

European Journal of Cancer 38 (2002) 99-166

European Journal of Cancer

www.ejconline.com

# Estimates of cancer incidence and mortality in Europe in 1995

F. Bray\*, R. Sankila, J. Ferlay, D.M. Parkin

Unit of Descriptive Epidemiology, International Agency for Research on Cancer, 150 cours Albert Thomas, 69372 Lyon Cedex 08, France

Received 10 April 2001; received in revised form 29 June 2001; accepted 1 July 2001

#### Abstract

Cancer incidence and mortality estimates for 1995 are presented for the 38 countries in the four United Nations-defined areas of Europe, using World Health Organization mortality data and published estimates of incidence from national cancer registries. Additional estimation was required where national incidence data was not available, and the method involved incorporating the high quality incidence and mortality data available from the expanding number of population-based cancer registries in Europe. There were an estimated 2.6 million new cases of cancer in Europe in 1995, representing over one-quarter of the world burden of cancer. The corresponding number of deaths from cancer was approximately 1.6 million. After adjusting for differing population age structures, overall incidence rates in men were highest in the Western European countries (420.9 per 100 000), with only Austria having a rate under 400. Eastern European men had the second highest rates of cancer (414.2), with extremely high rates being observed in Hungary (566.6) and in the Czech Republic (480.5). The lowest male all-cancer rate by area was observed in the Northern European countries, with fairly low rates seen in Sweden (356.6) and the UK (377.8). In contrast to men, the highest rates in women were observed in Northern Europe (315.9) and were particularly high in Denmark (396.2) and the other Nordic countries excepting Finland. The rates of cancer in Eastern European women were lower than in the other three areas, although as with men, female rates were very high in Hungary (357.2) and in the Czech Republic (333.6). There was greater disparity in the mortality rates within Europe—generally, rates were highest in Eastern European countries, notably in Hungary, reflecting a combination of poorer cancer survival rates and a higher incidence of the more lethal neoplasms, notably cancer of the lung. Lung cancer, with an estimated 377 000 cases, was the most common cancer in Europe in 1995. Rates were particularly high in much of Eastern Europe reflecting current and past tobacco smoking habits of many of its inhabitants. Together with cancers of colon and rectum (334 000), and female breast (321 000), the three cancers represented approximately 40% of new cases in Europe. In men, the most common primary sites were lung (22% of all cancer cases), colon and rectum (12%) and prostate (11%), and in females, breast (26%), colon and rectum (14%) and stomach (7%). The number of deaths is determined by survival, as well as incidence; by far the most common cause of death was lung cancer (330 000)—about one-fifth of the total number of cancer deaths in Europe in 1995. Deaths from cancers of the colon and rectum (189000) ranked second, followed by deaths from stomach cancer (152000), which due to poorer survival ranked higher than breast cancer (124000). Lung cancer was the most common cause of death from cancer in men (29%). Breast cancer was the leading cause of death in females (17%). Cancer registries are a unique source of information on cancer incidence and survival, and are used here with national mortality to demonstrate the very substantial burden of cancer in Europe, and the scope for prevention. Despite some provisos about data quality, the general patterns which emerge in Europe verify the role of past exposures and interventions, and more importantly, firmly establish the need for cancer control measures which target specific populations. In particular, there is a clear urgency to combat the ongoing tobacco epidemic, now prevalent in much of Europe, particularly in the Eastern countries. © 2002 Elsevier Science Ltd. All rights reserved.

Keywords: Neoplasms; Epidemiology; Registries; Incidence; Mortality; Data collection; Europe; Public health

#### 1. Introduction

Over one-quarter of the global burden of cancer occurs within Europe despite the fact that Europe's

E-mail address: bray@iarc.fr (F. Bray).

inhabitants comprise only approximately one-eighth of the world's population. The major public health challenges arising from an increasing cancer burden in Europe led the European Commission in 1987 to establish a collaborative policy on cancer control. The 'Europe Against Cancer Programme' identified four separate areas for action, namely data collection and research, information and health education, early

<sup>\*</sup> Corresponding author: Tel.: +33-4-7273-8375; fax: +33-4-7273-

detection and screening, and training and quality control.

The European Network of Cancer Registries (ENCR) is one of the main activities within the first area of the Programme, and seeks to improve the quality, comparability and availability of cancer data, promote their use in cancer control, healthcare planning and research, and provide regular information on the burden of cancer in Europe. Currently, the ENCR has a membership of 152 population-based cancer registries, who regularly submit information on the incidence and mortality of cancer in their catchment area to the ENCR secretariat, housed in the International Agency for Research on Cancer (IARC). The data are then formatted and included in the latest version of the EUROCIM software package [1]. EUROCIM provides ENCR members with a resource to compare their own incidence and mortality datasets with data from other European cancer registries, and a fundamental aim of the software tool is to promote communication and collaboration between members on issues such as data quality and cancer research. At present, approximately 30% of the European population of over 700 million reside in areas covered by cancer registries.

This paper examines the geographical variations in cancer burden and risk in 1995 in the European countries within the four United Nations (UN) defined regions (Eastern, Northern, Southern and Western Europe) using the most recent incidence and mortality data. To do this, we have complemented reported incidence figures from nationwide cancer registries and mortality data from the World Health Organization (WHO), with national estimates obtained using a method which incorporates the high-quality incidence and mortality data available from the cancer registries of Europe.

This report follows the methodology and style of presentation of several previous publications examining cancer burden in the European Union in 1980 [2] and 1990 [3]. The motivation behind this set of estimates for 1995 is the availability of more up-to-date information on cancer incidence and mortality in EUROCIM [1], as well as recent datasets published by national cancer registries. As part of the 'Europe Against Cancer' Programme, the ENCR is continually expanding, improving the quality of information on cancer burden in areas where previously less was known, such as in Eastern Europe. For the first time, we can provide estimates of the cancer incidence and mortality for the whole of Europe, using a consistent methodology, incorporating the many local and national cancer data sources available.

# 2. Patients and methods

Cancer incidence and mortality estimates in 1995 are reported for the 38 countries in the four areas of Europe for which the UN supplies population estimates and projections. Details are provided in the map of Europe (Fig. 1). Incidence and mortality data are summarised for 25 common cancer sites, together with an estimate of all cancers combined (excluding non-melanoma skin cancer, ICD-9 140-172, 174-208). The primary cancers considered are oral cavity (ICD-9 140-145), nasopharynx (147), other pharynx (146, 148, 149), oesophagus (150), stomach (151), colon and rectum (153, 154), liver and intrahepatic bile ducts (155), pancreas (157), larynx (161), trachea, bronchus and lung (162), melanoma of the skin (172), female breast (174), cervix uteri (180), corpus uteri (182), ovary and other uterine adnexa (183), prostate (185), testis (186), bladder (188), kidney and other and unspecified urinary organs (189), brain and other central nervous system (191, 192), thyroid (193), non-Hodgkin lymphoma (200, 202), Hodgkin disease (201), multiple myeloma (203), and leukaemia (204–208). The analyses involved 11 age groups; 0–14 years, 15–34 years, 35–39 years, 40–44 years, 45–49 years, 50–54 years, 55–59 years, 60–64 years, 65–69 years, 70–74 years and 75 years and over. Tables 1 and 2 summarise the sources and years of the mortality and incidence data, respectively, and where required, details of the estimation methods.

#### 2.1. Mortality

Mortality is well-recorded in most European countries, and the number of deaths in 1995 by age, sex and cancer site were available from the WHO Mortality Databank for most countries, originally coded (with the exception of Denmark, which used ICD-8) using ICD-9. There was no cancer death information for Bosnia and Herzegovina, nor for Yugoslavia, and estimates were provided by applying the age and sex-specific rates of Slovenia to the respective estimated populations in 1995 of these two countries.

For a number of countries, particularly in Eastern Europe, the original mortality coding system lacked, to varying degrees, the sufficient level of detail required in this study, and hence some additional manipulations were necessary to obtain the number of deaths from each individual site. In particular, mortality statistics for some countries were only available at the three-digit level outlined in the ICD-9 'Special Tabulation Lists', or only for the major primary sites, and hence the number of deaths from certain cancers were either not available (e.g. liver cancer) or only available as an aggregation of individual sites (e.g. oral cavity and pharynx, lymphatic and haematopoietic neoplasms).

To circumvent the latter problem, the grouped sites were split into their component parts by applying ageand sex-specific proportions obtained from the representative mortality data (see Table 1). Similarly, for neoplasms where no mortality data were available, the residual group 'all other sites' was subdivided into the missing sites required by applying site-specific propor-





Fig. 1. Map showing the four European areas studied.

tions based on appropriate death data (see Table 1), leaving a remainder representing 'other' cancers. In countries for which data up to 1995 was not available, the appropriate number of deaths was derived by applying the most recent age-specific mortality rates to the 1995 population estimates.

# 2.2. Incidence

National incidence data for 1995 were available for countries in Europe with nationwide cancer registration—Croatia, the Czech Republic, Denmark, Estonia, Finland, Iceland, Ireland, Malta, the Netherlands,

Table 1 Recorded data sources and methods of estimation of national cancer mortality

UN area	Country	Mortality: latest year available/method of estimation
Eastern Europe	Bulgaria	WHO Mortality 1995
		140-149 split into 140-145, 147 and 146, 148 and 149 using proportions in registries used in Model 1a
		155: proportion in Hungary and Latvia applied to residual in Bulgaria
	Belarus	WHO Mortality 1995
		140–149 split into 140–145, 147 and 146, 148 and 149 using proportions in registries used in Model 1a
		182, 189, 193: proportion in Hungary and Latvia applied to residual
	G 1 D 11	200 + 202, 201, 203: proportions in Hungary and Latvia applied to WHO mortality estimate of 200–203
	Czech Republic	WHO Mortality 1995
	Hungary	WHO Mortality 1995
	Republic of	140–149 split into 140–145, 147 and 146, 148 and 149 using proportions in registries used in Model 1a WHO Mortality 1995
	Moldova	140–149 split into 140–145, 147 and 146, 148 and 149 using proportions in registries used in Model 1 <sup>a</sup>
	Modova	182, 189, 193: proportions in Hungary and Latvia applied to residual
		200 + 202, 203: proportions in Hungary and Latvia applied to WHO mortality estimate of 200, 202, 203
	Poland	WHO Mortality 1995
		182, 189, 193: proportions in Hungary and Latvia applied to residual
	Romania	WHO Mortality 1995
		140-149 split into 140-145, 147 and 146, 148 and 149 using proportions in registries used in Model 1a
		182, 189, 193: proportions in Hungary and Latvia applied to residual
		200 + 202, 203: proportions in Hungary and Latvia applied to WHO mortality estimate of 200, 202, 203
	Russian	WHO Mortality 1995
	Federation	140-149 split into 140-145, 147 and 146, 148 and 149 using proportions in registries used in Model 1a
		155, 157, 172, 182, 183, 186, 189, 191, 193: proportion in Hungary and Latvia applied to residual
	G1 1:	200 + 202, 201, 203: proportions in Hungary and Latvia applied to WHO mortality estimate of 200–203
	Slovakia	WHO Mortality 1995
	Ukraine	WHO Mortality 1996
		140–149 split into 140–145, 147 and 146, 148 and 149 using proportions in registries used in Model 1 <sup>a</sup>
		155, 157, 172, 182, 183, 186, 189, 191, 193: proportion in Hungary and Latvia applied to residual 200+202, 201, 203: proportions in Hungary and Latvia applied to WHO mortality estimate of 200-203
		200 + 202, 201, 203. proportions in Trungary and Latvia applied to WTO mortality estimate of 200–203
Northern Europe	Denmark	WHO Mortality 1995
	Estonia	WHO Mortality 1995
		140–149 split into 140–145, 147 and 146, 148 and 149 using proportions in registries used in Model 1 <sup>a</sup>
		155: proportion in Hungary and Latvia applied to residual in Estonia
	Finland	WHO Mortality 1995
	Iceland	WHO Mortality 1995
	Ireland	WHO Mortality 1995
	Latvia	WHO Mortality 1995
		140–149 split into 140–145, 147 and 146, 148 and 149 using proportions in registries used in Model 1 <sup>a</sup>
	Lithuania	WHO Mortality 1995
		140–149 split into 140–145, 147 and 146, 148 and 149 using proportions in registries used in Model 1a
	NI	155: proportion in Hungary and Latvia applied to residual in Lithuania
	Norway Sweden	WHO Mortality 1995 WHO Mortality 1995
	United Kingdom	WHO Mortality 1995
	Ollited Killgdolli	WHO Mortality 1993
Southern Europe	Albania	WHO Mortality 1995
		140–149 split into 140–145, 147 and 146, 148 and 149 using proportions in registries used in Model 1 <sup>a</sup>
		155: proportion of 155 of all sites in Hungary and Latvia applied to residual in Latvia
	Bosnia and	1995 Slovenia mortality rates applied to population
	Herzegovina	
	Croatia	WHO Mortality 1995
	Greece	WHO Mortality 1995
	Italy	WHO Mortality 1995
	Malta	WHO Mortality 1995
	Portugal	WHO Mortality 1995
	Slovenia	WHO Mortality 1995
	Spain	WHO Mortality 1995
	FYROM (Magadania)	WHO Mortality 1995
	(Macedonia)	140–149 split into 140–145, 147 and 146, 148 and 149 using proportions in registries used in Model 1 <sup>a</sup> 155: proportion of 155 of all sites in Hungary and Latvia applied to residual in FYROM
	Yugoslavia	1995 Slovenia mortality rates applied to population
	1 ugosiavia	* * * * * * * * * * * * * * * * * * * *
		(continued on next page)

Table 1 (continued)

UN area	Country	Mortality: latest year available/method of estimation
Western Europe	Austria Belgium France Germany Luxembourg	WHO Mortality 1995 WHO Mortality 1995 WHO Mortality 1995 WHO Mortality 1995 WHO Mortality 1995
	The Netherlands Switzerland	WHO Mortality 1995 WHO Mortality 1994 140–149 split into 140–145, 147 and 146, 148 and 149 using proportions in registries used in Model 2 <sup>b</sup>

WHO, World Health Organization; UN, United Nations.

Norway, Slovakia, Slovenia and Sweden. In the UK, national incidence data was available for the populations of Scotland and Northern Ireland, but not, at the time of analysis, for all of the populations covered by the registries in England and Wales. Although nationwide cancer registration systems exist in Austria, Latvia and Lithuania, the recorded data were not used as they did not meet the data quality standards required for inclusion in the latest volume of Cancer Incidence in Five Continents [4]. There is also national incidence data available from Belarus, although the data available were considered too old for use in this study. Thus, for these countries, estimates of the number of new cases were obtained by utilising the data from the many nationwide and regional cancer registries within Europe, and the national mortality data available from the WHO. Specifically, national incidence  $(I_N)$  was estimated by applying a set of age, sex and site-specific incidence: mortality ratios  $(I_R/M_R)$ , obtained from the aggregation of representative cancer registry data, to the corresponding country's national mortality  $(M_N)$ :

$$I_{\rm N} = M_{\rm N} \times I_{\rm R}/M_{\rm R}$$

In practice, the  $I_{\rm R}/M_{\rm R}$  were obtained from a Poisson regression model of the selected registry incidence data offset by corresponding mortality data. Separate models for each country and cancer site were fitted to the data using GLIM [5], and the models included explanatory terms for sex and low-degree age polynomials (up to order five). Age was entered until two consecutive terms failed to provide a significantly improved fit to the data, or the maximum of five was reached. A comparison of the scaled deviance between sequentially-fitted nested models led to the best-fitting model. Although there was substantial extra-Poisson variation for models fitted to some cancer sites, a careful inspection of the age-specific

fitted values indicated that the overdispersion did not in practice adversely affect the estimates of incidence. Furthermore, the procedure has been used in previous studies estimating cancer burden in the European Union [2,3], and has been shown to estimate incidence fairly accurately [2].

To achieve a greater degree of stability in the resulting incidence estimates, average mortality estimates were calculated from the latest 3 years available, while the registry incidence:mortality ratios were based on aggregates of the latest 5-years of data (where available). Before aggregation, each registry dataset was weighted to take account of the relative size of the population covered and the number of years contributed. The predicted age-specific incidence rates were applied to the 1995 population figures to obtain an estimate of the number of new cases in 1995.

In Eastern Europe, the number of new cases in Bulgaria, Belarus, Hungary, Moldova, Poland, Romania, the Russian Federation and Ukraine, were derived using country-specific national mortality applied to the fitted incidence:mortality ratios of aggregated cancer registry data. The same process was applied to estimate incidence in the Northern European countries of Latvia and Lithuania. Such information was taken from registries thought to be representative of the areas they cover, and whom could provide reasonable incidence:mortality ratios covering periods reasonably near 1995. The registries of Belarus, the Czech Republic and Slovakia were used for this purpose, together with five Polish cancer registries (see Table 2 for details). Due to their relatively small populations, the 3-year average age and sex-specific numbers of deaths in Latvia and Lithuania lacked some precision, and mortality was therefore smoothed by fitting the average age-specific mortality rates of Bulgaria, Hungary and Poland to the overall numbers of deaths in each country. For Switzerland, incidence was calculated using a second model of

<sup>&</sup>lt;sup>a</sup> Poisson model of the log of incidence offset for the log of mortality adjusted for terms for sex and for age (polynomials of up to order 5) using site-specific aggregated incidence and mortality data from the following cancer registries: Czech Republic (1993–1997), Poland, Cracow City (1990–1992), Poland, Kielce (1992–1996), Poland, Lower Silesia (1990–1992), Poland, Opole (1990–1992), Poland, Warsaw City (1990–1992), Slovakia (1991–1995) and Belarus (1990–1992; for sites for which data available).

<sup>&</sup>lt;sup>b</sup> Poisson model of the log of incidence offset for the log of mortality adjusted for terms for sex and for age (polynomials of up to order 5) using site-specific aggregated incidence and mortality data from the following cancer registries in Switzerland: Basel (1992–1996), Geneva (1992, 1996), Grisons (1990–1992), Neuchatel (1990–1992), St.Gallen (1990–1992), Appenzell (1990–1992), Vaud (1990–1992), Zurich (1990-1992).

Table 2 Recorded data sources and methods of estimation of national cancer incidence

UN Area	Country	Incidence: latest year available/method of estimation
Eastern Europe	Bulgaria	WHO Mortality 1994–1996 and Model 1 <sup>c</sup>
		140-149 split into 140-145, 147 and 146, 148 and 149 using proportions in registries used in Model 1°
		155: proportion in Hungary and Latvia applied to residual in Bulgaria
	Belarus	WHO Mortality 1994–1996 and Model 1°
		140-9 split into 140–145, 147 and 146, 148 and 149 using proportions in registries used in Model 1°
		182, 189, 193: proportion in Hungary and Latvia applied to residual 200+202, 201, 203: proportions in Hungary and Latvia applied to incidence estimate of 200-203 from Model 1°
	Czech Republic	1995 available from source
	Hungary <sup>a</sup>	WHO Mortality 1994–1996 and Model 1 <sup>c</sup>
		140-9 split into 140-145, 147 and 146, 148 and 149 using proportions in registries used in Model 1°
	Republic of	WHO Mortality 1993–1995 and Model 1°
	Moldova <sup>a</sup>	140-149 split into 140-145, 147 and 146, 148 and 149 using proportions in registries used in Model 1c
		182, 189, 193: proportions in Hungary and Latvia applied to residual
	D 1 19	200 + 202, 203: proportions in Hungary and Latvia applied to incidence estimate of 200,202, 203 from Model 1°
	Polanda	WHO Mortality 1993–1995 and Model 1° 140–149 split into 140–145, 147 and 146, 148 and 149 using proportions in registries used in Model 1°
		182, 189, 193: proportions in Hungary and Latvia applied to residual
		200 + 202, 203: proportions in Hungary and Latvia applied to incidence estimate of 200,202, 203 from Model 1°
	Romaniaa	WHO Mortality 1993–1995 and Model 1°
		140-149 split into 140-145, 147 and 146, 148 and 149 using proportions in registries used in Model 1c
		182, 189, 193: proportions in Hungary and Latvia applied to residual
		200 + 202, 203: proportions in Hungary and Latvia applied to incidence estimate of 200, 202, 203 from Model 1c
	Russian	WHO Mortality 1994–1996 and Model 1°
	Federation	140–149 split into 140–145, 147 and 146, 148 and 149 using proportions in registries used in Model 1 <sup>c</sup> 155, 157, 172, 182, 183, 186, 189, 191, 193: proportion in Hungary and Latvia applied to residual
		200 + 202, 201, 203: proportions in Hungary and Latvia applied to incidence estimate of 200–203 from Model 1 <sup>c</sup>
	Slovakia	1995 available from source
	Ukraine	WHO Mortality 1992, 1996–1997 and Model 1°
		140-149 split into 140-145, 147 and 146, 148 and 149 using proportions in registries used in Model 1 <sup>c</sup>
		155, 157, 172, 182, 183, 186, 189, 191, 193: proportion in Hungary and Latvia applied to residual
		200 + 202, 201, 203: proportions in Hungary and Latvia applied to incidence estimate of 200-203 from Model 1 <sup>c</sup>
Northern	Denmark	1995 available from source
Europe	Estonia	1994–1996 available from source
•	Finland	1995 available from source
	Iceland	1995 available from source
	Ireland	1995 available from source
	Latvia <sup>b</sup>	WHO Mortality 1995–1997 and Model 1°
	Lithuania <sup>b</sup>	140–149 split into 140–145, 147 and 146, 148 and 149 using proportions in registries used in Model 1° WHO Mortality 1994–1996 and Model 1°
	Littiuallia	140–149 split into 140–145, 147 and 146, 148 and 149 using proportions in registries used in Model 1 <sup>c</sup>
		155: proportion in Hungary and Latvia applied to residual in Lithuania
	Norway	1995 available from source
	Sweden	1995 available from source
	United Kingdom	1995 estimate from EUCAN <sup>d</sup>
Southern	Albania <sup>b</sup>	1990 estimated rates applied to 1995 population
Europe	Bosnia and	1995 Slovenia incidence rates applied to 1995 population
Zurope	Herzegovina	1990 blovelina instalante rates appared to 1990 population
	Croatia	CI5 Vol. VII rates applied to 1995 population
	Greece	1995 estimate from EUCAN <sup>d</sup>
	Italy	1995 estimate from EUCAN <sup>d</sup>
	Malta	1995 available from source
	Portugal	1995 estimate from EUCAN <sup>d</sup>
	Slovenia	1995 available from source 1995 estimate from EUCAN <sup>d</sup>
	Spain FYROM	1990 estimated rates applied to 1995 population
	(Macedonia) <sup>b</sup>	1770 commerce rates applied to 1770 population
	Yugoslavia	1995 Slovenia incidence rates applied to population
Wast	A	1005timata farm FIJCANI
Western Europe	Austria Belgium	1995 estimate from EUCAN <sup>d</sup> 1995 estimate from EUCAN <sup>d</sup>
Larope	Deigium	(continued on next page)

(continued on next page)

Table 2 (continued)

UN Area	Country	Incidence: latest year available/method of estimation
	France	1995 estimate from EUCAN <sup>d</sup>
	Germany	1995 estimate from EUCAN <sup>d</sup>
	Luxembourg	1995 estimate from EUCAN <sup>d</sup>
	The Netherlands	1994 available from source
	Switzerland	WHO Mortality 1992–1994 and Model 2 <sup>e</sup>
		140–149 split into 140–145, 147 and 146, 148 and 149 using proportions in registries used in Model 2

UN, United Nations; WHO, World Health Organization; EUCAN, ?; ENCR, European Network of Cancer Registries; CI5 Vol. VII, Cancer Incidence in Five Continents, Volume VII.

