

¹ University of Torino² Cancer Registry of Torino and Regional Centre for Cancer Prevention of Piedmont, Torino

A short history of pathology registries, with emphasis on cancer registries

Summary

In the 1950s, major technical problems for ensuring quality and effectiveness of population based registration of cancer and other conditions had been faced and solved. Nevertheless, the classical epidemiological texts published in the 1960s and the 1970s gave little attention to and showed limited enthusiasm for population-based registries of pathology. The latter, in fact, have been marginal to the dramatic evolution of basic conceptual issues such as study design and causal inference. This perspective may change with the use of registries in order to assess quality of care in a public health perspective.

In looking retrospectively, marked changes occurred since the 1960s in distribution between countries and continents of cancer registries to the dataset known as "Cancer Incidence in Five Continents" (where worldwide data from cancer registries of quality converge). The number of countries with cancer registries approximately doubled vs. a fivefold increase in both the number of active cancer registries and the total population served by registration. Nevertheless the increases were concentrated in developed countries whereas in developing countries there was a substantial decrease in registration, attributable to the political and economical situation

Keywords: Population – Cancer registries – Epidemiology – Evaluation.

Background

The terms used in the present article are those indicated by Last (1988). A *registry* is a file of data concerning all cases of a particular disease or other relevant condition in a defined population, so that the cases can be related to a population base. The *register* is the actual document and the *registry* is the system of ongoing registration. A survey is an investigation in which information is systematically collected: it must

not necessarily be population based and is not a continuous ongoing exercise. In fact, the borderline between the mechanisms and purposes of surveys and registries is not always sharp. For instance, in the US, in the past, cancer and stroke surveys fulfilled functions which nowadays would be attributed to permanent registries.

A number of roles have been traditionally recognised to population-based disease pathology registries (Tuyns 1978). The primary function was (and is) the description of the frequency of disease in a population or in a set of sub-populations. Comparisons of rates with those produced by other similarly designed registries or within sub-populations served by the same registry provide clues for or evidence in favour of etiologic hypotheses. In fact, registries are also a database for investigating the natural history of disease. In public health, they have unique role for measuring the efficacy of screening programmes and for evaluating the effectiveness, coverage and overall quality of services.

The spectrum of health-related circumstances other than the occurrence of death or overt disease the registration of which may be useful is wide and heterogeneous. Etiological studies may benefit from registries of persons having experienced exposure to alleged or proven risk factors, either endogenous (e.g., twins) or exogenous (e.g., occupational exposures, environmental accidents). Similarly, identifying and counting – within a population – persons suffering from restricted individual performance, bed disability, inability to work etc. may be the purpose of a registry and contribute to health planning. It has been pointed out that for a registry the important point is to find a gauge whose definition is consistent (Riley 1993). This can be easy for standard gauges relying on diagnostic evidence, whereas individuals and societies make different decisions about the threshold between occurrence and non occurrence of health-related events – e.g., inability to work (Riley 1993).

In the present context, attention will be addressed to measurements of the number of persons with overt disease. It is

nowadays commonly accepted that a pathology-specific registry is justified in a given historical and societal framework when two conditions are met. Firstly, its *product* is of use in public health and/or for clinical and epidemiological research. Secondly, it can function effectively, i.e. the logistics for describing what it is expected to describe is adequate. Underlying *sine qua non* conditions include: (1) the specification of operational standards in order to characterise the individuals liable to registration; (2) the exhaustiveness of their identification (including estimates of cases lost to registration, if any), (3) the availability of adequate denominators in order to estimate rates; and (4) a favourable cost-benefit balance.

In fact, the term “registry” has been used to indicate the collection of individual nominal data within different contexts. Many initiatives were originally designed with the aim of assembling and managing data for the purpose of etiological or clinical studies, the estimate of occurrence on a population basis being a by product of the exercise. This has been the case of the registry of neurological diseases at the Mayo Clinic in Rochester, Minnesota (Kurland et al. 1982), which has been retrospectively extended back to 1907. Procedures of record linkage (of increasing sophistication throughout the decades) with the files of other institutions have been applied to such an extent that measures of disease occurrence in the area of Rochester and related trends have been available for almost half a century (Kurland et al. 1982).

