Health-related quality of life, fatigue and health behaviours in Australian adolescent and young adult cancer survivors.

Andrew Murnane[1, 2], Nicole Kiss[2, 3], Steve F Fraser[2] and Jeremy Lewin[1, 4, 5]

[1] ONTrac at Peter Mac Victorian Adolescent and Young Adult Cancer Service, Peter MacCallum Cancer Centre, Melbourne, Australia

[2] Deakin University, Institute for Physical Activity and Nutrition (IPAN), Geelong, Australia

[3] Allied Health Research, Peter MacCallum Cancer Centre, Melbourne, Australia

[4] Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia

[5] Sir Peter MacCallum Department of Oncology, The University of Melbourne, Parkville, Australia

Correspondence:

Andrew Murnane

ONTrac at Peter Mac Victorian Adolescent & Young Adult Cancer Service

Peter MacCallum Cancer Centre

305 Grattan St

Melbourne, VIC, 3000

T: +61 3 8559 6880| F: +61 3 8559 6229

E: Andrew.Murnane@petermac.org

- Abstract word count = 252 words
- Main text word count = 3695

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/pbc.29243.

- Short running title: Australian AYA cancer survivors health behaviours
- Key Words: Adolescent and young adult – Exercise – Diet – Quality of life – Fatigue
- Number of tables = 4 tables
- Number of figures = 1 figure
- Number of appendices (if applicable) = not applicable

Abbreviations:

AQoL-6D	The Assessment of Quality of Life-6D
AYA	Adolescent and Young Adult
FACIT-F	The Functional Assessment of Chronic Illness Therapy-Fatigue Scale
HR-QoL	Health Related Quality of Life
PA	Physical Activity
SF-36	Short Form 36v2

Meeting Abstract:

Murnane, A., et al., Diet quality, physical activity levels and other health behaviours in long-terms survivors of adolescent and young adult (AYA) cancer, in Clinical Oncology Society of Australia Annual Scientific Meeting 2019 (Adelaide), Asia-Pacific Journal of Clinical Oncology, Volume 15, Issue S9.

Abstract

Introduction:

Current knowledge of the long-term health behaviours and wellbeing of Adolescent and Yong Adult (AYA) cancer survivors is limited. The aim of this study was to evaluate the health behaviours of AYA cancer survivors compared to Australian normative data and describe their health-related quality of life (HR-QoL) and levels of fatigue.

Method:

A cross sectional online survey of participants aged 15-25 years at diagnosis and 2-7 years post-treatment completion was conducted at a comprehensive cancer centre. Validated questionnaires assessed health behaviours and functioning including current physical activity (PA) levels, diet quality, fatigue (FACIT-F) and HR-QoL (AQoL-6D, SF-36v2) was compared to Australian normative data.

Results:

Ninety individuals completed the survey (26% response rate) with a mean age of 25.4 years and median time post treatment of 61 months (24-85 months). Compared to normative data, a higher proportion of AYA cancer survivors were consuming the recommended daily serves of fruit and vegetables (16.7% vs 3.9%, $p<0.0001$), had a lower presence of overweight or obesity (46.7% vs 57.7%, $p=0.04$) and lower percentage of current smokers (2.2% vs 16.7%, $p<0.0001$). However, AYA cancer survivors reported increased fatigue ($t[df=596]=-4.1$, $p<0.0001$) and reduced HR-QoL

compared to normative data (t[df=533]=9.2, p<0.0001) along with a higher proportion suffering from one or more chronic health condition (65% vs 40%, p<0.0001).

Conclusion:

AYA cancer survivors from a single Australian institution, that were on average 5-years post-treatment, exhibited better health behaviours compared to Australian normative data, but still below recommended guidelines. However, they continue to experience issues with fatigue and reduced HR-QoL, especially in those not meeting the PA guidelines.

Introduction:

Approximately 1000 adolescent and young adults (AYA) aged 15-25 years are diagnosed with cancer each year in Australia [1]. Advances in cancer treatment and supportive care have led to serial improvements in five-year survival which now approaches 90% for the cohort [2]. The improving survival rate has resulted in an increasing number of AYA survivors living with the long-term consequences of cancer treatment and subsequent increased risk of morbidity and mortality [3, 4]. Compared to healthy peers, AYA cancer survivors are at increased risk of a number of chronic health conditions including cardiovascular disease, metabolic disease and secondary malignancies [2-12]. Alongside the significant physical morbidity experienced by AYA cancer survivors, there is also the psychosocial impact post treatment, with high rates of anxiety, depression, poorer mental health, impaired health related quality of life (HR-QoL) and ongoing fatigue [12-18].

The increased risk of chronic disease observed in AYA cancer survivors is hypothesized to be due to a number of factors, including pre-existing medical history, the direct effect of cancer treatment such as chemotherapy and radiotherapy, along with compounding health behaviours such as low levels of physical activity and poor dietary habits [3, 5, 6, 19-21]. Evidence more broadly suggests that cancer survivors who adopt healthy lifestyle behaviours following completion of cancer therapy (e.g. healthy dietary choices, regular physical activity, moderate alcohol consumption and smoking abstinence) have better health outcomes and in some tumour groups improved survival and decreased cancer recurrence [3, 22-24]. Therefore, understanding health behaviours that may contribute to these elevated risks is warranted.

Studies to date predominately undertaken in the USA, have identified that AYA cancer survivors (18-39 year age group) remain inactive post-treatment, consume diets low in fruits and vegetables, are overweight, regularly consume alcohol and continue to smoke [3, 25-32]. A paucity of research has examined the health behaviours of Australian AYA cancer survivors and in particular the 15-25 year age group [28, 33]. Also very little is known about the relationship between poor health behaviours and their potential impact on long-term HR-QoL or fatigue in AYA cancer survivors. Understanding the prevalence of these behaviours will support the development of targeted interventions to improve long-term health outcomes for AYA cancer survivors. The aim of this study was to explore physical activity levels, diet quality, fatigue and HR-QoL of AYA cancer survivors in a single Australian institution in comparison to Australian normative data.

Method:

Design and setting:

A cross sectional survey was undertaken within a single institution comprehensive cancer centre in Melbourne, Australia (Peter MacCallum Cancer Centre. Ethical approval was obtained via the local Human Research Ethics Committee (18/243L).

Patient population:

Eligibility criteria were as follows: aged 15-25 years at time of cancer diagnosis; referred to ONTrac at Peter Mac Victorian Adolescent and Young Adult Cancer Service (a specialist multidisciplinary state-wide cancer service, which focuses on supporting AYA with cancer, their families and healthcare professionals who provide

their care in Victoria, Australia); received their primary treatment at the Peter MacCallum Cancer Centre and still undergoing follow-up; and completed treatment between January 2011 and January 2017. Patients were excluded from the study if they were currently undergoing treatment for relapsed disease or those who had indicated previously that they did not wish to be contacted for research purposes.

