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## Original Paper

# Variation in Survival of Adult Patients with Haematological Malignancies in Europe Since 1978

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**Data on 73 070 patients for seven major haematological malignancies diagnosed in Europe between 1985 and 1989 from 39 population-based cancer registries in 17 countries are included in the EUROCARE database. Relative survival was analysed by country and age between 1985 and 1989 and time trends were analysed from 1978–1989 for 13 countries which collaborated in EUROCARE for this entire period. The European weighted age-standardised 5-year relative survival rate was 72% for patients with Hodgkin's disease (HD, ranging from 45 to 76% in 13 countries), 63% for chronic lymphocytic leukaemia (CLL, range 51–79%, 14 countries), 46% for patients with non-Hodgkin's lymphoma (NHL, range 25–63%, 17 countries), 31% for patients with chronic myelocytic leukaemia (CML, range 8–40%, 13 countries), 28% for patients with multiple myeloma (MM, range 18–36%, 14 countries), 25% for patients with acute lymphoblastic leukaemia (ALL, range 19–33%, 7 countries) and 10% for patients with acute myeloblastic leukaemia (AML, range 4–15%, 11 countries). In all countries, relative survival declined with age, most markedly for patients with acute leukaemias. Patients in Northern and Western Europe had better survival rates, particularly in younger patients (15–45 years of age), whilst those in Eastern European countries tended to have poorer rates. Compared with 1978–1979, relative 5-year survival improved in 1987–1989 for most haematological malignancies (relative risk (RR) of death for CLL 0.65, AML 0.75, HD 0.76, ALL 0.79, NHL 0.82), with only CML (RR 0.95) and MM (RR 1.00) showing little or no change. These results suggest that generally and particularly in Eastern Europe there is room for improvement in the diagnosis and treatment of haematological malignancies. The intercountry differences also highlight the importance of socio-economic conditions to health status.** © **1998 Elsevier Science Ltd. All rights reserved.**

**Key words: haematological malignancies, relative survival, Europe, registries**
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## INTRODUCTION

In 1990, haematological malignancies comprised approximately 7.5% of all new malignancies and 7% of cancer deaths in Europe, generally occurring more frequently among men than women [1]. The incidence rates of most haematological malignancies, except acute lymphoblastic leukaemia (ALL), increase with age after the age of 30 years and more than 60% of all patients are over the age of 60 years. As a proportion of all cancers, haematological malignancies decrease from approximately 40% of all childhood cancers to 10% of cancers in those aged 30 years and 5% of all cancers in the elderly. Haematological malignancies originate in the bone marrow and lymph nodes and are often systemic at diagnosis. Immunosuppression, benzene, nuclear irradiation and alkylating agents, used previously against other cancers, are established risk factors and viruses are also probably involved, but generally account for only a small proportion of the cases [2, 3]. Since the mid-1960s, increasingly effective (but aggressive) cytotoxic and radiation therapies have become

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available in parallel with increasingly sophisticated and refined methods of detection and classification [4, 5]. There are three major groups of haematological malignancies: lymphomas, leukaemias and multiple myeloma (MM). Lymphomas include non-Hodgkin's lymphomas (NHL), comprising almost 50% of all haematological malignancies, which can be subclassified into 3–10 or more subtypes [6, 7] and Hodgkin's disease (HD), with four histological subtypes. There are four main types of leukaemia: acute lymphoblastic (ALL), acute myeloblastic (AML), chronic lymphocytic (CLL) and chronic myelocytic (CML). Each of the leukaemias could be further classified into 2–7 subgroups, based on morphological, immunological or cytogenetic criteria with prognostic and possibly also aetiological relevance [8]. In total, more than 25 clinically relevant subcategories of haematological malignancies can be distinguished in adults, but the age-specific distribution is different.

Due to the rarity of the various haematological malignancies, certainly according to subtype, collaborative research is necessary to get stable results based on proper classification. Although possibly less accurate, population-based survival data usually give a more representative view of the state of medical management and also allow the assessment of improvements in treatment over time. In the first EUROCARE study, considerable variation in 5-year relative survival was observed from 1978–1985 across 11 countries for adult patients with HD (66–77%), ALL (13–28%) and AML (6–12%). This current EUROCARE II study updates those results, using data from approximately 122 000 adult cases with haematological malignancies, with at least 5 years of follow-up, registered between 1978 and 1989, with approximately 73 000 between 1985 and 1989. Detailed data at the registry level can be found in the special IARC monograph [10]. This article also contains the first analysis of relative survival of adult patients with NHL and MM in Europe, as these were not included in the first EUROCARE study.

## PATIENTS AND METHODS

Between 1985 and 1989, 39 cancer registries in 17 European countries contributed data, whereas only 21 registries from 13 countries contributed during the period 1978–1989. All newly diagnosed adult patients with any of the seven major haematological malignancies were included, classified according to ICD-9 as ALL (204.0), AML (205.0), CLL (204.1), CML (205.1), NHL (200, 202), HD (201) and MM (203). Cases of myelodysplasia, morbus Waldenström, monoclonal gammopathy of unknown significance (MGUS), polycythaemia vera, myelofibrosis and essential thrombocytaemia were excluded. Hairy cell leukaemia and the various skin lymphomas were included as NHL.

