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Physical activity level objectively measured by accelerometery in children undergoing cancer treatment at home and in a hospital setting: A pilot study

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ABSTRACT

Background: Over the last decades the number of childhood cancer survivors has increased. However, a significant number of childhood cancer survivors suffer from side effects of treatment. This results in a lower quality of life, reduced physical activity (PA), decreased muscle strength and cardiorespiratory fitness compared to healthy peers. To improve PA and to be able to set up and evaluate training programmes, it is necessary to study the feasibility of accelerometery and current objectively measured PA level of children with childhood cancer.

Methods: The PA level of twenty-five children undergoing cancer treatment was measured using accelerometery in a cross-sectional study design. Differences in PA levels were analysed by age, cancer type, sex, home or hospital setting and week or weekend days.

Results: All participants reported the Actical was well-accepted and the burden and risks associated with participation were negligible.The median of minutes was 1325 min/24hrs of Sedentary Behaviour (SB), 111 min/24hrs of light PA and 4-min/24hrs of moderate-to-vigorous PA (MVPA). In a hospital setting significantly lower levels of PA were achieved, in comparison to a home setting.

Conclusion: Accelerometery is feasible to objectively measure PA levels throughout the treatment, both in hospital or home settings. The level of PA per day of all participants was mostly SB, some light PA and hardly any MVPA. It is strongly recommended to determine benefits and limitations of PA in children during cancer treatment and to determine differences in perceptions of capability of PA of these children. With the growing population of childhood cancer survivors, substantiated PA guidelines and advices should be developed. PA for these children should be encouraged and stimulated to minimize the side effects during and after treatment.

1. Introduction

Of all diseases in children, cancer is the leading cause of mortality [1]. In the Netherlands each year approximately 600 of 3.5 million children (0–18 years) are diagnosed with cancer [2]. Over the past decades, the number of childhood cancer survivors (CCS) has been growing. Progress in multimodal treatment and supportive care has resulted in substantially improved 5-year survival rates in CCS from below 20% before 1950 to between 60% and 98% currently, depending on cancer type [3–5]. However, a significant number of children with childhood cancer are suffering from negative deficits and side effects of cancer treatment, for example educational problems, impairments in emotional health and physical performance [6–8]. Increased risks for health problems and physical functioning are reported, both during and even years

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after treatment [6,9,10].

More specifically: reduced physical activity (PA), decreased muscle strength and decreased cardiorespiratory fitness compared to healthy peers are found [11,12]. According to The Childhood Cancer Survivor Study the highest prevalence of physical performance limitations was found in patients with bone sarcoma and brain tumours [13].

Multiple national and international guidelines recommend a minimum of 60 min of moderate-to-vigorous intensity physical activity (MPVA) per day and muscle and bone strengthening activities three times a week for school-age children [14]. The average number of steps should be 12,000–16,000 steps per day for boys and 10,000–13,000 steps per day for girls [15]. These recommendations are considered to also be applicable to children with chronic disease [15,16]. However, childhood cancer is not mentioned in these studies. A long-term decline in PA in children can lead to a higher risk of depressive symptoms, lower aerobic fitness, lower insulin sensitivity, obesity and lower bone density. Studies have shown an association between reduced cardiorespiratory fitness and cardiovascular disease risk factors in childhood [17,18]. Studies assume that CCS are at greater risk of metabolic diseases and inactivity-related diseases such as diabetes, coronary artery disease, osteoporosis, hypertension, and recurrence of cancer later in life [19–24]. Elmesmari et al. [25] described in a review that children and adolescents with chronic diseases are currently not benefiting optimally of the potential effects of MVPA. In adults with cancer, scientific evidence about the benefits of PA on survival of cancer, chemotherapy tolerance during treatment and quality of life is already available [26–28]. In children with cancer the availability of scientific evidence about the effects of physical interventions during and after treatment is still limited [11,12,29–31]. The sample sizes in these studies are often small, only subsets of cancer types are included and a lot of variations in the exercise interventions are described. Also, the PA level of CCS is often estimated through self-reported questionnaires. Although this method is easy to administer, low in costs and feasible for large sample sizes; the validity and reliability is low to moderate, especially in small sample sizes [32,33]. In addition, PA levels are generally overestimated by children in self-reports [34]. Devices such as accelerometers measure PA more objectively than the participants themselves in self-reports [35,36].

