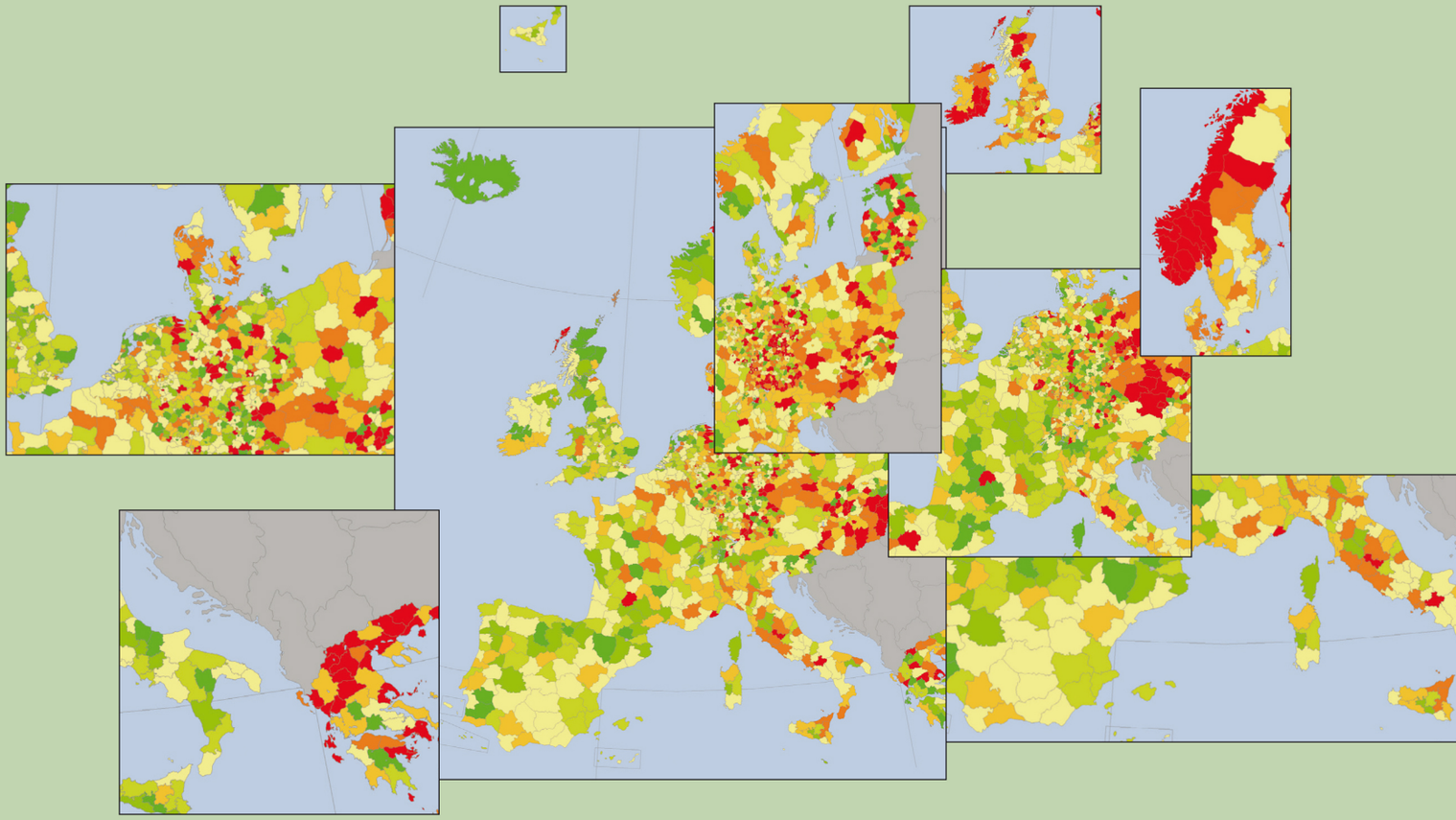
International Agency for Research on Cancer
Centre International de Recherche sur le Cancer



Atlas of Cancer Mortality in the European Union and the European Economic Area 1993-1997

Edited by
P Boyle and M Smans

IARC Scientific Publications No. 159

ATLAS

OF

CANCER MORTALITY

IN THE

EUROPEAN UNION

AND THE

EUROPEAN ECONOMIC AREA

1993-1997

Published by the International Agency for Research on Cancer,
150 cours Albert Thomas, 69372 Lyon Cedex 08, France

Distributed by
WHO Press, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland (tel: +41 22 791 3264; fax: +41 22 791 4857; email: bookorders@who.int).

IARC Library Cataloguing in Publication Data

Boyle, P. (Peter)
Atlas of cancer mortality in the European Union and the European Economic Area 1993-1997 / edited by P Boyle and M Smans

(IARC Scientific Publications ; 159)

1. Neoplasms - epidemiology 2. Neoplasms - mortality 3. Europe
4. European Union I. Smans, M. II. Title III. Series

ISBN 978-92-832-2159-3 (NLM Classification: W1)

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IARC Scientific Publications No. 159

International Agency for Research on Cancer
Lyon, France
2008

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FOREWORD

When the Europe Against Cancer programme was launched at a meeting of the Heads of State or Government of the European Economic Community countries in Milan, Italy, in 1985, it undertook an ambitious target to reduce cancer deaths in the Member States by 15% by the year 2000. During the lifespan of the Europe Against Cancer programme, cancer mortality in the (fifteen) Member States of the European Union started to decline and there were just over 935,000 cancer deaths in the European Union in 2000. This was about 98,000 (9.5%) fewer cancer deaths than expected had the original mortality rates not changed (Boyle, 2008) and it has been confirmed that downward trends are continuing in the current, enlarged, European Union (Bosetti et al, 2008).

Such progress against cancer is very reassuring.

The mortality rates of most cancers are falling in most countries, and in some countries rates which were rising have stabilised. While this is good news, it is tinged with the sad realisation that the stable rate achieved among men in Hungary is twice as high as that in Sweden (Quinn et al, 2003). These high rates are just part of the frightening picture of health disparities between "old" Europe (the first 15 Member States of the European Union: Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxemburg, Netherlands, Portugal, Spain, Sweden and the United Kingdom) and "new" Europe (Bulgaria, Czech Republic, Estonia, Hungary, Latvia, Lithuania, Poland, Romania, Slovakia and Slovenia).

Professor Witold Zatonski (Warsaw) has undertaken and completed a major study in central and eastern Europe (HEM Closing the Gap Project, EC action number 2003121) demonstrating that there is a huge gap in health between the ten accession countries in central and eastern Europe and the 15 Member States in western and northern Europe. These differences are frequently in evidence when the maps of cancer mortality presented in this atlas are examined. At the beginning of the 21st century, the extent of inequality in health status between new EU members from central and eastern Europe and the old EU members is not acceptable. The European Union is moving towards a "Single Europe", but there is an obvious two-speed track in Public Health which requires urgent and serious attention.

The issue is compounded by the ageing of the population in the European Union. Given the strong association of cancer incidence and mortality with age, this will lead to a substantial increase in the cancer burden (Quinn et al, 2003). There was an increase in the estimated number of cases of cancer diagnosed in Europe (all Europe, not only the EU) of 300,000 between 2004 (Boyle and Ferlay, 2005) and 2006 (Ferlay et al, 2007).

The decreasing risk of dying from most forms of cancer in the European Union is a major success but does not allow any room for complacency. The disparity between the health status in the populations of western and northern Europe compared with these of central and eastern Europe requires significant

and speedy remedial intervention. There is an urgent need to undertake research in central and eastern Europe to identify the causes of the excess cancer (and other chronic disease) mortality rates; to monitor through time changes in biomarkers of chronic disease in response to public health policy; and to create resources for capacity building in research and training of researchers in the whole of Europe. In addition, it is almost too late to take action to be in a position to cope with the increasing cancer burden which will arise throughout Europe due to the ageing population.

Umberto Veronesi MD
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EDITORS' FOREWORD

Cancer is the second-most common cause of death (after cardiovascular diseases) in the majority of European countries and cancer control is clearly one of the biggest challenges of the 21st century. It is an international issue and, thankfully, cancer epidemiology is one of the most fruitful areas of international cooperation in cancer research. The development of several new areas of cancer control, and in particular in cancer epidemiology and prevention, in Europe during the last few decades is closely related to co-operation among institutions and scientists from many countries.

One of the most interesting features of cancer in Europe is its geographical patterns. Studies of the geographical patterns of cancer distribution in Europe have been carried out for over twenty years now. After several national atlases published in the 1980s, international atlases were published in the early 1990s, covering the countries of the European Economic Community (Boyle, Smans and Muir, 1994) and those of central and eastern Europe (Zatonski et al, 1996). One clear message emerges from these works: that cancer risk does not respect national frontiers.

This atlas is the result of the collaboration of a Scientific Committee and the National Vital Statistics Offices in each of the 28 countries covered. The five years covered by the atlas (1993-1997) provide mortality rates based on 5.5 million cancer death, representing the cancer experience in a population with 2.2 billion person-years of risk. The aim of this publication is not only to present cancer patterns in Europe but also to stimulate further studies on cancer epidemiology and generate hypotheses for analytical epidemiological studies.

Modern cancer mapping and the introduction of international cancer atlases owe much to the pioneering ideas of Calum S Muir, formerly Chief of Descriptive Epidemiology at the International Agency for Research on Cancer. Many of the key participants in this project worked on the developments of cancer mapping with Calum. It is great pleasure to acknowledge his important contribution and to dedicate this atlas to his memory.

It was never our idea when mapping cancer to produce pictures suitable merely for a coffee table book. It is our intention and desire that this publication should draw the attention of medical practitioners, scientists, and politicians involved in public health care to important features of cancer in Europe, stimulate further study and lead to steps being taken to prevent the disease. Increasing prospects for prevention is, after all, a major goal in research on cancer.

Peter Boyle
Michel Smans

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CHAPTER I

AIMS AND OBJECTIVES

The aims and objectives of producing a cancer atlas have not changed in principle since the previous Cancer Atlas of the European Economic Community was completed (Smans, Muir & Boyle, 1992). But with rising trends in the incidence of many cancers, and the general shift in the age distribution of the population towards the elderly – in whom most cancers occur – it is essential that all available information be used to improve prospects for the prevention and control of cancer.

Maps may be topographic or thematic. The former display the physical features, the location of cities and towns, roads, railways, and the like, while the latter concentrate on displaying the geographical occurrence and variation of a single phenomenon – the *theme* of the map. In this atlas the theme is cancer mortality; the history of thematic mapping has been described in an outstanding monograph (Robinson, 1982).

The geographical representation of cancer on maps describes the *cancer scenery* of a country (Frenztel-Beyme et al., 1979). As cancer occurs in people, not geographical areas, the initial purpose of a cancer atlas lies in the identification of geographical areas that require more detailed study and, above all, the formulation of aetiological hypotheses to account for the observed differences. These hypotheses can then be pursued by appropriate analytical and environmental studies. Furthermore, priorities for cancer prevention can be better identified and tailored to the local needs.

These aims are attainable. Over 2,000 years ago, Hippocrates listed the kinds of question which should be asked when relating disease to environment and geographical distribution. A classical and frequently cited example comes from an outbreak of cholera in London in 1854. John Snow, by recording and mapping the addresses of the victims of the epidemic, was able to show that the disease was much commoner in people drinking water supplied by the Southwark and Vauxhall Water Company and, more precisely, from a pump in Broad Street, than in those drinking water from other sources. Removing the handle from the Broad Street pump effectively stopped the epidemic.

The first map for cancer was apparently produced for females in England and Wales by Haviland in 1875. Haviland, who observed that 'by studying the geographical laws of disease we shall know where to find its exciting as well as its predisposing causes and how to avoid it', was 'struck by the definite character of the arrangement that the mortality assumes throughout the country'. Stocks, who mapped cancer mortality in England and Wales in the 1930s, later attempted to correlate the distribution, as had Haviland (1875), with the mineral content, notably zinc and cadmium, of the soil (Stocks, 1928, 1936, 1937, 1939). Howe (1963, 1970) published national disease atlases in the United Kingdom, and described the historical mapping of disease.

There was a renaissance of cancer mapping when Burbank (1971) published computer-drawn maps of the distribution of cancer mortality for the 49 states which comprised the United States of America. The state was soon recognised as being too large an areal unit, which resulted in the publication of a County Cancer Atlas in two

volumes, one for whites and one for non-whites (Mason et al., 1975, 1976).

The present atlas, based on over 5.5 million deaths from cancer and 2.2 billion person-years of observation, reveals many distinctive patterns of cancer mortality distribution within the European Union and the European Economic Area (EU-EEA) Member States which clearly and urgently require further study from the standpoint of causation. The maps may also be used as an aid in planning the provision of the health services required to combat this disease and, importantly, identifying sub-national areas where specific interventions are required to reduce mortality from cancer.

The maps

The sources of the data and the methods of computation and technical details concerning the production of the maps are outlined in Chapter 2. The maps present age-standardised mortality rates by sex (see below) for 1,278 areas designated as being at levels II or III as defined by the European Commission (EC) statistical services. These areas, identified by a five-character code, frequently have a national equivalent such as Département in France, county in England and Wales, or Kreise in Germany. More details of the regions used in each country are given in the relevant country-specific section in Chapter 4 (below).

For a given cancer the main map shows the higher rates in shades of orange/red, the median rates in yellow and the lower rates in shades of green (see Kemp et al., 1985, for a fuller explanation). The distribution of the mortality rates is shown in the top right corner of each map. It should be borne in mind that in the main maps a given colour will represent a different range of values according to the site of cancer. In addition, a smaller map is presented (in the lower right of the chart) in which each colour represents the same range of values for every cancer site. This indicates whether mortality rates for that site were generally high (darker colours) or low (lighter colours). Information from the statistical tables on which the maps are based can be obtained from IARC.

Validity of the data in this atlas

Perhaps the most important requirement of a cancer mortality atlas is that it should present the geographical mortality patterns with a minimum of distortion. Chapter 3 thus contains information which will alert readers to possible sources of bias; many of the factors influencing interpretation are also examined in much greater detail elsewhere in the Atlas.

Availability of cancer mortality data

Mortality data were made available for the period 1993-1997 from all the 25 Member States of the European (as of May 2004) and three Member States of the European Economic Area (Iceland, Norway and Switzerland). This is a marked increase over the nine countries included in the previous atlas (Smans, Muir & Boyle, 1992). One important consequence is that there is much more comparable information available about cancer mortality rates and patterns in the Nordic Countries (Iceland, Norway, Sweden, Finland and Denmark), the Baltic States (Estonia, Latvia and Lithuania), central Europe (Czech Republic, Hungary, Poland, Slovakia and Slovenia) and around the Mediterranean (Cyprus, Greece, France, Italy, Malta and Spain). Geographically broader and more meaningful assessments of cancer risk can, therefore, be made now than previously.

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CHAPTER 2

THE MAPPING OF CANCER

Cancer is a group of diseases which possess a common feature – the uncontrolled growth of the cells that make up the part of the body affected (Cairns, 1977). The cancers described in this atlas are defined by the 9th Revision of the International Classification of Diseases (WHO, 1977), hereafter referred to as ICD-9 (Table 2.1). The ICD-9 code numbers for the cancers arising in the various sites (organs) are used in the text, tables and maps.

Table 2.1: Cancer sites and codes in ICD-8, ICD-9 and ICD-10

Cancer Sites	ICD8 code	ICD9 code	ICD10 code
Oral cavity and pharynx (Oral)	140-149	140-149	C00-C14
Oesophagus	150	150	C15
Stomach	151	151	C16
Small intestine	152	152	C17
Colon, rectum and anus (Large bowel)	153-154	153-154, 159.0	C18-C21, C26.0
Liver (primary)	155, 197.8	155	C22
Gallbladder and bile ducts	156	156	C23-C24
Pancreas	157	157	C25
Larynx	161	161	C32
Trachea, bronchus and lung	162	162	C33-C34
Pleura (mesothelioma)	163	163	C38.1-C38.4, C45
Melanoma of the skin	172	172	C43
Non melanoma skin cancer	173	173	C44, C46
Breast (female)	174	174	C50
Cervix uteri	180	180	C53
Corpus uteri	182	182	C54-C55
All uterus	180-182	179-182	C53-C55, C58
Ovary	183	183	C56, C57.0-C57.4, C57.8
Prostate	185	185	C61
Testis	186	186	C62
Bladder	188	188	C67
Kidney (urinary tract)	189	189	C64-C66, C68
Brain and central nervous system	191-192	191-192	C70-C72
Thyroid	193	193	C73
Hodgkin's disease	201	201	C81
Non-Hodgkin's lymphoma	200, 202	200, 202	C82-C85, C96
Multiple myeloma	203	203	C90
Leukaemia	204-207	204-208	C91-C95 less C91.4 & C94.4/5
Other and ill-defined	195-199	195-199	C76-C80
All forms of cancer	140-207	140-208	C00-C97

Mortality

Mortality is the number of deaths from cases of cancer occurring in a given population in a particular time period, usually expressed as a rate per 100,000 population per annum.

Choice of area size

There are constraints on the choice of areal unit that are outside the control of the cancer mapper. The intention was to choose the smallest administrative unit for which population information was available by sex and age group, subject to it being sufficiently large that it could be expected to provide reliable cancer mortality rates over a period short enough for time trends to be unimportant.

The areas mapped in this atlas conform to at least level II of the European Commission (EC) statistical services, with finer subdivision where population numbers are great enough. Only 47 of the 1,278 areas have less than 100,000 person years of risk, the smallest value (around 30,000 person years) occurring in Hiiuma Island to the west of the mainland of Estonia.

Use of age-standardised rates

The crude rate gives the burden of cancer in terms of the number of deaths from cancer per hundred thousand population in each area or country. However, rates of malignant disease are generally higher in older people and so comparison of the crude rates between areas can be misleading if the age structures of the populations in areas differ. Taking median age as a simple indicator of differences in age-structure between regions, for males the overall median age was 35.0 years with a range across the small areas of 25.8 to 43.5; for females, the overall median was 38.2 years with range of 27.2 to 48.8. The maps of the median ages for males and females illustrate the wide variation which exists within Europe (Maps 2.1 and 2.2).

To overcome this problem, age-standardisation is undertaken. There are two widely used methods of standardisation – direct and indirect, each with its own advantages and disadvantages. The resultant statistic – an age-standardised mortality rate per 100,000 population per annum – is taken to represent the risk of dying from cancer in a particular area. In this atlas all rates, unless otherwise stated, are average annual rates per 100,000 population, directly age-standardised to the world standard population (SICE, 1964) as used, after adaptation, in successive volumes of Cancer Incidence in Five Continents (Doll et al., 1966). The methodology of age-standardisation has been explained in detail elsewhere (Boyle & Parkin, 1991). For brevity they are presented in the text as figures only, e.g. "mortality from stomach cancer in females in Belgium was 3.5" rather than "the average annual age-standardised mortality from stomach cancer in females in Belgium was 3.5 per 100,000".

There is a great temptation, when a series of maps is being produced for a single country, to standardise to its own population, as this results in standardised rates which are close to the current crude mortality rates. However, for the present atlas this would have implied calculation of an EU-EEA standard population based on EU-EEA membership at the time of data collection. However, the age structure varies among the constituent countries, the EU has increased in size and is likely to expand further, and the age-structure of its constituent population changes over time. So such a solution has considerable disadvantages, principally lack of comparability of the standardised rates over time. Hence the use of the single and unchanging world standard population in this atlas; its use also permits comparison with a wide variety of data published elsewhere. Further, it is possible to compare not only the rates for one site of cancer in each of the areas mapped but also to compare them directly with those for another form of cancer. As the world standard population has a younger age structure than that of the EU-EEA, the age-standardised rates are usually lower than the corresponding crude (non-standardised) rates.

Indirect standardisation, as the name implies, also takes population age-structure into account. Here, the age-specific rates for a particular cancer for the EU-EEA as a whole are applied to the population of each area mapped and the number of cancer deaths to be expected if that region had the same mortality as the EU-EEA as a whole is computed. This number is compared with the number actually observed and the ratio of observed to expected is presented as a percentage. The

EU-EEA value is taken to be 100. The advantage of this method is that it reduces distortions associated with small numbers of cancers in small populations. However, as the populations for the area covered in this atlas generally yield a minimum of 100,000 person-years, this advantage is less important. The disadvantages of indirect standardisation are that it is not strictly valid to compare rates for individual areas for a particular cancer site; and it is not possible to compare rates for different cancer sites (as the standardised rates are all based on an overall average of 100 for every site). Also, it is difficult to follow trends over time, particularly when EU-EEA membership changes.

Illustrating differences between areas

The maps indicate the level of age-standardised mortality in the 1,278 areas mapped. Colour has been used to distinguish between districts with high, medium and low mortality rates. In the main maps for each cancer, a relative scale using seven classes for each cancer was based on the percentiles of the distribution of rates in areas weighted by the population size in each region. The following cut-off points were used: 5% of the population with the lowest rates, the next 10%, the next 20%, the middle 30%, the next 20%, the next 10%, and ending with the 5% of the population with the highest rates. The cut-off points for the seven classes differ from one cancer to another. The classes are depicted by three shades of orange-red for the higher rates, yellow for the mid-range and three shades of green for the lower rates. The scale at the top right-hand corner of each map shows the range of mortality rates for that site.

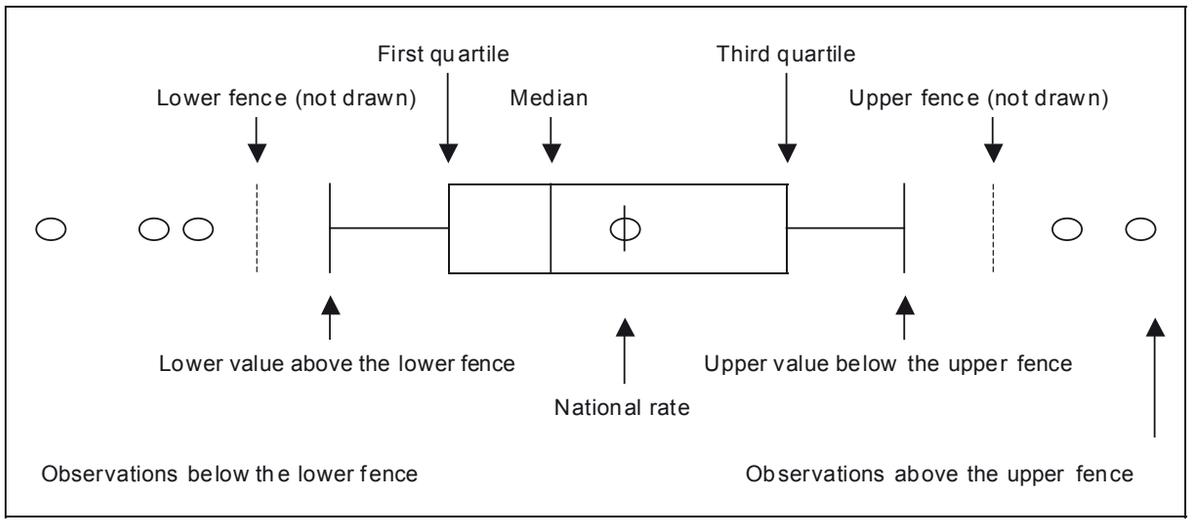
On all maps, the upper right hand figure presents box and whiskers plots for each country based on rates at the EU-EEA level II or III areas. The following statistics are represented: the national rate, median, first quartile and third quartile (Figure 2.1). Moreover, outliers are also shown that are outside the so-called fences (not drawn) which are defined as follows:

Inter-quartile range (IQR) = Third quartile – First quartile
Upper fence = Third quartile + 1.5 x IQR
Lower fence = First quartile – 1.5 x IQR

Finally, the two whiskers represent the lower value above the lower fence and the upper value below the upper fence.

It must be borne in mind that because the allocation of colour is relative to the median mortality rate for each cancer, all of the main maps contain roughly the same proportions of areas of each colour – whether the cancer has high or low average mortality, and whether the absolute range in variability is wide or narrow. The maps for the various cancers differ in appearance, principally of course because the high and low rates occur in different areas. But in addition the large, sparsely populated areas have greater visual impact than the smaller, less densely populated ones, so the proportions of high and low rates that are in these types of areas also affects the appearance of the maps.

Figure 2.1: Schematic representation of box and whiskers plots and location of fences



The smaller maps presented in the lower right of each chart also illustrate the variability in mortality rates, but using the *same* (21 point) colour scale for every cancer site. In this set of maps, those for cancers with generally low mortality rates are predominantly pale (yellow) and those for cancers with generally high rates are darker (red and brown). These maps enable rapid visual comparisons to be made between rates for males and females for the same cancer, and between different cancers. They also give an indication of the absolute range in the variability of mortality from each cancer: if the range in values is narrow, the map will be mostly one colour, but if the range is wide the map will be multi-coloured.

Patterns of cancer distribution

As will become evident in the descriptions of the cancer patterns in Chapter 6, emphasis has been placed on painting a broad canvas rather than picking out isolated areas of high mortality. However, while there is frequently a tendency to dismiss an isolated area of high mortality as being due to statistical chance, each such area should be examined critically to see whether any reasons for a high mortality are likely to exist. If a pattern for isolated areas becomes evident, then such close enquiry becomes all the more essential. For example, many years ago, the concentration of deaths from mesothelioma in towns with shipbuilding industries was eventually related to the industrial use of asbestos.

It is also instructive to look at the spatial distribution of cancer of the liver (ICD-8 155) in males in the 40 areas of the Netherlands depicted in the cancer atlas for that country (Netherlands Central Bureau of Statistics, 1980). This shows one area with a standardised mortality ratio which is significantly above the national average at the 5% probability level and a further area significantly above the national average at the 10% level. Similarly, there are two areas which were significantly lower at the 10% and 5% levels. Such a finding is exactly what one would expect from the laws of statistical probability and this phenomenon must constantly be borne in mind. In this atlas 1,278 areas are compared in each map: by chance alone around 60 areas in each map could be expected to have mortality rates significantly greater than the EU-EEA average for that cancer and a similar number to have rates significantly lower than the average at the 5% level of statistical significance.

The presence of a group of areas with higher or lower than average cancer mortality which are contiguous or close together is always of interest as this suggests the presence or absence of risk factors common to these areas. For further discussion, see Kemp et al. (1985).

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CHAPTER 3

CAUSE OF DEATH STATISTICS: PRODUCTION PROCESS, QUALITY AND INTERNATIONAL COMPARABILITY

Eric Jougla, Florence Rossolin, Gérard Pavillon

Background

The data analysed in this atlas are based on national causes of death (COD) statistics. COD statistics constitute a major source for comparing the health characteristics of European populations. The popularity of COD data as indicators for the status of health is readily explained by their availability. International cause of death data are published annually by international agencies such as the Statistical Office of the European Communities (EUROSTAT) or as the World Health Organization (WHO) using standardised lists of categories. COD data often provide the only information available for comparison of health status both between countries and within countries at a regional level. In each country, the production of these data involves two main stages: certification and coding of causes of death.

Results of comparisons presented in this atlas may be used as a starting point to investigate the sources of observed differences, (e.g. behavioural, cultural, ecological factors) or to assess the effectiveness of health prevention policies and the quality of health care. Because COD statistics include all deaths, the problems of bias and lack of representativeness due to sampling are avoided. Furthermore, some procedures for the collection of COD data are relatively homogeneous between European countries (WHO death certificate model, International Classification of Diseases, etc). In spite of these common features, important quality and comparability issues remain. Before attempting to interpret inter-country or regional differences in mortality rates in terms of aetiological factors, it is important to be aware of the possible biases affecting the comparability of the data.

Sources

This chapter is based on information collected through various studies undertaken within the context of the European Commission (EC), whose statistical agency, EUROSTAT has created a specific Task Force dedicated to cause of death statistics. The main objective of this Task Force is to improve the quality and comparability of cause of death data within the EU. DG SANCO (that part of the EC dedicated to health) has supported this type of research through the Health Monitoring Program. A specific recent DG SANCO project has focused on the problem of comparability of COD statistics (Jougla et al., 2001). The objective was to complete investigations on certification practices among EU members and to make recommendations to Member States on improvement in data quality and comparability. This work was carried out by a network of experts from all the EU countries. The information considered consisted of (i) a survey on certification practices in each country (situation and opinion); and (ii) an international literature review of papers on quality and comparability of cause of death statistics. For codification, EUROSTAT funded a specific study to describe the existing coding systems (Pavillon et al., 1998); it made a number of recommendations and guidelines for the implementation and use of automated coding systems.

Certification of cause of death

The certification process begins with the death and ends when the death certificate is completed. In every European country, the medical certification of death is a statutory requirement.

The document used to certify a death is the medical death certificate (in addition to the administrative death certificate that permits the notification of the death in the civil register). The objective of the medical death certificate is to allow the certifier to enter clearly and thoroughly the causes of death. Most of the time, physicians are in charge of the certification. In the case of non-natural deaths, the certification could be made by forensic physicians or in some countries by legal professionals, such as coroners in England. The international medical death certificate recommended by WHO (WHO, 1992; Figure 3.1) is divided into two parts, one designed for entering the sequence of diseases leading to death and the other for mentioning other contributing conditions. The certifier must also specify, for each cause of death entered, the time interval between onset and death.

Disparities between countries and possible biases

The overall implementation of the WHO international form of death certificate is on-going but the number of lines in part I, used to describe the morbid process leading to death, still varies across countries (from 2 to 4 lines).

Figure 3.1: International form of medical certificate of cause of death (WHO ICD-10)

Cause of death		**Approximate interval between onset and death**
I		
Disease or condition directly leading to death*	(a).....	.....
	due to (as a consequence of)	
Antecedent causes Morbid conditions, if any, giving rise to the above cause, stating the underlying condition last	(b).....	.....
	due to (as a consequence of)	
	(c).....	.....
	due to (as a consequence of)	
	(d).....	.....
II		
Other significant conditions contributing to the death, but not related to the disease or condition causing it	.....	.....
	.....	.....
* *This does not mean the mode of dying, e.g. heart failure, respiratory failure. It means the disease, injury, or complication that caused death.*		

The type of additional information available on the death certificate differs between countries (autopsy, surgery, work accident, pregnancy, occupation, etc). Information on autopsy is often collected on the death certificate but the results of autopsy are not systematically included in final statistics (except in Finland where the results of the autopsy must be included in the death certificate). Moreover, the proportion of autopsies varies substantially between countries, from 8% in The Netherlands and Germany to 35% in Sweden and Finland. The indication of surgery is listed in very few countries. In some countries, mainly in Scandinavia, these types of additional information can be available through specific registers. Risk factors such as alcohol abuse or drug addiction are rarely systematically collected. Among the countries using a specific certificate for death in very young babies, the definition of the considered age-period differs (stillbirth, perinatal, neonatal, infant).

In most countries, the death certificate includes guidelines to help certifiers. Usually, they consist of a text explaining the certification rules and of examples. The certification training practices vary markedly (from examples to video) as well as the procedures of queries to the physician when death certificates are incomplete or ambiguous.

Another factor that may result in an important source of bias in inter-country comparisons is the variation of the frequency with which ill-defined or unknown causes of death are reported. This frequency ranges from 1% in England, Finland and Sweden to 6% in Denmark and France. For age groups younger than 25 years, the disparities are even more marked: from 3% in Italy and Spain to 20% in France (Pavillon, Jougla & Maguin, 1994). In addition to these general differences in the percentage of imprecise conditions, there are also differences for unspecified causes within given chapters of the ICD classification of disease.

Specific studies on the certification process

The usual method of assessing inter-country variations in certification practices consists of asking a random sample of doctors to complete death certificates for the same case histories. This method can help to determine whether physicians from different countries differ in certifying and selecting the underlying cause of death for the same cases. The information presented to the physician is the diagnostic information that would normally be available to hospital doctors or general practitioners when certifying a death. These studies are primarily oriented towards assessing certification practices but they also allow the study of coding practices, since the certificates are coded both by national offices and by WHO reference centres. Such investigations are still rare (Gittelsohn & Royston, 1982; Jougla & Pavillon, 1997; Mackenbach, Van Duyne & Kelson, 1987). Before the 1980s, two studies had been performed, one in 1964 involving three countries (Reid & Rose, 1964) and the other by WHO in 1970 involving five countries (WHO, 1970).

More recently, the case history method has been used to investigate certification practices among EU countries for three types of cause of death: cancers (Kelson & Farebrother, 1987), respiratory diseases (Kelson & Heller, 1983) and diabetes (Balkau et al., 1993). For the study on cancers, a set of ten case histories was sent to samples of doctors in eight EU countries. After certification and coding by national coding offices, on average, 83% of all cases received a correct underlying cause code. There were important differences in certification between certain countries. The degree of inter-country variation was lower for cancers than for respiratory diseases. The study of cancer certification concluded that the differences observed may have serious implications for the international comparability of mortality data for cancers of the cervix and uterus (misclassifications between the two categories were attributable to doctors' entries). The main limitation of studies using case histories is the difficulty of ensuring external validity. Neither the case histories, in their content or complexity, nor the physician's responses are necessarily representative of the "real situation". Moreover, the analyses for cancer were restricted to fairly broad diagnostic categories and the case histories may not have been sufficiently sophisticated to enable the detection of subtle variations in diagnosis.

Studies have shown that the nature and amount of medical information entered on death certificates vary between countries, for example:

the way the diagnosis is established; the mean number of causes listed by the certifying physician in each certificate (Pavillon & Jougla, 1997); and the degree of consistency of the certification process. For example, in the context of a specific study concerning certificates mentioning diabetes, the proportion of certificates "properly completed" (i.e. for which coding required simply the application of the ICD general rule) varied from more than 90% for The Netherlands to 60% for Germany (Jougla et al., 1992). Other studies have noted marked differences between doctors' certificates and autopsy findings.

If international studies directly aimed at investigating the biases due to national differences in certification practices are rare, a number of studies, undertaken on a national basis, have examined the validity of COD data. These studies compare the diagnosis entered on the death certificate with the one found from other medical sources (e.g. autopsy findings, medical records, retrospective inquiry to the certifying physician). Some of these studies observed large discrepancies in the certification of cardiovascular diseases but fewer differences have been found for cancers. A general review of these studies is available from the SANCO project (Jougla et al., 2001). Pulmonary cancers, generally the most frequent type of cancer for males, are characterised by an acceptable concordance between mortality and morbidity information. In a longitudinal survey of an elderly population, 83% of the lung cancers identified by a registry or during hospitalisation were mentioned on the death certificate (Stang et al., 1999). These results have been confirmed by other longitudinal studies (Goldacre, 1993; Wells & Mannimo, 1996).

For breast cancer, the most frequent type of cancer for females, the studies based on a comparison of the underlying cause of death from the national statistical office with that produced by review of clinical care records concluded that the official statistics showed a slight underestimation of deaths (Garne, Aspegren & Balldin, 1996; Chamberlain et al., 1991; Brinkley, Haybittle & Alderson, 1984; Rutqvist, 1985; Nystrom et al., 1985).

For other cancer types, various biases may occur: imprecise diagnosis (pancreas, uterus cervix-corpus, thyroid); misclassification between sites (stomach-oesophagus, large bowel-small intestine, urinary bladder-kidney, liver-hepatitis-cirrhosis); sites leading to metastasis (prostate-bone, lung-brain, breast-bone); and co-morbidity in elderly populations (prostate, pancreas). Apart from these potential sources of biases, low rates such as those for cancers of the skin, larynx, testis and thyroid, may show wider fluctuations than those for cancers with higher rates because of random variability in the small numbers of deaths.

Coding of cause of death

The purpose of the coding process is to select the underlying cause of death and to translate the literal text of the listed conditions into ICD codes (WHO 1977, 1992). The selection of the underlying cause is an essential stage since the available international data used for between-country comparisons are based on this single underlying cause. The ICD international coding rules are intended to help to select this underlying cause in difficult cases.

All countries use the ICD codes to code the cause of death but they can apply different revisions of the ICD. In the 1990s, there were two revisions that were used in Europe (ICD-9 and ICD-10) that, in spite of common principles, have important differences – such as the number of codes (around 6,000 in ICD-9 and 12,000 in ICD-10). In the mid-1990s, most countries still coded using ICD-9; and the dates of any implementation of ICD-10 have varied across countries. This simultaneous use of different revisions of the ICD may lead to problems of comparability.

Most countries are now routinely coding causes other than the underlying cause. This multiple coding is very useful because it facilitates the assessment of the consistency of the certification process and permits comparability studies based on multiple cause analysis. However, the total number of coded causes varies (and only a few countries code *all* the causes of death).

In most countries the selection of the underlying cause of death in the mid-1990s was still done manually by trained coders using the ICD rules,

but an increasing number of countries began to use, or planned to implement, an automated coding system. This development is very important for two reasons. It will lead to marked improvement in the inter-country homogeneity of coding; and it will facilitate the coding of all the conditions for each death.

The usual method of assessing the between-country comparability of cause of death coding involves the submission of identical sets of certificates to different countries and comparing of the results of the national coding with a reference centre coding. Such testing is still rather rare. A first study in 1965 involved six countries and 1000 certificates (WHO, 1967). A more recent investigation studied the coding of certificates concerning cancer. This study compared the national coding of the underlying cause of death of a random set of 1243 death certificates that mentioned cancer. Seven countries participated in the test coding of these certificates in an initial study based on ICD-8 (Percy & Dolman, 1978). Results showed that for nearly half the certificates, the assigned underlying cause differed (at the 3-digit level of the ICD). As a result, ICD-9 contained more specific rules concerning cancer coding. The study was repeated after ICD-9 implementation and as part of the preparation of ICD-10 (Percy & Muir, 1989). Nine countries coded the original 1243 death certificates. Differences at the 3 digit-level ranged from 10% for England to 16% for Germany and indicated a marked improvement since the first study. The Netherlands selected cancer as the underlying cause least often (90% of the certificates) and France selected cancer most often (96%). To evaluate the statistical effect of these differences in coding practices on published international mortality data, "corrected" mortality rates were computed using the proportion of deaths coded to cancer by the US as the standard. French mortality rates were most affected with a decrease of 9% in death rates for cancer after correction.

Conclusions

The literature review has shown that, despite many recommendations, very few investigations have examined the international variation in certifying and coding practices and their consequences on published figures. These types of investigations may primarily focus on indicators specifically useful for health planners (e.g. premature deaths, avoidable deaths) or on causes of death with specific problems of comparability. These studies should be based on different types of methodologies such as certification of cases histories, confidential inquiries to the certifying physicians and recoding of samples of death certificates.

In this context, the SANCO project outlined important recommendations to improve the situation:

- the international form of death certificate with four lines recommended in ICD-10 should be adopted as widely as possible. The increased number of lines to describe the causes leading to death may allow for the death process to be more completely described, thus improving the quality of the certification and the validity of the coding process

- development of international guidelines for certifiers (medical examiners and coroners) will also improve homogeneity. Physicians need better initial and continuing training (medical school, occupational training, handbooks, etc) on how to complete the death certificate

- the querying of certifying physicians is recognised as an important method of improving data accuracy and training physicians about correct entry of causes of death

- information on autopsies should be systematically recorded on death certificates

- additional information should be collected to tackle the issue of unknown and ill-defined causes. It may include, in particular, specific national problems linked to legal investigations and confidentiality rules applied for certification

- the introduction of the 10th revision of the ICD should provide a good opportunity for

an international effort towards standardisation and improvement of mortality statistics. This revision is an important change compared to the 9th revision (the number of items doubled)

- the implementation of automated coding systems, similar to those used in the US to select the underlying cause of death, will markedly improve the international comparability of mortality statistics and also the quality and consistency of national statistics over time. At the same time, ad hoc national coding rules need to be discussed and bridge coding between ICD-9 and ICD-10 and between manual and automated coding should be implemented.

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CHAPTER 4

MEMBER STATES OF THE EUROPEAN UNION AND THE EUROPEAN ECONOMIC AREA

4.1: AUSTRIA

Introduction

Austria is situated in south-central Europe, constituting part of the Eastern Alps and the Danube region, extending 573 km from west to east and 294 km from north to south. It covers an area of 83,900 km^2 and its border has an overall length of 2,706 km, of which 816 km are shared with Germany, 466 km with the Czech Republic, 107 with the Slovak Republic, 356 km with Hungary, 330 km with Slovenia, 430 km with Italy, 166 km with Switzerland and 35 km with Liechtenstein.

Austrian territory can be divided into five sections: Eastern Alps (western, central and southern parts – about 60% of Austria), Alpine and Carpathian Foothills (central/northern parts), Pannonian Lowlands (eastern parts), Vienna Basin (surrounding Vienna), and Granite and Gneiss Highlands (Bohemian Massif in the north). The highest mountain is the Grossglockner (3,798 m) in the Hohe Tauern. The main river is the Danube with a 350 km section of its course running through Austria.

Austria is divided into nine administrative provinces: Burgenland, Carinthia, Lower Austria, Upper Austria, Salzburg, Styria, Tirol, Vorarlberg and Vienna. These provinces are further subdivided into administrative districts. In total there are 99 districts of which 15 are classified as urban and 84 as rural. Apart from the capital town of Vienna, with its 1.56 million inhabitants (population density 3,765 per km^2), there are 24 towns with over 20,000 inhabitants. Austria had a total population of about 8,030,000 in 2001. Since 1960 the population has increased by 14%, but a constant two-thirds of the population has been living in urban areas over the last 40 years. The overall population density was 96 per km^2 in 2001, but it varies among the provinces from 53 (Tirol) to 135 (Vorarlberg).

NUTS 2 level corresponds to the nine provinces, whereas NUTS 3 level divides Austria into 35 units, of which 27 consist of one or several administrative districts (note that Vienna represents only one unit) and eight consist of at least one administrative district and a part of another administrative district (judicial district).

The national language is German (spoken by about 90% of the population), but many other languages are spoken by various ethnic groups (e.g. Croatian, Hungarian, Slovenian, Turkish).

Mortality data collection

For each death, the registrar must draw up a death certificate which is to be filled in by the coroner stating the cause of death. This death certificate must then be forwarded to the Austrian Central Statistical Office, where the data are centrally processed and coded. The Austrian Central Statistical Office's data files on deaths cover all those persons listed in the resident population who have died in Austria.

In Austria coding is conducted according to the International Classification of Diseases (ICD) of the World Health Organization. Prior to 1979, cause of death was coded according to the 8th revision of the ICD, from 1980 to 2001 the 9th revision was used, and since 2002 the 10th revision has been employed. The coded cause of death is the *underlying cause of death*, or in cause of external causes, gives the circumstances of the accident or the effect of violence which caused the fatality.

The overall autopsy rate in 2001 was 24.5%. Among children under one year who died, an autopsy was performed in 67.4 % of the cases. The older the deceased were, the lower was the autopsy rate: only 13.5% of persons aged over 85 had an autopsy performed. The autopsy rates vary also by region: the east of Austria and large cities carry out more autopsies than the rest of Austria.

Population statistics

In Austria, censuses have been carried out every 10 years, the latest in 2001. For years between

the censuses, population size and composition were estimated by counting the births, deaths and migration reported to the Austrian Central Statistical Office. These estimates were revised after a new census. From 2002 onwards the population data have been extracted from the recently established Central Population Register (Zentrales Melderegister, ZMR)

Statistical publications

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4.2: BELGIUM

Introduction

Belgium has an area of 30,500 km^2 and extends over 230 km from north to south and over 290 km from east to west. About 60% of the land surface is used for agriculture and 20% is wooded (figures for 1990-2000). The Meuse flows out of the French Vosges, through eastern Belgium (Namur and Liege) into the Netherlands. About 45% of the land surface is used for agriculture and 20% is wooded. The capital is Brussels (population around 950,000 in the period 1993-1998).

The population of Belgium grew from 10,068,000 in 1993 to 10,192,000 in 1998, with an average density of 332 inhabitants per km^2 for that period. By 2007, the population had risen to 10,585,000, with a density of 347 inhabitants per km^2. Belgium is divided into three regions: the Flemish region, the Walloon region and the Brussels Capital region. In the Flemish region (58% of the population), the official language is Dutch; in the Walloon region (33%) it is French. The Brussels Capital area (9%) is a region where French and Dutch have an equal status. There is a fourth language region where German is spoken, in the North-East of the Walloon region (70,000 inhabitants).

Until the beginning of 1995, Belgium was also divided into nine provinces: Antwerp, Brabant, West Flanders, East Flanders, Hainaut, Liege, Limburg, Luxembourg and Namur. Since 1st January 1995, Belgium has consisted of 10 provinces: the province of Brabant was divided into 2 parts: the Flemish Brabant and the Walloon Brabant. In this atlas, the 10 provinces have been taken into account plus the region of Brussels Capital that is neither part of the Flemish Brabant nor of the Walloon Brabant.

Population estimates

Up to 1991, Belgium carried out a census of population every ten years. In October 2001, a large socio-economic survey, covering the whole population, was carried out.

Belgium has a centralised and computerised population register. It was created in 1970 with the collaboration of some communes (geographic entities) on a voluntary basis and was progressively developed. It became compulsory for all the communes on 1st January 1985 according to the law of 8th August 1983. Since 1st January 1989, population figures have been based on the data from the population register.

Each year, the National Institute of Statistics (NIS) receives in March all the population movements of the preceding year (births, deaths, migrations, nationality changes) from the National Population Register. New population figures are then estimated. These results are given the date of 1st January of the relevant year.

The communes have to transmit the data to the national register within 15 days of the declaration of the occurrence but, when the NIS receives the data from the National Register in March, some communes have not yet transmitted all their data from the preceding year. Therefore, a column called “statistical adjustment” has been added to the tables regarding population movements. In this column, we find the balance of the movements of two years earlier that could not be taken into account the year before when the NIS received the data.

Births must be declared at the commune where the event took place within 15 days and deaths within 3 days. For both, if the last day is a Saturday, a Sunday or a public holiday, the time limit is extended up to the following working day. If someone moves, he/she must declare it at the commune where he is moving. For all events, the commune of residence is informed through the register. Of course, not everyone respects the obligation of declaration. If the commune notices that a person has left the area of the commune without having declared his departure,

he/she will be officially struck off the population register after a police inquiry. These cases appear in a special column in the table regarding population movements.

Identity cards are renewed at least every ten years. This contributes to the update and some verification of the population register. No system is perfect, but Belgian population figures can be considered to be of good quality and reliable.

Some population features

Age distribution of the population

The average percentage of population in each age group for the period 1993 to 1998 is:

0-14	15-64	65 and over
18.0%	66.1%	15.9%

Life expectancy

According to life tables for 1995-1997, life expectancies (years) at different ages are:

At	Males	Females
Birth	74.3	80.9
20	55.2	61.6
40	36.4	42.2
60	19.1	23.9

Total fertility rate (births per woman)

1993	1994	1995	1996	1997
1.61	1.56	1.56	1.59	1.60

Infant deaths (per 1,000 live births)

1993		1994		1995		1996		1997	
M	F	M	F	M	F	M	F	M	F
9.44	6.52	8.52	6.52	7.31	4.64	6.06	4.47	6.02	5.09

Foreign population

The average foreign population in 1993 to 1998 was 912,800 or 9% of the total population. The population whose citizenship belongs to a member state of the EU represents just over 60% of the total foreign population. Those with French and Italian citizenship represent 56% of the EU foreign population (18% French and 38% Italian) while those with Moroccan and Turkish citizenship represent 62% of the foreign population outside EU (39% Moroccan and 23% Turkish).

Obtaining Belgian citizenship

From 1st January 1993 to the end of 1997, 124,560 foreigners obtained Belgian citizenship, an average of 24,900 per year. Even if they keep their former citizenship, they are included in the statistics as Belgian citizens.

Mortality data collection

Anonymous death certificates were introduced in Belgium in 1930, but were not in general use throughout the country until 1954. The death certificate in use in 1993-1997 (covered by this atlas) was introduced in 1979, and slightly modified in 1983. There are two versions – one for recording stillbirths and deaths of infants up to one year of age and the other for deaths of people older than one year.

The death certificate is divided into four sections (A, B, C and D). Only section A contains the name and address of the deceased. Sections B and D contain the information on age, sex, etc., necessary for compiling general mortality statistics. The certifying doctor, exclusively, uses section C to report the cause of death; the doctor seals this section.

Section A is detached from the death certificate and retained by the communal administration. Sections B, C and D are sent to the Health

Administration of the Ministry of the Flemish Community for deaths in the communes of the Flemish region, and to the Ministry of the French-speaking Community for deaths in the communes of the Walloon region. In 1993-1997, the communes of the Brussels capital region sent their certificates to a Health Inspector of the National Ministry of Health. In these administrations, a medical civil servant codes the underlying cause of death according to the International Classification of Diseases (ICD), 9th revision, and enters the code number on section B. Section C is then detached and sections B and D are sent to the National Institute of Statistics.

A few remarks about certification and coding of causes of death

A physician is the only person appointed by the law to fill out the death certificates. It can be the treating physician or a physician who comes to certify the death. Phone calls or faxes are used when the information about the cause of death is incomplete or poses an interpretation problem. The training of the students in medicine for certifying the causes of death is unsatisfactory. They receive only short information and vocational training on certification does not exist.

In 1993-1997, only two causes were registered for each death, the underlying cause of death and the immediate cause of death. The 9th revision of the International Classification of Diseases (ICD) was used. From 1st January 1998, new death certificates have been used. In accordance with the wishes of the World Health Organization, they ask the underlying cause of death and three antecedent causes of death and other significant conditions contributing to the death, but not related to the disease or condition causing it. The 10th revision of the ICD has been applied since 1998.

The comparability of the coding of causes of death between the north and the south of the country may be affected because different administrations are responsible for coding.

The proportion of ill-defined conditions (3.5%) is comparable with other countries, but the proportion of malignant neoplasms of other and unspecified sites (195-199) among the total of cancers is fairly high (9%: 7.9% for males and 10.5% for females).

Statistical publications

Tables of general mortality data (giving information on age, sex, civil status, residence, etc.) are published (in French and Dutch) by the Belgian National Institute of Statistics in a series of brochures entitled Demographic Statistics. The brochure on causes of death mainly contains information at the national level. Tables of causes of death classified according to abridged lists of mortality causes (the basic tabulation list of the 9th revision) are available down to the arrondissement level.

The results of the Health Interview Surveys 1997, 2001 and 2004 can be obtained on the web site of the Scientific Institute of Public Health: http://www.iph.fgov.be – choose Department of Epidemiology-Toxicology, Section of Epidemiology.
On the same main site causes of death for Belgium (registration years 1987 to 1997) are in an interactive way available on "Standardised Procedures for Mortality Analysis – Belgium (SPMA)":
http://www.iph.fgov.be/epidemio/spma/index.htm

The Flemish Region is publishing annually its own health indicators and causes of death since registration year 1993: "Gezondheidsindicatoren" en "Statistiek van de doodsoorzaken" (only in Dutch).

A Doneux
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4.3: CYPRUS

Introduction

Cyprus is a small island of 9,250 km^2 (3,570 sq miles), extending 240 kms (150 miles) from east to west and 100 kms (60 miles) from north to south. It is strategically situated in the far eastern end of the Mediterranean (35^o N 33^o E), on the busy trade routes linking Europe with the Middle East, Russia, Central Asia and the Far East.

The country is divided into six districts: Nicosia (Lefkosia) which is the capital, Limassol (Lemesos), Larnaca (Larnaka), Paphos (Pafos), Famagusta (Ammochostos) and Kyrenia (Keryneia). The former two of these districts are occupied by Turkish forces, partially and totally, respectively.

The official languages of the Republic of Cyprus are Greek and Turkish.

Cyprus gained its independence from Britain in 1960. In 1974 Turkey invaded Cyprus and occupied over a third of the island. The ceasefire line runs right across the island and cuts through the capital, Nicosia, dividing the city and the country.

Although the northern part of the island is still occupied by Turkish forces, the Republic of Cyprus is internationally recognised as the sole legitimate State on the island with sovereignty over its entire territory. In May 2004 the Republic of Cyprus became a full member of the European Union.

Mortality data collection in Cyprus

Law 141(I) of 2002 regarding the Population Register regulates the whole procedure of death certification and registration. Under this Law, medical certification of deaths is carried out when the deceased had been hospitalised, institutionalised or died elsewhere. The Law underlines the obligatory registration of all deaths, and specifies the relevant person for the death registration and the provision of any necessary additional information about the deceased. After the registration of the death, the death certificate is issued to the relatives of the deceased, since it is necessary for burial. Data from the District Registrar's Office is sent to the Statistical Service of Cyprus for processing.

The certification of deaths is conducted by a physician who completes three copies of the medical certificate of death. A medical certificate is necessary under any circumstances: if the deceased had been hospitalised because of the illness that finally caused the death, the doctor who was responsible for the patient during the hospitalisation would be responsible for certifying the death; if the deceased had not been hospitalised, a physician must examine the corpse in order to certify the death; if there are any doubts concerning the circumstances under which the person died, the case should be further investigated by the coroner. Specifically, autopsies are performed when the cause of death is not clearly identified or in cases when the death is sudden or violent or when an investigation is asked for by relatives.

One copy of the medical certificate is given to the relatives of the deceased who are obliged to notify the death, soon after the date of death, to the District Registrar's Office where the death certificate is issued. The second copy remains at the hospital or in the doctor's records. And the third copy is given to the authorised person who will conduct the burial. The medical certificate provides information on the name of the deceased, the date of death, age as stated, the place of death, last time the deceased was seen alive and the cause of death.

The Medical Death Certificate is available in both Greek and English. The diagnosis is described in text format and not in ICD codes. The physicians who fill the certificates have not undergone special training.

Since 2004, statistics on cause of death are compiled by the Statistical Service in collaboration with the Health Monitoring Unit (HMU) of the Ministry of Health. The HMU

is mainly responsible for collecting copies of the medical death certificates from the District Registration offices and coding the causes of death. The coding is performed according to ICD-10 rules and includes multiple cause coding and underlying cause coding.

Death statistics are published in the annual "Demographic Report" and "Health and Hospital Statistics", which are available on the website of the Statistical Service of Cyprus:

http://www.pio.gov.cy/mof/cystat/statistics.nsf/index_en/index_en?OpenDocument.

Population statistics

The population census is the main source of population statistics for Cyprus. Decennial censuses were undertaken from 1881 until 1931. In 1941 the census was not compiled due to the Second World War, but one was carried out in 1946. The next census was conducted in 1960, the year of the Independence of the Republic of Cyprus. In 1973 a census was conducted, but only amongst the Greek Cypriots, since the Turkish Cypriots were unwilling to provide data.

Censuses after 1974 refer to the Government Controlled Area. Four population censuses have been conducted since then: in 1976, in 1982, in 1992 and in 2001. The next population census is planned to be conducted in 2011.

For years between censuses, annual population estimates are published in the Demographic Report. These estimates are available by district of residence, age and sex.

E Kyriacou

4.4: CZECH REPUBLIC

Introduction and brief history

Until the end of 1918, the Czech Republic was a part of the Austro-Hungarian Empire. In 1918 the Czechs and Slovaks established a common state called Czechoslovakia. This state existed, with the exception of the period of the Second World War, until January 1993 (from 1968 under the name Czech and Slovak Federative Republic) when the country was peacefully divided into two independent states: the Czech Republic and Slovakia. The Czech Republic encompasses the territory of Bohemia, Moravia and Silesia. It acceded to the EU in May 2004.

The country and its people

The Czech Republic is situated in the middle of Europe between 48°33' and 51°03' N and between 12°05' and 18°51' E. The land boundaries total 2,290 km; the border countries are Germany with 810 km, Poland with 762 km, Austria with 466 km and Slovakia with 252 km. The Czech Republic covers an area of 78,900 km^2 including 1,590 km^2 of water. The country is surrounded by mountains, only the eastern border having several open valleys. Generally, the Czech Republic is a hilly country. The territory is formed by two different types of earth crust. The old earth crust forms the west part while the young crust and Carpathian mountains form the east part. The Czech highlands create a large hollow with border mountains on the west; the land gradually declines towards the Carpathian mountains in the east. Plains cover 15.5% of the territory and provide regions with the best condition for agriculture, the largest areas being hilly regions (39.6%), highlands (29.7%) and mountains (18.2%) which are used for less intense agriculture or are covered by forests, lakes, meadows and settlements. The lowest and highest points of the country are 115 m and 1,602 m above sea level. Natural resources of the country are hard and soft coal, kaolin, clay, graphite and timber. The country is highly industrialised and oriented mainly to metallurgy, machinery and equipment, motor vehicles, glass and armament production. There are areas with air and water pollution in northwest Bohemia and in northern Moravia, around Ostrava, which present health risks and resulting acid rains damage forests. The climate is determined by the position of the country between western Europe, with a maritime climate, and eastern Europe, with a continental climate. Most of the country belongs to the temperate warm zone with good conditions for growing nearly all cultivated plants, while the cold zone, including all the highlands, is exploited for forestry, pasture or foraging. The Czech Republic is administratively divided into 14 counties and 91 districts.

The total population in 1995 (estimate based on the 1991 census) was just over 10.3 million, consisting of 5.0 million males and 5.3 million females, with a density of 130 inhabitants per km^2. About 70% of the population lives in cities. Overall median age was 36.4 years, 34.4 for males and 38.4 for females. About 18% of the population was younger than 15 years, 68% in the age group 15 to 64 years and 14% were 65 and over (2004 estimate). There is a very high proportion of females in the highest age group. Life expectancy at birth has increased slowly but gradually and was estimated to be 72.5 years in males and 79.0 years in females in 2004. According to the 1991 census, just over 80% of the population are Czechs; the other groups are Moravians 13.2%, Slovaks 3.1%, Poles 0.6%, German 0.5%, Silesians 0.4%, Gipsies 0.3%, Hungarians 0.2% and other 0.5%.

The total labour force was around 4.8 million people in 2004; of these, 30% were employed in industry, 4% in agriculture, 7% in construction and 59% in various services. The official unemployment rate in the Czech Republic was 4% in 1995, one of the lowest rates among the countries of central and eastern Europe and below the EU average.

Mortality data collection

As in other countries which were once part of the Austro–Hungarian Empire, mortality statistics in the former Czechoslovakia have a long tradition: data on the main diseases (numbers) are mostly available from 1890. Great progress in this field was made in 1949 with the obligatory use

of the International Classification of Diseases 6th revision (ICD-6) in the whole of Czechoslovakia, together with the introduction of death certificates of international format. In Czechoslovakia the shortened version of ICD-6, with a list of diseases confined to about 200 items, was used in the period 1949-1974, but from 1975 the whole list of diseases of ICD-6 and of the subsequent revisions of ICD (ICD-7 from 1958, ICD-8 from 1968 and ICD-9 from 1979) has been used. Since January 1994, coding according to ICD-10 has been mandatory. In the National Cancer Registry, the International Classification of Diseases for Oncology 2nd Edition has been used for coding of morphology from January 1994. The mortality statistics are based on information present in death certificates and are compiled and published by the Czech Statistical Office. Data on cancer mortality are published also in the annual report "Malignant neoplasms" accompanying the data on incidence published for every year by the Institute of Health Information and Statistics, where the National Cancer Registry is situated. The legislation on the protection of personal data is strictly respected.

Population statistics

Annual estimates on the size and age-structure of the population (mid- and end-year), based on the results of the 1991 census, taking into account births, deaths and immigration of population, are provided and regularly published by the Czech Statistical Office.

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4.5: DENMARK

Introduction

Denmark has an area of 43,100 km^2. It consists of the major islands Sjælland and Fyn and the peninsula Jylland, which has a 68 km long border with north Germany at its base. Altogether there are 483 islands, of which about 100 are inhabited. The major islands are connected by bridges, the longest being the crossing over the Great Belt between Sjælland and Fyn (17km long). The pylons of the 6.8 km long suspension bridge are, at 254 m, the highest points in Denmark. The coastline along the North Sea, Skagerrak, Kattegat and the Baltic runs for 7,314 km. Denmark is a flat country, rising to only 173 m at its highest natural point. The longest river is the Gudenå (160 km) which rises in central Jylland and flows into Randers Fjord. About two thirds of the area is agricultural land, and some 11% is wooded. Of growing importance are the oil and natural gas deposits in the Danish waters of the North Sea.

The capital is Copenhagen (population around 1.2 million, including suburbs), the second largest city in the Nordic countries. It lies on the island of Sjælland and the nearby island of Amager.

Denmark has a population of 5.4 million, excluding Greenland and the Faeroes, and the average population density is 124 per km^2 (2001 figures). The population density on Sjælland is 302 per km^2.

Of the 206,000 migrants in Denmark, 30,000 come from the Nordic countries, 36,000 from EU countries, predominantly Britain and the Federal Republic of Germany, and the remainder mostly from Asia (56,000), Turkey (37,000) and the former Yugoslavia (35,000).

Denmark was divided into 14 counties plus the metropolitan region of Copenhagen with Frederiksberg, in 2008 counties were combined into 5 regions. The Faeroes have had home rule since 1948; they have their own assembly and are not in the EU. Greenland has belonged to Denmark since 1721; it obtained home rule following a referendum in 1979 and withdrew from the EU in 1985.

Mortality data collection

Death certification has been mandatory by law since 1871 and from 1875 onwards the National Board of Health has published annual statistics on the causes of death.

The international form of death certificate was introduced in Denmark in 1951. Anonymous death certificates were introduced in January 1966 and the current form was introduced in 1996 when processing of was automated including optical computer reading (OCR) technology.

The completed and sealed death certificate is given to the next of kin, who passes it to the local vicar who will be responsible for the burial. The vicar checks the name and personal number of the deceased and notifies the local population register of the death. He then sends the death certificate itself to the Department of Health Statistics at the National Board of Health (a division within the Ministry of the Interior and Health), where it is again checked and coded manually and computerised.

From the 1870s until 1931, a Danish classification system for deaths were used, followed by a Nordic classification in 1931-1940 and then one based on the Bertillion nomenclature until 1951. Since 1951 the WHO International Classification of Diseases (ICD) has been in use as follows: 6th revision 1951-1957, 7th revision 1958-1968, 8th revision 1969-1993, and since 1994 the 10th revision has been in use. Due to the modifications in the classifications over time, the data are not fully comparable, but a computerised system of fairly compatible categories of data was set up by the Danish Institute of Clinical Epidemiology (DICE) from 1943. From 1970 the register of causes of death has existed in a full and computerised form at the National Board of Health. The key identifier is the unique personal registration number given to all Danes since 1968. This number

facilitates easy linkages to other files and follow-up of questionable cases, e.g. in hospital files.

For all natural deaths, the death certificate is filled out by the physician of the deceased or, if the person was under treatment at the time of death, by the attending physician. If examination of the body raises doubt about the mode of death, the physician must inform the police, who must also be informed if there is suspicion that death was due to suicide, accident or criminal acts. In such cases, a legal examination must be undertaken. In 1984, legal examination took place following 11% of all deaths. If, after a legal examination, there is still doubt about the cause of death, an autopsy must be carried out. In 1984 an autopsy was performed for 33% of all deaths occurring in Denmark; this figure includes both legal and hospital autopsies.

The quality of the death certificates has been studied for cancer, heart diseases and other causes. It is obvious there is room for improvement even for cancer deaths, but the Danish death certificates are no worse than seen elsewhere in the developed world. Of importance has been the steep decline in autopsies from 45% of all deaths in 1970 to 12.5% in 1996. Ill-defined cause of death virtually did not exist in 1971 (1%) but accounted for 9% of deaths in 1996. This development in fact reflects more accurate coding and less guessing from the medical doctors filling in the certificates.

Danish population statistics

Data on the size, composition and mobility of the Danish population are compiled from entries in local (council) population registers, which contain, for each individual, information on place of residence, civil status, sex, age and nationality.

Information from all the local registers is collected together in the Central Population Register. The local registers are updated as births, deaths, changes of address, marriages and divorces are notified; all such changes must be reported to the Central Population Register within 40 days. Information from the Central Population Register is transferred to the Central Bureau of Statistics, which is responsible for publishing population statistics. These are available at http://www.dst.dk.

Statistical publications

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H Storm

4.6: ESTONIA

Introduction

Estonia was occupied for several centuries by Denmark, Germany, Sweden, Poland-Lithuania and Russia and attained independence only in 1918. At the beginning of the Second World War, Estonia was annexed by the USSR and regained its independence only in 1991, after the dissolution of the USSR. Subsequently, Estonia was able to undertake real political and economic transformation and to restore ties with Western Europe. The country acceded to the EU in May 2004.

The country and its people

Estonia is situated in Northern Europe between 57°3' and 59°5' N and between 21°5' E and 28°1' E. The area of the country is 45,200 km^2, including 43,200 km^2 of mainland and 2,000 km^2 of water; there are also over 1,500 islands in the Baltic Sea. Land boundaries with neighbouring countries total 633 km: the length of the border with Latvia in the south is 339 km, and in the east that with the Russian Federation is 294 km, while in the north and east of Estonia are the Baltic Sea and the Gulf of Finland. The mainland terrain is flat in the north with marsh and boggy lowland, and there are low hills in the south where the highest point is 318 m. Forests cover around half and arable land represents only just over a quarter of the country's area. Natural resources are oil shale, peat, phosphorite, clay, limestone, sand, dolomite and sea mud. Industry is oriented mainly to engineering, electronics, wood and wood products, textile, information technology and telecommunications. There is some air pollution with sulphur dioxide from oil-shale power plants but the amount of pollutants emitted to the air is falling gradually and emissions in the year 2000 were only 20% of the amount in 1980. Also, the amount of non-purified wastewater discharged to water bodies was only 5% of the level discharged in 1980 as a result of the building of new water purification plants; coastal waters are polluted in certain locations. The climate is temperate, with relatively warm summers and moderate but sometimes severe winters. The whole country is divided administratively into 15 counties. There are 254 local municipalities, of which 207 are rural and 47 urban.

The total population in 1995 (estimate based on the census in 1988) was 1,485,000 inhabitants (692,000 males and 793,000 females). In 1998 the majority, 64%, were Estonians; 29% were Russians, 3% Ukrainians, 2% Belarusians and 2% other ethnic minorities. The density of population was nearly 33 per km^2 in 1995. Over 70% of inhabitants live in urban areas. Overall median age was 38.8 years, 35.1 years for males and 42.1 for females. The age structure of the population (2004 estimate) was 16% in the age group 0-14 years, 67.5% 15-64 years, and 16.5% 65 years and over with a prevailing majority of females (about twice of the number of males, owing to the very short life expectancy of males in Estonia). The life expectancy at birth was 65.5 years for men (one of the lowest in Europe) and 74.3 years for women. The lowest rates of life expectancy in males, less than 63 years, were recorded around 1994, after a gradual decrease beginning in the mid-1980s. The sex difference in life expectancy has increased to 9.5 years and is above the EU average (6.4 years in 1997).

The labour force contains more than 600,000 people, of which 20% are employed in industry, 11% in agriculture and 69% in services (1999 estimate). The official unemployment rates in Estonia reached 12.3 % in 1998, which is relatively high in comparison with neighbouring countries as well as with the other countries of eastern and central Europe.

Mortality data collection

Mortality statistics in Estonia are compiled from information provided by physicians on death certificates, which in recent decades have been based on the international model proposed by WHO. All deaths are confirmed by physicians, including the selection of the underlying cause of death. Main and immediate causes of death together with co-morbidity (accompanying diseases) present on the

death certificate are coded using the codes of ICD-9. For cancer incidence and mortality, in addition to ICD-9 (and recently ICD-10) codes, the International Classification of Diseases for Oncology (ICD-O) has also been introduced in the National Cancer Registry; this has enabled the participation of Estonia in several international projects and studies. The data file for all death certificates issued in Estonia is produced annually by Statistics Estonia. The Population Registry was founded in 1992, when the national identification number was introduced. Legislation regulates access to mortality data as well as to the National Cancer Registry data, by decree No. 21 of the Minister of Social Affairs in February 2001 in accordance with the Personal Data Protection Act.

Population statistics

Demographic data are based on information from censuses. The last census was carried out in 2000. For years between censuses population, size, age structure and composition are estimated by counting the births, deaths and migrations reported to the Statistics Estonia (now the Estonian State Department of Statistics). The mid- and end- year population size and structure is published annually, together with mortality and other demographic statistics.

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4.7: FINLAND

Introduction

Finland has an area 338,000 km^2, of which inland waters form 33,600 km^2. From the southern coast to the border in the north is 1,157 km, and the country's greatest width is 542 km.

The length of the land boundary with Sweden is 586 km, with Norway 727 km and with Russia 1,269 km. In the south is the Gulf of Finland, opposite Russia and Estonia; in the west the Gulf of Bothnia; opposite Sweden; and in the southwest the Baltic Sea.

Forests and other wooded land cover 68%, and water 10%, of the country. About 8% of the land surface is used for agriculture. Gross national income per capita was US$ 22,600 in 1999.

The capital is Helsinki, located on the south coast, with 0.5 million inhabitants. In 1999, Finland had a population of 5.2 million and average population density of 15 inhabitants per km^2 (1999). The official languages are Finnish and Swedish. The Swedish-speaking minority is 6% of the total population. The proportion of foreigners is 2.6%, a quarter of them from Russia.

Cause of death statistics

Finland has since 1987 had two separate death certificate forms: one for persons aged 28 days or more, and one for stillbirths and infants who died under the age of 28 days. The death certificate is approved by the Ministry of Social Affairs and Health and is in accordance with the recommendation of the World Health Organization in its International Classification of Diseases, 9th Revision.

The certifier declares the causes of death with a text describing the diseases, conditions or external causes and with the corresponding code of the Finnish Classification of Diseases. At maximum there are four causes leading to the death and four contributing causes on the death certificate. In addition, the death statement is further supported by free text under the section "Circumstances of death".

If the determination of the causes of death necessitates forensic autopsy or medical autopsy, the death certificate, on which the statistics are based, is made out once the results of the autopsy have been released. The proportion of forensic autopsies is 20% of all deaths. The proportion of medical autopsies is lower, around 10% of all deaths. The rest of the death certificates are based on clinical examinations.

The doctor signing the death certificate sends the certificate to the legal medical officer at the county administration office to be checked. This officer then forwards the certificate to Statistics Finland.

In drawing up cause of death statistics, Statistics Finland uses both death certificates and the Population Information System available from the Population Register Centre where the death is registered by the notification of death (given in most cases by the same doctor who completes the death certificate). Statistics Finland links the death certificate data with the data from the Population Information System by means of the personal identification code of the deceased. This method ensures complete coverage of the statistics on deaths. It also reduces the volume of data handled by Statistics Finland because the vital events and the demographic personal data are included in the Population Information System.

The cause of death statistics covers the death in Finland or abroad of persons who were residents in Finland at the time of death. All causes of death are coded centrally by Statistics Finland. The International Statistical Classification of Diseases and Related Health Problems, 10th Revision, was introduced in 1996. Other variables coded from death certificates are manner of death (disease, occupational disease, accident, work accident, suicide, homicide, war, undetermined

intent), place of death, place of accident, activity during accident, medical operation before death, and code of the institute or hospital of the certifier. Additionally, the files of cause of death statistics include many demographic data from the Population Information System, for example name of the deceased, date of death, marital status, personal identification code of the spouse, and place of residence.

Because of the two sources of data – the death certificate and the Population Information System – the coverage of deaths is practically 100%. The non-response rate for death certificates was 0.1% of all deaths in 2000. These deaths occurred abroad, or when death certificates were still missing by the deadline for the production of the statistics.

In all, 6.1% of death certificates were specially processed. Inquires were sent in respect of total of 1.2% of all death certificates, either to the issuing physician, or in case of multiple poisonings to the forensic medical register. The rest of the specially processed death certificates were coded with the assistance of the medical experts of Statistics Finland.

In the Finnish cause of death statistics the number of ill-defined causes is very low. The categories R96-R99 included only 92 cases, 0.2% of all deaths.

For epidemiological uses such as this atlas, the death certificates from Statistics Finland are sometimes linked with the data base of the Finnish Cancer Registry to get some additional variables related to cancer diagnosis, or to ascertain the place of residence at the time at cancer diagnosis. If the place of residence at death is used, migration close to the main hospitals because of cancer treatment may falsify the geographical pattern.

Population statistics and censuses

Statistics concerning the structure of population and families, housing conditions or vital events are produced by Statistics Finland based on data from the Population Information System. All Finnish population files use the personal identification code, which makes possible versatile statistical production by combining individual data with the personal identification code.

Nation-wide population censuses were carried out in 1950, 1960 and 1970, and every fifth year from 1975 onwards. The 1990 census was the first which was entirely based on administrative registers. Data on occupation is included only in the censuses.

Since 1987, Statistics Finland has compiled annual Employment Statistics based on several administrative registers such as those of taxation, pensions, unemployment and welfare benefits. Other annual statistical data support the improvement of the databases based on censuses or Employment Statistics.

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Hilkka Ahonen (Statistics Finland),
Eero Pukkala (Finnish Cancer Registry)

4.8: FRANCE

Introduction

France has a surface area of 550,000 km^2 and is a maritime and continental crossroads between North European and Mediterranean European countries. With 60 million inhabitants, France has the third largest population in the EU. The mean population density is 107 inhabitants per km^2. Three quarters of the people live in cities and towns.

About 70% of the active population, more than 18 million people, work in the tertiary sector (transport, trading, service) that represents 71% of the gross domestic product. In 1998, unemployment affected 12% of the population. Migrants represent 6% of the population. Just over half of the surface area is used for agriculture. The most important crop is wheat, followed by oats and maize. Fruits and vegetables are grown in all regions, but particularly in the south. Vines cover extensive areas, especially in Languedoc, Bourgogne and around Bordeaux. Woodland covers 30% of the country.

People under 20 years of age currently represent a quarter of the population, compared with one third 20 years ago. The proportion of the population aged 65 and over (16%) continues to increase. Following a decrease which began in the 1960s, the fertility rate is now stable at 1.8 child per woman. The number of births, 745,000 in 1999, ranks third in the EU after Ireland and the United Kingdom.

In 1999, 540,000 deaths occurred, a mortality rate of 9.1 per 1000 inhabitants. The life expectancy at birth of French women, 82 years, is the highest in the EU, but male life expectancy, 75 years, is the same as the EU average.

With one physician for 338 inhabitants, France follows Spain (237), Germany (293) and Great Britain (310), but is above The Netherlands (396).

The French capital is Paris (population: city 2.1 million and Ile de France 11 million). Metropolitan France is divided into 22 regions and 96 departments. The regions are: Nord-Pas-de-Calais, Ile-de-France, Centre, Picardie, Basse Normandie, Haute Normandie, Bretagne, Pays de la Loire, Poitou-Charentes, Limousin, Aquitaine, Midi-Pyrénées, Champagne-Ardennes, Alsace, Lorraine, Bourgogne, Auvergne, Franche-Comte, Rhone-Alpes, Languedoc-Roussillon, Provence Alpes-Cte-d'Azur, and Corse. The overseas departments and territories are not represented in this Atlas.

Mortality data collection

The death certificate currently used in France was introduced in 1958. The physician can indicate one or more diseases leading directly or indirectly to death. Causes of death are coded according to the International Classification of Diseases (ICD). The ninth revision of the ICD (ICD-9) was used from 1979 to 1999. The present system for recording death information has been used since 1968.

When someone dies, a physician fills in a two-part death certificate: the date and time of death, identification information (name, surname, age, residence) are entered in the first part; and the place and date of death, and medical causes of death are entered in the second part – this part is sealed by the physician to preserve confidentiality.

The physician certifies the death and fills in the medical certificate. The medical certificate is sent to the town council of the place of death, where the nominal part is separated from the medical part. Another document, called bulletin 7, is completed by the town council. It contains information on socio-professional status, place of residence and places and dates of birth and death (but no information on identity). The sealed part of the death certificate and the corresponding Bulletin 7 are sent to the Direction Departementale de l'Action Sanitaire et Sociale (DDASS), which opens the anonymous death certificate in order to follow trends in important diseases.

The anonymous Bulletin 7 and the corresponding medical certificate are finally sent

by the DDASS to the department of the National Institute of Health and Medical Research (CépiDc-INSERM) responsible for the national statistics and the analysis of the medical causes of death. INSERM codes the causes of death according to ICD-9 (since 2000, ICD-10). The INSERM data base is then matched to the sociodemographic database of the National Institute of Statistics and Economic Studies (INSEE). INSEE performs the final checking of the data and sends back the final file to INSERM (socio-demographic information and medical causes of death for each death). This database does not contain the name of the decedent but is not completely anonymous, because dates and places of birth and death may be sufficient to identify an individual.

Since 1997, the French death certificate has been based strictly on the international form recommended by WHO. A first part with four lines describes the morbid process leading to death and a second part includes the contributing causes of death. Moreover, since 2000, the production process has been completely modified with the aim of improving the quality and the comparability of the data. This involved digitalisation of all the death certificates with the creation of a picture database, and implementation of an automatic coding system for medical causes of death (software STYX), implementing ICD rules for the selection and modification of the underlying cause. A bridge coding exercise has been performed on a sample of 50,000 certificates to document the changes in trends due to the new classification (ICD-9 versus ICD-10) and to the change in the coding mode (manual versus automated coding).

Deaths are recorded very accurately in France, but the quality of data on causes of death may vary according to age and region. The proportion of undefined causes of death decreased from 10.4% in 1970 to 6.3% in 1999 at the national level, but this proportion varies according to death place and age. In 1999, it ranged from 3.7% in Bas-Rhin to 12.6 % in Paris. In the same year, the proportion of undefined causes was 9.3 % for persons less than 45 years, 4.9% between 45 and 65, 4.4% between 65 and 84 and 8.7% for persons 85 and over.

Population statistics

Information on the size and composition of the resident population of France is gathered by census, carried out under the supervision of INSEE. From 1815 to 1936, a national census was carried out every five years. However, because of wars, the 1916 and 1941 censuses were not carried out. Since 1946, censuses have been carried out at intervals of 6-8 years; the most recent was in 1999. Data are collected by investigators specially employed by INSEE and the quality of these data is high. National Population statistics (census results) are published by INSEE (mean population by 5 year age group). For the years between census, populations at regional or departmental levels are estimated by INSEE.

Publications on mortality and population statistics

General Census of the Population of 1975, 1990 and 1999. [in French]. Paris, INSEE.
La situation démographique en France –Mouvement de la population (1979-1999) [in French]. Paris, INSEE.
Statistics of Medical Causes of Death. Data for the Whole of France and data by * Region and departement (for years 1968 to 1999) [in French], Paris, INSERM
Atlas de la santé en France. John Libbey ed., 2000.

Website CépiDc INSERM (Causes of death data): http://www.cepidc.vesinet.inserm.fr

Website INSEE (Demographic data): http://www.insee.fr

Eric Jougla

4.9: GERMANY (FEDERAL REPUBLIC)

Introduction

The description that follows refers to the Federal Republic of Germany as constituted at the period covered by the data in this atlas (1993-1997) after the unification with the German Democratic Republic in 1990.

Germany covers an area of 357,000 km^2, made up of mountain areas, uplands and plains. To the north the country is bounded by the North Sea and the Baltic Sea, and to the south by the Alps, Lake Constance and the Rhine – which also forms the border in the south-west. The main rivers are the Rhine, the Danube, the Elbe, the Weser and the Moselle. The highest mountain is the Zugspitze (2,962 m) in the Alps. Other upland areas rise to 1,500 m. About half the land is used for agriculture and 31% is wooded. Mineral resources include iron ore, potash, lignite, uranium, copper and natural gas.

The capital is Berlin (population 3,382,000) and the total population of Germany is 82.2 million, with an average density of 230 inhabitants per km^2 (2000).

The number of foreign residents stood at 7.3 million (8.9%) in 2000. Among these, the most common nations of origin were Turkey (1 998 000), Serbia and Montenegro (662 500), Italy (619 000), Greece (365 000), Poland (300 000) and Croatia (217 000).

The Federal Republic of Germany is a democratic, parliamentary State with a federal constitution. It is divided into 16 laender: Schleswig-Holstein, Hamburg, Niedersachsen (Lower Saxony), Bremen, Nordrhein-Westfalen, Hessen, Rheinland-Pfalz (Rhineland-Palatinate), Baden-Wuerttemberg, Bayern (Bavaria), Saarland (Saar), Berlin, Brandenburg, Mecklenburg-Vorpommern, Sachsen, Sachsen-Anhalt and Thueringen. For all but two laender (Hamburg and Schleswig-Holstein) data in the atlas are published at level III (*Kreis*), so that in total 448 different regions are shown. The biggest region (by population) is Schleswig-Holstein with an average of 2,717,000 inhabitants in the years 1993-1997. The smallest area is Zweibruecken with 36,000 inhabitants. The average for all regions is just over 182,000 inhabitants.

Mortality data collection

In the Federal Republic of Germany, mortality statistics are collected by each of the 16 laender independently. Statistics are compiled from information provided by physicians on death certificates which vary among the laender, but are mainly based on the international model proposed by the World Health Organization. From 1979, cause of death was coded according to the 9th revision of the International Classification of Diseases (ICD). In 1997 the 10th revision of the ICD was introduced. Mortality statistics are based solely on underlying cause of death.

The death certificate consists of two parts: an *open part* containing identification data (name, sex, date of birth, place of residence, place and time of death, and mode of death – natural, violent or unknown), and a *confidential part*, on which the physician indicates all causes contributing to the death. In the case of accidental death (for example, following a road accident) the physician must indicate the type of accident. In most laender, the physician may also make a request for an autopsy on the death certificate. Once filled in, the confidential part is sealed.

The physician who certifies the death sends the death certificate to the registrar's office of the town where the person died. A registration sheet, containing identification data and a registration number, is set up for every death; information on this sheet is used to compile population statistics. The death certificate is then sent to the Local Health Authority (*Gesundheitsamt*), where the information on the confidential part is checked by a physician (requests for clarification are rare). Violent deaths and deaths from unknown causes must be reported to the police or public prosecutor's office.

In most laender, the Local Health Authority sends the confidential death certificate to the State Board of Statistics (*Statistisches Landesamt*) where cause of death is coded; in Hamburg, deaths are coded by the Health Authority itself. The ICD code corresponding to the underlying cause of death is entered; contributing causes are not recorded but are considered for the choice of the underlying cause of death. The data are then exchanged between the regional statistical offices according to the place where the deceased person was last resident.

Once checked and corrected, data are pooled monthly, quarterly and annually in the state mortality statistics. On an annual basis, each of the laender transfers pooled data (on laender of residence, year of death, sex, nationality, cause of death (four digits), age (in standard age classes), type of accident and civil status) to the Federal Board of Statistics (*Statistisches Bundesamt*), which uses these data to compile and publish annual mortality statistics.

Validity

To guarantee the homogeneity of death coding in the different Federal States, and to ensure the correct application of WHO instructions for selecting the underlying cause of death, programs with plausibility checks are unified. The Federal Board of Statistics also runs annual training courses for coders.

Population statistics

Demographic data other than age, sex and civil status are only available through the census. The last two censuses, covering all residents in the Federal Republic of Germany, were held in 1970 and in 1987. For years between censuses, population size and composition are estimated by counting the births, deaths and migration reported to the State Boards of Statistics, and relating these figures to the last census data available. As for mortality statistics, population statistics are compiled by each federal state independently. The information from each of the State Boards of Statistics is reported to the Federal Board of Statistics, pooled and then published. As changes of residence are not always reported to the population registry, population data based on this information might be slightly overestimated.

Statistical publications

Each State Board of Statistics publishes its own mortality and population statistics annually in a series of Statistical Reports.

The Federal Board of Statistics publishes national statistics annually. Mortality statistics are published in Fachserie 12, Gesundheitswesen, Reihe 4, Todesursachen (Public Health – Causes of Death), and population statistics in Fachserie 1, Bevoelkerung und Erwerbstaetigkeit, Reihe 1.

The results of the 1987 census were published separately by the Federal Board of Statistics in Fachserie 1, Bevoelkerung und Erwerbstaetigkeit, Volumes 1 to 12.

