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University of Turku

ASSESSMENT AND PROMOTION OF PHYSICAL ACTIVITY IN CHILDREN – WITH SPECIAL REFERENCE TO CHILDREN DIAGNOSED WITH CANCER

Lotta Hamari

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To Jarkko and Heino

ABSTRACT

Lotta Hamari

ASSESSMENT AND PROMOTION OF PHYSICAL ACTIVITY IN CHILDREN – WITH SPECIAL REFERENCE TO CHILDREN DIAGNOSED WITH CANCER

University of Turku, Faculty of Medicine, Nursing Science
Annales Universitatis Turkuensis, Turku, 2018

The aim of this study was to explore how to assess and support physical activity of children diagnosed with cancer, and to describe the physical activity levels in children diagnosed with cancer compared to healthy children.

Healthy children's physical activity was explored with a longitudinal cohort study (study I). The proportion of those who spent less than 1 hour in leisure-time physical activities weekly was 17% at the age of 10-years, 12% at the age of 12-years, and 38% at the age of 15 (n=571). Self-perceived physical competence was positively associated with physical activity ($p<0.05$), and the association was strengthened with age.

At study II FitbitOne® step counts were compared to ActiGraph with an experimental design in 9-to-10-year old children (n=34). Positive correlations were consistent, r=0.94, but FitbitOne® overestimated the step counts significantly when compared to ActiGraph.

At study III, effectiveness of active video games was studied with randomised controlled trial in 3-to-16-year old children diagnosed with cancer (n=36). The intervention was not effective in physical activity (p=0.63), or motor performance (p=0.77), nor in reducing fatigue (p=1.00). Small sample size and large standard deviations may have hidden the effective results. Physical activity did not differ either by diagnosis or gender. The difference between younger children (aged 3–8) and older children (aged 9–16) was significant for step counts (p=0.028) and physical activity min/day (p=0.042).

At study IV the physical activity levels (p=0.56) or self-perceived physical competence (p=0.78) did not differ between children diagnosed with cancer and healthy children (data from studies I and III). The promotion of physical activity both in healthy children and in children diagnosed with cancer is warranted.

Keywords: physical activity, childhood cancer, active video games, motor performance, fatigue, self-perceived physical competence, randomized controlled trial

TIIVISTELMÄ

Lotta Hamari

LASTEN FYYSISEN AKTIIVISUUDEN ARVIOINTI JA EDISTÄMINEN – ERITYISENÄ KOHDERYHMÄNÄ SYÖPÄÄ SAIRASTAVAT LAPSET

Turun yliopisto, lääketieteellinen tiedekunta, hoitotiede
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Tutkimuksen tarkoituksena oli selvittää miten syöpää sairastavien lasten fyysistä aktiivisuutta voidaan arvioida ja tukea. Lisäksi tarkoituksena oli tutkia syöpää sairastavien lasten fyysisen aktiivisuuden määrää ja verrata sitä terveiden lasten fyysisen aktiivisuuden määrään.

Terveiden lasten fyysistä aktiivisuutta arvioitiin pitkittäis-kohorttitutkimuksella (osatutkimus I). Tutkimukseen osallistuneista lapsista (n=571) liikkui vapaa-aikanaan alle tunnin viikossa 10-vuotiaina 17%, 12-vuotiaina 12% ja 15-vuotiaina 38%. Lasten kokema fyysinen pätevyys oli yhteydessä fyysisen aktiivisuuden määrään kaikissa ikäpisteissä ($p<0.05$) ja yhteys vahvistui iän myötä.

Toisessa osatutkimuksessa FitbitOne® kiihtyvyysmittarin askelmääriä verrattiin ActiGraph kiihtyvyysmittarin antamiin askelmääriin kokeellisella asetelmalla 9–10-vuotiailla lapsilla (n=34). Laitteiden antamat askelmäärät korreloivat keskenään (r=0.94) mutta FitbitOne® yliarvioi askelmäärän verrattuna ActiGraphiin.

Tutkimuksen kolmannessa osatutkimuksessa aktivoivien videopelien vaikutuksia tutkittiin 3–16-vuotiailla syöpää sairastavilla lapsilla (n=36) satunnaistetussa ja kontrolloidussa asetelmassa. Interventiolla ei ollut vaikutusta syöpää sairastavien lasten fyysiseen aktiivisuuteen (p=0.63), motoriseen suoriutumiseen (p=0.77) tai itsearvioituun uupumukseen (p=1.00). Diagnoosi tai sukupuoli eivät olleet yhteydessä fyysisen aktiivisuuden määrään. Kuitenkin 3–8-vuotiaat liikkuivat enemmän kuin 9–16-vuotiaat (askelmäärä p=0.028 ja aktiivinen aika min/päivä p=0.042).

Neljännessä osatutkimuksessa syöpää sairastavien lasten ja terveiden lasten fyysisen aktiivisuuden määrää ja koettua fyysistä pätevyyttä verrattiin keskenään (aineistot osatutkimuksista I ja III). Fyysisen aktiivisuuden määrä (p=0.56) tai koetun fyysisen pätevyyden arvot (p=0.78) eivät eronneet syöpää sairastavien lasten ja terveiden lasten välillä. Sekä terveiden lasten että syöpää sairastavien lasten fyysisen aktiivisuuden edistäminen on perusteltua.

Avainsanat: fyysinen aktiivisuus, lapsuusiän syöpä, aktivoivat videopelit, motorinen suoriutuminen, uupumus, koettu fyysinen pätevyys, satunnaistettu koe-kontrollitutkimus

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ABBREVIATIONS

ALL	Acute lymphoblastic leukemia
AVG	Active video game
CRF	Cardiorespiratory fitness
DLW	Double labelled water
GEE	Generalised estimating equation
LTPA	Leisure-time physical activity
M-ABC2	Movement ABC-2
MET	Metabolic equivalent
PA	Physical activity
PAQ	Physical activity questionnaire
PedsQL™	Pediatric Quality of Life Inventory™
QOL	Quality of life
RCT	Randomised controlled trial
SDT	Self-determination theory
SPPC	Self-perceived physical competence

LIST OF ORIGINAL PUBLICATIONS

Hamari L., Heinonen O.J., Aromaa M., Asanti R., Koivusilta L., Koski P., Laaksonen C., Matomaki J., Pahkala K., Pakarinen A., Suominen S. & Salantera S. (2017) Association of self-perceived physical competence and leisure-time physical activity in childhood – A follow-up study. The Journal of School Health 87(4), 236–243. (Study I, article I)

Hamari L., Kullberg T., Ruohonen J., Heinonen O.J., Diaz-Rodriguez N., Lilius J., Pakarinen A., Myllymaki A., Leppanen V. & Salantera S. (2017) Physical activity among children: objective measurements using Fitbit One® and ActiGraph. BMC Research Notes 10(1), 161-017-2476-1. (Study II, article II)

Kauhanen L., Jarvela L., Lahteenmaki P.M., Arola M., Heinonen O.J., Axelin A., Lilius J., Vahlberg T. & Salantera S. (2014) Active video games to promote physical activity in children with cancer: a randomized clinical trial with follow-up. BMC Pediatrics 14, 94-2431-14-94. (Study III, article III)

Hamari L., Jarvela L., Lahteenmaki P.M., Arola M., Heinonen O.J., Axelin A., Lilius J., Vahlberg T. & Salantera S. The effect of an active video game intervention on physical activity, motor performance, and fatigue in children with cancer: A randomized controlled trial. (Submitted) (Study III, article IV)

 The thesis contains also unpublished material (study IV).

1 INTRODUCTION

Childhood cancer affects children and their families in many ways. Despite of the life-saving effects of the cancer treatment, aggressive treatments leave children at risk for negative physical and psychosocial early and late effects (Gawade et al. 2014, de Fine Licht et al. 2017, Huang et al. 2017). Common concerns among childhood cancer survivors are becoming overweight or obese, osteoporosis, reduced cardiopulmonary and musculoskeletal capacity, health-related quality of life and cardiovascular health (Kelly 2011, Green et al. 2013, Ness et al. 2015, Beulertz et al. 2016, Deisenroth et al. 2016), which all may be positively influenced by physical activity (Braam et al. 2013, Götte et al. 2013).

Physical activity in children diagnosed with cancer is reduced due to the disease itself, treatment-related side-effects, and isolation from everyday activities (Castellino et al. 2005, Florin et al. 2007, Winter et al. 2010, Stolley et al. 2010, Kelly 2011, San Juan et al. 2011, Tan et al. 2013, Götte et al. 2013). Also, parents of children diagnosed with cancer experience many psychosocial issues related to their child's condition and treatment (Raber et al. 2016), which may decrease parental support on the child's physical activity. Furthermore, treatment-related impairments in cardiorespiratory and muscle function may further worsen the decreased levels of physical activity after the treatment (Järvelä et al. 2010, Wong et al. 2014). Neither childhood cancer survivors nor the general child population meet the physical activity recommendations (Stolley et al. 2010, Winter et al. 2010, San Juan et al. 2011, Tremblay 2014).

Physical activity is an important part of healthy lifestyle. It has been connected to prevention, treatment and rehabilitation of several diseases and conditions (Lee et al. 2012, Eime et al. 2013, Andersen et al. 2016, Ekelund et al. 2016), and it has a significant role in securing the motor development of a child (Gallahue 2012). In healthy children, physical activity is usually a normal part of everyday life but during illness, it may become neglected (Winter et al. 2009, Fuemmeler et al. 2013, Tan et al. 2013).

Studies have shown that physical activity and exercise interventions are safe and beneficial even during the cancer treatment (Braam et al. 2013, Baumann et al. 2013, Wong et al. 2014, Grimshaw et al. 2016). However, it is still unclear when and how physical activity should be promoted during the cancer treatment.

The starting point of this study was the need to activate children diagnosed with cancer in a fun, entertaining and effective manner as part of an effort to improve their health and wellbeing in hospital and at home. That is how we settled upon building a physical activity intervention around active video games.

To understand physical activity habits during cancer, it is important to understand children's physical activity in general. This aim led us to also examine physical activity in healthy children. Healthy children's data enabled us to make comparisons of physical activity in healthy children and in children diagnosed with cancer. The results of this study may be used in developing, targeting and implementing physical activity interventions for healthy children and especially for children diagnosed with cancer.

2 BACKGROUND OF THE STUDY

2.1 Physical activity in children

2.1.1 The definition and importance of physical activity

Before going deeper into the phenomenon of physical activity in children diagnosed with cancer, it is indispensable to understand why physical activity is important in children in general. Physical activity is defined as “any bodily movements produced by skeletal muscles that result in a substantial increase over the resting energy expenditure” (Caspersen 1985, Dishman 2006, WHO 2015).

Physical activity has several benefits to health and wellbeing, and in childhood, it is essential to achieving healthy lifestyle (Lee et al. 2012, Eime et al 2013, WHO 2017c). Physical activity is associated with developing healthy musculoskeletal and cardiovascular systems, to developing neuromuscular awareness and motor skills, and to maintaining a healthy body composition and energy balance (Kohl & Hobbs 1998, Gallahue 2012, WHO 2017c). Conversely, physical inactivity is a risk factor for many chronic conditions, and non-communicable diseases in adulthood such as type two diabetes and cardiovascular diseases, obesity, osteoporosis, some cancers and potentially depression (Lee et al. 2012, Andersen et al. 2016). In addition, motor difficulties and low levels of psychosocial well-being, cognitive functioning and educational achievement are associated with physical inactivity (Williams et al. 2008, Piek et al. 2008, Cliff et al. 2009, Kantomaa et al. 2013). From the perspective of society, physical inactivity cost billions to health care systems worldwide each year (Ding et al 2016).

Low amounts of physical activity and high amounts of sitting time are associated with increased risk of mortality (Ekelund et al 2016). It is estimated that three-to-five million deaths each year worldwide are attributable to physical inactivity (Lee et al. 2012, Wen & Wu 2012, WHO 2017a), and about 2.6 million people die as a consequence of being overweight or obese each year (WHO 2017b). This further highlights the need to promote physical activity in childhood, since the foundation for health choices later in life are built in childhood. A physically active lifestyle is shown to develop early in childhood and the persistence of physical activity from youth to adulthood is moderate or high (Telama et al. 2014).

The prevalence of obesity in children has risen sharply in recent decades, and it has been estimated that in 2014, approximately 41 million children under five years of age were overweight or obese (Ebbeling et al. 2002, WHO 2016). As is the children's physical inactivity, childhood obesity is a public-health crisis (Ebbeling et al. 2002, Chan & Woo 2010). Obesity is preventable by dietary and physical activity behaviours (Sallis & Glanz 2009, Chan & Woo 2010, WHO 2016).

In addition to the physical health benefits of physical activity and the risks of inactivity, physical activity has several psychological and social benefits (Eime et al 2013). Physical activity is associated with better sleep quality, improved cognitive function and academic performance, as well as beneficial effects on self-esteem, and control over symptoms of anxiety and depression (Strong et al. 2005, Lee et al. 2012, Eime et al 2013, WHO 2017c). Physical activity has also been suggested to support the social development of children by providing possibilities for self-expression, feelings of relatedness and social interaction (Eime et al 2013, WHO 2017c).

2.1.2 Recommended levels of physical activity

The World Health Organization's (WHO) recommendations on physical activity for health for 5–17-year-old children states that children should accumulate at least one hour of moderate- to vigorous-intensity physical activity every day. Daily physical activity should be mostly aerobic (WHO 2010). Also based on a comprehensive review, school-age children should participate at least 60 minutes of moderate- to vigorous-intensity physical activity daily. Physical activity is suggested to be enjoyable and involve different kind of activities. (Strong et al. 2005.) Activities that strengthen muscle and bone should be implemented at least 3 times per week. (WHO 2017c.)

In Finland, at least one to two hours of age-appropriate and diverse physical activities every day are recommended for children aged 7–18 (Tammelin & Karvinen 2008, UKK institute 2017). Based on the Finnish recommendations, sedentary time should be limited to two hours at a time, and screen time should be limited to two hours per day (Tammelin & Karvinen 2008). For younger children, at least three hours of physical activity each day is recommended by the Finnish Ministry of Education and Culture (2016). The intensity of physical activity is recommended to vary during the day, but also high-intensity bursts are recommended to be included in each day (Janssen & Leblanc 2010, WHO 2010, Ministry of Education and Culture, Finland 2016).

2.1.3 The levels of physical activity in children

Even though the knowledge of the recommendations of physical activity and the benefits of physical activity are available worldwide, only a small number of children in the high-income countries carry out the recommended levels of physical activity (Tremblay 2014, Cooper et al. 2015). Children under 10 years of age tend to have higher levels of physical activity, but the physical activity levels decrease significantly between ages 11 and 15 and through adolescence (Riddoch et al. 2004, Dumith et al., 2011, Currie et al. 2012). This decrease in physical activity in adolescence is also called as drop-off phenomenon (Aira et al. 2013). Another phenomenon that is linked to children's physical activity behavior is polarisation. Those children that are physically active are very active (Jayanthi et al. 2015), and on the other extremity, children have high levels of sedentary behavior. (VLN 2013.) In 2010, over 80% of 11-to-17-year-old adolescents were insufficiently physically active (WHO 2017d). Girls are less physically active than boys both in childhood and in adolescence (Ekelund et al. 2012, Hallal et al. 2012, Soini et al. 2014, WHO 2017d). The low physical activity levels and the decrease in physical activity during adolescent years is a global phenomenon that is also strongly evident in Finnish youth (Currie et al. 2012, Aira et al. 2013, WHO 2017d). The reasons for children being physically active or inactive varies, but some determinants of physical activity in children have been recognised by previous research. These are described in the next paragraph.

2.1.4 Correlates and determinants of physical activity

Correlates and determinants of physical activity may be placed into five categories: demographic or biological, psychosocial, behavioural, social and cultural, and environmental factors (Trost et al. 2002, Bauman et al. 2012).

Of biological factors, male gender is a consistent positive determinant of physical activity in children and adolescents (Craggs et al. 2011, Bauman et al. 2012).

Of psychosocial factors, self-efficacy and perceived behavioural control are positive determinants of physical activity in children and adolescents (Craggs et al. 2011, Bauman et al. 2012). Some psychosocial determinants are inconclusive in children and adolescents. These inconclusive findings are regarding valuing physical activity for health status, perceived barriers to physical activity, perceived competence and attitude (Sallis et al. 2000, Van Der Horst et al. 2007, Bauman et al. 2012). In adolescents, physical or sports competence have been found to be associated with physical activity (Sallis et al. 2000, Van Der Horst et al. 2007), but also inverse findings have been presented (Craggs et al. 2011). Factors that motivates children and adolescents to be physically active are skill development, physical fitness, fun and enjoyment, social cohesion, appearance, challenge and success (Biddle & Murtie 2008, Aaltonen et al. 2014).

Strong behavioural predictors of physical activity are previous physical activity, and participation in community sports (Sallis et al. 2000, Cox et al. 2009, Craggs et al. 2011, Bauman et al. 2012).

Of social and cultural factors, social support and influences are considered to be determinants of physical activity (Sallis et al. 2000, Biddle et al. 2005, van der Horst et al. 2007, Craggs et al. 2011, Bauman et al. 2012). It means that friends, family, and different community groups have influence on a child's self-identity, thoughts, behaviour and feelings, which further predicts the physical activity behavioural patterns in adulthood (Kohl & Hobbs 1998, ACSM 2015). Parental support is significantly associated with children's physical activity (Trost & Loprinzi 2011). Especially mothers' activity habits are associated with daughters' physical activity (Pahkala et al. 2007). When children grow older, parental support becomes less prominent, and peers' and siblings' influence become more consistent (Sallis et al. 2000, Heitzler et al. 2006). It has also been suggested that parental support is not a determinant of children's physical activity (Craggs et al. 2011).

Environmental influences associated with physical activity behaviour include access to physical activity resources, safety and structure of the environment (Ferreira et al. 2007). The time spent outdoors is positively influencing to the amount of physical activity in children (Sallis et al. 2000, Soini et al. 2014).

2.1.5 Assessment of physical activity in children

A valid and reliable assessment of physical activity is important to understand physical activity behaviour in children, to evaluate the prevalence of children meeting the physical activity recommendations, and to be able to evaluate the effectiveness of physical activity interventions. Valid instruments are needed by both clinical and research communities. (Wareham 1998, Welk 2002.)

Physical activity can be evaluated by both subjective and objective methods (Trost 2007). Subjective methods are physical activity questionnaires (PAQs), and diaries, sometimes called logs (Trost 2007). PAQs are suggested to be the most feasible in large-scale studies, because they are of low cost and are convenient. However, PAQs have limitations and only a few PAQs are reliable and valid, even in adult populations (Helmerhorst et al. 2012). Physical activity diaries are studied more rarely than PAQs, but in some studies activity diaries, it has been shown to be feasible in hospitalised adult populations for determining sedentary, moderate, and total physical activity (Vanroy et al. 2014). Activity diaries have also been used to evaluate sedentary behaviour in children (Lubans et al. 2011), but when validated against objective criterion measure, they have been suggested to have lower levels of validity than objective methods (Wen et al. 2010).

The objective methods of assessing physical activity in children include direct observation, measures of energy expenditure (doubly labeled water, measurement of respiratory gas exchange, calorimeters), physiological measures (heart rate monitoring), motion sensors (pedometry and accelerometry), and a combination of these (Trost 2007, Strath et al. 2013). Double labelled water (DLW) is considered to be the golden standard and the most accurate measure of total energy expenditure. However, DLW is quite rarely used in research studies, because it is expensive and time-consuming, it has high subject burden, and it cannot capture the type of activity (Schoeller et al. 1986, Melanson et al. 1996, Plasqui & Westerterp 2007, Westerterp et al. 2009).

Amongst physiological metrics, heart rate monitoring has become popular, although it is problematic at low-intensity levels of activity (Strath et al. 2013). At the moment, accelerometry is the most commonly used and recommended objective measure of physical activity in children and adults (Trost 2007, Hildebrand et al. 2016). Accelerometers have widespread potential in practical applications provided that their costs keep becoming reasonable (Hallal et al. 2012).

Direct observation has been suggested to be valid and reliable in assessing physical activity in children (McKenzie et al. 2002). However, this method is time-consuming, and thus, expensive. The advantages of direct observation includes the possibility to record factors related to physical activity (such as type of activity, equipment used, environmental and social context) in addition to the duration, frequency and intensity of activity. (Trost 2007.)

Measuring physical activity in children is a complex procedure and challenges the research community (Helmerhorst et al. 2012, van Sluijs & Kriemler 2016). It is recommended that objective measurement devices (such as accelerometers) are used in conjunction with subjective measurements, at least when measuring low intensities of activity, and to be able to collect information of the type and context of behaviour (Lubans et al. 2011). Physical activity measurement should be able to catch the activity during daily life and long periods of time to ensure representativeness (Plasqui & Westerterp 2007).

2.1.6 Promotion of physical activity in children

Research assessing and describing physical activity, its correlates and physical activity interventions in children have increased greatly over the past two decades (Rhodes & Nasuti 2011, van Sluijs & Kriemler 2016). Evidence shows that the majority of children do not carry out the recommended levels of physical activity (Riddoch et al. 2004, Currie et al. 2012, Tremblay 2014). Yet, we do not know enough of the promotion of physical activity. Some evidence exists for potentially effective strategies (van Sluijs et al. 2007), but the evidence base is still fragile (van Sluijs & Kriemler 2016), and the changes in physical activity have been modest (Mehtälä et al. 2014).

