



How physically active do Australian and New Zealander childhood cancer survivors perceive themselves? A report from the ANZCHOG survivorship study

David Mizrahi^{a,b,*}, Joanna E. Fardell^{b,c}, Claire E. Wakefield^{b,c}, David Simar^a, Ann M. Maguire^{d,e}, Gill Hubbard^f, Richard J. Cohn^{b,c}, on behalf of the ANZCHOG survivorship study group

^a School of Medical Sciences, UNSW Medicine, UNSW Sydney, Australia

^b Behavioural Sciences Unit, Kids Cancer Centre, Sydney Children's Hospital, Sydney, Australia

^c School of Women's and Children's Health, UNSW Medicine, UNSW Sydney, Australia

^d Institute of Endocrinology and Diabetes, The Children's Hospital at Westmead, Sydney, Australia

^e Discipline of Child and Adolescent Health, Sydney Medical School, The University of Sydney, Sydney, Australia

^f Department of Nursing, Centre for Health Sciences, University of the Highlands and Islands, Inverness, United Kingdom

ARTICLE INFO

Keywords:

Exercise
Physical activity
Radiotherapy
Chemotherapy
Survivorship
Complementary medicine

ABSTRACT

Purpose: Childhood cancer survivors are at risk of treatment late-effects. Physical activity represents a necessary complementary therapy and modifiable risk-factor across all ages for many cardio-metabolic late-effects. This study assessed perceived physical activity in Australian and New Zealander childhood cancer survivors.

Methods: We recruited parents of survivors aged < 16 years, and adult survivors of childhood cancer aged ≥ 16 years, ≥ 5 years since diagnosis, with age-matched controls for comparison. We compared perceived moderate-vigorous physical activity between survivors and controls, using regression to identify associations with physical activity.

Results: We recruited 914 participants (570 childhood cancer survivors and 344 age-matched controls). Parents of survivors perceived more moderate-vigorous physical activity than child controls (248 ± 218 , 95% Confidence Interval (CI) = 218–280 vs 185 ± 214 min/week, 95% CI = 144–225, $p = 0.036$), with no perceived difference between adult survivors and controls (125 ± 152 , 95% CI = 108–140 vs 160 ± 201 min/week, 95% CI = 132–187, $p = 0.477$). Twenty-seven percent of child survivors (vs. 14.5% controls) and 30% of adult survivors (vs. 39.4% controls) met recommendations. Adult survivors who received radiotherapy (OR = 0.585, 95% CI = 0.343–0.995, $p = 0.048$) or not completed university (OR = 1.808, 95% CI = 1.071–3.053, $p = 0.027$) were less likely to meet recommendations.

Conclusions: Over two-thirds of Australian and New Zealander childhood cancer survivors across all ages are perceived to not meet physical activity recommendations. Adult survivors who had radiotherapy or did not complete university appeared at-risk for low physical activity.

Practical implications: Physical activity is important for everyone, but critical among childhood cancer survivors due to increased late cardio-metabolic risks. Monitoring survivors' perceived but also objectively measured physical activity as complementary to routine care is warranted, to provide education and motivate survivors to take control of their health.

1. Introduction

Advances in cancer treatment and supportive care have contributed to increasing survival rates among childhood cancer survivors (CCS),

with over 80% becoming five-year survivors.¹ Late-effects of treatment are common, with nearly all CCS experiencing at least one chronic health condition in adulthood.² Up to 20% of CCS develop cardiomyopathy 15–20 years after anthracycline treatment.³ Survivors of

Abbreviations: ANZCHOG, Australia and New Zealand Children's Haematology and Oncology Group; UNSW, University of New South Wales; HREC, Human Research Ethics Committee; POWH, Prince of Wales Hospital; CCS, Childhood cancer survivor; MVPA, Moderate to vigorous physical activity; BMI, Body mass index; STROBE, Strengthening the Reporting of Observational Studies in Epidemiology; ANOVA, Analysis of Variance

* Corresponding author at: Behavioural Sciences Unit, Kids Cancer Centre, Sydney Children's Hospital, Level 1 South Wing, Randwick, NSW, 2031, Sydney, Australia.

E-mail address: D.Mizrahi@unsw.edu.au (D. Mizrahi).

<https://doi.org/10.1016/j.ctim.2019.04.020>

Received 12 February 2019; Received in revised form 24 April 2019; Accepted 24 April 2019

Available online 25 April 2019

0965-2299/ © 2019 Elsevier Ltd. All rights reserved.

childhood cancer treated with radiotherapy over the heart are twice as likely to develop cardiac morbidity compared with the general population.⁴ In addition, 34% of adult CCS experience metabolic syndrome,⁵ with a recent study reporting the incidence of overweight and obesity at 37% in adult female and 61% in adult male CCS.⁶ Cancer treatment and co-morbidities can contribute to 5–15 times increased risk of developing cardiovascular disease compared with the general population.⁷ This is concerning given that cardiovascular disease is the leading non cancer-related cause of morbidity and mortality among CCS.⁸

In the general population, physical activity is a strong predictor for cardiovascular disease, cancer and mortality.⁹ Among adult cancer survivors, participation in physical activity can reduce cancer recurrence risk and mortality.¹⁰ Survivors of adult cancers who exercise experience improved physical well-being, psychological function, and quality of life compared with survivors who did no physical activity.¹¹ Evidence among CCS suggests young survivors who exercise regularly after treatment may improve their cardiorespiratory fitness,¹² body composition,¹³ muscular strength,¹⁴ and flexibility.¹⁴ These changes may mitigate risks associated with developing metabolic syndrome and cardiovascular disease, compared with survivors who do less physical activity.^{15–18,6}

Based on this evidence surrounding physical activity, the Australian Government recommends children (420 min) and adults (150 min) achieve sufficient moderate-vigorous physical activity (MVPA) each week.¹⁹ Despite the importance of maintaining physical activity during survivorship, there is limited research investigating physical activity among Australian and New Zealander CCS. Concerningly, this could be further compounded as healthy Australian and New Zealander children reported less physical activity (D- rating) compared with children from other high-income countries (C- average rating).²⁰ Adult CCS appear less likely to meet physical activity recommendations than their healthy siblings,²¹ with treatment-related side-effects including fatigue commonly reported barriers to initiating or maintaining physical activity.²² Reduced physical activity among acute lymphoblastic leukemia survivors contributed to increased body-fat percentage and reduced cardiovascular fitness.²³ Childhood cancer survivors may experience decreased ability to exercise due to their accumulating burden of treatment late-effects. The late-effects burden on younger and older CCS may differ due to the evolution of treatment protocols over time impacting on future cardiometabolic risk due to exposure to different agents.²⁴

Increased understanding of the associations with physical activity could allow doctors and exercise professionals to educate individuals who are at increased risk of not meeting these recommendations. A review focusing on child and adult CCS showed younger white males, with an education above high-school level were more likely to exercise.²⁵ However, survivors who were overweight or underweight, smoked, and had poor diets were less likely to meet physical activity recommendations.²⁵ Further, survivors who have been shown to have a fear of recurrence are more likely to engage in positive rather than negative lifestyle changes.²⁶ While this data is useful, there is a dearth of literature on the levels and predictors of perceived physical activity across the CCS population, especially across age groups covering early through to very long-term survivorship. There is also minimal data on perceived physical activity levels in child and adult Australian and New Zealander CCS.