Most of the studies using accelerometery describe PA of adult CCS. A systematic review from Elmesmari et al. [25] included three studies that objectively measured PA in CCS [33,37,38] and mentioned, “that despite the apparent similarity between the studies, the methodology was considerably different in sample sizes, age and place of the studies, differences in the stage of treatment, or differences in accelerometer methodology”.

With the growing population of CCS and a significant number of survivors suffering from negative long-term defects, side effects of treatment and decreased physical fitness, it is necessary to gain insight in device-based PA levels in Dutch children during cancer therapy. The trend in Dutch childhood cancer treatment is that children receive their treatment increasingly on an ambulatory basis, during a day stay or short overnight stays in the hospital which makes it difficult to get a full picture of their PA levels and therefore it is important to explore the use of accelerometery to objectively measure PA levels throughout the treatment phase of their disease.

To increase PA levels and to be able to set up and evaluate PA interventions, it is necessary to know the current levels of device-based PA level of children with childhood cancer during treatment. In exploring that, accelerometery is feasible to objectively measure PA levels of CCS during treatment. A longitudinal, prospective study design with a larger sample size can be set up in the future.

The primary objective of this study was to investigate the feasibility of accelerometery to measure PA levels in children with childhood cancer and to determine PA levels during treatment measured by accelerometery in both hospital and home settings. The secondary objective was to analyse differences in PA level by age, cancer type, sex, setting (hospital or home setting) and week or weekend days.

2. Material and methods

2.1. Study design and setting

PA Level in children undergoing cancer treatment was objectively measured using accelerometery, in hospital and home settings, in an observational cross-sectional study design. The study took place at the childhood oncology department of the Princess Máxima Center located in the Wilhelmina Children’s Hospital, UMC Utrecht, The Netherlands. This was before the centralization of specialized care and the opening of the new building of the Princess Máxima Center, Utrecht, The Netherlands. The principal investigator (W.P.B.) approached all eligible subjects and provided information about the study. Informed consent was obtained from all children and parents included in this study. The STROBE statement checklist for cross-sectional studies was used for transparent reporting.

2.2. Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study was registered under 17–346/C at the institutional research ethics board.

2.3. Participants

Patients were included from November 2017 until April 2018 if (i) they were under the age of 18 years, (ii) they were undergoing active cancer treatment according to the appropriate protocols of the Dutch Childhood Oncology Group (SKION) at the childhood oncology department of the Princess Máxima Center located in the Wilhelmina Children’s Hospital, UMC Utrecht, the Netherlands, (iii) they were able to walk and (iv) they agreed to wear an accelerometer for seven days in either a hospital and/or a home setting. Children were not included if they had comorbidities that could also have a major impact on walking and PA.

2.4. Data collection

2.4.1. Anthropometric measurements

Body weight was determined to the nearest 0.1 kg using a SECA electronic scale Model 877 (SECA, Germany). Height was measured to the nearest 0.1 cm using a SECA wall-mounted stadiometer Model 206 (SECA, Germany). Body Mass Index (BMI) was calculated as body weight (Kg) divided by square height (m^2). Age, sex, cancer type, according to the International Classification of Childhood Cancer (ICCC-3) [39] and types of treatment were extracted from the Electronic Patient Record.

2.4.2. Physical activity level

The level of PA and SB were assessed using the Actical (Philips Respironics, Mini Mitter Co, Inc., Bend, OR). The Actical is a child-friendly device that has been validated for measuring PA in

children in free-living conditions [36]. The main study parameters were, (i) Actical-counts per 15 s epoch measured, an epoch is a predetermined time period over which Actical data is summarised, (ii) the level of PA described and classified as a percentage of counts per minute (cpm), classification for participants aged < 7 years old was based on cut off points by Pfeiffer et al. [40] and for participants aged ≥ 7–18 years old it was based on Puyau et al. [36] (Table 1.), (iii) data in cpm were defined by averaging the four 15 s epoch counts over each minute [40] and (iv) daily number of steps.

Participants were instructed to wear the Actical for seven consecutive days for a minimum of 8 h during daytime. After initialization, the device was fastened to an elastic waist belt strap and worn on the participant's right hip. Parents or participants kept up a 'wearing time' activity diary in which they recorded start and end time of wearing, non-wearing time and the reason(s) for not wearing (e.g. nap, swimming, shower, etc.). The setting, in a hospital or home setting, had to be filled in each day. Parents or participants were asked to report the feasibility of wearing the Actical. For the wearing time validation, non-wearing time needed to be identified and labelled. The minimum wearing time of 8 h per day was required, and the minimum number of 4 valid days a week was required. If the wearing time of the Actical did not comply with these criteria, the data were withdrawn from the study. SB was defined as < 100 cpm for all age groups [36,40].

