

THE IMPORTANCE OF GLOBAL SURVEILLANCE OF CANCER SURVIVAL FOR CANCER CONTROL: THE CONCORD PROGRAMME

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CONCORD is a prize-winning¹ programme for the global surveillance of cancer survival. It started in 1999, with the aim of monitoring population-based cancer survival trends worldwide. The CONCORD Working Group now includes over 500 collaborators.

Why population-based survival?

Population-based survival is a key measure of the overall effectiveness of the health system in managing cancer in a given country or region.

Randomized trials tell us if a new treatment is better than the current standard treatment, but patients recruited to trials are not representative of all cancer patients: they are usually selected on age, stage of disease and lack of comorbidity and they are treated with close adherence to protocol in specialized cancer units by the most research-active physicians. Typically, also, fewer than 5% of adult cancer patients are treated in clinical trials (1), although for children in developed countries, the proportion may be 70% or more.

By contrast, population-based cancer survival reflects the overall effectiveness of the health system in dealing with cancer (2). It is a measure of the average survival achieved by *all cancer patients*, young and old, rich and poor, with and without comorbidity, and with early or advanced disease at diagnosis.

Population-based survival is estimated from data provided by population-based cancer registries, which routinely collect, on a continuous basis, a basic data set on every person diagnosed with cancer in a defined population, typically residents of a country, or a defined geographical area such as a province or state. The basic data set covers the patient's date of birth, sex and place of residence; the topography, morphology and behaviour of the tumour; the basis of diagnosis and the date of diagnosis. Most long-standing cancer registries also collect information on each patient's last known vital status (alive, dead, emigrated) and the date of the last known vital status. This information on the follow-up of cancer patients is crucial

to estimate survival.

Follow-up can be determined actively (*active follow-up*), by direct contact with the patient, their family or their GP, or passively (*passive follow-up*), by performing a record linkage between the cancer registry database and a national database of all deaths, such as the National Death Index (NDI) in the United States. With active follow-up, it is possible to determine exactly the date of the last known vital status for patients who are dead and those who are alive. With passive follow-up, the date of death of patients who have died is exactly determined when a record in the cancer registry is successfully linked to a death record for the same person in the national death index. Patients whose cancer registration record could not be matched to the national death index during record linkage are presumed to be alive at the date on which the linkage was performed (3, 4). Passive follow-up is widely used because it is cheaper than active follow-up and it is known to be efficient if the infrastructure is adequate (3).

Cancer survival and the stage of disease at diagnosis

The stage of disease at diagnosis is a key determinant of long-term survival for almost all malignancies. Differences in population-based cancer survival between population sub-groups (e.g., rich and poor (5), black and white (6), Maori and non-Maori (7)) within a country, or differences between countries (8), may be explained, at least in part, by differences in the stage of disease at diagnosis in the cancer patient populations being compared. The survival for all women

¹ <https://betterhealthforall.org/2016/05/16/fph-global-public-health-award-global-surveillance-of-population-based-cancer-survival/>

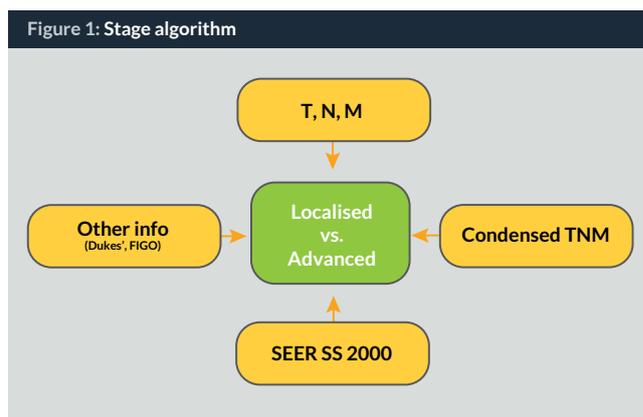
with breast cancer, for example, may be lower in one country than another because women in that country are generally diagnosed with more advanced disease that is less susceptible to treatment of curative intent. Alternatively, their survival may be poorer at each stage of disease, which may imply that optimal treatment is not available in that country, particularly for early-stage tumours: survival for very advanced tumours is similar in most countries. More advanced disease and lower stage-specific survival may both play a role in international differences in survival.

During the past two decades, most cancer registries have begun collecting information on the stage of disease at diagnosis, and whether the patient received surgery, radiotherapy, chemotherapy, hormonal or other systemic therapy, and if so, the date of first treatment. However, the proportion of registrations with incomplete data on stage and treatment is still very high, even in some developed countries.