Table 1 indicates the number of patients by country for each of the seven haematological malignancies. Table 2 details the quality of the data and shows that the proportion of histologically verified cases was generally more than 75%, a criterium for inclusion in the survival analysis. The death certificate only (DCO) cases and those lost to follow-up were excluded from the survival analysis. The registries of Denmark, Estonia, Finland, Iceland, Scotland, Slovakia and Slovenia cover the entire population of these countries, the English registries cover almost 50% and registries in Sweden (south), Austria (Tirol), Switzerland (Cantons of Geneva and Basel), Spain (4 registries), France (7 registries), Italy (9 registries), The Netherlands (southeast), Poland (Cracow and Warsaw) and Germany (Saarland), up to one-fifth of the

*Table* 1. *Number of adults with haematological malignancies, diagnosed in Europe,* 1985–1989 *according to country (EUROCARE* II*)*

| | ALL | AML | CLL | CML | NHL | HD | MM | Total |
|---|---|---|---|---|---|---|---|---|
| Northern Europe | | | | | | | | |
| Iceland | 6 | 23 | 22 | 10 | 78 | 14 | 57 | 210 |
| Finland | 167 | 515 | 621 | 207 | 2348 | 528 | 1168 | 5554 |
| Sweden* | 48 | 192 | 331 | 77 | 896 | 151 | 453 | 2148 |
| Denmark | 142 | 945 | 1271 | 336 | 2868 | 602 | 1239 | 7403 |
| U.K. | | | | | | | | |
| Scotland | 119 | 644 | 723 | 264 | 2902 | 625 | 1192 | 6469 |
| England | 627 | 2890 | 3370 | 1579 | 12 854 | 2929 | 5720 | 29 969 |
| Western and Central Europe | | | | | | | | |
| The Netherlands* | 24 | 79 | 92 | 45 | 388 | 87 | 152 | 867 |
| Germany* | 37 | 96 | 151 | 92 | 388 | 122 | 169 | 1055 |
| Austria* | 10 | 29 | 45 | 15 | 130 | 25 | 41 | 295 |
| Switzerland* | 25 | 82 | 132 | 65 | 472 | 107 | 136 | 1019 |
| France* | 55 | 234 | 392 | 219 | 983 | 249 | 346 | 2478 |
| Southern Europe | | | | | | | | |
| Spain* | 67 | 161 | 292 | 125 | 862 | 292 | 408 | 2207 |
| Italy* | 151 | 525 | 636 | 369 | 2562 | 712 | 1095 | 6050 |
| Eastern Europe | | | | | | | | |
| Slovenia | 56 | 136 | 321 | 121 | 541 | 142 | 222 | 1539 |
| Slovakia | 119 | 368 | 811 | 331 | 1069 | 448 | 686 | 3832 |
| Poland* | 30 | 83 | 86 | 48 | 341 | 156 | 158 | 902 |
| Estonia | 22 | 88 | 301 | 78 | 267 | 174 | 143 | 1073 |
| Europe | 1705 | 7090 | 9597 | 3981 | 29 949 | 7363 | 13 385 | 73 070 |

* < 20% of the national population covered. ALL, acute lymphoblastic leukaemia; AML, acute myeloblastic leukaemia; CLL, chronic lymphocytic leukaemia; CML, chronic myelocytic leukaemia; NHL, non-Hodgkin's lymphoma; HD, Hodgkin's disease; MM, multiple myeloma.

national population. The proportion of cases over 75 years of age was generally highest for MM and did not differ greatly for AML and NHL. The relatively small proportion of elderly patients in Eastern European countries is due to demographic factors, but in Spain and Austria, it could also be due to incompleteness.

Despite larger older female populations, there was a slight male predominance for all haematological malignancies, except MM: men comprised $\geq 60\%$ of all cases of CLL in 9 countries, of CML in 5 countries, of ALL in 3, of HD in 2, and of AML and NHL in only one country (data not shown).

Because of low numbers of patients in some countries (especially Iceland and Austria and sometimes Poland, The Netherlands and Switzerland), survival data are not always shown for them. For each type of malignancy, survival rates were calculated for the most recent 5-year period, i.e. 1985–1989 by age group and country. Trends in relative survival were also analysed from 1978–1980, 1981–1983, 1984–1986 and 1987–1989. Relative survival rates were calculated using the Hakulinen program [12], defined as the ratio of the observed to the expected survival rate, the latter calculated from regional or national mortality tables. Age-standardised survival rates were calculated from age-specific rates directly, taking the age distribution of the whole European sample as the standard. The general European estimates were weighted according to the national incidence, reflecting also the size and age-distribution of that population [11].

For an immediate comparison of survival differences and trends, the relative risk (RR) of death was calculated as the ratio of the logarithm for relative survival of the category of interest to that of a reference category, the European rate or rate from a previous period.

## RESULTS

*The effect of the type of malignancy on survival*

For adult patients diagnosed between 1985 and 1989 the European weighted average 5-year relative survival was highest for HD (72%) and lowest for AML (10%; Figure 1, Table 3). One-year relative survival was also low for patients with acute leukaemias: 29% for AML and 51% for ALL, but ranged from 65 to 88% for patients with chronic leukaemias, lymphomas and MM. Similarly, for all countries, age-standardised 5-year survival rates for ALL and AML were inferior to those for chronic leukaemias and lymphomas and MM (Figure 1, Table 3).

*Intercountry variation in survival*

*Acute leukaemia.* For ALL, the highest relative 5-year survival rate was reported in Sweden (33%), the lowest in Finland (19%), but none of the countries had a rate that was significantly different from the European average (Figure 1a). Generally, 5-year survival rates for adults with AML were low (less than 10% in five countries), whereas the rate seemed elevated in France (15%) (Figure 1b).

*Chronic leukaemia.* Five-year relative survival for patients with CLL was generally favourable throughout Europe, but there were major differences between countries (Figure 1c). The highest rates (70–79%) were seen in France, The Netherlands, Germany, Switzerland and Spain, whilst rates for patients in Eastern and Northern countries ranged between 47 and 63%. For CML (Figure 1d), the highest rates occurred in France (40%), Spain (38%) and Slovakia (34%), all above the European average (31%), but elsewhere survival was generally below this, particularly in Poland (8%).