Conversely, projects originally addressed to disease specific measurements evolved in other directions. In 1971, WHO launched a project for registering the occurrence of stroke over a 4-year period in 17 areas in Europe, Asia and Africa (Thorvaldren et al. 1995). This initiative led to what nowadays is known as MONICA. In fact, the representativeness of the population and the comparability of findings between areas has been problematic. In some countries MONICA evolved to more elaborated experiences: this occurred in Finland, where linkages between a variety of databases have been undertaken in the last decade, with the perspective of a reciprocal validation with mortality data (Tuormilehto et al. 1996).

The role of disease registers in the transition to modern epidemiology

Admittedly, the expansion of population-based registries and surveys has been relatively marginal to the dramatic evolution of epidemiological thought during the last decades. Basic conceptual issues such as study design and causal inference seem to have been in the forefront of modern epidemiologists to a much greater extent that the refine-

ment of registration techniques (among which the current possibility of storing and processing a huge number of files is a major but not the exclusive one) and the updating of nosological classifications. As recently as 1985, in his seminal review, Marvin Susser, while focusing on the theories and *techniques* used to cope with the changed spectrum of diseases and on the relevance of population research, barely mentions disease registries (Susser 1985).

During decades, disease registries were felt less promising tools for epidemiological research than long-term community studies (the origins of which can be traced to Sydenstricker's study in Hagerstown, Maryland, in the 1920s (Sydenstricker 1926)) or prospective studies on cohorts of persons exposed to exogenous agents.

This lack of enthusiasm transpires from the major epidemiological texts published up to the 1970s, with the exceptions of books addressed to the epidemiology of conditions particularly liable to registration, such as Lilienfeld's (Lilienfeld & Lilienfeld 1979). Otherwise, it is worth noticing that the alphabetical index of the first edition of the “Epidemiological methods” of the Harvard School of Public Health (MacMahon et al. 1960) does not include the term “register” or “registry”. The text mentions and acknowledges the role of two disease registries, i.e., cancer registration in Connecticut and the pulmonary tuberculosis register in Copenhagen (no mention of the Danish Cancer Registry!), but does not address the methodological problems inherent to the collection, processing and interpretation of data.

In the introductory chapter of the second edition of “Principles of Epidemiology”, Taylor and Knowlton (1964) addressed in general terms the issue of mechanisms (and shortcomings) of notification of infectious and industrial diseases and cancer registration. Clinical follow-up and measure of the results of therapy is specifically mentioned as a purpose of cancer registration (started in the UK in 1947 by the General Register Office) whereas it is acknowledged that registration “may ... provide information of epidemiological interest (but) at present it has not been used for this purpose”. Approximately in the same period, another “classical”, Morris (1970) commented that morbidity studies were becoming a main interest of public health since mortality seemed to be progressively less useful in the diagnosis of community health. Nevertheless “the cancer register and some hospital figures for psychosis apart, there are little data even on a national scale of the incidence and prevalence of the chronic diseases that now dominate the practice of medicine”. Morris acknowledged the potentialities of the National Cancer Registration Scheme in England and Wales, but he commented on the shortcomings – for aetiological research – created by the limited number of individual data which were

recorded. While emphasising the need for a community (as opposed to hospital) approach, the scenario depicted by Morris, was that of a *chronic disease register* (as opposed to a registry addressed to a specific condition) in order to study the transition of subclinical to clinical conditions.

