The top half of the image features a vibrant blue background with a textured, watercolor-like appearance. Overlaid on this background is a white line-art illustration of a person's head and shoulders in profile, facing right. The person is wearing a headset with a microphone. Surrounding the central figure are five white-outlined rectangles, each representing a mobile device (smartphone or tablet). These devices are connected to the central figure by thin white lines, suggesting a network or telehealthcare system. The devices are positioned at the top left, top right, bottom left, bottom center, and bottom right.

JOSIEN TIMMERMAN

CANCER REHABILITATION AT HOME

The potential of telehealthcare to support
functional recovery of lung cancer survivors

PROPOSITIONS

1. Physical activity should not be described as a single measure, but can best be understood as a complex and multidimensional behavior (*this thesis*).
2. Personalized coaching and care require appreciation of variation and heterogeneity in patterns of outcomes (*this thesis*).
3. Leading innovation is not about getting people to follow you into the future, it is about getting people to co-create it with you (*Linda A. Hill*).
4. Lung cancer survivors are able and feel competent to use technology; therefore, use of technology in cancer rehabilitation should not be feared (*this thesis*).
5. E-Health is health care transformation, not "an IT project" (*Salah Mandil*).
6. Rather than seeing implementation as a post-design activity, implementation conditions should be considered from the beginning and be intertwined with design and evaluation (*this thesis*).
7. Technology is not the problem (*this thesis*).
8. The process is testing you as well as teaching you (*Robert Kiyosaki*).
9. Progress is impossible without change (*George Bernard Shaw*).
10. If you want to go fast, go alone; if you want to go far, go together (*African proverb*).

CANCER REHABILITATION AT HOME

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Josien Timmerman

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CANCER REHABILITATION AT HOME

The potential of telehealthcare to support
functional recovery of lung cancer survivors

PROEFSCHRIFT

ter verkrijging van
de graad van doctor aan de Universiteit Twente,
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in het openbaar te verdedigen
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geboren op 22 oktober 1981
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SOLI DEO GLORIA

To Rebecca and Ruben -
That you may work hard,
be loved, find wisdom,
and prosper
wherever you go.

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1

GENERAL INTRODUCTION

Lung cancer is the most commonly diagnosed malignancy among adults worldwide, and leading cause of cancer-related death [1]. In the Netherlands, lung cancer accounted for 12% (12.6 thousand) of all new cancer cases and 25% (10.7 thousand) of cancer-related deaths in 2016 [2]. Approximately 85% of lung cancer patients are diagnosed with non-small cell lung cancer (NSCLC), and around 25% do have early-stage, operable disease [3]. Curative lung resection is the preferred treatment for early-stage lung cancer [4], significantly improving 5-years survival rates in this population [5, 6]. Although being the preferred treatment, lung resection causes a considerable decay of lung function, cardiorespiratory fitness, symptom burden, and Health Related Quality of Life (HRQOL) [7-11]. Characteristics of this population, such as high age, smoking-related comorbidities, poor performance status, and long-term physical inactivity may further aggravate the impact of resection [12, 13]. Even two to three years after lung resection, patients report persistent disability in daily functioning such as mobility, sleeping, breathing, and overall Quality of Life [14-16].

Rehabilitation for operable lung cancer survivors

Cancer rehabilitation aims to promote recovery, prevent deterioration and improve health in all stages of the cancer continuum. Accessibility to cancer rehabilitation, offered in a tailored and timely manner, is therefore advocated for all cancer survivors [17, 18]. Exercise or increasing physical activity is regarded a crucial component of cancer rehabilitation [17, 18]. In NSCLC survivors undergoing lung resection, exercise rehabilitation or physical activity programs have shown to improve treatment- and health-related outcomes, including exercise capacity, symptom burden, HRQOL, length of hospital stay, and postoperative complication risk [19-26]. Increasing physical activity may especially benefit NSCLC survivors to prevent or break through a vicious circle of deterioration of physical activity levels, functional capacity and symptom burden, which is often observed following diagnosis and treatment of lung cancer [27-29].

Since its introduction, the accessibility and tailoring of rehabilitation programs for cancer survivors have been discussed. Although supervised rehabilitation ensures adequate performance of the exercises, control of physical activity intensity, and support from specialized healthcare professionals, it may also hamper adherence and compliance, due to commuting problems, limited availability of professionals and location, and high symptom burden [17, 30]. Next to that, providing tailored and timely treatment and feedback - that is, providing a patient with the most effective treatment and coaching that fits their specific needs on the time that it is preferred - remains a challenge due to a lack of appropriate tools and outcome measures [31, 32].

Potential of telehealthcare in cancer rehabilitation

With the coming of internet and mobile technologies it is considered that rehabilitation for cancer survivors can be provided more tailored and timely using this technology, also called telehealthcare. Telehealthcare is defined as “the provision of personalized healthcare by a healthcare professional over a distance using Information and Communication Technology” [33]. Using the internet, smartphones and sensors, telehealthcare services are accessible on patients’ demand, wherever and whenever they need, providing continuous monitoring of health and behaviors, timely support, and easy access to specialized professionals [31-36]. The potential of telehealthcare services to improve cancer care throughout the entire continuum – including supportive care – has been recognized [37, 38] and various studies showed that telehealthcare applications are acceptable for patients and considered clinically safe [39].

Despite the potential of telehealthcare to improve cancer rehabilitation, the use of tailored telehealthcare services in lung cancer survivors to provide personalized rehabilitation has been limited. While the advantage of exercise or physical activity programs in the home environment to improve program adherence and physical fitness in NSCLC survivors compared to supervised training has been reported [17], only few studies have actually applied technology as part of home-based rehabilitation in operable lung cancer survivors [40-42].

Aim and outline of the thesis

The overall aim of this thesis is to gain knowledge on how to improve the quality and accessibility of home-based cancer rehabilitation that aims to improve functional recovery following lung resection using telehealthcare. To do so, this thesis consecutively addresses the design, evaluation and adoption of a telehealthcare service for NSCLC survivors undergoing lung resection.

The first part of this thesis describes the design of the telehealthcare service for which a user-centered, iterative design approach was used to come to proper functional requirements for the telehealthcare service that fit the actual needs of the users [43].

The design of the telehealthcare application built on existing technology that was already available for other chronic diseased populations such as COPD and chronic fatigue [44-46], as to speed up the first phase of the design process. Next to that, in project conception explicit choices were made to focus on physical activity behavior, given its potential as a therapeutic option to improve functional outcome following cancer diagnosis and treatment [18, 24, 47]. The content of this thesis can therefore best be viewed and understood in the context of these choices.

In **chapters 2 and 3** the potential of ambulatory monitoring of physical activity behavior and symptom burden in daily life of cancer survivors was explored. More specifically, **chapter 2** establishes the advantage of ambulatory monitoring methods and outcomes for personalized cancer rehabilitation as compared to the use of retrospective, questionnaire-based measures of physical activity behavior and fatigue in long-term cancer survivors. In **chapter 3** insight in the physical activity behavior patterns of operable NSCLC survivors from preoperative to six months postoperative are provided, using accelerometry. Also, this chapter addresses the usefulness of ambulatory monitoring for post-surgery rehabilitation of NSCLC survivors from a clinical point of view by evaluating the association between patterns of physical behavior early following surgery with perceived symptoms and Quality of Life at 6 months post-surgery.

In **chapter 4** the needs of both operable NSCLC patients and healthcare professionals involved in the care of these patients regarding technology-supported cancer rehabilitation were captured through interviews and focus groups. The fourth chapter also describes how these findings culminated in a list of functional requirements and a first prototype of the telehealthcare application.

The second part of this thesis focuses on the evaluation and adoption of telehealthcare in clinical practice. As a first step, the usability of the telehealthcare is investigated in **chapter 4**. **Chapter 5** continues with evaluation of acceptability and feasibility of the developed telehealthcare application in clinical practice. To do so, expectations, experiences and actual use of the service by NSCLC survivors and their healthcare professionals were evaluated with the service being offered as an addition to standard post-surgery follow-up care.

In **chapter 6**, the barriers and facilitators for successful adoption of telehealthcare services by healthcare professionals are clarified, providing guidance to promote acceptance, adoption and, thereby, successful implementation of telehealthcare services in clinical practice.

In the final chapter (chapter 7), the results of the studies are integrated, and their relevance for clinical practice as well as needs and possibilities for future research are discussed.

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2

RELATIONSHIP BETWEEN PATTERNS OF DAILY PHYSICAL ACTIVITY AND FATIGUE IN CANCER SURVIVORS

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ABSTRACT

Purpose: This study investigated: (1) physical activity behavior of cancer survivors throughout the day, (2) the relationship between objective and subjective measures of physical activity, and (3) the relationship between daily physical activity and fatigue.

Method: Physical activity was measured objectively using 3D-accelerometry (expressed in counts per minute (cpm)), and subjectively using a Visual Analogue Scale (VAS; 0-10) implemented on a smartphone in 18 cancer survivors (6 male; age 55.7 ± 10.2 yrs; free from cancer, last treatment three months previously), and matched controls. Fatigue was scored thrice daily on a smartphone (0-10 VAS).

Results: Mean daily physical activity of cancer survivors did not deviate from controls (1108 ± 287 cpm versus 1223 ± 371 cpm, $p = .305$). However, in cancer survivors physical activity significantly decreased from morning to evening ($p < .01$) and increased levels of fatigue throughout the day were reported ($p < .01$). Furthermore, a positive correlation was found between levels of fatigue and the magnitude of the decline in physical activity from afternoon to evening ($p < .05$). Objective and subjective measured physical activity showed low correlations.

Conclusions: This study demonstrated imbalanced activity patterns in cancer survivors. Also, the more a survivor felt fatigued, the greater the decline in activity behavior throughout the day. The low correlation between objective and subjective physical activity suggests low awareness in cancer survivors about their daily physical activity performed. Ambulatory monitoring provides new insights in both patterns of physical activity and fatigue, which might be a valuable tool to provide activity management more efficiently during treatment of fatigue.

INTRODUCTION

Cancer-Related Fatigue (CRF) often interferes with the performance of daily activities [1], can have devastating social and economic consequences [2] and may even hinder the chance of remission or cure as a result of its demotivating effects [3]. Not surprisingly, CRF is perceived by both patients and caregivers as a highly distressing and debilitating symptom.

It is generally believed that physical activity (PA) is important in the treatment of CRF [4]. Existing guidelines state that improvements to a patient's level of physical fitness and normalization of levels of daily activity, a process termed activity management, are important treatment goals for CRF management [5-7]. Moderate PA is associated with the alleviation of cancer-related symptoms such as fatigue [4], and the beneficial effect of activity management on fatigue in patients undergoing cancer treatment has been demonstrated in several randomized controlled studies [8-10].

Most of the studies examining PA and fatigue in cancer survivors have used retrospective outcome measures, such as questionnaires, to capture the extent and the nature of PA. Although these measures provide a general idea of the amount of PA performed, previous studies involving cancer survivors demonstrated a discrepancy between PA measured retrospectively with questionnaires and PA measured using objective measures such as accelerometers [11-14]. A likely explanation for the discrepancy is that questionnaires are prone to recall bias. When people are asked to recall past behavior, only a part of that behavior will be recalled, depending on the question asked, the frequency, severity, or impact of the behavior in question [15]. For example, for PA behavior it is known that light or moderate PA is difficult to measure using questionnaires [16]; one is likely to forget 'normal', daily PA, but will recall high intensity bouts of activity.

