

NAACCR Town Hall
Q&A Session for CONCORD-2 Study - Worldwide Surveillance of Cancer Survival
June 17, 2010

Q: Vital record/ndi linkage is going to be needed for this project, for those of us who have not done this before what kind of guidance and or training will you be able to provide.....prior to the need for the data in November

A: There will be two webinars this summer. The first webinar will discuss the process of preparing and sending data for NDI linkages. The second webinar will discuss the process for resolving the linkage results when the data are returned from NDI. We also encourage registries to apply to the NAACCR mentorship program. This program helps registries with less experience find a more experienced registry. The program provides funds to help travel staff from one registry to the other.

There are resources available to registries on the NPCR-CSS website (on the NDI page) to help facilitate the NDI linkage process (e.g., edit program, data extraction programs, and a SAS program to help process the NDI results).

In addition, there are a number of registries with NDI experience that are willing to work with less experienced registries. Please contact Hannah Weir if you would like to find a registry willing to assist you with these linkages.

Q: Given the differing definitions for date at diagnosis, I don't quite understand the emphasis on complete dates of diagnosis and last contact.

A: It is essential to have complete dates of diagnosis and last contact because the difference between them is the observed duration of survival until death or loss to follow-up, and the distribution of that interval in the cancer patient population is the end-point of survival analysis. Yes, the definition of the date of diagnosis varies somewhat between registries, but we will know how each registry defines that date and selects hierarchically from among two or more alternative dates if more than one date is recorded (e.g. date of pathology report, date of surgery, date of admission), and will adapt data preparation routines or comment accordingly. In the end, however, we can only measure survival between dates that are accepted locally as the point of diagnosis even if their definition does in fact vary slightly. In fact, a similar point applies to the definition of disease, where not all registries (or pathologists) interpret the ICD or the TNM manuals in identical fashion, but we still request full details on site, morphology, behaviour and stage.

If complete dates are not supplied, however, it is impossible to produce accurate (unbiased) estimates of survival, especially for the first few months after diagnosis when the rate of change of the excess hazard of death is usually maximal. The central purpose of international surveillance of survival is to obtain accurate and comparable estimates for all participating jurisdictions. Restriction of dates disables this purpose and devalues the study, and it calls into question why full dates are collected if they cannot be used for one of the core purposes for which cancer registries operate, namely public health surveillance of the burden and outcome of disease.

Q: With the conversion to v. 12, it will be extremely difficult if not impossible to do the required NDI linkage by 30 November 2010. At the NPCR PD meeting, Hannah mentioned that data might be accepted later. Please comment.

A: We will discuss this with individual registries. If a registry sends their data too far past the submission deadline of 30 November 2010, they run the risk of not having their data included in the CONCORD-2study. Please contact us if you expect to miss this deadline. Please note, it is not necessary to convert your data to v12 prior to sending the data to NDI.

Q: In practice, how much extra work will be needed at each registry; does each registry need local IRB approval, and are there funds to cover additional work, if additional work is not trivial?

A: The amount of work required to conduct NDI linkages will depend on the case load of the registry, the number of years to be searched and the quality and completeness of the matching variables. There are no additional funds available to conducting NDI linkages because this activity falls within the scope of the surveillance activities that are supported through NPCR funding. However, we do have a number of resources available to registries on the NPCR-CSS website (on the NDI page) that help facilitate the linkage process (e.g., edit program, data extraction programs, and a program to help process the NDI results). And there is a NAACCR mentorship program that will help match registries according to experience and support travel of staff from one registry to another.

The need for local IRB is determined by individual registry data release policy. Many states consider these activities to be part of public health surveillance and thus exempt. We will provide you with an IRB-approved protocol in September 2010.

Q: Are we looking at 5 year survival?

A: Yes, but we will report one-year survival, five-year survival and conditional five-year survival (survival up to five years after diagnosis amongst those patients who were survivors at the first anniversary of diagnosis). We will also examine time trends in these parameters where registries provide sufficiently long data series.

Q: I am wondering if our IRB would need to clear Concord 2 before participating....what has your experience with other states (USA) regarding this?

