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Comorbidities contribute to the risk of cancer death among Aboriginal and non-Aboriginal South Australians: Analysis of a matched cohort study

David Banham[a,b,*], David Roder[b], Alex Brown[a,c], for the CanDAD Aboriginal Community Reference Group and other CanDAD investigators

[a] Wardliparingga Aboriginal Research Unit, South Australian Health and Medical Research Institute, North Terrace, Adelaide, SA, 5000, Australia
[b] Centre for Population Health Research, School of Health Sciences, Sansom Institute for Health Research, University of South Australia, North Terrace, Adelaide, SA, 5000, Australia
[c] Aboriginal Health Research Group, Sansom Institute for Health Research, University of South Australia, North Terrace, Adelaide, SA, 5000, Australia

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ABSTRACT

Background: Aboriginal Australians have poorer cancer survival than other Australians. Diagnoses at later stages and correlates of remote area living influence, but do not fully explain, these disparities. Little is known of the prevalence and influence of comorbid conditions experienced by Aboriginal people, including their effect on cancer survival. This study quantifies hospital recorded comorbidities using the Elixhauser Comorbidity Index (ECI), examines their influence on risk of cancer death, then considers effect variation by Aboriginality.

Methods: Cancers diagnosed among Aboriginal South Australians in 1990–2010 (N = 777) were matched with randomly selected non-Aboriginal cases by birth year, diagnostic year, sex, and primary site, then linked to administrative hospital records to the time of diagnosis. Competing risk regression summarised associations of Aboriginal status, stage, geographic attributes and comorbidities with risk of cancer death.

Results: A threshold of four or more ECI conditions was associated with increased risk of cancer death (sub-hazard ratio SHR 1.66, 95%CI 1.11-2.46). Alternatively, the presence of any one of a subset of ECI conditions was associated with similarly increased risk (SHR = 1.62, 95%CI 1.23-2.14). The observed effects did not differ between Aboriginal and matched non-Aboriginal cases. However, Aboriginal cases experienced three times higher exposure than non-Aboriginal to four or more ECI conditions (14.2% versus 4.5%) and greater exposure to the subset of ECI conditions (20.7% versus 8.0%).

Conclusion: Comorbidities at diagnosis increased the risk of cancer death in addition to risks associated with Aboriginality, remoteness of residence and disease stage at diagnosis. The Aboriginal cohort experienced comparatively greater exposure to comorbidities which adds to disparities in cancer outcomes.

1. Introduction

Despite being diagnosed at younger average ages, Australia's Aboriginal and Torres Strait Islander peoples (respectfully referred to here as Aboriginal) have poorer cancer survival and increasing rates of disease burden from cancer compared to other Australians [1–3]. These disparities are influenced by relatively more diagnoses involving high mortality cancers and at later stages [1–3]. Nevertheless, adjusting for such risks does not fully explain the differences in survival outcomes.

The number and severity of health conditions coexisting, or co-morbid, at the time of incidence also impede cancer detection [4], prognosis [5], treatment [6] and subsequent survival outcomes[5] for cancer generally and for particular sites such as ovarian [7], cervical [8], colorectal [[4],9–12] and breast [13,14] cancers. In questioning the contribution of comorbid conditions to ethnic differences in cancer survival, international studies [[8],9,13,14] consistently report a higher prevalence of chronic conditions among disadvantaged ethnic and Indigenous groups. However, whether these comorbidities influenced the risk of cancer death among ethnic groupings was not clear. Those studies reporting differential effects by ethnicity [[8],9] did not appear to adjust for the competing risk of death from other causes.

In Australia, comorbidities are highly prevalent among cancer survivors with four in five people reporting two or more chronic diseases [15]. Little is known about comorbidities among Aboriginal Australians diagnosed with cancer or their influence on cancer survival. This is in spite of administrative hospital records being an accessible, useful source of information on comorbidities [16]. Two inter-related, matched cohort studies [17,18] in Queensland assessed such comorbidities

* Corresponding author at: The South Australian Health and Medical Research Institute, North Terrace, Adelaide, SA, 5000, Australia.
E-mail addresses: david.banham@sahmri.com, david.banham@unisa.edu.au (D. Banham).

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using public hospital records. While Aboriginal people had more comorbid conditions and higher scores on the Charlson Comorbidity Index [19] (CCI) than their non-Aboriginal contemporaries at time of diagnosis, no discrete effect of CCI score on outcomes were reported for all cause [18] and cancer [17] survival. In the interim, the Elixhauser Comorbidity Index [20] (ECI) has shown superior performance compared to the CCI in quantifying the effect of comorbidities on cancer patients' outcomes [21] and other hospitalised groups across countries and conditions [22].

Improved understanding of the comorbid conditions Aboriginal Australians experience at the time of cancer diagnosis and their influence on cancer survival is needed. The state of South Australia (SA) in southern, central Australia is developing an advanced cancer data system within a wider Cancer Data and Aboriginal Disparities [23] (CanDAD) project. CanDAD has previously described the role of Aboriginality, geographic remoteness and cancer stage at diagnosis in cancer outcomes [2]. The system now facilitates the inclusion of comorbid disease in that aetiological pathway and will contribute critical information for subsequent evaluations of the uptake and effectiveness of hospital-based and other cancer treatments.