- <sup>a</sup> Due to relatively few deaths associated with testes cancer, thyroid cancer and Hodgkin disease, the age and sex-specific average mortality data used in the estimation of incidence for these countries was smoothed using the combined mortality data of Bulgaria, Hungary and Poland.
- <sup>b</sup> Due to relatively small population sizes, the age and sex-specific average mortality data used in the estimation of incidence for these countries was smoothed using the combined age-specific mortality rates of Bulgaria, Hungary and Poland.
- <sup>c</sup> Poisson model of the log of incidence offset for the log of mortality adjusted for terms for sex and for age (polynomials of up to order 5) using site-specific aggregated incidence and mortality data from the following cancer registries: Czech Republic (1993–1997), Poland, Cracow City (1990–1992), Poland, Kielce (1992–1996), Poland, Lower Silesia (1990–1992), Poland, Opole (1990–1992), Poland, Warsaw City (1990–1992), Slovakia (1991–1995) and Belarus (1990–1992; for sites for which data available).
- <sup>d</sup> Poisson model of the log of incidence offset for the log of mortality adjusted for terms for sex and for age (polynomials of up to order 5) using site-specific aggregated incidence and mortality data from selected registries. See the "EUCAN Database" option on the Internet version of EUCAN, available on the ENCR website (http://www-dep.iarc.fr/eucan/eucan.htm).
- <sup>e</sup> Poisson model of the log of incidence offset for the log of mortality adjusted for terms for sex and for age (polynomials of up to order 5) using site-specific aggregated incidence and mortality data from the following cancer registries in Switzerland: Basel (1992–1996), Geneva (1992–1996), Grisons (1990–1992), Neuchatel (1990–1992), St.Gallen (1990–1992), Appenzell (1990–1992), Vaud (1990–1992), Zurich (1990–1992).

aggregated incidence and mortality based on eight Swiss regional cancer registries (see Table 2 for details).

The application of this method resulted in incidence having the same lack of detail as mortality in countries which coded deaths using the ICD-9 'Special Tabulation Lists'. Essentially the same procedures used in estimating missing site-specific mortality were employed to derive corresponding estimates of the number of new cases (see Table 2). Thus, for sites where incidence data were not available, appropriate cancer-specific incidence proportions were applied to the residual number of cases of 'all other cancers' to obtain the appropriate subdivision. Grouped sites were split according to the incidence proportions in the same manner. As no mortality data were available in Bosnia and Herzegovina and in Yugoslavia, incidence was estimated by applying the 1995 cancer incidence rates of Slovenia to their respective 1995 population data. In Croatia, incidence was estimated using the rates in Cancer Incidence in Five Continents Volume VII [4] applied to the 1995 population data. In a like manner, the number of new cases in Albania and FYROM (Former Yugoslav Republic of Macedonia) were calculated by applying the respective 1995 populations to rates estimated previously for 1990 [6]. It is for these countries—for which there have been large population migrations as a result of war or the local situation—that one must adopt particular caution when interpreting estimates of incidence in 1995.

For the remaining countries, Austria, Belgium, France, Germany, Greece, Italy, Luxembourg, Portugal, Spain and the UK, incidence estimates for 1995

were taken directly from the EUCAN software package [7], which gives statistical and graphical information on cancer incidence and mortality for the 15 Member States of the European Union. The methodology used to compile these estimates is consistent with the modelling approach described above. Details of the data sources and methodology are available in the 'Help' section of the EUCAN CD-ROM, or via the Internet version of EUCAN available on the ENCR website (http://www.dep.iarc.fr/eucan/eucan.htm).

The ratio of mortality to incidence  $(M/I \text{ or } 1/\{I/M\})$  is an indicator of the completeness of the cancer registry data [8]. To ensure that the datasets used in the analysis were of the highest possible quality, a systematic inspection of the sex-specific M/I ratios for each primary site was made. Registries were excluded from the model datasets if the M/I ratios were considered unreasonably high or low for the primary site in question.

Within Europe, there are large variations in the accuracy of death certificates related to cancer of the uterus, with many deaths recorded as 'uterus cancer, not otherwise specified' (ICD-9 179) rather than to the subsites of uterine cervix (ICD-9 180) and uterine corpus (182). In line with earlier studies [2,3], an adjustment to allow for this misclassification was made. The number of deaths coded as 'unspecified' were reallocated to either uterine cervix or uterine corpus cancer according to estimates of the age-specific proportions specified as 180 and 182 in each country. For consistency, incident cases were also reallocated in the same way from the rubric 179 to 180 and 182.

### 3. Results

Figs 2-47 display the sex-specific incidence and mortality rates (age-standardised using the European standard population) sorted by country within European area for all cancers combined, and for the 25 most common primary sites. The annual number of cancer cases and deaths in 1995 in Europe, the European Union, and the four European regions are presented in Tables 3 and 4, respectively, by sex and primary site. The figures are also expressed as a percentage of the total estimated number of cancer cases/deaths. Equivalent tables by sex, plus charts of the age-standardised incidence and mortality rates, the cumulative risk of incidence and mortality, and colour maps of Europe depicting the variations in age-standardised rates, for the primary sites studied, can be found at the ENCR website (http://www.dep.iarc.fr/encr/europe95.htm).

There were just over 2.6 million new cases of cancer (excluding non-melanoma skin) in Europe in 1995, 53% (1.4 million) occurring in males and 47% (1.2 million) in females. The number of deaths exceeded 1.6 million, of which 56% (0.9 million) were in men and 44% (0.7 million) in women. There were over one million new cases of just three cancers—lung (377 000), colon and rectum (334 000), and female breast (321 000), representing approximately 40% of the total number of incident cases in Europe.

The most common primary sites in men were lung (22% of all cancer cases), colon and rectum (12%), prostate (11%), stomach (9%) and bladder (7%). In females, the principal cancers were breast (26%), colon and rectum (14%), stomach (7%), lung (6%), and cervix uteri and corpus uteri (6% each).

The number of deaths reflected the cancer prognosis; by far the most common cause of death was from lung cancer (330 000)—approximately one-fifth of the total number of cancer deaths in Europe in 1995 and, due to poor prognosis, almost matching the number of incident cases. Deaths from cancers of the colon and rectum (189 000) ranked second, followed by deaths from stomach cancer (152 000), which due to poorer survival ranked higher than breast cancer (124 000).

Lung cancer continued to be the most common cause of death from cancer in men (29%) followed by stomach and colorectal cancers (10% each) and prostate cancer (8%). Breast cancer was the leading cause of death in women (17%), followed by colorectal cancer (14%) and lung and stomach cancers (9% each).

# 3.1. All cancers excluding non-melanoma skin cancer (ICD-9 140–208 except 173)

After adjusting for differing population age structures, overall incidence rates in men were highest in the Western European countries (420.9 per 100000), with

only Austria having a rate under 400 (Fig. 2). Eastern European men had the second highest rates of cancer (414.2), although there was a great deal of variation by country—extremely high rates were observed in Hungary (566.6) and in the Czech Republic (480.5) contrasting with much lower rates found in Romania and Bulgaria (313.0 and 321.1, respectively). In Southern Europe, rates also varied considerably between countries—high rates in Italian men (438.0) contrasted with rates for men in FYROM (281.5)—the lowest in Europe. The lowest all-cancer rate by area was observed in the Northern European countries with fairly low rates observed in Sweden (356.6) and the UK (377.8).

In females, and in contrast to men, the highest rates of cancer were observed in Northern Europe (315.9) and were particularly high in Denmark (396.2) and the other Nordic countries, with the exception of Finland (Fig. 2). The second highest rates were seen in Western Europe (286.8), where there was less variability between countries. The highest and lowest rates were observed in the Netherlands (331.0) and France (266.6), respectively. Rates were third highest in Southern European women (257.5), although the rates did not exceed 300 per 100 000 in any country. FYROM had the lowest agestandardised rates (190.4), while the rates in both Malta and Italy were high relative to the region, but not notably so when compared with Europe as a whole. The rates of cancer in Eastern European women were lower than in the other three areas, although as with the rates observed for men, rates in women were very high in Hungary (357.2) and in the Czech Republic (332.6). The incidence rate of female cancers in Belarus (207.2) was particularly low in comparison with other Eastern European countries.

The rank order of incidence rates by country reflect the frequency of the most common cancers, while death rates also reflect their fatality. For instance, the high all-cancer mortality rates observed for a number of Eastern European countries reflects both the large burden of lung cancer in these countries (due to current and previous smoking patterns) and the poor survival of the lung cancer cases (Figs. 2 and 3). Five countries in the region had mortality rates in men exceeding 300, and Hungary had a death rate (392.1) almost double that of neighbouring countries, Bulgaria (211.9) and Romania (210.7).

## 3.2. Oral Cavity (ICD 140–145)

This group include neoplasms of the lip, tongue, major salivary glands, gum, floor of mouth and other unspecified parts of the mouth. There were just under 50 000 new cases of oral cavity cancer in Europe in 1995, approximately 2% of all cancer cases. Differences in lifestyle with respect to the predominant risk factors for several of these neoplasms, namely cigarette and

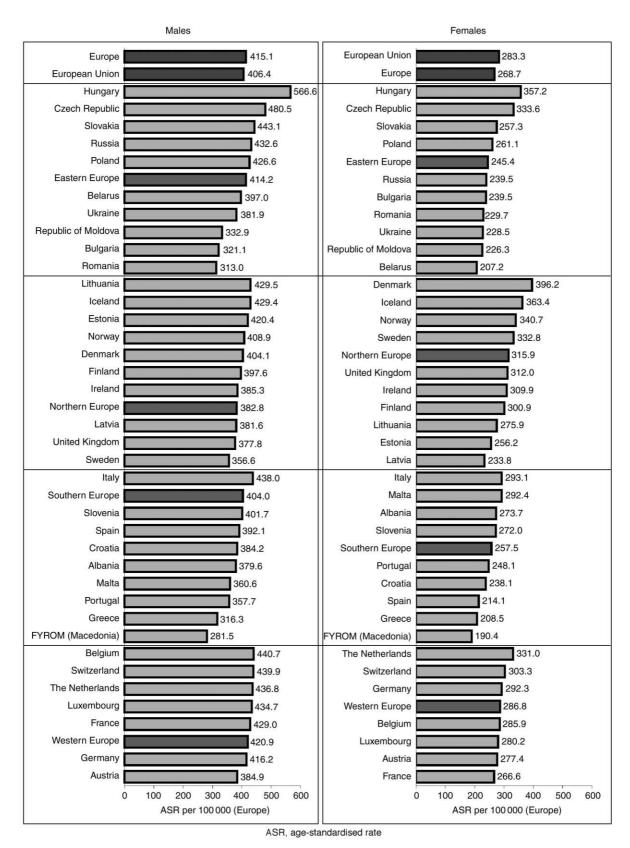


Fig. 2. Age-standardised incidence rates by area and country in Europe 1995: all cancer sites but skin.

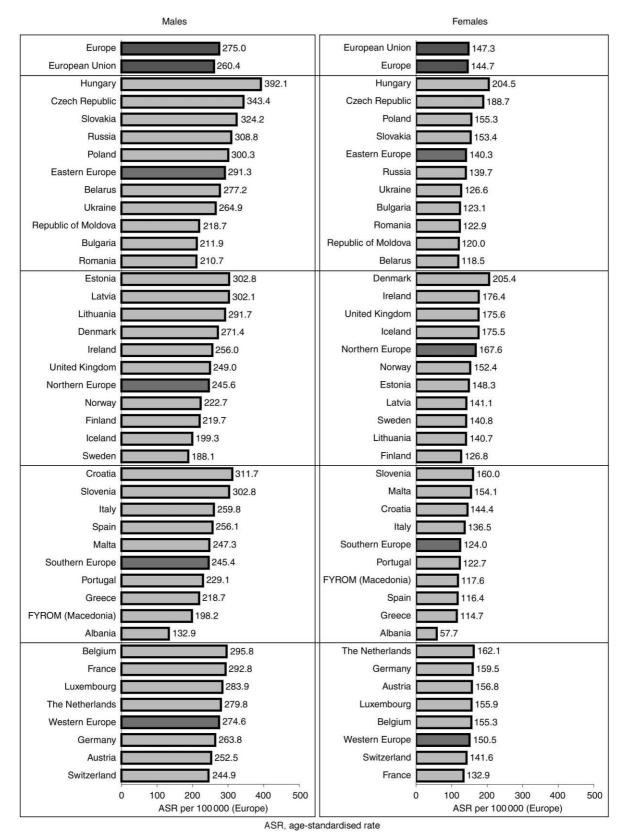


Fig. 3. Age-standardised mortality rates by area and country in Europe 1995: all sites but skin.

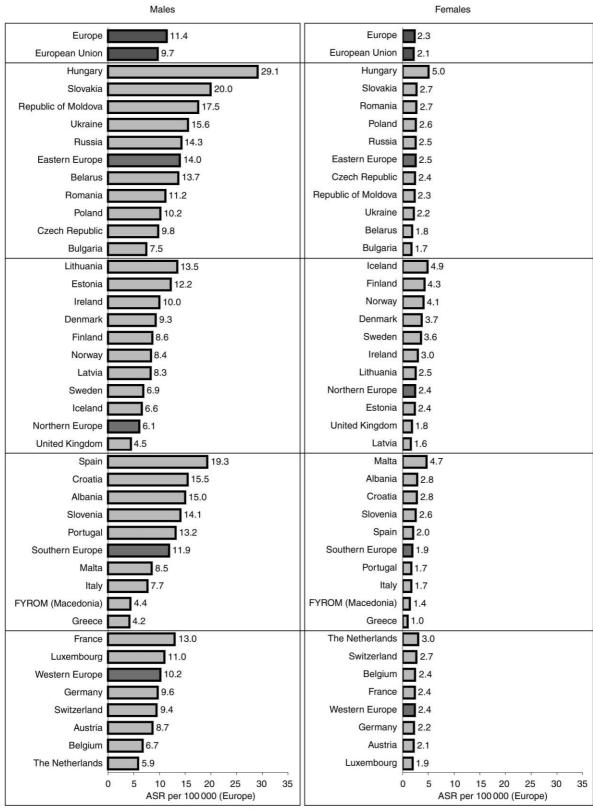


Fig. 4. Age-standardised incidence rates by area and country in Europe 1995: cancer of the oral cavity.

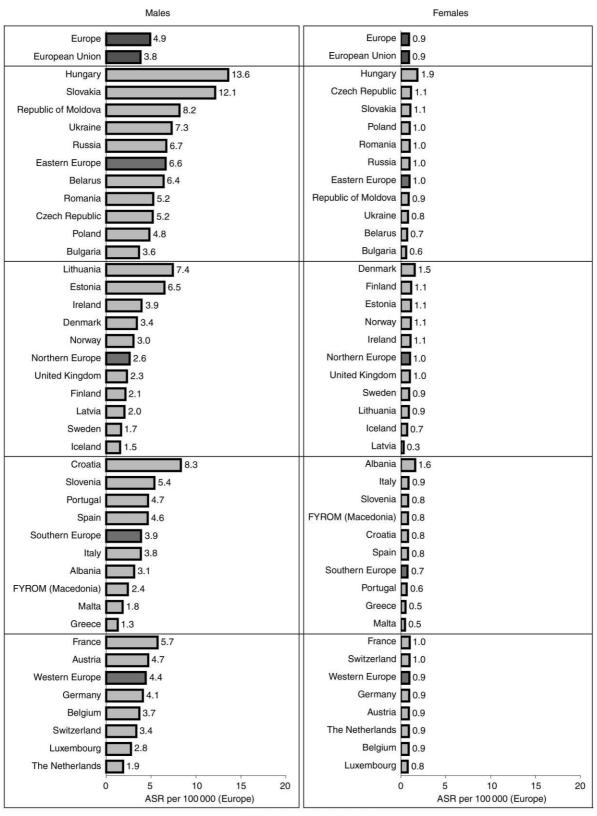


Fig. 5. Age-standardised mortality rates by area and country in Europe 1995: cancer of the oral cavity.

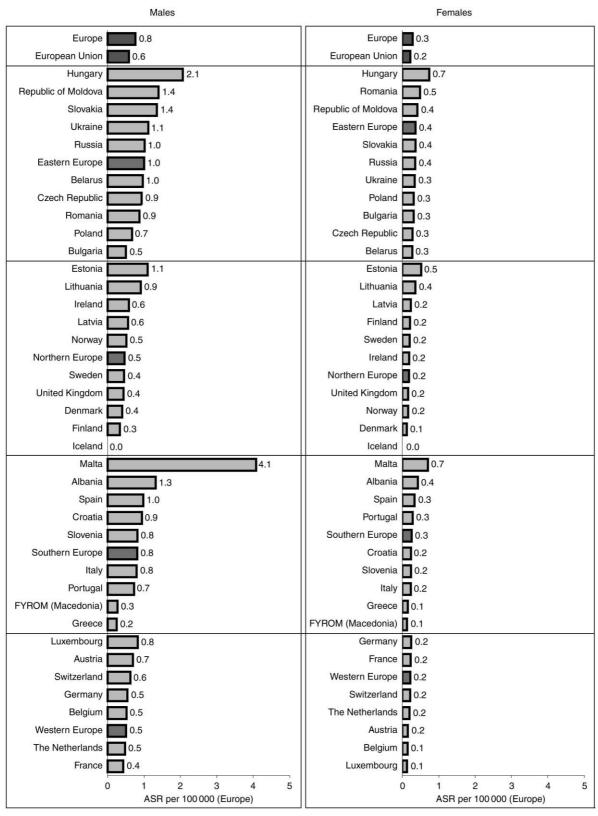


Fig. 6. Age-standardised incidence rates by area and country in Europe 1995: nasopharyngeal cancer.

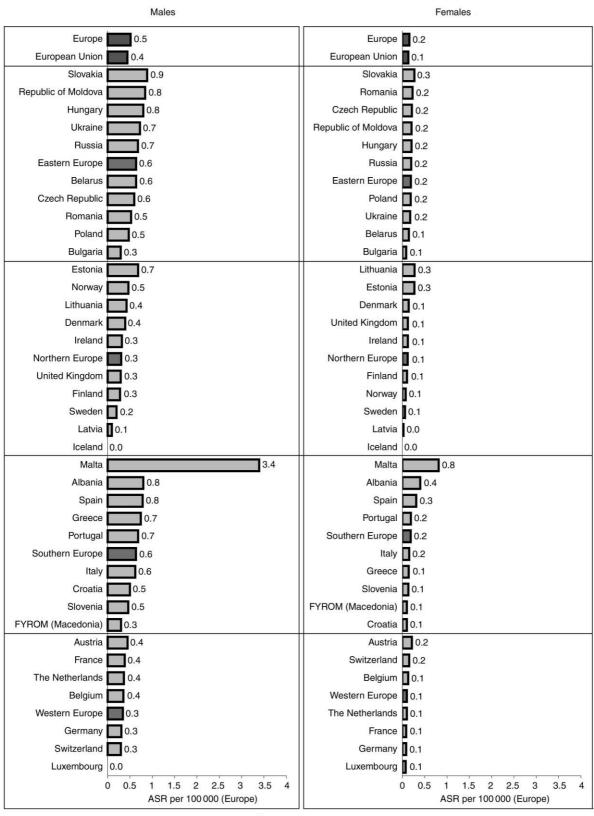


Fig. 7. Age-standardised mortality rates by area and country in Europe 1995: nasopharyngeal cancer.

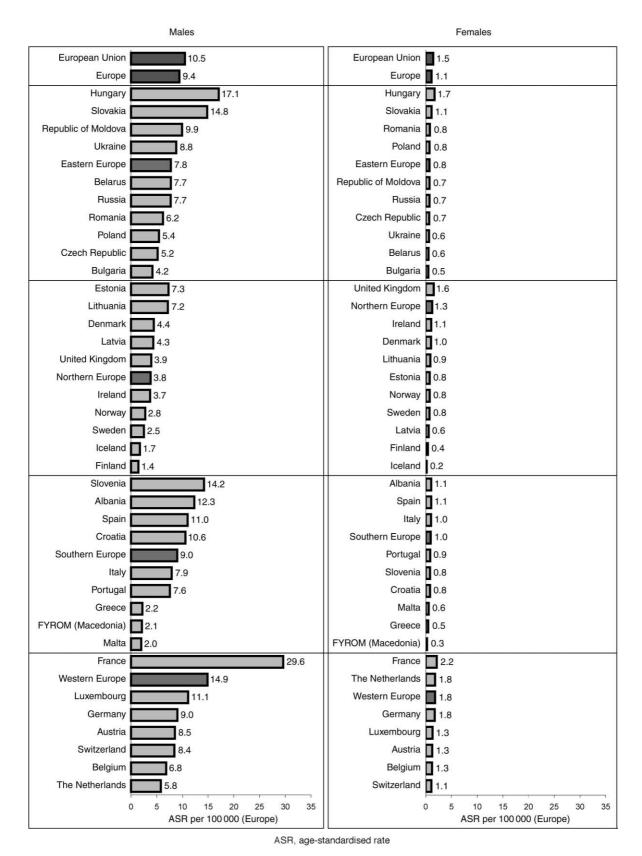


Fig. 8. Age-standardised incidence rates by area and country in Europe 1995: other pharyngeal cancer.

