MASTER THESIS

PHYSICAL ACTIVITY OF CHRONIC CANCER RELATED FATIGUE PATIENTS

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COLOPHON

PHYSICAL ACTIVITY OF CHRONIC CANCER RELATED FATIGUE PATIENTS

Analysis of daily patterns and identification of treatment goals

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Abstract

BACKGROUND: Fatigue is known as a frequent and invalidating residual symptom of cancer. More than 20% of cancer survivors report severe persistent fatigue after one year of treatment. Chronic cancer-related fatigue (CCRF) occurs as a consequence of the cancer itself, and, as a side effect of cancer treatment. However, the precise underlying etiology is unknown. The number of cancer survivors who suffer from cancer related complaints such as CCRF, will increase. This substantially increasing prevalence creates a major problem for cancer care, as it raises the pressure on both the care and the aftercare. It is the aim of this study is to analysing the physical activity patterns of CCRF people and investigates whether treatment goals can be defined which are more personalised and as such useful for better treatment programs.

OBJECTIVES: The objectives of this research are: (1) examination of the physical activity level and distribution of the CCRF patients during the day, (2) are these two parameters different in other groups and which treatment goals apply and (3) are the defined treatment goals, based on the physical activity level corresponding with the treatment goals defined by the physiotherapists.

METHOD: Objective one, solely focuses on the physical activity level from all included measurement days of the CCRF study population which have 6 hours of data (n=305 days). The physical activity distribution is determined on all participants which have accelerometer data of 7 days with 6 hours a day (n=35 participants), and determined by means of a theoretical, linear physical activity line and by subdivision the day in three parts. Objective two is a literature study of three chronic disease; COPD, CFS and CLBP. The physical activity level, pattern and treatment goals are investigated. Objective three focuses on the classification of the treatment goals by means of the description of the treatment goals and compared it with the physical activity level of the AAF participants.

RESULTS: The physical activity level of the CCRF study population were 203,592 IMA a day. This is lower than the defined physical activity norm of 7,000 steps (213,360 IMA-counts). The physical activity distribution, based on the linear line and calculated per part of the day, showed a lower physical activity level in the evening relative to the morning and afternoon. The physical activity level in morning and afternoon varied to each other. The analysis of the relative physical activity increase during the day showed an hourly physical activity increase until mid-afternoon, with subsequently an hourly physical activity decrease until the end of the day. The literature study of the other chronic

diseases showed two out of three chronic diseases a lower physical activity level compared to healthy people. Further, the physical activity level of the COPD GOLD II and CFS population corresponded with the level of the CCRF study population. The physical activity distribution was varied in all diseases but all of them, included CCRF, had a low physical activity level in de evening. Several literature studies suggest general treatment goals. Based on the corresponding physical activity patterns of the CCRF study population with the other chronic diseases, it can be suggested that the literature recommended treatment goals of chronic diseases can also be used in CCRF patients. As regards to the defined treatment goals by the physiotherapists and the physical activity level, it can be concluded that there exists an inconsistency between the defined treatment goals by the physiotherapists and the results physical activity level.

CONCLUSION: The physical activity level of the CCRF study population are lower than the Dutch norm for healthy physical activity and corresponded to other chronic diseases. The physical activity distribution during the day can be parameterized by determining the physical activity deviation of three parts of the day, in ratio to a normal linear physical activity distribution. Further, physical activity levels of several chronic diseases are corresponded with the physical activity level of the CCRF study population. As final, the treatment goals defined by the physiotherapists are not consistent with the measured physical activity levels and patterns.

Samenvatting

ACHTERGROND: Vermoeidheid is bekend als een frequente en belemmerend symptoom van kanker. Meer dan 20% van de overlevenden van kanker rapporteert, een jaar na behandeling, blijvend ernstige vermoeidheid. Chronische kanker gerelateerde vermoeidheid (CCRF) treedt op als gevolg van de kanker, maar ook als een neveneffect van de kankerbehandeling. De precieze onderliggende etiologie is onbekend. Het aantal overlevenden van kanker die lijden aan kanker gerelateerde klachten zoals CCRF, zal komende jaren toenemen. Deze aanzienlijk toenemende prevalentie veroorzaakt grote problemen voor de kanker zorg, het verhoogt de druk op zowel de zorg als op de nazorg. Het doel van deze studie is het analyseren van de fysieke activiteitenpatronen van mensen met CCRF met daarnaast onderzoeken of er gepersonaliseerde behandeldoelen gedefinieerd kunnen worden die bruikbaar zijn voor een beter behandeling.

DOELSTELLINGEN: De doelstellingen van dit onderzoek zijn: (1) het onderzoeken van het fysieke activiteiten niveau en de fysieke activiteiten verdeling over de dag van de CCRF patiënten, (2) onderzoeken of deze twee parameters verschillend zijn ten opzichte van andere ziekte populaties en welke behandeldoelen hebben deze, (3) zijn de gedefinieerde behandeldoelen, gebaseerd op het fysieke activiteiten niveau, in overeenstemming met de opgestelde behandeldoelen door de fysiotherapeut.

METHODE: Doelstelling 1 richtte zich op het fysieke activiteiten niveau van de CCRF studiepopulatie gemeten met een versnellingsmeter, waarbij alle meetdagen minimaal 6 uur aan meetgegevens had (n = 305 dagen). De fysieke activiteiten verdeling over de dag werd bepaald over alle deelnemers die 7 meetdagen hadden en tevens ook 6 uur per dag aan meetgegevens had (n = 35 deelnemers). De verdeling werd uiteindelijk bepaald aan de hand van een theoretisch lineaire lijn en berekend per dagdeel. Doelstelling twee is een literatuurstudie van de drie chronische ziekte; COPD, CFS en CLBP. Het fysieke activiteiten niveau, patroon en de behandeldoelen zijn onderzocht. Doelstelling drie richtte zich op de classificatie van de behandeldoelen en deze werden vergeleken met het fysieke activiteiten niveau de AAF deelnemers.

RESULTATEN: Het fysieke activiteitenniveau van de CCRF onderzoekspopulatie was 203.592 IMA per dag. Dit is lager dan de gedefinieerde fysieke activiteit norm van 7.000 stappen (213.360 IMA-tellingen). De fysieke activiteiten spreiding over de dag, gebaseerd op lineaire lijn en berekend per

dagdeel, vertoonde een lagere fysieke activiteiten niveau in de avond opzichte van de ochtend en middag. Waarbij het fysieke activiteiten niveau tussen de morgen en middag verschillend waren. De analyse van de relatieve toename van de fysieke activiteit tijdens de dag toonde per uur een toename tot halverwege de middag, met vervolgens elk uur een daling van de fysieke activiteit tot aan het einde van de dag. De literatuurstudie van de andere chronische ziekten vertoonden twee van de drie ziekten een lager niveau van fysieke activiteit in vergelijking met gezonde mensen. Verder komt de lichamelijke activiteiten niveau van de COPD GOLD II en CVS populatie overeen met de CCRF onderzoekspopulatie. De fysieke activiteiten verdeling van de onderzochte chronische aandoeningen waren verschillend van elkaar, maar ze hadden allen, inclusief de CCRF populatie, een laag fysiek activiteiten niveau in de avond. Diverse studies suggereren algemene behandeldoelen. Op basis van de overeenkomstige fysieke activiteitenpatronen van de CCRF studiepopulatie met andere chronische ziekten, kan worden gesuggereerd dat de behandeldoelen dit door de literatuur worden aanbevolen ook kunnen worden gebruikt bij patiënten met CCRF. Met betrekking tot de gedefinieerde behandeldoelen door de fysiotherapeuten en het niveau van fysieke activiteit, kan worden geconcludeerd dat er sprake is van een inconsistentie tussen de gedefinieerde behandeldoelen door de fysiotherapeuten en de resultaten van de fysieke activiteit niveau.

CONCLUSIE: Het fysieke activiteiten niveau van de CCRF studiepopulatie is lager dan de Nederlandse Norm voor Gezond Bewegen en komt overeen met de andere chronische ziekten. De fysieke activiteiten verdeling over de dag kan worden geparametriseerd door berekening van de hoeveelheid fysieke activiteiten afwijking op de drie dagdelen ten opzichte van een normale lineaire lichaamsbeweging verdeling. Verder, het fysieke activiteiten niveau van verschillende chronische ziekten komen overeen met het fysieke activiteiten niveau van de CCRF studiepopulatie. Tot slot, de gedefinieerde behandeldoelen door de fysiotherapeuten zijn niet in overeenstemming met de gemeten fysieke activiteiten niveaus en patronen.

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List of abbreviations

AAF	Ambulant Activity Feedback
CBT	Cognitive Behaviour Therapy
CCRF	Chronic Cancer Related Fatigue
CRF	Cancer Related Fatigue
PA	Physical Activity
PDA	Personal Digital Assistant
MBCT	Mindfulness-Based Cognitive Therapy
NCCN	National Comprehensive Cancer Network
NNGB	Nederlandse Norm Gezond Bewegen (Dutch norm for healthy physical activity)
RRD	Roessingh Research and Development, Enschede, the Netherlands
SD	Standard Deviation
MET	Metabolic Equivalent of Task
WHO	World Health Organization

Chapter 1

Introduction

Fatigue and cancer

Fatigue is known as a frequent and invalidating residual symptom of cancer. According to Goedendorp et al. (2013) it is estimated that more than 20% of cancer survivors report severe persistent fatigue after one year of treatment,[1 2 3] with major effects on the quality of life of these survivors. Fatigue seems to be elicited during the cancer treatment. More notably, chronic cancer-related fatigue (CCRF) occurs as a consequence of the cancer itself, and, as a side effect of cancer treatment. However, the precise underlying etiology is unknown.[2 4 5]

In general, cancer has become chronic of character through the increased life expectancy of cancer patients by the improved treatment opportunities for several cancer types. With this in mind, the number of cancer survivors who suffer from cancer related complaints such as CCRF, will increase.[6] It is estimated that between 2010 and 2020, the number of cancer patients who will have completed primary cancer treatment and engaged in the aftercare within the Netherlands will increase by 61%. At the same time, the number of (ex-)cancer patients in the Netherlands will rise from 579,000 to 905,000.[6] This substantially increasing prevalence creates a major problem for cancer care, as it raises the pressure on both the care and the aftercare.[7 8] Aftercare consists of rehabilitation, related to residual complaints of the cancer treatments. This aftercare differs from medical follow-up care which exists from medical check-ups by the specialists.

Pressure on after-care

The pressure on the aftercare in the secondary care thanks to the estimated rising prevalence of cancer survivors coupled with the growing demand for care. For this reason, the Dutch fund 'KWF kankerbestrijding' recommends a partial shift of the oncological aftercare to the primary (trans mural) care, as well as to improve patient self-management with respect to their complaints.[6] A potential primary aftercare is, for instance, ambulant care or a home-based program. Through this shift of the oncological aftercare, it is expected that the care will be more accessible for a larger group of patients.

Physical activity

In the case of cancer survivors and their corresponding fatigue, the physical activity level of the survivors is remarkable in comparison to healthy people. In detail, several researchers indicated a

lower physical activity level after cancer treatments in comparison with the physical activity level before the cancer diagnosis.[9-11] A decreased physical activity level during the cancer treatment with subsequent an increase of physical activity level post-treatment is notable and furthermore, the physical activity level before the diagnosis is often not reached anymore.[9] The physical activity level after the treatment is often even below the level recommended by the World Health Organization (WHO)[12], which suggests a moderate-to-vigorous intense physical activity level[13 14]. In opposite to this, a sufficient physical activity level is effective in handling cancer residual symptoms, and should therefore be stimulated. Specifically, a sufficient level of physical activity is effective in order to reduce cancer related fatigue.[15-21] To clarify, the researchers Lee(2013) and Pinto(2005; 2008; 2013) have shown that in breast and colorectal cancer survivors, there has been a positive effect on reduced fatigue by using a home-based program which focused on an increased physical activity level.[22 14 23 24]

Treatment goals

Most home-based interventions provide general treatment goals, such as an increase in frequency and duration of physical exercises, an increase in the Metabolic Equivalent of Task (MET) value. However it has been shown that self-defined treatment goals are more effective in reaching higher level of physical activity.[25] Austin et al.(1996) explained this by the fact that in case of self-defined goals patients have more focus on their goals and are therefore more likely to reach their goals.[26] This is supported by the research of Abraham et al. (2009) and Rabin et al. (2011) which results indicate that when patients are aware of their own personal treatment goals, then they are more likely to be able to realistically reach these goals.[27-29]

Currently, there is a study on-going about an mHealth home-based intervention for cancer patients with persistent fatigue (RCT 'Fitter na kanker'). The study included an mHealth ambulant activity feedback intervention which consists of an ambulant activity coaching system with the aim to improve balance, perception and the level of physical activity of former cancer patients in order to decrease the level of fatigue.[30]

It is the aim of this study to investigate whether or not the ambulant mHealth intervention is effective to reducing CCRF and what are the treatment mechanisms.

1.1 Problem definition

This thesis fits within this project and aims at analysing the physical activity patterns of CCRF people and investigates whether treatment goals can be defined which are more personalised and as such useful for better treatment programs.

To be more specific, the following research question and related sub-questions can be formulated:

> *How can the activity behaviour of former cancer patients with chronic cancer related fatigue be parameterized and which treatment goals can be defined based on this activity behaviour?*

Sub questions

1. What is the absolute cumulative IMA-value a day and what is the distribution of physical activity during the day, measured according to the IMA-values, for this patient group?

2. Are these parameters different for patients compared to other groups which are described in the literature and, if so, which treatment goals apply?

3. Do the defined activity goals, based on the physical activity level measured by the IMA-values, correspond with the activity goals formulated by the physiotherapist?

Chapter 2

Background

This chapter presents several topics useful for getting an overview on the background of the study as well as on the overarching RCT 'Fitter na kanker'.

2.1 Definition of chronic cancer related fatigue

Chronic cancer related fatigue (CCRF) is derived from cancer related fatigue (CRF). CRF is defined as a fatigue that occurs during and after cancer treatment and differs from every day or normal fatigue. The National Comprehensive Cancer Network (NCCN) defined CRF as "*a distressing persistent, subjective sense of physical, emotional and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning".* [31] [32] CRF is characterised by feelings of tiredness and weakness despite amount of sleep and rest, whereas normal fatigue is due to overexertion or lack of sleep. Based on the research of Goedendorp(2013), chronic CRF is defined as a persistent fatigue that lasts for more than three months after successful cancer treatment has been endured.[1] This definition is based upon the finding that there is a minimal chance of fatigue decreasing after more than three months following treatment.[1]

2.2 Treatment methods

A number of treatments is available for complaints of fatigue from cancer patients, such as: cognitive behavioural therapy (CBT), physical exercises, stress management[33] and several researches[34-38] indicate the effectiveness of these different treatments:

- Gielissen et al.(2006) report a highly effective specially designed cognitive behaviour therapy (CBT) in reducing CCRF.[34] This therapy consists of individual sessions with a therapist which is focus on six perpetuating factors of CCRF. The number of sessions varies between five and 26 in a six months period, depending on whether or not the goal was reached. They showed an improvement in fatigue severity compared to patients waiting/control group by using the Checklist Individual Strength (CIS). However, it is unclear which aspect of CBT caused a reduction in the fatigue. Many studies assume that a decrease in fatigue is caused by an increase in physical activity (PA) levels, but CBT did not cause any change in physical activity.[36 39 40]

- Buffart et al.(2013) claim that physical training has a positive effect on fatigue.[38] The therapy consists of twice weekly group training and personalised physical exercises to improve exercise capacity, muscle strength, reduced physical limitations and fatigue as well as an increase in physical activity levels. The physical training has both a direct and indirect effect; it improves physical activity as well as reducing fatigue.

The work of Van Weert et al. (2010) supports also the effectiveness of both of the above mentioned treatments in reducing fatigue.[35] They studied the effectiveness of physical training and the combination of physical training with CBT in comparison with a control/waiting group. It resulted in a significant and beneficial effect on fatigue compared with no intervention at all.

2.3 Measurement of physical activity

There are several methods to assess physical activity. One that is widely used is a self-report method that uses questionnaires that are simple and cheap but the reliability and validity is limited.[41 42] In addition, the use of the pedometer provides a measure on the count of steps per day. It does not, however, measure the intensity, duration or frequency of the activity. Another objective method is the use of an accelerometer which measures the intensity, duration and frequency of the activity and such as gives a more details evaluation of PA in comparison with the use of self-report questionnaires.[43] For the ranking of the different measurement tools see Figure 1.

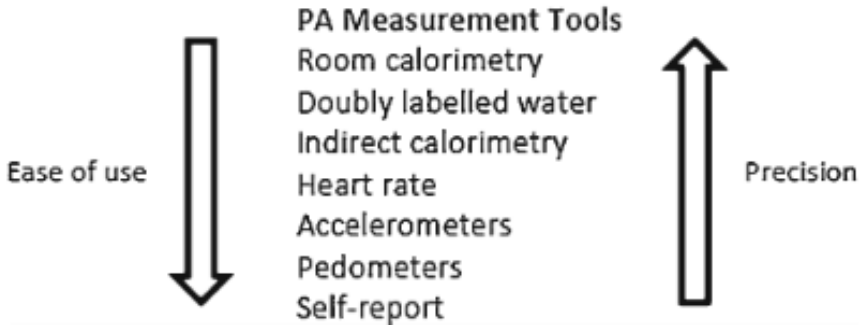

Figure 1 Precision and ease of use of physical activity measurement tools[43]

In the Fitter na kanker-project, an accelerometer is being used. The output of such a device is the Integral of the Modulus of body Acceleration (IMA) which is expressed as IMA-counts per minute and, moreover, higher IMA indicates a higher level in activity. This is a unit which has been scientifically proven to correlate to energy expenditure.[44 45]

2.4 Study 'Fitter na kanker'

The study 'Fitter na kanker' compares three groups. One was a control group and the other two groups received a different e-therapy that had the aim to reduce chronic cancer related fatigue. One of the e-therapies is the Ambulant Activity Feedback (AAF) treatment which focuses on physical activity. The RCT study itself was performed by Roessingh Research and Development (RRD) in Enschede alongside the Helen Dowling Institute in Bilthoven.[30] In addition, these two research institutes worked closely together with the Paramedical Institute Rembrandt in Veenendaal. The

study is being carries out at the moment whereby the inclusion was started in April 2013. Participants were acquired on a national basis from all former cancer patients who had suffered from CCRF. They were informed about the RCT study, in particular, from advertisement on patient websites, patient e-magazines, newsletters, and social media. The patients and medical care workers were also informed by national newsletters regarding the study.

The RCT group was formed from three groups which consisted of a web-based mindfulness-based cognitive therapy program (MBCT), ambulant activity feedback therapy (AAF) and a control/waiting group. The intervention period of the study was nine weeks that was supplemented with a post-measurement and two follow-up measurements, that consisted of two weeks post-treatment (T1), six months (T2) and 12 months (T3) after the baseline, respectively. For an overview of the RCT study, see Figure 2.

