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# The advantage of women in cancer survival: An analysis of EUROCARE-4 data

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ABSTRACT

We analysed 1.6 million population-based EUROCARE-4 cancer cases (26 cancer sites, excluding sex-specific sites, and breast) from 23 countries to investigate the role of sex in cancer survival according to age at diagnosis, site, and European region. For 15 sites (salivary glands, head and neck, oesophagus, stomach, colon and rectum, pancreas, lung, pleura, bone, melanoma of skin, kidney, brain, thyroid, Hodgkin disease and non-Hodgkin's lymphoma) age- and region-adjusted relative survival was significantly higher in women than men. By multivariable analysis, women had significantly lower relative excess risk (RER) of death for the sites listed above plus multiple myeloma. Women significantly had higher RER of death for biliary tract, bladder and leukaemia. For all cancers combined women had a significant 5% lower RER of death. Age at diagnosis was the main determinant of the women's advantage, which, however, decreased with increasing age, becoming negligible in the elderly, suggesting that sex hormone patterns may have a role in women's superior ability to cope with cancer.



## 1. Introduction

Women have a longer life expectancy than men[1] and better survival of chronic diseases like cardiovascular disease[2] and cancer.[3–5] The EUROCARE-2 study analysed survival in 1 million European cancer cases diagnosed in 1985–1989; it found that sex was a predictor of survival, and suggested women had a *biological* advantage over men in coping with cancer.[6] Other evidence supports the idea that women are more attentive to their health than men indicating a *cultural* rather than biological advantage.[7] Nevertheless, neither biological nor cultural factors have been clearly established as responsible for the longevity and survival advantage of women. If cultural factors were important then interventions to reduce the male disadvantage might be proposed; if biological factors were important, then studies to better understand the bases of these differences would be useful.

We analysed the latest release of the EUROCARE-4 dataset[8,9] which contains standardised population-based information on about 3 million cancer cases from 82 cancer

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registries (CRs) in 23 European countries.[10] Our aim was to further examine the role of sex in determining cancer survival, investigating whether the female advantage was present in all ages, cancer sites and European regions, and hence suggest possible reasons for the survival differences between the sexes.

## 2. Patients and methods

We considered 1,668,872 cancer patients (40% women) diagnosed between 1995 and 1999 in European adults (15–99 years).[8,9] For 13 participating countries (Austria, Denmark, England, Finland, Iceland, Ireland, Malta, Norway, Sweden, Scotland, Wales, Northern Ireland and Slovenia) the entire population is covered by cancer registration; the other 10 countries (Belgium, the Czech Republic, France, Germany, Italy, The Netherlands, Poland, Portugal, Spain, and Switzerland) are represented by CRs covering variable proportions of the population.[10] The countries were grouped into five European regions (footnote Table 1).

Detailed information on data collection and standardisation procedures is given elsewhere.[9] We considered only first primary malignant cancers. Second cancers, *in situ* tumours and those of uncertain or borderline malignancy were excluded. The third revision of the International Classification of Diseases for Oncology (ICD-O-3)[11] was used as reference coding system:[9] the cancer site nomenclature (see Table 1) follows that used in the EUROCARE-4 database presenting article.[9] Histologically verified and non-verified cases were included, but cases known to registries only by death certificate or discovered at autopsy were excluded. Non-melanoma skin cancer, sex-specific cancers, and breast cancer were also excluded: breast cancer because it is rare in men and aetiology and biological behaviour differ between the sexes.[12] We thus analysed 26 cancer sites defined according to ICD-O-3[11] together with all cancers combined (Table 1).

Overall, most (83%) patients were diagnosed at 55–99 years of age (Table 1, column c); of these 41% were women (not shown). The five most common cancer sites considered were: colon and rectum (24% of total cases), lung (17%), stomach (7%), kidney (7%), and melanoma of skin (5%) (Table 1, column d) in women; and lung (29%), colon and rectum (18%), bladder (9%), stomach (7%), and kidney (6%) in men (Table 1, column e).

The survival analyses were performed on pooled cases from all CRs (the European pool) by cancer site and for all cancers combined. Analyses by European region and for Europe (see below) were also performed.

We estimated non-age-adjusted (crude) and age-adjusted 5-year relative survival for men and women separately. We also estimated survival by age at diagnosis, for which patients were grouped into five age categories: 15–44, 45–54, 55–64, 65–74, and 75–99 years. For age adjustment we used the International Cancer Survival Standard (ICSS)[13] and five broad age categories. However, for an ancillary analysis of all cancers combined, the data were age-adjusted using narrower (5-year) age categories.

Relative survival was determined in order to take account of the risk of competing mortality (risk of death for causes other than cancer) which varies between CR areas. Relative survival, conventionally expressed as a percentage, is the ratio of the observed survival in a group of patients to the survival expected in a comparable group from the general population, with the same composition by sex, age and year of death.[14] Relative survival was calculated by the Hakulinen method[15] from sex-, age- and calendar year-specific lifetables for each CR population.

For several cancer sites (Table 3, columns a and b) some female and male age categories in Eastern Europe had no patients, so age-adjusted relative survival could not be estimated. For this reason the all cancers combined category of Eastern Europe does not include these non-estimable sites, and Eastern Europe data are excluded from the Europe estimates (Table 3, columns c and d). For the pleural site, no male patient was present in the 15–44 age category for Northern Europe and relative survival for this category was assumed to be that of the European pool.

In deriving estimates of survival for Europe (Tables 3 and 4), region-specific relative survival estimates were also weighted by the mean population size of each region in 1995–1999.[9] Because cancer site specific incidence rates differ between sexes, when comparing relative survival for all cancers combined, we also adjusted by case mix using as reference the estimated number of patients (men and women) diagnosed in 1995–1999 by cancer site.[9]

Percentage point differences in crude, age-specific or adjusted 5-year relative survival between women and men constitute the main indicators of between-sex differences in cancer survival.

To model the simultaneous effects age and region have (and case mix for all cancers combined) on survival differences we used generalised linear models (regression models) with a Poisson error structure based on grouped data.[16] The models estimated the relative excess risk of dying (RER) of women with men as reference (Model 1); 95% confidence intervals (95% CI) were also estimated. To assess the effect of the regional covariate on the RER, we used a reduced model that excluded this covariate (Model 2). The regression analyses were performed on all ages combined and on the 15–54 and 55–99 year age categories. In a few cases the Eastern data were not included in the analyses because iterative procedures did not converge (Table 4).

The SEER*Stat statistical software (version 6.3.6)[17] was used to estimate relative survival; the Z test (univariate analysis) was used to compare survival estimates. Stata software (version 9.0)[18] was used for the regression analyses.

