The evolution of the population-based cancer registry

Donald M. Parkin

Abstract | The idea of recording information on all cancer cases in defined communities dates from the first half of the twentieth century, and there has been a steady growth in the number of such cancer registries since. Originally, they were concerned primarily with describing cancer patterns and trends. Later, many were able to follow up the registered patients and calculate survival. In the last 20 years the role of registries has expanded further to embrace the planning and evaluation of cancer control activities, and the care of individual cancer patients. This Review looks at the current status of cancer registration practice and use from an international perspective, mindful that the registration of cancer has expanded into a global activity.

In their introduction to the first volume of the *Cancer Incidence in Five Continents* series, Doll *et al.*[1] discuss the role of comparisons of disease frequency, between different places and over time, in developing knowledge of the causes of cancer. They concluded that among the available statistics for studying cancer, "the most valuable data are, undoubtedly, the rates obtained by recording the occurrence of every case of cancer over a specified period." This is the basic function of a population-based cancer registry (PBCR, known in the United States as a central cancer registry), which is defined by Jensen *et al.*[2] as one that "records all new cases [of cancer] in a defined population (most frequently a geographical area)."

The core activity of a PBCR is to generate statistics on the incidence of cancer, and, by relating these to a population of known size, to calculate rates of incidence. Although this was the focus of the first registries to be established in Europe and North America in the 1940s and 1950s, their use to provide information on other aspects of cancer occurrence and on the control of the disease has developed progressively. This was initially through the need for information on survival from cancer at the population level, and later to study the effects of various aspects of services for prevention, early diagnosis, treatment and care. This template has been applied to a greater or lesser extent in other world regions, and the steady increase in the number of cancer registries attests to their value in cancer research and control (BOX 1).

The work of cancer registration

Technical aspects of cancer registration have been described in several manuals[2,3,4]. The idea is to collect a set of variables on every case of cancer diagnosed in the target population. But what is a case of cancer? Generally speaking, registrable cases include all malignant (invasive) tumours, although most registries exclude certain cancers, especially non-melanoma skin cancers, and include some benign tumours (especially intracranial) and/or carcinomas *in situ* (non-invasive) detected during screening (for example, of the breast and cervix).

The list of variables recorded in each case depends on the feasibility of capturing the required information in a large proportion of cases, and the resources available for doing so. BOX 2 lists the so-called essential variables (the minimum required to achieve a population-based registry) and those considered very desirable. The various national and international registry groups (see below) prescribe data sets for their members that are more complex than this.

PBCRs seek information from multiple sources — ideally, all those in which cancer cases may be diagnosed or treated. In practice, the principal sources are hospital records and records from diagnostic departments, particularly histopathology and cytopathology. When possible, death certificates in which cancer is included as a main or contributory cause of death are also used. An important step is to link together all of the records pertaining to an individual (or, rather, an individual tumour), to avoid duplicate registration. Personal identification numbers (if known and widely used) are ideal for this purpose; however, in practice cancer registries in many countries must rely, at least in part, on names (and sex, date of birth or age and place of residence) for linkage purposes.

Clinical Trials Service Unit & Epidemiological Studies Unit, University of Oxford, Richard Doll Building, Old Road Campus, Oxford, OX3 7LF, UK.
Correspondence to D.M.P.
e-mail: max.parkin@ctsu.ox.ac.uk
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At a glance

- Population-based cancer registries (PBCRs) aim to identify all cases of cancer that occur in a defined population. A defined set of variables is recorded for each case; the minimum number is 10, but most registries have a more extensive dataset.
- The basic role of PBCRs is to calculate the incidence of cancer at different sites, but most can provide more extensive information (for example, on tumour histology, stage at diagnosis, place and nature of treatment, and survival).
- Incidence of cancer is synonymous with diagnosis, and the number of cases detected is influenced by diagnostic practices, especially with respect to screening. This must be considered when comparing incidence rates between populations and over time.
- Cancer registries have been widely used in epidemiological research. Descriptive studies use the registry database to examine differences in the incidence (or survival) of cancer, according to variables associated with place (of residence, or of birth), time and personal characteristics (such as sex, ethnicity and social status). They are also widely used to follow up specific groups of individuals (cohorts) to detect the occurrence of new cases of cancer.
- PBCRs are an essential component of a fully developed cancer-control programme. In addition to providing information on current and future needs for services, they are used to monitor programmes of prevention, early detection and cure (treatment).
- PBCRs are becoming more widely involved in studies of the process of clinical care of cancer patients. Lack of clinical detail on cases is offset by the representative nature of the patients studied.
- The first PBCRs were established over 60 years ago. Their numbers have increased progressively; In 1966, 32 registries reported their results in volume I of *Cancer Incidence in Five Continents*, and 40 years later, there were 449 members of the International Association of Cancer Registries covering 21% of the world population.