We therefore aimed to 1) assess perceived physical activity levels in long-term Australian and New Zealander CCS across all ages and establish whether these levels differed compared with age-matched controls, and 2) investigate whether perceived physical activity differed across age groups. We finally aimed to 3) investigate the impact of clinical and sociodemographic associations for whether survivors met the Australian Government's physical activity recommendations.

2. Methods

2.1. Participants

We recruited CCS diagnosed with any cancer ≤ 16 years, ≥ 5 years after diagnosis, completed treatment, and in remission for the larger ANZCHOG Survivorship Study²⁷, with data extracted for this research paper. Participants' ≥ 18 years at the time of the study completed questionnaires themselves, whilst parents of children aged < 16 participated on their behalf. For participants aged 16–18 years, invitation letters were addressed to themselves and their parents, with the decision of who participated made by the family. We recruited a control group where participants chose to 'opt-in', which was randomly group matched to the CCS group on age and rurality, including adults aged ≥ 16 years and parents with a child aged 7–16 years. Exclusion criteria for all participants was not being proficient in English. Exclusion criteria for the control group included caring for a child with a history of cancer (for parents) and being a survivor of childhood cancer (for adults).

We identified eligible participants through medical records of 11 paediatric hospitals in Australia and New Zealand. We mailed consent forms, information sheets, questionnaires, and reply-paid envelopes, or gave participants the option to complete the questionnaire online. We followed up non-respondents with a phone call after four weeks, for a maximum of four attempts. We recruited community participants as controls online, advertising the study online (Pureprofile Pty. Ltd.), who were reimbursed approximately \$5AUD for participating. Control recruitment was 'opt-in', which excluded the possibility for calculating the control response rate.

The study was approved by human research ethics committees for each hospital and UNSW Sydney (HREC/12/POWH/345), which was endorsed by Australian and New Zealand Children's Haematology Oncology Group. Informed consent was obtained from all participants.

2.2. Measures

2.2.1. Physical activity measures

We used the International Physical Activity Questionnaire²⁸ to quantify perceived physical activity. We modified the questionnaire to ask participants in a single-item, 'over the past week, how much time did you spend doing moderate or vigorous exercise?'. A single-item physical activity questionnaire has been shown to perform as well as short questionnaires in terms of reliability and concurrent validity.²⁹ We categorized participants into two groups: currently meeting physical activity recommendations, or not, according to The Department of Health (Australian Government; ≥ 420 min per week (min/week) of MVPA for children < 18 years old; and ≥ 150 min/week of MVPA for adults ≥ 18 years old).¹⁹

2.2.2. Clinical measures

Parents and survivors' self-reported initial cancer diagnosis, (categorized into hematological, solid, and brain tumours), treatment completion date, and treatment history (chemotherapy, radiotherapy, surgery and/or bone marrow transplantation). Previous history of cardiac issues was self-reported. We calculated body mass index (BMI, kg/m^2) from self-reported height (m) and weight (kg).

2.2.3. Socio-demographic measures

We asked parents and adult survivors to report the survivor's age and sex. We obtained residential postcode to determine rurality status using the Accessibility/Remoteness Index of Australia lookup tool³⁰ and Statistics New Zealand Data Service.³¹ Rurality status was classified as major city, inner regional, outer regional, remote, and very remote,

dichotomized into major city and regional/rural. Adult survivors and parents of survivors reported their annual household income and education, dichotomized to above or below \$60,000 AUD and completing university, respectively.

2.2.4. Health status

We asked adult survivors to complete a single-item regarding mobility from the EuroQol EQ-5D-5 L quality of life survey.³² Assessed on a 5-point scale, we assessed mobility (no problems, slight problems, moderate problems, severe problems, unable to walk), dichotomized into ‘no problems’ versus ‘problems’ in accordance with the EuroQol EQ-5D-5 L scoring instructions if the number of reported problems was low.³² We asked parents and adult participants whether they worried about late-effects and cancer recurrence on a 5-point scale (‘not at all’ to ‘a great deal’), dichotomized into ‘not worrying’ versus ‘worrying’.

2.3. Data management and statistical analyses

We aligned reporting with the ‘Strengthening the Reporting of Observational Studies in Epidemiology’ (STROBE) statement for cross-sectional research. We performed statistical analyses using SPSS Version 24.0 (IBM Corp., New York). For question 1, we compared child and adult survivor participants with control and non-participant demographics using Chi-squared tests for categorical and independent sample t-tests for continuous variables. We truncated perceived physical activity data at 1260 min/week, according to the International Physical Activity Questionnaire.²⁸ We controlled for significant differences in demographic and outcome data when comparing perceived physical activity in survivors and controls. For question 2, we examined differences in perceived physical activity across different age groups (i.e. puberty phases and young adulthood) by conducting a two (cancer x control) by six (ages 7–11 × 12–16 × 16–20 × 21–30 × 31–40 × ≥41) analysis of variance with mean physical activity as the outcome. Post-hoc contrasts were conducted using Bonferroni correction. We used simple regression to determine mean differences in perceived physical activity between age groups when there was a significant group interaction. For question 3, we used binary logistic regression to identify clinical (cancer type, treatment, time since treatment), socio-demographic (age, sex, income, education, rurality) and outcome (mobility, past cardiac issues, BMI, health status, worry about late-effects and recurrence) associations for whether child and adult survivors met physical activity recommendations. Variables with $p < 0.2$ in the univariate analysis were included in the multivariable model. Variables with $p < 0.05$ in the multivariable model were considered significant. We used backwards stepwise regression to eliminate coefficients that did not contribute significantly to the model. We excluded cases with missing data from the regression analysis, and missing physical activity data from all analyses.