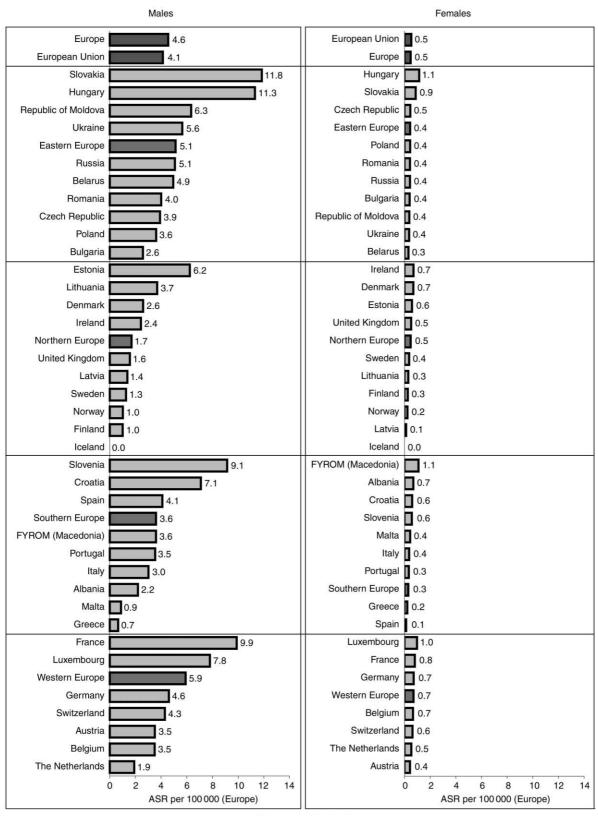


Fig. 9. Age-standardised mortality rates by area and country in Europe 1995: other pharyngeal cancer.

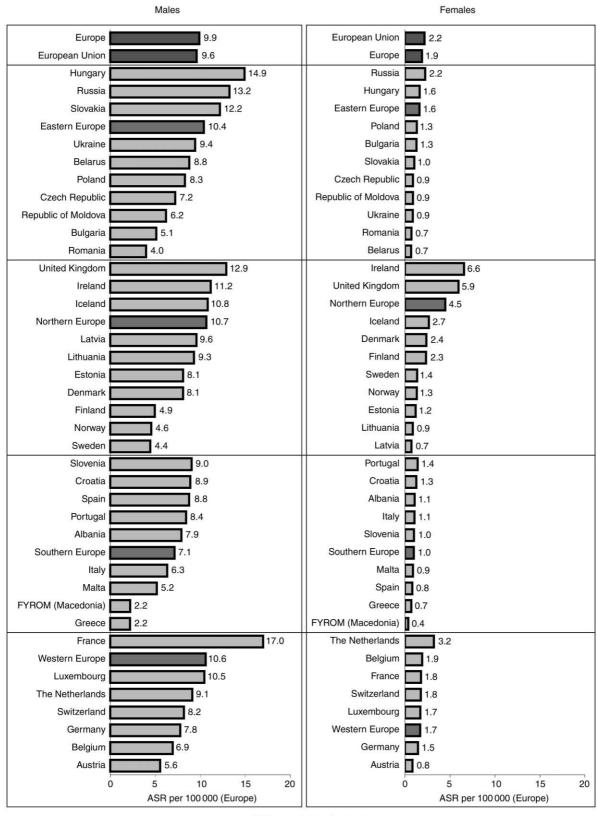


Fig. 10. Age-standardised incidence rates by area and country in Europe 1995: oesophageal cancer.

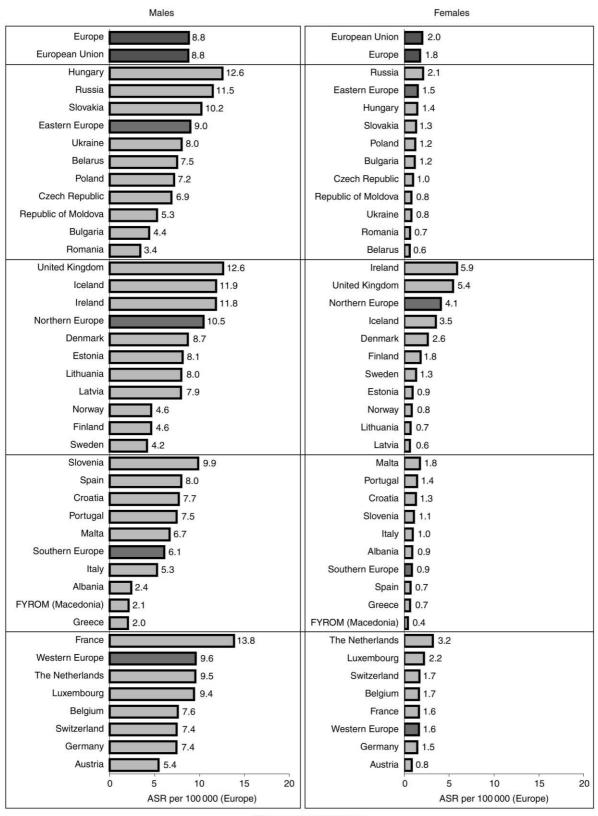


Fig. 11. Age-standardised mortality rates by area and country in Europe 1995: oesophageal cancer.

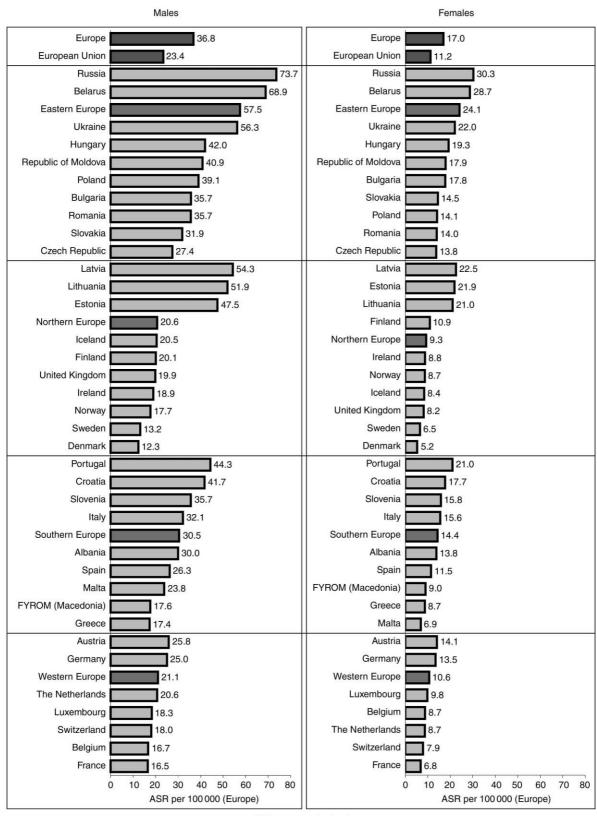


Fig. 12. Age-standardised incidence rates by area and country in Europe 1995: stomach cancer.

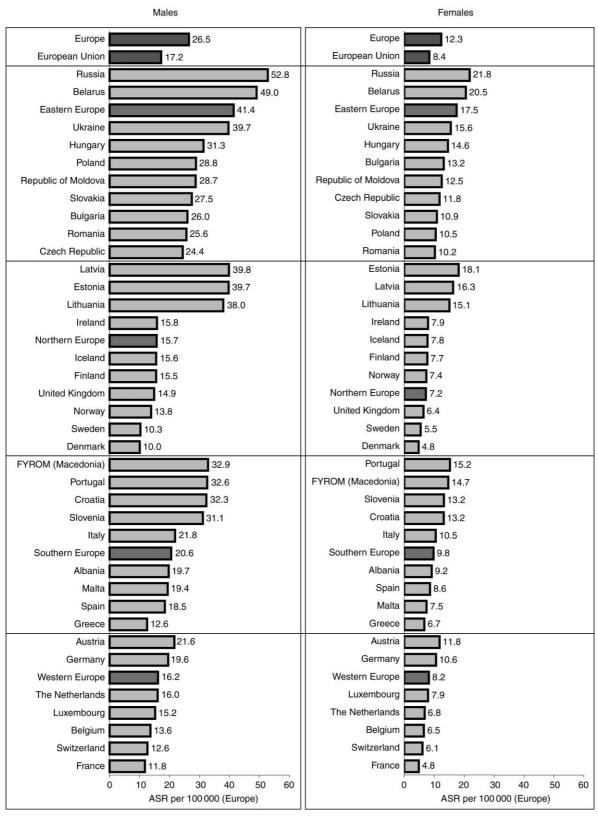


Fig. 13. Age-standardised mortality rates by area and country in Europe 1995: stomach cancer.

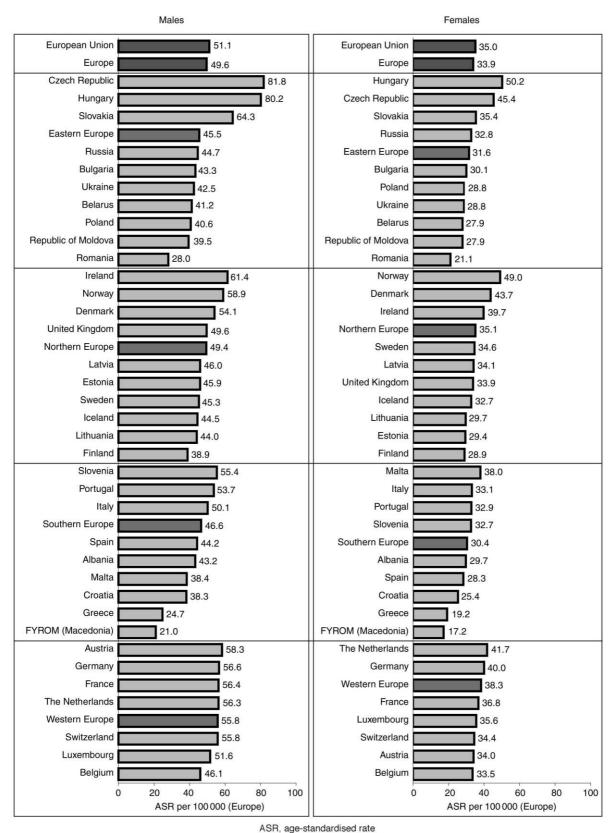


Fig. 14. Age-standardised incidence rates by area and country in Europe 1995: colorectal cancer.

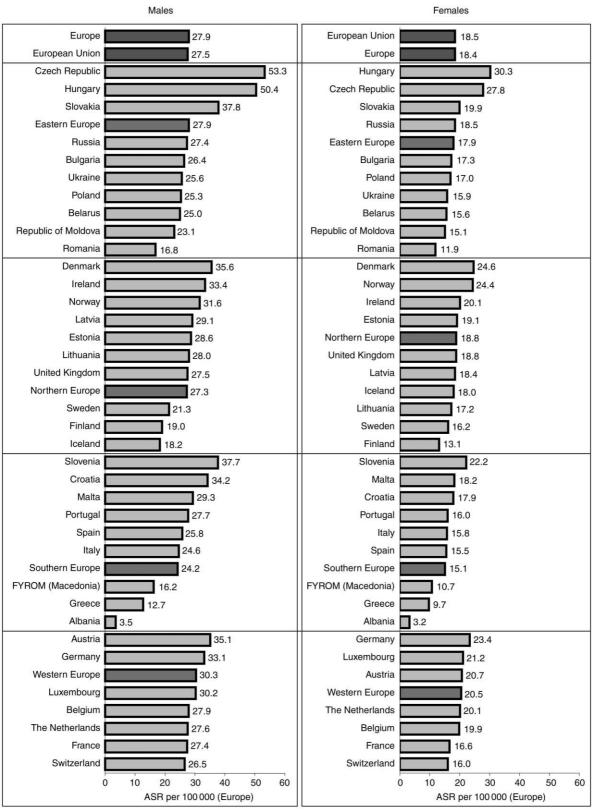


Fig. 15. Age-standardised mortality rates by area and country in Europe 1995: colorectal cancer.

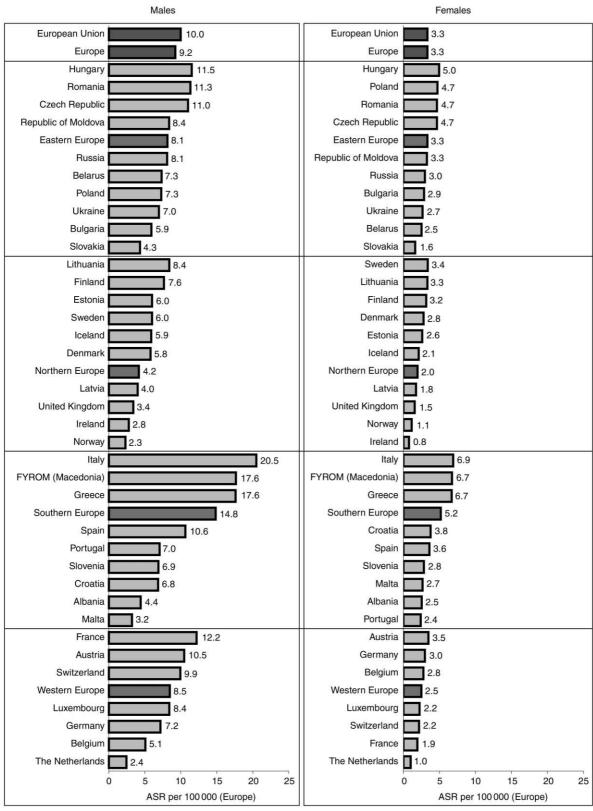


Fig. 16. Age-standardised incidence rates by area and country in Europe 1995: cancer of the liver.

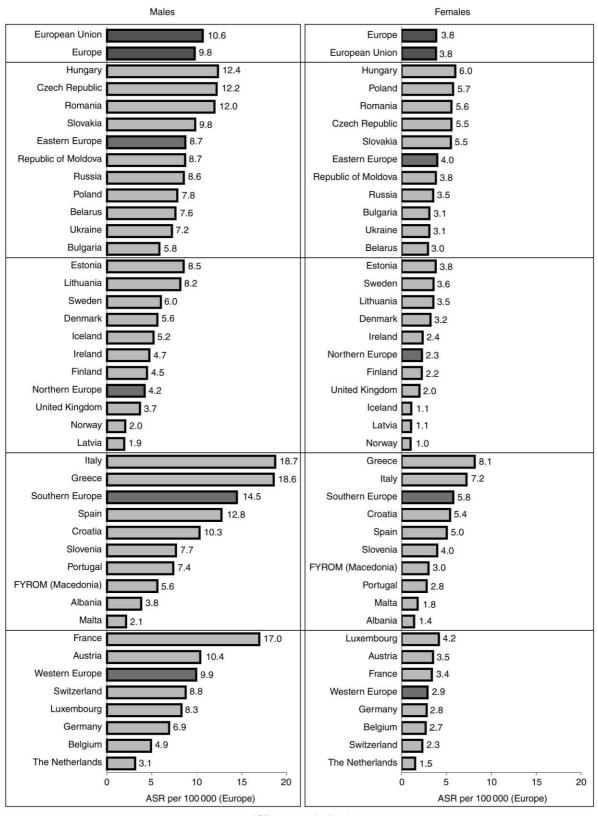


Fig. 17. Age-standardised mortality rates by area and country in Europe 1995: cancer of the liver.

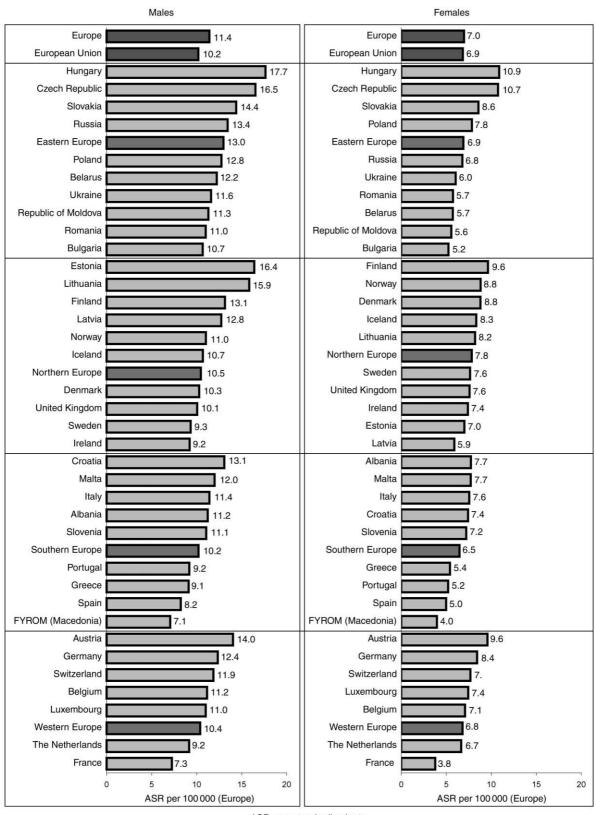


Fig. 18. Age-standardised incidence rates by area and country in Europe 1995: pancreatic cancer.

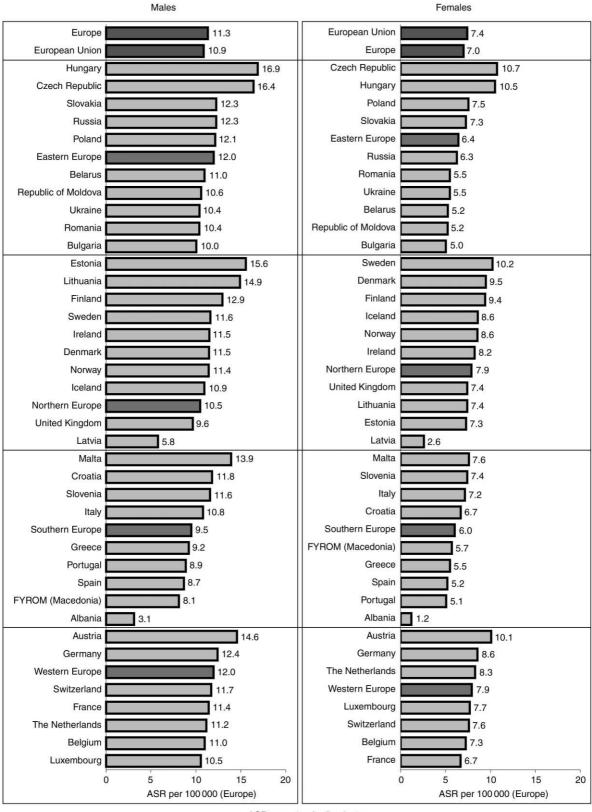


Fig. 19. Age-standardised mortality rates by area and country in Europe 1995: pancreatic cancer.

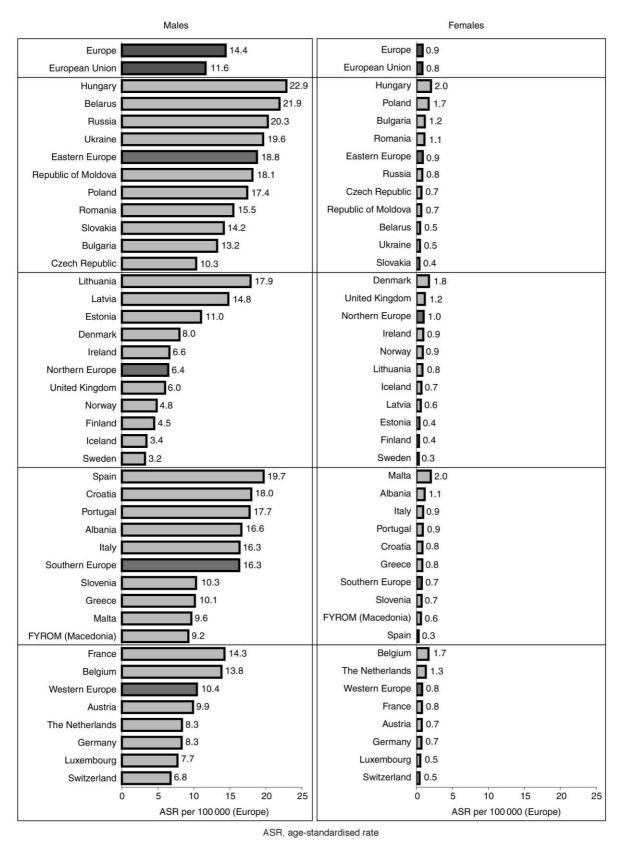


Fig. 20. Age-standardised incidence rates by area and country in Europe 1995: laryngeal cancer.

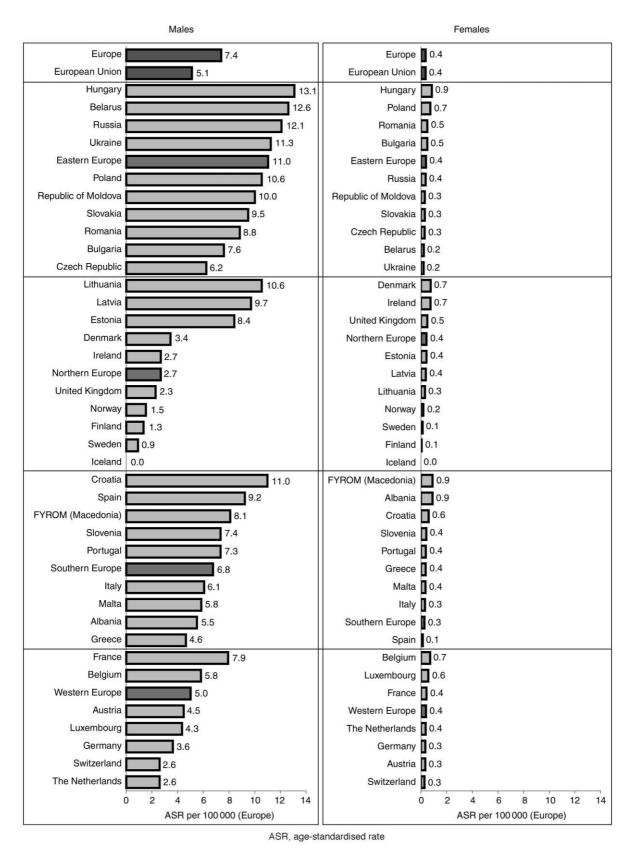


Fig. 21. Age-standardised mortality rates by area and country in Europe 1995: laryngeal cancer.