Ambulatory monitoring techniques can provide more accurate and detailed information on daily PA behavior and fatigue [17]. Ambulatory monitoring uses objective methods (e.g. accelerometers), subjective methods (e.g. symptoms scored several times during a day), or a combination of both, to capture behavior as it occurs in patients' daily life. So far, only a few studies have employed ambulant monitoring, such as accelerometry, to capture PA in cancer survivors [17]. The results are surprising, as contrary to the studies using questionnaires, only a minority of these studies report lower levels of PA in cancer survivors as compared with healthy controls [18], while the majority report no differences in PA level [12, 19, 20]. Even so, the expected relationship between PA and fatigue is scarcely observed when evaluated using

ambulant monitoring. Only one study reported a significant - but low - correlation between an increase in daily steps and a decrease in fatigue in adult survivors of childhood cancer [21].

Most of the studies that objectively assessed PA in cancer survivors used parameters that related to the *amount* of PA performed (such as intensity, number of steps, or total amount of daily PA). However, PA is not only a 'multi-dimensional construct incorporating frequency, time, type and duration' [17], but also a behavioral construct, concerned with patterns of PA within a specific time period [17]. To illustrate, for other populations who suffer from chronic disease, it has been reported that not the amount of PA, but PA *behavior* might be a useful predictor of health outcomes [22, 23]. So far, there are no studies evaluating patterns of PA reported in the cancer literature. Therefore, better insights into both PA behavior in cancer survivors and its relation to self-reported fatigue are desirable.

When discussing the role of PA behavior in CRF management, another important aspect is 'awareness'. Awareness is considered essential for effective behavior change [24], and is therefore a prerequisite for treatments that aim to change activity behavior such as activity management. No previous study could be found that explicitly evaluated awareness of daily PA behavior in cancer survivors.

Therefore, to explore the potential value of PA behavior in CRF treatment, this study: (1) assessed PA behavior throughout the day in a pilot group of cancer survivors; (2) compared objective and subjective ambulatory monitoring techniques to gain insights into the level of awareness of cancer survivors with regard to their daily PA performed; and (3) explored the relationship between specific parameters of daily PA pattern and self-reported fatigue in cancer survivors.

METHODS

A cross-sectional study was performed at the Roessingh Center for Rehabilitation, Enschede, the Netherlands. The experimental protocol was approved by the Twente Medical Ethics Committee, and informed written consent was obtained from each participant before enrolment.

Participants and setting

Cancer survivors were recruited from the Roessingh Rehabilitation Center Enschede, the Netherlands. Inclusion criteria were: (1) formerly diagnosed with cancer; (2)

completed cancer treatment (i.e. surgery, chemo- and/or radiotherapy) ≥ 3 months previously; (3) ability to read and speak Dutch; and (4) aged 18 or above. The exclusion criteria were: (1) use of wheelchair; (2) terminal or progressive disease; and (3) participation in a rehabilitation program in the previous three months.

For comparison of *daily activity behavior*, a sample of healthy controls was included in the study. Controls were recruited by asking the patients to ask their spouses to participate. The sample of healthy controls was supplemented with controls selected from a database available at the research center. This database consisted of family members from both patients included in other studies and from employees or students working at the research center. The controls were selected from the database based on their age and sex, so that the two groups were comparable in terms of age and sex. Inclusion criteria for healthy controls were: (1) 18 years or older; (2) subjective report of being healthy; (3) no history of cancer. The same exclusion criteria applied for the controls as for the main cancer survivor group.

Procedures

Eligible cancer survivors and controls were approached by the first and second authors, who provided verbal and written information about the study. Subjects who were willing to participate were asked to fill in an informed consent. On the morning of the first day, the procedure was explained and demographic characteristics were recorded for each participant. After that, participants filled in a questionnaire about fatigue. Instructions were given about the use of the equipment, namely an activity sensor and a smartphone. Instructions covered the correct placement of the accelerometer and the wearing schedule. Participants were asked to wear the accelerometer and smartphone for five consecutive days from 8:00 until at least 22:00, excluding time spent bathing or participating in water activities. Participants were also asked to perform their normal, daily routine, and to not change their physical activity pattern. After instruction, the accelerometer and smartphone were given to the participants, and returned by post or in person to the research center after five days of monitoring.

Study measures

For each participant, the following personal information was recorded: age, sex, BMI, and current work status. For survivors, the following information was added: treatment received, location of cancer and months passed since final cancer treatment.

Ambulatory measures - Cancer survivor and controls

Objective PA behavior was assessed using the MTx inertial 3-D motion sensor (XSens Technologies B.V., Enschede, the Netherlands), which is a tri-axial piezoelectric

accelerometer that measures accelerations in the x, y, and z-axis. This sensor was attached to the waist by means of an elastic belt. Data were transmitted wirelessly through a Bluetooth connection and stored on a smartphone. The output measure was calculated following the method described by Bouten et al. [25], which is highly related to measuring energy expenditure [26]. The accelerometer data were bandpass filtered through a 4th order Butterworth filter (.11- 20 Hz). The absolute value of the acceleration of each of the axes was integrated over time periods of 60 s and summed thereafter. The resulting data was expressed in counts per minute (cpm).

Ambulatory measures - Cancer survivors only

Fatigue was rated three times a day (13:00, 17:00 and 20:00) on a Visual Analogue Scale (VAS) by the cancer survivors, to rate fatigue in the morning, afternoon, and evening, respectively. In a previous study that employed the same activity monitoring method [22], it was shown that especially early in the morning activity data was missing, because patients turned on the system late in the morning. Therefore, it was chosen to schedule morning fatigue rating at 13:00, so sufficient morning activity data would be available to correlate with the morning fatigue scores. Scores could range from 0 ("I am not tired at all") to 10 ("I am totally exhausted"). The VAS has been previously successfully applied and validated in heterogeneous cancer populations [27].

Self-rated level of PA was assessed at the end of each measurement day (20:00). Cancer survivors were asked to rate their level of activity during that day on a VAS, ranging from 0 ("not active at all") to 10 ("maximum level of activity").

Retrospective self-report measures - Cancer survivors only

The Multidimensional Fatigue Inventory (MFI) questionnaire [28] was used to measure fatigue retrospectively in cancer survivors, as experienced over the previous days. This 20-item questionnaire covers five dimensions: General Fatigue, Physical Fatigue, Reduced Activity, Reduced Motivation, and Mental Fatigue. The MFI has been previously and successfully validated in cancer patients with various diagnosis sites [27].

Data analysis

Ambulatory measures

Objective PA behavior (accelerometer). Three days per participant with at least 420 minutes per day was set as the minimum to be included in the data analysis. Matlab algorithms were written to allow calculation of: PA level per hour, per day part and per whole day. For each group, the mean and standard error of the mean (SEM) per hour were calculated. Only those hours for which at least 30 minutes were measured, were included for analysis. The mean PA level per hour was used to calculate PA per day part; morning (8:00-12:00), afternoon (12:00-17:00), and evening (17:00-20:00). Only day parts for which at least 50% of the total data was available were included in the analysis. Finally, mean daily activity was calculated for each participant by averaging the mean activity of all the measurement days. To represent the PA pattern, the change in the PA between day parts was calculated, being the difference in cpm between (a) morning and afternoon ($\text{cpm}_{\text{afternoon}} - \text{cpm}_{\text{morning}}$); (b) afternoon and evening ($\text{cpm}_{\text{evening}} - \text{cpm}_{\text{afternoon}}$); and (c) morning and evening ($\text{cpm}_{\text{evening}} - \text{cpm}_{\text{morning}}$).

Daily fatigue. For each participant, scores of all measurement days were averaged into overall mean and standard deviation (SD) fatigue scores per day part (morning, afternoon, evening). To describe daily fatigue levels, a VAS fatigue score of ≥ 4 (out of 10) was used to represent a moderate to high level of fatigue [29].

Self-rated activity. Scores from all the measurement days were averaged, resulting in a mean score of self-rated activity for each participant, ranging from 0 to 10.

Retrospective fatigue (MFI)

A score for each dimension of the MFI was calculated, with higher scores indicating more fatigue [28].

Statistical analysis

IBM's Statistical Package for the Social Sciences (SPSS, 20.0) was used for the statistical analyses of our data. Descriptive statistics were used to summarize the characteristics of the sample. For all statistical analyses, a significance level of $p < .05$ was used. Normality of the outcome measures was tested using P-Plots, and histograms. Friedman's ANOVA was used to test the change in fatigue throughout the day in cancer survivors.

An independent t-test was performed to compare differences between survivors and controls in mean daily PA level. Secondly, differences in PA between day parts were

tested using repeated measures ANOVA for both groups independently. Thirdly, to test group differences in PA patterns throughout the day (i.e. between day parts), repeated measures ANOVA (RMANOVA) with a grouping factor (survivors versus controls) were performed, with PA per day part being the repeated measure.

Level of awareness was tested by calculating Kendall's Tau correlation between objective PA per day (accelerometer) and self-rated PA (VAS physical activity). To explore the *relationship between daily fatigue and activity patterns*, correlations (Kendall's Tau) were calculated between objective PA per day part and fatigue per day part.

For all correlations, cutoff scores of <0.3 , $0.3 \leq r \leq 0.8$, and >0.8 were used to represent low, moderate and high correlations, respectively.

RESULTS

Participants

Forty-four cancer survivors were approached for participation. Twenty-three cancer survivors participated in the study, of whom 18 survivors (6 male; mean age 56.7 ± 10.2 yrs) provided sufficient accelerometer data to be included in the final data-analysis. The most important reasons for exclusion of survivors were no interest in study, current participation in a rehabilitation program or progressive disease. Most survivors were women diagnosed with breast cancer, resulting in twice as many women than men in the study sample. Scores on the domains of the MFI varied between 10 and 13, which is relatively high compared to literature [30]. The sample of healthy controls comprised nine spouses of included survivors, and nine healthy subjects selected from the database. Characteristics of the included survivors and matched healthy controls are presented in Table 1. There were no significant differences found for age, sex, BMI or work status between the survivors and the controls.