3. Results

3.1. Participant characteristics

We invited 2590 survivors (735 parents, 1855 adult survivors) and had 344 controls opt-in (111 parents, 233 adults) between May 2013 and February 2016. We were unable to contact 432 survivors, while 1320 received the questionnaire but did not complete it, 18 were ineligible, and 3 were reported as deceased. Of the remaining 709 eligible survivors, 108 declined for a total of 570 CCS included (Supplementary Fig. 1; response rate of contactable parents of child survivors and adult survivors = 80%, with an overall response rate = 27%). The final sample for analysis included 914 participants (Table 1). The four participant groups included:

1) 192 parents of CCS (child mean age = 12.9 ± 2.3 years, age at diagnosis = 4.5 ± 1.9 years, 8.5 ± 2.7 years since treatment; Table 2), 2) 378 CCS (mean age = 26.2 ± 7.6 years, age at diagnosis = 9.2 ± 5.0 years, 17.0 ± 7.9 years since treatment), 3) 111

parents of child controls (child mean age = 12.3 ± 2.7 years), and 4) 233 adult controls (mean age = 27.2 ± 8.8 years)

Among child survivors, participants and non-participants did not differ by sex (43.8% vs. 49.2% female, $p = 0.210$), age at study (12.9 ± 2.3 vs. 12.8 ± 2.3 years, $p = 0.527$), time since diagnosis (10.4 ± 2.3 vs. 10.1 ± 2.3 years, $p = 0.782$), or diagnosis ($p = 0.667$). Among adult CCS, participants were more likely to be female (55.9% vs. 48.7%, $p = 0.015$), older (26.1 ± 7.6 vs. 24.3 ± 6.2 years, $p < 0.001$), and further from diagnosis (19.2 ± 8.1 vs. 17.6 ± 6.8 years, $p < 0.001$) compared with non-participants, but did not differ by diagnosis ($p = 0.551$).

Parents’ reports showed that child survivors and controls did not differ by sex, mobility and BMI, with no difference in parental income (Table 1). Parents of child survivors had higher education levels than parents of controls ($p = 0.032$). Parents reported that child survivors had history of cardiovascular abnormalities ($p = 0.009$) compared with controls. Adult survivors of childhood cancer and controls did not differ by sex, education level, or BMI. Adult CCS had lower household income ($p < 0.001$), reduced mobility ($p < 0.001$), and history of cardiovascular abnormalities ($p = 0.003$) compared with controls.

3.2. Perceived physical activity levels of Australian and New Zealander survivors

Parents reported that child survivors participated in higher MVPA than controls (248.4 ± 217.6 , 95% Confidence Interval (CI) = 218–280 vs 184.8 ± 213.6 min/week, 95% CI = 144–225, $p = 0.036$; Fig. 1A). More child survivors met physical activity recommendations compared with controls (26.6%, 95% CI = 20–33, vs 14.5%, 95% CI = 8–21, $p = 0.016$; Fig. 1B).

Adult survivors did not differ in MVPA compared with controls (125.3 ± 151.8 , 95% CI = 108–140 vs 160.5 ± 200.7 min/week, 95% CI = 132–187, $p = 0.477$; Fig. 1C), meeting recommendations at a similar rate (30.4%, 95% CI = 26–35, vs 39.4%, 95% CI = 33–46 $p = 0.804$; Fig. 1D).

3.3. Investigating perceived physical activity levels across age groups

With a 2-way ANOVA, there was no effect of group on perceived physical activity ($p = 0.965$), however there was an age effect ($p < 0.001$), and a significant interaction ($p = 0.010$) (Fig. 2). Therefore, we conducted two post-hoc contrasts to compare children vs adults (ages 7–16 vs > 16) and the child age groups (7–11 vs 12–16) across physical activity. Mean perceived physical activity was lower in adults compared with children ($p = 0.001$), however the magnitude of this difference was greater for CCS ($p = 0.006$). Perceived physical activity was lower in all adolescents compared with younger children ($p = 0.015$), however after Bonferroni correction, this was not significant. There was no interaction between cancer survivors and controls ($p = 0.137$), suggesting an absence of differences in physical activity between child and adolescent survivors and controls. Taken together, these results suggest that the high perceived physical activity level achieved in childhood by survivors (ages 7–11 = 289.8 ± 257.9 , ages 12–16 = 233.4 ± 199.9 min/week), compared with controls, was reduced in older survivors (ages 16–20 = 148.4 ± 206.5 , ages 21–30 = 125.4 ± 133.7 , ages 31–40 = 104.1 ± 107.7 , ages $\geq 41 = 84.8 \pm 99.9$ min/week). A follow-up analysis for each decade of increasing age revealed that CCS reduced their perceived physical activity by 68 min/week/decade ($p < 0.001$), however there was no interaction for the physical activity reduction with age in controls ($p = 0.194$).

3.4. Associations for whether survivors met physical activity recommendations

At the univariate level, cancer type did not influence whether child

Table 1

Demographic and outcome differences using Chi-squared and independent sample t-tests between child and adult survivors of childhood cancer and age-matched controls.

| Variable | Children (parent-proxy) | | | Adults (self-reported) | | |
|---|-------------------------|------------|---------|------------------------|-------------|---------|
| | Survivors | Control | p-value | Survivors | Control | p-value |
| Sex, female n(%) | 84 (43.8) | 57 (51.4) | 0.201 | 212 (56.1) | 133 (57.1) | 0.809 |
| Age, n(%) | | | 0.621 | | | 0.456 |
| 7-11 | 52 (27.1) | 33 (29.7) | | | | |
| 12-16 | 140 (72.9) | 78 (70.3) | | | | |
| 16-30 | | | | 287 (75.9) | 183 (78.5) | |
| ≥ 30 | | | | 91 (24.1) | 50 (21.5) | |
| Annual household income ^a , n(%) | | | 0.063 | | | 0.000 |
| < \$59,999 | 43 (22.4) | 34 (30.6) | | 200 (52.9) | 77 (33.0) | |
| > \$60,000 | 132 (68.7) | 62 (55.9) | | 117 (31.0) | 105 (45.1) | |
| Prefer not to answer | 16 (8.3) | 15 (13.5) | | 53 (14.0) | 51 (21.9) | |
| Missing | 1 (0.5) | | | 8 (2.1) | | |
| Highest education level ^b , n(%) | | | 0.032 | | | 0.770 |
| No university | 110 (57.3) | 78 (70.3) | | 238 (62.9) | 153 (65.7) | |
| University degree | 80 (41.7) | 33 (29.7) | | 131 (34.7) | 80 (34.3) | |
| Missing | 2 (1.0) | | | 9 (2.4) | | |
| Rurality ^c , n(%) | | | 0.182 | | | 0.193 |
| Urban | 134 (69.8) | 91 (82.0) | | 277 (73.3) | 194 (83.3) | |
| Rural | 44 (22.9) | 20 (18.0) | | 74 (19.6) | 39 (16.7) | |
| Missing | 14 (7.3) | | | 27 (7.1) | | |
| Current mobility issues, n(%) | | | | | | 0.000 |
| No problems | | | | 276 (73.0) | 200 (85.8) | |
| Slight to severe problems | | | | 102 (27.0) | 33 (14.2) | |
| Past cardiac issues, n(%) | 18 (9.4) | 2 (1.8) | 0.009 | 50 (13.2) | 14 (6.0) | 0.003 |
| Missing | 7 (3.6) | | | 13 (3.4) | | |
| Body Mass Index (kg/m ²), mean (SD) | 20.4 (5.5) | 20.3 (4.9) | 0.793 | 24.47 (5.1) | 24.32 (6.5) | 0.754 |
| Missing/self-report error | 56 | 8 | | 36 | 2 | |

Chi-square value for categorical data, with t-value for continuous data.