*Lymphomas and MM.* For patients with NHL, 5-year rates ranged from 42 to 50% in most Northern, Western and

*Table 2. Data quality for haematological malignancies in Europe,* 1985–1989 *(EUROCARE* II*)*

| | ≥ 75 years of age | | | | | |
|---|---|---|---|---|---|---|
| | AML % | NHL % | MM % | % HV | % DCO | % Lost to follow-up |
| Northern Europe | | | | | | |
| Iceland | 39 | 27 | 25 | 95 | 0 | 0 |
| Finland | 26 | 24 | 34 | 94 | 1 | 0 |
| Sweden* | 28 | 31 | 43 | 98 | 0 | 0 |
| Denmark | 28 | 27 | 34 | 100 | 0 | 0 |
| U.K. | | | | | | |
| Scotland | 30 | 28 | 39 | 81 | 2 | 0 |
| England | 31 | 27 | 38 | 74 | 9 | 0 |
| Western and Central Europe | | | | | | |
| The Netherlands* | 29 | 24 | 33 | 95 | 0 | 3 |
| Germany* | 25 | 24 | 28 | 96 | 9 | 0 |
| Austria* | 3 | 30 | 16 | 95 | 6 | 0 |
| Switzerland* | 34 | 33 | 43 | 100 | 0 | 3 |
| France* | 32 | 27 | 35 | 96 | 0 | 0 |
| Southern Europe | | | | | | |
| Spain* | 16 | 23 | 29 | 97 | 5 | 0 |
| Italy* | 23 | 24 | 37 | 77 | 2 | 0 |
| Eastern Europe | | | | | | |
| Slovenia | 24 | 19 | 18 | 99 | 0 | 1 |
| Slovakia | 14 | 17 | 22 | 99 | 6 | 0 |
| Poland* | 18 | 18 | 23 | 85 | 3 | 2 |
| Estonia | 17 | 15 | 13 | 99 | 0 | 1 |

* < 20% of the national population covered. HV, histologically verified; DCO, death certificate only; AML, acute myeloblastic leukaemia; NHL, non-Hodgkin's lymphoma; MM, multiple myeloma.

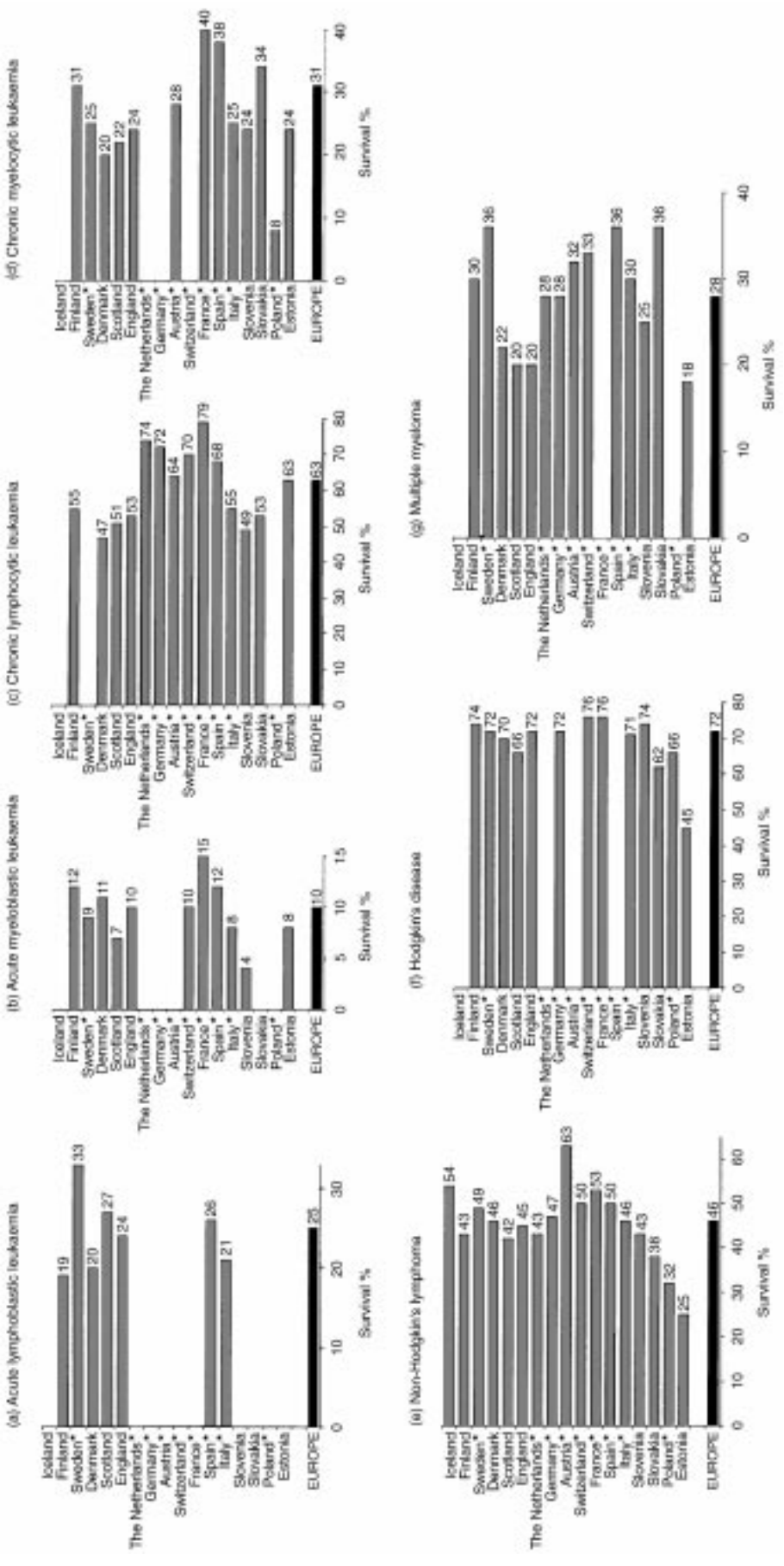


**Figure 1. Age-standardised 5-year relative survival rates for adults with haematological malignancies, 1985–1989 (EUROCARE II). * < 20% of the national population covered. Rates are not shown for countries with an insufficient number of cases.**