To be able to build effective interventions for physical activity promotion in children and adolescents, multilevel approaches needs to be considered: 1) physiological and developmental factors, 2) environmental factors, and 3) psychological, social, and demographic factors (Kohl & Hobbs 1998, Sallis et al. 2016). Multicomponent interventions, which include both school or daycare and family, are potentially effective and should be promoted (van Sluijs et al. 2007, Trost & Loprinzi 2011, Mehtälä et al. 2014, Soini et al. 2014, Sallis et al. 2016). Three settings, schools, homes, and health care settings, have been considered as best practice or the most promising settings (Trost & Loprinzi 2008). Evidence suggests that school-based physical activity interventions have positive effects on behaviour and physical health status (Dobbins et al. 2013). It is also suggested that when building the intervention, the views of those who are expected to deliver and participate in the intervention should be integrated into the development process from early in the process (van Sluijs & Kriemler 2016). Small children's interventions should focus on increasing children's free play, outdoor time, and positive encouragement by daycare personnel and teachers (Soini et al.2014).

When considering what makes children and adolescents get up and be active, above all is the component of making it fun (Neumark-Sztainer et al. 2000, van Sluijs & Kriemler 2016). Interventions are suggested to invest in sustained engagement rather than momentary enjoyment (van Sluijs & Kriemler 2016). Different psychological theories, for example, Self Determination Theory, have been used in intervention studies to sustain enjoyment and increase autonomous motivation (Deci & Ryan 2007, 2012, Plotnicoff et al. 2013). Self Determination Theory has been successfully used in promoting physical activity behaviour of children and adolescents (Plotnicoff et al. 2013). Also, Bandura's social cognitive theory, and other explanatory frameworks of human behaviour are useful in physical activity research (Young et al. 2014). Generally, it is suggested that theory-based physical activity interventions are more effective than interventions with no theoretical framework (Michie & Abraham 2004, Plotnicoff et al. 2013, Young et al. 2014).

Today, research community and health care professionals have begun to study and use digital solutions, such as digital games, to promote physical activity among children (Kharrazzi et al. 2012, Parisod et al. 2014). One innovative solution that has been under several evaluations are active video games (AVG) (Biddiss et al. 2010, Barnett et al. 2011, Primack et al. 2012, Parisod et al. 2014). In AVGs, the gaming is based on the player's movements, and playing these games equals to light-to-moderate physical activity. In more detail, playing active video games with light or moderate effort equals 2.3–3.8 metabolic equivalents. (Ainsworth et al. 2011.) They have become popular among children and adolescents, since they are attractive and fun to play (Penko et al. 2010). Examples of active video games include Nintendo Wii™ (Nintendo Co., Ltd., Kyoto, Japan) Xbox Kinect (Microsoft Co., Redmond, WA, USA) and Konami Dance Dance Revolution (Harmonix Music Systems Inc., Cambridge, Massachusetts, USA). These games have also been used in health care in promoting physical activity in different populations (Kharrazzi et al. 2012, Primack et al. 2012, Parisod et al. 2014).

2.1.7 Summing up the background of physical activity in children

To sum up the previous chapter, only a small proportion of children in the high-income countries carry out the recommended levels of physical activity (Tremblay 2014, Cooper et al. 2015, WHO 2017d). Physical activity participation is essential for normal development and physical and psychosocial health and wellbeing of all children (Gallahue 2012, Eime et al. 2013). Therefore, despite the challenges in assessing physical activity and finding the right ingredients in an effective intervention, physical activity should be promoted in healthy children and in children with disabilities whenever possible as a lifelong positive health behaviour (Trost & Loprinzi 2008, van Sluijs & Kriemler 2016, WHO 2017c).

2.2 Childhood cancer

Childhood cancer is a life-threatening condition, and an estimated of 300,000 children aged 0–19-year-old are diagnosed with cancer every year worldwide (ACCO 2018). In western countries, cancer is also the second most common cause of death in children (Buka et al. 2009, Pizzo & Poplack 2016, SVT 2017, CHOC 2018).

In Finland, approximately 200–250 children and adolescents ages 0–19 are diagnosed with cancer every year. The incidence rate of cancer cases by age-categories are 0–4 years: 20.4, 5–9 years: 14.5, 10–14 years: 11.7, and 15–19 years 17.6. per

100,000. (Finnish Cancer Registry 2016a, 2016b, 2018). In resource-rich countries, like Finland, and most European countries, the five-year survival rate is over 80% (Gatta et al. 2009, Howlader et al. 2016, Madanat-Harjuoja et al. 2014). This means that approximately 7,000 Finns have had and survived from cancer before their 25th birthday (Madanat-Harjuoja 2016).

The causes of the majority of childhood cancers are largely unknown and thought to be either sporadic or multifactorial (Lichtenstein et al. 2000, Buka et al. 2009). Genetic factors have a minor contribution (Lichtenstein et al. 2000), and approximately 1–10% of all childhood cancer patients have been affected due to a genetic syndrome or inherited susceptibility (Narod et al. 1991, Strahm & Malkin 2006). Environmental factors, such as radiation exposure (radioactivity, electromagnetic fields, UV), chemicals related to environmental pollution or early exposure to virus infections (for example, Epstein Barr virus, hepatitis B, and HIV) have been linked to some types of childhood cancers (Belpomme et al. 2007, Buka et al. 2009, Pizzo & Poplack 2016, American Cancer Society 2017).

The most common cancer types in children are leukemias, central nervous system tumours and lymphomas (Madanat-Harjuoja et al. 2014, Finnish Cancer Registry 2016a, 2016b, Pizzo & Poplack 2016, NIH 2017). Other common cancer types in children are kidney tumours, neuroblastoma, soft tissue sarcomas and bone tumours (Madanat-Harjuoja et al. 2014, Finnish Cancer Registry 2016a, 2016b, NIH 2017). The treatment regimens and five-year survival rates differ between cancer types (Madanat-Harjuoja et al. 2014). Survival figures are over 80% in resource-rich countries (Gatta et al. 2009, Howlader et al. 2012, Madanat-Harjuoja et al. 2014).

2.3 Life during the treatment of childhood cancer

The length and type of treatment depends on the type of cancer, the location and stage of disease at the time of diagnosis (Madanat-Harjuoja et al. 2014, Pizzo & Poplack 2016). Depending on the protocol, chemotherapy, radiotherapy, surgery or combinations of these are excessive treatments that children and their family need to go through during the child's disease. The average treatment time varies between two months and 2.5 years. The most common cancer in children, acute lymphoblastic leukemia, is treated for 2.5 years. Considering the typical age (2–4 years) at leukemia diagnosis and the length of the treatment, these children have been treated for cancer for half of their lives. (Pizzo & Poplack 2016.) In every case, the cancer disease and its treatment means immeasurable burden on the family and the child's life during their years of growth, and also the normal child development is at risk of being affected.

In Finland, the treatment of children diagnosed with cancer is centralised into five tertiary hospitals. The treatment protocols of leukemias follow the Nordic Society of Pediatric Hematology and Oncology (NOPHO) regimens. (Pihkala 2013, Madanat-Harjuoja et al. 2014.) Based on certain risk features at diagnosis, the NOPHO treatment regimen is dividing the treatment into three intensity groups: standard risk, intermediate risk and high risk. In the NOPHO protocol, the treatment duration for all risk groups is 2.5 years. (NOPHO – ALL 2008.) For other malignancies, even broader international groups are guiding the therapies.

Despite the life-saving effects of the cancer treatment, aggressive treatments leave children at risk of negative physical and psychosocial early and late effects (Gawade et al. 2014, de Fine Licht et al. 2017, Huang et al. 2017). These negative effects can occur within hours, days, weeks or even years of initial treatment (Pihkala 2013, Lähteenmäki & Minn 2013). The physical side effects of chemotherapy include pain, nausea, vomiting, tiredness, fatigue, infections, anemia, thrombocytopenia, peripheral neuropathy (vinca-alkaloids), musculoskeletal morbidity, motor difficulties, malnutrition, hair loss, (Cella et al. 2002, Pizzo & Poplack 2016, Elonen & Bono 2013, Lähteenmäki & Minn 2013), hyperinsulinemia and dyslipidemia (Cohen et al. 2010, Mohn et al. 2004). Corticosteroids are associated with unfavorable directions of body composition and caloric intake (Reilly et al. 2001). High cumulative doses of anthracyclines cause cardiac dysfunction (Elonen & Bono 2013).

In addition, various lifestyle changes are inflicted by the cancer treatment. Psychosocial hindrances are foreseeable due to the life-threatening disease, its treatment including long hospital stays and being away from family members and peers. Some children may have fear of death, and a various range of emotions are conceivable. (Lähteenmäki & Minn 2013.) During the intense phase of the treatment, children are at risk of being depressed and having anxiety (Myers et al. 2014). These adverse effects may negatively influence children's social life, emotional health and physical performance (Ness et al. 2008).

During cancer treatment, infections are a threat. Hence, the family is guided to avoid possible sources of infections. This means that the family cannot participate in their normal activities without thinking through the risks of infections. A normal visit to a grocery store and many other activities may be forbidden. Due to the dangerousness of infections, feverish child with cancer are always treated at the hospital. (Lähteenmäki & Minn 2013, Pihkala 2013.) Families of children diagnosed with cancer are therefore living at a continuous alert mode, and the malignant disease and its treatment dramatically affects the family's daily life and participation (Götte et al. 2013). Living long periods in the hospital isolates the child and his/her family from life outside the hospital. Travelling to the treating hospital and back home becomes part of their life. Since the care of children diagnosed with cancer is highly specialised and centralised, the distance between the hospital and family home may be hundreds of kilometers. (Lähteenmäki & Minn 2013.) All in all, the time of treatment is a distinct situation, while the treating professionals need to put effort in addition to the life-saving treatment into maintaining all possible 'normal' routines and improve the function and participation of the child and his/her family (Lähteenmäki & Minn 2013, Wong et al. 2014).

3 REVIEW OF LITERATURE OF PHYSICAL ACTIVITY IN CHILDREN DIAGNOSED WITH CANCER

3.1 Search strategy

The aim of the literature review was to provide an overview of research in the field of physical activity in children diagnosed with cancer, and to identify the needs and possibilities for future research. I included both studies that investigate physical activity levels and their effects during the acute phase of the treatment as well as after the treatment.

Since there are several reviews conducted in the field of physical activity in children diagnosed with cancer, the methodology of systematic review of reviews was adapted in this literature review. Systematic reviews of reviews are a logical and appropriate method to assemble findings of separate reviews to be able to collect existing evidence of the area of interest. (Smith et al. 2011.)

A systematic search was conducted in seven (7) relevant databases: PubMed (Medline), Embase, Scopus, Web of Science, Cinahl, Cochrane Library, and PEDro in May 2017. The search queries included Mesh terms and free words such as physical activity, motor activity, exercise, physical therapy modalities, physical fitness, rehabilitation, muscle training, resistance training, neoplasms, leukemia, lymphoma, child and adolescent. The full search queries are reported in Appendix 1. Inclusion criteria for selection were: 1) concepts of physical activity, motor activity, physical therapy, physical function, physical fitness, rehabilitation or exercise mentioned in the title and being the primary scope of the study, 2) the subjects of the study were children diagnosed with cancer and mean/median age ≤18, and 3) the publication is any type of review or book section. All types of reviews were included to gain a broad view of the current literature. Exclusion criteria were studies that included only studies in central nervous system tumours, since in this study those diagnoses were excluded. The flow of the literature is reported in Figure 1. Twenty-two articles met the inclusion criteria, and were included in this review of reviews. The selected reviews included altogether 251 articles where the subjects of the study were children diagnosed with cancer or childhood cancer survivors and the mean age was ≤18. Both reviews and the original papers included in the reviews are referenced. The literature review was supplemented with manual search from the reference lists of the included articles but no other reviews were included.

The included articles were analysed with computer-assisted qualitative data analysis software QSR NVivo 11 (QSR International Pty Ltd. 2017). NVivo is a qualitative research software programme that is designed to handle large amounts of unstructured data (QSR International Pty Ltd. 2017).

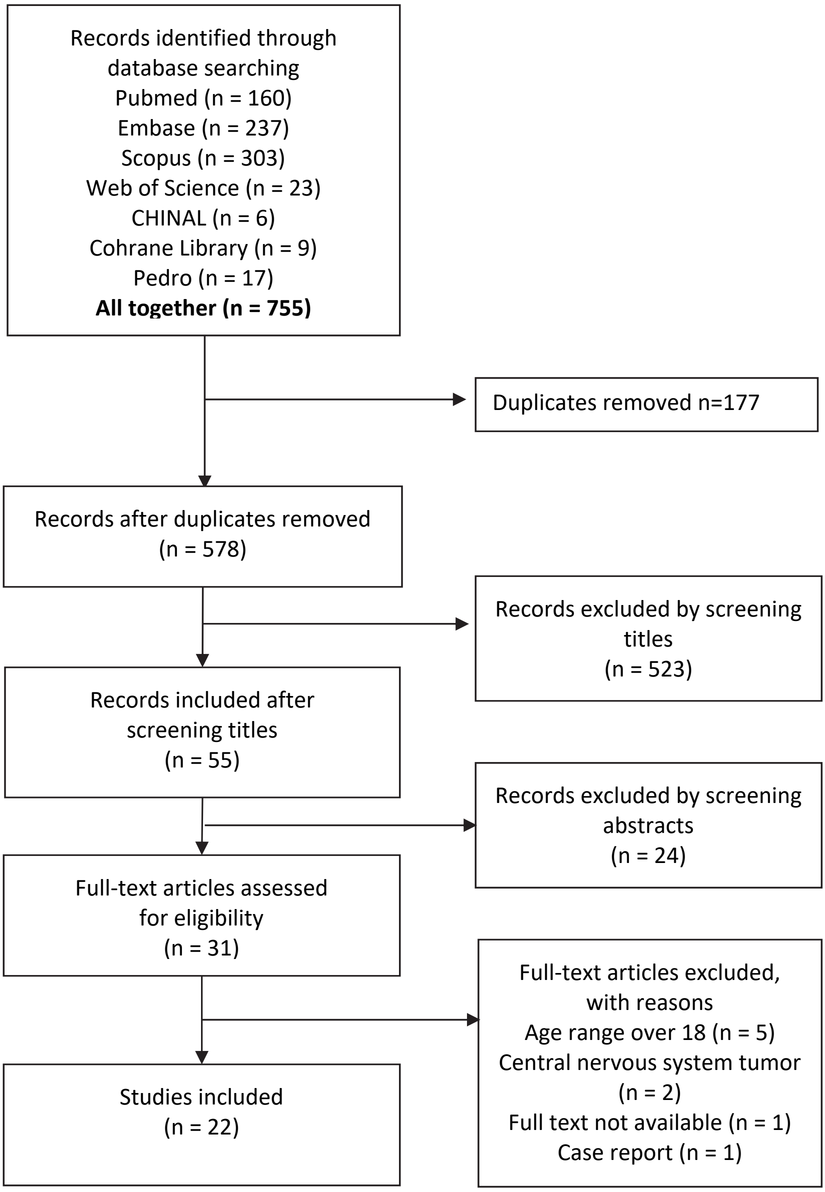

Figure 1 The flow of citations identified in the review of reviews

3.2 Basic characteristics of the included studies

The basic characteristics of the included reviews are presented in Table 1. The publication year range of the included reviews were 1996–2017. The oldest empirical study that were included in the reviews was conducted in 1993, meaning that physical activity promotion in children diagnosed with cancer has been investigated to date for over a quarter of a century.

The literature search revealed one Cochrane review, one meta-analysis, six systematic reviews, ten non-systematic reviews, one book section and three general overviews or discussion papers. Table 1 is organized based on the type of review. Some of the reviews included studies both in children and adults and both children undergoing acute treatment phase and survivors of childhood cancer. The reviews included both observational and intervention studies investigating physical activity levels and effects.

The selected reviews included altogether 251 papers where the subjects of the study were children diagnosed with cancer or childhood cancer survivors whose mean age was ≤18. However, most of the reviews included the same empirical studies, meaning that the real number of empirical studies in the field is much less. The most comprehensive selection and loose selection criteria for papers was in the book section "Physical activity and pediatric cancer survivorship" by San Juan et al. (2011), which included 42 empirical studies.

Both the reviews and the empirical studies of the reviews are cited in the following chapters. A table of the aims and main conclusions of the included reviews are reported more detailed in Appendix 2.

Table 1 The basic characteristics of the included reviews

Author (year)	Type of review	Number of included studies*	Year range of included studies**	Age range of participants**	Sample size range of included studies**	Intervention length range of included studies***
van Brussel et al. (2005)	Meta-analysis	3	1997-2002	6-13	58-78	N/A
Baumann et al. (2013)	Systematic review	17	1993-2011	1,3-19	U, altogether 282 participants	2 days - 2 years
Grimshaw et al. (2016)	Systematic review	12	2007-2015	<5-20	U, altogether 278 participants	3 weeks - 3 months
Kruijsen-Jaarsma et al. (2013)	Systematic review	3 (21)	1999-2010	7,5-14	10-20	30 min - 12 weeks
Liu et al. (2009)	Systematic review	2 (10)	2004-2007	4-18	7-28, altogether 35 participants	16-36 weeks
Raber et al. (2016)	Systematic review	25	1993-2014	1 - 30	6,0-266	≤ 1 week - ≥ 1 year
Wong et al. (2014)	Systematic review	13	1999-2012	U	U, altogether 345 participants	6 weeks - 3 years
Braam et al. (2013)	Cohrane review	5	2004-2011	4-18	13-64, altogether 131 participants	10 weeks - 2 years
Berkman et al. (2016)	Review	14	2005-2015	4-38	5-365 (intervention studies 5-17)	8-16
Culos-Reed (2002)	Review	4 (13)	1993-1999	U	U	U
Galvão & Newton (2005)	Review	1 (26)	1993	19	10	12
Gilliam et al. (2013)	Review	6 (17)	2001-2010	6-20	10-59	N/A
Huang & Ness (2011)	Review	17	1993-2011	4-29,8	4-51	30 min - 2 years
Stolley et al. (2010)	Review	15 (26)	1999-2009	U	U	10-16 weeks
van Brussel et al. (2011)	Review	17	1993-2009	U	U	U
Winter et al. (2010)	Review	28	1993-2009	5,1-29,8	4-2648	8-16 weeks
Wolin et al. (2010)	Review	13 (37)	1993-2010	U	U	U
Zhang et al. (2017)	Review	14	2007-2014	4-15,3	7-51	6 weeks - 2 years
San Juan et al. (2011)	A book section	42	1993-2010	4-35	6-2658 (intervention studies 6-51)	30 min - 3 years
Götte et al. (2013)	General overview	U	N/A	N/A	N/A	N/A
Heath (1996)	Discussion paper	U	N/A	N/A	N/A	N/A
Kelly (2011)	Discussion paper	U	N/A	N/A	N/A	N/A

* The number of studies including children and/or adolescents with cancer and PA being the main focus of the article. The number in parenthesis is the number of articles included in the review altogether, including adult participants and other focuses of interest than PA.
** the information includes only studies in child and adolescent participants with cancer
*** the information includes only studies including PA interventions
U = Unknown
N/A = Not applicable

3.3 Justification for physical activity in children diagnosed with cancer

Children diagnosed with cancer and childhood cancer survivors are at risk for many health issues related to both cancer and the side effects of cancer treatment (Kelly 2011, Armstrong et al. 2014). These secondary health issues and side effects include obesity, reduced cardiopulmonary capacity, cardiovascular diseases, osteoporosis, fatigue, decreased health-related quality of life (Kelly 2011) and musculoskeletal morbidity (Ness et al. 2015, Beulertz et al. 2016, Deisenroth et al. 2016), including motor difficulties (Green et al. 2013).

Below, the secondary health issues and side effects of cancer and its treatment are reviewed. These may positively be influenced by physical activity during and after treatment (Braam et al. 2013, Götte et al. 2013).

Obesity

Childhood cancer and some cancer treatments have been shown to increase the risk of obesity (Kelly 2011). The cause of increased obesity is multifactorial. For example, the corticosteroid treatment may be involved in disturbing energy intake and storage. Corticosteroids are also associated with unfavorable directions of body composition and caloric intake. (Reilly et al. 2001.) Also the decreased physical activity levels influence on weight gain (Kelly 2011). The weight gain starts as early as 6 to 12 months from the beginning of the treatment, and continues usually at least a year after the treatment (Reilly et al. 2001, Baillargeon et al. 2005, Nathan et al. 2006, Baillargeon et al. 2007, Esbenshade et al. 2011, Zhang et al. 2014). Survivors of cancer, especially adolescents, have higher BMI than their peers (Zhang et al. 2014). Therefore, physical activity is an essential part of weight control of children diagnosed with cancer during and after treatment (van Brussel et al. 2011).

Cardiovascular health

Cardiovascular diseases and cardiac mortality in cancer survivors are more common than in general population (Armstrong et al. 2009, Bhakta et al. 2016). Especially metabolic syndrome, which further increase the risk for cardiac events, is significantly more common in childhood cancer survivors than in general population (Oudin et al. 2011, Järvelä et al. 2013, Kero et al. 2014). Childhood cancer survivors have lower cardiorespiratory fitness when compared to the general population (van Brussel et al. 2005, Järvelä et al. 2010, van Brussel et al. 2011, Berkman et al. 2016), which further highlights the importance of physical activity in this population.