The Tumour Nodes and Metastasis (TNM) classification has been recognized as the gold standard for the collection of data on stage of disease for many years (9, 10), but it is still not sufficiently widely used. Several other stage classifications are still used in many countries. Surveillance, Epidemiology and End Results Summary Stage 2000 (SEER SS 2000) (11) is used in the United States, Australia and Israel, and a simplified form of TNM (condensed TNM) is used in many European countries (12). Several cancer-specific stage classifications are also widely used, such as Dukes' stage for colorectal cancer (13, 14), FIGO stage for cancers of the ovary and cervix (15), and Ann Arbor stage for lymphomas (16). Furthermore, some cancer registries still use local classifications. Data on stage in some of these classifications can be converted into equivalent categories in the TNM classification, but the conversions can be complex and time-consuming, especially when the cancer data being analysed cover long periods of time, during which both TNM and the parent classification may have undergone revision.

Long-term trends in stage-specific survival may also be affected by coding conversion issues. In recent analyses of survival trends by race and stage at diagnosis in the United States, patients were grouped by year of diagnosis into two calendar periods (2001–2003 and 2004–2009) to reflect changes in the methods used by United States registries to collect data on stage at diagnosis (17). From 2001, most registries coded stage directly from the source data to SEER SS 2000 (11). From 2004, all registries began to derive Summary Stage 2000 from 15 pathological and clinical data items, using the Collaborative Staging System (18).

To address these problems in international comparisons of cancer survival, the CONCORD Central Analytic Team has developed a complex algorithm that is designed to harmonize



as far as possible all the available data on stage at diagnosis. This is based on our previous work in the EUROCARE and CONCORD high-resolution studies (19–22). The algorithm summarizes all the data on stage into two broad categories, localized and advanced. It gives priority to TNM stage (pathological and clinical), then compensates for any missing information on TNM stage with the size of the tumour and/or the number of positive lymph nodes, then with SEER SS 2000, or condensed TNM, or FIGO or Dukes' stage, depending on the tumour (Figure 1 shows a simplified version of the CONCORD stage algorithm).

This algorithm enables much wider international comparison of cancer survival by stage than would otherwise be possible. In an ongoing study of breast cancer survival by stage at diagnosis, for example, restriction of the analyses to data sets in which at least 70% of tumours had been staged to the TNM classification would have limited the comparison to 34 cancer registries and 19 countries. After deployment of the algorithm to assign localized or advanced stage by integrating all the available data from each registry, it was possible to include data sets with at least 70% of staged tumours from 109 registries and 39 countries.

For international comparisons of cancer survival by stage on a worldwide scale, our main goal is to be able to categorize stage as localized and advanced. This simple dichotomy is helpful for comparisons of stage distributions between populations, as well as for stage-specific survival comparisons. It offers an opportunity to compare the distribution of stage at diagnosis in both developed and developing countries using a categorization which is likely to be more robust than if we pretended that stage could be precisely assessed for all cancer patients in every population we are comparing.

However, a much wider international implementation of the TNM stage classification would be most desirable.

The CONCORD programme

The first CONCORD study (23) produced five-year survival estimates for 2 million patients diagnosed with breast,

colorectal or prostate cancer during 1990–1994 and followed up to 1999. The data were provided by 101 cancer registries in 31 countries, 16 of which with national coverage. Global variation in survival was very wide: generally higher in North America, Australia and Japan, and in northern, western, and southern Europe, and lower in Algeria, Brazil and countries in eastern Europe.

In 2015, the second cycle of the programme (CONCORD–2) established long-term surveillance of cancer survival worldwide, for the first time (24). CONCORD-2 provided cancer survival trends for 25,676,887 patients diagnosed during the 15-year period 1995–2009 with one of 10 common cancers (stomach, colon, rectum, liver, lung, breast (women), cervix, ovary and prostate, and leukaemia) that collectively represented 63% of the global cancer burden in 2009. The data were provided by 279 population-based cancer registries that covered a total population of 896 million people in 67 countries. In 40 of those countries, the data provided 100% coverage of the national population.