Table 1 Characteristics of the study population

	Cancer survivors (n=18)	Healthy controls (n=18)
Age, mean (SD)	56.7 (10.2)	55.2 (8.2)
Sex, <i>n</i>		
Male	6	6
Female	12	12
Body mass index, mean (SD)	25.2(3.9)	25.3 (2.9)
Employed, <i>n</i> (%)		
Yes	8 (44)	12 (67)
Location of cancer, <i>n</i> (%)		
Breast	12 (66)	NA
Testicular	2 (11)	NA
Lung	2 (11)	NA
Skin	1 (6)	NA
Colon	1 (6)	NA
Treatment, <i>n</i> (%)		
Surgery	2 (11)	NA
Radiotherapy	1 (6)	NA
Surgery + Radiotherapy	4 (22)	NA
Surgery + Chemotherapy	3 (17)	NA
Chemotherapy + Radiotherapy	2(11)	NA
Surgery, chemotherapy + radiotherapy	6(33)	NA
Time since final treatment		
< 12 months, <i>n</i> (%)	10 (56%)	NA
Multidimensional Fatigue Inventory, mean (SD)		
General fatigue	12.9 (3.8)	NA
Physical fatigue	11.8 (3.8)	NA
Reduced activity	11.1 (3.7)	NA
Reduced motivation	10.1 (3.5)	NA
Mental fatigue	11.2 (3.8)	NA

Physical activity behavior

From the included cancer survivors, 85 days (i.e. 94% of all possible measurement days), and from the healthy controls 83 days (92%) were suitable for analysis. Reasons for missing data were technical failure, incorrect use of the system, and insufficient time for PA monitoring. It was found that the mean daily activity level of cancer survivors ($M = 1108$ cpm, $SD = 287$ cpm) did not deviate significantly from daily PA levels in the control group ($M = 1223$ cpm, $SD = 371$ cpm) ($p = .305$). Daily activity patterns of both

groups are visualized in Table 2 and Figure 1. Cancer survivors exhibited a significant decrease of PA during the day ($p = .001$; Greenhouse-Geisser corrected), while the PA level between day parts did not differ significantly in controls ($p = .147$). However, the group $\times$ time interaction failed to reach significance ($p = .199$, Greenhouse-Geisser corrected).

Table 2 Day part activity (in counts per minute) in both cancer survivors and controls

Day part activity (mean $\pm$ sd)		Morning	Afternoon	Evening
Cancer survivors	(n=18)	1364 $\pm$ 480	1034 $\pm$ 415	835 $\pm$ 353
Controls	(n=18)	1285 $\pm$ 517	1291 $\pm$ 402	1065 $\pm$ 453

Figure 1 Ambulatory activity. Activity patterns of cancer survivors (n=18) and controls (n=18)

Awareness daily activity levels

A low correlation of .193 ($p = .270$) was observed between self-rated VAS activity scores and mean daily PA as measured by the accelerometer, suggesting a low awareness of actual physical activity level in cancer survivors.

Patterns of fatigue

Of all VAS fatigue scores, 94% were available for analysis. Missing values occurred primarily for the evening hours, and were caused by technical failures (empty battery before the question was asked; question did not appear on the smartphone, or system was shut down before fatigue was scored due to connection failures with the activity sensor). Cancer survivors reported a significant increase in fatigue levels during the

day ($p = .006$), with 89% of participants reporting a VAS fatigue score of >4 during the evening (Figure 2). Ambulatory fatigue rated with the VAS fatigue did not correlate with fatigue measured with the MFI.

Figure 2 Daily fatigue pattern measured with the VAS fatigue in cancer survivors ($n=18$)

Relationship between PA behavior and fatigue

Both PA in the morning and PA in the afternoon were moderately and positively correlated with fatigue in the evening (Table 3), meaning that the higher the physical activity in the morning and afternoon, the higher the level of fatigue in the evening. Furthermore, moderate negative correlations were found between levels of fatigue in the afternoon and evening and the magnitude of the decrease in PA from afternoon to evening. That is, the more the survivors felt fatigued, the higher the decrease in activity throughout the day.

No significant correlations were found between subscales of the MFI and ambulant measured PA behavior, either accelerometry nor daily reported VAS activity.

Table 3 Correlations between ambulatory PA behaviour (accelerometry) and fatigue (VAS fatigue) in cancer survivors (n=18)

	VAS fatigue		
	Morning	Afternoon	Evening
Day part activity			
Morning	-.007	.076	.326 [†]
Afternoon	-.146	.149	.454 ^{**}
Evening	-.292	-.092	.133
PA pattern			
Afternoon - Morning	-.232	-.107	-.074
Evening - Afternoon	-.097	-.428 [*]	-.430 [*]
Evening - Morning	-.213	-.226	-.336 [†]

*p value < .05; **p value < .01; †p value < .10

DISCUSSION

This study has explored the potential value of PA behavior in CRF treatment, through investigation of daily activity behavior and its relation to fatigue in cancer survivors by using ambulatory monitoring techniques. Furthermore, we investigated whether cancer survivors are aware of their own daily activity behavior.

Our results show that, on average, daily activity levels of cancer survivors from this sample are comparable to those of age- and gender-matched controls. This finding is in line with the study of Servaes et al., who also found no difference in daily activity levels between post-treatment breast cancer survivors and healthy controls [13]. However, distribution of physical activity throughout the day turned out to be less balanced in cancer survivors as compared to the healthy controls; with the cancer survivors displaying a significant decrease in physical activity from morning to evening. This is the first known study to show imbalances during the day in PA behavior in cancer survivors. Imbalances in PA behavior have also been reported for other chronic patient groups, such as COPD, chronic low back pain and chronic fatigued patients [22, 31]. In those studies, the existence of symptoms, for example fatigue, pain or dyspnea, was suggested as a possible cause of altered PA behavior. That assumption is supported by the results of the present study: cancer survivors reported a significant increase in levels of fatigue from morning to evening. Furthermore, the more the survivors felt fatigued, the greater the decline in activity behavior from afternoon to the evening displayed by the cancer survivors.

Both the level and pattern of fatigue observed in our sample of cancer survivors are consistent with a previous study in which fatigue was assessed multiple times daily in breast cancer survivors [32], showing high levels of experienced fatigue from late morning to evening. Although increasing fatigue levels from late morning to evening are considered normal, and are also observed in healthy persons [32], cancer survivors seem more 'fatiguable' with overall higher levels of fatigue, except when getting up in the morning directly after a night's sleep [32].

In our study, the relation between PA behavior and fatigue patterns suggests that cancer survivors might be performing too much activity in the morning, resulting in increased fatigue levels, which in turn results in a relapse in activity from the afternoon going into the evening. One possible explanation for this specific pattern of PA is that cancer survivors are not aware of their PA behavior and the effect that certain activities have on their energy and fatigue levels. This phenomenon has been previously observed in other populations suffering from chronic disease [31, 33, 34].

For example, as described in the paragraph above, cancer survivors might feel 'good', that is not fatigued directly after waking up, and start with their 'normal' routine of daily activities. In healthy persons, this would not result in any significant increase in fatigue, whereas due to the high 'fatiguability' of cancer survivors [32], energy levels are quickly depleted in cancer survivors, resulting in increased levels of fatigue. This supports the assumption that balancing activity patterns, that is activity management, might reduce the experience of fatigue. Therefore, the role of PA as part of CRF treatment should not be limited to increasing the daily PA level, for example by exercise programs, but should also incorporate advice and tools for balancing activities over a day. In our study, we did not monitor fatigue levels directly following a night's sleep, and therefore cannot draw conclusions about whether or not this hypothesis holds for our sample of cancer survivors. Therefore, future research should further explore the interplay and cause-and-effect between changes in PA patterns and experienced fatigue.

The relationship between PA behavior and fatigue in the present study is in contrast with previous studies that reported no causal relationship between ambulant measured PA level and fatigue [11, 35]. As discussed in the introduction, these contradicting findings might result from the use of different outcome measures to represent PA and fatigue between the present and previous studies. In the present study, ambulant monitoring techniques were used to assess both PA and fatigue, while previous studies correlated retrospective measures for fatigue with ambulant measured PA. Information gathered by means of ambulatory monitoring is likely to be different and result in other conclusions than when the outcomes are assessed by means of retrospective questionnaires, since ambulatory assessment is less subject to recall bias, but more importantly, provides more and more detailed outcome parameters, which allows for in-depth analysis of actual PA patterns in relation to fatigue. Servaes et al. (2002) have already demonstrated that both retrospective measured PA and fatigue were correlated, as were ambulant measured PA and fatigue, while retrospective measures correlated poorly with ambulant outcome measures [13]. This was supported by the findings of our study, as no significant correlations were found between retrospective measured fatigue (i.e. MFI) and ambulant measured fatigue, or between retrospective fatigue and ambulant measured PA behavior. This emphasizes the importance of choosing suitable assessment methods when examining the relation between PA and fatigue.

As indicated by behavior change theories (e.g. Cognitive Behavioral Theory), awareness of a subject's own PA behavior is very important, otherwise PA behavior change programs are unlikely to be successful [24]. In the present study, awareness was operationalized by the relationship between the daily PA level measured using

an accelerometer, and the PA level rated by the cancer survivor at the end of each measurement day on an 11-point scale. By using this approach, the recalled period of PA behavior matches the period of objectively assessed PA. Also, both the score on self-rated PA and the resulting correlation will be less biased by recall problems than when measured using a questionnaire. Therefore, this approach is considered more advantageous than comparing objective PA with retrospective questionnaires, and a better indicator for the mismatch between perception of and the actual PA behavior. The results demonstrate low awareness in cancer survivors, suggesting that the survivors' perception of the PA performed on a particular day deviates from the actual level of PA. Therefore, for activity management to be successful, treatment should also focus on increasing awareness of actual activity behavior.

This study provides evidence of the value of ambulatory monitoring in the management of both PA and fatigue. As reported previously by Hermens et al., the use of ambulatory monitoring and feedback applications is a promising approach to monitoring, increasing awareness of, and thereby positively influencing daily activity behavior [36]. By using these applications, activity behavior is measured using ambulatory monitoring techniques, for example an accelerometer. By receiving personalized feedback messages on a smartphone, patients can be informed about their activity behavior, and are provided with advice about how to optimize activity behavior. Previous research demonstrated that giving real-time feedback on actual activity behavior can positively influence the activity behavior in patients suffering from chronic fatigue and chronic pain [37, 38]. The use of ambulatory monitoring and feedback applications might also be a promising approach to providing activity management efficiently in the treatment of CRF.

Our study provides new insights into daily activity behavior and its relation with self-reported fatigue in cancer survivors. However, potential limitations should be considered to help interpret the results. First, selection bias might be present due to the sampling method chosen for this study. We included cancer survivors who voluntarily applied for a cancer rehabilitation program to improve their physical and mental recovery following cancer treatment. It is likely that people who start a rehabilitation program, will experience a higher burden of symptoms and functional limitations in daily life compared to survivors who do not apply for supervised rehabilitation. It remains unknown how representative the findings of this study are regarding daily activity and fatigue for cancer survivors in general. Therefore, caution should be taken in generalizing the findings. Second, the small sample resulted in low statistical power, which might result in spurious effects or correlations. However, by using the mean value of a minimum of three days in the analysis, the probability of

the disproportionate influence of a single extreme measurement on the end result was reduced. Future research should further test the observed relationship between PA behavior and patterns of fatigue in a larger, adequately powered study. Last, although the present study suggests that daily physical activity patterns are associated with self-reported levels of fatigue in cancer survivors, no causal relationship between physical activity and fatigue could be established due to the cross-sectional nature of the study design. One further step would be to investigate whether activity coaching in daily life decreases self-reported fatigue in cancer survivors.

CONCLUSION

This is one of the first studies reporting on daily PA patterns in cancer survivors. Cancer survivors demonstrated imbalanced PA patterns as compared to those shown by the controls, while the overall level of PA was comparable between groups. Also, in cancer survivors PA behavior was associated with the experience of fatigue during the day; the more the survivors felt fatigued, the greater the decline in activity behavior from afternoon to the evening. This implies that providing survivors with advice and tools for balancing activities efficiently over a day might be of importance in the treatment of CRF. Furthermore, the observed low awareness in cancer survivors regarding the daily PA performed suggests that during treatment attention should be paid to making patients aware of their activity behavior. The use of ambulatory monitoring techniques is a promising method to employ activity management more efficiently in cancer survivors. These methods enable daily monitoring of PA and fatigue, and can provide survivors with real-time feedback on their behavior, improving both awareness and the ability to change PA behavior. Future research should determine if balancing activity through the use of ambulatory techniques indeed reduces the experience of fatigue in cancer survivors.

