When do I know I am cured? Using conditional estimates to provide better information about cancer survival prospects

Peter D Baade, PhD

Senior Research Fellow

Viertel Centre for Research in Cancer Control, Cancer Council Queensland

School of Public Health, Queensland University of Technology

peterbaade@cancerqld.org.au

Danny R Youlden, BSc

Biostatistician

Viertel Centre for Research in Cancer Control, Cancer Council Queensland

dannyyoulden@cancerqld.org.au

Suzanne K Chambers, PhD

Director of Research and General Manager Services

School of Psychology, Griffith University

Viertel Centre for Research in Cancer Control, Cancer Council Queensland

suzannechambers@cancerqld.org.au

Word count:

Manuscript: 1,494 words (excluding references, tables, figures, acknowledgements, title page)

Abstract : 239 words

References: 23

Sources of Funding: No external funding was required for this study

Ethical approval: Since this study utilised non-identifiable data from a routinely collected population-based cancer registry with no patient contact, ethical approval to conduct this study was not required.

Conflict of Interest: The authors declare no conflict of interest.

ABSTRACT

Objective: Conditional survival has been shown to provide much more useful and clinically reliable estimates of survival probability for cancer survivors than standard survival estimates. We report the latest conditional survival estimates for Queensland, Australia.

Design: Descriptive population-based study using data from the Queensland Cancer Registry.

Setting: Queensland, Australia.

Patients, Participants: Patients aged 15-89 years diagnosed with invasive cancer between 1982 and 2007.

Main Outcome Measure: Conditional 5-year relative survival for selected types of invasive cancer.

Results: The prognosis for cancer patients generally improves with each additional year they survive. Survivors of stomach cancer, colorectal cancer, melanoma, cervical cancer and thyroid cancer do not experience a significant excess in mortality within 10 years after diagnosis compared to the general population, with conditional 5-year relative survival of at least 95% after 10 years. For the remaining cancers, conditional 5-year relative survival estimates (at 10 years post diagnosis) ranged from 82% to 94%, suggesting that patients in these cohorts continue to have poorer survival compared to the age-matched general population.

Conclusions: Estimates of conditional survival have the potential to provide useful information for cancer clinicians, patients and their carers as they are confronted by personal and surveillance-related decisions. This knowledge may be effective in building realistic hope and assisting people to manage uncertainty about the future. To facilitate this process, we suggest measures of conditional survival be incorporated into routine statistical reporting avenues within Australia.

Introduction

The number of Australians being diagnosed and living with cancer is rising sharply.^[1, 2] Typically, newly diagnosed patients are informed of their prognosis according to published Australian estimates of observed or relative survival estimates calculated from the date of diagnosis. As time passes standard relative survival estimates are of limited relevance because they include survival information for people who have already died. However these initial survival estimates continue to loom large in patients' minds. A more relevant and useful question may be: "Now that I have survived for x number of years, what is the probability that I will survive another y years?".

Conditional survival directly addresses this question, and has been shown to provide much more useful and clinically reliable estimates of survival probability for cancer survivors.^[3]

While estimates for conditional survival have been reported in the international literature for a range of cancers,^[3-10] only limited estimates have been published using Australian data.^[11, 12] In this paper we present population-based conditional survival estimates for cancer patients diagnosed in Queensland, Australia.

Methods

Data required for this study was non-identifiable so no ethics committee involvement was necessary. No external funding was obtained.

Cancer cohort

De-identified case records were obtained from the population-based Queensland Cancer Registry (QCR). Notification of invasive cancers is required by law^[13]. We restricted our cancer cohort to patients aged 15-89 years at diagnosis. Survival status is obtained through routine record linkage with the National Death Index which enables interstate deaths to be identified.