Probably, there were two reasons for this limited interest in population-based pathology-specific registries. One was scepticism on the ability of registries to produce reliable and exhaustive data. The other was mistrust for a practice which had proved to be able to work but which was still looking for a function. This was well expressed by Harold Dorn (who was a pioneer of the national cancer survey of cancer in the US, and later of international comparisons of incidence rates), in 1950, at the 77th meeting of the American Public Health Association (Dorn 1951):

“Universal reporting, wherever it has been partially successful, has been required for administrative or legal purposes. This is true for ... infectious diseases and occupational diseases. The statistical data resulting from the registration arise as by-products of the system and are not the primary reason for its existence. As yet, the principal reason for the reporting of chronic diseases has been the statistical data which would be obtained. Until registration of cases of disease can be justified for reasons other than the statistics which will result, the universal reporting of chronic disease is not likely to be a useful source of morbidity data.”

In fact, Dorn (1951) intended to be more benevolent than critic: he was searching for justifications for registries (or large surveys) of chronic diseases to exist and went as far as to hypothesise “direct services” to be given to suspected cases in such an exhaustive form that record keeping would be tantamount to the creation of a registry producing morbidity data. Dorn was also concerned by the logistic and financial problems created by the huge volume of records, the possible heterogeneity in quality of data, if registration was exhaustive or – alternatively – the bias the likely selective identification of cases.

Rather than reviewing systematically the conditions for which population-based registration has been suggested, attempted or implemented, in the next paragraph, we concentrate on the history of cancer registration. This choice does not merely reflect our field of investigation. Indeed, cancer has probably been the condition for which the cultural gap nicely described by Harold Dorn half a century ago has been abridged to a greater extent. Perhaps more than registration of other conditions, for cancer registries it has become clear that their “descriptive” function is only a part of the game: their product has been the object of the application of sophisticated techniques based on elaborated conceptual thought, such as analysis of time trends and survival data, as

well as international co-ordination, thanks to the International Association of Cancer Registries (IACR) and to the International Agency for Cancer Research (IARC) (Wagner 1991).

It is acknowledged on the other hand that comparable efforts regarding a number of conditions such as congenital malformations, diabetes, neurological disease and others have been effective in producing epidemiological and clinical knowledge in those areas.

Cancer registration

In the first decade of this century, surveys measuring the point prevalence of cancer were reported from a number of European countries (Wagner 1991), including one in Baden in 1906, in which it was required that physicians should report all cases observed within a period of one year. All these “censuses” failed to reach their purpose, because of the high number of missing reports and the inability to match obtained from different sources regarding the same individual. It was also soon realised that compulsory notification would be unfeasible in most circumstances.

In Europe, permanent registration systems were implemented in Hamburg in 1926 and in Mecklenburg in 1937, both being discontinued during the second World War (Lilienfeld & Lilienfeld 1979), in North America, permanent registries were started in 1927 and 1935, respectively in Massachusetts and in Connecticut, whereas the first national survey on a significant sample of the US population (10 metropolitan areas) was carried out by Dorn in 1937–38 (and repeated in 1947–48) (Dorn & Culter 1959). It has been suggested by Dorn (1951) that the achievements of the application of statistical methods in social research influenced the decision of implementing the survey in health research.

By the end of the late forties, the four population based registries (those serving the populations of Hamburg, Connecticut, New York and Denmark, the latter having been created by J. Clemmesen in 1943) and the survey system (10 metropolitan areas in the US) had faced and solved most technical problems (exhaustiveness/representativeness, merging of data from different sources, development of nosological classifications, use of appropriate statistical indicators etc.). The concepts underlying these achievements have been valid for the subsequent half century. The first experiences of using nominal rosters of cancer patients for analytical studies or for linkage with other registries are dated in the late 1940s (Busk et al. 1948).

