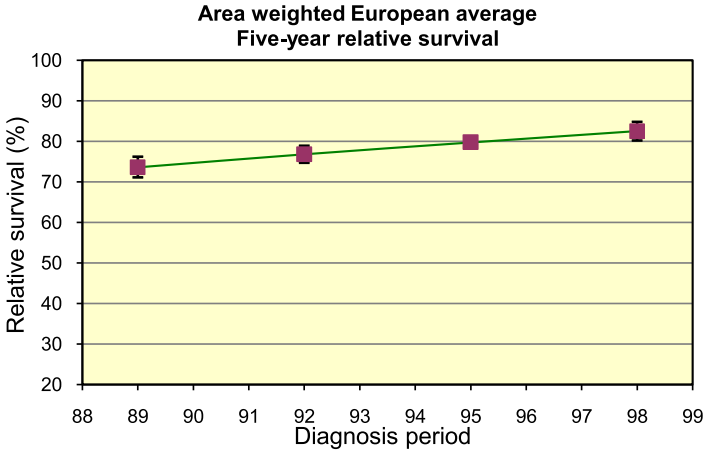


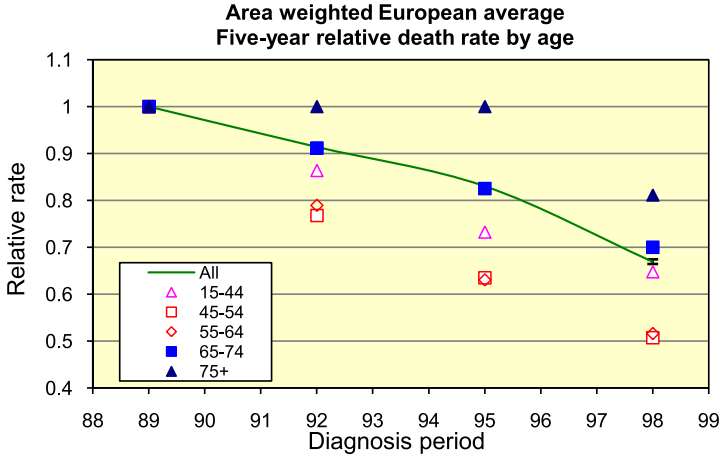


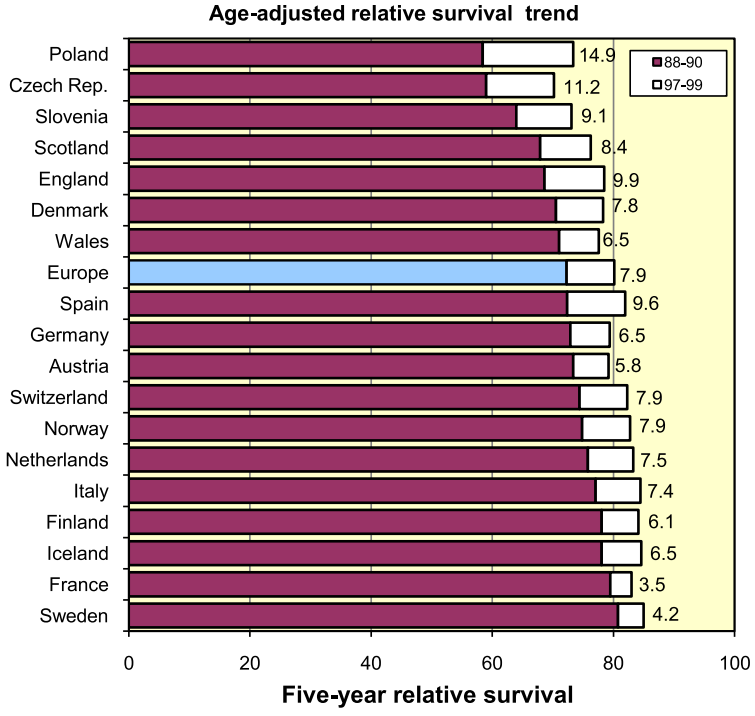




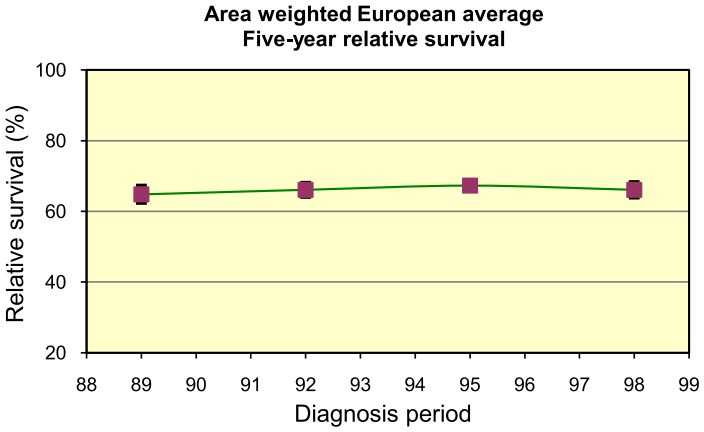
FEMALE BREAST

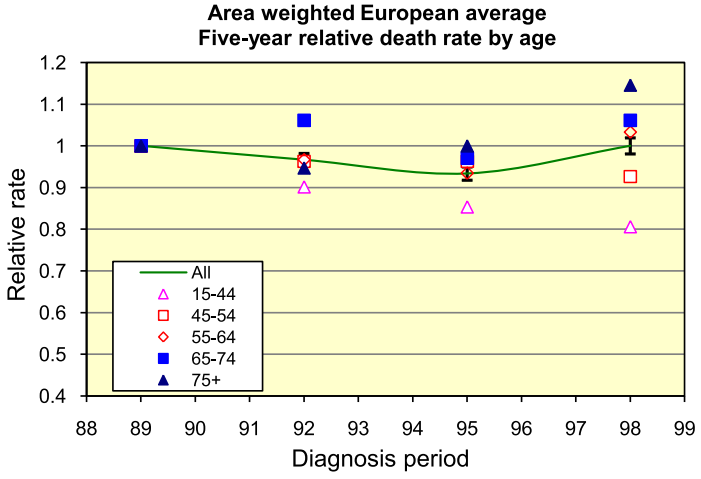


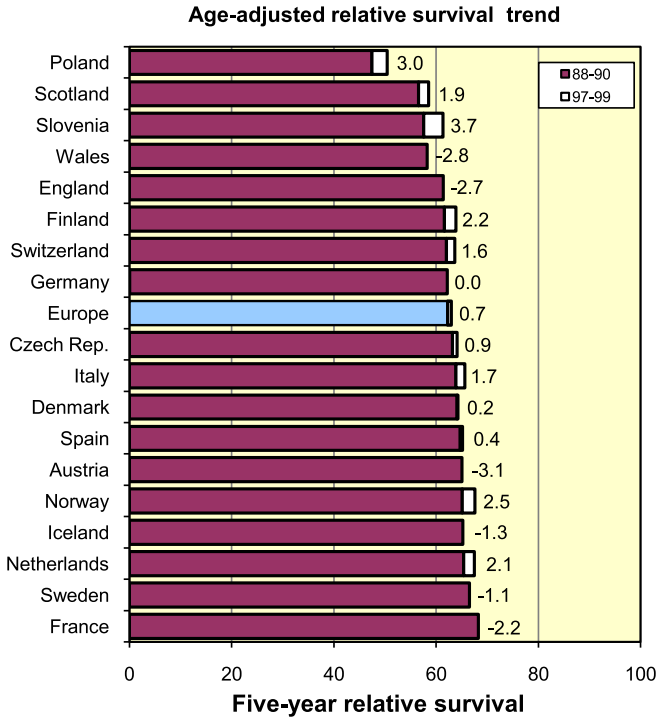




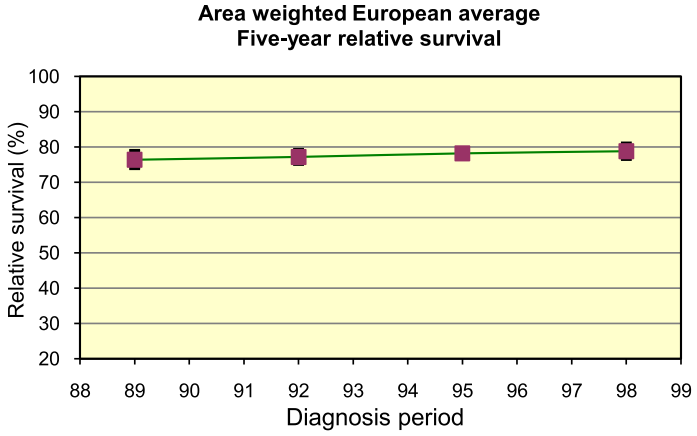
CERVIX UTERI

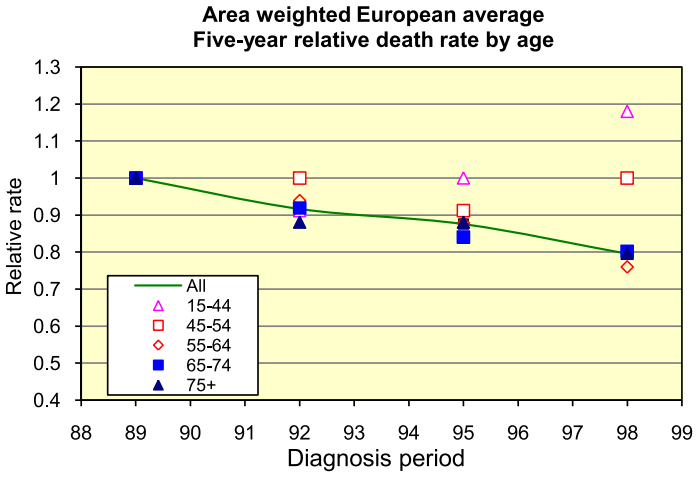


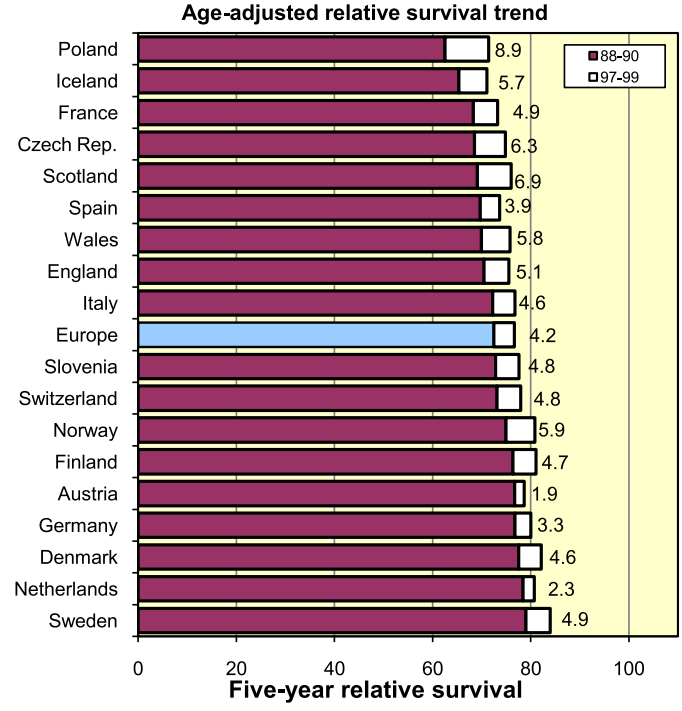




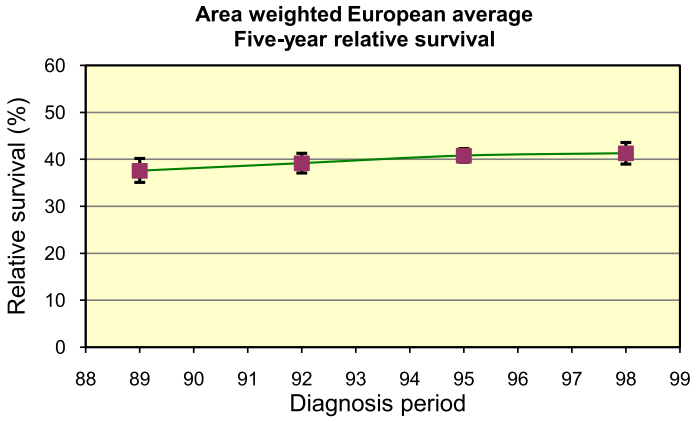
CORPUS UTERI

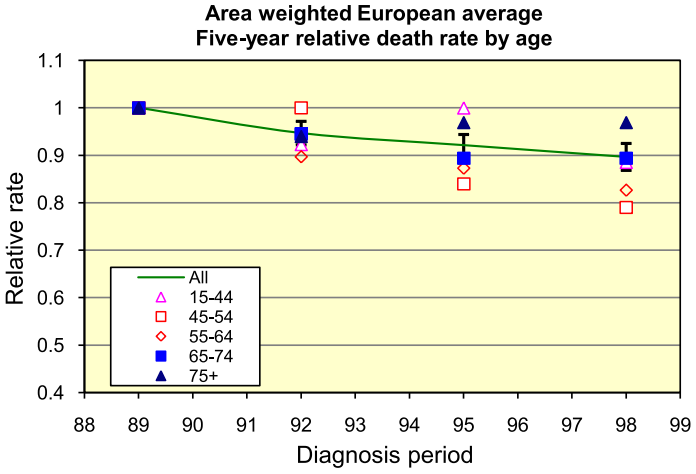


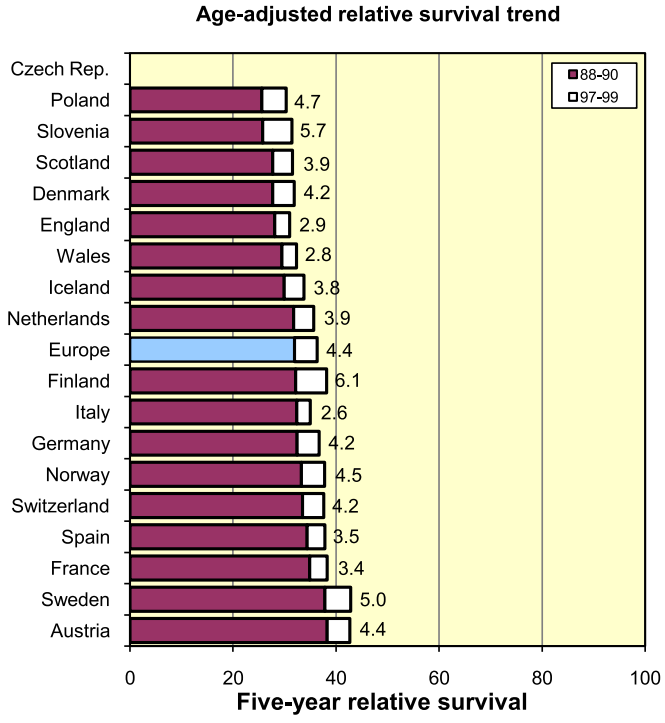




