Received: 19 September 2022 | Revised: 25 October 2022 | Accepted: 14 November 2022

DOI: 10.1002/pbc.30136

Pediatric Blood & Cancer | SIOP International Society of Paediatric Oncology | aspho The American Society of Pediatric Hematology/Oncology | WILEY

BRIEF REPORT

Long-term childhood cancer survival in Australia using period estimation

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Abstract

Estimates of childhood cancer survival are usually reported at 5 years after diagnosis only. Using cases prevalent between 2014 and 2018 from the population-based Australian Childhood Cancer Registry, we used the period method to calculate relative survival up to 20 years post diagnosis by cancer type. Twenty-year relative survival for all childhood cancers combined (n = 14,353) was 83.8% (95% confidence interval [CI] = 82.6%–85.0%). Survival decreased only slightly after 10 years for most childhood cancers, except for some types of brain and liver tumours. These contemporary estimates of long-term survival provide valuable information to assist childhood cancer patients and their families in planning for the future.

KEYWORDS
Australia, cancer, childhood, long-term survival, population based

1 | INTRODUCTION

Survival estimates from population-based cancer registries are typically expressed in terms of 5-year survival. This is primarily because most excess mortality due to cancer occurs in the first year or two following diagnosis, especially for most childhood cancers. After 5 years, estimates of continuing survival following most types of childhood cancer generally return to levels that are similar to the broader population.[1]

Nonetheless, 5-year survivors of childhood cancer are known to be at continuing risk of late effects from treatment, including conditions that may be life-threatening.[2,3] In the current study, we assess longer term relative survival for childhood cancer in Australia, using a statistical method designed to produce the most contemporary results possible.

2 | METHODS

De-identified unit record data for children aged 0–14 at the time of cancer diagnosis were extracted from the Australian Childhood Cancer Registry (ACCR). The ACCR operates with ethics approval from the Children's Health Queensland Hospital and Health Service Human Research Ethics Committee (HREC) (reference HREC04/QRCH/18) along with numerous HRECs representing each of the state/territory cancer registries and major paediatric treating hospitals throughout Australia (full details are available on request). Cancer is a notifiable disease in all Australian states and territories; therefore, the ACCR is understood to include all cases of cancer diagnosed among Australian children. Cases from the ACCR are matched annually against the National Death Index using a unique identifier to ensure that mortality status is complete up to the censor date.

Relative survival at 10 and 20 years from the date of diagnosis was estimated from the period method by type of cancer, defined using diagnostic groups and diagnostic subgroups according to the International Classification of Childhood Cancer, version 3 (ICCC-3).[4] Survival estimation using the period method involves a rolling group of patients during a specified 'at-risk' window of time. In contrast, the more traditional cohort method follows a set group of patients over time.[5] This distinction is particularly important when calculating longer term survival for many types of childhood cancer for which the prognosis has improved dramatically over recent decades.[6]

Abbreviations: ACCR, Australian Childhood Cancer Registry; CI, confidence interval; HREC, Human Research Ethics Committee.

TABLE 1 Ten- and 20-year relative survival for childhood cancer by ICCC-3 diagnostic group/subgroup, Australia, 2014–2018[a]

