The first year counts: cancer survival among Indigenous and non-Indigenous Queenslanders, 1997-2006

Cramb S, Garvey G, Valery P, Williamson D, Baade P.

ABSTRACT

Objective: To examine Indigenous persons' cancer survival differentials across time after diagnosis, remoteness and area-disadvantage in Queensland, Australia.

Design, Setting and Participants: Descriptive study of population-based data covering all Queensland residents of known Indigenous status aged 15+ years who were diagnosed with a primary invasive cancer during 1997-2006 (n=150,059).

Main Outcome Measures: Hazard ratios for the categories of area disadvantage, remoteness and Indigenous status as well as conditional 5-year survival estimates.

Results: Five-year survival was lower for Indigenous people diagnosed with cancer (50.3% [95% CI: 47.8-52.8]) compared to non-Indigenous people (61.9% [61.7-62.2]). There was no evidence that this differential varied by remoteness (p=0.780) or area disadvantage (p=0.845). However, the Indigenous survival differential varied by time after diagnosis. In a time-varying survival model stratified by age, sex and cancer type, the 50% excess mortality in the first year (adjusted HR=1.50 [1.4-1.6]) reduced to near unity at two years post-diagnosis (HR=1.03 [0.8-1.4]).

Conclusions: Indigenous cancer patients who survive two years after diagnosis have a similar outlook to non-Indigenous patients. There is, however, a strong call to action because of the unacceptably wide disparity in the first two years after diagnosis. It is unlikely that access to services or socio-economic factors are the main causes of the initial Indigenous survival inequality, since the patterns were similar across remoteness and area-disadvantage. There is an urgent need to identify the factors leading to poor outcomes immediately after diagnosis among Indigenous people diagnosed with cancer.

INTRODUCTION

Compared to non-Indigenous people, Aboriginal and/or Torres Strait Islanders (referred to here as Indigenous Australians) have poorer cancer survival.[1] Due to incomplete Indigenous ascertainment in routinely collected data sources, analysis of population-based cancer registry data has been largely restricted to those known to have high quality data ascertainment, such as Queensland, Northern Territory, South and Western Australia.[2] The limited data available show a consistent picture of similar overall cancer incidence, but lower incidence of some cancers with better prognosis, such as melanoma, and higher incidence of cancers with poorer prognosis.[3]

Recent studies have highlighted significantly lower survival among Indigenous cancer patients compared to non-Indigenous patients.[1,4-8] Indigenous people are more likely to be diagnosed at advanced stages for certain cancers, or receive poorer treatment, yet this does not completely explain the survival disadvantage.[5-7] A matched case-case study in Queensland found Indigenous patients treated in the public health system were 30% more likely to die from their cancer than non-Indigenous patients after adjusting for stage, cancer treatment and comorbidities.[8]

The proportion of Indigenous Australians living in remote or very remote areas is higher than for non-Indigenous Australians.[9] Many remote areas are also characterized by socioeconomic disadvantage, with both remoteness[10,11] and area-disadvantage[12] associated with lower cancer survival. There is however currently limited information on how the Indigenous survival differential varies across remoteness and area-disadvantage categories. This population-based study sought to address this lack of knowledge, and thus inform further research, policy and clinical priorities aimed at addressing the survival inequalities currently experienced by Indigenous people diagnosed with cancer.

METHODS

Data were provided by the population-based Queensland Cancer Registry (QCR),[13] under an agreement between Cancer Council Queensland and Queensland Health allowing access to non-identifiable data. For these analyses all persons of known Indigenous status aged 15 years and over that were diagnosed with a primary invasive cancer

(ICD-O3 C00-C80) during 1997-2006 were included. We excluded persons with unknown age or residential location at diagnosis, or whose diagnosis was based on death certificate or autopsy only. Included cases were followed to December 31st 2007, with matching to the National Death Index. Those that were still alive at 31st December 2007 were censored at that date, while those who died from a cause other than the diagnosed cancer were censored at the date of death.