## 3. Results

### 3.1. *European pool: Crude analyses (column b, Table 2)*

Crude 5-year relative survival for all cancers combined was significantly higher in women than men by 4.9 percentage points. The advantage for women was significant for 11 of the 26 cancer sites. For liver, biliary tract, bladder and leukaemia, women had a significant survival disadvantage.

**Table 1 – Numbers of patients (columns a) and percentages of women (W%, columns b) considered in the analyses, in each regional European grouping and in the European pool, by cancer site – The percentage of patients aged 55–99 years at diagnosis (column c) is also given for the European pool – Columns d and e indicate the percentages of women (w%) and men (m%) diagnosed with each cancer as a proportion of all cancers combined (as defined in the footnote).**

| ICD-O-3 Site | Cancer site | Northern Europe[a] | | UK & Ireland[a] | | Central Europe[a] | | Eastern Europe[a] | | Southern Europe[a] | | European pool[a] | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Patients a | W% b | Patients a | W% b | Patients a | W% b | Patients a | W% b | Patients a | W% b | Patients a | W% b | 55–99% c | w% d | m% e |
| C00 | Lip | 2,099 | 26.4 | 1,768 | 28.3 | 1,228 | 24.9 | 163 | 25.8 | 2,367 | 16.1 | 7,625 | 23.4 | 87.8 | 0.3 | 0.5 |
| C079-C089 | Salivary gland | 1,026 | 47.2 | 2,406 | 47.0 | 964 | 42.7 | 146 | 43.2 | 1,085 | 44.1 | 5,627 | 45.6 | 71.2 | 0.4 | 0.4 |
| C01-C06, C09-C14 | Head and neck | 6,729 | 34.9 | 18,054 | 34.9 | 11,808 | 21.3 | 1,078 | 24.6 | 11,900 | 20.3 | 49,569 | 27.9 | 68.2 | 1.8 | 3.6 |
| C15 | Oesophagus | 4,719 | 30.0 | 31,219 | 39.6 | 6,578 | 22.1 | 557 | 20.1 | 5,280 | 19.1 | 48,353 | 33.8 | 87.3 | 0.8 | 2.0 |
| C16 | Stomach | 13,919 | 39.9 | 45,180 | 36.0 | 18,742 | 42.5 | 2,501 | 37.0 | 31,567 | 41.1 | 111,909 | 39.0 | 89.4 | 6.5 | 7.0 |
| C17 | Small intestine | 1,604 | 47.7 | 2,941 | 46.2 | 1,303 | 45.7 | 64 | 40.6 | 1,331 | 45.2 | 7,243 | 46.2 | 80.4 | 0.2 | 0.2 |
| C18-C21,C260 | Colon and rectum | 59,633 | 50.2 | 159,244 | 47.0 | 68,923 | 47.8 | 7,515 | 46.0 | 72,855 | 45.9 | 368,170 | 47.4 | 88.9 | 24.1 | 18.1 |
| C22 | Liver, primary[b] | 3,913 | 39.3 | 7,650 | 39.0 | 6,210 | 28.2 | 258 | 43.0 | 14,787 | 30.9 | 32,818 | 33.4 | 89.2 | 0.8 | 0.7 |
| C23-C24 | Gallbladder and biliary tract[b] | 4,256 | 63.6 | 6,077 | 58.2 | 4,623 | 64.2 | 1,204 | 69.9 | 7,619 | 63.0 | 23,779 | 62.5 | 92.2 | 5.9 | 1.6 |
| C25 | Pancreas | 12,458 | 52.2 | 28,201 | 51.1 | 11,445 | 51.9 | 1.603 | 49.7 | 13,990 | 50.0 | 67,697 | 51.2 | 89.7 | 5.6 | 3.6 |
| C30-C31 | Nasal cavities and sinuses[b] | 829 | 40.8 | 1,847 | 42.3 | 864 | 32.5 | 69 | 31.9 | 850 | 32.2 | 4,459 | 38.0 | 78.1 | 0.2 | 0.2 |
| C32 | Larynx | 3,138 | 15.3 | 10,611 | 18.3 | 5,357 | 11.1 | 1,055 | 13.3 | 9,827 | 7.2 | 29,988 | 12.9 | 79.5 | 1.0 | 4.1 |
| C339, C34 | Lung,bronchus, trachea[b] | 44,158 | 35.7 | 168,201 | 37.1 | 54,291 | 22.2 | 8,972 | 27.1 | 63,133 | 17.6 | 338,755 | 30.6 | 88.9 | 16.9 | 29.2 |
| C384 | Pleura | 1,484 | 16.0 | 6,765 | 16.8 | 1,650 | 20.3 | 78 | 43.6 | 1,871 | 27.0 | 11,848 | 19.0 | 87.7 | 0.2 | 0.2 |
| C40-41 | Bone and cartilages[b] | 775 | 40.4 | 1,947 | 42.2 | 881 | 45.4 | 114 | 40.4 | 996 | 45.1 | 4,713 | 43.1 | 41.8 | 0.3 | 0.3 |
| C380, C47, C49 | Soft tissue | 2,679 | 45.6 | 5,758 | 43.7 | 2,755 | 44.8 | 271 | 54.2 | 2,438 | 46.0 | 13,901 | 44.9 | 62.4 | 1.0 | 0.6 |
| C440, C449 | Melanoma of skin | 18,506 | 52.3 | 29,128 | 58.3 | 13,458 | 55.8 | 1,258 | 56.4 | 11,370 | 55.3 | 73,720 | 55.8 | 55.4 | 5.0 | 2.4 |
| C67 | Bladder | 19,754 | 25.1 | 59,082 | 28.1 | 20,230 | 23.4 | 2,536 | 24.5 | 28,300 | 19.2 | 129,902 | 24.9 | 91.1 | 4.3 | 8.5 |
| C64-C66,C68 | Kidney | 12,418 | 41.8 | 25,213 | 37.8 | 14,186 | 40.8 | 2,364 | 39.5 | 15,341 | 34.8 | 69,522 | 38.5 | 81.9 | 6.5 | 6.4 |
| C693 | Melanoma of choroid | 331 | 45.6 | 1,068 | 47.4 | 410 | 48.0 | 19 | 52.6 | 379 | 45.9 | 2,207 | 47.0 | 71.6 | 0.1 | 0.0 |
| C71 | Brain | 6,983 | 43.9 | 17,770 | 42.2 | 6,318 | 43.5 | 962 | 46.9 | 8,028 | 44.9 | 40,061 | 43.4 | 63.0 | 3.1 | 2.3 |
| C739 | Thyroid | 4,359 | 74.1 | 5,846 | 71.3 | 4,833 | 74.1 | 668 | 81.1 | 7,207 | 76.7 | 22,913 | 74.4 | 43.3 | 3.8 | 0.6 |
| | Hodgkin's disease | 2,340 | 42.4 | 6,664 | 43.6 | 2,496 | 44.1 | 351 | 49.3 | 3,258 | 46.5 | 15,109 | 44.3 | 27.3 | 1.2 | 0.8 |
| | Non-hodgkin's lymphoma | 15,635 | 47.5 | 39,995 | 47.4 | 14,509 | 47.5 | 1,261 | 50.8 | 19,126 | 48.4 | 90,526 | 47.7 | 74.1 | 4.5 | 2.8 |
| | Multiple myeloma | 6,086 | 47.6 | 15,786 | 48.0 | 5,476 | 50.7 | 565 | 50.1 | 7,173 | 49.6 | 35,086 | 48.7 | 88.6 | 2.0 | 1.3 |
| | Leukaemia | 10,831 | 43.7 | 27,955 | 43.6 | 10,713 | 43.8 | 1,106 | 46.2 | 12,767 | 44.3 | 63,372 | 43.8 | 78.8 | 3.6 | 2.7 |
| | All cancers combined[c] | 260,662 | 43.2 | 726,376 | 41.3 | 290,251 | 38.5 | 36,738 | 39.0 | 354,845 | 36.1 | 1,668,872 | 40.0 | 83.1 | 100.0 | 100.0 |