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3

PHYSICAL BEHAVIOR AND ASSOCIATIONS WITH HEALTH OUTCOMES IN OPERABLE NSCLC PATIENTS: A PROSPECTIVE STUDY.

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ABSTRACT

Objectives: Our objectives were to 1) characterize daily physical behavior of operable non-small cell lung cancer (NSCLC) patients, from preoperative to six months postoperative using accelerometry, and explore if physical behavior preoperative or one month postoperative is associated with better health outcomes at six months postoperative.

Methods: A prospective study with 23 patients (13 female) diagnosed with primary NSCLC and scheduled for curative lung resection was performed. Outcome measures were assessed two weeks preoperative, and one, three and six months postoperative, and included accelerometer-derived physical behavior measures and the following health outcomes: six-minute walking distance (6MWD), questionnaires concerning health-related quality of life (HRQOL), fatigue and distress.

Results: On group average, physical behavior showed significant changes over time. Physical behavior worsened following surgery, but improved between one and six months postoperative, almost reaching preoperative levels. However, physical behavior showed high variability between patients in both amount as well as change over time. More time in moderate-to-vigorous physical activity in bouts of 10 min or longer in the first month postoperative was significantly associated with better 6MWD, HRQOL, distress, and fatigue at six months postoperative.

Conclusion: As expected, curative lung resection impacts physical behavior. Patients who were more active in the first month following surgery reported better health outcome six months postoperative. The large variability in activity patterns over time observed between patients, suggests that physical behavior ‘profiling’ through detailed monitoring of physical behavior could facilitate tailored goal setting in interventions that target change in physical behavior.

INTRODUCTION

Physical activity (PA) is recognized as an important health-promoting behavior throughout the entire cancer continuum [1]. Higher levels of PA are associated with less negative treatment side effects, improved exercise capacity and patient reported outcomes measures (PROMs), and lower risk of recurrence and mortality in various cancer types [1-4]. Independent of time spent in PA, increased time spent in sedentary behavior (SB) is related to lower health related quality of life (HRQOL), and higher mortality rates for cancer survivors [2, 5, 6]. Self-reported measures are often used to capture the extent and nature of PA. However, considerable discrepancy between self-reported PA and objectively measured PA is reported in patients in general [7], and those with cancer [8], including non-small cell lung cancer (NSCLC) [9]. Despite this discrepancy, the number of studies in operable NSCLC patients that measure PA using objective measures is limited [9-13]. The few studies available show that lung cancer patients have low levels of PA at diagnosis, which further decline in the first months following surgery.

In these studies, PA was represented by a single measure such as number of steps [9, 11, 12] or overall physical activity level (PAL)[13], while more and more evidence stresses the importance of including other, additional measures that characterize physical behavior more precisely [10, 14]. Especially time spent in SB and moderate to vigorous PA (MVPA) and how this time is accumulated are considered clinically relevant, due to their association with health and PROMs in cancer survivors [14]. So far, pre- to postoperative patterns of physical behavior of operable NSCLC patients and their relation to health and PROMs are lacking from literature. Inclusion of these additional measures will provide a more comprehensive description of physical behavior of operable NSCLC patients and their clinical relevance for recovery following resection, which might reveal new targets for rehabilitation.

Following this, the primary objective of this study was to characterize daily physical behavior of operable NSCLC patients, from preoperative to six months postoperative using accelerometry. Secondary objective was to explore if physical behavior preoperative and in the first month following surgery is associated with better health outcomes at six months postoperative.

METHODS

Participants and study design

A prospective study was performed at the Netherlands Cancer Institute (NKI), Amsterdam, the Netherlands from July 2012 to July 2014. Ethical approval was obtained (PTC12.0835/P12RQL) and all participants provided written consent. Eligible participants were Dutch speaking adults aged 18 years or older, diagnosed with primary non-small lung cancer (NSCLC) and scheduled for curative lung resection. Participants were identified during the multidisciplinary meeting at the NKI. Participants were excluded if they were unable to walk independently (with or without walking aid), exhibited severe cognitive disorders or emotional instability, suffered from uncontrolled comorbidities, received palliative treatment or recurrence of cancer.

A study information letter was sent to eligible patients, after which patients were contacted by the first author. Patients were measured at four time-points: at baseline (2–4 weeks prior to surgery, t0), and one (t1), three (t2) and six months (t3) after surgery. All patients received standard care at the hospital, which included outpatient appointments with the physician (thoracic surgeon or pulmonologists) (at t0, t1, t2 and t3), and the physiotherapist (at t0 and t1). Measurements were synchronized with standard appointments at the hospital. Structured instruction or education about PA or rehabilitation was not part of standard care.

Primary outcome: physical behavior

A waist-worn accelerometer was used to measure physical behaviors (ProMove 3D, 63 × 96 × 16 mm, 67 g, Inertia Technology, Enschede, The Netherlands, output being ‘integral of the modulus of acceleration per minute’ (IMA) comparable to the study of Bouten et al. [15], and referred to as ‘counts’; for detailed description see [16]). Participants were asked to wear the accelerometer prior to each physician appointment (at t0, t1, t2 and t3) for a minimum of three days during waking hours, excluding time spent bathing or participating in water activities. Instructions to patients also included to perform their normal, daily routine, and not change their physical behavior pattern. Several measures were derived from the accelerometer, reflecting characteristics of physical behavior (Fig. 1). Overall physical activity level (PAL) is the average counts per minute (cpm) of all valid days, calculated from total number of counts divided by the time the accelerometer was worn (i.e. wear time).

Intensity levels were divided in sedentary behavior (SB), light PA (LIPA) and moderate-to-vigorous PA (MVPA). Cutoff values for intensity levels were used as described by Wolvers et al. [14](Fig. 1).

Figure 1 Physical behavior outcome measures calculated from the accelerometer. *Abbreviations:* LIPA, low intensity physical activity; MVPA, moderate to vigorous activity; PAL, physical activity level; pLIPA, prolonged LIPA bouts; pMVPA, prolonged MVPA bouts; pPA, prolonged PA bouts; pSB, prolonged SB bouts; SB, sedentary behavior. Cut points intensity levels: sedentary < 1303 cpm; light PA 1303-< 2588 cpm; MVPA ≥ 2588 cpm.

Bout duration is the percentage of wear time spent in uninterrupted bouts of an intensity level. Time in prolonged SB bouts (pSB) is the total SB time accumulated in uninterrupted bouts of 30 min or longer [17]. Time in prolonged LIPA (pLIPA) and prolonged MVPA (pMVPA) is the total time in LIPA or MVPA accumulated in uninterrupted bouts of 10 min or longer [17]. Time in prolonged PA (pPA) is the total time in PA (i.e. LIPA and MVPA) in uninterrupted bouts of 10 min or longer.

Analysis data accelerometer

Raw IMA-data were processed in Matlab version R2015b (The MathWorks Inc., Boston, MA, USA). Data was scanned for non-wear, using the activity diary if they were available. Non-wear was removed, except when patients reported resting while placing the sensor on the bedside or table in their activity diary. For these cases, the data was maintained and treated as sedentary time. Data were analyzed separately per time-point and averaged across valid days. Due to the explorative nature of this study, a minimum of two days (per time-point) with ≥8 h/day of data were required to be included in the analysis.

Secondary outcomes

We assessed functional capacity using the Six Minute Walking Distance (6MWD), which was performed according to published guidelines [18]. The parcours for the 6MWD measured 10 m x 2.5 m x 10 m x 2.5 m.

With the European Organization for the Research and Treatment of Cancer Questionnaire (EORTC QLQ-C30) we assessed HRQOL over the previous week using the 'physical functioning' (5 items), 'global QOL' (2 items) and 'pain' subscale (2 items) [19]. The EORTC scoring procedures were followed resulting in a composite score ranging from 0 to 100 for each subscale. For the subscales physical functioning and global QOL, higher scores represent higher level of functioning and QOL. For the pain subscale a higher score represents higher level of pain.

Subscales of the Multidimensional Fatigue Inventory (MFI)-20 were used to assess 'general fatigue', 'physical fatigue' and 'reduced activity' [20]. Each subscale contains four items, with scores ranging from 1 to 5 per item. Scores per scale can range from 4 to 20, with higher scores representing higher level of fatigue.

Psychological distress was assessed using the sum score of the Hospital Anxiety and Depression Scale (HADS) [21, 22]. The HADS consists of 14 items. Item scores range from 0 to 3, with higher score indicating higher symptom level. Consequently, the sum score of the HADS may range from 0 to 42, with higher scores representing more distress.

At baseline, socio-demographics were obtained including age, gender, smoking status, marital status, and employment status. We extracted the following clinical information from the patient record: extent and technique of resection, body mass index (BMI), pack years, preoperative lung function (percentage of predicted 1 s forced expiratory volume (FEV1%pred), percentage of predicted diffusing capacity for carbon monoxide (DLCO%pred)), cardiorespiratory fitness (VO2peak), presence of COPD and presence of other comorbidities such as cardiovascular disease, diabetes mellitus, and renal insufficiency.

Statistical analysis

IBM's Statistical Package for the Social Sciences (SPSS, 23.0) was used for the statistical analyses of all data. Descriptive statistics and graphs (PP-Plots and histograms) were used to assess normality of the outcome measures. Continuous variables were expressed as mean with standard deviation (SD) or median with interquartile range (IQR), categorical variables as counts with corresponding percentages.

To present change in physical behavior over time, a mixed-model analyses for repeated measures (normally distributed or transformed variables) or Friedman's ANOVA (non-normally distributed; transformation not successful) was performed with time of measurement (t0-t3) as a within-subjects factor for each outcome separately. Mixed models were estimated by maximum likelihood and a heterogeneous first-order autoregressive structure variance-covariance matrix was used. If significant, the

analyses were followed by a post-hoc pairwise analysis (SIDAK corrected) to test for significant differences between any combination of time of measurement.

To investigate if preoperative and early postoperative physical behavior relates to health outcomes six months postoperative (t3), first Spearman's correlations were calculated between selected physical behavior measures preoperative and health outcomes at six months postoperative (t3), and between physical behavior measures at one month postoperative (t1) and health outcomes at six months postoperative (t3). To limit the number of tests, we calculated the association between the physical behavior measures PAL, SB, pSB, and MVPA, since their relevance in cancer rehabilitation has previously been reported [14]. Second, for pMVPA, patients were classified into three groups based on the international guidelines for PA in cancer survivors, that is a minimum of 150 min of MVPA per week [6]. This was translated to a daily amount of $150/7 = 21$ min per day. Based on the time spent in prolonged bouts in MVPA, patients were classified as 'no MVPA' (no minutes spend in pMVPA); 'some MVPA' (> 0 min/day but < 21 min/day in pMVPA) and 'sufficient MVPA' (≥ 21 min/day in pMVPA). The Jonckheere-Terpstra test was used to examine the relationship between group category at t0 and health outcomes at T3, and between group category at t1 and health outcomes at T3. For all statistical analyses, a significance level of $p < 0.05$ was used.