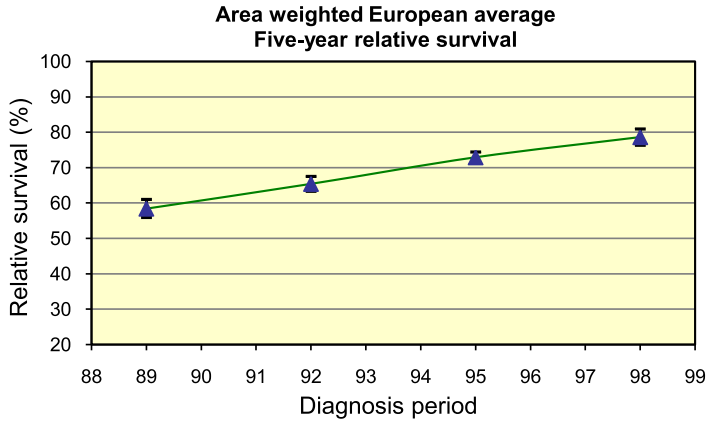
OVARY

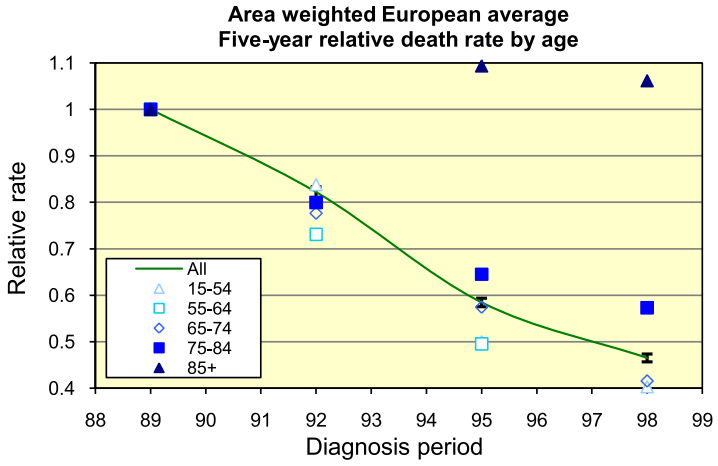

Area weighted European average
Five-year relative survival
Relative survival (%)
0
10
20
30
40
50
60
88
89
90
91
92
93
94
95
96
97
98
99
Diagnosis period

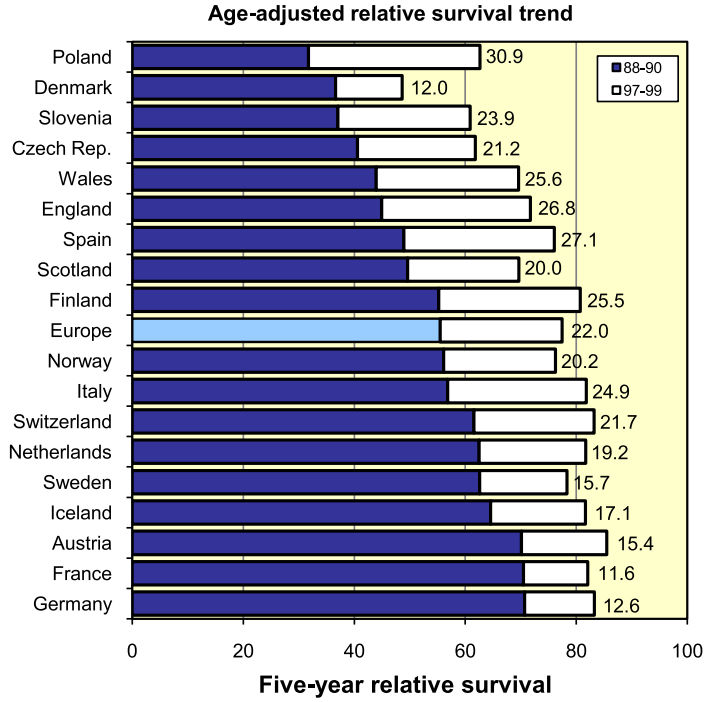

Area weighted European average
Five-year relative death rate by age
Relative rate
0.4
0.5
0.6
0.7
0.8
0.9
1
1.1
All
15-44
45-54
55-64
65-74
75+
88
89
90
91
92
93
94
95
96
97
98
99
Diagnosis period


Age-adjusted relative survival trend
