Hodgkin's disease mortality in Europe

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Summary

Trends in mortality from Hodgkin's disease between mid 1950s and the late 1980s have been analysed for Western European and seven Eastern European countries. In all western countries there were substantial falls in mortality from the mid 1960s onwards, for an overall mean decline of 50% in both sexes, although these falls were somewhat larger in Nordic countries (approaching 70% in Denmark and Sweden), and more limited (20 to 30%) in Portugal, Spain and Greece. The reductions in Hodgkin's disease mortality were evident both in younger (under 35) and middle age (35 to 64 years), as well as in children under 15 and, in several countries, in the elderly (above 65), too. They were persistent up to the most recent calendar periods, with no evidence of flattening off. The pattern of trends in Hodgkin's disease mortality was largely different in Eastern Europe. Among seven countries examined, some fall was observed only in Bulgaria and Czechoslovakia, but other countries showed no consistent pattern and there was some increase, too. In absolute terms, the reductions in Hodgkin's disease mortality in Western Europe correspond to the avoidance of over 3,000 deaths per year. This stresses the importance and urgency of improving the availability of currently defined knowledge and resources for treatment of Hodgkin's disease in Eastern Europe.

Effective therapies for Hodgkin's disease have been available for over 30 years (Rosenberg, 1989). These therapeutic successes have been based on a combination and integration of better diagnostic methods to evaluate the extent of the disease (lymphography, diagnostic laparotomy with splenectomy, bone marrow biopsy and computerised tomography), of technical advancements in radiotherapy (supervoltage machines and linear accelerators, allowing the delivery of tumoricidal doses to well identified lymphoid fields) and the development of combination chemotherapy, particularly MOPP (mechloretamine, vincristine, procarbazine, and prednisone) and ABVD (doxorubicin, bleomycin, vinblastine and dacarbazine) (De Vita et al., 1965, 1970, 1980; Bonadonna, 1982; Rosenberg, 1989). Still, availability and utilisation of curative treatments is not homogeneous, and a surveys on the status of Hodgkin's disease (ICD) were used, but there were no changes in the definition or coding of the disease between various Revisions.

Estimates of the resident population, generally based on official Censuses, were obtained from the same WHO data bank. From the matrices of certified deaths and resident populations age-standardised rates (using the World Standard Population) were computed (Doll & Smith, 1982). Besides overall age-adjusted rates, four different (age-standardised) truncated rates (0–14, 15–34, 35–64 and 65 and over) were chosen for presentation.

In a few countries, data were missing for part of the calendar period. When a single year was missing within a quinquennium, numerators and denominators were interpolated linearly from the previous and subsequent calendar years. No extrapolation was made for missing data at the beginning or the end of the calendar period considered, or when data on one or more quinquennia were not available.

For countries covered by national cancer registration schemes, mortality rates were contrasted with incidence trends, derived from subsequent volumes of 'Cancer Incidence in Five Continents' (Doll et al., 1966, 1970; Waterhouse et al., 1976, 1982; Muir et al., 1988).

Results

Trends in mortality from Hodgkin's disease are presented in Figure 1 for Western Europe and in Figure 2 for Eastern Europe in males and females of all ages and in two separate age groups (0–34 and 35–64 years). Rates for the first (usually 1955–59) and last (usually 1985–88) calendar period, together with the corresponding average absolute number of deaths per year and per cent changes, were further tabulated in Table I for population of all ages, in Table II for children under age 15 and in Table III in the oldest age group (65 years and over).

In all western countries there were substantial declines in mortality. The declines in all age mortality from Hodgkin's disease between the late 1950s and the mid 1980s were somewhat lower in both sexes (Table I) and most countries, except for Nordic Countries (and particularly Denmark and Sweden, whose fall approached 70%), and Portugal, Spain and Greece (with falls between 20 and 30%).