Recruitment and assessment procedures:

Eligible participants were identified via the ONTrac at Peter Mac database and were mailed, or emailed (if available), a personalised invitation letter. The letter contained information regarding the purpose and requirements of the study along with a unique study code that allowed for data linkage with medical records. Those wishing to participate, completed the survey via REDCap [34]. The invitation letter and landing page of the online survey, informed participants that consent was assumed by completing the survey and that it would take approximately 30 minutes to complete. Fourteen days after the initial mail out, non-responders were sent a reminder letter to maximise response rates. Recruitment was undertaken between March and April 2019.

Measures:

Demographic questionnaire:

Participants completed a self-report demographic questionnaire that was developed for this study and adapted from previous work [33, 35]. Data collected included age, sex, marital status, highest education level obtained, current living arrangement, location of residence, comorbidities (classified as 0, 1-2, >3) and smoking status. Body mass index (BMI) was calculated from self-reported height and weight.

Physical activity:

The Godin leisure time exercise questionnaire (GLTEQ) assessed participant PA behaviour over the previous week [36-38]. Additional questions were added to GLTEQ to assess number of minutes/days of physical activity undertaken each week and to assess participation in resistance exercise. Based on Australian weekly PA recommendations, (with high intensity/vigorous weighted by two, participants were classified into four groups; sedentary, insufficiently active (0-149mins per week), partly meeting exercise guidelines (>149mins aerobic activity and <1 resistance training sessions per week) and sufficiently active (>149mins per week and >2 resistance training sessions per week) [38, 39].

Diet habits:

The rapid eating assessment for participants (REAP) was used to assess dietary intake and quality [40]. This validated survey contained 27 questions scored one to three to assess consumption of fruits and vegetables, fat, whole grains, calcium rich food, sodium, sugary drinks and foods, and alcohol intake [41].

Health related quality of life:

The SF-36v2 and The Assessment of Quality of Life-6D (AQoL-6D) were used to assess physical and mental health domains of health and wellbeing [42-44]. The SF-36v2 comprises eight health domains Physical Functioning (PF), Role Physical (RP), Bodily Pain (BP), General Health (GH), Vitality (VT), Social Functioning (SF), Role Emotion (RE) and Mental Health (MH)]. The eight scales can be combined into

summary measures providing overall estimates of physical health [Physical Component Score (PCS) and mental health [Mental Component Score (MCS)] and scores are reported as *T*-scores as per recommendation by Ware et al [45]. The SF-36v2 has been widely utilised for routine monitoring and assessment of HR-QoL with higher scores the less disability [43].

The AQoL is a multi-attribute utility instrument of 20 items organized into scales assessing the six domains of independent living, relationships, mental health, coping, pain and senses (seeing, hearing and communication) with a higher standardised score indicating better overall quality of life. The AQoL-6D version of this tool has been validated with adolescents and young adults in various healthcare settings [44, 46]. Both the SF-36v2 and AQoL-6D have been included as they each measure different domains of HR-QoL. The SF-36v2 has a greater emphasis upon physical dimensions, such as walking and the ability to work. The AQoL-6D has a relatively greater emphasis upon psychological and social dimensions such as depression/anxiety and social relationships respectively.

Fatigue:

The Functional Assessment of Chronic Illness Therapy -Fatigue Scale (FACIT-F) is an assessment of fatigue related to chronic illness therapy and has demonstrated reliability and sensitivity to changes in fatigue for a variety of chronic health conditions, the general population and in specific populations including cancer [47]. The FACIT-F contains 13 items that measures a person's level of fatigue over the past week and higher scores represent better functioning or less fatigue [48, 49].

Information collected from participant's medical record:

Data collected directly from the participants' medical records included age at diagnosis, cancer type and stage, treatment received, comorbidities at diagnosis, weight and BMI at diagnosis.

Normative data source:

The 2017/2018 National Health Survey, conducted by the Australian Bureau of Statistics, was used to compare AYA cancer survivors' results [50]. The survey collected information on the health status of the population, including long-term health conditions; health risk factors including; physical activity levels, diet, alcohol, smoking, BMI; along with socioeconomic and demographic factors [50]. The survey was conducted throughout Australia between July 2017 and June 2018 and contained information on approximately 21,000 people [50]. Current smoking was defined as those smoking some/every day vs previous smoking history and never smokers. Exceeding weekly alcohol intake was confirmed when more than >14 standard alcoholic drinks were consumed per week as per Australian Guidelines at the time of undertaking the survey [51].

Participants self-report dietary intake assessed how many serves of vegetables was usually consumed each day (1-6, less than 1 serve, does not eat); with the same question repeated for serves of fruit. The criterion for meeting daily fruit and vegetable intake was consumption of two or more serves of fruit and five or more serves of vegetables per day as per Australian Guidelines [52]. BMI was calculated from self-reported weight (in kilograms, stones, pounds); and height without shoes (centimetres, feet/inches).

Physical Activity levels were collected using the following questions; how many times in the last week did you *walk* for fitness, recreation or sport for at least 10 minutes continuously; what was the total amount of time undertaking activity past week (hours and minutes); in the last week; did you undertake any exercise that may have caused a moderate increase in heart and breathing (if yes – how many times and total time spent); the same question was repeated for vigorous /high intensity exercise. The final question looked at strength training and participants were asked; including activities already mentioned in the last week how many strength or toning activities undertaken in past week (if yes – how many days). To meet Australian Physical Activity Guidelines participants needed to undertake ≥150mins of moderate intensity physical activity per week and or 75mins of vigorous intensity physical activity per week along with two muscle strengthening exercises per week [53].

Data analysis:

Descriptive statistics were used to summarise AYA cancer survivor characteristics. Recruitment bias was assessed by comparing participants with non-participants for age, sex, residential location and cancer diagnosis with Pearson's chi-squared, Fisher's exact or independent samples t-tests as appropriate. One-sample t-tests were used to compare the sample means for continuous outcomes, while chi-squared tests were used for categorical outcomes. Unpaired t-tests were performed to compare AYA survivor results to normative data along with comparing means between those who completed the aerobic component of the physical activity (PA) guidelines (>149mins per week) vs those not meeting PA guidelines. Pearson's chi-squared test was performed to compare AYA survivors' results to Australian normative data (National Health Survey 2017/2018) [50]. Statistical analysis was

conducted using Stata v15 software [54]. An alpha level of 0.05 was used to determine statistical significance.