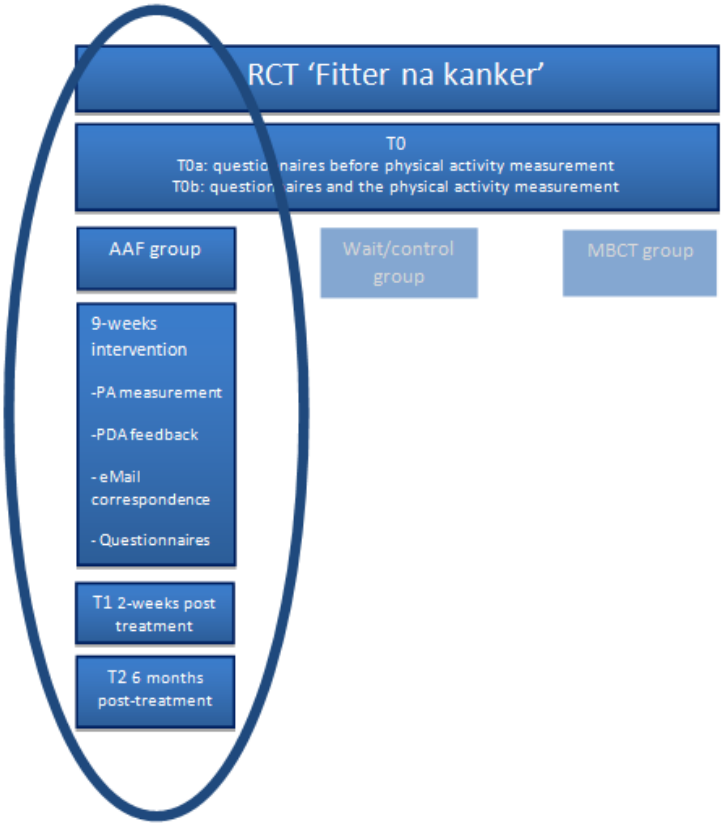

Figure 2 Structure of the RCT 'Fitter na kanker'

The intervention included an ambulant activity coaching system which consisted of a Personal Digital Assistant (PDA) and a ProMove 3D-accelerometer. During the nine-week intervention, the system gave the participant hourly feedback messages based on the measured activity level. At the same time, the participants were supported by a physiotherapist through weekly e-mail contact and one phone call. Overall, the aim of the intervention was to provide participants with an insight into their activity pattern and to balance out or increase their activity levels for improved energy.

2.5 Outcome measurements

All participants had a baseline physical activity (PA) measurement with regards to the objective activity level. The baseline consisted of daily PA that was measured by using an accelerometer between 8.00AM and 10.00PM during a seven days period. The data of the baseline was sent to a portal of the RRD and was made available to the researchers. Furthermore, to answer the third question about the comparison of treatment goals and the physical activity patters, the treatment goals of the AAF group, defined in the second week of the AAF intervention by the physiotherapists, were collected.

Chapter 3

Materials and methods

3.1 Research design

This study was being designed as cross-sectional that solely focused on the physical activity baseline measurements from all included CCRF participants. The baseline data consists on the accelerometer data of seven days. The baseline period is performed after the inclusion and before the randomization (T0) (Figure 2).

In addition to the baseline data from all included participants, the data of the participants that were randomized into the AAF intervention were also collected up to week three of treatment. This data consisted of treatment goals established by physiotherapists in consultation with the patient, which were focussed on the physical activity level.

3.2 Study population

In current research, former cancer patients have participated who have suffered with chronic fatigue as residual symptom of cancer. The in- and exclusion criteria were identical to those that were used in the overarching RCT. People who met the following criteria were eligible for participation.

- Completed the curative treatment for cancer at least three months ago and, this has to be approved by the referrer. For this study; surgery, chemotherapy, radiotherapy, immunotherapy, and/or stem cell transplantation, the use of anti-inflammatories and monitoring visits were considered treatment. But this did not include hormonal therapy.
- Disease-free, as defined by the absence of cancer activity parameters, which has to be approved by the referrer.
- The patient had complaints of severe fatigue for at least the last three months.
- CIS-fatigue severity subscale with a score of 35 or higher.[46] (See Appendix I)
- Older than 19 years of age (at registration).
- Age at disease onset minimal 18 years.
- Capable of reading and writing the Dutch language and to be able to use the Internet.

In addition to the inclusion criteria, people were excluded from participation if they had formerly had severe psychiatric morbidity, were dependent on a wheelchair in daily life, were pregnant, or had a recurrence of cancer. The exclusion criteria reduced the risk of confounding variables.

3.3 Materials

3.3.1 Activity monitoring system

The ambulant activity coaching system of the study consists of different components. These components are necessary for the measuring and registration of PA.

The ProMove3D (63 x 96 x 16 mm, 67 g, Inertia Technology, Enschede, the Netherlands, (Figure 3) is an accelerometer physical activity sensor. It communicates with the Personal Digital Assistant through Bluetooth. The output of the accelerometer data is the Integral of the Modulus of body Acceleration (IMA). This data was converted into IMA-values by the embedded software on the accelerometer and was calculated per minutes in metric units (10^{-3} m/s^{s}) with sample frequency f_s=100 Hz and time interval T=60 s.[47] The data was filtered by a high-pass filter with a cut-off frequency at 0.25Hz. The equation was similar to Bouten et al.:[48]

Equation 1.

$$IMA = \frac{1}{f_s T} \sum_{n=n_0}^{n_0+f_s T} |a_x[n]| + |a_y[n]| + |a_z[n]|$$

Bouten et al. (1994; 1996) suggest that IMA correlates to energy expenditure (R=.95).[44 49] Notable, sedentary activities have a lower correlation compared to e.g. walking. This difference might be explained by the difficulty of measuring physical activity at low levels of activity.[49]

The accelerometer must be worn laterally on the hip by using a clip on the waist belt. This position causes a low variability of the output from the sensor. Furthermore it is a user -friendly position. If the sensor will nevertheless hamper the mobility (e.g. if the arm swings alongside the body and touches the sensor), the sensor can be replaced. There is a minimal change in the reliability, when the sensor is bringing slightly forward into a more central position. Additionally, a suggestion of a tighter fixation of the sensor to the body has been made, in order to obtain the best results.[47]

Figure 3 ProMove 3D accelerometer

Figure 4 Personal Device Assistent

The Personal Digital Assistant (PDA) is the second part of the system, and is in fact, an HTC smartphone which communicates with the accelerometer by Bluetooth (Figure 4). The PDA registers the accelerations and sends it three times a day by a wireless internet connection to a secured web server at Roessingh Research and Development. The PDA must be near the accelerometer to achieve a sufficient Bluetooth connection.

3.3.2 Web portals

The participants had their own personal login to the project's web portal. This portal was made available on the project website www.fitternakanker.nl and presented the questionnaires (T0 – T3). Through this web portal, researchers could plan the moment at which a certain questionnaires could become available for a specific participant.

The participants who were randomised in the AAF intervention also received a login for the AAF web portal which was available on https://fitternakankerportal2.rrdweb.nl/ (Figure 5). The personal cumulative PA level of the measured days is shown in this portal.

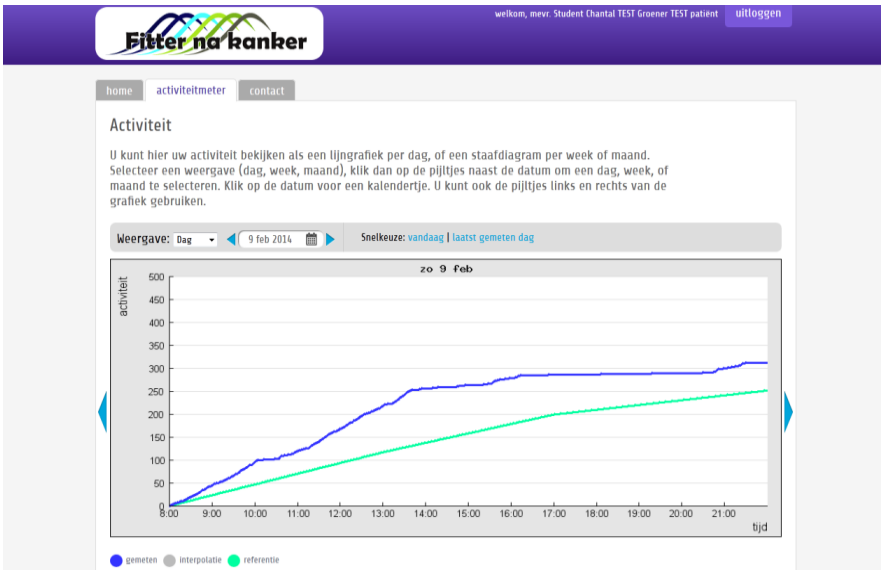

Figure 5 Web portal for the Ambulant Activity Feedback intervention group, it shows the amount of physical activity over the day. The blue line is the measured physical activity and the green line is the reference line.

3.4 Assessment protocol

3.4.1 Procedure

The people who registered online through the project website received patient information and an informed consent form by e-mail. The people also received an e-mail with their login details for the patient's web portal on the project website. They were requested to fill out the questionnaires (T0a) which were decisive for the inclusion procedure.

Whenever someone fulfilled the inclusion criteria, they personally received the activity monitoring system by a researcher. All participants wore the system for as much as possible over seven consecutive days, from 8.00AM until 10.00PM. The system must be worn lateral of the waist belt; this instruction is previously described in section 3.3.1 Activity monitoring system. In the case of activities being undertaken, such as, swimming or taking a shower; the accelerometer could not be worn. To gain insight into the missing physical activities, participants kept an activity diary for tracking these activities. When participants were randomly grouped into the AAF intervention, treatment goals were established by the physiotherapist in consultation with the participant in the second week of the intervention.

3.4.2 Data collection of the physical activity

The accelerometer data was collected and analysed to obtain an overview of the physical activity level and pattern of the CCRF study population. For this study, we used data from the overarching RCT 'Fitter na kanker' which was obtained between May 2013 and mid-May 2014.

3.4.3. Literature study of physical activity levels from chronic diseases

In order to answer research question 2, obtaining the physical activity patterns of other chronic diseases, literature was studied. By means of literature, find out the 'normal' physical activity level for the Dutch population as well as other patient groups, more specifically the Dutch norm of healthy physical activity (Nederlandse Norm Gezond Bewegen). Because of the chronic component of CCRF it was interesting to see whether or not other chronic diseases achieved the norm and which PA pattern the different chronic patient populations showed i.e. Chronic Obstructive Pulmonary Disease (COPD), Chronic Fatigue Syndrome (CFS) and Chronic Low Back Pain (CLBP). The aim of this information was to identify similarities and differences within the CCRF study population and the already studied chronic diseases, in regards to the PA level. In addition to the amount of PA level, the PA pattern during the day showed information about the distribution level over the day. Based on the PA level and the PA distribution over a day, treatment goals can be established in relation to the PA level of the corresponding chronic disease.

Search strategy

First, regarding the general physical activity norm, potentially relevant articles were retrieved from the databases; PubMed, Science Direct as well as databases from the National Ministry of Public Health. The literature search was limited to articles published between 2000 and 2014. The following

keywords were used: PHYSICAL ACTIVITY and (NORM or STANDARD or PREFERENCE or PREFERRED) and STEPS, either in full title or in abstract. This search resulted in 267 articles. By adding the keywords STEPS/DAY, it reduced down to 30 hits. A new search strategy was then formulated to obtain articles that related to the amount of steps per day with a sufficient physical intensity level. STEPS/DAY and MODERATE VIGOROUS PHYSICAL ACTIVITY were the used keywords in full title or in abstract. This resulted in 20 hits. However, in general, studies about the PA level of children were excluded.

Secondly, the different chronic diseases and the corresponding PA levels were searched in the same databases as the first search. The keywords for the three chronic diseases were substantially the same. COPD or CHRONIC OBSTRUCTIVE PULMONARY DISEASE and PHYSICAL ACTIVITY and STEPS/DAY were the keywords used for COPD. This resulted in 13 hits.

Results for CFS emerged by using the keywords: CFS or CHRONIC FATIGUE SYNDROME and PHYSICAL ACTIVITY and STEPS/DAY, and this resulted in two hits. Therefore, the keywords were adjusted into CFS or CHRONIC FATIGUE SYNDROME and PHYSICAL ACTIVITY LEVEL, which resulted in 94 hits which focused on a broader aspect of the PA.

For the last chronic disease, CLBP, the following search strategy was performed. The keywords CLBP or CHRONIC LOW BACK PAIN or LOW BACK PAIN and PHYSICAL ACTIVITY and STEPS/DAY also resulted in two hits. By using a broader search strategy, the number of hits increased to 339 by using the keywords: CLBP or CHRONIC LOW BACK PAIN or LOW BACK PAIN and PHYSICAL ACTIVITY LEVEL.

Furthermore, the reference lists of articles which met the inclusion criteria were manually searched for to ensure other relevant articles were not omitted.

3.4.4 Data collection of the treatment goals from the AAF intervention.

The AAF intervention focused on the physical activity level of the CCRF population. The participants were treated by four physiotherapists. These treatment goals were defined by means of e-mail contact and one telephone call in the second week of the AAF intervention. The treatment goals were subdivided into groups based on the corresponding descriptions of the treatment goals by the physiotherapist and participant. After that, the physical activity level of the measurement days of the AAF participants were collected and grouped based on the corresponding treatment goal description.

3.5 Data analysis

3.5.1 Physical activity parameters

To answer the question about the physical activity pattern of the CCRF population, two parameters were used; the absolute cumulative PA level per day and the distribution of the PA during the day. These parameters provided insight of the physical activity on two different manners and was already proven suitable for the analysis of PA patterns of the COPD population[50]. In general, previous studies have indicated a low physical activity level in cancer survivors with a more variable activity pattern compared to those of healthy people. [9-11 13]

Data which was derived from the accelerometer was used for analysis. The used data presented the average IMA-value per minute and the number of measured minutes per day.

Before the analysis of the physical activity level and distribution, the validity of the physical activity data was examined. Therefore the relation between the amount of system wear time and the amount of IMA-counts per day was analysed. The question was how much the amount of IMA-counts is explained by the wear time of the accelerometer.

3.5.2 Calculation of absolute cumulative physical activity level

The absolute cumulative physical activity level was analysed of means of three different approaches. First of all, the mean absolute cumulative physical activity level over all measured days was calculated. As additional calculation, the mean absolute cumulative physical activity level was also calculated over the mean PA level of each participant. As final, the correlation between the degree of variability of PA level between the participant's days and the mean participant's PA level over the days were analysed.

For the purpose of data analysis of the absolute cumulative physical activity level per day the number of measured hour is important for a realistic impression of the PA level. A study of Tabak(2014) used a minimum of six hours of data.[50] Days with less than six measured hours were excluded for analysis. The calculation of the absolute cumulative physical activity level was performed over each separate measurement day instead of an average physical activity level of the measurement days of each participant. In this way, the result will not be influenced by the variability of participants' PA level between the days and shows the actual physical activity level per single day. On the other hand, the PA value of the days could be dependent to each other because each participant represented more than one day. The absolute cumulative PA level per day was obtained by multiplying the average IMA-value per minute by the number of measured minutes per day. These results were expressed in IMA-counts and were reported as a mean and standard deviation.

As additional analysis, an impression of the physical activity level of the participants was obtained by calculation the mean PA level per participant. Data of all participants was included, regardless the number of measurement days. The distribution of the mean PA per participant was shown in a histogram.

Besides, the degree of variability of a participant's PA level between the days relative to the entire study population was analysed. It provided more information about the PA level of the study population. Related to this, it was interesting whether a correlation between the degree of variability and the mean PA level of a participant occurs. The hypothesis was: the PA level is explicable by the degree of variability. When a correlation occurs, the variability of the PA level could be an important aspect for improvement the balance of PA between the days and it could be important for defining of personal treatment goals. Literature is not yet available about a correlation between the variability of PA and the degree of PA level. In this way, possible determinations of physical activity level were described.

3.5.3 Calculation of the distribution of physical activity

In addition to the absolute cumulative physical activity level per day, also the PA distribution was analysed. The distribution of physical activity was analysed by means of two different approaches. The first approach was the degree of deviation of different parts of the day in comparison with, an in proportional linear PA distribution, derived from the total PA level of that individual's day. The second approach was the relative physical activity increase during the day. Both approaches used the hourly IMA-values. This was calculated by multiplying the average IMA-value per minute by the number of measured minutes of the corresponding hour.

At first, the method for data selection is described. Subsequently, the data analysis for the two approaches is described.

Selection of accelerometer data

For the analysis of the physical activity distribution of the CCRF study population, data of the same days were used as for the absolute cumulative physical activity, but a new data selection was performed. The analysis of the absolute cumulative physical activity included days with at least six hours of measurements, which previous literature used also this number of minimum hours[50].

The data represent hourly IMA-values per day as well as the number of measured minutes of the corresponding hour. The data we would use for the current analysis was selected on three aspects. The first aspect was that each hour should consist at least 30 minutes of data. Data less than 30 minutes represent an unrealistic physical activity of that hour, and were therefore excluded for analysis.

The second aspect is excluding erroneous data, by visually checking for erroneous data by the use of the RRD toolkit. The RRD toolkit was designed by programmers at the Roessingh Research and Development in Enschede (Figure 6). This tool showed the measured PA by means of the data outputted via the Integral of the Modulus of body Acceleration (IMA). Figure 6a is a graphical representation of the measurements taken from one participant over a period of one day. It shows the activity accelerations generated, per 10 seconds (the green line). Whereas, the blue line shows the cumulative activity over the same day. Figure 6b reveals a statistical overview over the corresponding day as well as the mean physical activity per hour.

6a

6b

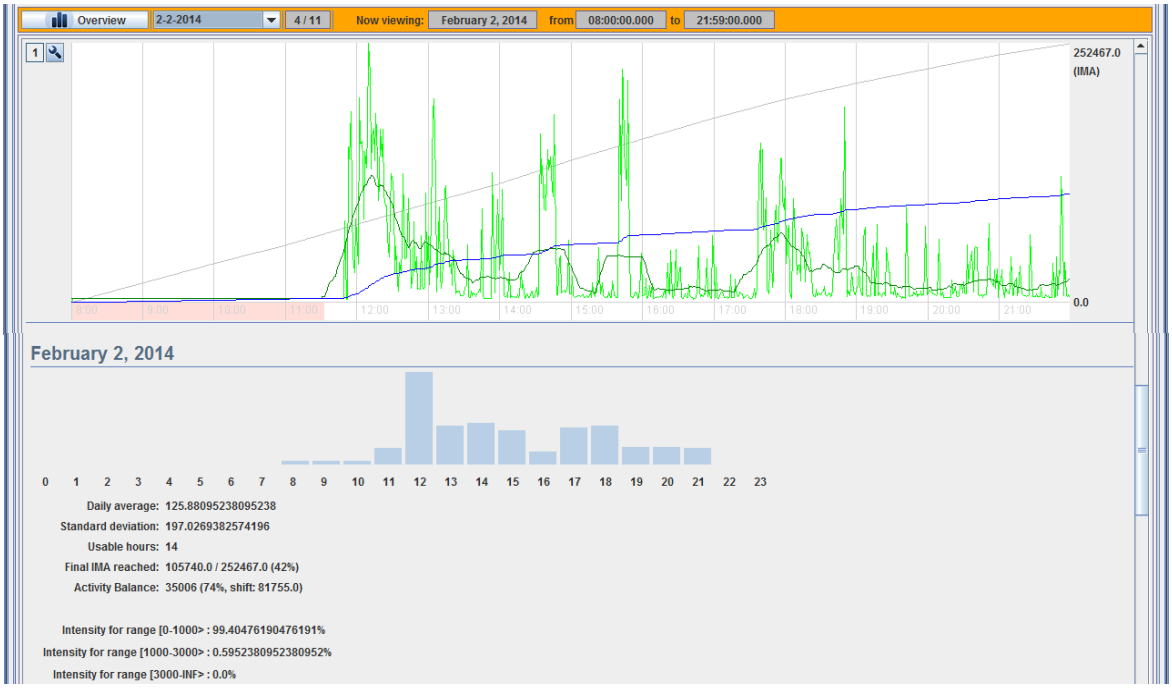

Figure 6 RRD toolkit; 6a: the graphic representation of the physical activity over a day. 6b: the statistical representation of the physical activity over a day.

These erroneous data (pink marked in Figure 6a) could be for instance, several consecutive hours with nil physical activity data at beginning of the day suggests erroneous data or participant is still sleeping (e.g. see figure 6a: 8.00AM – 11.30AM). Erroneous data at beginning and end of the day could be interprets as data which is not a part of participant's day or no physical activity, in contrast erroneous data during the day could be interpret as missing physical activity such as swimming or showering.

The last aspect for the current analysis, a participant's data should also consist of at least seven measurement days. So, all participants with fewer days were excluded for this analysis. Trost et al.[51] suggest a reliable estimation of the PA behaviour with seven days of data.[52] So there are three criteria used for selecting data and this data were used for the two approaches.

