



Childhood cancer mortality in Europe, 1955–1995

F. Levi^{a,*}, C. La Vecchia^{b,c}, E. Negri^c, F. Lucchini^a

^aRegistre Vaudois des Tumeurs, Unité d'Épidémiologie du Cancer, and Institut Universitaire de Médecine Sociale et Préventive, CHUV-Falaises 1, 1011 Lausanne, Switzerland

^bIstituto di Statistica Medica e Biometria, Università di Milano, Via Venezian 1, 20133 Milan, Italy

^cIstituto di Ricerche Farmacologiche "Mario Negri", Via Eritrea 62, 20157 Milan, Italy

Received 27 September 2000; accepted 5 January 2001

Abstract

Childhood cancer (0–14 years) mortality rates for six cancer sites, including bone, kidney, eye, Hodgkin's disease, non-Hodgkin's lymphomas, leukaemias, plus total cancer mortality were computed for subsequent calendar periods from 1955 to 1997, and graphically presented for 16 Western European countries, seven Eastern European countries, plus the European Union as a whole. All Western European countries showed substantial declines in mortality from leukaemias and from all neoplasms considered from the mid-1960s onwards, for an average fall over 60%, and an estimated total number of approximately 4500 avoided deaths per year. Favourable trends were observed also in Eastern Europe, but the declines started later (i.e. around the mid-1970s or the late 1980s), and were only approximately 30%. © 2001 Elsevier Science Ltd. All rights reserved.

Keywords: Childhood malignancies; Death rates; Leukaemia; Trends

1. Introduction

Mortality from childhood leukaemias and other childhood cancers showed substantial declines, from the early 1960s onwards, in developed areas of the world, including North America, Western Europe, Japan and Oceania, whereas favourable trends were observed later, and were smaller, in Eastern Europe, South America and other less developed areas of the world [1,2]. In the absence of substantial changes in incidence [3], changes in mortality are essentially attributable to improved treatment.

In developed countries, the downward trends were approximately linear, leading to a decline by around or over 50% for all childhood neoplasms, and by over 60% for childhood leukaemias compared with rates registered in the early 1960s [4–8]. The downward trends were however larger (approximately 60% in overall cancer mortality) in North America, compared with about 50% in Western Europe and Japan, and 55% in Oceania [1,2].

Since the late 1980s, rates have continued to decline, though with a less steady pattern in a few countries [9–11]. It is therefore interesting to update trends in Europe up to the mid-1990s. This has been carried out in the present report, by considering childhood cancer mortality between 1955 and 1995 in 23 European countries, as well as in two broad geographical areas, including (1) the European Union and its 15 member states, and (2) four countries from Eastern Europe. A comprehensive picture of the pattern of variation of mortality from leukaemias and other major childhood cancers across Europe is also given.

2. Patients and methods

Cancer death certification data and estimates of the resident population at age 0–4, 5–9 and 10–14 years for the period 1955–1997 were derived from the World Health Organization (WHO) database. Childhood cancer mortality rates for six cancer sites, including bone, kidney (predominantly Wilm's tumour), eye (predominantly retinoblastoma), Hodgkin's disease, non-Hodgkin's lymphomas (i.e. ICD-9 200 and 202, which on mortality data may include other and not specified lymphomas), leukaemias, plus total cancer mortality

* Corresponding author. Tel.: +41-21-314-7311; fax: +41-21-323-0303.

E-mail address: fabio.levi@inst.hospvd.ch (F. Levi).

Table 1

Average annual population (age 0–14 years) in 23 selected European countries (1990–1994)

Country	Boys	Girls
Austria	710 100	672 600
Belgium	932 900	888 500
Bulgaria	865 100	820 800
Czech Republic	1 073 400	1 022 400
Denmark	450 900	429 900
Finland	494 200	473 000
France	5 656 400	5 398 400
Germany	6 724 600	6 379 200
Greece	970 600	917 000
Hungary	1 017 000	971 500
Ireland	477 200	452 500
Italy	4 621 400	4 391 800
Norway	420 800	399 700
Poland	4 768 900	4 553 600
Portugal	971 200	927 800
Romania	2 619 600	2 510 400
Slovakia	631 900	604 500
Slovenia	200 100	189 900
Spain	3 700 600	3 483 500
Sweden	816 400	774 700
Switzerland	610 400	580 700
The Netherlands	1 419 600	1 357 700
United Kingdom	5 730 900	5 437 200

(age-standardised 0–14 and age-specific 15–19 years on the world standard population) [12] were computed for 16 Western European countries (excluding a few small countries such as Iceland, Liechtenstein, Luxembourg, Malta, etc.), four Eastern European countries which remained intact across the calendar period were considered (Bulgaria, Hungary, Romania and Poland), plus the European Union (EU) as a whole and Eastern countries as a whole. Germany includes the Federal Republic, plus the former Democratic Republic since 1970. Age-standardised mortality rates were computed for nine subsequent 5-year calendar periods, i.e. 1955–1959 to 1990–1994, plus, whenever available, subsequent calendar years up to 1997. For three additional countries recently established (Czech Republic, Slovakia, Slovenia), rates for the period 1990–1994 were also obtained. Table 1 gives the average annual population for the 23 European countries considered in the calendar period 1990–1994, and Table 2 gives the average annual number of certified deaths from most relevant cancers and all cancers in 1990–1994.

During the calendar period considered, three different Revisions of the International Classification of Diseases (ICD) were in operation [13–15]. None the less, there were no major changes in the classification or coding of

Table 2

Average annual number of certified deaths from most relevant cancers and all cancers at age 0–14 years in 23 selected European countries (1990–1994)

Country	Boys					Girls				
	Bone	Kidney	All other lymphomas	Leukaemias	All cancers	Bone	Kidney	All other lymphomas	Leukaemias	All cancers
European Union (incl. Luxembourg)	61	35	97	511	1561	60	44	46	360	1224
Austria	1	1	0	8	26	1	1	0	6	25
Belgium	2	1	0	13	45	3	0	0	11	34
Denmark	1	0	1	8	23	1	1	0	5	18
Finland	0	0	1	4	17	0	0	1	5	15
France	13	5	13	83	264	7	6	11	60	208
Germany	8	6	10	86	269	8	8	7	55	215
Greece	4	1	2	13	41	2	1	1	12	30
Ireland	1	0	1	4	17	0	1	0	2	13
Italy	10	5	21	93	270	11	8	7	46	198
Portugal	3	2	6	20	62	4	2	3	20	57
Spain	8	3	19	75	208	11	4	7	57	158
Sweden	2	1	3	11	33	2	0	1	8	29
The Netherlands	1	2	5	17	59	1	2	2	11	48
United Kingdom	8	6	14	79	244	8	10	5	49	190
Norway	0	0	1	5	15	1	0	0	3	12
Switzerland	1	1	2	11	26	1	1	1	7	25
Eastern European countries										
Bulgaria	2	2	4	22	64	2	1	2	10	42
Czech Republic	2	3	7	22	71	3	3	3	15	46
Hungary	2	1	5	19	60	3	1	3	15	47
Poland	10	NA	NA	83	272	8	NA	NA	56	211
Romania	9	NA	NA	70	238	11	NA	NA	57	183
Slovakia	1	1	1	7	20	1	0	1	4	16
Slovenia	0	0	1	2	7	0	1	0	3	9

NA, not available.

the cancers or groups of cancers considered between the sixth and the ninth revision of the ICD. It was impossible, however, to obtain meaningful death certification data for neoplasms of the nervous system, on account of difficulties in histopathological classification and of changes in the classification of neuroblastoma, which is coded in part to the organ affected (chiefly, the adrenal gland, i.e. with cancers of endocrine organs), in part to connective and soft-tissue sarcomas, and in part to the nervous system. Data for kidney, eye and non-Hodgkin's lymphomas were unavailable for Romania throughout the study period, and for Poland during more recent years. For some other countries also, data were not available for the whole study period for certain sites.

Mortality rates are graphically presented in the form of histograms, including, for each site or group of sites considered, the most recent complete (i.e. 1990–1994) quinquennial calendar period available (Fig. 1) for each gender, respectively. Fig. 2 gives trends in age-standardised (0–14 years; world standard) mortality rates from 1955 to 1995–1997 for all childhood cancers and each separate cancer or groups of cancers considered, whereas Fig. 3 gives trends for all childhood cancers and leukaemias in the EU and Eastern Europe.

3. Results and comments

Fig. 1 gives age-standardised 0–14 years death mortality rates from all neoplasms and six selected cancers or groups of cancers in various European countries in 1990–1994. The variation for total cancer mortality approached a factor of approximately 3, with the highest rates (9.41/100 000 boys, 7.65/100 000 girls) being registered in Romania, in most other Eastern European countries, and in Portugal, Italy and Spain, and the lowest ones in Ireland (3.58/100 000 boys, 2.75/100 000 girls), and several other Northern European countries. A similar pattern was reproduced for leukaemias, Hodgkin's disease, i.e. the neoplasms more amenable to treatment, and also for other lymphomas, whereas the picture was much less clear for bone, eye and kidney, possibly on account of smaller absolute numbers and consequently resulting in greater random variation. For leukaemias, however, Poland had intermediate rates (1.77/100 000 boys, 1.27/100 000 girls), between 2.72 for Romania and 0.87 for Ireland in boys, and 2.39 for Romania and 0.46 for Ireland in girls. Figures for smaller countries, however, are based on limited absolute numbers (Table 2), and are consequently subject to substantial random variation. The average numbers of deaths in the EU within the period 1990–1994 were around 900 for leukaemias and 2800 for all childhood cancers (Table 2). Corresponding numbers for the seven Eastern European countries considered were around 400 for leukaemias and 1300 for all childhood cancers.

Fig. 2 gives trends in age-standardised death certification rates between 1955 and 1997 for all neoplasms and selected sites for which data were available in various countries. Fig. 3 gives trends in mortality at ages 0–14 years and 15–19 years for bone, kidney, Hodgkin's disease, other lymphomas, leukaemias and all neoplasms in the EU and in the four Eastern European countries considered.

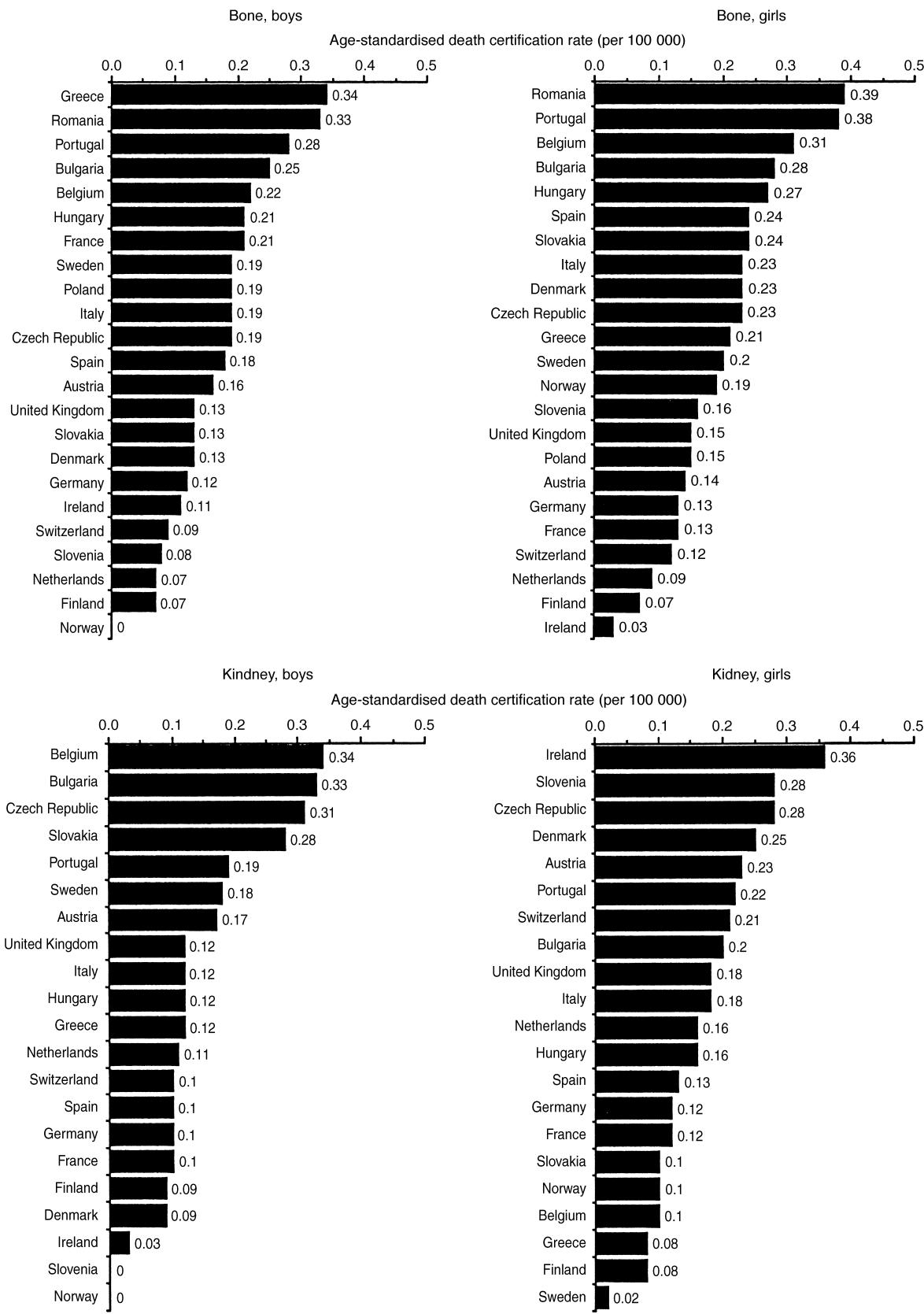
In general, all Western European countries showed substantial declines in mortality from leukaemia and from all neoplasms considered over the last decades (i.e. from the mid-1960s onwards), for an average fall of over 60% in both genders, and an estimated total number of approximately 4500 avoided deaths per year, based on proportional differences in age-specific rates. Apart from leukaemias, other neoplasms showing consistent declines in most countries were Hodgkin's disease and other lymphomas, and bone [16]. Other neoplasms showed no consistent pattern in each single country, probably on account of small numbers. This includes bone, and mostly eye, for which some indication of favourable trends was evident only for larger countries, such as Germany, Italy and the UK, while the pattern was inconsistent for most smaller countries.