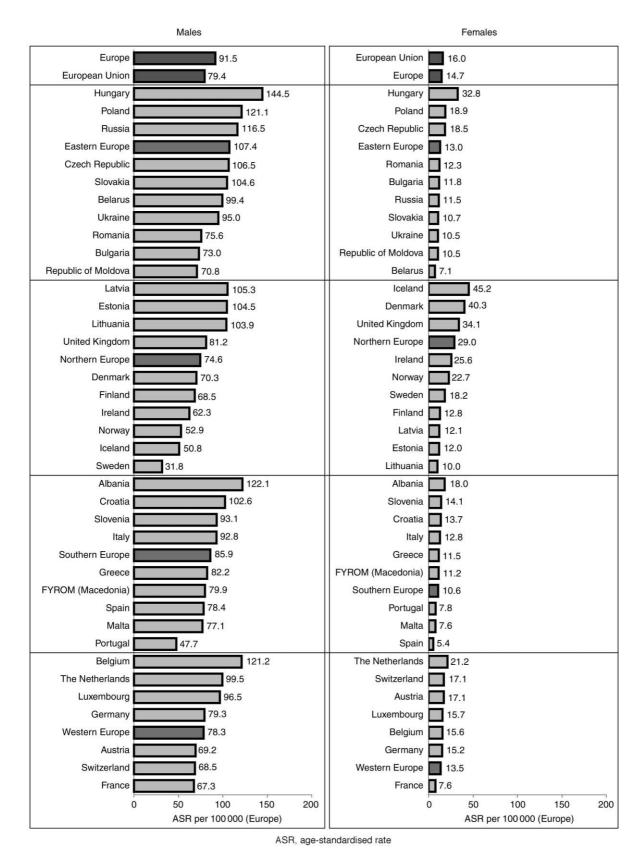


Fig. 22. Age-standardised incidence rates by area and country in Europe 1995: cancer of the lung.

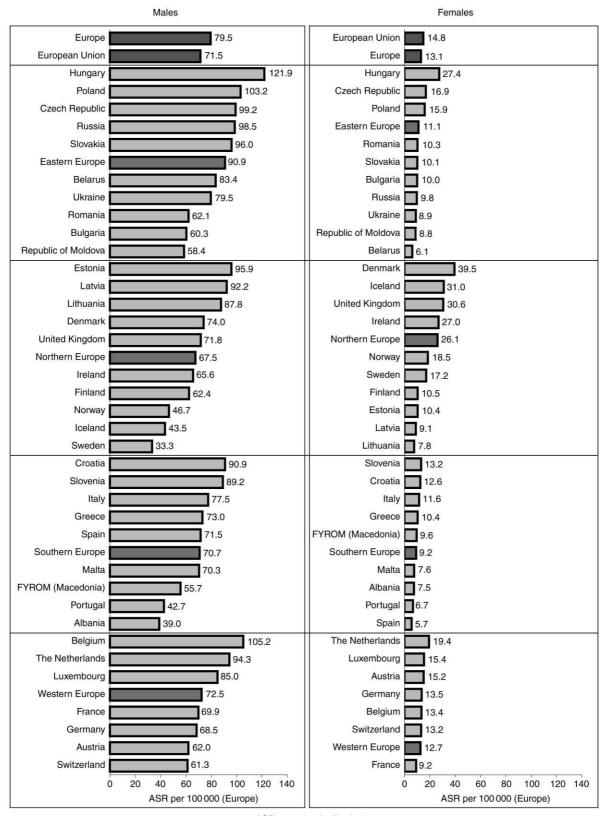


Fig. 23. Age-standardised mortality rates by area and country in Europe 1995: cancer of the lung.

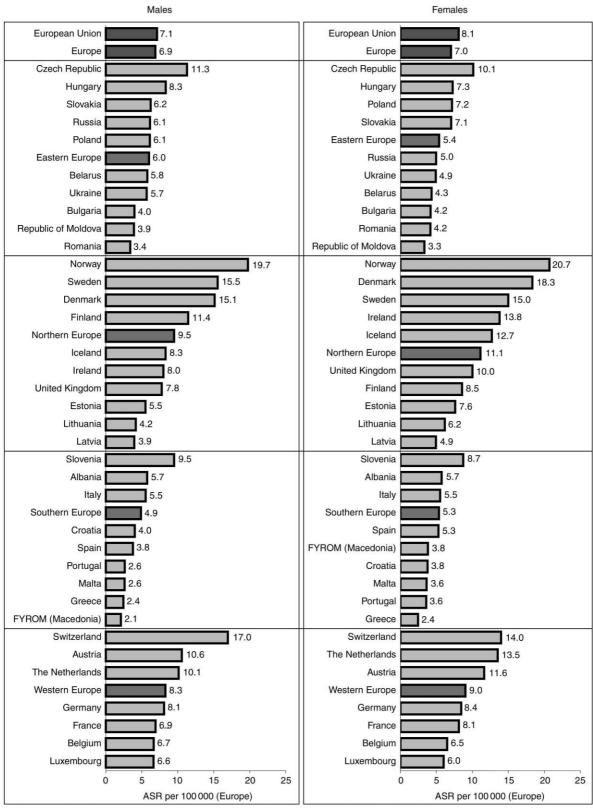


Fig. 24. Age-standardised incidence rates by area and country in Europe 1995: melanoma of the skin.

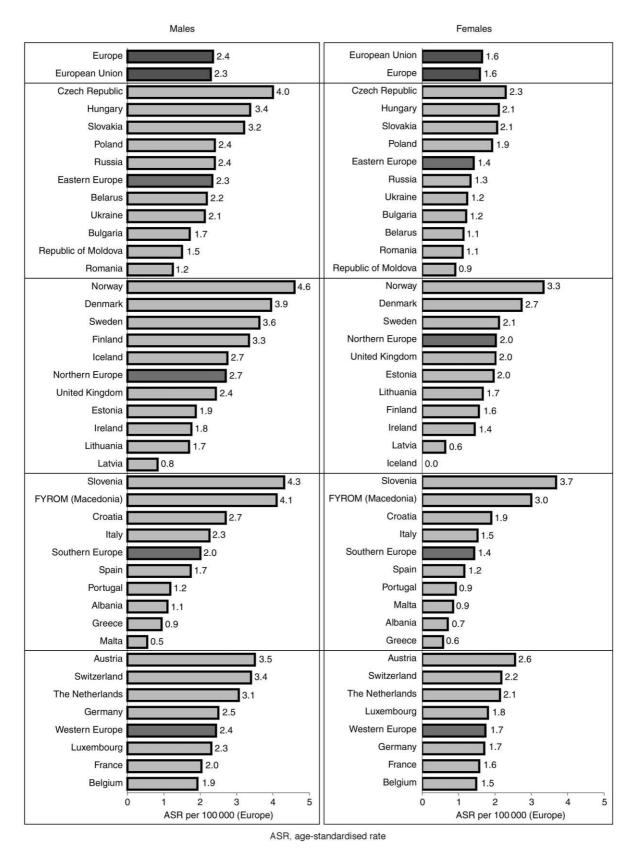


Fig. 25. Age-standardised mortality rates by area and country in Europe 1995: melanoma of the skin.

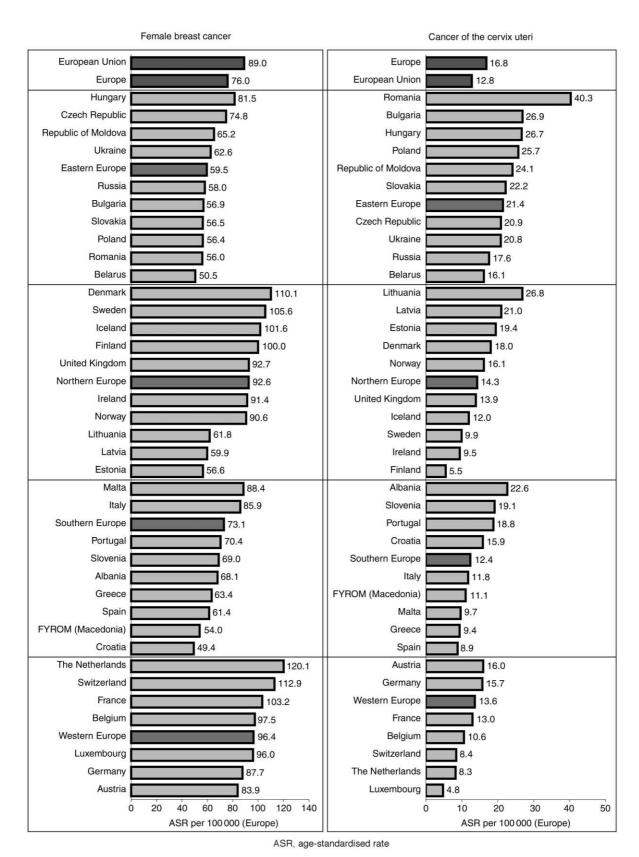


Fig. 26. Age-standardised incidence rates by area and country in Europe 1995.

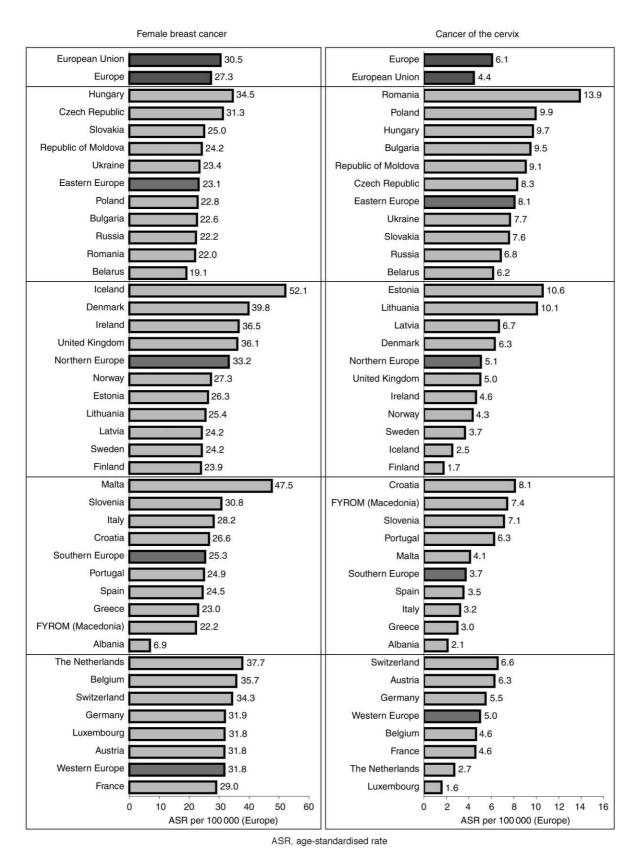


Fig. 27. Age-standardised mortality rates by area and country in Europe 1995.

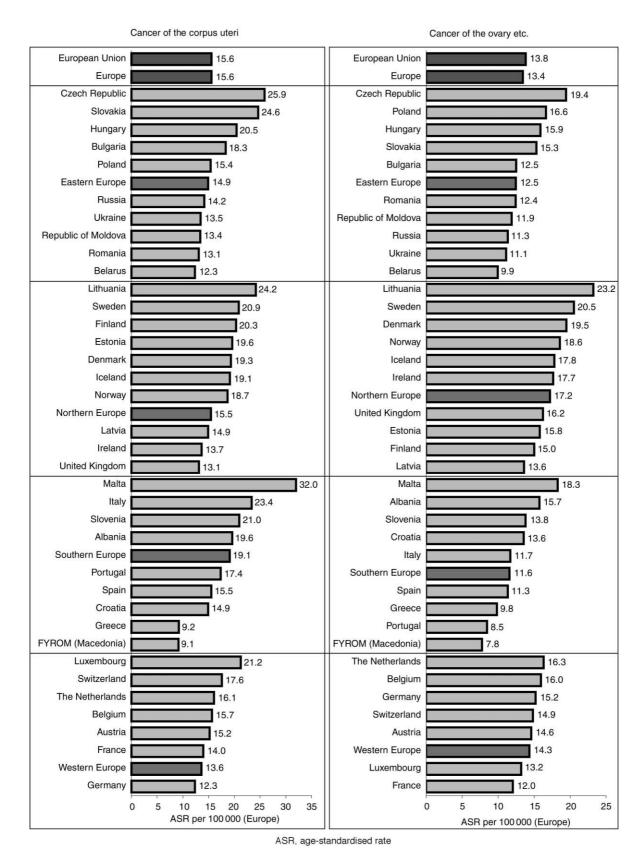


Fig. 28. Age-standardised incidence rates by area and country in Europe 1995.

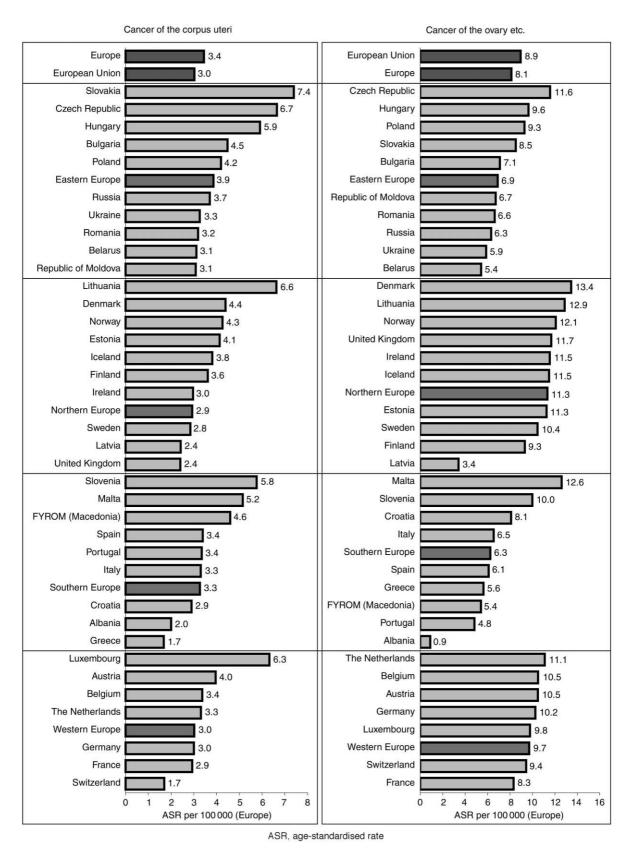


Fig. 29. Age-standardised mortality rates by area and country in Europe 1995.

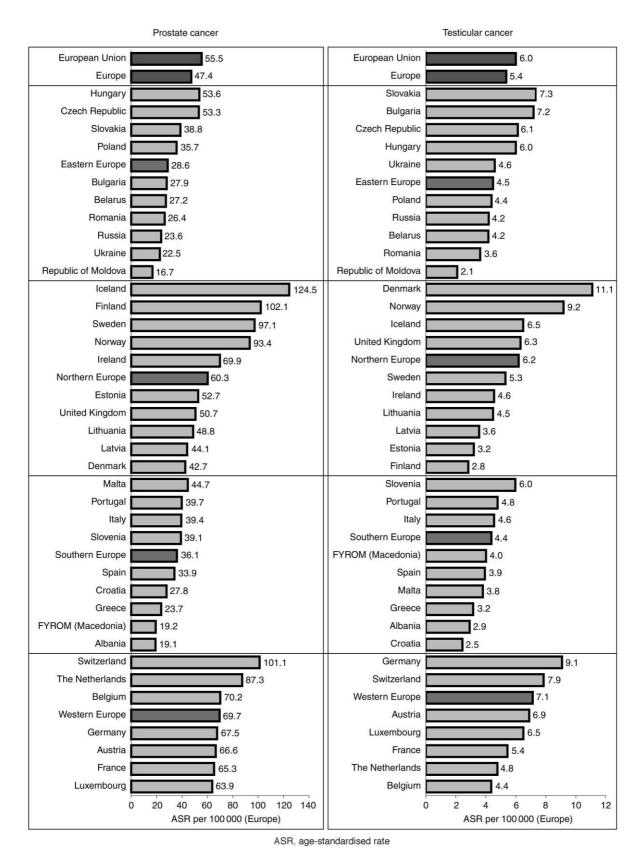


Fig. 30. Age-standardised incidence rates by area and country in Europe 1995.

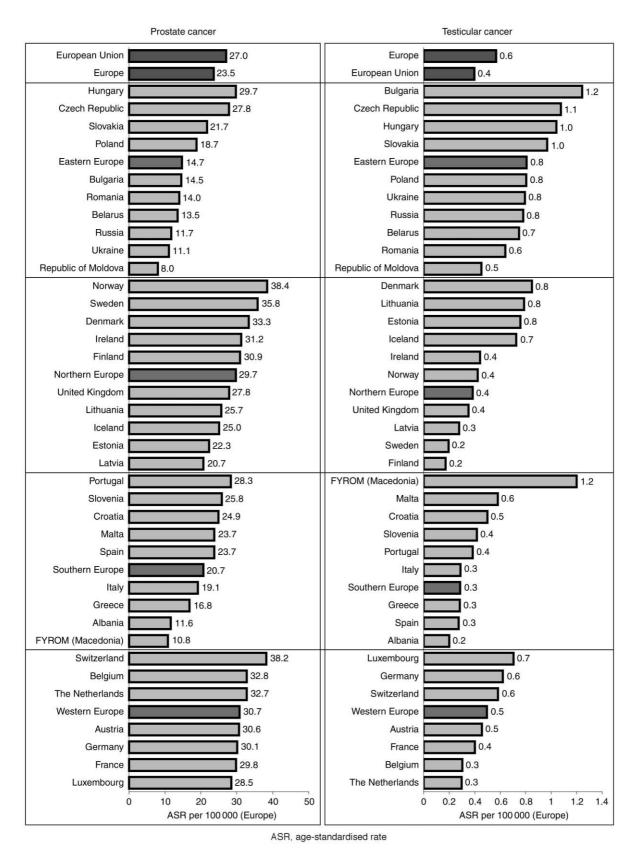


Fig. 31. Age-standardised mortality rates by area and country in Europe 1995.

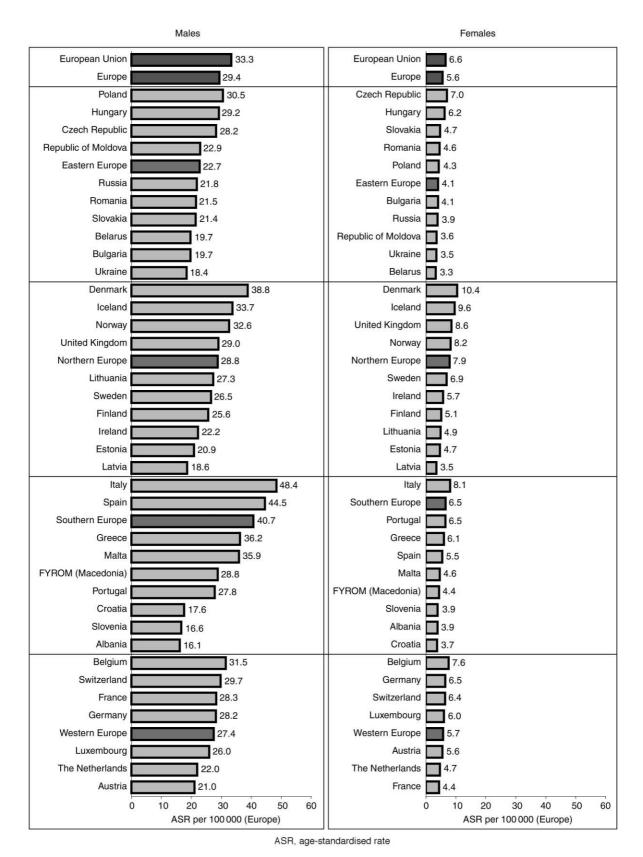


Fig. 32. Age-standardised incidence rates by area and country in Europe 1995: bladder cancer.

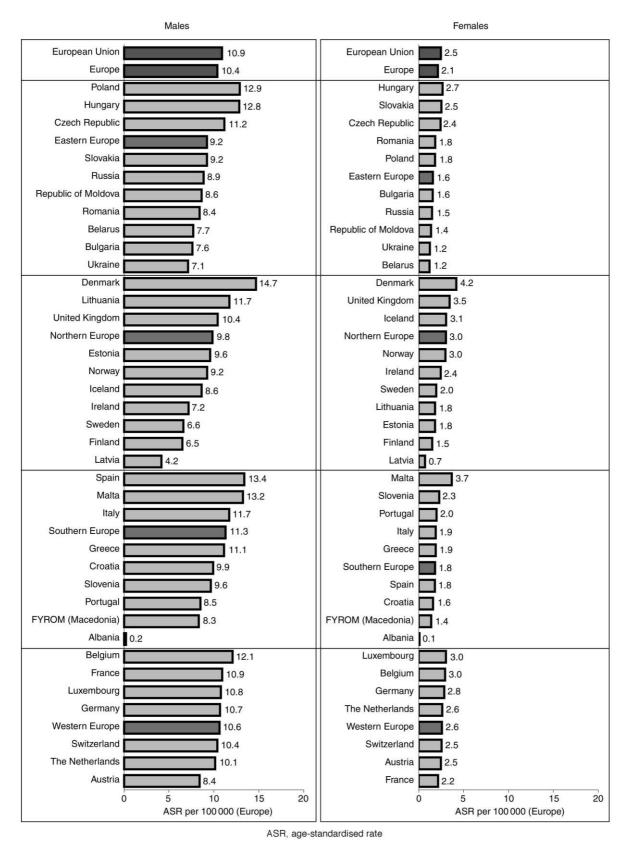


Fig. 33. Age-standardised mortality rates by area and country in Europe 1995: bladder cancer.

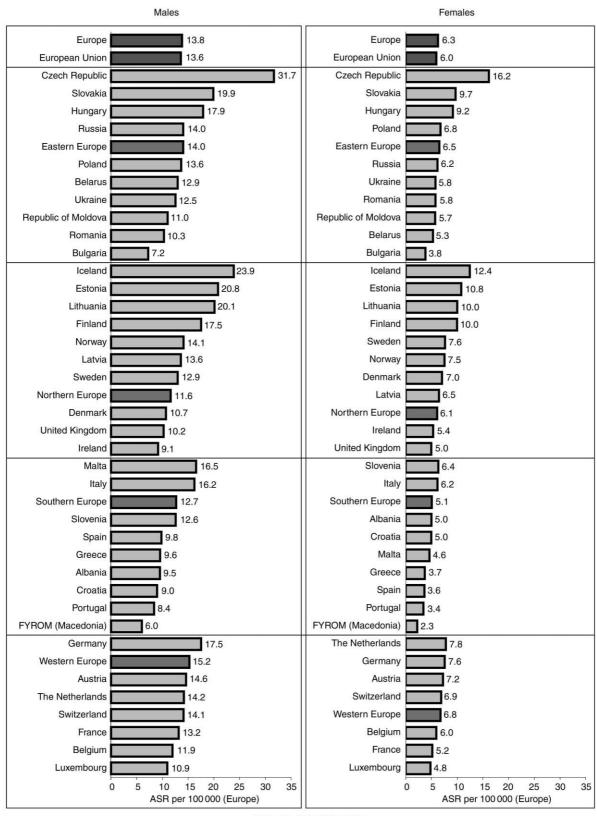


Fig. 34. Age-standardised incidence rates by area and country in Europe 1995: cancer of the kidney, etc.