The increasing availability of computerized databases that can be linked with cancer registries has enabled the capture of information on cancer patients that goes beyond the traditional registry dataset, including, for example, details of treatment and clinical status through health insurance records[5] or hospital information systems[6]. Another frequently used technique to extend the dataset is geocoding to permit the linkage of census information from the same small area as the patient to impute personal characteristics; it has been widely used to derive indicators of social status (or deprivation, in UK parlance)[7].

The quality of cancer registry data is evaluated by its completeness, validity and timeliness[8]. Completeness of ascertainment of cases should be as close to 100% as possible, so that the comparison of incidence rates between registries and over time reflects true differences in cancer risk. Although the target is 100%, an overall achievement of 90% can be considered satisfactory, provided that there are not substantial differences by cancer site or age group. Validity (the accuracy of the recorded data) can be increased by logical and consistency checks on recorded data; these are familiar checking procedures for all computerized databases.

The interpretation of cancer registry data

Cancer registries provide information on the incidence and survival (and sometimes mortality) of cancers classified according to their site of origin and histology, and usually on other aspects relevant to planning and evaluating cancer-control activities, such as stage at diagnosis and the nature of treatment received. The uses of such data are described below; however, in interpreting cancer registry data there are several important limitations that should be kept in mind.

Technical problems. Incidence and survival statistics from cancer registries have been criticized, especially the validity of the information they provide on the actual risk of developing (or dying from) a cancer for individuals in different populations, or living at different periods of time (see especially, Doll and Peto[10]). Although incompleteness and inaccuracy are issues of quality control that can be quantified and evaluated[8,9], there are other structural and technical difficulties that need to be taken into account.

A minor problem, common to all comparative studies, is the effect of changes in disease classification and coding over time — for example, the inclusion of borderline ovarian cancers as malignant tumours in the second edition (1990–1999) of the International Classification of Diseases for Oncology (ICD-O 2), but not in the first (1976–1989) or third (current) editions. This requires knowledge of the principles of cancer classification, and care in ensuring that similar disease entities are used in time-trend studies.

Potentially more serious is the fact that one individual can have more than one cancer. With improving survival, this is becoming more and more common — about 16% of new cancers in the United States are second (or higher order) cancers in the same individual[11]. Incidence rates (and survival) relate to a specific cancer, so that a new case must be distinguished from the extension, recurrence or metastasis of an existing case. Cancer registries adopt various rules to define a new cancer for inclusion in the registry database, but for international studies of incidence or survival a single set of rules is available[12], which enables comparison between different datasets.

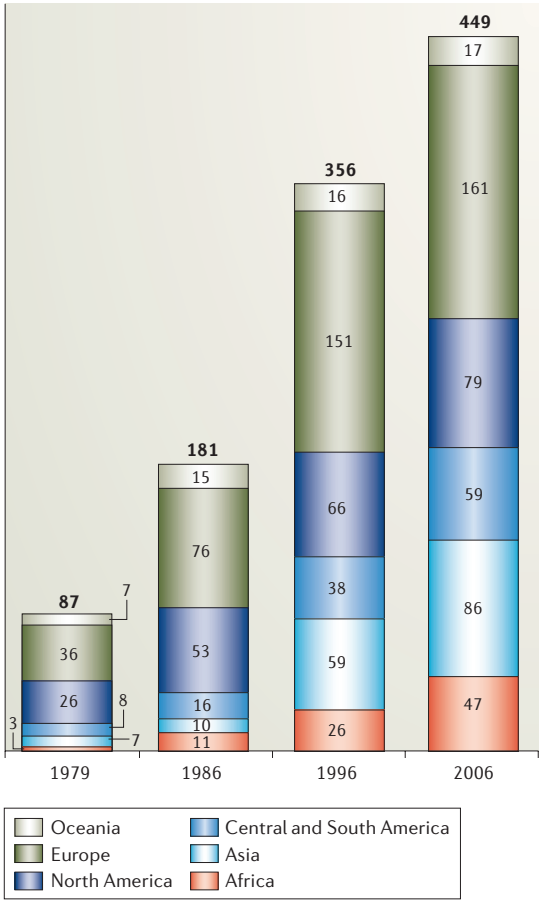
A more serious problem arises with respect to the definition of a case of cancer. Cancers are malignant tumours, and malignancy, although originally a clinical concept, is defined by pathologists in terms of the extent of invasion of the tumour (beyond the basement membrane, for carcinomas). Many studies attest to the fact that there is not complete concordance between pathologists in the diagnosis of cancer[13]. But, finding evidence of invasion will also depend, in part at least, on the diligence with which it is sought in histological specimens. Therefore, tumours of the bladder, in which malignant cells are observed at histology, are often defined as cancer even though invasion beyond the lamina propria is not observed. This is because such tumours are known to often be multifocal, with a strong potential for invasion even if invasion is not observed in a particular specimen or section. Statistics on the incidence of bladder cancer are therefore particularly prone to non-comparability of definition[14].