One of the many merits of the late J. Clemmesen was that of convening a meeting of experts (in those days, they would not call themselves epidemiologists but rather “cancer

statisticians”), who debated about the usefulness of population-based cancer data and compared the respective advantages and disadvantages of registries and surveys (Clemmesen 1974). The group acknowledged the potential for descriptive epidemiological information of mortality statistics and clinical findings: rates for a number of cancer sites varied according to occupation and social status, the number of deaths classified as carcinoma of the lung was increasing in several countries, geographical differences regarding carcinoma of the stomach had become obvious and a number of studies had associated cancer of the cervix and cancer of the corpus to ethnicity and parity. Thus, incidence and mortality statistics should not be considered as alternatives: the latter are largely credible but the former can provide information on treatment and follow up. In conclusion:

“the collection of accurate statistics of cancer incidence and mortality among different ... people and ... countries may lead to important indications for experimental (sic! – ndr) studies ... (whereas) the information (provided by mortality statistics) ... is becoming increasingly inadequate, owing to growing numbers of patients successfully treated and thus not registered in the statistics of death

(Thus), we ... make the following suggestions:

1. Great benefit would follow the collection of data about cancer patients from as many different countries as possible.
2. Such data should be recorded on an agreed plan so as to be comparable.
3. Each nation should have a central registry to arrange for recording and collection of such data.
4. There should be an international body whose duty should be to correlate the data and statistics obtained in each country”.

These recommendations had a great impact. The World Health Organisation, in 1950, created a Subcommittee on the Registration of Cases of Cancer (World Health Organisation 1950). Within a few years, European Nordic countries, Great Britain and Canada launched programs which led to national coverage of registration (Wagner 1991). The model followed in the US was different: no national coverage was attempted, whereas a number of country- or state-based registries were created and the surveys on samples of the population were converted – in the early 1960s – in the Surveillance, Epidemiology and End Results (SEER) program which has regularly produced incidence and survival rates broken down by ethnic groups.

Whereas the public health impact of cancer registration was immediately perceived in North America, UK and European Nordic Countries, in other industrialised nations, such

as Southern European countries, expansion of cancer registration occurred later and was slower. A major reason for this was the limited availability of epidemiologically-oriented skills within programmes for cancer control. In addition, in those countries, the medical milieu was reluctant to accept the role of exogenous agents in cancer aetiology and the need for investigations in this area. This attitude also reflected a paralysing interpretation of medical secrecy and some reluctance in adopting internationally validated classifications of disease. These problems were shared by most Southern European countries, where, in the late 1960s, a handful of pioneers (including some clinicians) realised that an exchange of experiences would have been profitable. Their effort led to the creation of the Group for Cancer Registration and Epidemiological Studies in Latin Language speaking Countries, which has successfully accomplished its mission during the last 25 years (it has also been a useful tool for the identification of exogenous cancer risk factors typical of these countries).

The need for international comparisons was implicit in the cultural pressure for the creation of cancer registries. The first world-wide analysis appeared in the 1960s, with the stimulating and ambitious (for those days) title of “Cancer incidence in five continents” (Doll et al. 1966). This marked the beginning of a series of publications appearing at 5-years intervals, taken care of by UICC, IARC and IACR (International Association of Cancer Registries, which was created after the International Cancer Congress in Japan in 1966). In 1997, the series has reached its 7th update (Parkin et al. 1997). Contrary the publication of mortality data by WHO, this editorial programme does not simply and passively accept data, but revises them and controls their quality. Two by-products of this strategy have been a world-wide standardisation of the activity of registration and the provision (in recent times through IARC) of technical advice to developing cancer registries.

In the early 1960s, 32 registries in 24 countries served 3 % of the world population: around 1990, 143 registries in 55 countries served 9 % of the world population (Fig. 1–3). Within this conspicuous increase, the relative contribution of cancer registries operating in developing continents has decreased in time, leading to the inequalities reported in Table 1. This dynamics has been driven by at least two components. One is the political and economical situation (which explains the appearance and disappearance of registries of small and medium size in Africa and South America). The other component is structural: the current overall picture has derived, in temporal order, by the national registries in Northern Europe in the 1950s, registries in North America and Japan in the 1960s, some large registries in