Table 1
Cut off points and classifications of PA level by counts per minute (cpm).

PA	SB	Light PA	Moderate PA	Vigorous PA
Children < 7 years old [40]	<100	100–2860	>2860	>5644
Children > 7 years old [36]	<100	100–1499	1500–6500	>6500

PA is expressed as counts per minute measured by the Actical; PA=Physical Activity; SB = Sedentary behaviour.

2.5. Data analysis

To describe the confidence level (%) of PA level of participants, a confidence interval of 90% with an absolute level of precision of 0.15 was used [41]. Data analyses were performed using IBM SPSS Statistics for Macintosh (Version 22.0. Armonk, NY: IBM Corp). The Shapiro-Wilk normality test showed that data were not normally distributed and that they were skewed. Descriptive and statistical values were expressed by graphic display; median and interquartile range (IQR) was reported for the data. The continuous data in cpm of the Actical were classified by cut-off points (Table 1) and described in minutes per day. Intergroup comparison of significant differences ($p < 0.05$) in PA level by age (age < 4, 4–12 and >12 years old), cancer type (Haematological malignancy or Solid tumours), sex (male or female), setting (home or hospital) and week or weekend days was analysed with the Mann-Whitney test or the Kruskal-Wallis test for not normally distributed data.

3. Results

A total of 46 children met the eligibility criteria, 15 children or parents chose not to participate. Reasons for not participating were (i) parents experienced too much emotional stress, (ii) children refused to wear the accelerometer. There were 6 dropouts out of the recruited participants. (Fig. 1. Participant recruitment).

A total of 25 children participated in the study, 17 participants with haematological malignancy and 8 participants with solid tumours. All participants that had met the eligibility criteria for recruitment were undergoing cancer treatment in the Princess Máxima Center and signed informed consent. Anthropometric characteristics of the participants are shown in Table 2.

All participants reported the Actical was well-accepted and the burden and risks associated with participation were negligible.

All 25 participants scored below the recommended minimum of 60 min of MPVA each day for school-age children, in duration as

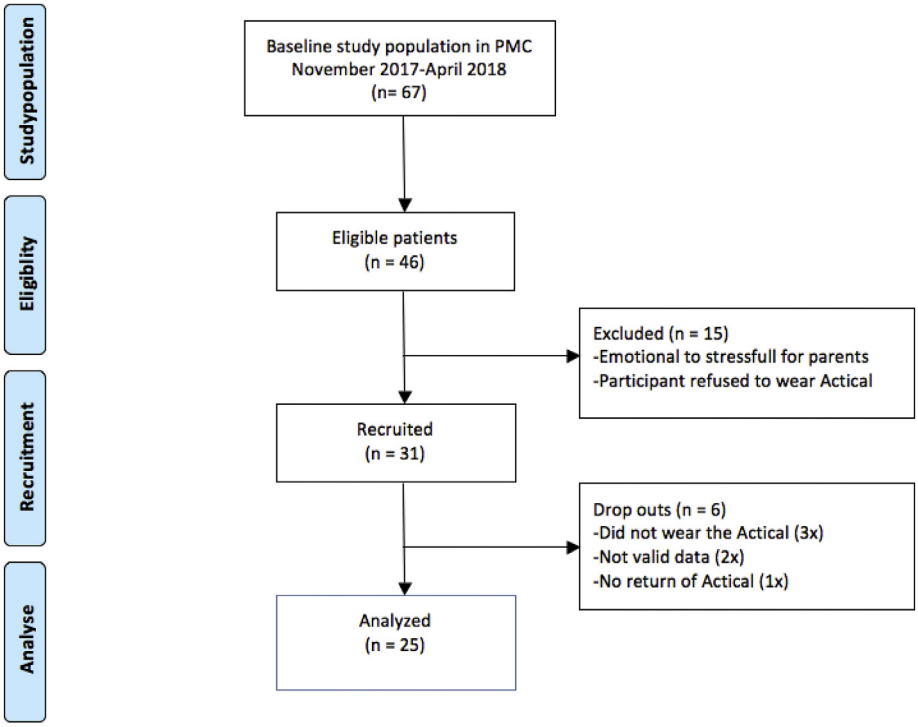

Fig. 1. Participant recruitment.