Incidence (unlike death) is clearly an arbitrary concept. It is a point somewhere in the continuum of the natural history of a cancer at which diagnosis takes place. Histological specimens taken from individuals in whom there were no symptoms, or no clinical suspicion of cancer, can reveal foci of malignant cells,

Box 1 | **The history of cancer registration**

The historical development of population-based cancer registration has been described by Wagner[77]. Although what constitutes a true population-based cancer registry (PBCR) could be debated, it is clear that the earliest registries that attempted to cover defined populations using multiple-source reporting were in Hamburg (established in 1927), New York (1940), Connecticut (1941) and Denmark (1942). A WHO (World Health Organization) subcommittee on "the registration of cases of cancer" was set up in 1950, and provided the first set of methodological guidelines for cancer registration[78]. At the International Symposium on Geographical Pathology and Demography of Cancer, arranged by the International Union Against Cancer (UICC) in 1950, the need for enumeration of all new cases of cancer in a defined geographic area was emphasized, and a Committee on Geographic Pathology was established[79]. From this initiative emerged the first volume of the *Cancer Incidence in Five Continents* series[1], and, following a meeting in Tokyo in the same year, the International Association of Cancer Registries (IACR) was founded. The IACR serves as a membership organization for PBCRs worldwide, and is concerned with establishing standards for cancer registration, training, the publication of registry data and holding scientific meetings. The figure shows the growth in the number of members of the IACR, as an indication of the spread of cancer registries during the last 27 years.

This growth in cancer registration has been, for the most part, unplanned. Occasionally a national policy has guided the process (for example, in the former Soviet Union[80]), but more often the process has been haphazard, and registries have been founded (and funded) through various organizations, including local government, health departments (at city, state and provincial level), non-governmental organizations (especially anticancer societies) and universities. Government policy has often followed *post hoc*, with an attempt to systematize or rationalize an existing situation (for example, in the United Kingdom, United States, France and Japan). In the United States, two government agencies have been involved. First, following three national cancer surveys (1937–1939, 1947–1948 and 1969–1971), the US National Cancer Institute set up the ongoing Surveillance, Epidemiology and End Results Program (SEER) in 1973. This has collected detailed and high-quality information from a number of cancer registries nationwide (8 initially, 18 today) on an ongoing basis, providing a reasonable (although non-random) sample of the population of the United States. Then, in 1992, the Center for Disease Control established the National Cancer Registry Program (NCRP), which aimed for a PBCR in every state of the Union, a goal that has now more or less been achieved[81].



and these 'cancers', when recorded, will inflate registration rates. This can occur during cancer-screening programmes. Screening aims to advance diagnosis, and so when introduced it will give rise to a temporary rise in incidence and a prolongation of survival (lead time). The effect on incidence will be more than temporary if a proportion of the cancers detected would never have surfaced clinically during an individual's lifetime. This is termed overdiagnosis, and probably accounts for some of the increase in incidence of breast cancer that has been observed following the introduction of systematic mammographic screening[15]. Similarly, readiness to biopsy thyroid nodules has probably inflated the rates for thyroid cancer[16].

Most striking, however, are the effects of screening with prostate-specific antigen (PSA), which has resulted in dramatic increases in the apparent incidence of prostate cancer in several countries[17]. In the United States, recorded rates doubled between 1986 and 1992 in whites and 1993 in blacks, since when incidence rates have declined[18]; this is probably because, by this time, most of the PSA tests being carried out were repeat examinations, and most of the latent cancers in the subset of the population reached by opportunistic screening had already been detected[19]. Nevertheless, incidence remains substantially higher than before screening was introduced[18], and Etzioni *et al.*[20] estimated that 29% of the prostate cancers detected in whites and 44% of those detected in blacks in 1988–1998 represented overdiagnosis.

Although these various problems can make it difficult to interpret incidence rates in terms of variation in individual risk between populations or over time, in a planning context the enumeration of newly diagnosed

Box 2 | **Variables recorded by cancer registries**[2,82]

Essential variables

- Personal identification (names (in full) and/or unique personal identification number).
- Sex.
- Date of birth or age.
- Address (usual residence).
- Ethnic group (when the population consists of two or more groups).
- Incidence date.
- Most valid basis of diagnosis (enables cases to be registered with a non-histological diagnosis).
- Topography (site) of primary cancer.
- Tumour morphology (histology).
- Tumour behaviour (benign, uncertain, *in situ* or malignant).
- Source of information.

Recommended variables

- Date of last contact.
- Status at last contact (at least dead or alive).
- Stage or extent of disease at diagnosis.
- Initial treatment.

cases is clearly relevant to defining the need for services or care for cancer patients.