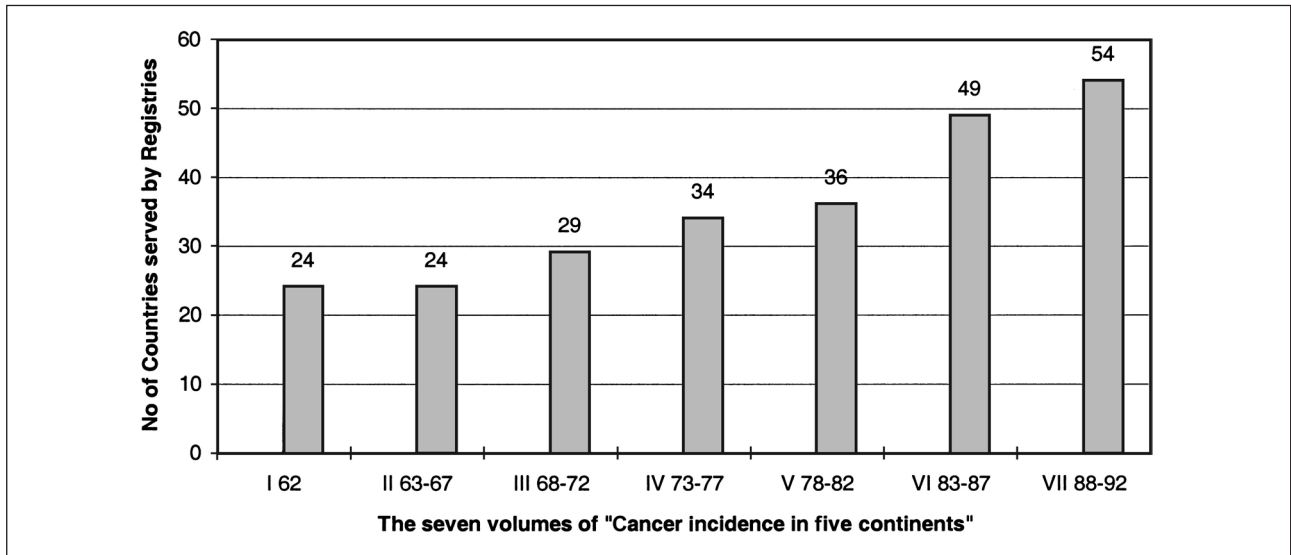


Figure 1 Number of countries served by population-based cancer registries reported in the volumes of "Cancer incidence in five continents" 1960–1992 (Doll et al. 1966; Doll et al. 1970; Waterhouse et al. 1976; Waterhouse et al. 1982; Muir et al. 1987; Parkin et al. 1992; Parkin et al. 1997)