Table 2
Anthropometric characteristics of participants.

	N[a]	SD[b]	Median	Min-Max
Total	25			
Age (years. months)		4.7	8.2	3.1–17.0
<4 years old	4			
4–12 years old	13			
>12 years old	8			
Sex				
Boy	16			
Girl	9			
Body weight (kg)		19.1	25.1	14–74
Height (cm)		30.8	128	93–191
BMI (kg/m^2)		2.2	16.6	13.6–20.9
Cancer type				
Haematological malignancy	17			
Solid tumours	8			
Type of treatment				
Chemotherapy	17			
Radiotherapy	–			
Surgery	–			
Combination	8			
Number of valid wear days	138			
Home setting	105			
Hospital setting	24			
Week days	94			
Weekend days	41			
Average steps per day	3374	2698	3564	4-9172
Average MVPA in min per day	7	9	4	0-2

[a] N = number of participants.
[b] SD = standard deviation, ^min-max = minimum-maximum.

well as in intensity of PA (Fig. 2 and Table 3). The median daily minutes per PA level was 1325 min of sedentary behaviour (SB), 111 min of light physical activity (PA) and 4 min of moderate-to-vigorous physical activity (MPVA). The average MPVA was 7 min of MPVA per 24 h with a minimum of 0 and a maximum of 27 min of MPVA per 24 h (Table 3). The average percentage of minutes of PA per 24 h was 91,7% SB, 7,8% light PA and 0,5% MVPA (Fig. 2.). All of the participants scored below the recommended average number of steps per day for boys and girls. The average steps per day were 3374 with a minimum of 4 and maximum of 9172 steps per day (Table 3). 5 of the 25 participants scored an average above 5000 steps per day.In the hospital setting the participants achieved significantly lower levels of PA compared to the children assessed in the home setting (Table 4). In other subgroups there were no significant differences.

4. Discussion

The primary objective of this study was to explore whether accelerometery is feasible to measure PA levels in children with childhood cancer and to determine device-based PA levels of these children during treatment in hospital or home settings. We found that accelerometery seems to be suitable for the objective assessment of PA in children with childhood cancer during their treatment. The data give a presentation of their PA behaviour during the day. Accelerometers provide an objective assessment of PA and can be applied with different kinds of patients.

We found that all participants spent their awake time mostly sedentary, some light PA was performed and almost no MVPA was performed. During treatment children with childhood cancer performed only 4 min of MVPA per day in the home setting and almost no MVPA in the hospital setting. The children in the hospital setting scored lower in PA level in comparison to the children in the home setting.

PA levels in our population are comparable with device-based measured PA levels reported in other studies in paediatric oncology [33,37,38,44]. These studies found PA levels below the recommendations of the guidelines for PA and lower intensity of PA, especially in MVPA. Compared to the current data, Winter et al. [44] and Aznar et al. [38] found higher intensities of PA levels or steps per day in the leukaemia group compared to our data. The data of Tan et al. [37] and Gotte et al. [33] are more comparable to our data in MVPA. In the study of Tan et al. [37] only in-hospital leukaemia patients were included. Overall our study population showed lower PA levels in both duration and intensity compared to the other studies [28,33,34,40]. According to Winter et al. [43], an important factor to compare data of PA level in individual children undergoing cancer treatment is the stage of cancer treatment the children are in. However, in our study we did not take into account the date of diagnosis or the duration of cancer treatment because of the heterogeneity of the group.

