

Population-based cancer registration and research in Switzerland: examples, limitations and perspectives

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Introduction

Cancer registries are unique in being able to provide population-based data to monitor geographic variation and changes in cancer risk or survival over long periods of time. Historically, the role of cancer registries has been to collect population-based data on all cancers being diagnosed, treated or dead within a well-defined population. In recent years the work of all registries has expanded to include the analysis of aspects of cancer prevention, treatment and care. Registries can assess how local and national targets for cancer services provision are met, and can contribute important information to the planning of services. Cancer registration is not an end in itself. Its tasks are closely linked to the scientific research and practical fight against cancer diseases and are adapted in parallel.

Cancer registration in Switzerland

Registration of cancers in Switzerland is primarily organised at the cantonal level. The cantonal or regional registries maintain links with all hospitals and pathology laboratories in their catchment area. In addition, the registries can contact the civil registry offices to approve cantonal residence and regularly check the vital status of each patient. Data of patients residing in other cantons will be forwarded to the competent registry. Reporting of cancer cases to the registry by physicians is either mandatory or voluntary based on cantonal regulations. The persons concerned can veto their data from being recorded in the registries' databases. Registration follows international recommendations for data collection procedures and contents.

The first tumour registry was created in 1970 in Geneva, followed by the cantonal registries of Vaud and Neuchâtel (1974), Zurich, St. Gallen-Appenzell (1980), Basel-Stadt and Basel-Landschaft (1981)¹, Valais, Graubünden (1989), Glarus (1992), Ticino (1996), Jura (2005) and

Fribourg (2006). More recently, registration has been introduced in Lucerne (2010), Nidwalden, Obwalden, Uri, Zug (2011), Thurgau (2012), Aargau (2013), and Berne (2014). As of 2016, nationwide population coverage of 94% has been achieved. Currently, only three cantons (Schwyz, Solothurn and Schaffhausen) are not covered by population-based cancer registration. The data of all cantonal registries are aggregated at the National Institute for Cancer Epidemiology and Registration (www.nicer.org). Paediatric tumours are registered for the whole country by the Swiss Childhood Cancer Registry (www.childhood-cancerregistry.ch).

National Institute for Epidemiology and Cancer Registration (NICER)

In 1978, the Swiss Association of Cancer Registries (SACR) was formed to harmonise data collection, to create an inter-cantonal database and to promote research on cancer epidemiology at the national level. In 2007, this association became the National Institute for Epidemiology and Cancer Registration (NICER), based at the University of Zurich. Its organisational structure brings together representatives of universities, social and preventive medicine institutions at the federal and cantonal level, registries as well as a scientific advisory committee composed of international experts. Functioning as a central scientific and administrative secretariat, NICER provides assistance to cantonal registries and has the following tasks:

- define standards and recommendations for collecting and coding data,
- check the quality of registered data,
- estimate national cancer incidence, survival and prevalence,
- coordinate epidemiological research, particularly in collaborative studies conducted between the registries or external partners.

¹ The Cancer Registry Basel (BL/BS) was already established in 1969 but electronic data are only available since 1981.

Objectives of cancer registration

Cancer registration is not an end in itself. Its tasks are closely linked to cancer research and cancer control and undergo constant development. A «systematic collection on cancer and cancerous diseases» was already suggested in 1901 by the German physician Ernst von Leyden: «... Death will be inevitable for the vast majority of cancer patients. Can we hope to create cure through collaboration? Such a claim is to be rejected from the beginning because this task is currently unsolvable. But some kind of prophylaxis is possible by knowing the distribution, the causes, and lethal factors of cancer». [1]

An accurate population-based (epidemiological) registration of incident cases including mortality was the beginning of the development of cancer registration and represents its core until today. With improvements in medical diagnostics and therapy, «cure» has become a realistic goal for many cancer cases. This development also expanded the tasks of cancer registries beyond the area of health monitoring towards evaluation of screening programs as well as in evaluating the quality of oncological care at the population level. The range of these various tasks will be outlined below.