RESULTS

During the study, 105 patients underwent lung resection for NSCLC in the NKI. Of these patients, 34 (32%) were approached, and twenty-nine consented to participation (Fig. 2). Reasons for non-consent were ‘feeling too emotional’ (n =2), ‘it will be too much’ (n =2), or ‘don’t want to monitor PA at home’ (n = 1).

Figure 2 Flow of participants through the study. *Abbreviations:* 6MWD, six minute walk distance; Insuff., insufficient.

In total, seven patients dropped out during the course of the study, primarily due to recurrence of cancer. Patients who dropped out during the study had comparable baseline characteristics to those who remained in the study.

Table 1 shows the main characteristics of the patients included in at least one of the analyses. Mean age of the patient group was 59 years, and more women than men were included. Most patients lived at home with family, were not employed and ex-smokers. The majority of the group had early stage disease and most underwent lobectomy.

Physical behavior

Twenty-five patients monitored physical behavior at one or more time points during the study, resulting in 256 monitoring days. During analysis, 37 days with less than 480 min of data were removed. Median wear time (per time point) of included days varied between 13 h/day and 14 h/day. Twenty-three patients had valid data for at least one of the time points; 10 (43%), 16 (70%), and 21 (91%) patients had valid physical behavior data at four, three, and two time point(s), respectively.

PAL and time spent in SB, LIPA, MVPA and pPA all showed significant changes over time (Table 2). Overall, patients tended to accumulate more sedentary time and less time being physically active, at one month postoperative (t1) compared to baseline (t0). At one-month postoperative, median percentage of time in SB and pSB increased to 80% and 44% respectively (compared to 74% and 37% at t0), while median percentage of time in MVPA and pPA both dropped just to below 5% (compared to 8% and 9% at t0) (see Table 2 and Fig. 3). At three months (t2) and six months (t3) following surgery, PAL and time spent in SB, LIPA, MVPA and pPA gradually improved, almost reaching preoperative levels at t3. Time spent in pSB, pLIPA and pMVPA showed no significant changes over time.

At baseline, four patients (22%) spent more than 21 min/day in pMVPA. Postoperative, four (25%), six (33%) and five patients (28%) spent more than 21 min/day in pMVPA at t1, t2 and t3 respectively.

Table 1 Sample characteristics at baseline.

	TOTAL (N=23)
	Mean $\pm$ SD / Median [IQR]
Age, years	59 $\pm$ 10
BMI	26 [24-28]
VO ₂ peak, ml/min/kg (n=17)	23.0 $\pm$ 4.2
Lung function	
FEV ₁ (L)	2.8 $\pm$ 0.8
FEV1%pred	99 $\pm$ 18
DLCO%pred	81 $\pm$ 12
Pack years	30 [14-40]
	N (%)
Gender, female	13 (57)
Social situation	
Home alone independent	6 (26)
Home with family	17 (74)
Employment status	
Working (payed)	5 (22)
Temporary/permanent sick leave	6 (26)
Home duties	1 (4)
Not employed/retired	11 (48)
Smoking status, n (%)	
Never smoker	3 (13)
Current smoker	3 (13)
Ex-smoker	17 (74)
Comorbidities	
None	5 (22)
1	5 (22)
≥ 2	13 (57)
Previous malignancies	5 (22)
Cancer diagnosis	
Squamous cell carcinoma	3 (13)
Adenocarcinoma	9 (39)
Large cell carcinoma	3 (13)
Other	5 (22)
Missing	2 (9)
Stage	
Stage I	11 (52)
Stage II	6 (24)
Stage III	4 (16)
Stage IV	1 (4)
Missing	1 (4)
Type of surgery	
Segmentectomy	2 (12)
Lobectomy	20 (84)
No resection	1 (4)
Surgery technique	
Thoracotomy	15 (65)
VATS	8 (35)
Neo-adjuvant CCRT	5 (22)
Adjuvant chemotherapy	4 (17)

Abbreviations: BMI, body mass index; CCRT, concurrent chemoradiotherapy; DLCO%pred, percentage of predicted diffusing capacity for carbon monoxide; FEV₁, 1 second forced expiratory volume; FEV1%pred, percentage of predicted 1 second forced expiratory volume; IQR, interquartile range; kg, kilogram; L, liter; min, minute; ml, milliliter; n, number; SD, standard deviation; VATS, video-assisted thoracoscopic surgery; VO₂peak, peak oxygen consumption.

Table 2 Physical behavior measures over time reported as median [interquartile range].

	Preoperative (t0)	1 month post (t1)	3 months post (t2)	6 months post (t3)	p-value
Physical behavior					
PAL [cpm]	897 [733-1169]	677 [544-859]	799 [736-1042]	782 [680-1059]	.005 ^{a,b,d}
Time in					
SB [%]	74 [67-79]	80 [75-87]	80 [69-83]	75 [70-81]	.011 ^{a,b,e}
LIPA [%]	16 [14-22]	12 [10-17]	13 [11-20]	19 [12-21]	.015 ^{a,b,f}
MVPA [%]	8 [6-11]	5 [2-9]	6 [5-10]	7 [5-12]	.031 ^{a,b}
Time in prolonged bouts of					
SB [%]	37 [24-45]	44 [34-56]	40 [23-47]	34 [23-45]	.057 ^{a,b}
LIPA [%]	1 [0-1]	0 [0-1]	0 [0-0]	1 [0-2]	.177 ^c
MVPA [%]	1 [0-2]	1 [0-3]	1 [0-3]	1 [0-4]	.973 ^c
PA [%]	9 [5-14]	5 [1-9]	6 [4-8]	6 [4-12]	.021 ^c

^a p-value based on transformed variables. ^b p-value of the mixed models analysis with time of measurement as within group factor (restricted maximum likelihood and a heterogeneous first-order autoregressive structure). ^c p-value from Friedman's ANOVA. Significant post-hoc comparisons (SIDAKcorrected): ^d t1-t0: p=.004; ^e t0-t1: p=.022; ^f t0-t1: p=.040.

Abbreviations: cpm, counts per minute; MVPA, moderate-to-vigorous physical activity; PAL, physical activity level; SB, sedentary behavior.

Individual patterns of physical behavior

On an individual level, we observed high variability within and between patients regarding the distribution of time spent active and sedentary and the patterns of change in physical behavior over time (Fig. 3). That is, at any one time, patients could be in different categories for different physical behavior outcomes. For example, some patients exhibited high levels of sedentary behavior together with low levels of physical activity, while others showed low levels of sedentary behavior but also low physical activity. Moreover, change patterns of physical behavior outcomes over time could occur in different combinations, for example increasing SB in combination with decreasing MVPA, but also less obvious combinations such as increasing SB together with increasing pPA or increase of total sedentary behavior (SB) together with a decrease of time spent in prolonged SB (pSB).

Relation between physical behavior at t0/t1 and health outcomes at t3

Patients experienced worsening of self-reported physical function, pain and general fatigue between t0 and t1. Postoperative, measures gradually improved again (see Table 3).

The Jonckheere-Terpstra test for ordered alternatives showed no difference in patients in higher pMVPA category (from 'no pMVPA', 'some pMVPA' to 'sufficient pMVPA') at t0 and health outcomes at t3. Contrary, patients in higher pMVPA category at t1

scored significantly better on 6MWD ($T_{JT}=63.000$, $z=2.967$, $p=.003$), HRQOL physical function ($T_{JT}=63.500$, $z=3.074$, $p=.002$), distress ($T_{JT}=16.000$, $z=-2.114$, $p=.034$), physical fatigue ($T_{JT}=15.500$, $z=-2.172$, $p=.030$) and reduced activity ($T_{JT}=16.000$, $z=-2.118$, $p=.034$), at t3.

For the other physical behavior outcome measures (i.e. PAL, SB, MVPA, pSB and pPA), only pSB at t0 showed moderate correlations with pain score at t3 ($r=0.47$). At t1, moderate correlations were found between: PAL and HRQOL (physical functioning, $r=0.50$; general QOL, $r=0.42$), MVPA and 6MWD ($r=0.48$) and HRQOL (physical function, $r=0.42$), pSB and HRQOL (physical function ($r=-0.49$). However, none of these correlations were significant (table included in Supplementary Materials).

Table 3 Health outcome measures over time reported as median [interquartile range] or mean $\pm$ standard deviation.

	Preoperative (t0)	1 month post (t1)	3 months post (t2)	6 months post (t3)
Health outcomes				
6MWD, metres	521 $\pm$ 78	444 $\pm$ 118	515 $\pm$ 87	537 $\pm$ 84
EORTC-C30				
Physical function	87 [80-95]	67 [60-83]	80 [73-93]	93 [77-93]
Global QOL	71 $\pm$ 19	60 $\pm$ 25	69 $\pm$ 21	77 $\pm$ 16
Pain	8 [0-33]	33 [17-54]	17 [0-50]	17 [0-33]
MFI				
General Fatigue	11 $\pm$ 5	14 $\pm$ 5	12 $\pm$ 4	10 $\pm$ 5
Physical fatigue	10 $\pm$ 4	13 $\pm$ 5	12 $\pm$ 4	10 $\pm$ 5
Reduced Activity	11 $\pm$ 5	14 $\pm$ 4	11 $\pm$ 5	10 $\pm$ 5
Distress (HADS)	8 [3-13]	7 [4-12]	7 [4-17]	6 [3-8]

Abbreviations: 6MWD, six minute walk distance; EORTC-C30, European Organization for the Research and Treatment of Cancer questionnaire; HADS, Hospital Anxiety and Depression Scale; MFI, Multidimensional Fatigue Inventory; QOL, quality of life.

Figure 3 Physical behavior patterns of NSCLC patients from preoperative to 6 months postoperative. The same color represents the same patient in each graph. Dotted black line is the median for that time point.

Abbreviations: mth, month; MVPA, moderate-to-vigorous physical activity; pMVPA, prolonged MVPA bouts; pPA, prolonged physical activity bouts; pSB, prolonged SB bouts; post, postoperative; SB, sedentary behavior.

DISCUSSION

This study is the first, to our knowledge, that explored physical behavior patterns in detail from preoperative to six months postoperative in resected primary NSCLC patients. In line with previous research [12], lung resection had significant negative impact on time spent in PA and SB. One month postoperative, patients spent on average more than 80% of the day in sedentary behavior, with almost half of this sedentary time accumulated in bouts with duration longer than 30 min. In the following months, time spent in SB declined, and PA levels recovered almost to preoperative levels. So

far, only Granger and colleagues reported longitudinal PA levels (as steps per day) in NSCLC patients from pretreatment (baseline) until six months following baseline [9]. In contrast to our study, they found no change in steps per day over time as compared to baseline. However, they included also non-surgical patients (50% of their sample) of which some received palliative treatment. Although non-surgical treatment modalities affect physical behavior patterns, the observed changes, both decline and recovery, may be less dramatic than following surgery [23].