88-90
97-99
Czech Rep.
Poland 4.7
Slovenia 5.7
Scotland 3.9
Denmark 4.2
England 2.9
Wales 2.8
Iceland 3.8
Netherlands 3.9
Europe 4.4
Finland 6.1
Italy 2.6
Germany 4.2
Norway 4.5
Switzerland 4.2
Spain 3.5
France 3.4
Sweden 5.0
Austria 4.4
0
20
40
60
80
100
Five-year relative survival

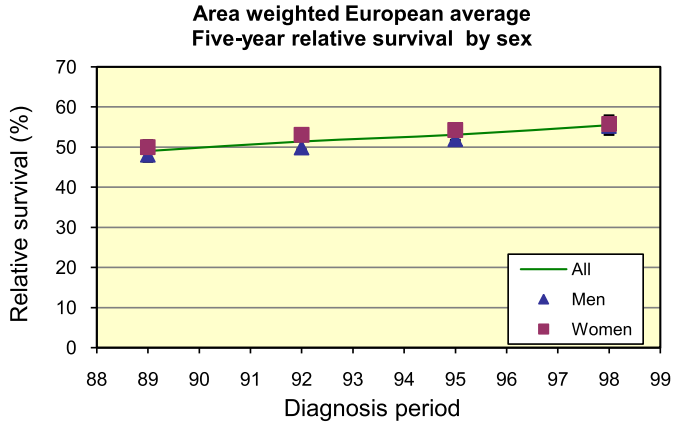
PROSTATE

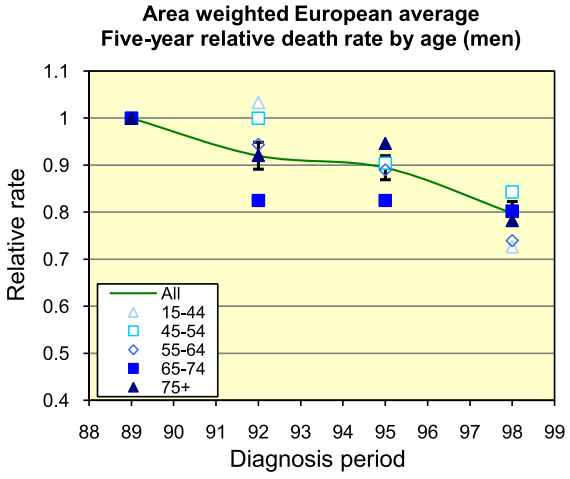

Area weighted European average
Five-year relative survival
Relative survival (%)
100
90
80
70
60
50
40
30
20
88
89
90
91
92
93
94
95
96
97
98
99
Diagnosis period