The first approach: the degree of deviation from a linear distribution

To answer the question about the physical activity distribution of the study population, we would like to compare the measured data with a theoretical line which represent a complete linear distribution. For each individual, and each day, a theoretical "normal" PA line was derived from the absolute cumulative PA value over the day. The normal PA line represents a linear distribution of the physical activity level over the measured hours of the day. The line consists of a maximum of 14 data points which represent the number of measured hours. In this line was corrected for the number of measured minutes per hour (31 – 60 minutes): the absolute cumulative PA value over the day was divided over all measured minutes per day and multiplied by the number of measured minutes per separate hour (see equation 2). An example is shown in Figure 7, via the red dots. The hours with

erroneous measurements or hours that represented less than 30 measured minutes, as described above, were registered as zero IMA-counts whether this occurred at the beginning or end of the day. These hours were excluded for analysis. When this occurred in the intervening hours during the day, the data were registered as missing data.

The days were subdivided into three fixed parts. These parts of the day were: morning (8.00AM to 1.00PM), afternoon (1.00PM to 5.00PM) and evening (5.00PM to 10.00PM). The division of the day in the current research consists of morning and evening five hours and the afternoon four hour, because the number of measured hours in the morning and evening are more variable compared to the afternoon. A day consists of a maximum of measured 14 hours (8.00AM - 10.00PM). A participant could start the day after 8.00AM (time of waking) and the day could be end earlier than 10.00PM (time of sleeping). A result is a more variability in the number of measured hours in the morning and evening, therefore the morning and evening have one hour more than the afternoon to compensate this variability. The chosen subdivision that was chosen for this analysis is in accordance with the literature that suggests that an analysis of fixed parts of the day is preferred over analysis per hour.[53 54] By choosing this defined day parts created the possibility to compare our results of the physical activity distribution analyses with literature of other populations.

$$Normal\ PA\ value\ for\ an\ hour = \frac{Absolute\ cumulative\ IMA\ per\ day}{Total\ measured\ minutes\ per\ day} * number\ of measured\ minutes\ for\ an\ hour$$

Equation 2.

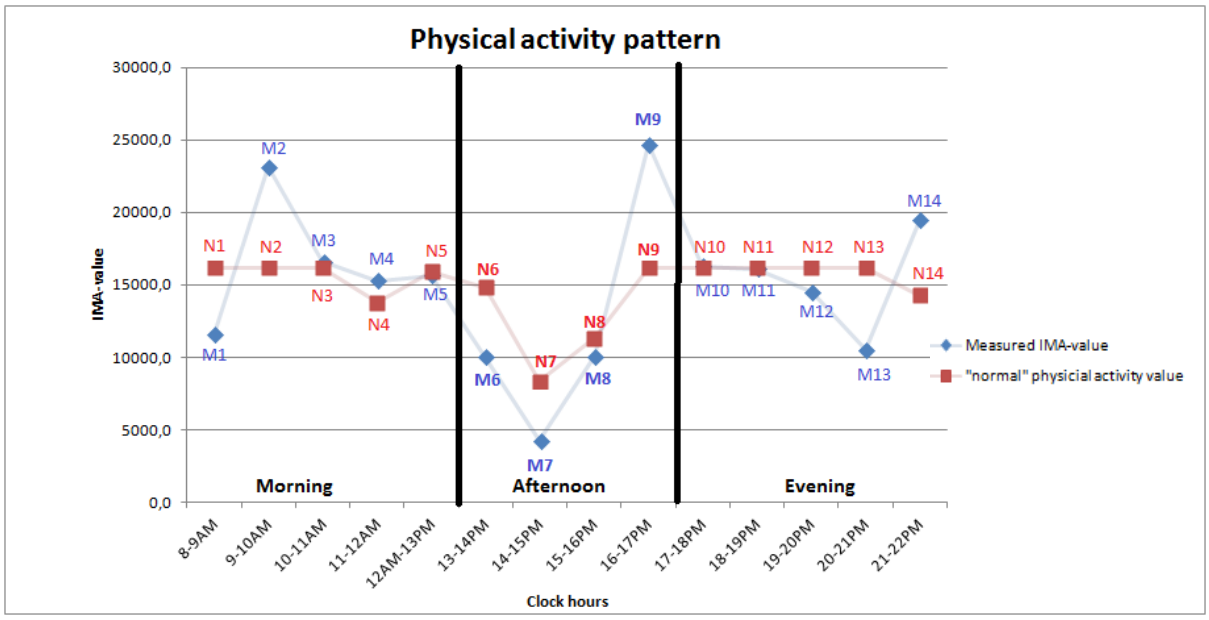

Figure 7 Physical activity pattern: the blue dots indicate the average measured IMA-value for each separate hour; the red dots are the normal PA value of the corresponding hour. Both values are corrected for the number of measured minutes of the corresponding hour.

Calculation of the degree of deviation from a proportional distribution

The degree of deviation relative to the normal PA line per part of the day was determined by calculation of the difference between the measured IMA-value of a part of the day e.g. the afternoon (Figure 7: M6-M9 =the afternoon) and the individual normal value of the corresponded part of the day (Figure 7:N6-N9 = the afternoon). By means of an equation of the measured IMA-value and the individual normal value of that particular part of the day and subsequently subtracting it with 100%, resulted it in a positive or negative percentage per part of the day (Equation 3). This percentage represented the degree of deviation from the normal value of each part of the day. This percentage could be infinitely negative and positive in which 0% meant a complete linear PA distribution with respect to the normal PA value over the corresponding part of the day. A negative percentage meant a lower PA level relative to the normal PA distribution of the corresponding part of the day. Whereby, a positive percentage meant a higher PA level with respect to the normal PA level. Summarized, a high negative or positive percentage meant a more imbalance PA distribution with respect to the normal PA distribution.

$$Deviation\ per\ part\ of\ the\ day\ (\%)\ e.g.the\ afternoon = \frac{Sum\ of\ the\ measured\ IMA\ values\ of\ one\ part\ of\ the\ day\ (M6-M9)}{Sum\ of\ the\ indivual\ normal\ PA\ IMA\ values\ of\ one\ part\ of\ the\ day\ (N6-N9)} * 100\% - 100\%$$

Equation 3

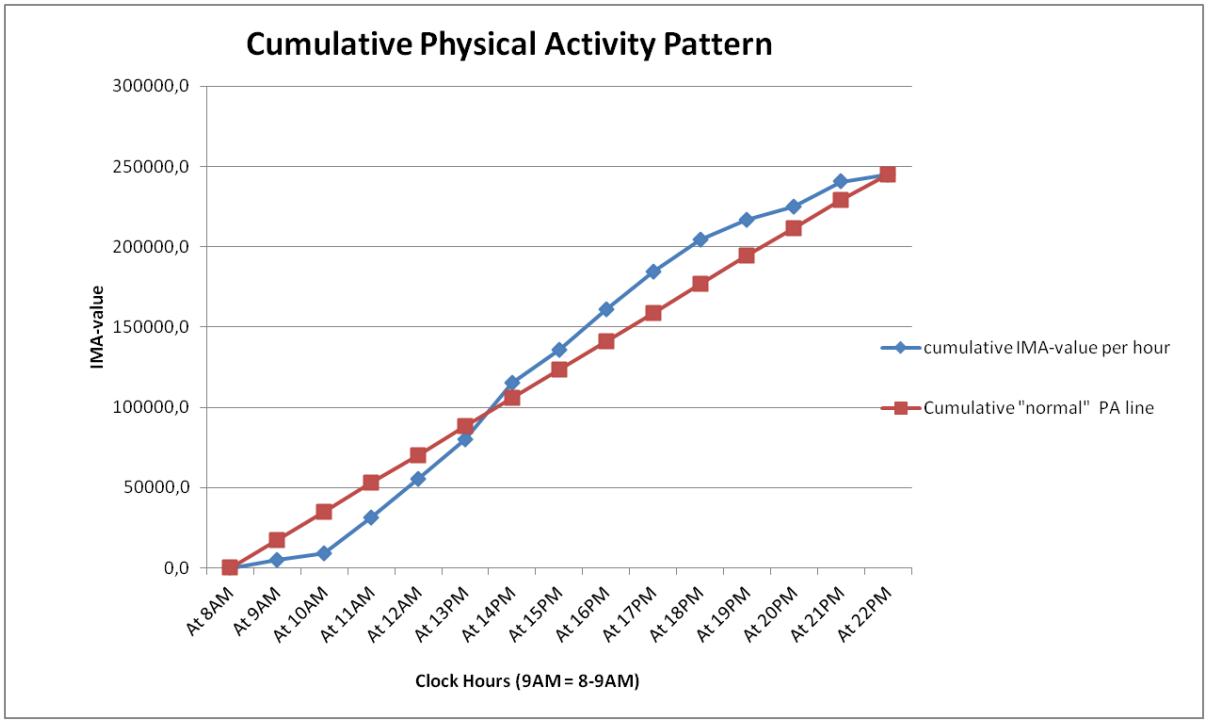

Figure 8 Cumulative representation of the physical activity over the day

With the calculated degree of deviation we want to answer the question what the physical activity distribution was during the day. Therefore, first to gain insight of the population we would like a calculation of a mean of each participant. In addition, we have calculated a mean over this to gain insight of the whole population whereby each participant has equally impact.

Interpretation of the degree of deviation from a proportional distribution

We now discuss what kind of consequences this type of calculation of a daily distribution has for this analysis. The calculated mean deviation of each part of the day represented a higher or lower PA level, in terms of a positive and negative percentage, with respect to the normal PA value (percentage of 0). The deviation percentage of the three parts of the day was together around the zero, because of the fact that the end value of the normal line (last measurement e.g. at 10.00PM) was corresponded with the absolute cumulative PA value (see Figure 8: the normal line (blue) and the absolute cumulative PA line (red) ending on the same value).

As final analysis for the PA distribution with regard to the normal PA line, the degree of deviation between the three parts of the day was compared. The question is whether a difference exists of the degree of deviation between the three parts of the day. In this case, it determined whether the physical activity during the parts of the day was (un)evenly distributed over the day. This suggested the deviation differences between the parts of the day which was based on the mean deviation of the study population. By observing the degree of deviation of the parts of the day of each participant separate, this enables to give more insight of the physical activity pattern.

The second approach: the relative physical activity increase during the day

Another way of approaching the physical activity distribution is to examine the degree of PA increase per hour during the day. The data selection criteria were the same as the first approach. The degree of PA increase during the day demonstrates the distribution by means of percentages. It provides more insight about the PA distribution during the day, because this approach shows the hourly PA distribution related to the daily PA level.

The degree of PA during the day was shown as cumulative percentage with a range between 0-100percent. Whereby, 0% represented no activity at the start of the day and the last measured hour ends always at 100%. All hours prior to the start of activity were reported as 0%, and the hours after the last measured hours were reported as 100% which represents the achieved day activity. On this way, these hours provide information about the daily schedule and PA distribution, for instance the start or ending of the day. Hours during the day with no data were reported as missing and were excluded for analysis.

The mean percentage of each hour was calculated over all participants, whereby the data of each participant consists of a mean of seven days. As a result, it presents the relative PA level on each hour of the day. In addition to this, the degree of increase per hour was also calculated, which was derived from the relative increase percentage. This represented the degree of hourly PA increase with respect to the previous hour and provides insight of the PA distribution over the day.

3.5.4 Interpretation of the literature study results of the PA patterns from chronic diseases

Before the literature study of the PA patterns of other chronic diseases, it is important to understand the physical activity outcome measure which is used in literature relative to the outcome measure of current study. This is also important for the interpretation and comparison of the literature with the current study. The physical activity level of the current study was reported in IMA-counts.

A study of Cabrita (2013) indicates an equation to convert the IMA-counts into a tangible and comprehensible interpreted measurement value; i.e. the number of steps (Equation 3).[45] This measurement value was multiple used in literature. With this in mind, other patient populations which use the number of steps as a measured outcome could be compared.

$$STEPS_{counts} = \frac{IMA_{counts} - 1680}{30.24}$$ **Equation 3.**

3.5.5 Data analysis physiotherapist treatment goals

First of all, the treatment goals defined by the physiotherapist and participant from all AAF participants were assessed. A classification was created based on the descriptions of the treatment goals. For instance, the classification of the treatment goals consisted of searching for meaningful words in the description. For example; a part of the treatment goal suggested a certain amount increase of physical activity in a period of nine weeks, this is related to a group with as aim to increase physical activity. Another treatment goal suggested maintaining of the physical activity level with a decrease fatigue level. Balancing of the PA level was in this case the main goal and was classified in a group with as goals to balancing the PA.

Second, the mean physical activity level of all participants was collected. All participants were collected in order to compare the PA levels of the AAF participants with respect to the whole study population. The PA level per participant was derived from the first sub question because the same participants were used in order to answer the question. In addition to the PA level, participant's degree of variability relative to individual mean PA level was calculated. This provided insight into the PA level distribution between the days. These two variables were used to evaluate and compare the defined treatment goals to the PA level.

3.6 Statistical analysis

The statistical analyses were performed using IBM SPSS (Statistical Packages for the Social Sciences, 19.0). For all analyses, statistical significance was set at an alpha level of $\alpha \leq .05$. The three sub questions from this research consisted of different statistical analyses. The normality for each variable was tested by the use of the Shapiro-Wilk test.

The first sub question was to identify the physical activity level and pattern of the CCRF study population. Different analyses will be performed to answer this question.

First, the correlation between the amount of system wear time and the amount of IMA value was analysed by means of a Spearman's rho or Pearson bivariate correlation (two-tailed), when the data were respectively non-normally or normally distributed. Subsequently, the coefficient of determination (R^2) was calculated for obtaining the degree of explanatory variance.

The absolute cumulative physical activity level was analysed by calculation the mean and standard deviation over each measurement day. The Shapiro-Wilk test was used to identify a normal distribution of the data. Outliers of the data were identified by the use of z-scores; the threshold-value of two standard deviations was applied[55].

Additional to the absolute cumulative physical activity level per day, the analysis of the physical activity levels of each participant (n=46) were analysed in the same way. Besides, the degree of physical activity variability between the days was analysed. The variability was calculated by means of the coefficient of variation. Subsequently, the correlation between this variability and the mean IMA value of the days were analysed by the use of the Pearson bivariate correlation (two-tailed) in normally distributed data, otherwise the Spearman's rho bivariate correlation (two-tailed) were used in non-normally distribution.

The physical activity distribution of the participants were analysed based on three parts of a day; morning, afternoon, and evening. These parts of the day were tested on normal-distribution by means of the Shapiro-Wilk test. The one-way ANOVA (two-tailed) was used to determine an overall difference of the mean deviation percentage among the three parts of the day. The Tukey post-hoc test was performed to confirm where the differences occurred between parts of the day.

The last sub question, about the comparison of the defined treatment goals and the physical activity level, were the relative variation of the physical activity level between the measured days for each participant calculated. This was calculated as a coefficient of variation by means of the equation: $Cv = \frac{\sigma}{\mu}$.

Chapter 4

Results

4.1 Participants characteristics

There were 46 participants which were included in the study and who all wore an accelerometer for a minimum of six hours a day. The absolute cumulative PA level determination is based on 305 valid measured days of these 46 participants. The determination of the PA distribution is based on an individual participant's data which fulfilled the required minimum seven days of wear time at the baseline. This resulted in data from 35 participants. The inclusion procedure is outlined in Figure 9.

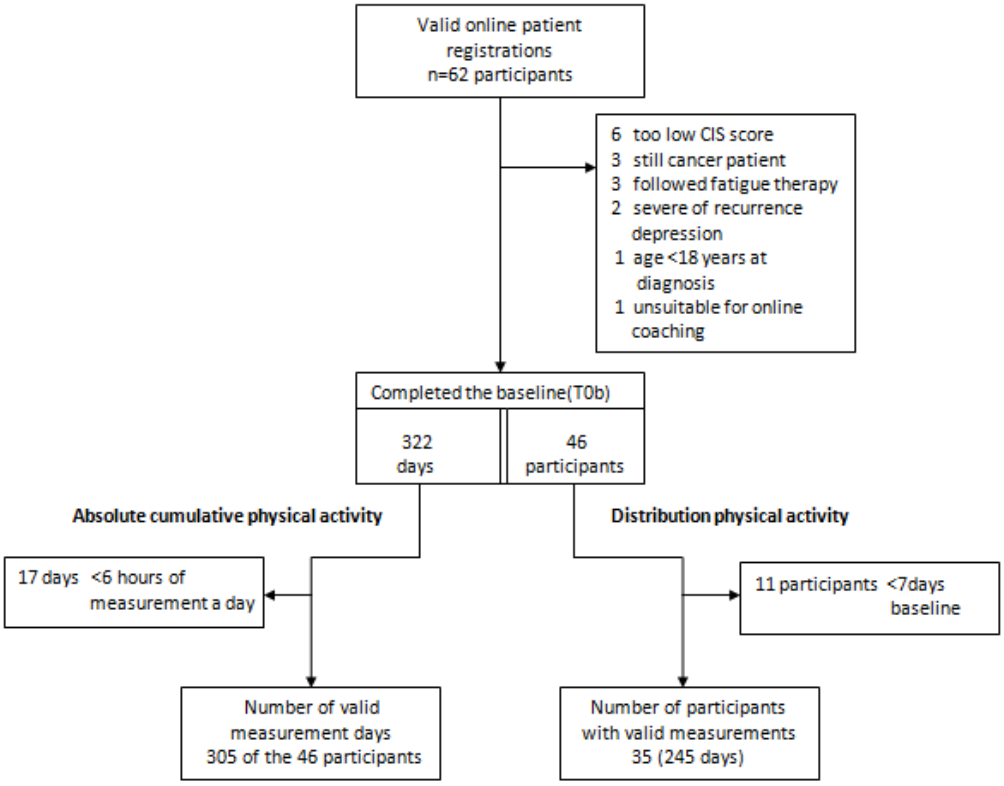

Figure 9 Flow-chart of the data inclusion procedure
Note: the inclusion has two outcomes: 1) 305 valid days for calculation of the absolute cumulative physical activity, 2) 36 participants which had seven valid measured days for determining the distribution of the physical activity.

Demographic and clinical characteristics of the participants are shown in Table 1. The mean age in the study is 55 (range 22-82). The extent of fatigue was measured by the CIS and has a mean score of 45.5 at registration (T0a), whereby, 35 is the required score for inclusion (range = 20-140)[46]. The CIS score at the start or during measurement (T0b) can be different from the first score that was taken (T0a) because the time between registration and the start of the measurement (T0b) could vary from one to 21 weeks.

Table 1 Characteristics of the participants

	CCRF participants (n=46)
Gender (n (%))	
Men	12 (26)
Women	34 (74)
Age (years)	54.8 (11)
Time between last cancer treatment and T0 (years)	5 (5.7)
CIS[1] score severity fatigue T0a	45.4 (6.1)
CIS score severity fatigue T0b	41.8 (8.8)
Living situation (n (%))	
Living alone	9 (20)
With partner	22 (48)
With child(ren)	3 (6)
With partner and child(ren)	10 (22)
Others, namely	
With parents and sister	1 (2)
LAT relationship	1 (2)
Work (n (%))	
Currently paid work	14 (30)
No currently paid work	12 (26)
Unknown	20 (44)
Ability to work compared to the best period of life, which indicates a score of 10 (self-rated) 1=not able, 10=able	2.5 (2.0)

Note: Presented as *mean* (SD) unless otherwise indicated. [1] CIS: Checklist Individual Strength (range 20-140)

4.2 Description of the data

The degree of dependence between the physical activity level and the amount of system wear time was calculated by means of a correlation coefficient. The absolute cumulative physical activity level, as it was measured in this study, correlated to the wear time of the accelerometer; R(305)=.198, p<.01 (Figure 10). With this method, it means that the wear time has a four per cent predictive value for the amount of PA (R^2=.04).