In addition, articles on specific topics of mortality statistics are published, irregularly, by the Federal Board of Statistics and the State Boards of Statistics. The following are some important publications, in German, from the Federal Board of Statistics in its series *Wirtschaft und Statistik*:
Causes of death 1990/91 in the unified Germany, Volume 4, 1993
Deceased 1993 by causes of death, Volume 12, 1994

Other important publications from the Federal Board of Statistics include the Statistical Yearbook of the Federal Republic of Germany.

To evaluate the quality of the cause of death statistics in Germany, several studies were carried out:

Mieller, W., Bocter, N.: Beitrag zur Abschaetzung der Aussagekraft der amtlichen Statistik. Schriftenreihe des Bundesministerium für Jugend, Familie, Frauen und Gesundheit, Band 253. Stuttgart, Berlin, Köln 1990.

Jahn, I., Jöckel, K.-H. et al: Studie zur Verbesserung der Validität und Reliabilität der amtlichen Todesursachenstatistik. Schriftenreihe des Bundesministerium für Gesundheit, Band 52. Baden-Baden, 1995.

Address: Statistisches Bundesamt, Gustav-Stresemann-Ring 11, 65189 Wiesbaden.

Stefan Dittrich

4.10: GREECE

Territory and population

Greece is bounded in the north by Albania, the Former Yugoslav Republic of Macedonia (FYROM) and Bulgaria, in the east by Turkey and the Aegean Sea, in the south by the Mediterranean and in the west by the Ionian Sea. The total area of Greece is 132,000 km^2, of which the islands account for 25,000 km^2.

The greatest length from north to south is 792 km and the greatest width from east to west is 992 km. The total length of the continental borders of Greece with neighbouring countries is 1,180 km, while the length of the coastline is 15,000 km.

The highest mountain in Greece is Olympos (2,904 m). The Aliakmon is the longest river in Greek territory (297 km). Among the lakes the largest is Trichonida (96 km^2).

Greece produces a variety of ores and minerals and the Greek economy was traditionally based on agriculture with the highest proportion exported of any EU member country.

The country is divided into 10 geographic departments or 13 regions (NUTS 2) and 51 departments, excluding Mount Athos, which is self-governed. The largest city (2001 housing and population census) is Athens (the capital) with 790,000 inhabitants; it is in the department of Attiki with a population of 3,895,000 millions.

According to the population census of March 2001, the usual resident population of Greece was 10.9 million, of which 5,413,000 were males and 5,521,000 females. The population average density was 83 inhabitants per km^2. The total population is mainly urban – 8,212,000, some 75% of the total.

About two thirds of the usual resident population (7,447,000 inhabitants) were aged 15-64 years (68%). The population aged under 15 years totals 1,661,000 (15%), with the remainder of the population, 1,827,000 (17%), 65 years or over.

The only official and written language is Modern Greek with Demotic as its core.

Mortality data collection

The register offices are the sources of information on vital statistics. Each municipality or commune constitutes a separate register area. The Registrar is the mayor or the president of the commune. Registrars are attached to the Ministry of Justice and are supervised by the local Public Prosecutor.

Legislation requires all deaths to be recorded at the regional register offices; official registration is needed for burial. A relative of the deceased, or a person present at the death, delivers the medical certificate, signed by the attending doctor and indicating the cause of death, to the Registrar's Office. Death should be reported within 24 hours of the event.

The register offices are required to send a report of all deaths to the local Regional Statistical Offices of the National Statistical Service of Greece (NSSG) during the month following the death. All the statistical forms are sent to the Central Statistical Office for coding and analysis. Any queries arising due to unclear indication of cause of death on the certificate are referred back to the certifying doctor for clarification. About 55% of deaths in Greece take place in hospitals and other institutions.

The NSSG provides mortality statistics every year to Eurostat and WHO, by sex and age at the NUTS 2 level. Causes of death are coded to the 9th revision of the International Classification of Diseases.

Population statistics

In order to plan for, and implement, economic and social development, administrative action or scientific research, it is necessary to have reliable and detailed data on the size, distribution and

composition of the population. The population census is the primary source of these benchmark statistics on persons, married couples, families and households for a wide variety of geographical units ranging from the country as a whole to small localities or city blocks.

Since the establishment of the Greek State (1828) there have been 29 population censuses (up to 2001) although the information collected has varied over time. Since 1951 the censuses have been on a decennial basis with questions in line with UN recommendations so the collected information is internationally comparable. The traditional complete census has been used for collecting population data, using enumerators and paper questionnaires. The data from the 2001 population census are available at LAU 1 and LAU 2 region levels.

Statistical publications (in Greek and English)

The Statistical Yearbook (annual)
News Release (annual)
The Concise Statistical Yearbook (annual)
Monthly Statistical Bulletin
Mouvement Naturel de la Population de la Grece (annual)

L Andritsopoulou

4.11: HUNGARY

Introduction

Hungary, unified under King Stephen 1st in 1001, was for many centuries an important part of the Austro-Hungarian Empire which was divided into several independent states after the First World War. The country came under the influence of the USSR after the end of the Second World War and achieved independence only in 1990, after the collapse of the USSR. In the same year Hungary held its first multiparty election and in May 2004 it acceded to the EU.

The country and its people

Hungary is situated in the south of Central Europe, lying between 45°05' and 48°45' N and between 16°05' and 22°05' E. The country is situated in the central part of the Carpathian basin encircled by the Alps, the Carpathian mountains and the Binaric Alps along the central parts of the rivers Danube and Tisza. These two rivers divide the country from north to south into three large regions. The area of Hungary is 93,000 km^2, with 690 km^2 of water. Lake Balaton (598 km^2) is the largest lake in Europe. The country's boundaries total 2,171 km; the length of the border with Austria in the west is 366 km, with Slovakia in the north 677 km, in the east with Ukraine 103 km and with Romania 443 km, and in the south with Croatia 329 km, Serbia 151 km and Slovenia 102 km. The largest part of the country is plain at about 200 m above sea level; only 2% is above 400 m. The mountains in the north, on the Slovakian border, are only of medium height with the highest point 1,015 m above sea level.

In the past, Hungary was mainly an agricultural country with a low level of industrialisation. Arable land forms about 52%, and forests about 15%, of the country. There has been a rapid decrease in the area of agricultural land, with corresponding increases in residential and industrial use. The main natural resources are bauxite, coal, natural gas, fertile soils and arable land. Industry is oriented to mining, metallurgy, construction materials, processed foods, textiles, chemicals, pharmaceutics and motor vehicles. About 13% of Hungary, containing nearly half its population, has high levels of air pollution; the main sources are road traffic, industry and heating. The emission of sulphur dioxide was more than twice the EU average. It has also been found that about 10% of children living in cities have relatively high concentrations of lead in blood.

The climate, due to the variable continental, oceanic and Mediterranean influences, is rather changeable with some very cold winters and extremely high temperatures in summer.

Hungary is divided administratively into 19 counties and the capital Budapest (which has county status). The counties are divided into towns and villages. There were 157 cities in 1990. The capital of the country, Budapest, is not only the seat of the government but also the site of many major factories.

The population of Hungary was 10,067,500 (mid-year population 1999) with an average density of 108 persons per km^2. Nearly 90% of the population are Hungarians; the main ethnic minorities in 1995 were Slovaks (0.8%), Romanians (0.7%), Germans (2.6%), Gypsies (4%), and Serbs (2%). On the other hand many Hungarians live in other countries. The median age of the population (2004 estimate) was 38.4 years, 35.9 for males and 41.1 for females. About 16% of the population were children under age 15 years, 69% were in the age group 15 to 64 years, and 15% were aged 65 or over. There were nearly twice as many females than males in the highest age groups. Life expectancy at birth was 66.2 years for men and 75.3 years for women in 1998, both lower than the averages for the countries of central and eastern Europe, including the Baltic states. The sex difference in life expectancy at birth increased from 8.1 years in 1985 to 9.2 years in 1998.

The labour force totalled 4.2 million in 1997, with 8% in agriculture, 27% in industry and 65% in various services. The official unemployment rate is declining and was 9.6% in 1998, lower than the EU average (11.1% in 1997).

Mortality data collection

Health statistics, including those of mortality from cancer, have a long tradition stretching back to the Austro-Hungarian Empire and are available from the end of the 19th century. In Hungary, the beginning of cancer control dates back to the beginning of the 20th century, with the collection of cancer statistics by Farkas in 1901. With the support of the Society of Physicians this work continued in 1904. Since the end of the Second World War, data on mortality have been collected from death certificates having the internationally accepted form and statistics are regularly published by the Hungarian Central Statistical Office. Data on cancer incidence, however, are collected only in smaller territories; the data for the longest period published in "Cancer Incidence in Five Continents" (Vol. I to Vol. VI) were provided by the registry covering the most eastern region of Hungary, Szabolz- Szatmar county.

I Plesko

Population statistics

Estimates of the size and age structure of the population are derived from censuses – the most recent in 1991 was performed together with a National representative survey – taking into account birth and deaths. All demographic data including the mid- and end-year population size and age structure in the whole country and in individual administrative units and regions are computed and published annually by the Hungarian Central Statistical Office in Budapest.

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European Commission on Public Health. *Health status overview for countries of Central and Eastern Europe that are candidates for accession to the European Union*. Geneva, WHO and European Commission, 2002.

Napalkov NP & Eckhardt S, eds. *Cancer control in the countries of the Council of Mutual Economic Assistance*. Budapest, Akademiai Kiado, 1982.

Napalkov NP & Merabishvili VM, eds. *Malignant tumours (According to the data of the CMEA members states)*. Leningrad, Petrov Research Institute of Oncology, 1986 (in Russian).

Parkin DM, Whelan SL, Ferlay J, Teppo L & Thomas DB, eds. *Cancer Incidence in Five Continents, Volume VIII*. Lyon, IARC, 2002 (IARC Scientific Publications No.155).

Pukkala E, Söderman B, Okeanov A et al. *Cancer atlas of Northern Europe*. Helsinki, Cancer Society of Finland, 2001.

Staneczek W, Gadomska H, Rahu M, Chaklin A, Shtraus Z & Plesko I, eds. *Atlas of cancer incidence in the population of the CMEA*. Moscow, CMEA, 1983 (in Russian).

Turner B, ed. The statesman's yearbook 2000. London, Macmillan, 1999.

Vagner RN & Merabishvili VM. *Cancer in selected territories (collection of scientific works)*. Leningrad, Petrov Research Institute of Oncology 1991 (in Russian).

Zaridze DG, Plesko I, Sidorenko JS & Sheliakina TV, eds. *Epidemiology of lung cancer*. Rostov on Don, Rostov University Press, 1990 (in Russian).

Zatonski W, Boyle P & Tyczynski J, eds. *Cancer prevention – vital statistics to intervention*. Warsaw, The Maria Sklodowska-Curie Memorial Cancer Centre and Institute of Oncology, 1990.

Zatonski W, Smans M, Tyczynski et al., eds. *Atlas of Cancer Mortality in Central Europe*. Lyon, International Agency for Research on Cancer, 1996 (IARC Scientific Publications No.134).

4.12: ICELAND

Introduction

Iceland is a volcanic island situated in the North Atlantic Ocean between Europe and America. The area of the island is 103,000 km^2, but the habitable part is only about 24,000 km^2, the rest being glaciers, lakes and wasteland.

The country is divided into eight constituencies. The capital area is located in two of those and consists of the capital city (Reykjavik) and Reykjanes.

Iceland is traditionally a European country, although recent geological studies have shown that the western part of the country is in fact situated on the North-American plate, moving westward, and the eastern part is situated on the Euro-Asian plate, moving eastwards.

Iceland is one of the smallest independent nations in the world. In 2001 the mean population was 285,050 individuals – 142,750 males and 142,300 females. Iceland was mainly settled from Norway 1,100 years ago, but to some extent also from the British Isles, where some Nordic-speaking people were residing. Celtic people were also among the first inhabitants, mostly slaves of the Vikings. Over 100,000 of the inhabitants live in Reykjavik. Reykjanes county includes six bigger districts (municipalities), with 5,000-25,000 inhabitants each, some smaller districts (fishing villages) and countryside. The rest of the inhabitants live in urban areas.

The nation is rather homogenous as there has been relatively little immigration since the settlement of the country. Icelanders have kept good family records since the country was settled.

Throughout the ages the main occupation was agriculture. Then in the 19th century fishing became more important, and migration from the rural areas to more densely populated areas started. This was on a small scale compared with the great migration to fishing and the fishing industry towns in the 20th century. At that time the migration was mostly to the capital area, where more than half of the population now lives. The main occupations have become commerce, services and industry, in addition to the traditional fishing and fish processing.

Mortality data collection

General registration of the underlying cause of deaths in Iceland began in 1911; from 1996 other underlying causes were also registered.

The death certificate is written by a medical doctor, who passes it to the local vicar who then conducts the funeral. The vicar sends the certificate to Statistics Iceland as soon as possible after the funeral has taken place. According to legislation (from 1998) the medical doctor gives the death certificate to the nearest relative, who sends it to the District Commissioner and from there it is sent to Statistics Iceland. In Iceland all information is entered on one form, but the form is folded and sealed so that the medical information is concealed and not available until it is used for statistical purposes.

At Statistics Iceland the name of the person and the personal identification number is checked. The underlying cause of death is coded (International Classification of Diseases (ICD) manually and then checked by a medical doctor, who can refer back to the certifying medical doctor for clarification. When the coding of death certificates is completed, the information is stored in a computerised database.

About 82% of deaths in Iceland (1998) take place in hospitals, nursing homes and other institutions. An autopsy was performed for 19-20% of all deaths occurring in Iceland in the period 1995-1998, but for 31% in the period 1971-1995.

In 1951-1970, the cause of death was coded according to the 7th revision of the ICD. In 1971-

1980 the 8th revision was used and in 1981-1995 the 9th revision. Since 1996, the cause of death has been coded according to the 10th revision.

Population statistics

The *National Register of Persons* within Statistics Iceland was founded 1952. A special census was taken in October 1952 to furnish a base for the new National Register, together with the general census of December 1950. Today the register is a computerised database, updated by means of notices of residence changes and the reporting of births, baptisms, marriages, deaths, etc. All such events must be reported to Statistics Iceland.

Sources of population data in Iceland are unusually rich and reach back three centuries. The first census was taken in 1703 (the inhabitants' names, age, sex and status, plus detailed livestock statistics) followed by a second census in 1769. At the same time the two bishops in the country were required to collect annual records from all parsons on births and deaths in their parishes, and later on confirmations and marriages too. Censuses were taken every ten years in the 19th century until 1960, followed by a long interval until the census of 1981. Since then no census has been taken.

Statistical publications

Statistics Iceland is responsible for publishing mortality and population statistics.
Hagtíðindi (Monthly Statistic) from 1916, includes summaries of statistics under preparation.
Landshagir (Statistical Yearbook of Iceland) from 1991
Hagskinna (Icelandic Historical Statistics) 1997

Icelandic mortality data are also published in:
Publications by *Directorate of Health*
Publications by *Eurostat*
Publications by *Nomesco*
Publications by *WHO*

In addition, information on cause of death is used for special research. The following are examples of such publications:
Björnsson J, Jónasson JG, Nielsen GP. Áreiðanleiki dánarvottorða (Accuracy of death certificates). *Læknablaðið* 1992, 78:181-185.
Tryggvadóttir L, Birgisson H, Jónasson JG & Tulinius H. Upplýsingar um dánarmein á dánarvottorðum (Information on the underlying cause of death from death certificates). *Læknablaðið* 1993, 79:313-320.

E Olafsdottir

4.13: IRELAND

Introduction

The total area of the Republic of Ireland is almost 70,000 km^2. The greatest length from north to south is 486 km and the greatest width from east to west is 275 km.

Ireland consists of a large central lowland of limestone with a relief of hills and a number of coastal mountains, the highest of which is Carantuohill (1,040 m). The Shannon is the longest river, 370 km. There are many lakes. Roughly 81% of the total land is used for agriculture, mostly for grassland pasture. About 5% is wooded. Ireland is a major base-metal producer. Water, peat and natural gas are important indigenous sources of energy.

The country is divided into four provinces (Connacht, Leinster, Munster and Ulster). Dublin, the capital, is in Leinster and is situated on the east coast at the mouth of the river Liffey. The population of the greater Dublin area is approximately 1 million. The Irish population has been increasing since 1961, reaching approximately 3.7 million in 1997, with an average density of 53 inhabitants per km^2. Ireland continues to have a young population with 22% of the population in 1997 aged under 15.

The official languages are Irish and English. Irish (Gaelic) is a Celtic language – one of the oldest written languages in Europe, and it is the first official language. All official documents are published in both languages.

Mortality data collection

General registration of deaths in Ireland began in January 1864, following the Births and Deaths Registration (Ireland) Act 1863. The responsibility for the administration of the registration system, the compilation of death records and the issuing of certificates is vested in the Registrar General, who in turn is responsible to the Minister for Health.

The registration service comprises local registrars in approximately 300 districts throughout the country, under the supervision of about 20 Superintendent Registrars responsible for all the registrations within larger areas, generally counties and county boroughs. Deaths are registered initially at local offices to where the death occurred and the Registrar's books are subsequently forwarded to the Registrar General.

Deaths must be registered within one year of occurrence. A relative of the deceased, or a person present at the death, delivers to the Registrar's Office the medical certificate, signed by the attending doctor and indicating the cause of death. The person registering the death also completes a special statistical form, which is sent, with any medical certificates, to the Central Statistics Office for coding and analysis. Any queries arising due to unclear indication of cause of death on the certificate are referred back to the certifying doctor for clarification.

In cases of sudden death a post-mortem may be required and the death may be registered on the basis of a coroner's certificate. About 10% of deaths in Ireland are registered following inquests or post-mortems.

About 70% of deaths in Ireland take place in hospitals, nursing homes and other institutions.

The coding and statistical analysis of deaths is carried out on behalf of the Minister for Health and Children by the Central Statistics Office. The causes of death in the data used in this atlas were coded in accordance with the 9th revision of the International Classification of Diseases.

Population statistics

The census of population is the main source of population statistics for Ireland. Decennial censuses were undertaken from 1821 until 1911 and, following a break in 1921, were resumed in 1926. Quinquennial censuses have been undertaken since 1946 with the exception of 1976, although a census with restricted content was

carried out in 1979. The usual range of questions on the census questionnaire cover such topics as age, marital status, sex, place of birth, principal economic status, occupation and industry.

For years between censuses, annual April population estimates are published by August of that year. These are available by sex, age, marital status and area of residence (NUTS 3) since 1986. The eight NUTS 3 regions are: Border, Midland, West, Dublin, Mid-East, Mid-West, South-East and South-West. There are two NUTS 2 regions in Ireland: Border, Midland and Western Region, and the Eastern and Southern Region. The latter is made up of the Dublin, Mid-East, Mid-West, South-East and South-West regions.

Statistical publications

Summaries of mortality data are compiled by the Central Statistics Office every quarter, approximately 18 weeks after the quarter to which they refer. A detailed report on each year is also prepared and published approximately two years after the year concerned.

Annual Report on Vital Statistics (published annually for the years 1864-2000), Department of Health and Children/Central Statistics Office.
Quarterly Report on Vital Statistics (published quarterly for the years 1899-2002), Department of Health and Children/Central Statistics Office.
Population and Migration Estimates (published annually for the years 1950-2002, Central Statistics Office.
Health Statistics (published annually for the years 1976-1999), Department of Health and Children.

Address: Central Statistics Office, Skehard Road, Cork or Ardee Road, Rathmines, Dublin 6.

M Heanue

4.14: ITALY

Introduction

The land area of Italy is just over 300,000 km²; it is divided into 20 regions and 103 provinces, eight of which were established after 1995, and 8100 communes.

The Italian regions are grouped in four large functional areas: North-East, North-West, Centre and South–Islands, which have different demographic and socio-economic characteristics.

Population

The population resident in Italy at the end of 2000 was estimated to be 57.8 million, 28.1 million males (51.4%) and 29.7 million females.

During 2000, 543,000 live births and 560,200 deaths were recorded, and about 1,572,000 immigrants and 1,391,000 emigrants were reported to the population registers. The population increase of 2.85‰ was due to the net migration – a natural decrease (more deaths than births) has been recorded in recent years.

The age structure of the Italian population continues to shift towards the elderly: the elderly (aged 65 and over) to child (0-14) ratio rose from 58% in 1980 to 125% in 2000. In 1999 Italy had the highest elderly to child ratio in Europe, 122%; the European average ratio was 96%.

Many factors contribute to this: the reduced level of fertility (1.25 children per woman in 2000, making the country one of the least prolific in the world); and the increase in longevity which results in a higher proportion of elderly people. During the past 20 years, a constant decrease in the proportion of children, from 23% in 1980 to 14% in 2000, has been recorded, together with an increase in the proportion of those aged 65 and over from 13.1% in 1980 to 18.2% in 2000. The proportion of the very elderly (over 80 years of age) has doubled during the last 20 years to more than 4% of the total population.

The age structure has shifted towards the elderly in all the regions, but there are important differences between north and south: in the South the elderly do not outnumber children (ratio 91%), in the North-Centre the ratio has reached 150%, and it has reached 157% in the North-East – more than three elderly people for every two children.

Survival patterns

Mortality trends have been showing decreases all over the country since the beginning of the 20th century. Life expectancy at birth for men was 69.4 years in 1975, increasing to 75.5 years in 1998; for women it was 75.7 and 81.8 years, respectively. The Italian population is consequently one of the oldest in Europe; it also had one of the highest life expectancies at 65 years of age (in 1998).

Male mortality is higher in the Northern regions while the highest female mortality is in the South. The Centre has the highest life expectancy for both sexes.

Mortality patterns

The main causes of death in 1998 were cardiovascular diseases (ICD-9 390-459), which accounted for 39% of male and 49% of female deaths. Cancer (ICD-9 140-239) was the second largest cause of death, being responsible for 32% and 23% of deaths for males and females, respectively. Respiratory diseases (ICD-9 460-519) and violent causes of death (ICD-9 800-999) each accounted for less than 8% of the total.

Mortality data collection

Demographic registries were first established in Italy in 1865, during the unification of the country. All deaths, from whatever cause, have been recorded for the whole country since 1887. All the Italian communes have their own registry office, where births, marriages and deaths are recorded. The death certificate currently used in Italy is based on the International model proposed by WHO.

Deaths must be reported to the communal registry office within 24 hours. When a death is notified, a two–part data form must be filled in. The first part is filled in by the medical practitioner who certifies the death; this part contains comprehensive medical data and specifies whether the death was due to a natural or a violent cause. In the former case, the initial (underlying), the intermediate and the final causes are recorded as well as any other relevant health conditions along with the time interval before death (in years, months and days).

For violent deaths, the violent cause and the description of the lesion are recorded, as well as the diseases or complications that occurred after the lesion, any other diseases before the accident together with the means and the modality of lesion; the date and place of accident and the time between action and accident, and between accident and death, are recorded as well.

Once this first part of the death form is filled in, the medical practitioner sends the form to the registry office of the commune in which the death took place. The registrar fills in the second part, with information on civil status and personal data of the deceased person and sends the form to the Italian National Census Bureau (ISTAT).

ISTAT produces the official mortality data; it codes the underlying cause of death reported on the form, as this one of the most important and demanding phases of the process. Until 1994, the coding was done directly by coders, who also selected the underlying cause of death. ISTAT subsequently introduced a new coding system using dedicated software.

Every year, 75% of the deaths forms are coded by use of the Micar-Acme software (Mortality Medical Indexing Classification and Retrieval – Automated Classification of Medical Entities), developed in the United States. This software is used in various countries (USA, Canada, Scotland, England and Wales, Sweden, Holland and Catalonia). The other 25% of deaths, including violent or AIDS deaths, for which the automated coding is not efficient, are coded manually.

The new system has optimised the production of official mortality data but there are inevitably differences between data coded up to and after 1995. For this reason, ISTAT carried out a bridge-coding exercise for a sample of about 300,000 deaths that occurred in seven months during 1995 (January, February, March, May, July, September, November) that provides both manual and automated classification.

The table below shows the distribution of the deaths in the sample by large groups of causes and by coding system, together with the coefficient of accordance (K) between the two coding systems.

The automated coding reduces the number of deaths attributed to ill-defined causes.

Only anonymous data are processed and published by ISTAT and the Istituto Superiore di

Cause of death	Code		K
	Manual (M)	Automated (A)	(A/M)
Infectious diseases	1230	1644	1.337
Cancer	90554	88850	0.981
Mental disorders, and nervous system and sense organs	10142	11138	1.098
Cardiovascular diseases	143481	143640	1.001
Respiratory diseases	19794	20722	1.047
Digestive system diseases	16676	15698	0.941
Other diseases	21010	21750	1.035
Ill-defined illnesses	4924	4369	0.887
Violent causes	16216	16216	..
Total	324027	324027	..

Sanità – aggregated by cause of death, age, sex, and region and province of residence. Scientists and researchers may have direct access to the anonymous and coded individual records.

Publications

(i) Population

Popolazione legale al 13° censimento della popolazione e delle abitazioni. 13° censimento generale della popolazione e delle abitazioni del 20 ottobre 1991. ISTAT, 1993.

Annuario Statistico Italiano 2001, ISTAT, 2001.

(ii) Mortality

La mortalità in Italia nel periodo 1970-1992: evoluzione e geografia. A cura di L. Frova, S. Prati, G. Boccuzzo, R. Capocaccia, S. Conti, M. Masocco, V. Toccaceli, A. Verdecchia. ISTAT (ed) Roma, 1999, pp 435.

Cause di morte. Anno 1995. ISTAT, annuario 11, 1999.

Cause di morte . Anno 1998. ISTAT, annuario 14, 2001.

La mortalità in Italia nell'anno 1993. A cura di R. Capocaccia, G. Farchi, S. Barcherini, A. Verdecchia, S. Mariotti, R. Scipione, G. Feola, G. Cariani. Roma: Istituto Superiore di Sanità, Rapporti ISTISAN (97/33), 1997.

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La mortalità in Italia nell'anno 1998. A cura di S. Conti, G. Farchi, R. Capocaccia, M. Masocco, G. Minelli, R. Scipione, V. Toccaceli, M. Vichi, R. Crialesi, L. Frova. Roma: Istituto Superiore di Sanità, Rapporti ISTISAN (in press).

Sources of data

Population data are from the ISTAT data bases.

Mortality data are from the Italian Mortality Data Base; they are collected by ISTAT and processed by the Laboratory of Epidemiology and Biostatistics at the Istituto Superiore di Sanità (Italian National Institute of Health).

Susanna Conti

4.15: LATVIA

Introduction

Like Estonia, Latvia obtained its independence only after the end of the First World War. At the beginning of the Second World War, Latvia was annexed by the USSR. Its independence was re-established only in 1991, following the break-up of the USSR. Latvia joined the EU in May 2004.

The country and its people

Latvia is situated in Northern Europe and is similar in many ways to the other Scandinavian countries. The country is located between 55°40' and 58°05' N and between 20°58' and 28°14' E. The land boundaries total 1,159 km: with Belarus 141 km, Estonia 339 km, Lithuania 453 km and the Russian Federation 212 km. The coastline (Baltic Sea) is 531 km long. The total area of Latvia is 64,600 km^2, of which surface water is about 1,000 km^2. Arable land forms about 29% of the territory. Most of the country consists of fertile, low lying plains with some hills in the east. The land in Latvia is often wet and in need of drainage. Approximately 16,000 km^2 or 85% of agricultural land has been improved by drainage during recent decades. Land resources are mainly peat, limestone, dolomite, amber, hydropower, wood and arable land. Industry, despite depending on imports of energy and raw material, includes production of buses, vans, street and railroad cars, synthetic fibres, agricultural machinery, fertilizers, washing machines, radios, electronics, pharmaceuticals, processed foods and textiles. On environmental pollution, the country benefited from the shift towards services industries after regaining its independence. The main priority in this field is improvement of drinking water quality and sewage systems, household and hazardous waste management and reduction of air pollution. The climate is maritime, temperate and continental. Winters are moderate and summers warm and wet, while warm and moist air coming from the Atlantic Ocean causes storms mainly in spring and autumn. Latvia is divided into 26 districts and seven cities. These are further divided into 481 municipalities (civil parishes).

The population of Latvia has decreased in recent decades. In 1990 it was 2,625,000 but decreased to 2,606,000 in 1994 due to Soviet military personnel leaving the country, and fell further to 2,458,000 at the end of 1997. Only just over half of the population is Latvian (55.5%), while Russians make up almost one third (32.4%). Smaller groups include Belarusians (3.9%), Ukrainians (2.9%), Poles (2.2%) and Lithuanians (1.3%). Around 70% of the population live in urban areas and 30% in rural areas; this distribution has not changed substantially during recent years. The average density of the population was 37 per km^2. The overall median age was 38.8 years – 35.6 for males and 41.9 for females. The age distribution was: children under the age of 15 15%; in the age group 15-65 years 69.2%; and in the age group 65 and over 15.8% (2004 estimate). The total labour force (2001 estimate) was about 1.1 million, with 25% employed in industry, 15% in agriculture and 60% in services. The official unemployment rate in Latvia increased from 2.3% in 1992 to 9.1% in 1999, still below the EU average (10.3% in 1999). Health status, including the cancer incidence rates, is closely related to the very short life expectancy in males which decreased in the 1970s but started to increase slowly from 1980. In 1987, male life expectancy started to decline once more and in 1994 fell to 59.5 years – the lowest in Europe with the exception of the Russian Federation. Since 1994 the mortality from main causes of death declined and 75% of the decline in life expectancy during previous seven years has been regained. The downward trend in life expectancy in females to 72.6 years in 1994 has also reversed to 75.4 years in 1999. The sex difference in life expectancy was 13.4 years in 1994 but declined to 10.7 years in 1999.

Mortality data collection

During the period 1993-97, death certificates of international format were used. For the period 1993-94 the codes of ICD-9 were used;

subsequently, ICD-10 was used for all health statistics in Latvia.

Deaths are confirmed, and the death certificates produced by, physicians; the death certificates are sent to the local district or city civil registry office, and then from there (in bulk) to the Central Statistical Bureau. After processing, the mortality data are published in a yearbook "The medical aspects of mortality in Latvia" by the Agency for Health Statistics and in the "Demographic Yearbook of Latvia" published by the Central Statistical Bureau of Latvia. According to the text about the contribution of the National Cancer Registry of Latvia to Volume VIII of Cancer Incidence in Five Continents, there were some difficulties in changing the morphology coding of numerous death cases coded up to 1996 using a system adapted from that used in the USSR. The confidentiality of personal data in Latvia is protected by law.

Population statistics

Annual population estimates based on the 1989 census were made for subsequent years, taking into account births, deaths and migration. The annual estimates of the size and structure of population are available and published every year by the Central Statistical Bureau of Latvia. in the above mentioned " Demographic Yearbook of Latvia". The last census was performed in 2000.

I Plesko

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4.16: LITHUANIA

Introduction

The Lithuanian nation came into being in the 13th to 15th centuries with the formation of the Grand Duchy of Lithuania. In the 16th century it was united with Poland to form a commonwealth. During the partition of this commonwealth by Russia, Prussia and the Austro-Hungarian Empire in the 18th century, Lithuania was absorbed into the Russian Empire. The country obtained its independence in 1918 after the end of the First World War, but was annexed by the USSR in 1940 at the beginning of the Second World War. On March 1990 Lithuania became the first of the former Soviet republics to declare its independence; it acceded to the EU in May 2004.

The country and its people

Lithuania is situated in north-eastern Europe bordering the Baltic Sea. The country lies between 49°15' and 57°30' N and between 49°15' and 57°34' E. Its land boundaries measure 1,747 km; border countries are Belarus (with a 724 km long border), Latvia (610 km), Poland (110 km), and the Kaliningrad region of the Russian Federation (303 km). The coastline is 99 km long. The country has an area of 65,300 km^2. The terrain of the country is mainly lowland, flat with many scattered small lakes; the highest point of the country is only 292 m above sea level. Areas with fertile soil in the central plains are separated by hilly uplands which are the remainders of ancient glacial deposits. Arable land covers about 45% of the country. Natural resources are peat and arable land. The industrial production of the country is rather diverse (in relation to the needs of the market of the former USSR) and oriented to metal-cutting machine tools, television sets, furniture, refrigerators and freezers, electric motors, petroleum refining, building of small ships, textiles, food processing, fertilizers, agricultural machines, optical equipment, electronic components, computers and products made from amber. The agricultural sector produces grain, potatoes, sugar beet, flax, vegetables, beef, milk and eggs. Lithuania is divided administratively into 10 counties, 44 regions, 111 towns and 449 wards (local administrative units).

The climate of the country is transitional, between maritime in the western parts adjacent to the Baltic Sea, and continental in the eastern part. There has been contamination of soil and ground waters with petroleum products and chemicals in the vicinity of the former military bases of Russian troops.

At the beginning of 1997, the estimated population of Lithuania was 3,588,000 persons, of which 1,685,800 were males and 1,902,200 were females, with a population density was 55 persons per km^2. Almost 68% of Lithuania's population lived in urban areas. The mean age of the population of Lithuania was 35.9 years. The mean age of males (33.5) was 4.5 years lower than that of females (38.0). The estimated age structure is 21.4% of the population younger than 15 years, 65.8% in the age group 15-64, and 12.8% in the age group 65 years and over, with the high proportion of females in the highest age groups. Nearly 80% of the population are Lithuanians, 9.4% Russians, 7.0% Poles, 1.7% Belarusians, 1.2% Ukrainians and 1.1% are members of smaller ethnic groups (1989 Population census data). Life expectancy at birth for men was 65.5 years and for women 76.6 years (in 1993 it was 63.2 and 75.0 years respectively). A quite significant difference between the life expectancy at birth for men and women remained: in 1997, life expectancy at birth for men was 11.2 years lower than that for women while in 1993 the difference was 11.8 years. Life expectancy of the rural population, especially of males, tends to be lower than that of the urban population. The largest differences between urban and rural areas were 4.2 years for males in 1997, and 2.2 years for females in 1993.

The total labour force is about 1.5 million; the main areas of occupation in 1997 were industry (about 30%), agriculture (20%), construction and building (15%) and the remainder in transport, communication and various services. Official

unemployment in Lithuania has increased continuously and according to the National Labour Exchange Information the rate in 1998 was 6.4%; by the end of 1999 this had risen to 8.4%.

Mortality data collection

The format of the death certificate is the common international model proposed by WHO and was introduced in 1975. All deaths are confirmed by physicians who also select the underlying and immediate cause of death as well as associated diseases (co-morbidity). The data in death certificates were coded using the International Classification of Diseases; the 9th revision (ICD-9) was introduced in Lithuania in 1978, and ICD-10 has been used since 1998. Death certificates are issued at primary health centres, hospitals or medico/legal departments. Mortality data are computed and published by the Lithuanian Department of Statistics in the annual "Causes of death of the Lithuanian population". The National Cancer Registry of Lithuania has responsibility at Lithuania's Department of Statistics to check the death certificates of cancer patients and examine them for validity of coding and completeness. Approximately 2% of cancer registrations are made from autopsy records and 6% from death certificates only. All institutions dealing with personal data are obliged to follow the recommendations of the Data Protection Agency and appropriate laws.

Population statistics

Demographic statistics are based on results obtained from censuses; the data used in this Atlas and in Volume VIII of Cancer Incidence in Five Continents were based on the 1989 census. The last census was performed in 2001. Population estimates are prepared every year taking into account births, deaths and migration. The size and age-structure of the population (mid- and end-year) in the whole country and in individual administrative regions are computed and published annually by the Department of Statistics.

I Plesko
L Kasparaviciene

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4.17: LUXEMBOURG

Introduction

The Grand Duchy of Luxembourg is a small country, tucked between Belgium, France and Germany. The country is 84 km long and 52 km wide, encompassing an area of 2,586 km^2. It shares borders with a total length of 356 km to the north and west with Belgium (148 km), to the south with France (73 km) and to the east with Germany (135 km).

The country is divided into two clearly defined regions:

1 the Eisléck or Öesling in the north, which is part of the Belgian and French Ardennes, on the western rim of the Eifel, and covers one-third of the territory; and

2 the Gutland or Good country in the centre and the south, covering the remainder of the territory, which is mainly rolling farmland and woods.

The highest point of the country (560 m) is Kneif in the northern village of Wilwerdange. Luxembourg is landlocked, but part of the eastern border (37 km) with Germany is a navigable river, the Moselle. Other important rivers are the Sûre, Our and Alzette. The capital is the city of Luxembourg with a population of 81,800 (2001 census).

According to STATEC (Service Central de la Statistique et des Etudes Economiques) the population of Luxembourg (2001 census) was 441,300. There were 164,700 foreign residents (37%), mainly Portuguese (13.2%), Italian (4.6%), French (4.6%), Belgian (3.4%) and German (2.4%).

Description of the mortality surveillance system

In Luxembourg, the mortality surveillance system – the collection, coding, transmission, analysis, interpretation and utilisation of mortality data – is centrally organised by the Directorate of Health/Ministry of Health. The death registration process has two stages:

1 certification of death (based on the international model proposed by WHO); and

2 coding of the cause of death.

As in all European countries, the medical certification of death is mandatory in Luxembourg. A physician is called to confirm the death; he fills out certain administrative information about the deceased person and certifies the cause of death. For confidentiality reasons, the physician seals the medical part of the death certificate involving the description of the cause of death before giving it to the family of the deceased, who take it to the town hall. Here, the civil registrar documents the death, and completes certain information related to the place of residence and the citizenship of the deceased. He sends a special form of declaration to the National Institute of Statistics and a notification to the municipality of residence. He forwards the death certificate to the Directorate of Health/Division of Sanitary Inspection.

The document used to certify a death has two separate parts: an administrative and a medical part. The administrative part, which is held at the civil registration office of the town hall, consists of identifying information including sex, age, residence, place (district) of residence, occupation, marital status, place of death (hospital, home, public street, etc), nature of death (known, unknown, suspected, etc). Usually, these official death records are directly collected via the death certificate. This part represents the socio-demographic variables and the mortality database. In the medical part of the death certificate, the certifying physician enters as clearly and completely as possible the causes of death, describing the sequences of diseases leading to death, mentioning other contributing conditions and specifying each cause of death involved. In case of a (suspected) non-natural death, the certifying physician will refer the death to the police, who contact the general prosecutor, and the latter decides whether further forensic investigation is needed. If so, the forensic physician can issue the death certificate after the autopsy.

The original death certificate is processed as follows:

-In the Division of Sanitary Inspection, the Inspector-Doctor, who has the exclusive right to open the sealed medical part of the death certificate, decides on the cause of death. He notifies the causes due to certain contagious diseases. He also fixes the conditions of burial (authorisation, transport to another country, prolongation of delay, etc).

-The certificate is then forwarded to the Service of Statistics of the Directorate of Health for the central coding of the mortality data.

-Finally, it is stored in the archive of the Directorate of Health (as an original document after being digitalised).

(See the diagram of the flow of death certificates, below.)

Practices of coding of cause of death and policy regarding corrections

The purpose of the coding process is to select the underlying cause of death and to translate the literal text of the listed conditions into ICD codes. From 1968 to 1970, cause of death was coded according to the 7th revision of ICD; the 8th revision of ICD was used until 1978; the 9th revision of ICD was used until 1997; and since 1998, the 10th revision has been used. These data are centrally processed and codified by the Service of Statistics in the Directorate of Health.

The last major change to the medical part of the general death certificate was made in 1980 when a specific form of infant death certificate was introduced. It covers the peri-natal period (up to 10 days of age) as recommended by WHO. The objectives were to facilitate the collection of mortality data and to improve the quality of infant mortality statistics. Generally, the administrative part of the infant death certificate is similar to the usual death certificate. The medical part requires additional details about the type of infant death (stillbirth, premature, or death at term), the period of gestation, the nature of labour (normal, forceps, caesarean, etc), and infant weight, as well as the cause of death (natural or violent).

About 1-3% of death certificates are queried by the Service of Statistics in order to improve the quality of the causes of death coded (in case of incoherent sequences, imprecise cause of death, etc). In the case of lack of clarity in the description of a specific cause of death, the physician responsible for the mortality statistics at national level asks the certifying physician for clarification.

Potential sources of biases

The completeness and coverage of the mortality register in Luxembourg is good – it is a small country, there are small numbers of deaths, and only one coder. Nevertheless, biases may occur in the process of coding or certification:

- The mortality data cover all those persons who died within Luxembourg's territory, whether listed in the resident population or holding foreign domestic residence. However, the data do not include those who died abroad – this can create a bias, particularly for certain rare causes of death or for deaths in certain groups of age (e.g. children aged 5 to 9).

-Under-declaration of suicide: for cultural, religious, moral or insurance reasons, suicide is sometimes denied by the family or the certifying physician.

-Autopsies are not very common in Luxembourg: the frequency of unknown causes of death has not improved in the past.

-Since there is no Faculty of Medicine in Luxembourg, our physicians have to be trained in different countries (Belgium, France, Germany, UK, etc). Therefore, their medical experience and their skill in filling out death certificates varies.

-An under-estimation of mortality due to alcohol abuse may exist, with such deaths recorded as complications such as liver cirrhosis, accidental falls, aspiration and asphyxia. Conversely, an over-estimation related to ischaemic heart diseases may exist, since these deaths are occasionally coded as an alternative to sudden death, unknown causes or cardiac arrest, mainly when the certifying physician of the emergency medical service did not know the patient.

Population statistics

Demographic data are provided by STATEC. The 35th and most recent census was carried

out in February 2001. Between two decennial censuses, the total population and the structure of this population are calculated by counting the births, deaths and migration reported to STATEC and combining these figures with those from the last available census data.

Statistical publications

Every year, STATEC publishes population statistics and many other statistical data in the "Annuaire Statistique du Luxembourg". Statec's address is

6, boulevard Royal, B.P. 304,
L – 2013 Luxembourg.
Tél: + 352 478 42 21
Fax: + 352 46 42 89
Email: statec.post@statec.etat.lu
Website: www.statec.lu (data available on this website)

National mortality data are published annually by the Directorate of Health:

Direction de la Santé, Service des Statistiques, Allée Marconi – Villa Louvigny, L – 2120 Luxembourg.
Tél: + 352 478 55 58 ;
Fax: + 352 478 50 599
Email: statinfo@ms.etat.lu
Website: www.etat.lu/ms

In addition, STATEC has also published various documents on specific topics:

- Trausch G., 1997, *La mortalité au Luxembourg : 1901-1995*, Cahiers Economiques n° 88, STATEC Editions, presenting mortality data in Luxembourg between 1901 and 1995.
- Statistiques du mouvement de la population – Volume III: 1954 – 1995, Statec Editions, 1996.

The « Registre Morphologique des Tumeurs » Association and the "Laboratoire National de la Santé" publishes morbidity data due to cancer every year.

The "Comité de Surveillance du SIDA" has, since 1984, published annually an activity report presenting morbidity and mortality data.

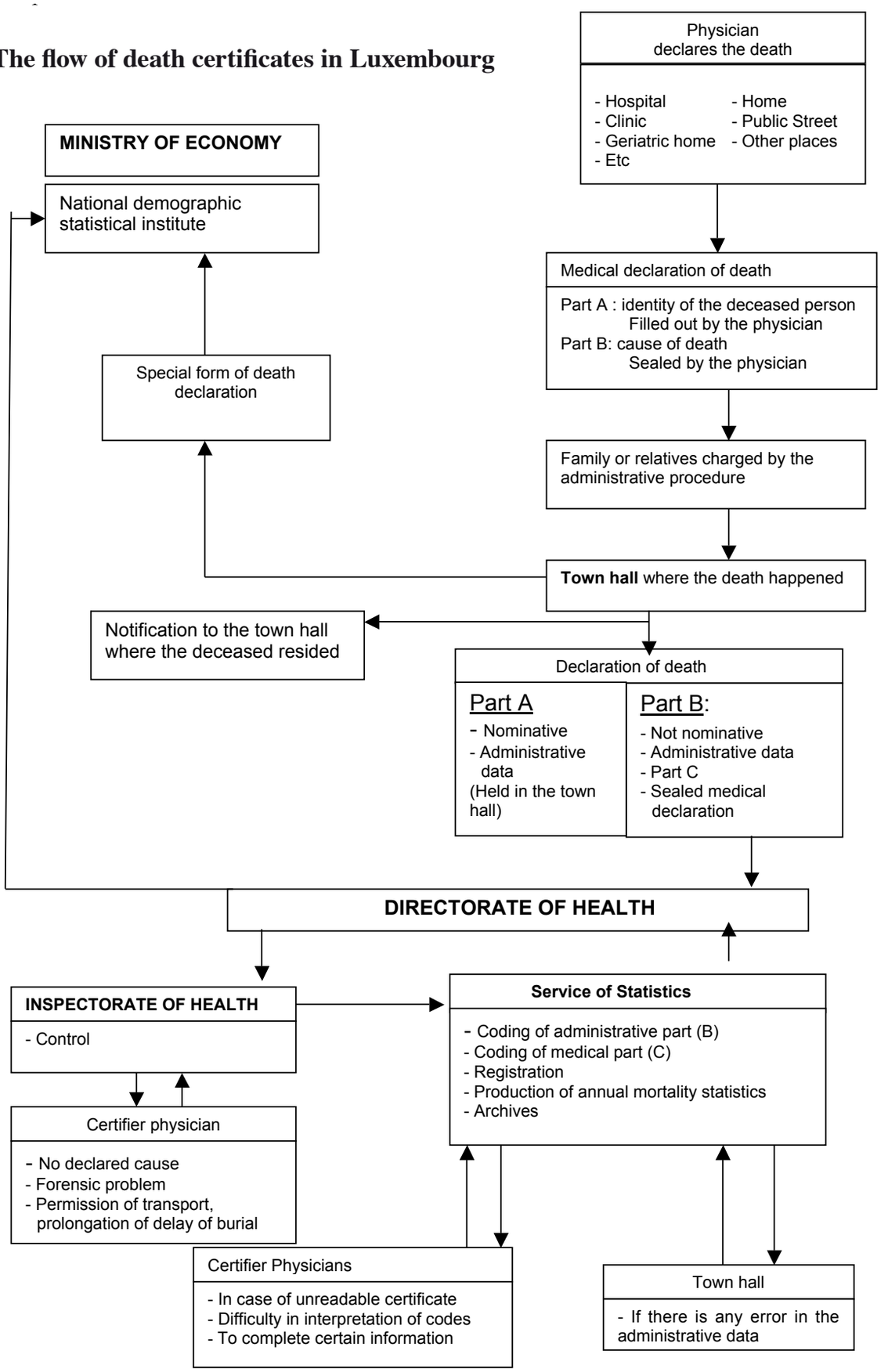
Quality of cause of death statistics

The quality of the national mortality data, particularly the reliability of the coding process, is due to:

- Centralisation of the surveillance system in terms of coding, registration, and processing of mortality statistics
- Coding and registration of the medical data of the death certificates is done by one health professional
- Double checking is always done to overcome possible human error in manual coding and registration
- Constant external contact and intense internal communication with all mortality data customers, for example certifying physicians, civil registrars, inspector-doctor, etc.
- Browsing the newspaper, looking for further information about certain causes of death caused by accidents, suicide, homicide, etc
- Tabulation of deaths for non-residents, in order to implement exchange of information between countries, for deaths occuring abroad
- Initiation of, and familiarisation with, the automated coding system, to improve the quality as well as to reduce the tedious work of manual coding
- International collaboration with WHO, the European Commision, INSERM, etc
- Finally, it is planned to develop the training of physicians in order to improve the certification process.

Guy Weber

The flow of death certificates in Luxembourg



4.18: MALTA

The Maltese Islands

Located in the Mediterranean Sea, just south of Sicily, the Maltese archipelago consists of three main islands: Malta, Gozo and Comino. The total population of the Maltese Islands in 1997 was estimated at 376,500. The distance between Malta and the nearest point of Sicily is 93 km, and from the nearest point on the North African mainland (Tunisia) is 288 km. Malta is the largest island measuring 27 kms by 14.5 km. The area of the Maltese Islands is 316 km^2. Malta is characterised by a series of low, flat-topped hills with terraced fields on their slopes. Malta's coastline is well indented with natural and man-made harbours, bays, creeks, several sandy beaches and rocky coves.

Malta's climate is strongly influenced by the sea and is typical of the Mediterranean. The islands have a very sunny climate with a daily average of five to six hours sunshine in mid-winter and more than 12 hours in summer. Annual rainfall is low, averaging 580 mm a year.

The strengths of the Maltese economy are its limestone, a favourable geographical location, its rich history and a productive labour force. The economy is dependent on foreign trade, manufacturing, tourism and financial services. The official languages are Maltese and English.

Mortality data collection

The National Mortality Registry, together with the National Cancer Registry, is housed within the Department of Health Information and Research (DHIR). The DHIR is one of the eight departments of the Health Division of the Ministry for Health. It is responsible for the management of national health data sets as well as for a number of other databases on health service activity. The department is also responsible for the National Health Interview Survey.

All death certificates of people who die in the Maltese Islands (around 3,200 each year) are received at the department where the National Mortality Registry is responsible for the coding, inputting, and verification of the information and analysing the data in order to produce mortality statistics which are as accurate and timely as possible. A copy of any death certificate in which cancer is mentioned is given to the National Cancer Registry.

Published mortality data by cause of death are available since 1872 in Malta. These were produced in the form of a fortnightly report published by the Chief Police Physician. Annual reports after 1896 were published by the Chief Government Medical Officer.

Main sources of information and reports received at the National Cancer Registry

Sources	Reported by	Notes
Clinical notification	Hospital doctors, GPs and others	Notification of Cancer Act, 1957
Copy of histology and cytology report	Pathology laboratories	State-owned (1) and private (8)
Copy of autopsy report	Pathology laboratories	Autopsies are only done in state-owned general hospitals
Death certificates	National Mortality Registry	Another registry at DHI
New referrals to Oncology Department	Oncologists	There is only one Oncology centre on the Islands

The Department of Health Information and Research and its forerunners have been responsible for keeping mortality data since 1983. Mortality data is available in electronic form from 1991. Mortality data have been coded using ICD-10 since 1995.

The National Cancer Registry is population-based and aims at covering all cancer diagnoses in residents of the Maltese Islands. These amount to about 1,200 new diagnoses each year excluding non-melanoma skin cancers. The main sources of information for the cancer registry are shown in the table below.

The first attempts at cancer registration in Malta were made in the mid-1960s. The present registry was started in 1985.

Statistical publications

The National Statistics Office came into being in March 1947, although official statistics had been compiled and published for a long time previously. In 1872, an official publication called The Malta Blue Book featured a statistical view of Malta and its Dependencies for the previous ten years – 1863 to 1872 – including time series for population, education, finance, sale of public sites, imports, exports and shipping. The National Statistics Office (NSO) is responsible for carrying out a census of the population every ten years. Mortality statistics are compiled by the DHIR and sent to the National Statistics Office on a yearly basis. Statistics regarding cancers are compiled by the National Cancer Registry.

Sources of Information:

Department of Health Information and Research, Malta: www.sahha.gov.mt/entities/healthinformation.html
National Statistics Office, Malta: www.nso.gov.mt

K England

4.19: THE NETHERLANDS

Introduction

The Kingdom of the Netherlands was formed in 1815. In 1830 Belgium seceded and formed a separate kingdom. A modern, industrialised nation, the Netherlands is also a large exporter of agricultural products. The country was a founding member of NATO and the EU, and participated in the introduction of the euro in 1999.

The Netherlands has an area of about 41,500 km^2, and extends roughly 300 km north to south and about 200 km east to west. Behind the North Sea coast lie the 'polders' – land partly reclaimed from the sea. The islands in Zeeland and South Holland provinces are linked by secure dikes to prevent the recurrence of disasters caused by storm tides. About 27% of the country's total area is below sea level, and the land is criss-crossed by a network of lakes, rivers and canals. Land over 100 m above sea level is to be found only in the south-east corner of the country.

About 70% of the land area (excluding water) is used for agriculture or horticulture and 9.5% is wooded. Mineral resources include coal, oil and natural gas.

The capital is Amsterdam (population 736,000), but the seat of government and the location of most central government departments is The Hague (population 458,000).

The Netherlands has a population of 16.1 million, with an average density of 475 inhabitants per km^2 (2002), making it one of the most densely populated countries in the world.

Dutch is the national language. There is a Frisian minority, speaking its own language, in the north of the country.

The Netherlands is divided into 12 provinces: Groningen, Friesland, Drenthe, Overijssel, Flevoland (established in 1986), Gelderland, Utrecht, North Holland, South Holland, Zeeland, North Brabant and Limburg. Each province has a Provincial Council and a Provincial Executive (responsible for day-to-day business), both chaired by a Queen's Commissioner appointed by the Government. The provinces are divided into 40 corop regions. These regions were set up in the early seventies for statistical and planning purposes. These regions consist of one or more centres and their surrounding areas. Corop regions are the NUTS level 3 subdivision of the Netherlands. Corop boundaries do not cross provincial and municipal boundaries, so that corops comprise several municipalities all contained within a single province.

Mortality data collection

The principles of the present system for notification of death and compilation of cause-of-death statistics date from 1927, modelled after the system of Switzerland. When a natural death occurs, the attending physician prepares two documents: a death certificate and a cause-of-death certificate (CoD-certificate). In the case of non-natural death, notification of death is given by the "legal physician". The CoD-certificate is a strictly confidential document on which the name of the deceased does not appear. It is inserted in an envelope which is then sealed. A perforated slip of paper attached to this envelope bears the name of the deceased. Civil registration of death takes place when both the death certificate form and the CoD-certificate are presented at the office of the Local Registrar of the municipality where the death occurred.

In the Local Registrar's Office, the data stream is split: demographic and medical data about the deceased go to Statistics Netherlands (CBS) separately, keeping the medical data confidential. At CBS these two data streams are merged again, using the entry number in the municipal death register. This number has been written on the envelope of the CoD-certificate.

At CBS the envelopes with the CoD-certificates are forwarded to the Medical Officer. After opening

of the envelopes the information on the cause of death in the CoD-certificates is coded – according to the 9th revision of the ICD in the period 1979-1995 and the 10th revision from 1996 onward.

Demographic data from the automated municipal population registers (date of death, date of birth, marital status, etc) concerning the deceased are meanwhile being processed by CBS.

After coding of the cause of death and processing of the demographic information have been completed, the two data sets are linked by means of the certificate number (and the number of the municipality where the death occurred). The final and complete data set on cause of death is used to produce statistics on cause of death differentiated by various characteristics.

Information on cause of death is available for the following characteristics: primary and secondary cause of death, municipality where the death occurred; date of death; date of birth; sex; nationality; country of birth; marital status; date of marriage or divorce; municipality of residence; municipality of birth (for infants only); place of death (hospital or at home); and whether a post-mortem examination was performed.

In some cases, the CoD-certificate contains incomplete or inconsistent information or is missing. Whenever possible, the Medical Officer of the CBS requests the attending physician to provide the missing information or to resolve inconsistencies. As a result of such efforts, more than 80% of these cases can be coded satisfactorily. The percentage of cases where the cause of death is described as 'unknown or badly described' (ICD-10 R95-R99) was 3% in 2002. The percentage of known autopsies in the Netherlands is around 5%; in 86% of the deaths, no post-mortem was held, while for 9% of deaths, no information was available (in 2002). About one third of the deaths (33%) occurred in hospitals in 2002; 60% occurred elsewhere and for the remaining 6% no information was available.

Population statistics

Information on the size and composition of the population of the Netherlands is based on the automated municipal population registers. In these registers information is stored on every inhabitant of the municipality. When an inhabitant undergoes a demographic event that results in the register being updated, Statistics Netherlands is informed directly by means of an electronic message. These messages are the building blocks for the population statistics.

This registration system is known as the GBA system, which stands for Gemeentelijke Basis Administratie persoonsgegevens, the municipal basic registration of population data. 'Basic' refers to the fact that the GBA serves as the basic register of population data within a system of local registers. Among these registers are the local registers on social security, the local registers of water and electricity supply, the local registers of police departments that are concerned with the foreign population in the Netherlands and the (national) registers of the old age pension fund system.

The GBA system was introduced on 1 October 1994. It is a fully decentralised, comprehensive and cohesive population registration system. Due to local provisions there is no central counterpart of these municipal registers. In this respect the system is unique in the world. Every municipality in the Netherlands has its own population register containing information on all inhabitants of that municipality. This information on each individual inhabitant is contained in a personal file (PL). In the registration system each inhabitant has been given a unique personal identification number (pin), which enables the municipal authorities to link his or her data to those on a spouse, parents and children. For this reason on each PL not only the inhabitant's pin is stored, but also those of the parents, the spouse and the offspring. This is done if these persons were in the population register of that municipality at any moment since 1 October 1994.

The personal file includes personal data, for example about the mother, father, citizenship, marriage, partnership, widowhood, divorce, death, registration, address, offspring, legal permit to stay in the Netherlands, legal restrains, passport and the right to vote.

Up to and including September 1994, the population registers were a paper card system.

These registers were maintained by the Local Registrars in the different municipalities and comprise all the personal cards of the de jure resident population of these municipalities. New personal cards were made out for births and migrants into The Netherlands. All changes in personal situation, such as marriage, divorce, change of residence or death, were entered on this card. When a person moved to another municipality his or her personal card was forwarded to the municipality of the new residence. In the case of emigration or death, the personal card was removed from the register. The population figures from the 1971 census (the last census in the Netherlands) were used as the base.

Over the years, a number of changes have occurred in municipal boundaries. The few small changes in boundaries do not affect the comparability of the data presented in this atlas.

Statistical publications

Data and articles on mortality by age, sex, region and cause of death are available in StatLine, the electronic databank of Statistics Netherlands at www.cbs.nl. It contains statistical information on many social and economic subjects in the form of tables and graphs. All the information in StatLine may be consulted, printed and downloaded free of charge.

The Atlas of Cancer Mortality in the Netherlands, 1979-1990 (in both English and Dutch) consists of maps, supplemented by graphs and tables, showing average standardised mortality ratios for the period 1979-1990 of cancers from a large number of sites by the 40 corop areas. The graphs and tables also show standardised mortality ratios of cancers of various sites for six two-yearly periods from 1979 to 1990 in corop areas, provinces and large municipalities.

Address: Division of Social and Spatial Statistics, Statistics Netherlands, Henri Vaasdreef 312, P.O. Box 24500, 2490 HA Den Haag.

J Hoogenboezem

4.20: NORWAY

Introduction

Norway is in the north of Europe between 57°58′ and 71°11′ N. The seaboard on the North Sea and North Atlantic Ocean is some 3,419 km long (excluding numerous islands and fjords). The mainland borders with Sweden, Finland and Russia are 2,542 km long and the land area is about 323,800 km^2. Approximately one-third of the mainland lies north of the Artic Circle and some 40 percent of its area is more than 600 m above sea level. Due to the prevailing westerly winds coming from the Atlantic and also the Gulf Stream, the country has a higher average temperature than one would expect given its latitude. These winds also make the annual precipitation higher in the western part of South Norway than in the rest of the country. Only 3% of the area is arable land and 27% is forests and woodland. The discovery of oil and gas in adjacent waters has been a main determinant of the Norwegian economy. Other natural resources are hydropower, timber and fish.

The majority of the Norwegian population are caucasians. The country has 4.5 million inhabitants. At present there are about 260,000 immigrants from all over the world (of whom 40,000 are second generation). Some 20% of the immigrants are from the northern parts of Europe and 50% from third world countries. Some 20,000 to 40,000 samis comprise a racial minority; their traditional homeland was in the northern part of Norway. There is a great variation in population density from 1,190 km^2 in the capital of Oslo to 1.6 km^2 in Finnmark, the northernmost county. Most cities and towns are situated on the coast. Norway is divided into 435 municipalities and 19 counties. The counties are: Østfold, Akershus, Oslo, Hedmark, Oppland, Buskerud, Vestfold, Telemark, Aust-Agder, Vest-Agder, Rogaland, Hordaland, Sogn og Fjordane, Møre og Romsdal, Sør-Trøndelag, Nord-Trøndelag, Nordland, Troms and Finnmark.

Health services are a part of the Norwegian welfare system and much is spent in maintaining equal opportunities for health services all over the country. Most hospitals are run by the government and the public health system covers all municipalities. For all inhabitants medical treatment is either free or only a modest payment is required. The country is divided into five health regions with responsibility for diagnosis and treatment of cancer, but patients with rare diseases or special needs might be transferred to other regions.

Mortality data collection

Since 1951, Norwegian cause of death statistics have been collected, classified and edited according to the International Classification of Diseases (ICD). The international form of medical certificate of cause of death recommended by the World Health Assembly is used. The present forms for certifying cause of death were introduced by Ministry of Social Affairs in 1983. Centralised coding of cause of death is performed at Central Bureau of Statistics (Statistics Norway). The coding was in accordance with ICD-9 in the period 1986-95 and with ICD-10 thereafter.

The law requires that when someone dies, a physician issues a medical death certificate. This includes demographic and medical information on the deceased. The certificate is taken to civilian authorities in the municipality who send it to the public health officer. The demographic information forms the basis for civil registration of deaths. In the case of deaths without medical information, the civilian authorities fill in a form with the demographic information and send it to the public health officer who has responsibility for the determination of cause of death. The public health officer regularly sends all death certificates issued in his/her municipality to Statistics Norway.

In the coding of cause of death, Statistics Norway has access to information from the Cancer Registry of Norway which includes incident cancer cases since 1953, the Medical Birth Registry which includes medical information on births since 1967, autopsy

reports from hospitals and forensic institutes, and information from statistics on road traffic accidents (from Statistics Norway).

The medical certificates are matched against the deaths in the civil registration of deaths in the Central Population Registry. If medical information on a death is lacking, a reminder is sent to the health authorities. Statistics Norway contacts the certifier in cases where the information is insufficient for coding the underlying cause of death. The coverage of the cause of death statistics is close to 100%. In 1997, 2.4% of all deaths, and 2.1% among people aged over 74 years, were classified as "Unknown and unspecified causes".

Population statistics

Information on the size of, and changes in, the resident population of Norway can be found in the Central Population Registry. Major demographic events such as birth, death, marriage/divorce and migration are recorded. Since 1964 all inhabitants of Norway have had a unique identification number. This is used in several areas of social life and enhances the linkage of different data sources. The Central Population Registry is run by the Directorate of Taxes and there are local population registries in each municipality.

The first national census was held in 1769, when there were 724,000 inhabitants in Norway. Since the Second World War there have been censuses in 1946, 1950, 1960, 1970, 1980, 1990 and 2000. From 1980 the Central Population Registry has provided the basis for the censuses.

Statistical publications

Statistics Norway is responsible for the publication of statistics on cause of death, population and censuses. From 1964 onwards, annual publications on cause of death have been issued. Earlier cause of death figures can be found in the series Health Statistics (1962-63) and Sundhedstilstanden og medicinalforholdene i Norge/ Rapport sur l`état sanitaire et médical (1854-1961). Annual figures for the population from 1986 can be found in three series: Changes in Municipalities, Population 1 January and Survey. Earlier important series are those on Vital Statistics and Migration Statistics which date back to 1866. For each census there are several publications on population by sex, age, marital status, education, occupation and industry for geographical subdivisions of the country. There are also publications on family/ household and housing statistics.

Statistics Norway publishes official statistics on their website (http://www.ssb.no).

Tor Haldorsen

4.21: POLAND

Introduction

The Polish nation was formed in Central Europe around the middle of the 10th century. After a long period of economic and political evolution, particularly in the 16th century, internal disorders weakened the country. In a series of agreements in the late 1770s, Russia, Germany and Austria divided Poland among themselves. Poland regained its independence in 1918, but was occupied by Germany and the USSR at the beginning of the Second World War. After the post-war years under the influence of the USSR, Poland regained its independence in 1990 and acceded to the EU in May 2004.

The country and its people

Poland is situated in the northern part of Central Europe between the Baltic Sea in the north and Carpathian mountains in the south. In the west its territory is limited by the river Odra and in the east by the river Bug. The territory is situated between 49°00' and 54°50' N and 14°07' and 24°08' E. The country covers an area of about 314,000 km^2. Poland's western neighbour is Germany with which it has a border of 470 km; in the south are the Czech Republic (border 558 km) and Slovakia (444 km); to the east are Lithuania (91 km), Belarus (407 km) and Ukraine (526 km); and to the north are the Kaliningrad region of Russia (206 km) and the Baltic Sea with a coastline of 524 km.

Poland is a lowland country, mostly flat and with 75% of its area less than 200 m above sea level; only 3% is above 500 m. The highest point in the Tatras Mountains reaches 2,499 m. Poland has many thousands of lakes with a total area of nearly 3,200 km^2.

In 1990, agricultural land covered about 60% of the country. The extent of agricultural land is diminishing gradually every year: about 9% has been converted to other purposes since 1946. Forested areas have increased from 21% in 1946 to 28% in 1990.

Poland is rich in resources including coal, sulphur, copper and iron ores, common salt, natural gas and arable land as well as lead, silver and amber. Polish industry is oriented to machine building, iron and steel, coal mining, chemicals, ship building, food processing, glass, beverages and textiles. About 40% of Polish industry is located in south-western Silesia, but Warsaw, the capital of Poland, is also a major industrial centre. Rapid industrialisation in the post-war years resulted also in growing environmental pollution, although this subsequently declined with reductions in heavy industry production and increased environmental concern of both the government and the population after 1989. Nevertheless, Poland is one of the leading emitters in Europe of sulphur dioxide (10% of total sulphur dioxide in Europe), and nitrous oxides (8%). Power engineering, chemical industry and metallurgy are responsible for about 65% of the total emissions. In 1990, 48% of industrial enterprises and 363 towns had no water treatment plants. Only 67% of the total sewage was treated while the remaining 33% was dumped into surface waters (rivers or lakes).

In 1975, the country was divided into 49 administrative provinces (voivodship). Voivodships are divided into communes (gminas) and towns. At the end of 1990 Poland had 830 towns, of which 20 were populated by more than 200,000 inhabitants, and 2,121 other gminas. In 1997, a new administrative division of the country was introduced with the number of provinces reduced to 16. The maps in this atlas are based on the administrative division in use from 1975 to 1996.

Poland has a mild climate characterised by the influences of the continental climate of eastern Europe and the maritime climate of western Europe and the Baltic Sea, so its weather is quite variable. The winters are often cold with frequent precipitation, while summers are mild with frequent showers and thunderstorms. The plains of central Poland have the lowest precipitation.

The total population of Poland in 1990 exceeded 38.2 million, 18.6 million males and 19.6 million females. By 2004 it had risen slightly

to 38.6 million. The density of population was 124 per km^2 with wide differences among the regions. Poland has an ethnically homogenous population – Poles make up 96.7%, with small ethnic groups of Germans, Belarusians, Ukrainians, Czechs and Lithuanians.

The median age of the population in 2004 was 36.2 years, 34.3 years for males and 38.2 for females. About 17% of the population was less than 15 years old, 70% in the age group 15 to 64 years, and 13% 65 and over. Life expectancy at birth was 68.9 years for males and 77.6 years for females in 1999. Life expectancy for women began to increase in the mid-1980s and is now some 2.5 years higher than in 1974. For men an earlier decline in life expectancy was reversed only in the 1990s. The sex difference in life expectancy in Poland was 8.7 years, more than two years greater than the average for the EU.

At the end of 1996 there were 20.1 million working people, of which 46% were women. About 30% were working in agricultural production (of these, about two thirds in small private farms), nearly 17% in industry and building, 18% in transport, communication, trade, education, or in financial, social or health services. The official unemployment rate in Poland increased from 6.3% in 1990 to 16.4% in 1993, then decreased to 10.5 in 1998, but rose again to 13.1% in 1999. Unemployment in most countries of eastern and central Europe may, however, be higher than the official rates.

Mortality data collection

Poland has had very good mortality statistics, including on cancer mortality, from the late 1950s. These data were regularly used in the first comparisons of cancer mortality in European countries in the post-war period after the end of the Second World War. Mortality statistics are based on the evaluation of data present in death certificates. All deaths in Poland are confirmed and the immediate and underlying causes of death are selected by physicians. The internationally accepted structure of the death certificate was introduced in Poland, as in the majority of the countries of central and eastern Europe, in the late 1950s, together with use of the latest revisions of the International Classification of Diseases (ICD). The data present in death certificates are completed in the local Registrar's Office and then compiled and regularly published by the Central Statistical Office. Several cancer mortality atlases covering different periods have been published. Introduction of the International Classification of Diseases for Oncology (ICD-O), together with data on cancer incidence derived from the national and regional cancer registries covering relatively long periods of time, enabled the presentation of incidence data from some regions in "Cancer Incidence in Five Continents" as well as the participation in, and use of the data for, several international projects in cancer epidemiology. Relatively high cancer incidence, and consequently cancer mortality rates, are a major influence on the low life expectancy figures, particularly in males.

Population statistics

Censuses were held in Poland in 1978 and 1988. Intercensual estimates were prepared for the years 1984 to 1995 based on census data and taking into account births, deaths, migration and administrative changes. Data on the size and age structure of the population for the whole of Poland and for smaller administrative regions are published annually in the Statistical Journal by the Central Statistical Office.

I Plesko

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4.22: PORTUGAL

Introduction

Located in southwest Europe, Portuguese territory is made up of a continental region, with an area of 89,000 km^2 and the archipelagos of the Azores (nine islands) and Madeira (two main islands and the small islets Desertas and Selvagens) situated in the Atlantic Ocean with areas of 2,320 and 800 km^2, respectively. Bounded by the Atlantic Ocean to the west and south, the continental territory has a coastline of 1,411 km, and a land border of 1,320 km with Spain to the north and east.

About 70% of the territory situated below 400 m, and only 12% above 700 m. The River Tagus crosses the Central Region, flowing from east to west into the Atlantic Ocean near Lisbon. North of the Tagus, 95% of the territory has an altitude above 400 m; 62% of the area to the south has an altitude below 200 m. The highest point is in the Azores (Pico Island, 2,351 m); within the continental territory the highest altitude is 1,993 m (Estrela Mountain) in the Central Region.

The climate is temperate and influenced by Atlantic characteristics which are more noticeable to the north of the Tagus River. In the South Region, summers are hot and dry, whilst winters are normally rainy. Over the last 15 years the average annual precipitation value has been about 850 mm, varying between 542 and 1,092 mm. Recorded average annual temperatures have varied between 14.9 and 16.6ºC. The highest mean monthly values of 30ºC have been registered during the months of July and August, and the lowest mean values around 4ºC during the winter months. The highest temperature variations are registered in the interior Central and Northern Regions.

The estimated Portuguese population at the end of 2005 was 10,570,000, with 5,116,000 males and 5,454,000 females. The population density in coastal areas, where the main urban centres are located, is higher than in the interior of the country. The two main cities are Lisbon with 520,000 inhabitants and Oporto with 233,000. However, their wider metropolitan areas contain 2.8 and 1.3 million inhabitants, respectively, almost 40% of the Portuguese population. According to the 2001 census, there were six cities with a population above 100,000 inhabitants, totalling around 1,326,000 people. There were 120 urban centres with a population of between 10,000 and 100,000 inhabitants with a total of 2,580,000 individuals; and 114 urban centres with a population between 5,000 and 10,000 inhabitants, in which 800,000 people lived. The remaining population lived in places with less than 5,000 inhabitants.

The average population density is 115 inhabitants per km^2. The highest values are in some districts of the metropolitan areas of Lisbon, Oporto and Braga (above 750 inhabitants per km^2); in most of the districts of the interior, the density is less than 60 inhabitants per km^2.

During the 20th century, in spite of several demographic upheavals the Portuguese population almost doubled, although with low growth rates: the 1900 census registered 5,447,000 inhabitants, while the 2001 Census registered 10,356,000.

The official language of the country is Portuguese. Most of the Portuguese (around 84% of the total population, according to the 2001 Census) consider themselves Catholic, with a minority that follow other Christian religions and other creeds.

According to the Constitution, the Portuguese Republic is based on the principles of sovereignty, freedom of speech and democracy. Administratively, the country is divided into 18 districts within the continental territory and two Autonomous Regions (Azores and Madeira). Districts are divided into municipalities, and these into parishes. In total, the country is made up of 308 municipalities and 4,257 parishes.

Mortality data collection

General registration of deaths in Portugal began in 1910 with the establishment of the Republic.

The responsibility for the administration of the registration system, the compilation of death records and the issuing of certificates is vested in the Registrar General, who reports to the Minister for Justice.

The registration service is based on local registrars in 308 municipalities throughout the country. They are also responsible for all the registrations in surrounding areas, generally counties and county boroughs. Deaths are registered initially in the local offices where the death occurred. The local officials make a hand-written copy of the Registrar's form, which is subsequently forwarded to the National Statistics Institute.

Deaths must be registered within two days of occurrence. A relative of the deceased or a person present at the death delivers the medical certificate, signed by the attending doctor and indicating the cause of death, to the Registrar's Office. The person registering the death also completes a special statistical form, which is sent to the National Statistics Institute for coding and analysis. The National Statistics Institute then sends those forms to the Directorate-General of Health for coding and analysis. Since 2002, any queries arising due to unclear indication of cause of death on the certificate have been referred back to the certifying doctor for clarification.

In cases of sudden death, a post-mortem may be required and the death may be registered on the basis of a certificate completed by a doctor after the post-mortem inquest. About 7% of deaths in Portugal are registered following post-mortems inquests. About 50% of deaths in Portugal take place in hospitals. Since 2002, cause of death has been coded in accordance with the 10th revision of the International Classification of Diseases.

Statistical publications

Summaries of mortality data are compiled by the National Statistics Institute every month. A detailed report for each year is also prepared and published approximately two years after the year concerned.

The Directorate-General of Health also publishes its own publications on these subjects, based on the same data, but with the distribution of deaths by district.

Health in Portugal 2007. Lisboa, Direcção-Geral da Saúde, 2007 (http://www.dgs.pt)

Anuário Estatístico de Portugal 2005. Lisboa, Instituto Nacional de Estatística, 2006 (http://www.ine.pt)

Censos 2001:Resultados definitivos; XIV Recenseamento Geral da População: IV Recenseamento Geral da Habitação. Lisboa, Instituto Nacional de Estatística, 2001 (http://www.ine.pt)

J Catarino

4.23: SLOVAKIA

Introduction

Until the end of the First World War, Slovakia was part of the Austro-Hungarian Empire. In 1918 Slovakia joined the closely related Czechs to form Czechoslovakia. In 1968 the political structure was changed and the state was transformed into a federation with the name Czech and Slovak Federative Republic. Following the collapse of the socialist system in 1989 the country regained independence through its peaceful "Velvet Revolution". In January 1993 the Czechs and Slovaks agreed to separate the country into the Czech Republic covering the territory of Bohemia and Moravia, and the Slovak Republic covering the territory of Slovakia. Slovakia joined the EU in May 2004.

The country and its people

The Slovak Republic (conventional short form Slovakia) is situated in central Europe in the Pannonian Basin. The territory of Slovakia has a broadly rectangular shape with gradual narrowing from the west to the east. The area of Slovakia is about 49,000 km^2; it lies between 47°43' and 49°36' N and between 16°54' and 22°34' E. The whole country is relatively small: the distances between the northern and southern borders vary from 76 to 195 km and the distance between extreme east and west is only 428 km. The neighbouring countries are: in the north Poland (with a border of 597 km), in the east the former USSR now Ukraine (98 km) and in the south Hungary (679 km) and Austria (76 km). The new western neighbour is now the Czech Republic with a border of 265 km.

About 40% of Slovakia is lowlands up to 300 m above sea level, 45% is between 300 and 800 m, 14% is between 800 and 1500 m, and only 1% is mountains above 1500 m; the highest point is 2,695 m above sea level. The fertile lowlands are situated in the south-western part of Slovakia in the northern extension of the great Western Pannonian Basin. This lowland is divided by the Carpathian Mountains into two parts, the smaller part lying in the extreme south-west of the country along the basin of the river Moravia and the larger in the northern part of the Danube basin. The lowlands situated in southeastern Slovakia are the northern extension of the Eastern Pannonian Basin. The central part of this lowland (100 to 120 m above sea level) is surrounded by hilly land (110 to 160 m). Arable land makes up about 30% of the country. The climate is continental with hot summers and cold and frosty winters, particularly in the mountainous regions.

Until 1996, the territory of Slovakia was divided into four counties, one of which was the capital Bratislava, and 38 districts. In 1996, new administrative boundaried were introduced, dividing the country into eight counties and 78 districts.

Natural resources are brown coal and lignite, small amounts of iron, copper and manganese ores, salt and arable land. Industry is oriented to the production of metal and its products, electricity, gas, coke, oil, nuclear fuel, chemicals and manmade fibres, machinery, paper, ceramics, transport vehicles, textiles, electrical and optical apparatus, rubber products, food and beverages. In some areas there is air pollution from metallurgical plants and the resulting acid rain damages forests. One small region in northwestern Slovakia is also polluted with arsenic from power plants which used coal with a high content of this element.

The total population of Slovakia in 1995 (estimate based on the census of 1991) was 5,359,000 – 2,610,000 males and 2,749,000 females.

During the period after the Second World War the population increased by more than 1.8 million – the population in 1945 had been only 3,459,000. The largest growth in the population (about 10%) occurred in 1970-1980; in the following decade, the increase slowed down 5.6% and was lower still in the 1990s. The density of the population increased from 70.5 per km^2 in 1945 to 107.5 per km^2 in 1991 and to 109.3 per km^2 in 1995. Overall median age is 35.1 years, 33.5 years for males and 38.9 for females.

The age structure is similar to that in other countries of central and eastern Europe: 17.5% are children aged under 15, 70.8% are in the age group 15-64 years, and 11.7% are 65 and over (2004 estimate). The proportion of females is nearly double that in males in the highest age groups – this is related to the difference in life expectancy at birth – 70.2 years in males and 78.4 years in females (2004 estimate).

The total labour force included about 3 million people in 1993. In 1994, 29% were employed in industry, 9% in agriculture, 8% in construction, 8% in transport and communication, and 46% in various services. The unemployment rate reached about 15% in 2003, but was very low in the western part of the country and high, about 20%, in some regions of northern and eastern Slovakia.

Mortality data collection

Mortality rates in Slovakia, as well as in the whole of the former Czechoslovakia, are available from the beginning of the 20th century owing to the highly efficient mortality statistics system in the former Austro-Hungarian Empire. Mortality rates from most important diseases, including cancer, in the former Czechoslovakia were published in 1926 with data beginning in 1890 for the Czech Republic and in 1900 for Slovakia. The importance of the availability of good mortality data was accepted in Czechoslovakia from its establishment. In the former Czechoslovakia (including Slovakia) ICD-6 was introduced in 1948, and during the period 1948 to 1974 the shortened form of ICD-6 was used. From January 1st 1975 use of the complete list of diseases of ICD-6 (and subsequent revisions) has been obligatory in all fields of health statistics. At the same time, death certificates of internationally accepted structure were introduced. The mortality data from Czechoslovakia were considered to be highly complete and reliable and were used in several international comparisons published by WHO and the UICC, mainly in the period after the end of the Second World War. All deaths in the post-war period were confirmed and the underlying and immediate cause of death was selected by doctors. In 1994, ICD-10 was introduced. Death certificates are used also in the National Cancer Registry of Slovakia (established in 1976) where the International Classification of Diseases for Oncology 2nd Edition (ICD-O-2) is also used.

Up to 1999, the collection of mortality data began with the "Letter of dead person examination" which is prepared immediately after death by a physician, while the completed death certificate was prepared in the local Registrar's office. There was the possibility of changing the cause of death within one month from death (e.g. after autopsy) using a special form for such correction. The death certificates are coded, and the mortality statistics are compiled and published annually, by the Statistical Office of the Slovak Republic. In 1999, the two documents were combined in one form "Letter of dead person examination and statistical notification of death", which is used as the only source of mortality statistics by the Statistical Office of the Slovak Republic. The protection of personal data is based on legislation and is strictly respected.

Population statistics

Information on the size and age structure of the population for the whole country and for counties and districts, together with other information and demographic data characterising the Slovak population, are compiled and published regularly by the Statistical Office of the Slovak Republic. The annual mid- and end-year estimates of the size and age structure of the population are based on the 1991 census taking into account the births, deaths and migration of the population.

I Plesko

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4.24: SLOVENIA

Introduction

Slovenia was part of the Holy Roman Empire in the distant past and of the Austro-Hungarian Monarchy until 1918 when the Slovenians joined the Serbs and Croats in forming a new state which was renamed the Kingdom of Yugoslavia in 1929. After the Second World War, Slovenia became the Socialist Federal Republic of Yugoslavia. Despite the socialist system, Yugoslavia was able to remain independent from the USSR. Slovenia established its independence in 1991, and renewed its ties with western European countries. In May 2004 Slovenia joined the EU.

The country and its people

Slovenia is situated in the southern part of central Europe, in the eastern Alps, bordering the Adriatic Sea in the west. The country lies between 45°15' and 48°30' N and between 13°10' and 16°05' E. The land boundaries are 1,370 km long; the bordering countries are Austria (with a 318 km long border) and Hungary (102 km) in the north, Croatia (670 km) in the south and Italy (280 km) in the west. The coastline is very short, only 47 km long. Slovenia covers an area of 20,273 km^2, including 63.3 % of wooded areas, 30.5 % agricultural areas, 1.6 % bar soils, 0.7 % water, 2.8 % built-up areas, and 1 % roads. With the exception of the short coastal strip on the Adriatic Sea, the prevailing terrain of the country is mountainous, lying in the alpine mountain region adjacent to Italy and Austria, with high mountains, deep valleys and numerous rivers. The highest point is Triglav (2,864 m). Arable land represents only 12% of the area, and the majority of the country's surface consists of forests and mountains. Natural resources are lignite coal, lead, zinc, mercury, uranium, silver, hydropower and forests. The industry of the country is oriented to ferrous metallurgy, aluminium products, lead and zinc smelting, electronics, trucks, electric power equipment, wood products, textiles, chemicals and machine tools. Agricultural products are potatoes, hops, wheat, sugar bets, corn, grapes, cattle, sheep and poultry.

Air pollution from metallurgical and chemical plants and the resulting acid rain causes damage to forests in some regions. The river Sava is polluted with domestic and industrial waste, and some parts of the coastal waters are polluted with heavy metals and toxic chemicals. The country has a mild, maritime climate on the coast and a hard, continental climate with mild to very hot summers and cold, frosty winters in the eastern mountainous regions. The whole country is divided into 210 administrative districts (municipalities) including 11 urban municipalities.

The mid-year total population in 1995 was 1,987,505, of which 965,650 were males and 1,021,855 females. The density of population was 98 per km^2. About 50% of the country's population lives in urban areas, but only 19% in cities with more than 100,000 inhabitants. According to the census in 1991 the bulk of the population (88%) was formed of Slovenians, 2.8% were Croats, 2.5% were Serbs, and there were small numbers of Hungarians, Montenegrins, Macedonians, Albanians and Italians.

According to the census in 2002 there were 83% Slovenians, 1.8 % Croats, 2% Serbs, 1.1% Bosnians, and small numbers of Muslims, Hungarians, Montenegrins, Macedonians, Albanians and Italians. In 1995 the median age of the total population was 36.1 years, 34.6 for males and 37.6 for females; the age structure of the population was: 17.9% were younger than 15 years, 69.6% in age group 15 to 64 years and 12.5% aged 65 years and over. In 2004 the median age of the population was 39.9 years, 38.4 for males and 41.4 for females; 14.3% were younger than 15 years, 70.6% in age group 15 to 64 years and 15.1% aged 65 years and over. The great majority of the population in the highest age groups were females. The life expectancy of Slovenians at birth in 1999 was the highest of the countries of central Europe and the Baltic states – 71.8 years for males and 79.5 years for females. The sex difference in life expectancy was 7.7 years (the smallest in the above mentioned countries).

The total labour force in 1995 was 952,000 of which 882,000 persons were in employment: 10% were working in agriculture, 43% in industry, and 46% in services. The service sector appears to be increasing as a proportion of the economic activity. The official unemployment rate in Slovenia rose from 1.5% in 1987 to 11.5% in 1992, but it fell to 7.4% in 1999, still among the lowest rates in the countries of central Eastern Europe and Baltic states.