ICCC-3 group/subgroup	*n*[b]	10-Year relative survival % (95% CI)	20-Year relative survival % (95% CI)
I. Leukaemias, myeloproliferative diseases and myelodysplastic diseases	4731	89.1 (87.2–90.8)	88.3 (86.2–90.0)
Ia. Lymphoid leukaemia	*3828*	*92.3 (90.3–93.8)*	*91.2 (89.1–92.9)*
Ib. Acute myeloid leukaemia	*591*	*73.4 (65.6–79.7)*	*73.6 (65.8–79.9)*
II. Lymphomas and reticuloendothelial neoplasms	1590	96.4 (93.1–97.3)	94.0 (90.8–96.2)
IIa. Hodgkin lymphoma	*607*	*97.8 (92.7–99.4)*	*97.4 (92.1–99.5)*
IIb. Non-Hodgkin lymphoma (except Burkitt lymphoma)	*499*	*89.4 (81.5–94.1)*	*85.8 (77.2–91.4)*
IIc. Burkitt lymphoma	*314*	*96.5 (89.1–99.0)*	*95.4 (87.0–98.7)*
III. CNS and miscellaneous intracranial and intraspinal neoplasms	3097	75.4 (72.4–78.2)	72.7 (69.5–75.7)
IIIa. Ependymoma and choroid plexus tumour	*300*	*77.6 (66.9–85.3)*	*74.1 (62.3–82.7)*
IIIb. Astrocytoma	*1465*	*81.8 (77.4–85.4)*	*80.1 (75.5–83.9)*
IIIc. Intracranial and intraspinal embryonal tumours	*465*	*58.1 (50.1–65.3)*	*52.0 (43.5–59.8)*
IIId. Other gliomas	*298*	*54.5 (44.3–63.6)*	*50.8 (40.4–60.2)*
IV. Neuroblastoma and other peripheral nervous cell tumours	822	78.0 (72.0–82.9)	76.4 (70.2–81.5)
V. Retinoblastoma	416	99.1 (92.7–100)	98.1 (91.3–99.9)
VI. Renal tumours	789	94.0 (89.6–96.6)	92.9 (88.0–95.9)
VII. Hepatic tumours	196	84.7 (71.6–92.1)	79.8 (65.3–88.9)
VIIa. Hepatoblastoma	*180*	*88.8 (75.0–95.3)*	*83.4 (67.9–92.0)*
VIII. Malignant bone tumours	532	70.6 (62.2–77.5)	69.3 (60.7–76.3)
VIIIa. Osteosarcoma	*234*	*54.4 (41.0–66.0)*	*52.8 (39.4–64.6)*
VIIIc. Ewing tumour and related sarcomas of bone	*254*	*83.1 (71.5–90.4)*	*81.9 (69.9–89.5)*
IX. Soft tissue and other extraosseous sarcomas	765	71.4 (64.8–77.0)	70.5 (63.8–76.3)
IXa. Rhabdomyosarcoma	*370*	*74.5 (64.8–81.9)*	*73.4 (63.3–81.1)*
X. Germ cell tumours, trophoblastic tumours and neoplasms of gonads	606	98.9 (94.9–99.9)	98.3 (93.5–99.8)
XI. Other malignant epithelial neoplasms and malignant melanomas	769	96.2 (91.6–98.4)	94.6 (89.3–97.4)
XId. Malignant melanoma	*293*	*94.9 (80.1–98.9)*	*91.8 (79.2–97.2)*

Abbreviations: CI, confidence interval; ICCC-3, International Classification of Childhood Cancers, version 3.
[a]Survival was calculated using the period method, with the 'at-risk' window from 1 January 2014 to 31 December 2018.
[b]'*n*' refers to the total number of children who contributed to the survival estimate.

Eligible patients in the current study were diagnosed from 1994 onwards and remained alive for at least some part of the 'at-risk' window from 1 January 2014 to 31 December 2018. The same 'at-risk' window was used for the estimation of 10- and 20-year relative survival. Survival time was censored at date of death, 10 or 20 years from date of diagnosis (depending on the estimate being calculated) or 31 December 2018, whichever occurred first.

3 | RESULTS

A total of 14,353 childhood cancer patients contributed to the survival estimates, including 7818 males (54%). Median age at diagnosis was 5 years. Children with leukaemia comprised one third of eligible patients (n = 4731, 33%), followed by tumours of the central nervous system (n = 3097, 22%) and lymphoma (n = 1590, 11%).

Relative survival for all childhood cancers combined was 85.4% (95% confidence interval [CI] = 84.2%–86.5%) after 10 years and 83.8% (95% CI = 82.6%–85.0%) after 20 years. Survival rates were lowest for children with intracranial and intraspinal embryonal tumours (mostly medulloblastoma), other gliomas or osteosarcoma, among whom 20-year relative survival was approximately 50% (Table 1). In contrast, 20-year relative survival exceeded 95% for those diagnosed with Hodgkin lymphoma, Burkitt lymphoma, retinoblastoma or germ cell tumours.

There was little difference between 10- and 20-year relative survival within most types of childhood cancer (Table 1). The biggest ongoing decrease in survival was reported for children with intracranial and intraspinal embryonal tumours or hepatoblastoma; for these two diagnostic subgroups, survival between 10 and 20 years after diagnosis was estimated to decrease from 58.1% (50.1%–65.3%) to 52.0% (43.5%–59.8%) and from 88.8% (75.0%–95.3%) to 83.4% (67.9%–92.0%), respectively.