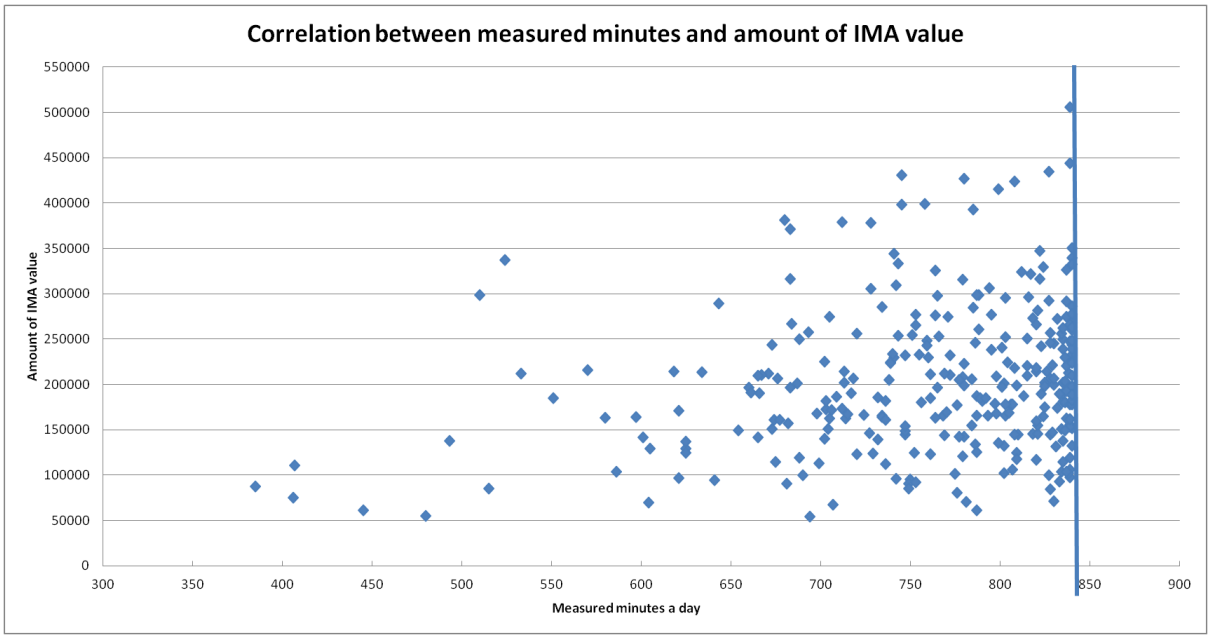

Figure 10 Scatter plot of the correlation of the measured IMA value and the number of measured minutes per day. *Note:* vertical line is the maximum measured wear time per day (840 minutes).

4.3 Absolute cumulative physical activity

The results of sub question 1 which presents the physical activity level per day are described. A total of 322 measured days were assessed for eligibility, of which 305 days fulfilled the six hours wear time, extracted from the total 46 participants. The average of the absolute cumulative physical activity level per day was 203,592 (79,662) IMA-counts, based on a minimum of six hours and the maximum of 14 hours wear time of the accelerometer per day. The data are non-normal distributed, it has a positively skewed distribution (W=.966, P=.001).

This skewed distribution is explicable by the fact that the data are finite towards zero IMA and the ascending data are infinite. There are 14 days which have a minimum of two standard deviations located of the mean, whereby, two participants accounted for four days. The values of these 14 outliers are between 370,869 and 506,917 IMA-counts (Figure 11). Related to the skewed distribution and the finite value toward zero, these 14 outliers represent more as 14 relative high values.

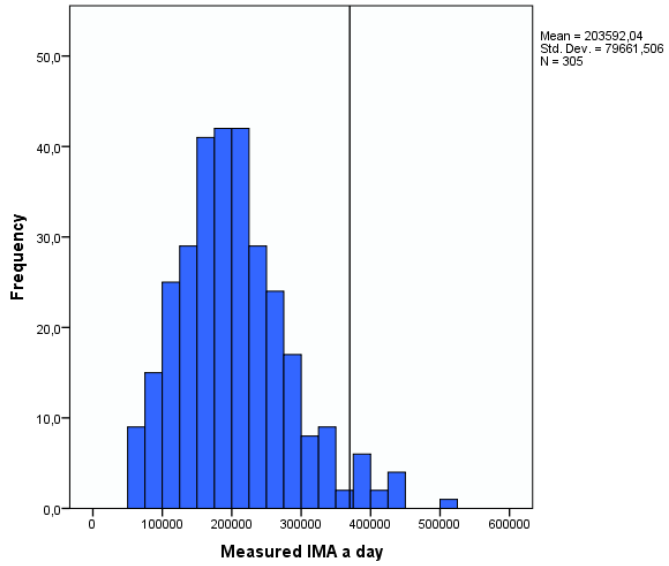

Figure 11 Distribution of the IMA values based on 305 measured days, extracted from the 46 participants.
Note: Vertical line has a value of 397,830 IMA, right side of the vertical line are the outliers.

As additional finding, the mean PA level of a participant, which was calculated over each participant's measured days, was 203,387 (60,681) IMA-counts per day. This data is normal distributed (W=.974, p=.393). Although, as a result of this distribution it can be suggested that the distribution consists of three divisions; IMA value till 200,000, between 200,000 and 300,000 IMA-values and IMA-values above the 300,000. Figure 12 showed these three divisions.

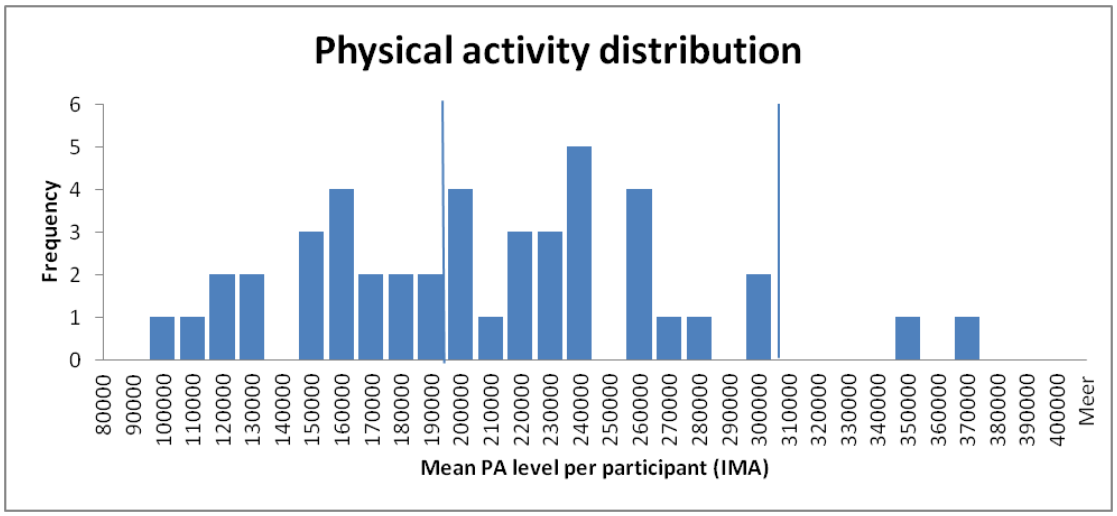

Figure 12 The distribution based on 46 participants

To gain more insight into the physical activity level of the study population, the relation between the degree of variability of PA level between participant's measured days and the amount of physical activity was examined. There is a weak negative non-significant relation between these two variables (R(45) =-.283. p=0.059). The hypothesis: the PA level is explicable by the degree of variability, can be rejected. In addition, Figure 13 shows the large differences of the degree of variability and the PA level between the participants.

Overall, it can be suggested that the identification of physical activity level can be approached in two different ways; the degree of PA variability between the days and the amount of PA level per day.

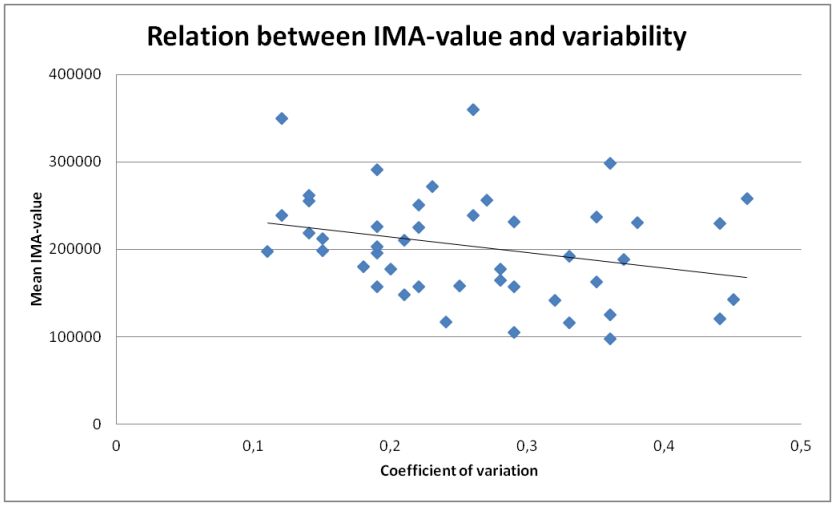

Figure 13 Scatterplot of the relation between the mean IMA-value over 7 days and the variability between the 7 days of the 46 participants.

4.4 Distribution of the physical activity per day

The results of the PA distribution are subdivided in two different approaches: the degree of PA deviation relative to a linear "normal" PA line per part of the day and the relative physical activity increase during the day (a percentage of the total daily PA level).

4.4.1 Degree of PA deviation

The degree of PA deviation is based on 35 participants. For each part of the day is the distribution of the degree of deviation presented. As presented in Figure 14, the mean deviation for the parts of the day; morning, afternoon and evening, are 11.44%, 17.55% and -21.41% respectively relative to the normal PA distribution. Appendix II shows the deviation of each participant. In addition to this, all three parts of the day are normally distributed; morning (W=.973, p=.538) afternoon (W=.982, p=.814) and evening (W=.976, p=.637).

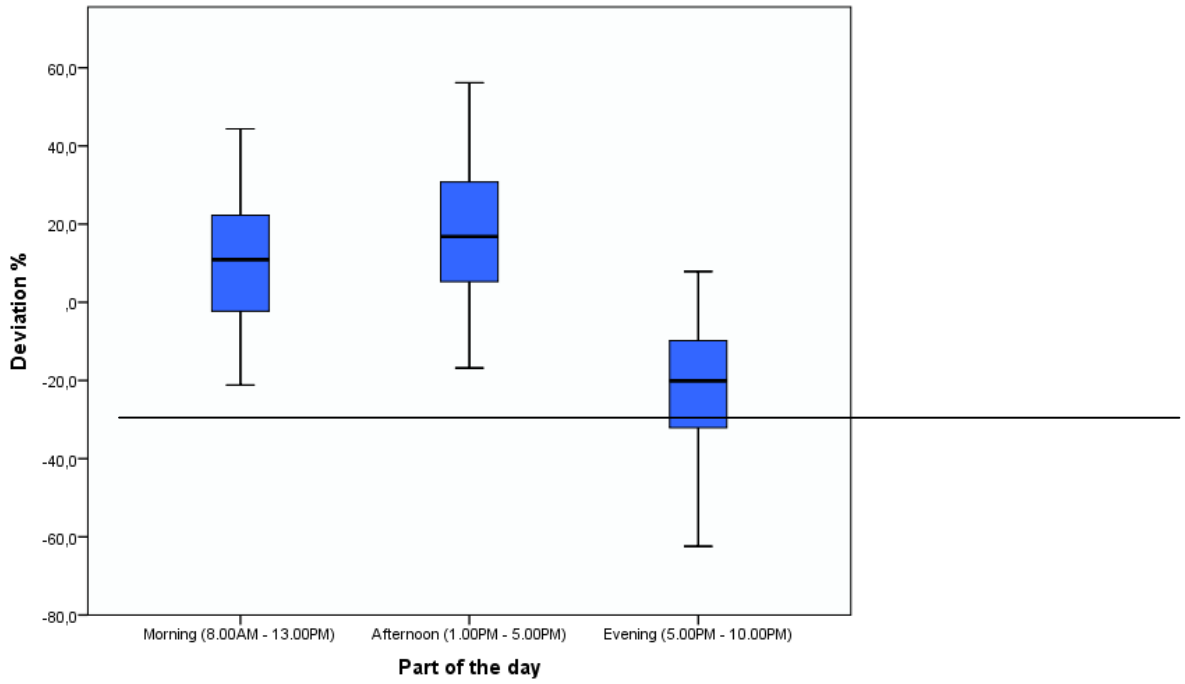

Figure 14 The PA deviation during the day with respect to the normal PA distribution of the CCRF study population. *Note:* mean deviation morning: 11.44%, afternoon: 17.55%, evening: -21.41%.

A comparison between the parts of the day provides more insight about the PA distribution over the day. First, there is a statistically significant differences between the three day parts (F (2,102) = 56.349, p=.001). In addition to this, a Tukey post-hoc test revealed that the mean deviation relative to the normal PA line was statistically significantly higher in the morning (11.4 ± 16.1%, p = .001) and afternoon (17.5 ± 18.3%, p = .001) compared to evening (-21.4 ± 14.9%). There were no statistically significant differences between the morning and afternoon (p = .274), which indicates that the mean amount of physical activity of this two parts of the day not differ much to each other. (See the first two box plots compared with the last box plot in Figure 14).

As the standard deviation of the mean deviation over the day is relatively large, an overview of the individual deviation provides more insight. Figure 15 shows the distribution of the parts of the day from each individual participant. The evening has in general a lower physical activity level relative to the normal PA line compared to the morning and afternoon. Remarkable, the deviation between the morning and afternoon are alternated for each participant. For instance, a participant with a high physical activity level in the morning has a lower physical activity in the afternoon, relative to the normal value, or vice versa. A high or low deviation value on both two parts of the day does not occur because the parts of the days form together a linear line.

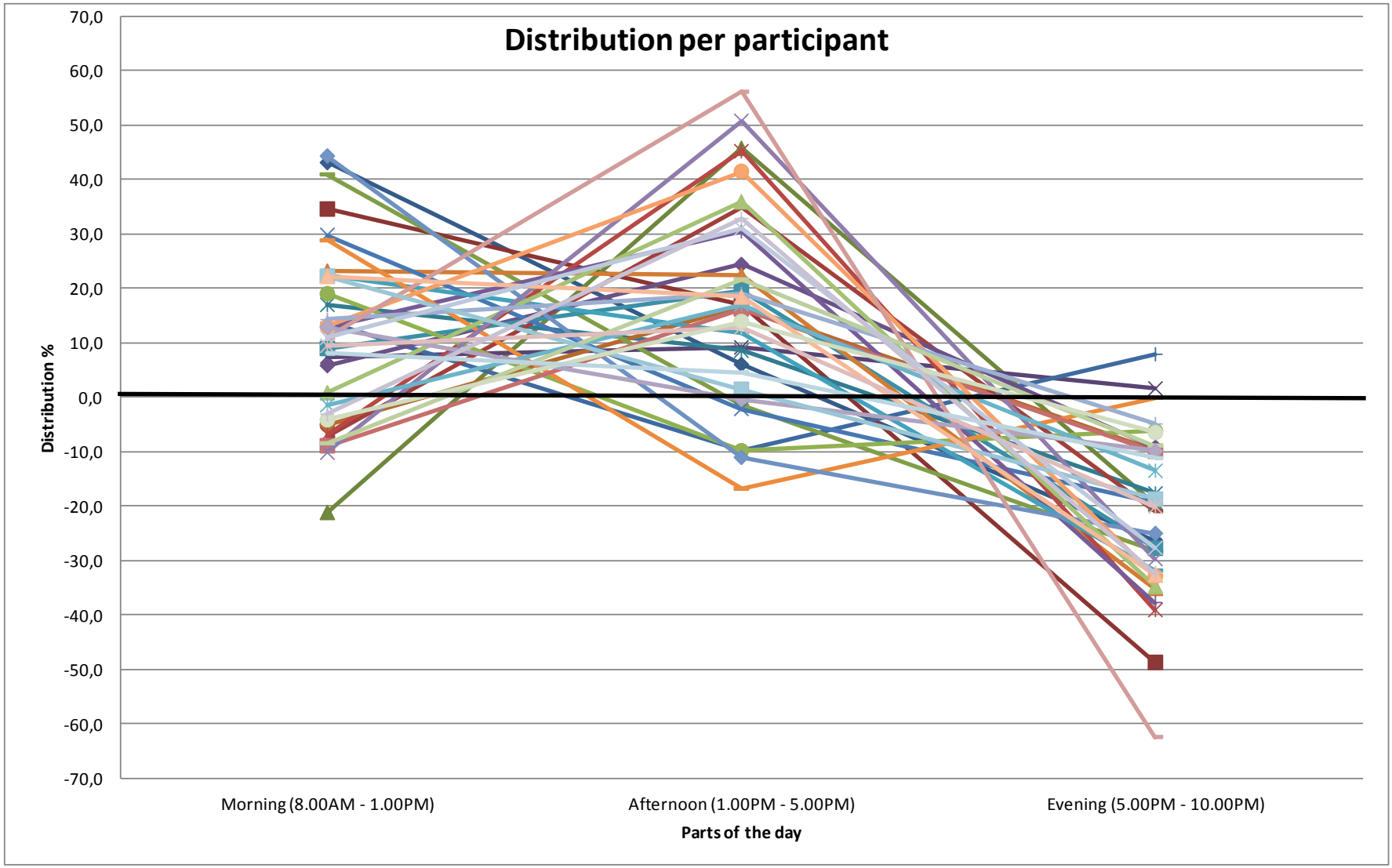

Figure 15 The degree of distribution over the day of each participant (n=35)

4.4.2 Relative physical activity increase during the day

To gain more insight into the PA distribution during the day, the mean PA level per hour relative to the total amount of PA of the day of 35 participants is analysed. First, the relative PA of each hour was cumulative shown in Table 2 and shows that the PA expenditure at 3.00PM was more than 50% of the total daily PA expenditure. This means that halfway through the measurement day (3.00PM) 50% of the total daily PA expenditure was used. In addition, at 1.00PM (end of the morning and at 5.00PM (end afternoon) is respectively 35% and 70% of the daily PA expenditure used. This results that the hours in the morning and afternoon had more PA expenditure compared to the evening which consists of the remaining 30%. This result is also shown in Figure 16, the flattering of the graph during the last few hours of the measurement day.

Second, the degree of increase per hour, which was derived from the cumulative PA level in percentages, is analysed. As shown in Figure 17 the hourly PA increase is ascended until 3.00PM and subsequently descended towards the end of the day.

Table 2 The mean percentage cumulative PA increase and the variable degree in PA increase during the day
Note: based on the mean of 35 participants.