Mortality data collection

Mortality statistics in Slovenia are based on the information present on death certificates. Medical death certificates are filled in by hospital physicians, GPs or specialists in forensic medicine. Civil death certificates are written in the Community registrar office. Medical and Civil death certificates are sent to Central Population Register of the Republic of Slovenia (RS), and forwarded to the Public Health Institute of the RS for coding of the underlying causes of death. Underlying causes of death (4-digits code) are coded according the rules described in the ICD. Data in this atlas were coded according to ICD-9 (1993-1996) and ICD-10 (1997). Obvious mistakes and incomplete information are traced back in hospitals, health centres, and also at the Cancer Registry of Slovenia founded in 1950 and producing traditionally highly reliable data on incidence. At the Public Health Institute of the RS a central mortality data-base has been created. Data since 1985 incl. are stored and analysed regularly. Data protection regulations are strictly respected during the coding and computation of mortality data as well as in the cancer registry.

Population statistics

Demographic data on the size and age structure on the population as well as on the other demographic information on the whole of Slovenia and on individual administrative regions are prepared and published regularly by the Statistical Office of the Republic of Slovenia in close collaboration with the Central Population Register of the Republic of Slovenia. The Central Population Register has been the source for the number of population and the number of the citizens of Slovenia since 1985. All inhabitants of Slovenia have a unique identification number.

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4.25: SPAIN

Introduction

Spain has a land surface area of 506,000 km^2 (just under 195,000 sq. miles), including mainland Spain, the Balearic Isles, the Canary Islands and the twin city enclaves of Ceuta and Melilla on the north African coast. Spain occupies 85% of the Iberian peninsula, with a shoreline extending 2,073 km along the Mediterranean, 1,682 km along the Atlantic and 1,075 km along the Bay of Biscay (Cantabria). The Spanish mainland has a perimeter 6,843 km long, made up of 4,830 km of coast and 2,013 km of land borders (France, Andorra, Portugal and Gibraltar). Five major mountain ranges traverse the country and almost 50% of its territory lies on high plateaux (*mesetas*).

Spain is divided administratively into 17 Autonomous Regions (*Comunidades Autónomas*): Andalusia, Aragon, Balearic Isles, Basque Country, Canary Islands, Castile-Leon, Castile-La Mancha, Catalonia, Galicia, the Principality of Asturias, Cantabria, La Rioja, Madrid, Murcia, Navarre, Valencian Region, Extremadura) that have their own organs of government and representative institutions. In addition, there are the two autonomous cities of Ceuta and Melilla.

Spain has a population of 40,500,000 (January 2000). At 80 inhabitants per km^2, Spain's population density is one of the lowest in Europe. The country's capital is Madrid. It is the largest city in Spain in terms of population, with 2,883,000 inhabitants in the metropolitan area and 5,205,000 in the Madrid Autonomous Region as a whole. Spanish is the official State language, along with *gallego*, *catalán* and *euskera* in their respective autonomous regions (Galicia, Catalonia and the Basque Country, respectively).

In 2000, the proportion of foreign residents in Spain was 2.3% (924,000 people). Of these, over 40% came from European countries, 20% from Latin America and 22% from African countries, principally Morocco. In 2001 the number of foreign residents was 1,370.000 people.

Spain has vast expanses of fertile areas, 54% of which are devoted to farming. Leading crops include citrus fruit, grapes and olives, the latter two being used for the production of wine and olive oil. The Spanish fishing fleet is one of the biggest in the world. The most important industries are the food and agriculture, automotive, chemicals, shipbuilding, steel, textiles, and footwear sectors. There is an economically active population of 16,844,000, with 14% being unemployed (2000).

Mortality data collection

In Spain, as in many other countries, death certificates are the only homogeneous and complete source of information that can be used for epidemiological studies of the whole country. The document used in Spain for certification of death is based on the WHO-recommended format introduced in 1951 (International Classification of Diseases (ICD) 6th Revision). Cause of death was coded in accordance with the International Classification of Diseases, the 7th, 8th, 9th and 10th revisions of which were introduced in 1961, 1968, 1980 and 1999, respectively. Certification of death is made in two documents, the death certificate and the death statistics report card (*Boletín Estadístico de Defunción* – BED). Both documents are compulsory. They must be completed by the medical practitioner who certifies the death and sent to the Civil Registry, which in turn forwards the BEDs to the statistics offices on a monthly basis.

When a violent death occurs, an Instruction Judge fills out a brief additional questionnaire about the external circumstances (accident, suicide, etc) that probably produced the injuries that caused death. This information is supplemented by the forensic information registered in the autopsy provisional report. This questionnaire is sent to the Civil Registries in order to be attached to the BED.

The information shown on the BED is: name and surname, ID number, date and place of birth, civil status, profession, nationality, municipality and province of residence, home address, date

and causes of death (immediate, intermediate and underlying history, other processes).

All regional authorities collaborate with the National Statistics Institute (*Instituto Nacional de Estadística* – INE) in producing population vital statistics and deaths by cause of death. When the data have been screened to detect errors and ensure quality control, the underlying cause of death is coded at the Regional Mortality Registries by trained teams applying common criteria in accordance with ICD-based international guidelines; national coding protocols were established to guarantee homogeneity of data (INE 1996). The decentralisation of the responsibility for the processing and management of deaths data has not only served to streamline the system, but has also enhanced overall quality. The Regional Authorities have implemented specific methods to validate the data in a systematic way (telephone interviews with doctors signing any certificate with ill defined or improbable causes of death; visits to Civil Registries or Courts to examine conflicting data) (García-Benavides 1991, Carballeira 1989, Regidor 1993, Saenz 1993, Cáffaro 1995), and have established courses for doctors to improve certification (Cirera 1998).

The files are sent to the central INE office, which releases them once they have been rendered 'anonymous', i.e. the death data are stripped of all information which might enable individuals to be identified (day of birth, day of death, months and days at death for older than 1 year, days at death for deaths between 1 month and 1 year old, municipality of residence in cases where there are fewer than 10,000 inhabitants). Access to the full uncensored register is, however, allowed for specific approved research purposes.

Quality of death statistics

The accuracy of cause of death reported in mortality statistics is very high in Spain and similar to that for other European countries, making this information suitable for geographical studies such as disease atlases (although there might be some inter-regional variability). Globally, the proportion of unspecified or ill-defined causes of death (ICD-9 780-799) fell from 4.6% of all deaths in 1975 to 2.0% in 1996; however, in 1996 the percentage varied across the Autonomous Communities from 1.0% to 4.3% for men and from 1.5% to 5.0% for women, with Navarre having the lowest values and Melilla the highest rates.

Neoplasms are among the best certified cause of death (García-Benavides 1989, Regidor 1993, Giménez 1998, Carballeira 1989). Overall, it has been estimated that medical death certificates in Spain might underestimate cancer deaths by 5%, with inaccuracies more frequently found in people of advanced age, women and home deaths (Cáffaro 1995, Cirera 2002). The proportion of ill-defined tumours (ICD-9 195-199) in 1996 was 7.4%, ranging from 4.4% in Navarre to 10.3% in Catalonia and 15% in Melilla (which has less than 0.2% of the Spanish population).

For all tumours as a whole, detection and confirmation rates have been found to be around 90 and 95 percent respectively. On mortality from specific cancers, concordance with clinical information has also improved over time.

In a study published by a Spanish Regional Authority, the proportion of agreement at the third digit of the ICD was close to 80% in 1992, and aggregation of data into 31 categories increased it to 83% (Cirera 2002); similar figures have been published for other parts of the country (Bosch 1981, García-Benavides 1989, Cáffaro 1995, Martínez 2000). Table 1 summarises available information about concordance by site in Spain. The highest concordance indices have been found for lung, breast, brain and haematological cancers, but some sites have low rates of agreement. Validation studies have shown some over reporting of larynx cancer due to misclassification of head and neck tumours, as well as underestimation of urinary bladder cancer, erroneously certified as prostate neoplasm (Cáffaro 1995, Cirera 2002, Martínez 2000). Also, unspecified uterus tumours are still over represented, including tumours of cervix, endometrium and ovary, while some declared cases of death due to ovarian cancer were really abdominal or uterus neoplasms (Cáffaro 1995, Sánchez Garrido 1996, Cirera 2002, Martínez 2000). However, "all uterus" as a category achieves good standards of certification. There is also some over reporting for oesophagus, which is due to inclusion of stomach cases and for

Table 1. Pooled analysis of published studies on accuracy of death certification for specific cancers in Spain according to Percy's criteria (Percy 1981).

Well-certified (DR>80 and CR>80)				Over-certified (DR>80 and CR<80)				Under-certified (DR<80 and CR>80)				Ill-certified (DR<80 and CR<80)			
Location	ICD-9	DR	CR	Location	ICD-9	DR	CR	Location	ICD-9	DR	CR	Location	ICD-9	DR	CR
Stomach	151	83	89	Oesophagus	150	87	78	Mouth & pharynx	140-149	59	85	Colon	153	72	70
Colon-rectum	153-154	83	90	Liver	155	85	45	Rectum	154	54	82	Gallbladder	156	58	79
Pancreas	157	84	80	Larynx	161	83	67	Skin	172-173	54	87	Corpus uteri	182	42	76
Lung	162	92	91					Melanoma	172	78	91	Ill-defined tumours	195-199	53	39
Breast-♀	174	90	98					Skin (non- melanoma)	173	42	80	L. Hodgkin	201	69	69
Uterus	179,180,182	82	83					Cervix uteri	180	51	91				
Prostate	185	89	82					Ovary	183	74	81				
Brain	191	96	85					Other genital-♂	186-187	69	82				
Lymphomas	200-202	86	80					Testicular	186	78	88				
Multiple Myeloma	203	96	94					Bladder	188	76	91				
Leukaemia	204-208	93	93					Kidney	189	76	83				
								Endocrine Glands	193-194	79	83				
								Thyroid gland	193	76	89				
								Lymphomas, Others	200,202	76	83				

Source: Pérez-Gómez B, Aragonés N, Pollán M, Suárez B, Lope V, Llácer A, López-Abente G. Accuracy of cancer death certificates in Spain: a summary of available information. Gac Sanit. 2006 Dec;20 Suppl 3:42-51.

liver due to misclassification of hepatic metastasis. Finally, the occurrence of childhood tumours is not well described in mortality data, due to the high survival rates than are found in Spain as in most other European countries (Gatta 2002).

Population statistics

Information on the composition of the population is drawn up on the basis of censuses. In Spain, Population & Dwelling Censuses must be conducted every ten years by law. The principal goal is: to ascertain the number of inhabitants, dwellings and buildings countrywide, both at a State level and in the various geographical and administrative areas; and to obtain a description of the structure of the country from different points of view to enable demographic, social and health, educational and environmental policies to be drawn up and assessed.

The task of conducting Population & Dwelling Censuses falls to the INE. In the last census, conducted in 2001, over 40,000 persons took part and for a period of some three months travelled to 21 million postal addresses, to gather information on buildings, occupied dwellings and the persons inhabiting same. A total of 13 million households were visited in this way and information was collected from approximately 40 million persons.

The taking of Spanish population censuses dates back to 1768. Since 1900, population censuses have been conducted every 10 years (1900, 1910, 1920, 1930, 1940, 1950, 1960, 1970, 1981, 1991, 2001). The quality of such census data is high.

Another source of demographic data is provided by the Municipal Rolls (*Padrón Municipal de Habitantes*), which currently take the form of an administrative register that is constantly being updated and lists all the inhabitants in the village, town or city in question.

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4.26: SWEDEN

Introduction

Sweden, which occupies the eastern part of the Scandinavian Peninsula, is the fourth-largest country in Europe with an area of over 410,000 km^2 – slightly larger than California. The country slopes eastward and southward from the Kjólen Mountains along the Norwegian border, where the peak elevation is Kebnekaise (2,123 m) in Lapland. In the north are mountains and many lakes. To the south and east are central lowlands and fertile areas of forest, valley, and plain where most of the population lives. About 65% of Sweden's land area is forested, and less than 10% is arable. Along Sweden's rocky coast, indented by bays and inlets, are many islands, the largest of which are Gotland and Öland. The country is divided into 24 provinces (*län*).

Sweden played a leading role in the second phase of the Thirty Years' War (1618–1648). By the Treaty of Westphalia (1648), Sweden obtained western Pomerania and some neighbouring territory on the Baltic. In 1700, a coalition of Russia, Poland, and Denmark united against Sweden and by the Peace of Nystad (1721) forced it to relinquish Livonia, Ingria, Estonia, and parts of Finland. The union between Sweden and Norway was an uneasy relationship, and it was finally dissolved in 1905. Sweden maintained a position of neutrality in both world wars.

In a 1994 referendum, voters approved joining the European Union. Although supportive of a European monetary union, Sweden decided not to adopt the euro when it was introduced in 1999 and rejected it again overwhelmingly in a referendum in September 2003.

Stockholm is the capital of Sweden and is one of Europe's leading economic regions with its high concentration of information technology, health care industry and research. Sweden is a monarchy and there are ten royal castles in the country. *Stockholm Palace* is the official residence of His Majesty King Carl XVI Gustaf. The Palace is situated in the Old Town, Stockholm's original city nucleus, and is built on the remains of its predecessor, Tre Kronor, which was destroyed by fire in 1697.

The population (July 2006 estimate) was 9,017,000 and the age structure was: 0-14 years 16.7% (male 775,400/female 732,800); 15-64 years 65.7% (male 3,002,000/female 2,918,000); and 65 years and over 17.6% (male 689,800/female 898,500). The great majority of the nation's population speaks Swedish. There is a sizable Finnish-speaking minority and a small Lapp-speaking minority. About 12% of the population is foreign born.

Mortality data collection

Swedish statistics on cause of death go back to 1749 when a nationwide reporting system was introduced. The responsibility was vested with the clergy until July 1860 when doctors were entrusted with the task of making out death certificates, especially in cities with medical officers of their own.

The most exhaustive way to establish the cause of death is autopsy. In Sweden, there are two different types, clinical and forensic. The clinical type is performed on the initiative of a doctor, the forensic type by the order of the police authorities. There has been a decrease in the number autopsies performed; this might lead to inaccurate statistics. Reasons for the decrease are new regulations that give relatives the right to refuse autopsies, amended rules for financial compensation for clinical autopsies and amended instructions for forensic autopsies.

American software (ACME – Automated Coding of Medical Entities) was incorporated fully into the Swedish coding system after the transition to ICD-10. Before that, Sweden used a version of ACME that was adapted to the Swedish system of coding.

Statistics on cause of death cover Swedish residents, whether the person in question was a

Swedish citizen or not and irrespective of whether the deaths occurred in Sweden or not. The quality of the statistics varies, due to the examinations made to define the underlying cause of death or the changes in the classification system or the processing methods.

The main variables included in the death register are: social security number, home district, sex, date of death, underlying cause of death, nature of the injury, multiple causes of death, marker if autopsied or not and if so what kind, marker if operated on within four weeks before death, marker if injury/ poisoning, marker if alcohol related, marker if narcotic related, and code for diabetes.

There were 93,000 deaths in Sweden in 2003, of which 47,600 were females and 45,400 males. To facilitate comparisons of mortality rates over time and between regions, age standardisation is used. In this publication the population in 2000 was used for both women and men as the standard population. The most common cause of death both for women and men was diseases of circulatory organs – almost half the deaths had these as the underlying cause of death (45% in women, 44% in men). The second most common cause of death was cancer (22% and 26%, respectively). Breast cancer was the most common cause of cancer death among women, and prostate cancer among men.

The trends for most causes of death fell in Sweden during the period 1987-2003. The trend was the same for males and females, although the absolute level was higher for males. The trends for diseases of the circulatory organs in those aged 15-74 have decreased continuously during this period, from 121 deaths per 100,000 females in 1987 to 69 in 2003, and from 337 to 166 for males. The overall cancer mortality trends are also falling. The figures show similar trends for most of the cancer sites, except for lung cancer for women which has increased.

Statistical publications

Statistics on cause of death have annually been published from 1911 to 1993 by Statistics Sweden (SCB). The National Swedish Board of Health and Welfare has been responsible for publication since 1994. Statistics Sweden had until recently been entrusted by the National Swedish Board of Health and Welfare with the compilation of the statistics. However, from 2003 onwards, all work on the cause of death registry and the related yearly publication was transferred to the Centre for Epidemiology at the National Swedish Board of Health and Welfare.

More information on publications and the Swedish cause of death registry is on the website: http://www.sos.se/epc/english/dorseng.htm

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4.27: SWITZERLAND

Introduction

Switzerland, which is landlocked, has an area of 41,300 km^2. In the west and southwest the Jura Mountains and the Lake of Geneva form the border with France (having a length of 572 km). In the north, it is separated from Germany by the River Rhine and Lake Constance (346 km). Its eastern neighbours are Austria (165 km) and Liechtenstein (41 km). In the southeast and south it is divided from Italy by the Alps and Lakes Lugano and Maggiore (734 km).

About 30% of the country is covered by forests and woods; 24% is cultivated land, 13% mountain farming, 7% settlements, 4% rivers and lakes, and 21% is unproductive. Switzerland's natural resources are hydropower potential, timber and salt.

The federal capital is Bern (population: 128,600 in 2000); the largest cities are Zurich (363,300), Geneva (178,000) and Basel (166,600).

Switzerland has a population of 7.2 million and an average population density of 175 inhabitants per km^2 (2000). The age structure is: 0-14 years 23.2% (male 641,500, female 605,800), 15-64 years 61.5% (male 2,427,000, female 2,420,000); and 65 years and over 15.3% (male 450,900, female 658,300). The proportion of foreign residents is around 20% and the net migration is rate 5.6 migrants/1,000 population (2001). The broad categories of employment are: agriculture and forestry 5%; industry 26%; services 69%. The official languages are German (64%), French (20%) and Italian (7%); Romanch is spoken by 0.5% and other languages by 9%.

Switzerland is divided into 26 cantons: Aargau, Appenzell AR, Appenzell IR, Basel-Land, Basel-Stadt, Bern, Fribourg, Genève, Glarus, Graubünden, Jura, Luzern, Neuchâtel, Nidwalden, Obwalden, St-Gallen, Schaffhausen, Schwyz, Solothurn, Thurgau, Ticino, Uri, Valais, Vaud, Zug and Zürich.

Mortality data collection

In Switzerland information on cause of deaths has been collected since 1876. Until 1969, a Swiss coding system was used. From 1969 to 1994, the 8th revision of the International Classification of Diseases was used, modified by country specific coding rules; from 1995 the 10th revision has been used.

Every case of death is certified by a licensed physician in a two step process. The fact of a death is communicated to the registry office of the local government within three days of its occurrence. The registrar registers the case of death with all the demographic information of the deceased person (date and time of death, sex, nationality, date of birth, marital state, number of dependent children, religion, job title of last performed occupation and job position) into a central database. On a daily basis, a list of cases with demographic information, but without the name of the deceased person, is sent to the Federal Statistical Office (FSO). From the electronic system the local registrar prints out a questionnaire for the collection of the causes of death and sends it to the certifying physician. The questionnaire comprises two pages: page 1 contains the name of the deceased person, place of residence, date of birth and a registration number. On page 2, the name of the physician who ascertained the death, the registration number, and date of birth are repeated. This form is then sent to the physician to complete page 2 of the form with the underlying illness or event having caused death, the direct cause of death and concurrent diseases. The physician will keep page 1 of the form containing the name of the deceased person in his files. He sends page 2 (without the name of the deceased person) to the FSO. There, both pieces of data are joined on the base of the unique registration number.

The information on cause of death is coded at the FSO according to the rules of the International Classification of Diseases and stored in a permanent data base. The FSO produces and publishes some standard reports and provides researchers and the public with specific summary information according to their needs.

Data quality is primarily dependent on the information provided by physicians. In more than 10 percent of cases the FSO asks the certifying physician to provide more information or to explain an incomprehensible expression or abbreviation. In the end, some 2 to 2.5% of cases are registered with unknown cause of death.

Data quality is checked routinely using plausibility checks. There is also internal supervision of the coding process. A major set of external validity studies was published in 1989 when ICD-8 was used. One study compared the reliability of the coding process through re-coding of 662 cases. An error rate of 3.8% of cases was found; an additional 2% of cases were coded differently because of the special coding rules mentioned above. A second study compared 12,478 death cases in 1979 from hospitals where data on the cause of death could be linked to diagnostic data from the Swiss hospital statistic (VESKA). The occurrence of the same code was strongly dependent on the diagnostic category: the best results, with rates over 90%, were obtained for malignant diseases, violent deaths, and perinatal causes.

Population statistics

Information on the size and composition of the resident population of Switzerland is provided by the FSO. The two main sources of data are the census and the yearly population estimates. From 1850 onwards a census was conducted in Switzerland every 10 years, the most recent in the year 2000. Data from the residents' registration offices and from the central Aliens Register are used to estimate monthly and annual population figures. The FSO establishes the size of the permanent resident population in Switzerland by using the census data, the figures on population movements (births, deaths, immigration, emigration) and the central Aliens Register data. The publication "Statistics of the yearly state of the population" (ESPOP) contains information on age, sex, marital state, community of residence, and nationality.

Statistical publications

The main population statistics are published regularly on the internet site of the Internet site of the BFS/OFS. All paper publications can also be downloaded in pdf files, free of charge, from this site.

Statistisches Jahrbuch der Schweiz (Statistical Yearbook of Switzerland) [published yearly in German and French (in one volume)] Neuchâtel, FSO and Zürich, Verlag NZZ
"Le portrait démographique de la Suisse", published every 2 years in German and French, presents and comments the main population figures for Switzerland. Neuchâtel, FSO
Todesursachenstatistik [Tables, published yearly, in German, French and Italian (in one volume)] Neuchâtel, FSO
Minder Ch.E. Zingg W.: Datenqualität der Todesursachen und der Berufsbezeichnungen / Qualité des données relatives aux causes de Décès et aux professions. Bern, FSO, 1989
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The collaboration of the following members of the Swiss Statistical Office should be acknowledged

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4.28: UNITED KINGDOM

Introduction

The United Kingdom of Great Britain and Northern Ireland (UK), which played a leading role in developing parliamentary democracy and in advancing literature and science, was the dominant industrial and maritime power of the 19th century. At its zenith, the British Empire stretched over a quarter of the earth's surface. The second half of the 20th century saw the dismantling of the empire and the rebuilding of the UK into a modern and prosperous European nation. Although a member of the EU, the UK is outside the European Monetary Union and its official currency is still the pound sterling, not the euro. Regional assemblies with varying responsibilities and degrees of delegated authority were established in Wales, Scotland and Northern Ireland in the late 1990s.

The UK has an area of around 245,000 km^2. Nowhere is further than 120 km from the sea. In general, a line from Bristol on the west coast to the Wash on the east divides mainland Britain into a hilly north-western zone and the lowlands of the south-east. The 240 km long Pennine Chain runs down from the Cheviot Hills on the Scottish border to the Midlands; north-western England is dominated by the Cumbrian Mountains of the Lake District where the highest point is Scafell Pike (977 m). Wales is dominated by the north-south range of the Cambrian mountains (Snowdon 1085 m). Scotland is also mountainous (Ben Nevis 1342 m), principally to the north of the central Forth-Clyde lowlands. The north-west highlands, deeply indented by sea lochs, are one of the most scenically impressive areas of Europe.

About 75% of the land surface is used for agriculture. There is relatively little heavily wooded country in Britain (10%), but there are large areas of heaths, moors and common land abound. Coal and iron were mined for centuries, but over the past thirty years natural gas and offshore oil deposits have been increasingly exploited.

London is the capital of England (mid-1990s population 7 million), Cardiff (300,000) of Wales, Edinburgh (450,000) of Scotland, and Belfast (300,000) of Northern Ireland.

The population of the United Kingdom in 1995 was almost 59 million, with an average density of nearly 240 inhabitants per km^2. About 83% of the total population lived in England, 5% in Wales, 9% in Scotland, and 3% in Northern Ireland. The age structure of the population, and its broad categories of employment are given in Table 4.28.1 below. At the end of the 1990s, the ethnic origin of about 90% of the population was White, 1% were Mixed, 4% Asian and 2% Black, with the remainder being Chinese, "Other", or "not stated" (3%).

Table 4.28.1: Age structure and employment status of the UK population, 1995

Age group	Population (000)	
	Males	Females
Under 1	376	358
1-4	1,589	1,513
5-9	1,980	1,880
10-14	1,882	1,785
15-19	1,781	1,682
20-29	4,406	4,211
30-44	6,415	6,294
45-59	5,201	5,244
60-64	1,358	1,427
65-74	2,330	2,797
75-84	1,147	1,907
85 & over	263	781
Total	28,728	29,879

Employment status	Numbers (000)	
	Males	Females
Employees in employment	11,083	10,869
Self-employed persons (with or without employees)	2,540	803
Work related Government training programmes	148	78
HM Forces	214	16
Workforce in employment	13,985	11,766
Unemployed	1,764	549
Total workforce	15,749	12,315

The official language is English, but Welsh is spoken in Wales. Gaelic speakers are found in western Scotland, particularly the Hebrides.

England had eight Standard Statistical Regions in the mid-1990s; there were 45 counties, consisting of 331 local authorities, plus 33 London Boroughs and the Isle of Wight which became a Unitary Authority in 1995. Wales had 22 unitary authorities. From 1974 to 1996, Scotland had 9 regions which were split into 53 local government districts and 3 island authorities. There were 26 districts in Northern Ireland.

Mortality data collection

The present system of registration of deaths in the United Kingdom dates from the Births and Deaths Registration Act 1836 for England and Wales, the Registration of Births, Deaths and Marriages (Scotland) Act 1854, and the Registration of Births and Deaths (Ireland) Act 1863. The responsibility for the processing and publication of information on deaths lies with the Office for National Statistics (ONS) for England and Wales, and the General Register Offices (GROs) for Scotland and Northern Ireland.

Most deaths in England and Wales – around 75% in the mid-1990s – were certified by a medical practitioner using the medical certificate of cause of death. The death certificate is then usually taken to a registrar of births and deaths by a person known as an informant, who is usually a near relative of the deceased. The informant is expected to provide information about the deceased, including date and place of birth, occupation and usual address.

In England, Wales and Northern Ireland, certain deaths are referred to, and sometimes then investigated by, a coroner who sends information to the registrar of deaths which is used instead of that from the medical practitioner. ONS encourages the prevailing practice of voluntary referral to the coroner by the certifying doctor who should consider whether the death was an accident, a suicide, or related to the deceased's employment; whether the death occurred during or shortly after detention in police custody; and whether the doctor himself, or another doctor, is legally qualified to certify the death. A registrar is legally obliged to refer a death to the coroner (unless it has already been so reported) if: (i) the deceased person was not attended during his or her last illness by a medical practitioner; (ii) the registrar has been unable to obtain a certificate of cause of death; (iii) information on the certificate of cause of death indicates that the deceased was not seen either after death or within 14 days before death by the certifying practitioner; (iv) the cause of death appears to be unknown; (v) the registrar has reason to believe that death resulted from an unnatural cause, violence, neglect, abortion or suspicious circumstances; (vi) death appears to have occurred from an operation or before recovery from an anaesthetic; or (vii) from the contents of the certificate, it appears that death was due to industrial disease or poisoning. Depending on the results of preliminary enquiries into whether death was from natural causes, the coroner may issue a notification of the cause of death without holding an inquest, having in some circumstances had an autopsy carried out. In fact, autopsies are performed for the majority of deaths referred to the coroner (about 80% in the mid-1990s). However, not all deaths referred to the coroner are certified by him; in 1995, just over 10% of the deaths initially referred to the coroner were finally certified by a doctor.

In some cases, additional information from the coroner's certificate is forwarded to ONS and the GRO for Northern Ireland by the registrar. Scotland does not have a system of coroners. However, cases such as those listed above are generally investigated by a procurator fiscal who may amend the cause(s) of death. The GRO for Scotland (GROS) records any such amendments. Coroners certify nearly a quarter of all deaths in England and Wales. The coroner does not hold an inquest if the pathologist's post mortem examination establishes a clear natural cause of death. About 40% of deaths from ischaemic heart disease, which may occur suddenly in people without previous symptoms, are certified by coroners in this way, but only about 5% of cancer deaths, where the course of the disease is often long and diagnosis is usually confirmed by biopsy or other tests before death.

Thus the information used in UK mortality statistics may have come from one of four sources: the doctor, the informant, a coroner or procurator fiscal, or derived from one or other of the above (for example, the age of the dead person is derived from date of birth and date of death).

Routine mortality statistics are usually based on a single cause for each death, the "underlying cause of death" as defined by the WHO [WHO 1977]. The medical certificate of death used in England and Wales has been in the format recommended by the WHO since 1927. Part I has three lines and Part II one line. Similar certificates are used in Scotland and Northern Ireland. If the death certificate has been properly completed, the underlying cause should be the condition entered in the lowest line of Part I. Various rules apply for determination of the underlying cause if the death certificate has not been completed correctly, or the conditions entered are not an acceptable sequence. In addition, there are modification rules which apply to particular conditions, combinations or circumstances. These rules are explained in the ICD9 manual Volume 1 [WHO 1977] with examples, but their interpretation and application is not always straightforward. It is clear from many studies [Percy & Muir 1989, Coleman & Aylin 2000] that the rules are not always applied uniformly in different countries, or even by different coders in the same country, or by one coder at different times. Using computer algorithms to apply the WHO selection and modification rules can increase uniformity and consistency – and so improve the spatial and temporal comparability of mortality statistics.

In the early 1990s, the Office of Population Censuses and Surveys (OPCS) – which merged with the Central Statistical Office in 1996 to form the Office for National Statistics – redeveloped its deaths registrations computer processing system. The main changes affecting the data included the progressive computerisation of local offices of registrars of births and deaths, and the automation of cause of death coding.

Since 1993, for a large and increasing proportion – over 90% by 1997 – of deaths in England and Wales the information from death certificates has been collected directly onto a personal computer by the registrar and forwarded to ONS on floppy disks at the end of each week. The remaining cases still sent as paper copies were keyed in at ONS using a clone of the software used by the registrars. This automation of the registration process, coupled with the change to the use of a relational database on the mainframe computer at ONS enabled the automation of the coding of causes of death in England and Wales from January 1993.

The automatic cause coding system (ACCS) consists of five main software components which take in the text for cause(s) of death from the death certificate and produce ICD9 codes for both underlying and multiple causes. The first module of ACCS (called TRACER) automatically splits the text into separate medical conditions and matches each recognisable word or phrase into an "entity reference number" (ERN) while retaining its position on the certificate. TRACER rejects non-standard text including spelling errors, or phrases which do not match its dictionary entries exactly. Rejected records are passed to clerical coders who can make corrections or select synonymous ERNs. The ERNs from TRACER are submitted automatically to a module (MICAR 200) which maps them to ICD9 codes. The output from MICAR passes directly to the next module (ACME) which applies the ICD9 general, selection and modification rules to select the underlying cause of death from all the conditions mentioned on the certificate. The final module (TRANSAX) sorts out linkages and repeat occurrences of codes to produce a set of multiple cause codes for each death.

The software was developed in the USA by the National Centre for Health Statistics. For technical reasons, the modules MICAR, ACME and TRANSAX were embedded in the ACCS as one automated unit with no intermediate input, output or clerical intervention possible. ICD9 codes for records rejected by MICAR or ACME therefore have to be coded clerically directly onto the deaths database. The database is "dynamic" in the sense that subsequent information, received for example after post mortem, can be used to produce final corrected multiple and underlying cause codes. Amended information is, however, not in the public domain, unlike the original death certificate, and is not stored as electronic text. The automated system does not deal adequately with external causes of death, which are certified after a coroner's inquest, and ONS has reverted to coding these clerically. Further details of the automated coding system have been published by ONS [Birch 1993; Rooney & Devis 1996; ONS 2001].

A full set of notes and definitions for mortality data has been published by ONS [ONS 2001]. This includes: base populations; occurrences and registrations; areal coverage; death rates and standardisation; certification of cause of death; coding the underlying cause of death; analysis of conditions mentioned on the death certificate; amended cause of death; accelerated registrations; legislation on registration of deaths; and the processing, reporting and analysis of mortality data. A paper describing the various processes by which deaths are certified and registered by doctors and coroners, and the many changes affecting registration and certification in recent years, has also been published by ONS [Devis & Rooney 1999].

A similar suite of automatic cause coding software has been used in Scotland since 1996; as in England and Wales, some manual coding is still required, particularly for external causes. Northern Ireland did not move to automatic coding for deaths until 2001.

UK Population statistics

(i) National population censuses

A national census has been held every 10 years since 1801, with the exception of 1941; there was an additional "mid-term" census in 1966 involving a 10% sample of the population.

The vast majority of the population are counted at the census in their (or someone else's) home, usually on a Sunday in April, by specially appointed enumerators. There are also arrangements for enumerating people present in institutions. The number of questions asked of respondents reached a peak of 30 in 1971, and was reduced to 21 in 1981. A major improvement in the 1966 census was the substitution of date of birth for the previous census question on age; this improved the accuracy of much of the age data. From the point of providing a denominator for calculating rates, the main demographic items are sex, age and marital status. More extended epidemiological analyses can be performed using the other material.

The initial coverage of the census is checked by attempting to repeat the enumeration for a sample of households, shortly after census day, using a skilled team of field staff. In 1981, it was estimated that 0.62% of people had been missed, but about 0.17% had been counted twice. This indicates that net under-enumeration was less than 0.5%. Under-enumeration in the 1991 census was thought to be just over 1%, but this varied by age and geographic area.

(ii) Annual population estimates

In years between censuses, annual population estimates are produced, which take account of the occurrence of births and deaths and migration into and out of the country or locality since the last census. These estimates have been prepared for the country and large towns since the 19th century, and for local authority areas since 1911; they have been produced for both levels in Scotland since 1901, and in Northern Ireland since 1926.

Occasional Paper 37 describes the methods used by ONS to produce annual mid-year estimates of the population of local and health authority areas in England and Wales has been published [the paper is available, price £4.00, from the address below; it and other papers on this subject are available on the National Statistics website – see below]. It includes historical background and methods used in the 1980s. Details are given of the components of change (births, deaths and migration), and of methods used to estimate some special groups in the population, such as students and armed forces.

At the time that this atlas was prepared, revised population estimates for the 1990s for small areas (such as NUTS 2 and NUTS 3 levels) based on the 2001 census were not available. The main differences at the national level between the population figures from the 2001 census and the population estimates "rolled forward" from the earlier censuses was in the younger age groups, particularly for men. Cancer is, however, generally a disease of the elderly, and checks have shown that the effects of (lower) population figures from the 2001 census on cancer mortality rates are very small.

Statistical publications

(i) England and Wales

From 1840 to 1974, the Registrar General published an Annual Report containing

statistics for England and Wales. After 1954, The Registrar General's Statistical Review of England and Wales was published in three parts – medical tables, population tables, and a commentary. Detailed tables were provided, giving particulars of deaths and death rates by cause, sex, age, locality, etc.

In 1974 this publication was replaced by an annual series of volumes containing subsets of the mortality statistics. The intention was that individual components of this series would be published with the least delay; individuals could acquire the subset of material that was of particular interest to them. This series, known as series DH, is now produced in four parts:

- DH1 – Mortality statistics: general
- DH2 – Mortality statistics: cause
- DH3 – Mortality statistics: childhood, infant and perinatal
- DH4 – Mortality statistics: injury and poisoning

A further volume, DH5 – Mortality statistics: area, was produced up to 1992, then replaced by sets of tables giving various aggregated mortality data for different geographical areas, on floppy discs or CD-ROM.

The main tables in the DH2 volume present the numbers of deaths by age and sex at ICD three and four digit levels, and rates for selected three digit codes or groups of codes; other analyses appear in the general DH1 volume.

Area and occupational mortality statistics have been published approximately every 10 years since 1851, initially as supplements to the Registrar General's Annual Reports, and later as specific decennial supplements produced by the Registrar General, OPCS or ONS. Those relating to the period of the data included in this atlas are:

DS 10 Occupational Health. Frances Drever (Ed). HMSO, 1995

DS 11 The health of our children. Beverly Botting (Ed). HMSO, 1995

DS 12 The Health of Adult Britain 1841-1994, Volume 1. John Charlton & Mike Murphy (Eds). HMSO, 1997

DS 13 The Health of Adult Britain 1841-1994, Volume 2. John Charlton & Mike Murphy (Eds). HMSO, 1997

DS 14 English Life Tables No.15, 1990-1992, England and Wales. TSO, 1997

DS 15 Health Inequalities. Frances Drever & Margaret Whitehead (Eds). TSO, 1997.

DS 16 Geographic Variations in Health. Justine Fitzpatrick & Clare Griffiths (Eds). TSO, 2001.

Until 1974, the Registrar General also published a Weekly Return and a Quarterly Return. In 1974 the Weekly Return was replaced by a monitor, particularly devoted to statistics on infectious diseases, and the Quarterly Return by a quarterly journal, *Population Trends*, which includes articles on specific topics and regular tables, with limited analyses on mortality. Since the beginning of 1999, ONS has also published the journal *Health Statistics Quarterly* which covers mortality and other health topics; the emphasis of *Population Trends* is now on population and demography, but it also includes some mortality data.

The National Statistics website www.statistics.gov.uk provides a comprehensive source of freely available vital statistics and ONS publications on other topics.

Address: Office for National Statistics, 1 Drummond Gate, London, SW1V 2QQ.

(ii) Scotland

The Registrar General for Scotland published an Annual Report every year between 1855 and 2000. The Report for 2001 (published in 2002) adopted a new style and approach to reporting vital events. Many of the tables previously published on a quarterly and annual basis are now available on the GROS website: www.gro-scotland.gov.uk.

Address: General Register Office for Scotland, Ladywell House, Ladywell Road, Edinburgh EH12 7TF.

(iii) Northern Ireland

From 1863 to 1921, Northern Ireland Statistics were included in the Annual Reports of the Registrar General for Ireland. After 1922, the Registrar General published

annual statistics for Northern Ireland, with detailed tables giving particulars of deaths and death rates by cause, sex, age, locality, etc. From 1924 to 1969, the Registrar General published weekly and quarterly returns, but from 1970 only quarterly returns have been published.

Address: General Register Office, Department of Health and Social Security, Oxford House, 49-55 Chichester Street, Belfast BT1 4HL.

MJ Quinn & A Baker (ONS), C Roberts (Welsh Assembly Government), I Brown (GRO Scotland), G Fegan (NISRA Northern Ireland)

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CHAPTER 5

REGIONAL VARIATION AND SPATIAL CORRELATION

Chris Robertson, Chiara Mazzetta, Alberto D'Onofrio

Age standardised rates

The age standardised rates presented in the maps are calculated using the world standard population and are given by

$$ASR_i = \sum_j w_j r_{ij},$$

where r_{ij} is the age specific mortality rate for age group j in region i, and w_j is the world standard population weight for age group j.

Regional variation

We used two methods to assess the strength of the regional variation in the age-standardised rates. The first was a method developed by Pennello, Devesa & Gail (1999) based upon a Poisson model for the observed number of cases together with a random effect for the regional variation. The second used a hierarchical regression model to partition the variation in the mortality rates among countries, among regions and within regions. In all of this work we used data from age groups 30-34 to 80-84 as there were few deaths from cancer in people under 30 and death certification is less reliable in those aged 85 and over.

Poisson Gamma model

The number of deaths in region i and age group j, d_{ij}, is assumed to follow a Poisson distribution, with mean depending upon the person years at risk, y_{ij}.

$$d_{ij} \sim Poisson\left(y_{ij}\xi_j\gamma_i\right)$$

where ξ_j is the age effect for age group j and γ_i is the random effect for region i. The random effect is assumed to follow a Gamma distribution,

$$\gamma_i \sim \Gamma(\alpha,\alpha)$$

which has a mean of 1 and a variance of $\frac{1}{\alpha}$.

The parameter estimates of this model, ξ_j and α, were obtained by maximum likelihood using specially written functions in R (Ihaka & Gentleman, 1996) and S-PLUS (Insightful Corporation, 2005).

As the γ_i are the relative risks in region i the square root of $\frac{1}{\alpha}$ is known as the relative risk standard deviation (RRSD). If the age effects, ξ_j, are known then $\sum_j y_{ij}\xi_j = E_i$ is the expected number of deaths in region i. Initial estimates of γ_i can be obtained by estimating ξ_j using the sum over all regions $\hat{\xi}_j^0 = \frac{\sum_i d_{ij}}{\sum_i y_{ij}}$, then calculating the expected number of deaths $E_i^0 = \sum_j y_{ij}\hat{\xi}_j^0$ and estimating $\hat{\gamma}_i^0 = \frac{O_i}{E_i^0}$, where $O_i = \sum_j d_{ij}$ is the observed number of deaths in each region. The standard deviation of the $\hat{\gamma}_i^0$ is an initial estimate of the RRSD. Using these initial estimates, maximum likelihood estimates are obtained by successively re-estimating ξ_j and

α until convergence. This was usually achieved within a few iterations. The estimated standard error of the estimated RRSD is calculated from the information matrix for α using the delta method.

This model is closely related to the empirical Bayes smoothing method of Clayton & Kaldor (1987). Neither model takes into account the geographical or spatial structure of the data. Randomly interchanging the regions would give exactly the same value for the RRSD. The RRSD is not a measure of spatial structure or correlation.

The RRSD is a measure of the regional variation both in the age specific rates and in the age standardised rates, as there is a constant multiplier for all age groups in the same region. The magnitude of the RRSD can be used to rank the cancer sites with the ones with larger values having more relative regional variation. More attention should be paid to the interpretation of the geographical distribution for cancer sites with larger values of the RRSD. If the RRSD is low then the common scale map at the bottom right of the chart will tend to be of one colour indicating little geographic variation even although the main relative map may have strong geographic patterns.

The RRSD is a measure of the variability in the distribution of age standardised rates illustrated in the boxplot for all Europe presented at the top of the boxplots beside each map and denoted 'All'. These boxplots are plotted on a different scale for each cancer site so it is not possible to use the boxplots to compare cancer sites. This can only be achieved with the RRSD and other measures of regional variation.

The RRSDs were calculated for each cancer site for males and females separately. Furthermore, for each cancer site we calculated the RRSD separately for each of the European countries. Generally, we would expect the RRSD for all Europe to be greater than the RRSDs for the individual countries. It is possible that the RRSD for a particular country will be larger than the RRSD for all of Europe, implying that there is extreme regional variation in that country. If the separate RRSDs for each country are similar in magnitude to each other then this implies constant regional variation over the countries of Europe. For the smaller countries with few regions and small populations the RRSD was not estimated for the rarer cancer sites. Convergence difficulties were noted due to the log likelihood function increasing monotonically as α increases.

Hierarchical modelling

In this framework, a three level multilevel model is used where the levels are country, region within country, and age group within region within country. The mean number of cases in age group j, in region i of country h, μ_{hij}, is written as

$$\ln\left(\mu_{hij}\right) = \ln\left(y_{hij}\right) + \rho_j + v_h + u_{hi}$$

where ρ_j are the age group effects, v_h the random effects associated with country, and u_{hi} the random effects associated with region within country. The ρ_j are fixed effects and are the same as $\ln\left(\xi_j\right)$ in the Poisson Gamma model.

The random effects are assumed to follow normal distributions with mean zero and variances σ_v^2 and σ_u^2, respectively. Similar models are used by Langford et al (1999), Leyland et al (2000) Langford & Day (2001).

At the lowest (age group) level the number of deaths is assumed to follow a Poisson distribution

$$d_{hij} \sim Poisson\left(\mu_{hij}\right)$$

which has expectation and variance $E\left[d_{hij}\right] = Var\left[d_{hij}\right] = \mu_{hij}$. This can be extended to include extra Poisson variation, Breslow (1984), through an over dispersion parameter, ϕ, where

$$Var\left[d_{hij}\right] = \phi\mu_{hij}.$$

The parameters are estimated using MLwiN, Rasbash et al (2000), using restricted iteratively reweighted least squares, partial quasi likelihood and a second order approximation. No major

estimation problems were encountered other than for mesothelioma for males where a first order approximation was used.

If the parameter, μ_{hij}, of the Poisson distribution is assumed to follow a Gamma distribution, as in Pennello, Devesa & Gail (1999), then a Negative Binomial distribution for the deaths, d_{hij}, results. This is an extension to the hierarchical Poisson regression model and has exactly the same level 2 and 3 structure but at the age group level has

$$d_{hij} \sim NBD\left(\mu_{hij}, \frac{\mu_{hij}}{\mu_{hij}+\nu}\right)$$

which, with a parameter for over dispersion, ϕ, has variance $Var\left[d_{hij}\right] = \phi\mu_{hij} + \frac{1}{\nu}\left(\mu_{hij}\right)^2$.

If we have only a two level model with age group nested within region then the Poisson model without the over dispersion parameter should be equivalent to the Poisson Gamma model, Pennello, Devesa & Gail (1999). The models are not algebraically identical, as the two level Poisson model assumes a normal distribution for the regional effects and so a log normal distribution for the exponential of these random effects. The exponential of the random effects serve the same purpose as the γ_i in the Poisson Gamma model which are assumed to follow a Gamma distribution. The hierarchical Poisson and Negative Binomial models are extensions to the two level Poisson Gamma model in that both regional variation and over dispersion can be estimated simultaneously.

The sum of the parameters, σ_v^2 and σ_u^2 is an estimate of the total regional variance and so performs a similar function to the RRSD of the Poisson Gamma model. We anticipate that $\sqrt{o_v^2 + o_u^2}$ would be strongly associated with RRSD. In fact the correlation over all sites investigated is 0.95 for males and 0.93 females. Usually the RRSD is slightly smaller than $\sqrt{o_v^2 + o_u^2}$ and the median ratio is 0.86 for males and 0.93 for females.

Only the results for the negative binomial model with over dispersion are presented. The regional and country variance parameters are similar for the Poisson and Negative Binomial models.

The important parameters for the assessment of regional variation are σ_v^2 and σ_u^2. When the rates tend to be higher in one country compared with other countries we would expect to see larger values for the between country variance, σ_v^2. In most cases σ_v^2 will be larger than the within country variance, σ_u^2; however if they are approximately the same size we would conclude that there was little evidence of geographical pattern associated with countries. If σ_v^2 is very much larger than σ_u^2 this is indicative of a geographical pattern associated with countries.

The geographical pattern need not be specifically associated with isolated countries but if there is a band of high rates in Scandinavia and lower rates in the Mediterranean countries this would be expected to manifest itself as between country variance larger than within country variance (σ_v^2 larger than σ_u^2). If there were areas of high rates and very low rates within a country with the same pattern in all countries then this would result in σ_v^2 being similar in magnitude to, or smaller than, σ_u^2.

As with the Poisson Gamma model, this is not a true model of spatial structure. It has a spatial structure in so far as regions are located within countries. However the countries could be randomly distributed in space and the regions randomly reordered within countries with exactly the same results.

The between country variance, σ_v^2, is a measure of the variability of the differences among the medians for each country as illustrated in the boxplots presented with the maps. The average variability within each boxplot is measured by σ_u^2.

Spatial autocorrelation

The spatial autocorrelation or association may be defined as "the phenomenon where locational similarity (observations in spatial proximity) is matched by value similarity (attribute correlation)" (Anselin 1995). Note that this matching may

be the result of a "true" interaction among the variables or as a sort of error due to the "artificial" administrative units such as provinces, counties, states etc. (Magalahes et al. 2002).

To quantify the strength of the autocorrelation of a given random variable in a given geographic map a number of statistics have been proposed (Gebhardt, 1998), including the Moran's I statistic (Cliff and Ord 1981):

$$I = \frac{r}{S_0} \frac{\sum_{ij} w_{ij} (z_i - \bar{z})(z_j - \bar{z})}{\sum_i (z_i - \bar{z})^2}$$

where there are r regions, with z_i denoting the age standardised rate in region i, and $\bar{z}$ is the average over all regions so that $\bar{z} = \frac{\sum_{i=1}^{r} z_i}{r}$. The neighbours of a particular region are denoted by a positive number w_{ij} if regions i and j share a common boundary, i.e. are neighbours, and $w_{ij} = 0$ if they are not neighbours, and $S_0 = \sum_{i=1}^{r} \sum_{j=1}^{r} w_{ij}$. Various forms have been used in the literature for w_{ij}, but the most important are $w_{ij} = 1$ and $w_{ij} = 1/\nu_i$, where ν_i denotes the number of neighbours of region i. We chose the latter form, which allows a simple geometrical interpretation for the statistic.

In fact, Moran's I statistic, with $w_{ij} = 1/\nu_i$, has similarities to the correlation coefficient and indeed may be interpreted as the slope of the regression line obtained from the scatter plot of $\bar{z}_i^*$ against $z_i - \bar{z}$, where $\bar{z}_i^*$ is the average of the age standardised rates in the regions neighbouring region i. This scatter plot has been proposed for its usefulness in exploratory spatial data analysis since it gives a synthetic graphical idea of the degree of correlation of the analysed map. It is possible to use the scatterplot to identify potential groups of regions having high (or low) values of the variable in study (Anselin, Sybari & Smirnov, 2002).

Moran's I statistic measures the similarity in age standardised rates between geographically close areas. If there is no spatial dependence, I will be close to zero, while values close to one indicate spatial clustering. Note that even if in theory the I statistic should be used only with identically distributed stochastic variables, it is often used also when the variables are not so distributed. As we are interested in assessing the spatial autocorrelation among neighbouring regions, the "mono-province" islands were not included in the computation since they have no neighbours. This means that Cyprus, Iceland and Malta were excluded from this analysis which is why they do not appear in Table 5.3. Furthermore, any other island with just one level 3 nuts region was also excluded. This means that Corsica, Orkney and Shetland, for example, were excluded but that Sicily, Crete and Sardinia were included.

We also used a bivariate version of this statistic to calculate the spatial association between the rates for males and females, and also between certain cancer sites. This is achieved by calculating the correlation between $\bar{z}_i^*$ for males and $\bar{z}_i^*$ for females. We would expect this correlation to be positive. If it is close to zero then this implies that the spatial structure is not the same for males and females. If it is close to one then the spatial structure is the same for males as for females. In these bivariate analyses we included also the "mono-province" islands, since the comparisons make sense also for regions without neighbours. The scatter plots associated with these correlations show, in particular, regions where the geographic pattern is not the same for males as for females.

Results

Across the cancer sites the magnitude of the overall variability (RRSD) ranged in males from 0.144 (leukaemia) to 0.755 (pleura) and in females from 0.138 (leukaemia) to 0.758 (oesophagus) (Figure 5.1, Tables 5.1 and 5.2). Among males, pleura (mesothelioma) exhibits the greatest regional variation (among females it has the third largest regional variation). This cancer site has very low rates in most areas but, relatively, very high rates in a few areas. A similar pattern is observed in most countries.

For both males and females, the cancer sites which have low regional variability are leukaemia, brain

and central nervous system, pancreas and multiple myeloma. There may still be a spatial structure but the relative spread of the age-standardised rates is small. Irrespective of the absolute level of the rates there is not much relative variation over all countries and NUTS regions in the maps for these cancers. There was also low variability for two major cancers – breast and prostate.

The cancer sites which have high regional variation are pleura, non-melanoma skin cancer, oesophagus, liver and larynx. These are sites where there is a relatively large range from the regions with low rates to the regions with high rates.

The model was fitted for each country for each cancer site. In some instances numerical problems were experienced when fitting the model as the log likelihood was monotonic in α and kept increasing while α tended to infinity. The reported value of the RRSD was consequently zero but no standard error could be calculated. This problem generally occurred among the cancer sites with fewer numbers of deaths and in the countries with fewer regions. Consistent results were obtained when using MLwiN in that the level 2 variance was estimated as zero. Individual countries with high regional variation are reported with the individual cancer sites in chapter 6. Results by country are given in Table 5.3 for males and females separately.

For the three level models, a negative binomial distribution was chosen, allowing for extra negative binomial dispersion: the addition of another component for the level 1 variation produced an extra negative binomial term which was smaller than the extra Poisson term. This happened in all sites, but such a reduction, although small, was present for both males and females. The estimates of the country variance and within country variance are not affected a great deal by the use of a Poisson or Negative Binomial level 1 structure.

The median variation associated with country is just over 80% in both males and females indicating substantial variation over large scale regions such as countries (Figure 5.2, Tables 5.1 and 5.2). This suggests that we should expect to see large scale regional patterns for most cancer sites. This may include high rates in just one country relative to all the others, or low rates in one country relative to the others. It may also manifest itself as lower rates in certain geographic areas, spanning more than one country. From the values of the statistic for the different cancer sites, such a large scale geographic pattern should be more evident for gallbladder, non-Hodgkin's lymphoma, large bowel, melanoma, liver, multiple myeloma and kidney. For males, the statistics is also high for prostate, oral cancer and larynx, while for females it is high for all uterus under 50, ovary, and all uterus. The sites where there may not be such a large scale pattern are bladder and Hodgkin's disease (in both males and females) and oral cancer in females, as these sites have the lowest percentages of variation associated with country.

For both males and females there is evidence of substantial extra Negative Binomial dispersion for lung cancer, where there are large numbers of deaths, and also for non-melanoma skin cancer. There is also over dispersion for pleura among males and all uterus among females. There is generally less over dispersion in rarer cancers such as melanoma, thyroid, testis and Hodgkin's disease. There is generally less over dispersion among females compared with males. For lung cancer, which has the greatest over dispersion for females, the estimate is 1.14 compared with 1.19 for males.

Moran's I statistic ranges from 0.18 (thyroid) to 0.82 (stomach) for males and from 0.16 (leukaemia) to 0.82 (oesophagus) in females (Figure 5.3, Table 5.4). The greatest spatial clustering is to be found in lung, liver, stomach, oesophagus and large bowel, for both males and females. There is also high spatial correlation in all uterus, breast and gallbladder for females, and in oral cancer and larynx for males. For these cancers we would expect to see areas of red clustered together on the maps and areas of green clustered together. Leukaemia, thyroid, brain, and Hodgkin's disease in both sexes, and testis all have very low spatial correlation and we should not find any spatial pattern.

For cancer sites which affect both males and females, the correlations between the smoothed rates

for males and females are also presented in Table 5.4. The highest correlations are for stomach, large bowel and gallbladder, indicating that the geographic pattern for males and females is similar. The lowest correlations are for lung, bladder and larynx.

For cancer sites which affect both males and females the values of the variability and correlation statistics are plotted for males and females in Figure 5.4. Generally, the magnitude of the RRSD is the same in males and females for cancers affecting both (Figure 5.4 (a)). Over the 20 common sites the median of the ratio of the RRSD for males to females is 0.99 ranging from 0.53 to 1.99, with an inter quartile range from 0.87 to 1.14. The main differences are lung and oesophagus, especially, and gallbladder and skin, also, which have a larger RRSD in females, and oral cancer, which has a larger RRSD in males. With the exception of these five sites there is a very strong agreement between the relative risk standard deviations in males and females. The rates may be higher for males (larynx, for example) than in females, but the magnitude of the relative geographic variability is the same.

The variation between countries (Figure 5.4(b)) is not always the same for males and females and the biggest differences occur for oral cancer and larynx, which have greater between country variation for males, and lung, oesophagus, skin and gallbladder, which have greater between country variation for females. The variation within a country is virtually the same for males and females over all cancer sites (Figure 5.4(c)). The only minor exceptions are for gallbladder, lung, and larynx which have higher variation within a country for females compared with males. The pattern for total variability from the multilevel model (Figure 5.4(d)) is similar to that for the RRSD (Figure 5.4(a)).

There is general agreement between Moran's I for males and for females for many sites (Figure 5.4(e)), but not for larynx and oral cancer which have a low Moran's I for females but high for males, and, to a lesser extent, for gallbladder and oesophagus which have a slightly higher Moran I for females compared with males. Also, for Hodgkin's Disease there is low spatial correlation for females but slightly higher for males.

The correlation between the smoothed rates for males and the smoothed rates for females is high (over 0.8) for cancers of the stomach, large bowel, gallbladder and kidney, non-Hodgkin's Lymphoma and low (under 0.3) for larynx, lung and bladder (Figure 5.4(f)). This implies that the spatial pattern among males and females is similar in some of the digestive tract cancers but not in three of the sites associated with smoking.

The measures of spatial variation and correlation are plotted pairwise against each other in Figure 5.5 for males and females separately. The three measures provide complementary information. The RRSD is a measure of relative spatial variation, Moran's I is a measure of spatial correlation through a chain of local correlations, and the percentage of variation associated with country is a measure of large scale correlation. Generally they are all weakly positively associated. The correlation between the RRSD and the percentage of variation associated with country is 0.08 for males and 0.13 for females; the correlation between the RRSD and Moran's I is 0.26 for males and 0.35 for females; and the correlation between the percentage of variation associated with country and Moran's I is 0.36 for males and 0.49 for females.

It is possible to find low RRSD and a high percentage of variation due to country (Figures 5.5(a) and 5.5(b)). Among females, this occurs for ovary, large bowel, multiple myeloma and leukaemia; among males, there is a similar pattern for non-Hodgkin's lymphoma, large bowel, multiple myeloma, prostate and leukaemia. This occurs when the relative regional variation is small but there are some countries with consistently higher or lower rates across their regions. When there was a relatively low percentage of variation due to country, as in the case of oral cancer and bladder among females, there was also a low RRSD. Those sites with strong overall variability (high RRSD) tended to have a higher percentage of variation due to country.

The overall association between RRSD and Moran's I is low (Figures 5.5(c) and 5.5(d)). There is however some similarity in the pattern for males and females. Both measures are low for leukaemia, brain and multiple myeloma and both

are high for liver. Pleura, skin and testis cancer (males only) have a high RRSD but low spatial correlation, while bowel, breast, prostate, lung (males), ovary, and uterus have relatively low RRSD but high spatial correlation.

If Moran's I is high, over 0.7, then the percentage of variation associated with country tends also to be high (Figures 5.5(e) and 5.5(f)). However it is possible to have a high percentage and a low Moran's I, for example for leukaemia. Also, we do not find a low percentage of variation explained by country differences and a very high Moran's I, as a strong local spatial correlation would imply differences between the countries. There are many sites where Moran's I is low but the country percentage is high. Often these are the same sites with RRSD low but the country percentage high such as leukaemia and multiple myeloma.

Summary

In this chapter we illustrate the use of summarising spatial variability and spatial correlation with a view to using these measures to assist in the interpretation of the maps. Throughout chapter 6 we discuss the interpretation of the maps in relation to these statistics. In the current chapter we have looked at the relationship among these statistics and have commented on the similarity between the maps for males and females for a number of, but not all, cancer sites.

If the RRSD is small then there is not a great deal of spatial variability in the rates even although the main map may have areas of red and green. In such cases it is prudent to pay attention to the absolute scale maps at the bottom right hand corner of the main maps. Furthermore, over-interpretation of the differences in rates between areas of the maps should be discouraged. If there is a large RRSD then there is a greater relative difference among the rates in the regions and for such maps the geographic differences are likely to be important.

Although we use a measure of the percentage of variation associated with country this has a broader interpretation of large scale correlation. When this percentage is low there is no large scale pattern in the rates. Moran's I statistic is high when there is high spatial correlation and this can occur even when the RRSD is low. Cancer sites with a high Moran's I and a high RRSD are the ones with the greatest geographic variation and pattern. Cancer sites with a low value for Moran's I and a low RRSD are the ones with little geographic variation and little geographic pattern.

Table 5.1: Spatial variation measures for males

Cancer site	Relative risk standard deviation		Countries		NUTS within countries		Extra Negative Binomial		%
	RRSD	SE	Var	SE	Var	SE	Var	SE	
Oral cavity and pharynx	0.552	0.011	0.375	0.107	0.0618	0.0038	1.083	0.018	85.9
Oesophagus	0.452	0.010	0.158	0.046	0.0643	0.0039	1.036	0.018	71.0
Stomach	0.395	0.008	0.194	0.055	0.0400	0.0022	1.004	0.016	82.9
Large bowel	0.251	0.006	0.082	0.023	0.0138	0.0009	1.025	0.016	85.7
Liver	0.602	0.012	0.328	0.093	0.0561	0.0034	1.075	0.015	85.4
Gallbladder	0.505	0.012	0.239	0.069	0.0218	0.0031	1.027	0.014	91.6
Pancreas	0.198	0.006	0.039	0.011	0.0148	0.0012	1.049	0.016	72.4
Larynx	0.617	0.013	0.573	0.163	0.0499	0.0038	1.050	0.016	92.0
Lung	0.294	0.006	0.111	0.032	0.0335	0.0017	1.188	0.026	76.8
Pleura	0.755	0.010	0.711	0.211	0.2327	0.0161	1.180	0.015	75.3
Melanoma	0.352	0.010	0.184	0.053	0.0312	0.0036	0.942	0.015	85.5
Non-melanoma skin cancer	0.555	0.010	0.185	0.064	0.0562	0.0101	1.161	0.015	76.7
Breast	..	..	..	..	..	..	..	..	..
All uterus	..	..	..	..	..	..	..	..	..
All uterus under 50	..	..	..	..	..	..	..	..	..
Ovary	..	..	..	..	..	..	..	..	..
Prostate	0.204	0.005	0.039	0.011	0.0068	0.0006	1.062	0.015	85.0
Testis	0.542	0.009	0.243	0.076	0.0711	0.0156	0.972	0.015	77.3
Urinary bladder	0.243	0.007	0.052	0.015	0.0256	0.0019	1.021	0.015	66.8
Kidney	0.334	0.008	0.127	0.036	0.0264	0.0021	1.062	0.016	82.8
Brain and CNS	0.183	0.007	0.026	0.008	0.0084	0.0012	1.019	0.016	75.7
Thyroid	0.365	0.008	0.083	0.028	0.0268	0.0086	1.019	0.013	75.6
Hodgkin's disease	0.475	0.010	0.153	0.047	0.0707	0.0097	0.920	0.015	68.4
Non-Hodgkin's lymphoma	0.273	0.008	0.118	0.034	0.0154	0.0017	0.991	0.015	88.4
Multiple myeloma	0.201	0.008	0.021	0.006	0.0036	0.0008	1.003	0.015	85.7
Leukaemia	0.144	0.006	0.047	0.014	0.0105	0.0019	0.988	0.014	81.7
All cancer (ICD-9 140-208)	0.174	0.004	0.042	0.012	0.0099	0.0005	1.284	0.032	80.8

Table 5.2: Spatial variation measures for females

Cancer site	Relative risk standard deviation		Countries		NUTS within countries		Extra Negative Binomial		%
	RRSD	SE	Var	SE	Var	SE	Var	SE	
Oral cavity and pharynx	0.278	0.009	0.049	0.016	0.0420	0.0049	0.945	0.015	54.0
Oesophagus	0.758	0.013	0.361	0.104	0.0672	0.0060	1.044	0.015	84.3
Stomach	0.384	0.008	0.156	0.045	0.0407	0.0024	1.037	0.016	79.3
Large bowel	0.236	0.006	0.051	0.015	0.0091	0.0007	1.038	0.016	84.8
Liver	0.538	0.012	0.249	0.072	0.0480	0.0036	1.079	0.015	83.8
Gallbladder	0.609	0.013	0.362	0.103	0.0517	0.0036	0.999	0.014	87.5
Pancreas	0.209	0.006	0.038	0.011	0.0144	0.0012	0.983	0.014	72.6
Larynx	0.503	0.008	0.236	0.074	0.0797	0.0136	0.874	0.013	74.7
Lung	0.554	0.011	0.252	0.072	0.0656	0.0035	1.144	0.020	79.3
Pleura	0.662	0.009	0.425	0.132	0.1873	0.0188	0.771	0.012	69.4
Melanoma	0.303	0.010	0.140	0.041	0.0265	0.0036	0.924	0.015	84.1
Non-melanoma skin cancer	0.667	0.009	0.297	0.092	0.0672	0.0136	1.099	0.015	81.6
Breast	0.201	0.005	0.035	0.010	0.0116	0.0007	1.067	0.018	75.1
All uterus	0.353	0.008	0.142	0.040	0.0224	0.0017	1.114	0.018	86.4
All uterus under 50	0.539	0.013	0.344	0.100	0.0410	0.0054	1.132	0.019	89.4
Ovary	0.257	0.006	0.067	0.019	0.0092	0.0010	1.043	0.017	87.9
Prostate	..	..	..	..	..	..	..	..	..
Testis	..	..	..	..	..	..	..	..	..
Urinary bladder	0.316	0.009	0.051	0.016	0.0348	0.0034	0.941	0.013	59.7
Kidney	0.361	0.009	0.146	0.042	0.0252	0.0025	0.996	0.015	85.2
Brain and CNS	0.202	0.007	0.037	0.011	0.0097	0.0015	1.035	0.016	79.1
Thyroid	0.319	0.010	0.063	0.020	0.0271	0.0057	1.002	0.014	69.9
Hodgkin's disease	0.415	0.010	0.113	0.037	0.0606	0.0109	0.928	0.014	65.1
Non-Hodgkin's lymphoma	0.307	0.009	0.160	0.046	0.0182	0.0019	1.020	0.015	89.8
Multiple myeloma	0.225	0.008	0.017	0.005	0.0036	0.0009	1.040	0.015	83.0
Leukaemia	0.138	0.006	0.066	0.020	0.0142	0.0022	1.046	0.015	82.3
All cancer (ICD-9 140-208)	0.166	0.003	0.026	0.008	0.0060	0.0003	1.264	0.024	81.6

Table 5.3: Relative risk standard deviation (RRSD) and standard errors (SE) for each cancer site by country

(a) Males

Country*	Oral cavity and pharynx		Oesophagus		Stomach		Large bowel		Liver		Gallbladder		Pancreas		Larynx		Lung		Pleura	
	140-149		150		151		153, 154 & 159.0		155		156		157		161		162		163	
	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE
Austria	0.205	0.062	0.141	0.071	0.112	0.033	0.170	0.048	0.184	0.056	0.302	0.095	0.110	0.039	0.063	0.064	0.088	0.024	0.198	0.097
Belgium	0.321	0.072	0.119	0.038	0.216	0.056	0.059	0.018	0.242	0.058	0.104	0.075	0.102	0.031	0.222	0.056	0.097	0.022	0.423	0.105
Czech Republic	0.168	0.039	0.152	0.039	0.137	0.030	0.113	0.024	0.186	0.043	0.061	0.038	0.026	0.038	0.123	0.041	0.166	0.032	0.000	0.055
Denmark	0.380	0.078	0.226	0.053	0.136	0.041	0.097	0.025	0.528	0.125	NA	NA	0.088	0.039	0.364	0.085	0.106	0.023	0.499	0.127
Estonia	0.248	0.077	0.174	0.125	0.218	0.058	0.097	0.069	NA	NA	0.129	0.026	0.000	0.043	0.188	0.080	0.093	0.030	0.726	0.052
Finland	0.209	0.063	0.275	0.068	0.127	0.036	0.056	0.042	0.257	0.064	0.171	0.093	0.098	0.034	0.166	0.142	0.083	0.022	0.451	0.115
France	0.283	0.022	0.319	0.024	0.186	0.016	0.114	0.010	0.249	0.019	0.090	0.031	0.109	0.013	0.230	0.020	0.186	0.015	0.376	0.037
Germany	0.209	0.012	0.184	0.013	0.176	0.009	0.096	0.006	0.212	0.014	0.174	0.019	0.051	0.014	0.190	0.018	0.212	0.008	0.464	0.021
Greece	0.008	1.234	0.210	0.050	0.438	0.049	0.206	0.032	0.276	0.035	0.094	0.015	0.297	0.048	0.268	0.053	0.260	0.028	0.001	0.000
Hungary	0.180	0.032	0.205	0.037	0.132	0.025	0.075	0.016	0.137	0.029	0.049	0.059	0.091	0.024	0.234	0.042	0.111	0.019	0.000	0.000
Ireland	0.075	0.075	0.075	0.049	0.120	0.045	0.000	0.072	0.077	0.078	0.000	0.046	0.000	0.022	0.282	0.109	0.166	0.045	0.572	0.134
Italy	0.412	0.032	0.567	0.041	0.299	0.022	0.171	0.014	0.326	0.025	0.125	0.022	0.244	0.020	0.259	0.023	0.230	0.018	0.681	0.052
Latvia	0.161	0.057	0.172	0.080	0.111	0.042	0.164	0.050	0.224	0.069	0.268	0.032	0.000	0.035	0.203	0.063	0.139	0.029	0.000	0.000
Lithuania	0.160	0.058	0.202	0.053	0.116	0.037	0.157	0.039	0.208	0.052	0.505	0.038	0.165	0.056	0.195	0.053	0.142	0.023	0.000	0.000
Netherlands	0.146	0.037	0.082	0.024	0.144	0.026	0.059	0.017	0.179	0.049	NA	NA	0.082	0.027	0.000	0.001	0.094	0.013	0.533	0.067
Norway	0.236	0.065	0.183	0.068	0.125	0.045	0.093	0.025	0.161	0.113	0.242	0.110	0.134	0.048	0.389	0.117	0.130	0.027	0.490	0.096
Poland	0.191	0.026	0.162	0.027	0.132	0.016	0.159	0.020	0.209	0.028	0.274	0.043	0.084	0.018	0.130	0.020	0.141	0.015	0.418	0.062
Portugal	0.274	0.053	0.241	0.052	0.222	0.038	0.149	0.033	0.234	0.051	0.185	0.072	0.154	0.042	0.344	0.063	0.371	0.060	0.000	0.000
Slovakia	0.264	0.038	0.238	0.046	0.138	0.031	0.133	0.027	0.217	0.055	0.369	0.058	0.201	0.047	0.299	0.051	0.127	0.020	0.335	0.041
Slovenia	0.195	0.079	0.109	0.140	0.190	0.070	0.155	0.059	0.174	0.106	0.000	0.140	0.034	0.200	0.106	0.131	0.154	0.048	0.943	0.036
Spain	0.296	0.035	0.290	0.033	0.221	0.026	0.134	0.017	0.227	0.028	0.098	0.039	0.126	0.019	0.218	0.026	0.232	0.026	0.466	0.055
Sweden	0.260	0.067	0.154	0.045	0.127	0.035	0.056	0.021	0.225	0.048	0.000	0.064	0.121	0.034	0.204	0.113	0.158	0.030	0.373	0.106
Switzerland	0.234	0.052	0.261	0.055	0.161	0.036	0.080	0.027	0.324	0.057	0.128	0.030	NA	NA	0.366	0.071	0.111	0.026	0.414	0.062
United Kingdom	0.290	0.023	0.148	0.013	0.217	0.016	0.115	0.009	0.227	0.020	0.162	0.031	0.054	0.015	0.336	0.027	0.220	0.014	0.690	0.041

* RRSDs cannot be calculated for Cyprus, Iceland, Luxembourg and Malta as they have only 1 or 2 regions

NA denotes situations where it was not possible to estimate the RRSD because of numerical problems see Results paragraph 4

Country*	Melanoma		Skin (other)		Breast		All uterus		All uterus Under 50		Ovary		Prostate		Testis	
	172		173		174		179-182		179-182		183		185		186	
	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE
Austria	0.000	0.026	0.000	0.070	..	..	..	..	..	..	..	..	0.084	0.027	0.475	0.119
Belgium	0.000	0.024	0.093	0.195	..	..	..	..	..	..	..	..	0.088	0.025	0.681	0.103
Czech Republic	0.085	0.065	0.085	0.134	..	..	..	..	..	..	..	..	0.059	0.024	0.000	0.052
Denmark	0.004	1.412	0.000	0.000	..	..	..	..	..	..	..	..	0.063	0.022	0.000	0.000
Estonia	0.174	0.042	0.000	0.000	..	..	..	..	..	..	..	..	0.122	0.070	0.000	0.000
Finland	0.107	0.077	0.454	0.060	..	..	..	..	..	..	..	..	0.098	0.034	0.356	0.051
France	0.116	0.032	0.233	0.037	..	..	..	..	..	..	..	..	0.112	0.010	0.197	0.020
Germany	0.142	0.023	0.487	0.014	..	..	..	..	..	..	..	..	0.069	0.008	0.369	0.012
Greece	0.312	0.031	0.431	0.045	..	..	..	..	..	..	..	..	0.156	0.028	0.453	0.025
Hungary	0.089	0.058	0.222	0.074	..	..	..	..	..	..	..	..	0.100	0.022	0.249	0.106
Ireland	0.103	0.136	0.000	0.112	..	..	..	..	..	..	..	..	0.011	0.079	0.371	0.114
Italy	0.288	0.033	0.188	0.046	..	..	..	..	..	..	..	..	0.102	0.011	0.189	0.016
Latvia	0.108	0.022	NA	NA	..	..	..	..	..	..	..	..	0.133	0.077	0.000	0.000
Lithuania	0.206	0.025	0.000	0.000	..	..	..	..	..	..	..	..	0.088	0.063	0.000	0.000
Netherlands	0.095	0.053	0.159	0.021	..	..	..	..	..	..	..	..	0.059	0.017	0.117	0.012
Norway	0.240	0.070	0.000	0.000	..	..	..	..	..	..	..	..	0.095	0.026	0.000	0.000
Poland	0.187	0.041	0.251	0.050	..	..	..	..	..	..	..	..	0.092	0.016	0.335	0.074
Portugal	0.296	0.105	0.151	0.079	..	..	..	..	..	..	..	..	0.151	0.030	0.000	0.000
Slovakia	0.000	0.000	0.334	0.048	..	..	..	..	..	..	..	..	0.056	0.057	0.230	0.026
Slovenia	0.000	0.081	0.335	0.108	..	..	..	..	..	..	..	..	0.000	0.051	0.476	0.100
Spain	0.169	0.043	0.336	0.049	..	..	..	..	..	..	..	..	0.100	0.014	0.263	0.031
Sweden	0.125	0.060	0.375	0.074	..	..	..	..	..	..	..	..	0.064	0.022	0.294	0.035
Switzerland	0.082	0.027	0.175	0.029	..	..	..	..	..	..	..	..	0.071	0.024	0.000	0.000
United Kingdom	0.230	0.025	0.176	0.024	..	..	..	..	..	..	..	..	0.063	0.008	0.216	0.021

* RRSDs cannot be calculated for Cyprus, Iceland, Luxembourg and Malta as they have only 1 or 2 regions

NA denotes situations where it was not possible to estimate the RRSD because of numerical problems see Results paragraph 4

Country*	Urinary bladder		Kidney		Brain and CNS		Thyroid		Hodgkin's disease		Non-Hodgkin's lymphoma		Multiple myeloma		Leukaemia	
	188		189		191 & 192		193		201		200 & 202		203		204	
	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE
Austria	0.069	0.035	0.079	0.053	0.102	0.043	0.000	0.081	0.859	0.243	0.165	0.052	0.023	0.160	0.000	0.036
Belgium	0.090	0.029	0.122	0.041	0.000	0.009	0.097	0.191	0.000	0.092	0.033	0.045	0.028	0.105	0.113	0.038
Czech Republic	0.141	0.037	0.130	0.031	0.069	0.038	NA	NA	0.174	0.078	0.055	0.068	0.000	0.052	0.049	0.036
Denmark	0.160	0.043	0.082	0.053	0.036	0.094	NA	NA	0.171	0.165	NA	NA	NA	NA	0.050	0.062
Estonia	0.000	0.119	0.000	0.038	0.073	0.162	0.000	0.000	0.000	0.000	0.239	0.134	0.200	0.066	0.000	0.018
Finland	0.000	0.043	0.040	0.096	0.000	0.011	0.000	0.000	0.000	0.000	0.014	0.257	0.000	0.076	0.000	0.039
France	0.184	0.017	0.111	0.016	0.102	0.017	0.064	0.009	0.301	0.035	0.055	0.017	0.027	0.063	0.037	0.022
Germany	0.222	0.013	0.186	0.012	0.099	0.015	0.305	0.014	0.346	0.014	0.121	0.016	0.274	0.019	0.045	0.022
Greece	0.200	0.036	0.157	0.055	0.173	0.036	0.591	0.033	0.226	0.042	0.174	0.047	0.094	0.031	0.144	0.040
Hungary	0.058	0.029	0.125	0.033	0.000	0.022	0.182	0.100	0.295	0.100	0.106	0.039	0.100	0.084	0.074	0.033
Ireland	NA	NA	0.053	0.102	0.154	0.062	NA	NA	0.323	0.168	0.000	0.006	0.128	0.070	0.000	0.015
Italy	0.145	0.014	0.289	0.025	0.058	0.020	0.158	0.041	0.165	0.046	0.191	0.019	0.117	0.022	0.071	0.014
Latvia	0.080	0.165	0.116	0.098	0.000	0.001	0.762	0.039	0.522	0.048	0.000	0.050	0.000	0.000	0.000	0.039
Lithuania	NA	NA	0.190	0.062	0.000	0.052	0.000	0.000	0.000	0.000	0.287	0.052	0.147	0.019	0.000	0.049
Netherlands	0.066	0.030	0.000	0.038	0.000	0.022	0.000	0.000	0.000	0.000	0.046	0.040	0.000	0.032	0.000	0.030
Norway	NA	NA	0.000	0.031	0.173	0.059	0.437	0.087	0.000	0.000	0.092	0.053	0.125	0.073	0.029	0.166
Poland	0.107	0.020	0.154	0.024	0.117	0.023	0.000	0.000	0.165	0.044	0.197	0.032	0.116	0.039	0.068	0.027
Portugal	0.302	0.058	0.290	0.072	0.085	0.050	0.000	0.000	0.174	0.123	0.225	0.059	0.039	0.083	0.163	0.042
Slovakia	0.112	0.065	0.121	0.063	0.146	0.087	0.341	0.032	0.259	0.029	0.129	0.026	0.186	0.059	NA	NA
Slovenia	0.209	0.100	0.000	0.041	0.315	0.146	0.000	0.000	0.000	0.000	0.158	0.119	0.000	0.165	0.000	0.058
Spain	0.212	0.025	0.217	0.029	0.098	0.026	0.000	0.000	0.194	0.044	0.191	0.030	0.083	0.034	0.057	0.020
Sweden	0.093	0.038	0.041	0.046	0.058	0.053	0.034	0.008	0.320	0.070	0.043	0.043	0.000	0.023	0.108	0.034
Switzerland	0.089	0.044	0.000	0.063	0.000	0.239	0.332	0.047	0.000	0.000	0.022	0.008	0.054	0.099	0.145	0.053
United Kingdom	0.126	0.014	0.068	0.017	0.113	0.017	0.128	0.010	0.184	0.021	0.111	0.014	0.061	0.025	0.039	0.024

* RRSDs cannot be calculated for Cyprus, Iceland, Luxembourg and Malta as they have only 1 or 2 regions

NA denotes situations where it was not possible to estimate the RRSD because of numerical problems see Results paragraph 4

(b) Females

Country*	Oral cavity and pharynx		Oesophagus		Stomach		Large bowel		Liver		Gallbladder		Pancreas		Larynx		Lung		Pleura	
	140-149		150		151		153, 154 & 159.0		155		156		157		161		162		163	
	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE
Austria	0.245	0.079	0.000	0.077	0.130	0.039	0.122	0.034	0.000	0.038	0.141	0.054	0.095	0.033	0.190	0.154	0.221	0.060	0.273	0.127
Belgium	0.321	0.083	0.194	0.071	0.149	0.040	0.063	0.020	0.173	0.052	0.045	0.083	0.052	0.030	0.178	0.098	0.221	0.049	0.460	0.109
Czech Republic	0.124	0.074	0.000	0.060	0.124	0.029	0.095	0.022	0.062	0.040	0.093	0.028	0.028	0.045	0.000	0.114	0.317	0.061	0.311	0.152
Denmark	0.166	0.071	0.082	0.087	0.085	0.051	0.062	0.026	0.158	0.092	NA	NA	0.080	0.034	0.000	0.000	0.126	0.027	0.000	0.000
Estonia	0.193	0.046	0.317	0.043	0.224	0.063	0.180	0.064	0.222	0.070	0.000	0.000	NA	NA	0.000	0.000	0.162	0.068	0.000	0.000
Finland	0.000	0.077	0.000	0.075	0.000	0.027	0.076	0.035	0.325	0.083	0.134	0.054	0.138	0.039	0.000	0.000	0.340	0.063	0.405	0.051
France	0.207	0.030	0.255	0.030	0.205	0.020	0.091	0.010	0.139	0.020	0.239	0.025	0.112	0.015	0.251	0.038	0.236	0.020	0.401	0.041
Germany	0.251	0.020	0.355	0.021	0.175	0.010	0.087	0.006	0.262	0.018	0.286	0.014	0.077	0.011	0.388	0.010	0.285	0.011	0.438	0.014
Greece	0.000	0.000	0.000	0.000	0.426	0.051	0.199	0.033	0.232	0.037	0.342	0.041	0.188	0.048	0.001	0.000	0.244	0.038	0.000	0.000
Hungary	0.236	0.053	0.290	0.076	0.071	0.020	0.069	0.017	0.140	0.038	0.118	0.027	0.137	0.031	0.265	0.077	0.210	0.052	0.000	0.000
Ireland	0.000	0.053	0.164	0.074	0.094	0.046	NA	NA	0.091	0.149	0.269	0.109	NA	NA	0.112	0.567	0.183	0.054	0.000	0.000
Italy	0.238	0.032	0.475	0.047	0.289	0.022	0.124	0.011	0.319	0.026	0.159	0.018	0.241	0.021	0.454	0.042	0.359	0.030	0.533	0.047
Latvia	0.305	0.044	0.471	0.041	0.247	0.056	0.149	0.044	0.522	0.101	0.363	0.047	0.160	0.073	0.513	0.039	0.326	0.075	0.754	0.033
Lithuania	0.370	0.039	0.000	0.000	0.172	0.043	0.154	0.033	0.000	0.147	0.140	0.032	0.073	0.088	0.000	0.000	0.278	0.061	0.401	0.022
Netherlands	0.234	0.064	0.149	0.051	0.125	0.028	0.072	0.018	0.019	0.296	0.085	0.058	0.074	0.024	0.369	0.045	0.195	0.028	0.294	0.041
Norway	0.285	0.092	0.188	0.060	0.079	0.047	0.116	0.028	0.065	0.307	0.228	0.089	0.098	0.045	0.000	0.000	0.215	0.044	0.082	0.020
Poland	0.159	0.046	0.155	0.044	0.120	0.018	0.136	0.018	0.155	0.023	0.239	0.030	0.117	0.020	0.261	0.064	0.346	0.038	0.151	0.030
Portugal	0.138	0.120	0.590	0.111	0.244	0.042	0.102	0.023	0.105	0.052	0.192	0.061	0.133	0.040	0.000	0.000	0.292	0.059	0.195	0.026
Slovakia	0.209	0.127	0.227	0.034	0.074	0.061	0.160	0.034	0.177	0.070	0.212	0.058	0.188	0.054	0.000	0.000	0.203	0.045	0.000	0.000
Slovenia	0.000	0.090	0.000	0.297	0.133	0.063	0.118	0.073	0.401	0.143	0.107	0.109	0.085	0.122	0.000	0.027	0.246	0.086	0.000	0.000
Spain	0.044	0.115	0.346	0.058	0.223	0.026	0.111	0.015	0.248	0.031	0.206	0.030	0.126	0.021	0.000	0.000	0.150	0.024	0.219	0.031
Sweden	0.192	0.075	0.035	0.012	0.131	0.042	0.052	0.023	0.165	0.051	0.091	0.036	0.065	0.029	0.250	0.032	0.190	0.038	0.136	0.046
Switzerland	0.224	0.040	0.204	0.037	0.124	0.045	0.014	0.099	0.217	0.049	0.197	0.060	0.070	0.039	0.555	0.049	0.204	0.043	0.578	0.052
United Kingdom	0.179	0.028	0.173	0.016	0.246	0.019	0.066	0.008	0.202	0.025	0.242	0.032	0.058	0.015	0.281	0.032	0.269	0.017	0.739	0.025

* RRSDs cannot be calculated for Cyprus, Iceland, Luxembourg and Malta as they have only 1 or 2 regions

NA denotes situations where it was not possible to estimate the RRSD because of numerical problems see Results paragraph 4

Country*	Melanoma		Skin (other)		Breast		All uterus		All uterus Under 50		Ovary		Prostate		Testis	
	172		173		174		179-182		179-182		183		185		186	
	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE
Austria	0.099	0.055	0.124	0.158	0.066	0.020	NA	NA	0.147	0.083	0.000	0.025	..	..	..	..
Belgium	0.169	0.069	0.000	0.093	0.066	0.018	0.090	0.033	0.100	0.098	0.135	0.036	..	..	..	..
Czech Republic	0.131	0.065	0.000	0.056	0.064	0.016	0.149	0.033	0.168	0.054	0.095	0.026	..	..	..	..
Denmark	0.000	0.043	0.000	0.069	0.091	0.022	0.092	0.038	0.053	0.206	0.055	0.035	..	..	..	..
Estonia	0.000	0.000	0.000	0.000	0.128	0.050	0.000	0.097	0.115	0.375	0.078	0.058	..	..	..	..
Finland	0.092	0.177	0.364	0.048	0.135	0.028	0.000	0.049	NA	NA	0.000	0.000	..	..	..	..
France	0.171	0.028	0.150	0.018	0.100	0.009	0.137	0.015	0.232	0.036	0.126	0.014	..	..	..	..
Germany	0.100	0.016	0.681	0.013	0.098	0.006	0.200	0.011	0.336	0.020	0.081	0.010	..	..	..	..
Greece	0.000	0.000	0.318	0.036	0.156	0.025	0.176	0.054	0.319	0.028	0.166	0.046	..	..	..	..
Hungary	0.000	0.045	NA	NA	0.122	0.022	0.096	0.024	0.164	0.054	0.105	0.029	..	..	..	..
Ireland	0.218	0.111	0.000	0.000	NA	NA	0.082	0.057	0.201	0.151	0.116	0.050	..	..	..	..
Italy	0.221	0.033	0.137	0.019	0.167	0.014	0.163	0.016	0.240	0.042	0.183	0.018	..	..	..	..
Latvia	0.000	0.000	NA	NA	0.101	0.030	0.155	0.055	0.352	0.122	0.000	0.049	..	..	..	..
Lithuania	0.265	0.031	0.000	0.000	0.119	0.028	0.147	0.046	0.251	0.061	0.076	0.035	..	..	..	..
Netherlands	0.125	0.060	0.281	0.033	0.055	0.012	0.015	0.126	0.052	0.215	0.029	0.028	..	..	..	..
Norway	0.221	0.072	0.000	0.000	0.069	0.023	0.114	0.045	0.219	0.135	0.137	0.043	..	..	..	..
Poland	0.108	0.052	0.181	0.052	0.136	0.017	0.142	0.018	0.131	0.031	0.091	0.018	..	..	..	..
Portugal	0.162	0.097	0.283	0.074	0.231	0.042	0.202	0.043	0.086	0.105	0.245	0.053	..	..	..	..
Slovakia	0.114	0.151	0.651	0.082	0.194	0.034	0.140	0.039	0.128	0.107	0.161	0.052	..	..	..	..
Slovenia	0.356	0.145	0.510	0.103	0.132	0.050	0.067	0.174	0.308	0.217	0.046	0.167	..	..	..	..
Spain	0.109	0.030	0.449	0.059	0.134	0.016	0.203	0.028	0.209	0.039	0.090	0.020	..	..	..	..
Sweden	0.000	0.158	0.321	0.059	0.103	0.024	0.180	0.044	NA	NA	0.086	0.034	..	..	..	..
Switzerland	0.000	0.000	0.001	0.000	0.058	0.020	0.000	0.019	0.247	0.046	0.095	0.034	..	..	..	..
United Kingdom	0.214	0.022	0.198	0.017	0.041	0.007	0.124	0.013	0.233	0.029	0.051	0.011	..	..	..	..