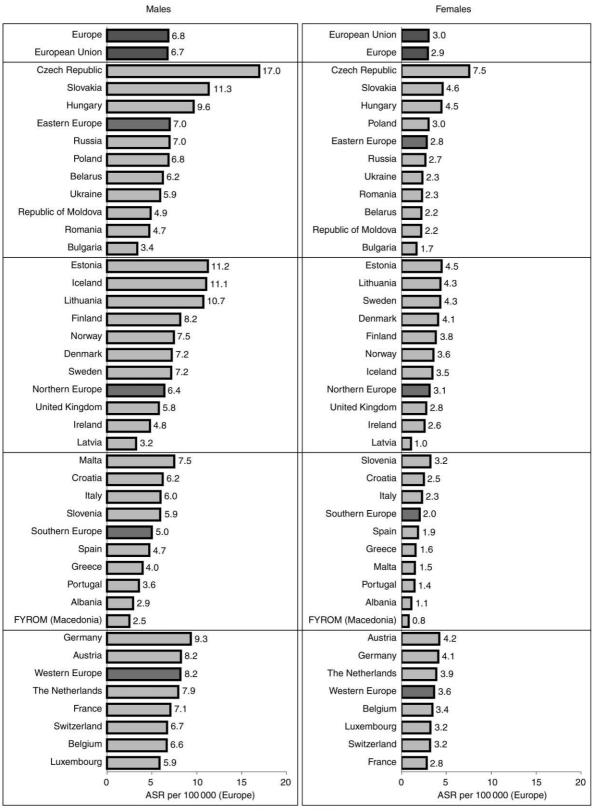
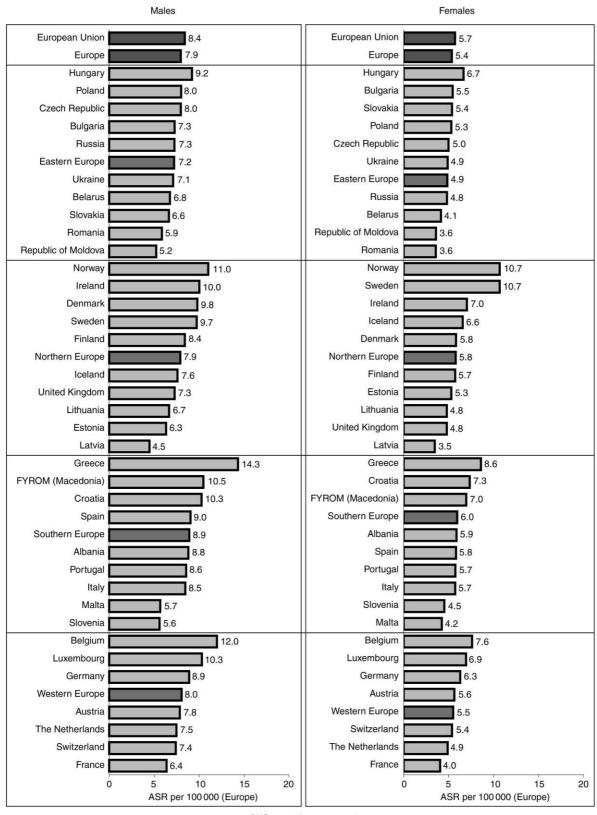
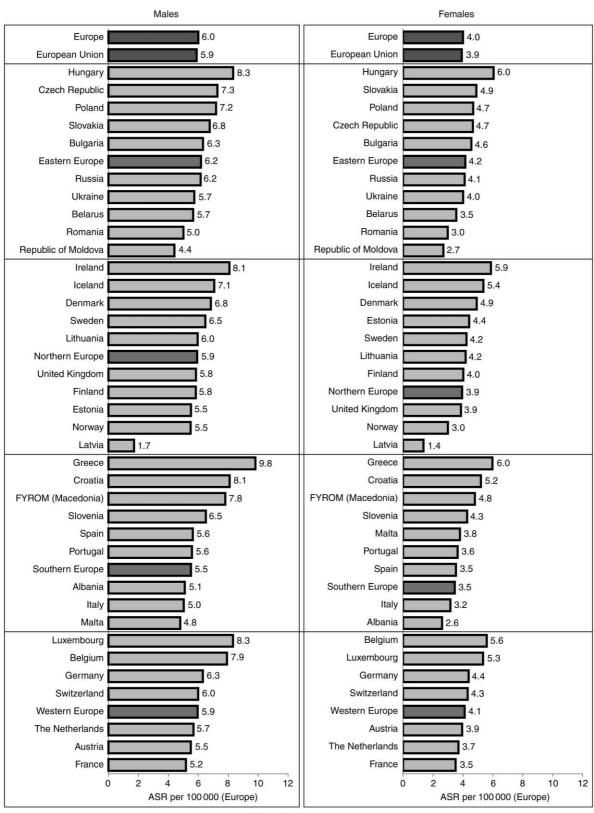


Fig. 35. Age-standardised mortality rates by area and country in Europe 1995: cancer of the kidney, etc.



CNS, central nervous system ASR, age-standardised rate

Fig. 36. Age-standardised incidence rates by area and country in Europe 1995: cancer of the brain and CNS.



CNS, central nervous system ASR, age-standardised rate

Fig. 37. Age-standardised mortality rates by area and country in Europe 1995: cancer of the brain and CNS.

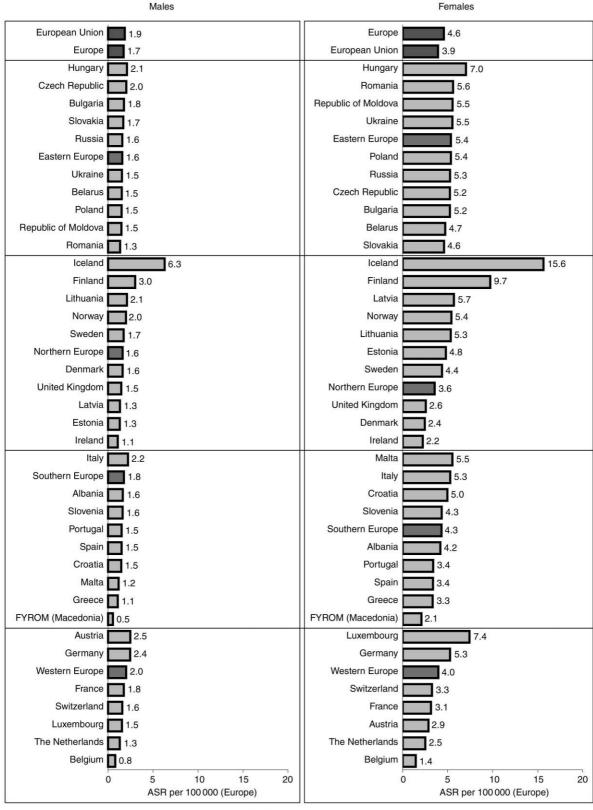


Fig. 38. Age-standardised incidence rates by area and country in Europe 1995: thyroid cancer.

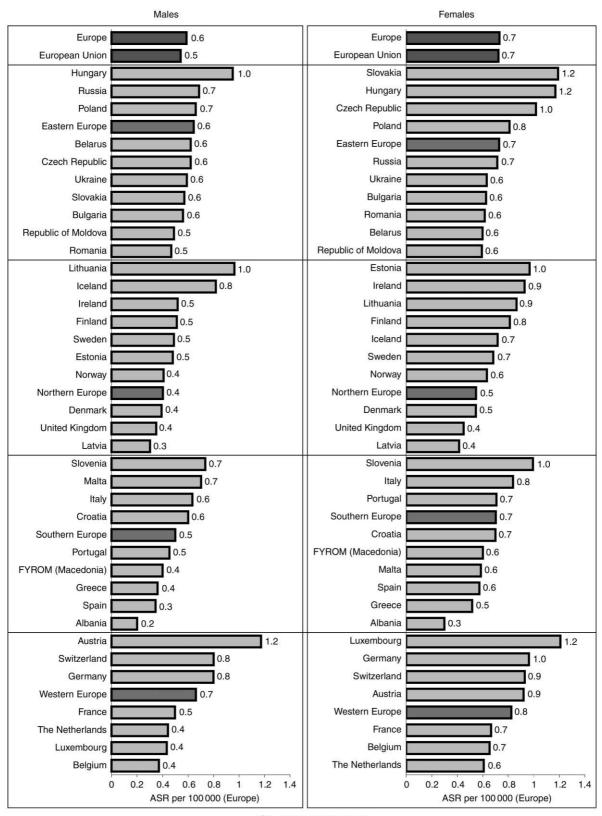


Fig. 39. Age-standardised mortality rates by area and country in Europe 1995: thyroid cancer.

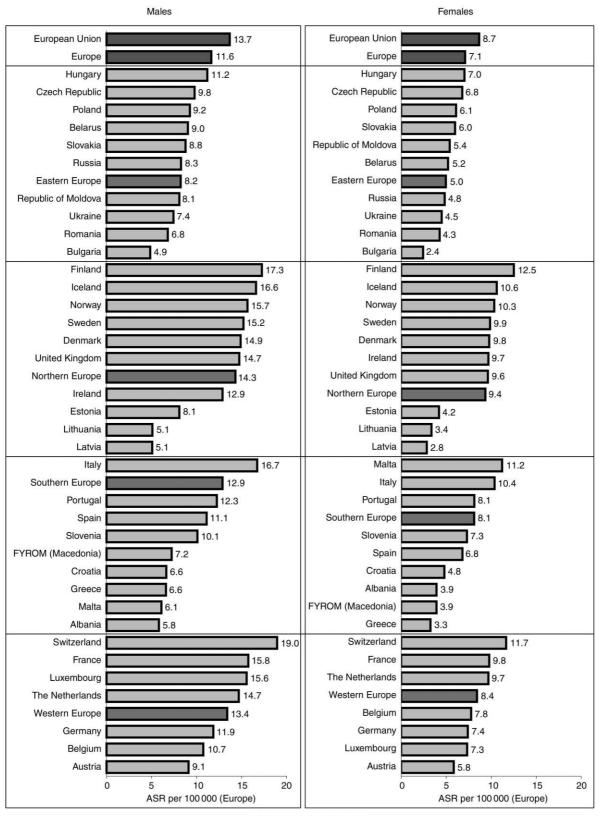


Fig. 40. Age-standardised incidence rates by area and country in Europe 1995: Non-Hodgkin lymphoma.

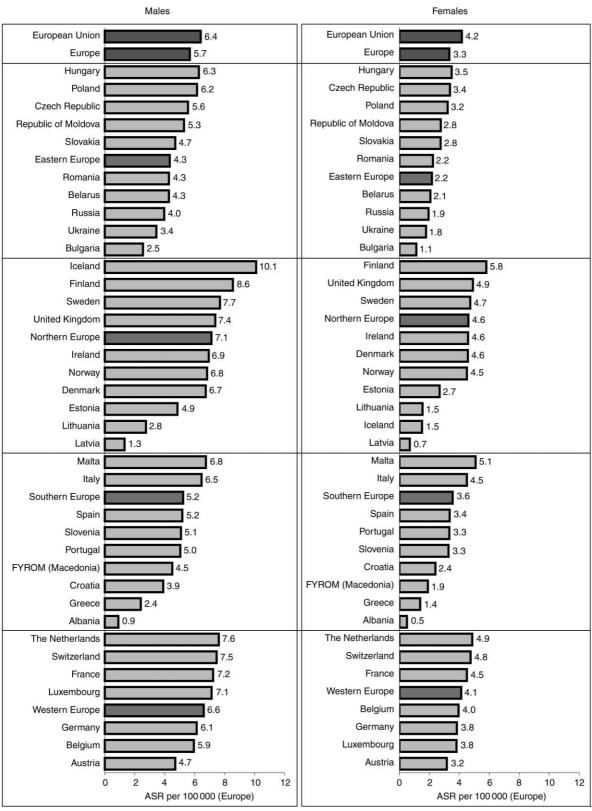


Fig. 41. Age-standardised mortality rates by area and country in Europe 1995: Non-Hodgkin lymphoma.

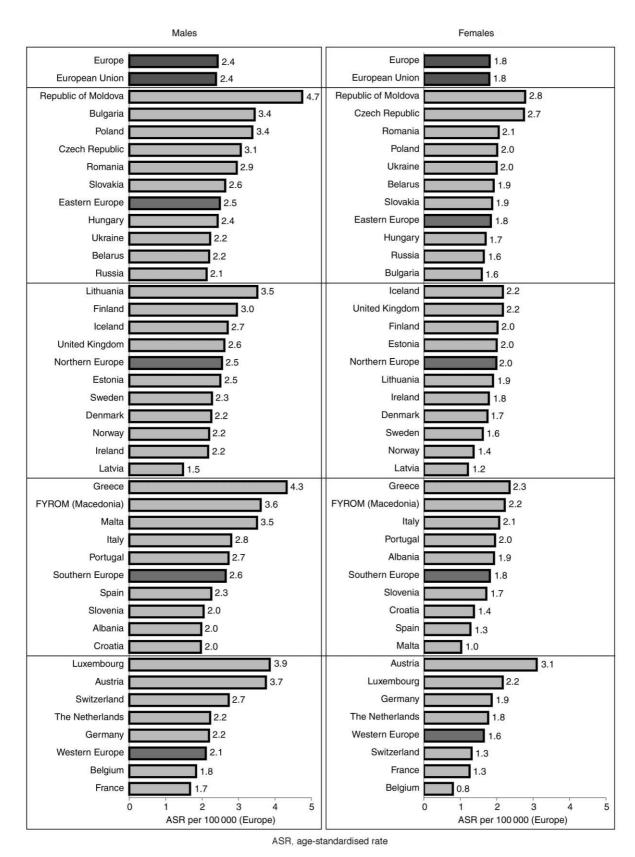


Fig. 42. Age-standardised incidence rates by area and country in Europe 1995: Hodgkin disease.

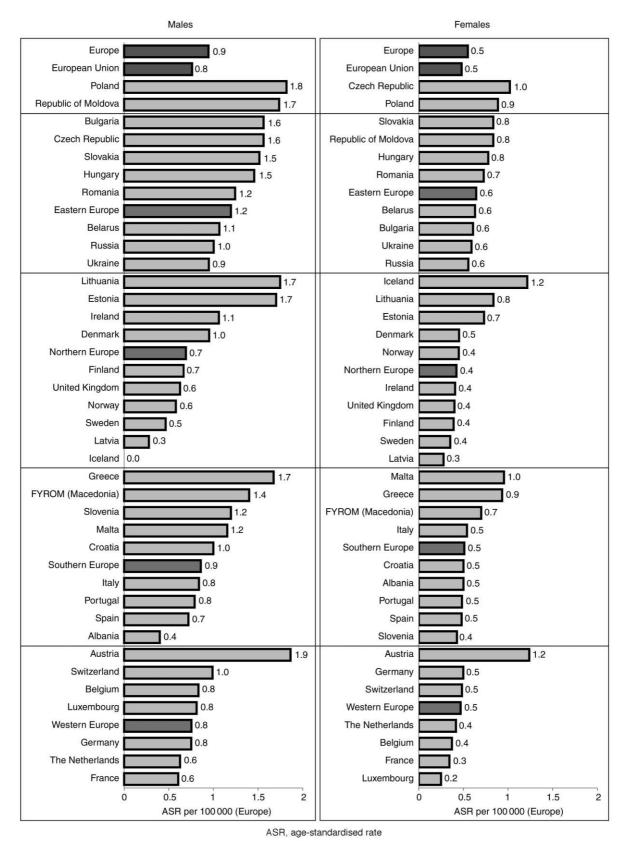


Fig. 43. Age-standardised mortality rates by area and country in Europe 1995: Hodgkin disease.

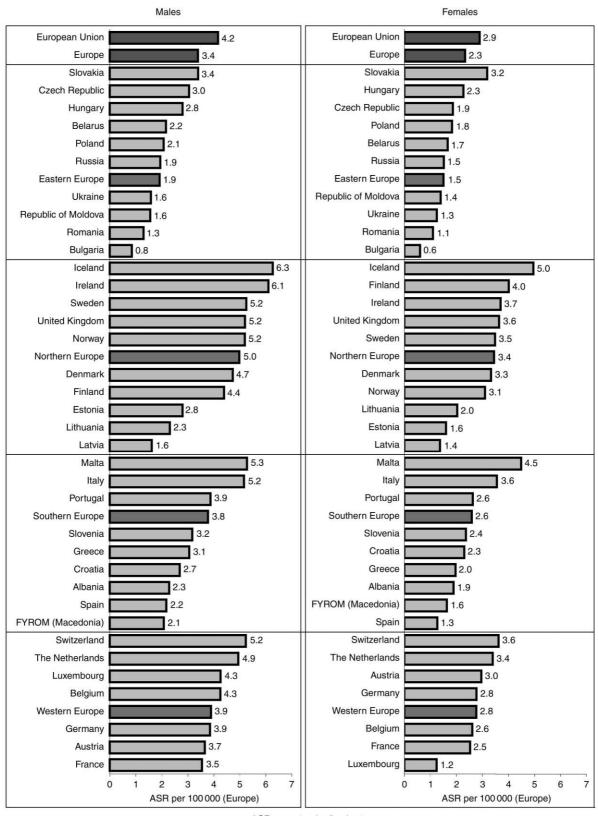


Fig. 44. Age-standardised incidence rates by area and country in Europe 1995: multiple myeloma.

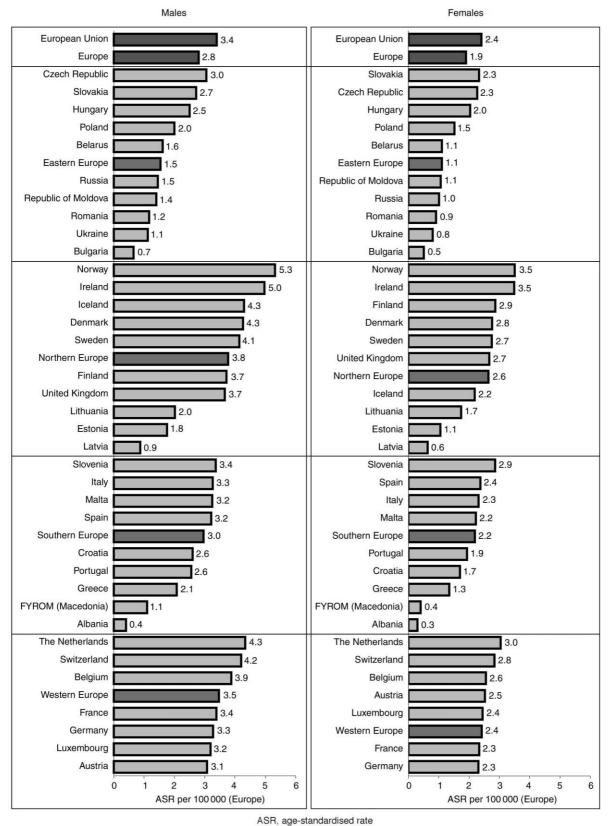


Fig. 45. Age-standardised mortality rates by area and country in Europe 1995: multiple myeloma.

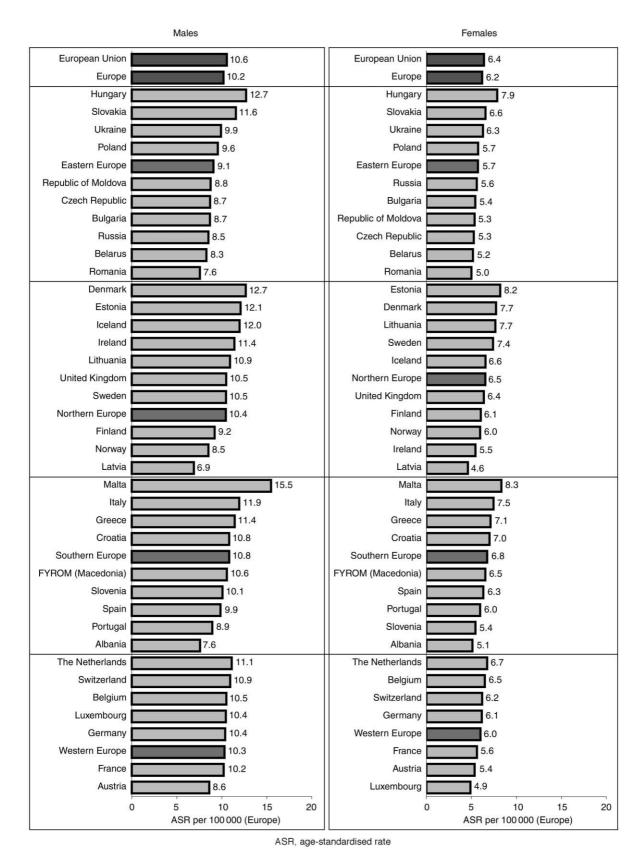


Fig. 46. Age-standardised incidence rates by area and country in Europe 1995: leukaemia.

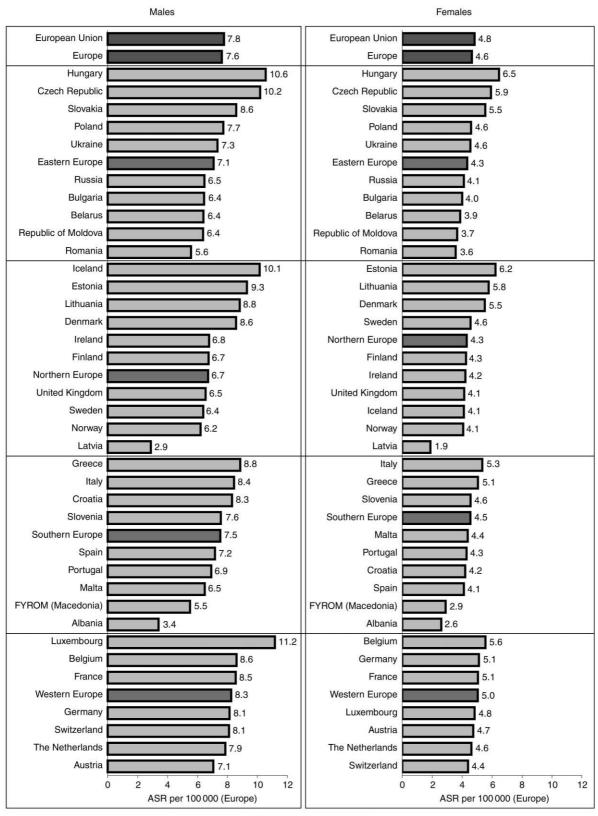


Fig. 47. Age-standardised mortality rates by area and country in Europe 1995: leukaemia.

alcohol consumption [9,10], probably explain much of the wide geographical variation in risk between and within European areas, and between the sexes. In the European Union, it has been estimated that approximately 60% of oral cancers in men and 30% in women could be attributable to smoking alone in 1995 [11]. Diet may also play a causative role—perhaps responsible for a further 10–15% of cases in Europe [12]. There were 3- to 5-fold differences in the risk in males in each region, with incidence rates ranging from over 29.1 per 100 000 in Hungary to around 4 per 100 000 in Greece, FYROM and the UK (Fig. 4). Similar magnitudes of geographical variation occurred in the incidence rates in women, although the risk of cancers of the oral cavity was generally much lower than that of men (male:female ratio = 3.5). Surgery and radiotherapy provide reasonable cure rates for most oral tumours, with the average European 5-year survival rates following oral cavity cancer diagnosis estimated to be 44% [13]. Therefore, death rates in 1995 were considerably lower than those of incidence there were some 21 000 deaths from oral cavity cancers, approximately 1% of all cancer deaths in Europe in 1995. Much of the regional patterns seen in incidence emerged in the distribution of the rates of mortality (Fig. 5).