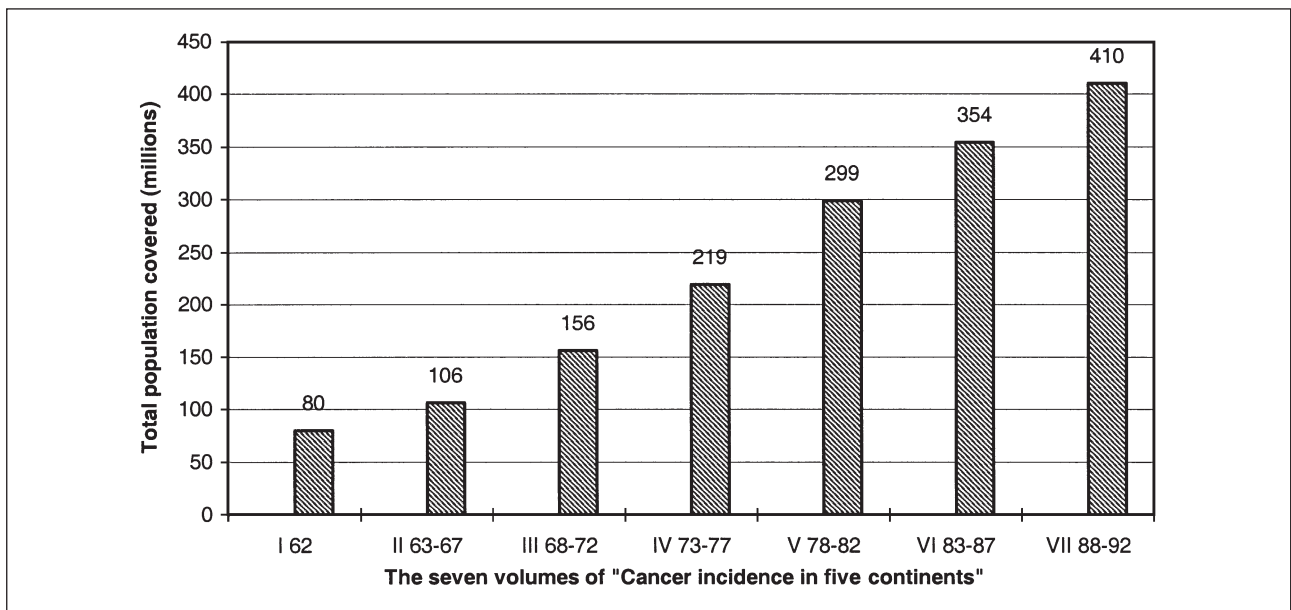


Figure 2 Total population served by population-based cancer registries reported in the volumes of "Cancer incidence in five continents" 1960–1992 (Doll et al. 1966; Doll et al. 1970; Waterhouse et al. 1970; Waterhouse et al. 1982; Muir et al. 1987; Parkin et al. 1992; Parkin et al. 1997)

Asia and national networks of registries in southern Europe starting in the 1970s. The current tendency to growth zero is partly attributable to the reduction in resources but also by the awareness that in a number of circumstances, incidence and prevalence estimates can be obtained indirectly from mortality and survival data, through validated methods (Parkin et al. 1993; International Agency for Research on Cancer 1995).

Comparing the geographical distribution of cancer registries in 1960 and in 1990 shows a strong polarisation in areas of major economical development. Elsewhere, registry implementation has been discontinuous and unstable, in both time and space. Whereas decades ago developing areas were supported (also in terms of public health programs) by the industrialised countries from which they traditionally depended, more recently registration seems to depend from local

