Appendix K

Methodological issues considered

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This appendix contains a discussion of the range of methodological issues involved in producing a cancer atlas, and explains the reasons behind our choice of methodologies.

Cancer incidence and mortality

For investigations of the aetiology (causes and risk factors) of cancer and for health care planning, incidence is the measure of primary interest, but mortality data are useful in planning resources for palliative care and hospices. Cancer incidence and mortality data each have their own advantages and disadvantages. The diagnostic accuracy is generally better for incidence than for mortality, and a much lower proportion of cases than deaths are 'unspecified' as to the type of cancer. Incidence data, however, may not be as complete or as timely as mortality data. The main problems with mortality data are that the trends and the geographical distribution reflect a combination of the incidence and the survival rates in each area; and for cancers with moderate or good survival, deaths in any one year result from cases diagnosed and treated many years earlier. Mortality data are therefore imperfect and 'fuzzy' indicators of trends and patterns related to the causes of cancer.[1] These and other aspects of data quality are discussed further below and in more detail in Appendix G.

There is strong evidence that survival rates for almost all cancers vary among the countries of Europe.[2-4] But the figures from the EUROCARE studies show that for the major cancers there was little variation between Scotland, Wales and the participating regions of England. There is also evidence that there is relatively little variation for any of the major cancers among all the regions of England[5] or among the health authorities of England.[6,7] To date (2005) all the cancer survival figures published separately for England and Wales, Scotland, Northern Ireland and Ireland have not been comparable owing to differences in the time periods covered, the exclusion criteria for the individual records (for example, relating to multiple tumours), the methodology used, the age groups used, and the weights for age standardisation (if any). A project is currently in progress to produce comparable survival figures for the five countries and the regions of England for 20 or so major cancers.[8] The inclusion of cancer survival figures at the health authority level would have required a substantial amount of further work.

We therefore chose to produce maps of both cancer incidence and mortality, but not of survival.

Time period covered by this atlas

We decided to use cancer incidence and mortality data that related mostly to the 1990s. The most recently available nine or ten years of data provided totals of around 2,400,000 cancer cases (all malignancies excluding non-melanoma skin cancer) and 1,600,000 deaths from cancer in the UK and Ireland. The inclusion of even more (earlier) years of data would have given further reliability to the rates for whichever type of small geographical area was chosen. There have, however, been noticeable long-term trends in both incidence and mortality for many cancers, and the inclusion of data from the 1980s might have obscured the more recent geographical patterns.

Types of cancer included in this atlas

This atlas covers in detail the 16 most common cancers in males and the 17 most common in females (20 separate cancers in total*) for which the average number of newly diagnosed cases each year in one or the other sex in England during the 1990s was at least 1,000. Hodgkin's disease was also included, despite the smaller number of cases (about 800 in males and 600 in females each year in the UK and Ireland), to give coverage of all the lymphomas and leukaemias. These cancers together constitute almost 90 per cent of all malignant cancers (excluding non-melanoma skin cancer – see Appendix G).

Mesothelioma was not included, despite an annual average incidence of about 1,000 cases in England during the 1990s, and rising numbers throughout the period.[9] This cancer is caused by exposure to asbestos.[10,11] The vast majority of such exposure occurred in an industrial setting in places where asbestos was processed, asbestos products such as brake linings for vehicles were manufactured, or asbestos was used, such as shipbuilding yards and railway carriage works.[12] Trends and the unique geographical patterns in this cancer have been described in many scientific papers.[13-16]

Data collection and quality

Incidence

The cancer incidence data included in this atlas were collected by the cancer registries in the UK and Ireland. There are nine population-based regional cancer registries in England; their

* *Counting as one type: cancers of the lip, mouth and pharynx; cancers of the colon and rectum (colorectal); and all leukaemias.*

data are collated by the National Cancer Intelligence Centre (NCIC) at ONS. There are population-based cancer registries in each of Wales, Scotland, Northern Ireland and Ireland. See Appendix G for descriptions of the operation of each national registry.

