**Global surveillance of trends in cancer survival 2000-2014 (CONCORD-3): analysis of individual records for 37,513,025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries**

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## 1    What is the CONCORD programme?

CONCORD is an international scientific collaboration designed to monitor trends in the survival of cancer patients world-wide. This has never been done before.

The CONCORD programme involves 600 investigators in over 300 institutions in 70 countries. It is designed to inform national and global policy on cancer control. It supports the over-arching goal of the World Cancer Declaration 2013, to achieve "major reductions in premature deaths from cancer, and improvements in quality of life and cancer survival".

## 2    What is CONCORD-3? Was there a CONCORD-1 and a CONCORD-2?

The first CONCORD study was published in 2008.[1] It brought together data from 101 cancer registries in 31 countries, on 1.9 million patients diagnosed during 1990-94 with a cancer of the colon, rectum, breast or prostate. It revealed very wide international differences in five-year survival at the end of the 20th century. It confirmed the well-known racial discrepancy in survival in the USA.

CONCORD-2 established world-wide surveillance[2] of cancer survival trends in 2015. That study:

- examined *trends* in 5-year survival for patients diagnosed during the 15 years 1995-2009
- included data on more than 25 million cancer patients, provided by 279 cancer registries
- covered 100% of the national population in 40 out of 67 countries
- included 10 common cancers, which collectively represented two-thirds (63%) of all cancer diagnoses world-wide every year around 2009, in both low- and high-income countries

## 3    Why has this study been done?

International trends in cancer patient survival reflect the comparative effectiveness of health systems in managing cancer patients. The results form part of the evidence that drives national and global policies on cancer control:

- The International Atomic Energy Agency is using the results in its campaign to highlight global inequalities in survival.
- The Organisation for Economic Co-operation and Development is using the results as indicators of the quality of healthcare in 48 countries in its *Health at a Glance* publications.
- The European Union is using the results in its Country Health Profiles for EU Member States.

## 4    Are the results up to date?

Yes.

CONCORD-3 adds five more years of cancer data (2010-2014), only 3 years after publication of CONCORD-2.

CONCORD-2 was published in 2015, within 6 years of the end of follow-up (1995-2009). With CONCORD-3, we have reduced that time-lag to 3 years.

CONCORD-3 brings the global surveillance of cancer survival trends right up to date.

## 5    Are the cancer survival figures from all these countries truly comparable?

CONCORD-3 is not a compilation of published reports, in which survival was estimated with different methods. Such results cannot be directly compared. CONCORD-3 is a systematic analysis of over 37 million individual cancer patient records in over 4,700 data sets, using a tight protocol, standardised quality control and centralised analysis with cutting-edge methods.

No study is perfect, and a study of this size will always have weaknesses. We believe the results are nevertheless comparable, within the limits of data quality.

We have flagged (§) survival figures that may be less reliable for international comparison, to help interpretation. We do this when we have to exclude more patients than expected from the survival analyses, usually because their date of diagnosis or death was not accurately known, or because some deaths may not have been recorded.

We made extraordinary efforts to ensure that the study protocol was correctly interpreted by all participants world-wide. We held face-to-face protocol workshops in several countries and in several languages. We held webinars and teleconferences. The protocol was translated from English into eight other languages by native speakers of **Arabic, Chinese (Mandarin), French, Italian, Japanese, Portuguese, Russian and Spanish**. The translations were checked by other native speakers.

We conducted extensive quality control of the data, in three phases. Standardised reports were sent to each cancer registry after each phase. Many data sets had very few significant errors, or even none. Where problems were identified, however, we liaised with the registry concerned in Chinese, Croatian, English, French, Italian, Portuguese or Spanish, as required, to discuss errors and to request correction of data where necessary.

## 6  Are the results representative? <span style="float:right">Back to top</span>

Population-based cancer survival estimates are often criticised as "unrepresentative" of the country (usually when survival is lower than in a neighbouring country). Curiously, this criticism is rarely heard for international comparisons of cancer *incidence*, even though those comparisons are derived from the same cancer patient data and the same cancer registries.