*Table* 3. *Age-standardised* 5*-year relative survival rates (%) for adults with haematological malignancies,* 1985–1989 *(EUROCARE* II*)*

| | ALL | | AML | | CLL | | CML | | NHL | | HD | | MM | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | RS | RR | RS | RR | RS | RR | RS | RR | RS | RR | RS | RR | RS | RR |
| Northern Europe | | | | | | | | | | | | | | |
| Iceland | † | | † | | † | | † | | 54 | 0.8 (0.5–1.1) | † | | † | |
| Finland | 19 | 1.2 (0.9–1.5) | 12 | 0.9 (0.8–1.1) | 55 | 1.3 (1.0–1.5) | 31 | 1.00 (0.8–1.3) | 43 | 1.1 (1.0–1.2) | 74 | 0.9 (0.8–1.1) | 30 | 0.9 (0.85–1.05) |
| Sweden* | 33 | 0.8 (0.6–1.1) | 9 | 1.1 (0.8–1.3) | † | | 25 | 1.2 (0.7–1.6) | 49 | 0.93 (0.8–1.1) | 72 | 0.9 (0.6–1.1) | 36 | 0.8 (0.7–0.9) |
| Denmark | 20 | 1.2 (0.9–1.5) | 11 | 1.0 (0.9–1.1) | 47 | 1.6 (1.4–1.9) | 20 | 1.4 (1.1–1.6) | 46 | 1.0 (0.9–1.1) | 70 | 1.1 (0.9–1.3) | 22 | 1.2 (1.1–1.3) |
| U.K. | | | | | | | | | | | | | | |
| Scotland | 27 | 1.0 (0.7–1.2) | 7 | 1.1 (1.0–1.3) | 51 | 1.4 (1.2–1.7) | 22 | 1.3 (1.0–1.6) | 42 | 1.1 (1.0–1.2) | 66 | 1.3 (1.1–1.5) | 20 | 1.3 (1.2–1.4) |
| England | 24 | 1.0 (0.9–1.2) | 10 | 1.0 (0.9–1.1) | 53 | 1.4 (1.2–1.5) | 24 | 1.2 (1.1–1.4) | 45 | 1.1 (1.0–1.1) | 72 | 1.0 (0.9–1.1) | 20 | 1.2 (1.2–1.4) |
| Western Europe | | | | | | | | | | | | | | |
| The Netherlands* | † | | † | | 74 | 0.7 (0.2–1.2) | † | | 43 | 1.1 (0.9–1.3) | † | | 28 | 1.0 (0.8–1.2) |
| Germany* | † | | † | | 72 | 0.7 (0.3–1.1) | † | | 47 | 1.0 (0.8–1.2) | 72 | 1.0 (0.6–1.4) | 28 | 1.0 (0.7–1.2) |
| Austria* | † | | † | | 64 | 1.0 (0.3–1.6) | 28 | 1.1 (0.7–1.5) | 63 | 0.6 (0.3–0.9) | † | | 32 | 0.9 (0.7–1.2) |
| Switzerland* | † | | 10 | 1.0 (0.7–1.3) | 70 | 0.8 (0.4–1.1) | † | | 50 | 0.9 (0.8–1.0) | 76 | 0.8 (0.6–1.1) | 33 | 0.9 (0.7–1.1) |
| France* | † | | 15 | 0.8 (0.7–1.0) | 79 | 0.5 (0.3–0.7) | 40 | 0.8 (0.6–1.0) | 53 | 0.8 (0.7–0.9) | 76 | 0.8 (0.6–1.0) | † | |
| Southern Europe | | | | | | | | | | | | | | |
| Spain* | 26 | 1.0 (0.7–1.3) | 12 | 0.9 (0.7–1.1) | 68 | 0.8 (0.6–1.1) | 38 | 0.8 (0.6–1.1) | 50 | 0.9 (0.8–1.0) | † | | 36 | 0.8 (0.6–0.95) |
| Italy* | 21 | 1.1 (0.9–1.4) | 8 | 1.1 (1.0–1.3) | 55 | 1.3 (1.1–1.5) | 25 | 1.2 (1.0–1.4) | 46 | 1.0 (0.95–1.1) | 71 | 1.0 (0.9–1.2) | 30 | 0.9 (0.8–1.0) |
| Eastern Europe | | | | | | | | | | | | | | |
| Slovenia | † | | 4 | 1.4 (0.9–1.8) | 49 | 1.5 (1.2–1.9) | 24 | 1.2 (0.9–1.6) | 43 | 1.1 (0.95–1.3) | 74 | 0.9 (0.6–1.2) | 25 | 1.1 (0.8–1.3) |
| Slovakia | † | | † | | 53 | 1.3 (1.1–1.6) | 34 | 0.9 (0.7–1.2) | 38 | 1.3 (1.1–1.4) | 62 | 1.4 (1.2–1.7) | 36 | 0.8 (0.7–0.9) |
| Poland* | † | | † | | † | | 8 | 2.1 (1.7–2.6) | 32 | 1.5 (1.2–1.8) | 66 | 1.3 (0.9–1.7) | † | |
| Estonia | † | | 8 | 1.1 (0.7–1.5) | 63 | 1.0 (0.7–1.3) | 24 | 1.2 (0.8–1.7) | 25 | 1.8 (1.5–2.1) | 45 | 2.4 (1.7–3.1) | 18 | 1.3 (1.0–1.6) |
| Europe | 25 | | 10 | | 63 | | 31 | | 46 | | 72 | | 28 | |

* < 20% of the national population covered. †not given because of low numbers. RR, relative risk of death (95% confidence intervals) in each country versus the European average; RS, relative survival; ALL, acute lymphoblastic leukaemia; AML, acute myeloblastic leukaemia; CLL, chronic lymphocytic leukaemia; CML, chronic myelocytic leukaemia; NHL, non-Hodgkin's lymphoma; HD, Hodgkin's disease; MM, multiple myeloma.