Time	Mean cum. PA %	SD	PA increase per hour %	SD
8-9AM	4.46	3.52	4.46	3.52
9-10AM	10.70	5.44	6.25	3.01
10-11AM	18.08	6.28	7.37	3.29
11-12AM	26.20	6.90	8.12	2.44
12AM-1PM	34.48	7.02	8.29	2.05
1-2PM	43.60	7.38	9.12	2.77
2-3PM	53.81	7.64	10.21	3.39
3-4PM	62.78	7.15	8.97	2.98
4-5PM	71.35	6.60	8.57	2.75
5-6PM	79.15	5.71	7.80	2.03
6-7PM	86.42	4.64	7.27	1.74
7-8PM	91.12	2.82	5.70	2.35
8-9PM	95.54	1.56	4.42	1.77
9-10PM	100	0	3.46	1.56

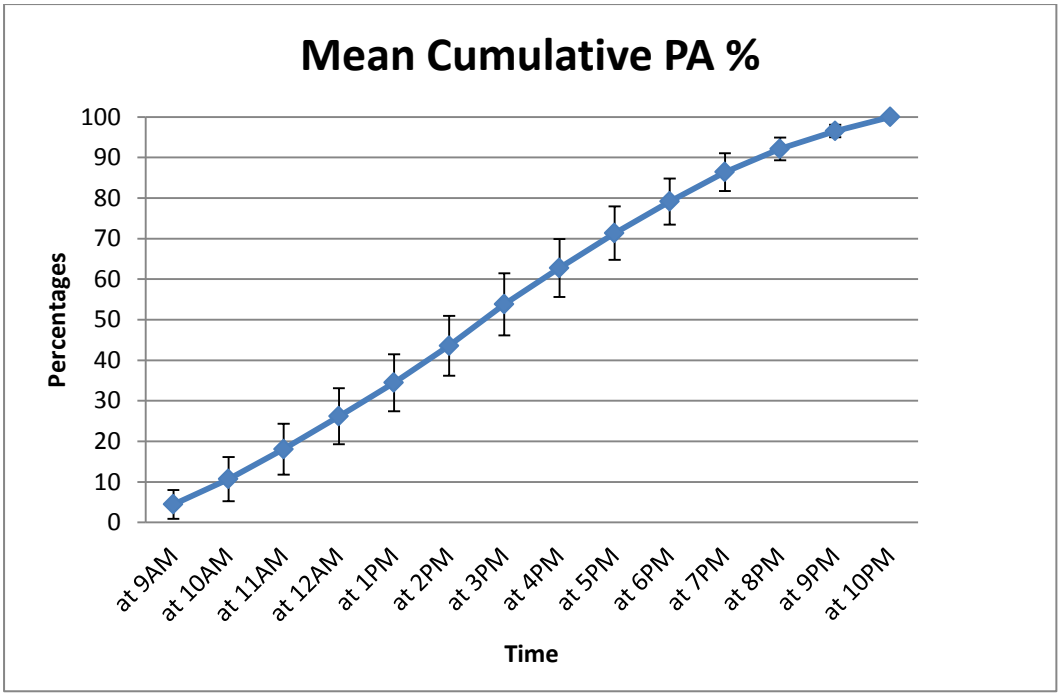

Figure 16 The PA distribution during the day, presented as cumulative percentages. *Note:* blue line is the mean PA percentage, the red and green line shows the standard deviation.

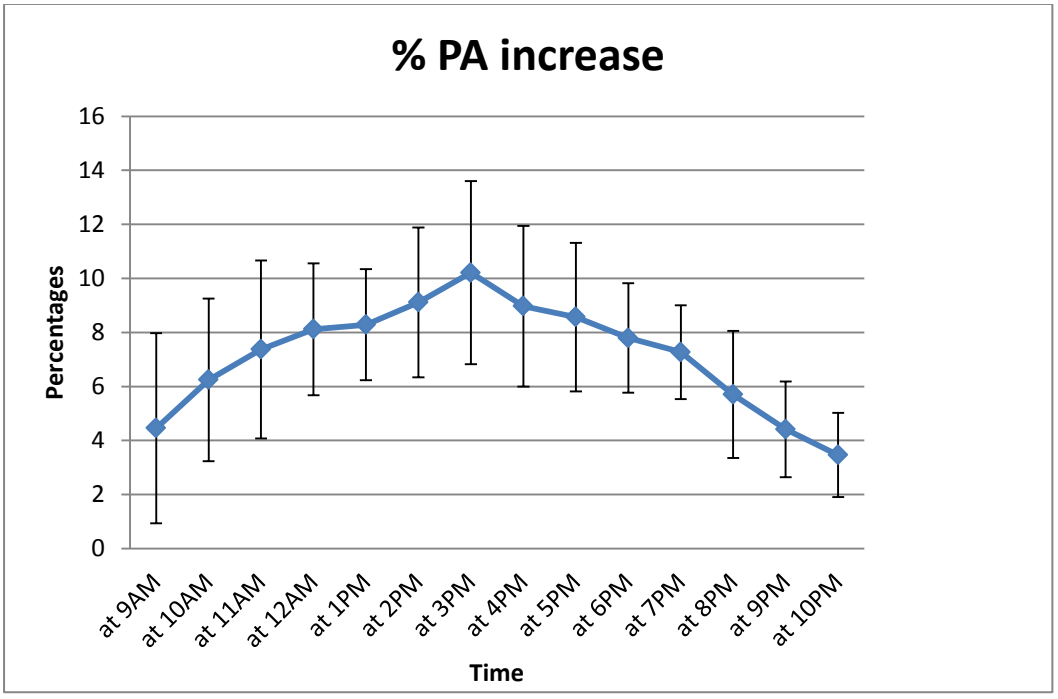

Figure 17 An overview of the amount of percentage increase per hour.

4.5 Results of the literature study from physical activity of other patient groups

The literature was studied answer of sub question 2; whether the PA level and distribution over the day of the study population are different compared to other groups. First, the results of the PA level norm for healthy behaviour are described; in addition, the literature research results of the PA behaviour of other chronic disease populations are reported.

4.5.1 General norm for physical activity level

The outcome measure of PA such as the amount of steps is a valuable method for indicating which amount of PA is sufficient for healthy behaviour. The Dutch norm for healthy physical activity (NNGB) was prepared in 1998 by the Dutch universities of Amsterdam (VU), Maastricht (UM), Groningen (RUG), Utrecht (UU), the National Institute for Public Health and Environment (RIVM), the Dutch Organization for Applied Scientific Research (TNO), and the Dutch Olympic Committee/Dutch Sports Federation (NOC*NSF).[56]

The NNGB for adults applies some norm of a PA for at least half an hour per day, with a minimum of five days a week with a moderate-to-vigorous physical activity (MVPA) level (≥ of 4 MET, Metabolic Equivalents of Task). Accordingly, the United States Department of Health and Human Services (HHS) defined the Activity Advisory Committee Report in 2008.[57] This report indicated a PA norm of 150 minutes of MVPA a week. Both are in compliance with the World Health Organisation, which prescribes at least half an hour of MVPA for minimum of five days a week.[12] The norm consists of physical activity of at least 30 minutes over a minimum of five days per week, and with a minimum MET value of three, but in the Netherlands a MET value of four or higher, is generally adopted.

4.5.2 The determination of a sufficient physical activity level

The 30 minutes of MVPA per day consists of 30 minutes of PA with minimum bouts of 10 minutes and on a cadence of 100steps/minute.[58] A study detected these cadences through a simultaneous comparison of the number of steps that were measured physical activity (reported in MET's).[59] This cadence represented a reasonable value for moderate-to-vigorous walking. By multiplying this cadence by the recommend 30 minutes, it resulted in a PA norm of 3,000 steps in 30 minutes. These 3,000 steps must be taken over and above a habitual activity level. Tudor-Locke and Bassett (2004; 2008) introduced a graduated step index for healthy adults based on current available evidence. [60] [61] Table 4 shows this index.

Table 3 Graduated step index for healthy adults (Tudor-Locke, 2004)

Steps/day	Descriptive category	
<2,500	Basal activity	Sedentary
2,500 – 4,999	Limited activity	
5,000 – 7,499	Low active	
7,500 – 9,999	(Somewhat) active	
10,000 – 12,500	Active	
12,500 >	Highly active	

Table 4 Revised step health index for healthy adults (Tudor-Locke, 2008)

Steps/day	Descriptive category
<1,499	No moving
1,500 – 3,499	Sedentary
3,500 – 4,999	Somewhat sedentary
5,000 – 7,999	Moderate
8,000 – 9,999	Somewhat active
10,000 – 11,999	Active
12,000 >	Special

As shown in Table 3 and 5, a PA lifestyle is defined as sedentary when it does not reach the 5,000 steps a day. This number of steps was most likely associated with various chronic conditions and an unfavourable state of health.[60] A PA level of 5,000 steps a day was perceived, by Tudor-Locke, as a baseline level which means that the amount of PA is exclusive to the 30 minutes recommended of MVPA. By adding the previous 3,000 steps of MVPA to the baseline of 5,000 steps, the healthy PA level leads to 8,000 steps per day. Although the 8,000 steps were calculated per day, the NNGB norm indicated 30 minutes of MVPA for a minimum of five of the seven days of the week, which corresponds with 7,000 steps a day.

The calculations in Equation 4 show the two calculations of steps a day; the number of steps for 30 minutes of MVPA every day (Equation 4a) and the number of steps which are corresponds with the NNGB norm of a minimum of five times a week 30 minutes of MVPA. This results in 8,000 and 7,000 steps a day.

$$7\ days * 5{,}000\ steps\ baseline = 35{,}000\ baseline\ steps\ a\ week$$
$$100\ steps\ a\ minute * 30\ minutes\ a\ day = 3{,}000\ steps\ MVPA\ a\ day$$

[a] 7 days 30 minutes of MVPA:

$$35{,}000\ steps\ a\ week + (3{,}000 * 7\ days) = 56{,}000\ steps\ a\ week$$
$$56{,}000\ steps\ a\ week / 7\ days = 8{,}000\ steps\ a\ day$$

[b] According to the norm; 5 days 30 minutes of MVPA:

$$35{,}000\ steps\ a\ week + (3{,}000 * 5\ days) = 50{,}000\ steps\ a\ week$$
$$50{,}000\ steps\ a\ week / 5\ days = 7{,}142\ steps\ a\ day$$

Equation 4 An overview of the two possible 'steps per day' calculations.
Notes [a] Based on the consideration of Tudor-Locke et al. [61]
[b] Based on the report of the U.S. Department of Health and Human Services[57]

In addition to the calculations of 7,000-8,000 steps for daily healthy behaviour, a Japan's doctor suggests another guideline with an amount of 10,000steps/day for a healthy behaviour. This guideline originates from the 1960s. The 10,000steps/day suggestion of this guideline was established by Japanese walking clubs and was studied by Japan's Dr. Hatano(2008).[62] The value of 10,000steps/day seems to be a good indication of daily activity for healthy adults. People who

reached this amount of PA were proven to be healthier, according to Hatano. This refers to lower blood pressure, reduced body fat, and body mass in comparison with healthy but less active people.[62 63]

The above norms and guidelines considered we choose the amount of daily steps which is most corresponding with the NNGB norm. The suggestion of Dr. Hatano, the goal of 10,000steps/day, is laudable. On the other hand, this guideline corresponds with 40-47 minutes of MVPA per day. In contrast, the calculation of the 7,000 and 8,000 steps/day is corresponding with the NNGB norm. In conclusion, we suggest in this study a minimum amount of PA for healthy adults between the 7,000 and 8,000 steps a day.

4.5.3 Physical activity levels of different chronic diseases

The physical activity patterns and the corresponding treatment goals of three chronic diseases are described. The outcome of the literature study was as following reported: first the description of the disease, subsequently the PA level, distribution and the (suggested) treatment goals.

Chronic Obstructive Pulmonary Disease

COPD is a progressive respiratory disease, characterised by persistent airflow limitation (dyspnoea) and a decrease in the capabilities of PA.[64 65] COPD is divided into four GOLD stages, ascending to degrees of severity. The level of PA depends on these GOLD stages.

Different studies have identified various PA levels. The level of PA was shown by using the outcome measurement: number of steps per day. In general, COPD patients with GOLD stage II have an daily PA level between 6,400 and 7,000 steps[66 67] The physical activity level of COPD patients with GOLD stages II and III have, studied by Schonhofer (1997) and Zwerink (2013), respectively a number of 3,781 and 4,857 steps per day.[68 69] GOLD stages III and IV have the lowest physical activity level with a mean level of ±3,500 steps per day, whereby GOLD stage IV has a level 2,750 steps per day.[70 71]

Overall, not all COPD patients had a daily PA level which complied with the NNGB norm, mainly patients with GOLD stage III and IV respectively. In addition, these two COPD groups showed sedentary behaviour in accordance with the graduated step-index of Tudor-Locke and Bassett (Table 3). Elderly and chronically ill people have typically a mean daily number of steps between 3,500 and 5,500, this is reported by findings from Tudor-Locke.[60] The PA level of COPD patients are in accordance with this finding.

Besides the evaluation of the total daily activity, the PA distribution over the day is also important. A study by Tabak (2012) identified a disrupted PA pattern over the day.[53] There is a remarkably visible relapse in the degree of physical activity in the early afternoon. This could be a consequence of too many activities in the morning. However, the PA level did recover after the relapse. The cause of the disrupted activity pattern is significant not due to the extent of fatigue or dyspnoea. Other causes should be investigated in further studies. In addition to this, several causes and opportunities are

possible for changing the physical activity patterns of COPD patients. The opportunities can be focused on for instance: motivating patients and behaviour change.[53]

As above mentioned, general treatment goals are established for chronic diseases, based on remarkable PA levels and distribution over the day which have a negative effect on the absolute PA level. By focusing on the recovery of the disrupted activity pattern, the treatment goals for the COPD population could be to improve the activity distribution and increase the total activity level.[53 72] The treatment goals of the two other described chronic diseases (CFS and CLBP) seem to be the same. The ultimate treatment goals to improve PA level are in compliance with those goals of COPD patients. Both diseases aim to improve the imbalanced daily PA pattern.

For an overview of all the outcomes of the parameters of the three chronic diseases with the corresponding treatment goals and the conclusions are presented in Table 5.

Chronic fatigue syndrome

The second chronic disease is chronic fatigue syndrome; CFS is a syndrome with persistent or recurrent fatigue for during at least six months, which is not related to physical limitations. Also, the fatigue is a new symptom, it is not proportional to recent activity, which is hardly improves with rest, and severely limits daily activities. Other symptoms can include; impairment of concentration, sore throat, myalgia, headaches and musculoskeletal pain.[73]

As a consequence of the limited daily physical activity level of CFS patients, it is expected that a reduction in the absolute PA level in comparison with healthy controls will be found. According to Newton (2011), the mean PA level is 7,100 steps a day for CFS patients. This amount of PA is at the lower limit of the NNGB.[74]

In regards to the PA distribution over the day, Evering (2011) suggests a less active period of time during the afternoon and evening.[75] The low activity level and the disrupted activity pattern could be caused by the alternating of physical activity during the afternoon.[75].

A study by Van der Werf (2000) suggested different types of CFS patients, related to the PA level: pervasively passive, moderately active, and pervasively active.[76] The PA pattern during the day of passive patients fluctuates more in comparison with the active patients.[77] A result of this, the different types of CRF require different treatment approaches. Van der Werf suggests a PA level increasing for passive patients and introduce a more PA regulated approach for active patients.[76] The overall treatment goal could be a total increase of the PA level because the absolute PA level was reached below the limit for healthy behaviour (NNGB). In addition to this, another goal could be to regulate the PA level during the day, especially in the afternoon.

Chronic Low Back Pain

The last comparison is regarding to the chronic low back pain (CLBP) patients. Chronic low back pain is defined by an existing pain that lasts longer than three months.

Regards to the PA level and pattern of the first two described chronic diseases, the expectation for CLBP patients would also be a lower absolute PA level per day relative to the NNGB. Some researchers suggest an identical PA level just like healthy people.[78-80] This is in contrast with the chronic diseases CFS and COP. On the other hand, there is limited evidence available which does indicates a lower PA level relative to healthy people.[81 82] As a result of this, there is no consistent evidence to suggest that CLBP patients are less active relative to healthy people and there is more evidence available that suggests that patients are just as physically active as healthy people.

In contrast to the absolute PA level, the distribution of the PA of this population is different compared to healthy people. A higher level of PA in the morning and a lower level in the evening is the daily distribution of CLBP patients. There is a suggestion that this patient population are, in proportional, more active in the morning and as a result of this, a lack of energy at the end of the day.[80 82] Figure 19 shows a global PA distribution level over the day of the three described chronic diseases.

Van Weering (2009) hypothesised a treatment goal about the regulating the PA level during the day[79]. The regulation is aimed at the concept of less activities being performed in the morning in order to remain at a higher capacity for the activities in the evening.

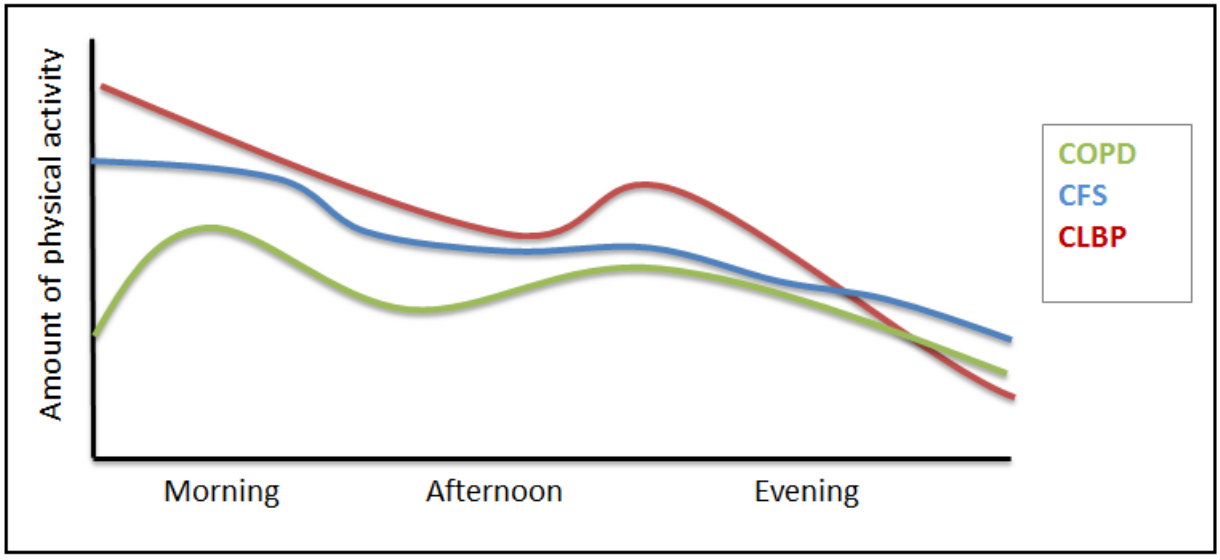

Figure 19 A global representation of the physical activity distribution over the day of the three chronic patient groups. *Note*: COPD: the curve is based on; 1) a relapse of activity in the early afternoon, 2) recovery of the relapse, 3) an increase in activity in the late afternoon. These results are based on Tabak (2012). CFS: the curve is based on; 1) no significant difference of physical activity during the morning compared with healthy controls, 2) significant less physical active which is based on the period of time between 2.00PM-3.00PM and 6.00PM-7.00PM, 3) a lower physical activity level during the evening. These results are based on Evering (2011). CLBP: the curve is based on; 1) a high activity level in the morning, 2) a decreased PA level in the afternoon and evening. This result is based on Van Weering (2009).

Table 5 An overview of the physical activity level of three chronic diseases.