All cancer patients diagnosed from 1982 through to 2007 were included in the cancer cohort, with follow-up to 31st December 2007. We restricted the cancer-specific analyses to all cancers combined, along with the 13 most common cancer types (Table 1) defined by ICD-0-3 codes.^[13]

Relative survival

Relative survival is used to approximate disease-specific survival, and is routinely reported by international cancer registries because it does not rely on accurate cause of death coding. Relative survival estimates were calculated using actuarial methods and based on the period approach,^[14] with cancer patients being at risk between January 1st 1998 to December 31st 2007. Expected survival was based on the Ederer II method.^[15] The survival time of patients who were not known to have died before the 31st December 2007 was censored as of that date.

Conditional survival

Conditional survival (CS) is the probability of surviving an additional y years given that the person has already survived x years. It is calculated by dividing the relative survival at $(x+y)$ years after diagnosis by the relative survival at x years after diagnosis.^[16] Confidence intervals can be calculated using the variance formula shown below.^[16]

$$Var[\bar{S}(t_j|t_i)] = [\bar{S}(t_j|t_i)]^2 = \sum_{k=i+1}^j \frac{d_k}{r_k(r_k - d_k)}$$

Given m time intervals, d_k and r_k are the number of deaths and number at risk respectively during the k^{th} interval. The probability of survival past time t is given by $S(t)$, so $S(t_j | t_i)$ is the probability of survival past time t_j , given they have already survived past time t_i . The 95% CIs are then constructed assuming that the conditional survival rates follow a normal distribution.

Results

Estimated relative survival at diagnosis and conditional relative survival curves calculated at 1-, 3- and 5-years after diagnosis are shown in Figure 1. For each type of cancer, the survival curves become progressively flatter and move closer to 1 the longer after diagnosis that the CS estimate begins. The differences in the survival curves are most pronounced when the initial survival prognosis is poorer, such as stomach cancer, pancreatic cancer and lung cancer. In contrast, the differences in survival curves are less substantial for cancers with a very good initial prognosis, such as melanoma and thyroid cancer. Figure 2 shows conditional 5-year relative survival for each additional year survived for selected cancers by age group. The improved survival prognosis at diagnosis for younger patients was generally maintained over time, but for most cancers the age-differential decreased.

Table 1 presents the 5-year relative survival estimates at diagnosis for each of the 13 selected cancer types, along with the 5-year conditional survival estimates for patients who have survived 1-year, 3-years, 5-years, 7-years and 10-years post diagnosis.

As an example, a person diagnosed with stomach cancer has an initial 5-year relative survival estimate of 29%. However, if this patient survives for one year, then their conditional 5-year relative survival percentage increases to 53%, and reaches 101% should they survive 10 years post diagnosis. In contrast, while 5-year relative survival is initially higher for leukaemia patients at diagnosis (58%), the 5-year CS estimate is lower than for stomach cancer patients 10 years after diagnosis (82%).

Discussion

Conditional survival estimates provide quantitative data for what is often observed anecdotally in clinical settings; that there is a subset of patients who survive beyond what would have been predicted at the time of diagnosis, and for these patients, their long-term prognosis continues to improve. This is critical information for cancer survivors to receive and understand. One of the most common unmet psychological needs cancer survivors report is fear of cancer recurrence,^[17] and fear of cancer recurrence is related to lower quality of life.^[18] A clearer understanding that survival after cancer is a conditional event may help cancer patients derive more hopeful appraisals about the future and potentially decrease the anxiety that often accompanies post-treatment surveillance.

It has been suggested that when conditional 5-year relative survival exceeds 95% (ie. survival is almost identical to the general population with the same age structure) the excess mortality is negligible.^[8, 9] In our study this was found within 10 years of diagnosis for all cancers combined, along with patients diagnosed with stomach cancer, colorectal cancer, melanoma, cervical cancer and thyroid cancer, similar to the results observed in international studies.^[8, 9, 19] People diagnosed with other cancers, and older patients continue to have poorer survival compared to the age-matched general population. Reasons for this continued excess mortality are varied, but would include late recurrences or adverse treatment effects, secondary tumours or increased co-morbidities leading to greater mortality.^[8, 9]

The value of the additional information provided by conditional survival estimates is greatest for people diagnosed with cancers having an initially poor prognosis. Unfortunately, the proportion of patients with these cancers who live to experience the improved survival outcomes is relatively low. However for those patients who do survive 1, 3 and 5 years after diagnosis, access to updated information for each point of their cancer recovery is important, providing scope for evidence-based optimism as they progress along the survivor's journey.