Southern countries, with the rates in Austria (63%) and France (53%), both significantly above the European average (46%) (Figure 1e, Table 3). Again, rates tended to be low in Eastern European countries, with Slovenia an exception. Generally for HD, 5-year relative survival rates for adults were relatively good ($\geq$ 70%, Figure 1f), with slightly lower rates (62–66%) observed in Scotland, Slovakia and Poland. The lowest survival for HD was seen in Estonia (45%), which was significantly lower than the European average (72%, Table 3). For MM, age standardised relative 5-year survival was significantly higher than the European average (28%) in Sweden (36%), Spain (36%) and Slovakia (36%), in contrast to those from the U.K. (20%) and Estonia (18%). (Figure 1g, Table 3).

*Age* 15–44 *years.* Small case numbers for some malignancies (CLL and MM) prevented age-standardised survival rates being calculated for all countries. Therefore, for a wider comparison, an analysis restricted to those aged 15–44 years was carried out for 5-year relative survival (Figure 2), enabling a more homogeneous comparison with respect to detection (and thus stage) and putative distribution according to subtype, so allowing an assessment of the influence of treatment in the various countries.

As expected, survival rates in the 15–44 age group were better than age-standardised rates for all malignancies analysed in all countries. For each type of malignancy, the inter-country variation seen with the age-standardised 5-year survival rates above was generally reduced. However, some

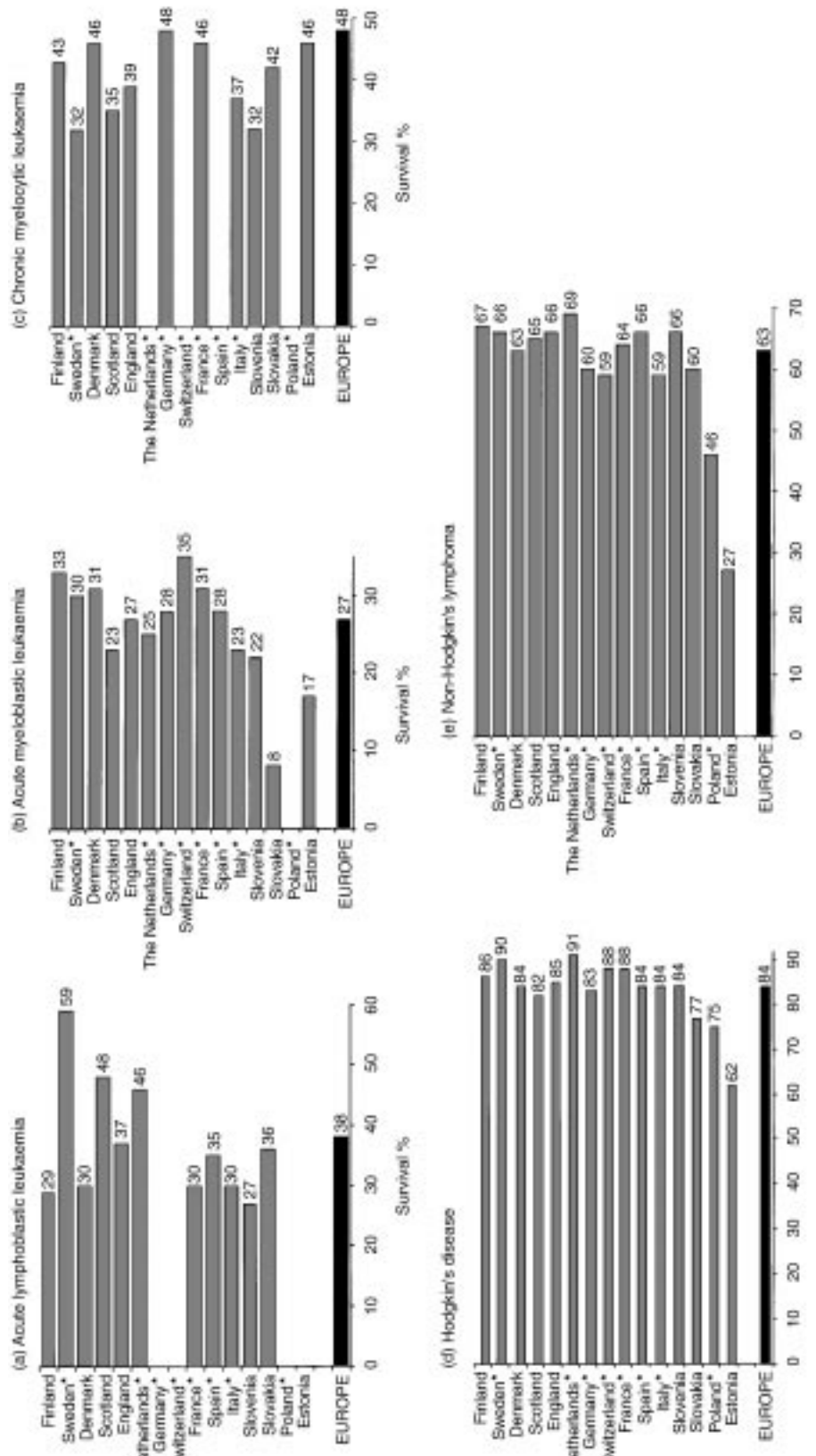


**Figure 2. Five-year relative survival rates for adults aged 15–44 years with haematological malignancies, 1985–1989 (EUROCARE II). * < 20% of the national population covered. Rates are not shown for countries with an insufficient number of cases.**

differences remained. For ALL, Sweden had a much higher rate than the other countries, whilst Slovakia, Finland and Denmark had the lowest rates (Figure 2a). For AML, Eastern European countries, particularly Slovakia, had the lowest rates (Figure 2b) although for CML their rates were similar to those in other countries, with few intercountry differences generally indicated (Figure 2c). For both NHL and HD, there were minimal differences, but lower survival in Eastern European countries was again evident (Figure 2d, e).