A: CONCORD falls into the domain of public health surveillance and most state registries would be expected to find exemption from the need for IRB approval on that basis (e.g. see the remark below from Nancy Cole in Missouri). However, an over-arching IRB approval is being sought for the study as a whole by the Cancer Research UK Cancer Survival Group at the London School of Hygiene and Tropical Medicine in London, UK, where the data will be prepared and the analyses performed.

Our experience from the first CONCORD study, involving both SEER and NPCR population-

based cancer registries from 16 states and 6 metropolitan areas in the USA, was that the IRB obtained from the CDC was sufficient to enable data transmission.

Q: Can the deadline for data submission be adjusted given our other calls for data?

A: If necessary, yes, but we would prefer to discuss this individually with registries that may find it impossible to meet the 30 November 2010 deadline.

Q: Please explain "population cure fractions"

A: The population 'cure' fraction is a public health estimate of the proportion (fraction) of the cancer patient population that can be said to have been cured, in the sense that the mortality of those patients who have survived to the point in time at which the relative survival curve reaches a plateau (the point of 'cure') is no longer different from that of the general population of the same sex, race/ethnicity and state from which they are drawn, given the distribution of age of the survivors. Alternatively, it is when the survivors no longer have any excess mortality over the background mortality; or the conditional relative survival is 100%. We will estimate the cure fraction in the US and other data sets where that is possible: for some cancers, no point of cure is discernible. There is an extensive literature on the subject, but we offer one research article and one methodological article:

S. Francisci, R. Capocaccia, E. Grande, M. Santaquilani, A. Simonetti, C. Allemani, G. Gatta, M. Sant, G. Zigon, F. Bray, M. L. G. Janssen-Heijnen, and EURO CARE-4 Working Group. The cure of cancer: a European perspective. *Eur.J.Cancer* 45:1067-1079, 2009.

P. C. Lambert, J. R. Thompson, C. L. Weston, and P. W. Dickman. Estimating and modeling the cure fraction in population-based cancer survival analysis. *Biostatistics* 8:576-594, 2007.

Q: What kind of assistance with NDI linkage is being offered?

A: Please see the first question.

Q: How many states are doing NDI linkages now?

A: Approximately 25-30 registries (SEER and NPCR) have either conducted NDI linkages or are in the process of conducting the linkages.

Q: When will 2008 deaths be available in NDI?

A: According to Robert Bilgrad at the National Center for Health Statistics, the data on 2008 deaths will be available in September 2010. Please note that to participate in CONCORD-2, you only need to conduct death linkages with NDI through 2007 (deaths in 2008 or later will not be core variables in the protocol).

Q: To ensure that inter-country comparisons are valid, has CONCORD studied the completeness of follow-up procedures in different parts of Europe, the US and other countries, Cuba, Brazil, etc.?

A: Yes; these have included the percentage of patients known to have been lost to follow-up, deaths within one month, and checks on the vital status of apparent long-term survivors. The bias in survival estimation from plausible proportions of incomplete follow-up is generally small in comparison with the international differences in survival; this issue was discussed in the first paper; measures by registry and cancer were also posted on-line from the first study. The international comparability of survival estimates in relation to differential completeness of follow-up is not likely to be worse than the international comparability of incidence rates (estimates) in relation to the estimated completeness of cancer registration, which is rarely reported in comparative studies. We will seek information by questionnaire from all participating registries on these issues.

Parenthetically, it may be observed that one can never completely “ensure that inter-country comparisons are valid”. The more appropriate question would be whether it can be ensured that international survival comparisons are fit for purpose, namely whether they are sufficiently robust and informative that actions may be taken or health policies devised that address observed inequalities or deficits in survival between countries or population groups. Evidence from Europe is that such survival comparisons are indeed fit for that purpose, having elicited explicit policy change and healthcare investments designed to reverse socio-economic inequalities and reduce international differences in survival.

Q: Will Hispanic ethnicity be considered as part of the life table requests from the States as opposed to white only?