Results:

In total, 944 potential participants were screened from the hospital database. Of these, 391 (41%) met the inclusion criteria and were mailed and/or emailed an invitation to participate in the study (Figure 1). Ten letters (3%) were returned undelivered. Of the 381 AYAs presumed to have received the invitation to participate, 97 (26%) attempted to complete the online survey, 6 started the survey but did not complete the first page of the questionnaire and 1 completed the questionnaire twice, leaving 90 complete data sets usable for final analysis (Figure 1). There were no significant differences between study participants and those who did not respond with regard to sex, age, cancer diagnosis and place of residence (all $p>0.05$, Table 1).

Participant characteristics:

Demographic and medical characteristics of study participants are summarised in Table 1. At time of questionnaire response participants were on average 25.4±3.8 years (range 17-33); predominantly female (51%) with a mean time since diagnosis of 61 months (SD 29.3 months). The most common cancer types were sarcoma (34%), lymphoma (28%) and germ cell (11%) and 81% underwent chemotherapy, 66% had surgery and 46% had radiotherapy as part of their primary treatment.

In regards to rating their health compared to their peers most AYAs (37%) indicated that their current health was the same ‘compared to peers’ or either ‘a little worse’ (26%) or ‘much worse’ (20%). A significantly higher proportion of AYAs reported

suffering from one or more chronic health condition in addition to their original cancer diagnosis compared to Australian normative data (65% vs. 40%, p<0.0001). The most common health problems reported by participants included anxiety (38%), depression (27%) and chronic pain (22%). Other conditions reported by AYA survivors that were all higher than Australian normative data [50] included hypertension (13% vs 9%), diabetes (7% vs 2%), asthma (16% vs 11%), osteoporosis (4% vs 1%), arthritis (9% vs 4%) and heart, stroke and vascular disease (3% vs 1%).

Health behaviours:

Health behaviours of participants are described in Table 2. There were no differences in the proportion of AYA cancer survivors meeting physical activity guidelines compared to Australian normative data (31% vs 23.7%, p=0.11). A higher proportion of AYA cancer survivors were meeting the recommended daily intake of fruit and vegetables compared to Australian normative data (16.7% vs 3.9%, p<0.0001), although still below the recommended intake of 5 or more serves of vegetables and 2 serves of fruit [52]. A similar finding was observed in regards to cigarette smoking, with a smaller proportion of AYA cancer survivors reporting they smoked than their non-cancer counterparts (2.2% vs 16.7%, p<0.0001). Furthermore, fewer AYA survivors had a BMI classified as overweight or obese (46.7% vs 57.7%, p= 0.04). In regards to alcohol intake, there was no difference in the proportion of AYA cancer survivors that exceeded recommendations for weekly intake of alcohol (>14 standard drinks per week) [51] compared to Australian normative data (16.7% vs 14.9%, p=0.65)

Health related quality of life and fatigue:

Results of the AQOL 6D, SF36v2 and FACIT-F along with associated normative data are reported in Table 3. On the AQOL 6D, the subscales with the highest scores reported by AYA cancer survivors were 'independent living' (86.1) and 'senses' (83.2), with the lowest scores reported for 'coping' (60.6) and 'mental health' (61.1). The mean overall HR-QoL for AYA cancer survivors was significantly worse than the normative sample 25-34 age group (M= 74.1, SD 15.3 versus M=85.9, SD=10.15, $p<0.0001$).

Compared to Australian normative data, the SF-36v2 showed that AYA cancer survivors had lower scores on five of the eight subscales including physical functioning (-3.8, $p<0.0001$), role physical (-3.8, $p<0.0001$), general health (-9.1, $p<0.0001$), vitality (-2.4, $p=0.02$), and social functioning (-3.6, $p=0.0005$). Of the two summary measures, overall physical health (PCS) was poorer in AYA compared to normative data (-4, $p<0.0001$). However, overall mental health (MCS) did not differ between AYA and normative data (-1.4, $p=0.28$). Fatigue scores were lower in AYAs compared to normative data ($t[df=596]=-4.12$, $p<0.0001$) indicating levels of fatigue having a greater impact on upon daily activities and function (M=35.1, SD=11.3)(M=40.3, SD=10.3).

In an exploratory sub-analysis, AYA survivors who met the aerobic component of the PA guidelines (n=48) had better HR-QoL on the AQoL6D ($t[df=88]=12.4$, $p<0.0001$) and less fatigue ($t[df=88]=3.4$, $p<0.0001$) than those who were not meeting PA guidelines (n=42) (Table 4). However, this difference was not observed on the MCS or PCS subscales of the SF36.

Discussion

This study reports the long-term health behaviours, HR-QoL and fatigue levels of Australian AYA cancer survivors, which is essential to inform strategies for improving long-term health outcomes in this cohort. Assessing lifestyle behaviours is crucial to identify potentially modifiable factors that may reduce the AYA's increased risk of co-morbid conditions, cancer recurrence and improve their overall quality of life [3, 4, 20, 22, 27, 55, 56]. While we hypothesized that survivors would be less likely to adhere to health behaviour guidelines, they were in fact better in a number of areas compared to their aged matched peers, however results were still below recommended guidelines. Our results also identified AYA cancer survivors, who were on average 5 years post-treatment, had persistent issues of greater levels of fatigue and poorer HR-QoL compared to the general population.

The main finding from this study was that Australian AYA cancer survivors were more likely to meet dietary recommendations for daily fruit and vegetable intake, less likely to be current smokers and less likely to be overweight or obese compared to aged matched Australian data. Although these results were encouraging, context is required when interpreting the results as the proportion of AYA cancer survivors meeting key recommended health behaviours was very low. Overall, 69% of AYA cancer survivors did not meet weekly physical activity guidelines, 83% did not meet dietary recommendations for daily fruit and vegetable intake and 47% were overweight or obese. The findings are similar to international data which has shown that very few AYA cancer survivors meet recommended physical activity, diet or weight recommendations [21, 25-29, 33, 57]. When combined with a cancer diagnosis and subsequent treatment, AYA's poor health behaviours may leave them

more vulnerable to developing chronic disease later in life, in particular obesity and cardiovascular disease [4, 55]. It is clear that most AYA survivors do not meet national health recommendations, and may benefit from interventions that promote healthy behaviours, which in turn reduce the risk of chronic disease development.