After earlier rises between 1955 and 1970, probably due to improved diagnosis and certification, favourable trends were observed also in Eastern Europe, but the declines started later (i.e. around the mid-1970s in most countries, and only in the late 1980s in Romania) and were only about 30%, corresponding, for the four countries considered, to an estimated number of about 500 deaths avoided per year, again based on proportional differences in age-specific rates.

4. Discussion

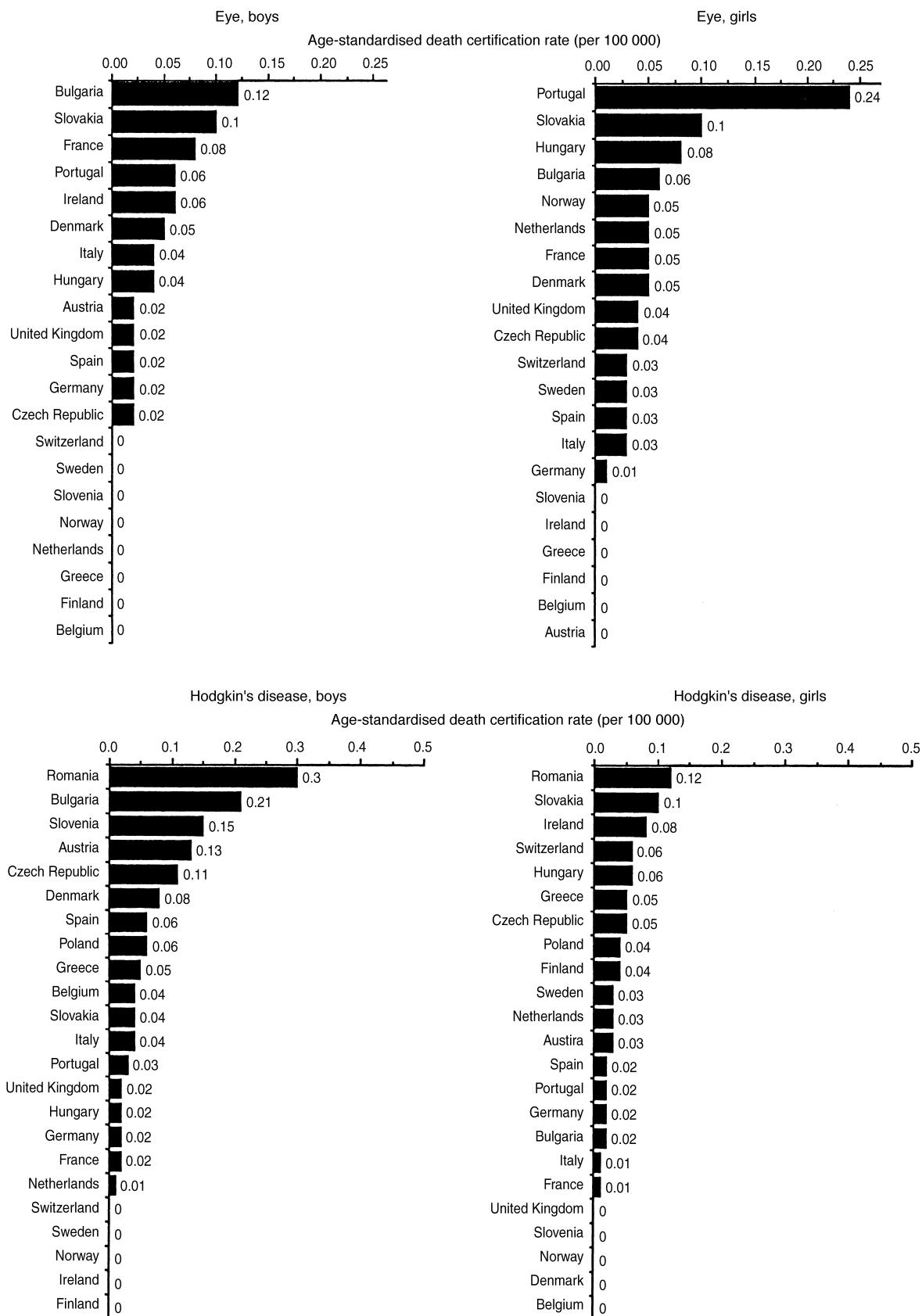
The declines in mortality, which were observed earlier at young ages since the survival of several tumour types decreases with age (and an initial postponement of death rather than cure is generally observed), can largely be attributed to the development of effective multidrug chemotherapy protocols, together with the introduction of various supportive measures to overcome toxicity, as well as to the availability of megavoltage radiation and improved diagnostic techniques.

It appears, therefore, that in acute leukaemias (which account for most childhood leukaemias), after the major therapeutic improvements which led the 5-year survival rate to increase from 20–30% in the 1960s to 60–75% in the 1980s [6,17–20], there is still some possibility of obtaining further improvement. Advancements have been achieved lately for the majority of good-prognosis children, while only a minority of bad-prognosis patients still await relevant improvements through newer treatment strategies.



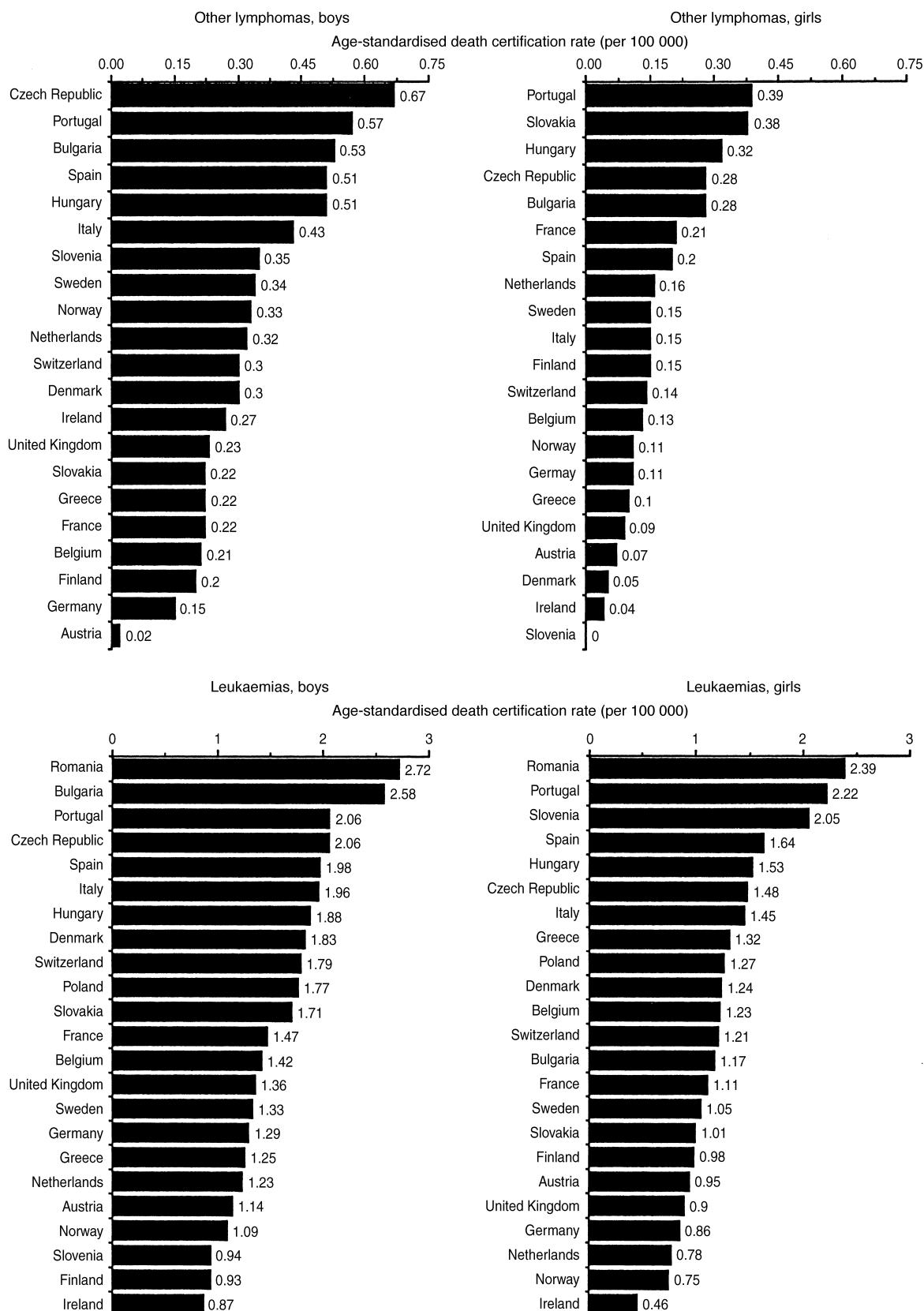
Source: World Health Organization

Fig. 1. Age-standardised 0–14 years (on the world population; rates per 100 000) death certification rates from selected childhood cancers in various European countries, 1990–1994.



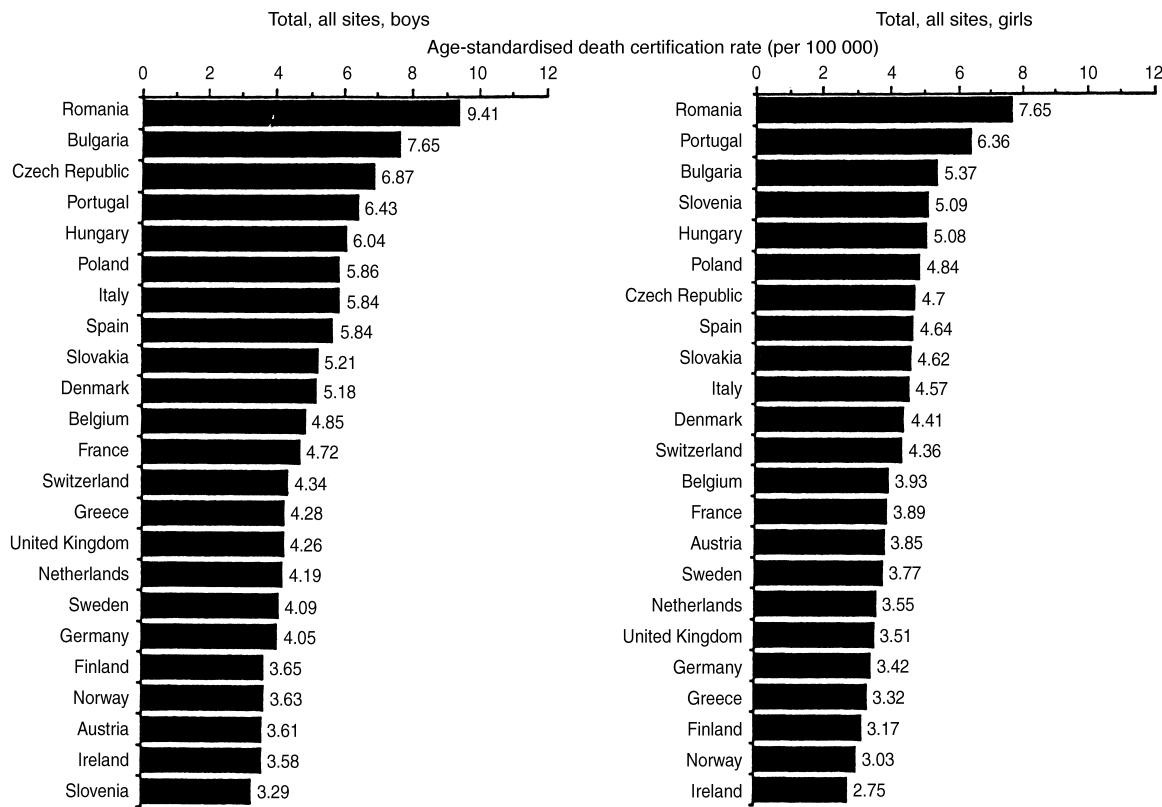
Source: World Health Organization

Fig. 1. (continued)



Source: World Health Organization

Fig. 1. (continued)



Source: World Health Organization

Fig. 1. (continued)

The declines observed in the EU and other Western European countries are of the same order of magnitude as those registered in the USA over comparable time periods [20,21]. The advancements registered in Western Europe, however, were somewhat later and are systematically smaller (by at least 10% for leukaemia, and 20% for all childhood neoplasms) than those observed in North America, pointing to some delay in the adoption and implementation of efficacious therapeutic approaches. Despite some differences in mortality registered by race and ethnicity in the US [22,23] between 1960 and 1993, in fact, mortality from childhood leukaemia declined by 73% in North America, but only by 67% in Western Europe, and that from all childhood neoplasms by 61% in North America and 49% in Western Europe [20]. Almost certainly, therefore, there is the possibility and scope for some further improvement in childhood cancer mortality in the EU and other Western European countries through a more widespread and better adoption of currently available techniques [24].