The secondary objective was to analyse differences in PA level by

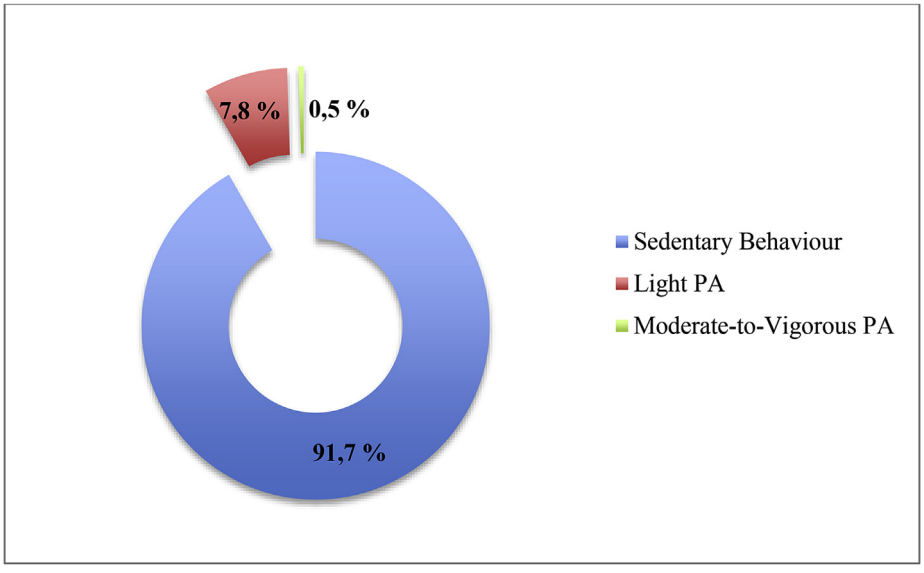

Fig. 2. PA level in average percentages per 24 h.

Table 3
PA level in minutes and amount of steps per 24 h.

PA	N=	SB	Light PA	MVPA	Steps
		Median (25th-75th quartile)	Median (25th-75t quartile)	Median (25th-75th quartile) Mean (min-max)	Mean (min-max)
All patients	25	1325 (1245–1410)	111 (28–187)	4 (0–12)[a] 7 (0–27)[a]	3374 (4–9172)

PA is expressed in minutes per 24 h measured by the Actical; PA=Physical Activity; SB = Sedentary Behaviour; Light PA= Light Physical Activity; MVPA = Moderate-to-Vigorous intensity of Physical Activity.
[a] Multiple guidelines recommend a minimum of 60 min of moderate-to-vigorous intensity physical activity (MPVA) every day for school-age children (14).

age, cancer type, sex, setting (hospital or home setting) and week or weekend days.

We found that participants in a hospital setting showed significantly lower levels of PA compared with children in a home setting. Winter et al. [44] also found significant differences between home and hospital setting. Participants were less active during hospital stays. In addition, Winter et al. [44] found a difference between PA levels in subgroups of types of cancer. Bone tumour patients had lower outcomes in PA than leukaemia patients [44]. In our study only participants with haematological malignancy and solid tumours were included. No significant differences between these two types of cancer groups were found. Tan et al. [37] only included leukaemia patients in a clinical setting. Data of PA level of the leukaemia patients in the study of Tan et al. [33] were comparable to our data of PA levels in the hospital setting. These data show the importance of a PA stimulating environment in paediatric oncology wards and hospitals. In the present study we found no significant differences between PA levels during week or weekend days. Children were very sedentary on both week and weekend days. Aznar et al. [38] also found no differences between groups during week or weekend days. However, on weekdays, all participants spent less minutes of MVPA, so they showed lower intensity compared to healthy peers.

Tan et al. [37] described two theories to explain reduced PA in CCS. The first is linked to the adverse effects experienced by patients due to chemotherapy, such as impaired pulmonary function, osteopenia and fatigue. Secondly the overprotective approach of many parents and caregivers is important. It influences the child's perception of its capability for PA. In a recent study from Ross et al. [43] PA barriers, preferences and beliefs are described for CCS. A large proportion of the participants in this study mentioned the safety concerns for doing physical exercise in relation to their diagnosis of childhood cancer [43]. It is our experience that in a clinical setting, active treatment and receiving infusion therapy also influences the capability of being physically active. Therefore, it was to be expected that participants in a hospital setting would even have a lower level of PA compared with participants living in a home setting.

One of the strengths of this study are the device-based measured PA levels by accelerometery during active cancer treatment. The used accelerometer, the Actical, is well-tolerated by children and has been validated for measuring PA among children in free-living conditions [36]. Another strength is that the level of PA was classified by age, based on cut off points for participants aged <7 years old by Pfeiffer et al. [40] and participants aged ≥ 7–18 years old by Puyau et al. [36] (Table 1), which makes the data more reliable per age group.

Choosing the Actical also introduced limitations, e.g. SB could be overestimated because during daytime children did not wear the Actical when taking naps or showers. We have corrected the data for the swimming time. The Actical does not measure the physiological demand of exercise (e.g. heart rate) and energy expenditure was not estimated using the data since no prediction equation for measuring activity energy expenditure in children with childhood cancer is available. These additional data could have provided more information about the energy costs and intensity of movement during PA.

Another limitation of this study is that the population studied

Table 4
Level of Physical Activity comparison per subgroup.