Nearly two-thirds of AYA cancer survivors reported at least one other comorbid condition and over a quarter reported three or more comorbid conditions. This was significantly higher than the Australian aged matched normative data where only three percent reported three or more comorbid conditions. Lifestyle interventions such as a healthy diet and regular physical activity can be utilised to prevent, treat and manage a number of chronic diseases including cardiovascular disease, type 2 diabetes and obesity along with improving mental health and well-being [3, 6, 19, 58]. Primary Care health teams are well prepared to take on this role when provided with adequate information and support from the treating team, with survivorship care plans being an important component of delivering post-treatment care [59]. The findings from our study suggest there is an important role for collaboration between cancer specialist treating teams and primary care professionals to enable AYA survivors to access information and specialised services that deliver tailored interventions that support patients to improve their health behaviours.

In our study only 2.2% of AYA cancer survivors reported to be current smokers. This is substantially lower than the results of a 2007 Australian study of 171 AYA cancer survivors (aged 18-39) where almost 43% of participants were current smokers [32]. High rates of smoking have also been reported in international studies in AYA cancer survivors in the USA, Canada, UK, and Europe with rates ranging between 16-26% [3, 28, 29]. These differences may be explained by the long history of public health

campaigns and government legislation aimed at reducing smoking rates over the past 10 years in Australia [44]. These measures have meant that smoking rates within the general population have almost halved over the past 20 years and these results are like to extrapolate to the AYA population [60].

Previous studies have found persistent fatigue to be a major and debilitating problem for AYA cancer survivors [12, 17, 61]. As many as 90% of AYA survivors report experiencing fatigue at some stage, and studies demonstrate this continues well into survivorship with 30% of survivors reporting fatigue persisting up to three years post treatment [12, 62]. Participants in our study were on average 5-years post completion of treatment and reported fatigue at a level that impacts on daily functioning, suggesting fatigue is a persistent long-term concern for AYA cancer survivors. This persistent fatigue that is seen in AYA cancer survivors may also in part explain the low scores seen across multiple domains on the AQoL6D and SF-36v2. Research has shown that cancer related fatigue in AYA cancer survivors to be a highly distressing and debilitating symptom, which can influence multiple facets of HR-QoL [12, 17, 63]. Interestingly, in an exploratory analysis, participants who met the aerobic component of the physical activity guidelines (>149mins per week) reported better HR-QoL and less fatigue then those who did not meet physical activity guidelines. Lifestyle changes such as undertaking regular physical activity and eating a healthy diet in adult cancer survivors have been shown to improve cancer related fatigue and HR-QoL [24, 64-71]. However, to date these positive effects have yet to be clearly established within the AYA setting [72]. It is therefore important that future research investigates the role of tailored interventions that

promote both physical activity and nutrition in AYA cancer survivors and the impact these can have on multiple domains of health.

Despite the health behaviours of AYA cancer survivors being better than normative data, HR-QoL scores were considerably worse across multiple domains. In particular, low scores were observed in domains of mental health and coping on the AQoL-6D, along with the mental health, general health and vitality domains on the SF-36v2. One potential reason for these observed scores was the prevalence of comorbidities within our sample compared to normative data. Multimorbidity is negatively associated with HR-QoL which increases over time after diagnosis even though the number of comorbidities remain unchanged [16, 73, 74]. Previous work undertaken in the area has shown that the survivorship phase poses a number of psychosocial challenges with survivors having worse physical and mental HR-QoL than peers [16, 75, 76]. AYA cancer survivors who undertake regular physical activity have shown to have better mental health and HR-QoL than those not meeting recommendations [25, 26, 33, 77]. While no studies to our knowledge have explored the impact of diet on HR-QoL in AYA cancer survivors, previous research has shown that nutrition plays an important role in maintaining good mental health in children, adolescents and adults without cancer, in particular diet quality [78, 79]. Future research in this area should explore the potential role of age specific physical activity and nutrition interventions on AYA cancer survivor's mental health and HR-QoL to enable survivors to transition successfully into adulthood.

This study has a number of important strengths and limitations. To the best of our knowledge this study is the first to focus on health behaviours, HR-QoL and fatigue levels in Australian AYA (15-25 years of age) cancer survivors. The study included

participants from a large specialist cancer institution within Victoria that contains a dedicated AYA service comprising of medical, nursing and allied health clinicians and has a systematised survivorship program. Therefore, due to its resourcing may not accurately represent the experiences and health behaviours of AYA cancer survivors in Australia more broadly. Selection bias may also have played a role in study findings, with survey responders who are more interested and educated in regards to their health behaviours completing the online questionnaire, which resulted in a healthier subset of AYA survivors. In addition, causality and pre-diagnosis levels of health behaviours cannot be inferred from a cross-sectional study design. The poor response rate (26%) may have introduced non response bias, and in part may have been due to potential participants not having an opportunity to complete the survey on hard copy and return via mail-in. However, the response rate is comparable to similar studies involving AYA cancer survivors where response rates range between 15-38% [25, 30]. Despite these limitations, our study provides some insight into the complex associations between physical activity levels and impact of HR-QoL and fatigue levels in AYA survivors.

Conclusion:

AYA cancer survivors within a single Australian institution showed better health behaviours (physical activity levels, dietary intake, smoking rates and BMI) compared to normative Australian data. However, the proportion of AYA cancer survivor's meeting recommendations for weekly physical activity and daily fruit and vegetable intake by guideline standards was still low, especially when burdened with the elevated risk of chronic disease. AYA cancer survivors report persistent fatigue

and reduced HR-QoL at five years post-treatment. This study adds to the growing body of international work showing the poor overall health behaviours of AYA cancer survivors. Future research should investigate targeted lifestyle interventions for AYA survivors as part of a wider collaboration between primary care, cancer specialists and cancer survivors that aim to promote better long-term health behaviours to ensure that AYA cancer survivors thrive in survivorship.