## 3.3. Nasopharynx (ICD-9 147)

Nasopharyngeal cancer is relatively rare in Europe, with some 4000 cases occurring in 1995. The aetiology of this cancer differs from the other alcohol- and tobacco-related malignancies of the oral cavity and pharynx—although tobacco smoking increases risk [14], genetic predisposition is important, as is infection with Epstein-Barr virus and, in some areas, dietary habits such as the high consumption of preserved or salted foods [15]. In Europe, there is an increasing risk gradient from north to south (Fig. 6), with relatively high rates observed in Malta in both sexes (males 4.1, females 0.7), as noted previously in Ref. [16]. Such observations point to ethnic origin as an important determinant. Several studies have shown Northern African migrants in France [17] and Israel [18] retain the high rates seen in their country of origin, and have approximately twice the risk of death relative to those locally-born. Women are less affected with a risk that is approximately 40% that of men. Approximately 2000 deaths occurred in 1995. Incidence:mortality ratios in both sexes were elevated in Eastern Europe (1.7) compared with elsewhere (e.g. 1.2 in Southern Europe), probably reflecting survival, which depends on the extent of disease following diagnosis. Mortality rates by area and country are shown in Fig. 7.

## 3.4. Other pharynx (ICD-9 146, 148 and 149)

An estimated 36 000 new cases of pharyngeal cancer occurred in 1995, over 85% in men. As with oral cavity

tumours, alcohol drinking and cigarette smoking play an aetiological role [9,10]. Dramatic differences in the rates of incidence were observed in each area of Europe (Fig. 8)—the risk in men was high in parts of Eastern Europe, particularly (as with cancers of the oral cavity) in Hungary (17.1) and Slovakia (14.8). Rates in Slovenia were also high (14.2). By far the greatest risk in Europe, however, occurred in France (29.6), where local rates in several northern regions of the country are extremely high, probably due to excess alcohol consumption, modified by smoking. In contrast, the risk in females is very low—as with men, the risk was highest in France (2.2), but still approximately 13 times lower than that of men. Approximately half as many deaths as new cases occurred in 1995, reflecting the possibility of cure if these tumours are detected early. Mortality rates by area and country are shown in Fig. 9.

#### 3.5. *Oesophagus (ICD-9 150)*

Although the incidence of adenocarcinoma of the oesophagus is increasing in several European countries [19], squamous cell carcinoma remains the predominant histological type, and hence the patterns which emerge are similar to those of oral cavity and pharyngeal cancers, which share the same established risk factors, tobacco and alcohol [9,10]. The multiplicative effects of tobacco and alcohol on the risk of squamous cell carcinoma are also well-established [20]. Some 63% of cases in men and 33% in women are estimated to be attributable to smoking in the European Union [11]. However, there are some differences—the UK, for instance, has the highest rate of this cancer in Northern Europe, yet the lowest rate of cancer of the oral cavity. Such contrasts can at least be partially explained by differences in the incidence of adenocarcinoma (particularly high in the UK), or misclassification between carcinomas of the lower third of the oesophagus and gastric cardia. Other putative risk factors, such as poor diet, may also explain some of the divergences [21,22]. Incidence rates in men are considerably higher in France (17.0) than elsewhere in Europe (Fig. 10), probably due to consumption of certain alcoholic beverages in the north west, notably in Calvados, for which an excess risk in men has been established [23]. Rates are also high in men in several Eastern European countries, notably Hungary (14.9) and Russia (13.2), presumably due to the joint effects of alcohol and tobacco, and possibly, diet-related factors. Rates are amongst the lowest in Southern Europe, between 2 and 9 per 100 000. The geography of oesophageal cancer in females is quite different from that in men, and their risk is much lower (sex ratio (male:female) = 3.3). Age-adjusted rates were well above the European average in both the UK and Ireland, suggesting a role for aetiological factors other than smoking and drinking, such as diet. Survival from

oesophageal cancer is poor—approximately 10% at 5 years [13]. Thus, death rates in both sexes were fairly close to the incidence rates (Fig. 11). French males had by far the highest mortality rate (13.8).

## 3.6. Stomach (ICD-9 151)

The steady decline in gastric cancer in Europe (and worldwide) in the last few decades can probably be

Table 3
Estimated number of new cases of cancer in 1995 in Europe, the European Union, and the UN-defined European areas (both sexes combined)

Cancer	New cases (thousands) percentage of total cancer burden							
	Europe	European Union	Eastern Europe	Northern Europe	Southern Europe	Western Europe		
Oral cavity	49.1	23.6	22.4	4.4	10.4	11.9		
	1.9	1.6	2.3	1.2	1.9	1.6		
Nasopharynx	3.8	1.6	2.0	0.3	0.8	0.7		
	0.1	0.1	0.2	0.1	0.1	0.1		
Other pharynx	36.3	22.8	11.3	2.5	7.3	15.1		
	1.4	1.5	1.2	0.7	1.4	2.1		
Oesophagus	42.6	24.5	16.2	8.5	6.2	11.7		
	1.6	1.6	1.7	2.2	1.2	1.6		
Stomach	207.3	79.0	118.1	17.0	37.7	34.4		
	7.9	5.3	12.3	4.4	7.0	4.7		
Colon and rectum	333.6	198.8	116.0	48.9	65.1	103.6		
	12.8	13.3	12.0	12.8	12.2	14.2		
Liver, etc.	47.8	29.1	16.5	3.4	16.7	11.2		
	1.8	1.9	1.7	0.9	3.1	1.5		
Pancreas	73.7	39.8	29.5	10.7	14.4	19.0		
	2.8	2.7	3.1	2.8	2.7	2.6		
Larynx	52.0	24.0	25.6	3.7	12.6	10.2		
	2.0	1.6	2.7	1.0	2.4	1.4		
Lung, etc.	377.1	196.5	159.3	55.9	74.5	87.3		
	14.5	<i>13.1</i>	16.5	14.6	13.9	12.0		
Melanoma of skin	53.4	31.4	17.6	10.6	8.0	17.2		
	2.0	2.1	1.8	2.8	1.5	2.4		
Breast	320.7	199.7	102.8	50.7	61.3	105.9		
	12.3	<i>13.4</i>	10.7	13.3	11.4	<i>14.6</i>		
Cervix uteri	68.0	27.2	36.6	7.3	9.8	14.2		
	2.6	1.8	3.8	1.9	1.8	2.0		
Corpus uteri	68.3	36.6	27.1	9.0	16.2	16.0		
	2.6	2.4	2.8	2.4	3.0	2.2		
Ovary, etc.	58.0	32.3	21.9	9.6	10.0	16.5		
	2.2	2.2	2.3	2.5	1.9	2.3		
Prostate	155.7	112.8	32.0	31.8	28.0	64.0		
	6.0	7.5	3.3	8.3	5.2	8.8		
Testis	20.0	11.5	7.1	2.9	3.3	6.7		
	0.8	0.8	0.7	0.8	0.6	0.9		
Bladder	126.6	85.1	35.7	20.0	37.6	33.3		
	4.9	5.7	3.7	5.2	7.0	4.6		
Kidney, etc.	75.6 2.9	41.5	29.8 3.1	9.4 2.5	14.1 2.6	22.3 3.1		
Brain and CNS	49.4	28.2	18.3	6.8	11.3	13.1		
	1.9	1.9	1.9	1.8	2.1	1.8		
Thyroid	24.3	12.1	10.9	2.7	4.8	6.1		
	0.9	0.8	1.1	0.7	0.9	0.8		
Non-Hodgkin lymphoma	71.9	48.0	19.8	12.7	16.9	22.5		
	2.8	3.2	2.1	3.3	3.2	3.1		
Hodgkin disease	15.8	8.3	6.6	2.2	3.4	3.6		
	0.6	0.6	0.7	0.6	0.6	0.5		
Multiple myeloma	22.7	16.1	5.3	4.8	5.4	7.2		
	0.9	1.1	0.5	1.3	1.0	1.0		
Leukaemia	62.1 2.4	36.6 2.4	22.0 2.3	9.2 2.4	1.0 14.1 2.6	16.7 2.3		
All sites excluding non-melanoma skin	2.4 2609.2 100.0	1495.0 100.0	963.7 100.0	382.5 100.0	535.4 100.0	727.5 100.0		

UN, United Nations; CNS, central nervous system.

attributed to better nutrition (e.g. a higher consumption of fruit and vegetables) and lower consumption of salt following the advent of refrigeration for the transport and storage of food stuffs [24]. A decline in the pre-

valence of *Helicobacter pylori* infection has also been implicated [25]. Nevertheless, stomach cancer remains the fourth most common cancer in Europe, with over 207 000 new cases in 1995. Approximately half of these

Table 4
Estimated number of deaths from cancer in 1995 in Europe, the European Union, and the UN-defined European areas (both sexes combined)

Cancer	Deaths (thousands) percentage of total cancer deaths							
	Europe	European Union	Eastern Europe	Northern Europe	Southern Europe	Western Europe		
Oral cavity	20.8	9.7	10.1	2.0	3.6	5.1		
	1.3	1.0	1.6	0.8	1.2	1.1		
Nasopharynx Other pharynx	2.4	1.2	1.2	0.2	0.6	0.4		
	0.1	0.1	0.2	0.1	0.2	0.1		
	17.3	9.0	7.3	1.1	2.8	6.0		
Oesophagus	1.1	1.0	1.2	0.5	0.9	1.3		
	38.6	22.9	14.1	8.3	5.4	10.8		
G. 1	2.4	2.5	2.3	3.5	1.7	2.4		
Stomach	151.5	60.0	85.0	13.3	26.1	27.1		
	9.3	6.5	13.7	5.6	8.4	6.0		
Colon and rectum	188.8	110.8	68.3	27.8	34.3	58.4		
Liver, etc.	11.6	12.0	11.0	11.7	11.1	12.8		
	52.6	32.4	18.4	3.7	17.2	13.2		
	3.2	3.5	3.0	1.6	5.6	2.9		
Pancreas	74.2	43.4	27.3	10.9	13.5	22.4		
	4.6	4.7	4.4	4.6	4.4	4.9		
Larynx	26.4	10.8	14.6	1.6	5.3	5.0		
Lung, etc.	1.6	1.2	2.3	0.7	1.7	1.1		
	330.0	180.5	134.4	51.2	62.5	81.9		
	20.3	19.5	21.6	21.6	20.2	18.0		
Melanoma of skin	15.2	8.5	5.6	2.5	2.8	4.3		
Breast	0.9	0.9	0.9	1.1	0.9	0.9		
	124.1	76.1	41.7	20.4	23.0	38.9		
	7.6	8.2	6.7	8.6	7.4	8.6		
Cervix uteri Corpus uteri	27.2	11.0	14.7	3.0	3.3	6.1		
	1.7	1.2	2.4	1.3	1.1	1.3		
	17.6	8.9	7.7	2.0	3.4	4.4		
Ovary, etc.	1.1	1.0	1.2	0.8	1.1	1.0		
	37.7	22.9	12.7	6.9	5.8	12.4		
	2.3	2.5	2.0	2.9	1.9	2.7		
Prostate Testis	75.4	55.2	15.5	16.0	15.9	28.0		
	4.6	6.0	2.5	6.7	5.1	6.2		
	2.1	0.8	1.2	0.2	0.2	0.5		
	0.1	0.1	0.2	0.1	0.1	0.1		
Bladder	46.1	30.3	13.7	7.6	10.8	13.9		
	2.8	3.3	2.2	3.2	3.5	3.1		
Kidney, etc.  Brain and CNS	37.6	21.8	13.9	5.3	5.9	12.5		
	2.3	2.4	2.2	2.2	1.9	2.7		
	37.6	20.3	15.6	4.9	7.1	10.0		
Thyroid	2.3	2.2	2.5	2.1	2.3	2.2		
	5.7	3.2	2.2	0.6	1.1	1.8		
Non-Hodgkin lymphoma	0.4	0.3	0.4	0.3	0.4	0.4		
	35.5	24.2	9.6	6.7	7.5	11.7		
Hodgkin disease	2.2	2.6	1.5	2.8	2.4	2.6		
	5.7	2.7	2.7	0.6	1.1	1.3		
	0.4	0.3	0.4	0.3	0.4	0.3		
Multiple myeloma Leukaemia	19.1	13.9	4.0	3.9	4.5	6.7		
	1.2	1.5	0.6	1.6	1.5	1.5		
	47.8	28.7	16.9	6.3	10.1	14.4		
	2.9	3.1	2.7	2.7	3.3	3.2		
All sites excluding non-melanoma skin	1624.0	924.2	622.7	237.5	309.2	454.7		
	100.0	100.0	100.0	100.0	100.0	100.0		

UN, United Nations; CNS, central nervous system.

occurred in Eastern Europe, where it is the second most frequent cancer in both sexes combined (118000 new cases), representing an estimated excess risk of developing gastric cancer 2 or 3 times that of the other areas (Fig. 12). Rates in males were particularly striking in Russia (73.7) and Belarus (68.9), while other high risk populations include the Ukraine (56.3), Latvia (54.3) and Lithuania (51.9). Such elevated rates may reflect the relatively low level of affluence in these countries in recent decades, and the resulting poor diet of their inhabitants. Rates in women were approximately half those of men, but the rankings by country were very similar, with women from Eastern Europe and the Baltic countries having the highest incidence rates. Despite improved surgical procedures and the widespread use of endoscopy, the prognosis for gastric cancer remains relatively poor, as diagnosis is often at later stages of the disease—relative survival at 5 years is approximately 22%. Consequently, mortality rates in 1995 were also high, and have a similar geographical pattern to those of the incidence rates (Fig. 13).

#### 3.7. Colon and rectum (ICD-9 153 and 154)

Although information on incidence and mortality from cancers of the colon and rectum were available (or estimated) separately, they were grouped together for the purposes of consistency with past publications and to avoid spurious differences in rates, caused by variations in practices with respect to allocating to one of the two 'sites'. Colorectal cancer ranked second in frequency of new cases in both men and women, with about 334 000 new cases estimated for 1995, distributed almost evenly between the sexes. The overall incidence rates of colorectal cancers are slightly higher in men due to a higher sex ratio of rectal cancer—the sex ratio of colon cancers is closer to unity (Fig. 14). There was very little variation in the rates in men and women between countries of Western Europe, where there was an excess risk of colorectal cancer (males 55.8, females 38.3) in comparison with the populations in Eastern (males 45.5, females 31.6), Northern (males 49.4, females 35.1), and Southern Europe (males 46.6, females 30.4). Nevertheless, by far the highest rates of incidence were observed (for both sexes) in Eastern Europe—especially in the Czech Republic (males 81.8, females 45.4), and Hungary (males 80.2, females 50.2). Slovakia also had a moderately high rate (males 64.3, females 35.4). As well as the Western and Eastern European countries, high rates were observed in Ireland, Norway and Denmark in the north, and in Slovenia, Portugal and Italy in the South. The populations of Romania, Greece and FYROM had the lowest incidence rates in Europe in 1995. Diets low in fruit, vegetables and unrefined plant food, and high in red meat and fat confer an increased risk of colorectal cancer [26]. Dietary differences may be

responsible for much of the incidence variation observed. Colorectal cancer has a relatively good prognosis—5-year relative survival is approximately 48 and 44% for cancers of the colon and rectum, respectively [13]—and thus mortality rates are considerably lower than those of incidence (incidence:mortality ratio = 1.8). Geographical patterns of mortality are similar to those of incidence—death rates were especially high in several Eastern European countries (Fig. 15).

## 3.8. Liver, etc. (ICD-9 155)

Cancer of the liver is extremely common in many developing countries [27], although in Europe there were just 48 000 new cases in 1995. Prognosis is very poor, with 5-year survival rates in Europe as low as 5% [13]. Men have approximately 3 times the risk of women (Fig. 16). Incidence rates were high in Southern Europe, particularly in Italy (males 20.5, females 6.9), FYROM (males 17.6, females 6.7), and Greece (males 17.6, females 6.7). Elsewhere, rates were high in French males (12.2) and in several countries in Eastern Europe— Hungary (males 11.5, females 5.0), Romania (males 11.3, females 4.7), the Czech Republic (males 11.0, females 4.7) and in women in Poland (4.7). Risk was lowest in Northern Europe relative to other areas, particularly in men (4.2). Mortality rates are more difficult to interpret, as differences between countries in the diagnosis and misclassification of secondary tumours are likely to have influenced the observed geographical patterns (Fig. 17). Thus, in common with other cancers with particularly poor survival, the estimated incidence was often lower than the reported mortality. None the less, the ranking of incidence rates does suggest that there are major variations in Europe with respect to the known risk factors for the disease. In European populations, alcohol consumption is a well-known cause of liver cancer [10], although the incidence and mortality patterns observed differ from the other alcohol-related cancers, suggesting modification by other factors. Hepatitis B, and more recently Hepatitis C are also established risk factors [28], and the prevalence of these infections may explain some of the geographical variation observed.

## 3.9. Pancreas (ICD-9 157)

With 74000 new cases in 1995, pancreatic cancer ranked eighth in frequency in Europe. There is perhaps less geographical variation in incidence than for the other cancers (Fig. 18). Rates in males were a little higher in Eastern Europe than elsewhere—13.0 per 100 000 compared with around 10 per 100 000 in the other three regions, but in females, the rates were close to 7 per 100 000 in all regions. Cigarette smoking increases the risk of cancer of the pancreas—approxi-

mately one-third of male cases and one-sixth of cases in women are thought to be attributable to tobacco in the European Union [11]. Yet the ranking of the rates observed in this study are somewhat different from those of lung cancer, suggesting that other factors are also associated with the disease. The role of dietary factors, alcohol and coffee consumption and diabetes are currently controversial, and further evidence is required to confirm any associations [29]. Prognosis is very poor—5-year survival from the disease is less than 5%. Thus, there were an estimated 75000 deaths from pancreatic cancer in Europe, a figure slightly higher than the number of incident cases most likely due to differing practices in defining the cause of death, with patterns of risk of death very similar to those characterised by the incidence rates (Fig. 19).

#### 3.10. Larynx (ICD-9 161)

Cancer of the larynx accounts for approximately 52 000 new cases, and is much more frequent in men than in women—92% of all cases occur in males. There was a large variation in risk in men between and within the areas of Europe (Fig. 20). Overall, male incidence rates were particularly high in Eastern Europe (18.8) and Southern Europe (16.3), moderate in Western Europe (10.4) and low in Northern Europe (6.4), although rates were high in the Baltic countries. The geographical variations are indicative of differences in alcohol and tobacco consumption [9,10] between countries—the joint effect of the two factors is multiplicative. However, patterns differed from those of other cancers related primarily to tobacco use, suggesting that alcohol is the more important determinant of the geographical patterns, either independently or jointly with tobacco. Thus, incidence rates were amongst the highest in countries where the consumption of alcohol (such as wine and spirits) is recognised as high.

Relative to men, cancer of the larynx in women is rare, ranging from 0.3 to 2 per 100 000. Prognosis depends on the sub-site involved, although overall 5-year relative survival is good—exceeding 60% in Europe [13]. Mortality rates from larynx cancer are prone to error due to difficulty in distinguishing between larynx and hypopharynx—but similar patterns emerge to those of incidence (Fig. 21). The ratio of incidence to mortality in men was notably higher in Northern Europe (2.4), than in Eastern Europe (1.7), reflecting the poorer prognosis amongst populations where alcohol consumption is high and the upper part of the larynx is most affected—such tumours are associated with lower survival.

## 3.11. Lung, etc. (ICD-9 162)

Lung cancer is the most common cancer occurring in Europe, and it accounts for nearly one-quarter of new cancer cases in European men (307 000). It was less common in women (approximately 70 000 cases, representing 6% of all cancers in women, fourth after cancers of the breast, colon and rectum and stomach. The differences in lung cancer burden within European areas (Fig. 22) illustrate the contrasts in the history of tobacco smoking in different populations. Previous estimates [30] indicate that smoking in European populations accounts for some 90% of new cases of lung cancer in men, and in women, from 30% (in Southern Europe) to 73% (in Northern Europe). In males, incidence was much higher in Eastern Europe (107.4) than elsewhere in Europe—with especially high rates in Hungary (144.5), but several other populations in the region also had rates over 100 per 100 000, namely Poland (121.1), Russia (116.5), the Czech Republic (106.5) and Slovakia (104.6). Rates were of the same magnitude in the Baltic countries of Latvia (105.3), Estonia (104.5), Lithuania (103.9), and in Albania (122.1) and Croatia (102.6). In Western European men, as noted previously in Ref. [3], rates in Belgium are strikingly high (121.2).

Rates are lower in women—although to a degree the patterns were akin to those seen in men—high rates were observed in women from many Eastern European countries, particularly in Hungary (32.8). The malefemale ratios varied greatly—the ratios tended to be high in areas where the impact of tobacco smoking has not yet been realised in women (for example, Eastern Europe), and low in Northern Europe, where, for some countries, the effects of smoking on subsequent lung cancer risk is currently at, or close to, its maximum level. Indeed, amongst European women, rates in Northern Europe (29.0) were amongst the highest, with very high rates observed in Iceland (45.2), Denmark (40.3) and the UK (34.1)—although time trend analyses suggest rates are peaking or have begun to decline in these countries [31], corresponding to decreases in smoking prevalence amongst women, and the use of lower tar cigarettes in more recent decades [32]. In many other countries in Europe, particularly in the East, incidence rates in both sexes are expected to continue to rise as the smoking epidemic advances.