* RRSDs cannot be calculated for Cyprus, Iceland, Luxembourg and Malta as they have only 1 or 2 regions
NA denotes situations where it was not possible to estimate the RRSD because of numerical problems see Results paragraph 4

Country*	Urinary bladder		Kidney		Brain and CNS		Thyroid		Hodgkin's disease		Non-Hodgkin's lymphoma		Multiple myeloma		Leukaemia	
	188		189		191 & 192		193		201		200 & 202		203		204	
	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE	RRSD	SE
Austria	0.287	0.093	0.092	0.066	0.088	0.042	0.248	0.086	0.811	0.223	0.164	0.049	0.000	0.027	0.000	0.029
Belgium	0.199	0.063	0.103	0.040	0.000	0.043	0.000	0.090	NA	NA	NA	NA	0.000	0.007	0.056	0.037
Czech Republic	0.273	0.076	0.177	0.041	0.126	0.038	0.184	0.092	NA	NA	0.073	0.052	0.096	0.055	0.029	0.052
Denmark	0.130	0.061	0.000	0.036	0.051	0.098	NA	NA	0.140	0.048	0.000	0.084	0.138	0.068	0.000	0.033
Estonia	0.000	0.000	0.000	0.000	NA	NA	0.526	0.061	0.000	0.000	0.267	0.063	0.000	0.000	0.000	0.067
Finland	0.215	0.088	NA	NA	0.000	0.027	0.270	0.131	0.393	0.050	0.000	0.041	0.089	0.115	0.094	0.082
France	0.122	0.025	0.138	0.022	0.098	0.021	0.143	0.056	0.198	0.029	0.054	0.020	0.055	0.029	0.061	0.018
Germany	0.263	0.017	0.169	0.015	0.230	0.019	0.230	0.019	0.230	0.019	0.103	0.017	0.311	0.018	0.044	0.028
Greece	0.194	0.050	0.000	0.000	0.166	0.047	0.268	0.027	0.071	0.009	0.000	0.000	0.149	0.036	0.056	0.019
Hungary	0.136	0.039	0.113	0.042	0.000	0.018	0.161	0.085	0.105	0.103	0.128	0.046	0.158	0.064	0.099	0.033
Ireland	0.000	0.057	NA	NA	NA	NA	0.000	0.074	0.000	0.223	0.046	0.136	0.000	0.263	0.123	0.072
Italy	0.154	0.024	0.305	0.029	0.101	0.022	0.066	0.050	0.124	0.029	0.232	0.022	0.141	0.023	0.061	0.017
Latvia	0.000	0.000	NA	NA	0.263	0.122	0.000	0.000	0.000	0.000	0.033	0.008	0.348	0.050	0.117	0.106
Lithuania	0.367	0.041	0.188	0.069	0.228	0.062	0.000	0.000	0.331	0.027	0.195	0.033	0.000	0.000	0.075	0.066
Netherlands	NA	NA	0.000	0.022	0.087	0.045	0.000	0.000	0.000	0.000	0.100	0.034	0.099	0.047	0.092	0.040
Norway	0.091	0.111	0.164	0.064	0.100	0.096	0.187	0.061	0.000	0.000	0.117	0.051	0.076	0.078	0.033	0.161
Poland	0.293	0.045	0.164	0.029	0.139	0.027	0.113	0.078	0.213	0.060	0.273	0.040	0.134	0.038	0.084	0.027
Portugal	0.210	0.067	0.181	0.069	0.165	0.063	0.375	0.083	0.122	0.145	0.207	0.054	0.205	0.060	0.057	0.040
Slovakia	0.119	0.163	0.139	0.070	0.000	0.000	0.000	0.000	0.048	0.008	0.280	0.072	0.346	0.077	0.000	0.082
Slovenia	0.000	NA	0.108	0.145	0.377	0.163	0.000	0.136	0.577	0.089	0.000	0.061	0.024	0.863	0.348	0.148
Spain	0.088	0.027	0.167	0.040	0.079	0.032	0.170	0.044	0.085	0.021	0.200	0.030	0.110	0.032	0.042	0.024
Sweden	0.122	0.084	0.091	0.042	0.000	0.003	0.000	0.000	0.189	0.061	0.050	0.065	0.112	0.054	0.087	0.063
Switzerland	0.000	0.056	0.157	0.036	0.067	0.065	0.132	0.021	0.273	0.032	0.156	0.050	NA	NA	0.080	0.067
United Kingdom	0.164	0.018	0.111	0.023	0.047	0.026	0.166	0.018	0.065	0.007	0.066	0.017	0.000	0.000	0.065	0.022

* RRSDs cannot be calculated for Cyprus, Iceland, Luxembourg and Malta as they have only 1 or 2 regions

NA denotes situations where it was not possible to estimate the RRSD because of numerical problems see Results paragraph 4

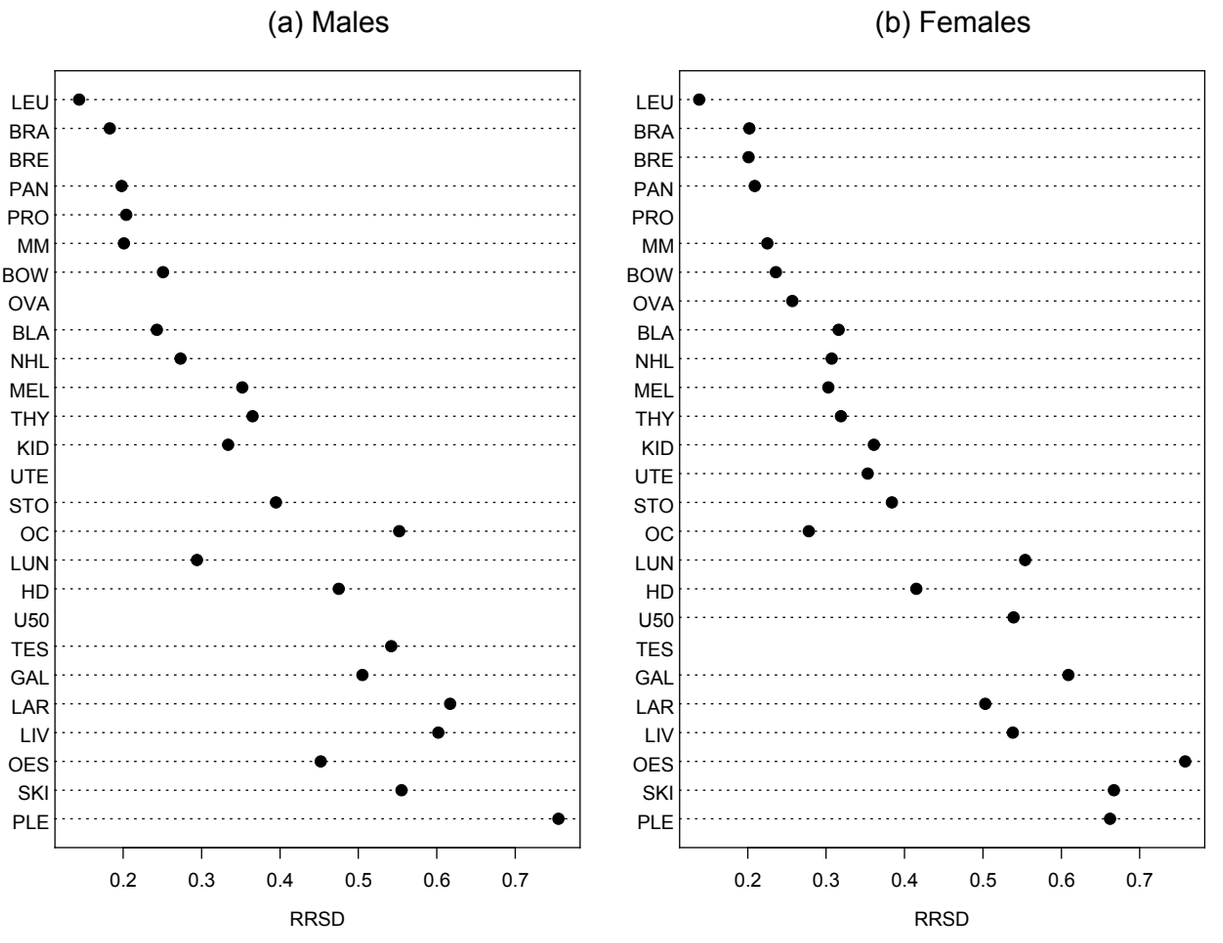
Table 5.4: Moran's I and correlations

Cancer site	Moran's I				Corr
	Males		Females		
	Value	Rank	Value	Rank	
Oral cavity and pharynx	0.794	3	0.236	19	0.407
Oesophagus	0.702	7	0.824	1	0.562
Stomach	0.816	1	0.715	6	0.897
Large bowel	0.736	6	0.700	8	0.830
Liver	0.802	2	0.736	5	0.730
Gallbladder	0.582	10	0.790	3	0.873
Pancreas	0.468	14	0.413	13	0.433
Larynx	0.756	5	0.206	21	0.289
Lung	0.761	4	0.793	2	0.187
Pleura	0.469	13	0.343	15	0.551
Melanoma	0.415	15	0.317	17	0.735
Skin (other)	0.401	16	0.387	14	0.737
Breast	..	..	0.700	7	..
All uterus	..	..	0.770	4	..
All uterus under 50	..	..	0.566	..	..
Ovary	..	..	0.573	9	..
Prostate	0.656	8	..	..	..
Testis	0.285	20	..	..	..
Urinary bladder	0.513	11	0.463	12	0.229
Kidney	0.630	9	0.537	10	0.838
Brain and CNS	0.287	22	0.251	22	0.683
Thyroid	0.184	19	0.203	18	0.526
Hodgkin's disease	0.351	17	0.213	20	0.559
Non-Hodgkin's lymphoma	0.508	12	0.507	11	0.808
Multiple myeloma	0.332	18	0.330	16	0.707
Leukaemia	0.195	21	0.163	23	0.520
All cancer (ICD-9 140-208)	0.773		0.776		0.439

Table 5.5: Cancer site codes for the Figures

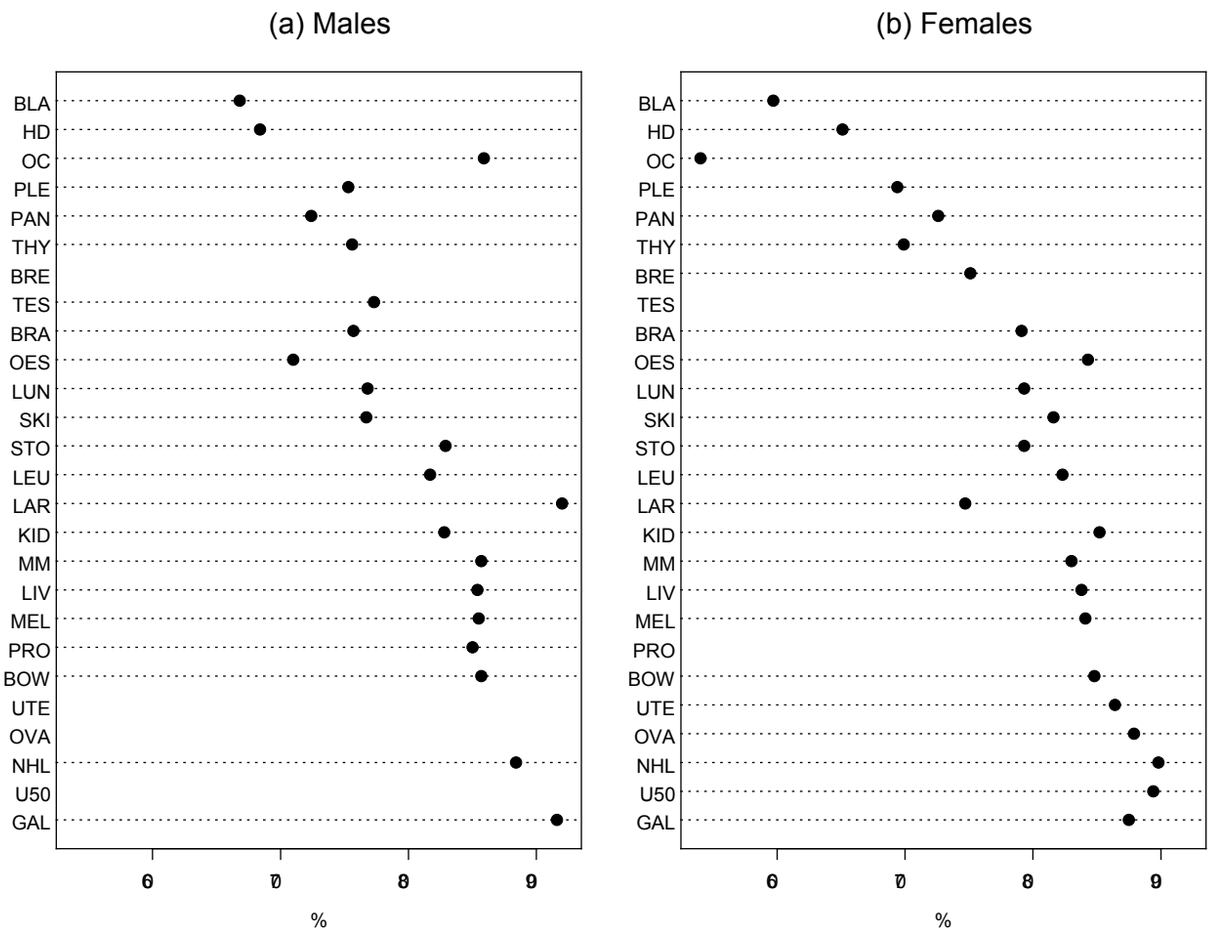
Cancer site	Figures 1 to 3	Figures 4 & 5
Oral cavity and pharynx	OC	OC
Oesophagus	OES	Oe
Stomach	STO	St
Large bowel	BOW	Bo
Liver	LIV	Li
Gallbladder	GAL	G
Pancreas	PAN	Pn
Larynx	LAR	La
Lung	LUN	Lu
Pleura	PLE	Pl
Melanoma	MEL	Ml
Skin (other)	SKI	Sk
Breast	BRE	Br
All uterus	UTE	U
All uterus under 50	U50	U50
Ovary	OVA	O
Prostate	PRO	Pr
Testis	TES	Ts
Urinary bladder	BLA	Bl
Kidney	KID	K
Thyroid	THY	Th
Brain and CNS	BRA	Bn
Hodgkin's disease	HD	HD
Non-Hodgkin's lymphoma	NHL	NHL
Multiple myeloma	MM	MM
Leukaemia	LEU	Le

Figure 5.1: Relative risk standard deviation (RRSD) for each cancer site*, ordered by the average value for males and females combined



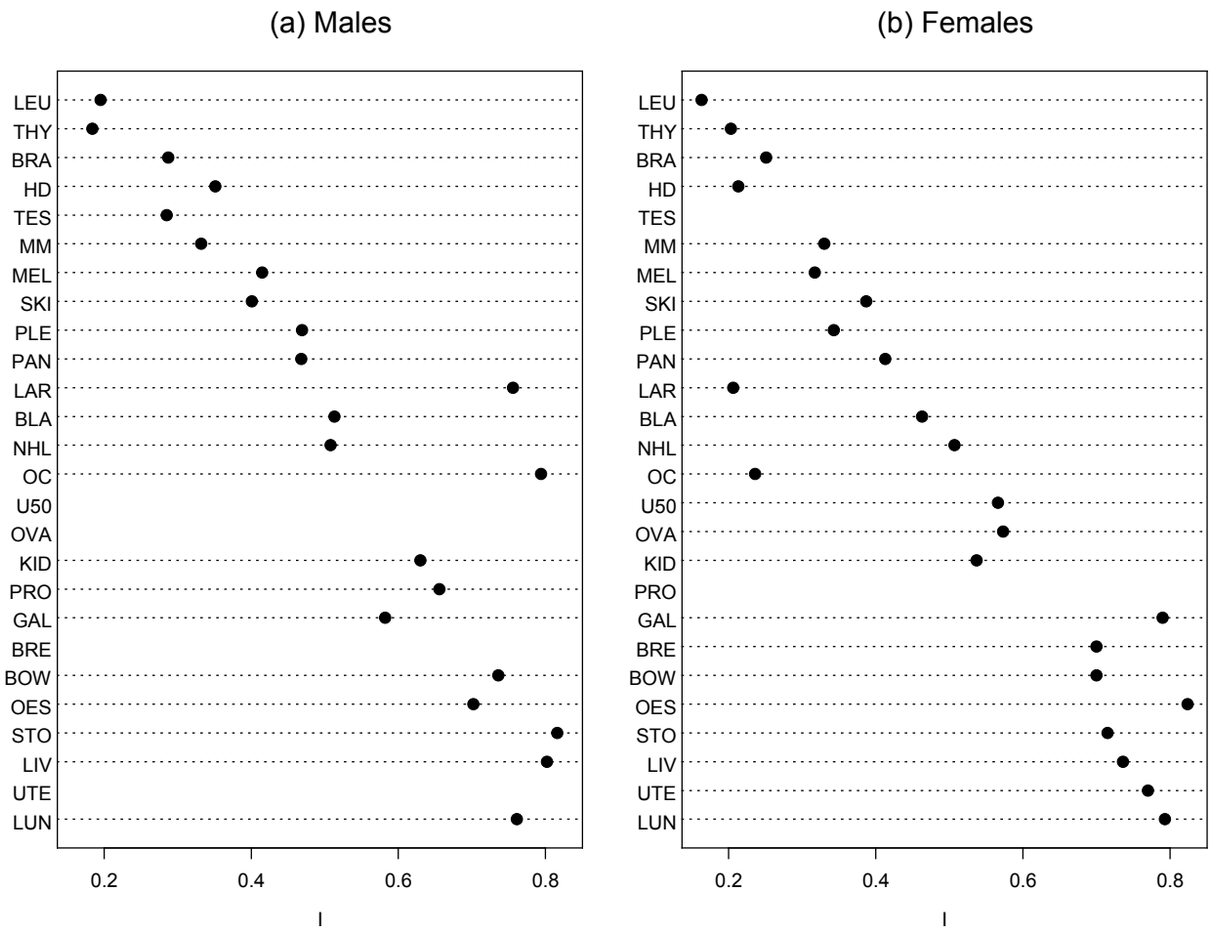
* See Table 5.5 for the cancer site codes

Figure 5.2: Percentage of variation associated with country for each cancer site*, ordered by the average value for males and females combined



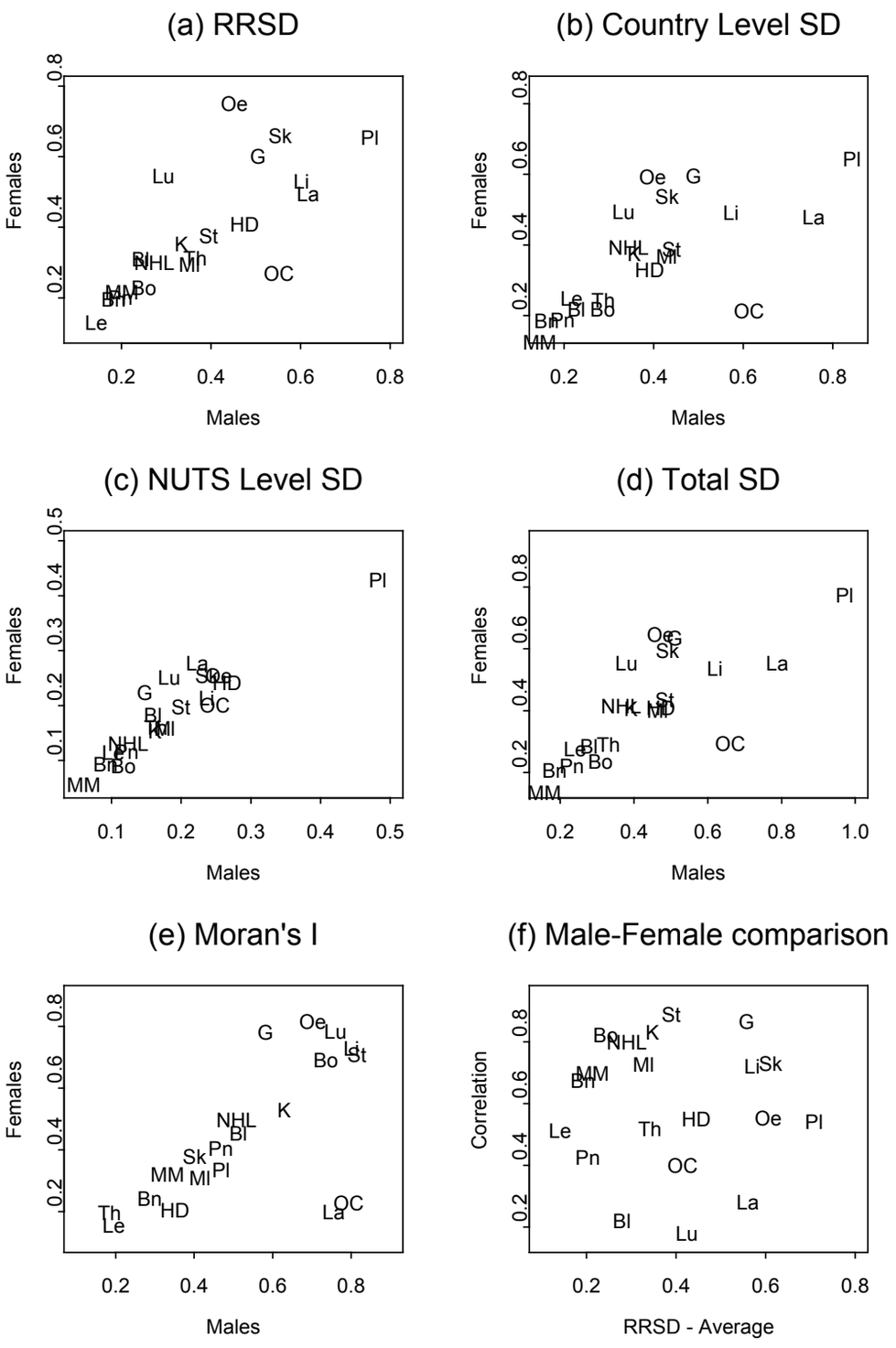
* See Table 5.5 for the cancer site codes

Figure 5.3: Spatial correlation – Moran's I – for each cancer site*, ordered by the average value for males and females combined



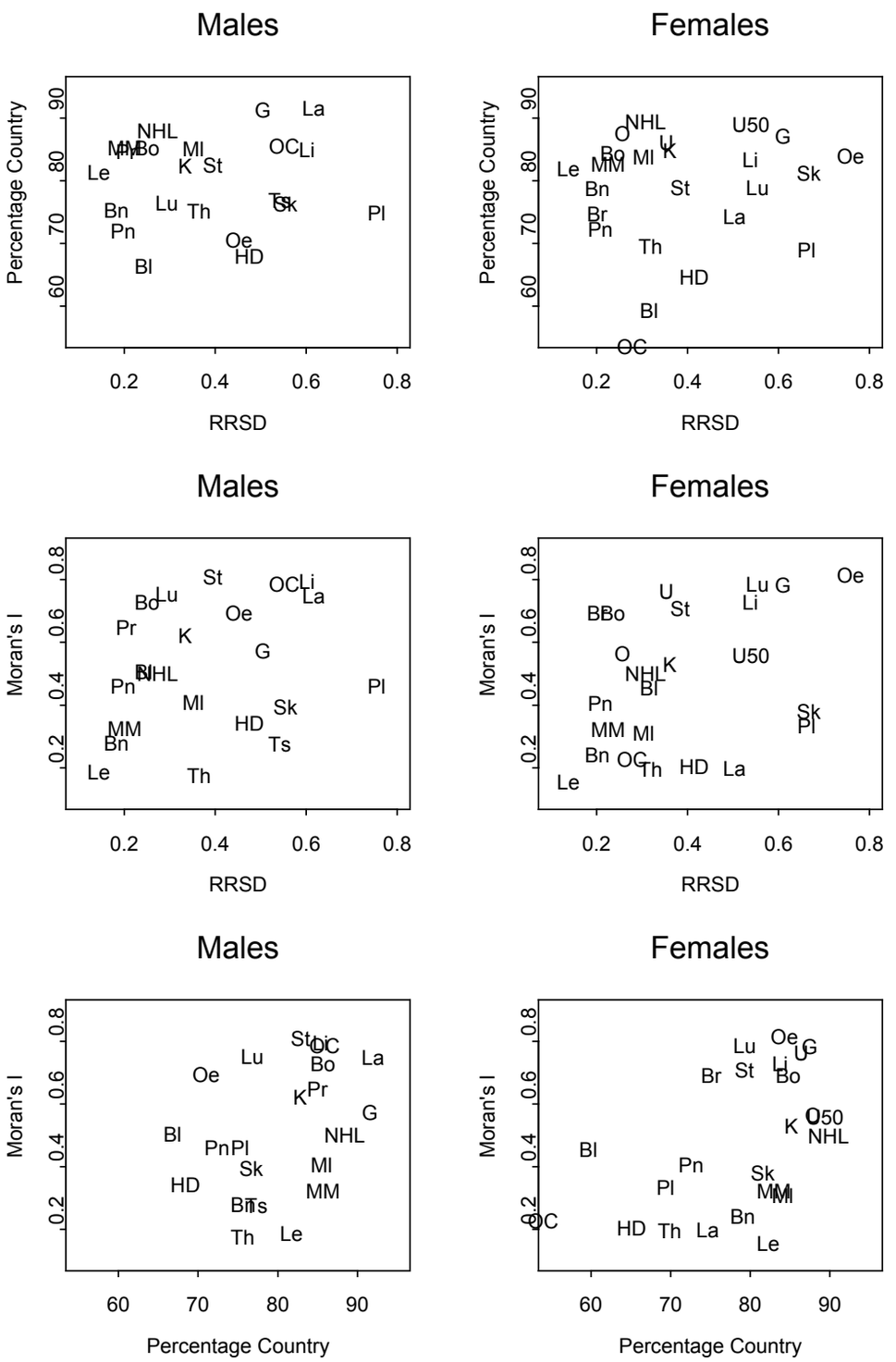
* See Table 5.5 for the cancer site codes

Figure 5.4: Comparisons between spatial statistics for males and females



See Table 5.5 for the cancer site codes

Figure 5.5: Comparisons of measures of variability and spatial correlation



See Table 5.5 for the cancer site codes

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CHAPTER 6

CANCER MORTALITY PATTERNS BY SITE

Introduction

In this chapter, the patterns of the distribution of cancer mortality throughout the 25 European Union (EU) and three European Economic Area (EEA) Member States are examined for the common forms of cancer, broadly following the numerical order of the codes in the 9th revision of the International Classification of Diseases (WHO, 1977).

Not all sites of cancer have been mapped, for three main reasons. First, the level of detail supplied by national vital statistics offices varies, which means that some data have had to be presented for broad groupings of cancer sites. Thus, ICD-9 codes 140-149, which cover such diverse cancers as those of the lip, mouth, tongue, salivary gland, nasopharynx and the various parts of the pharynx, have had to be presented as a group although, in the commentary, information is given about most of these sites separately.

Second, the numbers of deaths from a variety of cancers such as those of the small intestine (ICD-9 152), the mediastinum (ICD-9 164), male breast (ICD-9 175) and the eye (ICD-9 190) were too small to merit mapping. Any apparent variability in their mortality rates could well have been due solely to chance.

Third, for some cancers, the recorded cause of death is imprecise. Accurate recording of the precise site of cancer of the large bowel is often difficult, and so deaths from cancers of the colon (ICD-9 153) and rectum (ICD-9 154) have been combined along with cancers of the intestinal tract, part unspecified (ICD-9 159.0). Although maps of the mortality data for cancers of the cervix and the body of the uterus (ICD-9 180 and 182, respectively) have been presented separately, they have been combined as "all uterus" for descriptive purposes, as deaths from cancer of the cervix frequently appear as cancer of the uterus on death certificates (Cuzick and Boyle, 1988; Primic Žakelj et al., 2001). This inability to distinguish the cervix from the remainder of the uterus in mortality data in several countries is to be regretted, as the risk factors for these cancers are quite different. Results have, however, also been given for deaths from all uterus cancers in females under the age of 50. The vast majority of these deaths will have been from cervical cancer, as cancer of the body of the uterus occurs predominately in older females (Parkin et al., 2002).

In addition, although Hodgkin's disease (ICD-9 201) is mapped separately, the various forms of non-Hodgkin's lymphoma (ICD-9 200 and 202) have been grouped together as there are national differences in the nomenclature and classification of these forms of malignant disease. All the forms of leukaemia have had to be grouped together (ICD-9 204-208) because death certificates frequently cite *leukaemia* without further specification, the cell type involved not being mentioned.

Secondary cancers (metastases) and those of unknown primary site (ICD-9 195-199) are, however, mapped as these reflect the level of imprecision in certification of cancer deaths.

Following each cancer site title there appear two numbers, the overall average age-standardised mortality rates per 100,000 population for males and for females across the 28 EU-EEA countries. For

example: Trachea, bronchus and lung (ICD-9 162) (M 50.3; F 10.3). The national mortality rates for all the cancer sites are given in the table in Annex 2.

Following a description of spatial patterns, attention is drawn to the broad regions with the highest and lowest rates for each sex. For this comparison, in general only rates based on 100 or more deaths are presented. When two or more regions had the same mortality rate, the region with the greatest number of deaths has been chosen. All rates are age-standardised to the world standard population and are expressed as average annual rates per 100,000 population (see Chapter 2, and Boyle & Parkin, 1991).

To place the European mortality rates in a wider context, they are sometimes compared with those seen around 1995 in the USA, Japan and Australia, nations with a similar socio-economic level. Japan has been chosen as representing an industrialised country with a standard of living comparable to that of the EU-EEA, but with major differences in life-style and risk. Australia has sizeable communities of migrants from several EU-EEA countries.

In the descriptions that follow, the emphasis is on broad regional differences and patterns rather than dissection of variation at the EU-EEA level II or III areas. The reader should bear in mind that a given colour on the main maps may, for common cancers, embrace quite a large variation in level of mortality in absolute terms. Thus, for male lung cancer, the yellow areas that represent 30% of all values cover age-adjusted rates that lie between 37.5 and 55.0. Conversely, for infrequent cancers, the absolute range covered by one colour may be quite small – the yellow areas for male malignant melanoma represent the much narrower range of 5.0 to 7.6. Further, the ranges of mortality represented by a given colour may differ quite considerably between the sexes for the same cancer. So to enable rapid visual comparisons to be made between rates for males and females for the same cancer, and between different cancers, the smaller maps presented in the lower right of each chart also illustrate the variability in mortality rates, but using the *same* (21 point) colour scale for every cancer site (see Chapter 2 for further details).

In formulating their comments, the editors have ignored isolated 'hot spots', preferring to draw attention to regions where there seem to be groups of areas with high or low mortality rates (some problems in interpretation of these patterns are presented in Alexander & Boyle (1996)). For example, oesophageal and laryngeal cancer mortality is high in western and north-eastern France. Gastric cancer mortality is high in virtually all of the north of Italy and low in most of the south of France. Similarly, the higher levels of breast cancer mortality in Denmark, Ireland, The Netherlands and the United Kingdom contrast with the much lower levels in southern Italy, a contrast all the more interesting in that there is a gradient of mortality in-between. While describing the broad picture, the editors recognise that there may be local pockets of truly elevated risk which may be due to the presence of a relevant regional exposure.

It may be argued that many marked differences in cancer mortality rates seem to occur at national boundaries, and that this reflects habits of death certification rather than a true difference in risk (see Chapter 3). For example, oesophageal cancer, so common in west and north-east France, is much rarer on the other side of the border with Belgium. There may also be artefactual variations within countries. However, some of the variability is in opposite directions – for example, the higher levels of mortality from cancer of the stomach in Poland and the three Baltic Countries contrast with the lower rates for cancer of the large bowel in those countries. It is highly unlikely that these two sites would be confused with each other. Within Italy, the validity of the lower mortality rates for many sites in the south than in the centre or north has been examined as part of the DG SANCO project described in Chapter 3.

Interpretation of any apparent cancer mortality patterns is further complicated by the fact that mortality is influenced to a certain degree both by the stage of the disease at diagnosis and by the effectiveness of treatment. Hence the death rate for a cancer of equal incidence (i.e. of diagnosed cases) may be different from one country to another. Conversely, two countries with similar death rates may have quite different incidence. There is considerable evidence that both treatment and survival rates vary widely across Europe (Berrino et al., 2003).

Following the description of the patterns for each site, comments are presented on the

known causes of the respective cancer, and, where possible, on how they may relate to the mortality pattern observed. As many cancers have several component causes, it may not be possible to explain more than a proportion of the deaths seen. The comments are not meant to be exhaustive, and review papers have frequently been cited rather than original articles. Where possible, recent research undertaken in the EU-EEA is described.

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Cancer sites with the highest mortality rates in the EU-EEA

The form of cancer with the highest mortality rate in males was lung cancer (50.3 per 100,000) with large bowel (19.2) having the second highest rate (Figure 6.1 (a)). Prostate cancer (15.4) had the third highest rate, followed by cancers of the stomach (12.0), pancreas (7.5), liver (6.9) and bladder (6.8). The next highest rates of cancer mortality were in sites in the upper digestive tract: oral cavity and pharynx (6.5) and oesophagus (5.9). The leukaemias (5.5) had the tenth highest cancer mortality rate in males.

In females, breast cancer (20.6 per 100,000) had the highest rate of cancer death followed by cancer of the large bowel (12.4) (Figure 6.1 (b)). Cancer of the lung had the third highest rate (10.3) although the rate was only one fifth of that in males. The gynaecological cancers, ovary (6.3) and uterus (6) had the next highest rates, followed by cancers at the digestive sites of the stomach (5.5) and pancreas (4.8). The next highest mortality rates were for leukaemia (3.4), brain and central nervous system (3.2) and non-Hodgkin's lymphoma (2.7).

Mortality from "other and ill-defined" cancers

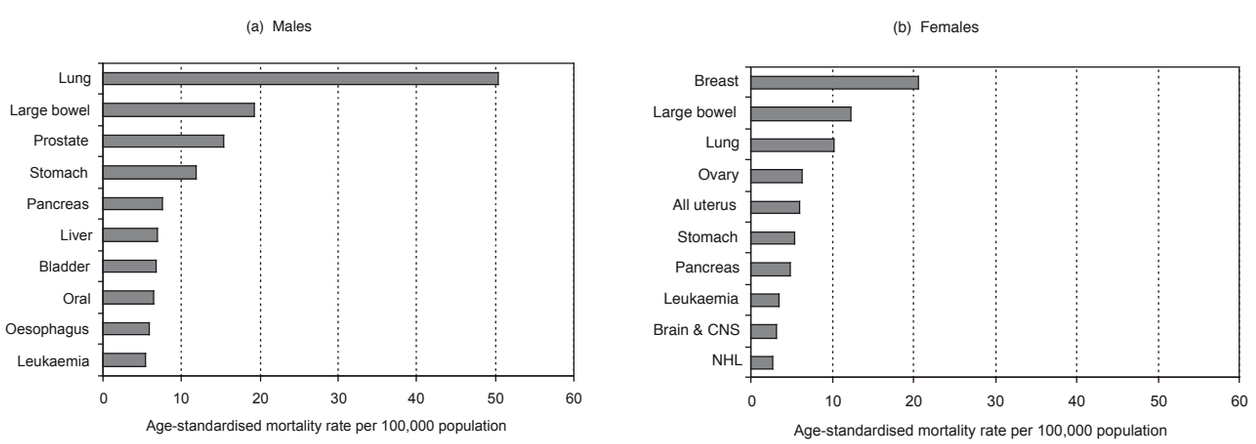
It is important have information on the pattern and rates of other and ill-defined cancer sites, because in areas where such cancers represent high proportions of the rates for all cancers combined, the rates for some (or many) individual cancers may appear to be lower than they really are.

Overall, the mortality rates for other and ill-defined cancers tended to be slightly higher at a national level in males than in females. The highest rates in males were found in the United Kingdom (15.0 per 100,000), Greece (11.8), Denmark (11.7), Ireland (11.1), Luxembourg (11.1), Spain (11.0) and The Netherlands (11.0); these rates represented 6% to 9% of the corresponding national mortality rates for all cancers. The lowest rates were in Latvia (3.0), Slovakia (3.1), Hungary (3.4) and Iceland (3.4); these represented 1 to 2% of the rates for all cancers.

In females, the highest national mortality rates for other and ill-defined cancers were found, as in males, in the United Kingdom (10.5), Denmark (9.9) and Greece (7.6), representing 9%, 7% and 10%, respectively, of the corresponding national rates for all cancers. The lowest rates were in Latvia (1.4), Lithuania (1.6), Slovakia (1.6) and Iceland (2.9), forming 1 to 2% of the rates for all cancers.

The maps [p.256-257] clearly illustrate the patterns of generally high rates of other and ill-defined cancer mortality in the United Kingdom, Ireland, Denmark and Greece, and the low rates in Austria, the Baltic Countries, the Czech Republic, Hungary, Iceland, Italy, Slovakia and Switzerland.

Figure 6.1: Cancer sites with the highest mortality rates



6.1: Oral cavity and pharynx (ICD-9 140-149)
(M 6.5; F 1.1)

This group encompasses cancers arising at all sites within the oral cavity and pharynx and will be referred to as *oral cancer*. Unfortunately, such a broad grouping of intra-oral sites may obscure important variations in both the mortality and the effect of aetiological factors for the different cancer sites.

Overall, the mortality rates for these cancers in the EU-EEA were about 4% of the rate for all cancers in males and about 1% of that in females.

International comparisons

Overall in the EU-EEA, the mortality rate for oral cancer was almost six times higher in males (6.5 per 100,000) than in females (1.1 per 100,000). In each of the 28 countries the mortality rate was considerably higher in males than in females, with large – almost 10-fold – variation in national rates in males but little in females (Annex 2).

In males, the highest rates were in Hungary (19.2) and neighbouring Slovakia (17.2) – both considerably higher than the countries with the next highest rates: France (11.3), Slovenia (11.1), and the three Baltic Countries – Estonia (9.3), Latvia (9.3) and Lithuania (8.6). The lowest rates were found in Greece (2.0), Sweden (2.2) and Finland (2.4).

In females, with the exception of the highest rate, in Hungary (2.4), there was relatively little variation, with the vast majority of countries closely grouped around a rate of 1 per 100,000. The ratio between the male and female rates in each country varied widely, from around 2:1 in several countries including Finland, The Netherlands, Sweden and the United Kingdom, up to more than 10:1 in Slovenia and Slovakia.

Regional variation (box and whisker plots)

In males, there was some variation both within and between countries, although there was little variation apparent in the countries with the lowest national rates [p. 210]. In females, while there was variation within most of the countries, there was little evidence of variation between the 28 countries (apart from the high rate in Hungary mentioned above) [p. 211].

Description of the maps

The outstanding features of the map depicting mortality from cancer of these sites in males is the higher levels of mortality in almost the whole of Hungary and Slovakia, in much of Slovenia, and France with concentrations of excess in the north-west and north-east of the country [p. 210]. There was also a belt of high rates extending across northern Germany and an aggregation of high rates in north-east Italy bordering Slovenia. Rates were generally low in the Nordic Countries, the United Kingdom and Ireland, much of Spain and Italy, and in Greece.

The geographical distribution of areas of high cancer risk for oral cancer demonstrate that while the higher mortality rates in France end abruptly at the border with Belgium – the risk being around one half in Belgium (5.9) of that in France (11.3) – this phenomenon is not seen in the south, with rates in south-east France and in the north of Italy, and in southwest France and northern Spain being at much the same levels. This suggests that there were likely to have been comparable exposures in the south, whereas exposures and/or protective agents may have been different in the north.

In looking at the map for females [p. 211], it must be remembered that the mortality rates were much lower than in males and that the range of mortality rates was very much narrower. Hence in contrast to the map for males, a false impression of important differences in level of mortality can easily be obtained. With the exception of the high rates across the whole of Hungary, there is no clear pattern apparent, although some of the

areas with higher rates in northern France in males also have higher rates in females.

Statistical aspects

The relative risk standard deviation (RRSD) for males was 0.55, the fifth highest of all sites considered, indicating substantial relative variation in the rates. The regional variance associated with country was high compared with most other sites at 0.38 (third highest) and 86% of the total regional variability was associated with differences between countries. This was associated with the higher rates throughout most of France and almost all of Slovakia, Slovenia and Hungary. The country with the most relative variation in the rates was Italy, with an RRSD of 0.41. This is seen in the map as a north-south gradient with high rates in northern Italy and low rates in the south. The Moran's I statistic was 0.79 (ranked 3) indicating substantial spatial autocorrelation; this is evident in the large tracts with low rates in the Nordic Countries, and central and southern Italy and Greece, in addition to the large areas with high rates mentioned above.

The results for females were quite different. There was much smaller regional variation, with the RRSD of 0.28 among the lower values for females. The regional variance associated with country was only slightly higher than that within countries, indicating that there was no strong pattern associated with countries and that there was as much variation within countries as between them. The highest RRSD values were in Belgium, Latvia and Lithuania. Spatial autocorrelation was estimated as 0.24, one of the smallest of all Moran's I values for females. It is common in the map to find areas of high rates bordered by areas of low rates and there is no clear spatial pattern in this map, except for the markedly high rates across most of Hungary. The correlation between the male and female rates was low at 0.41.

Comment

As noted above, the broad groupings of intra-oral sites may obscure important differences in both mortality and the effect of aetiological factors among the different cancers in this group. In addition, there may well be differences in the distribution of the different cancers across countries or regions which could also influence overall oral cancer mortality patterns. Tongue cancer, mouth cancer and pharyngeal cancer have been combined in the majority of analytical studies. These are important forms of cancer with incidence and mortality rates rising among younger persons in many parts of the world. However, several important risk factors have been clearly established.

It is estimated that between 25 and 30% of all cancers in developed countries are tobacco related. For both sexes combined, the proportion of cancers arising in the oesophagus, larynx and oral cavity attributable to the effect of tobacco, either acting singly or jointly with the consumption of alcohol is between 43 and 60%. Cigarette smoking and alcohol consumption have been found to be independent risk factors for oral cancer, and their combined effects seem to be multiplicative. After 5 or 10 years of smoking cessation, risk among ex-smokers reduces to a level similar to that in lifelong non-smokers.

Although the greatest hazard is caused by cigarette smoking, cigars are similar hazards if their smoke is inhaled, and cigar and pipe smoking are comparable hazards for cancers for the oral cavity, pharynx, extrinsic larynx, and oesophagus. Use of oral snuff and of a fine home-ground tobacco powder have been associated with an increased risk of oral cancer.

There is convincing epidemiological evidence that the consumption of alcoholic beverages increases the risk of cancers of the oral cavity, pharynx and larynx and of squamous cell carcinoma of the oesophagus. The risks tend to increase with the amount of ethanol drunk, in the absence of any clearly defined threshold below which no effect is evident. There is wide variability among EU-EEA countries in per capita average alcohol consumption and preferred type of alcoholic beverage.

Although alcohol drinking increases the risk of upper digestive and respiratory tract neoplasms, even in the absence of smoking,

alcohol drinking and tobacco smoking together greatly increase the risk of these cancers, each factor approximately multiplying the effect of the other. Compared with never-smokers and non-alcohol drinkers, the relative risk of these neoplasms is increased between 10- and 100-fold in people who drink and smoke heavily. Indeed, if there were total abstinence from drinking and smoking, the risk of oral, pharyngeal, laryngeal and squamous cell oesophageal cancers would be extremely low.

Poor dental hygiene may be an independent contributory factor. Oral cancer risk is reduced by frequent consumption of fruits and vegetables.

Nasopharyngeal cancer has a different epidemiological pattern from that for tumours of the mouth which have been discussed above. An association with Epstein-Barr Virus (EBV) infection has been suggested by a large number of ecological observations. Clinical progression of the disease is accompanied by increases in antibody levels and nucleic acid hybridisation has shown the presence of EBV DNA in squamous epithelial cells, this latter observation being a strong argument against the virus being only a passenger in the process of carcinogenesis. Despite the fact that nasopharyngeal cancer is smoking related, cigarette smoking seems not to be a major determinant of risk. Results from China and Hong Kong indicate increased risks of nasopharyngeal cancer linked to consumption of salted fish, notably in childhood, and preserved and fermented foods.

Taking account of known risk factors, the high levels in males appear to be generally in regions where there is a prevalent habit in the population of drinking strong alcoholic beverages. Reduction of this, together with avoidance of cigarette smoking, would lead to a large reduction in risk.

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6.2: **Oesophagus** (ICD-9 150)
(M 5.9; F 1.2)

The oesophagus is a 25 cm long tube which connects the pharynx with the stomach. Cancer of the upper third of the oesophagus is almost invariably *squamous cell carcinoma* while cancer of the lower third is usually *adenocarcinoma*.

Overall in the EU-EEA, the mortality rate for cancer of the oesophagus was around five times higher in males (5.9 per 100,000) than in females (1.2 per 100,000). In each of the 28 countries, the mortality rate was considerably higher in males than in females, but there was wider variation in national rates in males than in females (Annex 2). Mortality rates from cancer of the oesophagus represented about the same proportions of the rates for all cancer deaths as for oral cancer: 3% in males and 1% in females.

International comparisons

In males, the highest rate was in France (9.3), closely followed by Hungary (8.9), then the United Kingdom (8.5) and Ireland (8.0) (Annex 2). The lowest rates were in Greece (1.5), and Finland, Norway and Sweden (all 2.9 per 100,000).

In females, there was less variation in rates across the countries, except for three noticeably high rates in the United Kingdom and Ireland (both 3.4) and Iceland (2.9). The lowest rates were in Latvia and Greece (both 0.4) and in Estonia, Spain, Lithuania and Austria (all 0.5).

The pattern of the ratios between the rates in males and females in each country was closely similar to that for oral cancer (section 6.1 above): several of the same countries had ratios of around 2:1 and several others again had ratios of around 10:1.

Regional variation (box and whisker plots)

In males, as with oral cancer there was variation both within and between countries, although there was little variation apparent in the countries with the lowest national rates [p. 212]. In females, there was variation within each country and evidence of considerable variation between the 28 countries, with three countries having rates around 3.0 per 100,000, three in the range 1.5 to 2.0, and the remainder almost all at or below 1.0 [p. 213].

Description of the maps

In males, the feature of the map is the concentrations of very high risk in northern France, extending up to the border with Belgium; there were also contiguous areas of above-average risk in the northeast of Italy, Slovenia and Hungary. Rates were also generally above average in the United Kingdom, particularly in parts of Scotland, and in Ireland [p. 212]. Lower rates were concentrated in Norway, Sweden and Finland, Greece and central and southern Italy. The geographic distribution was thus similar, but not identical, to that for oral cancer (see section 6.1) the main difference being above average mortality from oesophageal cancer in the United Kingdom and Ireland.

High rates among females were also apparent in the United Kingdom and Ireland. There was a belt of slightly above average rates across northern France, Belgium, The Netherlands and Denmark, but no evidence of the excess risk in northeast Italy, Slovenia, Slovakia and Hungary that was seen in males [p. 213].

Statistical aspects

Cancer of the oesophagus in males had regional variation in the middle of the range (RRSD of 0.45). But it had the most regional variation for females, with a RRSD of 0.76. Among males there was a large amount of regional variation associated with country (71%) with higher rates in the United Kingdom, Ireland, France and Hungary and lower rates in Scandinavia and some of the Mediterranean countries. A high percentage of variation (84%) was associated with country for females. There were considerable differences

among the countries for females which is evident in the bimodal shape of the histogram and in the boxplots and maps [p. 213].

Italy had RRSDs of 0.57 for males and 0.48 for females, implying large regional variation; this is associated with low rates in most of the southern and central areas and high rates in the mountainous region in the north. Portugal also had large internal regional variation for females, associated with a small group of regions – mostly in the north of the country – with relatively high rates.

Moran's I for females was 0.82, the largest value, indicating the greatest amount of spatial correlation of all the cancer sites. For males, Moran's I was 0.70 (seventh largest). The correlation between the male and female rates was 0.56, which is not very high. However, there were moderately high rates for males and very high rates for females in Ireland and the United Kingdom and to a lesser extent in The Netherlands, and regions in France with very high rates in males but only average rates in females.

Comment

Much of the discussion of risk factors in the section on oral cancer (section 6.1) is applicable to oesophageal cancer. For both sexes combined, the proportion of cancers arising in the oesophagus, larynx and oral cavity attributable to the effect of tobacco, either acting singly or jointly with the consumption of alcohol is between 43 and 60%. Cigarette smoking and alcohol consumption have been found to be independent risk factors for oesophageal cancer; their combined effects seem to be multiplicative. Although the greatest hazard is caused by cigarette smoking, cigars can cause similar hazards if their smoke in inhaled, and both cigar and pipe smoking are comparable hazards for cancers of the oral cavity, pharynx, extrinsic larynx, and oesophagus.

A high prevalence of alcoholism among patients with oesophageal cancer and an apparent association between the disease and employment in the production and distribution of alcoholic beverages has long been noted. The role of alcohol consumption was most clearly demonstrated in the French département of Ille-et-Vilaine, where the risk rose steadily with dose of alcohol consumed. The highest oesophageal cancer mortality rates in Europe were to be found in males in France and it has been estimated that 85% of such deaths could be attributable to cigarette smoking and alcohol intake.

As noted in section 6.1 above, there is convincing epidemiological evidence that the consumption of alcoholic beverages increases the risk of cancers of the oral cavity, pharynx and larynx and of squamous cell carcinoma of the oesophagus. The risks tend to increase with the amount of ethanol drunk, in the absence of any clearly defined threshold below which no effect is evident. There is wide variability among EU-EEA countries in terms of per capita average alcohol consumption and preferred type of alcoholic beverage.

Although alcohol drinking increases the risk of upper digestive and respiratory tract neoplasms, even in the absence of smoking, alcohol drinking and tobacco smoking together greatly increase the risk of these cancers, each factor approximately multiplying the effect of the other. Compared with never-smokers and non-alcohol drinkers, the relative risk of these neoplasms is increased between 10- and 100-fold in people who drink and smoke heavily. The risk has been shown to be increased among non-cigarette smokers by consuming alcohol and among non-drinkers of alcohol by smoking cigarettes. In heavy smokers of cigarettes, relative risks of between 5 and 10 have been found. As for cancers of the oral cavity, the association is particularly strong for pipes and cigars and, among cigarette smokers, for high-tar/dark tobacco cigarettes. If there were total abstinence from drinking and smoking, the risk of oral, pharyngeal, laryngeal and squamous cell oesophageal cancers in European countries would be extremely low.

The increasing incidence of adenocarcinoma of the oesophagus, restricted largely to males, is one of the most interesting epidemiological changes in cancer recorded in recent decades. Indeed, as well as this increase there is also an increase in adenocarcinoma at the adjacent anatomical portion of the stomach (the gastric cardia). This rules out changes in diagnostic and recording practices being solely responsible. Tobacco smoking, but not alcohol consumption,

appear linked to this type of cancer and it appears that obesity and gastroesophageal reflux disease increase the risk of adenocarcinoma of the oesophagus. This trend could have been detected much more clearly, and unambiguously, if attention in recording had focussed on an entity composed of adenocarcinomas at or near the oesophagogastric junction.

The geographical pattern observed in males can be related directly to the patterns of smoking and alcohol intake (in terms of ethanol) throughout Europe. It is much more difficult to ascribe the pattern of oesophageal cancer observed in females to either these or other known risk factors. The similarity of the pattern in the ratios between the rates in males and females in each country with the corresponding pattern for oral cancer confirms that the risks arise from common aetiological and/or cultural factors. There has undoubtedly been a move in the distribution of cases of oesophageal cancer from the upper to the lower third of the oesophagus during recent decades. The reasons for this remain largely unknown and it seems important to try to elucidate the responsible factors and thereby help increase prospects for prevention of this highly fatal cancer.

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6.3: Stomach (ICD-9 151)
(M 12.0; F 5.5)

Mortality rates from stomach cancer have been falling in Europe for many years (for decades in some countries). What was the commonest fatal cancer in the early part of the 20th century now has only the fourth highest mortality rate in males and the sixth highest in females, representing about 7% and 6%, respectively, of the rates for all cancers. The mortality rate in males in any given area is generally double that in females.

Overall in the EU-EEA countries, the mortality rate for cancer of the stomach in males (12.0 per 100,000) was just over twice that in females (5.5 per 100,000).

International comparisons

In males, the three Baltic Countries all had rates over 25 per 100,000; rates were around 20 per 100,000 in Portugal, Hungary, Poland, Slovakia and Slovenia (Annex 2). Denmark (6.4), Sweden (6.6), France (7.1) and Switzerland (7.2) were the countries which had the lowest national rates.

In females, as in males, the highest rates were in the three Baltic Countries, Portugal, Hungary and Slovenia (around 10 per 100,000) with the Czech Republic, Poland and Slovakia having rates of around 7 per 100,000. The lowest rates were recorded in France (2.7), Denmark (3.1) and Switzerland (3.2).

The ratios between the national mortality rates in males and females were remarkably uniform, clustered very closely around the average of just over 2:1.

Regional variation (box and whisker plots)

In males, there was both variation between countries and between regions [p. 214]. In females, as in males, there was variation within each country and evidence of variation between the countries.

Description of the maps

There are very striking – and closely similar – geographic patterns for stomach cancer mortality in males [p. 214] and females [p. 215]. Moving broadly from southwest to northeast, there is a concentration of high rates in Portugal and much of the adjoining parts of central and northern Spain. Rates were below average in the United Kingdom and Ireland, and in most of the mainland of western Europe; rates were also low in Scandinavia. Rates were then above average in northern (but not southern) Greece, central and northern Italy, Austria, the east of Germany and the Czech Republic, and were highest across almost all of Slovenia, Slovakia, Hungary, Poland and the Baltic Countries.

Statistical aspects

There was moderate regional variation in both males and females with RRSDs of 0.40 and 0.38 respectively. Both Greece and Italy had large regional variation within country characterised by lower rates in the south and higher rates in the north. Other than these two countries there was generally low regional variation within each country. The percentage of variation associated with country was 83% for males and 79% for females. The spatial autocorrelation was high, with Moran's I of 0.82 and 0.72 for males and females, respectively (ranked 1 and 6, respectively).

The most striking feature was the very high correlation of 0.90 between male and female rates, confirming the visual impression that that the patterns in the two maps were very similar.

Comment

Some fifty years ago, stomach cancer was the leading cause of death from cancer in males. Since then, mortality and incidence have fallen virtually everywhere, even in high-risk Japan, but none the less this form of malignant disease remained the second commonest fatal cancer within the EU countries around 1990. By the mid-1990s, the period covered by this atlas, stomach cancer mortality was the sixth commonest fatal cancer in females and the fourth commonest in males.

The reasons for this worldwide decline are not known precisely, although it is strongly suspected that the wider availability of fresh fruit and vegetables and better food preservation (for example, refrigeration rather than salting and pickling) may be one of the major factors. Many studies have shown the risk of stomach cancer to be higher among members of the lower socio-economic classes. While this may be true within a country, the distribution of this disease within the EU-EEA strongly suggests that other factors operate. Tobacco is a risk factor for this form of cancer and this association may go some way to explaining the differences in disease risk between males and females. The distribution of blood group A, known to carry a 10% greater risk, is not likely to vary sufficiently for this alone to influence mortality substantially.

Attention for prevention should continue to focus on diet, notably encouraging higher consumption of fresh fruit and vegetables. It seems paradoxical that in northern Italy (where fresh fruit and vegetables are likely to be much more readily available than in, say, England and Scotland), the stomach cancer mortality should be so much higher. In a study of the role of diet and gastric cancer in this region of Italy, green vegetables were found to have a protective role, with the risk being three times greater in low consumers than in high consumers. Risk was increased in those consuming polenta (a maize porridge) and cured ham.

Intervention with beta-carotene, vitamin E and selenium has been shown to reduce the mortality and incidence of cancer of all forms and particularly stomach cancer in Linxian County in China, where the rates of oesophageal cancer and stomach cancer were extremely high. The results are in some sense proof of principle and confirm the importance of micro-nutrients in the determination of stomach cancer risk – although the direct significance to the European situation is tenuous given that this population suffered for decades from a marginally vitamin deficient diet.

Studies of occupational mortality in both Scotland and in England and Wales have shown excess risk of stomach cancer in workers exposed to chemicals and metals. The excess risk is not necessarily due to exposure at the workplace, as these individuals may eat less fresh fruit and vegetables than others. The risk of stomach cancer has been reported as being elevated among atomic bomb survivors, especially for those individuals exposed at ages of less than twenty years, and among persons treated for *ankylosing spondylitis.*

Some of the decline in gastric cancer mortality rates could be due to the decreased prevalence of *Helicobacter pylori* infection in the gastric mucosa, following reduced contamination of drinking water and control of other sources of infection. Serological markers of *Helicobacter pylori* have been consistently related to stomach cancer risk and there is now consistent epidemiological evidence that *Helicobacter pylori* is associated with an approximately 6-fold increased risk of non-cardia gastric cancer. In Europe, about two thirds of the new cases of gastric cancer every year may be attributable to *Helicobacter pylori* (assuming that the prevalence of *Helicobacter pylori* in the general population is about 35%). The current therapy for *Helicobacter pylori* infection, based on the use of proton-pump inhibitors and antibiotics, is efficacious but poor patient compliance, antibiotic resistance and recurrence of infection complicate the issue. Furthermore, although treatment of *Helicobacter pylori* infection can induce regression of gastric lymphoma, it has not yet been shown to reduce gastric cancer risk. Unfortunately, the natural history of *Helicobacter pylori* infection and the characteristics of an effective anti-*Helicobacter pylori* immune response are still poorly understood, limiting the development of an effective vaccine at present.

A clear message from this atlas is the close similarity of the geographic patterns observed in males and in females. This is present when considering the maps visually and is re-enforced when statistical analyses are conducted. There are traditional explanations put forward to explain some of the patterns apparent in the maps: the high rates in Portugal have been associated with the widespread practice of eating salted fish and the high rates in Italy, Germany and Austria have been associated with cured meats. These hypotheses need to be re-assessed

and tested as does the aetiology underlying the regional variation in Greece. The important aetiological role of *Helicobacter pylori* in the aetiology of stomach cancer provides an unusual opportunity for prevention via the development of an effective vaccine. Although the risk of stomach cancer is diminishing throughout Europe, pinpointing the risk factors responsible could help accelerate the decline of this form of cancer which has relatively poor survival (European average 22% in males and 26% in females at five years after diagnosis).

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6.4: **Large bowel** (ICD-9 153, 154 and 159.0) (M 19.2; F 12.4)

There have been several studies demonstrating the difficulties in accurate recording of the precise site of cancer of the large bowel on death certificates. Although resulting in some loss of information, the sites of colon and rectum have been combined as "large bowel" in this atlas as any misclassification is likely to be within this categorisation. Cancer of the large bowel (also known as colorectal cancer) is the second commonest form of cancer death in both sexes.

The overall EU-EEA mortality rate was considerably higher in males (19.2 per 100,000) than in females (12.4), a ratio of 1.6:1. In each of the EU-EEA countries the mortality rate was higher in males than in females, with a similar degree of variation present in the rates in males and females.

International comparisons

The highest national mortality rates in males were in the Czech Republic (34.2) and Hungary (33.1), followed by Slovakia (26.6), Ireland (25.4) and Slovenia (24.0). The lowest rates were in Greece (9.3), Finland (12.0), Iceland (13.8) and Sweden (13.8) (Annex 2).

In females, the highest national rates were recorded in Hungary (19.0) and the Czech Republic (17.5). The lowest national rates in females were in Greece (7.4), Finland (8.3), Switzerland (9.2) and France (9.6).

As with stomach cancer (section 6.3) there was remarkable consistency across the 28 EU-EEA countries in the ratios between large bowel cancer mortality rates in males and females: those for all but two of the countries fell in the narrow range 1.3 to 1.7:1

Regional variation (box and whisker plots)

In males, there was variation between countries and between regions, although there was little variation apparent in most of the countries with the lowest national rates [p. 216]. The patterns were broadly similar in females.

Description of the maps

It is apparent from the maps that the pattern of geographical distribution in both males [p. 216] and females [p. 217] is substantially the same, with a broad band of high rates running east-west across the middle of Europe. Higher than average rates were found in Ireland and the northern parts of the United Kingdom, Denmark, southern parts of Norway, Germany and eastern Austria. Rates were also above average in parts of northern Italy and southern Portugal – more markedly in males than in females. The highest rates were in the Czech Republic, Slovakia, Slovenia and Hungary. Low rates were found in Finland, Sweden and Poland, and in much of southern Europe: Greece and southern Italy, France, Switzerland and Spain.

Statistical Aspects

Cancer of the large bowel had quite low regional variation, with similar levels in males (RRSD = 0.25) and females (RRSD = 0.24). There was, however, evidence of regional variation associated with country (86% in males and 85% in females) associated with the high rates in the Czech Republic and Hungary and lower rates in Finland, Sweden and southern Europe.

Moran's Index was high at 0.74 for males and 0.70 for females, indicating strong spatial correlation. The correlation between the rates for males and females was very high at 0.83. Although there were strong geographic patterns, the range in the rates from the low areas to the high areas was quite narrow compared with liver cancer, for example, which also has a strong geographic pattern but has a bigger relative difference between the low and high rates.

Comment

Cancer of the large bowel is an important public health problem: there are nearly one

million new cases of colorectal cancer diagnosed world-wide each year and half a million deaths. Edwards et al recently reported that in the United States, colorectal cancer was the most frequent form of cancer among persons aged 75 and older. Given that the majority of cancers occur in older people, and with the ageing of the population in mind, this observation gives further impetus to investigating primary and secondary prevention and treatment strategies for this major cancer.

The disease is not uniformly fatal, although there are large differences in survival according to stage of disease. Five year survival in resected tumours at an early stage (Dukes' A) is around 80 per cent and survival following simple resection of an adenomatous pedunculated polyp containing carcinoma *in situ* (or severe dysplasia) or intramucosal carcinoma is generally close to 100 per cent. There is now firm evidence from randomised trials that faecal occult blood testing (FOBT) can lead to a reduction in mortality from cancer of the large bowel. Strong findings from observational studies indicate that endoscopic screening, either sigmoidoscopy or colonoscopy, also appears to have the potential to reduce mortality and incidence of the disease by diagnosing and removing polyps. Screening research, recommendations and implementation are obvious priorities.

A decade ago, the dietary aetiology of cancer of the large bowel seemed to be clearly understood: risk was increased by increasing consumption of dietary fat, particularly animal fat, and meat and was reduced by consumption of vegetables and fruits. Today this classical concept of risk is being increasingly challenged as more epidemiological data become available. It has been hypothesised that alterations to serum triglycerides and/or plasma glucose could be one possible vehicle for the effects of various aetiological factors.

The risk of cancer of the large bowel, and its precursor condition *adenomatous polyps*, is increasingly associated with physical activity and body mass index. For example, Giovannucci et al (1996) examined the influence of physical activity, body mass index and the pattern of adipose distribution on the risk of colorectal adenomas. After controlling for age, prior endoscopy, parental history of cancer of the large bowel, smoking, aspirin use and dietary intakes, physical activity was associated inversely with the risk of large adenomas (greater or equal to 1 cm) in the distal colon (RR=0.57, 95% C.I. (0.30, 1.08) – borderline significance), when those in the highest and lowest fifths of average weekly energy expenditure from leisure activities were compared. Much of this benefit came from activities of moderate intensity such as brisk walking. Additionally, body mass index was associated directly with risk of large adenomas in the distal colon (RR=2.21, 95% C.I. (1.18, 4.16)), for BMI 29 kg/m^2 or over compared with BMI values less than 21 kg/m^2. The relationships with BMI and physical activity were considerably weaker for rectal adenomas. This indicates that exercise appears to protect against adenomas and cancer of the large bowel, while increasing body mass index serves to increase the risk of both.

There is increasing evidence supporting an association between use of hormone replacement therapy (HRT) and a reduced risk of cancer of the large bowel. In an initial meta-analysis, the overall risk for cancer of the large bowel and oestrogen replacement therapy was 0.92 but this was not statistically significant (95% CI (0.74, 1.5)). There was also no apparent effect when colon and rectal cancer were considered as separate entities. Subsequent to this report there have been further studies published which have confirmed and extended the results. Despite these encouraging findings, it is important to emphasise that females using HRT tend to adopt life-styles choices that confer protection from colon cancer or other chronic conditions, and so confounding cannot be excluded with certainty from studies assessing HRT as a protective factor in colon cancer. For example, the practice of exercise involving increased physical activity, increased consumption of fruits and vegetables and reduced fat intake and/or past screening (colonoscopy, sigmoidoscopy or occult blood test) tend to be associated more with females who are HRT ever-users than with never-users. Beral and colleagues in their review of the use of HRT and the subsequent risk of cancer advocate caution in over-interpreting the suggested protective effect in colon cancer.

Thus there are prospects for primary prevention of cancer of the large bowel although it is difficult to know how to successfully

bring about such large-scale changes to large proportions of populations. The large bowel has not been traditionally considered as a site where the risk of cancer is linked to cigarette smoking although more recent evidence strongly points to the existence of such an association between cigarette smoking and an increased risk of both adenomatous polyps and colorectal cancer. There is also interesting evidence suggesting that specific chemopreventive strategies could prove useful in the prevention of colorectal cancer.

While there are many questions to be resolved, it is apparent that many facets of colorectal cancer are becoming increasingly understood and prospects for prevention are becoming apparent.

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6.5: Liver (classified as primary) (ICD-9 155)
(M 6.9; F 2.5)

The interpretation of data on primary cancer of the liver requires special attention, particularly regarding mortality, because the liver is an organ frequently attacked by metastases (secondary tumours). Observed mortality rates may be affected by the misclassification of primary and secondary neoplasms; the inclusion of the latter on death certificates will bias the mortality rates upwards and make any apparent geographic patterns difficult to interpret. In addition, in countries and regions covered by efficient cancer registries, the separation of metastases from primary liver cancers is likely to be better than elsewhere; this will be reflected on death certificates, resulting in lower mortality rates from liver cancer.

Overall in the EU-EEA countries, the mortality rate from primary liver cancer was almost three times higher in males (6.9 per 100,000) than in females (2.5). In all countries the national mortality rate was higher in males than in females (Annex 2) with a large degree of variation apparent between countries in both males and females. The mortality rates for liver cancer were about 4% of the rate for all cancers in males, and 3% of that in females.

International comparisons

In males, the national mortality rates were highest in Italy (13.1), Greece (13.0) and France (11.0), followed by Spain (8.4), Hungary (8.2) and the Czech Republic (8.0) (Annex 2). The lowest rates were recorded in Norway (1.4), Denmark (1.5), The Netherlands (2.1) and the United Kingdom (2.5).

In females, the highest national mortality rates were recorded in Greece (5.5) and Italy (4.7), followed by Poland (3.9), Hungary (3.8), Slovakia (3.6), the Czech Republic (3.5) and Spain (3.2). The lowest rates in females – as in males – were in Norway (0.8), Denmark (0.9), The Netherlands (1.0) and the United Kingdom (1.3).

The ratios between the mortality rates in males and females were generally close to the overall average, except for France where it was markedly above it (more than 5:1).

Regional variation (box and whisker plots)

In males, there was variation between countries and between regions, although there was less variation apparent in the countries with the lowest national rates [p. 218]. In females, while there was variation between the 28 countries, there was again less variation in countries with low rates.

Description of the maps

In males, higher than average rates were found in most of France, Italy and Greece and in southern Spain [p. 218]. In females, the higher rates were also found in most of Italy and Greece and in Spain – but not in France; there were also higher rates in the neighbouring countries of Hungary, Slovakia, the Czech Republic and Poland in central Europe, and in parts of Sweden but not elsewhere in Scandinavia [p. 219]. In both sexes, the lowest rates were to be found in the United Kingdom, Ireland, Belgium, The Netherlands, Denmark, Finland and Norway.

Statistical aspects

The RRSD was 0.60 (ranked third) for males, and 0.54 for females (seventh) indicating that there was substantial relative regional variation in the rates. There were also strong country patterns with 85% and 84% of the regional variation in the rates for males and females, respectively, associated with differences between countries. This is noticeable in the boxplots, which illustrate the low rates in northern Europe and higher rates in France (males only), Italy and Greece.

There was high spatial autocorrelation with Moran's I of 0.80 for males and 0.74 for females. The correlation between the rates for males and females was 0.73, which is high. In France, however, there were high rates for males but relatively low rates for females.

Comment

Patterns of hepatocellular cancer were generally related to the prevalence of chronic carriers of hepatitis B surface antigen (HBsAg) in the population. There is a strong and specific association between infection with hepatitis B virus (HBV) and hepatocellular carcinoma. The association is restricted to chronically active forms of HBV infection which are characterised by the presence in serum of HBsAg, commonly referred to as 'carrier status'. The association is strong: in a cohort study from Taiwan based on 22,707 subjects, of which 3,454 were HBsAg positive, the relative risk for hepatocellular carcinoma was found to be 104 (95% C.I. (51, 212)) and the calculated attributable risk was 94 per cent.

The relative risk is, however, about one order of magnitude smaller (i.e. by a factor of approximately 10) in studies conducted in Europe or the United States. This is probably related to some co-factors (particularly poorer diet in East Asia); but a different duration of exposure to the virus, which in the Far East is usually transmitted perinatally whereas in Europe and North America is contracted late in life, can by itself explain such a substantial difference. This hypothesis has found epidemiological support from a study conducted in Greece which demonstrated a tendency for cases of hepatocellular carcinoma to have a higher birth order. There does not appear to be an association with the presence of hepatitis B antibodies alone. With reference to implications for prevention, perinatal immunisation against hepatitis B could probably be the single most effective preventive action against cancer world-wide after the elimination of tobacco smoking.

Upward trends in incidence and mortality rates from liver cancer have been seen in the last two decades in males in France, Germany and Italy. Chronic infection with hepatitis B virus (HBV) and hepatitis C virus (HCV) accounts for the majority of liver cancer cases in Europe. In a large case-series of liver cancer from six European Liver Centres only 29% of 503 liver cancer patients had no marker of either HBV or HCV infection.

HCV represents an increasing problem in several areas of the EU (especially in Italy, Greece and Spain) and in some population groups, notably intra-venous drug users. A vaccine is not yet available, and the effectiveness of treating all HCV-RNA-positive individuals with pegylated interferon-2α with or without ribavirin is still under evaluation. Hence the prevention of HCV infection relies for the moment on a strict control of blood and blood derivatives and avoidance of use of non-disposable needles in medical and non-medical procedures (e.g. acupuncture, tattooing, etc).

An increased frequency of primary liver cancer has been observed among individuals with a high alcohol intake in a number of studies although this is not a universal finding. Of four published cohort studies, two found an increased risk with increasing consumption of alcoholic beverages while in a further study, elevated risk was restricted to a subgroup. An overview of published studies of alcoholics shows a general tendency for alcoholics to have a 50 per cent excess of liver cancer over non-alcoholics. These risks, however, may well be underestimated, since alcohol-induced liver damage may induce reduction or cessation of alcohol consumption before the diagnosis of liver cancer.

Part of the excess liver can risk in alcoholics could be attributable to dietary deficiencies, since it has been shown that a diet poor in vitamin A and other (micro)nutrients is related to an increased risk of hepatocellular carcinoma. In tropical areas of Africa and Asia, aflatoxin, a product of metabolism of *Aspergillus flavus* which contaminates foods, particularly cereals, has been related to elevated risk of primary liver cancer with a positive interaction with hepatitis B virus and alcohol. The risk of primary liver cancer has been found to be greatly elevated among subjects exposed to more than one factor.

The use of combined oral contraceptives (OC) substantially increases the risk of liver cancer, and OCs are effective in the process of hepato-carcinogenesis in rodents. An association between long-term oral contraceptive use and hepatocellular carcinoma has been observed in five out five studies conducted in developed countries (though not in a sixth based mainly on developing countries). Primary liver cancer is still extremely rare in young females, and the public health impact of such as association is

small (unless such an association persists when the same generation of females become older).

The patterns apparent in the maps are compatible with an alcohol and hepatitis aetiology in males, with high rates in France (alcohol) and Greece, Italy and (southern) Spain (hepatitis). In females, where alcohol consumption levels are much lower, the geographic pattern is compatible with a hepatitis aetiology. Hepatitis B, and particularly hepatitis C, should be regarded as public health priorities in southern Europe. The difficulties in separating the diagnosis of metastases from primary liver cancer in many countries must, however, be borne in mind.

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6.6: Gallbladder and bile ducts (ICD-9 156)
(M 1.6; F 2.3)

ICD-9 code 156 includes not only the gallbladder cancers but also those arising in the bile ducts outside the liver. Unfortunately, these are not separated in the available mortality data. In general, the frequency of gallbladder cancer is about the same as that of bile duct cancers in males but double in females. The mortality rates from these cancers in the EU-EEA represented about 1% of the rates for all cancers in males and about 2% in females.

Overall in the EU-EEA countries, the mortality rate in females (2.3 per 100,000) was almost 50% higher than that recorded in males (1.6). In most countries, the national mortality rate was higher in females than in males, with considerable variation present in the national rates in both males and females (Annex 2).

International comparisons

In males, by far the highest national rates were in the Czech Republic (3.9) and Hungary (3.6), followed by a group of countries with rates around 2.0: Austria (2.3), Slovenia (2.3), Germany (2.2), Slovakia (2.0), Italy (2.0) and Sweden (1.9) (Annex 2). The lowest rates were recorded in the United Kingdom (0.5), Greece (0.7) and Ireland (0.7).

In females, the highest national rates were also in the Czech Republic (5.9) and Hungary (6.1), but rates were also high in the eastern parts of Germany and in Poland. The lowest national rates in females were in the United Kingdom (0.6), Greece (0.8), Ireland (1.0) and Latvia (1.0).

Regional variation (box and whisker plots)

In both males and females, there was noticeable variation between countries and between regions [p. 220-221].

Description of the maps

The distribution of gallbladder and bile duct cancer mortality in the EU-EEA was quite unlike that for any other form of malignant disease, with generally lower than average rates in the west of Europe, including Iceland, Norway, the United Kingdom and Ireland, Denmark, The Netherlands, Belgium, France, Spain and Portugal. Rates were above average in a band across most of the centre of Europe, extending from Italy in the south through Germany to Sweden in the north [p. 220]. The high rates also extended eastwards into eastern Austria, the Czech Republic, Hungary and parts of Slovakia in both males and females, and into Poland for females.

Statistical aspects

There was substantial regional variation for cancer of the gallbladder: the RRSDs of 0.51 was the seventh highest for males and that of 0.61 was the fourth highest for females. There was substantial variation associated with country, with percentages of 92% for males and 88% for females. Variability between countries was more important than within country variation; this is clearly seen in the maps and boxplots [p. 220].

The spatial correlation (Moran's I) of 0.58 was near the middle of the range for males, but that of 0.79 for females was one of the highest. The male-female correlation was high at 0.87, similar to the values for cancers of the stomach, large bowel and kidney.

Comment

Knowledge of risk factors for gallbladder cancer continues to be incomplete. Epidemiological studies have focused on the relation between this disease and gall stones. In all analytical studies, gall stones are the most important risk factor. It is, however, difficult to establish whether it is a causative relation or only an accompanying one (*e.g.* both cancer and gallstones may be related to an infection). Apart from the role of gall stones in the development of this disease, obesity and hormonal status in females have also been associated with it. Gallbladder cancer incidence has been shown to decrease with the growth in the number of cholecystectomies performed in a given country or population. According to estimates, 100 cholecystectomies prevent one gallbladder cancer.

Cancer of the gallbladder is a rare disease with low survival, resulting in relatively high mortality. It is one of the few cancer sites which are diagnosed more frequently in females than in males. The higher predominance of gallbladder cancer and the increasing fraction of extrahepatic malignancies of the bile ducts and the Ampulla of Vater, in females has been noted in many countries. This disease is also more frequently found in some ethnic groups. The literature offers hypotheses linking gallbladder cancer in some ethnic groups with the type of metabolism which developed during evolutionary adaptation. The Czech Republic, Slovakia, Hungary, Austria and Germany are the European countries where the highest gallbladder cancer frequency is found. These findings correlate with the high frequency of gallstones which has been observed for at least a century in this part of Europe. Interestingly, Jews emigrating from Central Europe to Israel face a higher risk of this cancer. Among the lowest frequencies of gallbladder cancer in Europe are found in Ireland and the United Kingdom, where the incidence has also showed a decline over recent decades. The United Kingdom has in the past been a country with a low frequency of gallstones compared with the rest of Europe.

The frequencies of gallbladder cancer and of gallstones tend to run in parallel. Thus the high risk of gallbladder cancer seen among American Indians is reflected in a spectrum of gallstone-related disease in this population. The distribution of gallstones shares many of the features of gallbladder cancer, including female predominance. Most epidemiological studies have examined the characteristics of patients with gallstones rather than the much rarer gallbladder cancer. There have been a few reports of an excess of gallbladder and bile duct tumours in workers in a rubber plant consistent with the ability of several chemicals, including those used in rubber processing, to produce such cancers in laboratory animals.

The striking geographical distribution of gallbladder and bile duct cancer within the EU-EEA again offers opportunities for collaborative epidemiological studies and the prospect of significant prevention of the disease.

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6.7: **Pancreas** (ICD-9 157)
(M 7.5; F 4.8)

Cancer of the pancreas can frequently be difficult to localise and report correctly in both incidence and mortality statistics. In general terms, it will tend to be under-reported rather than over-reported. The disease is highly fatal, and in the EU-EEA the mortality rates from pancreatic cancer were about 5% of those for all cancers in both males and females.

Overall in the EU-EEA countries, cancer of the pancreas had the fifth highest cancer mortality rate in males (7.5 per 100,000) and the seventh in females (4.8). In all countries, the national mortality rate was higher in males than in females with more variability in the national rates in females than in males (Annex 2).

International comparisons

In males, the highest national mortality rates were in Latvia (12.0), Hungary (11.4), the Czech Republic (11.1), Estonia (10.6) and Lithuania (10.4) (Annex 2). The lowest national rates were in Spain (5.9), Greece (6.1), Portugal (6.1) and the United Kingdom (6.5).

In females, the highest national mortality rates were in Iceland (7.1), the Czech Republic (6.8), Hungary (6.7), Sweden (6.6), Denmark (6.2) and Austria (6.2). The lowest national mortality rates were recorded in Portugal (3.3), Spain (3.5) and Greece (3.5).

Regional variation (box and whisker plots)

In males, there is clear evidence of both the variation in the national rates and also in the rates within each country [p. 222]. There is also evidence of between and within country variation in females.

Description of the maps

In males, there were several distinct aggregations of high rates. One extended over northern Sweden and Norway; a second covered all three Baltic Countries; and a third extended from northern Italy into eastern Austria, the Czech Republic, Slovakia and Hungary [p. 222]. There is marked contrast between the high rates in the north of Italy and the very low rates in the south of the country; and there were low rates in Portugal, Spain and most of Greece and the United Kingdom.

In females, the broad pattern was similar, but there were some noticeable differences, with high rates over most of the Nordic Countries, particularly Sweden, and in Austria, the Czech Republic and Hungary, but only average rates in the three Baltic Countries [p. 223]. As in males, there were low rates throughout Spain, Portugal, southern Italy and much of Greece.

Statistical aspects

Cancer of the pancreas had low RRSDs in both males and females: 0.20 and 0.21, respectively. Within country variation was high in Italy for both males and females and high among males in Greece. These were all characterised by north to south gradients with higher rates in the north of both countries. Regional variation associated with country was at the low end of the range in both males (72%) and females (73%). For both males and females the higher rates were grouped together in Scandinavia, Austria, the Baltic Countries, the Czech Republic, Slovakia and Hungary, and the lower rates in Spain, Portugal and Greece.

Spatial correlation was relatively low with Moran's I of 0.47 for males and 0.41 for females. These values are consistent with the between and within country variances for males and females. There was a moderate correlation of 0.43 between the regional rates for males and females.