^a Parent's income.^b Parent's education level.^c Rurality status dichotomized into urban and rural (inner regional, outer regional, remote and very remote).**Table 2**

Clinical information among child and adult survivors of childhood cancer.

| Variable | Child survivors (parent-reported) | Adult survivors (self-reported) |
|---|-----------------------------------|---------------------------------|
| Cancer Type, n(%) | | |
| Hematological tumours | 110 (57.3) | 217 (57.4) |
| Solid tumours | 71 (37.0) | 109 (28.8) |
| Brain tumours | 9 (4.7) | 48 (12.7) |
| Missing | 2 (1.0) | 4 (1.1) |
| Treatment ^a , n(%) | | |
| Chemotherapy (yes/no) | 182 (95.3) | 339 (89.4) |
| Missing | 1 (0.5) | 11 (2.9) |
| Radiotherapy (yes/no) | 50 (26.6) | 182 (48.0) |
| Missing | 22 (11.5) | 33 (8.7) |
| Surgery (yes/no) | 78 (41.1) | 173 (45.3) |
| Missing | 13 (6.8) | 39 (10.3) |
| Bone Marrow Transplant (yes/no) | 36 (18.7) | 66 (17.4) |
| Missing | 24 (12.5) | 56 (14.8) |
| Years since treatment completion, mean (SD) | 8.45 (2.7) | 16.99 (7.9) |
| Missing | 8 | 29 ^b |
| Worry about late-effects? Yes, n (%) | 174 (90.6) | 269 (71.7) |
| Missing | 1 (0.5) | 5 (1.3) |
| Worry about recurrence? Yes, n (%) | 170 (88.5) | 260 (68.8) |
| Missing | | 2 (0.5) |

^a Treatments are not mutually exclusive.^b Missing data due to participants being unable to recollect the month/year of their cancer treatment.

($\chi^2 = 2.49$, $p = 0.535$; Fig. 3A) and adult ($\chi^2 = 0.33$, $p = 0.847$; Fig. 3B) survivors met physical activity recommendations. Among child survivors, there was no difference in meeting physical activity

recommendations by treatment, including surgery ($\chi^2 = 0.84$, $p = 0.435$), chemotherapy ($\chi^2 = 2.08$, $p = 0.561$), radiotherapy ($\chi^2 = 1.41$, $p = 0.237$) and bone marrow transplant ($\chi^2 = 0.64$, $p = 0.424$; Fig. 3C). Adult survivors who received radiotherapy ($\chi^2 = 6.94$, $p = 0.008$) or bone marrow transplant ($\chi^2 = 4.47$, $p = 0.035$) were less likely to meet the recommendations, whereas surgery ($\chi^2 = 0.03$, $p = 0.859$) or chemotherapy ($\chi^2 = 1.40$, $p = 0.236$; Fig. 3D) had no impact.

Among child survivors, the multivariable model for associations for meeting physical activity recommendations was significant ($r^2 = 0.043$, $p = 0.019$). The model included the non-significant association of parental worry about recurrence (Supplementary Table 1; OR = 6.91, 95% CI = 0.87–54.55, $p = 0.067$). Among adult survivors of childhood cancer, the multivariable model was significant ($r^2 = 0.075$, $p = 0.001$). The model included history of radiotherapy (OR = 0.585, 95% CI = 0.343–0.995, $p = 0.048$) and completing university (OR = 1.808, 95% CI = 1.071–3.053, $p = 0.027$). The final factor in the model, receiving bone marrow transplant did not reach significance (OR = 0.489, 95% CI = 0.223–1.070, $p = 0.073$).

4. Discussion and conclusions

4.1. Discussion

In this study, we established that the majority of both child and adult survivors of childhood cancer from all paediatric oncology centres around Australia and New Zealand did not meet the Australian Government's physical activity recommendations. Parents perceived that child survivors participated in more physical activity than healthy age-matched controls. The low perceived physical activity achieved among adult CCS were not significantly different compared with controls. We found that the higher perceived physical activity level