Cancer survivors are faced with increased uncertainty about their future at a time when they need to make important life decisions. Overall quality of life among cancer survivors has been shown to be influenced by the domains of control, uncertainty and the future.^[20] Levels of anxiety in each of these three domains may be alleviated, in part, by an understanding of the increased likelihood of continued survival over time.^[3] Thus, by acknowledging that risk profiles for cancer survivors change over time, conditional survival estimates have the potential to be especially relevant for survivors and their families as part of any mid- to longer-term follow up and support program.

Current Australian guidelines for the psychosocial care of adults with cancer^[21] advise that, when discussing prognosis, clinicians should provide examples of extraordinary survivors to give hope. By contrast, we suggest that it would be better if patients understood that the further they progress from the time of diagnosis, the greater their chance of surviving longer will become. This knowledge may be more effective in building realistic hope and assisting people to manage uncertainty about the future.

A strength of this study is the use of state-wide population-based data to calculate conditional survival estimates using information collected over a 26 year period. Applying a period analysis^[14] allowed us to calculate long-term conditional survival utilising the most recent outcomes available (i.e. patients at risk between 1998-2007), in recognition of the improvements that have been observed in cancer survival during the past two to three decades.

Limitations of this study include the lack of stage or treatment data. Stage at diagnosis is known to be an important prognostic factor for survival outcomes,^[22] its impact reduces and can disappear for long term conditional survival.^[9] Like all Australian cancer registries, the Queensland Cancer Registry does not routinely collect information about clinical stage, although NSW does collect some information about the spread of disease. Treatment can potentially have a dual effect on survival in terms of both remission and long term adverse effects.^[23] As is recommended for international cancer registries^[9], moves towards standardised collection and recording of stage and treatment information for population-based cancer registries in Australia should be a matter of priority.

Conclusions

Estimates of conditional survival have the potential to provide important information for cancer clinicians, patients and their carers as they face personal and surveillance-related decisions. To assist this process, we suggest measures of conditional survival be incorporated into routine statistical reporting avenues within Australia.

Figure 1: Conditional relative survival curves starting from 0-years (at diagnosis), 1-year, 3-years and 5-years after diagnosis, Queensland, 1998-2007.

Figure 1 (continued): Conditional relative survival curves starting from 0-years (at diagnosis), 1-year, 3-years and 5-years after diagnosis, Queensland, 1998-2007.

Footnotes:

1. Survival estimates are calculated using the Period method, including patients at risk from selected cancers between 1st January 1998 and 31st December 2007 in Queensland
2. Survival curves represent the percent of patients (y-axis) surviving the specified years after diagnosis (x-axis), given they have already survived a specified number of years (legend)
3. Vertical lines represent the 95% confidence intervals for the conditional survival estimates.

Table 1: Conditional 5-year relative survival estimates, with 95% confidence intervals, by type of cancer and number of years after diagnosis, patients aged 15-89 years at diagnosis, Queensland 1998-2007.