Several aspects of the cancer registration systems in the UK and Ireland that affect data quality and therefore the interpretation of cancer incidence (and survival) data have been discussed in detail by Swerdlow,[17] Swerdlow and dos Santos Silva[18] and Quinn et al.[19] These include geographic coverage; methods of data collection; ascertainment (or completeness of registration); completeness of recording of data items; validity; accuracy; late registrations, deletions and amendments; duplicate and multiple registrations; registrations made solely on the information from death certificates; clinical and pathological definitions and diagnoses; changes in coding systems; changes in the definition of resident population; and error. Brief details of these are given in Appendix G.

A report of a project to audit the quality and comparability of cancer registration data in the UK,[20] carried out under the aegis of the United Kingdom Association of Cancer Registries, found some variation among the registries in data quality for diagnostic factors, incidence date, stage of disease, treatment information and use of death information. It is known that there is some variation among the UK and Irish registries in, for example, the proportions of cases registered solely on the basis of information from death certificates (and these proportions vary within each registry across the different cancers, and over time).[21] There will be corresponding variations in the ascertainment of cases. A study in one English registry found that data quality varied by the age of the patient, the type of cancer, and area of residence.[22] However, a substantial audit of Scottish cancer registry data in the early 1990s,[23] in which information was re-abstracted from the available records, found that severe discrepancies had occurred in under 3 per cent of cases. During the 1990s, almost all of the registries were engaged in some type of ongoing audit of data quality, mostly involving re-abstraction of information from case notes. In addition, all registries receive continuous feedback on data quality from clinicians and other staff in health authorities, and from their own research and collaborative studies with other scientists. The review by Huggett[20] concluded that although comparisons between the various published studies of data quality was difficult, cancer registry records were largely complete, accurate and reliable.

Regional differences in the classification and registration of some cancers can, however, contribute substantially to the apparent geographical patterns. This is particularly a problem for bladder cancer (Chapter 3), for which a particular sub-type of the cancer was considered to be malignant by some registries but non-invasive (benign) by others. For cancer of the ovary (Chapter 18), cases judged to be of 'borderline' malignant potential were not classified as malignant under the Ninth Revision of the WHO International Classification of Diseases (ICD9)[24] but were under the Tenth Revision (ICD10).[25] Coding using ICD10 was introduced at different times in each of the national registries in the mid-1990s. For cancer of the uterus (Chapter 23), cases should not normally be registered without sufficient information being available to classify them to the cervix or body of the uterus. The proportion of cases assigned to the 'non-specific' code for uterus was only about 10 per cent overall, but this varied among the five countries and among the registries in England. The apparent geographical patterns in incidence may have been affected both by this and by the geographic variation in the prevalence of women who have had a hysterectomy.[26]

Mortality

Information on cause of death is obtained through the statutory process of registration of death.[27] In England and Wales, this is carried out by the Local Registration Service in partnership with the General Register Office (GRO), which is part of ONS. There are General Register Offices in Scotland, Northern Ireland and Ireland which operate in a similar way.[28-30] Cancer mortality figures are generally not affected by differences among the cancer registries, although there may sometimes be 'attribution bias' – an increased probability of a (registered) cancer being mentioned on a death certificate. But mortality data never were free from bias or criticism.[31] The diagnostic accuracy of cancer on death certificates is much less certain than for cancer incidence, and (in England and Wales) for about 10 per cent of deaths from cancer, a specific cancer site is not given.[32] Many studies have shown wide variability in death certification and coding, particularly between countries,[33-45] and there have been several changes in coding and other procedures in England and Wales during the 1990s[46-49] (see Appendix G).

The time periods covered by the cancer incidence and mortality data analyses in this atlas are described in detail in Appendix G. In brief, for incidence, data were included from 1991 onwards for England, Wales and Scotland. For Northern Ireland, data were available from the start of that registry's operation in 1993; and similarly for Ireland from 1994. The latest available complete year of data from all of the national registries when the work on the analyses began was 1999. Mortality data for England, Wales and Northern Ireland cover 1991 to 2000 (after which the basis of coding the cause of death changed), for Scotland 1991 to 1999 (after which coding changed there) and from 1994 to 2000 in Ireland.