Osteoporosis

Childhood cancer and its treatment have been associated with low bone density and osteoporosis (van der Sluis et al. 2008), and as a result, increased the risk of fractures (Högler et al. 2007). Although decrease in bone density are well known, Wilson et al. (2012) did not find an increase in the prevalence of fractures among adult survivors of childhood cancer compared with their siblings (Wilson et al. 2012). Almost 50% of children with ALL have decreased bone turnover and bone mineral density both at the time of diagnosis and during treatment (Jarfelt et al. 2006). Bone mineral density decrease may be due to cancer therapies, nutritional deficiencies and reduced physical activity (Wilson & Ness 2013). All in all, the reduced levels of physical activity impact bone density negatively (Kelly 2011). Physical fitness that is gained with physical activity and exercise is the most important factor in developing and maintaining bone mass in ALL survivors (Jarfelt et al. 2006).

Fatigue and health-related quality of life

Fatigue, antisocial behaviour, anxiety, and depression are significantly more commonly reported by childhood cancer survivors compared to healthy siblings or controls (Paxton et al. 2010). Especially fatigue is common in children during and after cancer treatment (Hockenberry et al. 2010, Clanton et al. 2011), and it has been reported to hinder normal life during and after the treatment. It is estimated that 14–96% of people with cancer suffer from fatigue (Cella et al. 2002), and that fatigue is present in 30–75% of all cancer survivors for months or even years after treatment (Prue et al. 2006, Liu et al. 2009). The presence and volume of fatigue may be different between different diagnosis groups (Mört et al. 2011). Wilms tumour or neuroblastoma may affect health-related quality of life more than leukemia diagnosis (Mört et al. 2011).

Parents of childhood cancer survivors experience many psychosocial issues related to their child's condition and treatment (Raber et al. 2016). Higher levels of parent's perceived child vulnerability and overprotection are associated with lower quality of life of the child (Hullmann et al. 2010). Parental stress is associated with poor behavioural and social adjustment of childhood cancer survivor (Colletti et al. 2008, Fedele et al. 2011, Wolfe-Christensen et al. 2010).

Physical activity is significantly associated with overall health-related quality of life among adolescent survivors of childhood cancer (Paxton et al. 2010). Preliminary evidence shows clinical exercise to have a positive impact on fatigue during medical treatment, as well as during survivorship (Blaauwbroek et al. 2008, Keats et al. 2008, Huang & Ness 2011, Yeh et al. 2011, Baumann et al. 2013). Fatigue reduction may, however, require training response in cardiopulmonary outcomes (Huang & Ness 2011).

Musculoskeletal morbidity

Physical activity is associated with motor skill development in children (Gallahue 2012), and in contrast, difficulties in motor performance negatively influence physical activity participation (Götte et al. 2013, Woodmansee et al. 2016, Oudenampsen et al. 2013). Motor performance has been reported to be reduced in children diagnosed with cancer when compared to the general population (van Brussel et al. 2011, Beulertz et al. 2013, Green et al. 2013, Kesting et al. 2015, Ness et al. 2015, Götte et al. 2015, Beulertz et al. 2016, Deisenroth et al. 2016). Muscle strength is often reduced, which may further complicate motor performance and every day functioning (Gocha Marchese et al. 2003, Hartman et al. 2006, Järvelä et al. 2010). Motor performance was, however, improved significantly after five years of completion of cancer treatment but functional exercise capacity was still significantly impaired (Hartman et al. 2013).

3.4 Physical activity levels and correlates in children diagnosed with cancer

Children diagnosed with cancer are suggested to have low levels of physical activity during and after the treatment (Castellino et al. 2005, Florin et al. 2007, Winter et al. 2010, Stolley et al. 2010, Kelly 2011, San Juan et al. 2011, Tan et al. 2013). A large portion of childhood cancer survivors do not meet physical activity recommendations (San Juan et al. 2011, Stolley et al. 2010, Winter et al. 2010) as it is with the general child population as well (Tremblay 2014). However, findings are partly contradictory (Winter et al. 2010, Stolley et al. 2010).

The time of diagnosis and the intense phase of cancer treatment is a challenging period for the child and the family. At this time, children are reported to have reduced physical activity levels (Winter et al. 2009, Fuemmeler et al. 2013). The cancer disease, its treatment and the infection control methods affect the children's possibility to take part in sports and physical education at school as well as in everyday activities (Götte et al. 2013). Furthermore, later during and after the treatment, protocol-related impairments in cardiorespiratory fitness and muscle function may further worsen the decreased levels of physical activity (Wong et al. 2014, Järvelä et al. 2010).

Physical activity behaviour is correlated with both background variables (for example age, gender, type of cancer and socioeconomic status) and dynamic variables (such as autonomous motivation, self-efficacy and perceived worries) (Cox et al. 2003, Finnegan et al. 2007, Gilliam et al. 2013). As in healthy populations as well (Strauss et al. 2001, Sallis et al. 2002), higher socioeconomic status of the family, male gender, previous physical activity behaviour, and younger age of the child predict greater physical activity levels in childhood cancer survivors, and the physical activity levels tend to decline in adolescence (Finnegan et al. 2007, Arroyave et al. 2008, Cox et al. 2009, Ness et al. 2009, Heath et al. 2010, Gilliam et al. 2013). Feelings of self-efficacy, autonomous motivation, perceived behavioural control, positive beliefs and attitudes are associated with higher physical activity behaviour and intentions to exercise in adolescent survivors (Finnegan et al. 2007, Keats et al. 2007, Keats & Culos-Reed 2009, Gilliam et al. 2013).

The diagnosis and treatment protocol are associated with physical activity levels. Central nervous system tumour, osteosarcoma and cranial radiation are associated with less physical activity than ALL, lymphoma or non-irradiated survivors (Florin et al. 2007, Arroyave et al. 2008, Nathan et al. 2009, Ness et al. 2009, Reeves et al. 2007, Winter et al. 2010, Gilliam et al. 2013).

Low physical activity levels are related to obesity (Florin et al. 2007), and reported fatigue (Cox et al. 2009). Low physical activity levels are also associated to perceived cons about physical activity and general worries (Finnegan et al. 2007). Generally, children are mostly positive towards physical activity during treatment, and they enjoy the possibility to exercise at the hospital (Götte et al. 2014). They think physical activity is important, but they experience different physical, psychological and organisational barriers. Physical barriers to engage in physical activity include fatigue (Arroyave et al. 2008, Götte et al. 2014), nausea, pain and motor difficulties (Götte et al. 2014). The lack of motivation has been the most important psychological barrier to physical activity (Götte et al. 2014). Lack of access to resources, for example, no gym or lack of exercise professionals to help to get started, were perceived as organisational barriers (Arroyave et al. 2008, Götte et al. 2014). The restrictions to engage in physical activity is a broad phenomenon, and within this special population, feelings of pain, exhaustion and weakness cannot be overlooked (Götte et al. 2013).

3.5 Physical activity guidelines and recommendations for children diagnosed with cancer

A large heterogeneity of previous physical activity literature in children diagnosed with cancer makes it impossible to determine evidence-based exercise recommendations (Baumann et al. 2013). Although there are currently no universally accepted physical activity guidelines or recommendations for children diagnosed with cancer (Takken & van Brussel 2015), general recommendations for physical activity can be provided. These physical activity and exercise guidelines have been provided by different research groups and generally physical activity is suggested both during and after treatment (Ness 2007, van Brussel et al. 2011, Chamorro-Viña et al. 2015a, 2015b).

It is suggested that before starting physical training, exercise testing should be performed by an exercise physiologist to be able to detect possible anthracycline cardiomyopathy. Gender- and age-specific hematological parameters should be followed to ensure the safety of physical activity. While these parameters are in appropriate ranges and without any dramatic changes in these values, physical activity is safe. (Van Brussel et al. 2011.) Van Brussel et al. (2011) suggest beginning aerobic training combined with strength training at the maintenance phase of the treatment (van Brussel et al. 2011.)

Some others indicate that interventions for physical activity and exercises should be initiated earlier than in the maintenance phase of the treatment (Zhang et al. 2017, Grimshaw et al. 2016). Justification of physical activity even with low thrombocytes or low hemoglobin is presented (Götte et al. 2013). The intensity of activities with low thrombocytes or hemoglobin should be light. Suggested low-intensity activities are, for example, games with the Nintendo Wii™ Fit balance board, flexibility and body awareness training. (Götte et al. 2013.) Significant increase in fatigue or nausea during exercise is a contraindication of training (van Brussel et al. 2011). Risk-benefit assessment of physical activity is suggested (Götte et al. 2013).

Children with ALL are recommended to engage in either light levels of or an individualised dose of aerobic exercise during induction and consolidation phase of the treatment (White et al. 2005, Ness et al. 2007). At the maintenance phase of the treatment, the aerobic exercise dose should become progressive and include resistance training some days of the week (White et al. 2005, Ness et al. 2007). van Brussel et al. (2011) are suggesting aerobic training and strength training at moderate intensity for all cancer patients starting at the maintenance phase of chemotherapy (van Brussel et al. 2011). Childhood cancer survivors are recommended to engage in 60 min of moderate-to-vigorous physical activity five days a week (Ness 2007).

A recently published pediatric oncology exercise manual for professionals indicate moderate-to-vigorous (40–85% VO2peak) aerobic training for children diagnosed with cancer, 2–5 times per week, 20–70 minutes at a time. The type of training can be, for example, running, jumping or cycling (Takken & van Brussel 2015). Alternatively, the training can be undertaken as aerobic interval training, 2–3 times per week, 20–70 minutes at a time with 1–3-minute-high-intensity-interval bouts (VO2peak >85% / rest at 20–59% VO2peak). Resistance training is suggested 2–3 times a week for 20–30 minutes at a time. Each principal muscle group should be trained for 2–3 minutes, 8–20 repetitions at a time. Aerobic and resistance training can be combined. The type of resistance training can be for example squats or sit-ups. (Takken & van Brussel 2015.)

3.6 Physical activity and exercise interventions in children diagnosed with cancer

There are several recommendations concerning physical activity and exercise interventions in children diagnosed with cancer. Gilliam et al. (2013) suggest that successful physical activity interventions in children diagnosed with cancer should include multiple components targeting behavioural, cognitive, emotional, environmental, and social factors rather than focusing on single domains (Gilliam et al. 2013). Zhang et al. (2017) suggest that lifestyle interventions should contain both components, physical activity promotion and improving dietary quality. An exercise programme should be developed individually for each survivor based on the type of cancer, treatments received, and fitness goals (Kelly 2011).

Setting of the intervention

Previous interventions have taken place in variety of settings (Baumann et al. 2013, Raber et al. 2016, Götte et al. 2013). These include hospital and care facilities, participants' homes and community locations. Short-term hospital-based programmes have been successful, even though they have faced many challenges to providers, since not even nearly all hospitals have relevant equipment like children's gyms at the oncology ward. (Raber et al. 2016.) Individually supervised interventions are suggested to have greater benefit than home-based programmes

(San Juan et al. 2011, Baumann et al. 2013). Combinations of supervised and non-supervised programmes exists (Baumann et al. 2013).

Interventions have also been initiated during stem cell transplantation in the patient room and in outpatient therapy (Götte et al. 2013, Kruijsen-Jaarsma et al. 2013).

Timing of the intervention

Interventions initiated early during the cancer treatment are less studied than interventions in the maintenance phase or following treatment. In the review by Wong et al. 2014, the interventions were offered during chemotherapy (studies n=5), during the maintenance phase (studies n=5), or after treatment (studies n=3) (Wong et al. 2014). They found that interventions during the maintenance phase of chemotherapy and after chemotherapy had more positive outcomes, compared to interventions during the course of chemotherapy (Wong et al. 2014). The latest review about physical activity interventions in children diagnosed with cancer is focusing on interventions placed at the beginning of cancer care to prevent the early onset of obesity and cardiovascular risk in this population (Zhang et al. 2017).

The type of exercise

Most exercise programmes have combined strength, endurance, and coordination training (Baumann et al. 2013). Examples of low intensity activities are games with the Nintendo Wii™ Balance Board, flexibility and body awareness training (Götte et al. 2013). Exercise types should be feasible during hospital stays and at home (Götte et al. 2013).

Adherence to physical activity interventions and psychological aspects

Adherence to exercise interventions ranges between 67–98% based on those studies where adherence has been evaluated (Baumann et al. 2013). Adherence has previously been examined within eight studies. When the duration of the exercise programme was over two years (Hartman et al. 2009), or programme was described as too demanding (Takken et al. 2009), compliance was unsatisfactory (Baumnn et al. 2013). Supervised programmes have higher adherence when compared with home-based programmes (Baumann et al. 2013).

Interventions designed to promote physical activity in children diagnosed with cancer should develop positive attitude towards physical activity and foster feelings of self-efficacy (Keats et al. 2007).

Theories behind the interventions

The previous literature on physical activity interventions has been described as atheoretical (Gilliam et al. 2013). This means that a majority of interventions have lacked a theoretical framework (Stolley et al. 2010). However, there are some theoretical backgrounds that have been adapted to physical activity research in children diagnosed with cancer. Interventions have been based on theory of planned behaviour (TPB) (Keats et al. 2007), social cognitive theory (SCT), transtheoretical model (TTM), and the health belief model (HBM) (Gilliam et al. 2013).

Gilliam et al. (2013) have presented a theoretical model explaining physical activity in childhood cancer survivors. The model is consistent with ecological systems theory (Bronfenbrenner 1979, 2001, Kazak, 1986) and includes intrapersonal, interpersonal, and environmental factors associated with physical activity (Gilliam et al. 2013). The model underlies the multiple interactive influences on children and adolescents' physical activity. Because behavioural changes are necessary when implementing physical activity and exercise interventions successfully, behaviour change theories should be incorporated (Liu et al. 2009).

We chose self-determination theory as a background theory in our intervention, since it has been successful in promoting physical activity behaviour of children and adolescents (Plotnicoff et al. 2013). This theory was chosen since it has been found effective in enhancing enjoyment and increase autonomous motivation in physical activity promotion (Deci & Ryan 2007, 2012, Plotnicoff et al. 2013).

Safety of physical activity during the treatment

Symptom-based approach and risk-benefit evaluation is suggested to determine the appropriateness for physical activity and physical therapy in populations with chronically low blood values such as children diagnosed with cancer (Peters & Tice 2011, Götte et al. 2013). Low hemoglobin concentration may lead to increased risk for minor events such as tachycardia (Peters & Tice 2011). Even with low thrombocytes, physical activity can be implemented with low intensities and when monitored (Götte et al. 2013). Significant nausea or fatigue and fever before or during the exercise is a contraindication of training (van Brussel et al. 2011). Children with significant thrombocytopenia should not perform strength training, but light aerobic activity is appropriate (Kelly 2011).

The appropriateness of physical activity may be evaluated based on objective values of patient's heart rate, blood pressure, cardiac status, oxygenation, respiratory pattern and blood glucose levels. However, subjective symptoms give important information of a patient's condition. Attention should be paid to a patient's emotional state, feelings of pain, pallor, facial expressions, anxiety, rate of perceived exertion, and excessive and abnormal sweating. (Peters & Tice 2011). Falling down and contact sports should be avoided during central venous catheter in place. Furthermore, surgery for bone or soft tissue, and brain tumours add a diversity of restrictions for physical activity with high individual variability. The children receiving anthracycline therapy should also be followed by a cardiologist and regular echocardiograms may be required. Severe exhaustion needs to be avoided. (Kelly 2011, Götte et al. 2013.) Chest radiation is associated with pulmonary fibrosis, which may cause reductions in lung function limiting the tolerance of high-intensity aerobic activity (Mertens et al. 2002, Kelly 2011). Children treated for brain tumours have a risk for neurological complications including poor balance, and different sensory deficiency, which need to be taken into account when developing the training programme (Kelly 2011). Individual risk assessment for physical activity is suggested and interdisciplinary work including treatment from a physiotherapist, a physician, and a sports scientist seems to be a precondition for safe and efficient exercise programmes (Götte et al. 2013).

Parental involvement

Lifestyle interventions in children diagnosed with cancer that include direct parental involvement are more effective than those with indirect or no parental involvement at all (Raber et al. 2016). In the general population, support and encouragement from parents are known to be associated with an increased amount of physical activity in children (Gustafson & Rhodes 2006, Heitzler et al. 2006, Sallis et al. 2000). Children diagnosed with cancer may be more strongly influenced by parental support across childhood and adolescence than healthy children, since family support has a major role during the treatment (Gilliam et al. 2013). The meaning of parental support to a child's physical activity behaviour may lessen with time since treatment, such that survivors who have completed treatment more recently may be more strongly influenced by parental encouragement, whereas children who are further from treatment may show associations similar to those in healthy youth. More evidence is needed to confirm these findings. (Gilliam et al. 2013.)

Parental involvement in physical activity and exercise interventions is even more important when considering the parents' overprotective attitude towards their child during the treatment. The border between overprotection and protection is hard to define. (Götte et al. 2013.) All in all, family should be involved in the rehabilitation process of the child (Heath et al. 1996). To help overcome a parent's fear regarding physical activity, interventions should begin at hospital as supervised (Kelly 2011). Parental fear may be attributed to lack of knowledge, and therefore the role of education and information given about physical activity during the treatment is essential. It is recommended that a psychosocial programme for parents and children should be included in the physical activity interventions. (van Brussel et al. 2011.)

Parental involvement can, for example, involve parents in developing the physical activity interventions and programmes for their children, discussing intervention materials and structures with parents or including exercises into the training programme that are conducted together with parents (Raber et al. 2016).

3.7 The effects of physical activity interventions on children diagnosed with cancer

Overall, physical activity interventions in children diagnosed with cancer have been beneficial, feasible, and safe during and after the intense phase of the treatment, but the evidence is still limited due to methodological limitations of the empirical studies (Braam et al. 2013, Grimshaw et al. 2016, Wong et al. 2014, Baumann et al. 2013, Kruijsen-Jaarsma et al. 2013, Liu et al. 2009, Zhang et al. 2017, Berkman et al. 2016, van Brussel et al. 2011, Huang & Ness 2011, Wolin et al. 2010, Winter et al. 2010, Galvão & Newton 2005, Culos-Reed 2002, Stolley et al. 2010, San Juan et al. 2011). Empirical studies have had small sample sizes (some of them being underpowered), many of them lack randomisation and blinding using single group designs, and they have concentrated on variety of interventions, settings, outcomes and outcome measures (Liu et al. 2009, Baumann et al. 2013, Braam et al. 2013, Gilliam et al. 2013, Kruijsen-Jaarsma et al. 2013, Grimshaw et al. 2016). Nevertheless, the evidence of the benefits of physical activity is generally accepted within the research community.

Physical activity in children diagnosed with cancer have been found to have positive effects on muscle strength (Baumann et al. 2013, Huang & Ness 2011, Wolin et al. 2010), physical fitness/capacity (Liu et al. 2009, Huang & Ness 2011, Berkman et al. 2016, Wolin et al. 2010, San Juan et al. 2011, Järvelä et al. 2012), flexibility, physical functioning (Huang & Ness 2011) and various immune parameters (Kruijsen-Jaarsma et al. 2013), as well as vascular endothelial function (Järvelä et al. 2013). Positive effects have been found also on psychological wellbeing (Liu et al. 2009, Culos-Reed 2002), fatigue (Baumann et al. 2013, Huang & Ness 2011, Culos-Reed 2002) and pain (Culos-Reed 2002).

Results of physical activity influencing quality of life are contradictory. Physical activity has been reported to improve health related quality of life (Baumann et al. 2013, Liu et al. 2009, Culos-Reed 2002, San Juan et al. 2011). However, Wong et al. (2014) reported that there is less support that physical activity would improve quality of life (Wong et al. 2014). The evidence of effects of physical activity on body composition (Baumann et al. 2013, Wolin et al. 2010), immune system, sleep, activity levels (Baumann et al. 2013), ankle dorsiflexion (Wolin et al. 2010), and different physical functioning measures, such as motor performance (Baumann et al. 2013, Wolin et al. 2010) somewhat exists, but the evidence base is still fragile.

Direct parental involvement may improve the effectiveness of the health promotion interventions for childhood cancer survivors (Raber et al. 2016). The evidence is more convincing when the intervention has been supervised in hospital settings (San Juan et al. 2011).

3.8 The gaps of knowledge in current literature

Even though evidence exists about the benefits of physical activity during and after cancer treatment, many issues regarding an effective physical activity intervention require further investigation. The type, frequency, duration, timing and intensity of effective physical activity intervention remains partly unsolved. (Kelly 2011, Braam et al. 2013, Qrimshaw et al. 2016, Wong et al. 2014, Baumann et al. 2013, Kruijsen-Jaarsma et al. 2013, Liu et al. 2009, Zhang et al. 2017, Berkman et al. 2016, van Brussel et al. 2011, Huang & Ness 2011, Wolin et al. 2010, Winter et al. 2010, Galvão & Newton 2005, Culos-Reed 2002, Stolley et al. 2010, San Juan et al. 2011). In addition, the overall methodological quality of the empirical studies in the field have been low (Braam et al. 2013), which somewhat weakens the generalizability and credibility of the findings.