Why is the criticism about the lack of representativeness of cancer survival misplaced?

- International differences in survival are typically smaller for cancers that are more readily treated (high survival), and for cancers with very poor survival. Such a pattern is difficult to explain on the basis of an artefact of cancer registration.
- Other studies suggest that the extent of disease (stage) at diagnosis and access to optimal treatment are major contributors to regional and international differences in survival.
- Clinical trials are excellent for deciding if one treatment is better than another, but they tell us nothing about the effectiveness of the health service in delivering those treatments to everyone who needs them. Clinical trials typically recruit less than 10% of all patients with a given cancer (although in some countries, 70% of children with cancer may be included in trials). Patients in trials are typically younger than 70, with little or no co-morbidity, and they are often selected by referral to the most research-oriented hospitals. Unlike trials, population-based survival comparisons *are* representative of the country or region covered by the cancer registry, because they include *all* cancer patients – young and old, rich and poor, black or white, with early or late-stage disease, and with or without serious comorbidity.
- This criticism misses the point of population-based cancer survival comparisons. These comparisons show that in some parts of the world — whether that is an entire country or a region of a country — the survival of all cancer patients is higher than in some other countries or regions. Where those differences are persistent, or affect many cancers, and cannot be explained by artefact, then we should be trying to understand how to reduce the deficit.

For CONCORD-3, in particular:

- For 47 of the 71 countries and territories, the data provided 100% population coverage.
- Survival in Europe is generally highest in the Nordic countries, all of which have national cancer registries, and generally lowest in eastern European countries, most of which also have national registries. These differences cannot be explained by lack of representativeness.

## 7   Some countries are very small: are their survival figures reliable?

Survival estimates based on small numbers of patients are less *precise* than estimates based on large numbers of patients. This is intuitively obvious, and it is reflected in the 95% confidence interval around each survival estimate. Thus, the confidence interval for survival estimates from Gibraltar (population 32,000) is much wider than for survival estimates from California (population 39 million).

However, precision is not the same as accuracy. Survival estimates are *not necessarily right (accurate, or reliable)* just because they are based on large numbers of patients and are statistically precise (narrow confidence interval). Complete registration and follow-up of cancer patients may be hard to achieve in big cities.

Equally, survival estimates are *not necessarily wrong (inaccurate, or unreliable)* just because they are based on small numbers of patients (wide confidence interval). It can be easier to achieve complete, high-quality registration and follow-up of all cancer patients in small populations or islands.

International comparisons of cancer survival should be interpreted in the light of data quality measures. We have indicated where the reliability of the survival estimates is affected by data quality. We have also provided the statistical precision of the estimates, with 95% confidence intervals for every survival estimate in tables and graphics.

## 8   "Two-thirds of the world's population." Really?

Yes.

The 71 participating countries and territories are home to a combined population of 4.9 billion (UN figures for 2014). That is two-thirds (67%) of the world's population (7.3 billion).

The 322 participating cancer registries contributed data on all cancer patients diagnosed among their combined resident population of almost a billion people (989 million). That's 20% of the combined population of those countries.

True, the figure of 4.9 billion in 71 countries is heavily influenced by the huge populations of China (1.37 billion) and India (1.30 billion). If we exclude China and India, the other 69 countries have a combined population of 2.2 billion. The participating registries in those countries cover a total population of 956 million, or 43%[a] of the combined population of those countries.

Population coverage of the data for China and India is low, at 2.3% and 0.1%, respectively. Even so, the participating Chinese registries cover a combined population of 31.7 million, more than the participating Canadian registries (27.2 million, 76.5% of the Canadian population).

**From the public health perspective, 71 countries now have internationally comparable population-based cancer survival estimates for at least part of their population – and for 47 of those countries, the data have 100% national coverage. These estimates are based on direct observation of the survival of over 37 million cancer patients – real data about real people. They are not derived by statistical models with data from other countries.**

## 9   Surely Cyprus is in Europe?

Cyprus is an EU Member State, but it is classified in Asia by the United Nations. We used the official UN classification of countries, regions and territories.