Given the load of new cases of the disease and its fairly poor prognosis—5-year relative survival is approximately 10% in Europe [13]—lung cancer was also the most common cause of cancer death in men in Europe, and the geographical patterns of mortality rates correspond to those of incidence (Fig. 23). Nearly one-third of all deaths from cancer in European men are due to lung neoplasms—approximately 266 000 deaths. As with incidence, geographical patterns in risk of death contrast markedly—in Sweden, for example, prostate cancer has replaced lung cancer as the leading cause of death in men. In women, the number of deaths due to lung cancer was much lower—64 000 (approximately 9% of all cancer deaths). In Northern Europe, the pro-

portion of deaths attributable to the disease was somewhat higher—estimated at around 15% of all female deaths from cancer in the region.

#### *3.12. Skin melanoma (ICD-9 172)*

Some 53 000 new cases and 15 000 deaths were estimated to have occurred in Europe in 1995. Incidence was similar in males and females. As previously demonstrated, rates are highest in the Northern parts of Europe. The main aetiological factor is exposure to the ultraviolet component of sunlight, particularly an intermittent but excessive exposure to pale skin—the wellabove average rates observed in the Nordic countries of Norway (males 19.7, females 20.7), Sweden (males 15.5, females 15.0) and Denmark (males 15.1, females 18.3) are probably explained by this factor (Fig. 24). Risks of the same magnitude were also present in parts of Western Europe, particularly Switzerland (males 17.0, females 14.0), as well as in Austria and The Netherlands. In contrast, incidence rates in Southern and Eastern European countries were fairly low, ranging between 2 and 8 per 100 000 in most countries. Survival is very good if the disease is diagnosed at a localised stage. Accordingly, death rates were much lower than incidence, although in contrast to incidence rates, mortality was generally lower in women (Fig. 25). The better prognosis in females is partly a consequence of the rather different site distribution of melanoma in the two sexes, with males having more melanomas on the back (with a consequently late presentation), and women having more leg tumours [33]. There is also evidence that there is better awareness of the disease among women [34].

## 3.13. Female breast (ICD-9 174)

By far the most common cancer in women in Europe is breast cancer. There were an estimated 321 000 cases in 1995, representing over a quarter of all new cancers occurring in females. There were approximately 124 000 deaths from breast cancer (17% of all female cancer deaths), and hence it was also the most common cause of cancer mortality in women. There were clear geographical differences in risk (Fig. 26); with high rates of incidence observed in Western Europe (96.4), notably so in The Netherlands (120.1), Switzerland (112.9) and France (103.2), and in Northern Europe, particularly the Nordic countries—Denmark (110.1), Sweden (105.6), Iceland (101.6) and Finland (100.0). In comparison, incidence rates in Eastern European countries were much lower (59.5), as were rates in Southern Europe (73.1). It is likely that the differing prevalence of the known risk factors for breast cancer between social classes—namely age at menarche and menopause, parity and body size [35]—explain much of the variation, while some of the excess incidence may be attributable to mammographical screening. Hence, the most affluent countries tended to have the highest rates in Europe. In Eastern Europe, for example, the risk of women developing breast cancer was approximately half that of women living in the Nordic countries.

Overall, prognosis in Europe is good—the relative survival rate is 65% for women at 5-years [13]. Geographical variations in mortality reflect not only levels of incidence, but also the relative affluence of the women in each country—there is poorer survival for women from lower social classes [36]. Rates of death were generally highest in countries where the risk of developing breast cancer was greatest, with the incidence:mortality ratios being slightly less favourable in Eastern Europe relative to elsewhere in Europe (Fig. 27). There is evidence that mortality rates in some Northern countries (e.g. Denmark, Norway, the Netherlands and the UK) are declining [37,38], as a consequence of the combined effects of earlier detection (in part due to screening), and improving treatment.

#### 3.14. Cervix uteri (ICD-9 180)

Cervical cancer is the second most common female cancer worldwide [27,56], but only 15% of cases occur amongst European women (68 000 in 1995). Rates varied a great deal between countries within each European area (Fig. 26), although the incidence was highest in the Eastern European countries including Romania (40.3), Bulgaria (26.9), Hungary (26.7), Poland (25.7), and in the Baltic country, Lithuania (26.8). The prognosis of cervical cancer is fair—the 27 000 deaths from cervical cancer is in line with the 5-year relative survival rate, approximately 62% in Europe [13]. Thus, mortality rates were approximately one-third those of incidence rates in 1995, with overall incidence:mortality ratios similar in each area of Europe (Fig. 27).

Infection with certain types of the human papillomavirus (HPV) is considered to be a necessary cause of cervical cancer [39], and the underlying risk for cervical cancer development probably largely reflects the prevalence of infection. The implementation of Papanicolaou (Pap)-smear screening in many European countries has also had a major impact on incidence and mortality—the low rates observed in Finland for example, points to the efficacy of a well-organised national screening programme, rather than an inherently low risk population.

## 3.15. Corpus uteri (ICD-9 182)

The number of new cases of cancer of the corpus uteri is approximately the same as for cancers of the cervix uteri. The highest reported incidence rates were in Southern Europe, particularly in Malta (32.0), although

age-adjusted rates above 20 years are observed in many countries (Fig. 28). Risk is enhanced by exposure to unopposed oestrogen [40], so that obesity, late menopause, and menopausal replacement therapy are thus associated with this cancer. The proportion of endometrial cancers due to excess weight in European women is estimated at 39% [41]. Relative survival is good, over 75% at 5 years in Europe [13], so that death rates are fairly low, with rates exceeding 5 per 100 000 in only a few countries, principally in Eastern and Southern Europe (Fig. 29).

## 3.16. Ovary, etc. (ICD-9 183)

Compared with other gynaecological cancers, invasive ovarian cancer has a fairly poor prognosis, relative survival estimated at approximately 30% in women 5 years from diagnosis [13]. There were an estimated 58 000 new cases and 38 000 deaths in 1995, ranking the disease as the seventh most common cancer and the fifth biggest killer from cancer of European women. Incidence rates are above the European average in all 10 Northern European countries (Fig. 28). In comparison, incidence is fairly low in many countries in Southern and Eastern Europe. In each region, the ranking of death rates by country tended to closely follow the patterns reported for incidence (Fig. 29). The role of hormonal and reproductive factors in the aetiology of ovarian cancer have been intensively studied; oral contraceptive use and hysterectomy have been shown to be protective, while nulliparity and refractory infertility may increase risk [42]. Mutations in the BRCA1 and BRCA2 tumour suppressor genes are also associated with an increased risk, but have only a small effect at the population level.

## 3.17. Prostate (ICD-9 185)

In 1995, prostate cancer was the third most common cancer in men in Europe, with some 156 000 new cases. Incidence rates have been influenced by the increased diagnosis of latent prostate cancers by the use of transurethral prostatectomy (TURP), and testing with prostate-specific antigen (PSA). Indeed, geographical variations in incidence probably relate more to the differing medical practices between countries than to any variation in the underlying risk. Rates were very high in many Northern and Western European countries, particularly so in the Nordic countries (with the exception of Denmark), probably due to the detection of latent prostate cancer cases (Fig. 30). Incidence rates were considerably lower in the majority of countries in Eastern and Southern Europe, where such clinical activities are not established. In comparison with incidence, there was less variability in death rates, although the risk of death was still considerably higher in Northern and Western parts of Europe, where detection rates are high

(Fig. 31). It could be that the excess risk of death in these countries arises simply from the increasing number of latent prostate cancers being recorded as an underlying cause of death, particularly when the cause is unknown [43]. The aetiology of prostate cancer remains unclear, although some studies have implicated a role for diet, in particular the high consumption of meat and dairy products [26]. Other studies have pointed to genetic factors, such as polymorphisms in genes controlling androgen metabolism [44].

#### 3.18. Testis (ICD-9 186)

Although testicular cancer is relatively rare in Europe, with an estimated 20 000 new cases in 1995, it is the most common cancer among men aged between 20 and 34 years. The age-standardised incidence rates were highest in Northern and Western Europe, particularly in Denmark (11.1), Norway (9.2) and Germany (9.1), with rates in many of the countries of Southern Europe and parts of Eastern Europe relatively low, in the 2–4 range (Fig. 30). The few deaths from testis cancer (estimated to be approximately 2000) reflect the favourable prognosis associated with this cancer, particularly when treated at an early stage—5-year survival in Europe is approximately 90% [13]. Yet the average mortality:incidence ratios in Eastern Europe indicate that the probability of death is 2 to 3 times higher in the male population than in other European areas, substantiating the need for a high level of resources in order to achieve the very good survival from this cancer. There are few clearly established risk factors associated with testicular cancer, although hormonal and genetic factors are likely to play a role [45]. Testis-related abnormalities such as cryptorchidism have been linked to the development of the cancer, although they can only explain a small proportion of cases.

## 3.19. Bladder (ICD-9 188)

Cancer of the bladder was the fifth most common malignancy in Europe and the sixth leading cause of cancer mortality, accounting for an estimated 127 000 new cases and 46 000 deaths in 1995. The risk of bladder cancer in men was elevated in several Mediterranean countries (Fig. 32), particularly Italy (48.4) and Spain (44.5). In contrast, rates were relatively low in many of the countries of Eastern Europe and within the Balkan and Baltic areas. Females are considerably less affected by the disease than males, the overall male:female ratio being approximately 5:1. Rates were elevated in Northern Europe, particularly in Denmark (10.4), Iceland (9.6) and the UK (8.6). Smoking has a causative role, and is estimated to cause up to 43% of cancers of the bladder in men and 16% in women in the European Union [11], as do some occupational agents [46]. However, some of the observed variation may be explained by differing coding practices between countries, especially with respect to non-invasive cases, which may be recorded as malignant bladder cases, along with invasive tumours. Prognosis is good provided the disease is diagnosed early. The overall relative survival rate in Europe is approximately 60% at 5 years [13], and consequently death rates are considerably lower than those of incidence (Fig. 33). The geographical patterns seen in the incidence rates are similar with regards to mortality, although the risk of death from bladder cancer by country is rather more homogenous.

### 3.20. Kidney, etc. (ICD-9 189)

There were 76 000 new cases of cancers of the kidney, renal pelvis and ureter, of which approximately fourfifths are renal cell carcinomas. Rates in men were approximately double those of women. Variation in the incidence rates between European countries was perhaps less marked than for most of the other cancers studied, with rates in the 10–20 range in men, and in the 5–10 range in women for the majority of countries (Fig. 34) Rates in the Czech Republic were, however, notably raised for both sexes (31.7 and 16.2 in males and females, respectively). They were also elevated in the Northern European countries of Iceland, Estonia and Lithuania, again the effect was seen in both males and females, rates being above 20 and  $\geq 10$  per 100 000, respectively. Relative survival from cancer of the kidney is fairly good, approximately 50% [13]. The overall patterns of mortality in European countries tend to reproduce the rankings seen in incidence (Fig. 35). Little is known about the risk factors involved, although cigarette smoking is causally linked to renal pelvis and ureter cancers. Overall, approximately 45% of kidney cancer cases in European men, but only 5% of cases in European women, may be attributable to smoking [11]. A further 25% may be due to obesity [41], an established risk factor for renal cell cancer.

# 3.21. Brain and central nervous system (ICD-9 191 and 192)

There were fewer than 50 000 cases of cancer of the brain and central nervous system in Europe in 1995. No real geographical patterns emerge and, as with cancers of the kidney, incidence and mortality rates within each European area do not vary much, with the majority of countries within the 4–10 per 100 000 range (Figs. 36 and 37). The mortality rates should be interpreted with caution as they may be inflated in some countries by the incorrect certification of metastasis as primary brain cancer. Thus, incidence rates may also be affected, given the number of new cases are calculated using national mortality data for countries where national incidence

data are not available. Given that the different histological types classified in this group are likely to have discordant aetiological factors, few risk factors have been determined at present.

#### 3.22. Thyroid (ICD-9 193)

Thyroid cancer is a relatively rare tumour in Europe, responsible for less than 1% of all new neoplasms in 1995. There were just over 24000 new cases and approximately 6000 deaths, with incidence 3 times higher in women than in men. The variation in risk within each region was around 3-fold, with most rates in women varying between 2 and 6, and in men between 1 and 3 (Fig. 38). Incidence rates in Iceland were exceptionally high for both women (15.6) and men (6.3), although the actual figures are based on rather few cases. Prognosis is good, with average five-year survival above 75% in Europe [13]. Thyroid cancer is also one of the few cancers for which there may well be sex-specific differences in risk of dying—survival rates are consistently higher in women than men for this cancer, particularly at younger ages. Thus mortality rates, which are less than 1 per 100 000 deaths in most countries, are of the same magnitude in both sexes (Fig. 39). Exposure to radiation and iodine deficiency are known risk factors [47], although only a minority of cases can be ascribed to them.

## 3.23. Non-Hodgkin lymphoma (ICD-9 200 and 202)

In Europe, slightly under 72 000 new cases of non-Hodgkin lymphoma occurred in 1995, approximately 3% of all cancers combined. In general, the risk was high in the Nordic countries, Italy and Switzerland. The lowest rates occurred mainly in Eastern European countries, with only Hungarian men having a rate above 10 per 100 000 (Fig. 40). Due to more effective chemotherapy and bone marrow transplantation, survival in Europe is now approximately 50% [13]; the annual number of deaths was therefore approximately half the number of new cases, approximately 36 000. The mortality rates displayed more or less the geographical patterns seen in the incidence rates (Fig. 41). The aetiology of Non-Hodgkin lymphoma, a very heterogeneous group of malignant diseases, remains largely unknown. Exposure to chemicals which impair the immune system have been implicated [48] and some cases are due to HIV infection [49].

### 3.24. Hodgkin disease (ICD-9 201)

Overall, Hodgkin disease is a rare neoplasm but, in the age group 15–29 years, it is one of the most common cancers, with similar rates for males and females. They diverge with increasing age, however, older men having a higher risk than women. For all ages combined, there were 16000 new cases in Europe in 1995 and approximately 6000 deaths, reflecting the good survival associated with the disease in Europe, estimated to be above 70% 5 years from diagnosis. There was less variation in the risk between European countries than for many other cancers, rates of Hodgkin disease were around 2–3 in men and 1-2 per 100 000 in women (Fig. 42). For both sexes, average rates in each area were similar high rates were however observed for both sexes in the Republic of Moldova (males 4.7, females 2.8) Greece (males 4.3, females 2.3) and Austria (males 3.7, females 3.1). A proportion of Hodgkin disease cases, particularly the mixed cellularity and nodular sclerosis subtypes, are associated with infection by the Epstein-Barr virus [50]. There appears also to be a familial aggregation of Hodgkin disease, related to cases occurring in young adulthood [51].

## 3.25. Multiple myeloma (ICD-9 203)

There were nearly 23 000 new cases in 1995, and just over 19000 deaths attributable to multiple myeloma. Myeloma mainly affects older individuals, is rare in younger people, and the overall burden in terms of absolute numbers is similar in men and women. No discernible geographical patterns emerge, other than rates in both sexes being somewhat elevated in Northern Europe as a whole, while Eastern Europeans tend to be less affected (Fig. 44). As the number of annual deaths relative to new cases in each region indicates, survival from myeloma varies considerably in Europe, the 5-year relative survival is estimated to range from below 10% in Estonia to up to 40% in Sweden (Fig. 45) [13]. The most widely-established risk factor associated with myeloma is exposure to ionising radiation, although certain chemicals and occupational exposures are suspected to increase risk [52].

#### 3.26. Leukaemia (ICD-9 204–208)

Leukaemias are responsible for 62 000 new cases and 48 000 deaths, representing nearly 2.5 and 3% of all cancer cases and deaths, respectively. The sex ratio is around 1.5. There was approximately a 2-fold difference in risk in men in each European region, rates in most countries ranging from 8 to 12 per 100 000, although rates are more constant between Western European countries (Fig. 46). In women, rates are relatively constant, with a range of approximately 5–8 per 100 000 observed for most parts of Europe. There are no clear geographical patterns regarding the incidence of leukaemia, which is fairly similar between regions for both sexes. 5-year survival is estimated as approximately 35%, although rates vary according to subtype—chronic lymphatic leukaemia is associated with a rela-

tively good survival of approximately 65%, contrasting with acute myeloid leukaemia for which only 1 in 10 European patients survives 5 years. As with lymphomas, leukaemias represent a diverse group of neoplasms with differing aetiologies. Well-known risk factors include radiation, several industrial chemicals, certain drugs, and a number of genetic conditions [53]. The possible role of an infectious agent in childhood leading to acute lymphoblastic leukaemia is not as yet confirmed [54].

#### 4. Discussion

This study provides an overview of the cancer incidence and mortality in European countries, documenting the extent of disease burden and the variations in the risk of developing and dying from cancer. The methodology is consistent with previous studies estimating cancer incidence within the European Union [2,3,7].

Several sources of data have been used in generating the statistics—for some countries, national incidence was available from national registries, for others, it was necessary to estimate incidence from national mortality data and incidence:mortality ratios of aggregated cancer registry data. A question that arises is the comparability of information between different countries. Although differences in practice do exist between cancer registries, for example, with respect to sources of data, definitions and processing methods, a great deal of care has been taken in ensuring completeness and validity of the registry data which has been used.

Mortality data have a lower accuracy (validity) than registry statistics, mainly because of the difficulties in ascertaining and certifying the cause of death, and a lack of comparability between countries in coding the underlying cause [55]. Inclusion of metastatic cancers along with primary neoplasms has been mentioned as a problem for some sites (especially liver, lung and brain). Even in this study, it is clear, on inspection of the national mortality rates, that there is a systematic underestimation of mortality for some countries (for example, Albania) and thus caution must be employed in interpretation.

With respect to incidence, comparability between countries may be a problem for some sites. The mortality:incidence ratios can vary considerably by registry, owing to different practices with respect to the detection (and registration) of preclinical prostate cancers, non-invasive tumours of the bladder, and non-invasive tumours of the brain and central nervous system.

The ENCR aims to ensure that registry data are of the highest quality and comparability, and provides common rules and definitions to meet this objective. The ENCR also supports the establishment of population-based national and regional cancer registries, particularly in areas where there has been little registry activity previously. This continuing process in harmonising registry practices, and the establishment of new registries in Europe has enabled us to provide estimates of cancer burden and risk for the whole of Europe. Nevertheless, less than one third of the population of Europe live in areas covered by cancer registration at the present moment, so that there is a clear need for further expansion.

Sound knowledge of the patterns of incidence and mortality is an essential basis for establishing policies for cancer control in the different countries and regions of Europe. Rates of lung cancer in men have began to decrease in some European countries, particularly in Northern and Western areas where the prevalence of smoking was first to diminish. This is not, however, the case for Eastern European males, whose rates are still rising. Incidence and mortality rates in women, who acquired the smoking habit later than men, are now on the increase in a number of European countries. Hence, lung cancer retains its status as the most common cancer in Europe, as well as the leading cause of cancer death. The lessons for primary prevention, through efforts to decrease tobacco smoking, are obvious. Such measures will have an impact upon other tobacco-related cancers too: oral cavity and pharynx, oesophagus, pancreas, larynx and urinary tract.

A reduction of alcohol consumption would reduce the risk of neoplasms of the upper digestive system and respiratory tract. There is scope for the avoidance of cancers of the colon and rectum and breast, the second and third most common cancers in Europe, respectively, through modification of diet, and for breast cancer, the reduction of the prevalence of obesity. Compared with previous estimates [2,3], there is also clear evidence that preventative interventions have had an impact on cancer incidence and mortality, particularly in the more affluent countries. For instance, the decline in cervical cancer observed in several of the Nordic countries can be attributed to the effectiveness of the national screening programmes. Similarly, effective treatment of testicular tumours has led to a reduction in death rates in many European countries during the last decade.

The important role of cancer registries in disease surveillance should not be taken for granted—cancer registration in Europe is at present facing an uncertain future in the wake of recent guidelines designed to protect the confidentiality of the patient. The requirement of obtaining informed consent from all patients before including their details in the registries has led to justifiable concern that cancer registration will collapse, no longer able to monitor cancer patterns and trends owing to the introduction of serious biases in the data, through the inevitable exclusion of a fraction of cases. If European governments consider the control of cancer an important issue, they must commit themselves to

investment in cancer registration and legislate to safeguard the registries' valuable contribution to the planning of public health services in Europe.

#### Acknowledgements

The research was undertaken with the support of the European Network of Cancer Registries project of the European Commission, Grant No. S12.299682 (2000CVG2—020). The estimates were made using incidence and mortality data from the EUROCIM database of the European Network of Cancer Registries. The contributions of the individual registries is gratefully acknowledged—a list of ENCR Members is attached as an Appendix. We would also like to thank Maria de Ia Trinidad Valdivieso Gonzalez of the Unit of Descriptive Epidemiology, IARC, Lyon for help with the graphical presentations of the results.

# Appendix A. European Network of Cancer Registries (ENCR): list of members

#### A.1. Full Membership

Austria—Cancer Registry of Tyrol, Innsbruck (Dr Wilhelm Oberaigner); Statistik Österreich, Wien (Dr Jeanette Klimont).

Belgium—National Cancer Registry, Brussels (Dr Margareta Haelterman); Limburg Cancer Registry, Hasselt (Dr Frank Buntinx).

Denmark—Department of Cancer Prevention & Documentation, Copenhagen (Dr Hans Storm).

Finland—Finnish Cancer Registry, Helsinki (Dr Lyly Teppo).

France—Registre des Cancers du Tarn, Albi (Dr Martine Sauvage); Registre du Cancer de la Somme, Amiens (Pr. A. Dubreuil); Registre des Tumeurs du Doubs, Besançon (Dr Patrick Arveux); Registre Général des Tumeurs du Calvados, Caen (Dr J. Mace-Lesec'h); Registre des Tumeurs de la Martinique, Fort-de-France (Dr H. Azaloux); Registre des Cancers du Limousin, Limoges (Prof. A. Vergnenègre); Registre des Cancers de l'Isère, Meylan (Dr François Ménégoz); Registre des Tumeurs de l'Hérault, Montpellier (Prof. Jean-Pierre Daurès); Registre des Cancers du Haut-Rhin, Mulhouse (Dr Antoine Buemi); Registre des Cancers de l'Ile de la Réunion, St Denis (Dr P. Grizeau); Registre Bas-Rhinois des Cancers, Strasbourg, (Prof. Paul Schaffer)

Germany—Gemeinsames Krebsregister der Länder Berlin, Brandenburg, Mecklenburg-Vorpommern; Sachsen-Anhalt und der Freistaaten Sachsen und Thüringen Registerstelle, Berlin (Dr Bettina Eisinger); Krebsregister Bremen/Registerstelle, Bremen (Dr Klaus Giersiepen); Krebsregister/Registerstelle, Darmstadt (Mr Wagner); Epidemiologisches Krebsregister Bayern, Erlangen (Dr Martin Meyer); Hamburg Cancer Registry, Hamburg (Dr Stefan Hentschel); Cancer Registry of Schleswig-Holstein, Lübeck (Dr Alexander Katalinic); Krebsregister Rheinland-Pfalz, Registerstelle, Mainz (Dr Irene Schmidtmann); Tumorregister München, München (Prof. D. Hölzel); Krebsregister Münster, Münster (Dr Volker Krieg); Epidemiologisches Krebsregister, Oldenburg (Mr Joachim Kieschke); Epidemiologisches Krebsregister Saarland, Saarbrücken (Mr Hartwig Ziegler); Epidemiologisches Krebsregister, Stuttgart (Mr Ulrich Batzler).