Columns a, b and c describe data by rows while columns d and e describe data by columns.

a The European regional groupings are[10]: Northern Europe comprising Denmark (26% of Northern European patients), Finland (19%), Iceland (1%), Norway (20%), and Sweden (34%); UK & Ireland comprising England (77%), Northern Ireland (3%), Wales (5%), Scotland (10%) and Ireland (5%); Central Europe comprising Austria (31%), Belgium (16%), France (17%), Germany (5%), the Netherlands (23%), and Switzerland (8%); Eastern Europe comprising the Czech Republic (31%) and Poland (69%); Southern Europe, comprising Italy (70%), Malta (1%), Portugal (5%), Slovenia (6%), and Spain (18%).

b Note that in the text 'liver, primary' is referred to as liver; 'gallbladder and biliary tract' is referred to as biliary tract; 'nasal cavities and sinuses' is referred to as nasal cavities; 'bone and cartilages' is referred to as bone; and 'lung, bronchus and trachea' is referred to as lung.

c All cancers in ICD-O-3[11] except non-melanoma skin cancer and cancers of the breast, cervix uteri, corpus uteri, ovary, vagina and vulva, prostate, testis and penis.

**Table 2 – Differences in 5-year relative survival between men and women for 26 cancer sites and for all cancers combined of the European pool.**

| Cancer site | No. of patients | All ages | | | | 15–44 years | | 45–54 years | | 55–64 years | | 65–74 years | | 75–99 years | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Crude RS(W)% a | Crude RS(W) minus Crude RS(M) b | Age-adj RS(W)% c | Age-adj RS(W) minus Age-adj RS(M) d | W% e | Specific RS(W) minus Specific RS(M) f | W% e | Specific RS(W) minus Specific RS(M) f | W% e | Specific RS(W) minus Specific RS(M) f | W% e | Specific RS(W) minus Specific RS(M) f | W% e | Specific RS(W) minus Specific RS(M) f |
| Lip | 7,625 | 93.8 | 0.2 | 94.2 | 0.7 | 24.8 | 2.9 | 23.0 | 1.6 | 15.0 | -0.5 | 17.9 | 1.8 | 32.3 | −0.4 |
| Salivary gland | 5,627 | 74.1 | 16.5* | 69.5 | 16.2* | 56.1 | 7.5* | 44.4 | 16.1* | 42.5 | 19.8* | 39.6 | 19.6* | 48.1 | 12.2* |
| Head and neck | 49,569 | 52.1 | 11.2* | 49.9 | 11.9* | 27.8 | 17.6* | 20.5 | 14.0* | 21.9 | 13.2* | 28.5 | 11.9* | 47.3 | 8.8* |
| Oesophagus | 48,353 | 10.9 | 0.5 | 12.6 | 2.6* | 19.3 | 7.8* | 20.5 | 4.1* | 21.9 | 4.6* | 29.7 | 2.0* | 49.0 | −0.4 |
| Stomach | 111,909 | 24.2 | 3.4* | 25.8 | 4.8* | 44.0 | 4.2* | 32.1 | 5.9* | 29.2 | 6.0* | 33.0 | 5.3* | 48.0 | 2.9* |
| Small intestine | 7,243 | 42.7 | −1.7 | 42.5 | 0.0 | 39.2 | 0.7 | 42.2 | 3.0 | 41.0 | 1.3 | 43.1 | 0.6 | 56.0 | −3.2 |
| Colon and rectum | 368,170 | 54.1 | 1.4* | 55.0 | 2.3* | 50.1 | 2.8* | 45.0 | 3.4* | 40.1 | 4.7* | 42.5 | 2.7* | 55.3 | −0.4 |
| Liver, primary[e] | 32,818 | 8.2 | −0.7* | 9.5 | 0.4 | 33.8 | 5.2 | 24.8 | 0.5 | 22.3 | 0.7 | 30.5 | 0.7 | 45.7 | −1.2* |
| Gallbladder and biliary tract[e] | 23,779 | 11.5 | −3.5* | 13.0 | −2.7* | 48.7 | −2.7 | 54.4 | −5.1* | 56.9 | −3.4* | 59.2 | −2.5* | 68.4 | −1.3 |
| Pancreas | 67,697 | 4.2 | −0.2 | 5.3 | 0.7* | 41.2 | 7.7* | 39.0 | −0.3 | 40.6 | 0.9* | 47.6 | 0.2 | 61.8 | −0.1 |
| Nasal cavities and sinuses[e] | 4,459 | 50.9 | 1.6 | 50.5 | 2.7 | 35.9 | 8.9 | 29.1 | 7.5 | 30.3 | 5.4 | 36.9 | 2.9 | 49.5 | −3.3 |
| Larynx | 29,988 | 63.4 | −1.9 | 61.8 | −3.0* | 15.9 | 5.7 | 11.4 | 6.9* | 11.4 | 2.6 | 12.1 | −7.0* | 17.4 | −9.7* |
| Lung, bronchus, trachea[e] | 338,755 | 10.6 | 0.8* | 11.2 | 1.2* | 40.8 | 6.5* | 33.2 | 1.9* | 27.6 | 2.0* | 28.7 | 0.1 | 33.7 | 0.1 |
| Pleura | 11,848 | 7.9 | 3.4* | 8.7 | 3.9* | 30.8 | 11.1 | 15.8 | 3.1 | 15.2 | 5.4* | 17.2 | 2.4* | 24.8 | 2.7* |
| Bone and cartilages[e] | 4,713 | 63.0 | 7.4* | 62.2 | 9.7* | 40.5 | 7.8* | 40.5 | 15.1* | 40.7 | 17.9* | 41.7 | 9.6* | 58.3 | −5.0 |
| Soft tissue | 13,901 | 59.9 | 1.4 | 61.1 | 2.5* | 44.1 | 6.1* | 43.2 | 8.1* | 41.1 | 0.4 | 44.1 | −0.8 | 50.1 | −3.6 |
| Melanoma of skin | 73,720 | 89.3 | 9.1* | 88.9 | 9.0* | 61.9 | 8.5* | 55.1 | 9.5* | 49.4 | 8.3* | 51.1 | 9.7* | 59.7 | 9.4* |
| Bladder | 129,902 | 62.3 | −6.2* | 65.3 | −4.2* | 27.9 | −8.0* | 20.9 | −2.4* | 19.9 | −0.6 | 21.6 | −3.3* | 30.6 | −7.9* |
| Kidney | 69,522 | 55.8 | 0.1 | 55.4 | 1.7* | 36.8 | 4.3* | 32.3 | 6.5* | 33.7 | 4.0* | 37.2 | 1.3 | 47.8 | −2.5* |
| Melanoma of choroid | 2,207 | 74.3 | −0.1 | 73.0 | 0.1 | 47.5 | −2.4 | 42.2 | 0.6 | 42.0 | −0.9 | 49.1 | 5.6 | 54.2 | −4.4 |
| Brain | 40,061 | 18.3 | 1.3* | 21.4 | 3.3* | 41.4 | 5.8* | 38.0 | 5.8* | 41.0 | 2.7* | 44.8 | 0.2 | 53.1 | 0.5 |
| Thyroid | 22,913 | 89.6 | 8.2* | 84.9 | 7.3* | 78.5 | 2.6* | 75.0 | 9.4* | 69.2 | 13.7* | 69.5 | 8.4* | 74.3 | 2.5 |
| Hodgkin's disease | 15,109 | 83.1 | 0.6 | 80.6 | 1.8* | 45.1 | 1.8* | 36.1 | 2.4 | 38.7 | 0.2 | 45.4 | 2.1 | 56.2 | 2.3 |
| Non–hodgkin's lymphoma | 90,526 | 55.9 | 2.1* | 54.1 | 4.7* | 38.2 | 7.5* | 42.1 | 8.6* | 44.5 | 7.3* | 48.1 | 4.1* | 56.6 | 1.1 |
| Multiple myeloma | 35,086 | 32.6 | −0.7 | 35.6 | 2.0* | 39.9 | 1.1 | 41.5 | 2.6 | 43.5 | 2.4 | 46.5 | 3.0* | 55.4 | 0.6 |
| Leukaemia | 63,372 | 43.0 | −2.3* | 43.1 | −0.4 | 42.4 | −2.2 | 39.9 | −1.0 | 37.6 | −3.3* | 40.2 | 1.7 | 51.3 | 0.7 |
| All cancers combined[a] | 1,668,872 | 42.7 | 4.9* | 42.2 | 5.0* | 47.1 | 11.9* | 37.1 | 10.0* | 33.4 | 7.0* | 35.8 | 3.6* | 47.4 | 1.3* |
| | | [b]39.9 | [b]1.1* | [d]40.6 | [d]2.2* | | [c]4.1* | | [c]3.6* | | [c]3.7* | | [c]2.1* | | [c]0.0 |