These declines tended to start between the late 1960s and the early 1970s in most countries, and were evident both in

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Figure 1 Trends in mortality from Hodgkin's disease in 16 western European countries from 1955 to 1988. Age-standardised (world) rates in males and females of all ages (□), at ages 0–34 (●) and 35–64 (■).
1b

MALES
FRANCE

Death rates/100,000 males

Calendar years

FEMALES
FRANCE

Death rates/100,000 females

Calendar years

WESTERN GERMANY

Death rates/100,000 males

Calendar years

WESTERN GERMANY

Death rates/100,000 females

Calendar years

GREECE

Death rates/100,000 males

Calendar years

GREECE

Death rates/100,000 females

Calendar years

IRELAND

Death rates/100,000 males

Calendar years

IRELAND

Death rates/100,000 females

Calendar years
The figure shows age-standardized death rates for males and females in Italy, the Netherlands, Norway, and Portugal from 1950 to 1990. The rates are presented per 100,000 population and are displayed for different age groups (55, 60, 65, 70, 75, 80, 85, 90 years). The data indicate a general decrease in death rates over time, with some variation by country and gender.
### HODGKIN’S DISEASE MORTALITY IN EUROPE

**MORTALITY IN MALES**

| Country   | 55 | 60 | 65 | 70 | 75 | 80 | 85 | 90 |
|-----------|----|----|----|----|----|----|----|----|
| SPAIN     |    |    |    |    |    |    |    |    |
| SWEDEN    |    |    |    |    |    |    |    |    |
| SWITZERLAND |   |    |    |    |    |    |    |    |
| UNITED KINGDOM | |    |    |    |    |    |    |    |

**MORTALITY IN FEMALES**

| Country   | 55 | 60 | 65 | 70 | 75 | 80 | 85 | 90 |
|-----------|----|----|----|----|----|----|----|----|
| SPAIN     |    |    |    |    |    |    |    |    |
| SWEDEN    |    |    |    |    |    |    |    |    |
| SWITZERLAND |   |    |    |    |    |    |    |    |
| UNITED KINGDOM | |    |    |    |    |    |    |    |

*Note: The data is presented in the form of line graphs for each country showing the death rates per 100,000 males and females across different calendar years.*
Figure 2 Trends in mortality from Hodgkin's disease in seven eastern European countries from 1955 to 1988. Age-standardised (world) rates in males and females of all ages (□), at ages 0–34 (●) and 35–64 (■).
Table I  Overall death certification rates* /100,000 people (and numbers of deaths) from Hodgkin’s disease in selected European countries, 1955–59 and 1985–88

| Country (year) | 1955–59 | 1955–59 | 1955–59 | 1985–88 | 1985–88 | Percent | Percent |
|----------------|---------|---------|---------|---------|---------|---------|---------|
|                | Rate    | Rate    | Percent | Rate    | Rate    | difference | difference |
|                | (No. of deaths per year) | (No. of deaths per year) | in rates | (No. of deaths per year) | (No. of deaths per year) | in rates | in rates |
| Western Europe |          |          |         |          |          |           |           |
| Austria        | 2.37 (93) | 1.15 (54) | -51     | 1.66 (79) | 0.68 (48) | -59      | -59      |
| Belgium        | 2.39 (127) | 1.18 (40) | -51     | 1.28 (70) | 0.85 (32) | -34      | -34      |
| Denmark        | 2.35 (58) | 0.79 (29) | -66     | 1.52 (39) | 0.33 (15) | -78      | -78      |
| Finland        | 1.88 (39) | 1.01 (30) | -46     | 0.78 (19) | 0.38 (17) | -51      | -51      |
| France         | 1.62 (387) | 0.75 (261) | -54     | 1.04 (273) | 0.36 (152) | -65      | -65      |
| W. Germany     | 2.08 (572) | 0.99 (397) | -52     | 1.19 (387) | 0.57 (321) | -52      | -52      |
| Greece (1965–69) | 1.86 (87) | 1.21 (81) | -35     | 0.87 (47) | 0.58 (42) | -33      | -33      |
| Ireland        | 2.08 (32) | 1.37 (26) | -34     | 1.02 (15) | 0.42 (11) | -59      | -59      |
| Italy          | 2.37 (615) | 1.16 (420) | -51     | 1.45 (414) | 0.67 (286) | -54      | -54      |
| Netherlands    | 2.08 (118) | 0.96 (86) | -54     | 1.40 (82) | 0.47 (56) | -66      | -66      |
| Norway         | 1.89 (37) | 0.72 (21) | -62     | 1.23 (26) | 0.51 (18) | -59      | -59      |
| Portugal (1980–84) | 0.94 (50) | 0.68 (40) | -28     | 0.45 (29) | 0.35 (25) | -22      | -22      |
| Spain          | 1.06 (155) | 0.82 (178) | -23     | 0.55 (91) | 0.45 (121) | -18      | -18      |
| Sweden         | 1.97 (86) | 0.59 (38) | -70     | 1.14 (55) | 0.38 (29) | -67      | -67      |
| Switzerland    | 1.90 (53) | 1.16 (51) | -39     | 1.46 (45) | 0.70 (39) | -52      | -52      |
| United Kingdom | 1.99 (570) | 0.85 (299) | -57     | 1.07 (358) | 0.49 (213) | -54      | -54      |
| Eastern Europe |          |          |         |          |          |           |           |
| Bulgaria (1965–69) | 1.45 (68) | 1.02 (57) | -30     | 0.74 (36) | 0.53 (30) | -28      | -28      |
| Czechoslovakia | 2.75 (192) | 1.54 (133) | -44     | 1.49 (116) | 0.84 (98) | -44      | -44      |
| E. Germany (1975–79) | 1.39 (132) | 1.33 (127) | -4      | 0.72 (93) | 0.81 (110) | +13      | +13      |
| Hungary (1970–74) | 1.06 (65) | 1.25 (80) | +18     | 0.58 (41) | 0.75 (64) | +29      | +29      |
| Poland (1960–64) | 1.62 (312) | 1.56 (309) | -4      | 0.66 (144) | 0.69 (166) | +5      | +5      |
| Romania (1965–69) | 1.25 (116) | 1.15 (138) | -     | 0.53 (63) | 0.57 (73) | +8      | +8      |