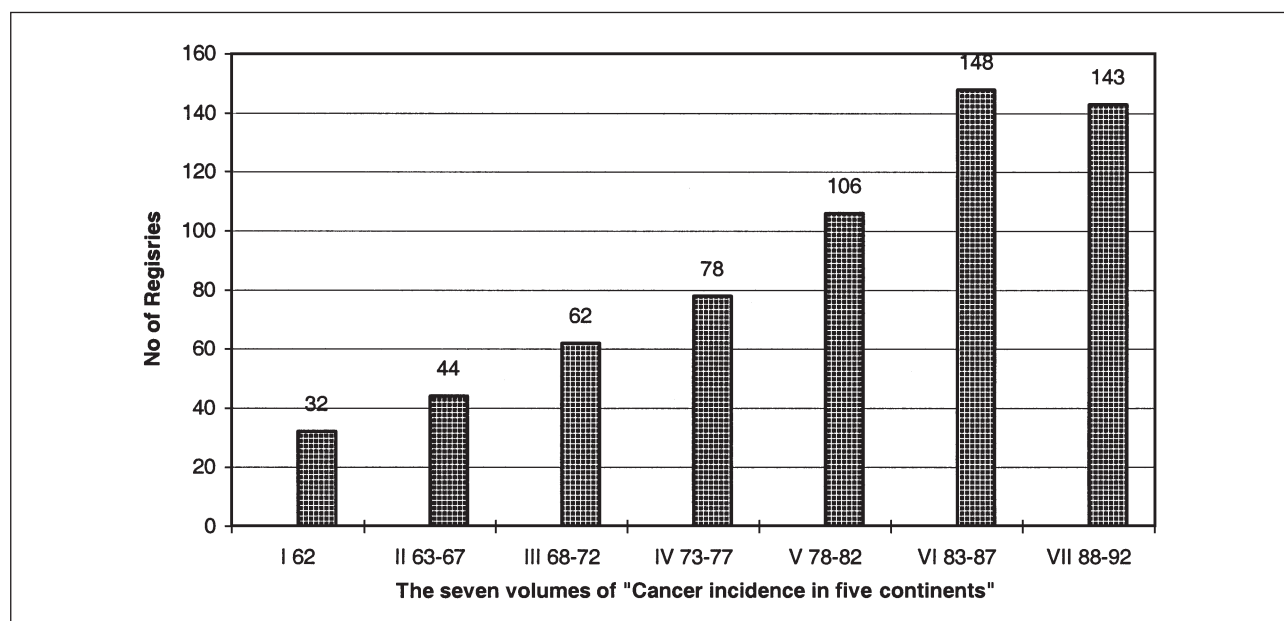


Figure 3 Number of population-based cancer registries reported in the volumes of "Cancer incidence in five continents" 1960–1992 (Doll et al. 1966; Doll et al. 1970; Waterhouse et al. 1970; Waterhouse et al. 1982; Muir et al. 1987; Parkin et al. 1992; Parkin et al. 1997)

Table 1 Coverage by Cancer Registries around 1992 (From Parkin et al. 1997)

Area	Number of registries	Population served by registration (m)	Total population around 1995 (m)	% served population
Africa	5	0.5	728	0.1
Central and Latin America	11	20.8	482	4.3
Canada and US	25 ^a	61.9	293	21.1
European Union	53	119.0	372	32.0
Other Western European Countries ^b	10	8.0	12	66.6
Other, Europe	10	45.6	344	13.2
Asia	24	71.4	3458	2.1
Oceania	9	18.5	29	63.8

^a Including SEER (Surveillance Epidemiology End Results) covering approximately 10% of the population.

^b Norway, Switzerland, Iceland.

initiatives, which find support in a complex programme launched by IARC some 10 years ago (International Agency for Research on Cancer 1995).

Throughout half a century, there has been an increasing production of conspicuous descriptive data by cancer registries. The fact that the use of nominal files for analytical studies (either etiological or clinical) has been more limited derives from several reasons. On one hand the design of most ana-

lytical studies does not require the files of a central registry, even if this implies duplication of data collection. In addition, the circumstances for the implementation of analytical studies (formulation of a hypothesis and availability of the epidemiological skill required to carry out the study) do not necessarily coincide with the presence of a registry or with an adequate update of the data which it contains.

Investigations on temporal trends have been a natural consequence of "ageing" of registries (those of Connecticut and Denmark have reached their 50th anniversary!). Adequate statistical tools have been available only since the 1970s. Limited international comparisons produced in 1980 (Magnus 1981) led to a more recent and methodologically rich comprehensive world-wide analysis of temporal variations of cancer incidence and mortality (Coleman et al. 1993).

At first sight, studies on geographical heterogeneity within the areas served by cancer registries would seem to be the natural evolution of their activity. Whereas "maps" and descriptive studies have been reported by many registries, it must be acknowledged that they did not add much to findings from corresponding analyses on mortality. In fact, with a few exceptions, confirming the existence of alleged clusters of incident (or lethal) cancers proved to be much more difficult than originally hoped as well as their interpretation in terms of association with environmental exposures (Elliott et al. 1992).

In the early 1980s, it became apparent that cancer registries provided the basis for a number of "clinical" uses, i.e., other

than the production of incidence data and clues for etiologic studies. Originally, the major effort was directed towards the evaluation of programs for the early diagnosis of cervical cancer with Pap-test, whereas more recently the attention was addressed to the evaluation of the efficacy of diagnosis of asymptomatic breast cancer through mammography (Tomatis 1990).

A logical expansion of this approach was the idea that population-based survival rates of cancer patients could be used as an indicator (not the only one, obviously) of the quality of cancer care in a given area and that cancer registries could have a major role in this direction. In fact, during the 1970s and early 1980s this potential was perceived in the US by SEER and by some registries in Northern Europe but not elsewhere. The limited interest for this approach may have

reflected the lack of resources for a systematic follow-up of the living status of the registered individuals. It can be traced back, however, also to an inadequate cultural co-operation between epidemiologists and clinicians, particularly in continental Europe. A major step to overcome the latter has been the Eurocare project, which published its first results in 1995 (Berrino et al. 1995). Undoubtedly, variations in survival after a diagnosis of cancer between populations served by registries must be interpreted with much caution. Nevertheless, the underlying comparisons may provide leads to the evaluation of cancer care (the same may well apply to other lethal conditions).