In our sample, patients who spent more time in MVPA in bouts of 10 min or longer in the first period following surgery had better functional performance, self-reported physical function, psychological wellbeing and fatigue six months postoperative. These findings are a first indication of a beneficial effect of adequate physical behavior following surgery on postoperative recovery and advocate further research and evaluation of interventions that improve physical behavior in this early postoperative period. If we want to intervene and improve physical behavior, then when should we intervene and what pattern of physical behavior should we aim for as to promote health? Regarding the timing of intervention, research suggests that pre- and postoperative exercise training both have advantages on health and recovery [24-27]. Preoperative exercise training seems promising to optimize physical fitness prior to surgery, which then might result in better outcomes early following surgery, such as reduced length of stay or decreased chance of complications [27]. However, evidence from a recent RCT demonstrated no long-term beneficial effect of preoperative exercise on recovery and health outcomes following surgery [28]. In contrast, postoperative exercise training may effectively improve postoperative functional recovery [24, 25, 29]. This supports the findings of our study, which show that physical behavior prior to surgery does not relate with health-related outcomes and PROMs at six months postoperative, while time spent in prolonged bouts of MVPA in the first month postoperative does. Therefore, to improve health-related outcomes and PROMs following resection, promotion of physical behavior in the early period postoperative might be more effective than interventions preoperative. Next to that, feasibility of preoperative interventions might be low due to the often small time window between diagnosis and actual surgery [30]. With regard to the desirable pattern of physical behavior, international guidelines recommend a minimum of 150 min per week of MVPA, preferably in bouts of minimal 10 consecutive minutes, for health promotion [6]. In line with these guidelines, our results show better health outcome at six months postoperative for patients that do perform some or sufficient MVPA in prolonged bouts compared to those patients who spent no time in prolonged MVPA early following surgery. However, only a minority of NSCLC patients meet these guidelines of MVPA postoperative [9, 31]. Therefore, instead of using the guideline as a fixed rule, which is possibly unrealistic and

demotivating for a majority of NSCLC patients, we advise to tailor physical behavior goals in the early postoperative period based on previous and current physical behavior patterns, preferences, and physical capabilities. Tailoring is especially relevant given the considerable variability in activity patterns between operable NSCLC patients. Some of the patients in our study spent relatively much time in moderate-to-vigorous activity, while at the same time accumulating considerable time in prolonged bouts of sedentary behavior; or vice versa. This supports the notion of individual variability, and emphasizes the need for so-called physical behavior ‘profiling’ to facilitate tailored goal setting in interventions that target change in physical behavior [14].

Tailored goal setting through physical behavior profiling is a promising new approach in cancer rehabilitation that acknowledges the individual variability in physical behavior and actually uses this variability for optimizing behavioral interventions [14, 32]. For operable NSCLC patients, this approach will require objective monitoring of physical behavior measures both prior to and postoperative, as to identify patients with disadvantageous physical behavior profiles. The physical behavior profile in combination with factors that cause this physical behavior profile can then form the basis for a tailored approach to improve physical behavior patterns. As a result, the actual intervention might differ between patients, varying from increasing time spent in prolonged bouts of MVPA in one patient, or breaking up prolonged bouts of sedentary behavior in the other, or starting with removing existing barriers for physical behavior change [33]. With increasing awareness of the complexity of physical behavior and how we might exploit this complexity for individual benefit, and given the recent advancements in technology, physical behavior could be a promising functional, patient-centered outcome in the treatment of operable NSCLC patients.

Nevertheless, further research is needed to live up to this promise. The present study was limited by a combination of small sample size and missing values at the different measurement occasions. Non-adherence to study protocols is a well-known problem in patients diagnosed with lung cancer, due to poor prognosis and high symptom burden [9]. It is possible that patients with worse physical behavior and worse health outcome were not included or non-compliant to the monitoring protocol, resulting in a bias of the results, such as over estimation of physical behavior and health outcomes. Also, because of the explorative nature of the study, we did not control for confounders that might influence both physical behavior early following surgery and better health outcomes at six months postoperative. Possible confounders might include a combination of personal, disease and treatment related factors, such as prior experience with exercising, age, comorbidities, smoking, surgery extent, complications, or (neo-) adjuvant treatment [2, 12, 13, 34-37].

Therefore, future longitudinal studies should confirm the existence of physical behavior profiles through objective monitoring of physical behavior, classify “problematic” physical behavior profiles, and identify predictors for these profiles. Second, experimental studies are needed that evaluate the acceptability and effect of tailored physical behavior interventions on both health outcomes and physical behavior on the short and long term, and how possible confounders may alter this effect in operable NSCLC patients.

CONCLUSION

Our study shows that, on average, curative lung resection has a negative impact on physical behavior. Patients who were more active in the first month following surgery reported better health outcomes six months postoperative. Due to the considerable variability in activity patterns observed between operable NSCLC patients, we would emphasize the need for so-called physical behavior ‘profiling’ through detailed monitoring of physical behavior to facilitate tailored goal setting in interventions that target change in physical behavior.

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SUPPLEMENTARY MATERIAL

Table A Moderate correlations ($r > .40$) between physical behavior measures at t0 and t1 and health outcomes at t3 (n=15).

Physical behavior measure t0	Health outcome t3	Spearman's rho	p-value
% Time in pSB	EORTC-pain	0.47	.079
Physical behavior measure t1	Health outcome t3	Spearman's rho	p-value
PAL	EORTC-PF	0.50	.057
	EORTC-QL	0.42	.124
% Time in MVPA	6MWD	0.48	.074
	EORTC-PF	0.42	.120
% Time in pSB	EORTC-PF	-0.49	.066

Abbreviations: t0, time two weeks preoperative; t1, time one month postoperative; t3, time six months postoperative; 6MWD, six minute walk distance; EORTC-PF, subscale physical functioning of the EORTC-C30; EORTC-QL, subscale general quality of life of the EORTC-C30; EORTC-pain, subscale pain of the EORTC-C30; HADS, Hospital Anxiety and Depression Scale; LIPA, low intensity physical activity; MVPA, moderate-to-vigorous physical activity; PAL, Physical activity level; pSB, prolonged SB bouts; SB, sedentary behavior.

4

CO-CREATION OF AN ICT-SUPPORTED CANCER REHABILITATION APPLICATION FOR RESECTED LUNG CANCER SURVIVORS: DESIGN AND EVALUATION

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ABSTRACT

Background: Lung cancer (LC) patients experience high symptom burden and significant decline of physical fitness and quality of life following lung resection. Good quality of survivorship care post-surgery is essential to optimize recovery and prevent unscheduled healthcare use. The use of Information and Communication Technology (ICT) can improve post-surgery care, as it enables frequent monitoring of health status in daily life, provides timely and personalized feedback to patients and professionals, and improves accessibility to rehabilitation programs. Despite its promises, implementation of telehealthcare applications is challenging, often hampered by non-acceptance of the developed service by its end-users. A promising approach is to involve the end-users early and continuously during the developmental process through a so-called user-centered design approach. The aim of this article is to report on this process of co-creation and evaluation of a multimodal ICT-supported cancer rehabilitation program with and for lung cancer patients treated with lung resection and their healthcare professionals (HCPs).

Methods: A user-centered design approach was used. Through semi-structured interviews (n = 10 LC patients and 6 HCPs), focus groups (n = 5 HCPs), and scenarios (n = 5 HCPs), user needs and requirements were elicited. Semi-structured interviews and the System Usability Scale (SUS) were used to evaluate usability of the telehealthcare application with 7 LC patients and 10 HCPs.

Results: The developed application consists of: 1) self-monitoring of symptoms and physical activity using on-body sensors and a smartphone, and 2) a web based physical exercise program. 71% of LC patients and 78% of HCPs were willing to use the application as part of lung cancer treatment. Accessibility of data via electronic patient records was essential for HCPs. LC patients regarded a positive attitude of the HCP towards the application essential. Overall, the usability (SUS median score = 70, range 35-95) was rated acceptable.

Conclusions: A telehealthcare application that facilitates symptom monitoring and physical fitness training is considered a useful tool to further improve recovery following surgery of resected lung cancer (LC) patients. Involvement of end users in the design process appears to be necessary to optimize chances of adoption, compliance and implementation of telemedicine.

BACKGROUND

Lung cancer is the most commonly diagnosed malignancy among adults worldwide, as well as the leading cause of cancer-related death [1]. Approximately 80% of lung cancer patients will be diagnosed with non-small cell lung cancer (NSCLC), and around 25% will present with early-stage, operable disease [2]. Curative lung resection is the preferred treatment for early-stage NSCLC [3], but is associated with a considerable symptom burden such as pain and fatigue, as well as decay of lung function, cardiorespiratory fitness, and Quality of Life (QOL) [4-8]. After hospital discharge, monitoring of self-reported symptoms and disability encountered in daily life is limited to a few, planned consultations. It is reported that clinicians systematically underestimate patients' symptoms, increasing the risk that crucial symptoms are overlooked [9]. In addition, NSCLC patients report high levels of supportive care needs [10], and often feel insecure about their health status and do not know what to do to improve their recovery [11]. These issues call for the development of new methods that enable better (objective) monitoring of the patients, as well as tools that increase the level of self-management of the patient in order to optimize post-surgery recovery of health status in NSCLC patients.

A promising method to improve survivorship care is the use of telehealthcare. Telehealthcare is 'the provision of personalized healthcare by a healthcare professional over a distance using Information and Communication Technology (ICT)' [12]. It is considered instrumental in maintaining good-quality patient care in the shift from inpatient to ambulatory care [13]. Next to that, telehealthcare has several advantages supplemental to face-to-face treatment. For example, it facilitates frequent monitoring of health status and patient-reported outcome measures, and can provide both the patient and healthcare professional with timely and personalized feedback [14-16]. It also supports patients to incorporate behavioral changes directly into daily life, improving their health-related self-management skills. The potential of telehealthcare applications to improve cancer care throughout the entire continuum - including supportive care - has been recognized [17, 18] and various studies showed that telehealthcare applications are acceptable for patients and considered clinically safe [19].

However, the number of tailored applications for resected NSCLC patients is limited, with as far as we know, only two single-component applications reported: a symptom management application [20], and a 6-week light-intensity, home-based exercise program using the Wii Plus [21, 22]. Each of these focusses on a single aspect of support, namely either symptom control or physical fitness. Considering the high number and complexity of supportive care needs, it could be expected that a

multimodal intervention would better meet the needs of NSCLC patients.

The primary objective of this study was 1) to develop a multimodal telehealthcare application that aimed at improving post-surgery rehabilitation and physical activity, in close cooperation with resected NSCLC survivors and their healthcare professionals (HCPs), and 2) to evaluate its usability. Through close involvement of the target users we aimed to explore potential new areas of care for lung cancer patients – from both an HCP and patient perspective – that might benefit from ICT-supported care. Next to that, we expected that this close cooperation would uncover requirements crucial for adoption early on in the project as to promote adoption and implementation on the long term.

METHODS

A promising approach, proven to successfully fit ICT- supported services to users’ requirements, is to involve the end-users early and frequently during the developmental process through a user-centered design (UCD) approach [23]. This is an iterative, cyclical process during which design and evaluation phases are alternated. In this way, systems and services can be developed step by step, so that changes in technology and work process can evolve together, and unforeseen challenges can be easily anticipated in future development steps. The followed process is visualized in Figure 1.