Comment

Analytical studies based on patients with pancreatic cancer consistently demonstrate that

cigarette smoking increases the risk. This appears to be the major clearly demonstrated risk factor. A dose-response relationship is found with increasing pancreatic cancer risk and lifetime reported cigarette consumption and the risk is found to reduce among ex-smokers to a level compatible with lifelong smokers fifteen years after quitting.

Although it had been speculated that there was a positive association with coffee consumption, the overall evidence available does not support this relationship. There is no convincing evidence linking alcohol consumption to an increased risk of pancreatic cancer.

It appears likely that dietary factors could emerge as influential in determining pancreatic cancer risk. The SEARCH study found positive associations between intake of carbohydrates and cholesterol and inverse associations with dietary fibre and vitamin C. These associations were generally consistent among the five centres which undertook the study and the consistency, strength and specificity appear to suggest underlying causal relationships. In a large cohort of females in the United States participating in the Nurses' Health Study (n = 88,800), 180 case subjects with pancreatic cancer were diagnosed during 18 years of follow-up. Carbohydrate and sucrose intake were not associated with overall pancreatic cancer risk in this cohort. A statistically borderline significant 53% increase in risk of pancreatic cancer (RR = 1.53, 95% confidence interval [CI] = 0.96 to 2.45) was observed among females with a high glycaemic load intake, and a similar association was observed for fructose intake (RR = 1.57, 95% CI = 0.95 to 2.57). The associations of glycaemic load and fructose intakes with pancreatic cancer risk were most apparent among females with elevated body mass index of 25 kg/m^2 or higher or with low physical activity. Among females who were both overweight and sedentary, a high glycaemic load was associated with an RR of 2.67 (95% CI = 1.02 to 6.99; highest versus lowest quartile of intake; P for trend =0.03), and high fructose was associated with an RR of 3.17 (95% CI = 1.13 to 8.91; P for trend =0.04). It would seem warranted to investigate further these findings that impaired glucose metabolism may play a role in the aetiology of pancreatic cancer.

Some aspects of medical history have been associated with pancreatic cancer risk. It has recently been demonstrated that patients with chronic pancreatitis have an increased risk of developing pancreatic cancer: ten years after the initial diagnosis of chronic pancreatitis, the risk was 8.5. In particular, besides pancreatitis, there is some evidence that diabetes and gastrectomy may be associated with elevated pancreatic cancer risk, while allergies may represent an indication of reduced risk.

In terms of the pattern in the mortality maps for males and females, it is difficult to propose a simple explanation based on the current state of knowledge of risk factors. Cigarette smoking, a long-standing history of chronic pancreatitis and familial pancreatitis are all the risk factors which are known with certainty. There is still a need for a great deal of epidemiological work on this topic before prospects for prevention improve.

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6.8: Larynx (ICD-9 161)
(M 3.9; F 0.3)

Cancer of the larynx has a high survival rate when the disease is diagnosed at an early stage. Differences in the sub-site distribution within the larynx may contribute partially to the variation in mortality from this cancer throughout Europe. Overall, the mortality rate from cancer of the larynx in the EU-EEA was almost 15 times higher in males than in females. The rate was just over 2% of the rate for all cancers in males, but less than 0.5% in females.

Cancer of the larynx was much commoner overall in males (3.9 per 100,000) than in females (0.3 per 100,000). In all countries, the national mortality rate was higher in males than in females, there was considerable variability in the rates between countries in males, and national rates in females were consistently very low (Annex 2).

International comparisons

In males, the highest national mortality rates were in Hungary (9.1), Lithuania (7.5), Slovakia (7.5) and Poland (7.4); the lowest rates were in Sweden (0.6), Norway (1.0) and Finland (1.0) (Annex 2). In females, cancer of the larynx is very rare and all national mortality rates – except that in Hungary (0.7) – were 0.5 per 100,000 or lower.

Regional variation (box and whisker plots)

In males, there was clear evidence of both the variation in the national rates and also within each country [p. 224]. There was also evidence of between and within country variation in females, but the numbers of deaths were all very small.

Description of the maps

The pattern in males has several features in common with those of oral cancer and cancer of the oesophagus. The outstanding feature of the map for laryngeal cancer is the two areas of generally higher levels of mortality [p. 224]. One covers parts of Portugal, Spain, France and northern Italy; and the second covers Hungary, Slovakia, Poland and the three Baltic Countries. Rates were low throughout in the Nordic Countries, the United Kingdom, Ireland and most of Germany. The areas of high cancer mortality from laryngeal cancer in northern France did not end abruptly at the borders with Belgium, Germany and Italy as did those for oral cancer (section 6.1), strongly suggesting that there are likely to be comparable exposures in these areas.

In looking at the map for females [p. 225] it must be remembered that the mortality rates were much lower than in males and that the range of mortality rates is very much narrower. Most of the apparent differences in rates among the small areas is simply due to chance variation because of the small numbers of deaths, but there are generally slightly higher than average rates across Hungary and parts of Poland.

Statistical aspects

Among males, 92% of the regional variation was associated with between country differences, while for females the figure was lower at 75%. The RRSDs were 0.62 and 0.50, respectively, making larynx the second most variable site for males and the eighth most variable for females. Among males the very strong country pattern was associated with low rates in north Europe, and Germany, and much higher rates in two areas: southwest Europe, especially in Spain, Portugal, France and northern Italy; and central Europe, especially Hungary, Slovakia and Poland, and the Baltic Countries.

There was little association between the rates for males and for females: the correlation was the third lowest of all sites at 0.29. The Moran index was quite high for males at 0.76, though it was much lower for females at 0.21. This implies that there was a different spatial pattern for males than for females. The relatively high rates in Ireland, the United Kingdom and Norway among females compared with the relatively low rates there for males, and the reverse in Spain and Portugal, are

major factors in the weak association in the rates between males and females. It was difficult to estimate the RRSD for several of the countries for females because their rates were so low.

Comment

As noted above, there may well be differences in the sub-site distribution in different countries or regions which could influence mortality patterns. Several important risk factors for laryngeal cancer have been clearly established. Much of the discussion about oral cancer (section 6.1) and oesophageal cancer (section 6.2) is equally relevant in this section.

It is estimated that between 25 and 30% of all cancers in developed countries are tobacco-related. For both sexes combined the proportion of cancers arising in the oesophagus, larynx and oral cavity attributable to the effect of tobacco, either acting singly or jointly with the consumption of alcohol is between 43 and 60%.

Although the greatest hazard is caused by cigarette smoking, cigars can cause similar hazards if their smoke is inhaled and both cigar and pipe smoker cause comparable hazards of cancers of the oral cavity, pharynx, extrinsic larynx, and oesophagus.

There is convincing epidemiological evidence that the consumption of alcoholic beverages increases the risk of cancers of the oral cavity, pharynx and extrinsic larynx and of squamous cell carcinoma of the oesophagus. The risks tend to increase with the amount of ethanol drunk, in the absence of any clearly defined threshold below which no effect is evident. There is wide variability among EU-EEA countries in terms of per capita average alcohol consumption and preferred type of alcoholic beverage.

The separate effects of alcohol and tobacco on laryngeal cancer are quite strong. The risk of extrinsic laryngeal cancer is 2.5 fold increased in heavy drinkers-non-smokers and over 9-fold among current smokers-non-drinkers. Although alcohol drinking increases the risk of upper digestive and respiratory tract neoplasms, even in the absence of smoking, alcohol drinking and tobacco smoking together greatly increase the risk of these cancers, each factor approximately multiplying the effect of the other. Compared with never-smokers and non-alcohol drinkers, the relative risk of these neoplasms is increased between 10- and 100-fold in people who drink and smoke heavily. If there were total abstinence from drinking and smoking, the risk of oral, pharyngeal, laryngeal and squamous cell oesophageal cancers in European countries would be extremely low.

Taking account of knowledge of risk factors, the high levels in males appear to be generally in regions where there is a prevalent habit in the population of drinking strong alcoholic beverages. The big difference between cancer of the larynx and oral and oesophageal cancers in males is the concentration of high rates in Spain: this could be due to the prominent habit of black tobacco use. Reduction of alcohol consumption, or avoidance of cigarette smoking, could lead to large reductions in risk.

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6.9: Trachea, bronchus and lung (ICD-9 162)
(M 50.3; F 10.3)

Cancer of the trachea, bronchus and lung (lung cancer) has by far the highest rate of cancer death in males in the EU-EEA, and the third highest rate in females. Overall, the mortality rate for lung cancer was around five times higher in males (50.3 per 100,000) than in females (10.3 per 100,000) (Annex 2). In all countries, the national mortality rate was higher in males than in females but there was considerable variability in the rates between countries in males. The ratios of the national rates in males and females ranged from around 2:1 to over 10:1.

International comparisons

In males, by far the highest national lung cancer mortality rate was in Hungary (84.8), followed by Poland (71.4), Belgium (69.1), the Czech Republic (68.3) and Estonia (65.6) (Annex 2). The lowest rates were in Sweden (22.3), Portugal (29.3), Iceland (30.8) and Norway (31.5).

In females, the highest national mortality rates were in Denmark (27.7), Iceland (26.2), the United Kingdom (20.5), Hungary (19.0) and Ireland (17.3). The lowest rates were in Spain (3.9) and Portugal (4.6).

Regional variation (box and whisker plots)

In males, there was clear evidence of variation both in the national lung cancer rates and in the rates within each country [p. 226]. The between-country variation in females appeared to be less marked than that observed in males, but there was again wide variation in rates within countries [p. 227].

Description of the maps

The most prominent feature of the geographical distribution of lung cancer in males is the large area of high rates which extends from northern Italy through neighbouring Slovenia into Hungary, Slovakia, the Czech Republic, Poland, parts of northeast Germany and the Baltic Countries. There was a second, smaller, area with higher than average rates covering The Netherlands, Belgium and northern France [p. 226]. There were also small numbers of areas with high rates in central Scotland, southern Spain and the northern mainland of Greece. Rates were generally low in Portugal, central and northern Spain, southern France, Switzerland, southern Germany and Austria, as well as in all the Nordic Countries.

The pattern of lung cancer mortality in females [p. 227] was quite different from that observed in males. The highest rates were in the United Kingdom (particularly the north), Ireland, Denmark and Iceland, and parts of Norway and Sweden, all of which had generally lower than average lung cancer mortality rates in males. There were, however, similar areas of higher than average rates in females as in males in Belgium and The Netherlands, in north and west Poland, and in Hungary. Low rates aggregated particularly in Portugal and Spain, but also in France, Greece, southern Italy and Finland.

Statistical aspects

There was relatively low overall regional variation for males (RRSD = 0.29) but relatively high regional variation for females (RRSD = 0.55, the fifth highest). Among females there was large regional variation within Italy, with an RRSD of 0.36 as a result of a north-south gradient with lower rates in the south. There was also a north-south gradient in Italy for males, but the regional variation was similar in magnitude to that in other Mediterranean countries. Portugal was the country with the highest internal regional variation among males.

The percentages of variation associated with differences between countries were in the middle of the range for both males (77%) and females (79%). But, as with cancer of the larynx, there was a big difference between the geographical patterns of lung cancer mortality in males and females by country, as described above.

For both males and females there was strong spatial correlation, with Moran's I of 0.76 for males and 0.79 for females, confirming the strong geographical patterns observed.

As a result of the widely different geographical patterns in the rates for males and females, the correlation between the regional rates was the lowest of all the cancer sites at 0.19. There were two main groups of countries: those where the ratio between the rate in males and females was low, such as the United Kingdom, Ireland, Denmark, Norway and Sweden; and those in which the ratio was high – of these, there were very high rates in males in parts of both Hungary and Poland, but relatively low rates in Portugal.

Comment

The 20th century witnessed a remarkable epidemic of lung cancer. The words of Adler, published in 1912, today make salutatory reading. *"Is it worthwhile to write a monograph on the subject of primary malignant tumours of the lung? In the course of the last two centuries an ever-increasing literature has accumulated around this subject. But this literature is without correlation, much of it buried in dissertations and other out-of-the-way places, and, with but a few notable exceptions, no attempt has been made to study the subject as a whole, either the pathological or the clinical aspect having been emphasised at the expense of the other, according to the special predilection of the author. On one point, however, there is nearly complete consensus of opinion, and that is that primary malignant neoplasms of the lungs are among the rarest forms of the disease. This latter opinion of the extreme rarity of primary tumours has persisted for centuries."*

Now at the beginning of the 21st century, lung cancer is the most common form of cancer worldwide. It is the most common cause of cancer death in males in North America and in virtually all European countries, west and east, and it is increasingly common as a cause of death in developing countries in Asia, Latin America and Africa, although comparable high-quality data are not available from many of these populations. From being virtually an unknown and rare disease at the beginning of the 20th century, lung cancer developed into a true epidemic.

It is estimated that between 25 and 30% of all cancers in developed countries are tobacco-related. From the results of studies conducted in Europe, Japan and North America, around 90% of lung cancers in males, and between 57 and 86% of lung cancers in females, are attributable to cigarette smoking. Because of the length of the latency period, tobacco-related cancers observed today are related to the cigarette smoking patterns over several previous decades. On stopping smoking, the risk of cancer induced by smoking rapidly decreases. Benefit is evident within five years and is progressively more marked with the passage of time.

Tobacco smoke released to the environment by smokers, commonly referred to as environmental tobacco smoke (ETS) and which may be said to give rise to enforced "passive smoking", has several deleterious effects on people who inhale it. It causes a small increase in the risk of lung cancer and also some increase in the risk of heart disease and respiratory disease and is particularly harmful to small children. Smoking during pregnancy increases the risk of stillbirth, diminishes the infant's birth weight, and impairs the child's subsequent mental and physical development, while smoking by either parent after the child's birth increases the child's risk of respiratory tract infection, severe asthma, and sudden death.

The situation regarding smoking in Europe is particularly worrying. Of the six World Health Organization (WHO) regions, Europe has the highest *per capita* consumption of manufactured cigarettes and faces an immediate and major challenge in meeting the WHO target for a minimum of 80% of the population to be non-smoking. In 1990-1994, 34% of males and 24% of females in the European Union were regular smokers. In females the overall rate was influenced by the low rates in southern Europe, but the rates there are rising and seem set to continue to rise over the next decade. In the age range 25-39 years, the smoking rates are higher than the average (55% in males and 40% in females) and this can be expected to have a profound influence on the future mortality from lung cancer, as well as other smoking-related cancers.

The importance of adequate intervention is shown by the decline to low lung cancer rates in those Nordic Countries which, since the early 1970s, have adopted integrated central and local policies and programmes against smoking. In the United Kingdom, tobacco consumption has also declined, by 46% since 1970 and lung cancer mortality among males has been decreasing since 1980, although the rate still remains high. In France, there was an 11% reduction in tobacco consumption due to the implementation of anti-tobacco measures introduced by the *Loi Evin* between 1993 and 1998.

In terms of our understanding of lung cancer aetiology, the current geographical patterns better represent the smoking habits in the various countries 20-30 years ago than those of today. In particular, the high mortality from lung cancer in females in Denmark and the United Kingdom reflects the early uptake of the smoking habit by large portions of females in those countries. An epidemic of tobacco-related lung cancer in females throughout Europe has yet to materialise (as it has previously in males) and effective intervention is now needed urgently to avoid this catastrophe.

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6.10: **Pleura** (ICD-9 163)
(M 1.0; F 0.3)

The pleura is the lining of the lung and hosts two distinct types of cancer: *adenocarcinoma of the pleura* and *pleural mesothelioma,* the latter being the dominant form. Pleural mesothelioma is one of the forms of cancer which has very strong links to occupational exposure (to asbestos). The majority of cancers recorded to this site will be mesothelioma. Although not a common form of cancer, it is likely to be correctly recorded on death certificates in view of its strong occupational determinant.

Overall the mortality rate in the EU-EEA was much higher in males (1.0 per 100,000 per annum) than in females (0.3) and the national mortality rates were higher in every country in males than in females. In males, there was a fair degree of variability in the rates between countries (Annex 2).

International comparisons

In males, the highest national mortality rates were in The Netherlands (2.7), France (1.5), Norway (1.3) and Italy (1.3) (Annex 2). The lowest rates were in Portugal (0.1).

In females, cancer of the pleura was quite rare and all the national mortality rates were 0.5 per 100,000 or lower.

Regional variation (box and whisker plots)

For males, in addition to the wide variation in national rates, there was considerable variability within many countries, particularly those with the higher average rates [p. 228].

Description of the maps

This is the only form of cancer presented in this atlas in which the local rates are more important than the general geographic picture. In males, high rates occur around the European coastline in regions where shipbuilding (and heavy engineering) have been traditional industries [p. 228]. Thus there were high rates in Trieste, Venice, La Spezia and Genoa in Italy; Marseilles, Saint Nazaire and Le Havre in France: Belfast, Glasgow, Newcastle, Sunderland, Barrow-in-Furness and Liverpool in the United Kingdom; Rotterdam and the Hague in The Netherlands; Hamburg in Germany; and Vestfold in Norway. Rates were also high in western Slovenia where asbestos was used in the production of fibre cement boards.

In females, there was little variation in the national rates which were all very low. The map for females appears to be broadly similar to that for males, as their rates are also below average in most of Portugal, Spain, Greece, Hungary, eastern Poland and the three Baltic Countries, and above average in much of France and northern Italy. The rates for females in most of the shipbuilding areas mentioned above were, however, not elevated as were the rates in males [p. 229].

Statistical aspects

This cancer had by far the highest RRSD for males at 0.76, and the third highest for females at 0.66. Within many countries, but excluding Ireland, Estonia, Hungary, Spain, Portugal and Greece, there were both extremely high rates and extremely low rates. The Moran Index was at the low end of the range for both males (0.47) and for females (0.34) and the male-female correlation in the rates was 0.55.

Comment

Asbestos exposure causes a number of benign conditions of the pleura including pleural effusions, diffuse pleural thickening and calcified pleural plaques; it has also been convincingly demonstrated that occupational exposure to asbestos causes mesothelioma of the pleura. Mesotheliomas of the pleura are so rare other than after occupational or other unusual asbestos exposure that any case that occurs after well attested and substantial exposure to asbestos is commonly accepted as being due to that exposure – the only qualification being that the time elapsed since the exposure and the disease being diagnosed is sufficiently long to permit the disease to

have been produced. This delay is important as the delay between the first exposure and the realisation of the effect is longer for mesothelioma than for many other cancers, being seldom less than 15 years and possibly never less than 10 years.

As with many other cancers, increasing exposure increases the risk of developing the disease but, in the case of asbestos exposure and mesothelioma, does not affect the length of the induction period. Periods of 30 or even up to 50 years are common and the risk apparently continues to increase indefinitely with the time since the exposure first occurred. Results of modelling of data obtained from occupational cohorts indicate that the risk of mesothelioma increases in proportion to the cube of the time elapsed since first exposure and that each brief period of exposure causes an addition to subsequent incidence which increases approximately as the cube of the time since the exposure occurred. The available data indicate also that exposure durations of between 10 and 20 years and longer intervals produce little difference in risk. However, risk caused by shorter durations of exposure may be lower than predicted.

Projections suggest that the number of males dying from mesothelioma in western Europe each year will almost double from (approximately) 5,000 in 1998 to about 9,000 in 2018. Thereafter there will be a decline with a total of around a quarter of a million deaths over the next 35 years. The highest risk will be suffered by males born around 1945-1950, with approximately 1 in 150 dying from mesothelioma. Asbestos use in western Europe remained high until 1980 and substantial quantities are still in use in several European countries.

Asbestos exposure has been highest historically in traditional shipbuilding and heavy engineering industries, but significant exposures occurred in the building industry during the post-WWII building boom. In the United Kingdom, an analysis of occupations recorded on death certificates with mesothelioma between 1968 and 1992 indicated that building workers, especially plumbers, gas fitters, carpenters and electricians were the highest risk group. These occupations account for a large proportion of deaths from mesothelioma.

In view of the striking association between mesothelioma risk and exposure to asbestos, the finding of the highest mortality rates around coastal areas of the EU-EEA with traditional port and shipbuilding facilities is not unexpected.

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6.11: Melanoma of the skin (ICD-9 172)
(M 1.7; F 1.2)

The incidence of cutaneous malignant melanoma is increasing in Caucasian populations around the world and these trends may be exacerbated by further increases in acute exposures to sunshine (sunbathing), together with, perhaps, the depletion of the stratospheric ozone layer. Thus melanoma has been identified as one form of cancer which will become very important in public health terms in coming decades in the absence of effective intervention today.

Overall, the mortality rate in the EU-EEA was around 40% higher in males (1.7 per 100,000) than in females (1.2). Rates in most countries were higher in males than in females (Annex 2) with considerable variation in the mortality rates between countries.

International comparisons

In males, the highest national mortality rates were in Norway (3.7), Slovenia (3.1), Denmark (2.8), the Czech Republic (2.8), Sweden (2.6) and Switzerland (2.6) (Annex 2). The lowest rates were in Greece (0.5) and Portugal (0.8).

In females, the highest national mortality rates were recorded in Slovenia (2.7), Norway (2.3) and Denmark (1.9). The lowest rates were in Greece (0.4), Portugal (0.7) and Spain (0.8).

Regional variation (box and whisker plots)

For both males and females there was considerable variation in the rates between countries; and the within country variability appeared wider in some of the countries with high average rates [p. 230-231].

Description of the maps

The prominent features of the geographical distribution of melanoma in males are the high levels across (southern) Finland, Norway, Sweden and Denmark and into northern Germany and The Netherlands, in Austria, Switzerland, the Czech Republic, Slovakia, Hungary and Slovenia, and in southern England. Rates were low in most of Spain, Portugal, southern Italy and Greece [p. 230].

In females, the pattern was quite similar in broad terms with higher than average levels across (southern) Finland, Norway, Sweden and Denmark and into northern Germany and The Netherlands, in parts of Austria, Switzerland, the Czech Republic, Hungary and Slovenia, and in southern England. As in males, there were lower than average rates in Spain, Portugal, southern Italy and Greece [p. 231].

Statistical aspects

For males, the RRSD was 0.35, towards the lower end of the range, but 86% of the regional variation was associated with differences between countries. For females, the RRSD was 0.30, again one of the lower values, and 84% of the between region variability was associated with differences between countries. This is noticeable in the maps with higher rates in Scandinavia, the United Kingdom, Switzerland, Austria, the Czech Republic, Slovakia, Hungary and Slovenia, and lower rates in southern European countries.

Spatial correlation was quite low with Moran's I at 0.42 males and 0.32 for females. The correlation between the rates for males and females was quite high at 0.74.

Comment

There remains no doubt that the major environmental cause of skin cancer is sun exposure. Skin cancer is predominantly, but not exclusively, a disease of white skinned peoples. Its incidence, furthermore, is greatest where fair skinned peoples live at increased exposure to ultraviolet light, such as in Australia. The type of sun exposure which causes skin cancer however appears to differ for the three main types.

Melanoma is more common in people of high socio-economic status who work inside but who have the opportunity to spend leisure time in the sun. A history of sunburn, which is associated with intermittent sun exposure, has repeatedly been described as a risk factor for melanoma. The latitudinal gradient within Europe is to some extent the reverse of what one sees in Australia: within Europe, the highest melanoma rates were in the Nordic Countries where intermittency of sun exposure is exemplified. There the people tend to have fair skin; and while the winters are long and dark, the summer lifestyle is characterised by outdoor lifestyles and holidays in the sun, frequently taken in southern latitudes where the sun is even stronger.

The incidence of melanoma doubled in Europe between the 1960s and the 1990s; this is attributed to increased intense sun exposure. There is some suggestion that this increased incidence is levelling off in some countries which might suggest that health education efforts to reduce sunburn may have had an effect. There are concerns however that exposure to the sun may still increase within Europe as a whole in years to come both as a result of increased affluence and possibly because of climatic change. It is conceivable, but as yet unproven, that depletion of the ozone layer may result in increased ultraviolet B (UVB) exposures at the earth's surface. There are also concerns that global warming may result in warmer summers in northern Europe leading to greater time periods spent outdoors and therefore greater sun exposure.

All Europeans, however, are not equally susceptible to melanoma. The fairest skinned are more susceptible, particularly (but not exclusively) those with red hair, freckles and a tendency to burn in the sun. Such fair skinned people are at increased risk of all types of skin cancer and because they burn quickly in youth, they usually do reduce their sunbathing activities through life. It is often their perspective therefore that their sun exposure has been reduced, and they are surprised when skin cancer ultimately occurs. The fair skinned should take continuous sun avoidance measures throughout life, rather than merely avoiding sun bathing.

The strongest phenotypic risk factor for melanoma however, is the presence of large numbers of moles or melanocytic naevi; there is strong evidence from studies of twins that the major determinant of the number of moles is genetic, with an added contribution from sun exposure. These naevi may be normal in appearance but are also usually accompanied by so-called atypical moles: moles which are larger than 5 mm in diameter with variable colour within them and an irregular shape. The phenotype is described as the atypical mole syndrome phenotype (AMS). AMS is present in something like 2% of the north European population and is associated with approximately a ten times increased risk of melanoma. Advice about sun protection is therefore particularly of importance to this sector of the population. Some patients with AMS report a family history of melanoma and overall a strong family history (three or more cases) is the strongest predictor of risk. These families should avoid the sun and should be referred to dermatologists for counselling.

The best protection from the summer sun is to stay out of it, but the following advice is given in order to allow safer enjoyment of the outdoors. Keeping out of the sun between 11 am and 3 pm (12 noon and 4 pm, Central Europe Time) is effective, as nearly three quarters of the total daily ultraviolet (UV) dose is delivered to the Earth's surface during this time. Scheduling outdoor activities for other times is therefore important, particularly for children. Using shade is allied to this and clothing remains the second most important protective measure. Close weave heavy cotton affords good protection although the clothing industry increasingly is developing UV protective cloths with sun protective factors (SPFs) of around 30 which are very valuable particularly where it is difficult to keep out of the sun.

Sunscreens are helpful for skin on parts of the body which cannot be protected with clothing, such as the face, the ears and the hands. Concerns have mounted in recent times, however, about the way in which sunscreens are used and which type of sunscreen is used. Sunscreen may protect against squamous cell carcinoma but there is currently inadequate evidence for their preventive effect against basal cell carcinoma and melanoma; prolongation of sun exposure may be responsible for an increase risk of melanoma.

In terms of our understanding of the risk factors for melanoma, the pattern is consistent with high

risk in those European populations with light skins and who rarely have their body exposed to the sun for most of the year but who experience intense intermittent sun exposure. There is very large scope for significant behavioural change to greatly reduce the incidence, and hence the mortality, rate of melanoma in European populations. In some countries, for example Slovenia, the mortality rate could be reduced by earlier diagnosis (and hence better survival).

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6.12: Non-melanoma skin cancer (ICD-9 173)
(M 0.6; F 0.3)

The incidence of malignant tumours of the skin other than melanomas, which include mainly basal and squamous cell carcinomas, shows wide geographical variation. Given their high frequency of occurrence, and the fact that an individual may have several basal cell carcinomas over a lifetime, many cancer registries choose not to record them. Even when registered, the true incidence is frequently difficult to assess, however, as these tumours are often subject to under-reporting. The generally high survival rates for these cancers makes it difficult to assess the effects of risk factors by examination of mortality data.

Overall, the mortality rate in the EU-EEA was around twice as high in males (0.6 per 100,000) as in females (0.3). In all countries except Latvia, the national mortality rate was higher in males than in females (Annex 2).

International comparisons

In males, the highest national mortality rates were in Hungary (1.2), Poland (1.1), Slovakia (1.1), Greece (1.0) and Estonia (1.0) (Annex 2). The lowest rates were in Iceland (0.2) and Germany (0.3); six countries had rates of 0.4.

In females, the highest rates were in Slovakia (0.8), Greece (0.8), Hungary (0.7), Poland (0.7) and Estonia (0.7); three countries had rates of around 0.4, and most of the remaining countries had rates of 0.2 or lower.

Regional variation (box and whisker plots)

In both males and females there was considerable variability both between and within countries. To some extent, the apparent within country variation is due to random fluctuations arising from rates being based on very small numbers of deaths [p. 232-233].

Description of the maps

In males, there were many regions with high mortality rates in Portugal, Spain, Greece, Ireland, Poland, the Czech Republic, Slovakia and Hungary [p. 232]. Low rates tended to aggregate in the Nordic Countries, France, Belgium, The Netherlands and large parts of Germany and western Austria.

The map for females is substantially similar to that for males, with areas of high rates aggregating in Portugal, Spain, southern Italy and Greece, Poland, the Czech Republic, Slovakia and Hungary [p. 233]. Low rates were noticeable in Sweden, Finland and a large part of northern Germany.

Statistical aspects

Although the mortality rates for non-melanoma skin cancer were low, particularly for females, they do exhibit strong regional variation. For males the RRSD was 0.56, which was the fourth highest; and 77% of the regional variation was associated with differences between countries. Similar results were obtained for females, where the RRSD was 0.67 (second highest) and 82% of the regional variance was associated with countries. The main country differences for males were due to the high rates in two groups of countries: Spain, Portugal and Greece; and Poland, the Czech Republic, Slovakia and Hungary, and generally lower rates elsewhere.

Spatial correlation was moderate to low with Moran's I of 0.40 for males and 0.39 for females. The spatial correlation between male and female rates was 0.74 which is reasonably high.

Comment

The major environmental cause of skin cancer is exposure to the sun. Skin cancer is predominantly, but not exclusively, a disease of white skinned people. Its incidence, furthermore, is greater where fair skinned peoples live at increased exposure to ultraviolet light. The type of sun exposure which causes skin cancer however appears to differ in the three main types. Squamous cell carcinoma shows the clearest relationship between cumulative sun exposure and risk. This form of skin cancer is therefore most common in outdoor workers and there is a linear increase with age. The recipients of transplanted organs are particularly at risk of these tumours as

a result of the combined effects of the unchecked growth of human papilloma virus in their skin due to immuno-suppression, and exposure to the sun.

Basal cell carcinoma (BCC) is the commonest type of skin cancer but it is the least serious as it is only a locally invasive disease. Extremely small numbers of people die from this cancer; as in addition there are very large numbers of cases, in some countries BCCs are not even recorded by the cancer registries. This form of skin cancer appears to share with melanoma an aetiological relationship to sun exposure. The case-control study evidence for both appears to suggest a non-linear relationship between cumulative sun exposure and risk. For both, intermittency of exposure seems to be important. Further discussion on exposure to the sun and protective measures is given in section 6.11 above

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6.13: Breast (female) (ICD-9 174) (F 20.6)

There was no country with a truly low mortality rate for breast cancer, for which the overall rate in the EU-EEA was 20.6 per 100,000. Breast cancer accounted for one fifth of all cancer deaths and was the most common form of cancer death in females.

International comparisons

The highest national mortality rates were in Denmark (27.4), The Netherlands (25.9), Belgium (25.3), Iceland (24.9), the United Kingdom (24.8) and Ireland (24.4) (Annex 2). The lowest national rates were in Greece (14.8), Poland (16.0), Finland (16.6), Sweden (16.7), Slovakia (16.9) and Spain (16.9).

Regional variation (box and whisker plots)

There was some variability in rates between countries, but only relatively small variations within countries [p. 234].

Description of the maps

There are several notable features of the geographic distribution of breast cancer mortality in females in the EU-EEA. There was an aggregation of high rates which covers Denmark and westwards through northern Germany, The Netherlands and Belgium and then across to the United Kingdom and Ireland; mortality was also slightly above average in parts of Slovenia and Hungary. Rates were low in the Nordic Countries (apart from Denmark), Portugal, Spain, France, southern Italy and Greece [p. 234].

Statistical aspects

Overall, the RRSD was very low at 0.20 (second lowest); within each country there was low regional variation in many countries, though it was a little higher in some of the Mediterranean countries. Of the regional variation, 75% was associated with differences among the countries of Europe. This is lower than for many other cancers, although the Moran Index of spatial correlation was quite high at 0.70. The geographic pattern was of relatively and uniformly low rates in the Mediterranean countries and Scandinavia (except Denmark), and high rates in the United Kingdom, Denmark, Belgium, The Netherlands and Ireland.

Comment

The risk of breast cancer is increased by around 50% in nulliparous compared with parous females. Risk increases with increasing age of the mother at first birth until a first birth occurring after the age of (approximately) 35 years carries a higher risk than nulliparity, indicating that first childbirth after this age no longer confers protection against breast cancer. It has been estimated that a 3.5% increase in relative risk is associated with every year of increase in the mother's age at first birth. Risk appears to be reduced by a late age at menarche and increasing parity, although the role of breast-feeding remain controversial. Risk is increased by a late age at menopause, and an early menopause, whether natural or artificial, contributes to reducing risk.

Breast cancer risk is increased among current users of oral contraceptives, although this risk returns to that of never users within five to seven years of stopping use. An anti-estrogenic effect of cigarettes could theoretically lead to some protection against breast cancer, but the majority of published studies have given null results. Radiation to the breast in high doses has been shown to increase the risk of breast cancer; exposure around the menarche is associated with a particularly high risk. Risk seems to be increased by obesity (in postmenopausal females) and decreased by regular exercise.

Over 100 studies have consistently shown a modest increased risk of breast cancer in postmenopausal females with a high body weight. Epidemiological studies have shown an increase in breast cancer risk above a body mass index (BMI) of, on average, 24 kg/m^2. A pooled analysis of eight cohort studies of about 340,000 females

showed an increase in risk of 30% in females with a BMI of 28 kg/m^2 or above compared with those with a BMI of under 21 kg/m^2. Factors that have been shown to attenuate the association between obesity and breast cancer include family history (heavier females with a family history have a higher risk than similar females without a family history) and the use of hormone replacement therapy (the risk of breast cancer associated with obesity is greater in females who have never used HRT). In contrast, among premenopausal females obesity is not associated with an increase in risk.

The association of breast cancer with diet remains the subject of much research and debate. There is at present little support for an association with fat intake in any form. However, the evidence is increasing that alcohol consumption increases the risk of breast cancer. Of the other factors for breast cancer studied, a positive family history has the effect of increasing the risk of breast cancer, with the maximum effect apparent in premenopausal females who have a first-degree relative with breast cancer at premenopausal ages.

An increased risk of breast cancer with alcohol consumption has been consistently reported in epidemiological studies conducted in different populations. Although not strong (increase risk in the order of 10% for each 10 g/day increase in alcohol intake, possibly reaching a plateau at the highest levels of intake), the association is of great importance because of the apparent lack of a threshold, the large number of females drinking a small amount of alcohol and the high incidence of the disease. Indeed, more cases of breast cancer than of any other cancer are attributable to alcohol drinking among European females. It has been suggested that alcohol acts on hormonal factors involved in breast carcinogenesis, but the evidence is currently inadequate to identify a specific mechanism.

Forty years of clinical trials, the contribution of hundreds of scientists and health workers and the dedication of hundreds of thousands of females to participate in studies lasting for decades has resulted in adequate evidence to support the efficacy of mammographic screening for breast cancer, which has allowed its transfer to the arena of public health policy. Doctors and females can be assured that participation in organised screening programmes, with rigorous quality assurance standards implemented, is of benefit, provided appropriate diagnostic investigation and treatment are available. Special efforts should be made to encourage screening among the more socio-economically deprived members of society. It is important not to over-emphasise the benefit of screening, and to appreciate that this is but one step in the total care of females with the disease. Females should, however, be informed clearly of the level of benefit and of potential risks and costs.

There is nothing known about the aetiology of breast cancer that can explain the geographic pattern demonstrated on the map. The pattern will change in the future as national breast screening programmes make their effects in reducing breast cancer mortality.

The similarities and differences between the geographical patterns in mortality from breast and ovarian cancers are discussed in the section on ovarian cancer (6.15, below).

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6.14: Uterus (ICD-9 179-182)
at all ages (F 6.0) and under 50 years (F 1.7)

Cancer of the cervix, endometrium and other parts of the uterus are very difficult to separate reliably on death certificates. The geographic patterns are therefore presented for all parts of the uterus combined, both for all ages and for females under 50 years. Such deaths in the latter group will overwhelmingly be cancer of the cervix, and will give a good picture of the mortality from this form of cancer in younger females in Europe.

International comparisons

Cancer of the uterus had the fifth highest mortality rate (all ages) in the EU-EEA of 6.0 per 100,000 (Annex 2). There was considerable variation in the national mortality rates with the highest rates in Lithuania (12.3), Hungary (11.2), Poland (11.1), Slovakia (10.9), Estonia (10.6), the Czech Republic (10.3) and Latvia (10.1); rates were also higher than in most of the other countries in Slovenia (8.7) and Denmark (8.4). The lowest national rates were recorded in Greece (3.3), Finland (3.7), The Netherlands (4.0) and Iceland (4.3).

The pattern in the national mortality rates for cancer of the uterus under the age of 50 was closely similar to that at all ages with the highest rates in Lithuania (4.5), Hungary (4.2), Poland (3.8), Slovakia (3.7) and Estonia (3.3). The lowest rates were in Finland (0.5), Iceland (0.7), Luxembourg (0.8), The Netherlands (0.8), Sweden (0.8) and Switzerland (0.9). The pattern was also closely similar to that for mortality from cervical cancer at all ages which showed high rates in most of the former communist countries in central Europe, including the eastern part of Germany, and the Baltic Countries; rates were generally low in the Nordic Countries and western and southern Europe.

Regional variation (box and whisker plots)

There was considerable variation in mortality from cancer of the uterus within countries as well as between countries [p. 235]. There appears to be less variation between countries for uterus cancer mortality rates in females under age 50, although there was still variation within each country [p. 236].

Description of the maps

For mortality from all cancer of the uterus at all ages, the most notable features of the geographic pattern were the aggregations of higher rates in Denmark, southwards through the eastern part of Germany and into Austria and Slovenia [p. 235], while to the east, rates were generally very high in the three Baltic Countries, some western (but not eastern) parts of Poland, and the Czech Republic, Slovakia and Hungary. Rates were also higher in some of the regions of Portugal, but Spain, Italy and Greece had generally low rates. Rates were also low in Sweden and Finland.

When consideration is restricted to mortality in females under the age of 50, the band of higher rates from Denmark southwards to Austria and Slovenia was still present but less prominent, as were the higher rates in Portugal. Rates were again highest in central Europe and low in Italy and Greece as well as Finland and Sweden [p. 236].

Statistical aspects

For cancer of the uterus at all ages, the RRSD was 0.35, in the middle of the range. The spatial correlation (Moran's I) was among the highest at 0.77; and 86% of the total variation over regions was attributed to differences among the countries. This is driven by higher rates in many of the former communist countries: the Baltic Countries, Poland, Hungary, the Czech Republic, Slovakia, Slovenia and eastern Germany. Within each country there was similar, low, regional variation.

For deaths in females under age 50, compared with the all ages results, the rates exhibited more regional variation, with an RRSD of 0.54. There was, however, a similarly high percentage of variation (89%) associated with country – the result of higher rates in the Baltic Countries, Poland, Slovakia and Hungary. Spatial correlation was lower than for cancer of the uterus all ages, at 0.57. Latvia and Germany had the highest RRSDs of 0.35 and 0.34, respectively, followed by Greece at 0.32.

Comment

About 90% of cancers of the body of the uterus occur in the inner lining of the womb (endometrium). The main risk factors are similar to those for cancers of the breast and ovary: early age at menarche, low parity and late age at menopause. These are all related to hormone levels, and result in the uterus being exposed to either prolonged or increased amounts of oestrogen. Another source of oestrogen is hormone treatments that contain only oestrogen. Oestrogen-only hormone replacement therapy (HRT) and unopposed oestrogen therapy used for alleviating the symptoms and harmful effects of the menopause increase the risk of endometrial cancer (among females who have not had a hysterectomy). HRT formulations that include progestin appear to reduce the risk. Sequential oral contraceptives (oestrogen followed by progesterone) increase the risk, but combined oral contraceptives that contain both the hormones have a long-lasting protective effect. There is a slight increased risk of endometrial cancer in females treated with tamoxifen for breast cancer.

Excess body weight and physical inactivity account for over a quarter of cases of endometrial cancer. Hormones in the body are affected by obesity. Fatty tissue contains important enzymes used in the production of oestrogen-like compounds. The more fat in a woman's body, the more oestrogen it can make and the greater the risk of endometrial cancer. Excess body weight is also associated with high blood pressure and diabetes; this association increases the likelihood that those with such conditions may develop endometrial cancer.

Changes in the prevalence of the above aetiological factors over time may be responsible for much of the observed increases in the incidence of uterus cancer which have been observed in many countries in Europe. Differences in the prevalence of the risk factors may in part explain the variations in mortality from cancer of the uterus seen in the EU-EEA. In addition, there is evidence that the higher mortality rates in central Europe may in part have resulted from lower survival rates there than in western Europe.

In 1996, the NIH Consensus Statement concluded that carcinoma of the cervix is causally related to infection with the human papillomavirus (HPV). Reducing the rate of HPV infection by changes in sexual behaviour in young people and/or through the development of an effective HPV vaccine would reduce the incidence of this disease.

A dozen types of human papillomavirus (HPV) have been identified in 99% of biopsy specimens from cervical cancer worldwide and, in Europe, HPV 16 has been reported in 56% of over 3,000 cervical cancer specimens. Five HPV types (HPV 16, 18, 31, 33, 45) account for more than 85% of European cervical cancer cases. In females without cervical cancer, the prevalence of the indicated HPV types is several dozen-fold lower. There is no effective medical treatment against HPV, but very sensitive and specific tests for the detection of HPV DNA in cervical cells have become available. There is sufficient evidence for recommending HPV testing among females who show borderline or low-grade cytological abnormalities. Additionally, HPV testing improves the follow-up of females who have been treated for cervical intraepithelial neoplasia (CIN) lesions and, pending results of ongoing trials, may offer a more sensitive alternative to cytology in primary cervical cancer screening.

A prophylactic vaccine, based on late (L) 1 HPV 16 proteins, has been shown to be safe, highly immunogenic, and efficacious in preventing persistent HPV infections in a trial of 1,523 HPV 16-negative young females in the United States. A multivalent vaccine against the most common oncogenic HPV types may thus ultimately represent the most effective way to prevent cervical cancer worldwide, either alone or in combination with screening. Vaccination would benefit females who do not attend screening programs in the EU-EEA and, if combined with current screening programs, it would allow substantial savings (i.e. less frequent screening tests, fewer treatments, etc.).

Screening for cervix cancer by examination of a cervical smear is now widely recognised as leading to a reduction in the mortality from cervical cancer. It has also been demonstrated to be cost-effective in older females, particularly among those who have not been screened regularly. The impact is greatest where organised screening programmes exist with personal letters

of invitation: this leads to improved attendance, particularly among those females who are at high risk of cervical cancer.

It has been shown, particularly from the Nordic Countries, that a population-based and well-organised screening programme with a valid target age range, the right frequency of screening, and built-in quality assurance programmes at each stage of the screening process, is more successful than opportunistic screening, and that such a programme can be effective in reducing both the incidence and mortality from invasive cervical cancer. It would appear that the most successful programme in terms of reduction in risk of cervix cancer is in Finland, with an official recommendation that a screening programme be started at age 30 and that the smear be repeated every five years. Finland has markedly lower rates of cervix cancer mortality than most of the countries in the EU-EEA.

If cytological screening programmes seem to be effective in preventing invasive cervical cancer and reducing cervical cancer mortality, numerous reports have underscored that that method may fail to detect a certain number of cervix cancers, mainly of the glandular type. It has been estimated that the number of cases of invasive cervical cancer in the UK would have been 57% greater if there had been no previous screening; and in females under 70 years it would have been approximately 75% greater. The study further estimated that full adherence to current screening guidelines could have prevented 1,250 cases of invasive cervical cancer in the UK in the same year but that further steps would have to be sought to prevent some of the remaining 2,300 cases in females under the age of 70. The most frequent reasons evoked to explain the lack of sensitivity of cytological screening are inadequate cell sampling with the spatula and errors in the reading of smear slides. However, even in the best hands, a certain number of false negative cytological tests cannot be explained by sampling or reading problems. Hence, there is a strong feeling in the medical community that besides searching to improve screening coverage, there is also a need for additional ways to improve screening methods for cervical cancer. The first could be the improvement of the spatula used for cell sampling (with current preference for instruments such as the extended tip spatula) and in the automation of cytological reading. It remains, however, to be assessed whether these improvements in cytological methods will prevent all types of false negative results.

Given the implication of HPV infection in cervical cancer, detecting HPV could represent an appealing screening method. A study of 2,009 females having routine screening in England and Wales revealed that 44% of CIN lesions of grade 2/3 detected had a negative cytology and were found only by HPV testing (for types 16, 18, 31 and 33): a further 22% were positive for HPV but demonstrated only borderline or mild cytological changes. However, 25% of CIN 2/3 lesions were not detected by the four HPV tests. Hence, there is convergence between the results obtained when comparing HPV testing with cytology, and cervicography with cytology. However, although appealing, routine HPV testing for cervical cancer screening is still controversial as HPV infection is very common in females under 30 years old, and the females at highest risk are those over the age of 30 with a HPV infection that persists over a long period of time. As it is impossible currently to identify those females with a HPV infection who will develop cervix cancer, HPV testing is proposed to be used in various ways, for example, as an adjunct to cytology for sorting out the cytological results classified as atypical squamous cells of undetermined significance (ASCUS), with referring to colposcopy-biopsy of those ASCUS lesions which are positive for HPV infection. Another proposal consists in testing all females over 30 years of age for HPV, and referring to cytology only those positive for HPV. HPV testing is still to be thoroughly evaluated in order to find the best role it could play in cervical cancer screening.

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6.15: Ovary (ICD-9 183)
(F 6.3)

Ovarian cancer was the fourth commonest form of cancer death in females in the EU-EEA with an annual mortality rate of 6.3 per 100,000.

International comparisons

The highest national mortality rates for ovarian cancer were in Lithuania (9.0), Denmark (8.6), the Czech Republic (8.5), Ireland (8.4), Latvia (8.3), Estonia (8.1), the United Kingdom (8.1) and Norway (8.0) (Annex 2). The lowest rates were in Portugal (3.5), Greece (3.6), Spain (4.2) and Italy (4.8). There was considerable variation in national mortality rates.

Regional variation (box and whisker plots)

There was more variation between countries for mortality from ovarian cancer than for breast cancer, but again relatively small variation within countries [p. 237].

Description of the maps

While there are certain similarities with breast cancer in the geographic distribution of mortality from cancer of the ovary, there are also some potentially interesting differences. As with breast cancer, there were lower than average rates for ovarian cancer in Portugal, Spain, Italy, Greece and much of France. Rates were similarly above average in the United Kingdom and Ireland, Belgium, The Netherlands and Denmark. But rates for ovarian cancer mortality were above average in the Czech Republic, western Poland, the three Baltic Countries, and parts of Norway and Sweden where breast cancer mortality rates were generally below average [p. 237].

Statistical aspects

The RRSD was 0.26, towards the lower end of the range. At 88%, this cancer had the third highest percentage of variation associated with country among cancers in females. This results from the strong geographic pattern, with rates generally low in southern Europe and consistently high over much of northern Europe. Moran's Index was 0.57, roughly in the middle of the range. The within country regional variation was similar to that for breast cancer, with low internal regional variation in most countries but slightly higher such variation among Mediterranean countries.

The correlation between the (smoothed) regional mortality rates for breast and ovarian cancers was 0.48. This confirms the visual impression from the maps [p. 237] that many areas that had relatively high mortality rates for breast cancer also had relatively high rates for ovarian cancer, for example in the UK, Ireland, Belgium, The Netherlands and Denmark, while many areas had relatively low rates for both cancers, for example in France, Spain, Portugal, Italy and Greece. Areas with relatively high ovarian cancer mortality but low breast cancer mortality included the Czech Republic, Estonia, Latvia, Lithuania, Norway and Sweden.

Comment

Epithelial ovarian cancer is the commonest type of ovarian neoplasm and the leading cause of death from gynaecological neoplasms in most western countries. As for other female hormone-related neoplasms, its age-incidence curve tends to flatten off around the age of the menopause. These cancers are more frequent in nulliparous than in parous females, with the former having an approximately two-fold elevated risk compared with multiparous females. Increased risks related to late age at first birth, early menarche and late menopause have not been found consistently.

Oral contraceptive use is protective, the incidence of invasive epithelial cancer being reduced by approximately 40% in females who have ever used oral contraceptives, and to a greater extent in long-term users. Combined oral contraceptives have probably been the major determinant of the decrease in ovarian cancer incidence rates observed in several western countries.

As with breast and endometrial cancer, nutrition and diet remain major open questions in ovarian cancer epidemiology, although nothing is certain at present and further research is required in this area because diet may be more amenable to intervention than reproductive or menstrual history.

There is nothing known about the aetiology of ovarian cancer (or breast cancer – section 6.13 above) which can explain the geographic pattern demonstrated on the maps. There is a large randomised trial of ovarian cancer screening underway in the United Kingdom (UKTOCS) that should quantify the advantages and risks of screening for this form of cancer.

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6.16: Prostate (ICD-9 185)
(M 15.4)

The overall prostate cancer mortality rate in the EU-EEA was 15.4 per 100,000, the third highest rate in males behind cancers of the lung and large bowel. There was, however, considerable variation in the national rates.

International comparisons

The highest national mortality rates were in Norway (23.8), Switzerland (20.1), Denmark (19.8) and Iceland (19.8), followed closely by Belgium (19.4), The Netherlands (19.2) and Ireland (19.0). The lowest national rates were in Greece (9.2), Poland (10.9), Italy (11.2) and Slovakia (12.3) (Annex 2).

Regional variation (box and whisker plots)

Although there was about a two-fold variation in the national mortality rates for prostate cancer, there was relatively little variability within countries.

Description of the maps

High mortality rates from prostate cancer are apparent in Iceland, Norway, much of Sweden, southern Finland and Denmark; there were also higher than average rates in The Netherlands, Belgium and northern France, and Ireland [p. 238]. There was also a band of high rates from Switzerland eastwards into Austria and western Hungary. Low rates are notable throughout Poland, Greece and Italy, and much of Spain.

Statistical aspects

The RRSD for prostate cancer was 0.20, one of the lowest values for cancers in males. The variation associated with differences between countries was, however, quite high at 85%. Rates were higher in north Europe, especially Norway, and lower in southern Europe. Moran's I was quite high at 0.66. Prostate cancer is an example of a site with low regional variation and high spatial correlation.

Comment

Prostate cancer has become the most commonly diagnosed cancer in males in several developed countries. With increasing age, most males will develop microscopic foci of prostate cancer whether or not they live in a population at a high or low risk for the invasive form of the disease. Although a majority of males will develop microscopic disease, only a small percentage of these slow-growing tumours will develop into invasive prostate cancer and an even smaller proportion will cause premature death. The principal focus of epidemiological investigations of prostate cancer, therefore, has to be the identification of factors – amenable to intervention – that cause the common microscopic form to progress to invasive disease.

Prostate cancer incidence is highest in western populations and particularly so among the black population of the United States. The disease is uncommon in populations of many Asian and other developing countries. Consideration of the public health importance of prostate cancer should be tempered with the observation that in many countries the average age at death from prostate cancer is approaching 80 years. Indeed, as data from England and Wales demonstrate, the average age at diagnosis of prostate cancer is greater by a considerable margin than that for other common cancers, such as breast and colorectal.

The epidemiology of prostate cancer has been notoriously difficult to study and the disease continues to present formidable challenges to epidemiologists. Much of the difficulty is linked with our lack of knowledge of disease specificity. Both the phenotype(s) and genotype(s) of prostate cancers are heterogeneous and studies that combine all forms of prostate cancer together are, therefore, likely to attenuate any associations that might only arise with particular sub-types. This problem has gained more widespread recognition in recent years and epidemiologists have attempted to increase disease specificity in their studies largely by stratifying on

severity e.g. histological grade, Gleason scores, stage of disease, progression and death. So far, although this approach has occasionally produced strengthened associations with various factors, it has not greatly advanced our understanding.

The causes of prostate cancer have been investigated in numerous case-control studies and a few prospective cohort studies. Apart from disease specificity, there have been other problems with epidemiological studies of prostate cancer, particularly small sample sizes and, therefore, poor statistical power, poor exposure measurement, and inappropriate study designs. The best available epidemiological evidence about prostate cancer is to be obtained from only a handful of large well-conducted case-control studies and cohort studies. Although historically case-control studies have identified numerous putative risk factors, only age and a family history of prostate cancer can be considered to have been well-established. During the 1990s, prospective studies suggested that specific fatty acids, antioxidant vitamins, and carotenoids may alter prostate cancer risk. There were also reports that changes in plasma levels of key hormones and associated molecules and naturally occurring variants in genes (polymorphisms) of the androgen, vitamin D and insulin like growth factor 1 (IGF-1) prostate cell growth regulatory pathways also alter risk, and conjectures that dietary factors may modulate risk by interacting with these pathways.

Although there are a number of new leads in regard to risk factors for prostate cancer, more research is required to confirm them. There is little purpose in conducting further case-control studies of prostate cancer, particularly since the widespread use of PSA testing, and much more attention will have to be paid in future epidemiological studies to prostate tumour sub-classification in terms of method of detection, markers of biological "aggressiveness" and genetic changes. Many of these new leads involve the possible influence of polymorphisms in key genes involved in important physiological processes in the prostate. To fully explore the complexity of interrelationships between the several elements in these pathways will require very large cohort studies in which blood is sampled prior to diagnosis. Such studies will be important for identifying which modifiable aspects of lifestyle (diet, alcohol, tobacco, physical activity etc.) might be targeted for intervention to reduce risk.

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6.17: **Testis** (ICD-9 186)
(M 0.4)

Testicular cancer mortality was very low – although the incidence was much higher and has been increasing. The successful outcome of treatment for testicular cancer was one of the major events in medical oncology during the last three decades of the 20th century.

International comparisons

Overall, the mortality rate for testicular cancer in the EU-EEA was 0.4 per 100,000. In all the countries of western Europe the national mortality rates were very low, less than 0.5 per 100,000, except in Denmark (0.7). Rates were, however, well above average in several of the countries in central Europe: the Czech Republic, Latvia and Hungary (all 0.9), and Poland, Slovakia, Lithuania and Estonia (all 0.7) (Annex 2).

Regional variation (box and whisker plots)

There were considerable differences between countries, with the rates clustering in two groups at 0.7 to 0.9 per 100,000 and around 0.3; as would be expected with generally very small numbers of deaths and low rates, there was wide variability in the values within countries [p. 239].

Description of the maps

The main feature of the geographic distribution of testicular cancer mortality is the grouping of areas with high rates in the former communist countries – the eastern part of Germany, Poland, the Czech Republic, Slovakia, Hungary, and the three Baltic Countries. The patchwork appearance of the remainder of the map simply reflects the wide random variation inherent in rates based on very small numbers of deaths [p.239].

Statistical aspects

There was moderate to high regional variation for cancer of the testis with an RRSD of 0.54 which gives it a rank of 6 out of 22. Moran's I statistic was 0.29 which is quite low and 77% of the total regional variation was associated with differences between countries. These statistics all confirm the visual impression of the map (described above).

Comment

The incidence rates of testicular cancer are increasing almost everywhere for reasons that are not entirely clear. Hypotheses to be studied are complicated and exposure assessment is difficult. For a form of cancer which is increasing so much, there is some degree of complacency in undertaking aetiological studies because of the very low, and generally declining, mortality rates.

A decline in mortality from testicular cancer has been widely demonstrated in many countries following the demonstration of effective therapy of platinum based drugs (in 1977) even against a background of increasing incidence. The decline in mortality rates from testicular cancer was evident in nearly all countries which adopted the new therapy between 1975 and 1985, with large decreases in the relative risk of death apparent almost everywhere. It is widely appreciated that the application of chemotherapy in the treatment of germ cell tumours exemplifies the best results to be expected from this approach to solid tumours, since the majority of patients treated are now cured. 80-90% of patients with testicular cancer could expect to be cured of their disease and in most countries this seemed to be so, but not in central Europe where about 1 in 2 cases were still dying in the mid-1980s. Any fundamental difference in biological behaviour in central Europe is unlikely and a more likely explanation is that the differences in mortality were related to lack of curative chemotherapy, including cisplatin, or to deficiencies in patterns of referral.

The poor outcome from testicular cancer in central Europe could be related to the lack of financial resources to purchase the expensive drugs necessary to treat disseminated testicular cancer.

The economic situation in many of these countries has been changing rapidly, including in Slovakia where there has been an effective population-based cancer registry for many years, making comparison of trends in incidence and mortality from testicular cancer possible. Another interesting aspect of testicular cancer treatment in Slovakia has been the establishment in 1982 of a specialist treatment centre for non-seminoma testicular cancer in the Department of Urology in the School of Medicine of Bratislava. This centre initially treated approximately 50 new patients per annum with this disease, employing a multidisciplinary approach. Following this, there has been the establishment of similar specialist units in the largest hospitals in central and eastern Slovakia and whereas the incidence rate of testis cancer has gradually increased between 1968 and 1990, the mortality rate has declined slightly since the early 1980s following an initial increase between 1968 and 1980. The gap between incidence and mortality is widening, indicating increasingly efficacious therapy of patients with testicular cancer in Slovakia.

In no country of central Europe was the economic change as rapid as in the former German Democratic Republic (DDR, known as East Germany). Mortality data from East Germany have become available since 1980. In the former Federal Republic of Germany (FRG, known as West Germany), the mortality rate from testicular cancer peaked around the mid-1970s and by 1995 had reached 0.4 per 100,000, less than one-third the mortality rate in 1977 (1.4 per 100,000) when details of treatment advances were first published. In East Germany, however, the mortality rate remained essentially unchanged until the opening of the border in 1989 (1.5 per 100,000) and has subsequently declined to almost the same level as in the former West Germany.

Thirty years ago, testicular cancer was almost invariably fatal, whereas today, in most developed countries, testicular cancer is almost always curable. This has been a major achievement for cancer control. Testicular cancer could become a very rare cause of death around the world if the knowledge currently available could be implemented world-wide. It is clear that when the economic situation is such that the necessary drugs become available, large reductions in mortality can occur quite rapidly. It is clear also than when treatment can be centralised, outcome also improves.

This emphasises the fundamental difference between the control of testicular and prostate cancers. Testicular cancer could be very nearly eliminated as a cause of death by implementing what is currently known.

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6.18: **Bladder** (ICD-9 188)
(M 6.8; F 1.4)

Bladder cancer had the seventh highest cancer mortality rate in males the EU-EEA, but was of far less importance in females. Overall, the mortality rate for cancer of the urinary bladder (bladder cancer) in the EU-EEA was about five times higher in males than in females. There was considerable variation in the national mortality rates in males, but little variation in females, in whom the rates were consistently much lower.

International comparisons

In males, the highest national mortality rates were in Denmark (9.1), Malta (8.5), Spain (8.5), Latvia (8.4), Poland (8.1), Hungary (8.1), Italy (7.7) and Lithuania (7.7) (Annex 2). The lowest rates were in Finland (4.0), Sweden (4.2) and Ireland (4.4).

In females, the highest national mortality rates were also in Denmark (2.7) and Malta (2.3), followed by the United Kingdom (2.0). A large number of countries had low rates of around 1.0: Finland, France, Greece, Italy, Poland, Portugal, Spain, Sweden, Estonia, Latvia and Lithuania.

Regional variation (box and whisker plots)

Although there was around a two-fold range in the national mortality rates for males, there appeared to be relatively low variability within countries [p. 240]. For females, there was much less between country variation, but there was wide variability within countries (partly due to the rates being based on much smaller numbers of deaths) [p. 241].

Description of the maps

An intriguing feature of the geographic map of bladder cancer in males is the high rates in coastal areas of Spain and parts of the Mediterranean coastlines of France (including Corsica) and Italy (including Sardinia and Sicily) [p. 240]. There were high rates in other regions of Spain, northern Italy and northern Greece. Rates were high in Denmark and in the northern part of the former East Germany and Poland, and in Lithuania and Latvia. There were low rates throughout the Nordic Countries (other than Denmark), Ireland, the south of Germany, Austria and Switzerland.

In females, rates were high in Denmark and northern Germany (as in males) but were also high in parts of the United Kingdom (especially Scotland) and The Netherlands [p. 241]. There were areas of low rates in the north of Europe except Norway: Sweden, Finland, the Baltic Countries and much of Poland; and in most of southern Europe: Portugal, Spain, France, Italy and Greece.

Statistical aspects

The three main spatial statistics all had similar values in males and females. The RRSD was 0.24 in males and 0.32 in females, both towards the lower end of the range. The variation explained by differences between countries was 67% in males and 60% for females, the lowest for males and second lowest for females. Spatial correlation was 0.51 in males and 0.46 in females, both in the middle of the range. Given these similarities, the correlation between the male and female rates was low at 0.23. This is because there were only relatively weak spatial patterns that were not the same in males as in females. There was relatively large within country variation in Germany in both males and females, and in Austria, the Czech Republic, Lithuania and Poland but only for females. In Germany this variation was associated with low rates in the south of the country and areas of high rates in the north and east.

Comment

The evidence for an association of bladder cancer with cigarette smoking is overwhelming: the only remaining question surrounds the strength of the association. In different regions of the world, smoking accounts for one third to a half of bladder cancers diagnosed among males and about one quarter of that among females. For all cigarette smokers, estimated relative risks for smokers (relative to non-smokers) have been generally

around 2.0, although some higher estimates have been reported. The large majority of studies find relationships between bladder cancer risk and 'dose' of cigarettes smoked. Furthermore, smokers of black tobacco appear to have around a 40% higher risk than smokers of blond cigarettes.

Cohort studies on mortality according to level of alcohol consumption find no excess of bladder cancer. A large number of case-control studies have also investigated the association between alcohol intake and bladder cancer risk and have found no association. Only a few studies conducted in Germany, France and Turkey reported some increased risk and an element of dose-response. Generally, the risk estimates in these studies were significant only for the heaviest drinkers. Taken together, the available data show no association between risk of bladder cancer and alcohol consumption.

Overall, the data from studies of coffee consumption are consistent with a weak positive relationship with the occurrence of bladder cancer, but the possibility that this is due to bias or confounding cannot be excluded. However, there is a certain amount of lack of internal consistency within most of the positive studies which should keep the question of a causal association open: in some studies the association is present in females but not in males and in others *vice versa* and there is a lack of a consistent dose-response relationship.

Several other factors are related to cancer of the bladder, including occupational exposure to aromatic amines, coal tar and, possibly, other chemicals; exposure to *Schistosoma haematobium* and other infectious agents; and exposure to some drugs such as phenacitin, chlornaphazine and cyclophosphamide. Occupational exposures have generally been considered to be the second most important risk for bladder cancer after smoking. The proportion of bladder cancers attributable to occupation ranges between 16 and 24 per cent in several investigations conducted in different countries. Among occupations most frequently reported to be associated with an increased risk of bladder cancer are printing, plastics and synthetics, rubber, mining, metal, and dyestuff industries, and those professions which involve exposure to dyes, spray paints, zinc, oils, petroleum stone dust, metal dust/fumes and herbicides. Relative risks for bladder cancer in males and females who are engaged in these occupations are generally around a factor of 2 with higher risk for chemical and metal workers, press operators, and those who exposed to dyes, paints and herbicides. The most common occupational carcinogens related to bladder cancer are benzidine 4-aminobiphenyl, 2-naphthylamine, aminobiphenyl, dichlorobenzidine, orthodianisidine and orthotolidine. Most of these exposures are regulated and occupational bladder cancer may be shrinking in importance in many western countries through a combination of legislation against carcinogens and a cleaner workplace: some of the practices responsible for bladder cancer in the west may, however, be in the process of being exported to the developing world where occupational hygiene standards may not be so rigorously enforced.

In terms of explaining the geographic pattern, the high rates in males in Spain could well be associated with the prevalent habit of smoking black tobacco, which carries an excess risk of bladder cancer over Virginia cured tobacco. The high rates in Denmark are a reflection of the high incidence rates which have persisted there for decades. The pattern of high risk areas in males – but not females – in areas around the Mediterranean coast is interesting and may be related to differences in smoking habits between the sexes.

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6.19: Kidney and other urinary organs (ICD-9 189)
(M 4.8; F 2.1)

Renal cell carcinoma in adults represents around 80% of the cancers of the kidney, renal pelvis and ureter that are grouped together under this ICD code. In general, rates for renal pelvis and parenchymal cancers correlate well. In children, most of the cancers are nephroblastomas.

Overall, the mortality rate in the EU-EEA for cancer of the kidney and other urinary organs (kidney cancer) in males (4.8 per 100,000) was over twice that in females (2.1). There appears to be considerable variation in the national rates between countries.

International comparisons

In males, by far the highest national mortality rate was in the Czech Republic (10.8); several countries had rates between 6 and 8 per 100,000: Estonia (7.9), Lithuania (7.6), Latvia (6.9), Iceland (6.8), Hungary (6.6), Slovakia (6.4) and Poland (6.3) (Annex 2). The lowest rates were in Portugal (2.3), Greece (2.6), Spain (3.3) and Ireland (3.5).

In females, the highest national mortality rate was also in the Czech Republic (4.9), followed by Iceland (3.7), Estonia (3.3) and Lithuania (3.1). The lowest mortality rates were recorded in Portugal (1.0), Greece (1.1) and Spain (1.2).

Regional variation (box and whisker plots)

There was considerable variation in national mortality rates in both males and females [p. 242-243]. The within country variability was generally small in countries with low rates, but was wider in some countries with higher rates, particularly in females.

Description of the maps

The strongest feature of the geographic distribution of kidney cancer mortality in males is the strong gradient from the low rates in Portugal, Spain, southern Italy and Greece through rates generally close to the average in France, northern Italy, Switzerland, Slovenia, Belgium, The Netherlands and the United Kingdom and Ireland, to high rates in eastern Germany and Austria, the Czech Republic, and western parts of Poland, Slovakia and Hungary. Rates were also generally high in all three Baltic Countries. Mortality rates in all the Nordic Countries were generally close to the average [p. 242].

The map for females shows that both the between- and the within-country variability in mortality rates were closely similar to the patterns in males. There were generally low rates in Portugal, Spain, Italy and Greece and around average rates in Ireland, the southern parts of the UK, France, Belgium and Switzerland. High rates, as in males, occurred in northeast Germany, the Czech Republic, eastern Austria, and western Poland, Slovakia and Hungary, and in the Baltic Countries. Many areas in the Nordic Countries had above average rates in females but not in males [p. 243].

Statistical aspects

Overall regional variation was not very high, with RRSDs of 0.33 for males and 0.36 for females. For both males and females, Italy had the highest internal regional variation (RRSDs of 0.29 and 0.31, respectively). There was almost as much relative variation in Italy as there was in the whole of Europe. From the maps [p. 242-243] it can be seen that this manifests itself as an increase in rates from south to north. The spatial correlation of the rates was 0.63 for males and 0.54 for females, both around the middle of the range, but there was a high male-female correlation of 0.84 in line with the similar spatial patterns visible in the maps.

Comment

The incidence of kidney cancer increased at the end of the 20th century, rising by 38% over the period 1974-1990. An increased detection rate, with the use of newer radiological imaging techniques, appears responsible for much of the increased incidence. The

five-year survival observed in kidney cancer patients has improved from 52%, in patients diagnosed in 1974-1976, to 57% among patients diagnosed from 1990 to 1994. The gain in survival is in great part due to an earlier detection of localised resectable tumours; mortality from this malignancy has not declined over the same period. A rise in the detection of advanced kidney cancer has also been reported, pointing to a genuine increase in kidney cancer incidence.

Cancers of the upper and lower urinary tracts are important, although somewhat neglected, public health problems. Currently there are over 100 population-based cancer registries providing cancer incidence data of recognisably high-quality; the most recent data available cover the period 1998-2002 (Curado et al., 2007). Out of a total of over 7,000,000 cancer cases (excluding non-melanoma skin cancers) registered in males there were around 450,000 bladder tumours (6.4% of all cancer in males), 200,000 kidney cancers (2.9%), 80,000 testicular cancers (1.1%) and 15,000 cancers of the penis (0.2%). In total, just over 10% of all incident cancers in males world-wide occur at urological sites (other than prostate). In females, there were a total of 6,500,000 incident cases of cancer in the same populations. Of these, around 150,000 were bladder cancers (2.3% of all cancers in females) and 125,000 were kidney cancers (1.9%). A total of just over 4% of all cancers in females were of urological origin.

Cigarette smoking is the best identified aetiological agent and a major cause of bladder cancer, cancer of the renal pelvis and adenocarcinoma of the kidney, although the latter association remains less well quantified. There is no consistent evidence on the role of alcohol or methylxanthine-containing beverages on the risk of renal cell cancer. Historically, occupational exposures have been investigated as causes of bladder cancer, although the proportion of bladder tumours related to such exposures is probably in decline. Hormonal influences are frequently cited as being aetiologically important in cancers of the prostate and testis although the precise hormonal determinant(s) remains unclear and further research is needed. Dietary and nutritional factors appear to have essential roles in the aetiology of most forms of urological tumours although the risks and the mechanisms have yet to be established and quantified. Recent studies have investigated the roles of obesity, physical activity, hypertension, diuretics, and phenacetin and paracetamol abuse. Within the constraints of our knowledge, up to one half of urological cancers could be avoided, about one-third by cessation of cigarette smoking alone. The increases in the incidence of urological cancers should serve to focus activity on the development of programmes focused on primary prevention.

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6.20: Brain and central nervous system (ICD-9 191 and 192) (M 4.6; F 3.2)

Primary tumours of the brain and nervous system are not uncommon, but their reported incidence depends to some extent on the standard of medical care which is available and the ability to exclude metastatic tumours. Most of these neoplasms are intracranial, with intraspinal tumours representing about ten percent of the total. This disease group includes a disparate range of tumour types (including gliomas and meningiomas which are derived from different tissues) and the various histological types have different prognosis and biological behaviour.

Overall, the mortality rate in EU-EEA from cancer of the brain and central nervous system (brain cancer) was about 50% higher in males (4.6 per 100,000) than in females (3.2).

International comparisons

In males, the highest national mortality rates were in Greece (7.3), Hungary (6.5), Ireland (6.1), Iceland (6.0) and Poland (6.0) (Annex 2). The lowest mortality rates were in France (3.9), Italy (4.0), Latvia (4.2), Spain (4.2), The Netherlands (4.2), Portugal (4.3), Austria (4.3) and Norway (4.4).

In females, the highest national mortality rates were in Iceland (5.1), Greece (4.6), Hungary (4.5), Ireland (4.4), Luxembourg (4.3), Belgium (4.1), Finland (4.1) and Estonia (4.1). The lowest national rates were in France (2.6), Italy (2.7), Portugal (2.7), Spain (2.7) and The Netherlands (2.9).

Regional variation (box and whisker plots)

For both males and females, there were only low levels of variability in the mortality rates, both between and within countries [p. 244-245].

Description of the maps

In males, rates were generally low in the south and west of Europe, including Portugal, Spain, France, Italy, Switzerland, Austria and southern Germany. Rates were noticeably higher than average in most of Greece, Hungary, the Czech Republic, Slovakia and Poland, and in parts of northern Germany and Belgium [p. 244]. The map for females shows both that the between- and within-country variability in the rates were very closely similar to those in males [p. 245].

Statistical aspects

The RRSD for males was 0.18 (rank 21 of 22) and 76% of the total variation was associated with differences between countries. For females, the RRSD was 0.20 (rank 22 of 24) and 79% of the variance was associated with differences between the countries. The high regional component associated with country is mainly due to the generally higher rates in Greece, Ireland, Poland and Hungary and lower rates in France, Portugal, Spain and Italy.

Moran's I was 0.29 for males and 0.25 for females, both values towards the lower end of the range, and there was a correlation of 0.68 between the rates for males and females.

Comment

Epidemiological study of cancers of the brain and nervous system is greatly impaired for two reasons. First, there is a wide variety of distinct clinicopathological entities which appear in this disease group, some of which may be associated to varying degrees with different aetiological factors. Second, there are problems associated with the diagnosis of intracerebral and intraspinal tumours including differentiation between primary and secondary neoplasms; there is a related issue that many apparently benign neoplasms can be fatal depending on the exact anatomical site of the tumour and in consequence the degree to which benign tumours are recorded as malignant may vary. Analytical studies can be further hampered by difficulties in interviewing patients who may

have difficulty remembering or communicating responses regarding recent exposures or exposures in the distant past. Gliomas, meningiomas and other intracranial neoplasms have generally been grouped together in epidemiological studies despite the fact that gliomas and meningiomas are derived from different tissues and the various histological types have different prognosis and biological behaviour.

Adult brain tumours have been noted to occur more frequently in a number of different occupational groups including a number of professional and managerial occupations; some occupations with potential carcinogenic exposures in the workplace such as rubber industry workers; and in farming and the electrical industries. When cancer incidence rates are examined subdivided by histology, it has been found that the risk of astrocytoma was elevated among automobile repair workers, workers in justice, public order and safety, police and fire protection officers, and machinists; farmers had an increased risk for non-astrocytoma cell types. The risk of brain tumours has been shown to be increased by cigarette smoking but this has not been a consistent finding.

Primary tumours of the brain and nervous system are the second commonest cancer in children. Exposure to ionising radiation appears to be a risk factor for this form of cancer. Increased risk was found among children exposed in utero when mothers had pelvimetry late in pregnancy and among cohorts of children who received X-ray treatment for ringworm of the scalp. Tobacco smoke contains several known carcinogens and can induce DNA adducts in human placenta and haemoglobin adducts in foetuses. In a large, multicentre study, there was no association between the risk of brain tumours in the child and parental smoking prior to pregnancy, maternal smoking or regular exposure to others' cigarette smoke during pregnancy at home or at work, or passive smoking by the child during the first year of life. These results did not vary with the child's age at diagnosis, the histological type of tumour, or study centre.

The use of cellular phones and possible adverse health effects related to their use, attract much attention. Reports on brain tumour excesses occurring among phone users, case stories in the press and reports on thermal as well as magnetic effects on exposed tissue hypothesised to stimulate tumour growth, combined with the explosion in subscribers to cellular phones, raise public concern. The radiation from cellular phones is characterised as non-ionising alongside that from radar, microwave ovens and electrical wiring configurations. The radio frequency signals emitted from the devices range between 450 and 2200 MHz, i.e. in the microwave region of the electromagnetic spectrum. A recent comprehensive review on the epidemiological literature has been carried out and published by the Swedish Radiation Protection Authority. They conclude after review of nine major studies that no significant association was present between brain tumours and use of cellular phones, irrespective of duration of use, type of phone (digital or analogue), tumour morphology or laterality. The conclusions are supported by observing that there is no biological mechanism which supports a causal relation and there is no evidence of adverse effects from laboratory animals.

At present only a small proportion of brain tumours can be attributed to a defined cause; and there is more suspicion than proof surrounding the nature and weight of several other risk factors for tumours of the nervous system. There is nothing known about risk factors and their distribution in the European population which can explain the strong geographic patterns – so closely similar in males and females – observed in the maps.

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Chapter 6.21: Thyroid (ICD-9 193)
(M 0.4; F 0.5)

Thyroid cancer is relatively infrequent on a world-wide basis, representing 1-2% of all cancers, although in adolescents and young adults it is one of the most frequent neoplasms. Incidence rates are approximately three times higher in females than in males; the excess in females varies with age, being greater in the young. The majority of thyroid cancers are not fatal and there is a wide gap between incidence and mortality which must be borne in mind when examining geographical patterns in mortality.

Overall, mortality rates for thyroid cancer were low, with similar rates in males (0.4 per 100,000) and females (0.5) in the EU-EEA.

International comparisons

In males, the highest national mortality rates were in Austria (0.7) and Hungary (0.6); all other national rates were 0.6 or lower (Annex 2).

In females, the highest national mortality rates were in Hungary (0.8), Latvia (0.7), Slovakia (0.7), the Czech Republic (0.7), Lithuania (0.7) and Poland (0.7). All other national rates were 0.6 or lower.

Regional variation (box and whisker plots)

For both males and females, there was some variability between countries. As would be expected for rates based on small numbers of deaths, there was considerable variability in rates within countries [p. 246-247].

Description of the maps

In males, there appears to be an aggregation of high rates in the centre of Europe – the neighbouring countries of Austria, central and southern Germany, Switzerland and the west of the Czech Republic [p. 246]. There were generally low rates in the United Kingdom, Spain, Portugal, France and Greece.

In females, there was the same pattern of generally higher rates in Austria and adjacent countries, and mostly lower than average rates in much of western Europe [p. 247]. However, it must be kept in mind that all these mortality rates were very low in absolute terms.

Statistical aspects

There was average regional variability with RRSDs of 0.37 for males and 0.32 for females. There was some evidence of a country based pattern, with 76% of the regional variation in the rates for males associated with country and 70% for females. There was a tendency for higher rates in both sexes in Austria and in the former communist countries of central Europe.

Spatial autocorrelation was very low for both males and females with Moran's I values of 0.18 and 0.20, respectively; these were the lowest value for males and the second lowest for females. It can clearly be seen in the maps that for both sexes there are very scattered patterns of red and green areas and no aggregations of higher or lower rates except possibly in Austria. In part, this is because the numbers of deaths in most regions were very low, resulting in apparent random variation in the mortality rates. There was a spatial correlation of 0.53 between the rates for males and females.

Comment

Thyroid cancer is a rare form of cancer in general, but it is characterised by the wide variation in the degree of malignancy exhibited by the various histological types ranging over a whole spectrum from relatively benign to rapidly fatal. There is evidence that in many developed countries mortality has been decreasing while incidence has been increasing. Many factors complicate the interpretation of thyroid cancer trends, in large part because of the widening of the concept of thyroid malignancy since the early 1960s with the increasing emphasis on cytological rather than on architectural features and the subsequent inflation of thyroid cancer incidence rates. This change in attitude has been paralleled

by the spread of scintigraphy and fine needle biopsy and the increasingly aggressive approach to the management of thyroid nodules.

Ionising radiation is the only definitely established cause of thyroid cancer in humans, although only a small proportion of thyroid cancers can be accounted for by radiation. The thyroid tissue is particularly susceptible to radiation at young ages, and considerable excess rates have been observed in Hiroshima and Nagasaki, as well as in subjects irradiated for thyroid hypertrophy during childhood. The risk was elevated 20-fold for the papillary type and 50-fold for the follicular type in subjects irradiated below the age of 20 years. The thyroid gland is highly susceptible to ionising radiation presumably because of its superficial location, high level of oxygenation, and high cell turnover rate.

A pooled analysis of seven studies revealed that thyroid cancer was induced even by low doses of brief external gamma radiation in childhood, but rarely developed after exposure in adulthood. Data from the atomic bomb survivors underline the strong modifying effect of age at exposure, with no excess risk seen in individuals older than 20 years. The Chernobyl nuclear accident in April 1986 led to a massive release of radionuclides into the environment. Although vast areas of Europe were affected by Chernobyl-related ionising radiation, the accident had the greatest impact in Belarus, Ukraine, and the Russian Federation. Epidemiological studies that have investigated the link between the Chernobyl accident and cancer have largely focused on malignant diseases in children, specifically thyroid cancer and leukaemia. During the first fourteen years after the Chernobyl accident, approximately 1,800 thyroid cancers were diagnosed in the three most contaminated countries among children younger than 15 years, whereas only 3-4 childhood thyroid cancers were registered in the same area annually before the accident. No increased thyroid cancer as a consequence of the Chernobyl accident has been identified in adults.

The major concern regarding medical use of ionising radiation has been the possibility that thyroid examinations or treatments using radioiodine causes thyroid cancer. The annual number of thyroid examinations using radioiodine is currently 5 per 1000 individuals in the western world. Patients treated with ^{131}I for hyperthyroidism are almost all adults and no increased risk of thyroid cancer is seen among these patients. A study which estimated thyroid cancer risk in a cohort of 35,074 Swedish subjects who had been subjected to diagnostic ^{131}I with an average dose of 1.92 megabecquerel (0.5 Gy to the thyroid itself) and followed up for 20 years found 50 incident cases of thyroid cancer compared with 39.4 expected (Standardised Incidence Ratio 127, 95% Confidence Interval (94, 167)). These results were fairly reassuring, although thyroid cancer risk was found to be highest among those receiving the highest dose of ^{131}I. However, such observations could be confounded by those individuals receiving the highest doses being suspected of having thyroid disease. Prior thyroid diseases, benign nodules and goitre are also associated with substantially elevated risk.

Differences in iodine intake may be one factor explaining the geographic variation in incidence, high iodine intake being associated with a slightly increased risk of developing thyroid cancer. In general, lifestyle factors have only a small effect on the risk of thyroid cancer. The thyroid gland is highly sensitive to radiation-induced oncogenesis. This is verified by numerous reports from survivors after Hiroshima and Nagasaki, and from the Nevada, Novaja Semlja and Marshal Island atmospheric nuclear tests, as well as by investigations of earlier medical use of radiation for benign diseases in childhood. The thyroid gland of children is especially vulnerable to the carcinogenic action of ionising radiation and there appears to be a dose-response relation for the risk of developing cancer after exposure to radioactive iodine.

Apart from these factors, there is little conclusively known about the aetiology of thyroid cancer. The long suspected influence of iodine deficiency is not totally understood. Two current areas of epidemiological interest are diet and female hormones, thyroid cancer being one of the few cancers where the incidence rate is higher in females. With reference to diet, the scanty available data tend to suggest that a poorer diet, particularly if containing natural goitrogens, is related with elevated risk. Positive associations have also been reported with nulliparity, late age at first birth and the use of oral contraceptives or menopausal replacement treatment, but the evidence on these is still open to debate.

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6.22: **Hodgkin's disease** (ICD-9 201)
(M 0.7; F 0.4)

Hodgkin's disease is nowadays a highly curable neoplasm. Development of successful therapy for this malignancy is a great success for medical oncology. Hodgkin's disease is unusual among human malignancies in that the epidemiology suggests an infectious aetiology.

Overall in the EU-EEA, mortality in males (0.7 per 100,000) was about 65% greater than in females (0.4). These overall rates were very low, representing less than 0.5% of those for all cancers in both males and females.

International comparisons

In males, the highest national mortality rates were in Lithuania (1.4), Poland (1.4), Estonia (1.3), Latvia (1.2), Austria (1.2), the Czech Republic (1.2) and Greece (1.1) (Annex 2). The lowest national rates were recorded in Sweden (0.3), Norway (0.4), France (0.4) and Switzerland (0.4). No deaths were recorded from this cause among males in Iceland during this period.

In females, the highest mortality rates were in the Czech Republic (0.8), Austria (0.8), Lithuania (0.8), Latvia (0.8), Estonia (0.7) and Poland (0.7). Rates in most of the other countries were 0.2 to 0.4 per 100,000.

Regional variation (box and whisker plots)

There was considerable variation, four- to five-fold, in rates between countries for both males and females [p. 248-249]. As would be expected because the rates for small areas were generally based on very low numbers of deaths, there was very wide variability in the rates between countries.

Description of the maps

High mortality rates for Hodgkin's disease in males were found in much of central Europe: the eastern parts of Austria, and across the former communist countries – the eastern part of Germany, Slovenia, Hungary, the Czech Republic, Slovakia, Poland and the Baltic Countries; rates were also high in many regions of Greece. Rates were generally low in the western parts of Austria and Germany, as well as in the rest of western mainland of Europe and all the Nordic Countries [p. 248].

In females, the pattern was closely similar to that in males, with high rates across the former communist countries in central Europe and in Greece, and generally low rates in western Europe and the Nordic Countries [p. 249].

Statistical aspects

For both males and females the regional variation in the mortality rates for Hodgkin's disease was in the middle of the range, with RRSDs of 0.48 in males and 0.42 in females. There was extremely high internal regional variation within Austria, with RRSDs of 0.86 for males and 0.81 for females, associated with high rates in two regions in the east compared with the low rates in the other regions in Austria. There was some evidence of mortality differences between the countries, with 68% of the total regional variation associated with between country differences for males and 65% for females.

Spatial correlation was low, with Moran's I of 0.35 for males (rank 17 of 22), and 0.21 for females (rank 21 of 24). The correlation between the male and female rates was moderate at 0.56.