These possibilities are even larger in Eastern Europe, where a substantial number of additional deaths from childhood cancer per year could be avoided, thus indicating the scope and importance for implementation in the treatment of these neoplasms.

Apart from the major East–West difference, some systematic variation in childhood cancer mortality is observed within Western Europe, too, with a tendency for some southern European countries, including Italy, Spain and Portugal, to share high mortality rates over the most recent calendar periods. Some of the differences within Western Europe are explainable in terms of random variation, but it is possible that some delayed or inadequate management of childhood leukaemias and other neoplasms has been registered in these areas of the continent too [9–11].

At ages 15–19 years, a different proportional composition of various neoplasms is observed, with a rise of testicular cancer in boys, germ cell ovarian neoplasms in girls and, mostly, bone cancer in both genders combined. None the less, mortality from all neoplasms, as well as from leukaemias, declined by almost 50% since the late 1960s, while in Eastern Europe some decline in cancer mortality (about 20% in boys, 25% in girls) was observed only over the last decade, again reflecting the delayed and inadequate adoption of efficacious treatment for various cancers in Eastern Europe. This is reflected also within each neoplasm, including the ones most amenable to treatment, such as Hodgkin's disease or leukaemias.

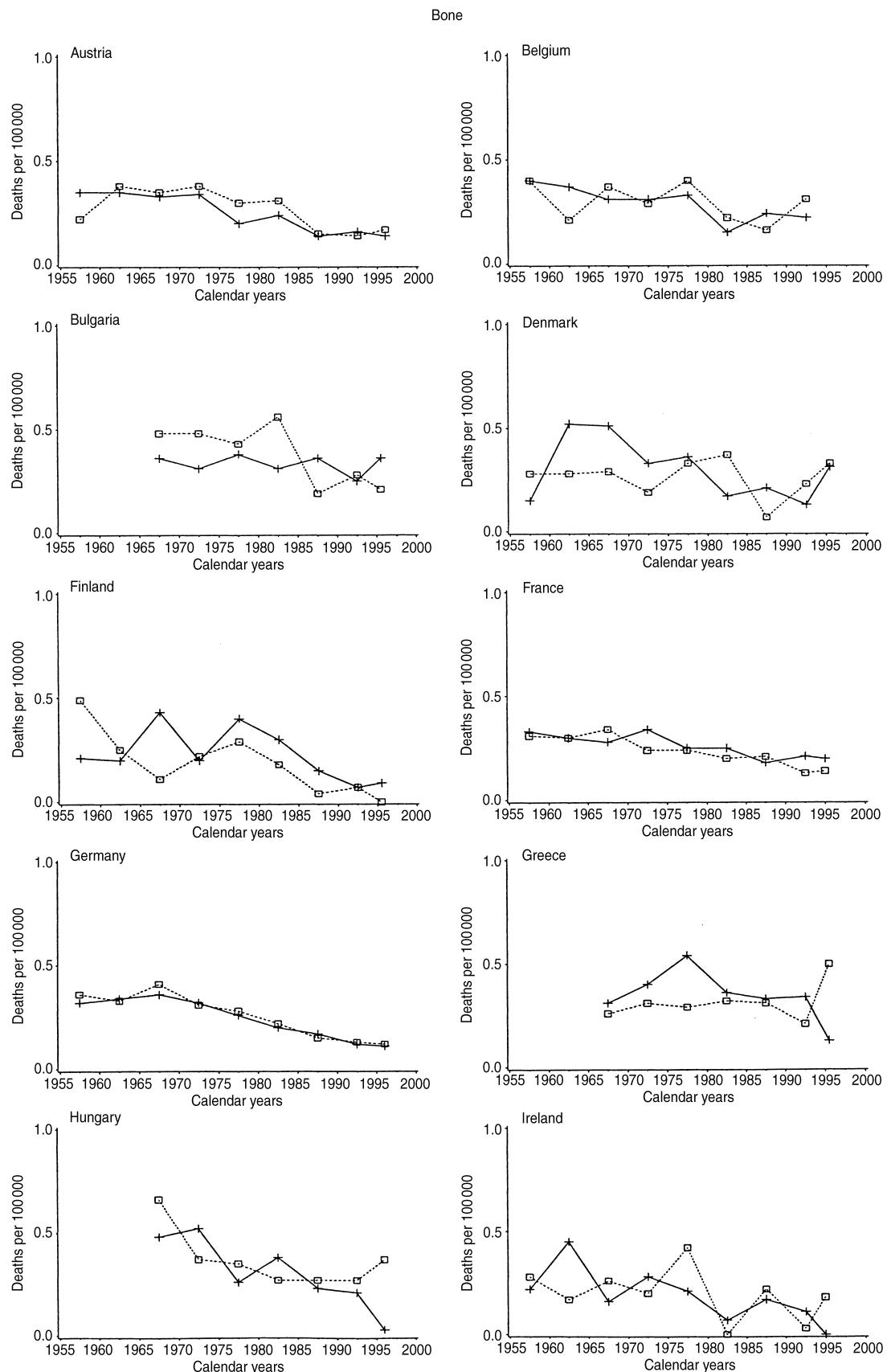


Fig. 2. Trends in age-standardised 0–14 years (on the world standard population; rates per 100 000) death certification rates from selected childhood cancers in various European countries, 1955–1997 (+ — + boys; - - - girls).

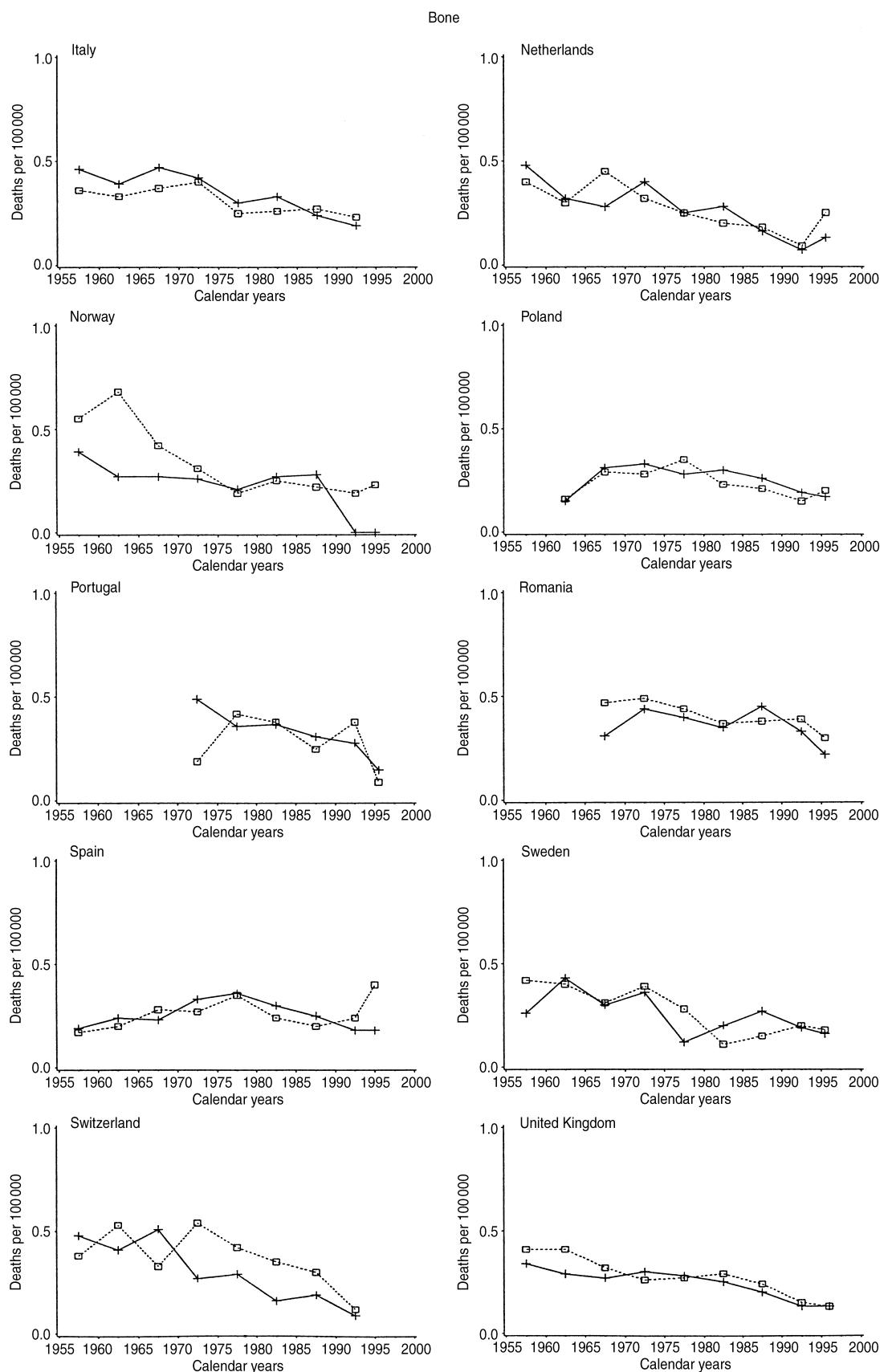


Fig. 2. (continued)