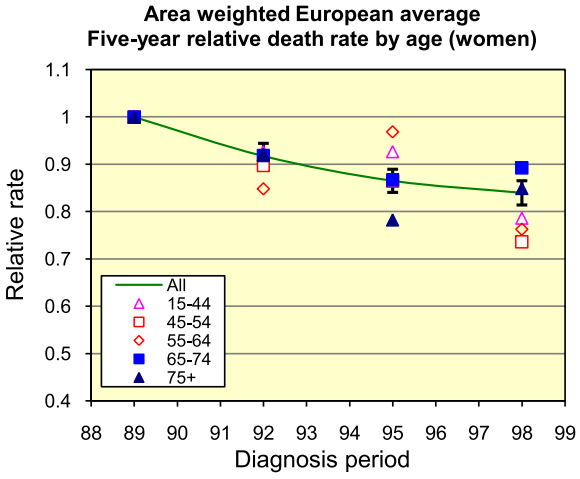

Area weighted European average
Five-year relative death rate by age
Relative rate
1.1
1
0.9
0.8
0.7
0.6
0.5
0.4
All
15-54
55-64
65-74
75-84
85+
88
89
90
91
92
93
94
95
96
97
98
99
Diagnosis period

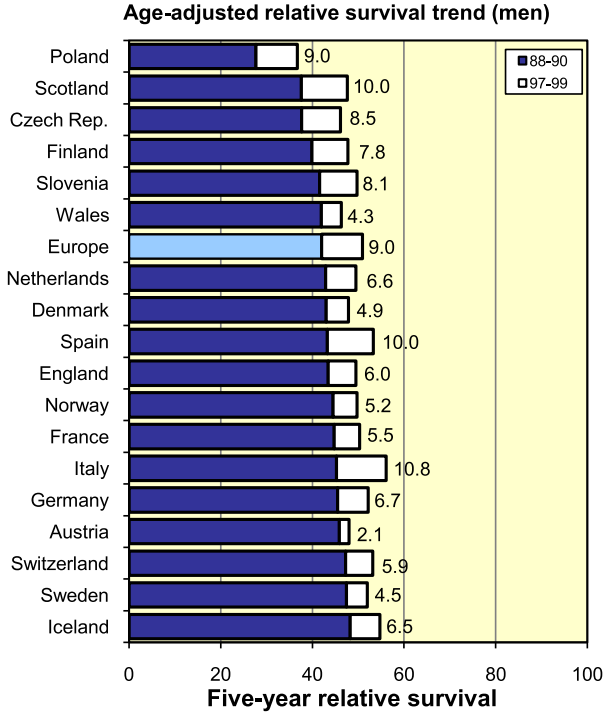

Age-adjusted relative survival trend
Poland 30.9
Denmark 12.0
Slovenia 23.9
Czech Rep. 21.2
Wales 25.6
England 26.8
Spain 27.1
Scotland 20.0
Finland 25.5
Europe 22.0
Norway 20.2
Italy 24.9
Switzerland 21.7
Netherlands 19.2
Sweden 15.7
Iceland 17.1
Austria 15.4
France 11.6
Germany 12.6
88-90
97-99
0
20
40
60
80
100
Five-year relative survival