This study firstly examines the amount and effect of hospital recorded comorbid health conditions on cancer death among a population-based cohort of Aboriginal cancer cases in South Australia and a matched cohort of non-Aboriginal cancer cases. It then considers whether the effect of comorbid conditions varied because of Aboriginality.

2. Method

2.1. Ethics approval and governance

CanDAD's Aboriginal Community Reference Group governed the project to ensure alignment with South Australian Aboriginal Health Research Accord principles [24]. The Aboriginal Health Council of South Australia (04-12-461), SA Health (HREC/12/SAH/35), the University of South Australia (30622) and the Central Australia (HREC-15-361) human research ethics committees approved the study.

2.2. Study design and participants

A retrospective cohort of all cancer cases diagnosed among Aboriginal South Australians in the period 1990–2010 (N = 777) matched one to one with a random selection of cancers among non-Aboriginal people according to: sex; birth year, primary cancer site; and, year of diagnosis.

2.3. Data sources and measurements

Cancer case data were obtained from the South Australian Cancer Registry (SACR), a population registry collating dates of International Classification of Diseases for Oncology (ICD-O-3) [25] coded diagnoses and death (coded as cancer or non-cancer death). Cancers of the head, oral cavity, and digestive and respiratory tracts are relatively over-represented within the study cohorts[2]. These sites are associated with increased likelihood of misattributing subsequent cause of cancer death to adjacent organs [26] so we adopted a broad definition of cancer death [27] to reduce the risk of inappropriately censoring and undercounting cancer deaths. CanDAD subsequently summarised each cancer's stage at diagnosis using SEER methodologies [28] as: *localised* – confined to tissue of origin; *regional* – invaded adjacent tissue or regional nodes; *distant* – spread to distant lymph nodes or other organ sites, or as leukaemia (C42.1); and *unknown* stage when insufficient staging data were available.

Identification of Aboriginal status from administrative records can be open to misclassification bias. We optimised the specificity of Aboriginal status by cross-referencing SACR records against other datasets available to the study through data linkage, including those traced through the SA-NT Datalink master linkage file, public hospital inpatient data, clinical information systems data, death records, and additional hand searching [23]. While expecting some false classification of Aboriginality to persist, we believe this would involve a very low proportion of cases classified as non-Aboriginal and cause little bias in assessing disparities.

SACR records postal area of residence categorised by remoteness (major city, regional country, and remote areas) using the Accessibility/Remoteness Index of Australia [29].

Person-linked private and public hospitalisations for cohort cases during the period 1 July 1991 to 30 June 2013 were extracted from the Integrated South Australian Activity Collection (ISAAC) and Alice Springs Hospital in the Northern Territory [23] (Supplementary Appendix A describes the study's record linkage protocol). Each record included up to 25 International Classification of Diseases (ICD-10-AM) [30] coded diagnoses. Each case's hospital records were then constrained to five years before, and one month after, a first hospitalisation with cancer as a primary diagnosis [31], or the SACR recorded cancer diagnosis date.

Comorbidities recorded within each case's inpatient administrative summary were determined after modifying the ECI to omit cancer related conditions (cancer, lymphomas and metastases [21]) and applying a condition hierarchy ensuring any individual with diabetes or hypertension would be further classified as either with *or* without complications. ECI scores are a simple count of comorbid conditions present, ranging from 0 (no comorbidities) to a maximum of 26, with further categorisation as 0, 1–3, and 4 or more comorbidities. Where no hospitalisation for a case was observed, we assigned an ECI score of 0 to prevent loss to missing data and unbalancing the study design.

2.4. Outcomes

The primary outcome was survival time from cancer diagnosis to cancer death or right censoring at 31st December 2011, whichever occurred first.

2.5. Statistical analysis

No formal power calculation was conducted as all identified Aboriginal cancer cases were included in the cohort. Demographic variables by categories of ECI score and Aboriginality were cross-tabulated with Pearson's Chi-Square Test used to determine the strength of relationships observed. The prevalence of discrete conditions included in the ECI were also cross-tabulated by Aboriginality.

Multivariate analysis begins with, then extends, our previously published regression model [2] describing the risk of cancer death. The approach accounts for the competing risk of mortality from non-cancer causes using Stata's *stcrprep* with *stcox* in order to provide estimates of sub-hazard ratios (SHR) consistent with Fine and Gray's [32] approach, and stratification using pairs of cohort cancer cases matched on the basis of sex, year of birth, year of diagnosis and primary cancer site. Our baseline Model 1 therefore included an interaction term of Aboriginality as the exposure variable with categories of area remoteness as covariates together with stage at diagnosis as moderator. Model 2 added the main effect of ECI category. Model 3 substituted ECI category with all discrete ECI conditions as potential new moderators and explored their contribution individually, and in groups. Conditions which did not significantly contribute were iteratively removed [33] and those conditions displaying a discrete, significant contribution to the risk of cancer death were retained. That subset of moderating conditions were subsequently included in a dichotomous variable (0 = none of these conditions present; 1 = one or more of these conditions present) which was added to Model 3. Potential interactions of predictor variables were assessed, including those of Aboriginality with comorbidities and stage at diagnosis. The adherence of Models 2 and 3 to the proportional

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