Cancer type

Since the Indigenous:non-Indigenous incidence differential depends on cancer type, with cancers common among Indigenous people more likely to have low survival,[14] we constructed a variable representing broad cancer groups based on 5-year cancer survival estimates for total Queensland[15] (i.e. <25% (e.g. oesophagus, liver, lung, pancreas, unknown site), 25-49% (e.g. stomach, ovarian, myeloid leukaemia, myeloma), 50-74% (e.g. colorectal, kidney, non-Hodgkin lymphoma) and 75-100% (e.g. breast, cervical, prostate, melanoma)) to include in the analysis.

Geographical areas

Residential location at diagnosis was obtained from the QCR according to Statistical Local Area (SLA). These SLAs were then grouped according to the level of geographic remoteness based on the Accessibility/Remoteness Index of Australia (ARIA+). Area-level socioeconomic disadvantage was measured by quintiles of the Index of Relative Socioeconomic Advantage and Disadvantage since it does not include Indigenous Status in its derivation.[16]

Demographics

Information on sex, age at diagnosis and Indigenous status was obtained from the QCR. Age at diagnosis was categorized into 5 age groups (15-49, 50-59, 60-69, 70-79 and 80+). The QCR obtains information about Indigenous status of cancer patients through the process of cancer notification from Queensland hospitals. Ascertainment of Indigenous status is based on an individual identifying as either Aboriginal, both Aboriginal and Torres Strait Islander or Torres Strait Islander only. As the focus of this analysis was on the Indigenous:non-Indigenous survival differential, we also excluded those patients who had unknown ethnicity.

Statistical methods

Cox proportional hazards models were used to quantify the differences in survival with Efron's approximation used to resolve tied data, i.e. multiple deaths at the same number of days from diagnosis.[17] Analysis was conducted using Stata v11.0 (StataCorp LP, College Station, TX, USA).

Variables considered for inclusion in the model were geographic remoteness (ARIA), area disadvantage (IRSAD), age group at diagnosis, sex, Indigenous status, and broad cancer group. Cancer stage could not be included as the QCR does not routinely collect data on spread of cancer at diagnosis. Interactions between covariates, including time-varying coefficients, were also considered.

A systematic process was used to develop the final model, considering the proportional hazards assumption, overall model fit and the influence exerted by individual cases. Scaled Schoenfeld residuals that test for non-zero slope over time were used to check if the proportional hazards assumptions were satisfied. Model goodness of fit was assessed by Cox-Snell residuals. Deviance residuals were then used to examine model accuracy. We considered the influence of individual cases to determine their impact on each of the estimated individual coefficients (using the DFBETA statistic) as well as their effect on the combined set of coefficients (using the LMAX statistic).[17,18]

Conditional survival, which is the probability of surviving a certain number of years given they have already survived for *x* years,[19] was calculated for both Indigenous and non-Indigenous cohorts.

RESULTS

Of the original 180,095 cases diagnosed in Queensland between 1997 and 2006 among those aged 15 years and above, 14.6% were of unknown ethnicity (Figure 1). A further 2.5% were excluded as they were either diagnosed at death (1.5%; Indigenous 2.9%, non-Indigenous 1.5%), did not contain information on the SLA of residence (0.8%; Indigenous 0.7%, non-Indigenous 0.8%) or the number of days between diagnosis and death (0.2%;

Indigenous 0.3%, non-Indigenous 0.2%), or did not have a SEIFA value assigned (0.0%; Indigenous 0.4%, non-Indigenous 0.0%). The final cohort size was 150,059 cancer diagnoses among individuals of known ethnicity, of which 1,819 (1.2%) were Indigenous (Table 1). The most common cancers among Indigenous people were lung, breast, colorectal, prostate and cervical cancers. Among non-Indigenous cases the most common cancer sites were colorectal, breast, prostate, lung and melanoma. A slight majority (55.5%) of cancers were diagnosed among males.