Health Monitoring

A key task of cancer registries is to describe the cancer landscape in space and time in terms of health monitoring. The object is processed by the registries on *the cantonal level*. At the *federal level*, the data of the regional cancer registries are aggregated by NICER. Updated national statistics are regularly published online (<http://www.nicer.org/en/statistics-atlas/>), in journals (<http://www.nicer.org/en/publications/>) by NICER or as «Swiss Cancer Report» in cooperation with the Federal Statistical Office (FSO) and the Swiss Childhood Registry. [2, 3]

Consolidation of cantonal and regional data continues on an *international level*. At the European level, the ENCR (European Network of Cancer Registries, www.enrcr.eu) together with the JRC (Joint Research Center, a research institute of the European Union) is responsible for joint evaluations. Data from all cancer registries worldwide that meet certain quality criteria are compiled by WHO's «International Agency for Research on Cancer» (IARC). IARC together with the International Association of Cancer Registries (IACR) publishes every five years the report «Cancer Incidence in Five Continents» (<http://ci5.iarc.fr>). These data also serve as the basis of the GLOBOCAN project which provides estimates of cancer incidence, mortality and prevalence on the global level (<http://globocan.iarc.fr>).

Research

For many years, the focus of cancer registration had been on performing regularly comparative studies of variation of incidence rates in time and place. Over time research involving cancer registries expanded from pure public health research to clinical and etiologic research spanning a wide range of topics such as

- Epidemiologic surveillance including trends and forecasting
- Aetiology
- Evaluation of impact of preventive interventions on populations
- Early diagnosis and mass screening (secondary prevention)
- Evaluation of cancer care including outcome research (effectiveness), pattern and quality of care
- Economic evaluation and planning of cancer care policies
- Prognosis, risk of secondary cancer, quality of life and other survivorship issues
- Registry methodology

An increasing number of European registries are now performing studies on survival, service evaluation of clinical practice, evaluation of mass screening programmes and etiological research. [4] In such studies the CR is either used as a sampling frame or linked to cohorts of screened or of more or less exposed persons who may develop cancer in due time.

Table 1 provides an overview of recent research activities in population-based cancer registries in Europe [5] and pertinent references from Swiss cancer registries. This overview demonstrates the potential of cancer registries and their multifaceted contribution to both public health and clinical research. Population-based cancer registries have adapted their registration to collect additional clinical variables to provide clinicians with unbiased population data on cancer treatment and survival. [6]

A selection of studies how cancer registries can provide evidence-based data to improve quality of care and prevent cancer deaths have been presented in a recent paper by Bouchardy et al. [Bouchardy, 2014 #27497]. Examples include:

- Impact on family history on breast cancer outcome [Ayme, 2014 #27499; Bouchardy, 2011 #27450]

- Excess of cardiovascular mortality among node-negative breast cancer patients irradiated for inner-quadrant tumours [Bouchardy, 2010 #27456]
- Merits of observational studies if clinical trials are not available [Merglen, 2007 #27737]
- Limitations of non-invasive treatment of precancerous lesions [Rapiti, 2012 #27483]
- Undertreatment among elderly cancer patients [Bouchardy, 2003 #27738]

Access to cancer registration data

Scientific use of cancer registration data is not limited to cancer registries. NICER was in part established to promote and support population-based epidemiological cancer research in Switzerland. The NICER Coordination Centre (NCC) maintains the NICER database (combined and harmonized individual registry data) as an authoritative national source of cancer information in Switzerland. The mission of the NCC in collaboration with partner registries is to bring NICER data to the public-health and research community. As a result, collaboration and cancer-related data are available for NICER-related epidemiological research through request. Each request will be approved based on its individual merit and resource availability. All single registry research requests (i.e. unpooled data) should be sent directly to the individual registry.

In principle, several different ways to access and use cancer registration have to be distinguished:

1. Aggregated data
2. Individual data
3. Individual patient access
4. Cohort linkage

1. Aggregated data

Individual data based on selected characteristics are aggregated into groups e.g. defined by year of incidence, age and sex. For the resulting groups different indicators such as the number of people in the relevant group and the incidence rate may be expelled. The only legal requirement is that from the created data set no individual can be identified.