Comment

Hodgkin's disease is characterised by the presence of the Reed-Sternberg giant cell. Hodgkin's disease has been one of the few neoplasms for which considerable advances in survival have been achieved over the past twenty years through the impact of effective treatment. The disease has a bimodal age curve: incidence rates rise early in life, peak in the late 20s and then decline to around age 45. Thereafter the incidence subsequently increases with age. One

suggested explanation this bimodal distribution is that Hodgkin's disease may be the result of two distinct aetiological processes. This notion is supported by the observation that among younger adults, 15 to 39 years of age, Hodgkin's disease of the nodular sclerosing type predominates but at older ages the predominant type changes to the mixed cellularity form.

MacMahon (1957) first made the observation that Hodgkin's disease in young adults could have an infectious aetiology; the similarity of its age distribution with that of paralytic poliomyelitis and Epstein-Barr Virus (EBV) infections led to the formulation of the 'late-host-response' model. This excludes the effect of direct contagion but proposes that early exposure to some relatively common agent is benign and confers subsequent immunity but later exposure can (although not commonly) lead to Hodgkin's disease. Evidence supporting this hypothesis is found in a variety of studies linking limitation of childhood social contacts and higher childhood social class with subsequent increased risk of Hodgkin's disease.

Studies of space-time clustering have generally been inconsistent but more recent investigations of purely spatial clustering have consistently shown evidence of weak clustering. The overall results available suggest that shared social experience during childhood and adolescence may be a feature of subsequent Hodgkin's disease. Elevated risks of disease have been recorded among agricultural workers, who presumably are more likely to live in isolated areas, although other possible aetiological factors such as exposure to pesticides have to be considered. Some studies have reported increased risk of Hodgkin's disease associated with employment in wood-related industries, the chemical industry and among schoolteachers, although the evidence is not conclusive. It is not possible to provide quantitative estimates of the attributable risk for various occupational exposures. Other factors investigated including reproductive patterns, motivated by the observation of a lower incidence in females during reproductive life, and tonsillectomy, offer little consistent support for association.

Infectious agents are known or suspected to play a major role in haemo-lymphopoietic tumours (non-Hodgkin's lymphoma, Hodgkin's disease and leukaemia). Certain viruses (Epstein Barr virus (EBV); human immunodeficiency virus (HIV); human-T-cell leukaemia/lymphoma virus 1; Herpes Simplex type 8; and HCV and HPV) account for an ill-defined proportion of non-Hodgkin's lymphoma and Hodgkin's disease. Highly active anti-retroviral therapy (HAART) has had a favourable impact on the occurrence of Kaposi's sarcoma, but not, for the moment, of non-Hodgkin's lymphoma in HIV-infected patients (International Collaboration on HIV and Cancer, 2000). Recognising and treating infections linked to haemo-lymphopoietic tumours is a priority in the EU, on account of the steady increase in the number of cases and high-risk individuals (e.g. iatrogenically immuno-suppressed and HIV-positive subjects).

To determine the incidence of non-Hodgkin's lymphoma (NHL) and Hodgkin's disease (HD) in the United Kingdom haemophilia population during the 22 year period 1978-1999, an analysis of patient data included on the UK Haemophilia Centre Doctors' Organisation Lymphoma Register was conducted. The incidence of NHL in the HIV-positive cohort was significantly increased, with a ratio of observed to expected cases of 84 ($P < 0.001$) in the period 1985-1996. The ratio reduced to 42 during the period 1997-1999, presumably as a consequence of the introduction of HAART. There was a significant excess of HD in HIV-positive patients, with an observed to expected ratio of 10.5 between 1985 and 1999 (based on five cases, $P < 0.001$). During the whole observation period, there was a significant excess of HD in HIV-negative patients, with an observed to expected ratio of 2.66 (based on eight cases, $P < 0.05$). The incidence of lymphoma is significantly higher in HIV-positive UK haemophilia patients compared with HIV-negative individuals. Since the introduction of HAART, the incidence of lymphoma has tended to fall in the HIV-positive group.

The Epstein-Barr virus (EBV) is associated with a proportion of cases and this association is believed to be causal. In these cases the Hodgkin and Reed-Sternberg (HRS) cells express the EBV-encoded proteins LMP1 and LMP2, which can mimic CD40 and the B cell receptor, respectively, and therefore may play a critical role in facilitating the survival of HRS cells. EBV-associated and

non-EBV-associated Hodgkin's disease cases have different epidemiological features and recent data suggest that delayed exposure to EBV is a risk factor for the development of EBV-associated Hodgkin's disease in young adults. It has been suggested that Hodgkin's disease can be divided into four entities on the basis of EBV status and age at presentation, with three groups of EBV-associated cases and a single group of EBV-negative cases. The aetiology of the latter cases is obscure although involvement of an infectious agent(s) is suspected.

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6.23: Non-Hodgkin's lymphoma (ICD-9 200 and 202) (M 4.3; F 2.7)

Historically, reticulum cell sarcomas were generally more common, by 30%, than lymphosarcomas in most populations, irrespective of the overall incidence. However, due to temporal and geographical variations in coding practice of non-Hodgkin's lymphoma it is difficult to make such comparisons at the present time with any degree of certainty. Burkitt's lymphoma remains a distinct pathological entity, arising from B-lymphocytes, occurring among children in both sexes and often involving the jaw or ovary. However, it is a rare cause of death in Europe.

Overall in the EU-EEA, the mortality rate from non-Hodgkin's lymphoma was about 60% higher in males (4.3 per 100,000) than in females (2.7), but in both sexes the rate was around 2.5% of that for all cancer deaths. In all countries, mortality was higher in males than in females and, apart from the very low rates in Greece, there was about a two-fold range in rates across the countries (Annex 2).

International comparisons

In males, the highest national mortality rates were recorded in Finland (5.6), The Netherlands (5.2), Sweden (5.1) the United Kingdom (5.1) and Norway (5.0) (Annex 2). The lowest rates were recorded in Greece (1.4), Slovakia (2.2), Lithuania (2.4) and Latvia (2.8).

In females, the highest national mortality rates were in Finland (3.9), Norway (3.4), The Netherlands (3.3), the United Kingdom (3.3) and Ireland (3.2). The lowest rates were recorded in Greece (0.9), Lithuania (1.3), Latvia (1.4), Slovakia (1.5) and Poland (1.6).

Regional variation (box and whisker plots)

There was moderate variation in national mortality rates for both males and females, but relatively little variation between countries for either sex [p. 250-251].

Description of the maps

In males, there were high regional mortality rates in the south of Norway, Sweden and Finland, in the United Kingdom and in northern Italy [p. 250]. There were aggregations of low rates in the Baltic Countries, much of central Europe including Austria, and southern Italy, Spain, Portugal and Greece.

The broad geographical pattern of the variability in mortality rates in females was very closely similar to that for males, with high regional rates in parts of Norway, Sweden and Finland, in the United Kingdom, and northern, but not southern, Italy [p. 251]. There were aggregations of low rates in central and southern Europe.

Statistical aspects

There was smaller regional variability in the mortality rates for non-Hodgkin's lymphoma than for Hodgkin's disease, but, as with Hodgkin's disease, the regional variability in males was similar to that in females, with RRSDs of 0.27 and 0.31, respectively. There was evidence of a regional pattern associated with countries as 88% and 90% of the regional variation was associated with differences between countries for both males and females, respectively.

There was moderate spatial correlation with Moran's I of 0.51 for both males and females. There was, however, a high correlation of 0.81 between the rates for males and females – this can be seen immediately in the maps.

Comment

This disease group includes a wide spectrum of cyto- (and almost certainly aetio-) pathological entities whose incidence and mortality have generally been rising in most developed countries during the past decades, possibly in association with generalised improvements in diagnosis and certification.

For some histological types there is a recognised viral aetiology, as, for example, in Burkitt's lymphoma. This disease is a well-defined patho-clinical entity comprising an undifferentiated, monoclonal lymphoma composed of malignant B-cells. It is common in children in many parts of sub-Saharal Africa where the incidence rate is up to 8 per 100,000 compared with the usual 0.1 to 0.3 per 100,000 in European populations of children. Burkitt's lymphoma has been associated with endemic malaria and there is evidence that successful chemotherapy for malaria is associated with a reduced incidence of the disease. Markers of Epstein-Barr Virus (EBV) (DNA or antigens) are found in 96% of tumours from subjects living in endemic areas of Africa but in only 15% of the so-called sporadic tumours: the corollary is that EBV is unlikely to be involved in the aetiology of Burkitt's lymphoma in 85% of the cases outside Africa.

B-cell lymphomas occur more frequently than expected in subjects with depressed immunological systems and most of these lymphoproliferations are (at least at the beginning of the disease) polyclonal B-cell malignancies – in contrast to the monoclonal Burkitt's lymphoma. The rate of these malignancies is observed to be considerably elevated in organ transplant recipients, who are treated with immunodepressants to reduce the risk of organ rejection, and among patients with virus-induced immunodeficiencies such as acquired immunodeficiency syndrome (AIDS) or genetic immunodeficiencies. Interestingly, the increased risk among transplanted organ recipients has a short latency of between several months and a few years after starting treatment. Aetiological links with aspects of disturbed or aberrant immunity were first suggested by a British case-control study which showed significant associations with past history of several diseases including skin conditions, malignancies, pneumonia, scarlet fever and diabetes.

Higher risk of non-Hodgkin's lymphoma has been associated with agricultural activity; this may be reconciled with a possible viral aetiology, although exposure to phenoxy-acid herbicides, chlorophenols, organic solvents and insecticides have also been postulated as being involved in the aetiology of this group of diseases. Increased risks have also been suspected among workers exposed to wood, meat and other food processing and certain chemical agents.

Cancer remains a significant burden for human immunodeficiency virus (HIV)-infected individuals. Most cancers that are associated with HIV infection are driven by oncogenic viruses, such as EBV, Kaposi's sarcoma-associated herpesvirus (KSHV) and human papillomavirus. Gaining insight into the epidemiology and mechanisms that underlie AIDS-related cancers has provided us with a better understanding of cancer immunity and viral oncogenesis. While Kaposi's sarcoma is the most common neoplasm that occurs in patients with AIDS (AIDS-KS), AIDS-lymphoma is a significant cause of morbidity and mortality in human immunodeficiency virus (HIV)-infected individuals. Over 50% of AIDS lymphomas are associated with EBV and/or KSHV infection. EBV activates B-cell precursors, leading to a transformed phenotype.

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6.24: **Multiple myeloma** (ICD-9 203)
(M 2.1; F 1.5)

Multiple myeloma, originally classified as a bone tumour, was recognised as a separate entity in the early 1950s. Diagnosis of multiple myeloma has greatly improved following the introduction of newer diagnostic techniques such as serum electrophoresis, in whose absence several deaths from multiple myeloma were missed and attributed to renal insufficiency or infections. There is a strong age dependence in incidence, with a rather late age of onset.

Overall in the EU-EEA, mortality from multiple myeloma was around 40% higher in males (2.1 per 100,000) than in females (1.5). Rates in each country were higher in males than in females; and across the EU-EEA the ratios of the rates in males and females were very close to the overall average of 1.4:1.

International comparisons

In males, the highest national rates were in Ireland (3.2), Norway (3.1) and Iceland (3.0) (Annex 2). The lowest rates were in Poland (1.4), Latvia (1.4), Greece (1.5), Lithuania (1.5) and Estonia (1.5).

In females, the highest national rates were in Norway (2.1), Ireland (2.1), and Iceland (2.0). The lowest rates were in Greece (0.7), Estonia (0.9), Latvia (1.0), Poland (1.1), Portugal (1.2), Lithuania (1.2) and Slovakia (1.2).

Regional variation (box and whisker plots)

There was about a two-fold range in the national rates in both males and females, and generally low levels of variability in regional rates within countries [p. 252-253].

Visual Description of the Maps

In males, regions with high rates were apparent in the Nordic Countries, Ireland and the United Kingdom, and in Belgium, The Netherlands and in northern Germany. In central and southern Europe, regional rates were generally low [p. 252].

The map for females shows substantially the same pattern of variability as that for males. There were high rates in Iceland, southern parts of Norway, Sweden and Finland, in northern Denmark and Germany, and in Ireland and the United Kingdom. Rates were low in most regions of central and southern Europe [p. 253].

Statistical aspects

Multiple myeloma exhibited a low level of regional variation: for males the RRSD was 0.20 (with rank 19 of 22) while for females it was 0.23 (rank 20 of 24). As with NHL and leukaemia, a large percentage of variation was associated with differences between countries: 86% for males and 83% for females. This is due to slightly, but consistently, higher rates in Scandinavia, the United Kingdom and Ireland, and lower rates throughout the Baltic Countries, Poland, Hungary and Greece. There was large internal variation within Germany, where the RRSDs were 0.27 for males and 0.31 for females. This was not associated with an obvious geographic pattern.

There was a low spatial autocorrelation of 0.33 for both males and females. The correlation between the rates for males and females was quite high at 0.71

Comment

Increases in the incidence of multiple myeloma during the 20th century implicate environmental factors as important causal agents. The molecular and cytogenetic alterations which occur in multiple myeloma are under investigation, but the precise causes of these abnormalities are largely unknown. Exposure to chemical substances and ionising radiation are associated with an increased risk of multiple myeloma. A single exposure is probably not sufficient to induce the disease, which results from the clonal expansion of an idiotypic plasma cell after cumulative mutational damage has altered its genetic makeup. Multiple myeloma does not have the same biology in all patients; it is best viewed as a heterogeneous disease with a different prognosis, clinical course, and response to therapeutic interventions in different subjects.

Ionising radiation is the single established risk factor for multiple myeloma. An overview of several cohorts of irradiated subjects has shown an approximately threefold elevated incidence of myeloma. As with many kinds of leukaemia, multiple myeloma can be produced by irradiation to the bone marrow. A small increased risk of multiple myeloma was observed in atomic bomb survivors and among patients treated by radiotherapy for cervical cancer. The increase became evident after a longer latent period than for leukaemia. Other studies carried out among personnel employed in the nuclear industry have not reported any consistent increase in multiple myeloma.

This association is interesting since, although radiation is linked to myeloid leukaemia, there is little evidence of association with chronic lymphatic leukaemia which, like myeloma, is a tumour of B lymphocytes. The elevated risk of myeloma becomes evident ten years after exposure, and persists up to 30 years.

Other risk factors are largely undefined. Occupational exposures to asbestos and lead have been sporadically reported, and an excess of myeloma in farmers, agricultural workers and wood workers has been found. This may be related to infectious agents, as are sporadic clusters of myeloma in families. Along the same lines, associations have been suggested with history of autoimmune diseases or other chronic antigenic stimulations, but the evidence on these is largely inconsistent.

Our current knowledge of aetiological factors for multiple myeloma cannot explain the geographic mortality patterns in the EU-EEA.

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6.25: Leukaemia (ICD-9 204-208)
(M 5.5; F 3.4)

The leukaemias are a group of cancers having their origin in cells that arise from bone marrow and circulate in peripheral blood. Leukaemias are classified by cell type in the International Classification of Diseases, distinction between the acute and chronic forms being made at the fourth digit level. However, the precise type of leukaemia is poorly recorded on death certificates and the enforced aggregation of data into a single group results in a considerable loss of information.

Overall, leukaemia had mortality rates in the EU-EEA of 5.5 per 100,000 in males and 3.4 in females. These rates were each just over 3% of the corresponding rates for all cancer deaths. Rates in each country were higher in males than in females and across the EU-EEA the ratios of the national rates in males and females were very close to the overall average of 1.6:1.

International comparisons

In males, the highest national mortality rates recorded were in Luxembourg (7.6), Hungary (7.2), the Czech Republic (6.8) and Lithuania (6.7) (Annex 2). The lowest rates were in Finland (4.4), Norway (4.4), Sweden (4.6) and the United Kingdom (4.6).

In females, the highest national mortality rates were in Hungary (4.6), Estonia (4.6), the Czech Republic (4.2), Lithuania (4.1) and Latvia (4.0). The lowest rates were in Iceland (2.3), Norway (2.8), Finland (2.8) and Switzerland (2.9).

Regional variation (box and whisker plots)

There was very little variation in the mortality rates between countries in either males or females, with the vast majority of rates clustered closely around the respective EU-EEA average. There was moderate variability in rates within countries [p. 254-255].

Description of the maps

In males, the features of the geographic distribution are the generally low rates in the Nordic Countries and most of the United Kingdom and Ireland, and the areas of above average rates in parts of the Baltic Countries (particularly Lithuania), the Czech Republic and Hungary, southern Belgium and Luxembourg, and central and northern Italy [p. 254].

The patterns in the variability in the rates in females were closely similar to those in males: generally low rates in the Nordic Countries (except Denmark) and the United Kingdom, and areas of high rates in the Baltic Countries, the Czech Republic and Hungary [p. 255].

Statistical aspects

Leukaemia exhibited the smallest RRSD of all the cancers, for both males and females, with values of 0.14 for both sexes, i.e. there was very low relative regional variation in the mortality rates. There was some evidence of differences among the countries with just over 80% of the variance associated with country differences for both males and females. This was associated with slightly higher rates in Hungary, the Czech Republic and Lithuania and slightly lower rates in the United Kingdom and the Nordic Countries (except Denmark).

Overall there was little spatial correlation, with Moran's I of 0.20 for males and 0.16 for females. These were the lowest value for females and the second lowest for males. The correlation between the mortality rates for males and females was 0.52. Overall, this cancer site had virtually no regional variation and no spatial aggregation.

Comment

Ionising radiation is an undoubted cause of leukaemia and the observations originally made from the survivors of the atomic bombs in Hiroshima and Nagasaki have never seriously been challenged. Age at exposure influences both the type of the resulting leukaemia and the latent interval: the younger the age at exposure the more likely it is that acute lymphoblastic leukaemia (ALL) will occur after a short latent period. With first exposure at older

ages, it is more likely that acute myeloid leukaemia (AML) will be produced after a much longer latency. Chronic myeloid leukaemia (CML) appears at any age and apparently the same rate. Approximately one in 450 of individuals exposed to radiation from the explosion of atomic devices in Japan developed leukaemia, as did subjects in the two major studies of iatrogenic radiation and its sequelae.

The situation regarding leukaemia risk and exposure to low doses of ionising radiation remains controversial. There is a degree of consensus regarding the increased risk of childhood leukaemia associated with in utero X-ray exposure. These X-ray exposures appear to confer a modest risk increase which has now largely disappeared as a result of a combination of changes in clinical practice and changes in the X-ray equipment which have resulted in lower doses. No excess leukaemia risk has been shown to result as a consequence of the similarly small doses received in diagnostic procedures by children postnatally or by adults. Similarly, the radiologists themselves have little or no apparent increase in risk nowadays.

Various studies have been carried out of cancer rates in the vicinity of nuclear installations in recent years, mostly in Western Europe and North America; there does not appear to have been a general increase in rates of adult cancers around nuclear installations. Some – but not all – studies have indicated increased rates of childhood cancers and particularly childhood leukaemia. The evidence for such increases has tended to be strongest in the vicinity of the nuclear reprocessing plants; in particular, Sellafield and Dounreay in the UK and, to a lesser extent, La Hague in France. Assessments of radiation doses to those living near these installations do not suggest that the raised childhood leukaemia risks can be explained on the basis of radioactive discharges. Non-radiation factors such as population mixing have been mentioned as possible explanations for the raised risks, but it is unclear whether these factors could explain all of the results.

Many studies have been carried out of cancer among nuclear industry workers. Some of the worker studies have been limited by relatively small population sizes and/or short follow-up periods. The larger studies include a combined analysis of about 95,000 workers in Canada, the US and the UK, and cohorts of over 100,000 nuclear workers in Japan (although with a short follow-up) and the UK. Most of the analyses have looked only at mortality. There has been some variation in the findings, which may be due in part to low statistical precision. However, mortality has often been lower than in the general population, due probably to factors associated with selection into and continuation of employment. The larger studies have tended to indicate an increasing trend in leukaemia risk with increasing dose, whereas the evidence for a dose-related increase in solid tumour risks has generally been less. However, the confidence limits for these trend estimates have been relatively wide, and encompass risks extrapolated from the Japanese atomic bomb survivors as well as a range of values, both higher and lower.

Power lines produce extremely low frequency (ELF) electromagnetic fields in range of 50 Hz to 60 Hz. Electric fields do not reach people inside houses but magnetic fields go through most materials and cause an additional exposure higher than the typical background field (about 0.1 μT) up to a distance roughly 50 meters from the power line, depending on the voltage and wire configuration. Health effects on humans related to this non-ionising type of radiation have been investigated in epidemiological studies for over two decades.

The first report of an association between childhood cancer and power line exposure was published in 1979, and after that at least 24 studies on the same topic have been published. There are two meta-analyses published lately which both show a significant 1.7 to 2.0-fold excess of childhood leukaemia in the extremely rarely existing fields above 0.3 or 0.4 μT. Part of the excess may be attributable to patient selection and publication bias, and a plausible biological mechanism is not known.

It appears on the basis of studies with large numbers of cancer cases that there is no excess risk of cancer among adults living close to power lines, but the results of occupational studies are suggestive of an association with some cancers including adult leukaemia. The results of epidemiological studies suggest that appreciable magnetic field effects, if any, are concentrated among relatively high and uncommon exposures.

A number of studies have examined possible links between various chemical exposures and several

types of leukaemias, producing an unconvincing array of positive, negative and null findings. The best known risks are those resulting from exposures to chemotherapeutic agents used in the treatment of prior malignant diseases, producing mainly adult acute myeloid leukaemia in adults, and the increased risks of a variety of adult leukaemias and myelodysplasias associated with chronic benzene exposures. A number of studies have suggested a link between employment in agriculture and increased risk of leukaemia.

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6.26: All forms of cancer (ICD-9 140-208)
(M 177; F 100)

Overall, in the EU-EEA, the mortality rate from all forms of cancer was almost 80% higher in males (177 per 100,000) than in females (100 per 100,000). Rates were higher in males than in females in every one of the EU-EEA countries. Rates in males were only 10-30% higher than in females in three of the Nordic Countries: Denmark, Iceland and Sweden; but were around twice as high as in females in France and Spain, and in most of the former communist countries in central Europe: the Baltic Countries, the Czech Republic, Hungary, Poland, Slovakia and Slovenia.

International comparisons

In males, the highest mortality rate for all cancers combined was in Hungary (268 per 100,000), around 20% higher than the rates in the Czech Republic (228) and Slovakia (218) (Annex 2). All the other former communist countries had rates around 200 per 100,000: Estonia (206), Poland (205), Slovenia (202), Lithuania (201) and Latvia (198). The highest rates in western Europe were in Belgium (194) and France (188). The lowest cancer mortality rates in males were in Sweden (121), Iceland (138) and Finland (139).

In females, the highest national cancer mortality rates were in Denmark (139) and Hungary (138). Rates were around 20% above the average in the Czech Republic (125), Iceland (122), Ireland (118) and the United Kingdom (117). The lowest rates were in Greece (76), Spain (78), Portugal (84), France (84) and Finland (85).

Regional variation (box and whisker plots)

There was variation in the mortality rates between countries for both males and females. There was much wider variability in rates within some countries than in others, particularly in males. The pattern of the variability in males, with high rates in all central Europe and generally low rates in western Europe was, however, not the same as that in females, where the rates in most of central Europe were around the average [p. 258-259].

Description of the maps

In males, the high total cancer mortality rates across the whole of Hungary extend both northwards into Slovakia, the Czech Republic (particularly its western part), western and northern Poland, northeast Germany and the Baltic Countries – and southeastwards into Slovenia and northern Italy. Rates were generally low in Greece, southern Italy, Portugal, large parts of Spain, and Switzerland, Austria and southern Germany as well as in the United Kingdom, Ireland and the Nordic Countries [p. 258].

The geographical pattern of the variability in the mortality rates for all cancers combined in females was similar to that in males in some respects, but very different in others. As in males, rates were high across all of Hungary, the Czech Republic (particularly its western part) and western and northern Poland; and low rates were found throughout Spain and Portugal, central and southern Italy, and Greece [p. 259]. Unlike in males, however, there were high rates in Denmark and in the United Kingdom and Ireland, the rates in the Baltic Countries were only around the average, and rates in almost the whole of France were low.

Statistical aspects

The regional variation in the mortality rates for all cancers was low (RRSDs of 0.17 in both males and females); and for both sexes just over 80% of variability was associated with differences between countries. This confirms the visual impression of the maps where the rates tend to be consistently higher or lower than average in any particular country, but there is general uniformity in the colours of the regions within countries. Exceptions to this were Italy, with lower rates in the south than in the north (especially for males), and Poland, with lower rates in the east than in the northwest.

There was evidence of spatial autocorrelation in males (Moran's I of 0.77) and in females (0.78).

The correlation between the rates for males and females was quite low at 0.44; this reflects the differences in the rates between the sexes described above.

Comment

The pattern of high cancer mortality rates in males appears to be dominated by those regions where mortality from smoking- and alcohol-related cancers was particularly high – such as in some, but not all, of the former communist countries in central Europe and in northern France. The pattern of high rates in females appears to be dominated by areas where lung cancer or breast cancer mortality (or both) was high – such as Hungary, parts of the Czech Republic and Poland, Denmark, the United Kingdom and Ireland.

ANNEXES 1, 2, 3

Annex 1: Map of the countries of the European Union and the European Economic Area

Annex 2: Table of national age standardised (world) cancer mortality rates by site and sex, 1993-1997

Annex 3: Table of populations by country, 1993-1997


Cyprus
Greece
Malta
Finland
Estonia
Latvia
Lithunia
Poland
Slovakia
Hungary
Czech Republic
Austria
Slovenia
Italy
Sweden
Germany
Switzerland
Norway
Denmark
Netherlands
Belgium
Luxembourg
France
United Kingdom
Ireland
Spain
Portugal
Iceland

Annex 2: National age standardised (world) cancer mortality rates by site and sex, 1993-1997														
Country		Oral		Oesophagus		Stomach		Large bowel		Liver		Gallbladder		Pancreas
	140-149	140-149	150	150	151	151	153-154.	153-154.	155	155	156	156	157	157
							159.0	159.0						
	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Austria	6.1	1.1	3.7	0.5	13.6	7.1	22.8	12.7	7.2	2.2	2.3	3.0	9.4	6.2
Belgium	5.9	1.3	5.5	1.1	8.1	3.5	19.4	13.0	4.2	1.9	1.1	1.2	7.4	4.8
Cyprus	0.0	0.0	0.2	0.1	2.9	1.3	4.7	2.8	1.2	0.6	-	-	1.3	0.5
Czech	6.8	1.1	4.8	0.6	15.1	7.3	34.2	17.5	8.0	3.5	3.9	5.9	11.1	6.8
Denmark	4.5	1.5	5.7	1.7	6.4	3.1	22.8	16.2	1.5	0.9	0.9	1.3	7.6	6.2
Estonia	9.3	1.3	5.4	0.5	25.7	11.3	18.2	12.0	4.8	2.1	1.1	1.3	10.6	4.6
Finland	2.4	1.1	2.9	1.2	10.2	5.2	12.0	8.3	3.1	1.5	1.7	2.6	8.1	5.9
France	11.3	1.3	9.3	1.0	7.1	2.7	16.6	9.6	11.0	2.1	1.2	1.4	7.4	4.0
Germany	6.5	1.2	5.2	0.9	12.1	6.4	21.3	14.6	4.5	1.8	2.2	3.1	8.1	5.3
Greece	2.0	0.6	1.5	0.4	9.2	4.8	9.3	7.4	13.0	5.5	0.7	0.8	6.1	3.5
Hungary	19.2	2.4	8.9	0.9	20.5	9.2	33.1	19.0	8.2	3.8	3.6	6.1	11.4	6.7
Iceland	2.1	1.0	5.7	2.9	11.6	5.9	13.8	10.1	3.0	1.7	0.5	1.4	8.3	7.1
Ireland	4.7	1.2	8.0	3.4	10.5	5.0	25.4	14.8	3.1	1.6	0.7	1.0	7.7	5.3
Italy	5.3	1.0	3.6	0.6	14.0	6.6	18.6	11.9	13.1	4.7	2.0	2.5	7.3	4.7
Latvia	9.3	1.1	5.2	0.4	25.4	10.7	18.3	11.8	3.6	1.7	0.9	1.0	12.0	5.4
Lithuania	8.6	0.9	5.6	0.5	25.9	10.2	18.0	11.5	3.4	1.6	1.1	1.8	10.4	4.7
Luxembourg	7.4	1.4	6.3	1.6	9.0	4.5	20.7	13.4	5.7	1.8	1.3	1.2	7.0	4.8
Malta	4.2	1.1	3.8	0.9	11.4	4.9	18.1	11.3	1.4	1.4	0.8	0.7	10.1	4.8
Netherlands	2.8	1.1	6.2	2.0	10.2	4.2	19.0	13.5	2.1	1.0	1.2	1.6	7.1	5.3
Norway	3.0	1.1	2.9	0.7	9.0	4.2	19.7	14.8	1.4	0.8	1.1	1.2	7.3	5.7
Poland	6.3	1.1	4.9	0.8	19.3	6.9	16.3	10.9	5.4	3.9	1.8	4.5	8.3	5.0
Portugal	6.5	0.8	5.4	0.9	21.5	10.0	19.8	11.8	4.9	1.9	1.4	1.5	6.1	3.3
Slovakia	17.2	1.3	7.2	0.8	17.3	7.0	26.6	12.9	6.7	3.6	2.0	3.9	8.9	4.7
Slovenia	11.1	1.0	6.5	0.7	20.6	8.8	24.0	13.9	5.0	2.4	2.3	3.2	7.9	4.9
Spain	6.9	0.9	5.5	0.5	12.4	5.4	16.9	10.4	8.4	3.2	1.3	1.9	5.9	3.5
Sweden	2.2	0.9	2.9	0.8	6.6	3.6	13.8	10.3	4.0	2.4	1.9	3.1	7.7	6.6
Switzerland	5.2	1.1	5.0	1.0	7.2	3.2	15.5	9.2	5.8	1.6	1.3	1.8	7.2	4.9
UK	2.9	1.1	8.5	3.4	9.6	3.9	19.6	12.7	2.5	1.3	0.5	0.6	6.5	4.7
EU-EEA	6.5	1.1	5.9	1.2	12.0	5.5	19.2	12.4	6.9	2.5	1.6	2.3	7.5	4.8
% of all cancer	4%	1%	3%	1%	7%	6%	11%	12%	4%	3%	1%	2%	4%	5%
'-' no data reported														

Annex 2: National age standardised (world) cancer mortality rates by site and sex, 1993-1997														
Country		Larynx		Lung		Pleura		Melanoma		NMSC	Breast	Cervix	Uterus	
	161	161	162	162	163	163	172	172	173	173	174	180	182	
	M	F	M	F	M	F	M	F	M	F	F	F	F	
Austria	3.1	0.2	42.3	10.2	0.7	0.3	2.4	1.7	0.8	0.3	21.2	2.7	1.3	
Belgium	4.0	0.5	69.1	9.8	1.2	0.2	1.4	1.2	0.5	0.2	25.3	2.2	1.2	
Cyprus	0.0	0.0	15.8	2.9	-	-	0.3	0.1	-	-	11.0	2.3	-	
Czech	4.4	0.2	68.3	11.1	0.7	0.3	2.8	1.6	0.8	0.5	21.0	5.1	3.5	
Denmark	2.4	0.5	49.1	27.7	1.2	0.3	2.8	1.9	0.4	0.2	27.4	4.0	2.5	
Estonia	5.7	0.3	65.6	7.3	0.2	0.0	1.5	1.6	1.0	0.7	18.4	6.0	2.0	
Finland	1.0	0.1	39.8	6.9	1.1	0.2	2.3	1.2	0.4	0.2	16.6	1.2	2.3	
France	5.5	0.3	46.5	6.1	1.5	0.4	1.4	1.1	0.4	0.2	19.5	1.5	0.8	
Germany	2.5	0.2	45.4	9.2	1.1	0.3	1.8	1.2	0.3	0.2	21.8	2.9	1.3	
Greece	3.4	0.2	50.0	6.3	0.0	0.0	0.5	0.4	1.0	0.8	14.8	0.9	0.4	
Hungary	9.1	0.7	84.8	19.0	0.3	0.1	2.4	1.5	1.2	0.7	23.9	6.4	3.4	
Iceland	0.4	0.1	30.8	26.2	0.3	0.3	1.7	1.3	0.2	0.1	24.9	1.8	2.5	
Ireland	2.1	0.4	42.7	17.3	0.5	0.1	1.3	1.2	0.9	0.2	24.4	3.1	1.6	
Italy	4.1	0.2	52.7	7.8	1.3	0.5	1.5	1.0	0.6	0.2	19.7	0.8	0.7	
Latvia	6.4	0.2	58.5	5.5	0.2	0.1	1.6	1.2	0.0	0.0	18.0	5.1	4.9	
Lithuania	7.5	0.2	61.2	5.5	0.2	0.1	1.2	1.2	0.7	0.4	18.8	7.7	4.5	
Luxembourg	3.1	0.4	55.9	10.6	0.8	0.1	1.6	1.2	0.5	0.2	22.0	1.2	4.1	
Malta	3.3	0.3	44.5	5.0	0.1	0.0	0.6	0.8	0.5	0.6	30.1	2.2	1.8	
Netherlands	1.7	0.3	61.1	13.7	2.7	0.3	2.2	1.6	0.4	0.2	25.9	1.8	1.8	
Norway	1.0	0.2	31.5	13.7	1.3	0.2	3.7	2.3	0.4	0.2	19.0	3.2	2.4	
Poland	7.4	0.5	71.4	11.0	0.4	0.2	1.7	1.4	1.1	0.7	16.0	7.3	2.5	
Portugal	5.4	0.3	29.3	4.6	0.1	0.1	0.8	0.7	0.9	0.4	17.5	2.6	1.1	
Slovakia	7.5	0.3	63.3	7.0	0.7	0.3	2.0	1.6	1.1	0.8	16.9	5.3	5.2	
Slovenia	4.8	0.3	61.2	9.2	1.1	0.4	3.1	2.7	0.3	0.2	22.3	3.8	2.7	
Spain	6.4	0.1	47.8	3.9	0.4	0.1	1.1	0.8	0.8	0.4	16.9	1.8	1.5	
Sweden	0.6	0.1	22.3	11.8	1.0	0.3	2.6	1.5	0.4	0.1	16.7	1.9	1.3	
Switzerland	1.6	0.2	37.9	9.1	1.2	0.2	2.6	1.5	0.7	0.3	21.7	2.0	2.2	
UK	1.6	0.3	47.5	20.5	1.1	0.1	1.8	1.4	0.5	0.2	24.8	3.1	1.2	
EU-EEA	3.9	0.3	50.3	10.3	1.0	0.3	1.7	1.2	0.6	0.3	20.6	2.7	1.5	
% of all cancer	2%	0%	28%	10%	1%	0%	1%	1%	0%	0%	21%	3%	2%	
'-' no data reported														

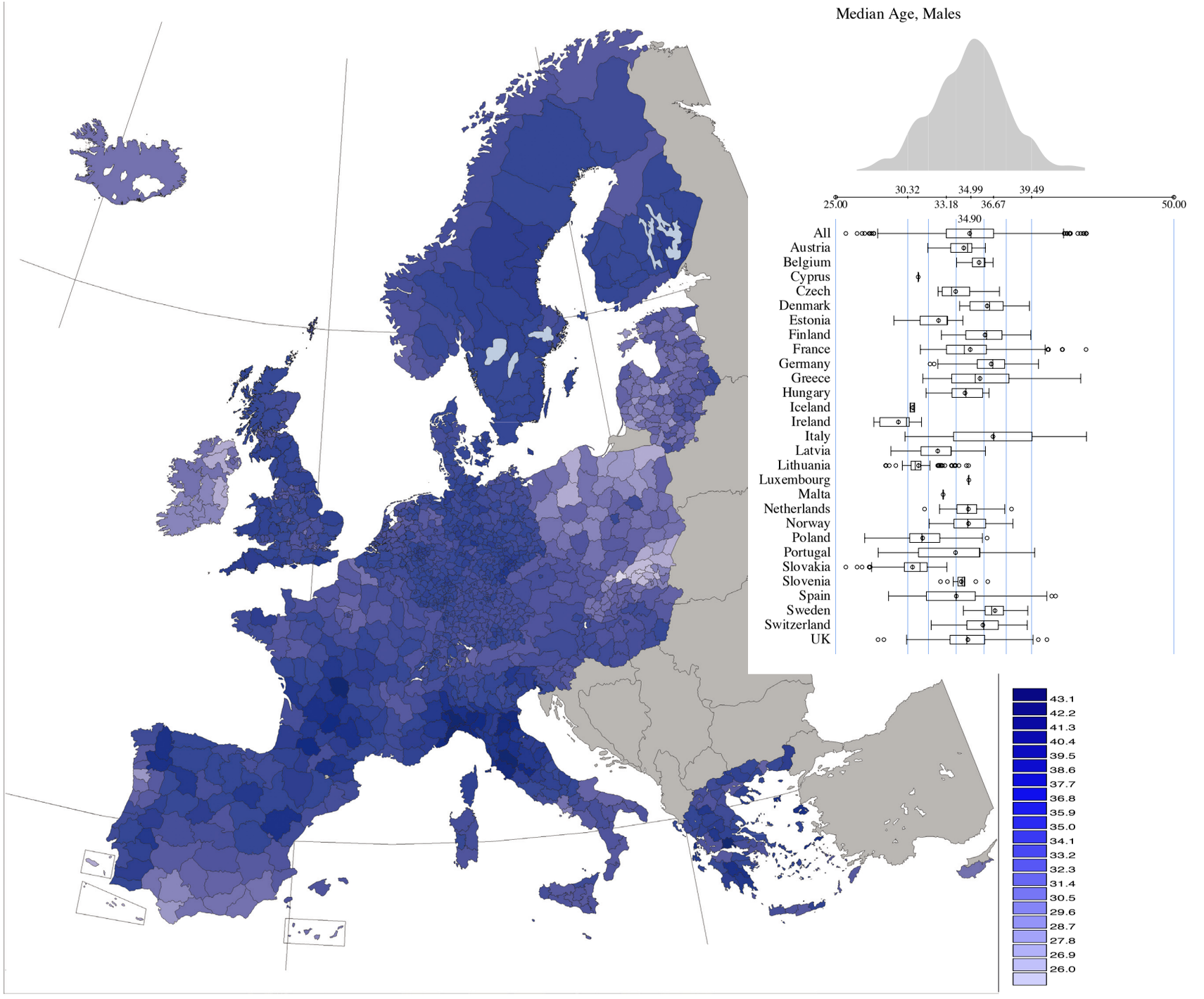
Annex 2: National age standardised (world) cancer mortality rates by site and sex, 1993-1997														
Country	All uterus	All uterus under 50		Ovary	Prostate	Testis	Bladder		Kidney		Brain & CNS		Thyroid	
	179-182	179-182	179-182	183	185	186	188	188	189	189	191-192	191-192	193	193
		Under 50	% total											
	F	F	F	F	M	M	M	F	M	F	M	F	M	F
Austria	6.8	1.9	28 %	7.0	17.5	0.4	5.1	1.4	5.5	2.7	4.3	3.0	0.7	0.6
Belgium	5.3	1.3	25 %	7.1	19.4	0.2	7.5	1.6	4.6	2.2	5.8	4.1	0.3	0.4
Cyprus	0.1	0.0	0 %	0.8	1.8	-	0.3	0.1	-	-	0.1	0.1	-	-
Czech	10.3	2.8	27 %	8.5	15.9	0.9	6.9	1.5	10.8	4.9	5.4	3.6	0.5	0.7
Denmark	8.4	2.0	24 %	8.6	19.8	0.7	9.1	2.7	4.8	2.8	5.5	3.7	0.3	0.4
Estonia	10.6	3.3	31 %	8.1	14.5	0.7	6.3	1.1	7.9	3.3	5.3	4.1	0.5	0.6
Finland	3.7	0.5	14 %	6.4	18.1	0.3	4.0	1.0	5.1	2.5	5.2	4.1	0.3	0.5
France	5.0	1.3	26 %	5.6	15.7	0.3	6.5	1.2	4.5	1.7	3.9	2.6	0.3	0.4
Germany	5.8	1.7	29 %	7.0	16.5	0.5	6.3	1.6	6.1	2.7	4.7	3.3	0.5	0.6
Greece	3.3	0.9	27 %	3.6	9.2	0.2	6.3	1.0	2.6	1.1	7.3	4.6	0.2	0.4
Hungary	11.2	4.2	38 %	6.4	17.5	0.9	8.1	1.6	6.6	2.9	6.5	4.5	0.6	0.8
Iceland	4.3	0.7	16 %	7.8	19.8	0.1	4.9	1.7	6.8	3.7	6.0	5.1	0.6	0.8
Ireland	5.2	1.6	31 %	8.4	19.0	0.3	4.4	1.6	3.5	1.7	6.1	4.4	0.3	0.6
Italy	4.7	1.1	23 %	4.8	11.2	0.2	7.7	1.2	4.1	1.5	4.0	2.7	0.4	0.6
Latvia	10.1	2.8	28 %	8.3	12.8	0.9	8.4	1.2	6.9	2.6	4.2	3.0	0.5	0.7
Lithuania	12.3	4.5	37 %	9.0	15.1	0.7	7.7	1.0	7.6	3.1	4.6	3.2	0.5	0.7
Luxembourg	5.3	0.8	15 %	6.2	15.4	0.6	6.3	1.7	3.9	2.1	5.7	4.3	0.2	0.8
Malta	6.6	1.2	18 %	7.5	13.6	0.2	8.5	2.3	4.2	1.3	3.7	3.2	0.6	0.3
Netherlands	4.0	0.8	20 %	7.3	19.2	0.3	6.3	1.6	5.0	2.4	4.2	2.9	0.3	0.4
Norway	5.9	1.3	22 %	8.0	23.8	0.3	5.6	1.8	4.6	2.2	4.4	3.1	0.4	0.4
Poland	11.1	3.8	34 %	6.8	10.9	0.7	8.1	1.1	6.3	2.7	6.0	4.0	0.4	0.7
Portugal	6.8	2.3	34 %	3.5	17.2	0.3	5.2	1.2	2.3	1.0	4.3	2.7	0.3	0.5
Slovakia	10.9	3.7	34 %	5.9	12.3	0.7	6.0	1.0	6.4	2.9	5.2	3.6	0.5	0.7
Slovenia	8.7	2.5	29 %	6.7	15.3	0.4	6.1	1.3	3.8	2.3	4.6	3.2	0.5	0.6
Spain	4.7	1.2	26 %	4.2	13.8	0.2	8.5	1.1	3.3	1.2	4.2	2.7	0.2	0.4
Sweden	4.5	0.8	18 %	7.3	17.1	0.2	4.2	1.2	4.7	2.7	4.9	3.4	0.3	0.4
Switzerland	4.6	0.9	20 %	5.8	20.1	0.4	5.3	1.5	4.1	2.0	4.7	3.1	0.5	0.5
UK	5.2	1.7	33 %	8.1	16.7	0.3	6.5	2.0	4.0	1.9	4.5	3.0	0.2	0.3
EU-EEA	6.0	1.7	28 %	6.3	15.4	0.4	6.8	1.4	4.8	2.1	4.6	3.2	0.4	0.5
% of all cancer	6%			6%	9%	0%	4%	1%	3%	2%	3%	3%	0%	1%
'-' no data reported														

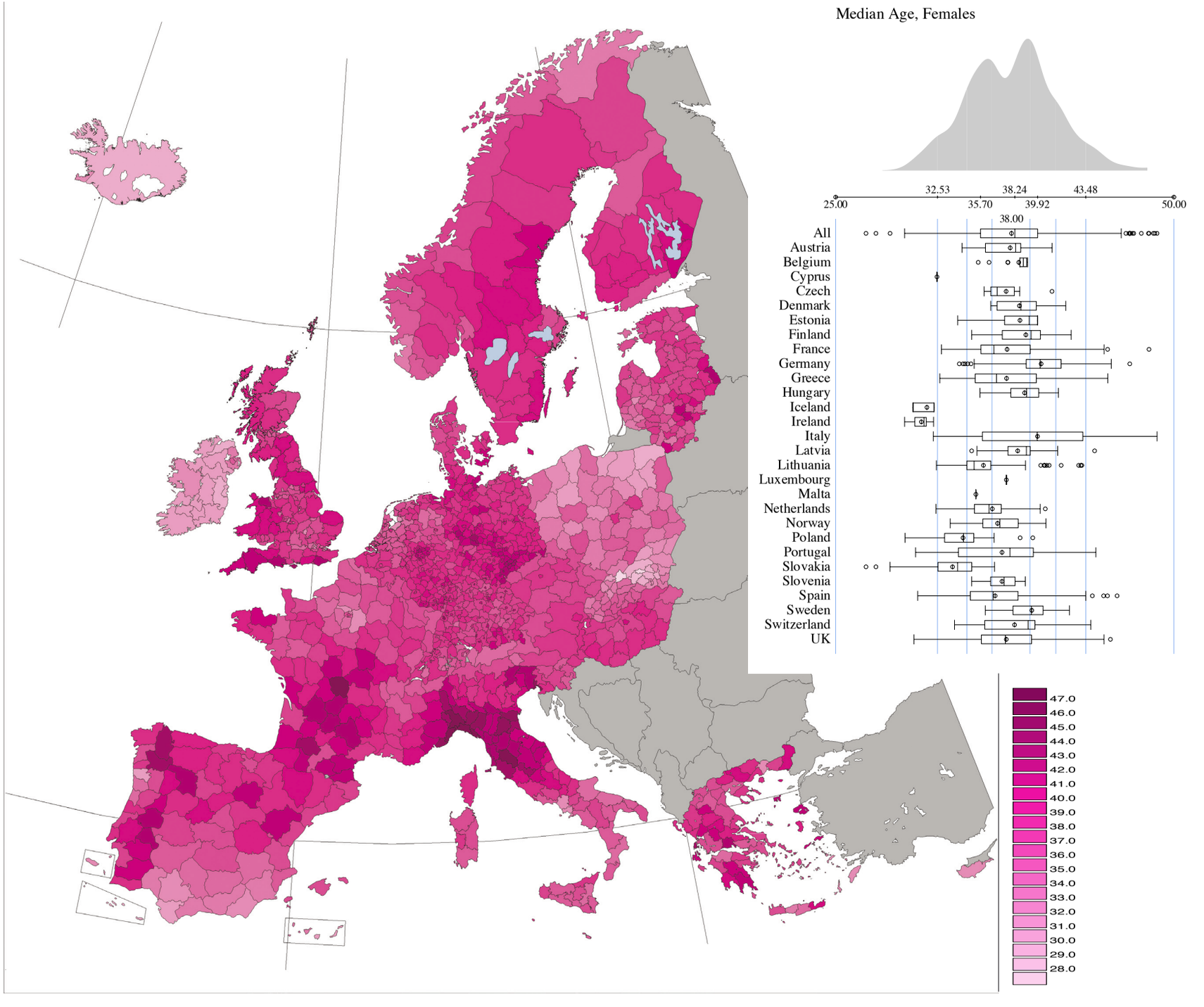
Annex 2: National age standardised (world) cancer mortality rates by site and sex, 1993-1997														
Country	Hodgkin's disease		NHL		Myeloma		Leukaemia		Other and ill-defined				All cancer	
	201	201	200 & 202	200 & 202	203	203	204-208	204-208	195-199		195-199		140-208	140-208
										%		%		
	M	F	M	F	M	F	M	F	M	140-208	F	140-208	M	F
Austria	1.2	0.8	3.2	2.2	2.1	1.6	5.1	3.4	4.2	2.5 %	3.0	2.9 %	166.5	101.9
Belgium	0.6	0.3	4.4	2.7	2.5	1.6	6.1	3.7	9.8	5.1 %	5.8	5.7 %	193.9	102.2
Cyprus	-	-	0.6	0.3	1.7	1.0	11.2	5.7	34.5	45.0 %	19.5	37.9 %	76.6	51.5
Czech	1.2	0.8	3.6	2.1	2.2	1.5	6.8	4.2	5.5	2.4 %	3.6	2.9 %	227.8	124.6
Denmark	0.6	0.4	4.4	3.0	2.7	1.7	6.2	3.8	11.7	6.6 %	9.9	7.1 %	177.4	139.3
Estonia	1.3	0.7	3.1	1.9	1.5	0.9	6.3	4.6	4.4	2.1 %	1.7	1.7 %	206.0	102.0
Finland	0.5	0.3	5.6	3.9	2.3	1.6	4.4	2.8	5.4	3.9 %	4.3	5.1 %	139.3	84.6
France	0.4	0.2	4.5	2.8	2.0	1.4	5.5	3.3	10.9	5.8 %	6.0	7.1 %	187.6	84.4
Germany	0.6	0.4	4.0	2.5	2.0	1.5	5.5	3.5	8.5	5.0 %	5.6	5.4 %	169.4	104.0
Greece	1.1	0.6	1.4	0.9	1.5	0.7	5.9	3.4	11.8	8.1 %	7.6	10.1 %	145.0	75.6
Hungary	1.0	0.6	4.3	2.6	1.7	1.4	7.2	4.6	3.4	1.3 %	2.5	1.8 %	268.0	138.4
Iceland	0.0	0.5	4.8	2.1	3.0	2.0	5.2	2.3	3.4	2.5 %	2.9	2.4 %	137.6	121.6
Ireland	0.8	0.3	4.9	3.2	3.2	2.1	5.2	3.1	11.1	6.5 %	7.8	6.6 %	170.4	117.6
Italy	0.6	0.4	4.7	3.0	2.1	1.5	6.1	3.7	5.5	3.1 %	3.3	3.6 %	175.2	92.2
Latvia	1.2	0.8	2.8	1.4	1.4	1.0	6.0	4.0	3.0	1.5 %	1.4	1.5 %	198.0	96.5
Lithuania	1.4	0.8	2.4	1.3	1.5	1.2	6.7	4.1	3.8	1.9 %	1.6	1.6 %	201.3	99.8
Luxembourg	0.6	0.3	4.8	1.9	2.0	1.5	7.6	3.2	11.1	6.1 %	6.3	6.2 %	181.4	101.6
Malta	1.1	0.5	4.4	3.3	1.9	1.5	4.7	2.7	10.9	6.9 %	6.4	6.4 %	158.1	100.6
Netherlands	0.5	0.3	5.2	3.3	2.7	1.9	5.4	3.1	11.0	6.1 %	7.0	6.5 %	181.6	108.4
Norway	0.4	0.2	5.0	3.4	3.1	2.1	4.4	2.8	8.7	6.0 %	6.8	6.6 %	146.2	103.7
Poland	1.4	0.7	3.0	1.6	1.4	1.1	5.6	3.5	8.8	4.3 %	5.2	4.8 %	205.0	107.6
Portugal	0.6	0.4	3.5	2.2	1.7	1.2	5.0	3.4	7.0	4.5 %	4.0	4.8 %	154.2	84.1
Slovakia	0.9	0.5	2.2	1.5	1.6	1.2	5.6	3.7	3.1	1.4 %	1.6	1.6 %	218.4	102.4
Slovenia	0.9	0.3	3.7	2.2	1.8	1.8	5.4	3.1	7.4	3.7 %	4.5	4.1 %	202.4	108.5
Spain	0.6	0.3	3.6	2.3	1.9	1.4	5.1	3.1	11.0	6.4 %	5.7	7.3 %	170.8	78.4
Sweden	0.3	0.3	5.1	3.1	2.7	1.7	4.6	3.1	5.5	4.5 %	4.9	5.3 %	121.4	93.3
Switzerland	0.4	0.3	4.8	3.1	2.4	1.7	5.2	2.9	5.0	3.3 %	3.5	3.9 %	151.0	89.2
UK	0.5	0.3	5.1	3.3	2.4	1.7	4.6	2.9	15.0	9.1 %	10.5	9.0 %	165.4	117.0
EU-EEA	0.7	0.4	4.3	2.7	2.1	1.5	5.5	3.4	9.3	0.1	5.8	0.1	177.0	99.8
% of all cancer	0%	0%	2%	3%	1%	2%	3%	3%	5 %		6 %		100%	100%
'-' no data reported														

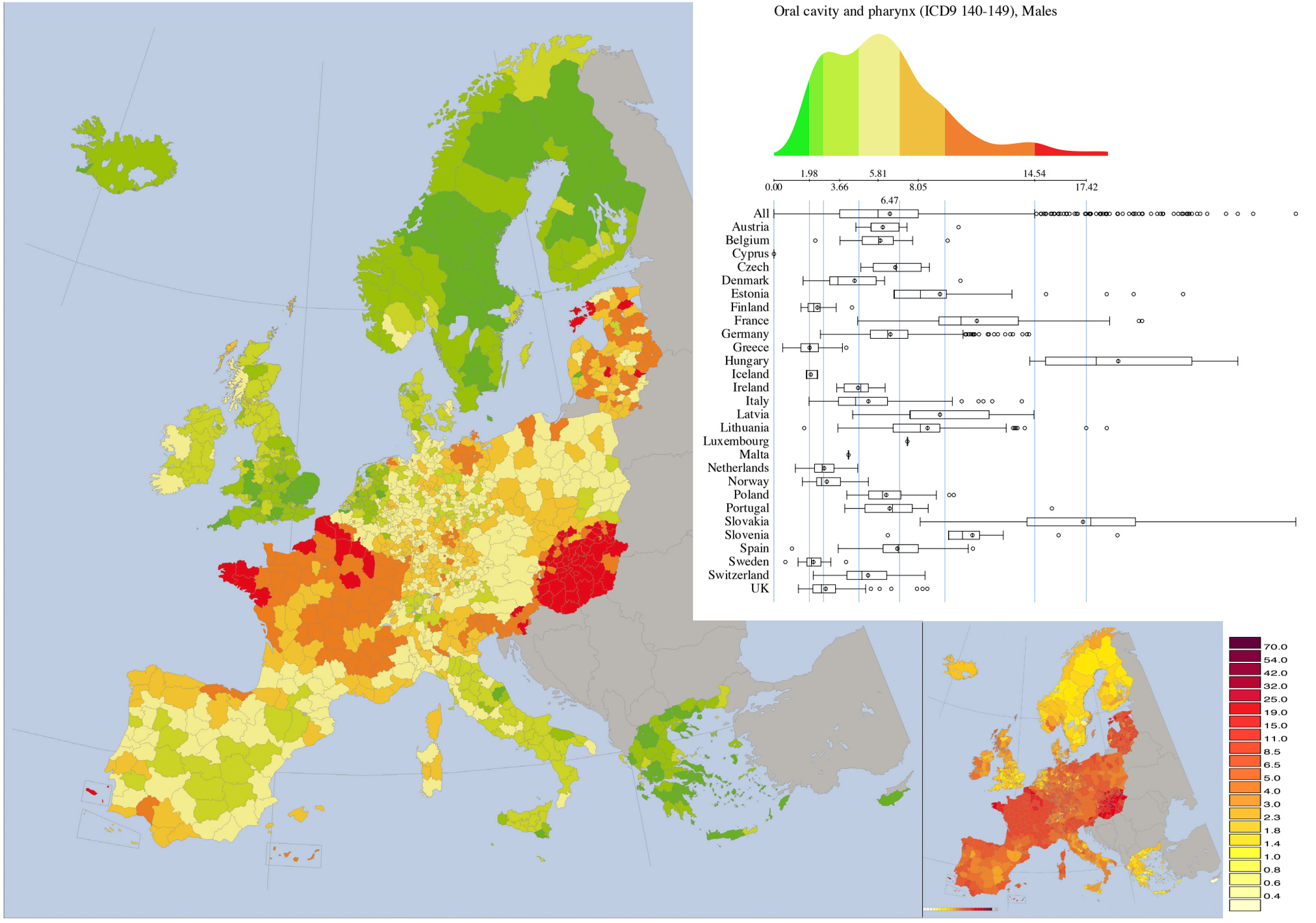
Annex 3 Populations by country, 1993-1997												
	Number of	Total	Pop 0-24	Pop 25-64	Pop 65+	Pop all ages	Pop 0-24	Pop 25-64	Pop 65+	Pop all ages	Lowest	Highest
Country	NUTS regions	population	male	male	male	male	female	female	female	female	NUTS pop	NUTS pop
Austria	9	7,943,417	1,235,863	2,162,868	432,036	3,830,767	1,186,995	2,156,438	769,217	4,112,650	135,007	824,641
Belgium	11	10,122,559	1,595,116	2,713,949	640,721	4,949,786	1,527,356	2,686,756	958,661	5,172,773	118,062	824,939
Cyprus	1	655,241	130,903	160,932	32,464	324,300	126,054	164,874	40,012	330,941	324,300	330,941
Czech	14	10,323,305	1,851,627	2,646,843	518,274	5,016,744	1,766,373	2,692,178	848,010	5,306,561	149,355	660,071
Denmark	15	5,233,591	820,721	1,432,710	329,555	2,582,986	784,511	1,397,929	468,166	2,650,606	22,396	314,264
Estonia	15	1,472,200	256,815	365,056	64,091	685,961	246,941	403,477	135,820	786,238	5,746	292,333
Finland	22	5,111,949	819,374	1,399,539	270,427	2,489,340	784,492	1,378,684	459,433	2,622,609	12,394	399,899
France	95	58,089,559	9,692,832	14,959,558	3,633,868	28,286,258	9,302,233	15,110,101	5,390,967	29,803,301	36,253	1,316,969
Germany	441	81,752,301	11,526,670	23,692,203	4,567,607	39,786,480	10,929,626	22,911,721	8,124,474	41,965,821	17,313	1,132,409
Greece	51	7,344,973	1,260,652	1,916,903	497,552	3,675,107	1,186,797	1,884,932	598,137	3,669,866	10,567	492,009
Hungary	20	10,226,254	1,774,971	2,574,877	543,364	4,893,212	1,693,113	2,741,947	897,983	5,333,043	107,190	1,045,924
Iceland	2	268,263	54,615	66,163	13,693	134,471	52,224	64,796	16,772	133,792	45,408	88,384
Ireland	8	3,609,560	773,040	843,840	176,500	1,793,380	734,280	846,900	235,000	1,816,180	100,700	545,460
Italy	95	57,204,249	8,458,930	15,434,043	3,871,880	27,764,854	8,079,272	15,713,938	5,646,185	29,439,395	44,925	2,029,742
Latvia	26	2,509,053	439,122	615,736	104,327	1,159,185	421,064	695,222	233,582	1,349,868	12,882	563,918
Lithuania	44	3,711,855	683,515	915,273	153,797	1,752,585	658,147	1,005,840	295,283	1,959,270	10,268	349,068
Luxembourg	1	409,611	63,192	116,013	21,928	201,134	60,363	112,727	35,387	208,477	201,134	208,477
Malta	1	370,340	69,940	95,820	17,560	183,320	66,060	97,180	23,780	187,020	183,320	187,020
Netherlands	40	15,454,223	2,493,184	4,326,442	822,059	7,641,685	2,391,925	4,195,923	1,224,689	7,812,538	26,865	664,286
Norway	19	4,370,366	735,627	1,137,551	288,072	2,161,250	701,660	1,101,496	405,960	2,209,117	37,022	255,148
Poland	49	38,551,960	7,594,753	9,579,826	1,589,818	18,764,397	7,261,208	9,893,213	2,633,142	19,787,563	122,984	2,012,262
Portugal	20	9,920,351	1,711,530	2,467,304	598,633	4,777,467	1,651,469	2,636,284	855,131	5,142,884	61,902	1,077,508
Slovakia	38	5,352,545	1,071,230	1,306,092	229,652	2,606,974	1,027,392	1,360,059	358,120	2,745,571	22,060	238,243
Slovenia	9	1,985,043	335,801	539,614	86,602	962,017	319,964	545,321	157,741	1,023,026	36,908	307,416
Spain	52	39,222,453	6,638,231	10,060,650	2,499,892	19,198,772	6,315,735	10,196,916	3,511,029	20,023,681	30,149	2,597,456
Sweden	21	8,802,661	1,403,181	2,294,022	652,047	4,349,249	1,335,858	2,229,337	888,217	4,453,412	28,715	880,975
Switzerland	26	7,026,701	1,066,118	1,952,262	413,275	3,431,655	1,021,773	1,949,921	623,352	3,595,046	7,244	601,591
UK	133	58,606,280	9,650,522	15,337,383	3,743,604	28,731,509	9,159,337	15,234,458	5,480,976	29,874,771	9,806	872,935
EU-EEA	1,278	455,650,861	74,208,074	121,113,472	26,813,298	222,134,844	70,792,222	121,408,570	41,315,225	233,516,017	5,746	2,597,456

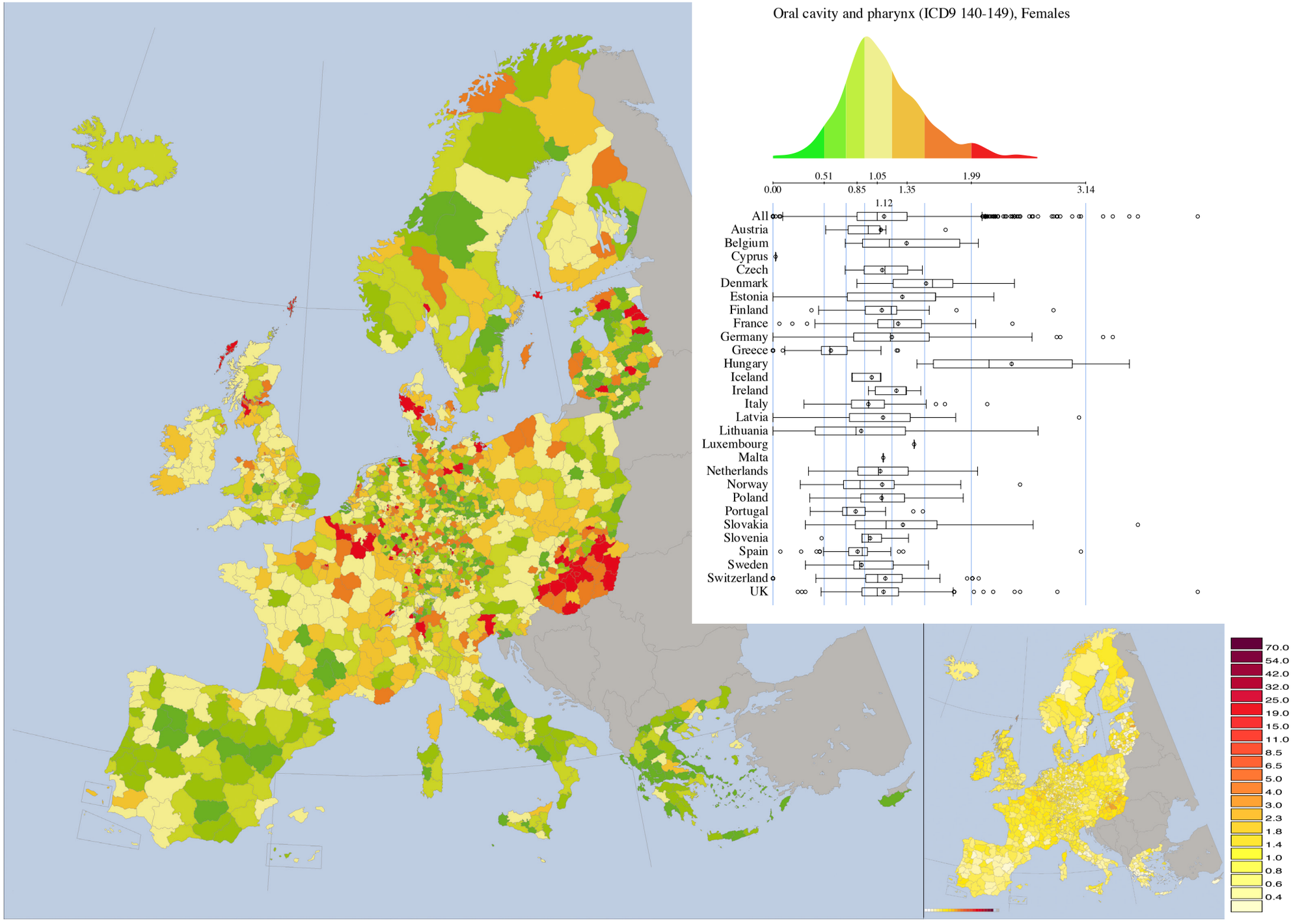
ANNEX 4

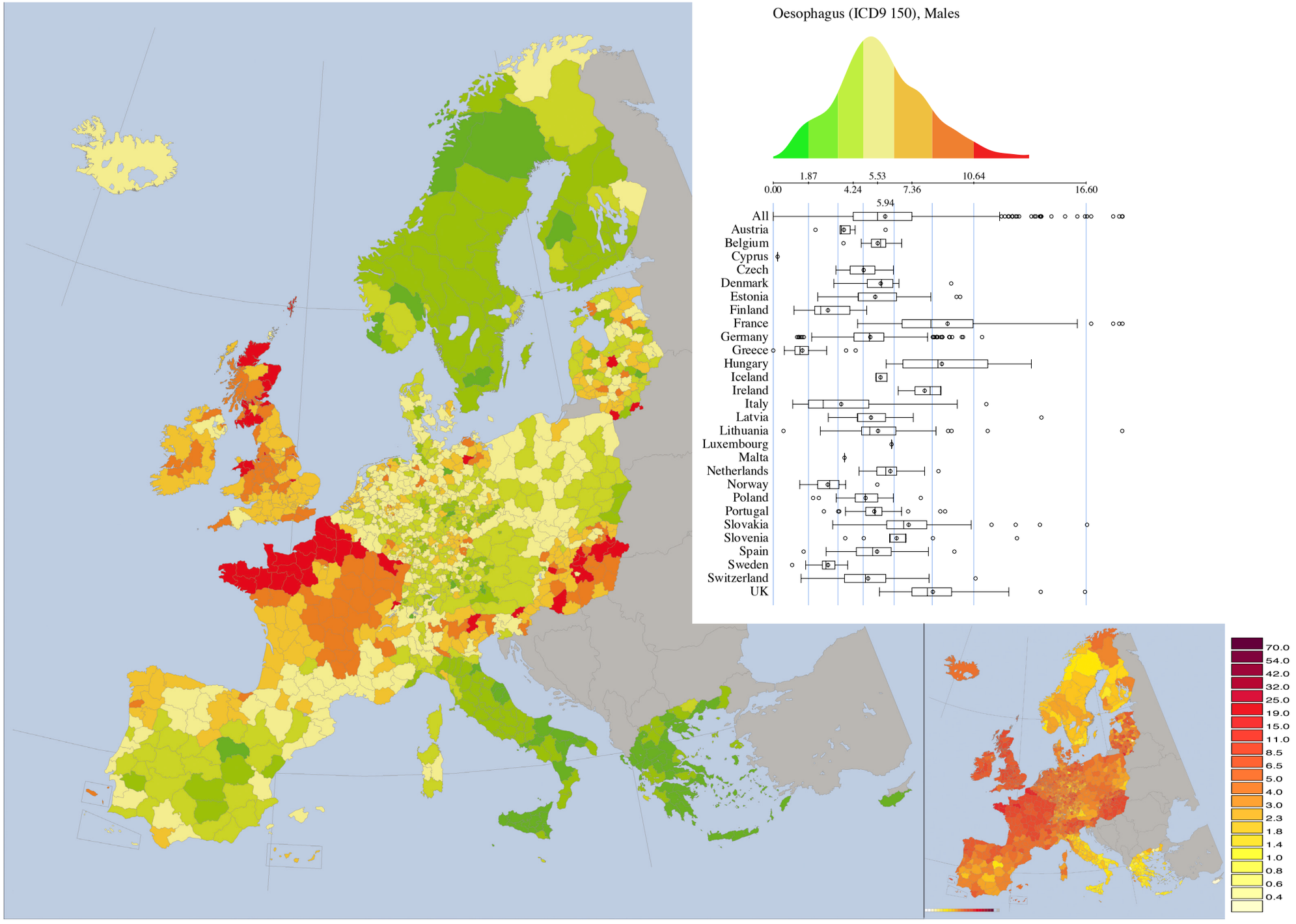
CANCER MORTALITY MAPS BY SITE

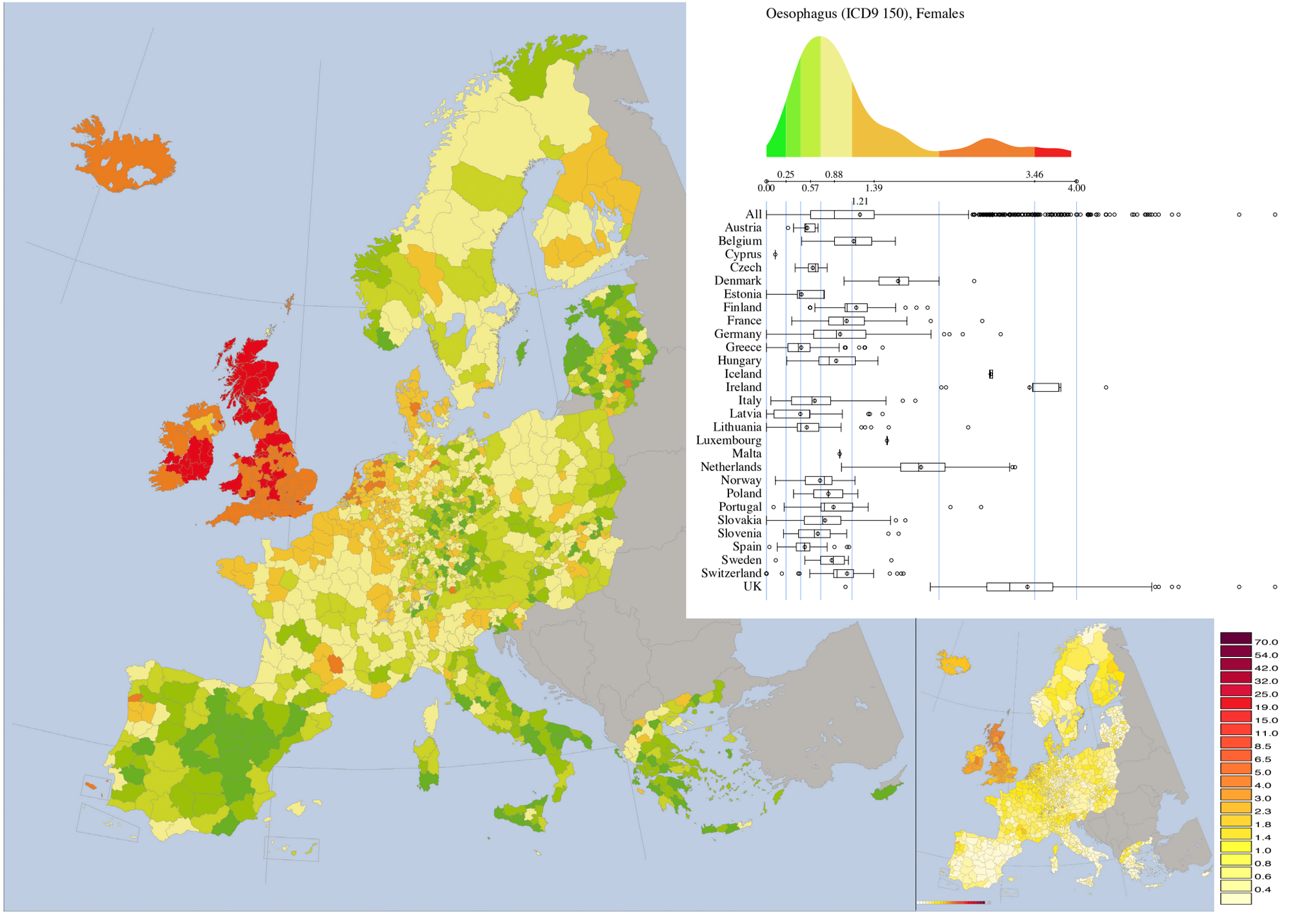

Median Age, Males
30.32
34.99
39.49
25.00
33.18
36.67
50.00
34.90
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
43.1
42.2
41.3
40.4
39.5
38.6
37.7
36.8
35.9
35.0
34.1
33.2
32.3
31.4
30.5
29.6
28.7
27.8
26.9
26.0

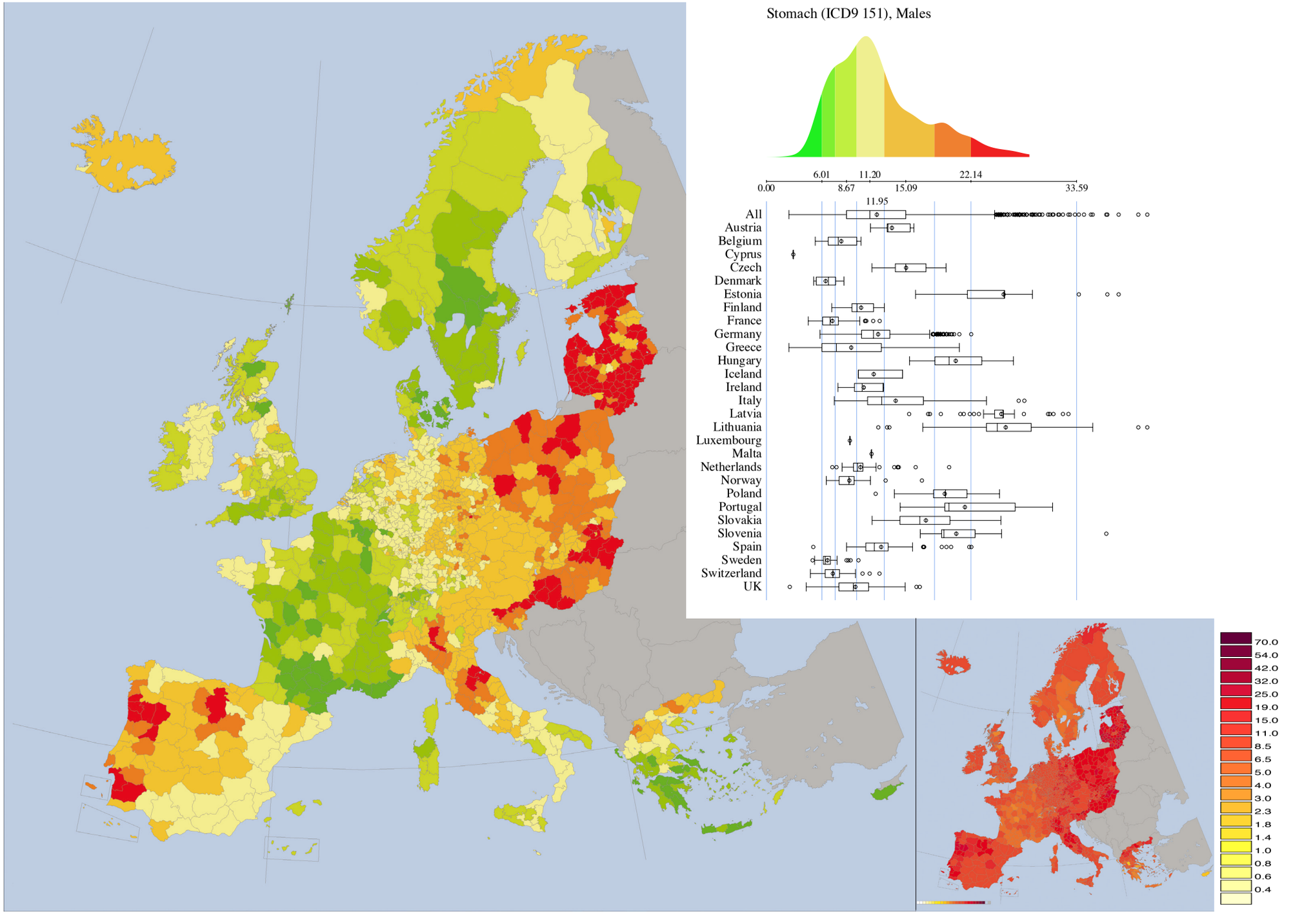

Median Age, Females
25.00
32.53
35.70
38.00
38.24
39.92
43.48
50.00
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
47.0
46.0
45.0
44.0
43.0
42.0
41.0
40.0
39.0
38.0
37.0
36.0
35.0
34.0
33.0
32.0
31.0
30.0
29.0
28.0

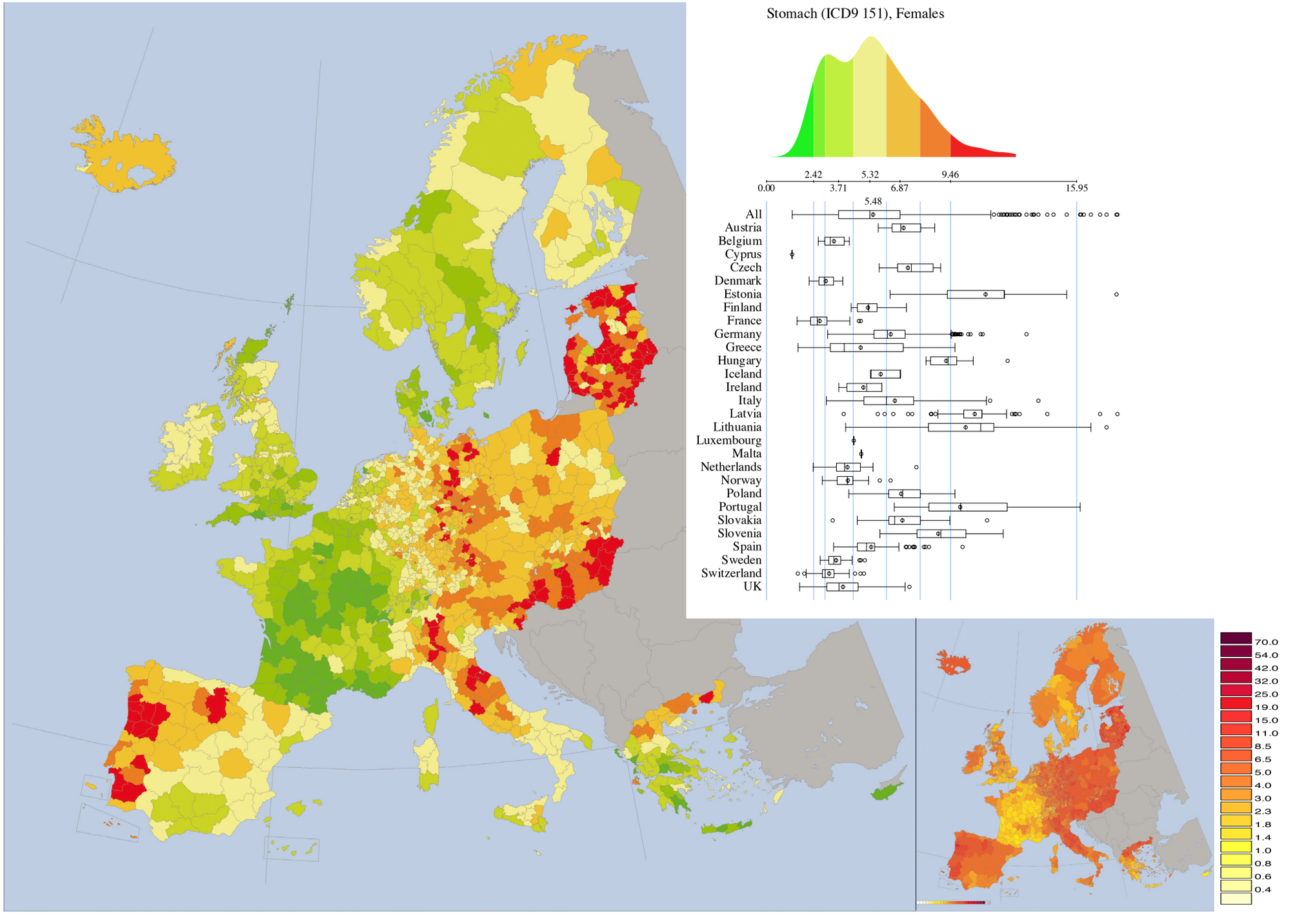

Oral cavity and pharynx (ICD9 140-149), Males
1.98
5.81
14.54
0.00
3.66
8.05
17.42
6.47
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4

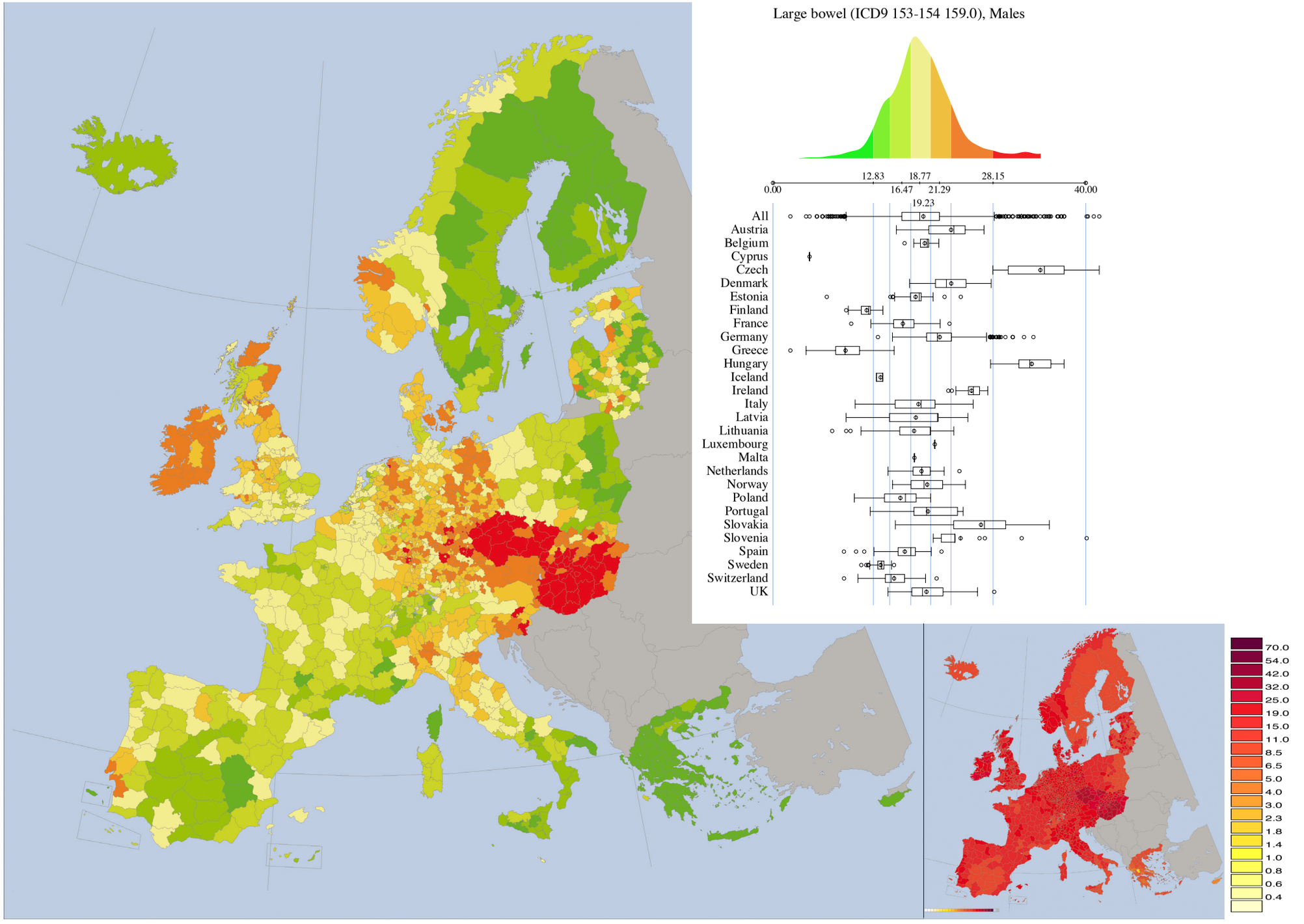

Oral cavity and pharynx (ICD9 140-149), Females
0.00
0.51
0.85
1.05
1.35
1.99
3.14
1.12
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4