Contextual (societal and political) problems. Cancer cases can only be recorded once they have been diagnosed, after a patient has presented themself to medical attention. It is possible that in rural areas of developing countries, people can die with their cancer never having been seen by a conventional medical practitioner, but this must be a rare occurrence in the urban populations of the twenty-first century[21]. In some countries, cancer registration (like the notification of communicable diseases) has a legal basis, but most registries have operated on a voluntary basis, relying on good will and the tradition of sharing of medical information among different specialties. However, this situation has changed with the rise of legislation on data protection and the proliferation of ethics committees, especially in the developed world (BOX 3).

Box 3 | **Legal and confidentiality issues**

Cancer registries have always operated under relatively strict conditions of respect for the confidentiality of medical information, particularly with regard to the physical security of their data files and the release of information to third parties[82,83]. Recent developments in the biological sciences have given rise to a growing range of ethical codes and guidelines, which propose ever more stringent regulation of the confidentiality of personal data, and the need for signed informed consent for its collection, storage and use. Although prompted by a concern for individual rights, this has often conflicted with social responsibilities, as reflected by disease notification and registration, including cancer. Peto *et al.*[84] have described the serious damage that the obstacles erected by recent legislation can cause to *bona fide* researchers, particularly epidemiologists, when they seek access to individual medical records.

Cancer registration is not feasible when individual consent must be sought from cancer patients, and ironically, the first cancer registry (in Hamburg) was the first victim of an attempt to make this mandatory. A sustained campaign by epidemiologists and public-health specialists has resulted in derogations to the informed-consent principle for information collected for public-health-related purposes — for example, in the United States[85], Japan and the European Union[86]. The International Association of Cancer Registries (IACR) has published a set of guidelines for cancer registries based on these principles[82]. Nevertheless, the local authorities and committees that produce ethical guidelines (see, for example, the Council for International Organizations of Medical Sciences[87]) continue to apply principles such as those in the Declaration of Helsinki[88], requiring that "in any human research, every potential participant … must be informed of the right to participate or not in the investigation and to withdraw his or her consent at any moment." This, in effect, makes accurate disease notification and registration impossible[89].

Geographic spread

PBCRs that are members of the International Association of Cancer Registries (IACR) cover around 21% of the population of the world, with a slightly uneven spread across the continents (FIG. 1). Some entire national populations are covered; in smaller countries (for example, Singapore, the Gulf States and the Nordic countries) this is possible with a single cancer registry, but larger populations pose considerable technical and logistical problems, and there are few registries that cover populations in excess of 10–15 million. National registries for the larger countries therefore rely on input from independent regional registries (as in the United Kingdom, Australia and Canada). In most countries one or more cancer registries are present, which provide coverage of a sample of the population, although this is by no means random. FIG. 2 shows, for example, the situation in Europe in 2004.

Not all of these cancer registries produce data of a sufficiently high quality to provide an accurate and unbiased estimate of incidence for their respective areas. Fortunately, the *Cancer Incidence in Five Continents* series of books provide incidence data that have been peer reviewed, and are considered to meet the requisite quality criteria for this purpose. There have been 8 volumes since the first, which was published in 1966 (REF. 1) (TABLE 1), with a progressive expansion in geographic coverage and diagnostic detail. The entire Cancer Incidence in Five Continents database, together with software for its analysis and presentation, is now available on CD[22] and, with more limited analysis options, on the Cancer Mondial web site. Around 9% of the world population is covered by the registries in the latest volume (VIII)[23].

Registry associations have grown up to deal with issues such as cross notifications (of cancer patients resident in one area but treated in another), common definitions and coding, quality-control procedures and staff training. There are many national associations (for example, the UKACR (United Kingdom Association of Cancer Registries), FRANCIM (France-Cancer-Iincidence et Mortalité), the AIRT (Italian Network of Cancer Registries) and the JACR (Japanese Association of Cancer Registries)), as well as groupings on a regional or linguistic basis (see online links box). Most hold training courses, sponsor joint research projects, and hold scientific workshops and meetings. Almost all PBCRs are members of the IACR, the role of which is summarized in BOX 1.

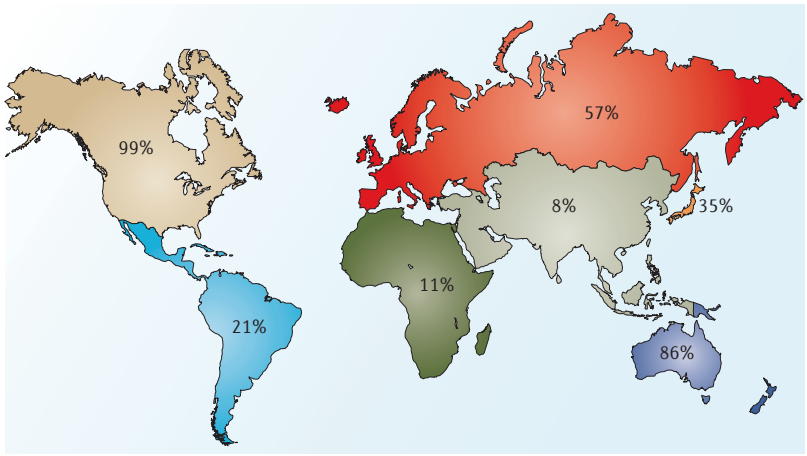


Figure 1 | **Cancer registry coverage; the geographic coverage (per cent of total population) of cancer registries by region.** The map includes all registries that are members of the International Association of Cancer Registries in 2006.