Bivariate comparisons of survival

There was clear evidence of lower cancer survival for Indigenous people compared to non-Indigenous (Figure 2). The survival curves in Figure 2a are the cumulative survival. The hazard function (Figure 2c) represents the mortality rate at each time, conditional on survival until at least that time.

Unadjusted survival curves by remoteness suggested lower survival for Indigenous people in outer regional and remote/very remote areas, but not in more urban areas (results not shown). The interpretation of survival curves by area disadvantage was difficult due to small numbers of Indigenous patients in more affluent areas. Nonetheless, differences in survival were not apparent until the disadvantaged and most disadvantaged quintiles, where Indigenous cancer patients had poorer survival than non-Indigenous patients.

Development of multivariate model

The initial model was created including all variables in the model (age groups, sex, rurality, area disadvantage, broad cancer site and Indigenous). However, proportional hazards assumptions were clearly not met for each broad cancer group (based on scaled Schoenfeld residuals, each $p < 0.001$), so the model was adjusted to include cancer site as a stratification variable.

The plot of the hazard function by Indigenous status (Figure 2c) revealed large initial differences in hazards, which decreased over time since diagnosis. Therefore time-varying components (Indigenous status by follow-up years

after diagnosis) were incorporated into the model. To prevent a few cases with longer follow-up exerting undue influence on survival estimates, time since diagnosis was categorized up to 5+ years follow-up.
Proportional hazards assumptions were not being met for the final age category ($p<0.001$) or sex ($p<0.001$). While including Indigenous-sex and Indigenous-age group interaction terms improved the model fit based on the likelihood-ratio tests, the proportional hazards assumptions were still violated (overall model $p<0.001$). To address this we instead included age and sex in the model as stratification variables.

The final multivariate model

The final model included rurality (ARIA+), area disadvantage (IRSAD), Indigenous status and time-varying Indigenous components, and was stratified by broad cancer site, sex and age groups. The graph of Cox-Snell residuals (not shown) indicated excellent model fit, and there was no evidence the parameter estimates were being overly influenced by outlying individual data points.

Survival estimates and the results from the final Cox hazard model are shown in Table 1. The results show poorer survival for Indigenous people during the first and second years following diagnosis after stratifying by age, sex and broad cancer sites, and adjusting for area-level disadvantage and remoteness. This disparity decreased with time since diagnosis, and after two years there was no survival disparity between Indigenous and non-Indigenous cancer patients.

Survival was lower for people living in less accessible areas and those in more disadvantaged areas. However there was no significant evidence for interaction found between Indigenous status and either remoteness ($p=0.780$) or area disadvantage ($p=0.845$).

Two sensitivity analyses were conducted. The first included patients with unknown Indigenous status in the non-Indigenous group, while the second included those diagnosed at death (by death certificate or autopsy) by assuming they had an average of one year survival. In both cases the analyses yielded similar results, with hazard ratios slightly higher when including those of unknown Indigenous status.

Conditional survival

Conditional survival estimates (Table 2) reinforce the time-dependent nature of the Indigenous:non-Indigenous survival differential. Indigenous cancer patients initially had poorer 5-year survival prognosis than non-Indigenous, but this disparity in survival expectations vanished once they had survived two or more years.

DISCUSSION

In this population-based study of cancer in Queensland, we found significant disparities between the survival outcomes for Indigenous and non-Indigenous people after their diagnosis. These differences remained after accounting for remoteness, area disadvantage, age group, sex and mix of cancers. However, this survival disparity was modified by time since diagnosis, with the comparative risk of death decreasing as the time from diagnosis increased. This varying time effect has not been previously noted in studies examining cancer survival among Indigenous people in Australia,[4,20] apart from a brief mention of time-varying Indigenous:non-Indigenous survival for colorectal cancer patients in the Northern Territory.[21]

This is important information for Indigenous cancer patients to know, because the longer they survive the greater likelihood they have of continuing to survive. Most of the currently published literature has focused on the poorer survival outcomes of Australian Indigenous people diagnosed with cancer. This is justifiably so, and has helped galvanise a concerted government, clinical and research effort to reduce this disparity in cancer survival. However, the perspective that Indigenous cancer patients have continued poorer prognosis cannot help but limit their own personal optimism and outlook for the future. It is for this reason that these results, based on the total Queensland population, provide an avenue for increased optimism for Indigenous cancer patients to successfully complete their cancer journey.