A great challenge for clinicians and researchers is to give reasons, to inform and to motivate children diagnosed with cancer and their families to stay active even during the treatment. Many children may not be interested in returning to hospital during or after treatment for physical activity intervention, and therefore home-based and community activities are suggested (Raber et al. 2016, Huang & Ness 2011). Supervised programmes in hospitals are expensive and often unrealistic for families who travel long distances to the treating hospital (Huang & Ness 2011). Nonetheless, supervised programmes have had higher adherence when compared with home-based programmes (Baumann et al. 2013), and the evidence is more convincing when the intervention is supervised in hospital settings (San Juan et al. 2011). Therefore, we built intervention, which is feasible in hospital and at home.

To summarise, effective, convenient, motivating and innovative physical activity-promoting interventions in children diagnosed with cancer still need to be developed, implemented and studied. The interventions should be feasible both in hospital settings and at home, and for better engagement, they should keep children of different ages interested in being active. Examples of interventions that could be interesting, fun and appropriate to conduct at hospital and home during the treatment are games on the Nintendo Wii^{TM} Balance Board (Götte et al. 2013).

Today, health technology is becoming more popular (Tucker 2011, STM 2016) and different applications and digital games are part of children's everyday life. This 'diginative' generation are eager to use digital solutions in many life situations, which provoked our research group to search knowledge of alternative digital possibilities to activate children during the treatment. After being convinced of the possible effects of active video games in promoting physical activity in other populations (Biddiss et al. 2010, Barnett et al. 2011, Primack et al. 2012, Parisod et al. 2014), we started to seek information of this intervention in children diagnosed with cancer.

The digital game industry is relatively new, and when considering the time-consuming research designs that are needed to prove the effectiveness of an intervention, no studies were found of the effectiveness of active video games in children diagnosed with cancer at the time of planning the study III. This led us to plan a study of active video games in promoting physical activity in children diagnosed with cancer. During the time our study was in progress, Sabel et al. (2016) published a study regarding active video games in childhood brain tumour survivors. Their findings indicate that active video gaming improved body coordination in survivors of childhood brain tumours, and that the active video gaming was equal to moderate physical activity in this population (Sabel et al. 2016).

To understand physical activity in children diagnosed with cancer, we investigated physical activity in healthy children as well. With this approach, we reached comparison data to better understand the possible targeting and rationale of physical activity promotion in children in general and in children diagnosed with cancer.

4 AIMS OF THE STUDY

The primary aim of this study was to explore how to assess and support physical activity of children diagnosed with cancer during hospitalisation and at home. The secondary aim was to describe the physical activity levels in children diagnosed with cancer compared to healthy children. The study comprises four sub-studies.

The aim of study I was to explore healthy children's physical activity, and to define the associations of self-perceived physical competence with physical activity. The aim of study II was to evaluate the validity of Fitbit One® accelerometer step counts compared to ActiGraph step counts in children. The aim of the study III was to pilot and evaluate the effectiveness of an active video game based physical activity intervention in children diagnosed with cancer. Finally, at the study IV the physical activity levels and self-perceived physical competence levels between healthy children and in children diagnosed with cancer were compared by using the data from studies I and III. The detailed research questions are described below.

Study I (article I)

1. What is the level of physical activity among a Finnish cohort at the ages of 10, 12, and 15-years?
2. How is self-perceived physical competence associated with physical activity at the ages of 10, 12, and 15?

Study II (article II)

3. Are Fitbit One® step counts comparable to ActiGraph step counts in measuring physical activity in 9-to-10-year-old children?

Study III (articles III and IV)

4. Is active video game based intervention effective in promotion of physical activity and motor performance, and in reducing fatigue in 3-to-16-year old children diagnosed with cancer?

Study IV (summary)

5. Do the physical activity levels of children diagnosed with cancer (mean age 7.8) differ from the physical activity levels of 10-year-old healthy children?
6. Do the self-perceived physical competence levels of children diagnosed with cancer (mean age 12.8) differ from the self-perceived physical competence levels of 12-year-old healthy children?

The results of this study may be used in developing, targeting and implementing physical activity interventions for healthy children and for children diagnosed with cancer.

5 SUBJECTS AND METHODS

The study was built according to the framework for developing and evaluating complex interventions by Medical Research Council (Craig et al. 2013). The four steps in developing and evaluating complex interventions according to this framework are development, feasibility and piloting, evaluation and implementation (Figure 2). In this study, we conducted the two first components of the framework: development (study I), and feasibility and piloting (studies II and III). After testing procedures (study II) and piloting the intervention (study III), the evidence base was supplemented by study IV, which is called here as a re-development phase.

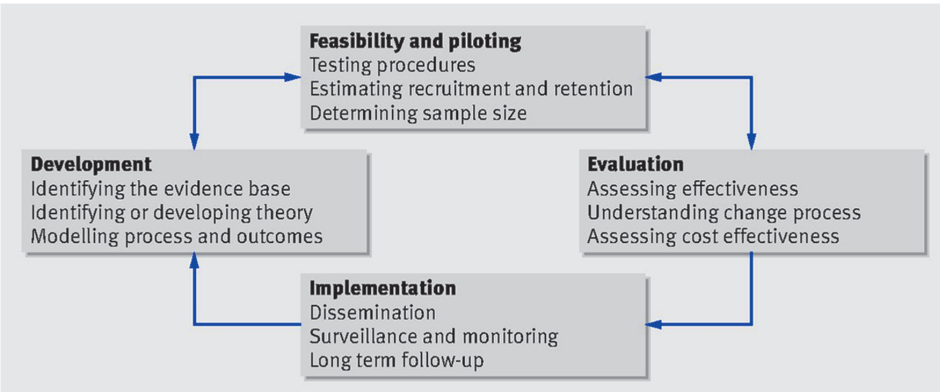

Figure 2 Key elements of the development and evaluation of complex interventions according to Craig et al. (2013)

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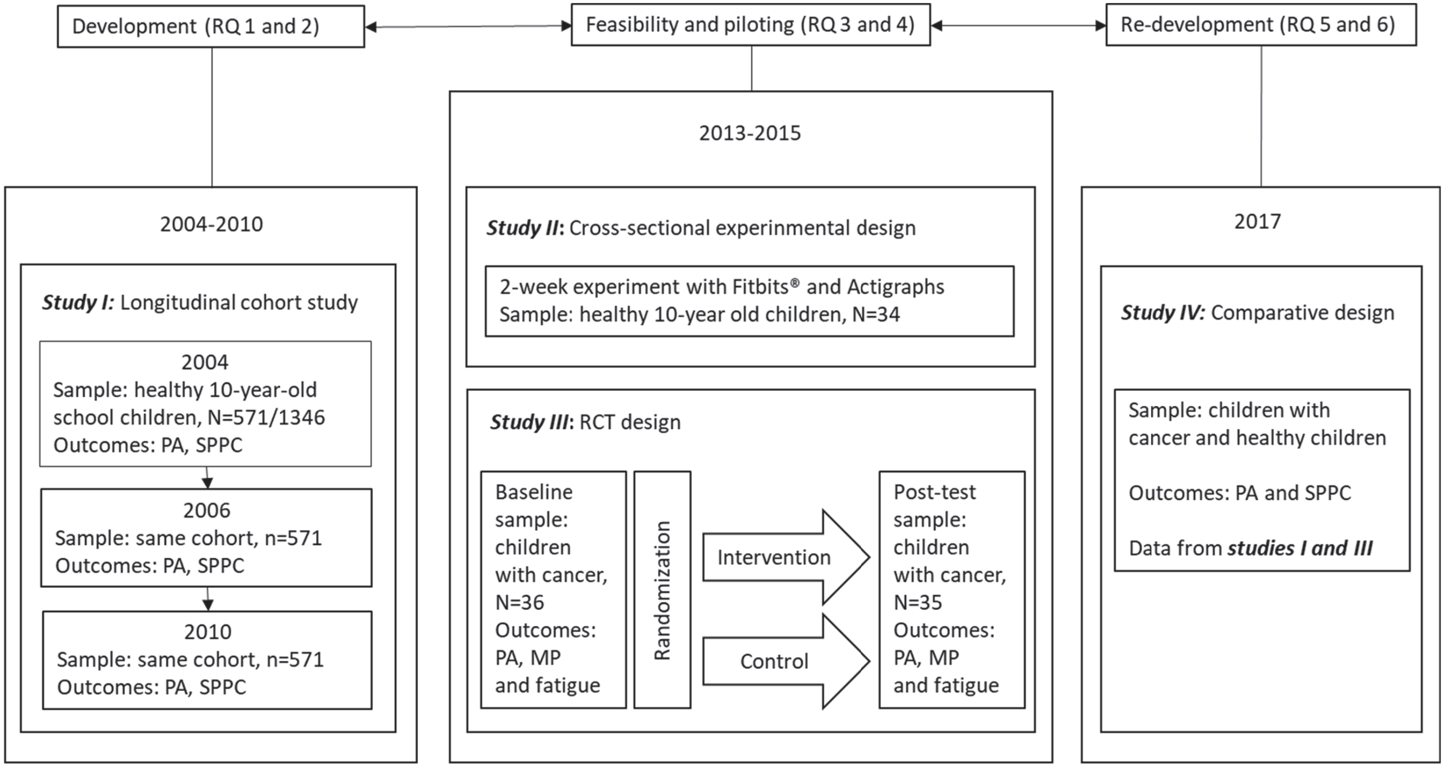
5.1 Study designs

This study contains four different study designs of which each was built to answer the detailed research questions described in the previous chapter. The study designs are illustrated in Figure 3.



RQ = Research question
PA = Physical activity
SPPC = Self-perceived physical competence
MP = Motor performance
RCT = Randomized controlled trial

Figure 3 The study designs of the studies I–IV

To describe the healthy children's physical activity at study I, a longitudinal cohort study design was used. The study I was planned and reported according to STROBE Statement (von Elm et al. 2007). Longitudinal methodology was chosen to gain knowledge of phenomenon that is intrinsically longitudinal, such as the development and behavior change of the child (White & Arzi 2005). In this study, magnitudes of the associations were measured as odds ratios (OR) and their 95% confidence intervals (CI).

At study II a cross-sectional experimental design was used to evaluate the validity of Fitbit One® step counts against Actigraph wActisleep-BT step counts for measuring habitual physical activity among children. This design was chosen based on the methodology for assessing agreement between two clinical measurements (Bland & Altman 1986).

To assesses and promote physical activity of children diagnosed with cancer we built the intervention around active video games and evaluated the preliminary effectiveness of the intervention with randomised controlled trial (RCT) design (study III). The RCT design is generally accepted to be the most reliable method to produce evidence of intervention effectiveness (Uhari & Nieminen 2001, Burns & Grove 2009, Moher et al. 2012, CEBM 2015). The study III followed the methodological guidelines for clinical trials outlined in the CONSORT statement (Schulz et al. 2010). The protocol of study III was reported according to SPIRIT statement (Chan et al. 2013).

To compare physical activity levels and self-perceived physical competence levels between healthy children and in children diagnosed with cancer at study IV, were used a comparative design with data from studies I and III. The study designs, sample, setting, data collection and analysis for all studies are reported in Table 2.

Table 2 The study designs, samples, settings, data collection and analysis for all studies

Study	*Design*	*Sample, Setting, Time*	*Data collection*	*Analysis*
I	Longitudinal cohort study	Healthy 9–10-year-old school children cohort from a city located in Southwest Finland followed-up in 2004 (N=571/1346), 2006 (N=571) and 2010 (N=571)	MET questionnaire, SPPC questionnaire in 2004, 2006 and 2010	Descriptive statistics, Mixed models, Cumulative logit models, GEE method
II	Cross-sectional experimental design	Healthy 9–10-year-old school children (N=34), 2015	Participants carried Fitbit One® and Actigraph wActisleep-BT accelerometers for five consecutive days, 2015	Descriptive statistics, Bland-Altman plots, Shapiro-Wilk normality test
III	Randomized controlled trial	Three-to-16-year-old patients with new cancer diagnosis treated at two tertiary hospitals in Finland (N=36), 2013–2015	Fitbit Ultra® accelerometer, PA diary, MET-, activity-, and SPPC questionnaires, Movement-ABC2, PedsQL™ Multidimensional Fatigue scale, 2013-2015	Descriptive statistics, Mann–Whitney U, Wilcoxon rank sum test
IV	Comparative study design	Sample from studies I and III	MET and SPPC questionnaires, 2006 and 2013-2017	Descriptive statistics, one-way anova, Wilxocon rank sum test, Kruskal-Wallis test

5.2 Participants

The next chapters are reported under subheadings based on the framework of Medical Research Council (Craig et al. 2013): development phase (study I), feasibility and piloting (studies II and III) and re-development phase (study IV).

Development phase (study I)

The study population at study I consisted of healthy nine-to-ten-year-old school children from a city in Southwest Finland (175 000 inhabitants, population data from the year of baseline data, 2004). The eligibility criteria for the schools were 1) Finnish speaking school, and 2) teaching mainly pupils without special needs. A total sampling of the children at fourth grade in eligible primary schools (N=31) were used at baseline. The same cohort was followed-up longitudinally in years 2006 and 2010. The cohort size at baseline was 1346 children. Altogether 571 (42,4%) children (girls N=299, 52.4%; boys N=272, 47.6%) finished the follow-up, had complete data set at all three time points, and were included in the analyses.

Feasibility and piloting (studies II and III)

For feasibility and piloting, the data were collected from two populations, healthy children and from children diagnosed with cancer. The accelerometers were tested with healthy children (study II) and the intervention was targeted for children diagnosed with cancer, and thus, piloted in this population (study III). The study populations, sample sizes and participants are described in more detail below.

At study II, the study population consisted of healthy nine-to-ten-year-old school children from a city in Southwest Finland. The eligibility criteria for participants were 1) 9–10-years of age, and 2) no chronic diseases. At study II, a purposive sampling method was used. The sample size was set on the basis of previous literature (Puyau et al. 2002, Evenson et al. 2008, Rothney et al. 2010, Takacs et al. 2014, Ferguson et al. 2015, Sasaki et al. 2015, Diaz et al. 2015) to be 30 participants. Finally, 34 children took part in the study, since all eligible children from three fourth grade classes were given the possibility to participate.

At study III, the study population consisted of 3-to-16-year old children with newly diagnosed cancer. The eligibility criteria were 1) 3-to-16 years of age at the time of recruitment, 2) the treatment regimen included vincristine, and 3) the treatment was given in either of the designated hospitals in Finland. Simple random sampling method was used in the designated hospitals—all new patients meeting the eligibility criteria were given the possibility to be included in the study.

Re-development phase (study IV)

At study IV we used data from studies I and III. The data used from study I was the baseline data, since at that time participants were 10-year-olds, and that was closed to the mean age of participants at study III (mean age 7.8, min–max 3–16). For comparison of self-perceived physical competence values between healthy children and children diagnosed with cancer, we used data from 12-year olds (study I), since at study III, self-perceived physical competence was asked only from those participants who were over 10-year old (n=14). The mean age for those participants who were over ten-years-old at study III was 12.8 (min–max 10–16).

Power calculation (study III)

The sample size at study III was defined by a power analysis based on a previous study in physical activity in children diagnosed with cancer by Winter et al. (2009). Winter et al. (2009) reported the mean gait cycles and standard deviations of children diagnosed with cancer during the treatment and with this information we estimated the baseline accelerometer counts (Winter et al. 2009). Based on these calculations, a total of 34 participants (17 to each group) was needed to provide 80% power with a 5% significance level. The intervention effect was set to 20% difference between the groups, meaning that we targeted 360 gait cycles per day mean difference (assuming SD of 360 for the mean change) in the change between groups.

Randomisation and blinding (study III)

Participants were randomly allocated to intervention and control groups. Computer-generated list based block randomisation was used. The block sizes were 2 to 4. After participant gave the informed consent to participate the group allocation was revealed to the researcher. Participants did not know whether they were in the intervention group or control group, since they only got the intervention or control advice but they did not know which advice was the intervention. Researcher (LH) could not be blinded to the group allocation, because researcher conducted the intervention education. Non-blinding of the researcher who carried out the intervention is acknowledged as a limitation. The physical therapists who conducted the motor performance testing were blinded to the group allocation. However, it was possible that participants revealed which advice they had got from the researcher during the motor performance testing.

5.3 Settings and data collection procedures

Development phase (study I)

At study I, the cohort data were collected in school settings during the normal school day at classrooms. The eligible schools were located in a city in Southwest Finland. There was a contact teacher in each participating school who handed the written research information over children and parents. The contact teacher ensured that all participants and their guardians gave a written informed consent to participate at all time points. Children filled in the research questionnaires either in electronic or paper form depending on the availability of computers at each classroom. Both versions, electronic and paper questionnaires, were piloted before the actual data collection. Pilot testing was conducted with one 4th grade class (10-year old children) outside the city where the study was conducted. Children who participated to the pilot testing were not included to the actual study. Overall, the questionnaires functioned well, but few questions were shortened and clarified after pilot testing.

Feasibility and piloting (studies II and III)

At study II, the data were collected during free-living conditions of the eligible children in Southwest Finland. A researcher (TK) gave the written information and initial information sheets to eligible pupils during a normal school day. Children were instructed to give the material to their parents and discuss the study with them. After these preliminaries, the researcher ensured that all participating children and their parents had given the written informed consent and collected the filled initial information sheets from the children. Based on the information at the initial information sheets, the researcher programmed the accelerometers individually and allocated them to each participant during a normal school day. Researcher (TK) also educated the children about the study procedures. After five days of data collection in free-living conditions, children returned the accelerometers to school where a researcher collected them. All participating children got an individual feedback sheet about their results and recommendations for future physical activity behavior.

At study III, the data were collected in two university hospitals in Finland. These two hospitals treat approximately one third of all child patients diagnosed with cancer in Finland. The treating oncologist screened children for eligibility and informed the researcher (LH) of eligible children. Researcher (LH) met each eligible child and his/her family, and gave oral and written research information to each family. All eligible families who got the information had to consider participation at minimum overnight before agreeing to participate. When meeting the eligible families again, the researcher answered the questions about the study if families wanted to discuss more. Children's own opinion was listened carefully when receiving the written informed consents from parents. Children over six years gave also own written informed consents to participate. According to Finnish law, children over 15 years of age were independently able to decide whether to participate.

After these preliminaries, the researcher (LH) contacted the physical therapists and research nurses about the new study participant. Designated physical therapists from each hospital scheduled an appointment with participating children, and conducted the motor performance testing at each time point (0, 2, 6, 12 and 30 months from the diagnosis). The designated research nurses also scheduled the metabolic risk factor outcome measures at each time points. The researcher allocated the questionnaires, diaries and accelerometers to each participant at specific measurement points (accelerometers at 0 and 12 months, and questionnaires and diaries at 0, 2, 6, 12 and 30 months from the diagnosis). The researcher allocated and educated the interventions to each participant after the baseline measure. All measurements were done at the hospital during the appointed treatment visits. After the first measurement point, the questionnaires were mailed to the participants. All questionnaires were instructed to be returned either to the hospital ward at hospital visits or by mail with self-addressed returning envelopes that were posted to participants with the questionnaires. All study participants received an individual study feedback and recommendations for future physical activity behavior from the research group after the study period of 2.5 years from the beginning of the data collection.

Re-development phase (study IV)

At study IV, the values of physical activity and self-perceived physical competence from healthy children (study I) and children diagnosed with cancer (study III) were collected from data files. The study settings and data collection of these two studies are reported above.

5.4 The intervention (study III)

The intervention is reported according to TiDieR (Template for Intervention Description and Replication) framework (Hoffmann et al. 2014).

Brief name

The brief name of the intervention was FUN as was the study brief name (FUN-project). The brief name is based on the assumption that intervention based on gaming is being fun and beneficial at the same time. The “FUN theory” is originally a campaign to Volkswagen designed by an agency called DDB Stockholm (Volkswagen 2009). The leading idea of “Fun theory” is that fun is seen as the easiest path to change people’s behavior for the better. This idea with the research evidence behind the study, led to naming the intervention as FUN.

Why

The rationale of the intervention raised from the evidence of four issues: 1) low levels of physical activity among children diagnosed with cancer (Winter et al. 2009, Winter et al. 2010), 2) the problems in musculoskeletal system caused by cancer treatments such as vinca-alkaloids (Diller et al. 2009, Järvelä et al. 2010),

3) benefits of physical activity and exercise interventions in children diagnosed with cancer (White et al. 2005, Braam et al. 2013, Sabel et al. 2016), and 4) the possibilities of active video gaming in hospital setting and therapeutic purposes (Parisod et al. 2014, Primack et al. 2012, Biddiss et al. 2010, Barnett et al. 2011, Sabel et al. 2016).

The self-determination theory (SDT) is a theory of motivation and was chosen to guide our intervention building (Self-determination theory 2015). Self-determination theory has been used as a theoretical background in interventions that are aiming behavior change in health care (Deci & Ryan 2012). It has been successfully used in promoting physical activity behavior of children and adolescents (Plotnicoff et al. 2013).

The important concepts of the theory are experience of autonomy, competence, and relatedness. These three aspects are suggested to foster the most volitional, and high-quality forms of motivation and engagement for activities (Self-determination theory 2015).