Ecological study
A study in which the exposure to and outcome of disease are measured on populations or groups, rather than on individuals.

The role of PBCRs in research

The original function of cancer registries was to calculate rates of incidence, so that the risk of various cancers in different populations could be compared. Although this still remains their most basic role, the activities of cancer registries have developed far beyond this to include studies of cancer cause and prevention, and to provide the information needed for the planning and evaluation of cancer-control programmes, although it has been pointed out that they are still an under-used resource in this respect[24–26].

Figure 2 | **Members of the European Network of Cancer Registres in July 2004.** The map shows regions of Europe that are covered by registries in green.

Descriptive studies

Descriptive studies use information from registry databases to examine differences in the incidence (or survival) of cancer, according to variables associated with place (of residence or of birth), time and personal characteristics (such as sex, ethnicity and social status). Classically, such descriptive studies are said to be 'hypothesis generating' — providing clues to aetiology, to be followed up in studies that focus on specific risk factors. For example, the role of diet in colon cancer was suggested by geographic variations[27,28], international correlations[29], migrant studies[30] and time trends[31]. The ongoing collection of statistics on cancer occurrence and outcome is an important component of cancer surveillance, but the term also encompasses the collection of data on the prevalence of causative (or preventative) factors in the population, and is concerned not only with identifying causes, but also with monitoring progress in prevention or screening[32], as described below.

There is an ongoing debate over the relative merits of registry (incidence) data and mortality statistics as measures of variation in individual risk. Mortality data are more widely available than incidence (although not for many developing countries)[33], but are less accurate (because of poorly specified causes of death)[34], and as a comparative measure of risk of disease are compromised by differences in survival, especially for less-fatal cancers. Therefore, comparisons using incidence and mortality data from the same populations can give different results (FIG. 3). On the other hand, death is a more objective and reproducible event than incidence, so that mortality data suffer less from distortions introduced by incidental or overdiagnosis (see above). Cancer registries do, however, record more detailed information about the patient and their cancer than is available on a death certificate, so that it is possible, for example, to examine risk according to histological subtype of cancer or stage of disease. In reality, the combination of data on mortality and on incidence, stage, distribution and survival from cancer registries will provide the best resource to interpret the relative contributions of differences in risk, earlier diagnosis and therapeutic success to cancer burden in different populations and over time.

Studies of cause

Cancer registries do not feature in most epidemiological studies of cause — except as a source of incidence rates for studies with an ecological study design. Because a registry includes all cases of cancer in the population, it is in theory an unbiased source of cases for case–control studies. In practice, the registry database is only complete several years after the incident date of the cases, so that individuals might be hard to trace (or have died), and random sampling of controls from the general population is difficult[35]. Some sort of 'rapid reporting' of cases to the registry is usually a prerequisite[36], but the need to identify population controls can

Table 1 | **Coverage of *Cancer Incidence in Five Continents* 1966–1992**

Volume	Year	Registries	Populations*	Countries	Period (approximate)
I	1966	32	35	29	1960–1962
II	1970	47	58	24	1963–1967
III	1976	61	79	29	1968–1972
IV	1982	79	103	32	1973–1977
V	1987	105	137	36	1978–1982
VI	1992	137	166	49	1983–1987
VII	1997	150	183	50	1988–1992
VIII	2002	186	214	57	1993–1997

* Populations defined in several ways, for example, ethnicity, birthplace and urban or rural.

result in low participation and possible bias[37]. Cancer registries have, however, been extensively used to follow up specific groups of individuals (cohorts) to detect the occurrence of new cases of cancer. This can involve the linkage of pre-existing databases with the cancer registry (for example, registries of specific occupations[38], or of HIV–AIDS[39]). A special example is the study of the risk of second cancers (in relation to the initial cancer and its treatment), where the assembly of the cohort, and its follow-up, make use of registry databases only. These studies are of interest in detecting the commonality of risk factors (or susceptibility to them), or the adverse effects of treatment[40].

PBCRs in cancer control

Cancer control is a term that encompasses all elements of prevention, early detection, treatment, rehabilitation and palliation. The World Health Organization recommends that cancer-control activities are best planned and delivered through a national cancer-control plan, and notes that PBCRs are a core component of cancer-control strategy[32].