Population	Parameters		Treatment goal	Conclusion
	Physical activity level	**Physical activity distribution**		
COPD	Level of activity of COPD patients is lower than healthy age- and sex-matched healthy people[68]. Total steps/day(SD) per GOLD class: GOLD I (25%) & II (75%) Fastenau[66] 6,459 (2,994) GOLD I (22%), II (61%), & III (17%) Hospes [67] 7,087 (4,058) GOLD II & III Schonhofer[68] 3,781 (2,320) Range ±2,000 – 6,250 GOLD II & III Zwerink[69] 4,857 (3,132) GOLD I(10%), II(39%), III(22%) & IV(29%) Moy[71] 3,596(1,532) GOLD III & IV Tudorache[70] 3,414(1,105) GOLD III ± 4,250 GOLD IV ± 2750	Tabak (2012) found a relapse of activity in activity in the early afternoon after a morning of high activity[53]. Pitta(2005) showed a less time of walking and standing and more time of lying and sitting in daily life, compared with sedentary elderly people[72].	Tabak(2012) indicates an improved activity behaviour and focuses on the distribution of physical activities over the day[53]. Pitta(2005) suggests a more active lifestyle in daily life because inactivity may influence the clinical evolution[72].	COPD patients are markedly inactive over the day compared to that of healthy people. The distribution of the physical activity is not optimal because of the higher activity level in the morning and a dip in the early afternoon. Treatment goals related to physical activity could be: - Improve the activity distribution - Increase the absolute activity level

	Parameters			
Population	**Absolute physical activity level**	**Physical activity distribution**	**Treatment goal**	**Conclusion**
CFS	CFS patients are less physically active [75]. Total steps/day (SD) CFS: 7,089 (3,096) Healthy controls (age-, sex-, BMI- matched): 10,270 (3,999) [74] Mean daily activity level (counts per minute) CFS: 957 (266) Healthy controls (age- and gender- matched): 1,129 (300) [75] and asymptomatic controls: 1,162 (282)[53]	Evering (2011) establishes that CFS patients are less active in the afternoon (between 2.00-3.00 pm) and in the evening (between 6.00-7.00 pm)[75]. Also, CFS patients show more variability of physical activities between different days. This is in relation to 'good' and 'bad' days of the patients. On a 'good' day, patients have a higher physical activity level in the afternoon and a lower level on a 'bad' day. Evering (2011) and Newton (2011) indicates a more reduced activity at a vigorous level [74 75]	Van der Werf et al. (2000) identified different types of CFS patients' related to physical activity. These types are 'pervasively passive,' 'moderately active' and 'pervasively active.' Van der Werf suggests different approaches for these groups. An increasing physical activity level for passive patients and a more regulated physical activity approach for active patients [76].	An imbalanced daily physical activity; a less absolute physical activity and the physical activity pattern are affected by the alternating afternoon patterns. Treatment goals related to physical activity could be: - A total increase in physical activity - More regulation of the physical activity throughout the day, especially in the afternoon.
CLBP	Different researches indicate no less physical activity in comparison with healthy controls [78 79 82].	Higher activity in the morning, lower activity level in the evening compared with controls [79 80 82].	Van Weering (2009) hypothesises to regulate the physical activity balance. The aim is to do less physical activity in the morning in order to have more capacity left in the evening[79].	CLBP patients have the same physical activity level in comparison with healthy controls. Treatment goals related to physical activity could be: - Less active in the morning and subsequently more activity in the evening.

4.6 Treatment goals and the physical activity level

In this section is the question whether the treatment goals defined by the physiotherapist corresponded with the activity goals based on measured physical activity level discussed.

The treatment goals from ten of the total 19 people, which have participated in the AAF intervention, are available. Nine were missing as one physiotherapist did not administrate the treatment goals yet. The treatment goals of the ten participants are shown in Appendix V. In addition to this, the treatment goals are classified in three different groups. The classification of the treatment goals into groups is obtained by searching meaningful terms or sentences. The words 'increase physical activity', 'more activity', 'increase in sport activities' and other related terms to increasing of physical activity level, resulting in the general group 'increase PA'.

Terms such as; 'decreased fatigue,' keep energy,' as well as 'improving PA pattern during the day/week' resulted in an overall group 'balancing of PA'. The physiotherapists were not consistent in defining treatment goal related to balancing of PA. Balancing of PA could be a treatment goal for a skewed PA distribution over the day or for a high variability of PA level between the days. In this research, a high variability of PA level over the week and a skewed PA level during the day were both classified in the group 'balancing of PA'.

When the description of the treatment goal includes a combination of the above terms, it could be conclude that the treatment goal is ambiguous. These ambiguous treatment goals are categorized as 'gaining insight of the PA level, balancing of PA and increase PA'.

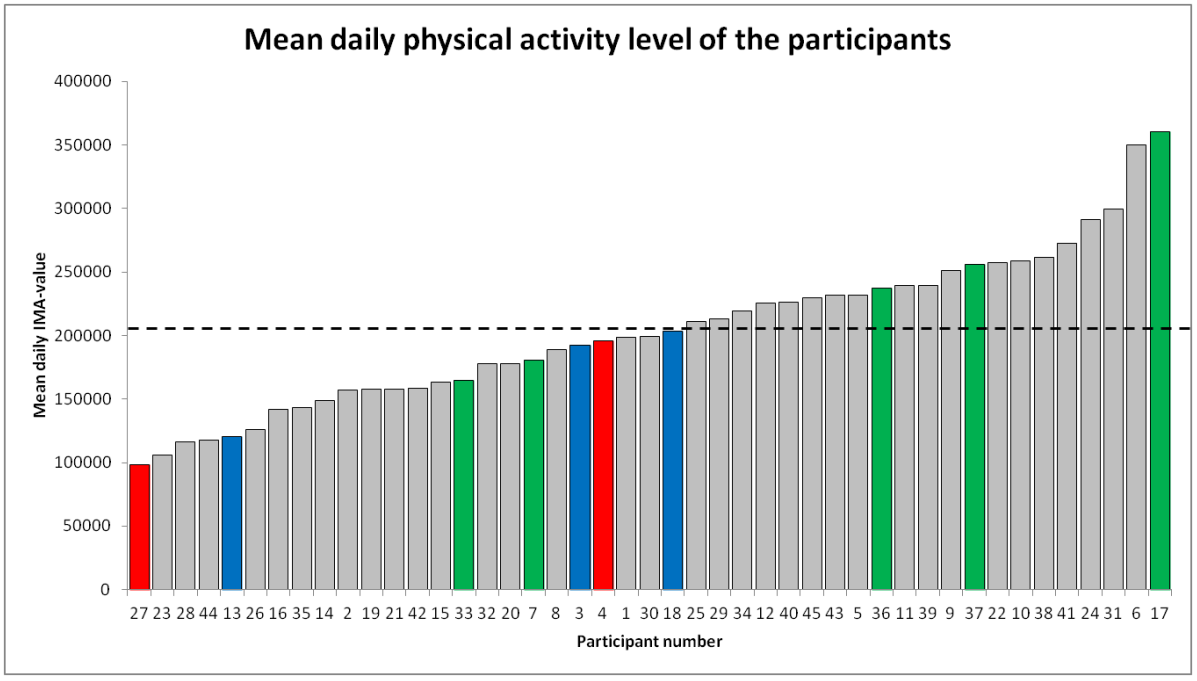

Figure 20 The mean physical activity level of the measured days (IMA). *Note:* blue bars are classified in group 'increase PA', green bars are classified in group 'balancing of PA', the red bars are classified in group 'gaining insight of the PA level, balancing of PA and increase PA' and the grey bars represents the remain participants of the study population. The horizontal line represents the defined healthy PA level of 7,000steps/day (213.360 IMA).

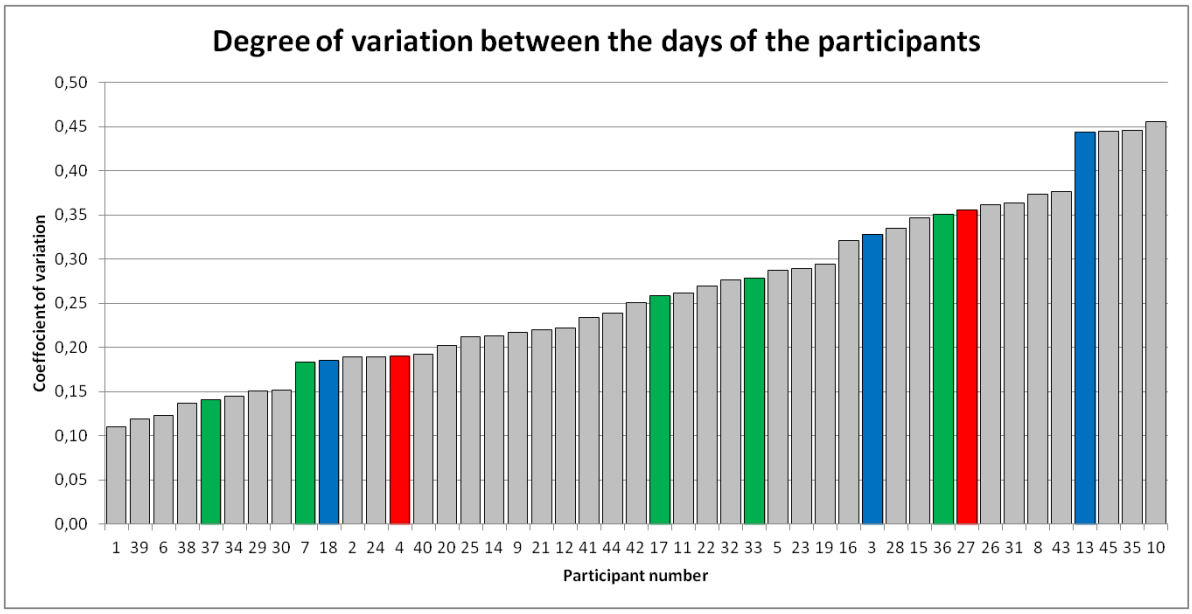

Figure 22 The variability of the physical activity level between the seven measured days.
Note: blue bars are classified in group 'increase PA', green bars are classified in group 'balancing of PA' and the red bars are classified in group 'gaining insight of the PA level, balancing of PA and increase PA'.

The treatment goals of the ten participants are classified as follows: three participants are classified in the treatment goal group 'increase PA', five of the ten participants are classified in a group with the general treatment goal 'balancing of PA', the remaining two participants are classified in the group 'gaining insight of the PA level, balancing of PA and increase PA'. The physical activity level and the degree of variability of the ten participants are compared with each other and relative to the whole study population. Thereby mentioned, there is no correlation between the degree of variability of PA level over the week and the daily PA level (R (46) =-.290, p=.053).

The three participants which are classified in the group 'increase PA', based on the description of the treatment goal, are shown in Figure 21 and Figure 22 as blue bars. One participant has a low physical activity level relative to the whole population and the variability of PA level between the days was relative high (participant 13). The other two participants have a mean PA level which was corresponded with the, in previous sub question defined, healthy PA level of 7,000 steps/day (213.360 IMA). In contrast, the degree of variability is different to each other (participant 3 and 18). In fact, all participants in the group 'increase PA' have a lower PA level with respect to the defined healthy PA norm of 7,000steps/day but vary, relative to the whole study population, in the degree of variability between the days.

The five participants which were classified in the group 'balancing of PA' (green bars), have high and moderate PA level relative to the study population. Based on the relative high PA level it is correct that these participants do not received a treatment goal to increase the PA. In addition, three participants fulfilled the defined healthy PA level of 213,360 IMA (7,000steps/day) (participants 36, 37, 17). In addition to this, the degree of variability between the days is varied. Three of the five have a high variability of PA level between the days, relative to the study population. Given these observations, participants which have been assigned the goal to balancing the physical activity level are varied in PA level and in the degree of variability. There is not consistency between the amount of PA level and the variability over the week; there consist cases with high PA level with low as well

as high variability between the days. This could be related to the previous described fact of no consistency of define treatment goals related to balancing of PA.

The last group, which the treatment goal consists of gaining insight of PA level and/or disease, balancing the PA and also to increase the PA, has two participants (participant 4 and27). Both have a lower PA level with respect to the defined healthy PA level but one participant has a sedentary level of PA while the second participant has a PA level to around the healthy PA level. In contrast, the degree of PA level variability between the days of these two participants is varying. One has a low variability and the other a high degree of variability relative to the whole study population.

Chapter 5

Discussion

The aim of the study was to investigate how behavioural activity of former cancer patients with chronic cancer-related fatigue can be parameterized and, which treatments goals can be defined based on the physical activity level. Result of this is the ability to standardize personalized treatment goals. Within this chapter, the results of the research questions will be presented and combined. Subsequently, the results will be discussed through existing literature. In addition to this, the strengths and the limitations of this study will be mentioned.

5.1 The results of the sub questions

Sub question 1). 'What is the absolute cumulative IMA-value a day and what is the distribution of physical activity during the day, measured according to the IMA-values, for this patient group?'
The results of this question was that the mean absolute cumulative IMA-value per day was 203,592 IMA-counts with a standard deviation of 79,662 IMA-counts, based on measured days with at least six hours of data.

In addition, the distribution of the physical activity during the day was also analysed and was subdivided into two approaches. The first approach focussed on the degree of deviation per part of the day relative to a linear "normal" PA line. The result of the analysis was a lower physical activity level in the evening relative to the morning and afternoon by which the PA level in morning and afternoon are varied to each other. So, the PA level is over an average in the morning and afternoon higher compared to the evening. Based on this analysis it is difficult to draw a strong conclusion, by the fact that the analysis was based on the mean deviation percentages as well as that the degree of deviation of the parts of the day are dependent to each other. The second approach was the relative physical activity increase during the day. The result of the analysis was an hourly physical activity increase until mid-afternoon, with subsequently an hourly PA decrease until the end of the day.

2). 'Are these parameters different for patients compared to other groups which are described in the literature and if so, which treatment goals apply?'
The results of the literature study about the physical activity level of the analyses chronic diseases; COPD, CFS and CLBP indicate a lower daily PA level for COPD and CFS patient relative to the defined healthy norm of 7,000steps/day. Literature is not consistent about the PA level of the CLBP population. Literature indicates for this chronic disease a lower than or equal PA level relative to the level of healthy controls. The structural lower daily PA level of these chronic diseases, relative to the defined healthy norm, was corresponding with the study population of this research.

On the other hand, the PA distribution over the day of the chronic diseases was different to each other. Apart from that, the chronic diseases have in general a higher variability and/or a relapse of activity during the day or over the week in comparison with healthy people. Several literature studies suggest general treatment goals for instance; to increase PA level, improve PA distribution over the week or over the day. Based on the corresponding PA patterns of the CCRF study population with the other chronic diseases, it can be suggested that the literature recommended treatment goals of chronic diseases can also be used in CCRF patients.

3). 'Do the defined activity goals, based on the physical activity level measured by the IMA-values, correspond with the activity goals formulated by the physiotherapist?'

First, the treatment goals were classified in three groups. Treatment goals which were classified for 'increase PA' have, relative to the study population and the defined norm of 7,000steps/day, a low PA level. The degree of variability is varied; there exists a low and high variability relative to the study population. The classified group 'balancing of PA' have a relative high PA level, it can be suggested that it is correct that these group does not have received the treatment goals 'increase PA'. The degree of variability between the days in this group is also varied. The last group 'gaining insight of the PA level, balancing of PA and increase PA' was inconclusive regards to the PA level and variability of PA level over the week.

Overall, it can be concluded that there exists an inconsistency between the defined treatment goals by the physiotherapists and the results of the two parameters; the daily PA level and the PA distribution over the week.

5.2 Discussion of the study

First of all, the degree of dependence between the physical activity level and the amount of system wear time were calculated. The outcome indicated a correlation between these two variables. Therefore we concluded that the PA levels are representative for the amount of physical activity. But there is a limitation to this analysis. In this analysis, only days were included which had a minimum of six hours and the amount of IMA was an average over the measured days. This can be a bias for the analysis.

5.2.1 Parameter: Absolute cumulative physical activity level

Description of the data

The distribution of the absolute cumulative physical activity per day was non-normal, whereby 14 relative high values of measured days existed. The distribution of the data was obtained by the use of the Shapiro-Wilk test ($p<.001$). It can be suggested that the calculated physical activity level is not valid because each participant are represented for more than one measurement day. This resulted that the measured days are not all independent of each other which can lead to a selection bias. Notably, it occurred twice that four relative high values were derived from one participant. The participant's characteristics of the relative high values are shown in Appendix IV. By excluding these relative high values, the distribution was still non-normal distributed ($p=.012$) and did not have a notable influence on the mean of the physical activity level. Important to realize is the fact that the minimum PA values cannot be negative or even on a low scale whilst the highest PA values can be

infinite. As a result of this, the infinite relative high values on the right side of the mean are realistic in comparison with the finite values on the left side of the mean. For this reason, relative high values were not excluded from the analysis. In addition to this, more of these extreme physical activity levels could exist amongst people with CCRF.

Amount of measurement hours

Regards to the wear time of the accelerometer, in this study was six hours of PA data used as cut-off point for analysis. This was based on the study of Tabak et al.(2014) which suggest at least six hours of data for analysis.[50] Due to this, we missed 18 hours a day, including night/sleeping hours. Related to this, Masse et al. (2005) suggest different minimal wear times as a cut off point for analysis.[52] They indicate a wear time of 10 or 12 hours a day, or 60% of the waking hours. Addition to this, in the current study was 305 days included for analysis which had at least six hours of data. The number of measured hours of the included days was as follows: 1 day of 6 hours (0.3%), 3 days of 7 hours (1%), 2 days of 8 hours (1%), 5 days of 9 hours (2%), 13 days of 10 hours (4%), 27 days of 11 hours (9%), 56 days of 12 hours (18%), 86 days of 13 hours (28%) and 112 days of 14 hours (37%). This means that 294 days current study fulfilled the 10 hours wear time criteria suggested by Masse et al. (2005). The current used cut-off point of six hours of wear time could be seen as a limitation in measuring the daily physical activity level. The physical activities which are missing could be lead to a structural underestimation of the daily PA level. In further research should the suggested 10 or 12 hours of data are examined as cut-off point for a more complete physical activity level estimation.

Defined healthy physical activity norm

The absolute cumulative physical activity of the participants has a range between 54,132 and 505,917 IMA-counts a day. Based on the literature study of sub question 2, a norm for a healthy PA level for the current research is defined. This norm is regarding to physical activity levels for healthy adults who have a PA level between 7,000 and 8,000 steps a day. These number of steps a day can be converted by an equation of Cabrita(2013) into 213,360 and 243,600 IMA-counts per day respectively.[45] Out of total 305 included days, 33 fulfilled the requirement daily steps between the 7,000 and 8,000 steps a day. In addition to this, in total 118 days had a PA level higher than 7,000steps/day. This means that a small 40% of all days reached the defined physical activity norm.

Besides to the defined daily physical activity norm, there exists a physical activity norm for a week. This norm was 50,000 steps a week, which was based on the NNGB. This norm was fulfilled by 11 participants which is 28% (n=37) of the study population. In line with this, studies by Courneya (1997) and Prinsen (2013) have indicated that a lower physical activity level occurred after cancer treatments in comparison with the levels that existed before the cancer treatment was undertaken.[9 10]

In this study, the physical activity level before the cancer diagnosis is unknown. A possibility could be to compare the PA level of the CCRF population with the PA level of Dutch healthy adults. With as assuming, the CCRF population belonged to the Dutch healthy population before their received the diagnosis of cancer. Healthy adults from the Dutch population fulfilled ±59% of the NNGB between 2006 and 2012. [83 84] Based on this, the CCRF population in the current study decreased the fulfilment of the NNGB by about a quarter compared to the Dutch population. Related to these 59% who achieved the NNGB for the diagnosis, it could be that a CCRF participant already before the cancer

diagnosis, as being healthy person, does not achieved the NNGB (41%). Subsequently, when the same person, as CCRF patient in current study, also does not fulfilled the NNGB (72%), the low PA level of this person is not remarkable. In general, the low PA level is not always directly related to CCRF, but could also be dependent on the physical activity level before the cancer was diagnosed.

A limitation is that the NNGB assumes that the 3,000 steps of MVPA, which are derived from the daily 7,000-8,000 steps, have occurred in bouts of minimal 10 minutes of PA on a cadence of a minimum of 100steps/minute. In the current research, only the number of steps was included for the defining of the healthy PA level norm. The previous described minimal bouts and cadence was not examined.

5.2.2 Parameter: distribution of the physical activity a day

In this section, the determination of the distribution is explained, which consists of the use of a sort of reference line and the selection of a subdivision of the days. Subsequently, the results of the analyses were compared with other populations and some recommendations for further research are proposed. After all, the final opinion of the used quantification of the distribution is described.

The determination of the distribution

Firstly, a reference was needed to evaluate the physical activity distribution during the day. Literature is not yet available regarding an obvious daily PA pattern for healthy people. For this reason, it was too ambitious and impossible to make a comparison of the daily PA pattern of the CCRF population with the daily PA pattern of healthy people who complies with the NNGB norm.[56] Most people do not have the same schedule every day, even if they did, it may not comply with the NNGB norm. The various daily schedules can consist of different work hours, home settings, and variations in sports and leisure activities.[85] In this case, the 'normal' PA line was based on the personal physical activity level. The individual 'normal' PA value was a theoretical, linear line; the 'normal' PA value per part of the day was corrected by the amount of wear time which resulted in a proportional PA value.