In the FUN intervention, autonomy was promoted so that the Wii^{TM} Fit games played were self-elected. The possibility to choose the games promotes the activity time and intensity especially within girls (Roemmich et al. 2012). Also, other studies have stated that when the physical activity intervention includes possibilities to choose, the total amount of physical activity increases compared to those interventions that includes no choices for activities (Wilson et al. 2005).

Relatedness was promoted with FUN intervention through connectivity via the Nintendo Wii^{TM} Fit games (if internet connection was available). Participants were encouraged to play with a peer, parent or siblings if possible.

The third important concept of SDT, competence, was taken into account so that the suggested games were age appropriately tailored.

What

Materials: The FUN intervention included Nintendo Wii^{TM} game console, Nintendo Wii^{TM} Fit balance board and Wii^{TM} Fit Plus game, including over 60 different game activities. Wii^{TM} Fit Plus categorizes activities in Strength Training, Yoga, Balance, Aerobics and Training Plus categories. The intervention included a written user instructions of Wii^{TM} Fit game console, recommendation to play 30 minutes per day (with information on contraindications), and age tailored game suggestions for ages 3–6, 7–10 and for 11–16.

Procedures: After the randomisation and baseline data collection, the researcher met all participants at the intervention group and their family members individually. The participants in the intervention group were educated to install and play the Nintendo Wii™ Fit Plus games. The written information and the equipment were delivered to the participants during the meeting. All participants were able to use the games at patient rooms at hospital and they also received the console and games to home for eight weeks. At this appointment, researcher also allocated the accelerometers and activity diaries to the participants. In addition, intervention included a phone call in the middle of the intervention (four weeks from the beginning of the intervention). The aim of the phone call was to encourage children to play and be active, and also to ask and discuss if the family had any problems with the intervention devices.

Researcher met all participants at the control group similarly as the intervention group. At the control appointment participants received general written instructions for physical activity for 30 minutes or more per day for eight weeks. Both intervention and control advices included following statement: "Being ill takes energy and sometimes physical activity is not possible due to daily condition. However, physical activity is recommended for children diagnosed with cancer similar than for healthy children, within the limits of the treatment and own condition. Listen to your feelings, since physical activity should feel good and bring positive feelings. Below you can see the general physical activity recommendations for children."

Who provided, how, and where

The intervention was provided by the researcher (LH) with background of physical therapist and master degree in health sciences. The intervention was delivered face-to-face individually to each participant and a family member at the hospital, with written instructions, intervention equipment (game console and games) and by a phone call in the middle of the intervention.

The intervention appointment was located at the treating hospital at participant's own patient room. The eight week intervention was located either at hospital or home depending on the individual treatment regimen. The relevant infrastructure included a television where the console was able to be installed. The internet connection was a positive addition, since it was supposed to encourage connectivity between the players, however it was not necessary.

When and how much

The intervention appointment was scheduled after the baseline assessment. The researcher met all participants once and the intervention group received a phone call in the middle of the intervention. The intervention appointment took about an hour with each participant in the intervention group and about a half an hour with the participants in the control group. All in all, the intervention lasted eight weeks.

The dose of recommended physical activity was 30 minutes per day for eight weeks. The physical activity intensity was recommended as light-to-moderate. The parents were guided that light-to-moderate intensity physical activity equals only to a slight increase in breathing rate, still feeling "easy to breathe" or "slight breathlessness". Parents were advised to monitor the child's condition before and during the physical activities.

Tailoring

The intervention was tailored according the written game instructions. The game suggestions for ages 3–6, 7–10 and for 11–16 were tailored age appropriately. Based on the easiest difficulty levels, games such as Hola hoop or Jogging were recommended for children aged 3- to 6-years. For children aged 7- to 10-years, the recommended games include Island Cycling, Rhythm Kung-Fu, Hola hoop and Jogging. For 11- to 16-year-old children games from all exercises categories (Aerobics, Balance, Strength training, Yoga) were recommended. Despite on the game suggestions, the participants were free to play any games they preferred.

Modifications

One obligatory modification to the intervention was that the Nintendo Wii™ game console that was used at the beginning of the intervention was no longer on sale when the consoles were needed to purchase during the study. The console changed to Nintendo Wii™ Mini which was compatible with the Wii™ Fit plus games. Wii™ Mini console, however, lack the internet connection possibility.

How well (intervention adherence)

The intervention adherence was followed with the self-administered activity diaries. Participants were advised to fill in an activity diary during the first week of the intervention. The diary included a category of playing active video games. Intervention group also received a special self-administered game diary where the specific games were supposed to be reported during the intervention. The phone call from the researcher was a strategy to maintain the fidelity to the intervention.

5.5 Outcomes and instruments

Development (study I)

At study I, the outcomes studied were self-perceived physical competence and leisure-time physical activity which were measured using questionnaires. The self-perceived physical competence was measured by questionnaire developed by Lintunen (1987). This questionnaire includes a total of ten questions and constructs of two sum variables: seven questions on self-perceived physical fitness and three questions on self-perceived physical appearance.

Self-perceived physical fitness sub-scale contains questions of physical skills, agility, flexibility, endurance, speed, strength and courage. Each question is estimated on a five-point Osgood semantic differential scale where number one indicates poor and number five indicates high perceived physical fitness. (Lintunen et al. 1995). The score of the subscale varies from seven to 35 points and 21 points equals a neutral perception (neither good nor poor) (Lintunen 1999).

The sub-scale of self-perceived appearance contains three questions of appearance, height and body weight. The subscale score varies from three to 15 points where 9 points indicate neutral value (Lintunen 1999).

Lintunen's (1987) questionnaire has been validated for 10–15-year-old healthy children (Lintunen 1987; 1995; 1999) and for 13–18-year-old children with disabilities (Lintunen et al. 1995).

Leisure-time physical activity was estimated with multiple-choice questionnaire developed by Raitakari et al. (1996). The questionnaire included three questions of the three dimensions of physical activity: frequency, duration and intensity of activities. Leisure-time physical activity was defined as time spent in physical activities outside school hours or commuting to school. The sum variable was formulated from these questions by multiplying the time spent in leisure-time physical activity per week and physical activity intensity. The sum variable is called the MET (metabolic equivalent) index and reported as MET hours per week (METh/week). (Raitakari et al. 1996.)

The physical activity duration and intensity were also reported independently. The duration was estimated by the question `How many hours per week are you physically active or exercise in your leisure time outside school?´ The choices were: (1) at least seven hours, (2) 4–6 hours, (3) 2–3 hours, (4) about an hour, (5) about a half an hour and (6) not at all. The weekly mean duration of leisure-time physical activity was reported so that the answer choices (4), (5), and (6) were combined as "about an hour or less", and other choices were reported independently.

Intensity of leisure-time physical activity was estimated by inquiring `Which of the following alternatives describes your physical activity the best? I engage in physical activity so that I´ : (1) sweat and become heavily breathless, (2) sweat and become somewhat breathless, (3) sweat but do not become breathless, (4) sweat and become slightly breathless, (5) do not sweat or become breathless, (6) don't do physical activity at all. The reported usual mean intensity of physical activity was reported so that the choice (1) was described as intense aerobic activity, choice (2) was described as moderate activity, choices (3), (4), and (5) were combined and described as light aerobic activity, and choice (6) was described as inactivity.

The questionnaire by Raitakari et al. (1996) has been validated against accelerometer and suggested to correlate reasonably well with the accelerometer data (Mansikkaniemi et al. 2012). Reporting the duration and intensity of leisure-time physical activity independently from the METh/week value is problematic, since physical activity consists of three dimensions: duration, frequency and intensity of physical activity. If these dimensions are reported independently, the interpretation of the overall view of physical activity results may become biased. This choice is further discussed and reasoned at the validity and reliability section.

Feasibility and piloting (studies II and III)

At study II, the main outcome measures were Fitbit One® (Fitbit® Inc., San Francisco, CA, USA) accelerometer and ActiGraph wActisleep-BT (ActiGraph, LLC, Pensacola, FL, USA) accelerometer. An initial information sheet and activity diary developed for the study were supporting the primary outcome measures.

The study II was originally planned to be conducted with the Fitbit Ultra® accelerometer which was used at study III as non-validated outcome measure in children. In the feasibility and piloting study (Craig et al. 2013) of this PhD study, the plan was to validate the accelerometer used at study III. However, Fitbit Ultra® was replaced by the manufacturer with the new equivalent model Fitbit One® resulting that Fitbit Ultra® was not available in the market at the time of study II data collection (2015). The manufacturer informed that Fitbit One® is identical to the older model Fitbit Ultra® but with new design and that is why we decided to conduct the validation study with Fitbit One®.

Consequently, the validation data were collected with Fitbit One® accelerometer and compared to the step counts collected with a research-grade accelerometer ActiGraph wActisleep-BT. The ActiGraph was chosen for the research-grade accelerometer, since at the time of study II, ActiGraph's products were the most widely used and validated accelerometer devices in studies exploring children's physical activity (Trost 2007, Cliff et al. 2009, ActiGraph 2016).

The initial information sheet contained questions of the child's name, date of birth, weight and height in order to program the accelerometers individually. The activity diary collected data of the times accelerometers were on and off to ensure more efficient data handling, and evaluation of the discrepancies in the accelerometer data (Sasaki et al. 2016).

At study III, the primary outcome was physical activity. Secondary outcomes were motor performance and fatigue. The primary outcome was measured with objective and subjective methods. The objective measure of physical activity was Fitbit Ultra® accelerometer and subjective methods were questionnaires and an activity diary which are described in detailed below.

The Fitbit Ultra® accelerometer (Fitbit Inc., San Francisco, USA) is a three-dimensional accelerometer that estimates data of step counts, calories burned, stairs climbed and distance travelled. In this study, only the step count data were used in analyses.

One of the two questionnaires were developed for this study. The questionnaire contained questions of physical activity habits (for example a question about being involved in supervised physical activity before the illness) and experienced importance of physical activity at baseline to be able to compare the intervention and control group at baseline. The second questionnaire used at study III was the same questionnaire as in study I and was developed by Raitakari et al. (1996).

Motor performance was measured with Movement ABC2 (M-ABC2) test battery by Henderson et al. (2007). The test is suitable for 3–16-year-old children, and measures standardised tasks in three categories: manual dexterity skills, ball skills and balance skills (Henderson et al. 2007). The M-ABC2 has been successfully used among children diagnosed with cancer (Hartman et al. 2006) and the validity of the instrument has been established by Croce et al. (2001).

Fatigue was estimated with standardised PedsQL™ Multidimensional Fatigue Scale by (Varni et al. 2002). These questionnaires were filled by all over five-year-old children and parents as proxy reports. The PedsQL™ Multidimensional Fatigue Scale has been suggested to show good internal consistency and responsiveness in measuring fatigue in children diagnosed with cancer (Tomlison et al. 2013).

Re-development (study IV)

At study IV, the outcomes studied were self-perceived physical competence and leisure-time physical activity, which were measured at studies I and III. The self-perceived physical competence was measured by questionnaire developed by Lintunen (1987), and leisure-time physical activity was estimated by questionnaire developed by Raitakari et al. (1996). These questionnaires are described before in the outcomes and instruments -section. Lintunen's (1987) self-perceived physical competence scale have not been validated for children with cancer which is acknowledged as a limitation regarding the study IV. The outcomes and instruments used in studies I–IV are summarised in Table 3.

Table 3 Outcomes and instruments used in studies I–IV

Outcome	*Instrument*	*Study*
Physical activity	MET questionnaire (Raitakari et al. (1996)	I, III, IV
	Fitbit One® (Fitbit Inc., San Francisco, CA, USA)	II
	Fitbit Ultra® (Fitbit Inc., San Francisco, CA, USA)	III
	Actigraph wActisleep-BT (ActiGraph, LLC, Pensacola, FL, USA)	II
	PA diary	II, III
	Activity questionnaire	III
	Initial information sheet	II
Self-perceived physical competence	SPPC questionnaire (Lintunen 1987)	I, III, IV
Motor performance	Movement ABC2 (Hendersson et al. 2007)	III
Fatigue	PedsQL^{TM} Multidimensional Fatigue scale (Varni et al. 2002)	III

5.6 Data analysis

The quantitative data from the MET questionnaire, activity questionnaire, Fitbit One®, Fitbit Ultra®, ActiGraph wActisleep-BT, PA diary, SPPC questionnaire, Movement ABC2 and PedsQL^{TM} Multidimensional Fatigue scale (studies I–IV) were analysed statistically. Parametric tests were used for normally-distributed data and non-parametric tests with non-normally distributed data. Normal distribution assumption was checked visually together with Shapiro Wilk's test.

Development (study I)

At study I, to describe the data and analyse the association between self-perceived physical competence and leisure-time physical activity, descriptive statistics, mixed models, cumulative logit models and GEE (generalised estimating equation) method were used. Mixed models with subject as a random effect were used to study the association of age and sex with physical activity and self-perceived physical competence. Cumulative logit models were used to study the associations between age and sex and the physical activity and self-perceived physical competence. A GEE method was used to account for repeated observations. The magnitudes of the associations were measured as odds ratios and their 95% confidence intervals. When the association between self-perceived physical competence and leisure-time physical activity was studied, age, sex, self-perceived physical competence, interaction between age and self-perceived physical competence, and interaction between sex and self-perceived physical competence were the predictor variables used in the model. The Statistical software SAS ® System for Windows (version 9.3) was used.

Feasibility and piloting (studies II and III)

At study II, to compare the two accelerometers studied, the mean bias and the limits of agreement between the Fitbit One® and ActiGraph accelerometer step counts were assessed with the Bland-Altman plot (Bland & Altman 1986). Shapiro-Wilk normality test was used to test the normality assumptions of the hourly differences and the hourly means of the step counts. Also, descriptive statistics were reported. The statistical computations were performed with R-language (R 3.2.0).

At study III, Mann–Whitney-U test was used to study the differences in outcomes between the groups during the intervention, at baseline and at post-test. The change between baseline and post-test values within groups was tested with the Wilcoxon signed-rank test. Also, descriptive statistics were reported to summarise the sample characteristics. Fisher's exact test and Chi-square test were used to study the differences between the groups regarding the categorical baseline variables. The statistical computations were performed with IBM SPSS Statistics for Windows 23 (IBM Corp., Armonk, NY). The statistical significance was set at $p < 0.05$ (two-tailed).

Re-development (study IV)

At study IV, the METh/week, and the self-perceived physical competence parameters were compared between healthy children and children diagnosed with cancer using one-way anova or Wilxocon rank sum test. For children diagnosed with cancer METh/week was compared within diagnosis classes with Kruskal-Wallis test.

6 ETHICAL CONSIDERATIONS

All studies were approved by the Joint Commission on Ethics of Hospital district of Southwest Finland (study I: 8/2004/232, study II: 12/2014/43, study III: 5/2012/153). The research approvals at all studies were obtained from participating institutions (24.9.2012 K66/12 No 13059 and 21.3.2013 65§ R13030). The permissions to use the validated instruments used in this study (MET questionnaire, SPPC questionnaire, Movement ABC2, PedsQL^{TM} Multidimensional Fatigue scale) were obtained from the instrument owner or developer.

Written informed consent is an essential ethical consideration in research and a legally defined process (9.4.1999/488). Medical research must be voluntary in all circumstances (The Medical Research Act 9.4.1999/488). In this study (studies I–III), the informed consents were asked from the child and his/her guardian if child was under 15. Written informed consent was asked from all participants over 6-years-old and oral acceptance from children under 6 years old. Written informed consent were asked from the caregivers of children under 15 years of age. The caregivers of children over 15 years were informed about the child's decision to participate. Families were adequately informed before asking the consent and they had time to consider their participation at least overnight, or for longer, if needed. They had an opportunity to ask questions before giving their consent.

According to the Medical Research Act, participation in the study could be withdrawn or cancelled at any time without the need to justify the decision (The Medical Research Act 9.4.1999/488). From an ethical point of view, the study procedures at data collection (studies I–III) did not encumber participants excessively. The collected data were stored using code numbers without personal identifiers. The statistical analyses were carried out using the code numbers. Individuals cannot be identified from the study reports.

The protocol of study III was published in order to increase the transparency of research trials, and thus, was part of the ethical deliberation. Publishing the protocol is part of the ethical deliberation, since medical research on vulnerable groups, such as children diagnosed with cancer, needs to be planned carefully (Chan et al. 2013). The study was also registered in the ClinicalTrials.gov -database with the identifier NCT01748058.

The researcher followed all good scientific practices during the study and took the special nature of the participants, age and illness, into account at every stage of the study (Research Ethics 2012, ETENE 2003).

7 RESULTS

7.1 Physical activity levels in healthy children

At study I, physical activity levels of healthy children were measured as METh/week (Raitakari et al. 1996) from the same cohort (n=571, 299 girls, 272 boys) longitudinally at ages 10- (n=529), 12- (n=515, and 15 (n=508). The results are reported as weekly duration of leisure-time physical activity, reported intensity of physical activity and as METh/week. The METh/week was calculated based on the three dimensions of physical activity, frequency, duration and intensity.

Based on the results, 27 % of the children at 10 years of age, 34 % of the children at 12 years of age, and 20 % of the children at 15 years of age spent at least one-hour physical activity per day at their leisure-time. At 15 years of age, the proportion of those children who were about an hour or less than one hour physically active per week was 38 %. Summary of time spent in leisure-time physical activities at 10, 12 and 15-years-of age are reported in Figure 4.

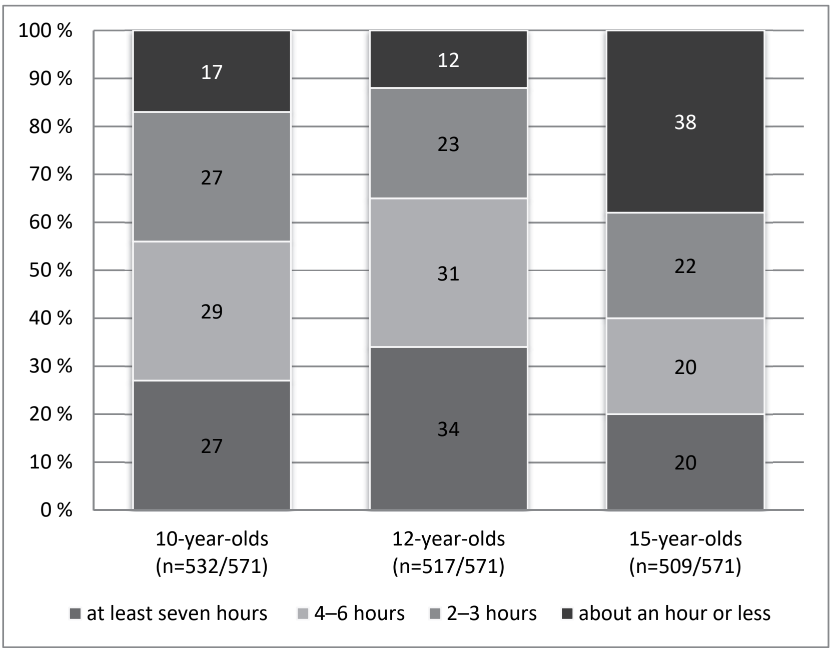


Figure 4 Reported weekly mean duration of physical activity of the studied children

While the time spent in leisure-time physical activities decreased with age (<0.0001), the physical activity intensity increased with age (<0.0001). The proportion of 15-year-olds in the highest, intense aerobic activity group, was 25% compared to 16% at age 12 and 11% at age 10 (Figure 5).

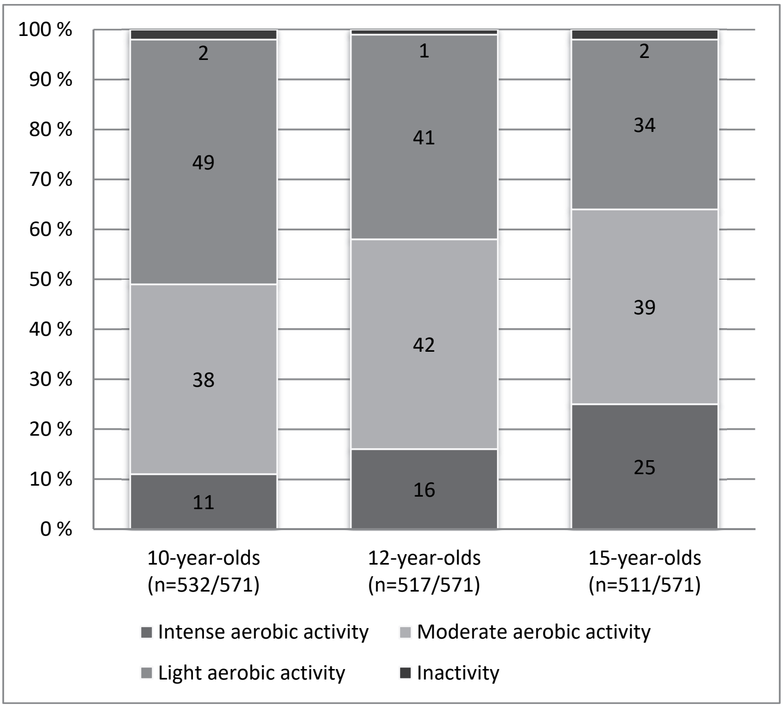


Figure 5 Reported usual intensity of physical activity of the studied children

When the weekly duration and intensity of physical activity were combined and analysed as METh/week, we noticed that the mean METh/week increased with age (Table 4). The increase in mean METh/week with age was explained by the increase in physical activity intensity with age.