In conclusion, through the decades, cancer registries have found a number of functions, thus reversing the state of affairs which was feared by Harold Dorn half a century ago.

Zusammenfassung

Ein kurzer geschichtlicher Überblick zu Krankheitsregistern, speziell Krebsregistern

In den 1950er-Jahren wurden wichtige technische Probleme in der Qualitätssicherung und Leistungsfähigkeit der bevölkerungsweiten Registrierung von Krebs und anderen Krankheiten festgestellt und gelöst. Dennoch wurde den bevölkerungsweiten Krankheitsregistern in den klassisch epidemiologischen Publikationen der 1960er und 1970er-Jahre wenig Beachtung geschenkt und nur begrenzt Enthusiasmus entgegengebracht. Krankheitsregister waren nur Randerscheinungen der dramatischen Entwicklung grundsätzlicher konzeptioneller Belange wie Studiendesign und kausaler Rückschlüsse. Diese Situation könnte sich ändern, soweit Register für die Beurteilung der Behandlungsqualität aus Sicht der öffentlichen Gesundheitspflege eingesetzt werden.

Rückblickend haben sich seit den 1960er-Jahren markante Veränderungen in der Verteilung von Krebsregistern über Länder und Kontinente vollzogen, dies mit Entwicklung des als „Krebsinzidenz auf fünf Kontinenten“ bekannten Datensatzes, in dem Krebsregisterdaten guter Qualität aus der ganzen Welt zusammenlaufen. Die Anzahl Länder mit Krebsregistern hat sich in etwa verdoppelt im Gegensatz zu einer Verfünffachung sowohl der aktiven Krebsregister als auch der Gesamtbevölkerung, die registriert wird. Allerdings betreffen diese Zunahmen vor allem entwickelte Länder, während in Entwicklungsländern die Krankheitsregistrierung aufgrund der politischen und wirtschaftlichen Situation wesentlich an Bedeutung verlor.

Résumé

Une brève histoire des registres de pathologie, et plus particulièrement des registres du cancer.

Dans les années 50, les principaux problèmes techniques pour assurer la qualité et l'efficacité de l'enregistrement des données concernant le cancer et d'autres maladies ont été résolus. Pourtant, les manuels d'épidémiologie classiques des années 60 et 70 ont accordé peu d'attention et montré un enthousiasme limité pour les registres de maladies basés sur les populations. Ces derniers n'ont en fait eu qu'un rôle marginal par rapport à l'évolution rapide des concepts fondamentaux tels que le dessin de l'étude ou l'inférence causale. Cette situation pourrait changer avec l'utilisation des registres pour évaluer la qualité des soins dans une perspective de santé publique.

Rétrospectivement, des changements importants se sont produits depuis les années 60 dans la distribution des registres du cancer dans différents pays et continents, tel que cela apparaît dans la base de données connue sous le nom de « Incidence du cancer dans cinq continents », qui regroupe les données mondiales des registres du cancer de qualité. Le nombre de pays ayant des registres du cancer a approximativement doublé alors que le nombre de registres du cancer actifs et la population qu'ils desservent ont quintuplés. L'accroissement s'est surtout produit dans les pays développés alors que dans les pays en voie de développement il y a eu une diminution substantielle des enregistrements, en raison de la situation politique et économique.

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Address for correspondence

B. Terracini
Dipartimento di Scienze Biomediche e Oncologia Umana
Università di Torino
Via Santena 7
10126 Torino, Italy

Tel.: +00 39 011 670 6526
Fax: +00 39 011 670 6692
e-mail terracini@etabeta.it