*The effect of age on survival*

Weighted European 1- and 5-year weighted relative survival rates for all patients in Europe were estimated for five age groups. For all haematological malignancies in all countries, survival declined with age (Table 4). The best survival rates were seen in those aged 15–44 years for all haematological malignancies. For ALL and AML, 5-year survival in the 45–54 year age group was almost half that in the 15–44 year group, with 1-year rates also showing a notable reduction. Generally, a steady decline was evident in most of the older age groups, with relatively poor rates (1 year $< 20\%$; 5 year $\leq 11\%$) occurring in the elderly (75+ years) (Table 4). A similar pattern was seen for CLL, NHL and MM, with the worst rates occurring in the two oldest age groups, although differences between the 15–44 year and 45–54 year age groups were much less marked, particularly for 1-year survival. For CML and HD, a different pattern was seen, with minimal differences between the two younger age groups, but large reductions in survival, particularly at 5 years, occurring in the 55–64 year group compared with the 45–54 year group, and again in the 65–74 year group versus the 55–64 year group. One year survival was further reduced in those in the 75+ age group, but 5-year survival was similar in the two older groups (Table 4).

*Table* 4. *Weighted European age-specific* 1- *and* 5-*year relative survival (%) for adults with haematological malignancies,* 1985–1989 *(EUROCARE* II*)*

| | 15–44 years % | 45–54 years % | 55–64 years % | 65–74 years % | 75+ years % | All % |
|---|---|---|---|---|---|---|
| (a) 1-year | | | | | | |
| Acute lymphoblastic leukaemia | 67 | 49 | 43 | 38 | 19 | 51 |
| Acute myeloblastic leukaemia | 56 | 37 | 31 | 17 | 11 | 29 |
| Chronic lymphocytic leukaemia | 95 | 94 | 91 | 87 | 72 | 84 |
| Chronic myelocytic leukaemia | 84 | 83 | 76 | 64 | 52 | 69 |
| Non-Hodgkin's lymphoma | 81 | 80 | 75 | 66 | 51 | 68 |
| Hodgkin's disease | 97 | 92 | 79 | 66 | 56 | 88 |
| Multiple myeloma | 78 | 78 | 75 | 66 | 52 | 65 |
| (b) 5-year | | | | | | |
| Acute lymphoblastic leukaemia | 38 | 20 | 21 | 7 | 11 | 28 |
| Acute myeloblastic leukaemia | 27 | 14 | 12 | 4 | 2 | 12 |
| Chronic lymphocytic leukaemia | 88 | 75 | 72 | 63 | 54 | 64 |
| Chronic myelocytic leukaemia | 48 | 47 | 32 | 20 | 24 | 30 |
| Non-Hodgkin's lymphoma | 63 | 59 | 53 | 42 | 31 | 48 |
| Hodgkin's disease | 84 | 77 | 58 | 39 | 32 | 73 |
| Multiple myeloma | 48 | 38 | 36 | 27 | 19 | 29 |

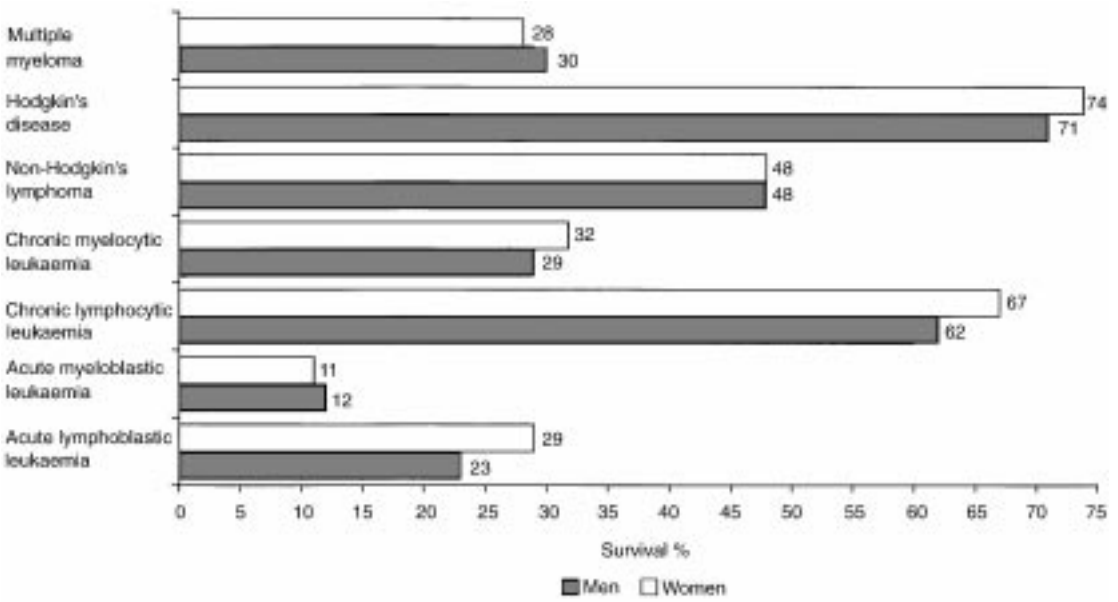


**Figure 3. Relative 5-year survival for adult patients with haematological malignancies in Europe by gender, 1985–1989 (EUROCARE II).**

An analysis for each country is not presented because there were small numbers within specific age groups making any comparison confounded by random variation. However, similar patterns were seen generally, with the best 5-year survival rates within countries seen in the 15–44 year group and the worst in the elderly (75+ years) (data not shown). Countries with some of the lowest rates in the elderly included Denmark (ALL, CLL, CML, HD), Slovenia (AML, CLL), Estonia (MM, NHL; rates were also poor for NHL for 15–44 and 55–64 year groups), Italy (AML, HD) and Scotland (CML, HD) (data not shown).