Figure 1: Flow of participants through the trial

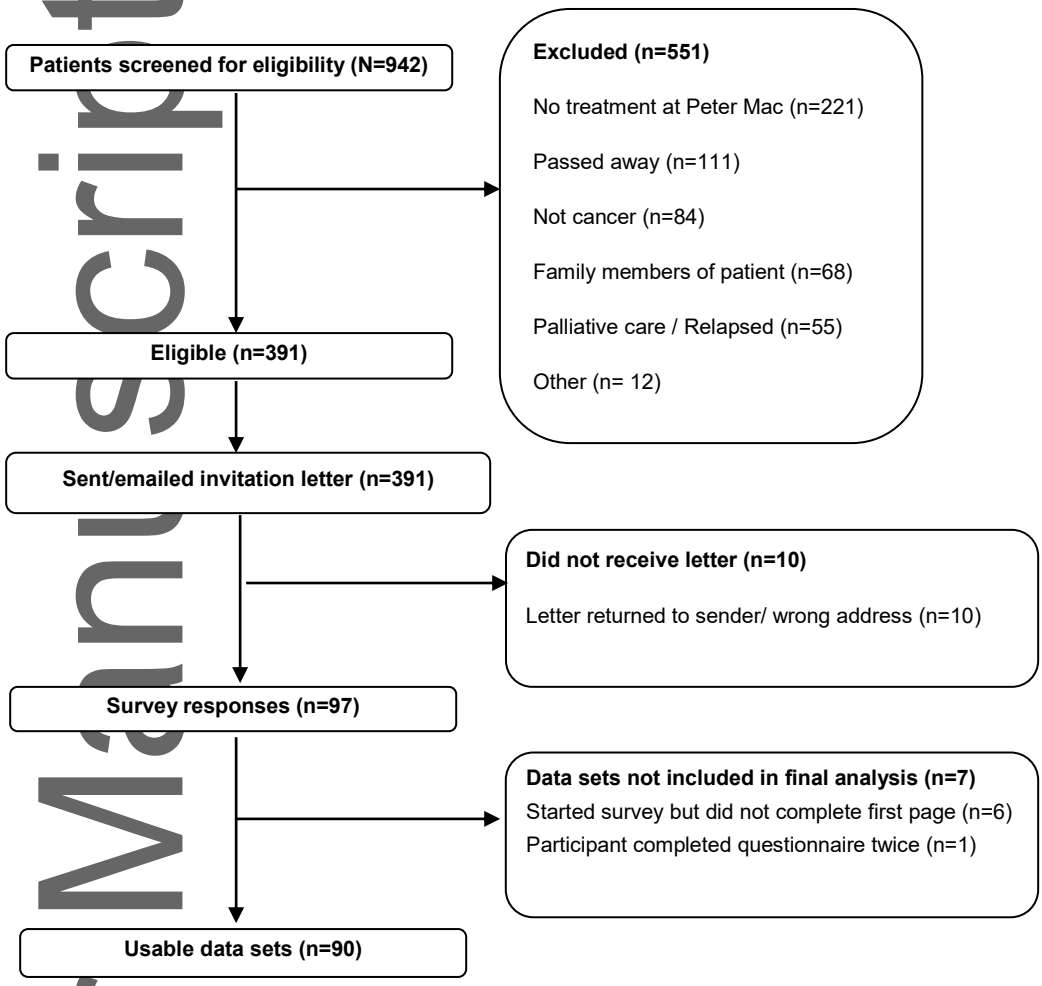

Table 1: Mean, SD, range and frequencies of demographic and medical and psychosocial characteristics of study participants and non-responders

	Participants		Non-responders		
	n	%	n	%	P
Current Age, years					
Mean (SD),	25.4 (3.8)		25.2 (3.7)		0.4
Range	17-33		17-34		
Months since diagnosis					
Mean (SD)	61 (19.3)				
Range	24-85				
Gender					
Male	43	47.8	156	51.8	0.3
Female	46	51.1	145	48.2	
Prefer not to say	1	1.1			
BMI					
Mean (SD)	25.7 (5.7)				
Range	14-41.2				
Relationship status					
Single	48	53.3			
Partner/Married/ De facto	39	43.3			
Other	3	3.3			
Residential location					
Metro	57	63.3	184	61.1	0.9
Rural	24	26.7	92	30.6	
Interstate	9	10	25	8.3	
Employment status					
Working full-time	37	41.1			
Working part-time	18	20			
Casual	18	20			
Sick leave (permanent)	5	5.5			
Not employed (study only)	10	11.1			
Home duties	2	2.2			
Study status					
Study only	10	11.1			
Work and study	17	18.9			
No study	63	70			
Highest education level completed					
Some high school (Year 10/11)	9	10			
Completed high school (Year 12)	19	21.1			
Trade/certificate/diploma	21	23.3			
Undergraduate degree	27	30			
Postgraduate degree	14	15.6			
Cancer diagnosis					
Sarcoma	31	34.4	55	18.3	0.1
Lymphoma	25	27.8	98	32.6	
Germ Cell	10	11.1	19	6.3	
Leukaemia	7	7.8	30	10	
Brain	6	6.7	23	7.6	

Other*	11	12.2	76	25.2
Treatment				
Chemotherapy	73	81.1		
Surgery	59	65.6		
Radiotherapy	41	45.6		
Stem cell transplant	8	8.4		
Other	3	3.3		
Number of other health conditions				
0 other health conditions	32	35.6		
1-2 other health conditions	35	38.9		
>3 other health conditions	23	25.5		
How would you rate your health compared to others your age				
Much worse	18	20.2		
A little worse	23	25.8		
The same	33	37.1		
A little better	12	13.5		
Much better	3	3.4		

^ Trade, community or TAFE college
* Melanoma, Colorectal, Breast, Head and neck

Table 2: Health behaviours and status of long-term AYA cancer survivors compared to Australian normative data

Characteristic	AYA cancer survivors (n=90)	Non-cancer comparisons$_1$ (n=2576)^	p
	Proportion of person (%)		
Physical activity levels			0.1
Meet guidelines	31.1	23.7	
Did not meet	68.9	76.3	
BMI		*(n=1733)*	0.04
Underweight / Normal	53.3	42.4	
Overweight/Obese	46.7	57.6	
Daily consumption of fruit and vegetables			<0.0001
Met guidelines	16.7	3.9	
Did not meet	83.3	96.1	
Smoking status			<0.0001
Never	92.2	63.1	
Current	2.2	16.7	
Ex-smoker	5.6	20.2	
Alcohol intake			0.6
Meet guidelines	83.3	85.1	
Exceeded guidelines	16.7	14.9	

Notes: $_1$ Age ranges used comparison group – Physical activity levels, BMI, Fruit and Vegetable intake Smoking (25-34 year)

^ n=2576 unless specified

Physical Activity Guidelines: 150mins-300mins of moderate intensity physical activity or 75-150minutes of vigorous intensity per week and muscle strengthening exercises 2 times per week [53]

Daily consumption of fruit and vegetables: 5 or more serves of vegetables and 2 or more serves of fruit [52]

Alcohol intake: Exceed guidelines >14 standard drinks per week [51]

Table 3: HR-QoL and fatigue levels of AYA cancer survivors as compared to normative data