Figure 1 Design approach for the co-creation of our telehealthcare application. The people-figures at the various steps indicate that target users were involved. The steps written in grey indicate future steps in our study

User needs and requirements

The first aim was to gain insight into the needs and requirements of HCPs and NSCLC patients after resection, regarding the content, the expected benefit on clinical outcome, and contextual aspects of use of a telehealthcare application designed to improve rehabilitation and stimulate physical exercise.

Semi-structured interviews were held with HCPs and NSCLC patients based on the framework of the Unified Theory of Acceptance and Use of Technology (UTAUT), since UTAUT has been proven to capture the users' intentions to accept ICT [24]. First, HCPs from the professional network of the authors MW and MV were approached by email for participation. In turn, participating HCPs were asked for other potential participants, both HCPs and NSCLC patients. Resected NSCLC patients were recruited via participating HCPs and via advertisement on the website of the Dutch patient association for lung cancer. The interviews were performed by the first author (PhD student, human movement scientist and occupational therapist), and lasted between 60 and 90 min. Prior to the interviews the researcher did not have any relationship with the participants, except for one HCP (i.e., the fifth author MW). Interviews took place at the patients' home or at the workplace of the HCPs. To familiarize participants with telehealthcare and its wide range of possibilities [18, 25], mock-ups were shown with potential functionalities: (1) tailored information about disease and treatment, (2) tailored lifestyle information, (3) ambulant monitoring of health status, (4) web based tailored exercise program, (5) contact with professional by means of ICT (e.g., e-consultation), and (6) contact with fellow lung cancer patients. The content of the mock-ups was based on existing applications that are already available for other chronic diseased populations such as COPD [26, 27]. During the interview needs and requirements regarding content (UTAUT component 'performance expectancy'), usability/ease of use ('effort expectancy'), influence of important others on use ('social influence'), facilitators and barriers for use ('facilitating conditions'), and intention to use the service were assessed.

Subsequently focus groups were held with HCPs in which the functionalities derived from the interviews were discussed, and specific requirements for both the technology and implementation in every day practice were defined in more detail. All HCPs approached for the interviews were contacted again for participation in the focus groups. Additionally, HCPs from the Netherlands Cancer Institute (NKI), a designated cancer center in the Netherlands, known to be involved in the post-surgery care for lung cancer patients were asked for participation by the first author. The focus groups were performed by the authors JT, TT (PhD student, background in biomedical engineering) and MD (PhD, human movement scientist). The focus groups were audio recorded and transcribed verbatim with participants' permission. Data were arranged in themes using the UTAUT components by authors JT and MD.

As a third step, a scenario was described, validating the requirements drafted from the interviews and focus groups. Scenarios are stories describing the activities, in detail, of persons when using the envisioned ICT application with a specific goal and

within a specific context [28, 29]. The scenario described: 1) a NSCLC patient using the telehealthcare application as part of her lung cancer treatment and recovery process, and 2) a visualization of the measurement protocol for homebased symptom monitoring. The written scenario was sent by email to ten HCPs employed at the NKI who are involved in the post-surgery care for lung cancer patients. Professionals were instructed to read the scenario in detail and to write comments, both positive and negative, as tracked changes in the text of the scenario. Comments were sent back to the first author via email.

Prototype design

Authors JT and TT selected relevant requirements from the interviews, focus groups and scenario comments. Authors MV and MD validated the selection. Considerations for requirement selection included (in order of importance): 1) context of use of the application, including aim for which the application will be used, overlap or integration with existing services and people involved, 2) technical feasibility and time available to realize the requirement, 3) the number of participants who mentioned it, and 4) factors influencing future dissemination possibilities in multiple institutions and other cancer diagnoses. As an example for our study, the NKI already hosted an interactive electronic patient record (EPR) including tailored information [30]. This contextual information was taken into account during development to optimize adoption and implementation of the application in the NKI. From the selected requirements, technical requirements were derived after which the first prototype was developed.

Evaluation of usability

Participants

HCPs from various disciplines and healthcare institutions were recruited, using the professional network of the authors MS, MW, and MV. Colleagues of participating HCPs were also asked for participation. NSCLC patients were recruited via HCPs who participated in this evaluation. Included NSCLC patients were 18 years or older, treated with lung resection within the previous two years (with or without adjuvant treatment), and had no recurrence of cancer at enrolment. Only HCPs who treated resected NSCLC patients at the moment of enrolment, were included.

Procedures

The interviews were performed by the first author at the patients' home and at the HCPs workplace. Each session lasted between 30 and 60 min. First, the aim and procedure of the session were explained after which the participants signed informed consent. Next, participants received a short introduction of the aim and content of

the telehealthcare application, together with a user manual of the modules. Then they interacted with the modules by completing several predetermined tasks while verbalizing their thoughts out loud ('thinking-aloud' method) [31]. After completion, semi-structured interviews were performed to evaluate the content (UTAUT component 'performance expectancy'), interface (visual design), ease of use ('effort expectancy'), and intention to use the modules. All interviews were audio-recorded and transcribed verbatim with participants' permission. Lastly, the participant completed the System Usability Scale (SUS) questionnaire. The SUS consists of ten statements to which the participant can agree or disagree on a 5-point scale [32]. All the responses are summed and multiplied with 2.5, resulting in a score between 0 and 100, with a higher score meaning better usability. Cut-off scores of ≤ 50 , 51–69, and ≥ 70 were considered 'not acceptable', 'OK' (i.e., 'moderately acceptable') and 'acceptable' usability, respectively as suggested by Bangor et al. [32].

Data-analysis

Comments on usability issues were extracted from the transcripts and classified by authors JT and MD through an inductive approach using the following classifications [33]:

- content & information: missing content such as relevant outcome variables, exercises, functionalities or written information.
- navigation & structure: problems with navigating through the portals. For example, location where information is located on the portal.
- design & presentation: representation of the available data and information. For example, color use, graphs, amount of text on a page or smartphone.
- ambulant devices: remarks regarding the use of the sensors (that is smartphone, activity monitor, heart rate sensor and oxygen saturation sensor).

In this early phase of evaluation the focus is on the reported points of improvements only, with the aim to generate redesign input [34]. Therefore, only the points of improvement are reported in this article. These comments were further classified as being critical, serious, or minor using the following definitions [34]:

- A critical problem prevented participants from completing tasks or was reported by all participants.
- A serious problem severely increased task completion time or was reported by $\geq 50\%$ of the participants. However, a serious problem did not prevent a participant from completing the task eventually.
- A minor problem increased task completion time slightly or was reported by $< 50\%$ of participants.

RESULTS

User needs and requirements

Semi-structured interviews

Ten NSCLC patients (mean age $\pm$ sd = 62 ± 11 years, 70% female, mean $\pm$ sd time since resection = 6 ± 3 months) treated with lung resection and six HCPs involved in post-surgery care of NSCLC patients (2 pulmonary rehabilitation specialists, 1 pulmonologist, 1 thoracic surgeon, 1 physiotherapist, 1 nurse practitioner; 50% female) from four different hospitals participated in the interviews.

All participants expected that a telehealthcare application would be of clinical benefit for resected NSCLC cancer patients. In particular, HCPs valued the application as a method to improve quality of current care, while patients considered it as a way to decrease their insecurity about experienced symptoms, their recovery, and healthy behavior.

"That fear [for recurrence], if you can put an end to that by surveillance, I would do anything. Even if it is not OK, that you know this in time...get a hint" (Patient 2, female, 59 years).

"I do not need to measure it [lung capacity] every day, but once a month, something like that. Especially when regular visits to the lung physician have ended, then I would like to know. To be reassured" (Patient 7, male, 48 years).

Other expected benefits were improved patient-HCP communication - since HCPs will have better insight in relevant issues - and improved accessibility to care provided by a specialized cancer center while being at home.

Figure 2 summarizes the functionalities that were regarded useful by the participants to improve survivorship care following lung resection. The majority of both patients and professionals considered ambulant monitoring of health status, tailored information about disease, treatment and lifestyle, and a web based tailored exercise program of added value. Additional ("other") functionalities mentioned were psychological education ($n = 4$), support for family or other caregivers ($n = 1$), and treatment of pain ($n = 1$). Although HCPs agreed that fellow patient contact might be beneficial, they voiced concerns regarding hosting such a service, since this would mean continuous moderation by a HCP to check statements posted by patients. The physicians also reported a negative attitude towards ICT-supported contact between HCPs and patients. They expected that the costs in time and money outweigh the added value

if patients are able to contact them by email, chat or web-based consultation. In contrast, the physiotherapist and nurse practitioner considered e-consultation as an opportunity to improve quick and easy access to the professional when needed. For patients, a positive attitude of the HCPs towards the service, as well as feedback from the HCP on results were considered essential to motivate use and compliance.

Figure 2 Functionalities for the telehealthcare application reported by resected LC patients and HCPs. Red bars = resected LC patients (n=10); blue bars = healthcare professionals (n=6).
Abbreviations: HCP = healthcare professionals

“That [the attitude of the HCP] will be important. If the physician isn’t motivated, they will not use it, and they will not motivate us, if they aren’t enthusiastic.” (Patient 3, female, 58 years).

Use of smartphones and computers were seen as barriers. However, this could be solved by good usability of the service and adequate instruction. All patients reported willingness to wear monitoring devices and complete questionnaires, as long as this would not restrict daily functioning and would be of clinical value for their HCP. For HCPs the most important barrier mentioned was the limited time available for preparation and patient consultation.

“We only have 10 minutes per patient. I am already lucky when I have time to consult the medical record of the next patient. If I have to log on in advance as well... I can’t imagine doing that. That would be too time-consuming” (pulmonologist, female).

“You have to connect with the electronic patient record, so you can consult all

information at once. If you have to switch between systems during a patient consult, that doesn't work very well" (thoracic surgeon, male).

Therefore, integration of the service with existing electronic patient records, as well as adequate summary of the measured outcome parameters into a coherent overview were regarded critical and were further defined during the focus groups.

Focus groups

Five HCPs (thoracic surgeon, pulmonologist, two physiotherapists, nurse; 60% female; all employed at the NKI) participated in the focus groups. The HCPs emphasized the importance of a flexible, modular system, that allows for quick and easy adjustment to various patients and patient groups. HCPs selected three main treatment modules: ambulant symptom monitoring, a web-based exercise program, and tailored information on disease and treatment. Since tailored information on disease, treatment and an active lifestyle were already available as part of the EPR in the NKI [30], this module was not developed further as part of our telehealthcare application. The content of the other two selected modules was discussed and defined as follows:

- Ambulant symptom monitoring aims to provide insight in the rate of recovery after surgery, by monitoring self-reported symptoms and physiological parameters at home and over time. For this, monitoring should integrate self-reported symptoms (pain, dyspnea and fatigue) with physiological parameters (heart rate and oxygen saturation).
- The web-based exercise module should enable the patients to recondition at home using a personalized set of exercises, which will be remotely supervised. Physiotherapists need to be able to easily select a specific set of exercises suited for resected lung cancer patients, and adapt training level and program from a distance.