However this optimism must be constrained by a strong call to action to understand what is causing the very wide disparity in survival in the first one or two years after diagnosis. A recent Queensland study[23] revealed an Indigenous survival differential for breast cancer that remained even after adjusting for spread of disease. This suggests other factors, such as the impact of poorer general health and increased co-morbidities among the

Indigenous population compared to the non-Indigenous population, also play an important role. There may be a healthy cohort effect, as those Indigenous patients who survive beyond two years after diagnosis may have less comorbidities or better general health than those who died earlier. Alternatively, Indigenous cancer patients in Queensland (all cancers) are less likely to undergo treatment for their cancer than other patients.[8] Indigenous patients who access services and adequate treatment may have better survival.[22] Until Australian cancer registries standardize collection and recording of stage and treatment data, it will be impossible to appropriately explore these factors.

We found no evidence that the Indigenous:non-Indigenous survival differential varied according to geographical area of residence. As the use of any area-based measure of socioeconomic status is likely to over-estimate the affluence of Indigenous people,[25] this reinforces the lack of evidence. This may indicate the Indigenous survival differential is not primarily related to access to treatment or socio-economic barriers, but that other as yet unknown factors are more relevant, including those related to culture and general health, and that these other factors have similar impact across geographical locations. Clearly having an almost 50% differential in cancer survival within the first 12 months of diagnosis is not acceptable, and our findings increase the motivation for further efforts in this area. Greater emphasis and research focus should therefore be placed on identifying the factors for the initial survival disparity.

Limitations of this study include the relatively small numbers of Indigenous cases, resulting in limited capacity to investigate differences for specific types of cancer. We were also unable to separate the effects of early diagnosis from other factors, including those of treatment differentials. Since not all Indigenous cases may have been identified, there is potential misclassification of true Indigenous status. However this misclassification is thought to be small,[8] and ascertainment is considered high.[2]

In conclusion, these results provide some cause for cautious optimism, as Indigenous patients in Queensland who have already survived two years following a cancer diagnosis are likely to have a similar outlook as non-Indigenous patients. However there is still an urgent need to address the unacceptable disparity in survival

outcomes immediately after diagnosis, and these results highlight the importance of making this important health issue a continuing priority.

References

1 Chong A, Roder D. Exploring Differences in Survival from Cancer among Indigenous and non-Indigenous Australians: Implications for Health Service Delivery and Research. 2010. Asian Pacific J Cancer Prev; **11**:953-961.

2 Australian Institute of Health and Welfare. 2010. Indigenous identification in hospital separations data - quality report. Health Services Series no. 35. Cat. no. HSE 85. AIHW: Canberra.

3 Cunningham J, Rumbold AR, Zhang X, *et al.* Incidence, aetiology, and outcomes of cancer in Indigenous peoples in Australia. 2008. Lancet Oncol; **9**(6):585-595.

4 Condon JR, Armstrong BK, Barnes T, *et al.* Cancer incidence and survival for indigenous Australians in the Northern Territory. 2005. Aust N Z J Public Health; **29**(2):123-128.

5 Condon JR, Barnes T, Armstrong BK, *et al.* Stage at diagnosis and cancer survival for Indigenous Australians in the Northern Territory. 2005. Med J Aust; **182**(6):277-280.

6 Condon JR, Cunningham J, Barnes T, *et al.* Cancer diagnosis and treatment in the Northern Territory: assessing health service performance for indigenous Australians. 2006. Intern Med J; **36**(8):498-505.

7 Hall SE, Bulsara CE, Bulsara MK, *et al.* Treatment patterns for cancer in Western Australia: does being Indigenous make a difference? 2004. Med J Aust; **181**(4):191-194.