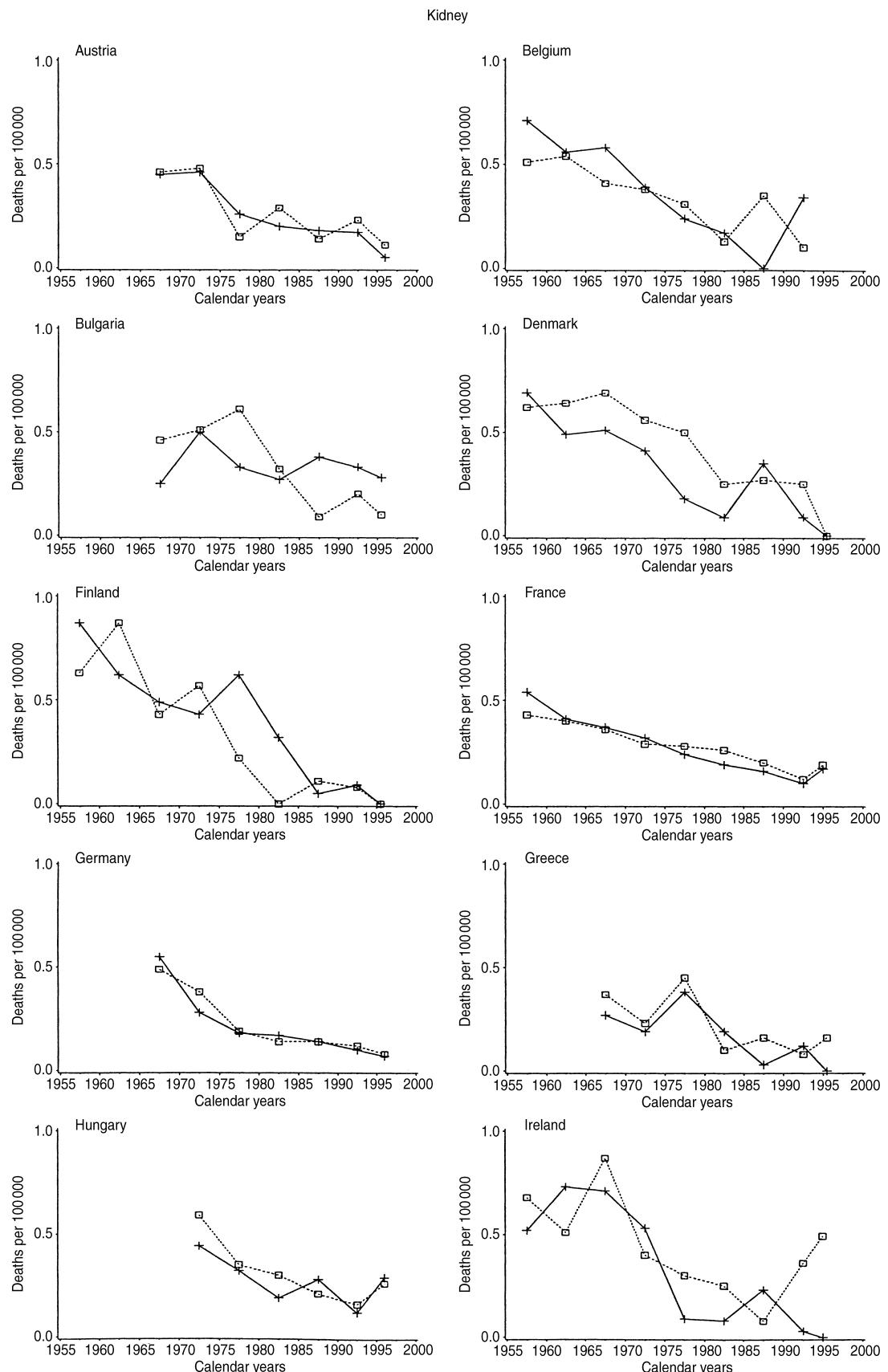


Fig. 2. (continued)

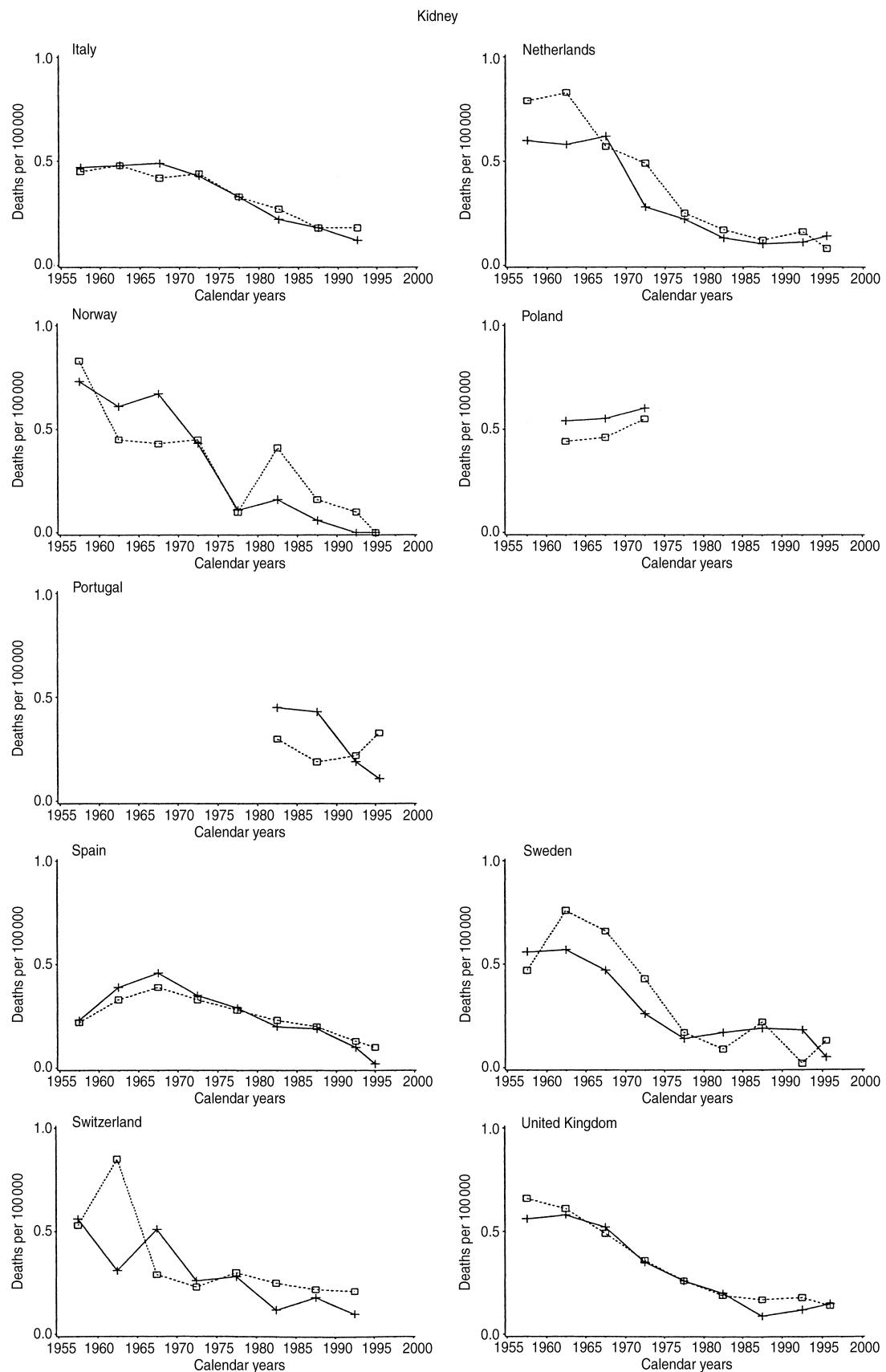


Fig. 2. (continued)

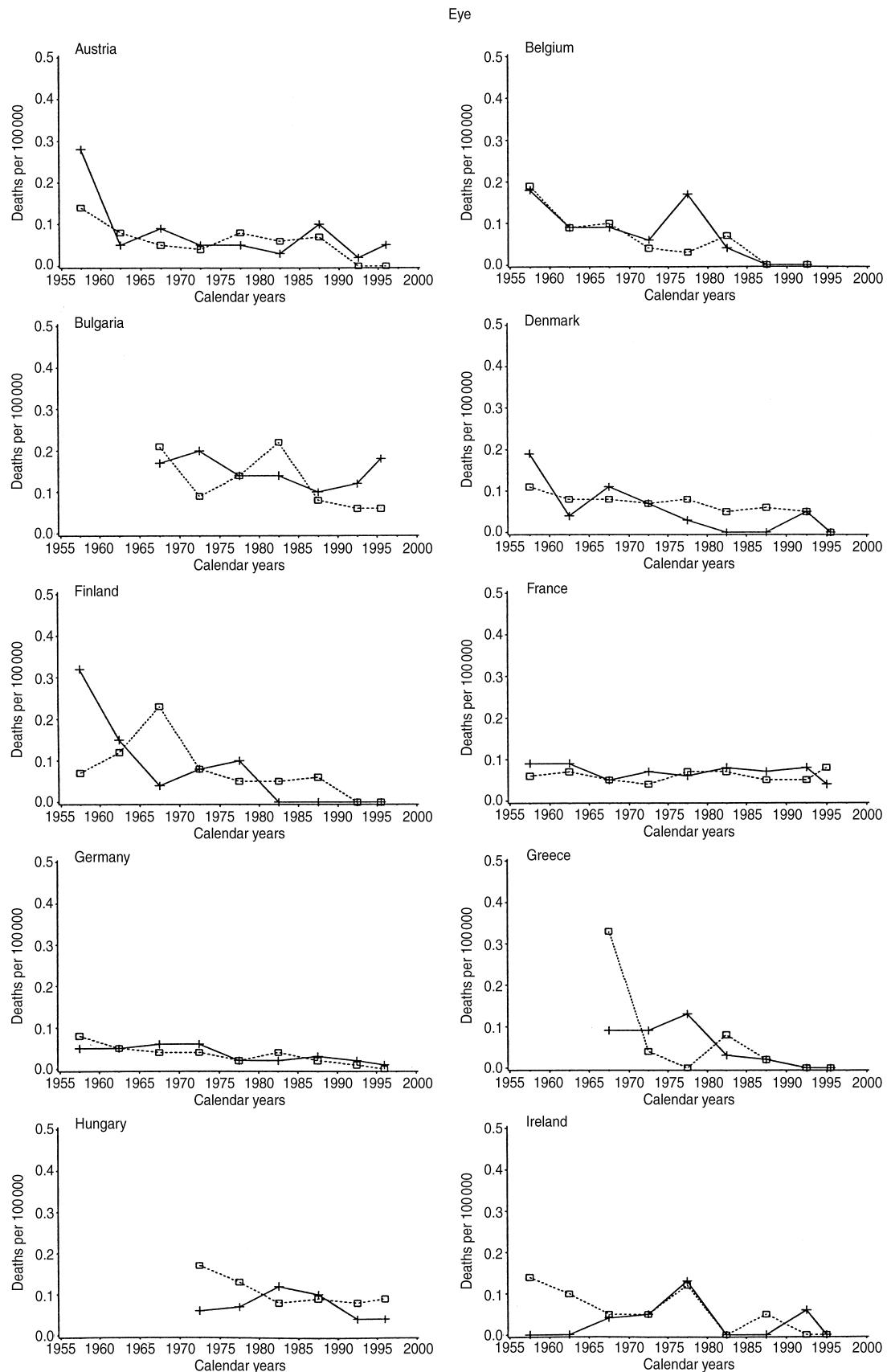


Fig. 2. (continued)

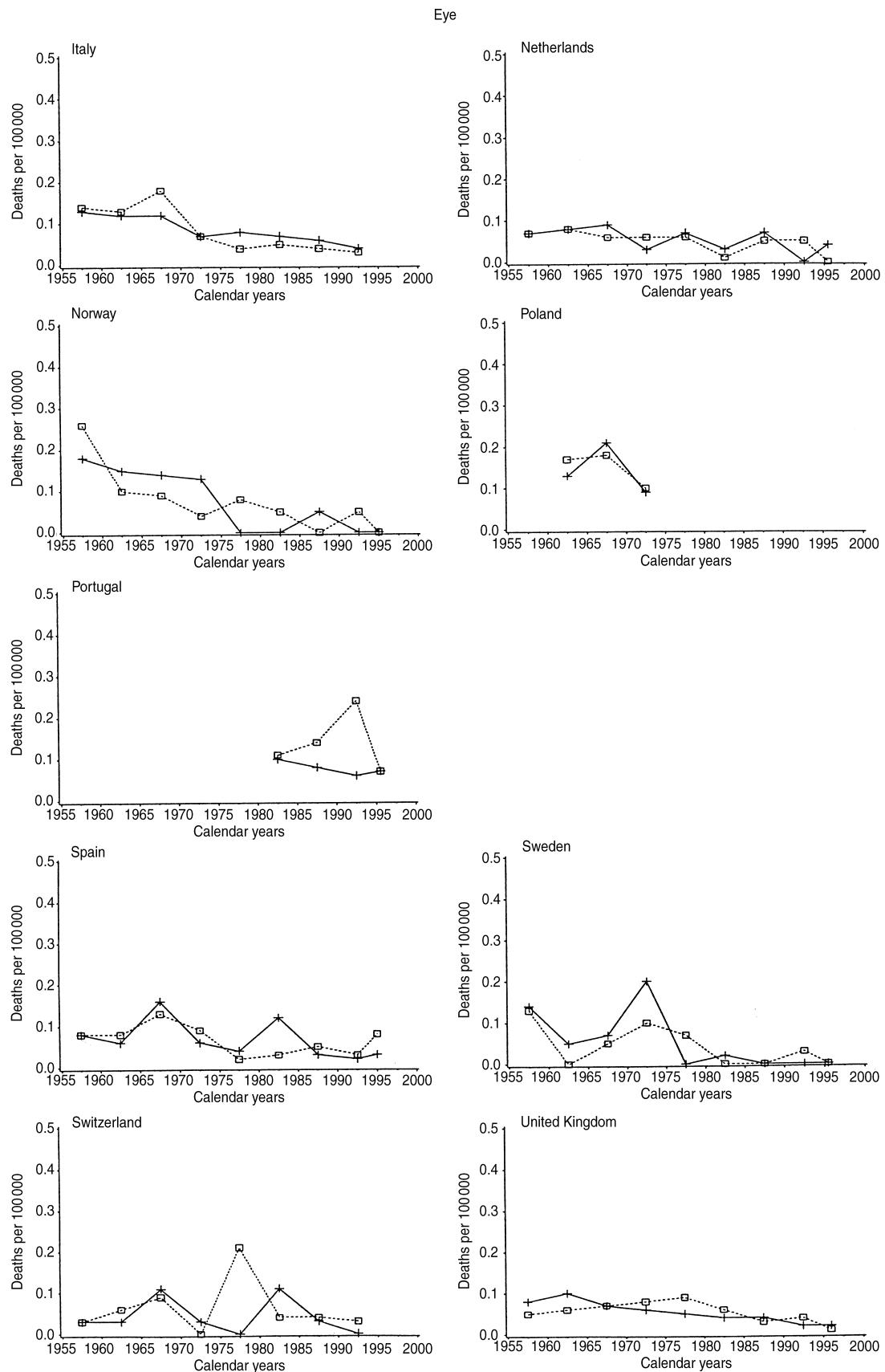


Fig. 2. (continued)