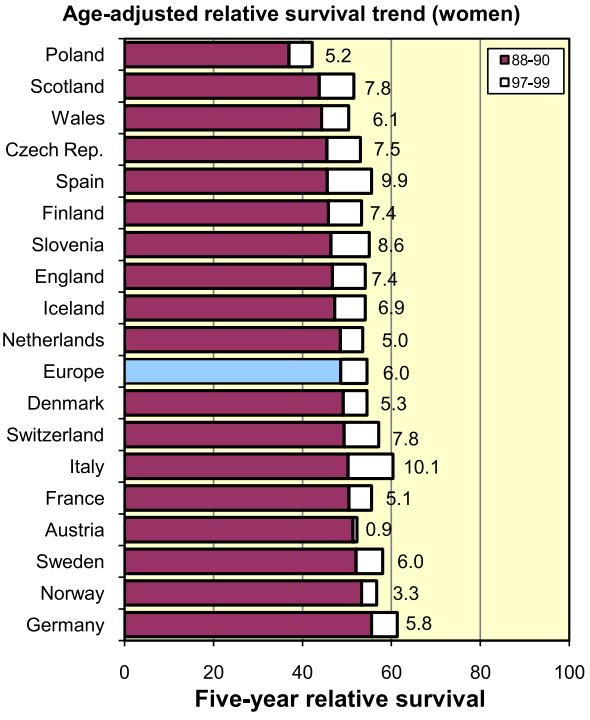
NON HODGKIN LYMPHOMA



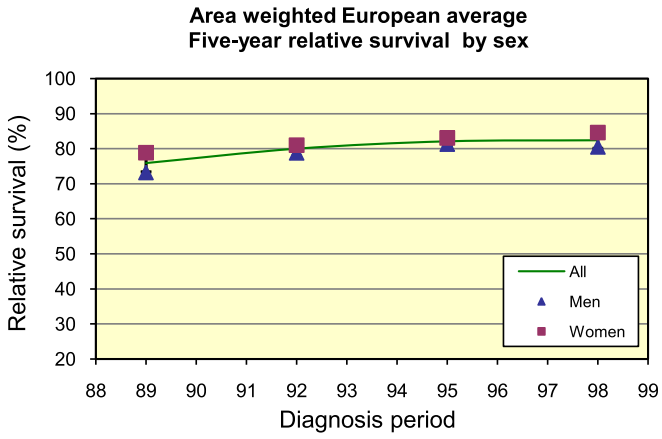


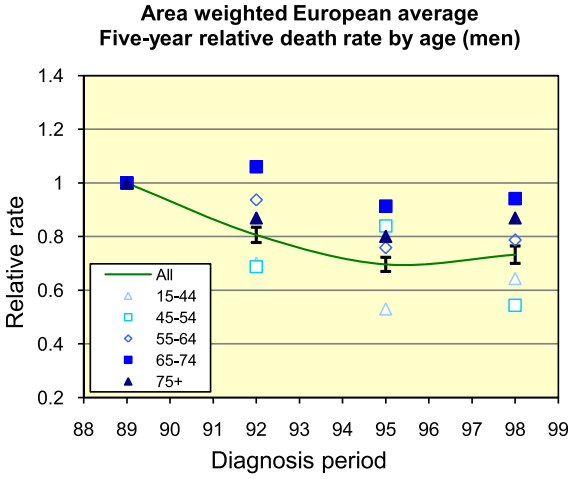


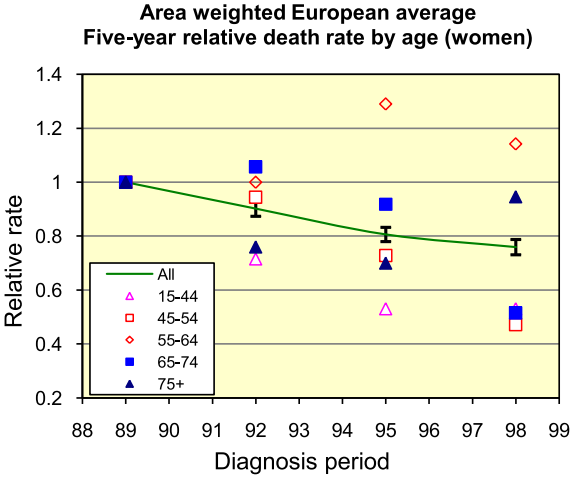


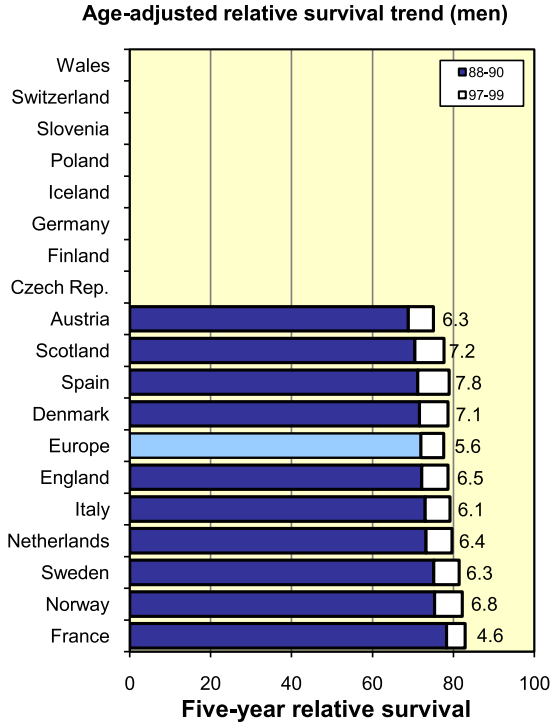


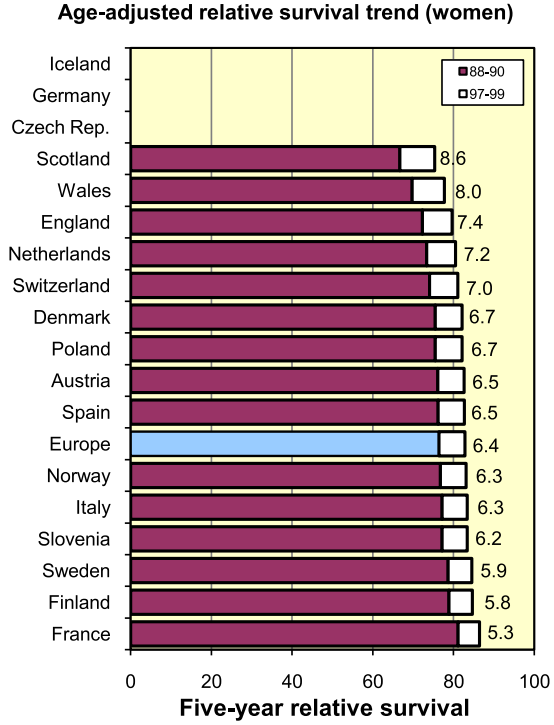
HODGKIN'S DISEASE



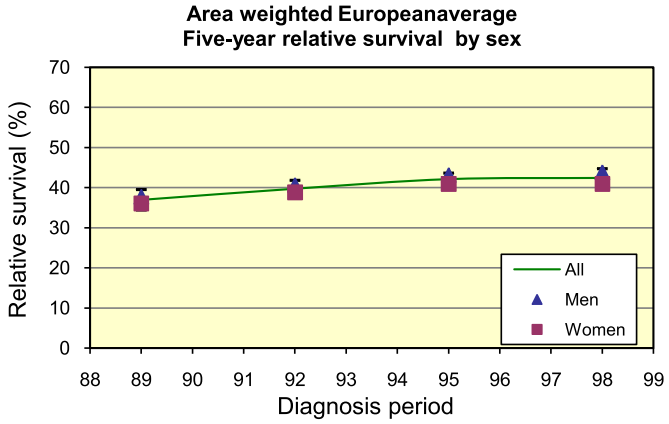


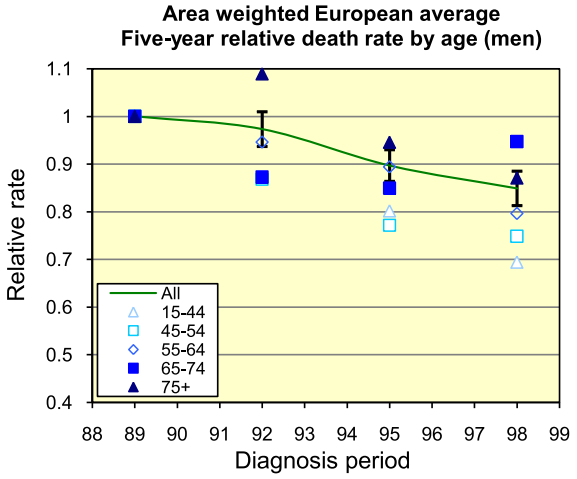


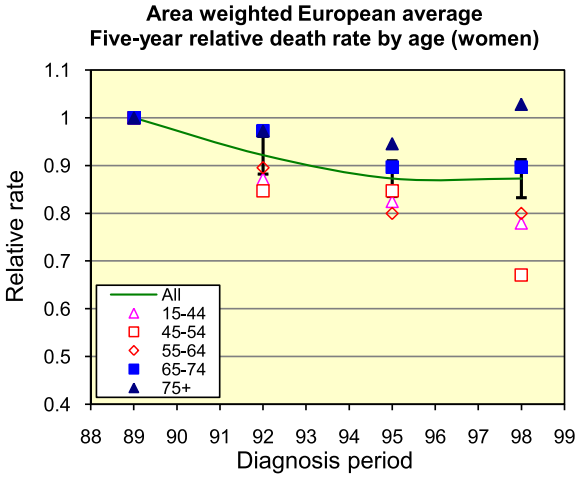


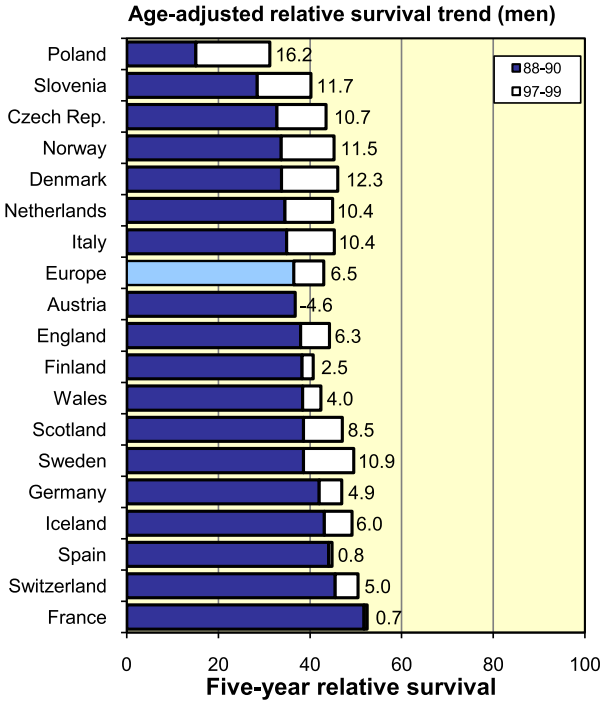


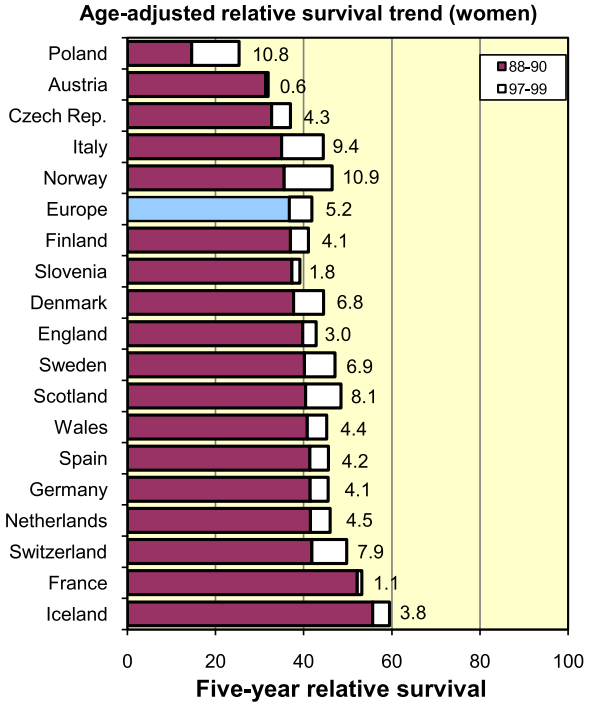
LEUKAEMIAS


Area weighted Europeanaverage
Five-year relative survival by sex
Relative survival (%)
70
60
50
40
30
20
10
0
88 89 90 91 92 93 94 95 96 97 98 99
Diagnosis period
All
Men
Women