Second, the degree of deviation in respect to the individual 'normal' PA value per part of the day was based on the defined fixed parts of the day of Tabak.[53] These parts are fixed to ensure the comparability between populations. Besides this, an hourly physical activity deviation is, in this case, not effective. In addition to this, an hourly deviation reported a highly variability between the hours, which was difficult to interpret. On the other hand, it gave more information about the PA variability between the hours as well as giving an insight into the fluctuations of the physical activities. This fact can be further investigated through additional research.

The analysis of the distribution

The deviations of the three parts of the day indicate a higher physical activity level in the morning and in the afternoon compared to the evening in regards to the defined normal linear physical activity distribution. In addition to this, a lower physical activity level in the evening also occurs in other chronic diseases, but the cause of these observations has not yet been investigated.[53 75 79] Correspondingly, the studies from Davis (2007) and Copeland (2009) reported the daily physical activity pattern of healthy people, both young and old. Both groups showed also a decreased level of

physical activity during the evening.[86 87] A decreased physical activity level in the evening of the CCRF study population seems for this reason not a remarkable observation compared to healthy people. With attention to the lower PA level in the evening, the differences of the degree of lower PA level between different populations is unknown.

The observation in this study about the high deviation differences between the evening and the first two parts of the day could be a reason to improve the PA distribution during the day with as result a higher PA level in the evening. This results in smaller PA level differences between the three parts of the day. In further research must be the improved PA distribution investigated related to degree of fatigue.

An observation of the current study population resulted in an alternating PA deviation between the morning and afternoon of the individual participant. In this way, it is hard to draw a conclusion about the deviation of the first two parts of the day. If the participants will be subdivided into groups for instance based on CIS score, living situation or work, there could be provide more insight about the PA distribution of different groups. Besides, by means of comparison of these groups there can be possible drawing improved conclusions and the treatment could be adjusted to the respective group. This subdivision analysis is a recommendation for further research.

Physical activity distribution and fatigue

In general as regards to the degree of deviation, it can be suggested that the variation between the parts of the day can be explained through different variables. A possible variable in current study population may be the occurrence of sudden fatigue during the day. Luctkar-Flude (2007) indicated an association between high fatigue and low physical activity levels.[88] Related to this, the NCCN defined cancer related fatigue as not proportional to recent activity and thus interferes with usual functioning.[32] The suddenly occurrence of fatigue during the day could be caused the variability of deviation between the parts of the day.

Overall, by the use of the theoretical linear normal PA line, it provides insight of which part of the day has relative high or low physical activity. Although the 'ideal' PA distribution is unknown, the distribution based on the normal PA line indicates a proper indication to compare it with healthy or other populations. In this way, there could be drawn a conclusion related to the distribution over the day. The physical activity level is not included in this parameter; the first parameter complements this analysis. With the above considerations and the existed literature in mind, the described quantification of the PA distribution a day is a representative parameter.

5.2.3 Physical activity pattern and treatment goals of chronic diseases

Physical activity norm

Before the physical activity level could be evaluated, a physical activity norm was determined. In this research, the PA norm for healthy PA level was determined the number of steps between 7,000 and 8,000.[63] Besides the amount of PA, the NNGB was an additional variable to examine the PA. This suggests minimal five days a week 30 minutes of MVPA, with a cadence of 100steps/minute and with minimal bouts of 10 minutes. In current research only the number of steps was observed for the evaluation of the amount of PA. The data was not examined on the requirement 30 minutes

MVPA with the related cadence and minimal bouts. When there is in future an interest in the specific fulfilment evaluation of the NNGB, a study of Whitt (2003) and Masse (2005) suggest a method to examine the PA data on these 30 minutes of MVPA.[52 89]

Comparison of PA levels of different populations

Based on the physical activity level of the CCRF participants and the literature study of the chronic diseases, it can be mentioned that the PA level is comparable with the physical activity level of COPD GOLD stage II and the CFS population.[66 75] These populations, including CCRF population, have structural lower compared to healthy people and lower than the defined norm of 7,000-8,000steps/day. Related to this, the studies of GOLD stage II were calculated based on the physical activity level during three days or, in other studies, were the number of wear time unknown. Meanwhile, the physical activity level in this research was based on seven measured days. It is important to realize that a minimum measured period of seven days is an acceptable and reliable estimation of gathering results regarding daily physical activities, suggested by Trost (2000).[51] The low number of measured days of the existing literature could be seen as a limitation for the analysis and comparison of physical activity levels. In this case, the studies of GOLD stage II have limited reliability in making a comparison with the CCRF population of this study.

The PA distribution

The PA patterns of the observed chronic diseases are different to each other, for instance a high PA peaks followed by PA dips during the day. Furthermore, some chronic diseases shows PA variability between the days, which was related to bad or good days.[75] The PA variability between the days also occurs in the CCRF study population but on an average is the PA variability low (Figure 22). A corresponding observation of all chronic diseases, including CCRF, is the lower PA level during the evening. Overall, it is hard to compare the PA patterns of the chronic diseases because of the variability of PA distributions. There could be suggested that the PA distribution of CCRF is in general are corresponded with other chronic diseased based on the PA variability during the day but not correspond with the pattern during the day.

Treatment goals

The majority of the described chronic diseases had certain level of disruptions of PA level during the day. As described above, the PA pattern of the chronic disease were disrupted over the day and had final a lower PA level in the evening. These chronic diseases had less energy capacity left at the end of the day through, potentially, too many activities being carried out in the morning or in the afternoon.[53 80 82]

Overall, all chronic diseases have their own specific mechanisms and symptoms, but it is quite a coincidence that all these diseases have the same PA level and patterns problems despite the underlying factors may differ. Based on this consideration it could be mentioned that balancing PA pattern (level and distribution) is an appropriate treatment goal. Though, the effectiveness of these treatment goals is not yet investigated. In addition to this, the disease related variables influences the PA level such as, depression, sleep problems or cognitive problems.

5.2.4 Physiotherapist treatment goals

In current study, the treatment goals, defined by physiotherapists, were compared to the PA level during the baseline. Based on the description of the treatment goals were defined three different classification groups. This is a quick and easy method to classify the treatment goals. Following, we will describe another method.

This study demonstrated inconsistency between the treatment goals, defined by the physiotherapists, and the PA level from the AAF participants. The evaluation of this PA level was determined by a comparison of the PA level relative to the whole study population, which is described above. The treatment goals were classified in groups based on the goal description by the physiotherapists. The inconsistency between the PA level and the treatment goals could be caused by the fact that the classification was derived from the description of the treatment goals and not by predetermined criteria. By the use of predetermined criteria for the classification of the treatment goals, there can occurs more specific classified groups for the subdividing of the defined treatment goals. This method may be more precise in the comparison and evaluation between the treatment goals and PA level relative to the classification based on the description of the treatment goals. This method is a recommendation and should be investigated in future research.

The three classification groups

Participants, which received the treatment goals to increase physical activity level, had a lower PA level than the defined PA norm.[62] This is corresponding with the proposed treatment goal from van der Werf.[76] Remarkable to this, participants with a low PA level received other treatment goals while they had approximately the same variability between the measurement days. This shows the described inconsistency.

The second treatment goal, 'balancing of PA' can be interpreted in different ways. Balancing the PA level can refer to balancing the PA during the day[79] as well as balancing the PA level during the week.[53 79] The physiotherapists are not consistence about these two approaches, the evaluation of the description of the treatment goals suggested treatment goals which are focussed on weekly PA improvement as well as daily improvement (Appendix V). In this research was assumed that both approaches are classified in the general group 'balancing of PA' with in mind that it could be balancing over the day or over the week. In future research is recommended that the treatment goals defined by the physiotherapists must be more specific. As final, with the current method it is hard to define treatment goals when the PA pattern of the participant shows no variability problem and the PA level are 'normal', it is hard to define treatment goals.

Chapter 6

Conclusion

It can be concluded that the physical activity level of people with chronic cancer related fatigue is lower compared to the Dutch norm for healthy physical activity but corresponds with the level of other chronic diseases. The physical activity distribution during the day can be parameterized by determining the physical activity deviation of three parts of the day, in ratio to a normal linear physical activity distribution. This approach showed, for the CCRF study population, in an on average lower physical activity level in the evening with respect to the morning and afternoon. In addition to this, the degree of physical activity increase during the day can be parameterized by calculation the hourly physical activity level relative to total physical activity level. The CCRF study population shows an hourly physical activity level increase till mid-afternoon and subsequently decrease of physical activity level. The treatment goals by the physiotherapists are not consistent with the measured PA levels and patterns. There is a difference between the treatment goals defined by the physiotherapists and the PA levels. Nevertheless, treatment goals can be equalled to the treatment goals from other chronic diseases because of the in accordance physical activity level of these groups, taking account to the disease related complaints.

There some recommendations for further research:

- For the analysis of the total physical activity level and pattern is a larger range of measurement hours desirable. In this way, it will provide more insight of the total PA level and pattern of a patient.
- Related to the above recommendations, the analysis of the PA level and pattern will be more reliable and accurate when the cut-off point will be increased to 10 or 12 hours for the analysis.
- To gain more insight and a more meaningful interpretation of the daily PA patterns of the population, the CCRF population must be subdivided in different groups, for instance: CIS score, (not) working, gender, living situation. By means of the differences of PA patterns between the groups, there will provide a more meaningful interpretation of the PA patterns of the CCRF population.
- Regards to the classification of the defined treatment goals by the physiotherapists, it is a recommendations to define predetermined criteria for the classification of the treatment goals.
- The last recommendation is to performing an evaluation of the PA distribution during the day and week, independent to each other, compared with the defined treatment goals by the physiotherapists.

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Appendices

Appendix I. Checklist Individual Strength (CIS)

Met behulp van de volgende 20 uitspraken willen wij een indruk krijgen van hoe u zich de **laatste twee weken** heeft gevoeld. Geeft u van iedere uitspraak aan in hoeverre deze op u van toepassing is.

Ja, dat klopt 1 2 3 4 5 6 7 Nee dat klopt niet

1. Ik voel me moe

2. Ik zit vol activiteit

3. Nadenken kost me moeite

4. Lichamelijk voel ik me uitgeput

5. Ik heb zin om allerlei leuke dingen te gaan doen

6. Ik voel me fit

7. Ik vind dat ik veel doe op een dag

8. Als ik ergens mee bezig ben, kan ik mijn gedachten er goed bijhouden

9. Ik voel me slap

10. Ik vind dat ik weinig doe op een dag

11. Ik kan me goed concentreren

12. Ik voel me uitgerust

13. Het kost me moeite ergens mijn aandacht bij te houden

14. Lichamelijk voel ik me in een slechte conditie

15. Ik zit vol plannen

16. Ik ben gauw moe

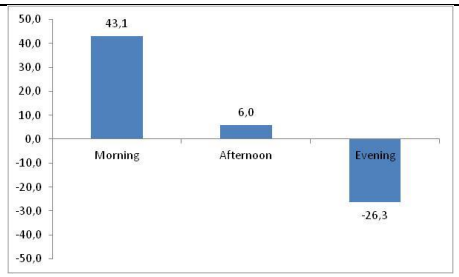
17. Er komt weinig uit mijn handen

18. De zin om dingen te ondernemen ontbreekt mij

19. Mijn gedachten dwalen gemakkelijk af

20. Lichamelijk voel ik me in een uitstekende conditie

Appendix II. Distribution of three parts of the day from all participants



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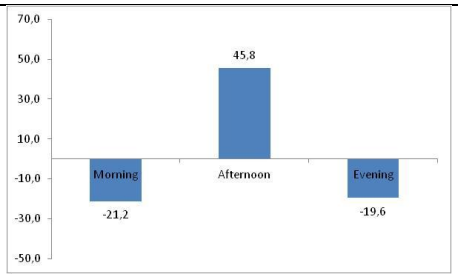

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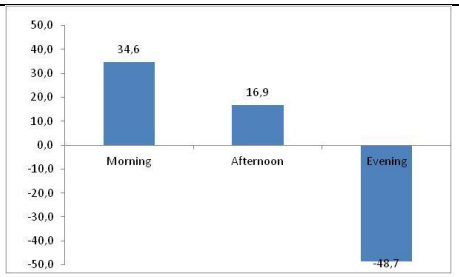

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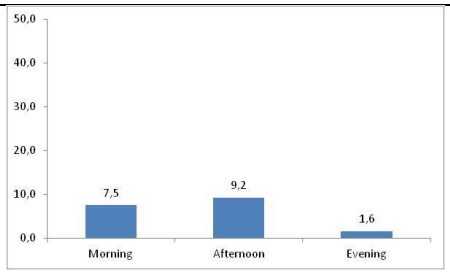

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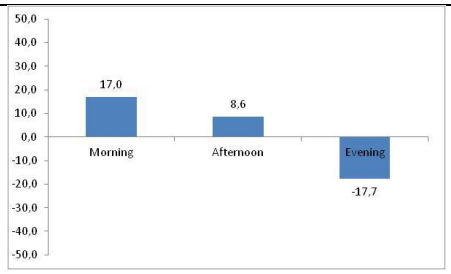

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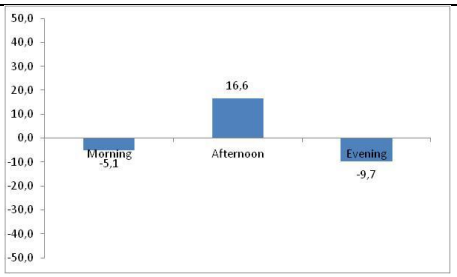

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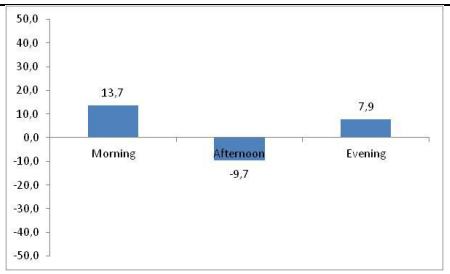

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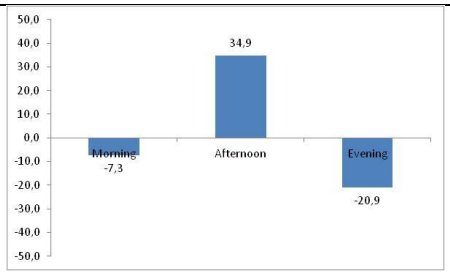

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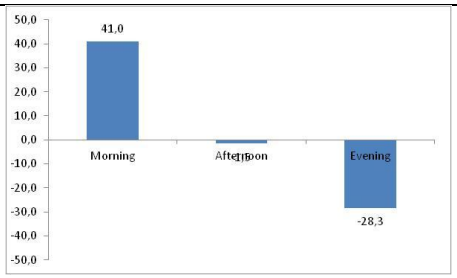

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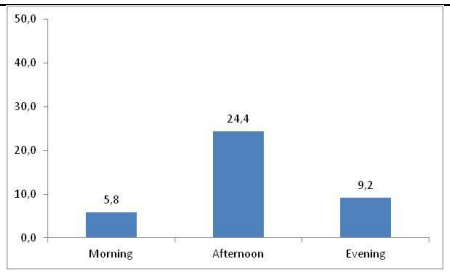

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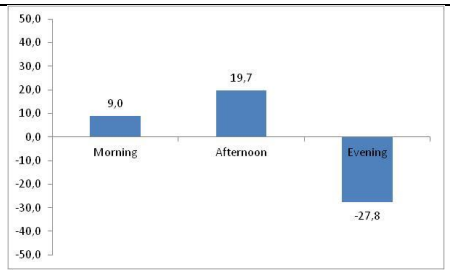

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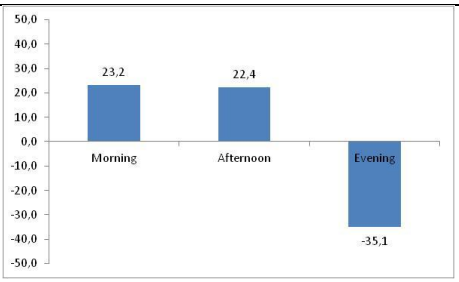

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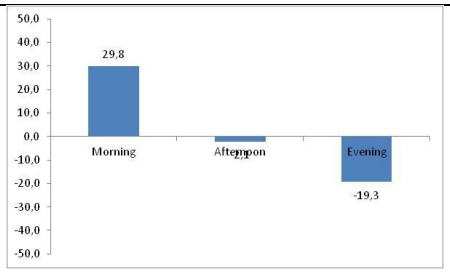

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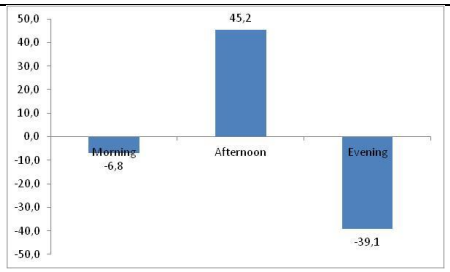

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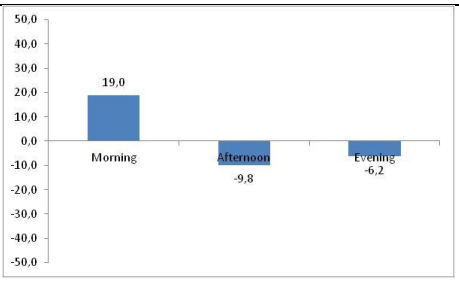

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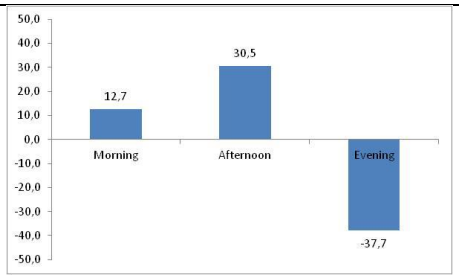

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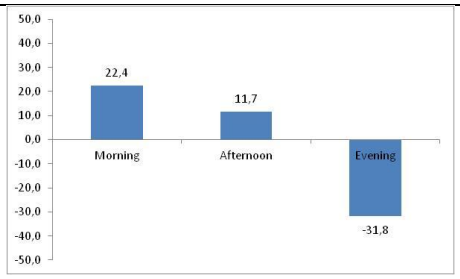

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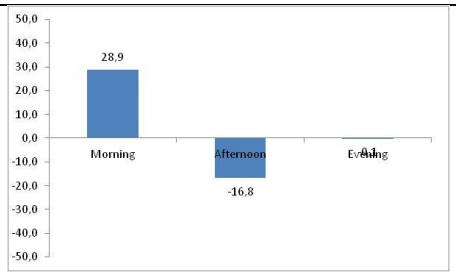

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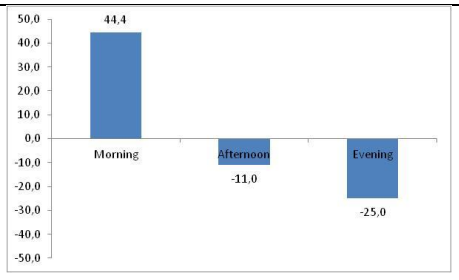

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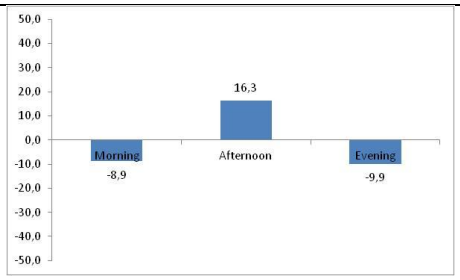

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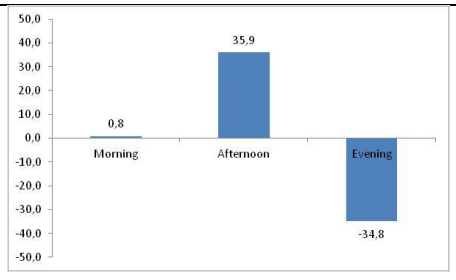

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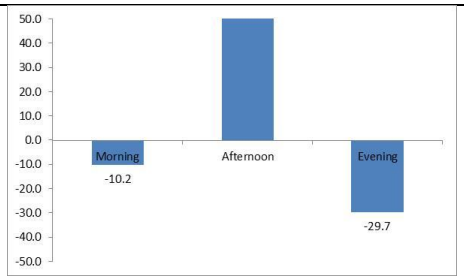