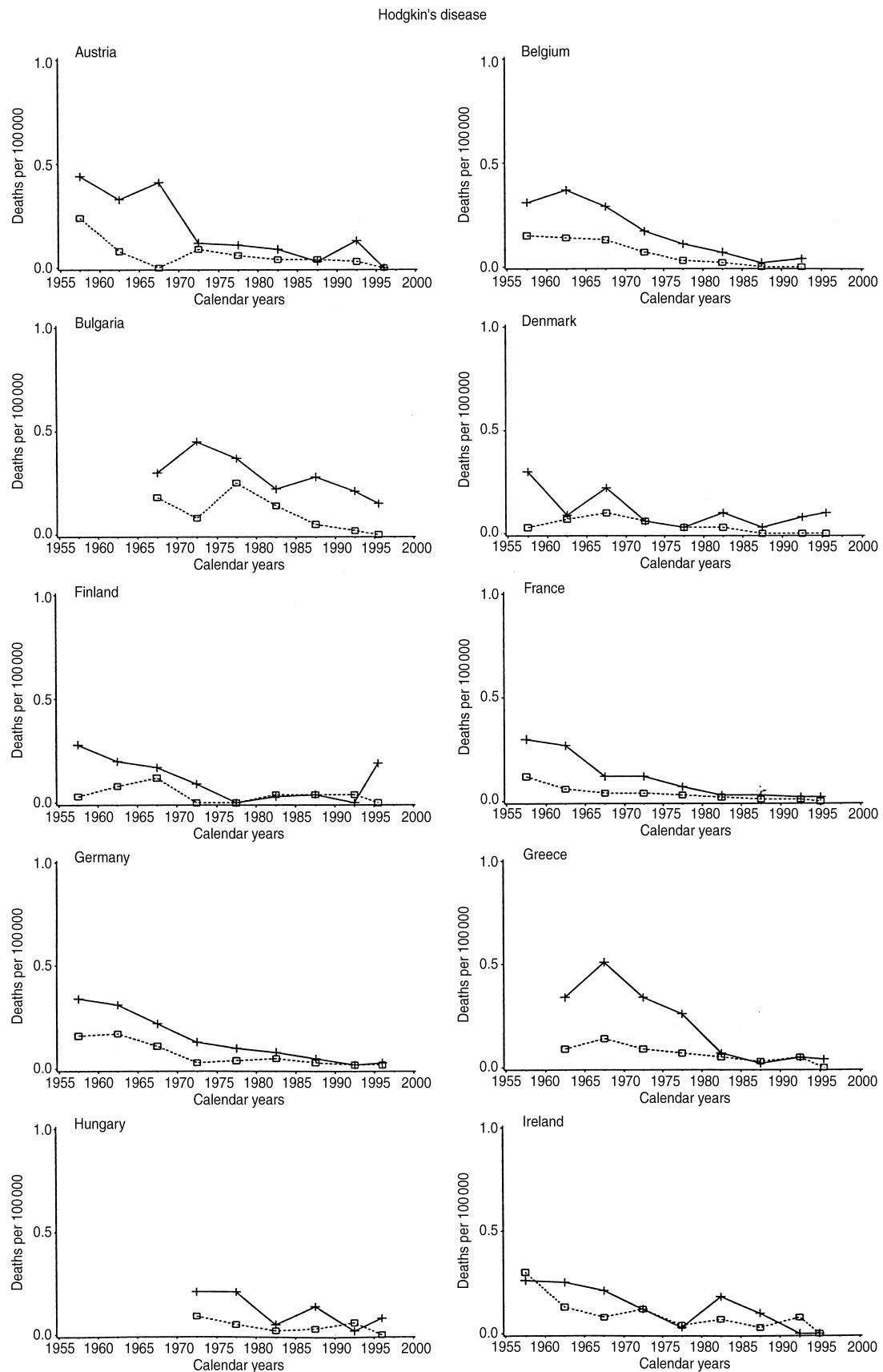


Fig. 2. (continued)

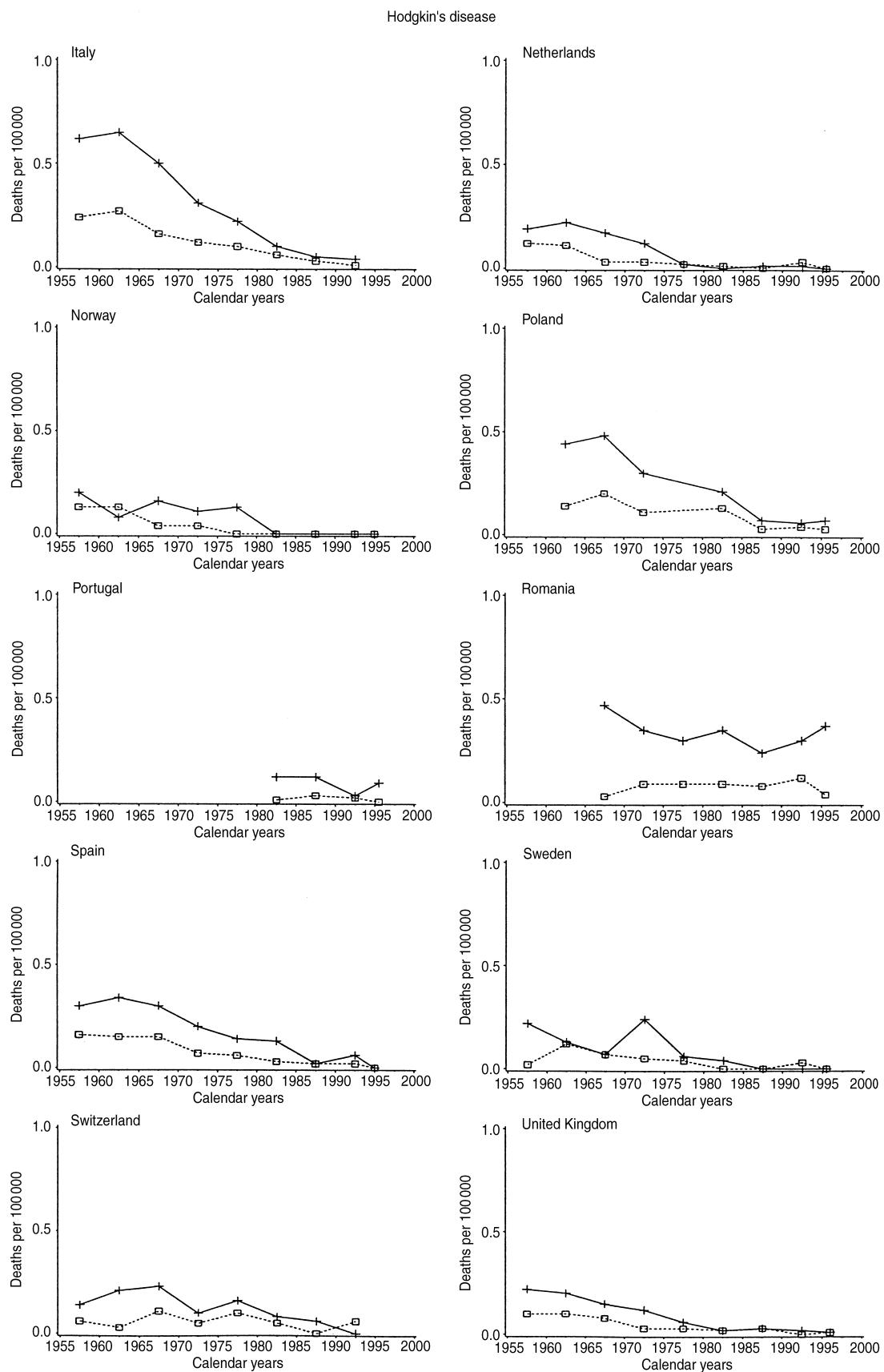


Fig. 2. (continued)

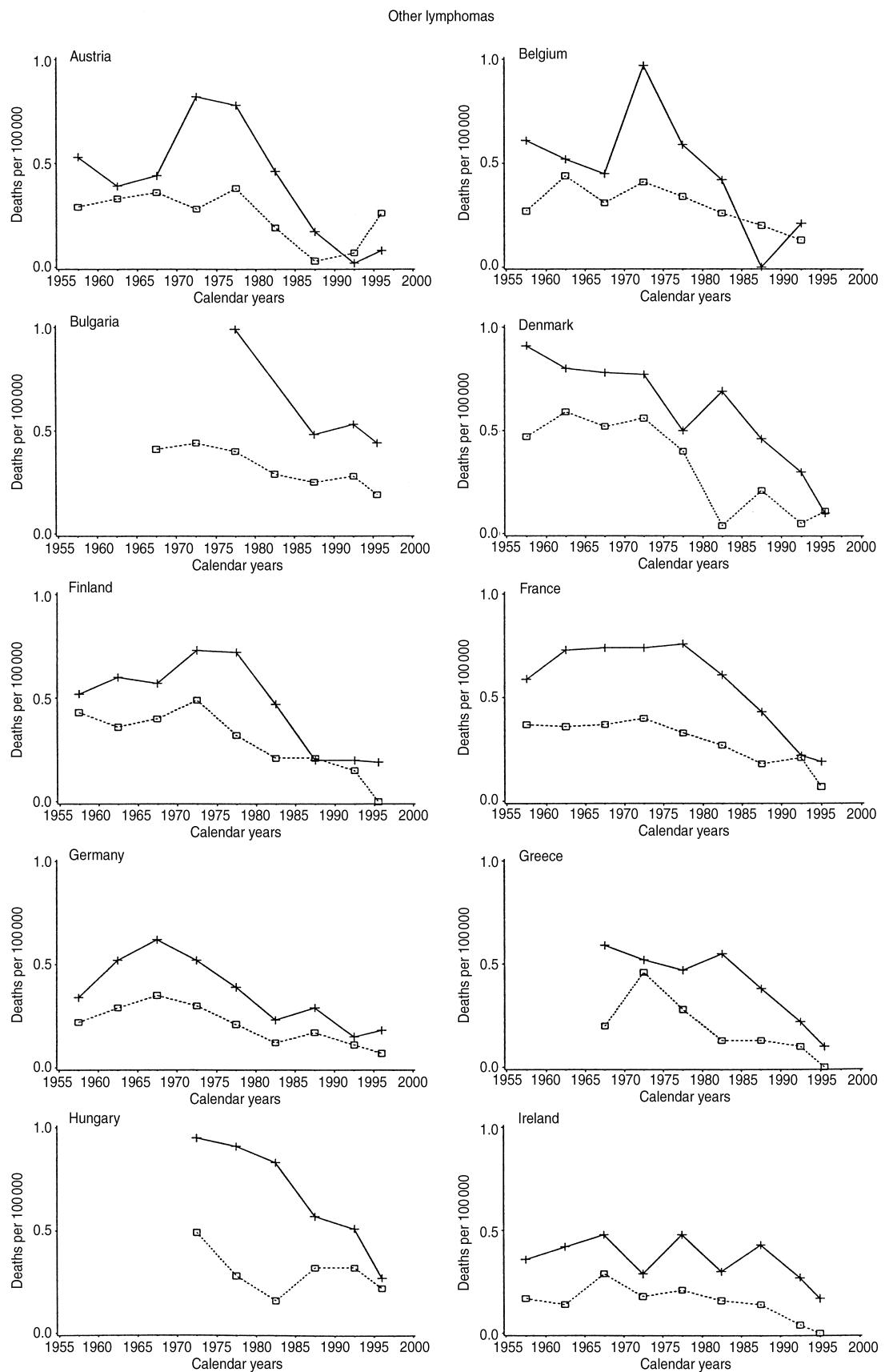


Fig. 2. (continued)