Column 2 shows the total number of patients (men and women combined). Subsequent columns show: (column a) non-age adjusted (crude) 5-year relative survival (RS) in women; (column b) the difference (percentage points) in non-age adjusted 5-year RS between women (W) and men (M); (column c) 5-year age-adjusted RS for women; and (column d) the difference in 5-year age-adjusted RS between women and men. Subsequent columns e and f refer to specific age classes and show the percentages of total patients who are women (columns e) and the difference (% points) in 5-year age-specific RS between women and men (participating countries are specified in Table 1).

* Significant between-sex difference in relative survival (Z test; $P<0.05$).

a All ICD-O-3[11] sites except non-melanoma skin, breast, cervix uteri, corpus uteri, ovary, vagina and vulva, prostate, testis and penis.

b Non-age-adjusted (crude) relative survival adjusted by case-mix for women with difference between sexes.

c Difference between sexes for age-specific relative survival adjusted by case mix.

d Age-adjusted relative survival adjusted by case-mix for women with difference between sexes.

e Note that in the text 'liver, primary' is referred to as liver; 'gallbladder and biliary tract' is referred to as biliary tract; 'nasal cavities and sinuses' is referred to as nasal cavities; 'bone and cartilages' is referred to as bone; and 'lung, bronchus and trachea' is referred to as lung.

**Table 3 – Differences in survival between women and men for 26 cancer sites and all these sites combined for each European region and Europe.**