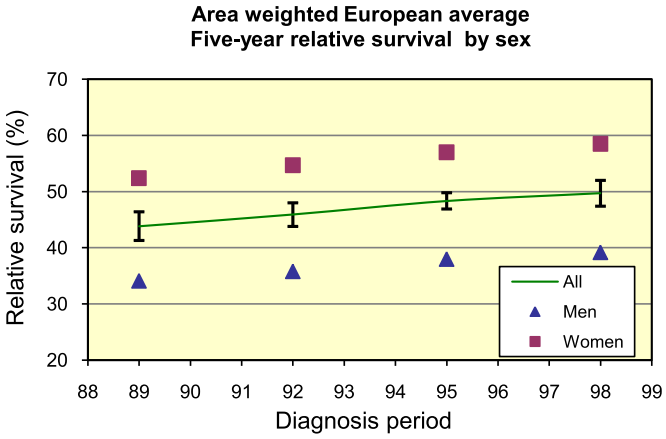

Area weighted European average
Five-year relative death rate by age (men)
Relative rate
1.1
1
0.9
0.8
0.7
0.6
0.5
0.4
88 89 90 91 92 93 94 95 96 97 98 99
Diagnosis period
All
15-44
45-54
55-64
65-74
75+

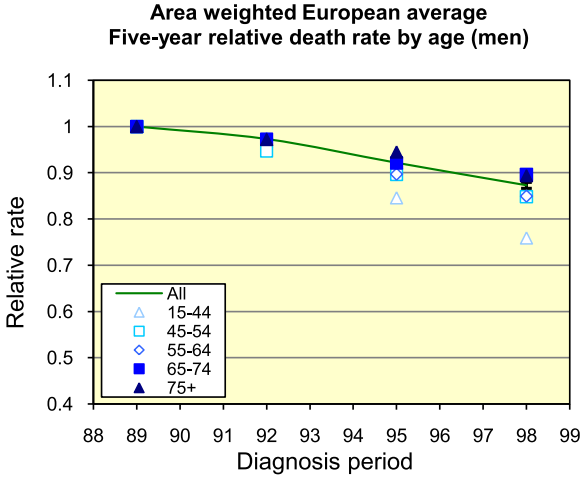

Area weighted European average
Five-year relative death rate by age (women)
Relative rate
1.1
1
0.9
0.8
0.7
0.6
0.5
0.4
88 89 90 91 92 93 94 95 96 97 98 99
Diagnosis period
All
15-44
45-54
55-64
65-74
75+

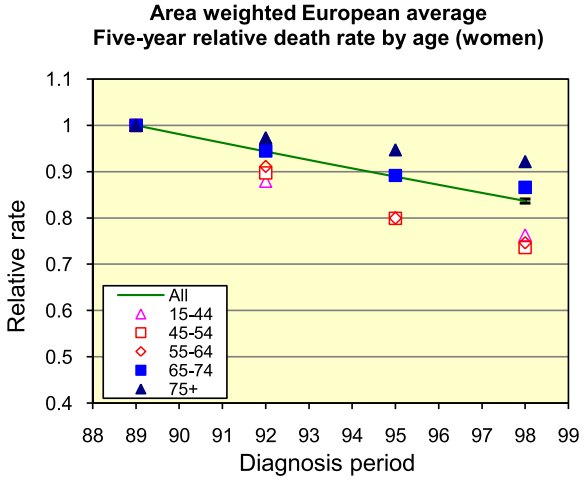

Age-adjusted relative survival trend (men)
88-90
97-99
Poland 16.2
Slovenia 11.7
Czech Rep. 10.7
Norway 11.5
Denmark 12.3
Netherlands 10.4
Italy 10.4
Europe 6.5
Austria -4.6
England 6.3
Finland 2.5
Wales 4.0
Scotland 8.5
Sweden 10.9
Germany 4.9
Iceland 6.0
Spain 0.8
Switzerland 5.0
France 0.7
0 20 40 60 80 100
Five-year relative survival

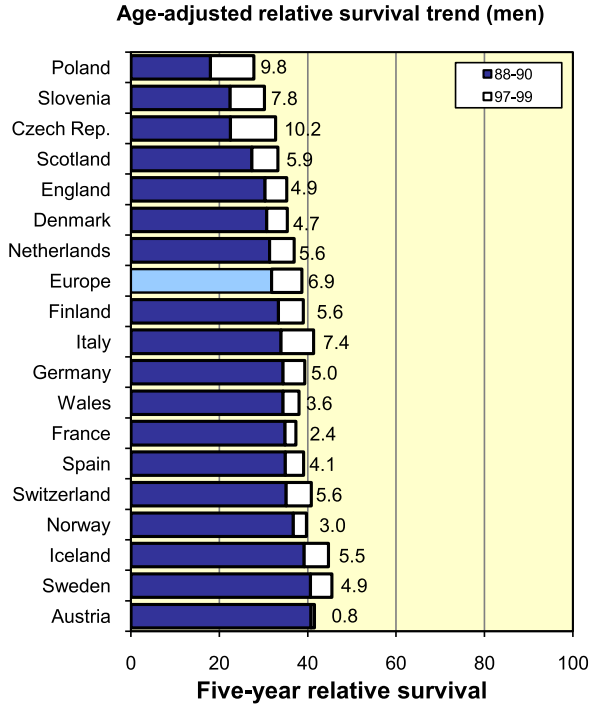

Age-adjusted relative survival trend (women)
88-90
97-99
Poland 10.8
Austria 0.6
Czech Rep. 4.3
Italy 9.4
Norway 10.9
Europe 5.2
Finland 4.1
Slovenia 1.8
Denmark 6.8
England 3.0
Sweden 6.9
Scotland 8.1
Wales 4.4
Spain 4.2
Germany 4.1
Netherlands 4.5
Switzerland 7.9
France 1.1
Iceland 3.8
0 20 40 60 80 100
Five-year relative survival

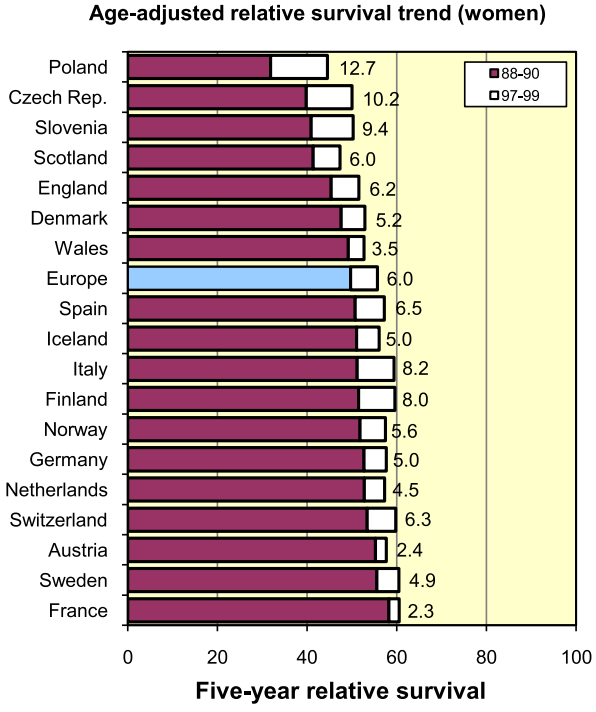
ALL CANCERS COMBINED











and women (16–31% for survival and from virtually zero to 5.7% for the increase). In Europe, survival for colon cancer increased from 48% to 54% in men and women over the study period. The decrease in relative risk of death was homogeneous across age groups for men, but not for women. There were large between-country differences in survival for colon cancer cases diagnosed in the latest period (1997–1999): from 38% in Poland to 60% in France, men and women. The between-country range of survival increase was fairly contained (range 5–9% points) for men, but more variable for women, and usually more marked for countries with poor relative survival at the beginning of the study period. The highest colon cancer survival by 1997–1999 was estimated in Italian women (61%), presenting 1 of the greatest increases in Europe.