4 | DISCUSSION

Results from the current study indicate that survival following a diagnosis of childhood cancer continues to slowly decrease up to 20 years after diagnosis for most types of cancer. Cancers with lower 5-year survival[7] tended to be the same ones where longer term survival declined the most, particularly for certain types of brain and liver tumours in children.

Fear of cancer recurrence is very real among survivors of childhood cancer,[8] with a recent Canadian study showing that over 40% of a sample of survivors expressed concern about this possibility and around 20% reported fear of recurrence to their clinical team on a regular basis.[9] It has also been associated with worse health-related quality of life among parents of survivors.[10] In addition, 5-year survivors of childhood cancer have been shown to experience more than a four-fold increased risk of non-cancer disease-related death compared to other people matched by age and sex, with a higher risk among patients who received more intensive treatment.[3]

Current literature on population-based long-term survival following childhood cancer is limited. Ten-year observed survival for all patients combined has been estimated at 82% in Canada (2013–2017, for ages 0–14),[11] 81% in France (2000–2015, for ages 0–14)[12] and 80% in the Netherlands (2010–2015, for ages 0–17),[13] compared to the 85% relative survival reported here for Australia (2014–2018, for ages 0–14). The reason for the higher overall survival in Australia compared to these other high-income countries is unknown. This may reflect a real difference in outcomes; however, the different time periods covered, differing methodologies and different mix of cancers (with a higher proportion of melanoma in Australia) make direct comparisons difficult.

Most studies on childhood cancer survival do not report 20-year estimates, underlining the value of our longer term results. A comparison of the current results against previous estimates of 20-year relative survival from the ACCR[14] show an increase for all childhood cancers combined, from 75% for prevalent cases between 1997 and 2006 compared to 84% for the current period (2014–2018). Some of the largest improvements in 20-year survival between the current and previous results in Australia are observed for lymphoid leukaemia (from 80% to 91%) and neuroblastoma (from 64% to 76%).

Annual matching with the National Death Index is a strength of the ACCR and allows for accurate long-term follow-up. Because survival is calculated cumulatively, with the estimate after year 1 feeding into the estimate for year 2 and so on, longer term survival may be unduly influenced by patients diagnosed many years previously. The period method better reflects temporal survival by focusing on patients diagnosed more recently.

Deaths that occur overseas will not be captured in the data; however, these are likely to be few. International immigration is likely to have a larger effect on long-term survival estimates compared to the traditional 5-year survival estimates, but we are not able to quantify the impact. Increasing the 'at-risk' window would allow for more patients to be included in the calculations leading to greater precision, but comes with the drawback of including cases diagnosed in an earlier time period, hence hindering the recency of the estimation process.

In summary, relative survival following childhood cancer in Australia generally remained high up to 20 years following diagnosis, although survival continued to decline throughout this period for some types of brain and liver tumours. With the possibility of delayed recurrence being a concern for many childhood cancer survivors and their families, these contemporary estimates of long-term survival provide an accurate picture that may assist childhood cancer patients and their families in planning for the future.

ACKNOWLEDGEMENTS

The authors wish to thank Leisa O'Neill, Chloe Henshaw, Leanne Keeley and Anne Currell for their work in the Australian Childhood Cancer Registry. We also acknowledge the assistance of staff at all Australian State and Territory Cancer Registries, the Australian Institute of Health and Welfare and the Medical Records Department at each of the major paediatric oncology treating hospitals throughout Australia.

Open access publishing facilitated by Griffith University, as part of the Wiley - Griffith University agreement via the Council of Australian University Librarians.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

DATA AVAILABILITY STATEMENT

Unit record data that support the findings of this study are not publicly available through the Australian Childhood Cancer Registry due to privacy and ethical restrictions but may be requested directly from the state and territory data custodians (subject to ethical approval). Please contact statistics@cancerqld.org.au for further details.

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How to cite this article: Youlden DR, Baade PD, Aitken JF. Long-term childhood cancer survival in Australia using period estimation. *Pediatr Blood Cancer*. 2023;70:e30136. https://doi.org/10.1002/pbc.30136