| Cancer site | Northern Europe[d] | | UK and Ireland[d] | | Central Europe[d] | | Eastern Europe[d] | | Southern Europe[d] | | Europe[d] | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Age-adj RS(W)% a | Age-adj RS(W) minus Age-adj RS(M) b | Age-adj RS(W) % a | Age-adj RS(W) minus Age-adj RS(M) b | Age-adj RS(W) % a | Age-adj RS(W) minus Age-adj RS(M) b | Age-adj RS(W) % a | Age-adj RS(W) minus Age-adj RS(M) b | Age-adj RS(W) % a | Age-adj RS(W) minus Age-adj RS(M) b | Age and region-adj RS(W) % c | Age and region-adj RS(W) minus Age and region-adj RS(M) d |
| Lip | 94.2 | 0.6 | 94.1 | −0.5 | 95.1 | 1.4 | n.e | n.e | 96.7 | 3.6 | 95.3 | 1.7 |
| Salivary gland | 68.5 | 8.8* | 68.6 | 16.5* | 74.4 | 23.0* | 60.7 | 25.7* | 69.3 | 16.8* | 71.6 | 19.2* |
| Head and neck | 53.6 | 12.7* | 48.9 | 8.4* | 49.5 | 13.7* | 36.0 | 4.3 | 51.3 | 15.0* | 50.2 | 13.1* |
| Oesophagus | 12.2 | 3.7* | 12.2 | 2.5* | 14.8 | 2.1 | 9.6 | n.e | 14.6 | 5.0* | 14.1 | 3.1* |
| Stomach | 25.3 | 5.0* | 18.3 | 3.1* | 29.6 | 4.5* | 17.6 | 3.9* | 32.7 | 4.7* | 28.3 | 4.3* |
| Small intestine | 46.8 | −2.9 | 37.4 | −0.5 | 45.5 | −0.8 | 27.4 | 1.9 | 45.8 | 3.6 | 44.3 | 0.4 |
| Colon and rectum | 57.5 | 2.7* | 52.0 | 2.3* | 59.0 | 2.1* | 41.1 | 0.4 | 56.4 | 2.0* | 57.0 | 2.2* |
| Liver, primary[e] | 07.2 | 1.8 | 07.7 | 0.3 | 09.3 | 0.3 | n.e | n.e | 11.7 | 1.0 | 9.6 | 0.6 |
| Gallbladder and biliary tract[e] | 11.1 | −1.0 | 14.7 | −1.5 | 14.3 | −4.3* | 8.1 | −1.1 | 13.1 | −3.2* | 13.8 | −3.3* |
| Pancreas | 03.6 | 0.1 | 04.6 | 0.2 | 07.0 | 1.3* | 5.8 | 0.7 | 07.0 | 2.0* | 6.4 | 1.2* |
| Nasal cavities and sinuses[e] | 57.0 | 3.5 | 50.3 | 4.6 | 48.1 | 1.8 | 51.1 | 20.3 | 44.6 | −5.1 | 48.0 | 0.4 |
| Larynx | 61.1 | −3.3 | 59.0 | −6.1* | 64.2 | 1.2 | 48.6 | −1.6 | 72.0 | 5.0* | 65.4 | 0.8 |
| Lung, bronchus, trachea[e] | 11.8 | 2.5* | 09.2 | 1.2* | 15.8 | 2.2* | 11.7 | 3.8* | 14.8 | 3.5* | 14.2 | 2.4* |
| Pleura | 9.4 | 5.7* | 07.1 | 3.0* | 11.9 | 6.2* | n.e | n.e | 09.3 | 2.4 | 10.2 | 4.5* |
| Bone and cartilages[e] | 66.7 | 9.6* | 60.1 | 9.8* | 67.2 | 10.0* | 40.7 | 22.6* | 61.1 | 8.9* | 64.2 | 9.6* |
| Soft tissue | 64.6 | 4.2* | 60.1 | 3.9* | 59.7 | −1.5 | 54.8 | −1.1 | 62.2 | 2.5 | 60.8 | 0.9 |
| Melanoma of skin | 91.1 | 7.4* | 89.3 | 10.8* | 88.4 | 8.3* | 74.9 | 16.5* | 86.9 | 8.1* | 88.3 | 8.6* |
| Bladder | 66.7 | −4.1* | 62.5 | −6.9* | 67.3 | −1.0 | 63.1 | −0.9 | 70.5 | 0.2 | 67.4 | −1.9* |
| Kidney | 53.8 | 2.3* | 46.3 | 0.5 | 63.3 | 2.9* | 54.4 | −1.1 | 63.7 | 1.6 | 60.0 | 2.1* |
| Melanoma of choroid | 67.7 | −6.5 | 77.2 | −0.3 | 68.6 | −1.1 | n.e | n.e | 70.5 | 7.4 | 70.5 | 1.1 |
| Brain | 23.5 | 3.0* | 20.3 | 3.4* | 22.4 | 3.4* | 22.9 | 5.9* | 20.5 | 2.7* | 21.6 | 3.2* |
| Thyroid | 86.5 | 6.4* | 79.4 | 5.5* | 85.3 | 7.2* | 81.7 | 6.7 | 88.0 | 8.5* | 85.2 | 7.3* |
| Hodgkin's disease | 83.7 | 2.2 | 78.3 | 0.8 | 82.9 | 3.1 | n.e | n.e | 81.7 | 2.8 | 81.8 | 2.6* |
| Non–hodgkin's lymphoma | 54.9 | 6.7* | 52.4 | 3.9* | 54.5 | 4.6* | 46.9 | 5.7 | 57.4 | 4.9* | 55.0 | 4.7* |
| Multiple myeloma | 37.3 | 2.3 | 31.7 | 2.0* | 36.6 | 0.5 | 25.9 | 2.7 | 41.5 | 1.6 | 37.2 | 1.2 |
| Leukaemia | 45.6 | −0.3 | 42.4 | −0.4 | 42.6 | −0.7 | 34.8 | −3.1 | 43.3 | −0.1 | 43.0 | −0.5 |
| All cancers combined[a] | 45.1 | 4.2* | 37.9 | 3.4* | 47.1 | 7.8* | 34.3 | 4.7* | 45.9 | 7.3* | 45.2 | 6.7* |
| | [b]41.7 | [b]2.5* | [b]37.9 | [b]1.7* | [b]43.4 | [b]2.7* | [b]34.7 | [b]2.7* | [b]43.4 | [b]3.5* | [b]42.4 | [c]2.7* |

For each region, columns a show the 5-year age-adjusted relative survival (RS) for women, and columns b the difference in survival between women and men in% points. For Europe, column c shows the 5-year age and region-adjusted survival (RS) for women, and column d the survival difference between women and men in% points.

* Significant difference between sexes (Z test; $P<0.05$).

a All sites in ICD-O-3[11] except non-melanoma skin, breast, cervix uteri, corpus uteri, ovary, vagina and vulva, prostate, testis and penis.

b Age-adjusted relative survival also adjusted by case-mix for women with difference between sexes.

c Age and region-adjusted relative survival for women also adjusted by case-mix with difference between sexes.

d Participating countries specified in Table 1. n.e., not estimable. For Eastern Europe all cancers combined does not include n.e. sites, and Europe does not include Eastern Europe.

e Note that in the text 'liver, primary' is referred to as liver; 'gallbladder and biliary tract' is referred to as biliary tract; 'nasal cavities and sinuses' is referred to as nasal cavities; 'bone and cartilages' is referred to as bone; and 'lung, bronchus and trachea' is referred to as lung.

**Table 4 – Relative excess risks (RER) of death for women compared to men for different age classes (with 95% confidence intervals in parentheses) in Europe.**