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[a]   Population coverage of 956,321,603 out of a total population of 2,225,137,385 = 43.0%

**What is "net survival"?**

Two companies each make $20 million gross profit. One has a gross income of $100 million, the other, $200 million. Their **net profits** are 20% (20/100) and 10% (20/200), respectively.

We intuitively divide each company's income into two categories, the "background" income required to cover costs and taxes, and the extra income (profit). We cannot reliably compare the two companies' profits ($20 million) unless we take account of their different levels of income.

Cancer patients have an extra risk of dying from their cancer, over and above the ordinary ("background") risk of death faced by everyone. In adults, the background risk of death varies more than 6-fold worldwide, and in children, more than 100-fold.

**Net survival** enables fair comparisons of cancer survival worldwide, because it allows us to take account of these international differences in the background risk of death.

11 **What are "life tables" and why do you need them?**

A life table is a set of death rates that reflect the background risk of death in a population (see Question 10). A life table will often contain 100 death rates, one for each single year of age 0-99 years. Life tables are always produced separately for males and females.

Cancer patients have an extra risk of dying, over and above the background risk of death, which affects everyone. This background risk varies with age and sex. It also varies widely between countries. Typically, it is also declining over time, and it will differ between racial or ethnic groups, as well as between states or regions within a country.

In an international comparison of trends in net survival among cancer patients, we must correct for all these differences in background mortality, at the finest level of detail possible.

For CONCORD-3, we produced more than 6,000 life tables of background mortality by single year of age (0-99 years), covering every combination of country or geographic region, calendar year (2000-2014), sex, and - where it was known for the cancer patients - race or ethnicity.

12 **Why are cancer survival estimates "age-standardised"?**

To enable us to compare cancer survival fairly between countries, between cancers, and over time.

Cancer survival varies with age at diagnosis. For most cancers, it is lower in older patients. The proportion of cancer patients who are younger or older – their age profile – differs between cancers, between countries or regions, and over time. Age-standardisation produces a weighted average of the survival figures for each separate age group. We use the *same* weights to produce the age-standardised survival for every country.

With age-standardisation, we avoid the mistake of concluding that there are international differences in cancer survival, or in survival trends, when the differences that we see could be due solely to international differences in the age profile of cancer patients, or changes in the age profile of patients within a country.

Where age-standardisation was not possible, usually because too few patients were available for analysis of survival in each age group, the survival estimates are flagged (†) in the tables and graphics, to aid interpretation.

13 **What is a "period" estimate of survival?**

Everyone is familiar with life expectancy at birth. We may say that a baby girl born today may expect to live 85 years, given current patterns of mortality. That is known as a "period" life expectancy. The principle of a "period" estimate of survival is identical, and it depends on the same assumptions. A parallel explanation may therefore help:

A "period" life expectancy at birth for babies who were *born* last year is derived from the latest available death rates for each sex, and for each single year of age, from birth to 99 years. But death rates at each age will most probably fall steadily over the next century, so babies born last year will generally live longer than this "period" estimate of their life expectancy at birth. So, even though – obviously – last year's babies have not yet been followed up for a lifetime, we still find a period estimate of life expectancy at birth useful, as a one-number summary of current patterns of mortality.

A "period" survival estimate for patients who were *diagnosed* last year is derived from the latest available survival estimates for each sex, and for each year since diagnosis up to (say) 5 years. But cancer survival at each age will most probably rise steadily over the next few years, so patients diagnosed last year will generally survive longer than this "period" estimate of their 5-year survival. So, even though – obviously – last year's cancer patients have not yet been followed up for 5 years, we still find a period estimate of 5-year survival useful, as a one-number summary of current patterns of survival.

"Period" estimates of survival provide useful (and reliable) predictions of survival for recently diagnosed patients.

We used period estimates to provide a short-term prediction of 5-year survival for patients who were diagnosed with cancer during 2010-2014.