Outcome	AYA survivors Mean (SD)	Normative Mean (SD)	Two-sample t-test*	P value
AQoL - 6D (overall score)	74.1 (15.3)	85.8 (7.7)	-9.2	<0.0001
Senses	83.2 (12.6)			
Pain	75.1 (25.1)			
Mental health	61.1 (21.6)			
Relationships	76.3 (21.2)			
Independent living	86.1 (16.7)			
Coping	60.6 (20.6)			
SF-36v2				
Physical functioning	50.2 (9.1)	54 (5.4)	-3.8	<0.0001
Role physical	48 (10)	51.8 (8)	-3.8	<0.0001
Bodily pain	50.8 (9.9)	51.4 (9.4)	-0.6	0.6
General health	43.3 (12.2)	52.4 (8.8)	-9.1	<0.0001
Vitality	48.8 (9.9)	51.2 (9.1)	-2.4	0.02
Social functioning	46.1 (10.5)	49.8 (9.1)	-3.8	0.0005
Role emotional	45.6 (11.5)	47.4 (12.6)	-1.8	0.2
Mental health	46.2 (9.6)	48.3 (10)	-2.1	<0.0001
MCS	45.2 (10.4)	46.6 (11.5)	-1.4	0.3
PCS	49.6 (9.5)	53.6 (7)	-4.0	<0.0001
FACIT-F (overall score)	35.1 (11.3)	40.3 (10.3)	-4.1	<0.0001

AQoL - 6D total Assessment of Quality of Life 6 dimensions (n=445 / age 25-34) [46]; SF36v2 – Short Form 36v2 (n=493 / ages 25-34) MCS=Mental Component Score and PCS= Physical component score [43, 45]; FACIT-F - Functional Assessment of Chronic Illness Therapy – Fatigue Scale (n=308 / ages 18-34) [47].

Table 4: HR-QoL and fatigue levels: meet/partly meet PA guidelines vs not meeting PA guidelines

Outcome	Meet/partly meet PA guidelines (n=48)	Do not meet PA guidelines (n=42)	Two-sample t-test	P value
AQoL - 6D	79.8 (11.5)	67.5 (16.5)	12.4	<0.0001
SF-36v2				
MCS	45 (9.5)	45.3 (11.4)	-0.2	0.9
PCS	50.4 (9.8)	48.7 (9.2)	0.9	0.4
FACIT-F	38.7 (9.2)	31 (12.2)	3.4	<0.0001

AQoL - 6D total Assessment of Quality of Life 6 dimensions; SF36v2 – Short Form 36v2 - MCS=Mental Component Score and PCS = Physical Component Score; FACIT-F - Functional Assessment of Chronic Illness Therapy – Fatigue Scale; PA = Physical activity, (Meet/partly meet PA = undertakes >149mins of aerobic activity per week)

Declarations:

Funding:

No funding was received for conducting this study

Conflicts of interest/ Competing interests:

The authors have no conflicts of interest to declare that are relevant to the content of this article.

Ethics approval:

This study was approved by the Peter MacCallum Cancer Centre Human Research Ethics Committee (approval date 18th December 2018). HREC reference number (LNR/46319/PMCC-2018) and the local reference number (18/243L)

This study was designed, based on knowledge of the literature, and conducted according to globally accepted standards of the Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) annotated with TGA comments (Australia, July 2000), in agreement with the Declaration of Helsinki (WHO, 2004), the National Statement (Australia, 2007) and in keeping with local regulations and institutional guidelines.

Consent:

Participants who meet inclusion/exclusion criteria were sent an invitation letter/and or email, outlining the purpose and requirements of study participation. The package contained the following information:

a) A letter of invitation to participate in the study on Peter MacCallum Cancer Centre letterhead (Participation Information Sheet).

b) A unique code that allowed the participant to complete the questionnaire package online via REDCap.

Those wishing to take part in the study completed the study questionnaires online via REDCap, a secure web application for building and managing online surveys. A reminder letter was sent to non-responders 3 weeks post the initial mail-out to assist with response rate. All participant data was de-identified prior to data analysis and study participants were instructed that *consent was assumed* based on completing the online survey.

Consent for publication:

Participants were informed that their privacy will be respected in any publication arising from this study. All data was de-identified and was reported as group data only. The project did not involve the collection, use or disclosure of identified or potentially identifiable information.

Availability of data and material:

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request

References:

1. Roder, D.M., et al., *Australian Adolescents and Young Adults-Trends in Cancer Incidence, Mortality, and Survival Over Three Decades.* J Adolesc Young Adult Oncol, 2018. **7**(3): p. 326-338.
2. Welfare, A.I.o.H.a., *Cancer in adolescents and young adults in Australia. Cat. No. CAN 110.*, in *Canberra: AIHW*. 2018.
3. Tai, E., et al., *Health status of adolescent and young adult cancer survivors.* Cancer, 2012. **118**(19): p. 4884-91.
4. Chao, C., et al., *Cardiovascular Disease Risk Profiles in Survivors of Adolescent and Young Adult (AYA) Cancer: The Kaiser Permanente AYA Cancer Survivors Study.* J Clin Oncol, 2016. **34**(14): p. 1626-33.
5. Carretier, J., et al., *A Review of Health Behaviors in Childhood and Adolescent Cancer Survivors: Toward Prevention of Second Primary Cancer.* J Adolesc Young Adult Oncol, 2016. **5**(2): p. 78-90.
6. Woodward, E., et al., *Late effects in survivors of teenage and young adult cancer: does age matter?* Ann Oncol, 2011. **22**(12): p. 2561-8.
7. Clinton-McHarg, T., et al., *Measuring the psychosocial health of adolescent and young adult (AYA) cancer survivors: a critical review.* Health Qual Life Outcomes, 2010. **8**: p. 25.
8. Rugbjerg, K., et al., *Cardiovascular disease in survivors of adolescent and young adult cancer: a Danish cohort study, 1943-2009.* J Natl Cancer Inst, 2014. **106**(6): p. dju110.
9. van Laar, M., et al., *Cardiovascular sequelae in long-term survivors of young peoples' cancer: a linked cohort study.* Br J Cancer, 2014. **110**(5): p. 1338-41.
10. Keegan, T.H.M., et al., *Cardiovascular disease incidence in adolescent and young adult cancer survivors: a retrospective cohort study.* Journal of Cancer Survivorship, 2018. **12**(3): p. 388-397.
11. Lee, J.S., et al., *Increased risk of second malignant neoplasms in adolescents and young adults with cancer.* Cancer, 2016. **122**(1): p. 116-23.
12. Nowe, E., et al., *Cancer-related fatigue in adolescents and young adults: A systematic review of the literature.* Crit Rev Oncol Hematol, 2017. **118**: p. 63-69.
13. Langeveld, N.E., et al., *Quality of life in young adult survivors of childhood cancer.* Support Care Cancer, 2002. **10**(8): p. 579-600.
14. Yi, J.C. and K.L. Syrjala, *Anxiety and Depression in Cancer Survivors.* Med Clin North Am, 2017. **101**(6): p. 1099-1113.
15. Sun, H., et al., *Fear of cancer recurrence, anxiety and depressive symptoms in adolescent and young adult cancer patients.* Neuropsychiatr Dis Treat, 2019. **15**: p. 857-865.
16. Quinn, G.P., et al., *Quality of life in adolescent and young adult cancer patients: a systematic review of the literature.* Patient Relat Outcome Meas, 2015. **6**: p. 19-51.
17. Spathis, A., et al., *Teenage and Young Adult Cancer-Related Fatigue Is Prevalent, Distressing, and Neglected: It Is Time to Intervene. A Systematic Literature Review and Narrative Synthesis.* J Adolesc Young Adult Oncol, 2015. **4**(1): p. 3-17.
18. Kosola, S., et al., *Early Education and Employment Outcomes After Cancer in Adolescents and Young Adults.* Journal of Adolescent and Young Adult Oncology, 2018. **7**(2): p. 238-244.
19. Ferioli, M., et al., *Impact of physical exercise in cancer survivors during and after antineoplastic treatments.* Oncotarget, 2018. **9**(17): p. 14005-14034.
20. Berkman, A.M. and S.G. Lakoski, *A Review of Cardiorespiratory Fitness in Adolescent and Young Adult Survivors of Childhood Cancer: Factors that Affect its Decline and Opportunities for Intervention.* J Adolesc Young Adult Oncol, 2016. **5**(1): p. 8-15.