| Cancer site | RER of death for women all ages | | | | RER of death for women age 15–54 years | | RER of death for women age 55–99 years | |
|---|---|---|---|---|---|---|---|---|
| | Model 1[a] | | Model 2[b] | | Model 1[a] | | Model 1[a] | |
| Lip | 0.91 | (0.62–1.35) | 0.86 | (0.57–1.30) | 0.61 | (0.36–1.78) | 1.02 | (0.66–1.58) |
| Salivary gland | 0.57 | (0.51–0.64) | 0.57 | (0.51–0.64) | 0.48 | (0.37–0.61) | 0.60 | (0.53–0.67) |
| Head and neck | 0.73 | (0.71–0.75) | 0.72 | (0.70–0.74) | 0.65 | (0.61–0.69) | 0.75 | (0.73–0.78) |
| Oesophagus | 0.95 | (0.93–0.97) | 0.97 | (0.94–0.99) | 0.85 | (0.79–0.91) | 0.96 | (0.94–0.99) |
| Stomach | 0.92 | (0.90–0.93) | 0.90 | (0.88–0.91) | 0.90 | (0.86–0.94) | 0.92 | (0.90–0.93) |
| Small intestine | 1.00 | (0.94–1.07) | 1.00 | (0.93–1.07) | 0.90 | (0.78–1.07) | 1.02 | (0.95–1.10) |
| Colon and rectum | 0.97 | (0.96–0.98) | 0.96 | (0.95–0.97) | 0.90 | (0.87–0.92) | 0.98 | (0.97–0.99) |
| Liver, primary[e] | 1.02 | (0.99–1.04) | 1.04 | (1.01–1.07) | 0.90 | (0.83–0.98) | 1.03 | (1.00–1.06) |
| Gallbladder and biliary tract[f] | 1.14 | (1.11–1.18) | 1.15 | (1.12–1.19) | 1.15 | (1.05–1.29) | 1.14 | (1.11–1.18) |
| Pancreas | 0.97 | (0.95–0.99) | 0.97 | (0.95–0.99) | 0.92 | (0.88–0.98) | 0.98 | (0.96–1.00) |
| Nasal cavities and sinuses[f] | 0.91 | (0.83–1.01) | 0.90 | (0.82–0.99) | 0.76 | (0.61–0.95) | 0.95 | (0.85–1.05) |
| Larynx | 1.04 | (0.98–1.11) | 1.07 | (1.00–1.13) | 0.76 | (0.65–0.87) | 1.13 | (1.06–1.21) |
| Lung, bronchus, trachea[f] | 0.95 | (0.94–0.96) | 0.99 | (0.99–1.00) | 0.88 | (0.86–0.91) | 0.96 | (0.95–0.97) |
| Pleura[e] | 0.86 | (0.82–0.91) | n.e. | n.e. | 0.85 | (0.73–0.99) | 0.87 | (0.82–0.92) |
| Bone and cartilages[f] | 0.74 | (0.68–0.82) | 0.75 | (0.68–0.82) | 0.73 | (0.64–0.84) | 0.77 | (0.67–0.88) |
| Soft tissue | 0.94 | (0.89–1.00) | 0.94 | (0.89–1.00) | 0.77 | (0.71–0.86) | 1.04 | (0.97–1.12) |
| Melanoma of skin | 0.49 | (0.47–0.52) | 0.50 | (0.48–0.53) | 0.42 | (0.39–0.45) | 0.56 | (0.53–0.60) |
| Bladder | 1.30 | (1.27–1.33) | 1.31 | (1.28–1.34) | 1.30 | (1.16–1.42) | 1.30 | (1.27–1.33) |
| Kidney | 0.97 | (0.94–0.99) | 0.97 | (0.94–0.99) | 0.80 | (0.75–0.86) | 1.00 | (0.97–1.02) |
| Melanoma of choroid[e] | 1.00 | (0.82–1.23) | 0.99 | (0.81–1.21) | 1.08 | (0.74–1.58) | 0.97 | (0.77–1.24) |
| Brain | 0.93 | (0.91–0.95) | 0.93 | (0.90–0.95) | 0.85 | (0.82–0.89) | 0.98 | (0.95–1.01) |
| Thyroid | 0.69 | (0.63–0.75) | 0.67 | (0.62–0.72) | 0.25 | (0.21–0.33) | 0.79 | (0.79–0.85) |
| Hodgkin's disease | 0.87 | (0.85–0.89) | 0.89 | (0.82–0.96) | 0.79 | (0.68–0.89) | 0.96 | (0.87–1.07) |
| Non hodgkin's lymphoma | 0.87 | (0.85–0.89) | 0.87 | (0.85–0.88) | 0.72 | (0.68–0.75) | 0.91 | (0.89–0.93) |
| Multiple myeloma | 0.94 | (0.91–0.96) | 0.93 | (0.91–0.96) | 0.95 | (0.86–1.05) | 0.94 | (0.91–0.96) |
| Leukaemia | 1.03 | (1.01–1.06) | 1.03 | (1.01–1.06) | 1.07 | (1.01–1.12) | 1.03 | (1.00–1.05) |
| All cancers combined[d] | [c]0.95 | (0.95–0.96) | [c]0.96 | (0.96–0.97) | [c]0.85 | (0.84–0.86) | [c]0.97 | (0.96–0.97) |

a Model 1 Adjusted by age and region.
b Model 2 Adjusted by age.
c Adjusted also by case–mix.
d All sites in ICD-O-3[11] except non-melanoma skin, breast, cervix uteri, corpus uteri, ovary, vagina and vulva, prostate, testis and penis.
e Eastern Europe was not included because of problems in modelling data.
f Note that in the text 'liver, primary' is referred to as liver; 'gallbladder and biliary tract' as biliary tract; 'nasal cavities and sinuses' as nasal cavities; 'bone and cartilages' as bone; and 'lung, bronchus and trachea' as lung.

### 3.2. *European pool: Age specific analyses (columns e and f, Table 2)*

Overall, less women than men were considered in the study in all age groups, but the proportion varied with cancer site and age, being highest at 47%, in both the youngest (15–44 years) and oldest categories (75–99 years). In the 75–99 year category, there were more women than men for 14/26 cancer sites; for cancers of biliary tract, thyroid, and melanoma of skin there were more women than men in most age classes.

Women had significantly higher survival than men for all cancers combined in each age class; however, this advantage reduced progressively with age: from +12.0% points at 15–44 years to +1.3% points at 75–99 years.

For 4/11 cancer sites where women had a significant advantage in crude 5-year relative survival (salivary glands, head and neck, stomach and melanoma of skin), women also had a significant survival advantage in each age group. For the other seven sites the survival advantage was present, but not significant, in all age groups. For biliary tract and bladder, women in all age groups had a survival disadvantage but it was not always significant.

### 3.3. *European pool: Age adjusted analyses (columns c and d, Table 2)*

After age adjustment, the significant women's survival advantage for all cancers combined was +5.0% points. For the 11 sites where the advantage was significant in the non-age-adjusted data, the advantage remained significant in the age-adjusted data, and became significant for six more sites (oesophagus, pancreas, soft tissue, kidney, Hodgkin's disease and multiple myeloma). The significant *disadvantage* for women in non-age-adjusted survival remained, in the age-adjusted comparison, only for biliary tract and bladder (no longer for liver and leukaemias); while a new significant survival disadvantage emerged for larynx.

### 3.4. *European pool: Age and case mix adjusted analyses (all cancers combined, Table 2)*

After case mix adjustment, the women's advantage reduced from +4.9 to +1.1% points in the analysis with non-age-adjusted survival and from +5.0 to +2.2% points with age-adjusted survival, but the difference remained significant in

both cases. In the age-specific analyses, the women's advantage remained significant (but at 75–99 years) after case mix adjustment but reduced dramatically, though not uniformly, with increasing age (+4.1% points at 15–44 years, +3.6% points at 45–54, +3.7% points at 55–64, +2.1% points at 65–74, and 0.0% points at 75–99).