*Age-standardised rates on the world standard population. b1980–84.
younger (under 35) and middle age (35 to 64 years), although generally larger, in proportional terms, in the young, but in absolute terms in middle age. Even more substantial declines were observed in childhood (Table II), too, and, in larger countries, some fall was discernible even in the more confusing pattern of trends in the oldest age group (over age 65) (Table III and Figure 3). The declines were steady and persistent up to the most recent calendar period, with no evidence of levelling of rates.

The pattern of trends in mortality from Hodgkin’s disease was largely different in the seven eastern and central European countries. Among them, some fall was observed only in Bulgaria (approximately 30%) and Czechoslovakia (44%), although there was some evidence of levelling of rates.
over more recent calendar periods. Other countries showed no consistent pattern, and some of them (Hungary and Yugoslavia) showed some increase. The overall mean difference of rates over the last few decades in the eastern block countries were −5% for males and +2% for females. Only in children before age 15 was some decline in rates evident in Eastern Europe, too.

Figure 4 contrasts incidence and mortality rates for five countries where national cancer incidence statistics have been available since 1960 (Denmark, Finland, Norway, Scotland and Sweden). In all countries, mortality declined while incidence showed little systematic change, leading to a substantial widening of the incidence/mortality ratios from an average of 1.35 in 1960 to 2.38 in 1980 (Table IV).

**Discussion**

This analysis of trends in Hodgkin’s disease mortality in 23 European countries shows a clear divergence between consistent declines over the last two decades in all western countries, and no evidence of systematic falls in Eastern Europe. It is unlikely that problems of diagnosis and certification of Hodgkin’s disease (particularly with respect to non-Hodgkin’s lymphomas) (Grufermann & Delzell, 1986; Glaser & Swartz, 1990), which might have somewhat influenced the rates, could explain the observed trends. The pathological entity of Hodgkin’s disease, with its pathognomonic Reed-Sternberg cell, has been recognised for almost a century now (Reed, 1902; Sternberg, 1893; Hellmann, 1991). In relation to these potential problems, it is also reassuring that the pattern of trends, in most countries, was similar at younger and middle age, when diagnosis and certification of the disease has long been more accurate (Doll & Peto, 1981).