Physical activity in childhood cancer survivors versus age-matched controls

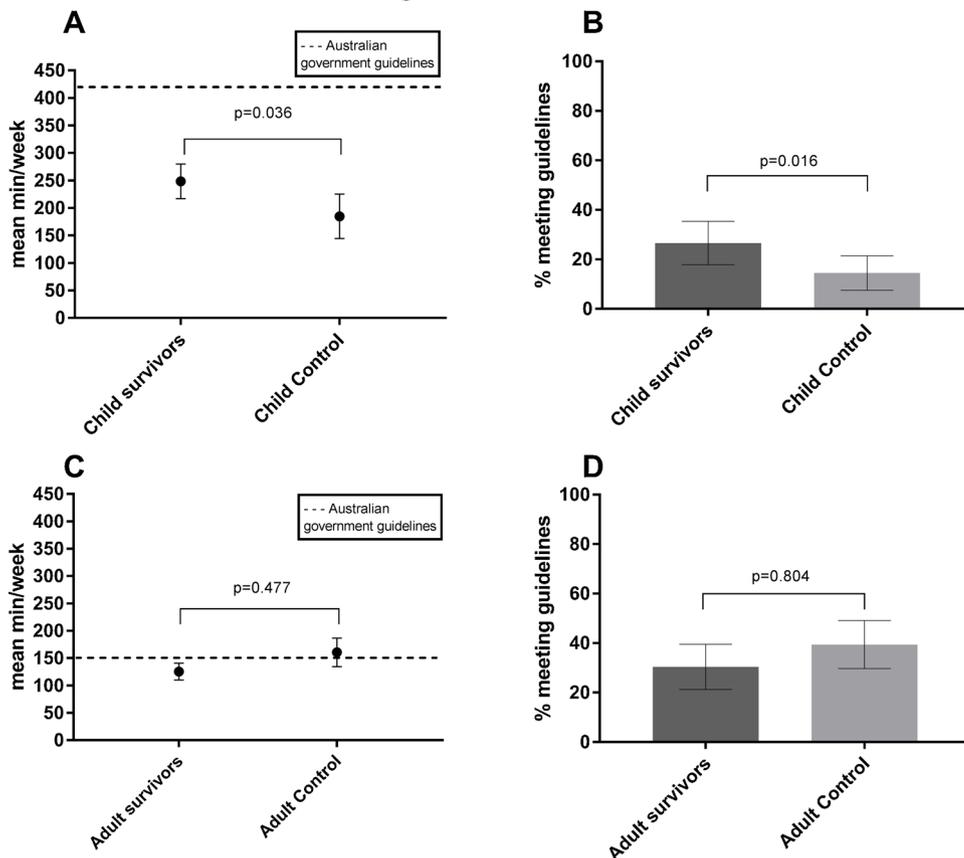


Fig. 1. (A) Moderate-vigorous physical activity weekly minutes (mean, 95% confidence interval) in child survivors of childhood cancer and age-matched controls. Grey line denotes physical activity recommendations according to guidelines (≥ 420 min/week). (B) The proportion of the entire cohort of child survivors of childhood cancer meeting the recommended physical activity guidelines compared with controls (bars indicate 95% confidence interval). Child data controlled for significant differences in education and cardiac co-morbidity history. (C) Moderate-vigorous physical activity weekly minutes (mean, 95% confidence interval) in adult survivors of childhood cancer and age-matched controls. Grey line denotes physical activity recommendations according to guidelines (≥ 150 min/week). (D) The proportion of the entire cohort of adult survivors of childhood cancer meeting recommended physical activity guidelines compared with controls (bars indicate 95% confidence interval). Adult data controlled for significant differences in income, mobility, and cardiac co-morbidity history. All graphs display means and 95% confidence interval.

observed in young survivors was lower in older age groups. We did not identify any predictors of physical activity among child survivors. Adult CCS who received radiotherapy, and who had not completed university were less likely to meet physical activity recommendations, highlighting two groups who may benefit from receiving education on the importance of improving their lifestyle.

Our study reported a smaller proportion of CCS meeting physical activity recommendations (27% of child and 30% of adult survivors)

compared with 55% of child and 44% of adult survivors of childhood cancer in America, with the investigators also indicating the need for lifestyle interventions among the CCS population.³³ Our control cohort was representative of the general population in terms of socio-demographics, with a similar proportion achieving recommended recommendations compared with other Australian adolescents (28%)³⁴ and adults (43%).³⁵ Due to the higher risk of late-effects experienced by CCS compared with the general population, it is imperative for

Physical activity by age in childhood cancer survivors and age-matched controls

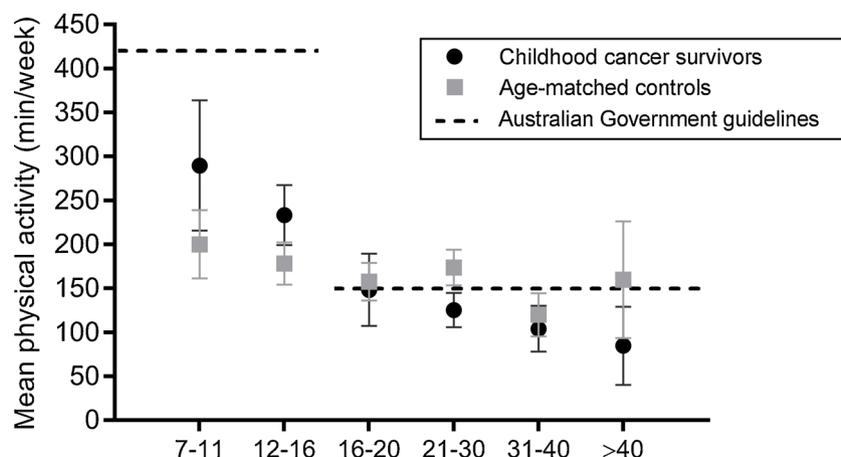


Fig. 2. Moderate-vigorous physical activity weekly minutes (mean, 95% confidence interval) in all childhood cancer survivors and controls. The lines at 420 min/week and 150 min/week represent the child and adult physical activity guidelines, respectively.

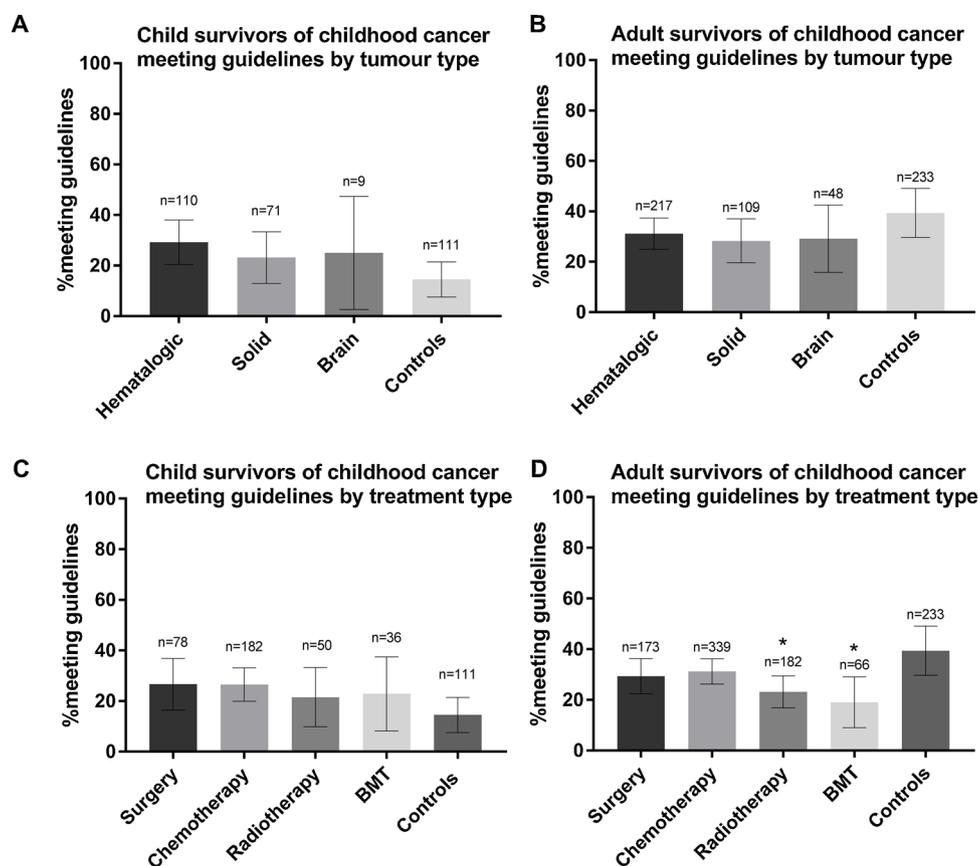


Fig. 3. The proportion of the survivor cohort meeting physical activity guidelines by tumour type in (A) children and (B) adults, and by treatment type in (C) children and (D) adult survivors of childhood cancer compared with controls (95% confidence interval). BMT = bone marrow transplant, * denotes $p < 0.05$.

survivors to be active as complementary to their usual care. Hence, survivors need to be educated appropriately to address this deficit.