### 3.5. *Europe and European Regions: Age and case mix adjusted analyses (Table 3)*

For all cancers combined both age-adjusted and age- and case-mix adjusted 5-year relative survival were significantly higher in women than in men in all regions. After case-mix adjustment, this women's advantage ranged from +1.7% points in the UK and Ireland, where women's case mix adjusted survival was low (37.9%), to +3.5% points in Southern Europe where women's case mix-adjusted survival was high (43.4%).

The women's advantage was significant in all European regions for six cancer sites (salivary glands, stomach, lung, bone, melanoma of skin and brain). For three of these sites (salivary glands, stomach, and melanoma of skin) the women's advantage was also significant for all age groups (Table 2). Women had a *disadvantage* in all regions only for leukaemias (always non significant) and biliary tract (significant in 2/5 regions); other significant *disadvantages* were for bladder in Northern Europe and UK and Ireland, and larynx in UK and Ireland.

Survival and the proportion of women constituting the total cases (not shown) varied considerably across European regions. When 5-year age and region-adjusted relative survival was calculated for Europe (Eastern Europe excluded), women had a significant survival *disadvantage* for biliary tract (–3.3% points) and bladder (–1.9% points), and an advantage for 15/26 cancer sites: salivary glands (+19.2% points), head and neck (+13.1% points), oesophagus (+3.1%), stomach (+4.3% points), colon and rectum (+2.2% points), pancreas (+1.2% points), lung (+2.4% points), pleura (+4.5%), bone (+9.6%), melanoma of skin (+8.6% points), kidney (+2.1%), brain (+3.2% points), thyroid (+7.3% points), Hodgkin disease (+2.6%) and non-Hodgkin's lymphoma (+4.7% points). For all cancers combined the women's advantage was +6.7% points and +2.7% points after adjusting for case mix (Table 3, column d).

### 3.6. *Multivariable analyses (Table 4)*

Two models are shown for the all-ages analysis: Model 1 with age at diagnosis and region as covariates, and Model 2 without the region covariate. For all ages, Model 1, women had a significantly lower RER of dying than men for 16/26 sites (salivary glands, head and neck, oesophagus, stomach, colon and rectum, pancreas, lung, pleura, bone, melanoma of skin, kidney, brain, thyroid, Hodgkin's disease, non-Hodgkin's lymphoma and multiple myeloma). For all of these sites, except for multiple myeloma, the age and region adjusted univariate analyses also showed a survival advantage (Table 3, column d). By Model 1 women had a significantly *higher* RER of dying than men for biliary tract and bladder (consistent with the age- and region-adjusted univariate findings) and also leukaemia.

When the analyses were restricted to older patients (55–99 years), for 12/16 sites noted above (except pancreas, kidney, brain and Hodgkin's disease) the women's RER of dying was again significantly less than that of men. Women had a significantly higher RER of dying for biliary tract, larynx and bladder. Among younger patients (15–54 years), women had a significantly lower RER of dying for 19 sites (all sites of the all-ages analysis except multiple myeloma, plus liver, nasal cavities, larynx and soft tissues). In this age class, women had significantly higher RERs of dying for biliary tract, bladder and leukaemia.

The results of Model 2, which omitted the region covariate, were closely similar to those of Model 1 (data not shown for young and old patients). However, the region covariate seemed to play a role in the lower RER of women dying from lung cancer and from laryngeal cancer in older age groups.

For all cancers combined, women's RERs of death were 0.95 for all ages, 0.85 for younger patients and 0.97 for older patients (by Model 1), in all cases significantly lower than men. These risks reduced by 1 percentage point when assessed by Model 2. Fig. 1 synthesises results for all cancers combined in univariate analysis. For women, 5-year relative survival was 42.7% in crude analyses and 42.4% when the age, case-mix and region adjustment was performed; on the other hand, for men, survival figures were 37.8% in crude data and 39.7% when the age, case-mix and region adjustment was considered. Thus, after all the performed adjustments (note that in this last analysis Eastern Europe data were not included), the female advantage reduced to 2.7 percentage points from 4.9 percentage points when crude data were compared.

Fig. 2 synthesises the results for all cancers combined in multivariable analysis, highlighting how the differences between male and female survival in all ages is mainly attributable to the female performance in younger ages.

## 4. Discussion

We have found that women had a survival advantage for most cancers. In the age-adjusted univariate analyses on the European pool, women had significantly better survival for 17/26 sites, and only for biliary tract, larynx and bladder was survival significantly worse in women (Table 2). In the analysis by region, the women's advantage was significant in all regions for six sites. Although the women's *disadvantage* for biliary tract, bladder and leukaemias was pervasive, for no site was a significant women's *disadvantage* present in all regions (Table 3). In the multivariable analyses the women's advantage (lower RER of dying) was significant for 16/26 sites. A significant disadvantage was found for biliary tract, bladder, larynx (older patients) and leukaemia (younger patients).

### 4.1. *Age at diagnosis*

Cancer survival decreases with age at diagnosis for both women and men, at least in Europe.[19] We found that age at diagnosis had a major effect on the women's survival advantage. This is evident from Fig. 2, which shows women had 5% lower RER of dying by Model 1 which was still 4% lower than men

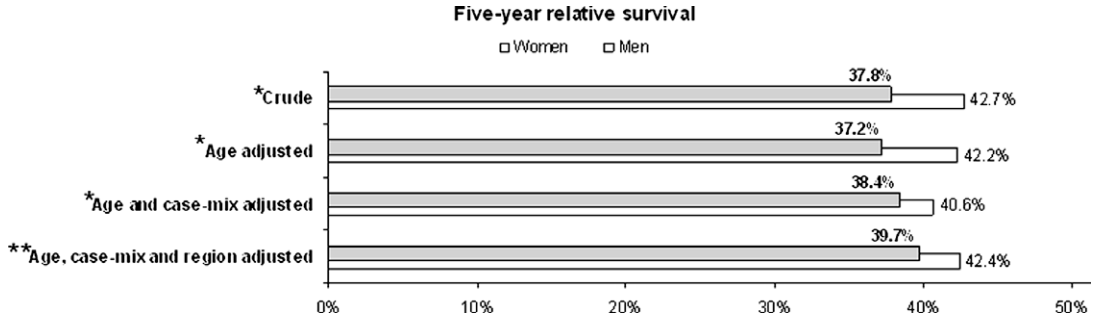


**Fig. 1 – Non age adjusted (crude), age adjusted, and age and case-mix adjusted in the European Pool; and age, case-mix and region adjusted 5-year relative survival for all cancers combined in Europe (Participating countries are given in Table 1). Figures are based on 1,668,877 cases except the age, case-mix and region adjusted figures that are based on 1,632,139 cases (see footnote in Table 3). * Figures from Table 2; ** Figures from Table 3.**