A: We will obtain or construct complete (single-year-of-age) life tables by sex, state, calendar year and race/ethnicity where it is possible to do so with adequate robustness. We will document all these life tables and tabulate standard measures to demonstrate their robustness or comparability. We will also produce graphical representations of them. In the first study, it was possible to produce life tables for whites for all 22 jurisdictions, but for blacks, it was not possible in five of the jurisdictions where the black population was small. We have better techniques for dealing with small populations now and may improve on that ‘score’. It remains to be seen whether it is possible to construct life tables for Hispanic and non-Hispanic ethnicity; that would only be done where the cancer patients are also so coded, and where the numbers of deaths and the populations are also available by the same parameters - age, sex and state or metropolitan area.

All the life tables will be made available to all participants.

Q: so conversion to v 12 would have to be done first before the ndi? or can these be done concurrently? (sorry for all the questions....you can email me later if you wish)

A: The programs that we have developed to facilitate NDI linkages are in NAACCR v11. You do not need to convert to v12.

Q: Hannah, will you be using cause specific survival in relation to SES for the U.S. monograph

A: We do not anticipate using cause-specific survival. We expect to construct SES- and state-specific life tables for participating cancer registries. That will enable us to use relative survival to examine survival in relation to SES. Cause-specific survival raises difficulties of interpretation related to unknown differences by SES in the quality of death certification and selection of the underlying cause of death, whereas relative survival not only avoids those problems (since the cause of death is not required), it also enables modelling of the excess hazard of death between socio-economic and/or racial groups. This achieves the same objective— quantifying SES differences in outcome – without raising these particular problems of interpretation.

Q: just a comment, re the timing & ver12: since we are only submitting thru 2007, we should already have this data. Theoretically, we could pull files today to prepare to submit to ndi and then to CONCORD-2.

A: Sounds good to me! You are correct.

Q: You didn't really answer my question! Perhaps participants in CONCORD-1 could answer? With other special studies there are usually extra requests eg for data cleaning or extra data. AFTER NDI linkage, how much extra work do you anticipate per registry?

A: We have developed a SAS program that helps process the results from the NDI linkages. This program will help identify matches, non-matches and possible matches that require clerical review. The amount of clerical review will be determined by the number of cases that are sent to NDI and the quality and completeness of the matching variables.

We will host a webinar later this summer to discuss processing the results from NDI linkage. Glenn Copeland from Michigan will discuss resources that can be used to help with the clerical review.

Q: If we find that we DO need to submit a local IRB and also get data release permission from our state, we're talking about several days of work. Can you provide funds?

A: We do not have funds but I (Hannah Weir) am willing to help in any way that I can. We will also make available the applications for statutory and ethical approvals in the UK being prepared by Michel Coleman.

Q: When will a list of requested data elements be made available? Will there be instructions on how to impute "day" for those instances in which the "day" portion is unknown or missing?

A: The list of data elements will be made available shortly. We will also provide a data extraction program that will take the NAACCR v11 data format and output a file in CONCORD-2 format.

We will ask registries not to impute any dates. This reduces the workload of data suppliers. Also, experience has shown us that such imputation is done differently in different registries. In such large studies, this complicates very greatly the work of data preparation. Instead, we will ask missing variables to be represented (for the day of a date, for example) as “99”. That way, all missing dates can be handled consistently.

Q: IRB approval will be required in Missouri but we anticipate that it might be classified as exempt.

A: That is helpful, thank you.

Q: What will be involved in providing additional data for the random sample of patients that Michel mentioned?

A: The “high-resolution” studies will require data collection in the field to a separate protocol: that work is likely to require local funding. Seven US states (Colorado, Louisiana, Illinois, California, Rhode Island, South Carolina, New York) have experience of HR data collection from the first CONCORD study.

High-resolution studies are designed to collect detailed and high-quality clinical data directly from the medical records in order to quantify the impact of covariables such as stage, the determinants of stage, treatment, race/ethnicity, socio-economic status and co-morbidity (etc.) on the regional and/or international differences in cancer survival observed in the main survival studies. Such studies require the collection of data that most registries cannot collect for all registered cancer patients on a routine basis. Funding will be sought for these studies.