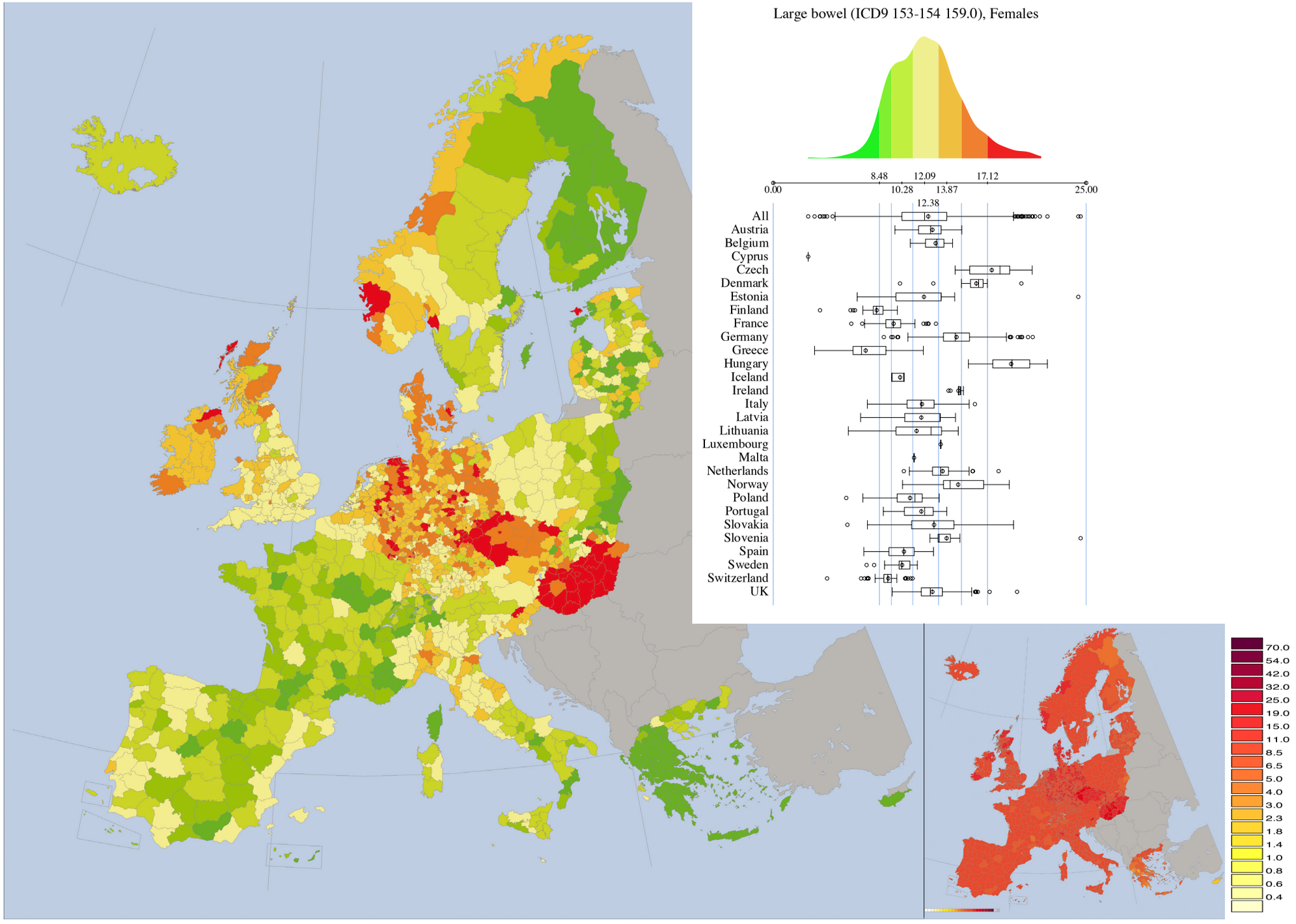

Oesophagus (ICD9 150), Males
1.87
5.53
10.64
0.00
4.24
7.36
16.60
5.94
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4

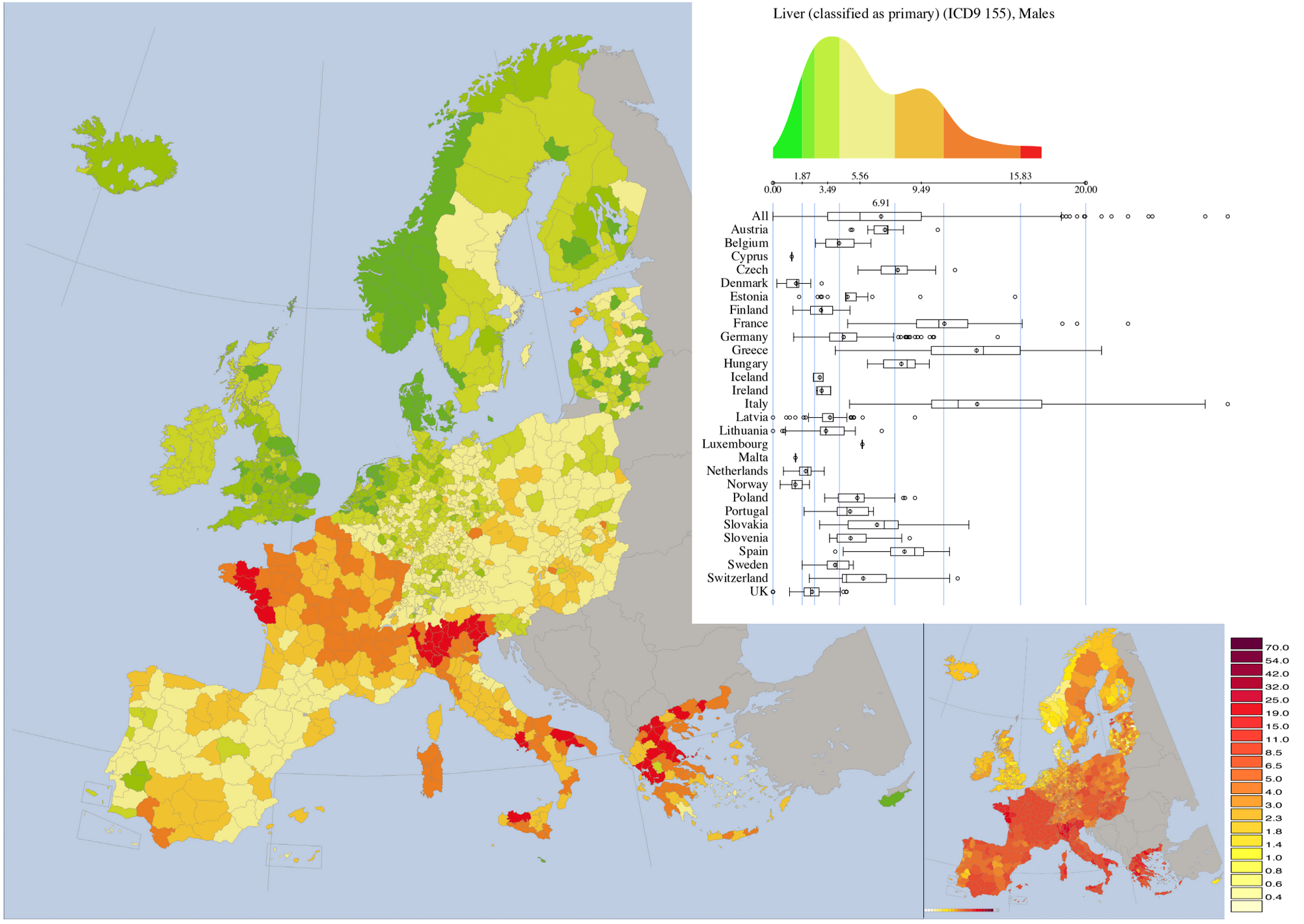

Oesophagus (ICD9 150), Females
0.25
0.88
3.46
0.00
0.57
1.39
4.00
1.21
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4

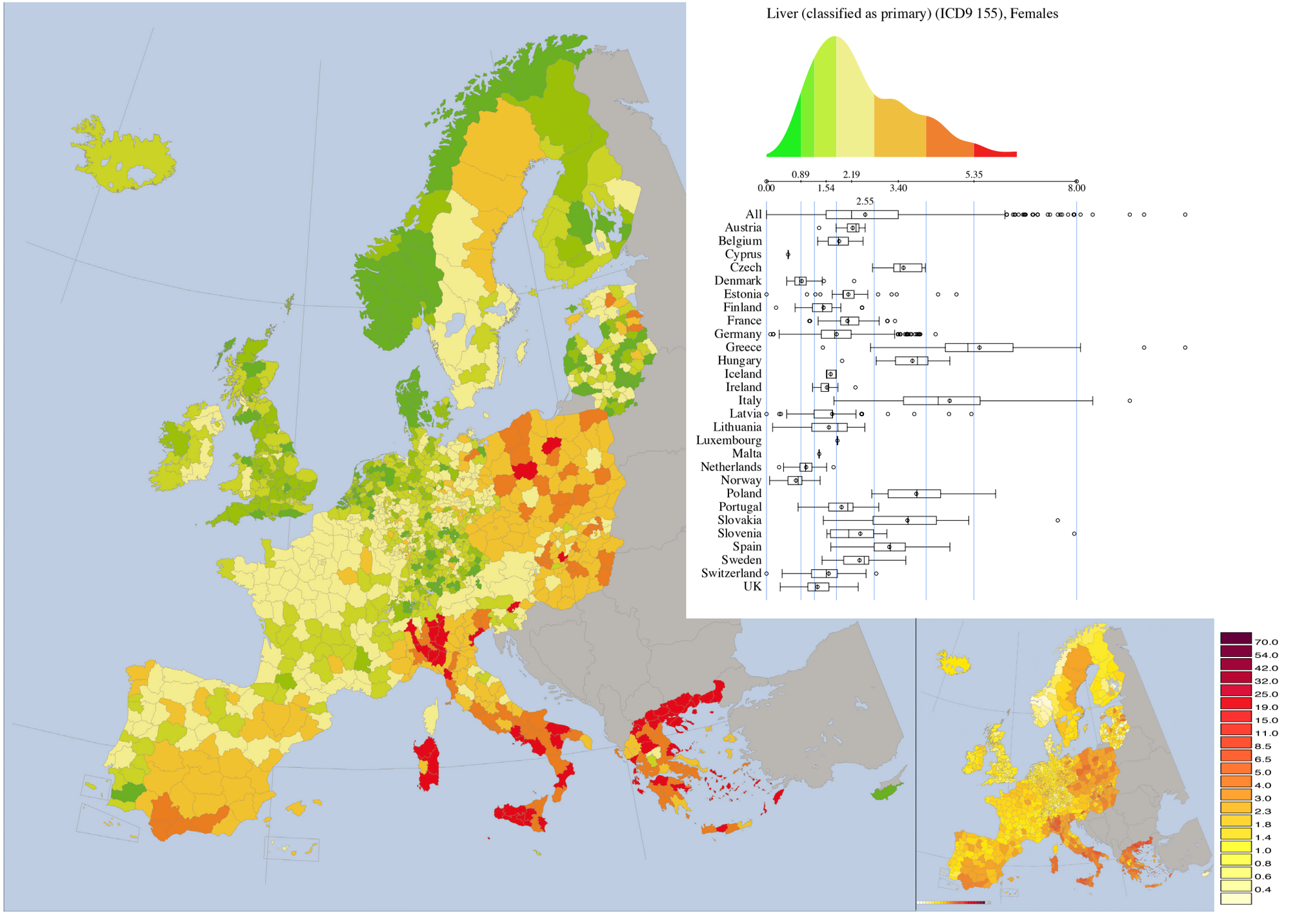

Stomach (ICD9 151), Males
6.01
11.20
22.14
0.00
8.67
15.09
33.59
11.95
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4

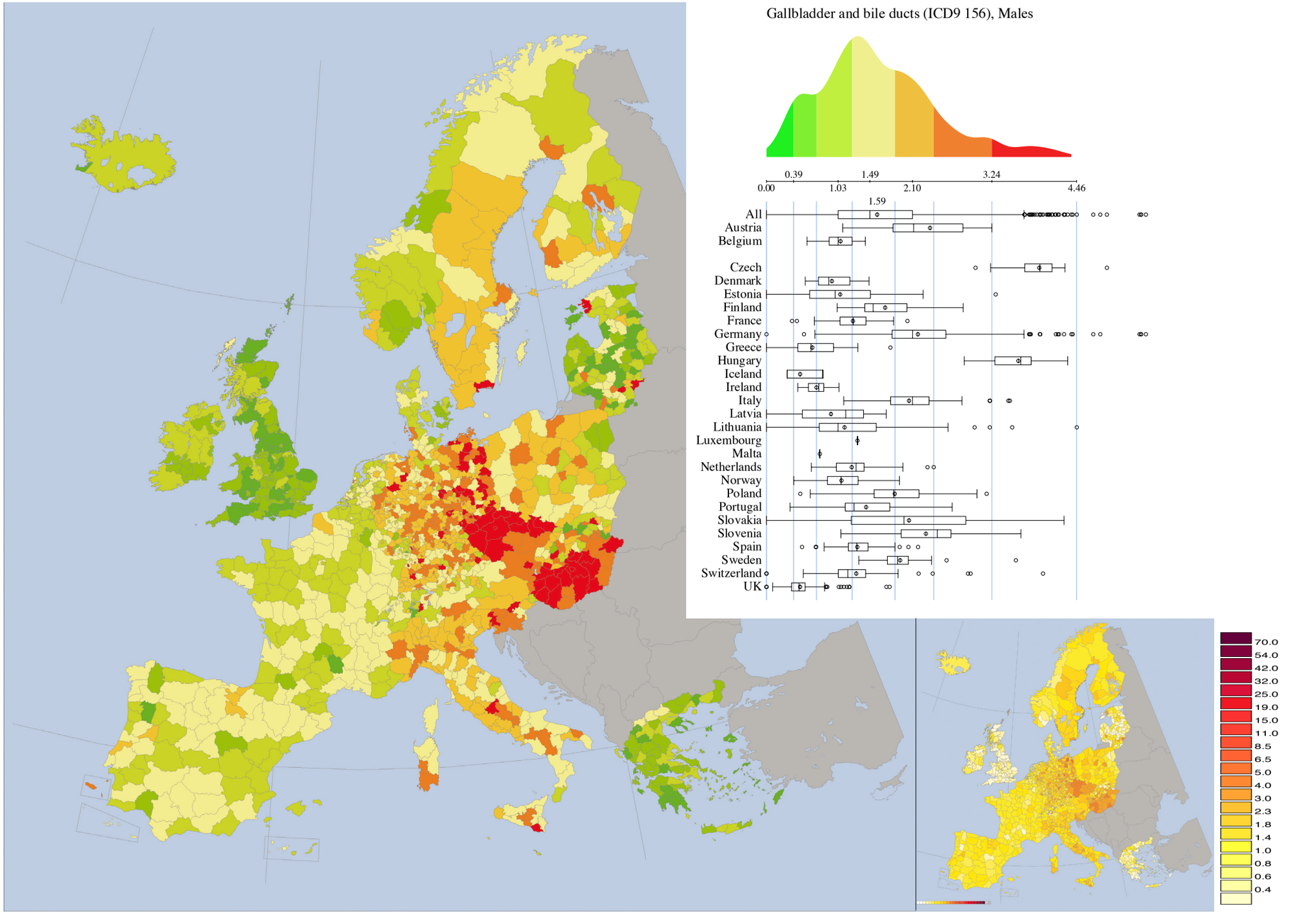

Stomach (ICD9 151), Females
0.00
2.42
3.71
5.32
6.87
9.46
15.95
5.48
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4

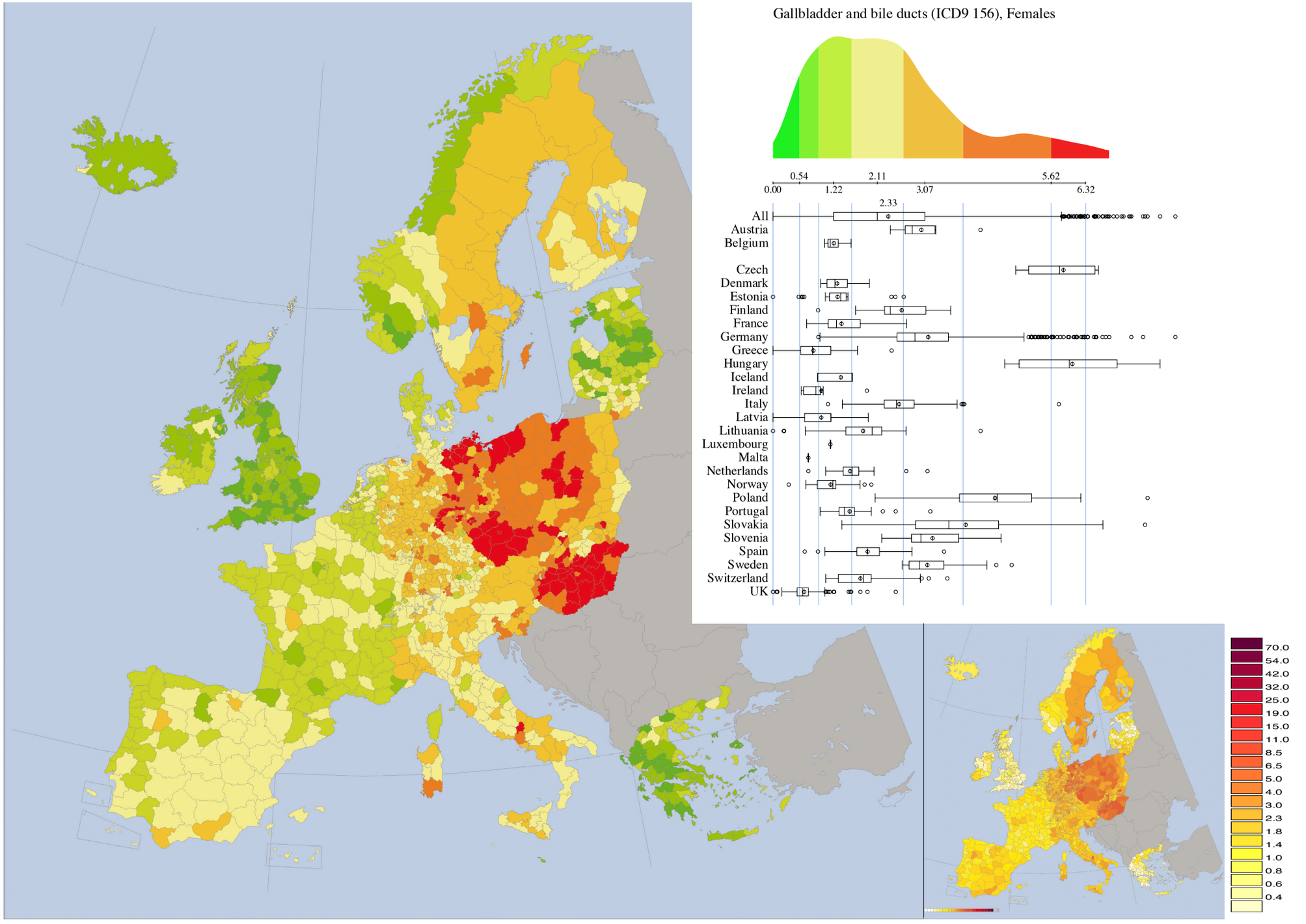

Large bowel (ICD9 153-154 159.0), Males
12.83
18.77
28.15
0.00
16.47
21.29
40.00
19.23
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4

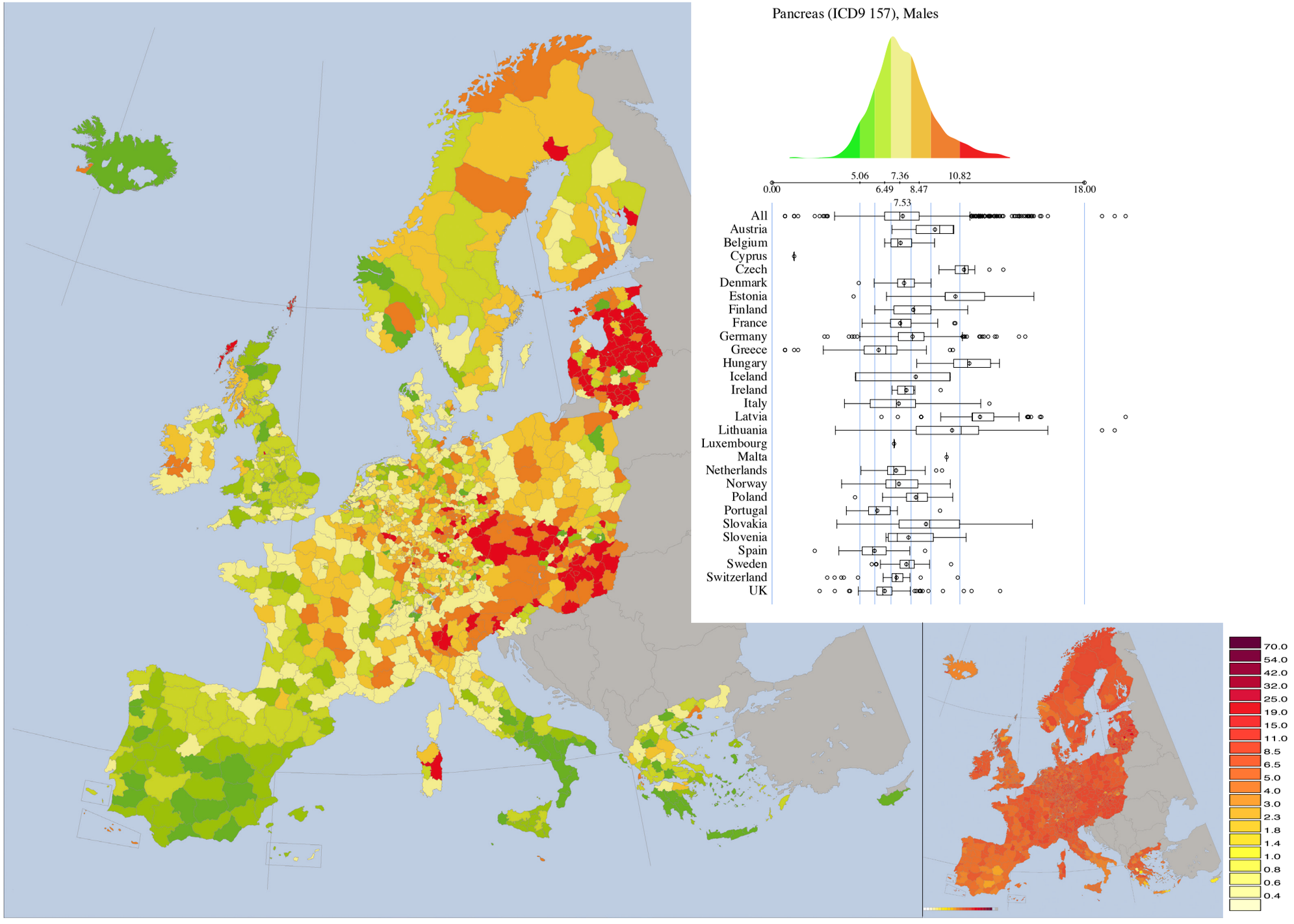

Large bowel (ICD9 153-154 159.0), Females
8.48
12.09
17.12
0.00
10.28
13.87
25.00
12.38
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4

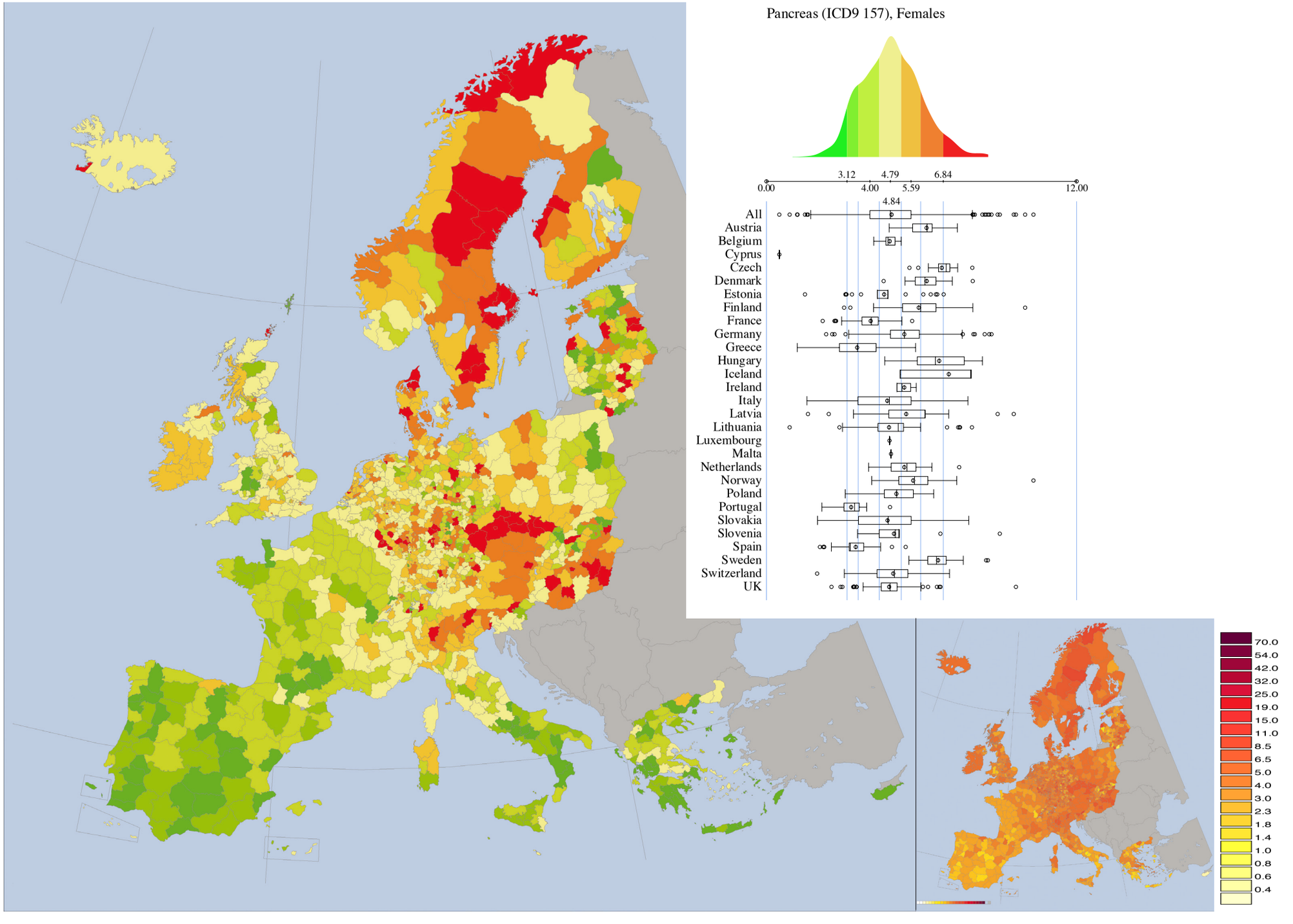

Liver (classified as primary) (ICD9 155), Males
1.87
5.56
15.83
0.00
3.49
9.49
20.00
6.91
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4

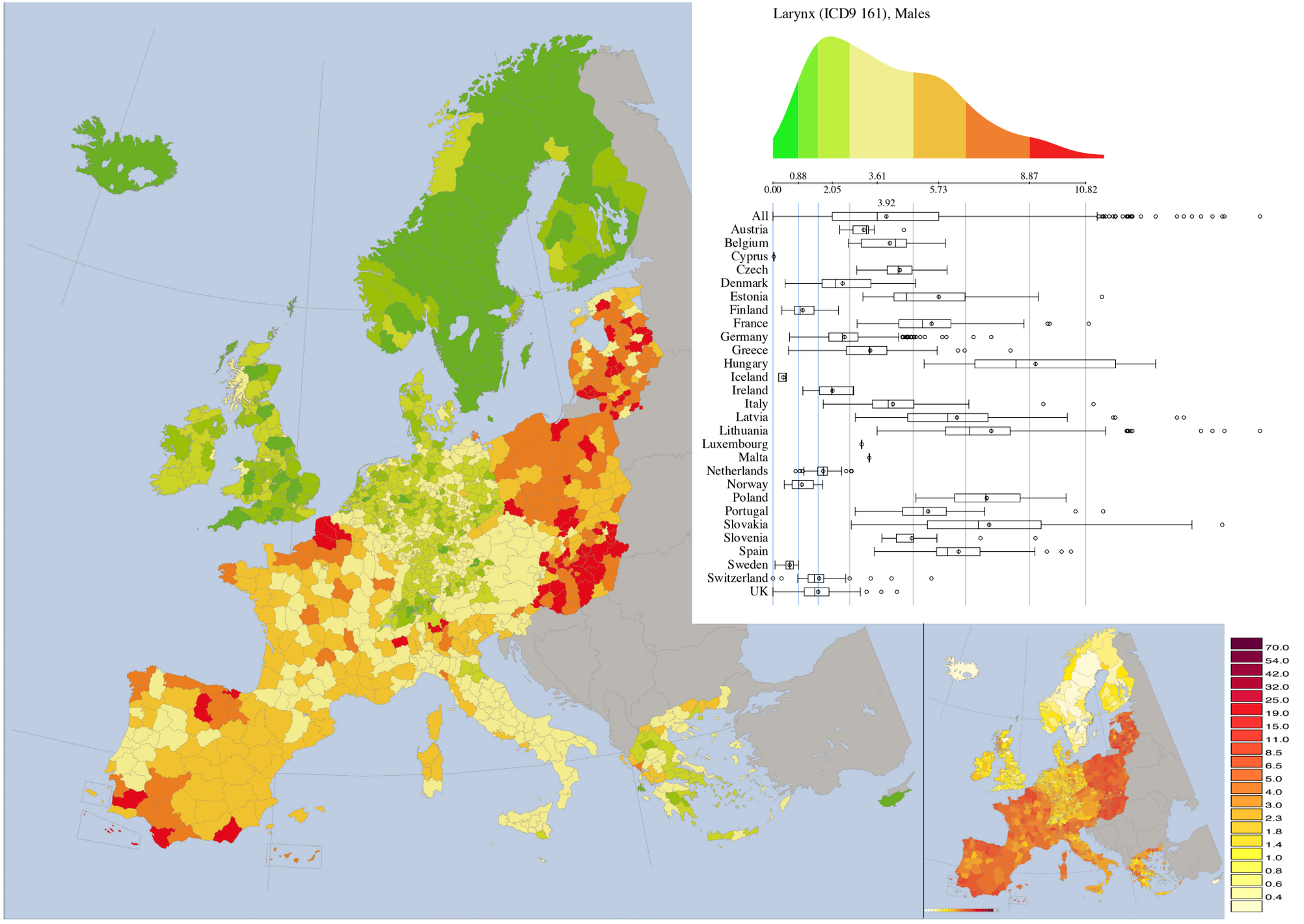

Liver (classified as primary) (ICD9 155), Females
0.00
0.89
1.54
2.19
2.55
3.40
5.35
8.00
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4

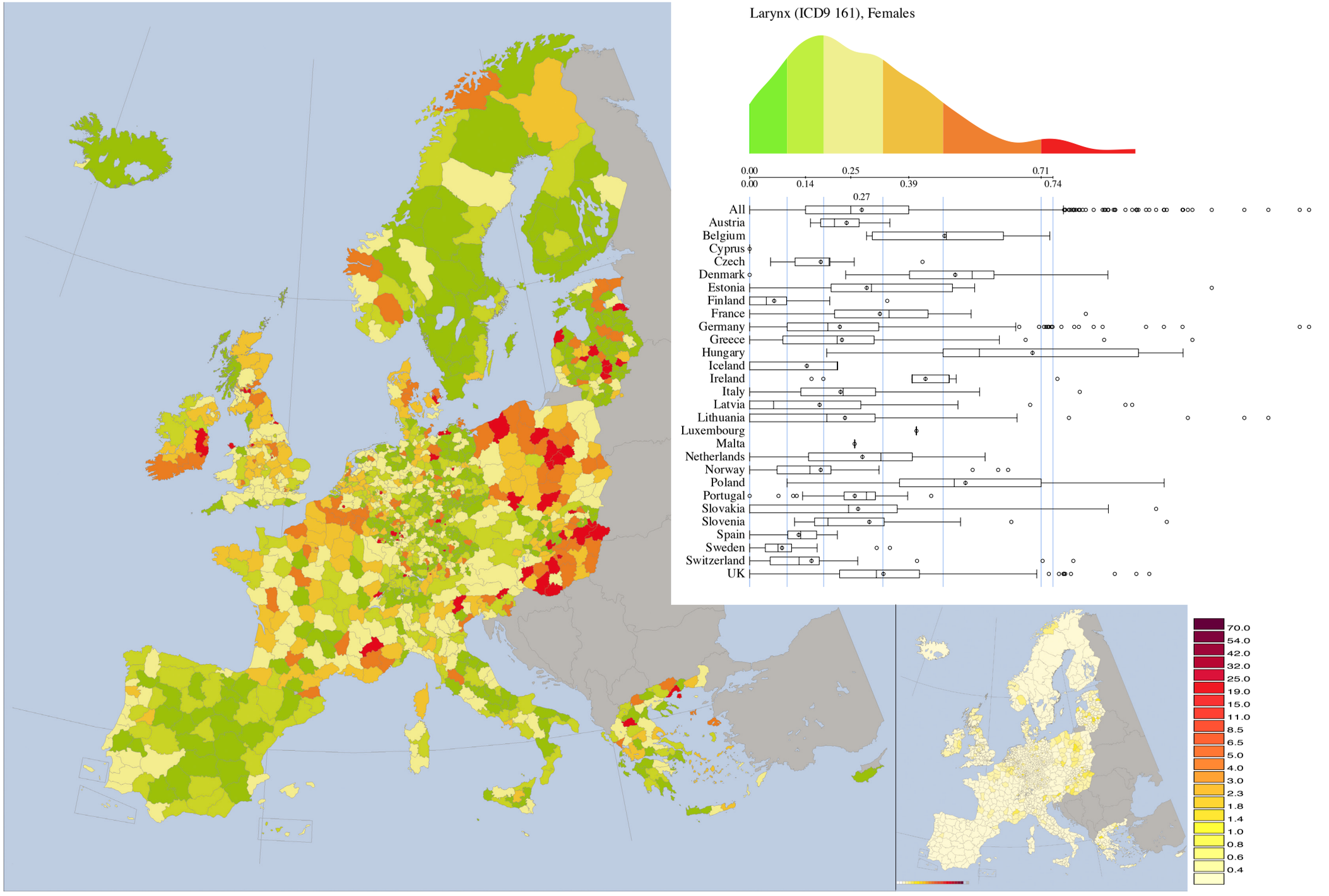

Gallbladder and bile ducts (ICD9 156), Males
0.00
0.39
1.03
1.49
2.10
3.24
4.46
1.59
All
Austria
Belgium
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4

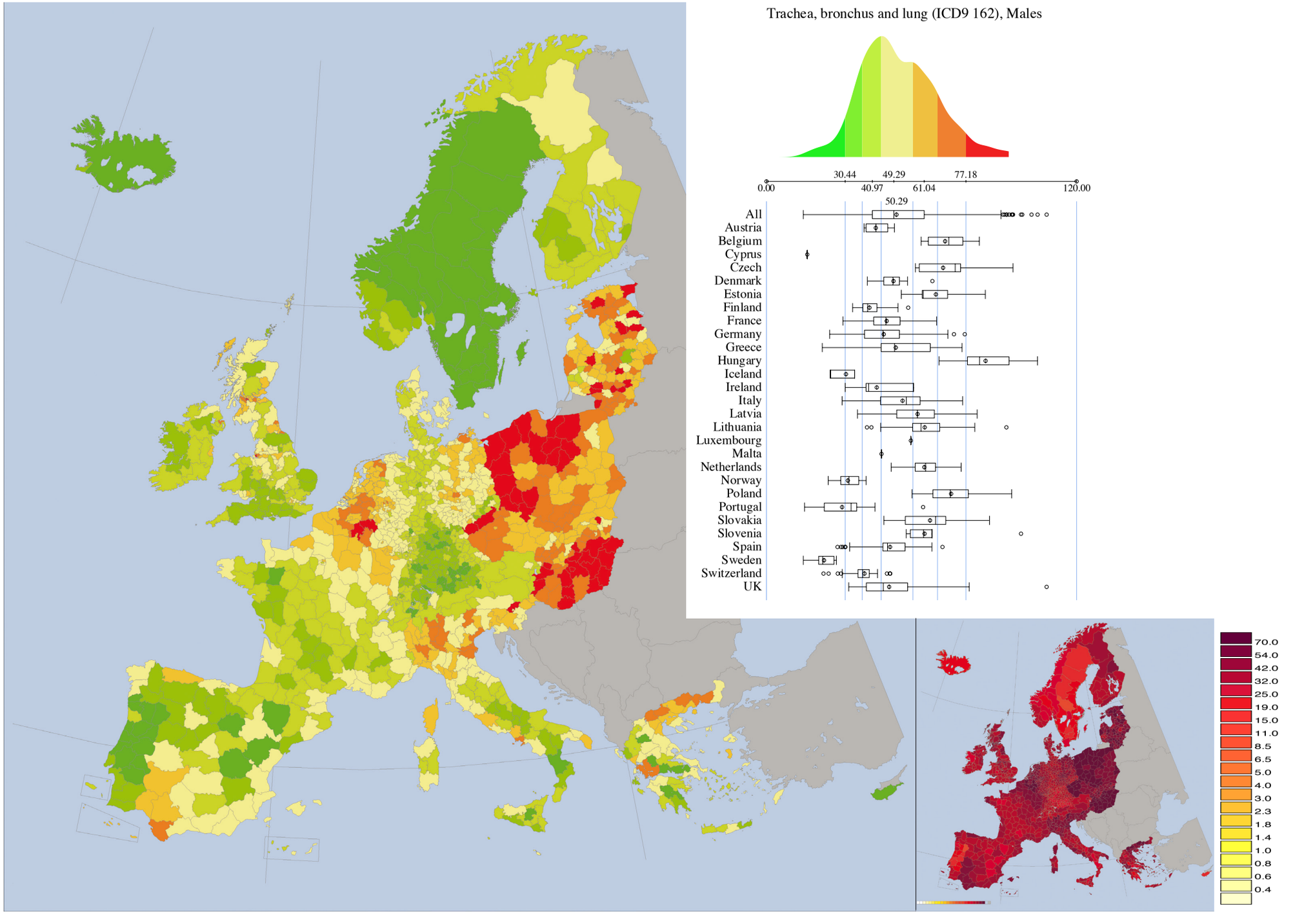

Gallbladder and bile ducts (ICD9 156), Females
0.54
2.11
5.62
0.00
1.22
3.07
6.32
2.33
All
Austria
Belgium
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4

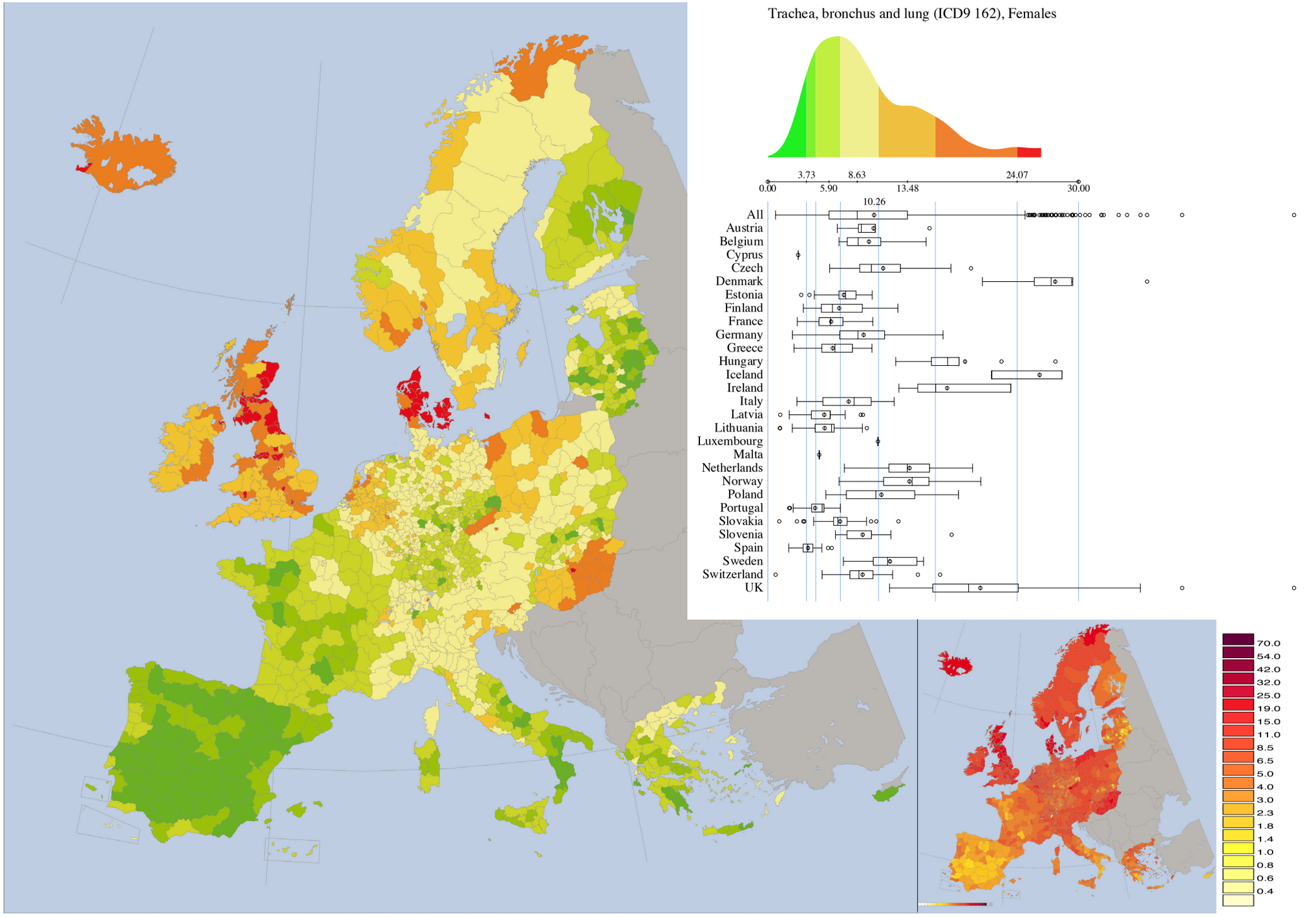

Pancreas (ICD9 157), Males
5.06
7.36
10.82
0.00
6.49
8.47
18.00
7.53
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4

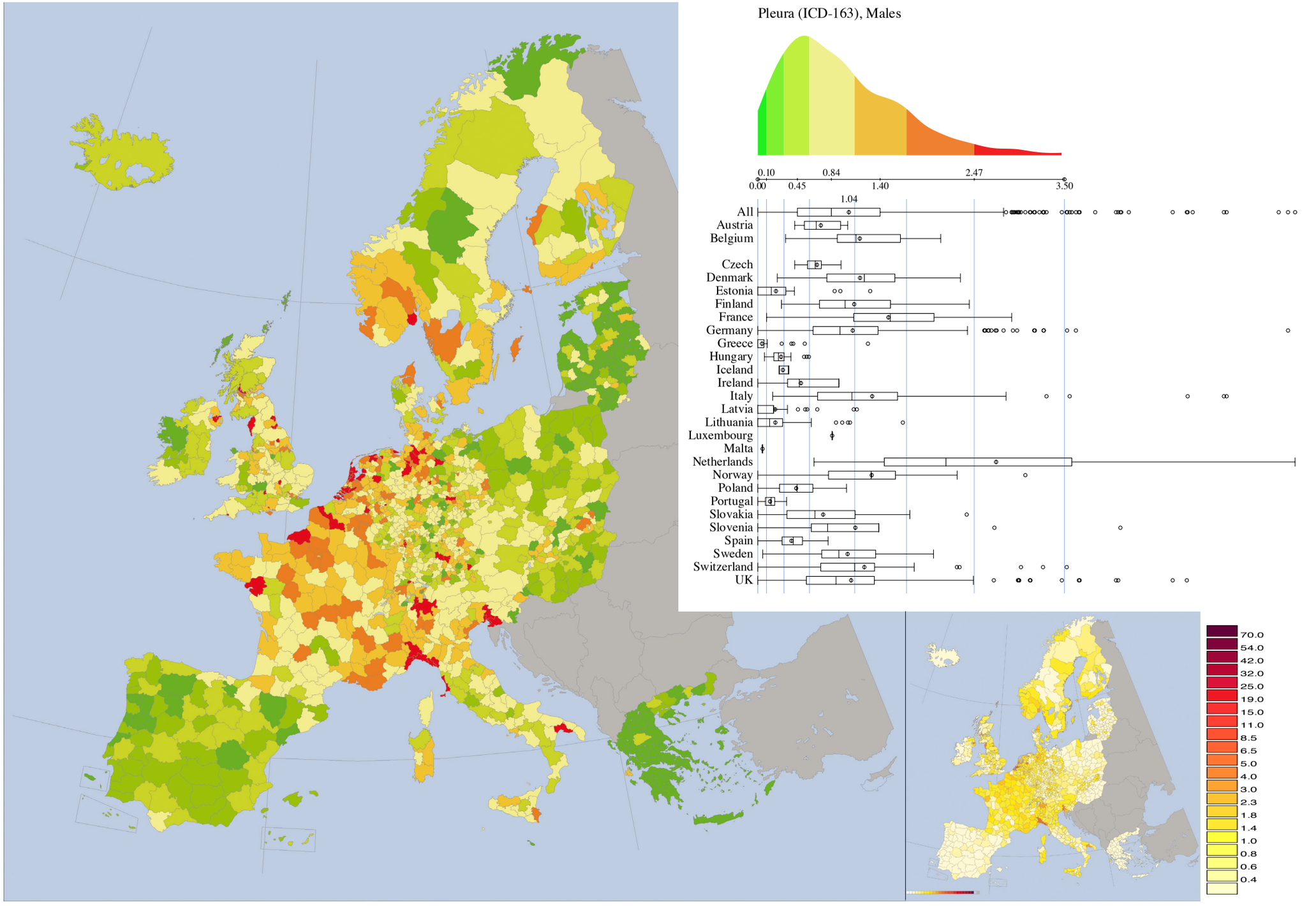

Pancreas (ICD9 157), Females
3.12
4.79
6.84
0.00
4.00
5.59
12.00
4.84
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4

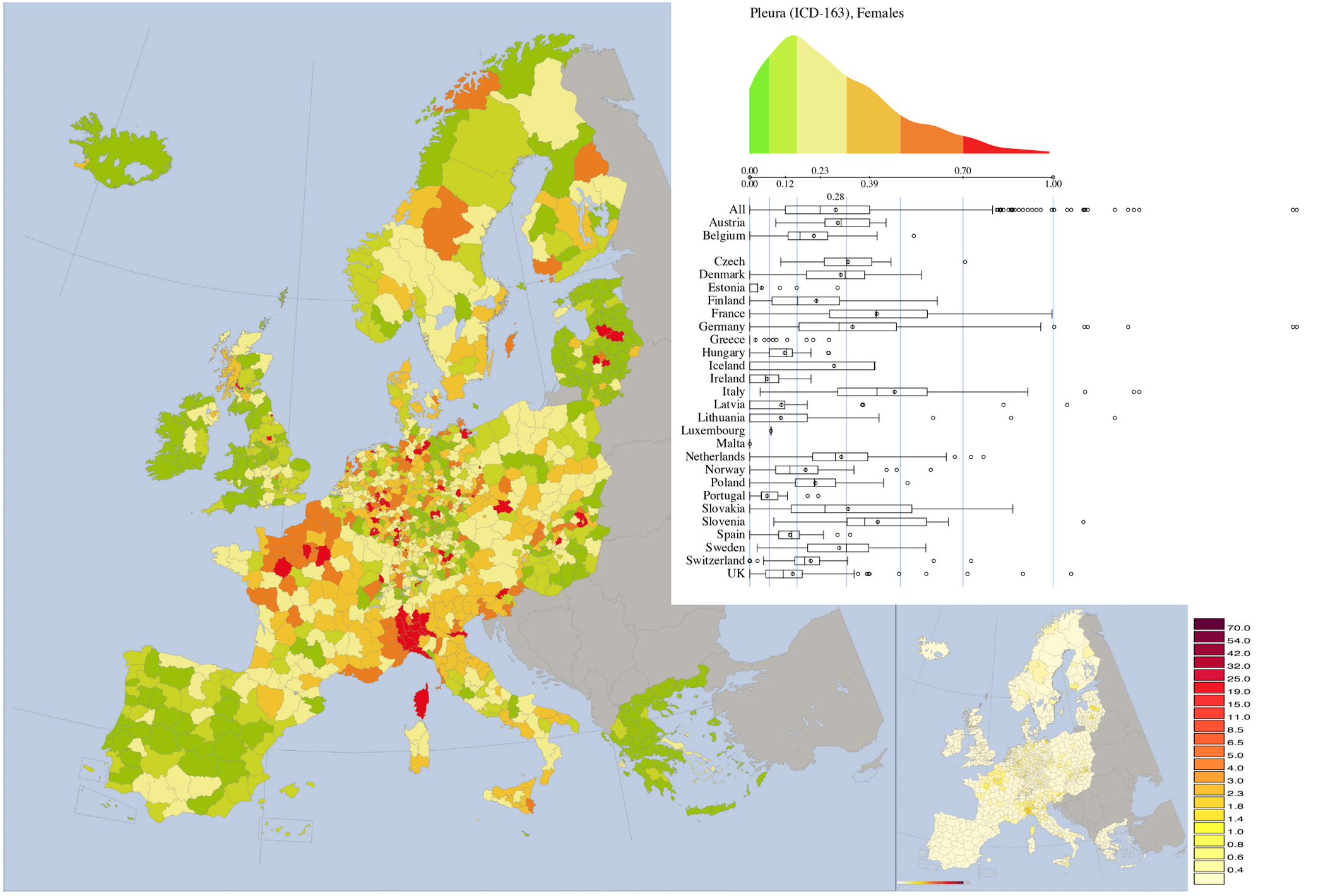

Larynx (ICD9 161), Males
0.00
2.05
0.88
3.61
5.73
8.87
10.82
3.92
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4

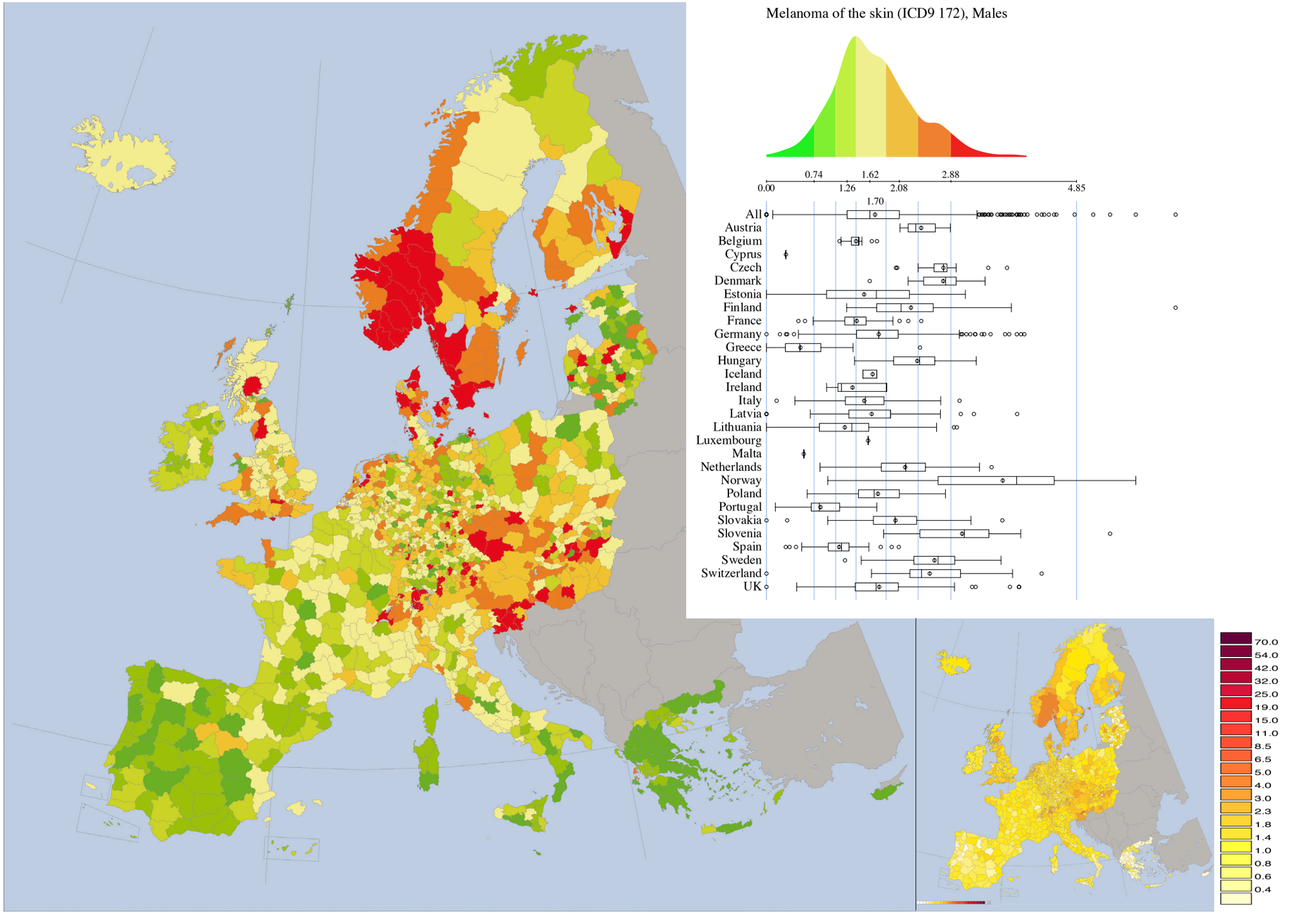

Larynx (ICD9 161), Females
0.00
0.25
0.71
0.00
0.14
0.39
0.74
0.27
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4

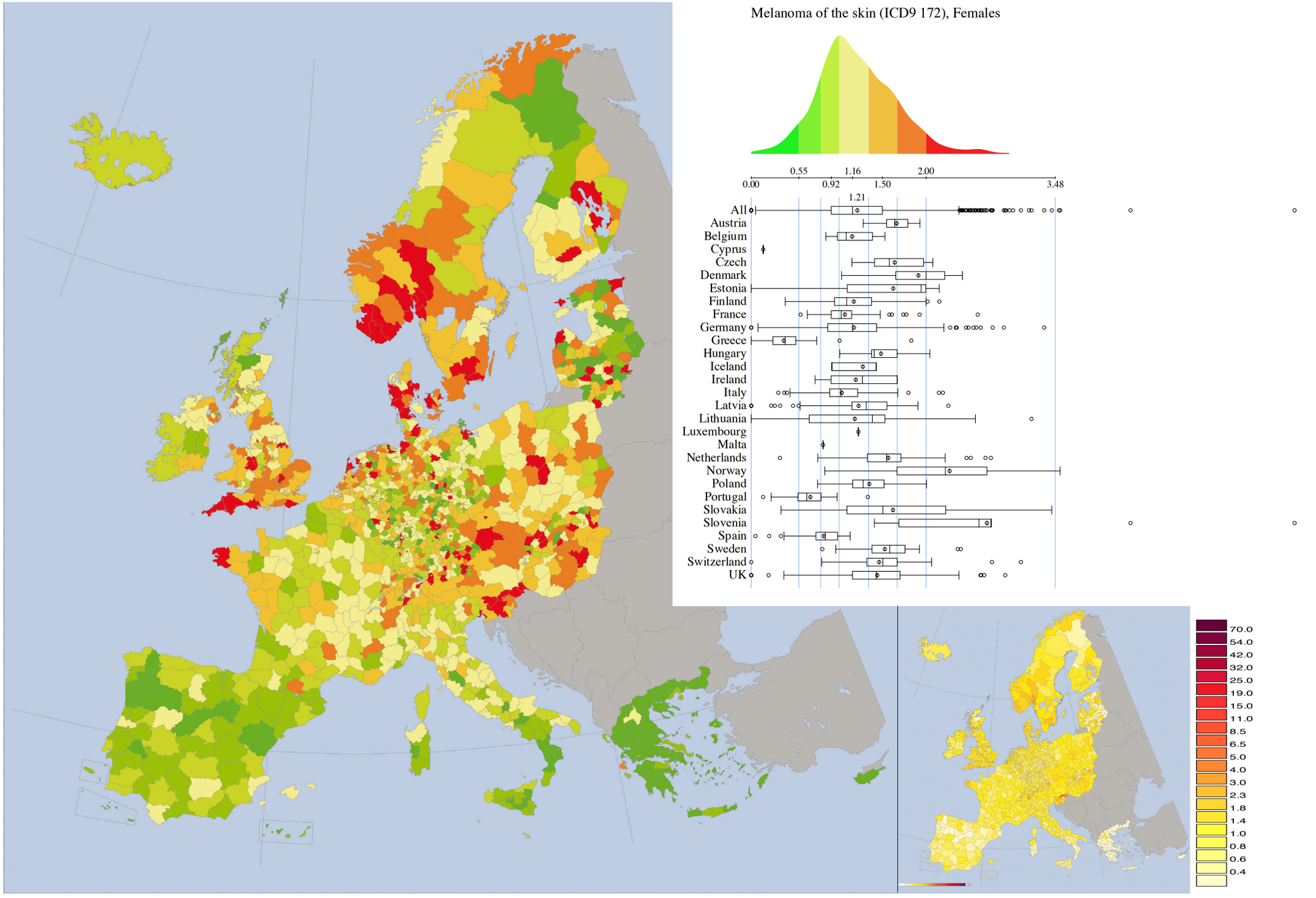

Trachea, bronchus and lung (ICD9 162), Males
30.44
49.29
77.18
0.00
40.97
61.04
120.00
50.29
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4


Trachea, bronchus and lung (ICD9 162), Females
3.73
8.63
24.07
0.00
5.90
13.48
30.00
10.26
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4


Pleura (ICD-163), Males
0.10
0.84
2.47
0.00
0.45
1.40
3.50
1.04
All
Austria
Belgium
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4


Pleura (ICD-163), Females
0.00
0.23
0.70
0.00
0.12
0.39
1.00
0.28
All
Austria
Belgium
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4


Melanoma of the skin (ICD9 172), Males
0.74
1.62
2.88
0.00
1.26
2.08
4.85
1.70
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4


Melanoma of the skin (ICD9 172), Females
0.55
1.16
2.00
0.00
0.92
1.50
3.48
1.21
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
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5.0
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2.3
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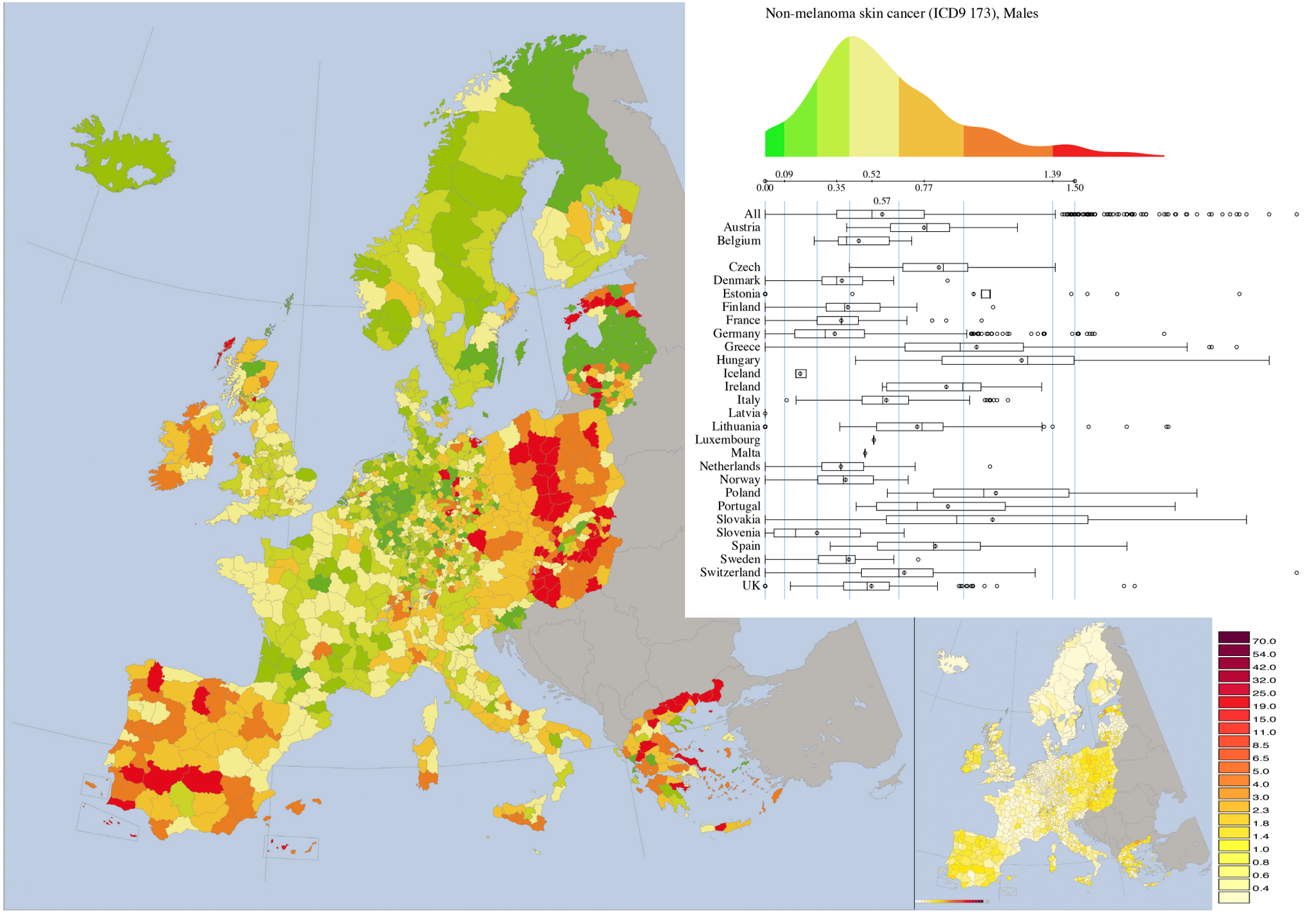
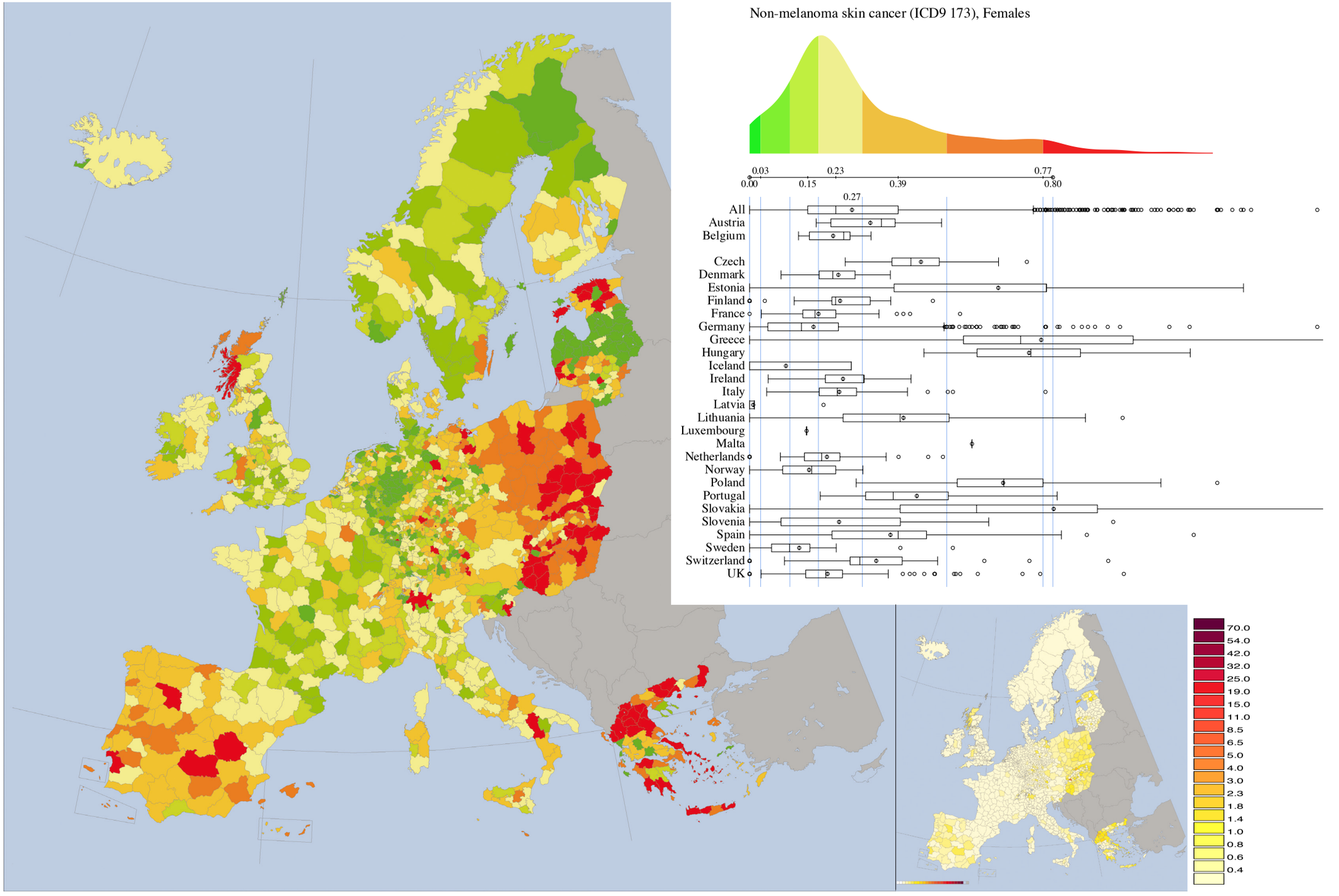
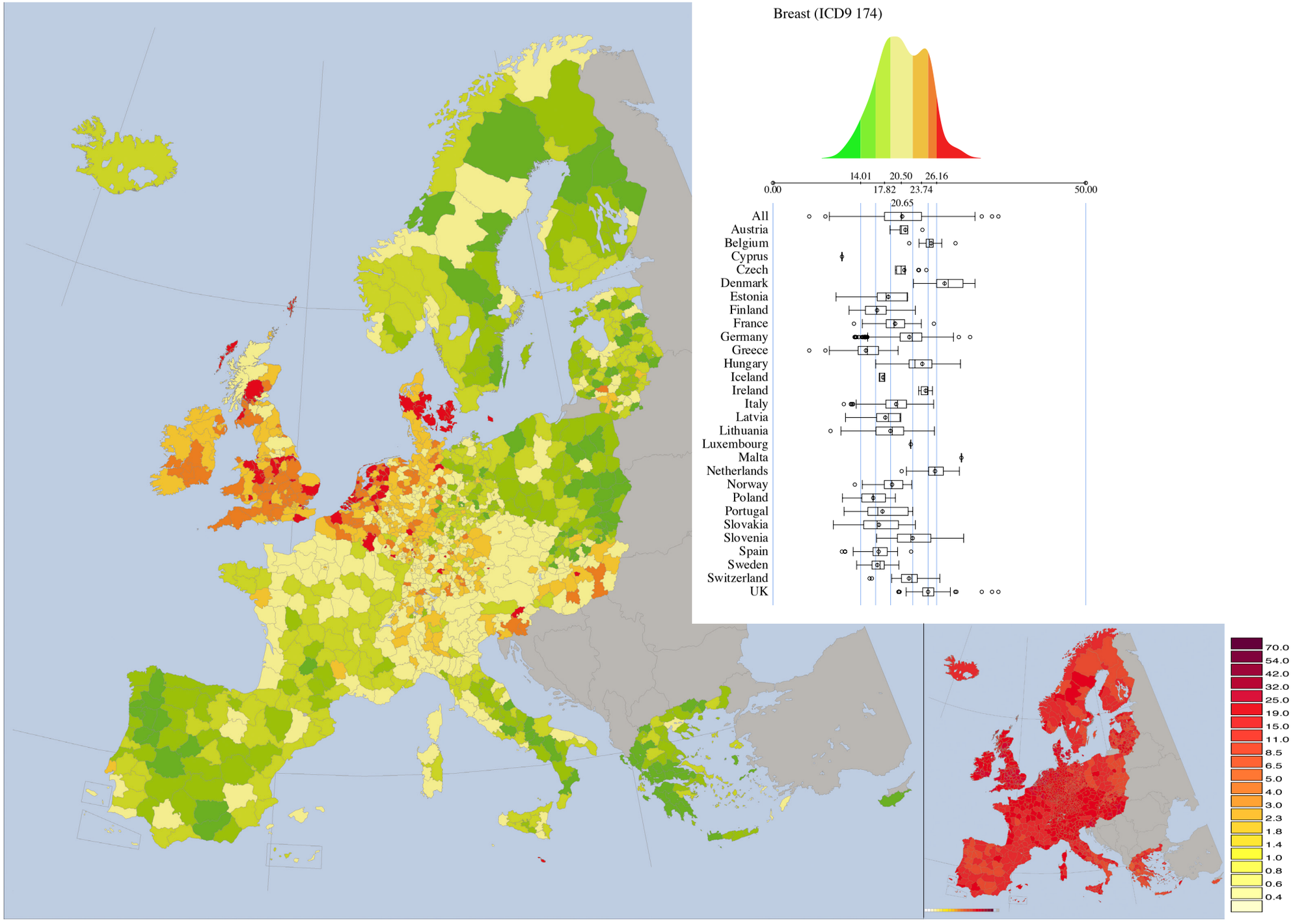
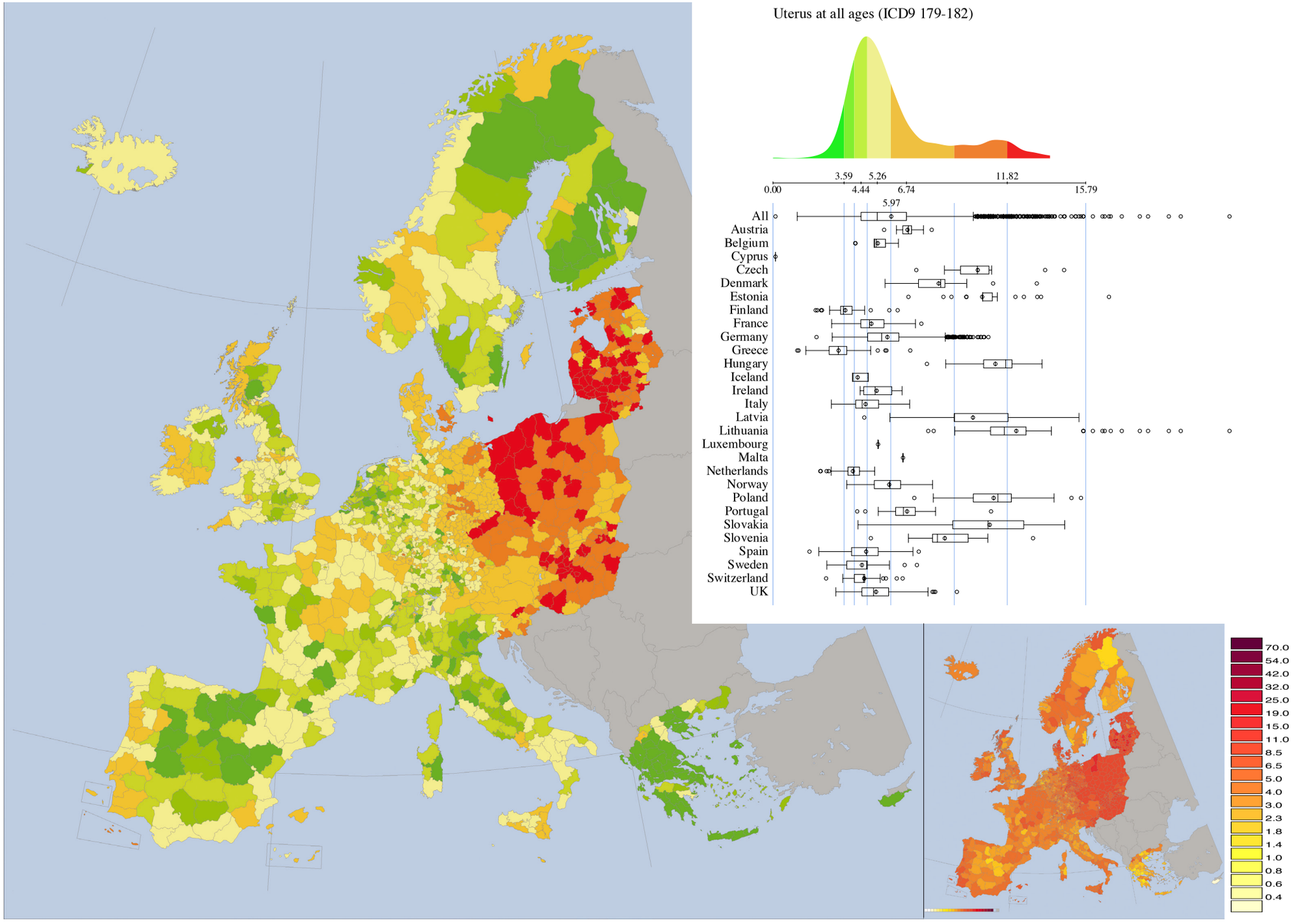
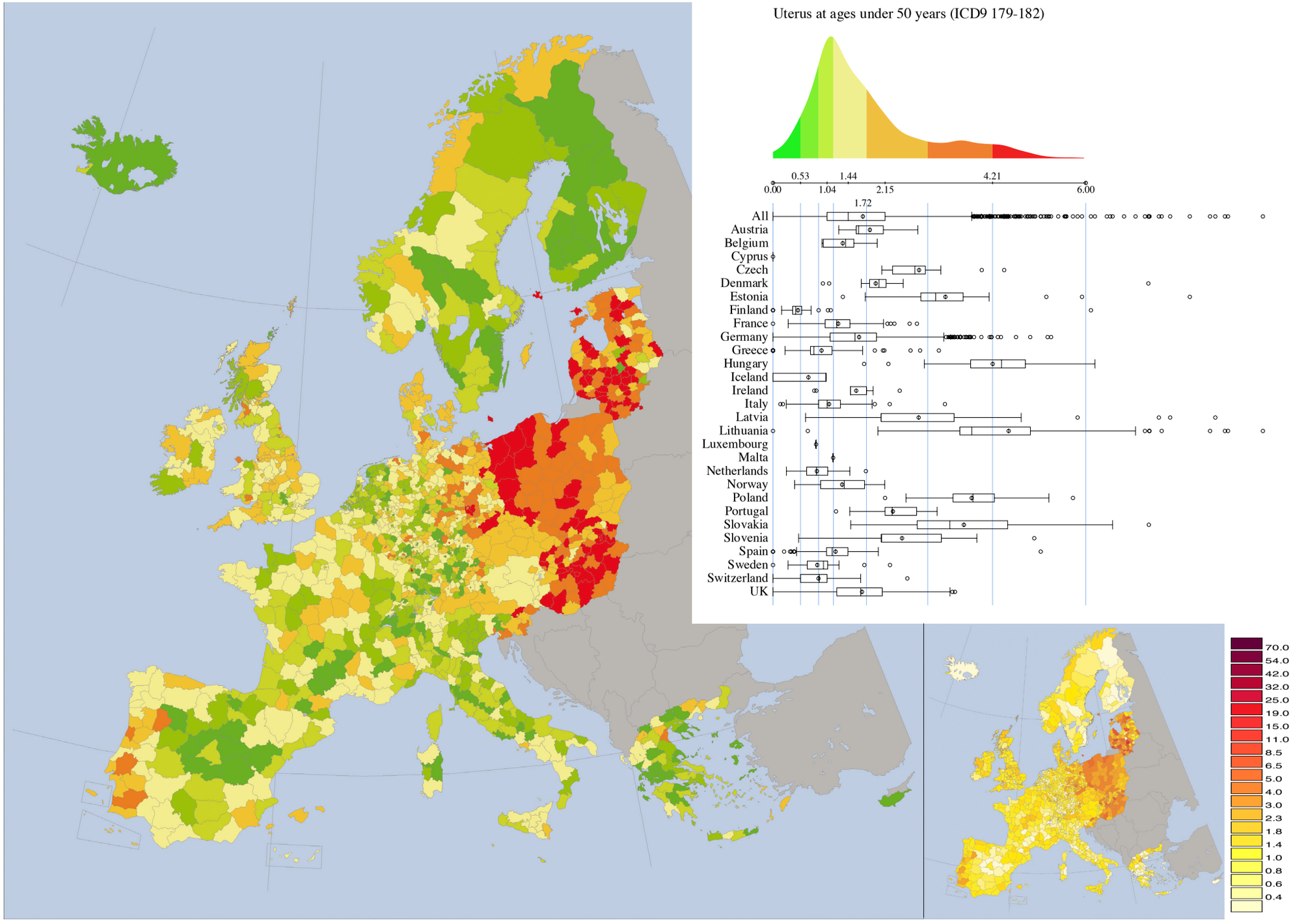
1.4
1.0
0.8
0.6
0.4

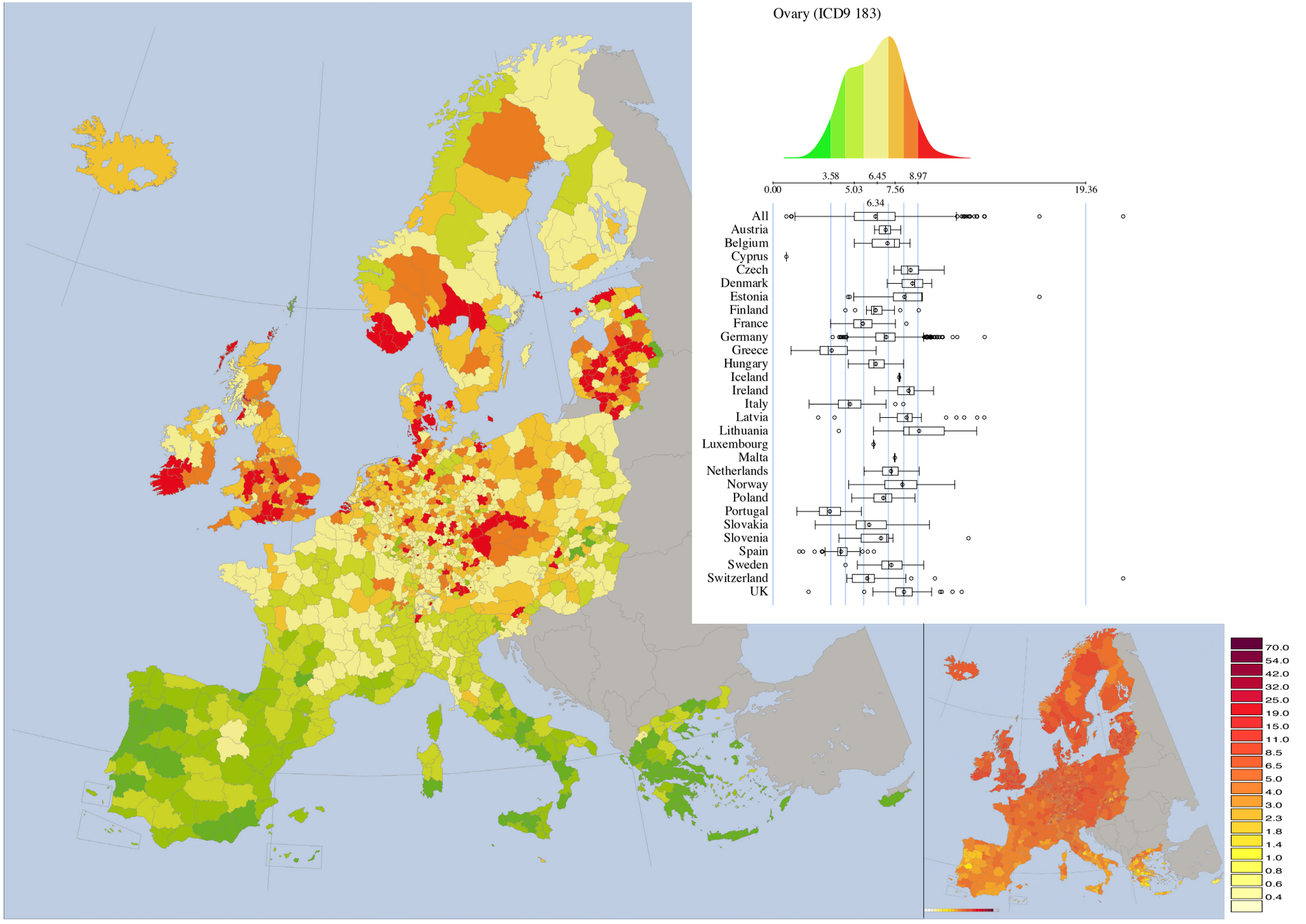

Non-melanoma skin cancer (ICD9 173), Males
0.09
0.52
1.39
0.00
0.35
0.77
1.50
0.57
All
Austria
Belgium
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4


Non-melanoma skin cancer (ICD9 173), Females
0.03
0.23
0.77
0.00
0.15
0.39
0.80
0.27
All
Austria
Belgium
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4


Breast (ICD9 174)
14.01
20.50
26.16
0.00
17.82
23.74
50.00
20.65
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4


Uterus at all ages (ICD9 179-182)
3.59
5.26
11.82
0.00
4.44
6.74
15.79
5.97
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4


Uterus at ages under 50 years (ICD9 179-182)
0.53
1.44
4.21
0.00
1.04
2.15
6.00
1.72
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4