Type of cancer (N)	Years since diagnosis					
	At diagnosis	1 year post-diagnosis	3 years post-diagnosis	5 years post-diagnosis	7 years post-diagnosis	10 years post-diagnosis
Stomach cancer (3,188)	28.5 [27-30]	52.5 [45-60]	78.9 [74-84]	89.7 [85-95]	92.8 [87-99]	101 [95-107]
Colorectal cancer (24,728)	65.9 [65-67]	77.1 [76-78]	87.1 [86-88]	93.2 [92-94]	96.4 [95-98]	99.2 [98-101]
Pancreatic cancer (3,244)	6.9 [6-8]	26.5 [18-35]	62.9 [53-73]	83.7 [73-94]	90.0 [80-100]	92.2 [80-105]
Lung cancer (16,054)	14.0 [13-15]	31.6 [30-33]	58.7 [56-62]	70.9 [68-74]	76.2 [72-80]	82.9 [78-87]
Melanoma (25,565)	93.9 [93-94]	94.8 [94-95]	96.4 [96-97]	97.1 [97-98]	98.2 [98-99]	99.4 [99-100]
Breast cancer: females (23,742)	88.0 [87-89]	88.4 [88-89]	90.1 [89-91]	91.8 [91-93]	93.0 [92-94]	93.9 [93-95]
Cervical cancer: females (1,764)	75.2 [73-77]	83.2 [81-86]	90.3 [88-92]	92.5 [91-94]	94.6 [93-96]	97.2 [96-99]
Prostate cancer: males (25,970)	85.6 [85-86]	86.0 [85-87]	87.3 [86-88]	87.3 [86-89]	86.3 [85-88]	87.7 [85-90]
Kidney cancer (5,058)	65.6 [64-67]	77.4 [75-80]	85.9 [84-88]	87.7 [85-90]	90.8 [88-94]	92.7 [89-96]
Bladder cancer (6,883)	75.5 [74-77]	83.5 [82-85]	89.6 [88-91]	91.4 [89-94]	92.0 [90-94]	93.5 [91-96]
Thyroid cancer (3,124)	96.6 [96-98]	98.2 [97-99]	98.6 [97-100]	98.2 [97-100]	98.3 [97-100]	99.2 [97-101]
Non-Hodgkin lymphoma (6,462)	65.9 [64-67]	76.3 [74-78]	82.0 [80-84]	85.5 [83-88]	86.9 [84-90]	88.9 [86-92]
Leukaemia (4,687)	58.3 [57-60]	69.8 [67-72]	75.6 [73-78]	77.1 [74-80]	79.4 [76-83]	81.6 [77-86]
All cancers combined (189,591)	67.0 [67-67]	79.9 [80-80]	87.8 [88-88]	90.8 [90-91]	92.5 [92-93]	95.0 [95-96]

Footnotes:

1. Survival estimates are calculated using the Period method, including patients at risk from selected cancers between 1st January 1998 and 31st December 2007 in Queensland
2. Survival estimates represent the percent of patients surviving an additional 5 years at the specified number of years following the original cancer diagnosis.
3. Unless indicated, estimates for males and females are combined.
4. N represents the number of cancer patients alive at the beginning of the 'at risk' period.

Figure 2: Conditional 5-year relative survival for every additional year survived after initial diagnosis of cancer, according to age group and cancer type, Queensland, 1998-2007.

Figure 2 (continued): Conditional 5-year relative survival for every additional year survived after initial diagnosis of cancer, according to age and cancer type, Queensland, 1998-2007.

Footnotes:

1. Survival estimates are calculated using the Period method, including patients at risk from selected cancers between 1st January 1998 and 31st December 2007 in Queensland
2. Survival curves represent the percent of patients(y-axis) of surviving the specified years after diagnosis (x-axis), given they have already survived 5 years after diagnosis
3. Vertical lines represent the 95% confidence intervals for the conditional survival estimates.
4. Numbers of stomach, pancreatic, thyroid and cervical cancers were not sufficient to provide stable long-term age-specific conditional survival estimates.