Priorities and targets, projections and predictions. An important role of PBCRs is to assess the current magnitude of the cancer burden and its probable future evolution. Burden can be evaluated in terms of incidence and mortality, but other dimensions are often considered, such as the prevalence of different cancers, person years of life lost, and quality or disability-adjusted life years. An appraisal of the current situation provides a framework for action, and the setting of targets enables the success (or otherwise) of these plans to be monitored. There have been several attempts to set goals for cancer control, both at national and international level[41–44]. Logically, target setting involves not only a sound knowledge of the present cancer situation, but also how it might be expected to evolve in future; prediction might simply involve the projection of recent trends into the future, or encompass the probable effects of changes in aetiological factors or proposed interventions[45]. Cancer projections that have been prepared as an aid to service planning have been published for the Nordic countries[46], Australia[47] and Scotland[48].

Prevention. The effectiveness of preventive interventions against cancer has rarely been evaluated by randomized controlled trials; more usually success has to be inferred from observations after the introduction of programmes[45]. This can involve comparing observed versus expected incidence rates (allowing for a time-lag for the effects to emerge), with the expected rates based on a prediction model of some kind. This approach has been widely used to evaluate the success of interventions against lung cancer[50,51]. An even more striking example[52] is the dramatic effect on the incidence of hepatocellular carcinoma recorded by the cancer registry in Taiwan after the introduction of a vaccination against hepatitis B in the 1980s, first to neonates born of HBsAg positive mothers, then, in 1984, for all new-borns. By 1994, it was possible to compare liver cancer incidence in children aged 6–9 who were born before vaccination was introduced, and

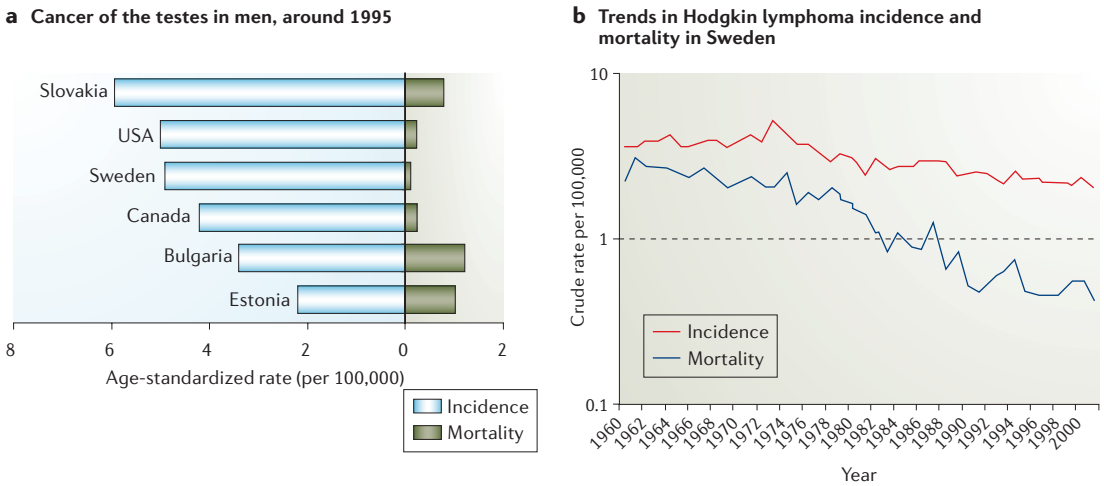


Figure 3 | **Differences between incidence and mortality rates. a** | Geographic variation in incidence and mortality from cancer of the testes in various countries around 1995. **b** | Time trends in incidence and mortality of Hodgkin lymphoma in Sweden. Data from REFS 22,23,90.

Disability-adjusted life years (DALY) The years of life lost to premature death and years lived with a disability of specified severity and duration. One DALY is therefore one lost year of healthy life.

Comorbidity
The presence of coexisting or additional diseases with reference to an initial diagnosis or with reference to the index condition that is the subject of study. Comorbidity can affect both the ability of affected individuals to function and their survival; it can be used as a prognostic indicator for length of hospital stay, cost factors and outcome or survival.

those who were born after. There was a fourfold decrease in incidence following the introduction of the vaccination. Another approach has been to compare incidence rates in areas with or without preventive programmes, or with different intensities of intervention[53,54].

Screening. Cancer registry data have been widely used for the evaluation and monitoring of screening programmes[55]. Although the effectiveness of screening can only be correctly judged by the extent to which the objective of reduced mortality (or reduced incidence, for cancer of the cervix) is achieved, if this has been demonstrated, intermediate endpoints (such as tumour size, stage and survival) can be used to monitor the screening process.

Ideally, information on the screening status of individuals from a suitable database can be linked to a cancer registry in order to study the outcome of individuals with different intensities of screening exposure. Thus, in monitoring breast cancer screening programmes the expected distribution of cancers by stage or the expected incidence rates (overall, by age group and/or by stage) can be obtained from a registry and compared with the observation of screened individuals[56]. The incidence of interval cancers (detected between screenings) is useful in decisions about the appropriate intervals between tests[57], and the incidence of advanced cancers provides an early surrogate for cancer mortality[58].