Leisure-time physical activity was different between boys and girls. Boys reported higher physical activity levels than girls at ages 12 and 15. The differences in METh/week between boys and girls are seen in Table 4.

Table 4 Mean leisure-time physical activity METh/week of the children studied and the comparison between girls and boys

	All participants Mean METh/week	***Girls*** Mean METh/week	***Boys*** Mean METh/week	***p (girls vs. boys)***
10 years	24.6 SD 19.4 (n=529/571)	23.2 SD 18.4 (n=280/299)	26.2 SD 20.4 (n=249/272)	0.1368
12 years	29.8 SD 21.4 (n=515/571)	25.9 SD 18.7 (n=278/299)	34.4 SD 23.5 (n=237/272)	<0.0001
15 years	33.9 SD 26.3 (n=508/571)	31.4 SD 25.2 (n=271/299)	36.9 SD 27.3 (n=237/272)	0.0082

The statistical differences of the changes in reported duration and intensity of leisure-time physical activity and METh/week across the ages of 10, 12 and 15 years are reported in Table 5. All other comparisons were statistically significant except the METh/week from 12 years to 15 years.

Table 5 Changes in reported duration and intensity of leisure-time physical activity and METh/week of the children studied across the ages of 10, 12 and 15 years

		LTPA duration	***LTPA intensity***	***METh/week***
10 vs. 12 years old	p	<0.0001 (12↑)	<0.001 (12↑)	<0.0001 (12↑)
12 vs. 15 years old	p	<0.001* (12↑)	<0.0001 (15↑)	0.06
10 vs. 15 years old	p	<0.0001 (10↑)	<0.001 (15↑)	<0.0001 (15↑)
	p**	<0.0001	<0.0001	<0.0001

** analysis of all three groups (10, 12 and 15 years old)
* corrected p-value from article I

To summarise, at 10-years of age boys and girls were equally active, but the differences between boys' and girls' activity were significant at the ages of 12 and 15. More than every third child reported to having spent less than an hour in leisure time physical activities per week at the age of 15. The reported intensity of leisure-time physical activity increased with age. The results are reported also in article I.

7.2 Self-perceived physical competence in healthy children

At study I, self-perceived physical competence was measured with Lintunen's (1987) scale from the same cohort than physical activity at the ages of 10-, 12-, and 15. Self-perceived physical competence was divided into self-perceived fitness and self-perceived appearance, which both are reported separately, and then together as self-perceived physical competence. The results are reported also in article I.

Self-perceived fitness

At the age of 15 years, 14% of the children were unsatisfied with their physical skills, as the corresponding percentage at the ages of 10 and 12 years was 7%. A total of 10–12% of 15-year-old children were unsatisfied with their agility, endurance, speed and strength when they compared themselves with others of their age. In mobility item, the percentage of those who perceived themselves low was 24% at the age of 15 years. The corresponding percentage of mobility item at the age of 10 years was 11% and at 12 years 15%. Children's age had a significant association with self-perceived physical fitness (p=0.0005).

Self-perceived appearance

A total of 54–69% of the 10-, 12- and 15-year-old children were satisfied with their appearance, and 22–31% felt neutral (neither good nor poor) about their appearance. At the age of 15 years 16% were unsatisfied with their appearance, and the corresponding percentage at the age of 12 years was 13% and at 10 years 9%. When asked about perceptions of their height and body weight, 57–64% of the 10-, 12- and 15-year-olds were satisfied with their height and body weight. Children's age did not have interaction with self-perceived appearance (p=0.554).

To summarise, children perceived their physical fitness to be lowest at the age of 15. Mobility was perceived the lowest of all the fitness items. Majority of children were satisfied to their appearance at ages 10, 12 and 15. Boys perceived their physical competence better as compared to girls (p=0.0006). The results are reported in more detailed in article I.

7.3 Association of physical activity with self-perceived physical competence in healthy children

At study I (article I), the association of leisure-time physical activity with self-perceived physical competence was assessed.

Leisure-time physical activity was significantly associated with self-perceived physical competence and with the subscale of self-perceived fitness at each time point of assessment (at 10, 12 and 15 years). The association was stronger at the age of 12 and 15 than at the age of 10 years. When the self-perceived physical competence score increased (compared to unchanged), leisure-time physical activity was more likely to increase. Odds ratios showed that a one-point increase in physical competence score and physical fitness score were associated with the probability of intense leisure-time physical activity by 11% (fitness 18%) at the age of 10, 16% (27%) at the age of 12 and 15% (28%) at the age of 15.

To summarise, children's positive perceptions of their physical competence, and especially their fitness, was related to higher leisure-time physical activity.

7.4 Physical activity assessment with Fitbit One® accelerometer

The study II (article II), contributed to the assessment of physical activity in children by comparing Fitbit One® step counts to a research-grade accelerometer ActiGraph wActisleep-BT step counts. The study was conducted with 9-to-10-year old children (n=26, 11 girls, 15 boys). The per-subject sample sizes varied between participants, and on average, the wear-time was 3581 minutes (range 2889–3 925) recorded by each participant.

Overall, Fitbit One® gave higher step counts for all but the least active (the smallest amount of step counts according to ActiGraph) participant. The results showed that the average per-participant daily difference between the step counts from these two devices was 1937 steps. The range was 116–5052. According to a Bland-Altman plot, the hourly step counts had a large mean bias across participants being 161 step counts. The 95 % limits of agreement ranged from 1.6 to 320.7 step counts per hour. The differences were explained by the activity intensity, since higher intensity of activity denoted higher differences between ActiGraph and Fitbit One®, and light intensity denoted lower differences.

To summarise, Fitbit One® step counts were comparable to ActiGraph step counts in healthy children's sample when studied in free-living conditions, when the intensity of activity was sedentary (0–100 counts per minute) or light (101–2295 counts per minute). However, in moderate-to-vigorous physical activity (2296–4012 counts or more per minute), Fitbit One® gave higher step counts when compared to ActiGraph. These results are reported more detailed in article II.

7.5 Physical activity levels in children diagnosed with cancer

Physical activity levels of children diagnosed with cancer were studied at study III. Study cohort consisted of 36 (10 girls and 26 boys), 3-to-16-year-old children diagnosed with cancer, mean age 7.8 (min–max 3–16). The most frequent diagnosis within the sample was acute lymphocytic leukemia (n=17). Other diagnoses within the sample were lymphoma (n=12), Wilm's tumor (n=2), and other neoplasms (n=5).

Physical activity was measured with accelerometers, PA diaries and MET questionnaires. The results are reported by step counts/hour (from accelerometer), PA min/day (from PA diaries), and METh/week values (from MET questionnaire). The accelerometer measure and PA diaries were conducted at the beginning of the treatment (baseline), and the MET questionnaire were filled at the beginning of the treatment (baseline), 2 months, 6 months and 1 year after the baseline, and 2,5 years from the baseline. The results are reported as mean values for the whole study period.

The results are reported for all participants together and for subgroups: acute lymphoblastic leukemia versus other diagnoses, age 3–8 versus 9–16 at the time of diagnosis and girls versus boys. The participants were divided into the subgroups by diagnosis, since the treatment protocols differ between diagnoses. The age groups (3-to-8-years and 9-to-16-years) were chosen based on previous literature on healthy children, which indicates that younger children tend to be more active than older children (Riddoch et al. 2004, Dumith et al. 2011, Currie et al. 2012), and we wanted to test this assumption with data from children diagnosed with cancer as well.

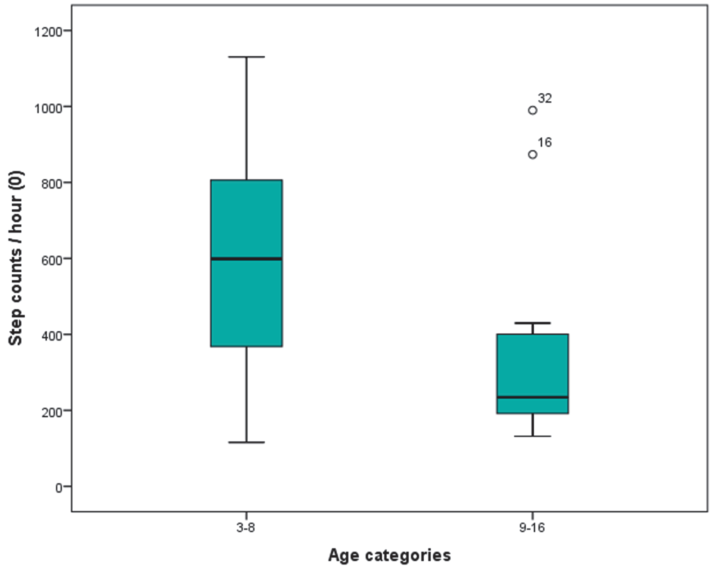
The results show that the median step counts/hour for participants were 401 (min–max 116–1130), and median PA min/day was 30 minutes (0–260). Median METh/week for the whole study period was 20 METh/week (3–79). The results show, that the physical activity values (step counts, PA min/day, METh/week) did not differ statistically significantly either by diagnosis (ALL versus other diagnoses) or gender (Table 6). The difference between younger children (aged 3–8) and older children (aged 9–16) was statistically significant for step counts (p=0.028) and PA min/day (p=0.042), but not for METh/week values for the whole study period. Children aged 3–8-years were more active than children aged 9–16. Boxplot of step counts and PA min/day by age group are seen in Figures 6 and 7.

Table 6 Physical activity in children diagnosed with cancer during the treatment

		Diagnosis median (min–max, n)			***Gender*** median (min–max, n)			***Age*** median (min–max, n)		
Sub-group	**All** n=36	**ALL*** n=17	**other** n=19	p	**Girl** n=10	**Boy** n=26	**p**	**Ages 3–8** n=21	**Ages 9–16** n=15	**p**
Step counts/ h	401 (116–1130, n=30)	300 (116–1012, n=15)	429 (142–1130, n=15)	0.512	368 (132–1012, n=9)	401 (116–1130, n=21)	0.894	599 (116–1130, n=17)	234 (132–990, n=13)	**0.028**
PA min/day	30 (0–260, n=28)	34 (0–260, n=14)	23 (0–80, n=14)	0.454	34 (0–260, n=8)	23 (0–150, n=20)	0.862	43 (0–260, n=16)	0.83 (0–89, n=12)	**0.042**
METh/ week	20 (3–79, n=32)	24 (4–79, n=15)	17 (3–79, n=17)	0.246	17 (3–59, n=10)	20 (4–79, n=22)	0.967	20 (3–79, n=20)	18 (4–59, n=12)	0.985

* ALL = Acute lymphoblastic leukemia

To summarise, younger children (3–8-year-old) were more active than older children (9–16-year old). The overall level of physical activity during the treatment was low (401 step counts / hour, and 30 minutes per day).



Horizontal lines = median
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Figure 6 Median (min–max) step counts for 3–8-year-old and 9–16-year-old participants

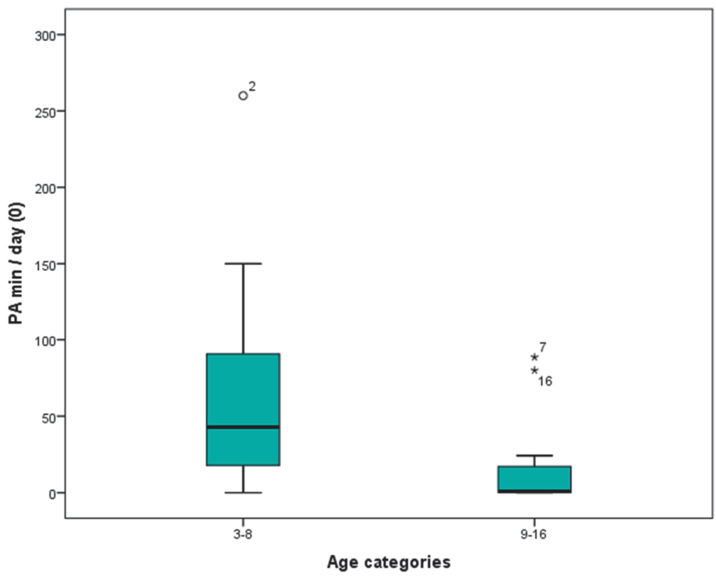

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Figure 7 Median (min–max) PA min / day for 3–8-year-old and 9–16-year-old participants

7.6 Active video games in promotion of physical activity, motor performance and reducing fatigue in children diagnosed with cancer

At study III (articles III and IV), participants were randomly allocated to intervention (n=17, mean age 7.8, 3–16) and control (n=19, mean age 7.9, 3–15) groups (difference between groups for age p=0.68). At baseline, we compared the intervention and control groups regarding of age, gender, physical activity habits, experienced importance of physical activity and experience of playing AVGs before the illness. From these not any of the comparisons were statistically significant. This comparison was done to be able to ensure that the groups were similar at baseline. The gender distribution, diagnoses, physical activity habits and experienced importance of physical activity are reported in Table 7.

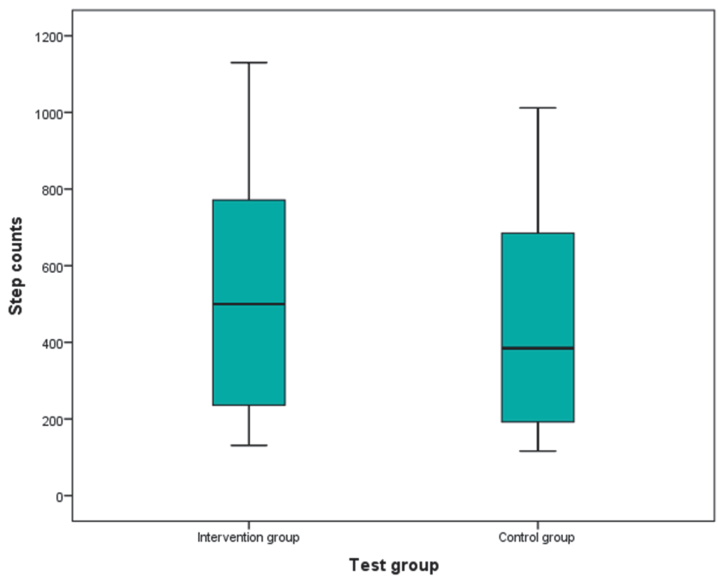
Table 7 Gender, diagnoses, physical activity habits and experienced importance of physical activity of study participants

	All (n = 36)	**Intervention group** (n = 17)	**Control group** (n = 19)	**Difference between groups**
Gender				p=1.000
Female	10 (28 %)	5 (29 %)	5 (26 %)	
Male	26 (72 %)	12 (71 %)	14 (74 %)	
Diagnosis				p=0.6800
Acute lymphocytic leukemia (SR:IR:HR*)	17 (47 %) (8:6:3)	7 (41 %) (4:2:1)	10 (52 %) (4:4:2)	
Wilms' tumor	2 (6 %)	2 (12 %)	0 (0 %)	
Non-Hodgkin lymphoma	9 (25 %)	4 (24 %)	5 (26 %)	
Hodgkin lymphoma	3 (8 %)	1 (5 %)	2 (11 %)	
Other neoplasm	5 (14 %)	3 (18 %)	2 (11 %)	
PA habits				p=0.948
The number of participants involved in supervised PA before the illness	20/33 (67 %)	9/15 (60 %)	11/18 (61 %)	
Experienced importance of PA				p=1.000
The number of participants who experienced PA as "very important"	26/32 (81 %)	11/14 (79 %)	15/18 (83 %)	
Experiences of playing AVGs				p=0.925
The number of participants who had experience in playing AVGs before the illness	13/31 (42 %)	6/14 (43 %)	7/17 (41 %)	

Intervention and control groups were also compared regarding of medication (vincristine/vinblastine doses), days admitted to hospital (overnight), hospital visits (visit the hospital but not admitted overnight) and physical therapy visits during the intervention. This information was collected and compared between groups since these parameters were deemed influential in terms of physical activity and physical functioning. This information was collected from the electronic patient records. The intervention and control groups did not differ regarding of vincristine/vinblastine doses (p=1.0), days admitted (p=0.38), hospital visits (p=0.35) or physical therapy visits (p=0.16) during the intervention. Based on the collected baseline characteristics the intervention and control groups were comparable in the RCT design.

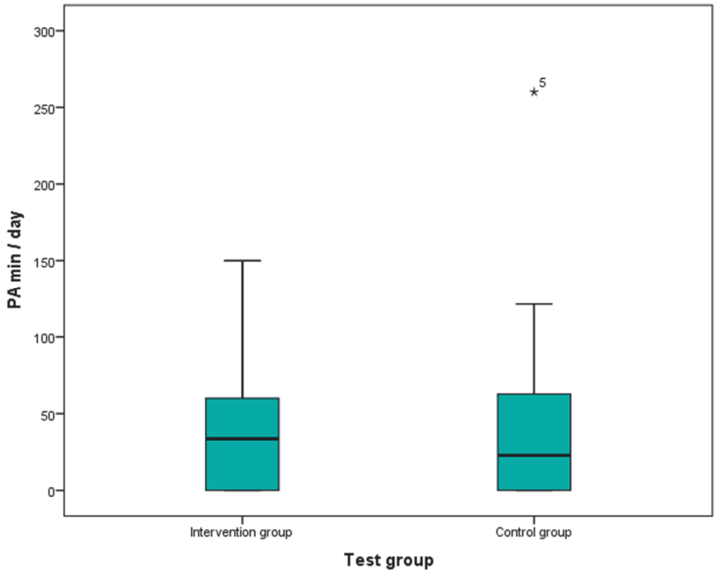
Physical activity between intervention and control groups

Physical activity was measured using the Fitbit Ultra® accelerometers, PA diary and MET questionnaire. The results from the accelerometers and PA diaries showed no statistically significant differences between the groups (p=0.63 and p=0.95 respectively) during the first week on the intervention. The median of accelerometer counts for the intervention group (n=12) were 500 counts/h (min–max 131–1130) and for the control group (n=18) 385 counts/h (116–1012) (Figure 8). The median of PA min/day for the intervention group (n=12), was 34 min/day (0–150) and for the control group (n=16) 23 min/day (0–260) (Figure 9).



Horizontal lines = median

Figure 8 Accelerometer step counts for the intervention and control groups



Horizontal lines = median

* = outliers

Figure 9 Physical activity min / day for the intervention and control groups

The METh/week values for the intervention and control group did not differ significantly at baseline (p=0.50) or after intervention (p=0.47). The median for change between the baseline and post-intervention measurement was -0.3 (-52–33) for the intervention group and 0 (-34–15) for the control group. The change in MET h/week was not statistically significantly different between the groups (p = 0.38).

Motor performance

The motor performance results are presented in percentiles and a higher number means better performance. The intervention and control groups did not differ statistically significantly in Movement-ABC-2 scores (percentile) at baseline [75 (5–99) vs. 50 (0–99), p=0.18] or after the intervention [63 (0–95) vs. 37 (1–98), p=0.59]. At baseline, 8% of the intervention group and 31% of the control group, and at post-intervention 21% of the intervention group and 29% of the control group were at risk of having or had movement difficulties. The change in motor performance between the baseline and post-intervention test did not differ between the groups (p = 0.77). The three components of motor performance, manual dexterity, aiming and catching and balance, tested with Movement-ABC2 at baseline and at post-intervention are illustrated by group in Figures 10 and 11.

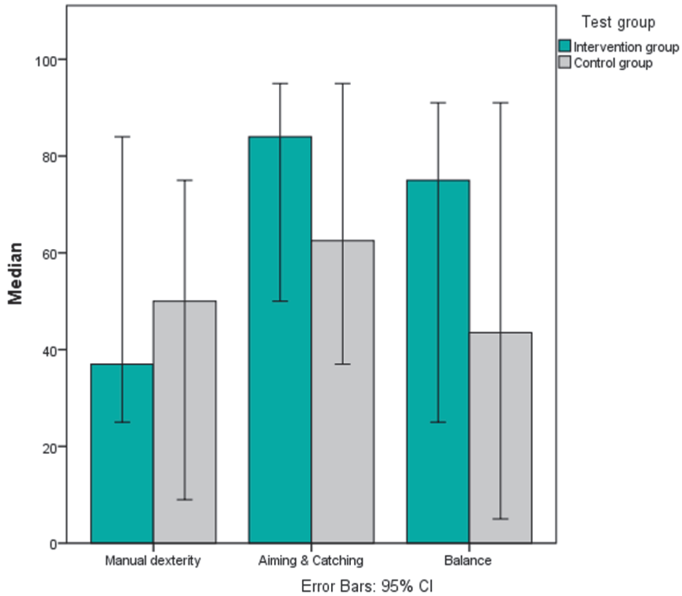


Figure 10 Median manual dexterity, aiming & catching and balance at baseline by group

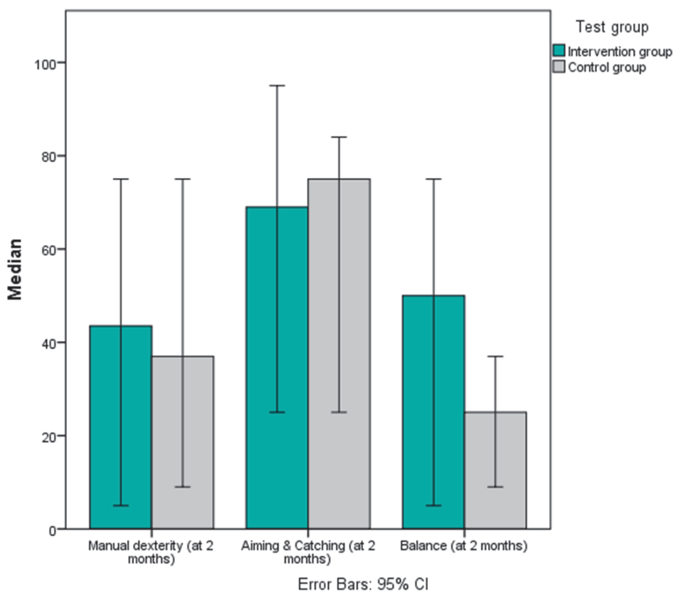


Figure 11 Median manual dexterity, aiming & catching and balance at two months by group

Fatigue

Parents filled the fatigue questionnaires as proxy reports thinking of their child. The higher fatigue score mean less fatigue (max 100).