2. Individual data

In addition to the aggregated data individual anonymised data can be provided for research purposes and collaboration under the condition that re-identification of an individual person from the requested data is not possible. Optionally, individual features are omitted or collapsed in broader categories.

Epidemiologic surveillance

- Exploring perceived or real environmental threats [on individual request]
- Monitoring time trends in incidence or mortality (by age and gender) [2, 3, 10-21]
- Monitoring social class differences and migration [16, 22-24]
- Monitoring prevalence [2, 3, 25, 26]

Hypothesis generating and testing

- Assessing new potential risk or prognostic factors [7-9, 27-49]
- CRs as follow-up source for epidemiologic cohort studies [7-10, 38, 44, 50-54]
- CRs as baseline source for epidemiologic cohort studies [30, 38, 39, 44, 49, 51, 53-56]
- CRs as source of cases for population-based case-control studies [8, 9, 27-29, 32, 34-37, 40-43, 45-48]
- Cross-sectional or longitudinal studies of variation in occurrence (incl. clusters) [15, 16, 18, 20, 33]

Evaluation of impact of preventive interventions on populations (scenario development and research)

- Primary prevention: e.g. smoking cessation and lung cancer risk [19, 20]
- Secondary prevention: (side)effects of mass, grey or targeted screening [14, 23, 24, 57-59]
- Anticipating and monitoring changes by new diagnostics [60]

Evaluation of cancer care

- Changing burden of cancer on health services [61-64]
- Treatment pattern and outcome [49, 52, 56, 61, 65-75]
- Assessing patient's preference in care [62-64, 76]
- Monitoring of process indicators and quality of information [65, 67]
- Translational research of prognostic biomarkers [39, 77, 78]
- Host determinants like co-morbidity, family history [50] [31, 33, 67]

Survival, quality of life, secondary primaries, recurrences

- Trends in survival [2, 3, 66, 79-93]
- Quality of life [work in progress]
- Risk of secondary cancers and recurrence [30, 38, 39, 51, 53, 54, 94-98]

Economic evaluation and planning of cancer care policies

- Scenario planning and resource allocation for specialised care/centres
- Contribution to cost-effectiveness analyses (or doing them)

Registry methodology

- Completeness/accuracy of population-based registration and statistics [99, 100]
- Survival analysis methods (relative survival, cured fractions, conditional, etc.)
- Validating classifications (ICD-O, Gleason score etc) [60, 101]

CRs: Cancer registries

Table 1: Research activities in Swiss population-based cancer registries 2010-2015 (research taxonomy adapted from Coebergh et al., 2015)[5]

3. Individual patient access

Direct (by name) access to individual data stored in the registers, e.g. for interviews or examinations of patients as part of a case-control study, is only possible with informed consent of the patient in accordance with the Human Research Act (HRA). As cancer registries in Switzerland are not entitled to contact the patient directly, informed consent has to be obtained via treating physician in addition to a study protocol that satisfies scientific requirements, the vote of an ethics committee and where appropriate, an opinion from the cantonal data protection authority.

4. Cohort linkage

The fourth possibility is to link individual data of an external cohort with the data stored in the cancer registry (e.g. linkage of the HIV-cohort [7-10]). In case of prior informed consent, deterministic linkage is feasible; otherwise the linkage has to be probabilistic based on anonymised data if possible (e.g. linkage of Swiss National Cohort (work in progress)).

A special case of the cohort linkage arises in the evaluation of organized screening programs. Here, participants in screening programs should be linked with the data from the cancer registry to identify interval cancers (i.e. discovered between two screening rounds).