8 Valery PC, Coory M, Stirling J, *et al.* Cancer diagnosis, treatment, and survival in Indigenous and non-Indigenous Australians: a matched cohort study. 2006. Lancet; **367**(9525):1842-1848.

9 Australian Bureau of Statistics, Australian Institute of Health and Welfare. 2008. The Health and Welfare of Australia's Aboriginal and Torres Strait Islander Peoples. ABS cat. no. 4704.0, AIHW cat. no. IHW 21. ABS & AIHW: Canberra.

10 Cramb SM, Mengersen KL, Baade PD. 2011. Atlas of Cancer in Queensland: geographical variation in incidence and survival, 1998 to 2007. Viertel Centre for Research in Cancer Control, Cancer Council Queensland: Brisbane.

11 Jong KE, Smith DP, Yu XQ, *et al.* Remoteness of residence and survival from cancer in New South Wales. 2004. Med J Aust; **180**(12):618-622.

12 Australian Institute of Health and Welfare, Cancer Australia & Australasian Association of Cancer Registries. 2008. Cancer survival and prevalence in Australia: cancers diagnosed from 1982 to 2004. Cancer Series no. 42, Cat. no. CAN 38. AIHW: Canberra.

13 Queensland Cancer Registry. 2011. Cancer in Queensland: Incidence, Mortality, Survival and Prevalence 1982 to 2008. QCR, Cancer Council Queensland and Queensland Health: Brisbane.

14 Condon JR, Armstrong BK, Barnes A, *et al.* Cancer in Indigenous Australians: a review. 2003. Cancer Causes Control; **14**(2):109-121.

15 Queensland Cancer Registry. 2010. Cancer in Queensland: Incidence, Mortality, Survival and Prevalence 1982 to 2007. QCR, Cancer Council Queensland and Queensland Health: Brisbane.

16 Australian Bureau of Statistics. 2008. Information Paper: An Introduction to Socio-Economic Indexes for Areas (SEIFA), 2006. ABS Cat. no. 2039.0. ABS: Canberra.

17 Cleves M, Gutierrez RG, Gould W, *et al.* An introduction to survival analysis using Stata. 3rd ed College Station: Stata Press; 2010.

18 Collett D. Modelling survival data in Medical Research. 2nd ed London: Chapman & Hall/CRC; 2003.

19 Baade PD, Youlden DR, Chambers SK. When do I know I am cured? Using conditional estimates to provide better information about cancer survival prospects. 2011. Med J Aust; **194**(2):73-77.

20 Roder D, Currow D. Cancer in Aboriginal and Torres Strait Islander People of Australia. 2009. Asian Pacific J Cancer Prev; **10**:729-733.

21 Condon JR, Barnes A, Armstrong BK, *et al.* 2005. Stage at diagnosis and cancer survival of Indigenous and non-Indigenous people in the Northern Territory, 1991–2000. National Cancer Control Initiative: Melbourne.
22 Coory MD, Green AC, Stirling J, *et al.* Survival of Indigenous and non-Indigenous Queenslanders after a diagnosis of lung cancer: a matched cohort study. 2008. Med J Aust; **188**(10):562-566.
23 Dasgupta P, Baade PD, Aitken JF, *et al.* Multilevel determinants of breast cancer survival: association with geographic remoteness and area-level socioeconomic disadvantage. In Press. Breast Cancer Res Treat.
24 Moore S. *A comparative study of cancer incidence, diagnosis, treatment and survival between Indigenous and non-Indigenous people in Queensland*. Brisbane: The University of Queensland; 2010.
25 Kennedy B, Firman D. Indigenous SEIFA - revealing the ecological fallacy. Population and Society: Issues, Research, Policy. 12th Biennial Conference of the Australian Population Association; 2004; Canberra. 2004.