References

- 1 AIHW. ACIM (Australian Cancer Incidence and Mortality) Books. (http://www.aihw.gov.au/cancer/data/acim_books/index.cfm - Accessed 2nd June 2010). 2010 [updated 2010; cited]; Available from.
- 2 AIHW & AACR 2008 Cancer survival and prevalence in Australia: cancers diagnosed from 1982 to 2004 (Cancer Series no. 42. Cat. no. CAN 38.) Canberra,
- 3 Xing Y, Chang GJ, Hu CY, *et al.* Conditional survival estimates improve over time for patients with advanced melanoma: results from a population-based analysis. 2010. *Cancer*; 116, 9: 2234-41.
- 4 Yang YH, Liu SH, Ho PS, *et al.* Conditional survival rates of buccal and tongue cancer patients: how far does the benefit go? 2009. *Oral Oncol*; 45, 2: 177-83.
- 5 Chang GJ, Hu CY, Eng C, *et al.* Practical application of a calculator for conditional survival in colon cancer. 2009. *J Clin Oncol*; 27, 35: 5938-43.
- 6 Alanee S, Shukla A. Paediatric testicular cancer: an updated review of incidence and conditional survival from the Surveillance, Epidemiology and End Results database. 2009. *BJU Int*; 104, 9: 1280-3.
- 7 Choi M, Fuller CD, Thomas CR, Jr., *et al.* Conditional survival in ovarian cancer: results from the SEER dataset 1988-2001. 2008. *Gynecol Oncol*; 109, 2: 203-9.
- 8 Janssen-Heijnen ML, Housterman S, Lemmens VE, *et al.* Prognosis for long-term survivors of cancer. 2007. *Ann Oncol*; 18, 8: 1408-13.
- 9 Janssen-Heijnen ML, Gondos A, Bray F, *et al.* Clinical relevance of conditional survival of cancer patients in europe: age-specific analyses of 13 cancers. 2010. *J Clin Oncol*; 28, 15: 2520-8.
- 10 Bowles TL, Xing Y, Hu CY, *et al.* Conditional Survival Estimates Improve Over 5 Years for Melanoma Survivors with Node-Positive Disease. 2010. *Ann Surg Oncol*; 17, 8: 2015-23.
- 11 Hahnel R, Spilsbury K. Oestrogen receptors revisited: long-term follow up of over five thousand breast cancer patients. 2004. *ANZ J Surg*; 74, 11: 957-60.
- 12 Woods LM, Rachet B, O'Connell D, *et al.* Large differences in patterns of breast cancer survival between Australia and England: a comparative study using cancer registry data. 2009. *Int J Cancer*; 124, 10: 2391-9.
- 13 QCR, CCQ 2009 Cancer in Queensland. Incidence and mortality 1982 to 2006 Brisbane; Queensland Cancer Registry and Cancer Council Queensland
- 14 Brenner H, Gefeller O, Hakulinen T. Period analysis for 'up-to-date' cancer survival data: theory, empirical evaluation, computation realisation and applications. 2004. *Eur J Cancer*; 40: 326-35.
- 15 Ederer F, Heise H 1959 Instructions to IBM 650 Programmers in Processing Survival Computations. Methodological Note No. 10, End Results Section. Bethesda, MD; National Cancer Institute
- 16 Skuladottir H, Olsen JH. Conditional Survival of Patients With the Four Major Histologic Subgroups of Lung Cancer in Denmark. 2003. *J Clin Oncol*; 21, 16: 3035-40.
- 17 McDowell ME, Occhipinti S, Ferguson M, *et al.* Predictors of change in unmet supportive care needs in cancer. 2009. *Psychooncology*; 19, 5: 508-16.
- 18 Hart SL, Latini DM, Cowan JE, *et al.* Fear of recurrence, treatment satisfaction, and quality of life after radical prostatectomy for prostate cancer. 2008. *Support Care Cancer*; 16, 2: 161-9.
- 19 Merrill RM, Henson DE, Ries LA. Conditional survival estimates in 34,963 patients with invasive carcinoma of the colon. 1998. *Dis Colon Rectum*; 41, 9: 1097-106.
- 20 Ferrell BR, Dow KH, Grant M. Measurement of the quality of life in cancer survivors. 1995. *Qual Life Res*; 4, 6: 523-31.
- 21 National Breast Cancer Centre and National Cancer Control Initiative 2003 Clinical practice guidelines for the psychosocial care of adults with cancer Camperdown, NSW; National Breast Cancer Centre
- 22 Greene FL, Sobin LH. The staging of cancer: a retrospective and prospective appraisal. 2008. *CA Cancer J Clin*; 58, 3: 180-90.

23 Miller KD, Triano LR. Medical issues in cancer survivors--a review. 2008. *Cancer J*; 14, 6: 375-
87.