14 **Why are patients whose cancer was registered as a "Death Certificate Only" (DCO) not included in survival analyses?**

Because we don't know how long they survived.

Most cancer registries use death certificates to register a new cancer patient, but only if no other information is available. Such patients can be included in the number of new cancer patients per 100,000 population a year (annual *incidence rates*), if one assumes that the date of death is acceptable as the date of diagnosis.

Death certificates do not record the date of diagnosis, though, so if a death certificate is the only evidence that a person has had cancer, we don't know how long the person survived. Therefore, they cannot be included in survival analyses.

15 **What is the "cancer burden"?**

This usually refers to the number of *new cancer patients* diagnosed each year (cancer incidence), e.g. 330,000 new patients each year in the UK. The most recent estimates of the global cancer burden are that over 14 million new cancer patients are diagnosed every year.

The "cancer burden" may also refer to the number of *cancer survivors* who have been diagnosed with cancer at any time in the past (cancer prevalence), e.g. 2 million cancer survivors in the UK, or 3% of the population.

16 **How is the confidentiality of the data sets maintained?**

We operate very strict security procedures, under a System-Level Security Policy approved by the UK's statutory Health Research Authority. All cancer data sets are anonymised (no name, no address, no ID number) and fully coded (no clear text). Only the cancer registry sending the

data knows the identity of the individuals. Files are transmitted with a secure 256-bit Advanced Encryption Standard utility with end-to-end encryption. We provide unique numeric codes for filenames that each registry must use. These codes have no meaning outside the CONCORD programme. Strong, random, one-time passwords are automatically generated by the utility for each file: the sender does not see the password, which is sent to a separate address. This eliminates the need to construct and exchange passwords by email or telephone. All data files are held in a secure facility and manipulated on secure computers. These computers are not linked to the intranet or the internet, and they are not wireless-capable. Backups are stored in a fireproof safe.

We maintain statutory and ethical approvals to conduct the study from the relevant bodies in the UK. Scientific journals require that these approvals are specified in publications. We maintain statutory or ethical approvals in more than 80 other jurisdictions world-wide. These approvals are based on our justification to each relevant authority of the need to analyse sensitive individual health data, as set out in the study protocol; on the impracticality of obtaining consent from millions of patients; on the public health importance of the study, and on independent review of our system-level security policy.

We provide a report and a request for renewal of approval to almost all these bodies every year.

17 **The article says:** *"Population-based cancer survival is increasingly recognised as a key indicator of the overall effectiveness of the health systems in managing care and treatment for all cancer patients… It has applications to cancer control and health policy at the state, national and global levels, in both high-income and low-income countries."* **Have the results had any impact so far?** Back to top

Cancer survival that is lower than expected has prompted national strategies for cancer control in many countries.

- CONCORD-3 results will stimulate national politicians to improve health policy and health-care systems if survival is low – or lower than in other countries with which they are usually compared.
- The World Health Organisation, the Organisation for Economic Co-operation and Development (OECD) and the World Bank have all confirmed that the results of CONCORD are an important stimulus for global cancer control policy.
- Childhood leukaemia is now a largely curable disease, but CONCORD-3 confirms that five-year survival is still less than 60% in some of the poorest countries, compared with 90% or more in wealthy countries.
- OECD's *Health at a Glance* series now includes 5-year survival figures from CONCORD-3 for acute leukaemia in children, and for cancers of the colon and rectum (large bowel) and breast (women only) in adults, as official indicators of healthcare quality in 48 countries.
- The overarching goal of the World Cancer Declaration 2013 is to achieve "major reductions in premature deaths from cancer, and improvements in quality of life and cancer survival." The CONCORD programme provides evidence on whether that goal is being achieved.
- Algeria is upgrading its national cancer strategy, in part because of low survival revealed in the first CONCORD study. It has now introduced a cervical screening programme and set up a nation-wide network of cancer registries to monitor progress.
- The US is using CONCORD cancer survival figures for blacks and whites in 37 states to document racial and socio-economic disparities in survival, as part of its public health policy.
- The UK, Canada, Malta, Poland and Brazil have also used results from the CONCORD programme in developing their cancer control policies.