Ovary (ICD9 183)
3.58
6.45
8.97
0.00
5.03
7.56
19.36
6.34
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
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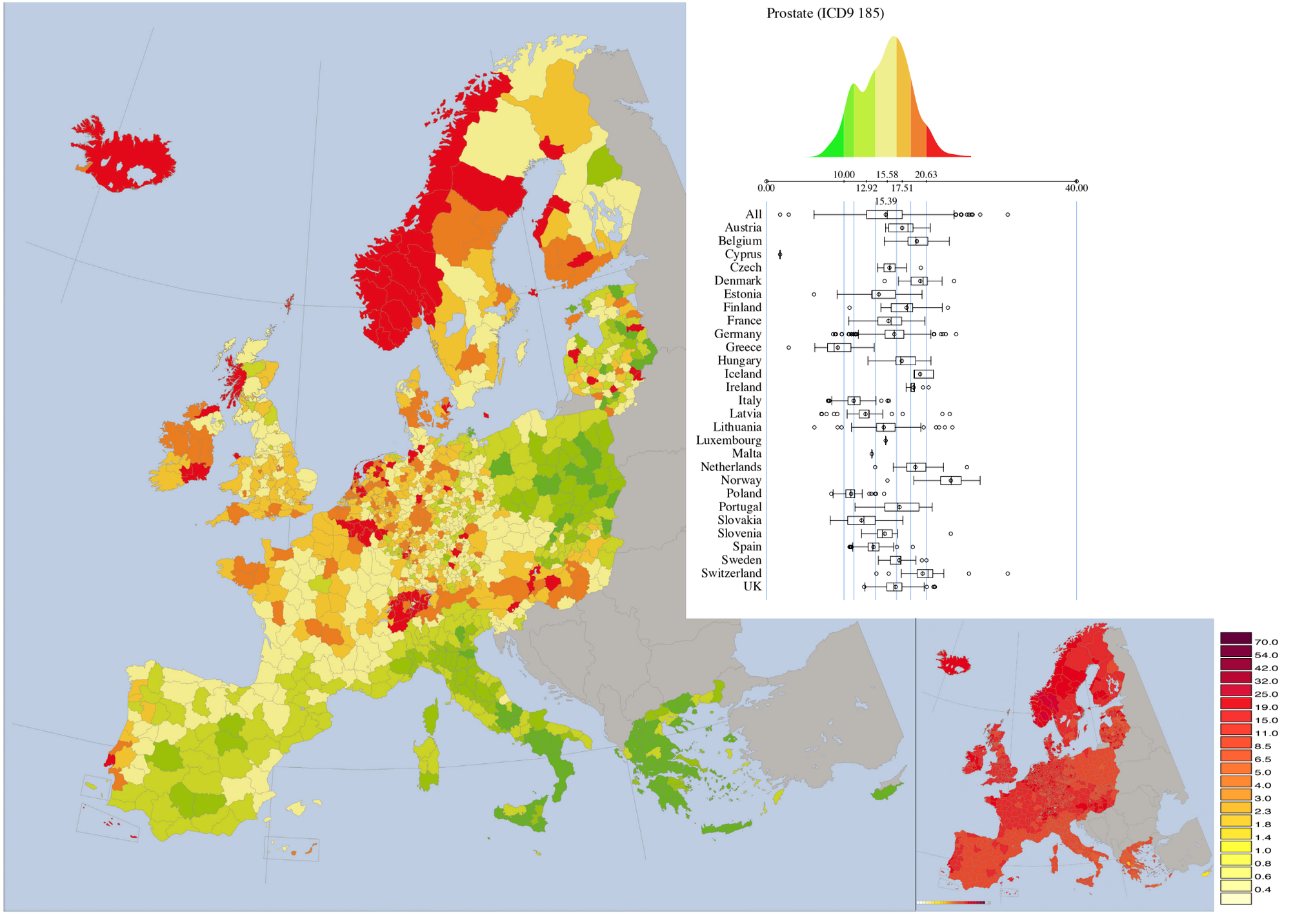
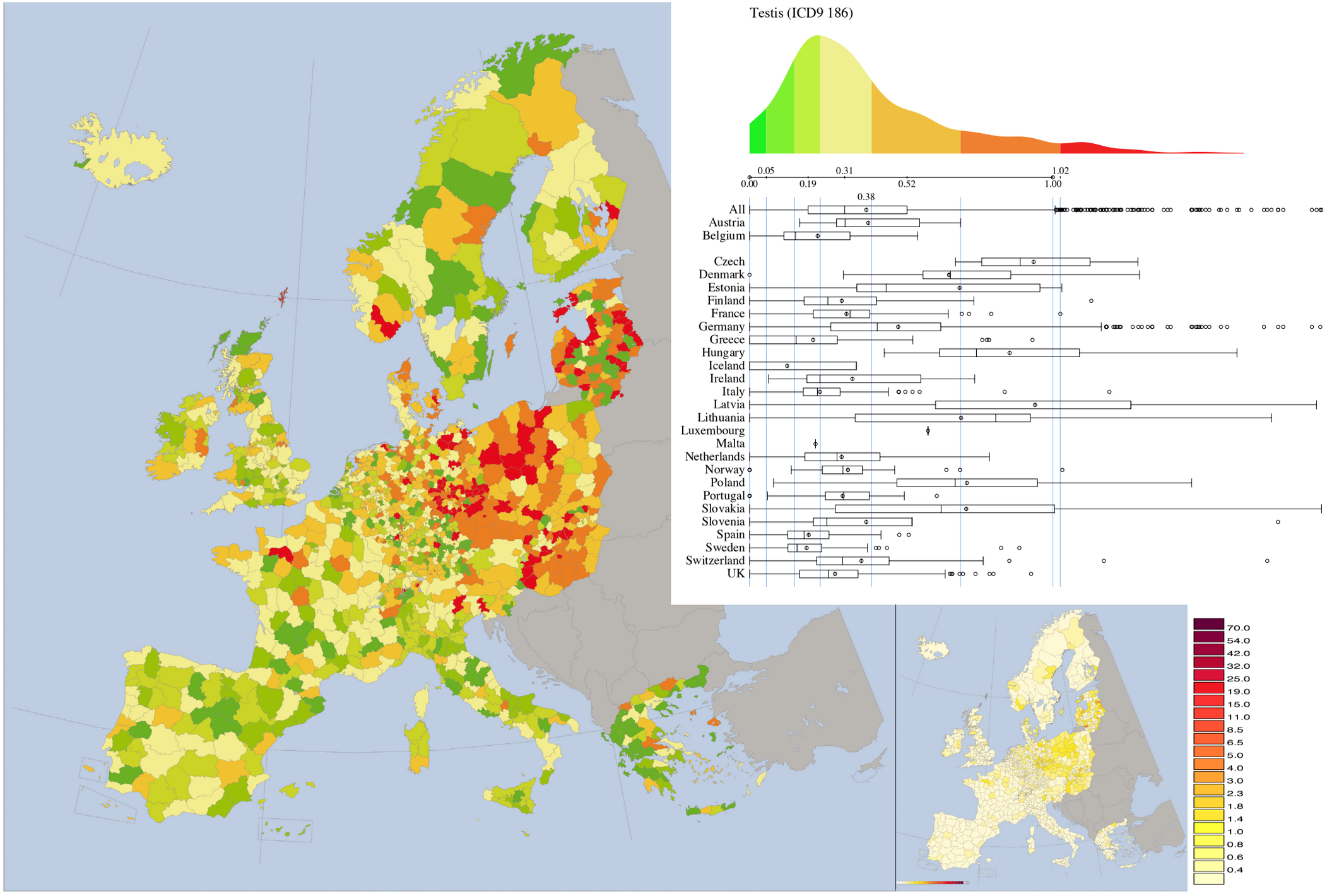
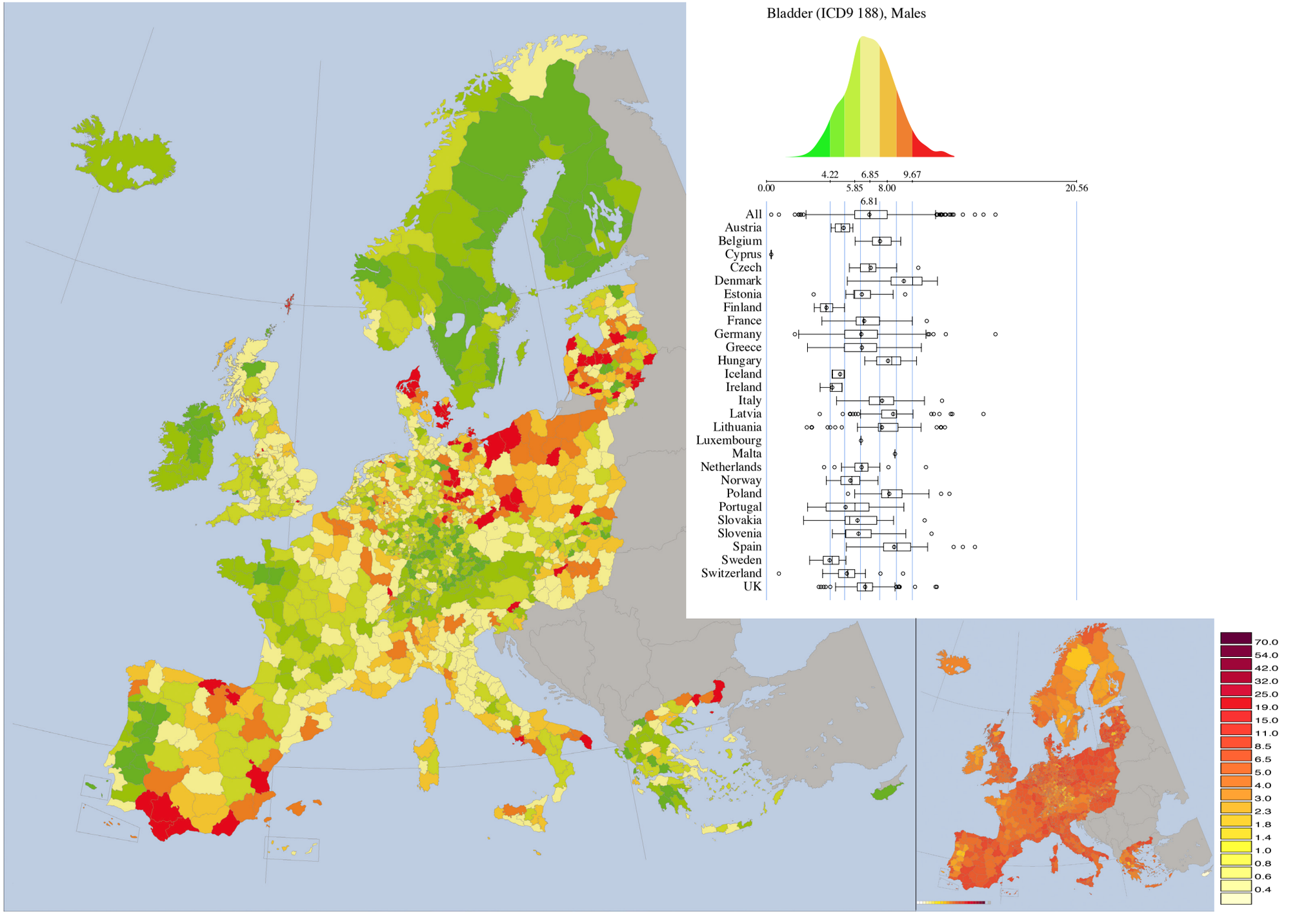
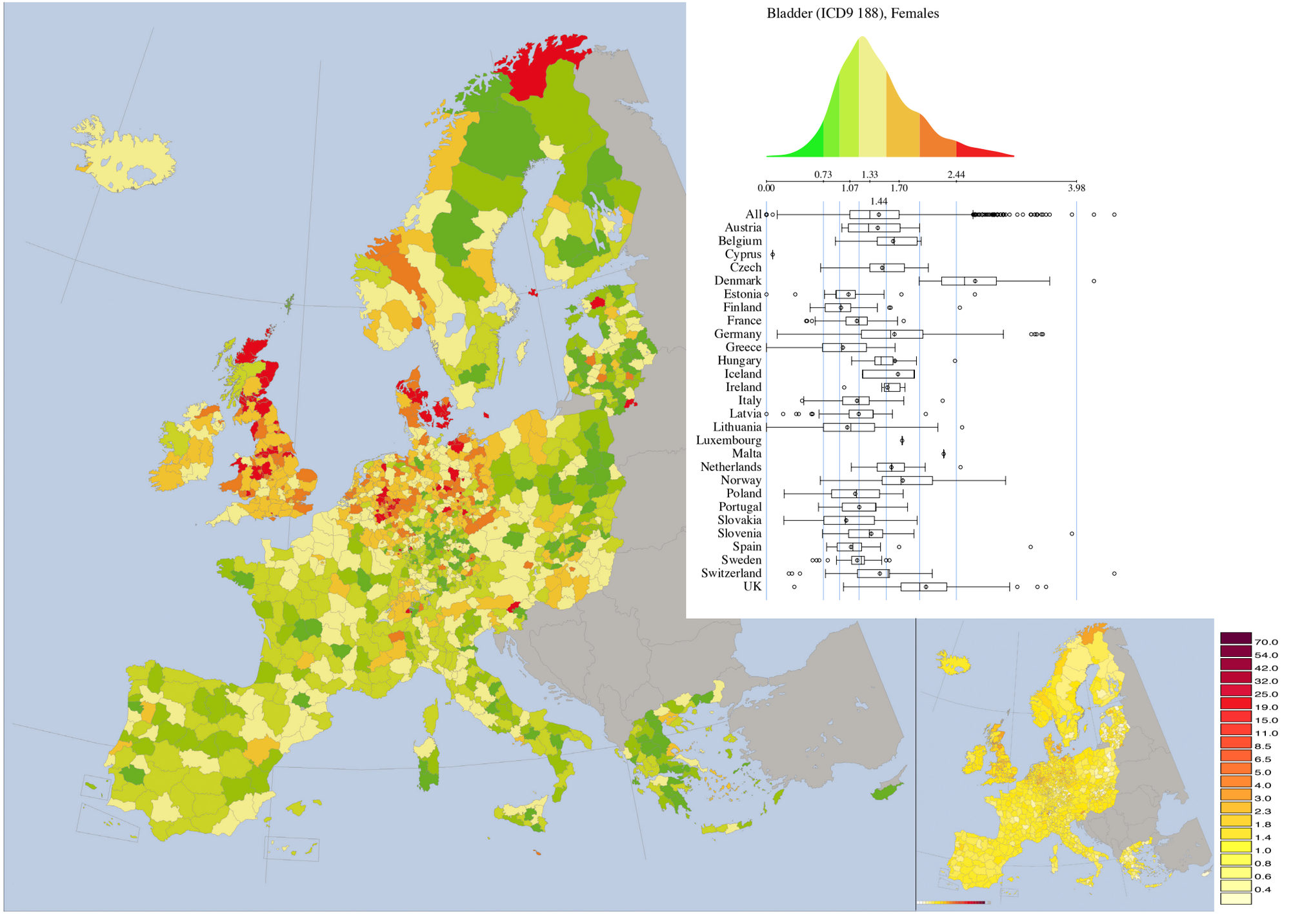
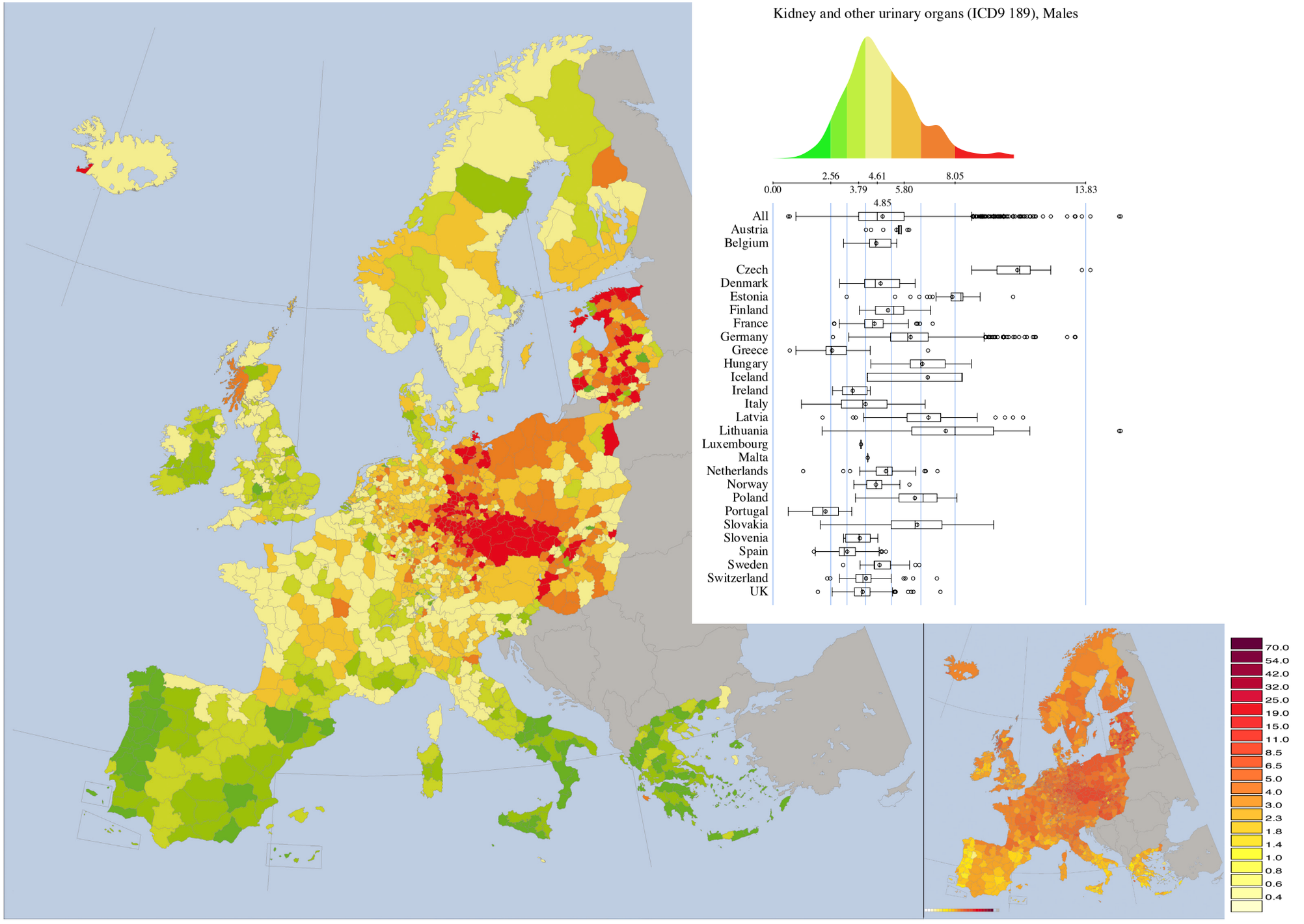
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4

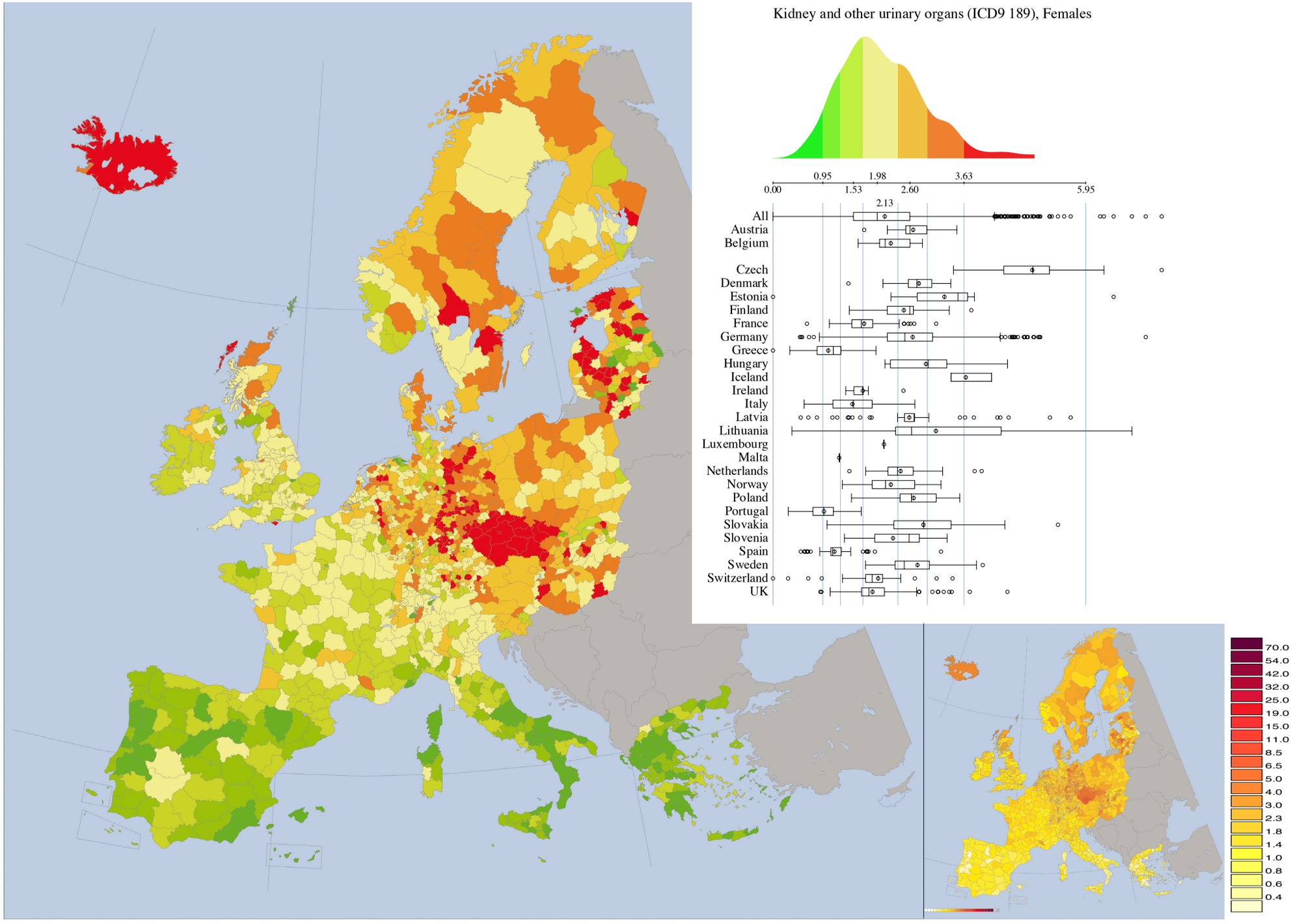

Prostate (ICD9 185)
10.00
15.58
20.63
0.00
12.92
17.51
40.00
15.39
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4

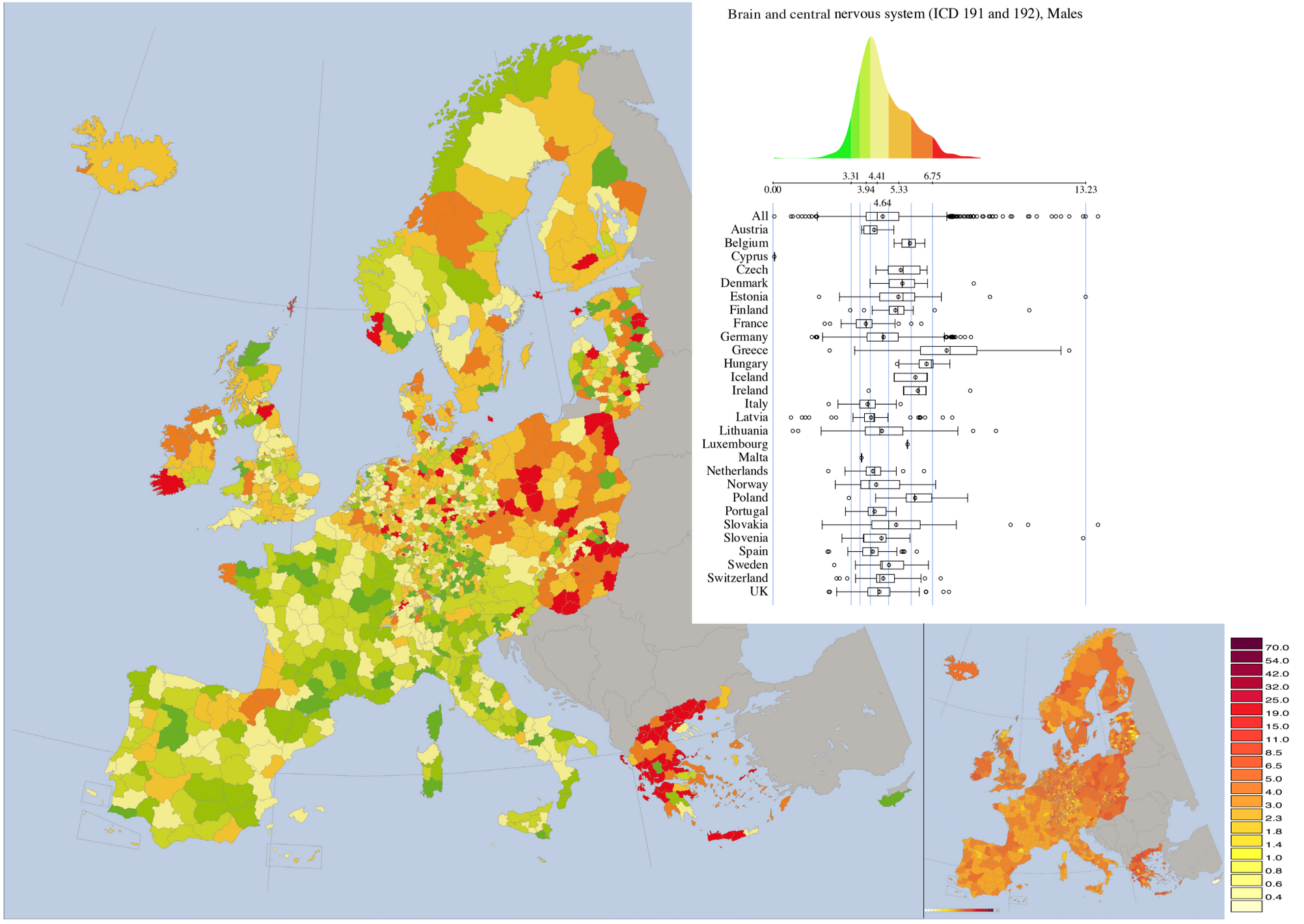

Testis (ICD9 186)
0.05
0.31
1.02
0.00
0.19
0.52
1.00
0.38
All
Austria
Belgium
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4

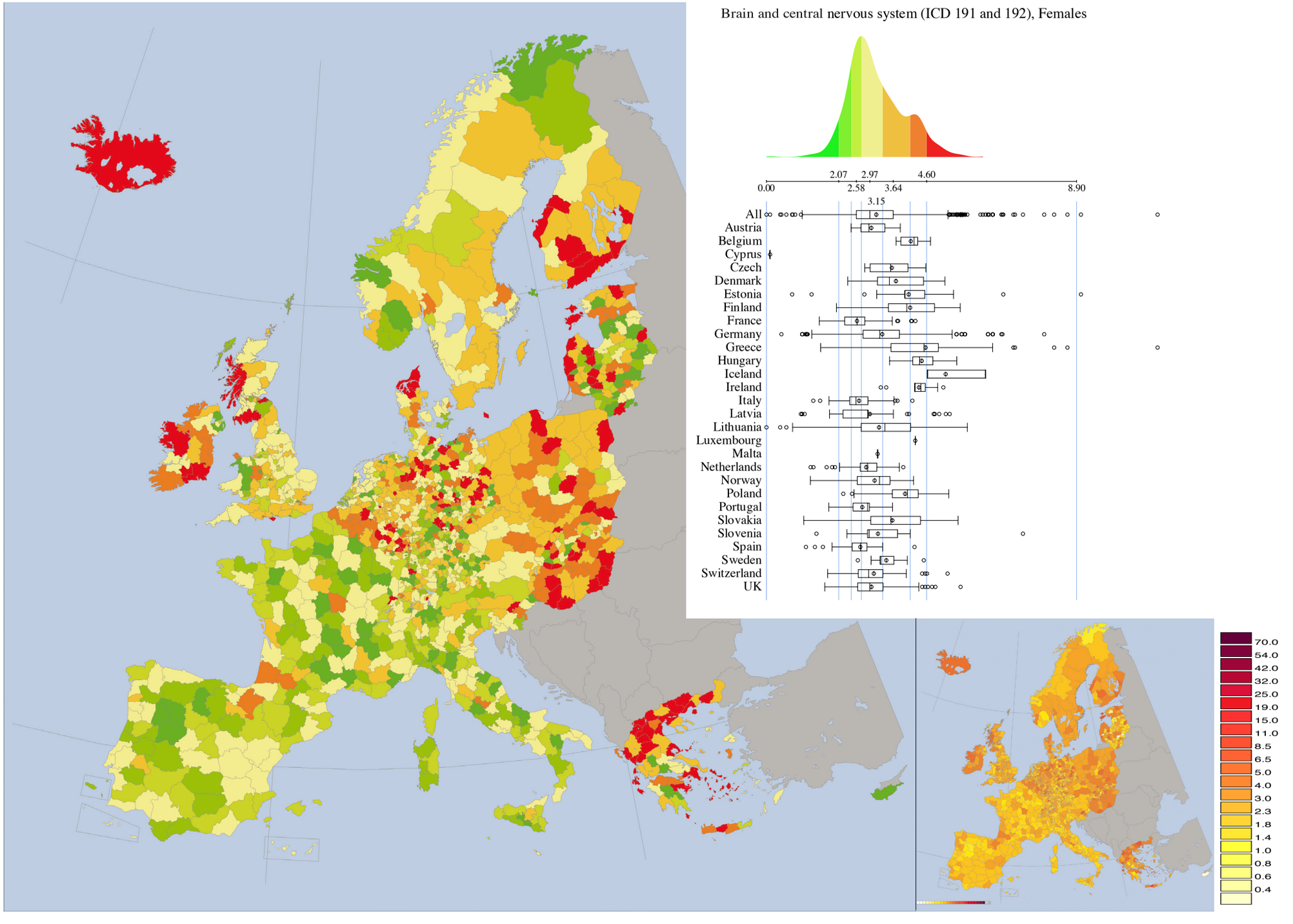

Bladder (ICD9 188), Males
4.22
6.85
9.67
0.00
5.85
8.00
20.56
6.81
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4

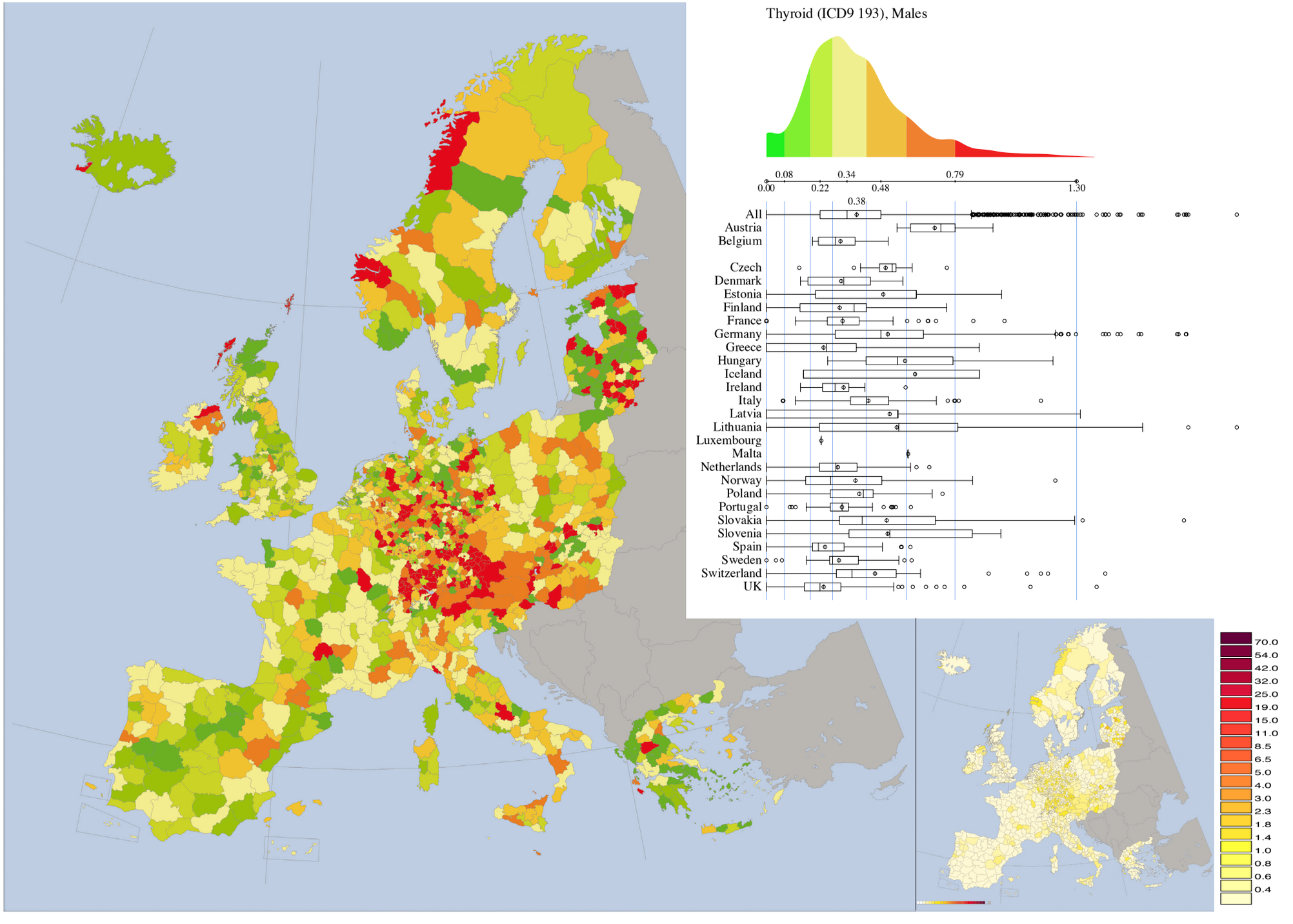

Bladder (ICD9 188), Females
0.00
0.73
1.07
1.33
1.44
1.70
2.44
3.98
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4

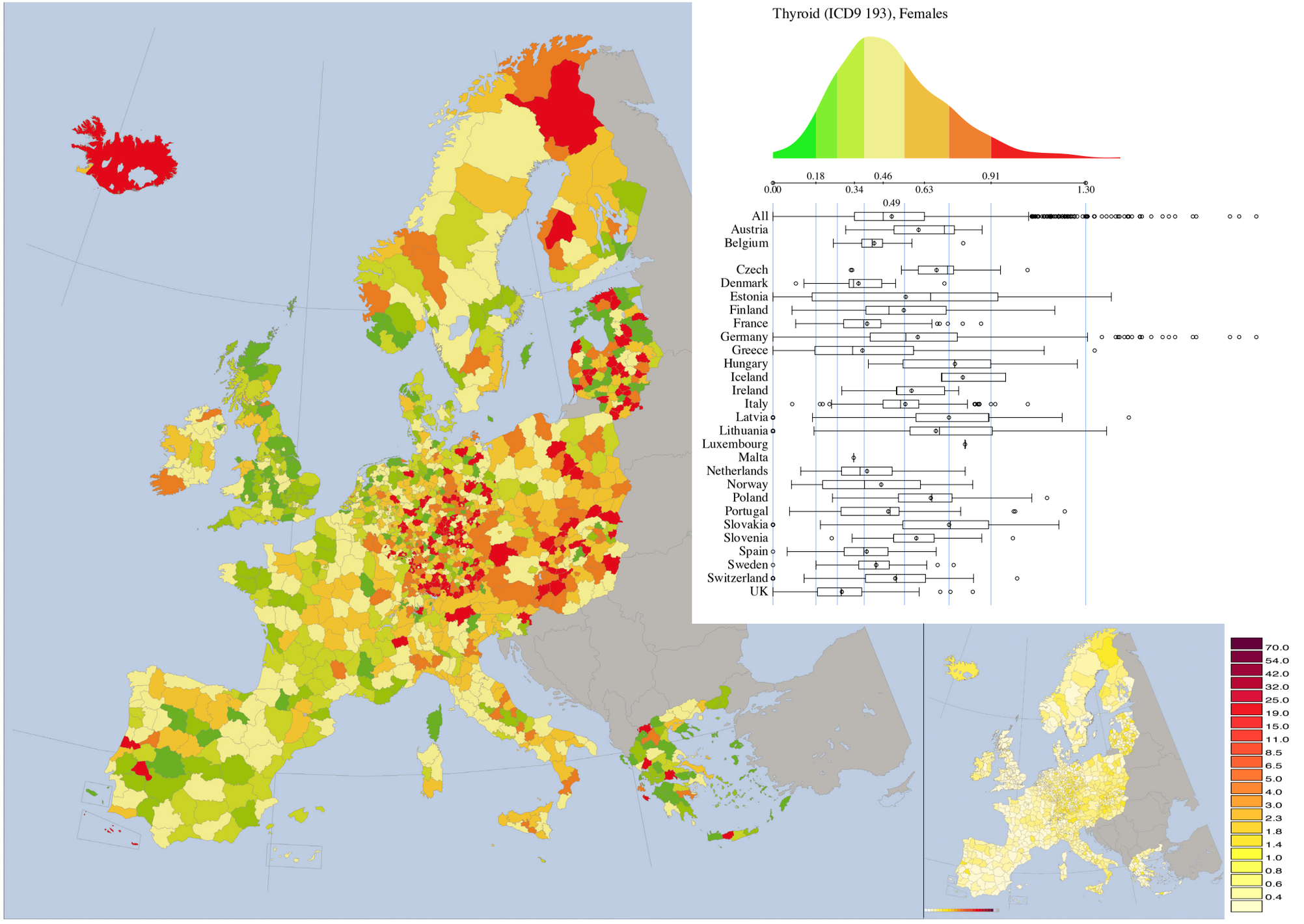

Kidney and other urinary organs (ICD9 189), Males
2.56
4.61
8.05
0.00
3.79
5.80
13.83
4.85
All
Austria
Belgium
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4

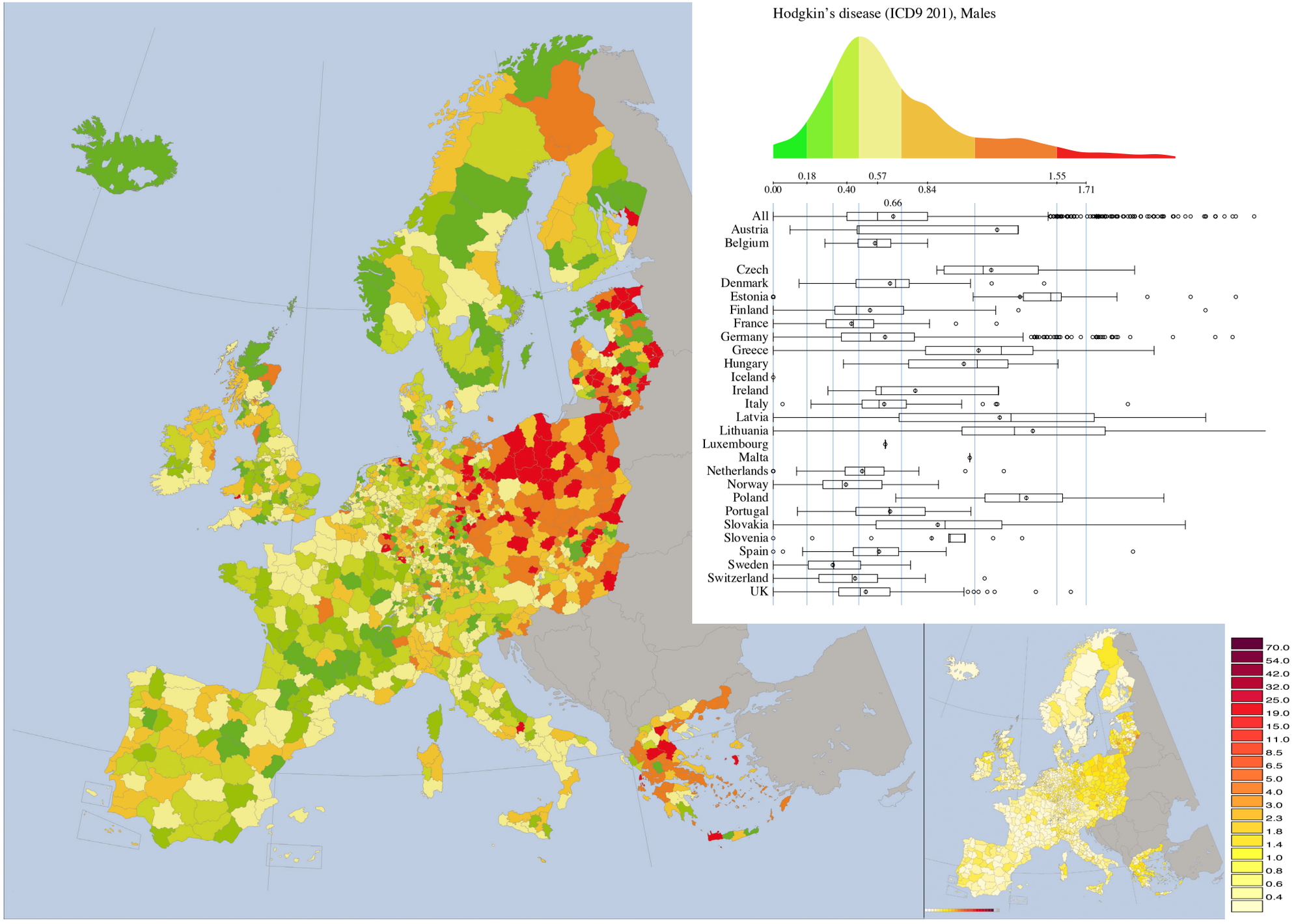

Kidney and other urinary organs (ICD9 189), Females
0.00
0.95
1.53
1.98
2.13
2.60
3.63
5.95
All
Austria
Belgium
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4

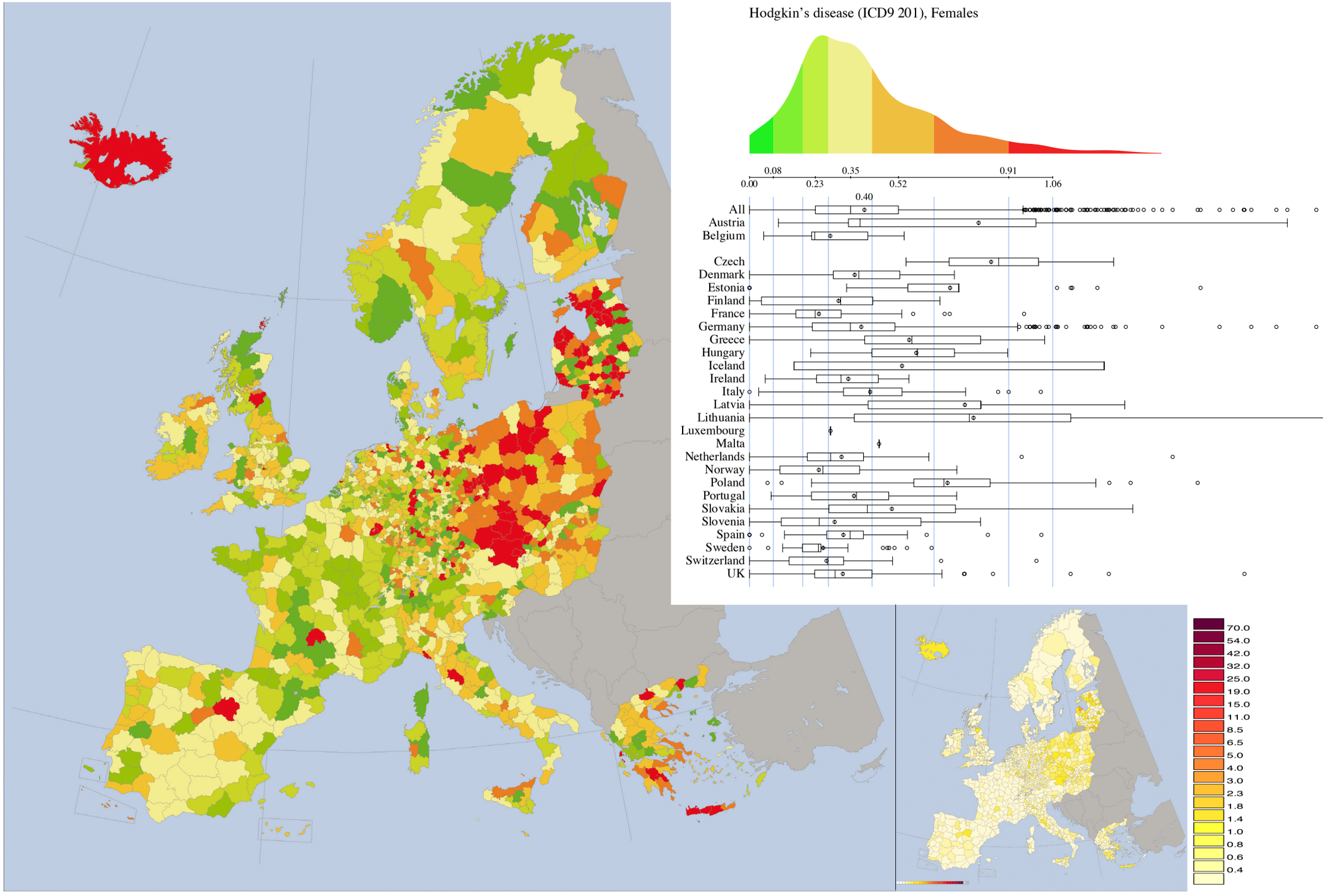

Brain and central nervous system (ICD 191 and 192), Males
3.31
4.41
6.75
0.00
3.94
5.33
13.23
4.64
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4


Brain and central nervous system (ICD 191 and 192), Females
2.07
2.97
4.60
0.00
2.58
3.64
8.90
3.15
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4


Thyroid (ICD9 193), Males
0.08
0.34
0.79
0.00
0.22
0.48
1.30
0.38
All
Austria
Belgium
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4


Thyroid (ICD9 193), Females
0.00
0.18
0.34
0.46
0.63
0.91
1.30
0.49
All
Austria
Belgium
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4


Hodgkin's disease (ICD9 201), Males
0.18
0.57
1.55
0.00
0.40
0.84
1.71
0.66
All
Austria
Belgium
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4


Hodgkin's disease (ICD9 201), Females
0.08
0.35
0.91
0.00
0.23
0.52
1.06
0.40
All
Austria
Belgium
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
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Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
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11.0
8.5
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5.0
4.0
3.0
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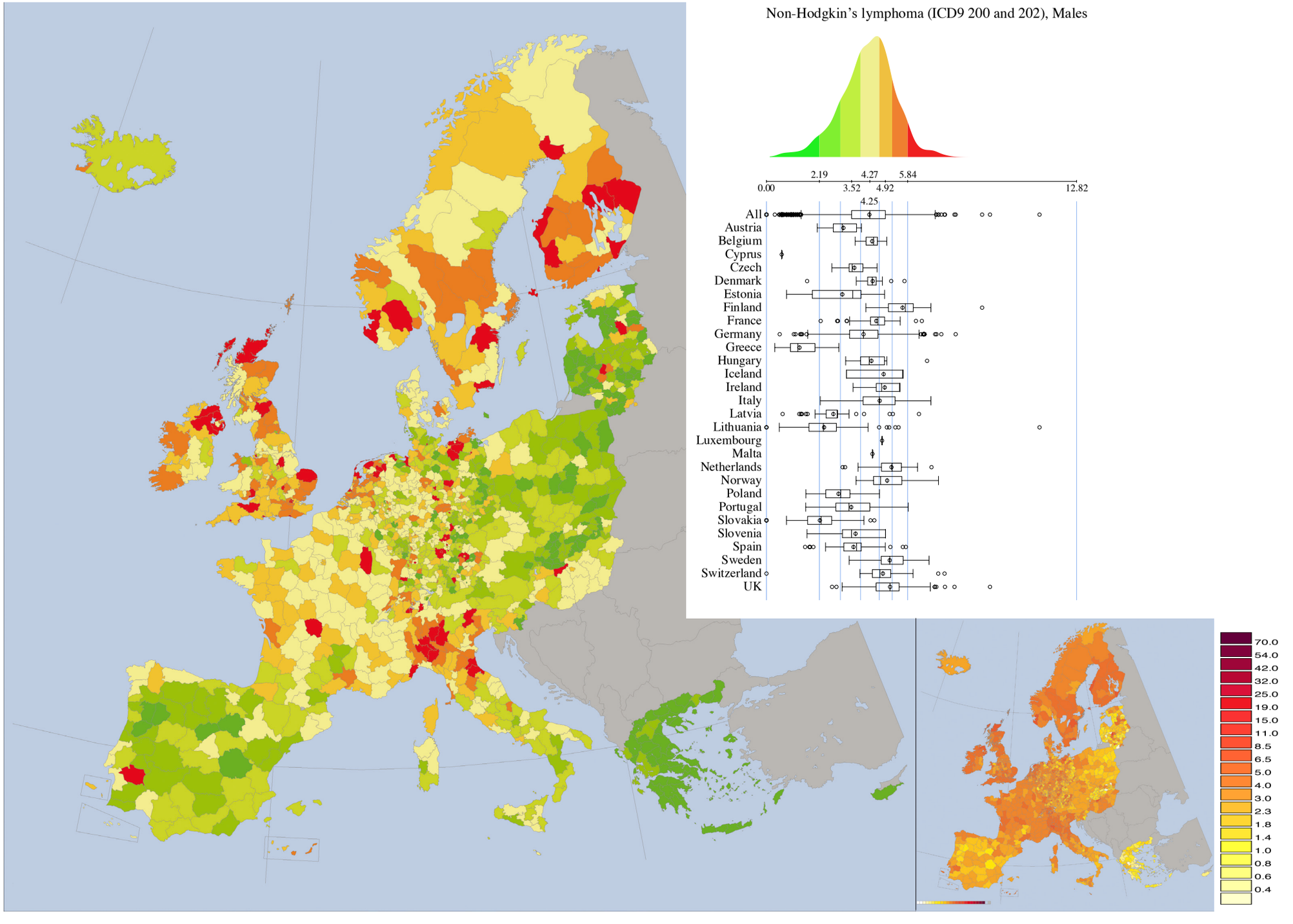
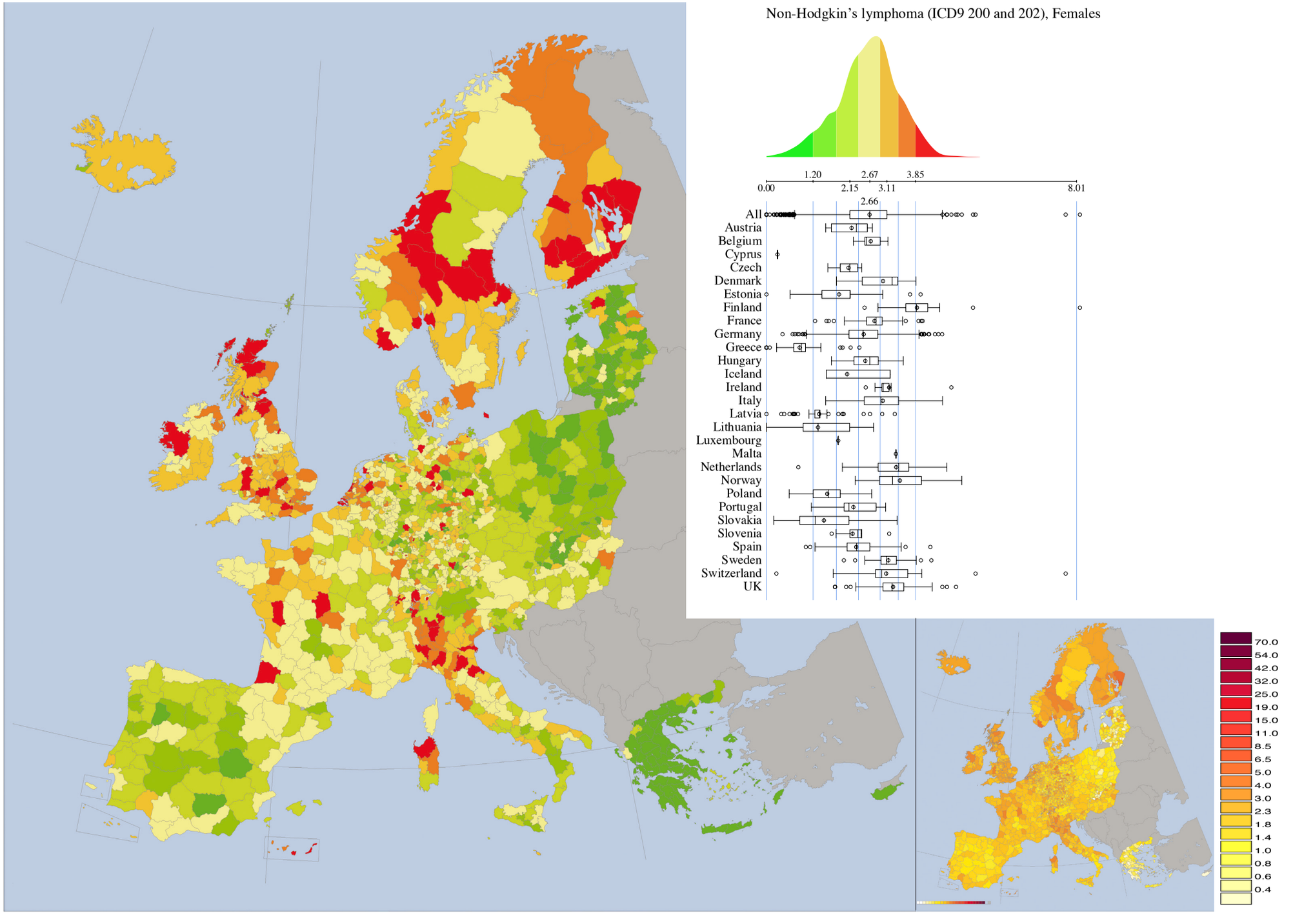
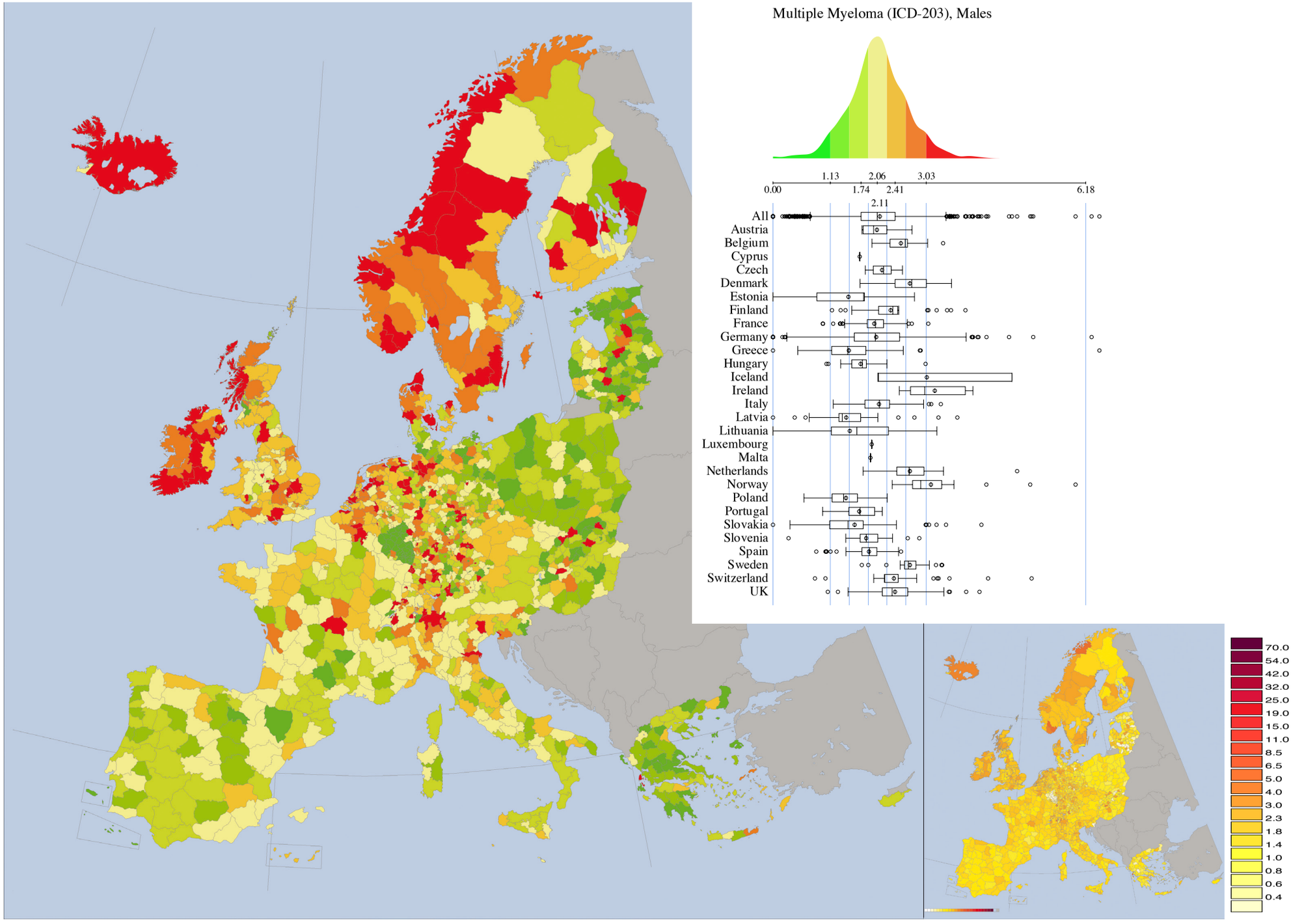
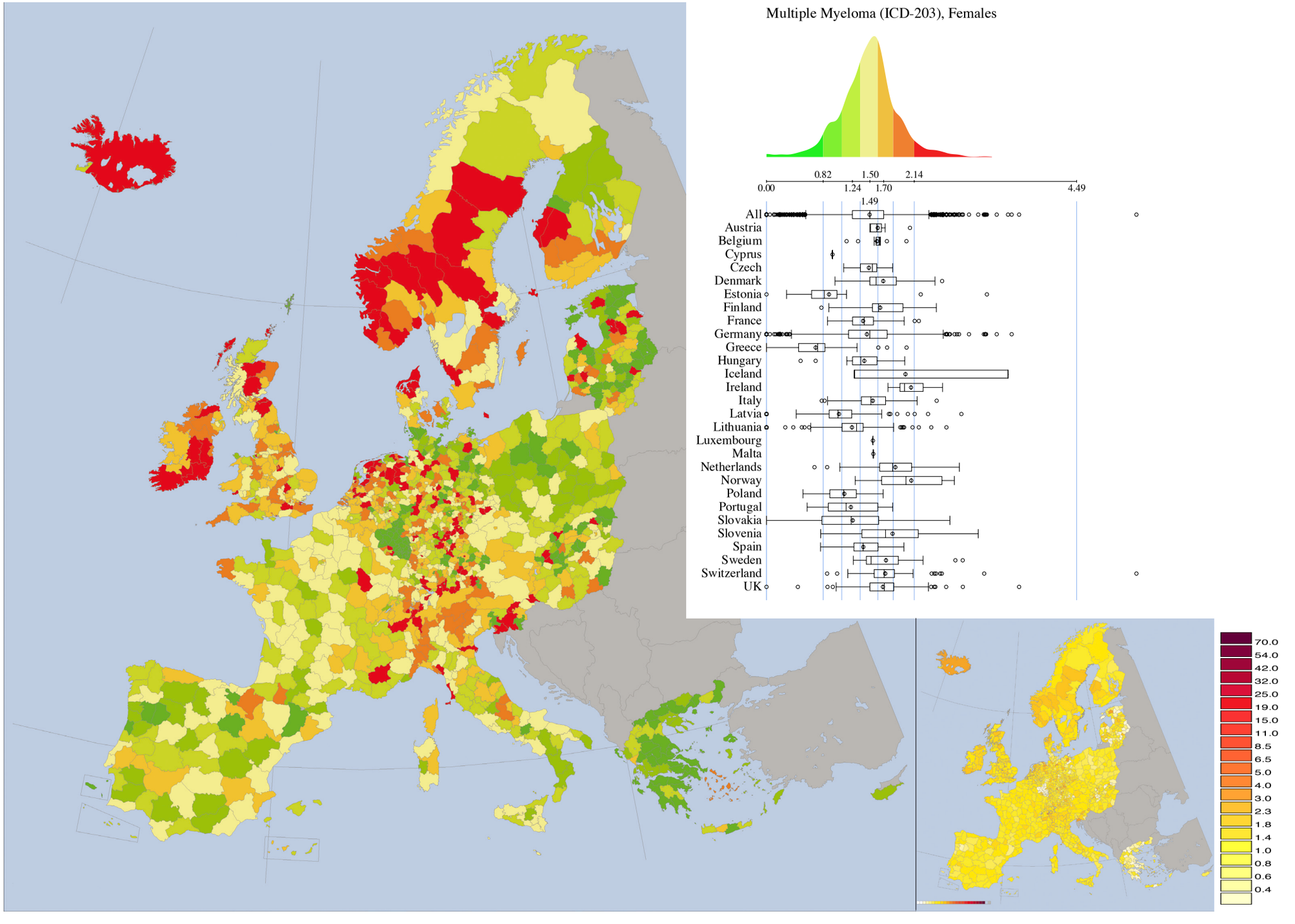
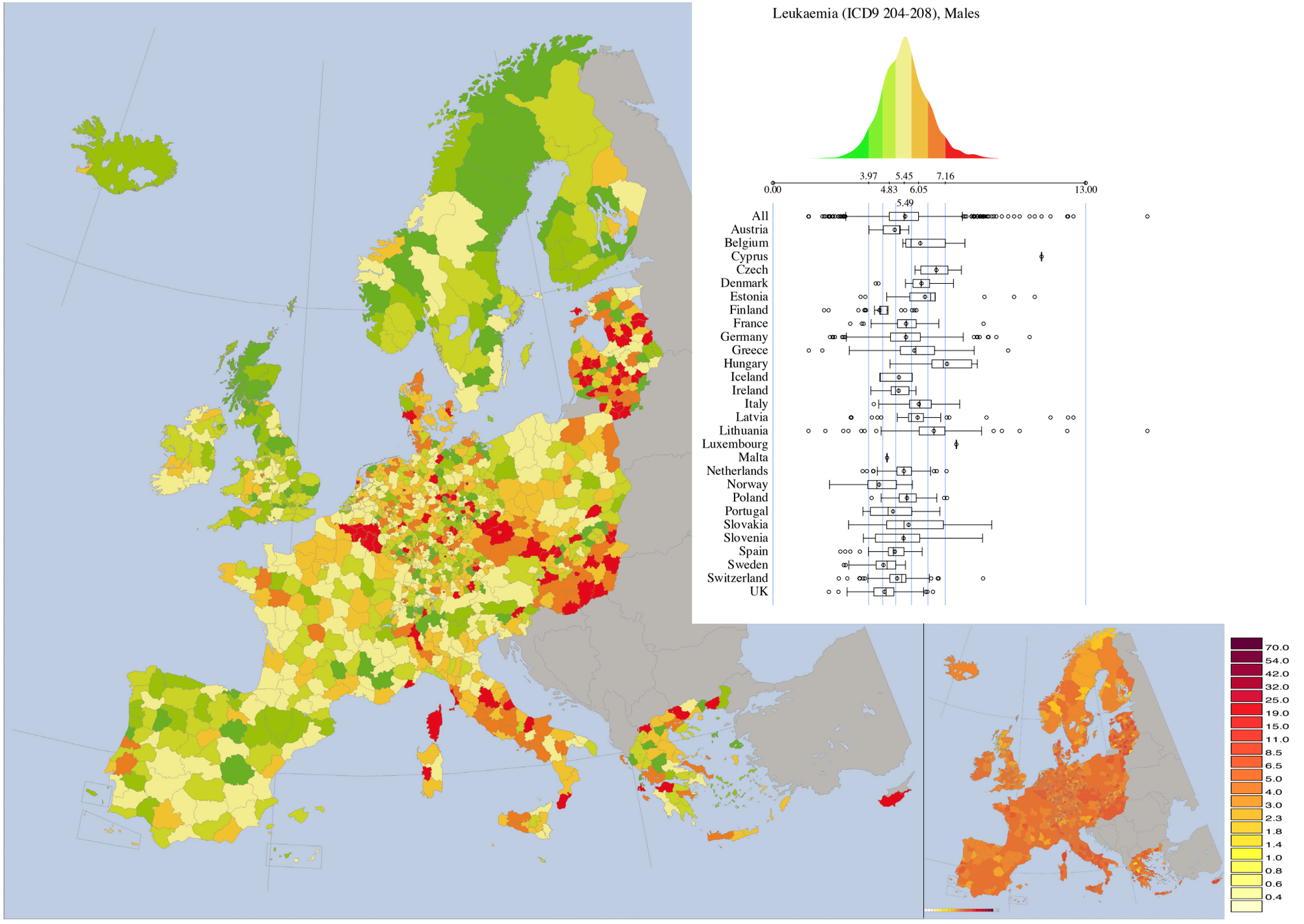
1.4
1.0
0.8
0.6
0.4

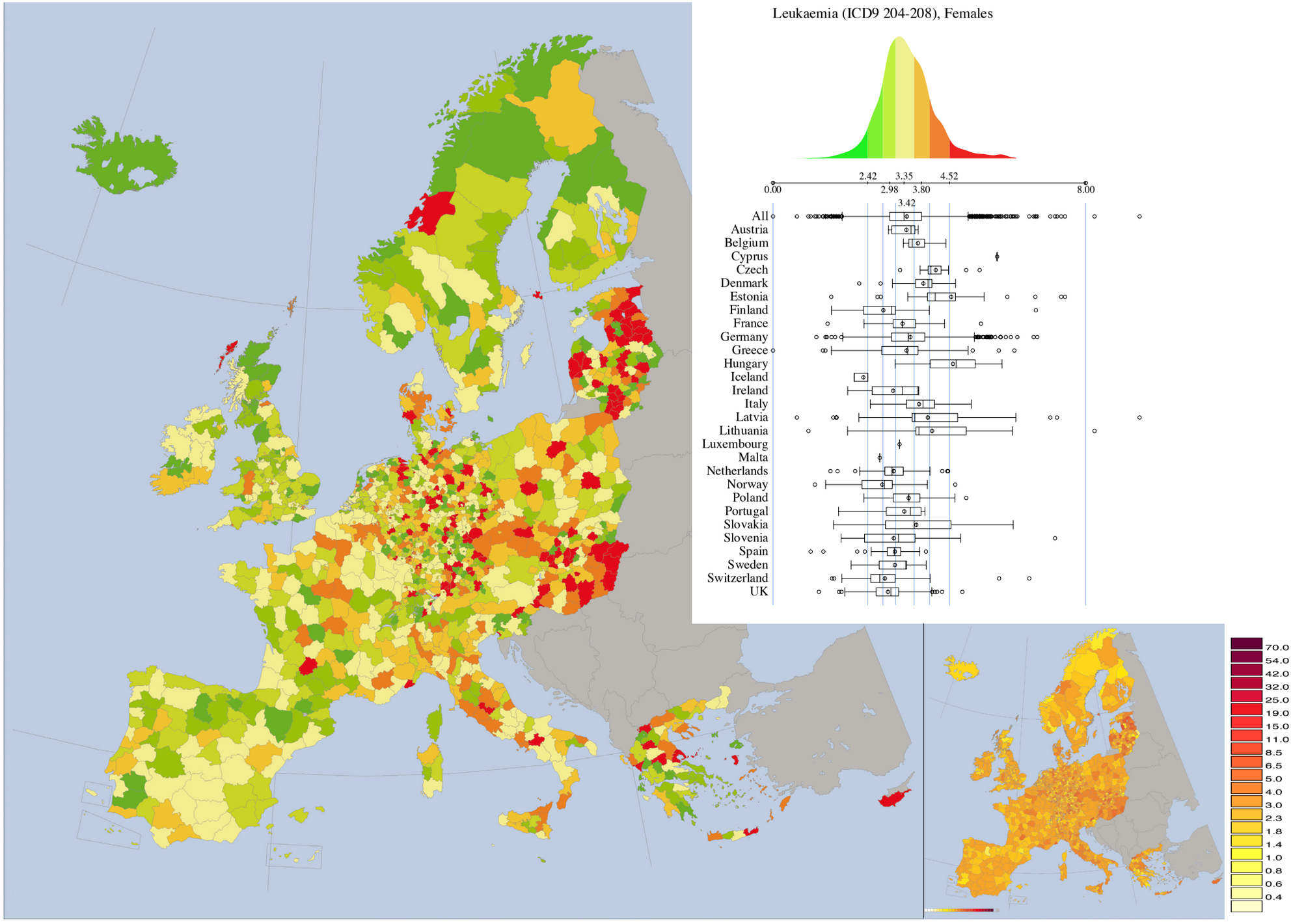

Non-Hodgkin's lymphoma (ICD9 200 and 202), Males
2.19
4.27
5.84
0.00
3.52
4.92
12.82
4.25
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4

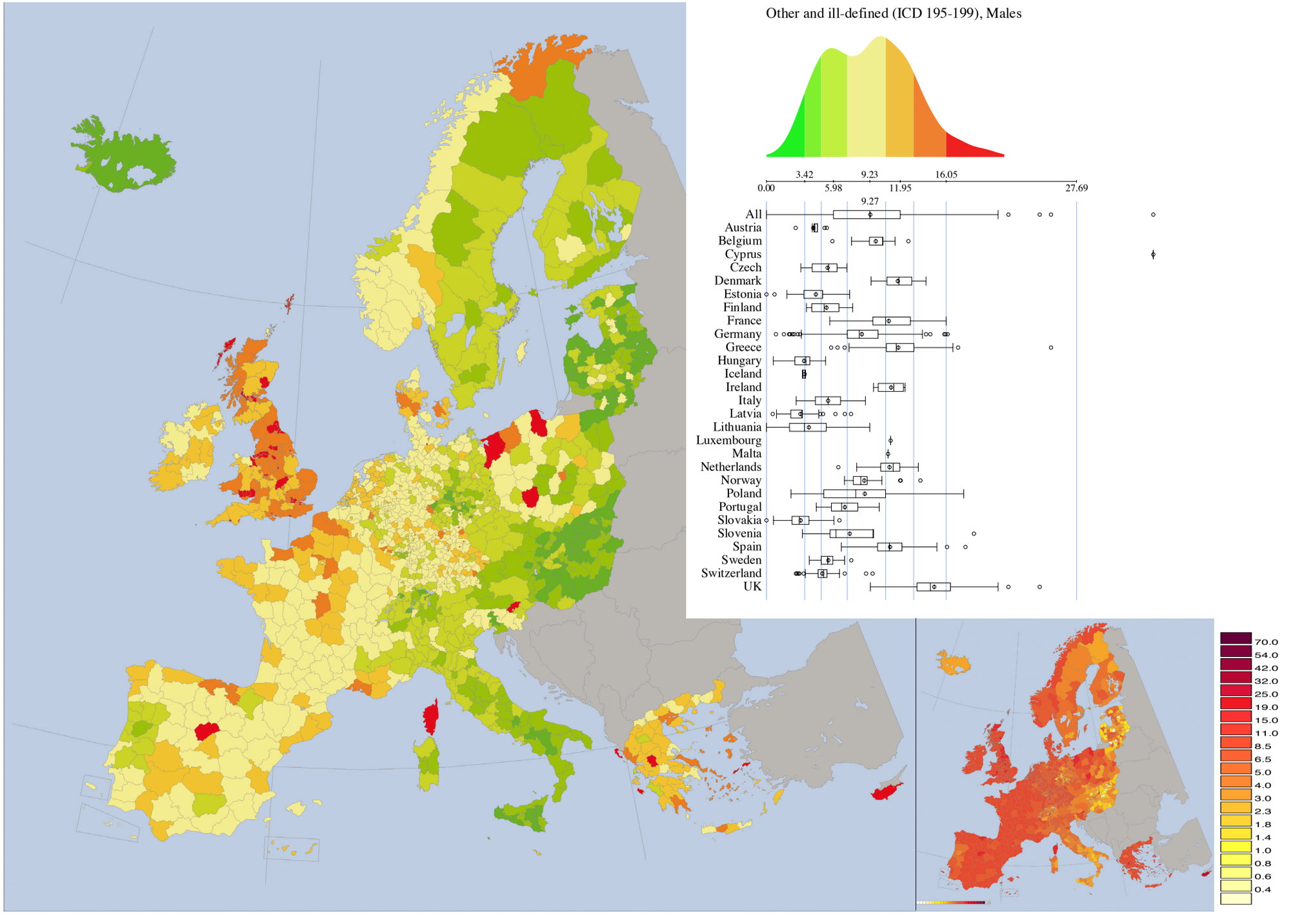

Non-Hodgkin's lymphoma (ICD9 200 and 202), Females
1.20
2.67
3.85
0.00
2.15
3.11
8.01
2.66
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4

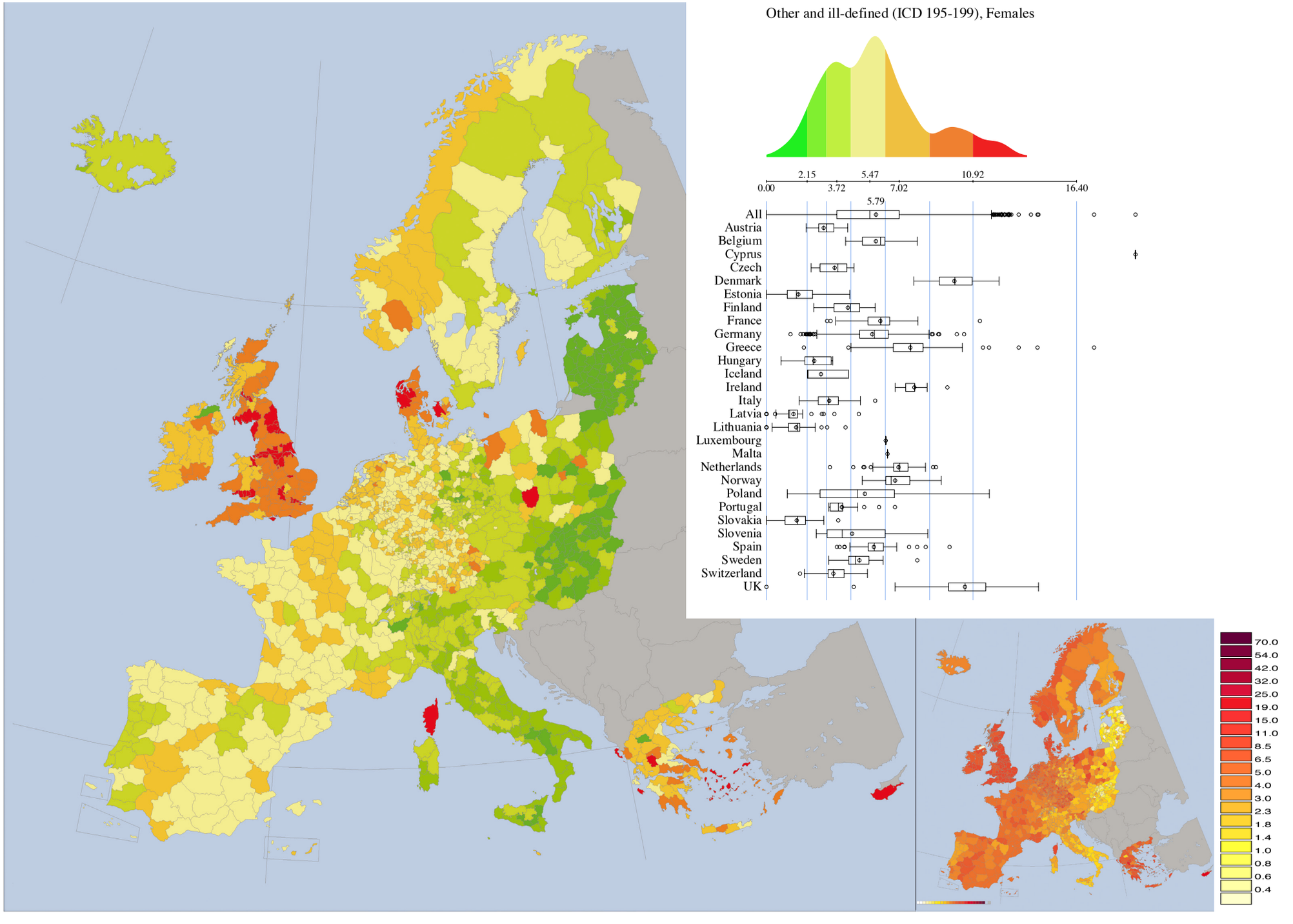

Multiple Myeloma (ICD-203), Males
1.13
2.06
3.03
0.00
1.74
2.41
6.18
2.11
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4

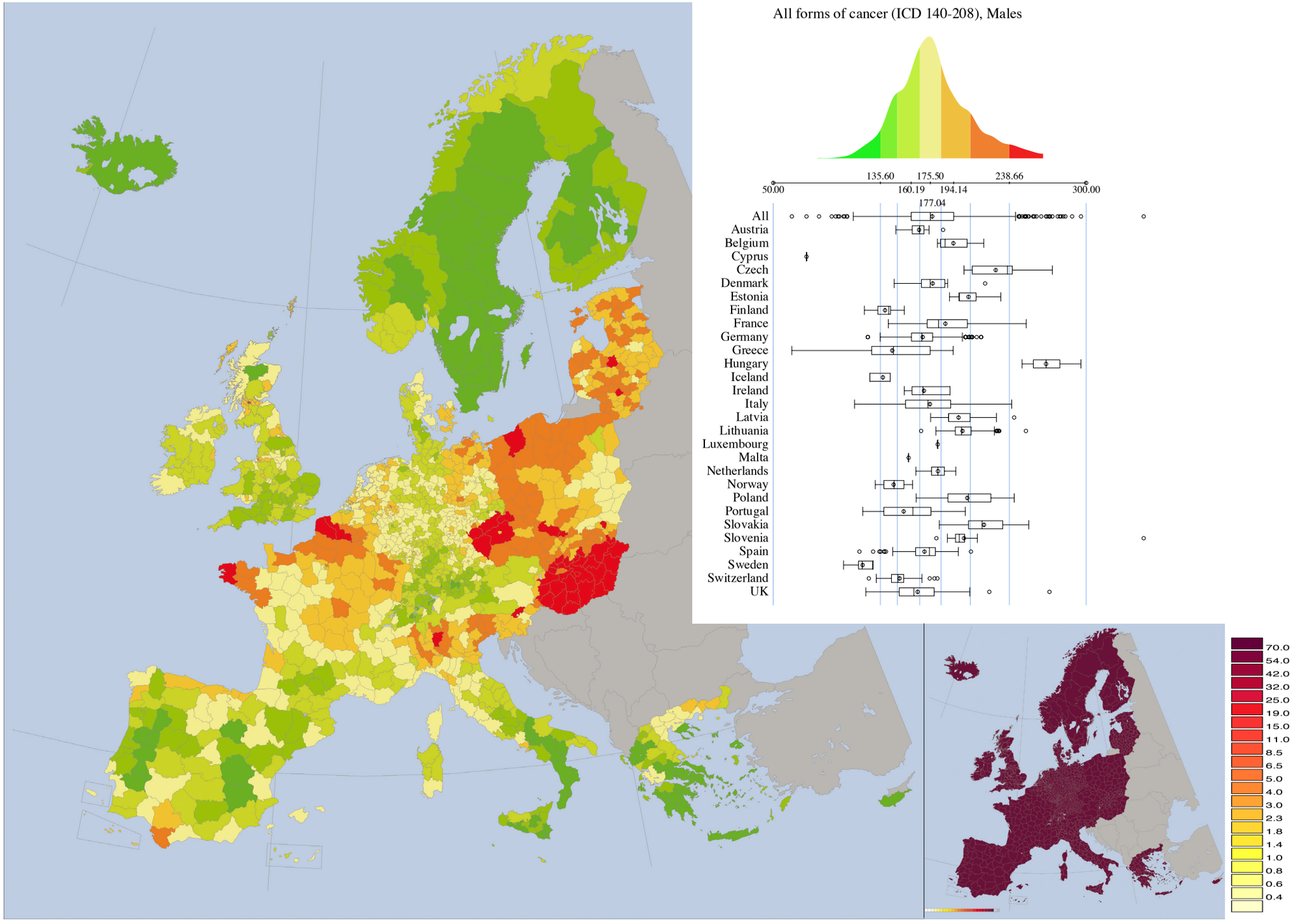

Multiple Myeloma (ICD-203), Females
0.82
1.50
2.14
0.00
1.24
1.70
4.49
1.49
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4

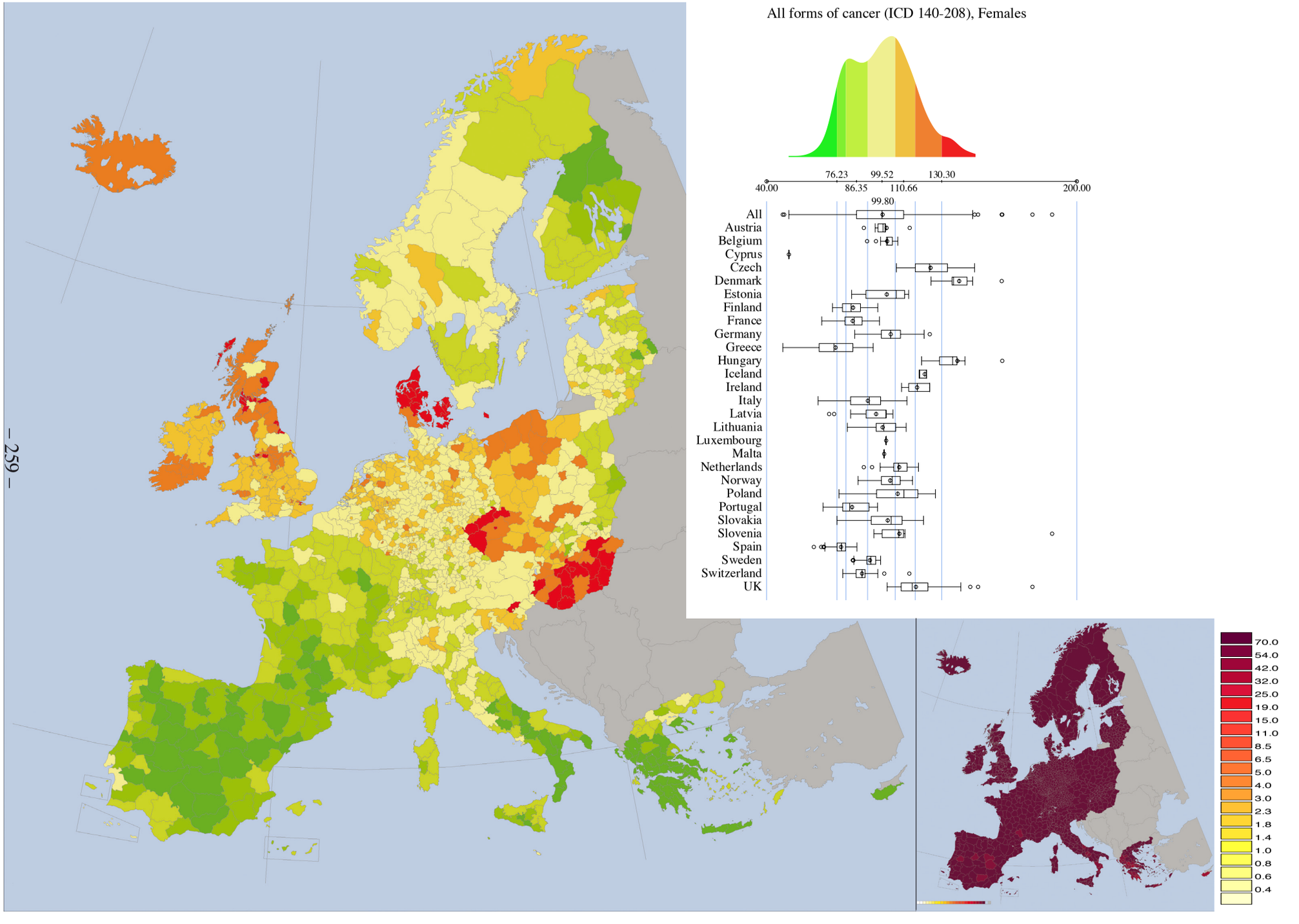

Leukaemia (ICD9 204-208), Males
3.97
5.45
7.16
0.00
4.83
6.05
13.00
5.49
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4


Leukaemia (ICD9 204-208), Females
2.42
3.35
4.52
0.00
2.98
3.80
8.00
3.42
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4


Other and ill-defined (ICD 195-199), Males
3.42
9.23
16.05
0.00
5.98
11.95
27.69
9.27
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4


Other and ill-defined (ICD 195-199), Females
2.15
5.47
10.92
0.00
3.72
7.02
16.40
5.79
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4


All forms of cancer (ICD 140-208), Males
135.60
175.50
238.66
50.00
160.19
194.14
300.00
177.04
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4


All forms of cancer (ICD 140-208), Females
76.23
99.52
130.30
40.00
86.35
110.66
200.00
99.80
All
Austria
Belgium
Cyprus
Czech
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Slovakia
Slovenia
Spain
Sweden
Switzerland
UK
70.0
54.0
42.0
32.0
25.0
19.0
15.0
11.0
8.5
6.5
5.0
4.0
3.0
2.3
1.8
1.4
1.0
0.8
0.6
0.4