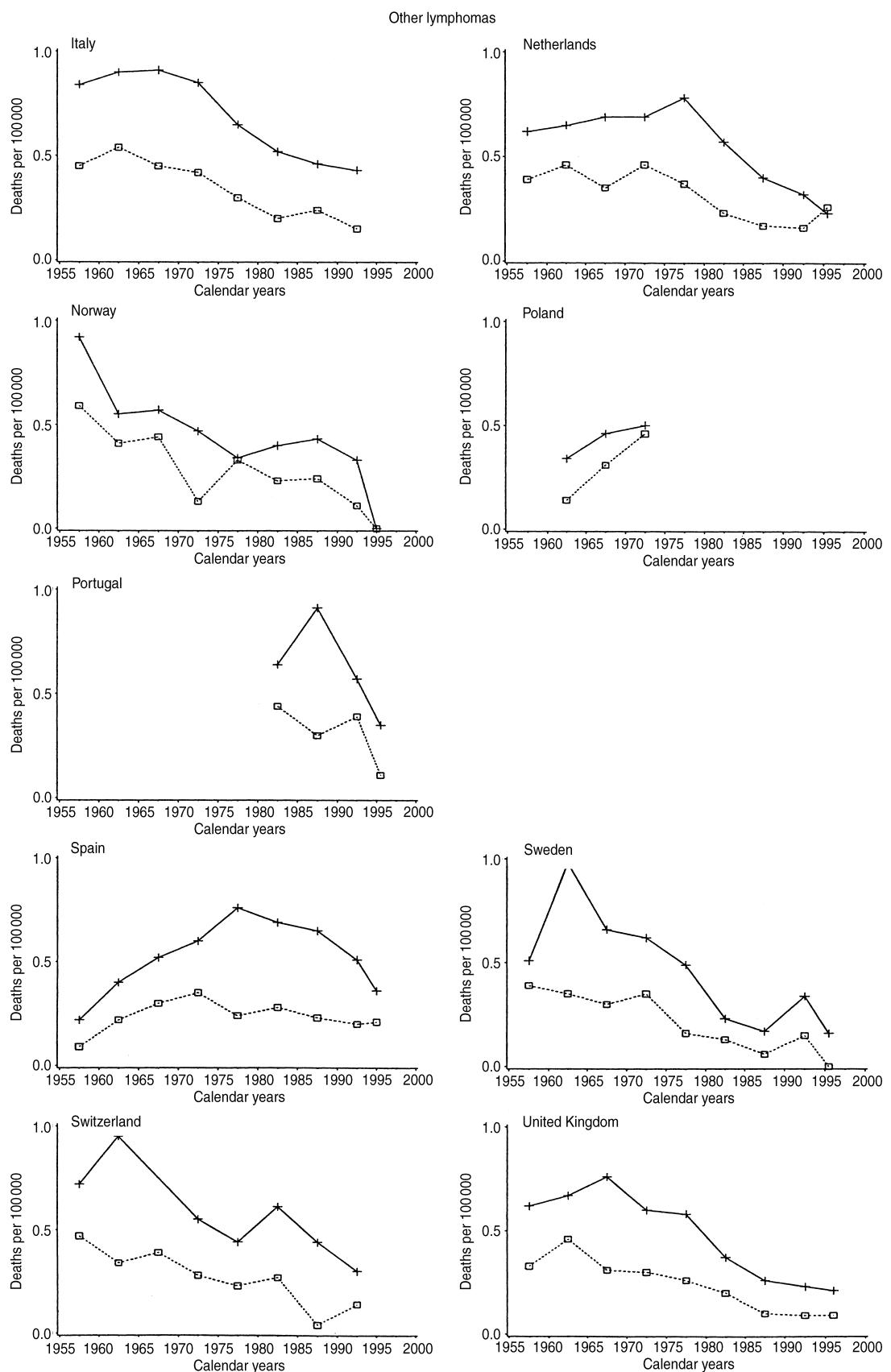


Fig. 2. (continued)

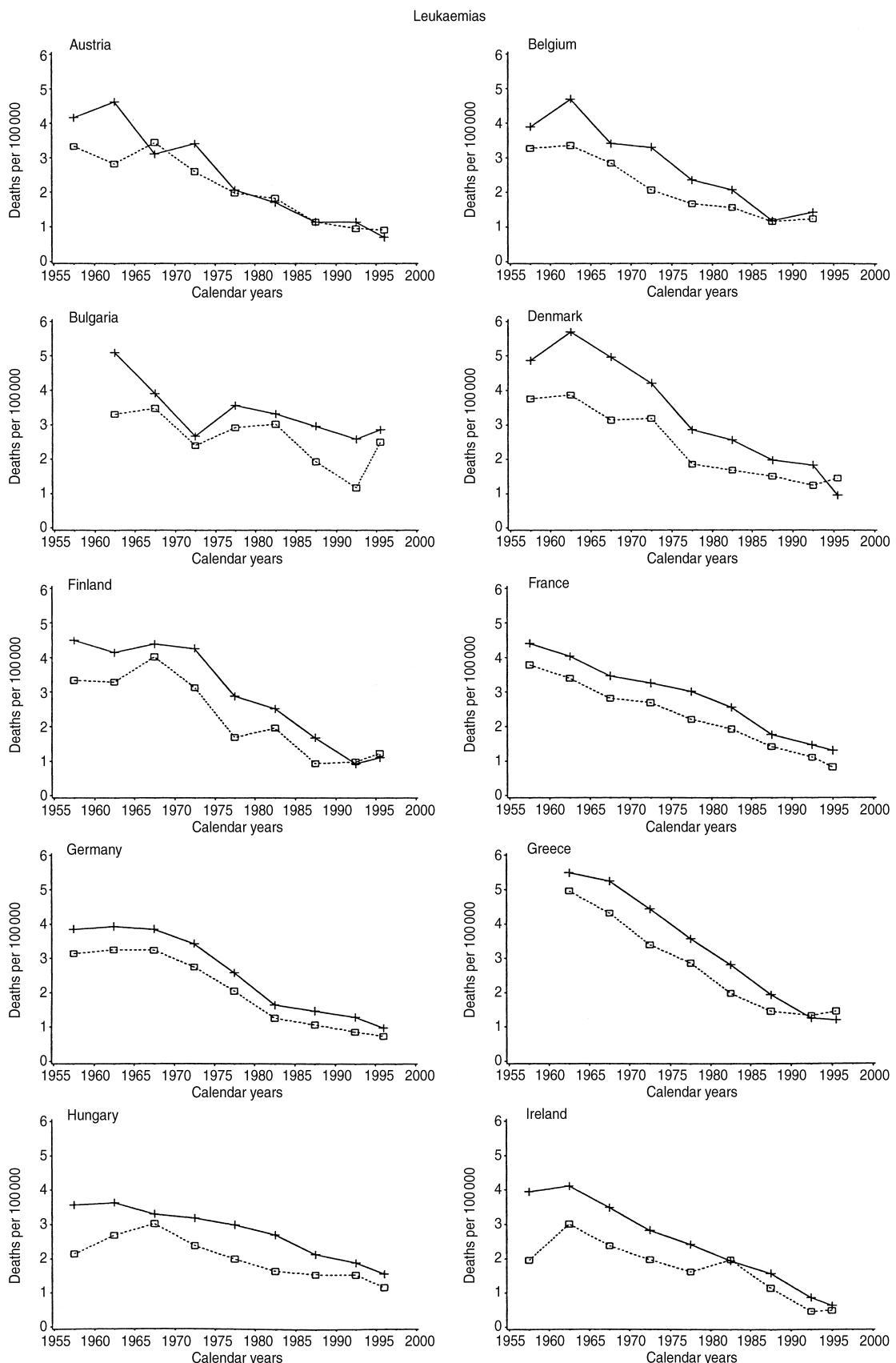


Fig. 2. (continued)

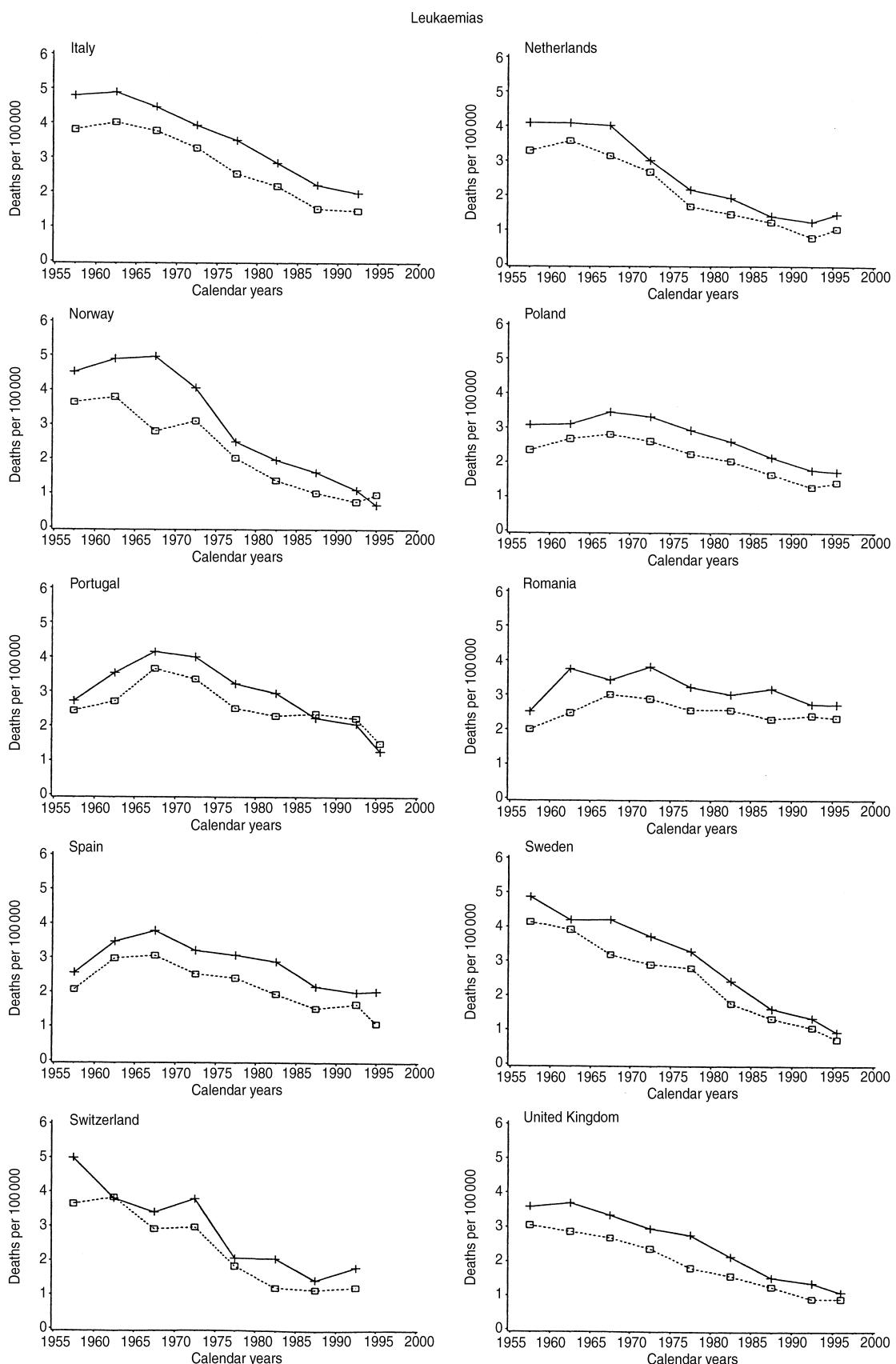


Fig. 2. (continued)