Populations

The calculation of area-specific rates requires accurate estimates of the population at risk.[50] In general, potential problems arising from inaccuracies in population data receive far less attention than those in the incidence or mortality data.[51] As the areas of interest become smaller, the problems become more acute, as small changes in the populations can have large effects on the resulting incidence and mortality rates.[52]

Scandinavian and some other European countries have population registers that are updated continuously, and so accurate population counts for small areas are always available.[50,53] In the UK and Ireland, the primary source of population data is the census. It is the only attempt at a complete count of the population and in theory gives true population counts at very small levels of aggregation. There are two main problems. The first is undercount: people are missed by the census, and the proportions missed are not uniform across geographical areas or socio-economic groups. For the 2001 census in the UK, the methodology was designed to integrate adjustments for undercount into the census database using information from a very large follow-up survey.[54] Census under-enumeration is generally highest for men and women in the 20-24 age group, particularly in inner city areas. This will only marginally affect the age-standardised rates for most cancers, as the age-specific rates in young people are very low; the principal exception is testicular cancer (Chapter 22).

The second problem is that the census is conducted only every ten years in the UK and every five years in Ireland, and estimates of the population therefore need to be made for the years between the censuses. This is done for England and Wales at the local and health authority levels by ONS.[55] Between censuses, quite substantial changes may occur in the size and composition of the population in a given area. The births and deaths in an area are readily accounted for, but the estimation of migration into and out of an area is usually imprecise. As much migration occurs within short distances, the smaller the areas being considered, the greater the migration problem.

The population denominators used in this atlas to calculate age-specific cancer incidence and mortality rates were the sums of the mid-year population estimates for each year of data included; as noted above the time periods covered by the data differed between the countries and between the incidence and mortality data. The mid-year population estimates for 1996, the approximate mid-point of the time period spanned by the vast majority of the data, are given in Appendix C as a guideline. For the UK, the original population estimates made in the 1990s were adjusted using information from the 2001 census (these were slightly revised subsequently for a few areas[56]). For Ireland, the 1996 populations are official national census figures published by the Central Statistics Office.

Measures of incidence and mortality for comparison of areas

It is clearly not valid simply to compare the numbers of cases of (or deaths from) cancer in one area with those in another, as the areas may have widely different total populations (for example, the population of England is about ten times that of Scotland). The *crude rate*, the total number of cases (or deaths) divided by the total population, takes the population sizes of different areas into account. But as cancer incidence and mortality rates generally increase with age, and populations in different areas usually have different age structures, it is essential to adjust, or standardise, any rates for age.[57,58]

The method of *indirect* standardisation takes the ratio of the observed number of cases (or deaths) in a given small area to the number that would be expected if the rates in a reference (usually the national) population applied in the small area. This ratio is usually multiplied by 100 and is called the standardised incidence (or mortality) ratio (SIR or SMR). A value of 132 means that 32 per cent more cases were observed in that particular small area than if the age-specific incidence rates had been the same as in the country as a whole. The SIR or SMR generally provides a more precise statistical estimate than the directly standardised rate[57] (see below). But the main problem with indirect standardisation is that comparisons of SIRs or SMRs between areas are not valid, and may be misleading. It is possible for all the age-specific rates in one area to be lower than those in a second area, yet the SIR or SMR in the first area is higher than that for the second because of widely different population structures in the two areas. Given that the invalidity of comparing SIRs or SMRs was recognised over 80 years ago[59-61] it is surprising how often it has been done in recent times.

The method of *direct* standardisation uses the age-specific rates in each small area concerned to determine the incidence (or mortality) rate that would be observed in that area if it had the same population structure as a given or standard (usually theoretical) population. The two most commonly used standard populations are the World and European standards[62] (see also Appendix C). As the World standard population is much more heavily weighted than the European towards younger ages, and cancer is mainly a disease of elderly people,

for most European countries the directly age-standardised cancer rates using the World standard tend to be about half the crude rates, whereas rates using the European standard are broadly comparable with the crude rates.