The median (min-max) fatigue scores between the intervention and control groups reported by parents were not different at baseline (median 67, min–max 35–100 versus 60, 39–97, p=0.44) or after the intervention (67, 40–92 versus 66, 47–90, p=0.82). The median change was 4 (-35–68) for the intervention group and 6 (-7–64) for the control group (p=1.00 for the difference in change between the groups).

7.7 Comparison of physical activity levels of children diagnosed with cancer and healthy children

Physical activity levels of children diagnosed with cancer were compared to physical activity levels of healthy children for understanding how the illness, heavy medical treatment and long hospital stays could possibly affect to the physical activity levels of children diagnosed with cancer. The data used of children diagnosed with cancer is from study III (the median values calculated from the whole study period at 0, 2, 6, 12 and 30 months from the diagnosis) and the data used of healthy children is from study I (baseline data). Both studies used the MET questionnaire. The METh/week values of healthy children and children diagnosed with cancer were compared using comparative analysis.

The results show that METh/week values did not differ between healthy children and children diagnosed with cancer (p=0.56) (Table 8).

Table 8 Overall level of physical activity (METh/week) among children diagnosed with cancer and healthy children

Level of physical activity *(METh/week) (median, min–max, n)*	***Children diagnosed with cancer*** *(n=36)*	***Healthy children*** *(n=571)*	***p***
Girls	20.4 (3-35) (n=9/10)	20.0 (0-80) (n=269)	
Boys	20.0 (4-79) (n=23/26)	20.0 (0-80) (n=238)	
Total	20.0 (3-79) (n=32/36)	20.0 (0-80) (n=529/571)	0.56

7.8 Comparison of self-perceived physical competence levels of children diagnosed with cancer and healthy children

Self-perceived physical competence levels of children diagnosed with cancer and healthy children were compared using comparative analysis. The data used was from study I and III. Both studies used the Lintunen's (1987) self-perceived physical competence scale.

The results show that the self-perceived physical competence values did not differ between healthy children and children diagnosed with cancer (p=0.78) (Table 9). Neither did the subscale (perceived fitness and perceived appearance) values differ between children diagnosed with cancer and healthy children (p=0.12, 0.08 respectively) (Table 9).

Table 9 Self-perceived physical competence among children diagnosed with cancer and healthy children

Component Median (lower quartile Q1- upper quartile Q3)	***Children with cancer*** (n=14)	***Healthy children*** (n=479)	***p***
			p
Perceived fitness (neutral value 21)	24.5 (22.4-27.2)	26.0 (23-30)	0.12
Perceived appearance *(neutral value* 9)	13.4 (11.5-14.2)	11.0 (9-14)	0.08
Perceived physical competence (neutral value 30)	37.1 (35.8-40.8)	38.0 (34-42)	0.78

8 DISCUSSION

8.1 Discussion of the results

In this study, the overall aim was to understand the assessment and promotion of physical activity in children with special reference to children diagnosed with cancer. The main findings of this study, and their relationship with previous literature are discussed below.

Physical activity in healthy children

Our findings indicate that there are a large proportion of children whose level of leisure-time physical activity is insufficient. This result is in accordance with previous findings, which indicates that only a small proportion of children in the high-income countries encounter the recommended levels of physical activity (Tremblay 2014, Cooper et al. 2015, Kokko et al. 2016).

Previous literature indicate, that younger children tend to be more active, but the physical activity levels decrease through adolescence (Riddoch et al. 2004, Dumith et al. 2011, Currie et al. 2012). In our study, the mean METh/week values actually increased from 10-years-of-age to 12-, and 15-years of age. This increase in mean METh/week values with age was explainable with the increase of the physical activity intensity with age. At the age of 15, children reported higher physical activity intensity than at the age of 10 or 12 years, whereas, children reported lower weekly duration of physical activity at 15 years than at 10 or 12 years old. This result might be partly due to the polarisation of physical activity in children. The group with high amounts of physical activity participates in more hours of organized sports per week than number of age in years, and also the training intensity in youth athletes increase in adolescence (Jayanthi et al 2015). In addition, parental support becomes less prominent as a correlate of physical activity in adolescence (Sallis et al. 2000, Heitzler et al. 2006). Thus, when children grow older, they become more independent and their responsibility for their own health increase.

Our result is partly contradictory and partly in accordance with previous findings (Telama et al. 2000, Corder et al. 2016, Kokko et al. 2016). A recent study that included data from 24 025 participants estimated that objectively-measured vigorous-intensity physical activity is reduced 6.9% each year of age (Corder et al. 2016). Another study with Finnish data, reported that the self-reported intensity of physical activity increased during adolescence, even though the overall physical activity decreased (Telama et al. 2000). In another Finnish nationwide study, the number of children who spent at least one hour in physical activities per day, increased from 2014 to 2016 (Kokko et al. 2016). These studies differ in methodology, since one is based on objectively measured physical activity (Corder et al. 2016), and the two others on self-reported data (Telama et al. 2000, Kokko et al. 2016), as is our study as well.

These studies referred here are not inclusive. However, they indicate that the phenomenon of physical activity in children is complex. There are differences in cultural and socioeconomic factors, study methodologies and subgroups across countries and studies, and a variety of correlates (biological, psychological, behavioral, social and environmental) of physical activity, which makes it challenging to compare results explicitly (Sallis et al. 2000, Van Der Horst et al. 2007, Biddle & Murtie 2008, Dumith et al. 2011, Corder et al. 2016). However, our results are quite parallel with other findings from Finnish children and youth (Telama et al. 2000, Aira et al. 2013, Kokko et al. 2016). Roughly one third of Finnish children and adolescents report to be physically active for an hour per day (Kokko et al. 2016). Therefore, children's physical activity should be promoted by different means both at school and outside school days. A special attention is suggested to be payed to prevent and decrease the polarisation of physical activity behaviors, and girl's physical activity. Preventing children's excessive sedentary behavior may be one solution to consider (van Grieken et al. 2012).

It is essential to decrease sedentary time during day care and at school (Dobbins et al. 2013, Mehtälä et al. 2014, Soini et al. 2014, Sallis et al. 2016). In Finland, one of the governmental key projects is Schools on the Move -project, which governs over 70 % of Finnish comprehensive school pupils at the moment. The project goal is that each child would exercise for at least 60 minutes per day, and this is aimed to achieve by sitting less during lessons and being more physically active during break times. (Ministry of Education and Culture, Finland 2018.) Also childcare centers offer great possibilities to decrease sedentary time and to promote physical activity in under school aged children (Mehtälä et al. 2014, Soini et al. 2014).

Association of physical activity with self-perceived physical competence in healthy children

The previous evidence of associations between self-perceived competence and physical activity has been described as indeterminate and inconclusive (Sallis et al. 2000, Van Der Horst et al. 2007). Some evidence exists that physical or sports competence is associated with physical activity, especially in adolescents (Sallis et al. 2000, Van Der Horst et al. 2007). Our study was clarifying this connection, and brings a new insight for the changes of association across adolescence. Our strength was the longitudinal cohort study design, including three measurement points.

Based on our findings, children who had more positive perceptions of their physical competence had higher leisure-time physical activity levels than those with poorer perception of their physical competence. We also found that the association was strengthened with age. The components that were perceived as being poorest were physical skills and mobility.

By promoting children's positive perceptions of their physical competence it is more likely them to be active, and thus, it is important to consider the psychological variables when promoting physical activity in children and youth.

Physical activity assessment with Fitbit One® accelerometer

Another finding from this study indicated that Fitbit One® accelerometer overestimates the step counts when compared to a research-grade accelerometer ActiGraph wActisleep-BT. In light activities, Fitbit One® may be considered as comparable to ActiGraph but in moderate-to-vigorous physical activity intensities the hourly step counts mean bias in our study was large according to the Bland-Altman plot.

Previous findings have had similar results than our study (Ferguson et al. 2015, Evenson et al. 2015, Middelweerd et al. 2017). Fitbit One® has been found to overestimate step counts compared to ActigGraph GT3X+ in adults when measured in free-living conditions (Ferguson et al. 2015, Middelweerd et al. 2017). When measured in laboratory, and when Fitbit One® step counts have been compared to manually counted steps, the results have been reverse (Diaz et al. 2015). These studies have been conducted with adults, and the evidence regarding Fitbit One® in children is lacking with the exception of our study. Further research is required to confirm our results.

Even though the use of Fitbit One® (or other devices meant for consumer use) as an outcome measure in physical activity research in children is still ambiguous, it must be noted that these devices may be suitable for use in interventions of behavior change (Price et al. 2017). These devices provide real-time feedback to user, and therefore may help in motivating people in behavior change (Gomersall et al. 2016, Middelweerd et al. 2017, Price et al. 2017).

Physical activity levels in children diagnosed with cancer

The results of the third study contributed to understanding physical activity levels of children diagnosed with cancer at the early phase of the treatment. The median level of activity at the beginning of the treatment was 401 step counts per hour. If the child is awake for example on average for 12 hours, this means as much as 4812 step counts per day. For children, this is very little, even though low levels of activity are understandable during the early phase of the treatment and, for example, on days of procedures or severe nausea. Our findings are in line with earlier findings. At the time of diagnosis and early during the treatment, children are reported to have reduced physical activity levels (Winter et al. 2009, Fuemmeler et al. 2013).

Although the median step count per hour was relatively low (401), the standard deviations in step counts were large, which reflects a wide distribution of physical activity behavior during the treatment. There were children whose activity was at a very high level (max 1130 step counts per hour) and, reversely, those whose activity was at very low level (116 step counts per hour). It should be noted that the accelerometer data were missing from 6 participants, which may bias the result. These missing 6 participants could have been those who lay in bed feeling sick. However, this is only a speculation, since we did not get this information after data collection. During the data collection, it was noticeable that children (and/or their parents) wanted to give “good” results to the researcher. This means that the accelerometers motivated children to be more active but also that despite the guidance, some parents chose not to put the accelerometer on the child when the child’s daily physical activity was “poor”. This indeed biased the results, and need to be taken into account when interpreting them. Physical activity in children diagnosed with cancer is however suggested to be assessed with accelerometers or other objective methods (Götte et al. 2017). Even though accelerometer’s motivational function may have biased the results, it is notable that based on our experience in this study accelerometers could be used as motivational means in the interventions in the future.

Furthermore, based on the physical activity diaries, children diagnosed with cancer were on average 30 minutes physically active per day. This is in line with the accelerometer data, since approximately 5000 steps at moderate-to vigorous intensity equals to 30 minutes of activity per day in 4–6-year-old children. In children aged 10–15, 3300–3500 steps at moderate-to vigorous intensity equals 30 minutes activity. (Tudor-Locke et al. 2011.) In Finland, children below school age are recommended to accumulate at least three hours of physical activity each day (Ministry of Education and Culture, Finland 2016). School-aged children are recommended to accumulate at least one to two hours of diverse physical activities per day (Tammelin & Karvinen 2008). These recommendations cannot directly be applicable to children diagnosed with cancer. However, physical activity recommendations for children with ALL indicate that at the maintenance phase of treatment they should progress to an activity level close to the recommendations set for healthy children (White et al. 2005). Even though there are currently no universal physical activity recommendations for children diagnosed with cancer (Takken &

van Brussel 2015) generally, physical activity is recommended both during and after treatment (Ness 2007, van Brussel et al. 2011, Chamorro-Viña et al. 2015a, 2015b).

The cancer disease, its treatment and the isolation due to infection control affect the children's possibility to take part in community sports, physical education or in everyday physical activities (Götte et al. 2013). Therefore, new, innovative ways to promote physical activity in children diagnosed with cancer at hospital and home are still highly needed.

Active video games in promotion of physical activity, motor performance and reducing fatigue in children diagnosed with cancer

In this study, we aimed to promote physical activity and motor performance, and to reducing fatigue in children diagnosed with cancer with an active video game based intervention. We did not find intervention effects on any studied outcomes, which needs to be further discussed.

The time of diagnosis and the intense phase of cancer treatment is a challenging time for the child and his/her family (Götte et al. 2013). This may be one reason, why the intervention was not fully followed by all participants in the intervention group. Even though the evidence base of physical activity in children diagnosed with cancer was strong enough to build an intervention study, many of the important references were published after 2013 when our study started recruiting. For example, Wong et al. (2014) suggests that physical activity and exercise interventions have more beneficial outcomes when implemented at earliest at the maintenance phase of the treatment (Wong et al. 2014). Therefore, our intervention might have been timed too early. Better timing would have been later during the treatment, and for ALL patients at the maintenance phase of the treatment.

One other reason why intervention was not fully followed could have been that the novelty and challenge of playing AVGs have been suggested to decrease dramatically over time (Sun 2013, Joronen et al. 2017). In our study, 43 % of the participants in the intervention group had experience on playing AVGs before the study (see Table 7). This might have lessen the feelings of novelty, challenge and enjoyment of playing AVGs during the intervention.

Also, many questionnaires and accelerometer or PA diary results were missed, since families had so much going on that time, and sometimes these extra procedures were possibly too much to remember. The lack of questionnaires, and accelerometer and PA diary data led to smaller analysed sample size than expected. It is worth noting, that the descriptive values tend to show higher amount of physical activity in the intervention than control group even though the differences were not statistically significant.

The data collection in the motor performance test were successful throughout the study since the test was conducted at the hospital during the normal treatment visits. The differences between the intervention and control groups in motor performance values were not statistically significant. The descriptive values of motor performance at baseline give an impression that participants in the intervention group could have been at better condition than participants in the control group. At post-intervention, the better values in the intervention group had been maintained only at balance component. This might be due the fact that the Nintendo Wii™ Fit games are mostly practicing balance and not that much manual dexterity or aiming & catching.

No statistical difference between intervention and control groups in fatigue scores was found. This was not surprising, since fatigue reduction likely require training effects in cardiopulmonary outcomes (Huang & Ness 2011). In our case, the physical activity levels did not differ between the groups, and we can assume that the training effects (if any) would also have been similar between groups. Nevertheless, physical activity promotion is important in fatigue reduction in children diagnosed with cancer, since there is some supporting evidence that exercise is effective in the management of fatigue during and after cancer treatment (Blaauwbroek et al. 2008, Keats et al. 2008, Huang & Ness 2011).

Finally, it must be noted that interventions that succeed in retaining the physical activity level or attenuate the decline of physical activity during the treatment, can be considered as effective, even without an increase in physical activity levels (Dumith et al. 2011). In addition, with the current knowledge of game and physical activity research, outcome measures like enjoyment, motivation, self-efficacy, acceptability and usability of the games, which we did not have, could have been useful when judging the value and usefulness of the intervention in this population (Finnegan et al. 2007, Keats et al. 2007, Barnum 2011, Craggs et al. 2011, Bauman et al. 2012, Gilliam et al. 2013, Plotnicoff et al. 2013, Götte et al. 2014). These evaluations remain unstudied and require further investigations.

Finally, even though many things could have been done differently in our study, it is worth noting that this was among the first studies investigating the effects of active video games in pediatric cancer population. Our results and lessons learnt can be actively taken into account in future projects.

Comparison of physical activity levels of children diagnosed with cancer and healthy children

The level of activity between healthy children and children diagnosed with cancer did not differ statistically. This finding was particularly alarming when considering the healthy children and their level of physical activity.

Our findings from the comparison of physical activity in healthy children and children diagnosed with cancer are in line with findings by Järvelä et al. (2010), who found that physical activity index did not differ between survivors of cancer and healthy controls (Järvelä et al. 2010). However, these studies had importantly different samples, since our study compared the levels of activity in children diagnosed with cancer aged 3–16 years during the treatment, and Järvelä et al. (2010) investigated survivors of cancer (n=21) aged 16–30 years. Also Heath et al. (2010) found that childhood cancer survivors (n=19, aged 6–18 years) were similarly active than previously documented healthy children when physical activity was measured using accelerometers (Health et al. 2010). Nevertheless, many previous studies report that children diagnosed with cancer have low levels of physical activity during and after the treatment, and that they do not meet the physical activity recommendations (Castellino et al. 2005, Florin et al. 2007, Winter et al. 2010, Stolley et al. 2010, Kelly 2011, San Juan et al. 2011, Tan et al. 2013). On the other hand, neither do all healthy children meet the physical activity recommendations or engage enough in physical activity (Tremblay 2014).

However, this finding should be interpreted with caution, since the result is based on a subjective instrument and not objectively measured data. The MET questionnaire (Raitakari et al. 1996) might be problematic with small children since it has previously been validated and used only in studies with adolescents (aged 9–16 years, Lehtonen-Veromaa et al. 2000) and young adults (aged 23–55 years, Mansikkaniemi et al. 2012).

Comparison of self-perceived physical competence levels of children diagnosed with cancer and healthy children

As did not the levels of physical activity differ between children diagnosed with cancer and healthy children, neither did the self-perceived physical competence differ between them. This was also slightly surprising since the treatment of cancer causes physical discomfort, musculoskeletal morbidity (Ness et al. 2015, Beulertz et al. 2016, Deisenroth et al. 2016), and unwanted appearance changes (Larouche et al. 2006). This result should be interpreted with caution as the sample of children diagnosed with cancer was small and the self-perceived physical competence questionnaire was intended only for those participants who were over ten years old. Therefore, this comparison needs to be replicated with a bigger sample.

8.2 Validity and reliability

In this chapter, the validity and reliability, and strengths and limitations of the literature review, study designs, samples, data analysis and instruments used in this study are discussed. The validity and reliability of the results in relation to earlier findings are discussed in above section.

The literature review

The literature review of this study was conducted with systematic approach, including the search process, review selection, and data extraction (Smith et al 2011). Although a systematic approach was used, it is possible that not all relevant studies were identified. The literature search was conducted from seven databases, and due to the overlap between search results in different databases, it is unlikely that relevant studies were missed. A systematic quality evaluation was not conducted, which is acknowledged as a limitation. The selection and review process of the reviews was done by only one researcher which may be considered as a limitation too.

The study designs

The study designs used in this study were longitudinal cohort study design, experimental design, randomised controlled trial, and comparative study design. With different research approaches, it is possible to obtain more complete picture of the studied phenomenon than with a single approach (Johnson & Onwuegbuzie 2004).

At study I, the longitudinal cohort study design enabled to describe and understand the phenomenon that is intrinsically longitudinal (White & Arzi 2005). The longitudinal cohort design can be considered as a strength, when studying associations in time (Caruana et al. 2015).

At study II, the experimental design was used to be able to collect data for Bland & Altman difference plot, which is a method to analyse agreement between two different measurements (Bland & Altman 1986) as was our aim at study II.

Randomised controlled trial is generally accepted to be the most reliable approach to produce evidence of effectiveness (Uhari & Nieminen 2001, Burns & Grove 2009, Moher et al. 2012, CEBM 2015). At study III, we followed the methodological guidelines outlined in the CONSORT statement (Schulz et al. 2010), and the protocol was reported according to SPIRIT statement (Chan et al. 2013), which makes the reporting of the study transparent. One limitation regarding the study design in study III, was that the researcher (LH) could not be blinded to the group allocation, because the researcher conducted the intervention education.

Samples and analysis

In this study, there were three different samples, two from healthy children, and one from children diagnosed with cancer. At study I, the sample consisted of a cohort of healthy 10-year old children from comprehensive schools (4th grade) in a city located in Southwest Finland. The cohort sample strengthens the statistical inference about the associations as the sampling errors are minimised (Friis & Sellers 2014). The sample is likely to represent the whole Finnish speaking child population of ages 10, 12 and 15 in Finland relatively well. However, a large number of cohort members were lost to follow-up, and this may lead to biases where only those who tend to be physically active answered the questionnaires.

The lack of subgroup analyses, i.e. how parental socioeconomic status reflects the results, may be considered as a limitation. However, the main focus of study I, was the association of self-perceived physical competence with leisure-time physical activity in three time points within the same cohort which already was an ambitious design. The analysis was done in co-operation with statistician, which strengthens the validity and reliability of the analysis.

At study II, the sample consisted of purposive sample of healthy 9-to-10-year-old children. The purposive sampling method was useful in this study, since we collected knowledge of the agreement between the two accelerometers (Bland & Altman 1986), and the participant's behavior was not in the main focus. The analyses were done in co-operation with information scientist, who had experience in time series analysis, which strengthens the validity and reliability of the analysis.