Results for rectal cancer were closely similar to those for colon cancer, with the consequence that results for large bowel cancer were also similar to those for colon and rectal cancers. The increase in mean European survival for rectal cancer was similar for both sexes (from 45% in 1988–1990 to 55% in 1997–1999); the range of survival increase was also similar for both sexes (6–12% points) and tended to be higher for countries with poorer relative survival.

3.2. *Larynx and lung*

There were few laryngeal cancer cases in women so survival estimates are somewhat unstable. The European average survival in men increased from 62% in 1988–1990 to 64% in 1997–1999. In women, survival improved up to 1995 but worsened in the latest period, with an increase in relative excess death rate from 1.0 to 1.3. There was a slight improvement (0.0–5.0% points) in most countries for men, but for all countries survival in women remained stable.

Although survival for lung cancer was poor, mean 5 year European survival increased from 11% in 1988–1990 to 13% in 1997–1999. The greatest increases were seen in Sweden and Italy, and were most marked in women.

3.3. *Melanoma of the skin*

Survival for skin melanoma was higher in women than in men, although the survival increase over the study period was similar for both sexes: from 70% to 79% in men and from 82% to 87% in women. Trends in relative risk of death were homogeneous with age for women, but not for men. The variation in 5 year melanoma survival between countries was striking (in 1997–1999 from 56% in Poland to 87% in Sweden, men; 70% in Poland to 94% in Sweden, women). Survival increases over the whole study period tended to be the greatest in countries with poorer survival at the beginning, so that the variation between countries reduced with time.

3.4. *Breast, cervix and corpus uteri, ovary*

In Europe, survival for female breast cancer increased from 74% to 83% over the study period. There was a considerable heterogeneity in survival in relation to age at diagnosis, and the increase in survival for the oldest ages (65–74 and 75–99 years) was less than for the 45–54 and 55–64 age classes. Survival was also significantly heterogeneous by country, ranging in 1997–1999 from 73% in Poland to 85% in Sweden. The improvement over the study period was greater in countries with poor survival at the beginning, so that between-country variation in survival reduced with time as noted previously.[6]

For cervical cancer, the area weighted European average 5 year relative survival improved slightly over the study period, from 64.8% to 66.1%, but there was a slight decline in the latest period. Relative risks of death decreased for young women over the entire study period, but increased for older women in the latest period. Survival ranged from 57% in Poland to 67% in France.

The European mean 5 year relative survival for corpus uteri cancer increased modestly from 76% to 79% over the study period. There was marked variation in the relative death risk of death with age over the study period, which increased in younger women (1.2), but decreased in older women (0.80). Survival by country in 1997–1999 varied from 71% to 84%. Survival by country increased in the range 1.9–8.9% points over the study period and again the increase was greater in countries with poorer survival at the beginning of the study period.

Five year average European survival for ovarian cancer increased slightly over the study period (38–41%). Survival trends did not differ with age, but varied markedly by country (29–43%). The largest increase in survival over the study period (6% points) occurred in Finland.

3.5. *Prostate*

European mean 5 year relative survival for prostate cancer increased more than that of any other cancer over the study period (58–79%). The increases were fairly homogeneous with age, except that there was no increase in the oldest age class (85–99 years). The decrease in relative death risk was most marked in the first 2-diagnosis periods. The absolute increase in survival varied markedly between countries, from 31% points in Poland to 12% points in France and Denmark. Five year survival in 1997–1999 varied from 51% in Denmark to 84% in Austria and Switzerland.

3.6. *Haematological malignancies*

Mean European survival was considerably lower for non-Hodgkin lymphoma than for Hodgkin lymphoma, but improved markedly (49–56%) over the study period, to a similar extent in both sexes. Relative risk of death lessened with a heterogeneous improvement in relation to age for men but not women. The risk of death in the latest period relative to the first was 0.80 for men and 0.84 for women. The largest increases in survival were in Italy and Spain (around 10% points) for both sexes. Survival in 1998 varied from 37% in Poland to 56% in Italy for men, and from 42% in Poland to 61% in Germany for women.

The average area weighted European 5 year relative survival for Hodgkin disease in Europe increased from 77% to 83% over the study period in a closely similar way for both sexes. Risk of death in the latest period compared to the first period was 0.75 in men and 0.78 in women. There was considerable survival heterogeneity by age for women, and less for

men. On the contrary, survival and survival trends by country were fairly homogeneous, and particularly in women, for which a unique average relative rate is estimated for all countries.

Mean European survival for all leukaemias increased from 37% in 1988–1990 to 42% in 1994–1996, but remained stable from then to 1997–1999. Survival levels and trends were similar for both sexes. The improvement was heterogeneous with respect to age, with average relative risk of death 0.87 in the latest period for both sexes. There was notable between-country variation in survival and survival time trends for leukaemias. In the latest period, survival varied from 31% in Poland to 53% in France for men, and from 25% in Poland to 60% in Iceland for women. The most marked survival increases occurred, most conspicuously in men, in countries with poor survival in 1988–1990. The largest increase occurred in Poland (16.2% points in men; 10.8% points in women).

3.7. *All cancers combined (excluding non-melanoma skin cancers)*

Mean European 5 year relative survival for all cancers combined (not adjusted for case-mix) increased significantly over the study period from 44% to 50%. The increase was almost linear up to 1994–1996, and then slowed. Survival for women increased from 52% to 59%, survival in men increased from 34% to 39%, with significant trend heterogeneity between the sexes. Survival trends were also heterogeneous with age in that younger patients had a greater increase in survival than older patients of both sexes. Countries with poor relative survival in the early period (e.g. Poland, Czech Republic, and Slovenia) had larger increases in survival for all cancers combined (6–10%) than countries with high levels at the outset (northern European countries and Switzerland), resulting in some reduction in between-country survival variation from 1988–1990 to 1997–1999.

4. Discussion

Five year age-adjusted relative survival in Europe increased in the period 1988–1999 for all 14 cancer sites considered. Major increases occurred for prostate, colon, breast and haematological sites; increases were small for lung and cervix.

These results derive from a wide database including information collected by 49 cancer registries in 18 European countries. The disadvantage of such a large participation is given by the potential heterogeneity in data quality (completeness of registration, quality of diagnosis and death certificates, completeness of follow-up) and by its impact on survival estimates. The quality of date of EUROCARE-4 participating registries is analysed elsewhere.[3] As a general consideration, poor data quality often leads to overestimate survival. Therefore, improvement in quality in particular areas tends to reduce this overestimation, partially hiding real trends for a better survival.