Figure 1. Flow chart for case ascertainment

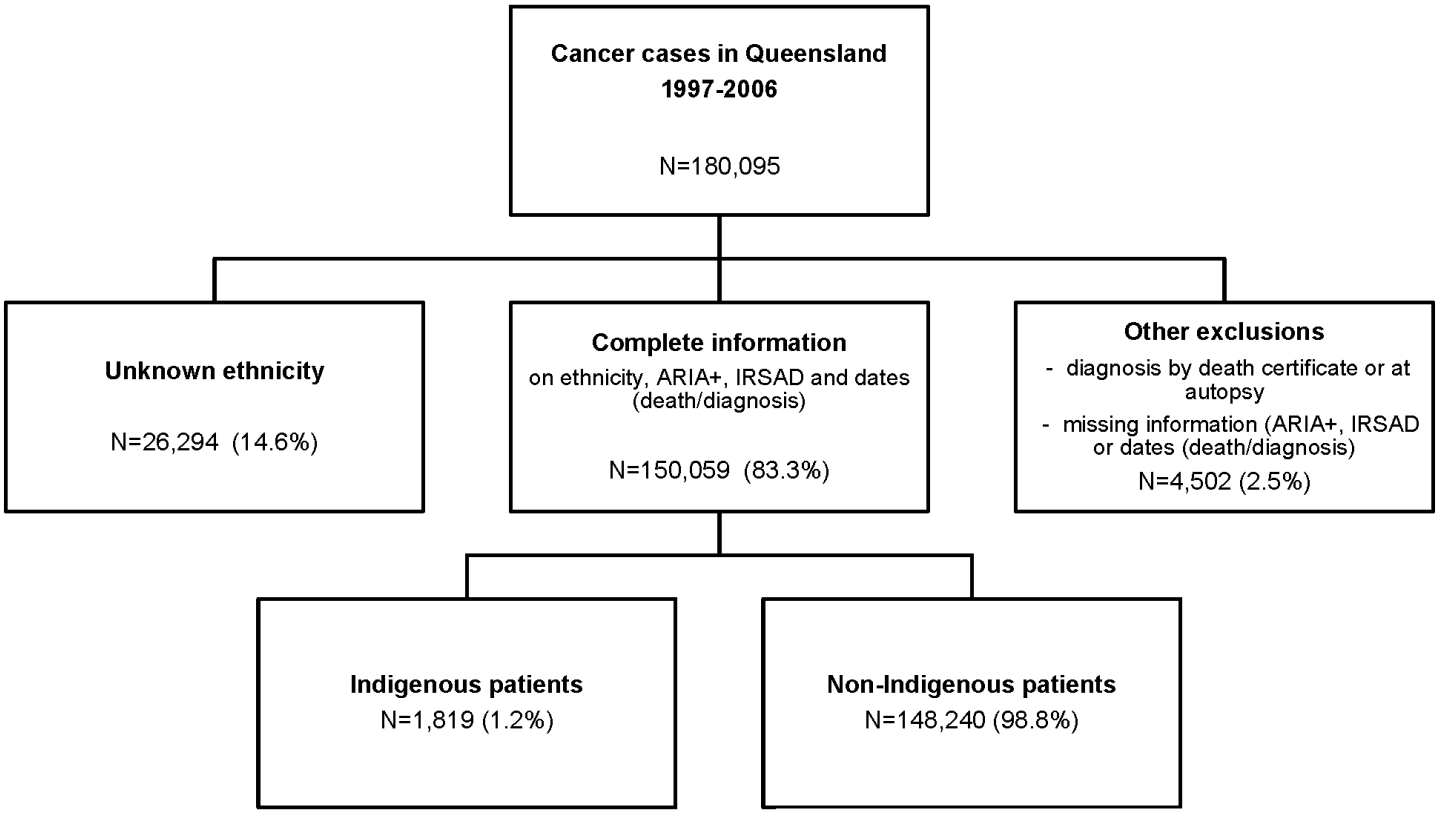

Figure 2. All invasive cancers by Indigenous status. A. Kaplan-Meier survival curve at diagnosis. B. Kaplan_Meier survival curve two years after diagnosis.