Our study identified higher perceived physical activity achieved in childhood by survivors compared with controls. This finding was surprising given the potential cardiometabolic and neuromuscular impairments experienced by survivors, although could also be explained by the general population experiencing a screen-time and obesity epidemic.³⁶ Although parents of survivors may take a protectionist approach and over-perceive their child's ability simply because they are thriving post-treatment. The decline by 68 min/week/decade among CCS saw the high physical activity in childhood drop below the control data from age 16 onwards, suggesting a potential intervention point. There are several explanations for the reduced perceived physical activity among our adult survivors such as study, employment and family commitments. However, older survivors may experience more late-effects due to increasing incidence of mild-severe chronic health conditions as they age.³⁷ Further, older survivors may have been exposed to more intensive therapy regimens, with a smaller percentage of child survivors treated with radiotherapy in our cohort due to clinical practice changes (50.9% adults vs 29.6% children). These changes may consequently lead to a reduction in cardiovascular and metabolic risk factors for those who received cranial, thoracic or total body radiotherapy.^{5,4} Although not investigated in our study, the impact of field-specific radiotherapy on physical activity warrants investigation due to differences in late-effects that may impact survivors' ability to exercise. As cranial and total body irradiation is shown to have higher risk for developing metabolic⁵ or cardiac dysfunction,⁴ these co-morbidities could negatively contribute to CCS capacity to regularly exercise.

Radiotherapy or lower education was associated with not meeting physical activity recommendations in adult survivors in our study. If survivors and parents can be educated and motivated early in

survivorship to adopt healthy behaviours, they may bridge this lifestyle gap into survivorship. Identifying survivors at-risk for low physical activity will allow medical teams to educate, monitor and refer these survivors into programs earlier. This is vital to increase the proportion of survivors meeting recommendations, thereby minimising the risk of developing particular late-effects that may be intensified by inactivity. Our findings support previous research which indicated that older survivors have lower physical activity than younger survivors,²¹ with survivors from a lower socio-economic status and treated with cranial irradiation likely to have lower physical activity.³⁸ We dichotomised income by \pm AUD\$60,000 (USD\$43,000) which is the approximate median Australian salary,³⁹ yet socio-economic status may have different implications on physical activity around the world. Unlike the Ness study, we did not find obesity was a contributing factor.²¹ The Ness study was substantially larger than our cohort, however their results emphasise the broad range of clinical, socio-demographic and contextual differences across countries affecting physical activity. Further, our identification of adult survivors who have not completed university being at-risk of low physical activity was similarly identified in the general population in the Netherlands.⁴⁰ Finally, we found that parents worrying about cancer recurrence did not appear to motivate increasing physical activity in child survivors, although this has been found to promote health behaviour change in adult cancer survivors.²⁶ Although this neared significance, there was little variability in the outcome (i.e. over 90% were worried) that associations were attenuated.

In our cohort, both adult and child survivors self-reported a higher incidence of cardiac issues compared with controls. With known risks of late-effects among CCS, and the majority of our cohort not meeting physical activity recommendations, strategies are needed to increase regular physical activity participation. Issues such as cardiovascular

disease, cancer recurrence and early mortality have been shown to be minimized with increased physical activity across many adult cancers.⁴¹ However, it is uncertain whether physical activity can prevent the onset of cardiac late-effects induced by treatment in CCS, despite the emerging positive benefits. Consideration to monitor and motivate survivors without additional hospital visits is required, which would be especially useful for the substantial group in our cohort who lived rurally. Increasing use of technology has shown that health promotion interventions to improve physical and psychological health can be delivered away from the hospital setting, using telephone and internet to connect health professionals with survivors.⁴² This guidance may minimise the 68 min/week/decade reduction seen in our cohort with increasing age, whilst mitigating the risk of developing late-effects.³⁷

4.2. Limitations and strengths

Our study was limited by relying on perceived parent or self-reported, cross-sectional data, preventing clear causality conclusions, whilst control data were self-invited and may induce selection-bias. Perceived parent and self-reported physical activity allows for intensity misinterpretation also considering we did not provide examples of different intensity activities.⁴³ Further, it is also plausible that social-desirability or over-reporting induces bias,⁴⁴ whilst parents of survivors could over-perceive how active their child is compared with parents of children without history or cancer based on their child thriving post-treatment. To overcome this, future research should investigate at what age CCS can self-report on their own physical activity levels accurately. These potential biases could be eliminated by using objective measures (i.e. accelerometers). Our physical activity survey combined moderate and vigorous physical activity intensities, making direct comparisons to other studies separating these intensities difficult. The physical activity guidelines used in our study vastly differed in duration between children (420 min/week) and adults (150 min/week). Future guidelines should aim at addressing these limitations and investigate the possibility of a transition phase during adolescence (e.g. progressively decreasing to 150 min/week). Our study was over-represented with leukemia survivors (57% vs 34%) and under-represented with brain tumour survivors (10% vs 23%) compared with the general Australian survivor population,⁴⁵ whilst the response rate (27%) may limit generalisability of the findings. The strengths of this study include containing the largest sample assessing perceived physical activity across survivors of all paediatric oncology centres in Australia/New Zealand. We also compared to an age- and gender-matched control group. Finally, we investigated both young survivors and older survivors to obtain data and specific challenges that survivors may experience in the formative years and later in life. We believe these strengths outweigh the limitations in providing informative information to identify survivors at-risk of not achieving physical activity recommendations.

4.3. Conclusions

We established that the majority of Australian and New Zealander survivors of childhood cancer do not meet the Australian Government's physical activity recommendations. While parents perceived child survivors participate in more physical activity than controls, this advantage appears to be reduced when survivors perceive their physical activity in adulthood. Adult survivors who received radiotherapy, or have not completed university are at increased risk of not being sufficiently active, suggesting the need for closer assessment of their physical activity during clinic visits. This provides opportunities for monitoring, education and motivation to help survivors work towards recommended guidelines. Due to increased risk of late-effects including obesity, metabolic syndrome and cardiovascular disease, it is more critical for survivors to participate in physical activity as a complementary therapy compared with the general population. To ensure the highest likelihood that a healthy lifestyle will be maintained long-

term, medical teams and exercise professionals should educate survivors at each opportunity about how to safely exercise, with the importance for long-term health.

Ethics approval and consent to participate

This study received ethics approval from human research ethics committees for each participating hospital and UNSW Sydney (HREC/12/POWH/345), obtained informed consent from all participants and was conducted in accordance with the Declaration of Helsinki.

Consent for publication

All participants information is de-identified in this study.

Conflict of interest

The authors declare that they have no conflict of interest.