Concurrent chat session

Q: If a registry submits a data set for the analysis, but is unable to do the work associated with one of the focus studies, can they still participate?

A: Yes. It is NOT a requirement for participation in the survival analyses for CONCORD-2 that a registry must also agree to do field-work for a high-resolution study. The obverse is also true: a state may choose to collect data and participate in a high-resolution study, but not to participate in the main survival analyses, and two states did just that in the first CONCORD study.

We would prefer, however, that states wishing to join high-resolution studies DO contribute data to the main survival study, because that enables a direct contrast between the results of modelling the high-resolution data and the results of the overall survival analyses [see response to previous question].

Thus, in the first CONCORD study, US registries from 16 states and 6 metropolitan areas contributed data for the main survival analyses. Of these, 5 states (Colorado, Louisiana, California, Rhode Island, New York) also participated in the high-resolution studies; but Illinois and South Carolina chose to participate in the high-resolution studies without contributing data for the main survival analyses.

Q: Will survival for Hispanics be studied separately from non-Hispanic Blacks and Whites in the Survival monograph

A: Yes, where possible. See response to Randi Rycroft (above).

Concurrent email

Dear professor Michel Coleman,

Thank you for the Web seminar for the CONCORD-2 Study - Worldwide Surveillance of Cancer Survival.

I have a question, is there any details stepwise, books, materials and procedures are available for calculating the overall 5-year relative survival rates for cancers.

Could you please send me some references?

Thank you so much.

Sincerely,

Sohrab

Yes. The methodology was mooted in the 1950s¹⁻³. It was used in 1964 in the first trans-Atlantic comparison of cancer survival⁴: oddly enough, until the first CONCORD study was published in 2008⁵, that was the only such comparison!

There is an extensive methodological literature - as a start, our monograph of 1999 carries a full-length description of the classical approach and formulae⁶. This should be available in US libraries. But you should look for more recent references by T Hakulinen, J Estève, G Hédelin, P Dickman, B Rachet, J Stare, M Pohar and H Brenner, all of whom have individually or jointly addressed methodological issues.

Paul Dickman, Timo Hakulinen and Paul Lambert have web-sites from which you can download survival analysis packages. Our own web-site also contains free, open-source STATA software for relative survival estimation (*strel*), including life tables and other tools, which you can download after registering at:

<http://www.lshtm.ac.uk/ncdeu/cancersurvival/>.

We run a one-week course on cancer survival each year (see same web-site). The course in June 2010 had 50 participants from 22 countries. We will run a one-day workshop prior to the IACR meeting in Yokohama, Japan, on Monday 11 October 2010.

1. Berkson J, Gage RP. Calculation of survival rates for cancer. *Proc Staff Meet Mayo Clinic* 1950; **25**: 270-86
2. Cutler SJ, Ederer F. Maximum utilisation of the life table method in analyzing survival. *J Chron Dis* 1958; **8**: 699-712
3. Ederer F, Axtell LM, Cutler SJ. The relative survival: a statistical methodology. *Natl Cancer Inst Monogr* 1961; **6**: 101-21

4. Cutler SJ, ed. *International symposium on end results of cancer therapy. NCI Monograph 15*. Bethesda MD: National Cancer Institute; 1964
5. Coleman MP, Quaresma M, Berrino F, Lutz J-M, De Angelis R, Capocaccia R, Baili P, Rachet B, Gatta G, Hakulinen T, Micheli A, Sant M, Weir HK, Elwood JM, Tsukuma H, Koifman S, Azevedo e Silva G, Francisci S, Santaquilani M, Verdecchia A, Storm HH, Young JL, CONCORD Working Group. Cancer survival in five continents: a worldwide population-based study (CONCORD). *Lancet Oncol* 2008; **9**: 730-56
6. Coleman MP, Babb P, Damiecki P, Grosclaude PC, Honjo S, Jones J, Knerer G, Pitard A, Quinn MJ, Sloggett A, De Stavola BL. *Cancer survival trends in England and Wales 1971-1995: deprivation and NHS Region. (Studies on Medical and Population Subjects No. 61)*. London: The Stationery Office, 1999, pp1-695.