21. Rabin, C., *Review of health behaviors and their correlates among young adult cancer survivors.* Journal of Behavioral Medicine, 2011. **34**(1): p. 41-52.
22. Smith, W.A., et al., *Lifestyle and metabolic syndrome in adult survivors of childhood cancer: a report from the St. Jude Lifetime Cohort Study.* Cancer, 2014. **120**(17): p. 2742-50.
23. Spector, D.J., et al., *Are lifestyle behavioral factors associated with health-related quality of life in long-term survivors of non-Hodgkin lymphoma?* Cancer, 2015. **121**(18): p. 3343-51.
24. Cormie, P., et al., *Clinical Oncology Society of Australia position statement on exercise in cancer care.* Med J Aust, 2018. **209**(4): p. 184-187.
25. Belanger, L.J., et al., *Physical activity and health-related quality of life in young adult cancer survivors: a Canadian provincial survey.* J Cancer Surviv, 2011. **5**(1): p. 44-53.
26. Warner, E.L., et al., *Health behaviors, quality of life, and psychosocial health among survivors of adolescent and young adult cancers.* J Cancer Surviv, 2016. **10**(2): p. 280-90.
27. Pugh, G., et al., *Health Behavior Change Interventions for Teenage and Young Adult Cancer Survivors: A Systematic Review.* J Adolesc Young Adult Oncol, 2016. **5**(2): p. 91-105.
28. Hall, A.E., et al., *Young adult cancer survivors' psychosocial well-being: a cross-sectional study assessing quality of life, unmet needs, and health behaviors.* Support Care Cancer, 2012. **20**(6): p. 1333-41.
29. Marjerrison, S., et al., *Smoking, Binge Drinking, and Drug Use Among Childhood Cancer Survivors: A Meta-Analysis.* Pediatr Blood Cancer, 2016. **63**(7): p. 1254-63.
30. Rabin, C. and M. Politi, *Need for health behavior interventions for young adult cancer survivors.* Am J Health Behav, 2010. **34**(1): p. 70-6.
31. Keats, M.R., et al., *An examination of physical activity behaviors in a sample of adolescent cancer survivors.* J Pediatr Oncol Nurs, 2006. **23**(3): p. 135-42.
32. Eakin, E.G., et al., *Health behaviors of cancer survivors: data from an Australian population-based survey.* Cancer Causes Control, 2007. **18**(8): p. 881-94.
33. Murnane, A., et al., *Adolescents and young adult cancer survivors: exercise habits, quality of life and physical activity preferences.* Support Care Cancer, 2015. **23**(2): p. 501-10.
34. Harris, P.A., et al., *Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support.* J Biomed Inform, 2009. **42**(2): p. 377-81.
35. Pugh, G., et al., *The Health Behavior Information Needs and Preferences of Teenage and Young Adult Cancer Survivors.* J Adolesc Young Adult Oncol, 2017. **6**(2): p. 318-326.
36. Godin, G. and R.J. Shephard, *A simple method to assess exercise behavior in the community.* Can J Appl Sport Sci, 1985. **10**(3): p. 141-6.
37. Jacobs, D.R., Jr., et al., *A simultaneous evaluation of 10 commonly used physical activity questionnaires.* Med Sci Sports Exerc, 1993. **25**(1): p. 81-91.
38. Amireault, S., et al., *The use of the Godin-Shephard Leisure-Time Physical Activity Questionnaire in oncology research: a systematic review.* BMC Med Res Methodol, 2015. **15**: p. 60.
39. AIHW, *Physical activity across the life stages*, AIHW., Editor. 2018: Canberra, ACT. p. 72.
40. Gans, K.M., et al., *REAP and WAVE: new tools to rapidly assess/discuss nutrition with patients.* J Nutr, 2003. **133**(2): p. 556s-62s.
41. Johnston, C.S., et al., *Rapid Eating Assessment for Participants [shortened version] scores are associated with Healthy Eating Index-2010 scores and other indices of diet quality in healthy adult omnivores and vegetarians.* Nutr J, 2018. **17**(1): p. 89.
42. Ware, J.E., *User's Manual for the SF-36v2 Health Survey*. 2008: Quality Metric.
43. Hawthorne, G., et al., *The SF36 Version 2: critical analyses of population weights, scoring algorithms and population norms.* Qual Life Res, 2007. **16**(4): p. 661-73.