More usually, there is no information on the screening status of individuals, and population-level analyses are used. The simplest are time-trends in incidence for cases in which screening should prevent invasive cancer, such as in the cervix, or mortality for programmes that are designed to detect early invasive cancers (for example, breast, colon and prostate). No reduction in incidence should occur in programmes to detect early invasive cancers; indeed, the introduction of screening should be followed by a rise in incidence (as prevalent, asymptomatic cases are detected), followed by a fall, with cumulative incidence unchanged over what it would have been without screening[59]. However, the cancers detected by screening must have a more favourable stage distribution, and be of a smaller size than those detected clinically (by symptoms) if the programme is to be effective. Cancer registry data have been used to examine the proportionate distribution, or incidence rates, by stage at diagnosis in relation to the presence of screening (or measures of screening intensity). Screening should lead to a reduction in the incidence of advanced cancers[60–63]. Stage at diagnosis might also improve over time as a result of better diagnostic technology, and the benefits of screening might be better quantified from comparisons of subpopulations that have or have not received screening (or different intensities of screening)[64], although there could then be other questions concerning the comparability of the populations.

The detection of cancers by screening will lead to improved survival, whether this results in a reduction in mortality (the goal of screening), or is simply due to advancing the date of diagnosis (lead time bias) or differential detection of slow-growing tumours (length bias). Survival trends, by age, have been studied in relation to the early diagnosis of breast cancer due to screening[63] or to improving breast cancer awareness[65], and in relation to the early detection of colon cancer[62]; the favourable trends in survival were due to a shift to earlier stage at diagnosis as well as better survival within stage.

Outcome: survival and quality of life. Although they are essential as a measure of the success (if any) of cancer-control activities in different populations, trends in mortality rates are not ideal, as they are influenced both by incidence and survival. Moreover, the effect of cancer-control activities on mortality will often be delayed, and data on both the detection and incidence, and on cancer patient survival, can give a more immediate insight into changes in outcome after diagnosis[66]. Randomized controlled trials (RCTs) are the recognized technique for the measurement of the precise effects of specific interventions on survival, but the outcomes shown in RCTs will rarely be evident at the population level, where the patients being treated are more heterogeneous, are generally elderly, have significant comorbidity and are less likely to derive benefit from the intervention[67]. In any case, the objective of measuring population-level survival is to give an indication of the possible role of the process of care,

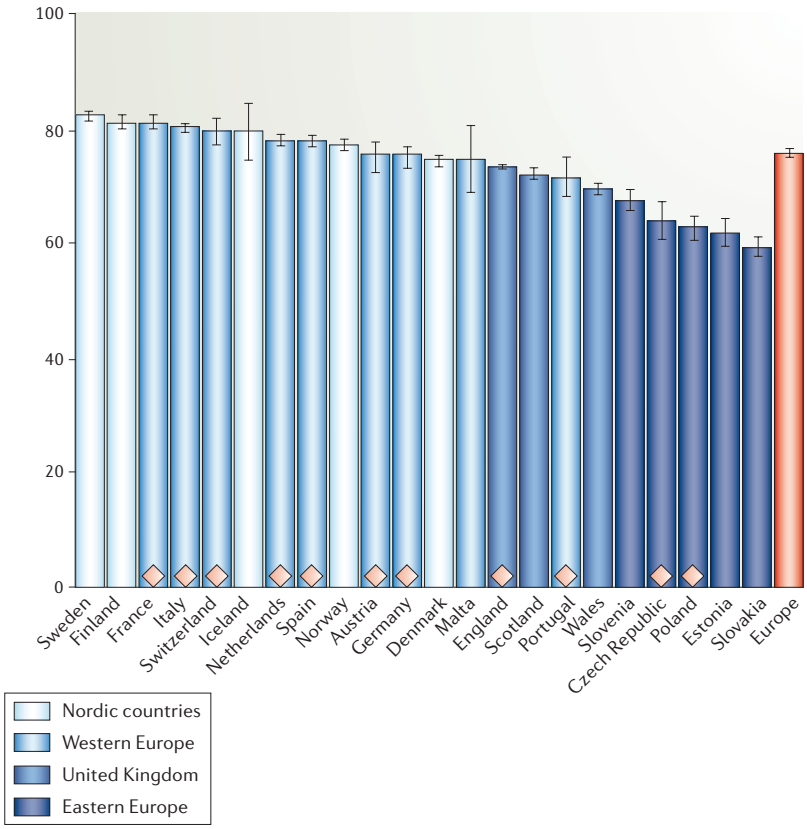


Fig 4 | **Survival from breast cancer in Europe.** Data from the European cancer registries study on cancer patients' survival and care (EUROCARE) III study shows the age-standardized 5-year survival (%) from breast cancer in European countries. Progressively darker shades of blue represent Nordic countries, Western continental European countries, components of the United Kingdom, and Eastern European countries. The European average is shown in orange. Diamonds represent countries for which the data represents only a sample of the population. Data from REF. 91.

and not simply the effectiveness of a specific treatment, as a determinant of survival differences.