PA	N=	SB		Light PA		MVPA	
		Median (25th-75th quartile)	Sign	Median (25th-75th quartile)	Sign	Median (25th-75th quartile)	Sign
All patients	25						
Age			*0,69*		*0,57*		*0,24*
< 4	4	1313 (1227–1338)		116 (101–211)		2 (0–2)	
4–12	13	1284 (1214–1417)		129 (23–209)		4 (0–18)	
> 12	8	1352 (1275–1392)		81 (46–151)		7 (2–10)	
Sex			*0,80*		*0,76*		*0,76*
Boys	16	1314 (1237–1413)		1312 (27–189)		4 (0–5)	
Girls	9	1342 (1245–1369)		98 (24–189)		4 (0–9)	
Cancer type			*1,00*		*0,84*		*0,80*
Haematology	17	1344 (1245–1410)		88 (28–187)		6 (1–13)	
Solid tumours	8	1322 (1221–1401)		117 (39–203)		1 (0–10)	
Setting			0,03*		0,04*		0,05
Hospital	24	1412 (1333–1431)		28 (9–104)		0 (0–4)	
Home	105	1302 (1218–1386)		112 (53–207)		4 (1–14)	
Days			*0,89*		*0,99*		*0,30*
Week days	94	1320 (1233–1400)		106 (35–181)		4 (0–16)	
Weekend days	41	1310 (1214–1418)		95 (30–184)		2 (0–8)	

PA is expressed in minutes per day measured by the Actical; PA=Physical Activity; SB = Sedentary Behaviour; Light PA= Light Physical Activity; MVPA = Moderate-to-Vigorous intensity of Physical Activity; Sign = significance.
* Significance difference intergroup comparison by Mann-Whitney test ($p < 0.05$).

was not representative for the Dutch population of children with childhood cancer. From the literature it is known that the highest prevalence of performance limitations can be found in patients with bone sarcoma and brain tumours and these children were not included in this study [13]. Therefore, the results of this study cannot be generalized to all children with childhood cancer, but only for the subgroups of children with haematological malignancy and solid tumours. The recruitment of participants had to end in May 2018 because of the opening of a new facility for paediatric oncology, the Princess Máxima Center, and this has limited the number of participants. Due to the limited sample size the confidence interval dropped just below 90% [41].

The study population of the feasibility study was heterogenic in age, stage and type of treatment. The side effects of treatment varied greatly and individual disease- or treatment related factors were not reported.

Now we find that accelerometery is feasible, recommendations for further research are, to set up a longitudinal, prospective study design with more homogenic groups with larger sample sizes to determine initial PA levels on an individual basis and to set up an exercise program based on this initial PA assessment and finally to evaluate the programme by comparing pre and post PA-assessments and to include other important factors like health-related quality of life. It is important to determine reasons of reduced PA in children during cancer treatment and study the benefits of PA in children during cancer treatment such as better toleration of chemotherapy treatment-induced effects and contribution to better quality of life as reported in adult oncology patient populations [26–28]. It is important to determine the differences between capacity and perception of capability of PA in these children and their parents. As there is still a safety concern towards exercise in relation to diagnosis in many parents according to a study from Ross et al. [42]. More research in the total population of childhood cancer patients is needed to get more insights. With the growing population of CCS, substantiated PA guidelines should be developed and PA for these patients should be encouraged. If it is evident to indicate that PA for these children needs to be encouraged and increased, to minimalize the negative long-term side effects and side effects of treatment, it is necessary to stimulate activity programmes.

Thereby parents and children should be informed about limitations and benefits of PA in children with childhood cancer and parents should be guided in encouraging and stimulating their children. In hospital settings the surroundings are important to challenge children in PA. Our policy is to encourage children to stay out of bed as much as possible.

The interior design of the Princess Máxima Center is purposefully developed to challenge children to be and become physically active. To stimulate movement, stairs, bicycles, a movement garden and activity rooms are provided. It would be interesting to repeat this study after transition into the new building to investigate the effects of this policy to stimulate PA in the vulnerable population.

5. Conclusion

This study measured PA level using accelerometery in children during cancer treatment in both home and hospital settings. All participants in our study had a severely reduced PA level compared to the general recommendations for PA in children. Significant differences in PA levels were found between home or hospital settings.

It is strongly recommended to determine benefits and limitations of PA in children during cancer treatment and differences in perceptions of capability of PA of these children. With the growing population of CCS, substantiated PA guidelines and advices should be developed. PA for these patients should be encouraged and stimulated to minimize the side effects during and after treatment.

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