44. Richardson, J., et al., *Measurement of the Quality of Life for Economic Evaluation and the Assessment of Quality of Life (AQoL) Mark 2 Instrument.* Australian Economic Review, 2004. **37**(1): p. 62-88.
45. Ware, J.E., M. Kosinski, and J.E. Dewey, *How to score version 2 of the SF-36 health survey: standars & acute forms*. 2001: QualityMetric.
46. Maxwell, A., et al., *Deriving population norms for the AQoL-6D and AQoL-8D multi-attribute utility instruments from web-based data.* Qual Life Res, 2016. **25**(12): p. 3209-3219.
47. Webster, K., D. Cella, and K. Yost, *The Functional Assessment of Chronic Illness Therapy (FACIT) Measurement System: properties, applications, and interpretation.* Health Qual Life Outcomes, 2003. **1**: p. 79.
48. Mulrooney, D.A., et al., *Fatigue and sleep disturbance in adult survivors of childhood cancer: a report from the childhood cancer survivor study (CCSS).* Sleep, 2008. **31**(2): p. 271-81.
49. Fortmann, J., et al., *Sleep Quality, Fatigue, and Quality of Life Among Teenage and Young Adult Cancer Survivors.* J Adolesc Young Adult Oncol, 2018. **7**(4): p. 465-471.
50. ABS, *National Health Survey 2017-2018.* 2018. **4364.0.55.011**.
51. (NHMRC), N.H.a.M.R.C., *Australian guideline to reduce health risks from drinking alcohol*, NHMRC, Editor. 2009: Canberra, NHMRC.
52. Council, N.H.a.M.R., *Australian Dietary Guidelines*, D.o.H.a. Ageing, Editor. 2013: Canberra.
53. Goverment, A., *Australia's Physical Activity and Sedentary Behaviour Guidelines and the Australian 24-Hour Movement Guidelines*, D.o. Health, Editor. 2017: https://www1.health.gov.au/internet/main/publishing.nsf/Content/health-pubhlth-strateg-phys-act-guidelines.
54. StataCorp, *Stata Statistical Software: Release 15*. 2017, StataCorp LLC.: College Station, TX.
55. Oeffinger, K.C., et al., *Chronic health conditions in adult survivors of childhood cancer.* N Engl J Med, 2006. **355**(15): p. 1572-82.
56. Slater, M.E., et al., *Physical Activity, Fitness, and Cardiometabolic Risk Factors in Adult Survivors of Childhood Cancer with a History of Hematopoietic Cell Transplantation.* Biol Blood Marrow Transplant, 2015. **21**(7): p. 1278-83.
57. Eakin, E.G., et al., *Health Status of Long-term Cancer Survivors: Results from an Australian Population-Based Sample.* Cancer Epidemiology Biomarkers & Prevention, 2006. **15**(10): p. 1969-1976.
58. Berkman, A.M. and S.G. Lakoski, *Treatment, Behavioral, and Psychosocial Components of Cardiovascular Disease Risk Among Survivors of Childhood and Young Adult Cancer.* Journal of the American Heart Association, 2015. **4**(4): p. e001891.
59. Jefford, M., et al., *Implementing novel models of posttreatment care for cancer survivors: Enablers, challenges and recommendations.* Asia Pac J Clin Oncol, 2015. **11**(4): p. 319-27.
60. Welfare, A.I.o.H.a., *National Drug Strategy Household Survey 2016: detailed findings.* 2017, AIHW: Canberra.
61. Erickson, J.M., *Fatigue in adolescents with cancer: a review of the literature.* Clin J Oncol Nurs, 2004. **8**(2): p. 139-45.
62. Poort, H., et al., *Prevalence and impact of severe fatigue in adolescent and young adult cancer patients in comparison with population-based controls.* Support Care Cancer, 2017. **25**(9): p. 2911-2918.
63. Bower, J.E., *Cancer-related fatigue--mechanisms, risk factors, and treatments.* Nat Rev Clin Oncol, 2014. **11**(10): p. 597-609.
64. Mock, V., et al., *Cancer-related fatigue. Clinical Practice Guidelines in Oncology.* J Natl Compr Canc Netw, 2007. **5**(10): p. 1054-78.
65. Campbell, K.L., et al., *Exercise Guidelines for Cancer Survivors: Consensus Statement from International Multidisciplinary Roundtable.* Medicine & Science in Sports & Exercise, 2019. **51**(11): p. 2375-2390.

66. Patel, A.V., et al., *American College of Sports Medicine Roundtable Report on Physical Activity, Sedentary Behavior, and Cancer Prevention and Control.* Medicine & Science in Sports & Exercise, 2019. **51**(11): p. 2391-2402.
67. Cramp, F. and J. Daniel, *Exercise for the management of cancer-related fatigue in adults.* Cochrane Database Syst Rev, 2008(2): p. Cd006145.
68. Mishra, S.I., et al., *Exercise interventions on health-related quality of life for cancer survivors.* Cochrane Database Syst Rev, 2012(8): p. Cd007566.
69. Arends, J., et al., *ESPEN guidelines on nutrition in cancer patients.* Clin Nutr, 2017. **36**(1): p. 11-48.
70. Isenring, E., et al., *Updated evidence-based practice guidelines for the nutritional management of patients receiving radiation therapy and/or chemotherapy.* Nutrition & Dietetics, 2013. **70**(4): p. 312-324.
71. Baguley, B.J., T.L. Skinner, and O.R.L. Wright, *Nutrition therapy for the management of cancer-related fatigue and quality of life: a systematic review and meta-analysis.* Br J Nutr, 2019. **122**(5): p. 527-541.
72. Munsie, C., et al., *The Benefit of Physical Activity in Adolescent and Young Adult Cancer Patients During and After Treatment: A Systematic Review.* J Adolesc Young Adult Oncol, 2019.
73. Brettschneider, C., et al., *Relative impact of multimorbid chronic conditions on health-related quality of life--results from the MultiCare Cohort Study.* PLoS One, 2013. **8**(6): p. e66742.
74. Schoormans, D., et al., *The impact of co-morbidity on health-related quality of life in breast cancer survivors and controls.* Acta Oncol, 2015. **54**(5): p. 727-34.
75. Smith, A.W., et al., *Health-related quality of life of adolescent and young adult patients with cancer in the United States: the Adolescent and Young Adult Health Outcomes and Patient Experience study.* J Clin Oncol, 2013. **31**(17): p. 2136-45.
76. Barnett, M., et al., *Psychosocial outcomes and interventions among cancer survivors diagnosed during adolescence and young adulthood (AYA): a systematic review.* J Cancer Surviv, 2016. **10**(5): p. 814-31.
77. Hauken, M.A., et al., *Working toward a good life as a cancer survivor: a longitudinal study on positive health outcomes of a rehabilitation program for young adult cancer survivors.* Cancer Nurs, 2015. **38**(1): p. 3-15.
78. Dalle Grave, R., *Nutrition and Fitness: Mental Health.* Nutrients, 2020. **12**(6).
79. Marx, W., et al., *Nutritional psychiatry: the present state of the evidence.* Proc Nutr Soc, 2017. **76**(4): p. 427-436.