A third measure is the *cumulative rate*,[57] which gives an approximation of the risk of being diagnosed with the cancer (in the absence of mortality) or of dying from the cancer, either before a given age or between two ages. It is calculated by summing the age-specific incidence or mortality rates over the desired age range. There are problems with doing this calculation over a whole lifetime because the last age group is open-ended; cumulative incidence rates are rarely calculated above 75 years, as competing causes of death then play a major role. The cumulative rate is proportional to the simple arithmetic average of the age-specific rates; in other words, it is effectively a standardised rate using a standard population in which every age group contains the same number of people. The interpretation of the cumulative rate assumes that the age-specific rates from the cross-sectional incidence or mortality age curve for a given time period correctly represent the risk for any one individual. But the risk estimate is actually for a fictitious person who synthesises the risks for various birth cohorts:[57] for example, using data for (say) 1996, the incidence rate for the 30-34 age group relates to those born in 1962-66, while the rate for the 65-69 age group relates to those born in 1927-31. The cumulative rate is the indicator that is the most readily interpretable on a probability scale: for example, the risk of being diagnosed with cancer of the colon up to age 75 in a given area may be 2.73 per cent. An alternative, but more complicated, calculation of the lifetime risk using the life table method[63] does not have a problem with the upper-most age group, and allows for competing mortality – but does require appropriate life tables. The widespread use of either the cumulative rate or lifetime risk would greatly increase the comparability of cancer maps and atlases.

In this atlas, all the incidence and mortality rates have been directly age-standardised using the European standard population. Further details are given in Appendix H.

Choice of 'small' geographical area

The potential types of sub-national area (below the very large regional level in England) that could be used for mapping cancer incidence and mortality include wards (either 'frozen' census wards, or boundaries at a particular (other) point in time), local authorities, counties, health authorities, primary care trusts (PCT), strategic health authorities (SHA), and cancer networks. Although cancer is a major cause of morbidity and mortality, in small geographical areas the numbers of cases of any particular type of cancer occurring each year can be quite low, and of course the corresponding numbers of cancer deaths are even lower.

There are about 10,000 wards in England and Wales with an average population of about 5,000 people, and so on average in each ward there would be just two cases of lung cancer diagnosed in males, and three cases of, and one death from, breast cancer in females each year. Even if ten years of data were aggregated, the numbers of cases of even the most common cancers would be small, and the corresponding numbers of deaths even smaller; for the less common cancers, with about 1,000 cases each year in England, there would be an average of only one case in each ward over the whole period. And many wards are much smaller than the average, with populations of only about 2,000 people. Even if reliable population estimates were available for wards for the years between censuses, all incidence and mortality rates would be highly unreliable, with very wide confidence intervals (see Appendix H).

Local authorities (LA), of which there are about 350 in England, have an average population of about 140,000 people, and much more reliable rates can be calculated for them than for wards. LAs were the geographical unit chosen as the basis for analysis in the book *Geographic Variations in Health*,[64] but this included only the three most common cancers in each sex. Uncertainty in the rates, as indicated by wide confidence intervals, would have been a problem for all of the cancers less common than these. As noted above, counties were used by Swerdlow and dos Santos Silva in their atlas of cancer incidence in England and Wales over the period 1962-85;[18] at that time there were about 60 counties in England and Wales (counting Greater London as one; and the three parts of Lincolnshire and Yorkshire and the two parts of Suffolk and Sussex separately), with an average population of just under 1 million people. But the boundaries of several counties were affected by the formation of unitary authorities during the 1990s. Also, most counties are quite large in terms of land area, and generally consist of a mixture of densely populated cities or large towns with relatively high levels of socio-economic deprivation, more affluent suburban areas, and sparsely populated rural areas. Real and important differences in cancer rates *within* counties could be obscured if this level were used for analysis. In addition, a major disadvantage of local government boundaries (both LAs and counties) is that they are generally not contiguous with the boundaries of the administrative units in the NHS which are responsible for delivering health care.