*The effect of gender on survival*

For all types of haematological malignancies (except MM), 5-year European relative survival rates were slightly better for women than for men (Figure 3). A better prognosis for ALL in women was mainly observed in England, Finland, Scotland and Spain, in contrast to Denmark (25% in males versus 13% in females) (data not shown). Women with CLL had better rates, particularly in Italy and Slovenia and this also pertained to women with CML in Finland, Denmark, France and Poland (>10%). Survival rates for women with NHL were only clearly superior to men in Slovenia and Estonia (>10%). Gender differences in relative survival for patients with MM only occurred in Spain (41% men versus 31% women) and in Germany (34% men versus 24% women), whereas the opposite was true in Slovakia (men 31% versus 41% women).

*Time trends in survival*

Five-year survival improved significantly for all haematological malignancies in 1987–1989 compared with 1978–1980, except for CML for which the change was non-significant and MM for which rates were unchanged (Table 5). This improvement over time was similar for both sexes (data not shown), although for men particular improvement was seen for ALL (men RR 0.60; women RR 1.13) and HD (men RR 0.72; women RR 0.86), and for women in AML (women RR 0.66; men RR 0.87) and CML (women RR 0.66; men RR 0.89).

Increases in 1- and 5-year relative survival rates sometimes only occurred in certain age-groups: for patients with ALL and AML, mostly in the 55–74 year age group, with CLL up to the age of 64 years; with CML mainly in the elderly (≥75 years) (RR = 0.52 for 1-year and 0.43 for 5-year survival); for HD 1-year survival rates improved in all age groups (least in 55–64 year old patients), but 5-year survival mostly between the ages of 45 and 74 years. Improvement in 1-year survival in MM occurred mainly in the youngest (RR 0.63) and oldest (RR 0.68) age groups.

The largest improvements (data not shown) were observed in France, Italy and The Netherlands, to a lesser extent in Finland, Sweden, Denmark and the U.K. and least in Poland and Estonia, where the initial 1978–1980 survival rate was also low. The detailed results for NHL, the most common haematological malignancy, is shown as an example. An increase in survival over time was observed in most countries, particularly in France, Italy, Sweden, Denmark, Finland and the U.K. (RRs of death varying from 0.69 to 0.85; Table 6). Improvement was significant for men but not for women, and was seen in all age groups, except the elderly (75+ years), although the greatest increase was seen in the 45–54 year age group (Table 6).

## DISCUSSION

This EUROCARE II study has shown the pattern of survival across Europe for each type of haematological malignancy, within age groups, with improvement in survival over time clearly indicated. The overall European age-standardised 1- and 5-year relative survival rates for adult patients were favourable for HD (88 and 72%, respectively) and CLL (84 and 63%, respectively), moderate for NHL (68 and 46%, respectively), poor for MM (65 and 28%, respectively), CML (69 and 31%, respectively), and ALL (51 and 25%, respectively), and very poor for AML (29 and 10%, respectively). The 5-year rates were similar to those reported in caucasians in the U.S.A. (Table 7); EUROCARE II rates were somewhat better for CML, but somewhat worse for HD, NHL and CLL [13].

There was some variation in age-standardised relative survival between different countries. Generally, relative survival was higher in Northern and Western European countries, more modest in Southern Europe and poor in Eastern European countries, although Slovenia had clearly better rates than Poland, Slovakia and Poland. It was encouraging to observe the improvement in survival with time for almost all

*Table* 5. *Trends in* 1- *and* 5-*year relative survival rates (%) for adults with haematological malignancies* in Europe,* 1978–1989 *(EUROCARE* II*)*

| | Years since diagnosis | 1978–1980 % | 1981–1983 % | 1984–1986 % | 1987–1989 % | RR (95% CI) |
|---|---|---|---|---|---|---|
| Acute lymphoblastic leukaemia | 1 | 52 | 48 | 55 | 56 | 0.89 (0.60–1.38) |
| | 5 | 20 | 18 | 29 | 28 | 0.79 (0.52–1.22) |
| Acute myeloblastic leukaemia | 1 | 21 | 29 | 29 | 29 | 0.80 (0.68–0.94) |
| | 5 | 6 | 9 | 11 | 12 | 0.75 (0.61–0.95) |
| Chronic lymphocytic leukaemia | 1 | 76 | 81 | 82 | 84 | 0.64 (0.49–0.83) |
| | 5 | 53 | 59 | 63 | 66 | 0.65 (0.53–0.82) |
| Chronic myelocytic leukaemia | 1 | 68 | 68 | 68 | 71 | 0.89 (0.67–1.21) |
| | 5 | 32 | 23 | 33 | 34 | 0.95 (0.74–1.22) |
| Non-Hodgkin's lymphoma | 1 | 64 | 67 | 68 | 69 | 0.83 (0.74–0.94) |
| | 5 | 43 | 46 | 46 | 50 | 0.82 (0.71–0.96) |
| Hodgkin's disease | 1 | 82 | 85 | 89 | 89 | 0.59 (0.42–0.81) |
| | 5 | 66 | 69 | 73 | 73 | 0.76 (0.57–0.98) |
| Multiple myeloma | 1 | 60 | 64 | 66 | 64 | 0.87 (0.76–1.01) |
| | 5 | 27 | 27 | 30 | 27 | 1.00 (0.87–1.15) |

*Only 20 registries from 13 countries contributed data for the whole period 1978–1989. RR, relative risk of death in 1987–1989 versus 1978–1980.