At study III, the study sample of children diagnosed with cancer was chosen with simple random sampling method, and the sample size was estimated with power analysis. Many questionnaires were not returned, and we missed accelerometer and PA diary data from some of the participants (see Figure 1, in article IV). Therefore, we had smaller analyzed sample than planned with the power analysis. We also expected smaller standard deviations than our data ultimately had. These are major limitations, and makes it difficult to draw firm conclusions of the results.

Even though the expected amount of data were not available for the analysis, the results are strengthening the evidence base of physical activity levels and motor performance levels of children diagnosed with cancer in general. In the most of the other studies of this population, the samples are unfortunately quite small as well (Braam et al. 2013). The data were collected from two of the five tertiary hospitals that are treating childhood cancer patients in Finland. This means that these two hospitals are treating approximately one third of all childhood cancer patients in Finland. With the sample expected, the results would have been generalized into all newly diagnosed childhood cancer patients in Finland. However, with this sample, the findings should be interpreted with caution. To summarise, the significant results were missed since 1) small analyzed sample size, and 2) larger standard deviations than expected.

The analyses were done in co-operation with two biostatisticians, which strengthens the validity and reliability of the analysis. Also the comparative analyses at study IV were done in co-operation with biostatistician.

The limitations regarding the samples and data collection at studies I and III are also limitations at study IV, since study IV used the same data.

Instruments

The instruments used at studies I and IV were validated instruments: Lintunen's (1987) Self-perceived physical competence scale, and Raitakari's (1996) MET questionnaire. The Self-perceived physical competence scale has been validated for 10–15-year-old healthy children (Lintunen 1987; 1995; 1999) and for 13–18-year-old children with disabilities (Lintunen et al. 1995). However, the Lintunen's scale has not been validated for children diagnosed with cancer, which is acknowledged as a limitation. The convergent validity of MET questionnaire has been tested with accelerometer data. The MET questionnaire correlated relatively well with the accelerometer data (r = 0.26–0.40) and pedometers (r = 0.30–0.39) (Mansikkaniemi et al.2012). It has been successfully used in earlier studies in children (aged 9–16 years) and adults (23–55) as well (Lehtonen-Veromaa et al. 2000, Pahkala et al. 2011, Mansikkaniemi et al. 2012). However, the MET questionnaire has not been validated for children diagnosed with cancer, which is acknowledged as a limitation. Although the MET questionnaire has been validated, the presentation of the results from the questionnaire in this study must be discussed. Originally the results are supposed to present as METh/week or METh/month values. In study I, we decided to report the duration of weekly physical activity and the intensity of physical activity as independent outcomes in addition to the METh/week value. This approach is problematic, since physical activity behavior consists of three dimensions: duration, frequency and intensity of physical activity. If these dimensions are reported independently, the interpretation of the overall view of physical activity results may become biased. The reason to report these dimensions independently from METh/week value was that with this approach it was possible to visualise the reason why METh/week increased with age. Even though children reported lower weekly duration of physical activity at 15 years than at 10 or 12 years of age, they reported higher physical activity intensity at 15 years of age than at the age of 10 or 12 years.

The Self-perceived physical competence scale, and the MET questionnaire were used also at studies III and IV. The validity considerations regarding MET questionnaire and Self-perceived physical competence scale are therefore regarding study IV as well. At study III, the MET questionnaire was modified for children under 10 years of age, and parents filled it as a proxy report of their child. This proxy version has not been validated, which is considered as a limitation.

Instruments that were developed for the purposes of this study, and therefore not validated before, were the PA diary (studies II and III), activity questionnaire (study III), and the initial information sheet (study II). These instruments were mostly used to collect baseline and additional data. For example, the initial information sheet (at study II) collected the information about the participant's name, date of birth, weight and height in order to program the accelerometers individually. The activity questionnaire (study III) was used, for example, to ask how much participants spent time in playing active video games in a week before starting the study. This was necessary to enable comparing the intervention and control groups at baseline, but naturally there was no validated questionnaires to this purpose before.

The results of the PA diary were used in evaluating the effectiveness of the intervention at study III, but it was not the only outcome measure for physical activity. Therefore, the results from the activity diary serve as an interesting add to the results from the more validated instruments. We have not validated the PA diary. However, it is interesting to remark that the PA min/day result from the PA diaries, and the step count data from the accelerometers were well in line. The median PA min/day results were 30 minutes a day, and the median step count data was 401 step counts/hour which is approximately 4812 step counts per day. Based on previous literature, approximately 5000 steps equal to 30 minutes of activity in 4–6-year-old children (Tudor-Locke et al. 2011). The validation of the PA diary against accelerometer data is planned to be studied in the future.

Since the validity of Fitbit Ultra® accelerometer, that we used at study III, was not previously been evaluated, we conducted the study II of this study. As mentioned in the methods section, Fitbit Ultra® was replaced by the manufacturer with the new equivalent model Fitbit One® before the data collection of study II was conducted. This unexpected circumstance, which was not depending on us, resulted to a situation where Fitbit Ultra® was not available in the market anymore, and we needed to conduct the validation study with the new variant Fitbit One®. The results of the validation study of Fitbit One® (study II) showed that Fitbit One® was comparable to ActiGraph in light physical activity intensities. Based on the fact that children diagnosed with cancer are not suggested to engage in vigorous physical activities at the beginning of the treatment (White et al. 2005, Ness et al. 2007, Götte et al. 2013), we may assume that Fitbit One® is a valid instrument in measuring physical activity in children diagnosed with cancer at the beginning of the treatment. This result may not directly be generalised to Fitbit Ultra®, which is a limitation regarding the study III.

Motor performance and fatigue were measured at study III with Movement ABC2 (M-ABC2) (Hendersson et al. 2007), and standardised PedsQL^{TM} Multidimensional Fatigue Scale (Varni et al. 2002) respectively. The validity of M-ABC2 has been proved by Croce et al. (2001), and it has been successfully used among children diagnosed with cancer (Hartman et al. 2006). The Fatigue questionnaire had also been validated, and it is suggested to show good internal consistency and responsiveness in measuring fatigue in children diagnosed with cancer (Tomlison et al. 2013).

8.3 Implications and future research

The United Nations Convention on the Rights of the Child declare that children have the right "to engage in play and recreational activities appropriate to the age of the child" (OHCHR 1996-2017). This declaration is concerning children at all ages and conditions, meaning that it is children's right to participate in play and physical activity even when being ill or being hospitalised. Adults – parents, decision-makers and health care professionals – have the responsibility to ensure the accessibility of play spaces, and to promote physical activity of children at all times (Götte et al. 2013). The following suggestions for future are given based on this study:

1. ***Promoting physical activity in healthy children***

   There are a large proportion of children whose level of leisure-time physical activity is insufficient. Children's, especially girls' physical activity should be promoted both at school and outside school days.

   Self-perceived physical competence should be enhanced to promote physical activity, especially in adolescence. This may be enhanced by providing experiences of success in physical activities, by offering the possibility of a wide range of physical activity experiences, and the possibility for individual choices.

2. ***Promoting physical activity in children diagnosed with cancer***

   The level of physical activity during the cancer treatment was low, and one fourth of the children were at risk of having or had motor difficulties. Therefore, physical activity should be promoted during the treatment both at hospital and at home. More innovative ways, using new technology to promote physical activity should be developed.

   To ensure access to play spaces at hospital means that these places exists. More effort should be made on building spaces where children's natural physical activity is enhanced at hospital. This may mean, for example, a children's gym on the ward or more possibilities to borrow physical activity equipment to the patient rooms.

To promote physical activity of children may need a change in the care culture and attitudes. Unnecessary restrictions to physical activity should be avoided.

3. ***Using games and technology in health promotion in children diagnosed with cancer***

   Additional selection of novel games are suggested to be included to the interventions to keep players motivated.

   The level of difficulty of the games should be age appropriate, meaning to be challenging enough, but not too hard to play. Young (three-to-four-year old) children need easier games than what Nintendo Wii^{TM} Fit offered.

   The majority of active video games are being released and played with game consoles. This highlights the potential of designing physical activity promoting games in other platforms, such as mobile devices as well, without increasing passive screen time.

   Accelerometers motivated children to be active during the treatment. These devices could be included in the physical activity interventions as a motivational mean.

4. ***Assessment of physical activity in children***

   Accelerometers give valuable objective data of children's physical activity. The choice of the device is important, and based on the results of this study, ActiGraph remains as a preferred choice.

   The Fitbit One® accelerometer needs further evaluations in measuring physical activity in children.

   The physical activity diary developed in this study is worth of being developed and tested further. The validity of the PA diary should be evaluated against direct observation or objective measurements.

5. ***Future directions in research***

   The active video game based intervention evaluated in this study is suggested to be replicated with larger sample size, and with different timing. Outcome measures like enjoyment, motivation, self-efficacy, acceptability and usability of the games require further investigations.

The international physical activity recommendations (Pediatric Oncology Exercise Manual) (Chamorro-Viña et al. 2015a, 2015b) for children diagnosed with cancer are planned to be validated, and implemented into Finnish health care.

The self-perceived physical competence in children diagnosed with cancer needs further evaluation in larger sample sizes.

9 SUMMARY AND CONCLUSIONS

The main results and conclusions of this study are summarised in Table 10.

Table 10 Summary of results and contribution of each studied research question (RQ)

RQ	*Research question*	*The main results*	*Conclusions*
1	What is the level of physical activity among Finnish 10, 12, and 15-year old children?	A total of 27 %, 34 %, and 20 % (10-, 12-, and 15-years-of-age respectively) of the children spent at least one-hour physical activity per day at their leisure-time. More than every third 15-year old child reported less than one hour leisure time physical activities per week. Boys were more active than girls at ages 12 and 15.	There is a large proportion of children whose level of leisure-time physical activity is insufficient at ages 10, 12, and 15. Children’s (especially girls’) physical activity should be promoted also outside school days.
2	How is self-perceived physical competence associated with physical activity at the ages of 10, 12, and 15?	The self-perceived physical competence was positively associated with leisure-time physical activity at all ages, and the association was strengthened with age.	By influencing children's perception of their physical competence they are more likely to be active.
3	Are Fitbit One® step counts comparable to ActiGraph step counts in measuring physical activity in children?	The hourly step counts mean bias across participants was 161 step counts. Higher intensity of activity denoted higher differences than light intensity. Fitbit One® gave higher step counts for all but the least active participant.	Fitbit One® gives higher step counts than ActiGraph. However, at light intensities of activity Fitbit One® may be considered as comparable to ActiGraph.

4	Is active video game based intervention effective in promotion of physical activity and motor performance, and in reducing fatigue in children diagnosed with cancer?	Active video game based intervention was not effective in physical activity promotion, and it neither had effect on motor performance nor in reducing fatigue. The median values of physical activity were low. One fourth of the children had or were at risk of having motor difficulties at two months from diagnosis.	The early active video game based intervention was not effective in studied outcomes. However, the descriptive values of physical activity and motor performance (especially balance) were promising. Physical activity promotion and ways to support motor performance during the treatment are warranted. The intervention is suggested to be scheduled later during the treatment (maintenance phase) and tested with larger sample size.
5	Do the physical activity levels of children diagnosed with cancer differ from the physical activity levels of healthy children?	Physical activity levels did not differ between children diagnosed with cancer and healthy children.	Cancer disease and its treatment does not necessarily diminish children's physical activity levels when compared to healthy children. Methods to promote physical activity both in healthy children and children diagnosed with cancer are needed.
6	Do the self-perceived physical competence levels of children diagnosed with cancer differ from the self-perceived physical competence levels of healthy children?	Self-perceived physical competence did not differ between children diagnosed with cancer and healthy children.	Cancer disease and its treatment does not necessarily impair children's self-perceived physical competence when compared to healthy children. Methods to promote self-perceived physical competence in healthy children and children diagnosed with cancer are needed.

A supplementary result, which this study contributed was that younger children's (aged 3–8) physical activity levels were significantly higher than older children's (9–16) physical activity levels during the cancer treatment. Therefore, the older age group (9–16) needs a special attention when promoting physical activity in children diagnosed with cancer

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APPENDICES

Appendix 1 Databases, search queries and search results

Database	Search query	Search focus and limits	Search result
PubMed (Medline)	((((((((("Physical Activity") OR ("Motor Activity"[Mesh]) OR ("Exercise"[Mesh]) OR ("Physical Therapy Modalities"[Mesh]) OR ("Physical Therapy Department, Hospital"[Mesh]) OR ("Physical Fitness"[Mesh]) OR ("Rehabilitation"[Mesh]) OR ("Resistance Training"[Mesh]) OR ("Exercise Movement Techniques"[Mesh]) OR ("Exercise Therapy"[Mesh])))) AND ((("Neoplasms"[Mesh]) OR ("Leukemia"[Mesh]) OR ("Lymphoma"[Mesh])))) AND ((("Child"[Mesh]) OR ("Child, Preschool"[Mesh]) OR ("Adolescent"[Mesh])))))))	Filters activated: Review, English	160
Embase	'physical activity'/exp/mj OR 'motor activity'/exp OR 'exercise'/exp OR 'physiotherapy'/exp OR 'kinesiotherapy'/exp OR 'fitness'/exp OR 'rehabilitation'/exp OR 'resistance training'/exp OR 'muscle training'/exp AND 'neoplasm'/exp OR 'leukemia'/exp OR 'lymphoma'/exp AND'child'/de OR 'adolescent'/de OR 'preschool child'/de	Publication types: 'conference review'/it OR 'review'/it Language: English	237
Scopus	(TITLE-ABS-KEY ((("Physical Activity") OR ("Motor Activity") OR ("Exercise") OR ("Physical Therapy") OR ("Physical Fitness") OR ("Rehabilitation") OR ("Resistance Training") OR ("Exercise Therapy")))) AND (TITLE-ABS-KEY ((("Neoplasms") OR ("Leukemia") OR ("Lymphoma")))) AND (TITLE-ABS-KEY ((("Child") OR ("Child, Preschool") OR ("Adolescent"))))	Search focused on title, abstract and keywords Document type: "reviews" and language "English"	303
Web of Science	(((("Physical Activity") OR ("Motor Activity") OR ("Exercise") OR ("Physical Therapy") OR ("Physical Fitness") OR ("Rehabilitation") OR ("Resistance Training") OR ("Exercise Therapy")) AND (("Neoplasms") OR ("Leukemia") OR ("Lymphoma")) AND (("Child") OR ("Child, Preschool") OR ("Adolescent"))))	Search focused on topic Document type: “review” Language: “English”	23
Cinahl	((MM "Physical Activity") OR (MH "Motor Activity") OR (MH "Exercise") OR (MH "Therapeutic Exercise") OR (MH "Physical Therapy+") OR (MH "Physical Fitness") OR (MH "Rehabilitation+") OR (MH "Resistance Training") OR (MH "Muscle Strengthening")) AND ((MM "Neoplasms") OR (MH "Leukemia+") OR (MH "Lymphoma+")) AND ((MH "Child") OR (MH "Child, Preschool") OR (MH "Adolescence"))	Publication Type: Review	6
Cochrane Library	((((((((("Physical Activity") OR ("Motor Activity") OR ("Exercise") OR ("Physical Therapy Modalities") OR ("Physical Therapy Department, Hospital") OR ("Physical Fitness") OR ("Rehabilitation") OR ("Resistance Training") OR ("Exercise Movement Techniques") OR ("Exercise Therapy")))) AND ((("Neoplasms") OR ("Leukemia") OR ("Lymphoma")))) AND ((("Child") OR ("Child, Preschool") OR ("Adolescent")))))))	Search focused on Title, Abstract and Keywords Limits: Cochrane Reviews' and Other Reviews'	9
PEDro	physical activit* and child* with cancer	Language: English	17
All together			**755**

Appendix 2 Aims and main conclusions of the included reviews

Author (year)	**Aim of the review**	**Main conclusions**
Baumann et al. (2013)	To compile, structure and evaluate current literature of the effects of exercise interventions in pediatric oncology.	Clinical exercise interventions are safe and feasible during treatment. Positive effects were found on fatigue, strength, and QOL and limited evidence on the immune system, body composition, sleep, activity levels, and physical functioning.
Berkman et al. (2016)	To demonstrate low cardiorespiratory fitness (CRF) and factors contributing to low CRF in childhood cancer survivors (CS).	CS have lower CRF than general population, maybe due to cardiac, pulmonary, vascular and musculoskeletal limitations. CRF can be improved with exercise.
Braam et al. (2013)	To evaluate the effect and adverse effects of exercise interventions on physical fitness, fatigue, anxiety, depression, self-efficacy, and health-related QOL of children diagnosed with cancer.	Modest but positive effects of physical exercise training interventions exist and interventions are feasible.
Culos-Reed (2002)	To examine the evidence of PA in rehabilitation behavior in youth cancer populations.	PA may have beneficial outcomes, such as reduced fatigue and pain, enhanced QOL and improved self-esteem.
Galvão & Newton (2005)	To present an overview of exercise interventions in cancer patients during and after treatment, and to evaluate type, frequency, vol., and intensity of training.	Recent evidence supports the preliminary positive physiological and psychological benefits from exercise during or after treatment. Most of the studies was done in adult populations.
Gilliam et al. (2013)	To adopt the socio-ecological framework of PA correlates in healthy children to childhood cancer survivors.	The review presents a model to explain childhood cancer survivors' PA. The six domains are: 1) demographic, 2) medical, 3) cognitive/emotional, 4) behavioral, 5) social/cultural, and 6) environmental.
Götte et al. (2014)	To analyse and discuss the pros and cons of PA of children diagnosed with cancer.	Even though the evidence of benefits of PA in children diagnosed with cancer is limited, positive effects on physical and psychosocial outcomes is suggested both on acute side effects as well as late effects.
Grimshaw et al. (2016)	To investigate the feasibly of PA interventions during intense cancer treatment for children and adolescents.	Preliminary evidence supports PA interventions to be safe, feasible, and beneficial during the intense phase of treatment and attendance rates were high.
Heath (1996)	To demonstrate the potential and developmental needs for childhood cancer rehabilitation.	The author represents a modified model from Optimal Functioning Plan. Adoption of the model could help ensuring that rehabilitation occurs for all children diagnosed with cancer to the same standard.
Huang & Ness (2011)	To summarise literature of the effects of exercise on health and physical function among children diagnosed with cancer during and after treatment.	Early evidence indicates that exercise improves cardiopulmonary fitness, muscle strength, flexibility and physical function and reduces fatigue.
Kelly (2011)	To discuss PA levels, exercise effects, safety and participation in childhood cancer survivors, and how treatment side effects might be influenced by PA.	Cancer survivors are at risk for many secondary health conditions. Exercise program should be developed individually for each survivor based on the type of

		cancer, treatments received, and fitness goals.
Kruijsen-Jaarsma et al. (2013)	To systematically review changes in immune parameters after acute and chronic exercise in cancer patients and to offer a critical analysis of this literature and outline directions for future research.	Various immune parameters improved after exercise, however, the knowledge is still limited.
Liu et al. (2009)	To define the methodological quality of findings of exercise interventions, aimed at improving physical function or psychological well-being in patients treated for hematological malignancies.	A variety of exercise interventions were applied and encouraging results were found on physical fitness, health-related QOL and psychological wellbeing. The trials were of poor methodological quality.
Raber et al. (2016)	To determine if and to what extent parents were included in diet and PA interventions for childhood cancer survivors and whether parent involvement had a significant effect on behavioral outcomes or adiposity.	Studies including direct parental involvement improved all study measures. Adding a parental involvement component may improve health promotion interventions for childhood cancer survivors.
San Juan et al. (2011)	To provide a general overview and summarise the current literature of PA in children diagnosed with cancer.	Regular PA can improve the overall health status, functional capacity, and QOL of children diagnosed with cancer during and after treatment. Individually supervised interventions are suggested to have greater benefit than home-based programs.
Stolley et al. (2010)	To review literature regarding diet, PA, and related interventions among childhood cancer survivors.	Children diagnosed with cancer are insufficiently physically active, but the results are partly contradictory. Some of the interventions were beneficial.
van Brussel et al. (2005)	To determine whether physical fitness (VO2peak) is reduced in survivors of ALL compared to healthy children.	Physical fitness tends to be reduced in survivors of ALL. Regular physical activities are suggested for this population.
van Brussel et al. (2011)	To summarise and discuss current evidence of clinical pediatric exercise physiology in a variety of chronic childhood conditions, including childhood cancer.	Supervised exercise training, especially during maintenance phase and after, is beneficial and feasible in children diagnosed with cancer. PA is essential part of weight control of children diagnosed with cancer.
Winter et al. (2010)	To provide a survey of studies investigating PA and exercise interventions during and after childhood cancer treatment.	Reduced PA is highly probable during and after treatment. However, findings are not unanimous. Results of the interventions are promising, but also many challenges were reported.
Wolin et al. (2010)	To summarise the research of exercise interventions in hematological cancer survivors.	Strong evidence exists for a benefit of exercise on muscle strength and cardiorespiratory fitness. Evidence is weak for ankle dorsiflexion, physical functioning and body composition.
Wong et al. (2014)	To examine the effects of exercise on strength, function, and endurance, during and following chemotherapy, in children with ALL	Therapeutic exercises were safe and beneficial for patients with ALL.
Zhang et al. (2017)	To review lifestyle interventions in childhood cancer survivors and discuss implications of the findings for clinical care.	Lifestyle interventions are safe and feasible during cancer treatment.

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