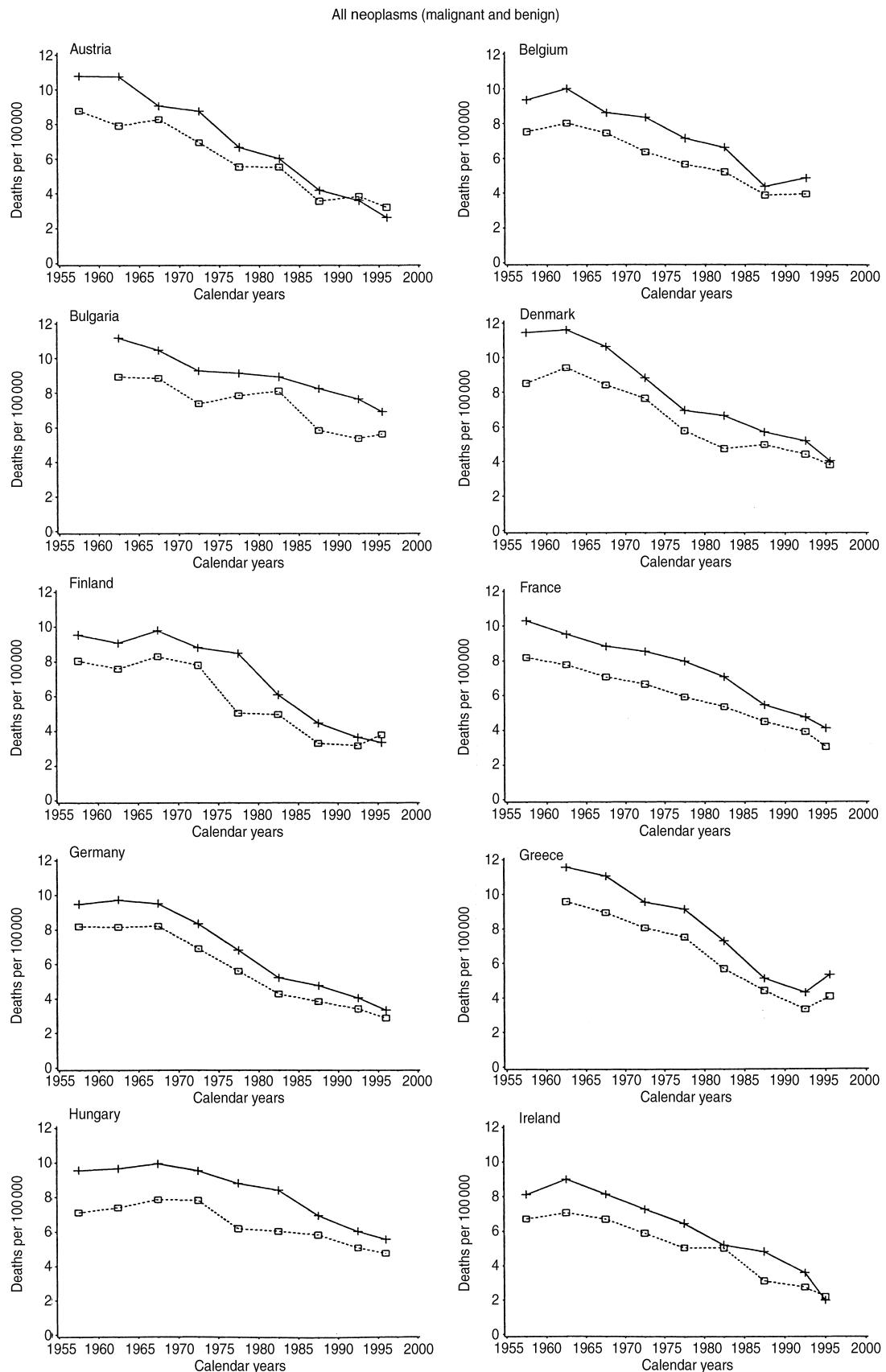


Fig. 2. (continued)

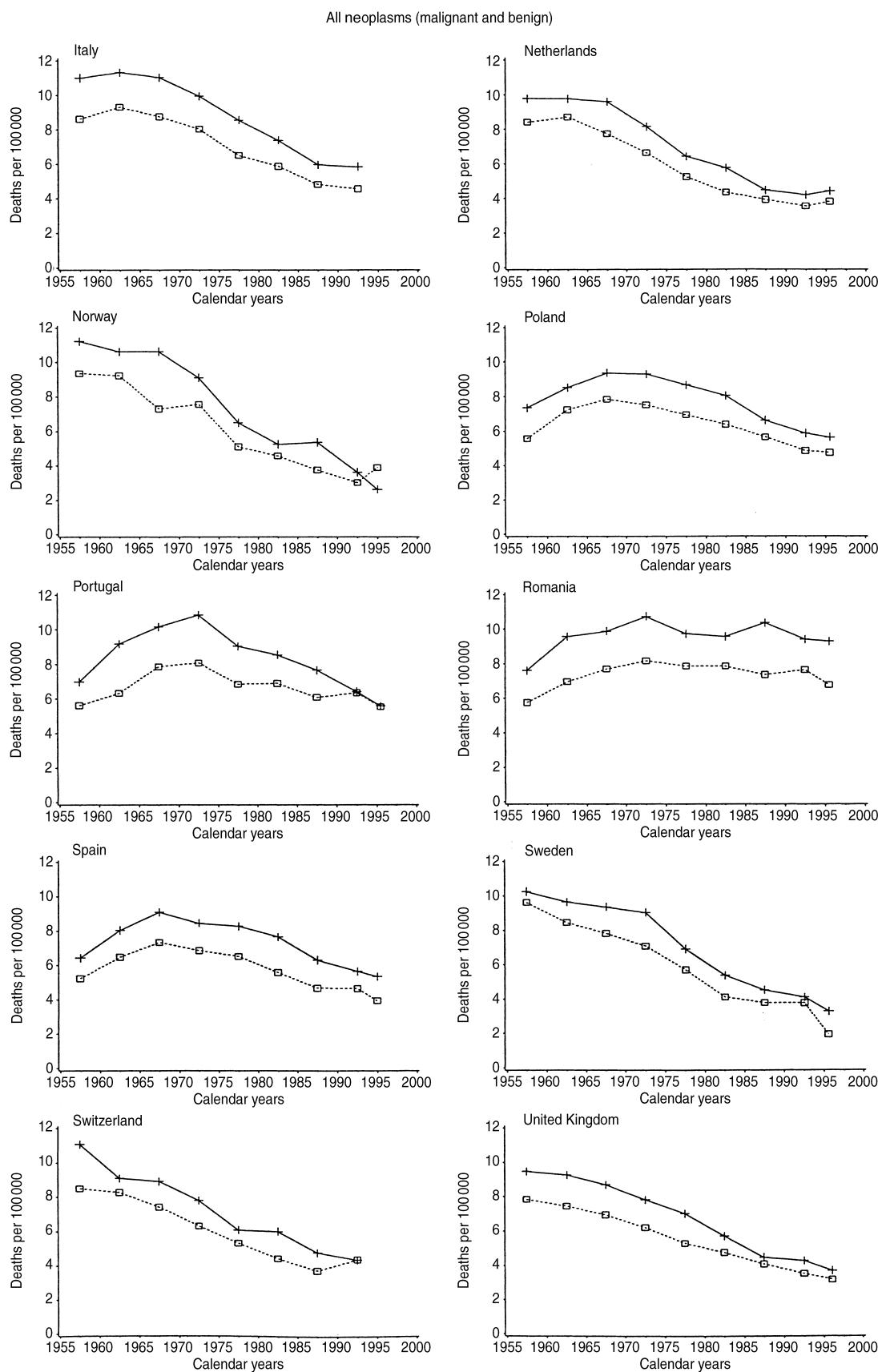


Fig. 2. (continued)

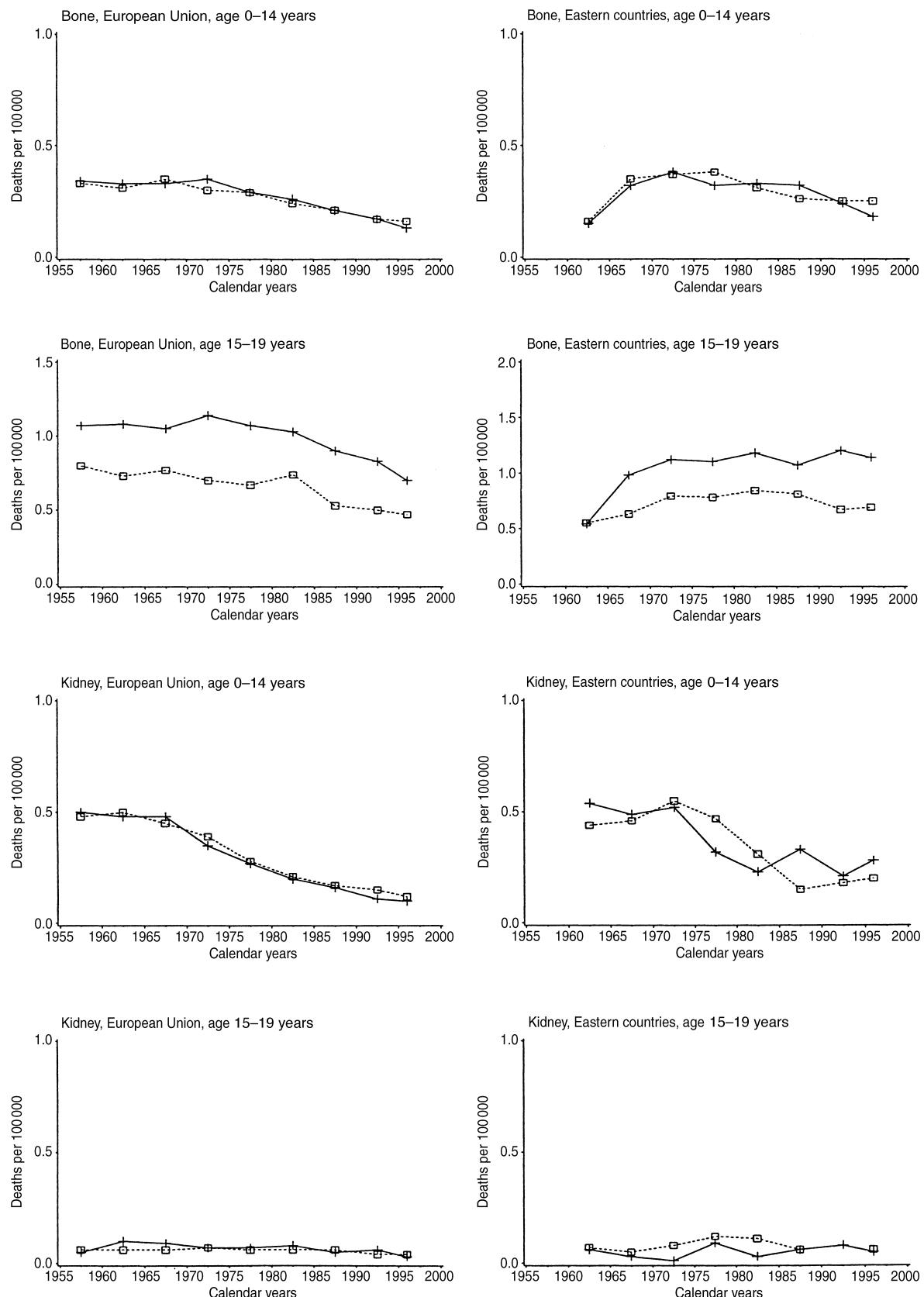


Fig. 3. Trends in age-standardised 0–14 years and 15–19 years (on the world standard population; rates per 100 000) death certification rates from childhood bone, kidney, Hodgkin's disease, other lymphomas, leukaemias and all childhood cancers in European Union and Eastern European countries (Bulgaria, Hungary, Poland, Romania), 1955–1997 (+ — + boys; - - - girls).

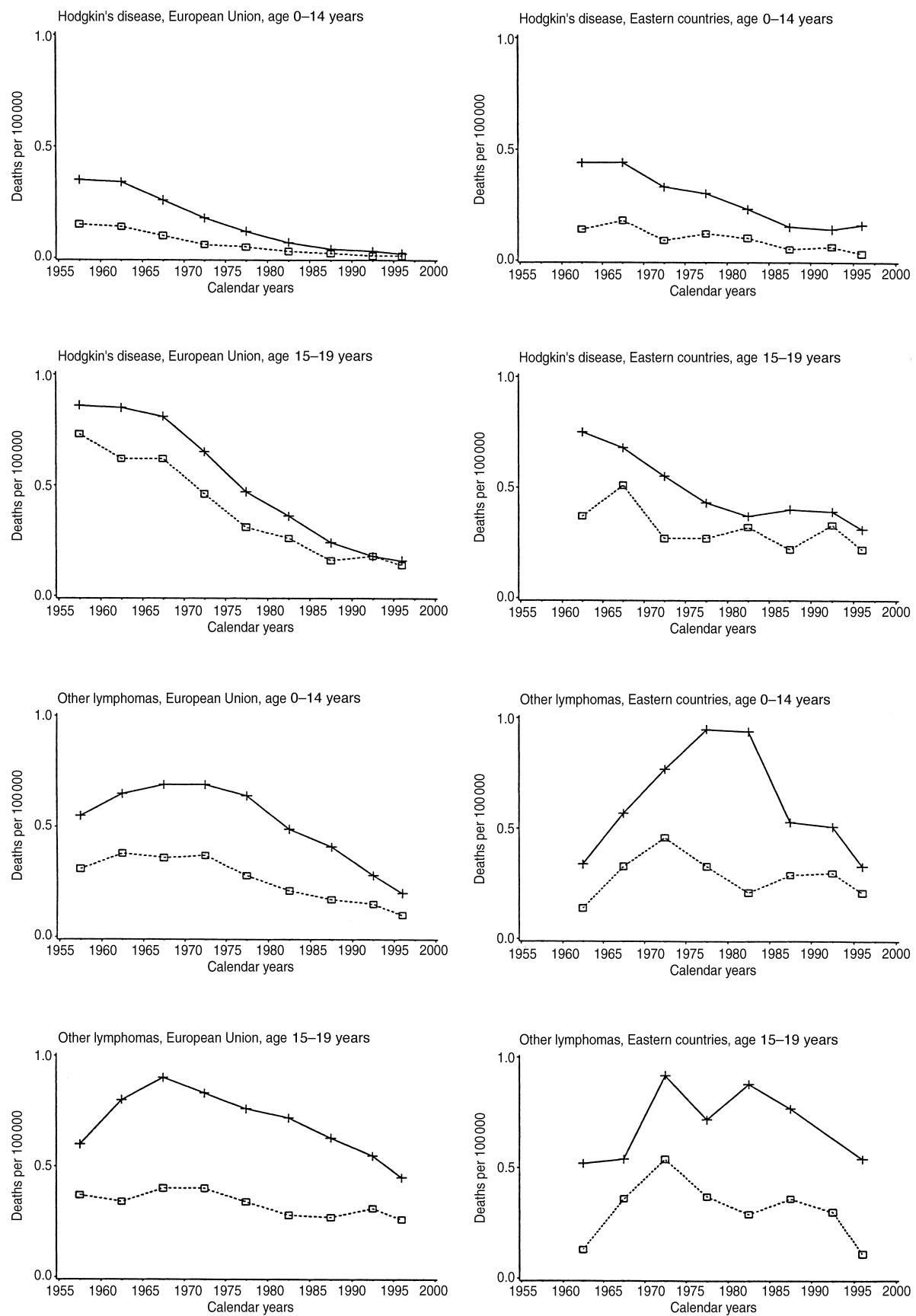


Fig. 3. (continued)