We used a modelling approach to estimate survival and survival trends, and thereby taking account of random variation in survival. Modelling was also used to test the significance of differences by sex, age class, and country, and to assess whether the observed increases in survival over the study period were real or random. The empirical Bayesian method adopted to compare countries had the advantage of smoothing variation in survival rates, especially for small cancer registries. We also used imputation of survival when data are missing, particularly when populations were small or for rare cancers, such as laryngeal cancer in women. We only imputed 1 missing value on the basis of the data available from other 3-periods.

Another limitation of the study is that, in countries with incomplete cancer registration, survival in the areas covered may not be representative of survival in the country as a whole. This is likely to be the case for Germany (1% coverage), Poland (6%) and Spain (8%), and our results must therefore, be treated with caution.

We used, for each site considered and for all cancers combined, the area weighted average survival of the 18 participating countries as an indicator of survival for all Europe. These 18 countries constitute a considerable fraction of the European population, and survival estimates in this pool of countries are therefore, a useful indicator of survival in Europe as a whole, and a reference against which survival in individual countries can be compared.

4.1. *Digestive tract*

The prognosis for stomach cancer remains poor, and 5 year mean European survival increased only modestly (by 3% points) from 1989 to 1998. Some studies suggest that the decline in stomach cancer incidence – evident in most western countries[7,8] – is largely confined to cancers of the distal stomach,[9] which are less aggressive than those arising in the cardia or fundus, and which are usually diagnosed in older patients, at advanced stage, and with diffuse/signet ring morphology.[10,11] Thus, the fact that the improvement in stomach cancer survival is only slight, which may be related to reduced incidence of less aggressive cancers, while the incidence of more aggressive forms remains constant. Earlier diagnosis, allowing radical surgery, may have contributed to the survival increase, as there have been no major improvements in systemic treatment for stomach cancer over the last 20 years.[12] This may be particularly the case for Italy which registered a fairly marked increase in survival (about 4% points). Stomach cancer incidence is high in northern and central Italy, where health facilities are well developed.[13] Finland had the greatest improvement in stomach cancer survival over the study period.

Survival for colon and rectal cancers increased remarkably over the study period probably because these cancers are diagnosed at earlier stages allowing more effective treatment.[14] Increased survival for these sites may also be due to advances in the treatment of advanced non-localised disease.[15] The large increases in UK survival (approximately 8%) may be in relation to the initiative, started in the late 1990s, to promote early diagnosis and to shorten diagnostic delay, as reported in.[16]

4.2. *Larynx and lung*

Survival figures for women with laryngeal cancer are unstable because of the low numbers of cases. However, our data sug-

gest that although survival is better in women than in men, there has been a tendency to worsening survival among women in the recent years. This decline is plausibly related to the increased smoking among European women.

Lung cancer survival remains poor. The small increases in survival seen in many countries may be due to earlier diagnosis and more accurate staging than in the past. Better staging allows a better selection of patients who may benefit from surgery with curative intent.[17] The use of low-dose computer tomography screening in high risk populations as way of reducing lung cancer mortality is being investigated in the United States of America (USA)[18] and in Europe.[19] However, lung cancer remains the most conspicuously preventable cancer and efforts to reduce smoking should be redoubled, since although smoking is decreasing among adult European males, it is increasing in women, and young Europeans of both sexes.[20] Lung cancer incidence is declining in men, but not in women in most western countries.[8] It has been shown that lung cancer patients who continue smoking after diagnosis have a worse prognosis than those who stop smoking.[21]

4.3. *Breast, cervix and corpus uteri, ovary*

Breast cancer screening was introduced to many European countries during the study period[22] and undoubtedly contributed to the increase in survival evident in Europe overall and in several countries. Breast cancer survival increased less in Sweden or Iceland, where screening has been in place since the beginning of the 1980s. Survival was already high in these countries at the beginning of the study period, and may represent the highest levels attainable with current diagnostic and treatment methods. It has been noted that in addition to its direct effect on diagnosis, screening also drives improved treatment of symptomatic cancers.[23] In France, nationwide screening was not in place during the study period, nevertheless survival was among the highest in Europe. In Slovenia, Czech Republic, Poland, England and Scotland, where survival was low in 1989, the survival increase (10% points or more) may be attributed to a wider availability of adequate treatments, as well as earlier diagnosis.

The slight decline in survival for cervical cancer, evident for the latest diagnosis period in several countries and affecting also the European average, may actually reflect the success of the screening programmes. Screening has a beneficial effect on the population at risk by identifying pre-malignant lesions and removing them from incidence statistics. The cases that remain include both early stage cancer and aggressive malignancies (the so-called interval cases). The latter tend to be present at an increased proportion, and therefore, have an adverse effect on survival figures. Also, the widespread introduction of population-based screening has prevented the rise in cervical cancers incidence rate which would be expected with the increased tendency for multiple sexual partners.[24] However, lower survival in some countries could be caused by a group who have this increased risk and who do not attend for cervical cancer screening and who present with late disease. Stage at diagnosis remains the main prognostic factor for all gynecological cancers, and the slight increase in survival is likely to be mostly related to earlier diagnosis than in the past. Ovarian cancer treatment improved from the 1980s thanks to the introduction of platinum-containing chemotherapy regimens.[25] However, stage at diagnosis is a major determinant of ovarian cancer survival[26] for a disease that typically remains asymptomatic until it is fairly advanced. The large variation in ovarian cancer survival across Europe at the end of the study period is probably attributable to variation in extent to which diagnostic examinations are applied to non-symptomatic women.

4.4. *Prostate*

Although incidence and survival of prostate cancer have increased in most western countries, mortality rates remain constant, or have declined only slightly.[27] In France, Germany and Austria, high survival in the earliest part of the study period, with comparatively small increases over the study period, suggests that dissemination of the PSA test started earlier than in other countries. Low survival in Denmark, associated with a small increase over the study period, suggests that the PSA test is still not widely used, apparently because of insufficient evidence it can reduce mortality.[28,29]

4.5. *Haematological malignancies*

The evolving classification and the poor standardisation of morphology data on haematological malignancies complicate comparisons of survival over time and between countries. In the present study, we considered Hodgkin's disease, NHL and leukaemias without breaking them down into morphology subtypes, which are known to have differing prognoses. The survival increase for these malignancies may be partly due to earlier stage at diagnosis, making them more treatable, and partly to improvements in treatment. In the recent years, so-called targeted treatments have been introduced for the treatment of subtypes of chronic myeloid leukaemia,[30] B lymphomas[31] and multiple myeloma.[32] The high cost of these new treatments is likely to generate inequalities in availability and access, and should be carefully monitored.

4.6. *All cancers combined*

Cancer is a general category universally used to group together a wide set of diseases, even though they present a high degree of etiologic, biological and treatment variability. How many cancer patients survive in a given population and how much their survival chances are increasing are legitimate questions requiring direct replies. Survival for all cancers combined is therefore, a useful measure of the relative performance, in cancer care, of the health care systems of the participating European countries,[33] even in the presence of a substantial variation in case-mix both in time and across Europe. In the previous EUROCARE-4 publications[2,34] case-mix adjusted survival for all cancer combined has been presented. In this paper, as well as in several papers published in this monograph, we choose to present relative survival data for all cancer combined without

adjustment, in order to reflect also the different site distributions in different countries and its changes over time. In any case, the survival ranking of countries shown for all cancers combined is similar to the ranking for most specific sites.

For countries with poorer survival in the early part of the study period, there were major improvements in relative survival for most cancer sites by the end of the study period, so that between-country survival variation in the most recent period (1997–1999) reduced compared to the first period (1988–1990). This is an encouraging result for Europe as it suggests a reduction in cancer care inequalities among European citizens of differing nationality.

Conflict of interest statement

None declared.

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