In England and Wales the latest of several major re-organisations in the NHS, to the current (2005) PCT and SHA boundaries, took place in 2001, after the period to which all of

the incidence and mortality data relate. And there have been several boundary changes in PCTs and SHAs since 2001. There are about the same number of PCTs (about 300) as LAs in England, and slightly fewer SHAs (28) than counties, so these units suffer from the same problems as LAs and counties of being too small and too large, respectively. Before the re-organisation of the NHS organisations and boundaries in 2001, there had been about 100 health authorities with an average population of about half a million people. With ten years of aggregated data, these areas would have sufficient numbers of cases and deaths, even for the less common cancers, to enable the calculation of reliable directly age-standardised rates. And they were the areas that were in existence for most of the period covered by the data. In addition, most of the current SHAs consist of aggregations of the former health authorities, and most of the current PCTs aggregate to the former health authorities. We therefore decided to present the data at the health authority level for England.

In consultation with our colleagues in Wales, Scotland, Northern Ireland and Ireland, and taking into account the implications of the various possible geographical sub-units, we decided to use the 'small' areas based on health administrative boundaries in this atlas as summarised in the table below. For simplicity and convenience, these slightly different types of areas are referred to as 'health authorities' throughout this atlas. A 'key' map to the 127 health authorities is given in Appendix A.

Tables of cancer incidence and mortality, and populations, by health authority

Mid-year population estimates for 1996 for the 127 health authorities, by sex and age group, are given in Appendix C. The age-standardised rates adjust for differences in the age structure of the population between countries, regions and health authorities, and hence they allow unbiased comparisons of the rates across areas (see Appendix H).

We had estimated that nine or ten years of data would give an average of over 100 newly diagnosed cases of all the different types of cancer at the health authority level, and hence reasonably reliable directly age-standardised rates, with quite narrow confidence intervals – except for Hodgkin's disease, for which the average numbers would be only about 55 in males and 40 in females. The numbers of cases are also small for several cancers for some of the health authorities with small populations, especially three in Scotland: the Western Isles, Orkney and Shetland. We decided not to omit either incidence or mortality rates for these three areas from the charts and maps; but it must be borne in mind that for the less common cancers, and particularly for mortality, the rates for these areas are based on relatively small numbers (of cases or deaths) and therefore have very wide confidence intervals.

Tables giving the numbers of cases and deaths, and the corresponding directly age-standardised rates, together with the ratio of the mortality to incidence rates, by cancer, by sex where appropriate, for all 127 health authorities, the eight regions of England, and the five countries, are given in Appendix B. These tables also indicate where the 95 per cent confidence interval about a country, regional or health authority rate does not overlap the 95 per cent confidence interval about the corresponding average rate for the UK and Ireland. This is *not* equivalent to the area rate being statistically significantly different from the average at the 5 per cent level – see Appendix H for further details.

Table K1

Health authority areas and their equivalents by country, UK and Ireland

Country	Area	Number of areas	Average population
England	Health authority	95	510,000
Wales	Health authority	5	577,000
Scotland	Health board	15	340,000
Northern Ireland	Health and social service board	4	415,000
Ireland	Regional health board[1]	8	453,000
Total		127	

1 Except for the Eastern Regional Health Authority, which includes Dublin, and is divided into three area health boards – this subdivision was not used.

Divergence from the methodological guidelines of Walter and Birnie[65]