The striking global inequalities revealed by the CONCORD programme support the need for continuous, world-wide surveillance of cancer survival, as a contribution to cancer control policy.

The CONCORD programme currently has funding from [alphabetical order]:

American Cancer Society® (Atlanta GA, USA)
Centers for Disease Control and Prevention (Atlanta GA, USA)
Institut National du Cancer (Paris, France)
Ligue contre le Cancer (Paris, France)
National Cancer Institute (Washington DC, USA)
Rossy Family Foundation (Montréal QC, Canada)
Susan G Komen Foundation® (Dallas TX, USA)
Swiss Cancer League (Bern, Switzerland)
Swiss Cancer Research foundation (Bern, Switzerland)
Swiss Re (London, UK)

19  **Who endorses the CONCORD programme?**                          Back to top

CONCORD is also endorsed by the following agencies [alphabetical order]:

1.  Asociación Española contra el Cáncer (aecc) (Madrid, Spain)
2.  Association of European Cancer Leagues (ECL) (Brussels, Belgium)
3.  Canadian Association of Provincial Cancer Agencies (CAPCA) (Toronto, Canada)
4.  Canadian Council of Cancer Registries (Toronto, Canada)
5.  Childhood Cancer International (CCI) (Nieuwegein, the Netherlands)
6.  Children with Cancer UK (London, UK)
7.  Danish Cancer Society (Copenhagen, Denmark)
8.  European CanCer Organisation (ECCO) (Brussels, Belgium)
9.  European Cancer Patient Coalition (ECPC) (Brussels, Belgium)
10. European Institute for Women's Health (Dublin, Ireland)
11. European Society for Medical Oncology (ESMO), (Lugano, Switzerland)
12. Fondation de France (Paris, France)
13. International Agency for Research on Cancer (IARC) (Lyon, France)
14. International Atomic Energy Agency (IAEA) (Vienna, Austria)
15. International Network for Cancer Treatment and Research (INCTR) (Brussels, Belgium)
16. International SOS (Papua, Indonesia)
17. Israel Centre for Disease Control (Tel-Hashomer, Israel)
18. Jolanta Kwaśniewska's Foundation (Warsaw, Poland)
19. Liga Argentina de Lucha contra el Cancer (LALCEC) (Buenos Aires, Argentina)
20. Members of the European Parliament Against Cancer (MAC) (Brussels, Belgium)
21. National Cancer Institute (NCI), Center for Global Health (Washington DC, USA)
22. National Cancer Research Institute (NCRI) Consumer Liaison Group (Leeds, UK)
23. National Institute for Cancer Epidemiology and Registration (NICER) (Zürich, Switzerland)
24. NCD Asia Pacific Alliance (NCDAPA) (Tokyo, Japan)
25. North American Association of Central Cancer Registries (NAACCR) (Springfield IL, USA)
26. Organisation for Economic Co-operation and Development (OECD) (Paris, France)
27. Société Internationale d'Oncologie Pédiatrique (SIOP) (Geneva, Switzerland)
28. Union for International Cancer Control (UICC) (Geneva, Switzerland)
29. WHO Regional Office for Europe (WHO-EURO) (Copenhagen, Denmark)
30. World Bank (Washington DC, USA)

**References**                                                        Back to top

1.  Coleman MP, Quaresma M, Berrino F, et al. and CONCORD Working Group. Cancer survival in five continents: a worldwide population-based study (CONCORD). *Lancet Oncol* 2008; **9**: 730-56.
2.  Allemani C, Weir HK, Carreira H, et al. and CONCORD Working Group. Global surveillance of cancer survival 1995-2009: analysis of individual data for 25,676,887 patients from 279 population-based registries in 67 countries (CONCORD-2). *Lancet* 2015; **385**: 977–1010.