The analysis and publication of survival data by cancer registries has a history as long as cancer registration itself. But, although the black–white disparities in cancer survival in the United States had been the subject of comment for many years[68], population-based survival statistics had attracted little attention at policy-making level until the publication of international comparisons of survival by the European cancer registries study on cancer patients' survival and care (EUROCARE) group[69]. The results, which showed substantial international variation (FIG. 4), had a galvanizing effect, and profoundly influenced policy making in some countries, such as the United Kingdom and Denmark. Although there has been some justified criticism of the fixation on improvement in survival as the target for cancer services[70–72], the findings from studies such as EUROCARE have at least focused attention on the reasons for the observed differences in survival.

Of course, survival in terms of the average number of years lived after diagnosis is a very crude indicator of outcome, albeit a relatively easy one to measure. Years of life are of little value if they are accompanied by disability and pain. For this reason, survival measures have been refined, either into medico-surgical categories such as disease-free survival (before any recurrence) or metastasis-free survival, or by evaluating the quality of life lived between treatment and death in terms of, for example, disability or the side effects of treatment. The measurement of health-related quality of life is not part of routine cancer registration; it requires complex data collection, by interview or observation, from individual patients[73]. However, quantification of the outcome of cancer care is important when considering alternative strategies of intervention, as are the economic considerations with respect to the inputs (costs) required to achieve given improvements in outcome.

Clinical care. A range of indicators of the quality of the process of clinical care has been used in different studies[74]. The location (for example, type of hospital) of treatment for specific cancers has been found to vary considerably for different groups of patients, and this probably reflects the type of facilities available and the level of expertise of the therapists. The technical expertise of physicians and surgeons can be a function of their familiarity with the appropriate diagnostic and therapeutic methods, as measured in terms of case load. The importance of these admittedly indirect indicators of quality of care in determining outcome has been shown in the pioneering work of Gillis[75] and others. Simple measures such as delay (for example, between diagnosis and therapy) provide information on equity and access, as well as potentially influencing outcome. Auditing the nature of the diagnostic and therapeutic procedures that are actually performed provides a more direct indication of the quality of care; if the focus is effectiveness of care, then the choice of indicators should be known to have an effect on its outcome. However, the dataset collected by PBCRs is limited with respect to the variables suitable for clinical-care studies. The usual variables that are available are hospital, specialty of treatment, nature of first therapy (radiotherapy, chemotherapy) and outcome (dead or alive). It is difficult for PBCRs to expand their dataset, like those of hospital database systems[76], to capture information on comorbidity, diagnostic and staging procedures, extent of disease at diagnosis and at surgery, the nature and sequence of treatment and follow-up in terms of recurrence and metastasis. It might be possible by linkage with other files of clinical data (see above), and such studies normally use samples of the registry database — confined to selected cancers, for limited periods of time and for representative samples of cases. The advantage of using population-based data in this way is that they relate to the whole community of cancer patients, rather than a single institution, or self-selected and often atypical subgroups of patients (such as those reaching comprehensive cancer centres).

Implications and future directions

Cancer registries are recognized as being more or less indispensable components of national cancer-control programmes, and are likely to be founded in countries that implement such programmes if they do not already exist. There are several advantages to the ongoing registration of cancers, rather than one-off surveys, but the desirability of national coverage, rather than sample sites, is less obvious. A limited geographic coverage is adequate for many descriptive and surveillance activities, and although national data are clearly superior, especially if follow-up of specific cohorts is required (to avoid losing track of migrating subjects), the costs involved should be weighed against the benefits. The expanding roles of registries in monitoring factors that influence outcome (survival and quality of life), and the nature and quality of the care received by cancer patients, demands a dataset that includes many more variables than has traditionally been collected. Sometimes this can be achieved through linkage to other files; sometimes an in-depth study of sample cases will be the more reasonable approach. Cancer registration has come a long way in the last 60 years, and future expansion in geographic coverage and scope of work seem reasonable predictions, unless registries fall foul of the objections to their work by the informed-consent ethicists.

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Competing interests statement
The authors declare no competing financial interests.

DATABASES
The following terms in this article are linked online to:
National Cancer Institute: http://www.cancer.gov
breast cancer | colon cancer | hepatocellular carcinoma | prostate cancer

FURTHER INFORMATION
Association of Nordic Cancer Registries: http://ncu.cancer.dk
Australasian Association of Cancer Registries: http://www.aihw.gov.au/cancer/aacr/index.html
Cancer Mondial: http://www-dep.iarc.fr
European Network of Cancer Registries: http://www.encr.com.fr
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Gulf Center for Cancer Registration: http://www.gccr.org/main.html
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