Greece—Greek Cancer Registry, Athens (Dr E. Stavrakakis).

Crete—Cancer Registry of Crete, Heraklion (Dr I.G. Vlachonikolis).

Ireland—National Cancer Registry, Cork (Dr Harry Comber).

Italy-Registro Tumori di Popoazione, Napoli (Dr Mario Fusco); Cancer Registry of Macerata Province, Camerino (Prof. F. Pannelli); Registro Tumori della Provincia di Ferrara, Ferrara (Dr Stefano Ferretti); Registro Tumori Toscano, Florence (Dr Eugenio Paci); Romagna Cancer Registry, Forli (Dr Dino Amadori); Ligurian Cancer Registry, Genoa (Dr Marina Vercelli); Cancer Registry of Latina Province, Latina (Dr Ettore Conti); Registro Tumori Lombardia, Milan (Dr Franco Berrino); Tumour Registry of Modena Province, Modena (Dr M. Federico); Registro Tumori del Veneto, Padova (Director); Parma Province Cancer Registry, Parma (Dr Giorgio Cocconi); Umbrian Population Cancer Registry, Perugia (Prof. Francesco La Rosa); Ragusa Cancer Registry, Ragusa (Prof. Lorenzo Gafà); Tumour Registry of the Province of Salerno, Salerno (Dr Andrea Donato); Registro Tumori della Provincia di Sassari, Sassari (Dr Mario Budroni); Trieste Cancer Registry, Trieste (Dr Giorgio Stanta) Piedmont Cancer Registry, Torino (Dr Roberto Zanetti); Friuli-Venezia-Giulia Cancer Registry, Venezia (Dr Lorenzo Simonato).

Luxembourg—Registre Morphologique des Tumeurs, Luxembourg (Dr Catherine Capesius).

The Netherlands—Comprehensive Cancer Centre Amsterdam (IKA), Amsterdam (Dr Otto Visser); Comprehensive Cancer Centre South (IKZ), Eindhoven (Dr Jan Willem Coebergh); Comprehensive Cancer Centre Stedendriehoek Twente (IKST), Enschede (Dr Sabine Siesling); Comprehensive Cancer Centre North (IKN), Groningen (Dr Renée Otter); Comprehensive Cancer Centre West (IKW), Leiden (Mrs M.J. Oostindiër); Comprehensive Cancer Centre Limburg (IKL), Maastricht (Dr Sjoerd Adema); Comprehensive Cancer Centre East (IKO), Nijmegen (Dr Jos van Dijck); Comprehensive Cancer Centre Rotterdam (IKR), Rotterdam (Dr Ronald Damhuis); Comprehensive Cancer

Centre Midden-Nederland (IKMN), Utrecht (Dr V.C.M. Kuck-Koot).

Portugal—Registro Oncológico Regional-Zona Centro, Coimbra (Dr Manuel Antonio Silva); Regional Oncological Register, Lisbon (Dr Ana da Costa Miranda); RORENO-Registo Oncológico Regional do Norte, Porto (Dr Ricardo da Luz); Vila Nova de Gaia Cancer Registry, Vila Nova de Gaia (Dr J. Teixera Gomes).

Spain—Registro de Cáncer de Albacete, Albacete (Dr Enrique Almar Marques); Registre de Càncer de Girona, Girona (Dr Angel Izquierdo); Granada Cancer Registry, Granada (Dr Carmen Martínez Garcia); Registro de Cáncer de La Rioja, Logroño (Dr Josefina Perucha González); Registro de Cáncer de Murcia, Murcia (Dr Carmen Navarro Sánchez); Registro de Tumores del Principado de Asturias, Oviedo (Dr Alvaro Cañada Martínez); Registre de Cáncer de Mallorca, Palma de Mallorca (Dr Isabel Garau); Registro de Cáncer de Navarra, Pamplona (Dr Eva Ardanaz); Registro de Cáncer de Guipuzcoa, San Sebastien (Dr María Jesús Michelena): Registro Poblacional de Cáncer de la Comunidad Autónoma de Canarias, Tenerife (Dr Araceli Alemán Herrera); Tarragona Cancer Registry, Tarragona (Dr Joan Borràs); Registro de Cáncer de Euskadi, Vitoria-Gasteiz (Dr Isabel Izarzugaza); Dirección General de Salud Pública, Zaragoza (Dr Julián de la Bárcena Guallar).

Sweden—Oncological Centre, Göteborg (Dr Per-Olof Brogren); South Est Sweden Cancer Registry, Linköping (Dr Kerstin Nordenskjöld); Southern Swedish Regional Tumour Registry, Lund (Dr Torgil Möller); Swedish Cancer Registry, Stockholm (Dr Lotti Barlow); Stockholm-Gotland Regional Tumour Registry, Stockholm (Mrs Shiva Ayoubi); Regional Cancer Registry for Northern Sweden, Umeå (Dr Lena Damber); Regional Oncological Centre, Uppsala (Dr Jörgen Strömquist).

United Kingdom—Northern Ireland Cancer Registry, Northern Ireland (Dr Anna Gavin); West Midlands Cancer Intelligence Unit, Birmingham (Dr G.M. Lawrence); East Anglian Cancer Registry, Cambridge (Dr Tom Davies); Wales Cancer Intelligence & Surveillance Unit, South Glamorgan (Dr J. Steward); Scottish Cancer Intelligence Unit, Scotland (Dr David Brewster); Northern and Yorkshire Cancer Registry and Information Service, Leeds (Prof. David Forman); Mersey and Cheshire Cancer Registry, Liverpool (Dr E.M.I. Williams); Thames Cancer Registry, London (Professor Henrik Møller); Office for National Statistics, London (Dr Michael Quinn); North Western Cancer Registry, Manchester (Prof. Ciaran Woodman); Oxford Cancer Intelligence Unit, Oxford (Dr Monica Roche); Trent Cancer Registry, Sheffield (Dr Hannes Botha)South and West Cancer Intelligence, Winchester Unit (Dr Jenifer Smith)

#### A.2. Associate Membership

Albania—Cancer Registry, Tirana (Dr Ferdinant Jorgoni).

Armenia—Department of Genetics and Cytology, Yerevan (Dr Armen Nersesyan).

Belarus—Belarus Cancer Registry, Minsk (Dr A.E. Okeanov).

Bermuda—Oncology Services, Hamilton (Ms Margo Rego).

Bulgaria—Bulgarian National Cancer Registry, Sofia (Dr Shemuel Danon).

Croatia—Croatian National Cancer Registry, Zagreb (Dr Marija Strnad).

Cyprus—Cyprus Cancer Registry, Palouriotissa (Dr M. Boyiadzis).

Czech Republic—Cancer Registry of South Moravia, Brno (Dr Edvard Geryk); Univ. Hospital Oncology Institute, Ostrava-Poruba (Dr Frantisek Beska); Czech National Cancer Registry, Prague (Dr V. Mazankova).

Estonia—Estonian Cancer Registry, Tallinn (Dr Tiiu Aareleid).

France—Registre des Tumeurs Digestives, Caen (Dr Hacina Lefèvre); Registre des Hémopathies Malignes en Côte d'Or, Dijon (Dr P.M. Carli); Registre Bourguignon de Pathologie Gynécologique, Dijon (Dr Gilles Chaplain); Registre Bourguignon des Cancer Digestifs, Dijon (Dr Jean Faivre); Registre des Cancers des Voies Aérodigestives Supérieures des Départements du Nord-Pas de Calais, Lille (Prof. Jean-Louis Lefebvre); Registre des Cancers de l'Enfant PACA et Corse, Marseille (Dr J.L. Bernard); Registre des Cancers de Loire-Atlantique, Nantes (Dr Ana Maria Chouillet); Association du Registre des Cancers de l'Enfant de la Région Rhône-Alpes, Saint Etienne (Prof. Fernand Freycon); Service de Pédiatrie Professeur Lauras, Saint Etienne (Dr Claire Berger); Registre des Cancers Digestifs de la Haute-Garonne, Toulouse (Dr P. Pienkowsky); Registre Pédiatrique des Cancers de Lorraine, Vandœuvre (Dr D. Sommelet-Olive); Registre national des leucémies de l'enfant, Villejuif (Dr Jacqueline Clavel) Georgia; Georgian Network of Cancer Registries, Tbilisi (Dr Vasili T. Tkeshelashvili).

Germany—German Register of Childhood Malignancies, Mainz (Prof. J. Michaelis).

Gibraltar—Gibraltar Health Authority, Gibraltar (Dr Vijay Kumar).

Hungary—Hungarian Society for Paediatric Oncology, Budapest (Dr D. Schuler); County Vas Registry, Szombathely (Dr Eszter Kocsis).

Icelandic—Icelandic Cancer Registry, Reykjavik (Dr Hrafn Tulinius).

Italy—Registro dei Tumori Infantili del Piemonte, Torino (Dr C. Magnani).

Kyrgyzstan—Kyrgyz Cancer Registry, Bishkek (Dr Elmira Erkinbayeva).

Latvia—Latvian Cancer Registry, Riga (Dr Aivars Stengrevics).

Lithuania—Lithuanian Cancer Registry, Vilnius (Dr Juozas Kurtinaitis).

Malta—Malta National Cancer Registry, Guardamangia (Dr Miriam Dalmas).

Norway—The Cancer Registry of Norway, Oslo (Dr Aage Andersen).

Poland—Cracow City and District Cancer Registry, Cracow (Dr Jadwiga Rachtan); Katowice District Cancer Registry, Gliwice (Prof. Brunon Zemla); Cancer Registry of Kielce, Kielce (Dr Ryszard Mezyk); Regional Cancer Registry, Opole (Dr Kazimierz Drosik/Dr Teresa Gebauer); Warsaw Cancer Registry, Warsaw (Professor Zbigniew Wronkowski/Dr Maria Zwierko); Polish Cancer Registry, Warsaw (Prof. Witold Zatonski); Lower Silesian Cancer Registry, Wroclaw (Mr Jerzy Blaszczyk).

Romania—Institute of Public Health, Bucharest (Dr Magdalena Patruleasa); Cluj County Cancer Registry, Cluj-Napoca (Dr Adreana Porutiu); Territorial Cancer Registry, Oradea (Dr Vasile Pacurar).

Russian Federation—Cancer Registry of St Petersburg, St Petersburg (Dr V.M. Merabishvili).

San Marino—San Marino Cancer Registry, Borgo Maggiore (Dr Stefano Pretolani).

Slovakia—National Cancer Registry of Slovakia, Bratislava (Dr Ivan Plesko).

Slovenia—Cancer Registry of Slovenia, Ljubljana (Prof Vera Pompe-Kirn).

Spain—Childhood Cancer Registry of Valencia Province, Valencia (Dr Juanjo Abellán); Spanish National Childhood Cancer Registry, Valencia (Prof. Rafael Peris-Bonet).

Switzerland—Basel Cancer Registry, Basel (Prof. Joachim Torhorst); Kantonales Krebsregister Graubünden und Glarus, Chur (Dr Jürg Allemann); Registre Genevois des Tumeurs, Genève (Dr Christine Bouchardy); Registre Vaudois des Tumeurs, Lausanne (Dr Fabio Levi); Registro dei Tumori del Cantone Ticino, Locarno (Dr Andrea Bordoni); Registre Neuchatelois des Tumeurs, Neuchâtel (Dr Fabio Levi); Registre Valaisan des Tumeurs, Sion (Dr F. Joris); Krebsregister St Gallen Appenzell, St Gallen (Dr Thomas Fisch); Cancer Registry of the Canton of Zürich, Zürich (Dr George Schüler).

Turkey—Izmir Cancer Registry, Izmir (Dr Caner Fidaner).

Ukraine—Childhood Cancer in the Donetsk Region, Donetsk (Dr I. Zhurilo) Ukrainian National Cancer Registry, Kiev (Dr Luidmila Goulak).

United Kingdom—Childhood Cancer Research Group, Oxford (Dr Gerald Draper).

Yugoslavia—Cancer Registry of Voivodina, Serbia (Dr Marica Mikov) Cancer Registry for Central Serbia, Belgrade (Dr Andjelka Vukicevic).

#### References

- 1. European Network of Cancer Registries. *EUROCIM Version 4.0*. *European Incidence Database V2.3*. Lyon, ENCR, 2001.
- Jensen OM, Estève J, Møller H, Renard H. Cancer in the European Community and its member states. Eur J Cancer 1990, 26, 1167–1256.
- Black RJ, Bray F, Ferlay J, Parkin DM. Cancer incidence and mortality in the European Union: cancer registry data and estimates of national incidence for 1990. Eur J Cancer 1997, 33, 1075–1107.
- Parkin DM, Whelan SL, Ferlay J, Raymond L, Young J. Cancer Incidence in Five Continents, vol. VII. IARC Scientific Publications No. 143. Lyon, IARC Press, 1997.
- Francis B, Green M, Payne C, eds. The GLIM System. Release 4 Manual. Oxford, Clarendon Press, 1993.
- Ferlay J, Parkin DM, Pisani P. GLOBOCAN 1: Cancer Incidence, Mortality and Prevalence Worldwide, Version 1.0. IARC Cancer Base No. 3. Lyon, IARC Press, 1998.
- Ferlay J, Bray F, Sankila R, Parkin DM. EUCAN: Cancer in the European Union, 1995. Version 2.0. IARC Cancer Base No. 4. Lyon, IARC Press, 1999.
- Parkin DM, Chen VW, Ferlay J, Galceran J, Storm HH, Whelan SL, eds. Comparability and Quality Control in Cancer Registration. IARC Technical Report No. 19. Lyon, IARC, 1998.
- International Agency for Research on Cancer. Tobacco Smoking. Evaluation of Carcinogenic Risks to Humans, vol. 38. Lyon, IARC Press, 1986.
- International Agency for Research on Cancer. Alcohol Drinking. Evaluation of Carcinogenic Risks to Humans, vol. 44. Lyon, IARC Press, 1988.
- Pisani P. Avoidable Cancer in Europe: Estimating Avoidable Fractions. Europe Against Cancer Programme (EU contract SOC 96 200504). Lyon, December 2000.
- La Vecchia C, Tavani A, Franceschi 5, Levi F, Corrao G, Negri E. Epidemiology and prevention of oral cancer. *Oral Oncol* 1997, 33, 302–312.
- Berrino F, Capocaccia R, Estève J, et al. Survival of Cancer Patients in Europe: The EUROCARE-2 Study. IARC Scientific Publication No. 151. Lyon, IARC, 1999.
- Vaughan TL, Shapiro JA, Burt RD, et al. Nasopharyngeal cancer in a low-risk population: defining risk factors by histological type. Cancer Epidemiol Biomarkers Prev 1996, 5, 587–593.
- Hildesheim A, Levine PH. Etiology of nasopharyngeal carcinoma: a review. *Epidemiol Rev* 1993, 15, 466–485.
- Hirayama T. Descriptive and analytical epidemiology of nasopharyngeal cancer. In de Thé G, Ito Y, eds. Nasopharyngeal Carcinoma: Etiology and Control. IARC Scientific Publications No. 20. Lyon, IARC, 1978, 167–189.
- Bouchardy C, Parkin DM, Wanner P, Khlat M. Cancer mortality among north African migrants in France. *Int J Epidemiol* 1996, 25, 5–13.
- Parkin DM, Iscovich J. Risk of cancer in migrants and their descendants in Israel: II. Carcinomas and germ-cell tumours. *Int* J Cancer 1997, 70, 654–660.
- Ekstrom AM, Signorello LB, Hansson LE, Bergstrom R, Lindgren A, Nyren O. Evaluating gastric cancer misclassification: a potential explanation for the rise in cardia cancer incidence. *J Natl Cancer Inst* 1999, 91, 786–790.
- Castellsague X, Munoz N, De Stefani E, et al. Independent and joint effects of tobacco smoking and alcohol drinking on the risk of esophageal cancer in men and women. Int J Cancer 1999, 82, 657–664.
- Steinmetz KA, Potter JD. Vegetables, fruit, and cancer. I. Epidemiology. Cancer Causes Control 1991, 2, 325–357.

- Brown LM, Swanson CA, Gridley G, et al. Adenocarcinoma of the esophagus: role of obesity and diet. J Natl Cancer Inst 1995, 87, 104–109.
- Launoy G, Milan C, Day NE. Diet and squamous-cell cancer of the oesophagus: a French multicentre case-control study. *Int J Cancer* 1998, 30, 7–12.
- Correa P, Chen VW. Gastric cancer. Cancer Surv 1994, 19-20, 55-76.
- Correa P. Human gastric carcinogenesis: a multistep and multifactorial process—First American Cancer Society Award Lecture on Cancer Epidemiology and Prevention. *Cancer Res* 1992, 52, 6735–6740.
- World Cancer Research Fund. Food, Nutrition and the Prevention of Cancer: A Global Perspective. Washington, World Cancer Research Fund/American Institute for Cancer Research, 1997.
- Ferlay J, Bray F, Pisani P, Parkin DM. GLOBOCAN 2000: Cancer Incidence, Mortality and Prevalence Worldwide, Version 1.0. IARC CancerBase No. 5. Lyon, IARC Press, 2001.
- International Agency for Research on Cancer. Hepatitis Viruses. Evaluation of Carcinogenic Risks to Humans, Vol. 59. Lyon, IARC, 1994.
- Boyle P, Hsieh CC, Maisonneuve P, et al. Epidemiology of pancreas cancer. Int J Pancreatol 1989, 5, 327–346.
- Parkin DM, Pisani P, Lopez AD, Masuyer E. At least one in seven cases of cancer is caused by smoking. Global Estimates for 1985. *Int J Cancer* 1994, 59, 494–504.
- Lopez-Abente G, Pollan M, de la Iglesia P, Ruiz M. Characterization of the lung cancer epidemic in the European Union (1970–1990). Cancer Epidemiol Biomarkers Prev 1995, 4, 813–820.
- Wynder EL, Muscat JE. The changing epidemiology of smoking and lung cancer histology. *Environ Health Perspect* 1995, 103, 143–148.
- Elwood JM, Gallagher RP. Body site distribution of cutaneous malignant melanoma in relationship to patterns of sun exposure. *Int J Cancer* 1998, 78, 276–280.
- Richard MA, Grob JJ, Avril MF, et al. Delays in diagnosis and melanoma prognosis (I): the role of patients. Int J Cancer 2000, 89, 271–279.
- McPherson K, Steel CM, Dixon JM. Breast cancer-epidemiology, risk factors, and genetics. Br Med J 2000, 321, 624–628.
- Thomson CS, Hole DJ, Twelves CJ, Brewster DH, Black RJ. Prognostic factors in women with breast cancer: distribution by socioeconomic status and effect on differences in survival. *J Epi*demiol Community Health 2001, 55, 308–315.
- 37. van den Akker-van Marie E, de Koning H, Boer R, van der Maas P. Reduction in breast cancer mortality due to the introduction of mass screening in The Netherlands: comparison with the United Kingdom. *J Med Screen* 1999, 6, 30–34.
- 38. Blanks RG, Moss SM, McGahan CE, Quinn MJ, Babb PJ. Effect of NHS breast screening programme on mortality from breast cancer in England and Wales, 1990–8: comparison of observed with predicted mortality. *Br Med J* 2000, 321, 665–669.
- Walboomers JM, Jacobs MV, Manos MM, et al. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. J Pathol 1999, 189, 12–19.
- Kelsey JL, Whittemore AS. Epidemiology and primary prevention of cancers of the breast, endometrium, and ovary. A brief overview. *Ann Epidemiol* 1994, 4, 89–95.
- Bergstrom A, Pisani P, Tenet V, Wolk A, Adami HO. Overweight as an avoidable cause of cancer in Europe. *Int J Cancer* 2001, 91, 421–430.
- Holschneider CH, Berek JS. Ovarian cancer: epidemiology, biology, and prognostic factors. Semin Surg Oncol 2000, 19, 3–10.
- Feuer EJ, Merrill RM, Hankey BF. Cancer surveillance series: interpreting trends in prostate cancer—part II: cause of death misclassification and the recent rise and fall in prostate cancer mortality. J Natl Cancer Inst 1999, 91, 1025–1032.

- 44. Shibata A, Whittemore AS. Genetic predisposition to prostate cancer: possible explanations for ethnic differences in risk. *Prostate* 1997, **32**, 65–72.
- 45. Buetow SA. Epidemiology of testicular cancer. *Epidemiol Rev* 1995, **17**, 433–449.
- Johansson SL, Cohen SM. Epidemiology and etiology of bladder cancer. Semin Surg Oncol 1997, 13, 291–298.
- 47. Franceschi S, La Vecchia C. Thyroid cancer. *Cancer Surv* 1994, 19-20, 393–422.
- 48. Hardell L, Lindstrom G, van Bavel B, Fredrikson M, Liljegren G. Some aspects of the etiology of non-Hodgkin lymphoma. *Environ Health Perspect* 1998, **106**(Suppl. 2), 679–681.
- Obrams CI, Grufferman S. Epidemiology of HIV associated non-Hodgkin lymphoma. *Cancer Surv* 1991, 10, 91–102.
- 50. Harris NL. The many faces of Hodgkin disease around the

- world: what have we learned from its pathology? *Ann Oncol* 1998, **9**(Suppl. 5), S45–S56.
- Ferraris AM, Racchi O, Rapezzi D, Gaetani GF, Boffetta P. Familial Hodgkin disease: a disease of young adulthood? *Ann Hematol* 1997, 74, 131–134.
- 52. Cuzick J. Multiple myeloma. Cancer Surv 1994, 19-20, 455-474.
- 53. Kinlen U. Leukaemia. Cancer Surv 1994, 19-20, 475-491.
- Greaves MF, Alexander FE. An infectious etiology for common acute lymphoblastic leukemia in childhood? *Leukaemia* 1993, 7, 349–360.
- Percy C, Muir C. The international comparability of cancer mortality data. Results of an international death certificate study. *Am J Epidemiol* 1989, 129, 934–946.
- 56. Parkin DM, Bray FI, Devesa SS. Cancer burden in the year 2000. The global picture. *Eur J Cancer* 2001, **37**(Suppl. 8), S4–S66.