Limitations and perspectives

Cancer registries are a rich source of population-based information on cancer incidence, management, treatment, and outcomes. However, there are problems of comparability because of large differences in the completeness of these data between registries. Each cantonal cancer registry is autonomous, being commissioned regionally, with different financial resources and legal mandate. A common minimum dataset, which includes registration and death details, has been used since 2011 and subsequently developed. Although this dataset fulfils the national requirements for cancer monitoring it cannot answer all of the management and treatment questions posed to cancer registries by health authorities, pharmaceutical industry and researchers.

Most registries hold more information than the common minimum dataset. Additional data may include demographic factors such as socioeconomic and ethnic status, smoking status, occupation, and detailed treatment data). For some cancer sites additional variables are recorded by some registries, such as family history of cancer, comorbidities, body mass index, and recurrence. Not only do the data items vary between registries and within registries over time. For example, the extent of treatment data

(not yet part of the minimum data set) is collected differentially between registries depending on resources and legal mandate. Also, death and second primary cancers are usually the only outcome measures routinely collected by cancer registries. So far, information on disease-free survival, tumour recurrence, functional status or quality of life is lacking in most cases.

As compared to Nordic countries, the possibilities of linkage cancer registration data with other population data (such as detailed information of socio-economic status, education, job history, family history, and other health care data such as comorbidities and vaccinations), are very limited.

The completeness of the registration and the quality of follow-up information in the registries is also a crucial factor for the feasibility and quality of research projects. Despite that reporting of cancer cases to the registry by physicians has been on voluntary basis in most cantons up to now, all established Swiss registries have reached sufficiently high completeness for most cancer entities. However, research projects relying on up-to-date incident data (e.g. for direct patient access via patient survey) should consider delays in reporting and subsequent availability of data for research projects. A delay of two to three years after diagnosis is not uncommon.

Perspectives with the new cancer registration law

Many of the aforementioned limitations have been addressed in the new cancer registration law which will be effective presumably in 2019. Enhancements within this new law include

- a systematic cancer registration in all cantons
- mandatory reporting unless veto of patient
- basic data set contains some clinical data
- collection of supplementary data (progression, recurrence, treatment, screening) possible
- automatic access to population registry data
- right of cantons to give feedback to providers

Despite these obvious improvements with respect to cancer registration, the enhancements for cancer research are limited as pseudonymized linkage on national level of cancer registration data with other data will be only partially possible and other prognostic and treatment affecting variables such as information regarding comorbidities will have to be collected under HRA regulations and are not included in mandatory registration. Likewise, no provisions were made to contact patients directly by the registry in order to collect additional patient data (including

patient reported outcome) for research purposes. Nevertheless, the new law will enable a broader and systematic collection of clinical variables which will allow a better monitoring of treatment pattern in cancer patients.

Future challenges

Information coming from genome wide association studies will play a pivotal role in understanding not only carcinogenesis but also drug effectiveness/resistance or occurrence of side effects in the near future. Cancer registries will have to prepare how to collect data of cancer patient's genetic profiles and/or linking with available biobanks. Likewise, it will become increasingly important to collect comprehensive data on risk factors including environmental exposures, personal habits, familial links as well as treatment details like palliative care, costs, and quality of life. New strategies and technologies to facilitate the integration of this information will be needed as well as an open discussion regarding ethical problems and data protection requirements. Cancer registries will continue their important activities, adapting to medical progress and future challenges in cancer research.

Summary

Cancer registries are a vital source of information on cancer epidemiology and cancer services. Their role has changed dramatically over the past 25 years. A number of factors will affect their future role, including health service changes, information technology, development of clinical datasets and greater demand for both health service and public information. The potential of cancer registration needs to be realized by clinicians and health authorities: how they can use the data, its limitations, and how they can support and influence it through this period of change.

Disclaimer

The views and opinions expressed in this article are those of the author and do not necessarily reflect any official policy or institutional position.

Acknowledgement

The author thanks Andrea Bordoni (TI), Isabelle Konzelmann (VS), Christine Bouchardy (GE), Mohsen Mousavi (BS/BL), and Sabine Rohrmann (ZH) for providing details of current research activities in Swiss cantonal cancer registries and stimulating input for this article.

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