Title: Adolescent and young adult (AYA) malignant bone tumour survival in New Zealand, 2000-2009: A retrospective case review.

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The spectrum of cancers occurring in the AYA population (15-29 years) uniquely reflects the biological developmental stage of this age group. AYA cancers encompassed a mixture of childhood cancers and adult carcinomas. In addition, some types of cancers, such as bone tumours, peak in incidence during this period. While overall survival rates for all cancers continue to rise, this benefit seemingly has not been extended to AYA patients, particularly for those with malignant bone tumours. In the New Zealand AYA population, the predominant sub-types of malignant bone tumours are osteosarcoma (46%) and Ewing’s sarcoma (48%).

A recent study, ‘AYA Cancer Incidence and Survival in New Zealand 2000-2009’ using New Zealand Cancer Registry (NZCR) data, has found unexpectedly low survival rates in AYA with malignant bone tumours. Even though the overall incidence of malignant bone tumours was relatively rare (12% of all AYA cancers), it had the lowest 5-year survival (46% for 15-29 year olds) and the highest number of deaths out of all the AYA cancer diagnostic groups in the 15-19 year cohort. Compared with the same diagnostic category cohort in 1988-2002, the 5-year relative survival has decreased by 11% in the 15-19 age group and by 19% in the 20-24 group whilst overall survival in overall AYA cancers was improving. Compared with survival reported by America (63%), Scotland (67%), and Canada (68%), New Zealand’s 5-year survival for malignant bone tumours is considerably lower. This suggests New Zealand AYA patients suffering from malignant bone tumours have a poorer outcome and are well below international benchmarks. Furthermore, more attention should be paid to the ethnic disparity in survival particularly for AYA of NZ Maori descent experiencing only 33% 5-year survival. Data on New Zealand AYA in the 25-29 age group are being collected concurrently to this study but unpublished results show only 31% 5-year survival for the bone tumour group. Compared to 66% 5-year survival for malignant bone tumours in the 25-29 age group in Australia, we are clearly not doing as well.

Following on from the previous study, we hope to gain more comprehensive data not routinely collected by the NZCR, and have been unreported in similar survival studies in other countries, in order to find any potential contributing factors to the poor survival of AYA malignant bone tumour patients. We conducted a retrospective case review of the clinical records of all AYA receiving treatment in the South Island and a sample from the North Island for a malignant bone tumour within the period between January 2000 and December 2009. Comprehensive data about onset of symptoms, presentation, histology, site, disease staging at diagnosis, chemotherapy, radiotherapy, clinical trial participation, surgery, disease recurrence, secondary malignancies, and cause of death were collected. Our aim was to examine the modifiable factors in the most crucial early period before disease progression. Therefore we have not reviewed palliative type treatments. As the cause of death was not reported from the previous study, we have collected this data from the Ministry of Health to confirm whether bone cancer was the primary cause. The final date of follow up was the 31st December 2013. Although we have tried to review a representative sample, the North Island data has yet to be completed due to time constraints, and therefore we are unable to draw any reliable conclusions from the data at this time.

Of the 122 AYA (15-29 years) diagnosed with malignant bone tumours between 2000 and 2009, 63 patient records have been reviewed to date. One patient was excluded because their disease was only notified by death certificate. South Island treated patients (n=26) have been completely reviewed and 36 of the 94 North Island treated patients
have been reviewed. Of these 62 patients, 47% were diagnosed with a Ewing sarcoma and 45% with osteosarcoma. This is very comparable to the whole malignant bone tumour group. None of deaths of patients reviewed were contributed by causes other than their malignant bone tumour.

An aspect of hospital presentation for bone tumours in the youth that has been thought to influence outcome is the time the individual takes to present. Therefore we recorded the subjective amount of time the individual had experienced symptoms expressed at their first hospital consultation. These patients presented to a tertiary care facility a median of 69 days after symptom onset. However those presenting under the median number of days (n=31) had 5-year survival of 48% compared with 65% 5-year survival of the patients presenting later than 69 days (n=31). Compared with early presenters, late presenters in this study group showed no difference in disease progression at presentation. Of the 19 patients with metastatic disease at presentation, 53% presented later than the median presenting time.

The individual’s socioeconomic status has also been thought to influence their survival due to a variety of reasons such as access to primary and tertiary healthcare. Patient address at diagnosis was used to derive scores based on the New Zealand Deprivation scale 2006 (NZ Dep). The scale ranges from 1 (least deprived) to 10 (most deprived). Those with a score between 1-5 (n=26) had a 5-year survival of 69% and those that had scores of between 6-10 (n=36) had 5-year survival of 47%. It was found that between the two groups, there was no difference in the percentage receiving treatment in a specialist sarcoma multidisciplinary treatment centre (Auckland, Middlemore, Christchurch) or the median number of days for presentation. However, the majority (n=10, 83%) of NZ Maori patients included in this review belonged to the 6-10 NZ Dep group. Further statistical analysis will be needed once collection is completed to separate the effects of the two variables.

AYA NZ Maori diagnosed with malignant bone tumours in 2000-2009 had particularly poor survival. In this project we have only reviewed 12 of the 33 Maori patients, therefore conclusions cannot be drawn until the review is completed. Metastatic disease at presentation was very similar between NZ Maori and non-Maori patients, as was the median time between symptom onset and presentation. However, we found only 50% (n=6) of NZ Maori patients received surgery as a form of treatment compared with 80% (n=40) of non-Maori patients receiving surgery. Ethnic variation in survival and its possible causes will be further examined once the dataset is complete.

As participation in clinical trials has been suggested in the literature as a factor influencing outcome, we collected detailed chemotherapy protocol information. While 57 patients received curative chemotherapy, 26% did not complete treatment due to disease progression or chemotoxicity and 9% of patients chose to not complete chemotherapy. Only 60% of these patients were treated on a named protocol, and only 21% participated in a clinical trial. However, in this group, participating in a clinical trial did not confer better survival as suggested by the literatures.

Another variable thought to influence survival was the place of treatment. 21 patients from this group were treated in paediatric oncology (Christchurch and Starship hospitals). Their 5-year survival was 71% and those treated in the adult service had a 5-year survival of 49%. This possibly reflects the biological differences in disease progression of the different age groups presenting to the two services. Furthermore, treatment in multiple centres did not seem to influence survival. The 12 patients treated in multiple treatment centres (of different cities) reviewed, had 75% 5-year survival while those treated in single centres only had 52% 5-year survival.

We do not yet have an answer to why New Zealand adolescents and young adults with malignant bone tumours have poorer survival compared to those AYA in similar countries. Nonetheless, this study has provided some ideas. The data will be further consolidated once the North Island data collection has been completed. It is expected that the completed dataset and subsequent statistical analysis will highlight potential areas of improvement to the future service delivery for AYA diagnosed with malignant bone tumours.