Funding

The Behavioural Sciences Unit at Sydney Children's Hospital is supported by the Kids with Cancer Foundation. The Behavioural Sciences Unit's survivorship research program is funded by Kids Cancer Alliance, The Kids' Cancer Project and a Cancer Council NSW Program Grant (PG16-02) with the support of the Estate of the Late Harry McPaul. David Mizrahi is supported by the Research Training Scheme. Joanna Fardell is supported by the Kids' Cancer Project. Claire Wakefield is supported by a Career Development Fellowship from the National Health and Medical Research Council of Australia (APP1067501).

Authors' contributors

DM was responsible for the cleaning and analysis of the data, preparing the figures and tables. JEF contributed extensively to the statistical analysis plan, preparing the figures and tables. CEW and RJC were responsible for the conception of the study, and data collection. All authors were responsible for writing and editing the manuscript.

***The members of the ANZCHOG Survivorship Study Group in alphabetical order:** Dr Frank Alvaro, Prof Richard Cohn, Dr Rob Corbett, Dr Peter Downie, Ms Karen Egan, Ms Sarah Ellis, Prof Jon Emery, Dr Joanna Fardell, Ms Tali Foreman, Dr Melissa Gabriel, Prof Afaf Girgis, Ms Kerrie Graham, Ms Karen Johnston, Dr Janelle Jones, Dr Liane Lockwood, Dr Ann Maguire, Dr Maria McCarthy, Dr Jordana McLoone, Dr Françoise Mechinaud, Ms Sinead Molloy, Ms Lyndal Moore, Dr Michael Osborn, Ms Christina Signorilli, Dr Jane Skeen, Dr Heather Tapp, Ms Tracy Till, Ms Jo Truscott, Ms Kate Turpin, Prof Claire Wakefield, Dr Thomas Walwyn, Ms Jane Williamson, and Ms Kathy Yallop.

Acknowledgements

We thank the participants and their parents for participating in this study, as well as all of the participating sites. We also thank Emma Doolan for her assistance with the statistical analysis. A sub-analysis of this research has been presented in 2017 as an oral presentation at the Clinical Oncology Society of Australia, Sydney, Australia, and as a poster presentation at the American College of Sports Medicine in Denver, United States.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.ctim.2019.04.020>