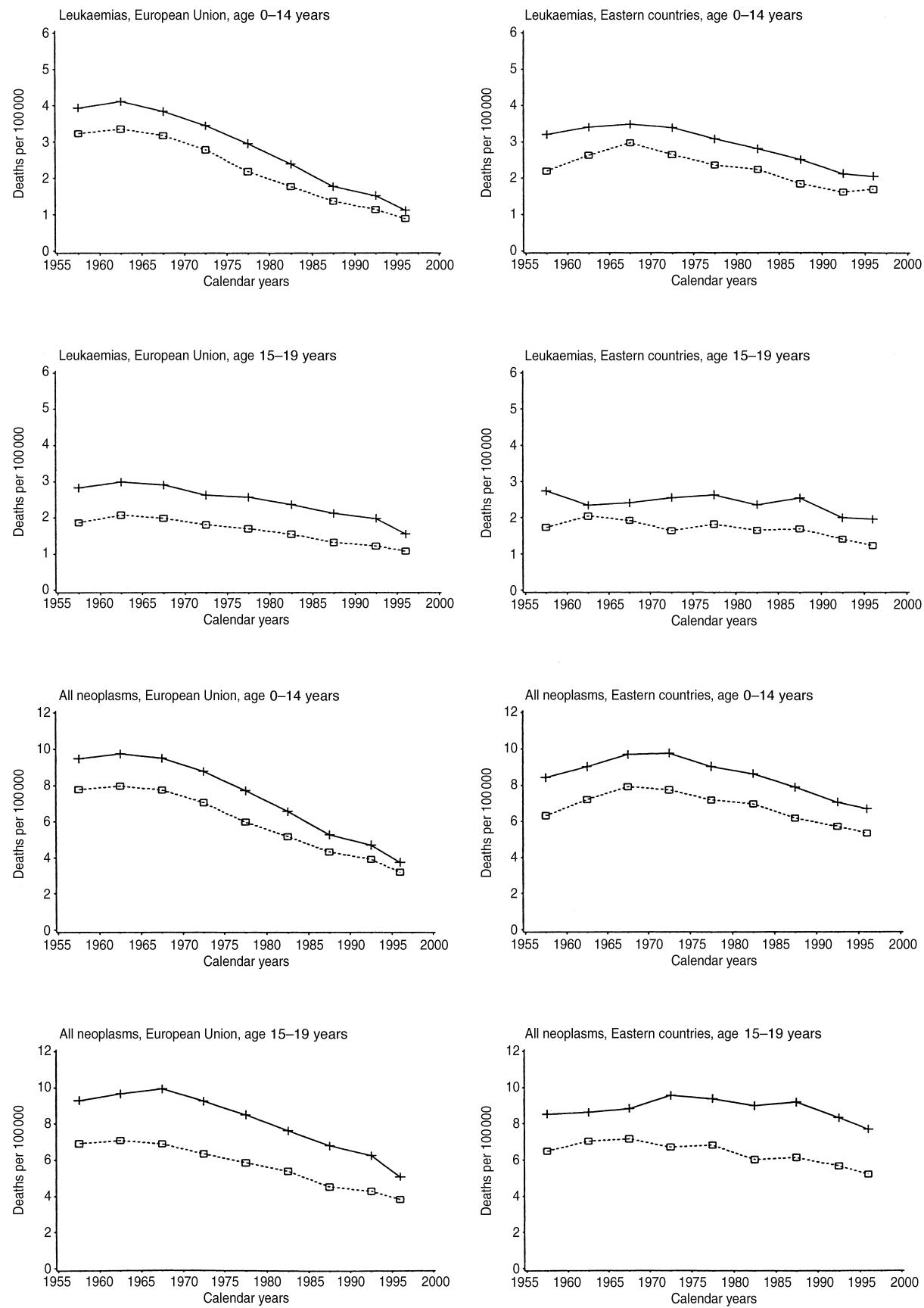


Fig. 3. (continued)

5. The EUROCARE Working Group for this study

Austria: W. Oberaigner (Cancer Registry of Tirol). *Denmark:* H. Storm (Danish Cancer Society 'Institute of Cancer Epidemiology'). *Estonia:* T. Aareleid (Estonian Cancer Registry). *Finland:* T. Hakulinen (Finnish Cancer Registry). *France:* J. Mace-Lesec'h (Calvados General Cancer Registry), P. Arveux (Doubs Cancer Registry), N. Raverdy (Somme Cancer Registry). *Germany:* P. Kaatsch, J. Michaelis (German Registry of Childhood Malignancies). *Iceland:* L. Tryggvadottir, H. Tulinius (Icelandic Cancer Registry). *Italy:* P. Crosignani (Lombardy Cancer Registry), E. Conti (Latina Cancer Registry), M. Vercelli (Liguria Cancer Registry — NCI, Genova), M. Federico, L. Mangone (Modena Cancer Registry), V. De Lisi (Parma Cancer Registry), C. Magnani (Piedmont Childhood Cancer Registry), L. Gafà, R. Tumino (Ragusa Cancer Registry), F. Falcini (Romagna Cancer Registry), A. Barchielli (Tuscan Cancer Registry), *Poland:* J. Pawlega, J. Rachtan, (Cracow Cancer Registry), M. Bielska-Lasota, Z. Wronkowski (Warsaw Cancer Registry). *Slovakia:* A. Obsitnikova, I. Plesko, (National Cancer Registry of Slovakia). *Slovenia:* V. Pompe-Kirn (Cancer Registry of Slovenia). *Spain:* I. Izazugaza (Basque Country Cancer Registry), C. Martinez-Garcia (Granada Cancer Registry), I. Garau (Mallorca Cancer Registry), E. Ardanaz, C. Moreno (Navarra Cancer Registry), J. Galceran (Tarragona Cancer Registry). *Sweden:* T. Möller (Southern Swedish Regional Tumour Registry). *Switzerland:* C. Bouchardy, L. Raymond, (Geneva Cancer Registry). *The Netherlands:* J.W. Coebergh (Eindhoven Cancer Registry). *Scotland:* R. Black, A. Gould (Scottish Cancer Registry). *England and Wales:* CA. Stiller (Childhood Cancer Research Group, Oxford).

Study Coordinator, Data Centre and Steering Committee: F. Berrino (Project Leader), G. Gatta, A. Micheli, M. Sant (Division of Epidemiology, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan, Italy), R. Capocaccia, M. Santiquilani, F. Valente, A. Verdecchia, (Dept. of Epidemiology and Biostatistics, Istituto Superiore di Sanita, Rome, Italy), J.W. Coebergh (The Netherlands), M.P. Coleman (UK), J. Estève (Service de Biostatistique, Centre Hospitalier Lyon, France), J. Faivre (France), D. Forman (UK), T. Hakulinen (Finland), C. Martinez-Garcia (Spain).

Acknowledgements

This work was supported by the Swiss League against Cancer and the Italian Association for Cancer Research.

References

- Levi F, La Vecchia C, Lucchini F, Negri E, Boyle P. Patterns of childhood cancer incidence and mortality in Europe. *Eur J Cancer* 1992, **28**, 2028–2049.
- Levi F, La Vecchia C, Lucchini F, Negri E, Boyle P. Patterns of childhood cancer mortality: America, Asia and Oceania. *Eur J Cancer* 1995, **31**, 771–782.
- Kaiser J. No meeting of minds on childhood cancer. *Science* 1999, **286**, 1832–1834.
- UK Childhood Cancer Study Investigators. The United Kingdom Childhood Cancer Study: objectives, materials and methods. *Br J Cancer* 2000, **82**, 1073–1102.
- Birch JM, Marsden HB, Morris Jones PH, Pearson D, Blair V. Improvements in survival from childhood cancer: results of a population based survey over 30 years. *Br Med J* 1988, **296**, 1372–1376.
- Stiller CA, Bunch KJ. Trend in survival for childhood cancer in Britain diagnosed 1971–1985. *Br J Cancer* 1990, **62**, 806–815.
- La Vecchia C, Levi F, Lucchini F, Garattini S. Progress of anticancer drugs in reducing mortality from selected cancers in Europe: an assessment. *Anti-Cancer Drugs* 1991, **2**, 215–221.
- Martos MC, Olsen JH. Childhood cancer mortality in the European Community, 1950–1989. *Eur J Cancer* 1993, **29A**, 1783–1789.
- La Vecchia C, Negri E, Decarli A. Childhood cancer mortality in Italy. *Lancet* 1996, **347**, 1633–1634.
- Henze G. Childhood acute lymphoblastic leukaemia. *Eur J Cancer* 1997, **33**, 8–9.
- La Vecchia C, Negri E, Decarli A. Childhood cancer mortality in Italy. *Rev Epidemiol Santé Publ* 1994, **45**, 93–97.
- Doll R, Smith PJ. Comparison between registries: age-standardized rates. In Waterhouse JAH, Muir CS, Shanmugaratnam K, et al., eds. *Cancer Incidence in Five Continents*, vol. IV. IARC Scientific Publication. No. 42. Lyon, IARC, 1982, 671–675.
- World Health Organization. *International Classification of Diseases*, 7th revision. Geneva, World Health Organization, 1957.
- World Health Organization. *International Classification of Diseases*, 8th revision. Geneva, World Health Organization, 1967.
- World Health Organization. *International Classification of Diseases*, 9th revision. Geneva, World Health Organization, 1977.
- Stiller CA, Craft AW, Corazziari I. Survival of children with bone sarcoma in Europe since 1978: result from the EUROCARE study. *Eur J Cancer* 2001, **37**, 760–766.
- Gatta G, Luksch R, Coleman MP, Corazziari I and the EUROCARE Working Group. Survival from acute non-lymphocytic leukaemia (ANLL) and chronic myeloid leukaemia (CML) in European children since 1978: a population-based study. *Eur J Cancer* 2001, **37**, 695–702.
- Stiller CA. Population based survival rates for childhood cancer in Britain, 1980–91. *Br Med J* 1994, **309**, 1612–1616.
- Pui C-H. Childhood leukaemias. *N Engl J Med* 1995, **332**, 1618–1630.
- La Vecchia C, Levi F, Lucchini F, Lagiou P, Trichopoulos D, Negri E. Trends in childhood cancer mortality as indicators of quality in medical care in the developed world. *Cancer* 1998, **83**, 2223–2227.
- Linet MS, Ries LAG, Smith MA, Tarone RE, Devesa SS. Cancer Surveillance series: recent trends in childhood cancer incidence and mortality in the United States. *J Natl Cancer Inst* 1999, **91**, 1051–1058.
- Singh GK, Yu SM. US childhood mortality, 1950 through 1993: trends and socioeconomic differentials. *Am J Public Health* 1996, **86**, 505–512.
- Gloeckler Ries LA. Childhood cancer mortality. In *National Cancer Institute (NCI) Monograph, Cancer Incidence and Survival among Children and Adolescents: United States SEER Program, 1975–1995*. National Cancer Institute, 2000, 165–174.
- Coebergh J-W, Pastore G, Gatta G, Corazziari I, Kamps W and the EUROCARE Working Group. Variation in survival of European children with acute lymphoblastic leukaemia, diagnosed in 1978–1992: the EUROCARE study. *Eur J Cancer* 2001, **37**, 687–694.