*Table* 6. *Time trends in age-standardised* 5*-year relative survival (%) for adults with NHL in Europe,* 1978–1989 *(EUROCARE* II*)*

| | 1978–1980 % | 1981–1983 % | 1984–1986 % | 1987–1989 % | RR (95% CI) |
|---|---|---|---|---|---|
| (a) By country | | | | | |
| Northern Europe | | | | | |
| Finland | 33 | 40 | 43 | 43 | 0.76 (0.69–0.84) |
| Sweden* | 37 | 43 | 50 | 49 | 0.72 (0.61–0.84) |
| Denmark | 38 | 41 | 44 | 48 | 0.76 (0.69–0.83) |
| U.K. | | | | | |
| Scotland | 34 | 36 | 40 | 42 | 0.80 (0.73–0.89) |
| England | 39 | 41 | 43 | 45 | 0.85 (0.82–0.88) |
| Western and Central Europe | | | | | |
| The Netherlands* | 42 | 38 | 41 | 43 | 0.97 (0.76–1.24) |
| France* | 43 | 50 | 50 | 56 | 0.69 (0.57–0.82) |
| Italy* | 39 | 44 | 48 | 51 | 0.72 (0.60–0.85) |
| Germany* | 49 | 47 | 45 | 50 | 0.97 (0.72–1.27) |
| Eastern Europe | | | | | |
| Poland* | 41 | 36 | 23 | 29 | 1.30 (0.94–1.98) |
| Estonia | 26 | 28 | 27 | 25 | 1.03 (0.78–1.34) |
| Europe | 42 | 44 | 45 | 48 | 0.85 (0.75–0.96) |
| (b) By age and gender | | | | | |
| 15–44 years | 57 | 57 | 58 | 66 | 0.74 |
| 45–54 years | 49 | 58 | 55 | 65 | 0.60 |
| 55–64 years | 45 | 51 | 50 | 54 | 0.77 |
| 65–75 years | 37 | 38 | 40 | 46 | 0.78 |
| 75 + years | 34 | 28 | 32 | 28 | 1.18 |
| Men | 39 | 42 | 43 | 47 | 0.81 (0.69–0.96) |
| Women | 45 | 46 | 46 | 50 | 0.88 (0.74–1.05) |

* < 20% of the national population covered. RR, relative risk of death 1987–1989 versus 1978–1980; CI, confidence interval (not available for age groups).

the haematological malignancies (MM excepted), with the best improvements observed in France, Italy and The Netherlands, to a lesser extent in Finland, Sweden, Denmark and the U.K., and least in Poland and Estonia. As with other malignancies, the combination of prosperity and access to appropriate specialised centres will influence survival within a particular country. The higher rates, as seen particularly in those 15–44 years of age, are similar to those reported in clinical series [14], although selection according to subtypes and stage does not allow easy comparisons [15]. A recent publication from the U.K. for the same period reported rates of 39% for ALL and 36% for AML (patients aged 15–44 years) [16].

*Table* 7. *Comparison of* 5*-year relative survival for adults with haematological malignancies from EUROCARE* II (1985–1989) *and the SEER programme* (1986–1991)

| | | EUROCARE (%) | SEER Caucasian (%) |
|---|---|---|---|
| ALL | All | 25 | 24 |
| | 15–44 years | 38 | 35 |
| AML | All | 10 | 11 |
| | 15–44 years | 27 | 28 |
| CLL | All | 63 | 70 |
| | 15–44 years | 88 | 75 |
| CML | All | 31 | 27 |
| | 15–44 years | 48 | 41 |
| NHL | All | 46 | 52 |
| | 15–44 years | 63 | 51 |
| HD | All | 72 | 81 |
| | 15–44 years | 84 | 88 |
| MM | All | 28 | 28 |
| | 15–44 years | 48 | 48 |

For abbreviations, see Table 1.

For ALL, AML and CML intercountry differences were minimal, but the relatively low rates seen throughout indicate that the effectiveness of chemotherapy was still limited. These were confirmed in two well documented population-based series [17, 18]. For CLL more variation was seen with higher rates in France, The Netherlands, Germany, Switzerland and Spain (Figure 1), all countries with a high proportion of histologically verified cases ($\geq$ 95%). It is known that relative survival for CLL can be increased by extensive detection and a shift in classification to NHL (the survival rate of which would then also be improved). Lower survival rates for CLL in Nordic countries and the U.K. may reflect a more stringent definition of the disease in those countries.

For all countries, a decline in survival with age was evident, particularly for ALL, AML and HD (Table 4). This probably reflects not only a declining effectiveness of aggressive chemotherapy in older patients, but also suboptimal treatment or a lack of therapy given to these patients, even though this may not be warranted. In this respect, further analysis of differences in the treatment of older patients with cytotoxic therapy in different countries would be worthwhile.

Finally, some comment is needed on the completeness and accuracy of the EUROCARE II data, which are likely to vary between countries (Table 2). In addition to random variation due to the rarity of most haematological malignancies, other common biases which occur in registry-based analyses of survival may exert a greater influence on outcome assessment

for patients with haematological malignancies than for those with solid tumours [19]. These include:

(1) Greater variation in approaches to diagnosis, classification and staging (for example more cytological than histological diagnosis of leukaemias and myeloma).
(2) Incomplete inclusion of patients, especially in areas with poor access to specialised care, where some patients may not be recognised, 'hidden' by infectious or bleeding complications or even myocardial infarctions related to anaemia.
(3) Differential medical and registry practices may have existed with respect to patients who, before diagnosis of the haematological malignancy, suffered from relatively mild conditions such as anaemia, myelodysplasia, MGUS (monoclonal gammopathy of unknown significance) [20] or macroglobulaemia. In these cases, the date of diagnosis, if recognised at all, may be somewhat arbitary.
(4) There is the influence of appropriate classification: if a more aggressive subtype is excluded from a category and shifted to another, then the result may be that survival of both categories is improved, such as may have happened with CLL when some of these leukaemias were classified as low grade NHL.

Nevertheless, despite all these potential inadequacies and uncertainties, results of this EUROCARE II analysis are derived from all haematological malignancies together. The variations in survival between countries and age groups suggest room for improvement generally, and particularly in Eastern Europe. Further population-based studies of patterns of diagnosis and treatment in subgroups of patients with haematological malignancies in Europe are likely to provide additional information, highlighting those areas where improvement in specialised care has clearly been obtained [21–25].

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## APPENDIX

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