Much thought has been given by many authors to the methodological issues involved in disease mapping.[66-70] This atlas meets most, but not all, of the methodological guidelines for health atlases set out by Walter and Birnie.[65] For five reasons, we have not indicated on the maps in each of the cancer-specific chapters where the incidence and mortality rates are statistically significantly different from the relevant overall UK and Ireland average. First, the choice of significance level is arbitrary. Second, allowance has to be made for the very large numbers of comparisons of rates in any one area for the different cancers, some of which will be related to each other, for example, where there is a common aetiological factor or a similar relationship with socio-economic deprivation. Also, the rates for incidence and mortality in any one area will often be closely related to each other. These factors would tend to cause statistical tests to give a falsely high level of significance. Third, statistically significant deviations in risk (from the average) are more likely to occur in areas with large populations, even if the actual deviations are small.[71] Fourth, it is clear from the charts of rates by health authority for most cancers that there is a relatively narrow range of values, and most rates do not differ widely from those in the other health authorities in their own countries and regions or elsewhere. Any rates which are not quite statistically significantly different from the average (or from each other) would probably become so if two or three more years of data were included. But fifth, and most important, we were interested in the broad geographical patterns in each cancer, how the patterns in incidence generally related to those in mortality, and how the patterns in both were related to known aetiological factors and to socio-economic deprivation. For these purposes, the statistical significance (or otherwise) – even if this could be accurately assessed – of a rate of either incidence or mortality for a particular cancer in a given small area is not highly relevant.

We have included descriptions of any broad time trends in incidence and mortality in each of the cancer-specific chapters – but we have not investigated temporal changes in geographic patterns over what is a relatively short period (mostly ten years) covered by the data.

We have not formally analysed the spatial structure in the data. There are several statistical measures available,[72-81] but, as mentioned above, we were principally interested in relating the broad geographical patterns in incidence to those in mortality and to aetiological (risk) factors and socio-economic deprivation. With about ten years of both incidence and mortality data, the health authority areas we used as the basic unit for analysis were individually generally large enough to give reliable age-standardised rates. Health authorities were also large enough that real differences between them could exist both in the underlying levels of the relevant risk factors and in the levels of the disease. Any artificial measure of 'association' in rates for adjacent areas was therefore not of great interest. For similar reasons, we have not geographically 'smoothed' the data. As noted above, rates for small areas, especially wards, would be highly unreliable, even with the large amount of available data, and would need to be smoothed.[82-87] Using health authorities as the lowest level of geography, with an average population of about half a million people (in England), and ten years of data, effectively smoothes the results to a large extent. There would be a danger in smoothing the data further, by Bayesian or other statistical techniques including 'head banging',[88-91] of obscuring real differences in rates between adjacent areas, especially, for example, where one area was a highly industrialised and socio-economically deprived city with high population density, and the other a large, relatively affluent and sparsely populated rural area.

We have not included maps of potentially relevant aetiological factors. A comprehensive (although now slightly out of date) guide to information on geographical variations in a very large number of risk factors for cancer was given by Swerdlow and dos Santos Silva,[18] including abortions; age at first birth; air pollution; alcohol consumption; asbestos; blood group; diet; education; ethnicity; fallout from nuclear explosions; geochemistry; height, weight and obesity; hepatitis B; immigration; income; indoor radiation; medical conditions; nuclear installations; occupation and industry; operated conditions (surgical interventions); overcrowding; parity; population mobility; post-neonatal mortality (four weeks to one year); rainfall; screening; smoking (cigarettes); social class; sunshine; venereal diseases; and Welsh language speaking (which it was thought 'might correlate with other cultural behaviours'). The analyses presented in Chapters 3 to 23 show that for many cancers the known risk factors could explain only a small proportion of the incident cases, and so the geographical distribution of these factors could not greatly influence the observed patterns. For those cancers related to smoking and/or drinking alcohol and related 'lifestyle' factors, overall measures of socio-economic deprivation are often a highly accurate marker. For example, the strength of the relationship of the incidence of lung cancer with deprivation[19] measured on a small-area basis by the Carstairs index[92] is closely similar to that with social class measured on an individual basis in the Longitudinal Study;[93,94] and the prevalence of smoking is much higher in social classes IV and V than in classes I and II.[95] Details of the Carstairs index are given in Appendix F, along with a map showing its distribution at the LA level in Great Britain.

Finally, we have not included tables of age-specific numerators. Such tables for all of the 21 cancers by sex where appropriate for all of the 127 health authorities, the eight regions of England, and the five countries, would require considerably more pages in what is already a thick book. We expect that not many readers would be interested in such detail, or would want to calculate age-standardised rates using a different standard population. These tables are available, however, on request from the NCIC at ONS.

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