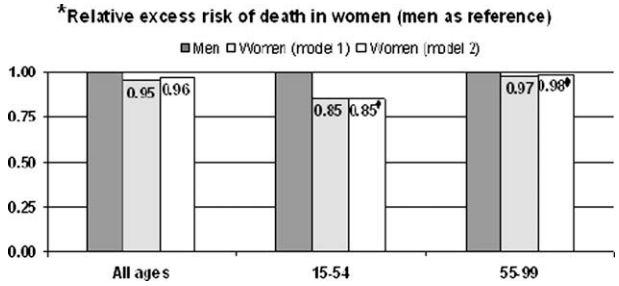


**Fig. 2 – Relative excess risk of death in women compared to men for all ages, 15–54 years and 55–99 years, for all cancers combined in Europe (Participating countries are given in Table 1). Figures are based on 1,668,877 cases. *Figures from Table 4 except '♦'data.**

when the region variable was excluded (Model 2). As shown in Table 2 (age and case-mix adjusted relative survival for all cancers combined), this advantage was most marked in young adults, declined in middle ages and reduced dramatically in the oldest patients. We used broad age-adjustment categories because early censoring or lack of cases produced missing values in one or more narrower age-classes. However, we were able to use narrower (5-year) age adjustment categories in the pooled analysis for all cancers combined. This more precise age adjustment produced substantially similar figures to the case-mix adjusted results shown in Table 2: the women's survival advantage was +3.6% points in 45–54 and +3.7% in 55–64 (middle ages), and +2.2% points and +0.6% points in the oldest patients (significant in all cases). In young adults (15–44) this advantage was not estimable because of missing values in the 15–19, 20–24 and 25–29 age groups.

Health systems may tend to favour younger over older patients, at least in Europe.[20] However, it is difficult to conceive how this phenomenon acts differentially in the two sexes as age increases. The most likely explanation is that age at diagnosis is a proxy for biological factors that change more markedly in women than men as age advances. The biological factor that immediately suggests itself is hormonal status. As women progress from mature fertility through peri-menopause to menopause, their sex hormone status changes profoundly; similar dramatic changes do not occur in men. It seems probable, therefore, that sex hormones are the prime mediators of the female cancer survival advantage.

### 4.2. *Regional differences between women and men*

It seems likely *a priori* that genetic heterogeneity across Europe will contribute to regional differences in the risk of dying from cancer; however, this heterogeneity should affect both sexes to the same extent. The regional variations we found in female versus male cancer survival may therefore to be due to non-genetic factors: perhaps women tend to take better care of their health, and these tendencies vary with region. However, as noted, regional variation (Fig. 2) can explain only a limited part of the women's advantage.

### 4.3. *Cancer site*

Survival varies markedly with cancer site.[19] Our findings are in general supported by published population-based investigations.[21–27,29,30] A study on EUROCARE-2 data noted that women with lung cancer have better survival than men;[21] A recent study on a population-based sample of 19,000 Surveillance Epidemiology and End Results cases found that elderly women with early lung cancer had better risk-adjusted survival than men, both when untreated and when treated, and regardless of treatment type, suggesting that the natural history of lung cancer may differ in women and men.[22] In a EUROCARE-2 study on 35,000 European head and neck cancer patients, women had better 5-year, but not 1-year survival than men.[23] A EUROCARE-2 study on 20,000 oesophageal and 66,000 gastric cancer patients found slightly better survival for women than men in most European countries.[24] Five-year age-standardised relative survival in 2000 EUROCARE-2 bone cancer cases was 51% in women and 45% in men.[25] Analysis of 16,000 EUROCARE-2 brain cancer patients revealed better survival in women than men in all countries except Switzerland and Austria, and that the advantage was present in all age classes.[26] A study on 73,000 EUROCARE-2 haematological cancer patients found that 5-year relative survival was slightly better for women than for men except for multiple myeloma.[27] A review on the effect of gender on cutaneous melanoma reported that most epidemiological data indicated a survival advantage for women with primary melanoma, and

suggested a role of sex hormones in mediating this advantage.[28] A 1990 population-based investigation of 6300 cancer cases which were under 20 years of age at diagnosis in Sweden revealed an advantage in 5-year survival for women which increased with increasing age. The authors suggested that sex hormones had a role in this advantage.[29]

One factor that may contribute to explaining the women's survival advantage found in this and other studies is that the distribution of cancer morphologies (with differing prognoses) varies between men and women – perhaps in relation to different exposure to risk factors. However, morphology (together with stage at diagnosis and treatment) must be studied on a site-per-site basis and is outside the scope of the present survey. Another factor that may contribute is co-morbidity, particularly for cases in which a given risk factor is associated both with cancer and co-morbidities. Smokers have higher incidences of (and death risks of) cancer and cardiovascular diseases than non smokers. Hence, relative survival for cancer patients might be underestimated because they die more often than expected of cardiovascular diseases. The prevalence of smoking is higher in men than women; e.g. women account for only 30% of all lung cancer patients (Table 1, column b of European pool), thus biasing the survival difference between sexes and contributing to the male disadvantage for tobacco-related cancers.

The biliary tract was one of the few sites in the present study where survival was consistently better in men than women. In a previous EUROCARE-2 study on 11,500 patients with biliary tract cancer, survival rates were closely similar in men and women.[30]

## 5. Conclusions

Our previous study on the prognostic role of sex in cancer survival investigated 1 million EUROCARE-2 cases.[6] Multivariable analysis showed that the relative risk of dying was 2% lower in women after adjusting for age, case-mix and country population (not regional population as in the present study).[6] The women's advantage was most evident in the young, reduced in middle age, and reversed in the oldest patients when men had better prognoses.[6] We concluded that women might be intrinsically more robust than men in coping with cancer.

In the present multivariable analyses we investigated the same age categories and practically the same sites as in EUROCARE-2. Like EUROCARE-2 we found pervasive and significant female advantages for head and neck, oesophagus, stomach, and pancreas. We also found significant women's advantages for salivary glands, colon and rectum, lung, pleura, bone, melanoma of skin, kidney, brain, thyroid, Hodgkin's disease and non-Hodgkin's lymphoma, that were not significant in EUROCARE-2. Finally, we uncovered a significant female disadvantage for biliary tract, leukaemia and bladder – a disadvantage for the latter site was also found in EUROCARE-2.

The present study supports our previous results, with the analysis by age and across European regions suggesting that biological factors are more important that cultural factors in determining the women's advantage. The novelty of the present study is that it has characterised this advantage as a plateau in middle age followed by a marked decline as age progresses beyond menopause, suggesting that female hormonal status is a major factor and certainly merits further investigation. Finally, a likely implication of our findings is that changes in male behaviour (such as increasing concern with health and body) can reduce only a part of the male disadvantage.

## Conflict of interest statement

None declared.

## EUROCARE-4 Working Group

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