A further support to the existence of a major role of therapy, rather than diagnostic artifacts, on these trends comes from a comparison of incidence and mortality rates for European Community Members States in 1980–84, since incidence rates were two to three times higher than the corresponding mortality, the differences being greater in younger ages (Jensen et al., 1990). In the early 1980s, the differences between incidence and mortality were systematic.
ally smaller in areas covered by cancer registration from Eastern Europe (Levi et al., 1989). Further, no major and systematic change was observed in non-Hodgkin’s lymphoma mortality over the same calendar period (unpublished data from the WHO databank). Socio-demographic changes may influence sub-type and age distribution of Hodgkin’s disease, since nodular sclerosis is more common at younger age and among higher social classes (Glaser, 1990; Serraino et al., 1991). This may well influence survival rates, but is unlikely to largely explain the mortality trends observed.

Registered mortality trends were less consistent above age 65, but this is compatible with generalised decline in reliability and validity of cancer death certification in the elderly (Doll & Peto, 1981). In addition, experience from all countries indicates that the prognosis for elderly patients with Hodgkin’s disease remains poor, despite clear improvements in therapy. Still, this is less important for Hodgkin’s disease than for epithelial cancers, since Hodgkin’s disease incidence does not rise with a power of age (Cook et al., 1969; Doll, 1971), and the proportion of cases in the elderly is consequently smaller than for epithelial neoplasms.

The major determinant of the favourable trends in mortality in Western Europe has been improved treatment of the disease, as confirmed also by comparison of incidence and mortality trends in selected areas. These clear successes notwithstanding, the present data gives scope for a few critical considerations. First, advancements in radiotherapy have been available since the 1950s, and effective chemotherapy in clinical series from research settings has been available since the early 1960s (De Vita et al., 1965; Rosenberg, 1989). Only from the late 1960s or early 1970s onwards, however, improvements became evident in national mortality data from more advanced western European countries, and in a few countries rates started to fall only during the late 1970s. This is consistent with a modelling of survival data from the US National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) program, which showed that dissemination of improved survival took approximately 11 years for Hodgkin’s disease (but only three for testicular cancer; Feuer et al., 1991). This longer delay was attributed to the difficulty in replicating the very positive results of the original MOPP trial, of staging Hodgkin’s disease, and to the fact that treatment of Hodgkin’s disease is less frequently referred to specialist centres. Thus, the most likely interpretation of this pattern is that the utilisation of effective treatments of Hodgkin’s disease, which have been established since over two decades now, has been different in various parts in Europe. In absolute terms, the reductions in Hodgkin’s disease mortality in Western Europe correspond to the avoidance of over 3,000 deaths per year, which is the major established therapeutic advancement for any cancer site (Cairns & Boyle, 1983; Boyle et al., 1988; La Vecchia et al., 1989). This figure could well approach 4000 deaths avoided per year if the larger advancements observed in a few Scandinavian countries had been registered in other western European countries, too.

Table IV Incidence/mortality ratios for Hodgkin’s disease in selected European countries, circa 1960 and 1980

| Country   | Incidence/mortality ratios for: | 1960 | 1980 | 1960 | 1980 |
|-----------|---------------------------------|------|------|------|------|
|           | Males, circa                    |      |      |      |      |
|           | Females, circa                  |      |      |      |      |
| Denmark   | 1.28                            | 2.36 | 1.27 | 2.29 |
| Finland   | 1.32                            | 1.43 | 1.63 | 2.43 |
| Norway    | 1.35                            | 2.17 | 1.31 | 2.67 |
| Sweden    | 1.45                            | 2.30 | 1.58 | 2.50 |
| Scotland  | 1.05                            | 3.00 | 1.22 | 2.60 |
Even within Western Europe, there is certainly scope for future progress, as indicated by the different patterns of trends in various countries and by the observation that rates are still downwards in most recent periods in most areas. A major indication emerging from this analysis, moreover, is on the importance and urgency of improving the availability of currently defined knowledge and resources for the treatment of Hodgkin's disease, as well as of other types of curable cancers (Boyle et al., 1990), in Central and Eastern Europe.

Further study in these countries will determine whether the major problem relates to a failure to refer patients for treatment at specialised cancer centres, where the results of treatment for curable neoplasms such as Hodgkin's disease may be expected to be superior to those in non-specialist centres. An alternative explanation could be the lack of availability of certain cytotoxic agents, and this would be particularly regrettable, as the drugs involved have been widely used for several years.

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