References

- Smith MA, Seibel NL, Altekruse SF, et al. Outcomes for children and adolescents with cancer: Challenges for the twenty-first century. *J Clin Oncol*. 2010;28(15):2625–2634. <https://doi.org/10.1200/jco.2009.27.0421>.
- Bhakta N, Liu Q, Ness KK, et al. The cumulative burden of surviving childhood cancer: An initial report from the St Jude Lifetime Cohort Study (SJLIFE). *Lancet (London, England)*. 2017;390(10112):2569–2582. [https://doi.org/10.1016/S0140-6736\(17\)31610-0](https://doi.org/10.1016/S0140-6736(17)31610-0).
- Mulrooney DA, Yeazel MW, Kawashima T, et al. Cardiac outcomes in a cohort of adult survivors of childhood and adolescent cancer: Retrospective analysis of the Childhood Cancer survivor Study cohort. *BMJ*. 2009;339. <https://doi.org/10.1136/bmj.b4606>.
- Mertens AC, Yasui Y, Neglia JP, et al. Late mortality experience in five-year survivors of childhood and adolescent cancer: The Childhood Cancer survivor Study. *J Clin Oncol*. 2001;19(13):3163–3172.
- Nottage KA, Ness KK, Li C, Srivastava D, Robison LL, Hudson MM. Metabolic syndrome and cardiovascular risk among long-term survivors of acute lymphoblastic leukaemia - from the St. Jude Lifetime Cohort. *Br J Haematol*. 2014;165(3):364–374. <https://doi.org/10.1111/bjh.12754>.
- Warner EL, Fluchel M, Wright J, et al. A population-based study of childhood Cancer survivors' body mass index. *J Cancer Epidemiol*. 2014;2014:531958. <https://doi.org/10.1155/2014/531958>.
- Chow EJ, Chen Y, Kremer LC, et al. Individual prediction of heart failure among childhood cancer survivors. *J Clin Oncol*. 2015;33(5):394–402. <https://doi.org/10.1200/jco.2014.56.1373>.
- Lipshultz SE, Adams JM. Cardiotoxicity after childhood cancer: Beginning with the end in mind. *J Clin Oncol*. 2010;28(8):1276–1281. <https://doi.org/10.1200/jco.2009.26.5751>.
- Hu FB, Willett WC, Li T, Stampfer MJ, Colditz GA, Manson JE. Adiposity as compared with physical activity in predicting mortality among women. *N Engl J Med*. 2004;351(26):2694–2703. <https://doi.org/10.1056/NEJMoa042135>.
- Holmes MD, Chen WY, Feskanich D, Kroenke CH, Colditz GA. Physical activity and survival after breast cancer diagnosis. *JAMA*. 2005;293(20):2479–2486. <https://doi.org/10.1001/jama.293.20.2479>.
- Mishra SL, Scherer RW, Geigle PM, et al. Exercise interventions on health-related quality of life for cancer survivors. *Cochrane Database Syst Rev*. 2012;8:CD007566. <https://doi.org/10.1002/14651858.CD007566.pub2>.
- Oldervoll LM, Kaasa S, Knobel H, Loge JH. Exercise reduces fatigue in chronic fatigued Hodgkins disease survivors—results from a pilot study. *Eur J Cancer (Oxford, England: 1990)*. 2003;39(1):57–63.
- Hartman A, et al. A randomized trial investigating an exercise program to prevent reduction of bone mineral density and impairment of motor performance during treatment for childhood acute lymphoblastic leukemia. *Pediatr Blood Cancer*. 2009;53(1):64–71. <https://doi.org/10.1002/psc.21942>.
- Marchese VG, Chiarello LA, Lange BJ. Effects of physical therapy intervention for children with acute lymphoblastic leukemia. *Pediatr Blood Cancer*. 2004;42(2):127–133. <https://doi.org/10.1002/psc.10481>.
- Jones LW, Liu Q, Armstrong GT, et al. Exercise and risk of major cardiovascular events in adult survivors of childhood hodgkin lymphoma: A report from the childhood cancer survivor study. *J Clin Oncol*. 2014;32(32):3643–3650. <https://doi.org/10.1200/jco.2014.56.7511>.
- Gibson TM, Ehrhardt MJ, Ness KK. Obesity and metabolic syndrome among adult survivors of childhood leukemia. *Curr Treat Options Oncol*. 2016;17(4):17. <https://doi.org/10.1007/s11864-016-0393-5>.
- Tonorezos ES, Jones LW. Energy balance and metabolism after cancer treatment. *Semin Oncol*. 2013;40(6):745–756. <https://doi.org/10.1053/j.seminoncol.2013.09.011>.
- Armstrong GT, Stovall M, Robison LL. Long-term effects of radiation exposure among adult survivors of childhood cancer: Results from the childhood Cancer survivor study. *Radiat Res*. 2010;174(6):840–850. <https://doi.org/10.1667/RR1903.1>.
- The Department of Health, Australian Government. *Australia's physical activity and sedentary behaviour guidelines*. 2017; 2017.
- Aubert S, Barnes JD, Abdeta C, et al. Global matrix 3.0 physical activity report card grades for children and youth: Results and analysis from 49 countries. *J Phys Act Health*. 2018;15(S2):S251–S273. <https://doi.org/10.1123/jpah.2018-0472>.
- Ness KK, Leisenring WM, Huang S, et al. Predictors of inactive lifestyle among adult survivors of childhood cancer: A report from the Childhood Cancer survivor Study. *Cancer*. 2009;115(9):1984–1994. <https://doi.org/10.1002/cncr.24209>.
- Clifford BK, Mizrahi D, Sandler CX, et al. Barriers and facilitators of exercise experienced by cancer survivors: A mixed methods systematic review. *Support Care Cancer*. 2018;26(3):685–700. <https://doi.org/10.1007/s00520-017-3964-5>.
- Warner JT. Body composition, exercise and energy expenditure in survivors of acute lymphoblastic leukaemia. *Pediatr Blood Cancer*. 2008;50(2 Suppl):456–461. <https://doi.org/10.1002/psc.21411> discussion 68.
- Schultz KR, Pullen DJ, Sather HN, et al. Risk- and response-based classification of childhood B-precursor acute lymphoblastic leukemia: A combined analysis of prognostic markers from the Pediatric Oncology Group (POG) and Children's Cancer Group (CCG). *Blood*. 2007;109(3):926–935. <https://doi.org/10.1182/blood-2006-01-024729>.
- Stolley MR, Restrepo J, Sharp LK. Diet and physical activity in childhood Cancer survivors: A review of the literature. *Ann Behav Med*. 2010;39(3):232–249. <https://doi.org/10.1007/s12160-010-9192-6>.
- Hawkins NA, Smith T, Zhao L, Rodriguez J, Berkowitz Z, Stein KD. Health-related behavior change after cancer: Results of the American Cancer society's studies of cancer survivors (SCS). *J Cancer Surviv*. 2010;4(1):20–32. <https://doi.org/10.1007/s11764-009-0104-3>.
- Vetsch J, Fardell JE, Wakefield CE, et al. "Forewarned and forearmed": Long-term childhood cancer survivors' and parents' information needs and implications for survivorship models of care. *Patient Educ Couns*. 2017;100(2):355–363. <https://doi.org/10.1016/j.pcc.2016.09.013>.
- Craig CL, Marshall AL, Sjostrom M, et al. International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc*. 2003;35(8):1381–1395. <https://doi.org/10.1249/01.mss.0000078924.61453.fb>.
- Milton K, Bull FC, Bauman A. Reliability and validity testing of a single-item physical activity measure. *Br J Sports Med*. 2011;45(3):203–208. <https://doi.org/10.1136/bjism.2009.068395>.
- ARIA lookup tool user guide [database on the Internet]. School of Psychology, The University of Sydney; 2012 Accessed:.
- Service SNZD. *Meshblock 2013*. 2015; 2015 (Accessed 13 March 2017). <https://datafinder.stats.govt.nz/layer/8347-meshblock-2013/data/>.
- Herdman M, Gudex C, Lloyd A, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res*. 2011;20(10):1727–1736. <https://doi.org/10.1007/s11136-011-9903-x>.
- Demark-Wahnefried W, Werner C, et al. Survivors of childhood cancer and their guardians. *Cancer*. 2005;103(10):2171–2180. <https://doi.org/10.1002/cncr.21009>.
- Ridgers ND, Timperio A, Crawford D, Salmon J. Validity of a brief self-report instrument for assessing compliance with physical activity guidelines amongst adolescents. *J Sci Med Sport*. 2012;15(2):136–141. <https://doi.org/10.1016/j.jsams.2011.09.003>.
- (ABS) ABoS. *Australian health survey: Physical activity, 2011-12*. ABS catalogue number 4364.0.55.004. 2013; 2013.
- LeBlanc AG, Katzmarzyk PT, Barreira TV, et al. Correlates of total sedentary time and screen time in 9–11 year-old children around the world: The international study of childhood obesity, lifestyle and the environment. *PLoS One*. 2015;10(6):e0129622. <https://doi.org/10.1371/journal.pone.0129622>.
- Oeffinger KC, Mertens AC, Sklar CA, et al. Chronic health conditions in adult survivors of childhood cancer. *N Engl J Med*. 2006;355(15):1572–1582. <https://doi.org/10.1056/NEJMsa060185>.
- Devine KA, Mertens AC, Whitton JA, et al. Factors associated with physical activity among adolescent and young adult survivors of early childhood cancer: A report from the childhood cancer survivor study (CCSS). *Psycho-oncology*. 2017. <https://doi.org/10.1002/pon.4528>.
- ATO. Office AGATed. *Australian government Australian taxation office: taxation statistics 2014-15*. 2018; 2018.
- Droomers M, Schrijvers CT, Mackenbach JP. Educational level and decreases in leisure time physical activity: Predictors from the longitudinal GLOBE study. *J Epidemiol Community Health*. 2001;55(8):562–568.
- Cormie P, Zopf EM, Zhang X, Schmitz KH. The impact of exercise on Cancer mortality, recurrence, and treatment-related adverse effects. *Epidemiol Rev*. 2017;39(1):71–92. <https://doi.org/10.1093/epirev/mxx007>.
- Mizrahi D, Wakefield CE, Fardell JE, et al. Distance-delivered physical activity interventions for childhood cancer survivors: A systematic review and meta-analysis. *Crit Rev Oncol Hematol*. 2017. <https://doi.org/10.1016/j.critrevonc.2017.08.008>.
- Götte M, Seidel CC, Kesting SV, Rosenbaum D, Boos J. Objectively measured versus self-reported physical activity in children and adolescents with cancer. *PLoS One*. 2017;12(2):e0172216. <https://doi.org/10.1371/journal.pone.0172216>.
- Bender JM, Brownson RC, Elliott MB, Haire-Joshu DL. Children's physical activity: Using accelerometers to validate a parent proxy record. *Med Sci Sports Exerc*. 2005;37(8):1409–1413.
- Baade PD, Youlden DR, Valery PC, et al. Trends in incidence of childhood cancer in Australia, 1983–2006. *Br J Cancer*. 2010;102(620) <https://doi.org/10.1038/sj.bjc.6605503>.