Worldwide differences in survival were striking. Age-standardized five-year net survival from colon, rectal and breast cancers had increased steadily in most developed countries up to 2009, reaching 60% or more in 22 countries for colon and rectal cancers, and up to 85% or more in 17 countries for breast cancer in women. For cancers of the liver and lung, however, 5-year survival was still below 20% everywhere. Striking rises in prostate cancer survival were seen in many countries, but survival still varied from less than 60% in Bulgaria and Thailand to 95% or more in Brazil, Puerto Rico and the United States. Survival from cervical cancer also ranged widely, from below 50% to over 70%, and improvements over the 15 years to 2009 were generally small. For women with ovarian cancer, 5-year survival was above 40% in only 20 of the 67 countries. For stomach cancer, 5-year survival was very high in Japan and South Korea (54–58%), but less than 40% in all other countries. Five-year survival from adult leukaemia in Japan and South Korea (18–23%) was lower than in most other countries. This striking contrast may be attributable to differences in the distribution of the main types of leukaemia between Asian and Caucasian populations: survival from chronic lymphocytic leukaemia is generally very high, but it is comparatively uncommon in Asian populations. More detailed analyses of leukaemia survival are in progress.

For acute lymphoblastic leukaemia in children, survival was less than 60% in several countries, but close to 90% in Canada, the United States and four European countries, suggesting major deficiencies in many countries in the management of what is now considered a largely curable disease (25).

CONCORD–2 was covered by TV, radio, press and wire services worldwide. The Altmetric score of 800, reflecting

social media impact, is higher than 99.98% of 6.5 million articles evaluated to date. Results have been incorporated into the American Cancer Society's *Cancer Atlas* (26). The article has been cited over 750 times since 2015 (Google Scholar).

Impact on cancer control strategies

With publication of the CONCORD–2 study, health ministers in 67 countries – home to two-thirds (4.8 billion) of the world's population – finally obtained cancer survival estimates that are methodologically rigorous and internationally comparable, to help them prioritize and formulate cancer control strategies (27). For some countries, this was the first time such data had been available.

The US National Cancer Institute recognized the impact of CONCORD–2 in an invited commentary for *The Lancet*, noting that global analyses of cancer survival provide an opportunity for lessons from countries with successful cancer control initiatives to be applied to other regions. They added that the availability of better data “provides a clearer picture of the effect of cancer control programmes on the ultimate goal of improving survival and reducing the effect of cancer on the social and economic development of countries” (27).

The US Centers for Disease Control (CDC) described CONCORD–2 as the start of global surveillance of cancer survivalⁱⁱ, with survival estimates “that can be compared, so scientists can begin to determine why survival differs among countries. This could lead to improvements in cancer control programmes”.

CONCORD–2 results underpinned new cancer strategy in England in July 2015 (28, 29).

In September 2015, the International Atomic Energy Agency's Programme for Action on Cancer Therapy (PACT) used CONCORD–2 results to launch an ambitious worldwide campaign to highlight the global divide in survival and to raise awareness of persistent inequalities in access to life-saving cancer services (30).

CONCORD–3

The third cycle of the CONCORD programme updates worldwide surveillance of cancer survival trends to include patients diagnosed during 2010–2014, with follow-up to 31 December 2014. It includes 15 malignancies that represent 75% of the global cancer burden: oesophagus, stomach, colon, rectum, liver, pancreas, lung, melanoma of the skin, breast (women), cervix, ovary and prostate in adults (15–99 years), and brain tumours, lymphomas and leukaemias in both adults and children (0–14 years) (33). We have examined geographic variation and time trends in cancer survival for 70

ⁱⁱ <https://www.cdc.gov/cancer/dcp/research/articles/CONCORD-2.htm>

or more countries. Where adequate data are available, we will examine survival by stage at diagnosis, morphology and race/ethnicity. We will also include information on the first course of treatment for each patient.

The results of CONCORD-3 can be expected to have a substantial impact on the public, in the media and in the scientific and public health community.

CONCORD and OECD

From 2017, the Organisation for Economic Co-operation and Development (OECD) will include survival estimates from the CONCORD programme for 48 countries in its biennial publication series *Health at a Glance* (31), and regional online versions for Asia, Europe and Latin America. This represents formal recognition by an international agency of the global coverage, methodological rigour and international comparability of the CONCORD survival estimates, which will become crucial for the evaluation of health systems

performance in all OECD Member States. Survival estimates from the CONCORD programme will therefore become the *de facto* standard for international cancer survival comparisons. The results will also help monitor progress toward the overarching goal of the 2013 World Cancer Declaration (32), to achieve major improvements in cancer survival by 2020. ■

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