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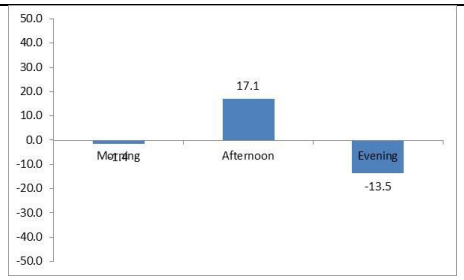

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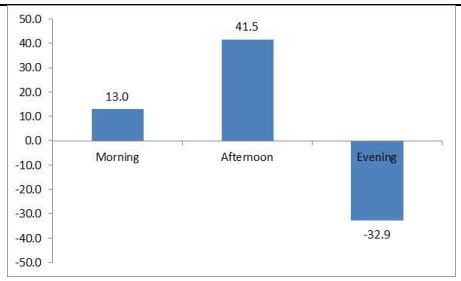

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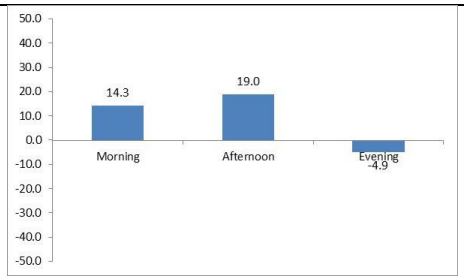

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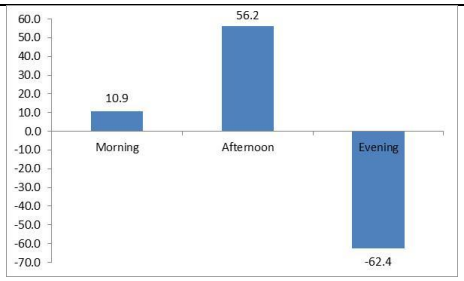

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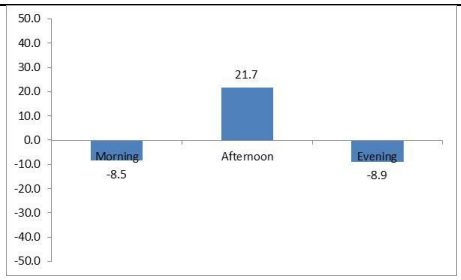

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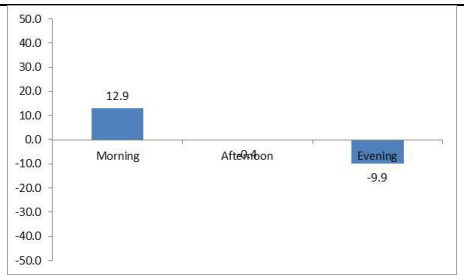

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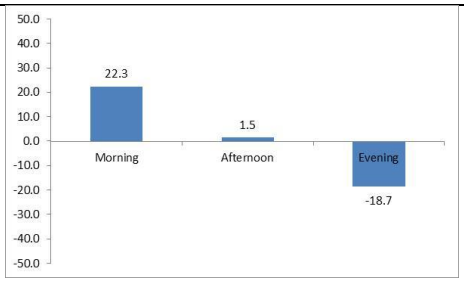

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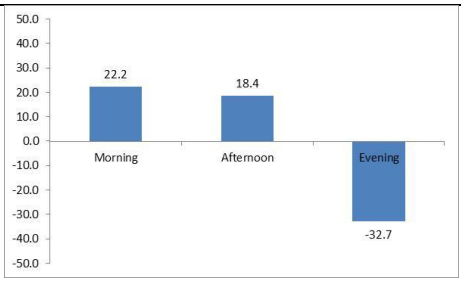

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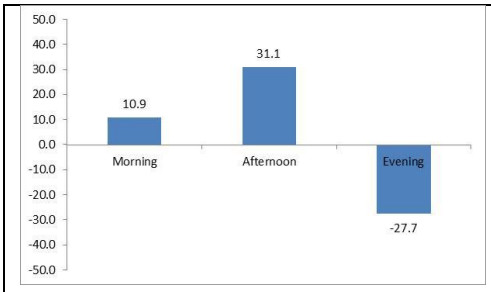

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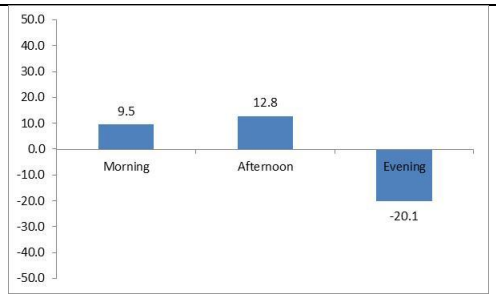

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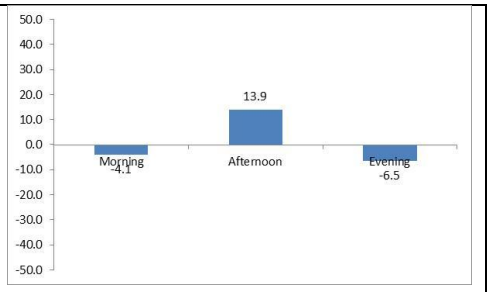

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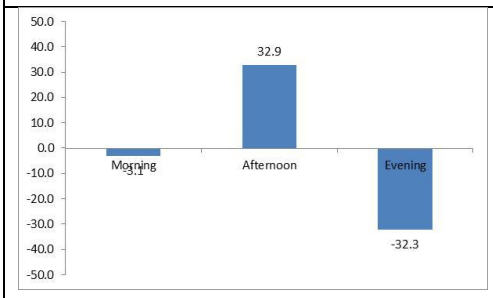

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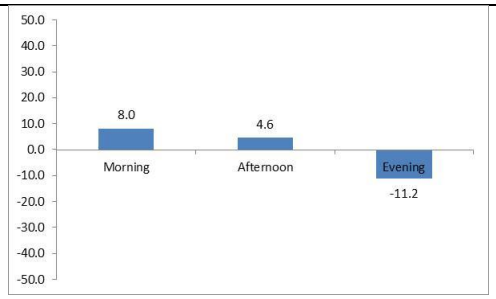
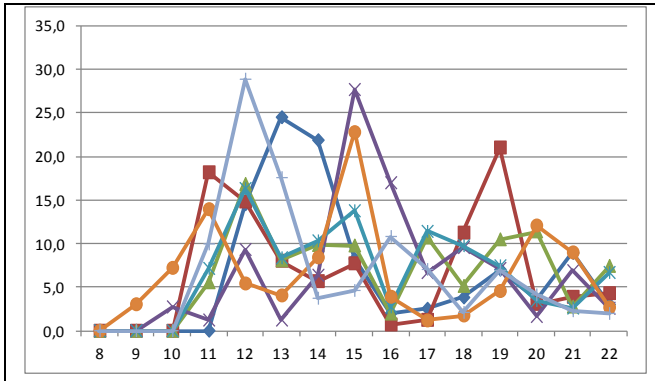


Participant 35

Appendix III. The physical activity increase per hour of the measured days of 12 participants (percentages)



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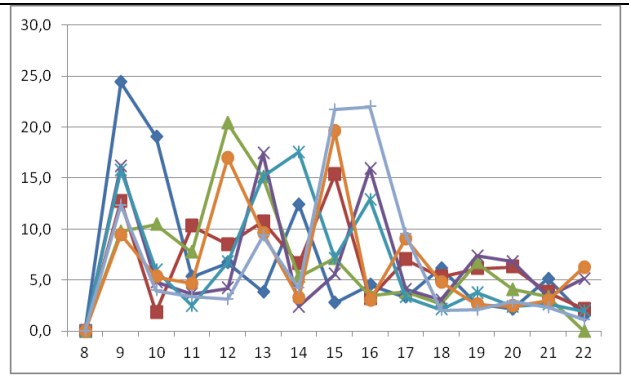

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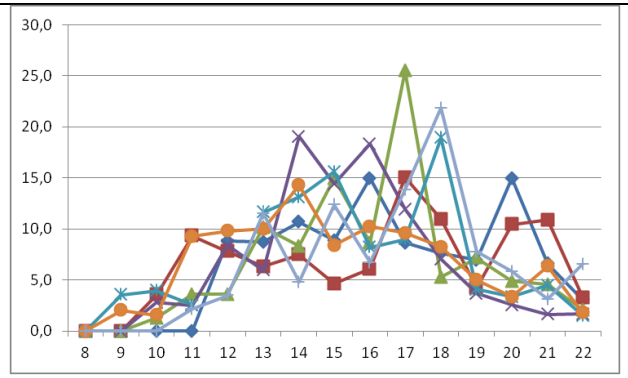

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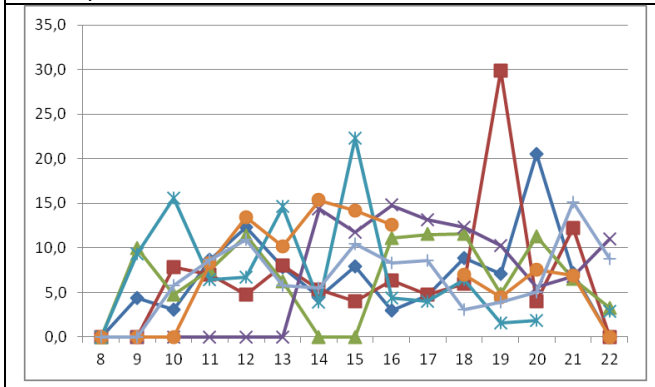

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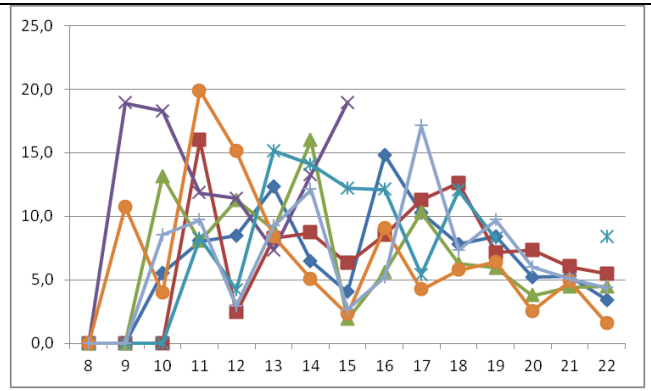

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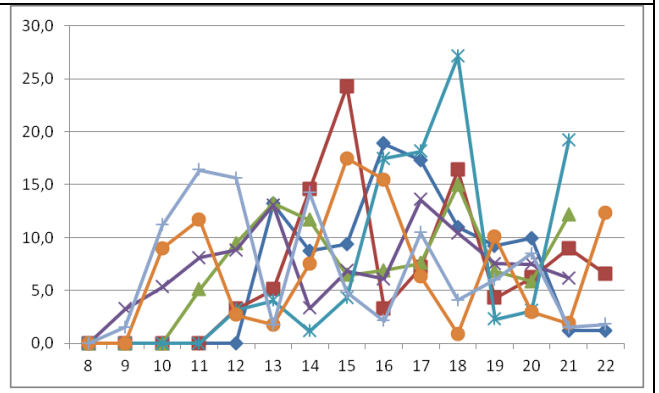

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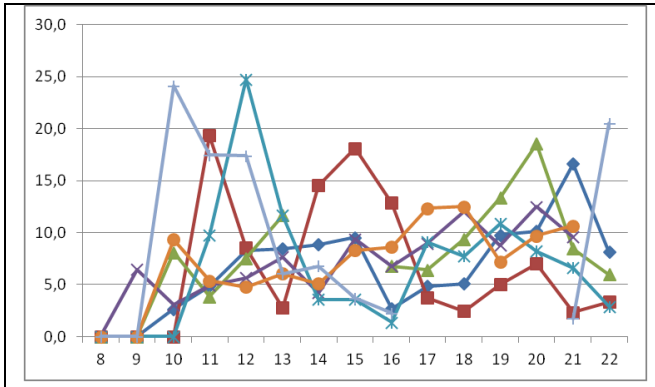

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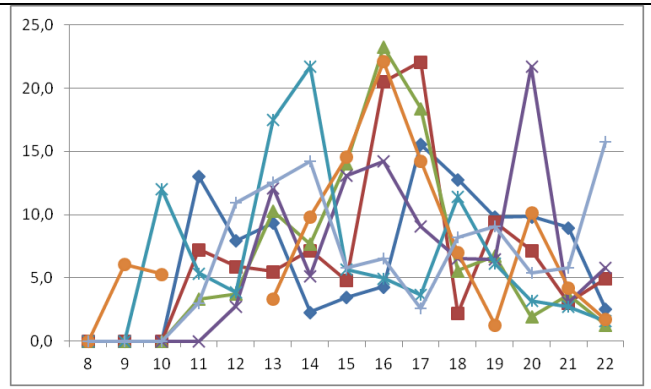

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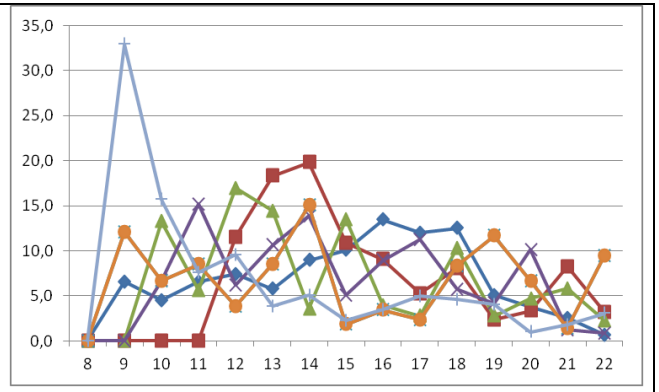

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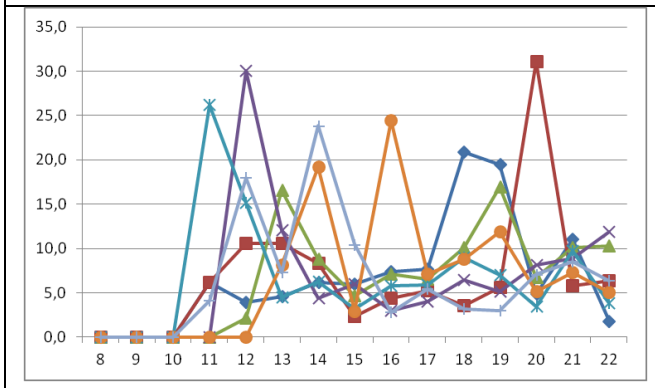

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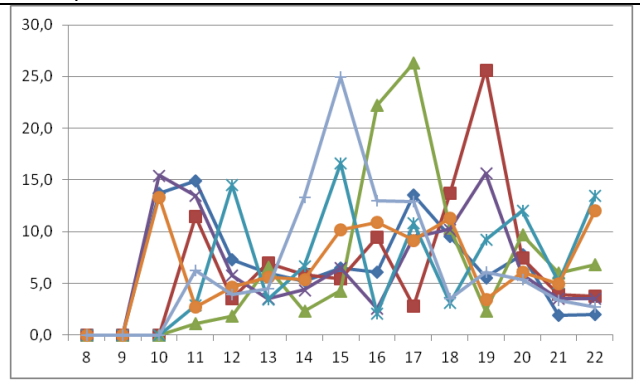
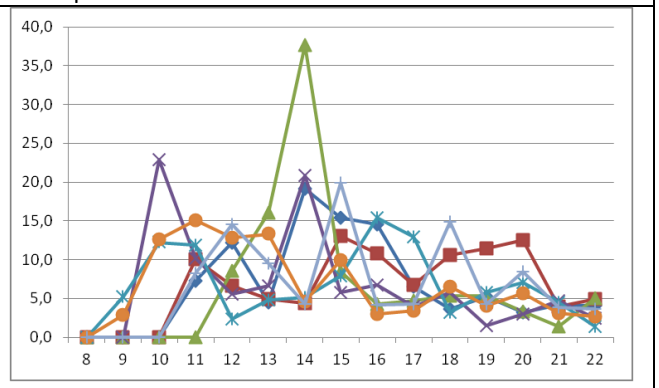


Participant 11



Participant 12

Appendix IV. Relative high values characteristics

Number of days outliers	Gender	Age(years)	Last cancer treatment (years)	CIS score	Living situation
1	Male	49	1,5	35	With partner + child(ren)
1	Female	21	0,4	37	With parents + sister
1	Female	51	-	52	With partner + child(ren)
2	Female	41	5	45	With partner + child(ren)
4	Female	55	4	51	With partner
4	Male	35	4,8	46	With partner + child(ren)
1	Female	54	2	39	With child(ren)

Appendix V. Defined Treatment goals by the physiotherapist and participant

Participant number	Treatment goal(s) (defined by the physiotherapist and participant)	Summary treatment goal
1.	Je wilt graag aan het einde van deze therapie weer 32 uur kunnen werken en daarbij 2 uur in de week kunnen sporten (1 uur bodyshape and 1 uur bodybalance OF 2x hardlopen.	Increase PA
2.	Inzicht in de oorzaken van vermoeidheid, optimalere dagindeling en handvatten om na de 9 weken therapie op de goede voet verder te gaan. Verbeteren van uithoudingsvermogen (toename in wandeltijd)	Gaining insight of PA + balancing of PA + increase PA
3.	Je wilt dezelfde hoeveelheid activiteit blijven uitvoeren als je op dit moment doet, maar hierbij minder vermoeidheid voelen. Dit wil je bereiken door de activiteiten beter over de dag/week te verdelen, waardoor je vermoeidheidsscore aan het eind van de week (vrijdag) teruggebracht word van een 7 (op een schaal van 0-10 op dit moment) naar een 5 (schaal van 0-10) over 9 weken.	Balancing of PA
4.	De vermoeidheidsscore is gemiddeld over de dag 3 bij een zelfde activiteit (200) over 6 weken. Aan het eind van week 9 haal je een hoeveelheid activiteit van 350 met een vermoeidheidsscore aan het eind van de dag van 5.	Increase PA
5.	Inzicht verkrijgen in de oorzaken van vermoeidheid, signalen herkennen en handvatten verkrijgen in het zelfstandig continueren van de therapie na afloop van de therapie. Door middel van inzicht verkrijgen in oorzaken van vermoeidheid een gezondere/betere dag- en weekindeling kunnen maken waardoor vermoeidheidsscore aan het eind van de week daalt van 6 naar 3 (op een schaal van 0-10). Opbouw in loop- en fietsbelasting, zonder hierdoor extra vermoeid te raken. Fietsbelasting opbouwen van 1,5km achtereenvolgend naar 7,5km.	Gaining insight of PA + balancing of PA + increase PA
6.	Inzicht en handvatten verkrijgen om grenzen te herkennen en daarmee om te gaan. Daarbij inzicht krijgen in hoe de vermoeidheid ontstaat en wat eraan te doen in de komende periode. Je wilt graag na een dag werken nog gezellig op visite kunnen gaan bij vriendinnen en dan niet zo uitgeput thuiskomen dat je er de volgende dag nog last van hebt, maar maximaal een score van 7 op 10 van vermoeidheid.	Balancing of PA
7.	Een vaster activiteiten- en rustpatroon te krijgen en verschil voelen tussen lichamelijke mentale moeheid. Mijn grenzen leren voelen aankomen, zodat ik er niet overheen ga.	Balancing of PA

8.	Kan ik in 9 weken met behulp van het Fitter na Kanker en met de goede informatie een dag goed doorkomen zonder extreme vermoeidheid.	Balancing of PA
9.	Zonder al te veel klachten meer fietsen zowel recreatief als functioneel naar het werk heen en weer. Streven dat ik buiten mijn werk om meer energie heb om samen met mijn gezin dingen te ondernemen.	Balancing of PA
10.	Je voelt je zeker genoeg om rustig aan weer in de sportschool te gaan beginnen met sporten. Je kunt een uurtje wandelen. Je kunt drie kwartier op de hometrainer fietsen (minimaal stand 2).	Increase PA