Scenario evaluation

Five HCPs provided feedback on the written scenario; a rehabilitation physician, a thoracic surgeon, two physiotherapists, and a nurse. All were optimistic about the telehealthcare application as described in the scenario, and expected that it would benefit recovery following lung resection. The feedback given by the professionals primarily concerned implementation issues. For example, one of the professionals questioned the feasibility of ambulant monitoring in this population:

"I find this a good idea. However, I believe this [use of the application] comprises too much 'activities', especially in such a pre-post-surgery trajectory. I am curious about its

feasibility” (rehabilitation specialist, male).

No specific comments were given on the technology described in the scenario.

Table 1 Requirements for the telehealthcare service reported by LC patients and HCPs
The requirements reported in this table are summarized from the interviews, focus groups and scenario evaluation

GENERAL REQUIREMENTS
<p>General service requirements</p> <ul style="list-style-type: none"> • Integration with existing (hospital) electronic patient records • Flexible service to facilitate individual tailoring • User-friendly for (elderly) patients and HCPs • Helpdesk for ICT-related problems
AMBULANT MONITORING
<p>Monitoring of recovery, perceived symptoms and physical activity</p> <ul style="list-style-type: none"> • High mobility to facilitate independent and home-based use by an elderly population without restricting daily activities • Connect and disconnect sensors on patients' demands • Parameters: physiological, physical activity, weight, symptoms, pain medication use, experienced QOL and daily disability.
WEB BASED EXERCISE
<p>Promote physical activity and improve physical fitness pre- and post-surgery</p> <ul style="list-style-type: none"> • Quick and easy selection of exercises and weekly program • Minimally once face-to-face contact with healthcare professional • Supervised and supported by healthcare professionals (from a distance) • Individually tailored based on patient-reported difficulty of performance of exercises
DATA ACCESS AND REPRESENTATION
<p>Facilitate adequate data access and interpretation</p> <ul style="list-style-type: none"> • Integration of outcome parameters to facilitate interpretation • Summary of most relevant outcome parameters at top of page • Data available to HCPs prior to planned consultations • Pre-surgery measures as baseline to compare post-surgery recovery

Application requirements

A summary of the selected requirements is given in Table 1. These application requirements were used for the development of the first working prototype of the telehealthcare application.

Prototype design

The telehealthcare application is a modular system, consisting of two treatment modules. For the first evaluations, the modules will run independent from each other. The modules run from the Continuous Care and Coaching Platform ("C3PO"), hosted at the research institute [35].

Monitoring system

The monitoring module is a combined system consisting of an Android smartphone application and an internet web portal accessible via internet. The monitoring system of the patient consists of an android smartphone and three on-body sensors, i.e., accelerometer, heart rate sensor and an oxygen saturation sensor. The sensors transmit the measurement data wirelessly to the smartphone over a Bluetooth connection. The smartphone stores the data and transmits it to the C3PO server - using a secure connection - at set time intervals. The smartphone is used as input device for answering questions about dyspnea, fatigue, pain, medication use and type of activity performed. Once a week the weight of the patient is asked as input. When connection with a sensor is lost or the data are of non-acceptable quality, the smartphone will give instructions on how to improve data quality. To facilitate integration of the symptom scores with physiological parameters, a predefined monitoring protocol is used. Figure 3 describes an example of the monitoring protocol established with HCPs from the NKI. The gathered data are summarized into graphs, combining symptoms with activity intensity. The data are accessible for both patients and HCPs via a web portal. The web portal is integrated with existing EPRs at the hospital using a single sign on, to improve insight in the change of health status and recovery process. On the portal, the graphs most relevant for clinical care are shown first and can be viewed on one page. To increase security, no personal information is stored in the C3PO platform that can directly link the data with a user (e.g., no name, social security number or address information). In the C3PO platform users are identified by a system-id and patient-id. Only within the EPR, accessible within the hospital, the system can link these id's with the real user.

Figure 3 Example monitoring protocol for monitoring health status and recovery in operable lung cancer patients.

Abbreviations: SpO₂ = blood oxygen saturation.

Web-based exercise module

The web-based exercise module consists of a patient portal and a professional portal, both accessible through the internet. The starting point of development was an existing web-based exercise module, developed and validated as part of the CoCo portal for COPD patients [36]. In close cooperation with physiotherapists of the NKI, the content of the existing web portal was adapted based on selected requirements and exercise protocol deemed relevant for NSCLC patients. The portal is a website hosted at a server at the research center. The physiotherapist manually selects relevant exercises for the patient from a predefined set. Exercises and exercise intensity are chosen based on the face-to-face intake. The training program is aimed at maintaining or improving overall physical fitness. To minimize the time needed for exercise selection the therapist can define a training level from 0 (easy) to 5 (hard) which results in a pre-selection of exercises corresponding to this training level. Each exercise is illustrated by a movie with spoken instructions, and supported by written text (Fig. 4). The patient can access the training program online via the patient portal, and perform the exercises independently at home. The patient reports the number of exercises performed, the number of exercises successfully completed, and the experienced difficulty of the exercise on a scale from 0 (not difficult at all) to 10 (extremely difficult). After completion of an exercise, patients are asked to indicate whether intensity or difficulty for that exercise could be higher in the training program for the next 4 weeks. This information is summarized in a feedback report available to both the therapist and

the patient. Based on this report, the therapist will adjust the training level and select relevant exercises each month. When needed, the patient can select an “emergency” button at the web portal, which results in a standardized email sent to the responsible professional with instructions for the HCP to contact the patient.

Figure 4 Screenshot of the web-based exercise module

Usability

Seven resected NSCLC survivors (mean $\pm$ sd age = 64 ± 9 ; 57% female; mean $\pm$ sd time since diagnosis = 9 ± 7 months), and 10 HCPs (6 physiotherapists, 2 thoracic surgeons, 1 pulmonologist, 1 oncology nurse; 40% female) from two different hospitals participated in the usability study.

System usability score

Based on the defined cut-off scores for the SUS, moderate to high acceptable usability scores were given for the symptom monitoring module (median: 69; range patients 68-95; range HCPs 63-78). For the web-based exercise module usability was more variable, ranging from non-acceptable ($n = 4$) to acceptable ($n = 5$) (median: 70; range patients: 35-80; range HCPs: 45-80).

Interviews

All participants voiced positive intentions to use the symptom monitoring module, while only half of participants felt this way about the web-based exercise module. In total, 75 usability issues were identified; of which 10 were critical, 25 serious, and 40 were minor issues. HCPs reported 63% of these issues. The issues critical for efficient use and long-term adoption will be reported here.

Symptom monitoring

Design & Presentation – 21 (4 critical) usability issues were reported. Both HCPs and patients experienced the visualization of results as “cluttered” with a lot of numbers and

dots, making interpretation of the data, especially for patients, somewhat problematic.

"I don't think this is very clear with all those dots and numbers" (patient 2, 61 years, female).

Missing graph legends and introductory texts at each page further hampered quick interpretation of the graphs.

Content & Information – Seven (3 critical) usability issues were identified. Both HCPs and patients lacked detailed information on pain medication use (i.e., medication category and amount used on a measurement day). Next to that, HCPs disagreed on the relevancy of the outcome measures included. For example, fatigue was regarded non-relevant by surgeons, but clinically relevant by pulmonologists and the oncology nurse.

"I don't think fatigue is useful; as a surgeon I don't use this" (thoracic surgeon, male).

Likewise, surgeons and pulmonologists requested overall daily activity level, while pattern of activity throughout the day was of interest for the oncology nurse.

"I primarily consider the patient; as a human being. For humans the consequences of daily activity influence how you feel; that you feel pain, dyspnea and fatigue due to too much activity. [...] So, from my perspective this has added value" (oncology nurse, female).

Ambulant devices – Only two usability issues (none critical) were reported by patients. No usability issues were reported relating to "Navigation & Structure" or "Other".

Web-based exercise

Design & Presentation – 20 (3 critical) usability issues were reported. HCPs had difficulty interpreting both training compliance and the results of exercise-related questions (e.g., 'How difficult was this exercise for you?'), due to faulty visualization of these results in their respective tables. For patients, lack of instruction about using features of the portal (for example difficulty playing exercise video) was rated critical. Both patients and HCPs experienced problems with reading and leaving new messages. For example, it was unclear which of the messages was new (HCPs) or where to click to send a new message (patients).

Content & Information – 19 issues were detected; 14 by HCPs, 5 by patients. None of these issues were rated critical, that is the issues did not prevent task completion or

were reported by a minority of the participants.

Navigation & Structure – In total four (one critical) issues were identified. For HCPs navigation through the portal in general was rated critical, since all HCPs had difficulty finding one or more components on the site, for example where to select adequate exercises or where to add exercise instructions.

“So, where can we select the exercises? And the overview? [...] This is not logical, I can’t find it” (Physiotherapist 3, female).

Other – Two usability issues (not critical) were reported by the HCPs. Although it did not hamper task completion, HCPs believed that accessibility through smartphone and tablet would promote use and access of the portal in future.

DISCUSSION

This paper presents the co-creation process of a telehealthcare application for NSCLC patients treated with lung resection. Results of the needs and requirement elicitation study show that both patients and HCPs have positive intentions to use an application that supports post-surgery recovery. For HCPs, improving quality of care was the primary reason to embrace telehealthcare applications. On the other hand, patients valued the increased sense of self-control as a result of insight in patterns of experienced symptoms, as well as easy access to advice and treatment that promotes recovery.

During this first phase of needs and requirement elicitation we presented a broad spectrum of possible applications to participants. Nonetheless, HCPs mainly selected applications that are comparable to existing interventions for lung cancer patients, such as exercise and symptom monitoring [20, 22, 37]. There are several possible reasons why HCPs selected these specific - already available and evidence-based - applications. First, in clinical practice HCPs work with evidence-based treatments to ensure high-quality patient care. This preference for evidence-based practice might have caused the selection of already tested applications [25, 38]. Second, the clinical context of HCPs and their role in the clinical care of lung cancer patients possibly steered the choice of applications that comply with these existing processes and roles. A nice example from the present study is ICT-supported peer support between NSCLC patients. Such an application was regarded valuable, but - from a HCPs point of view - did not fall under the responsibility of the hospitals. Third, our method of providing explicit examples of telehealthcare applications might have hampered creative processes to envision 'out of the box' ideas. Despite these drawbacks, our approach ensured selection of relevant treatment applications that have high chance of adoption since they fit the requirements and expectations of the target users [28].

The close cooperation with patients and HCPs gave us valuable insight into critical requirements for both the development and implementation of the telehealthcare application. Two requirements will be discussed further, because of their importance for future adoption and implementation. Patients indicated willingness in using a telehealthcare system given that results were actively used by the HCP in treatment. This is in agreement with findings from the study of Basch et al. [39]. In their study a decreased motivation in lung cancer patients for using electronic symptom-reporting was reported when the results of these reports weren't used during consultation [39]. The influential role of HCPs on perceptions, motivation and treatment adherence of their patients regarding telehealthcare services has been previously recognized

[40]. It can be expected that this influence will be present between cancer patients and their professionals as well. Especially in acute cancer care where the emotional impact of the diagnosis, together with the amount of and difficulty in understanding details of treatment and outcome, can cause high dependence on the attitudes of the HCP. This also emerged in our interviews with patients, who stated that they would do anything as long as it would help their HCP to improve treatment and recovery. Critical requirements mentioned by HCPs primarily related to their limited time available for preparation of patient consultations. Therefore, integration of the telehealthcare application with existing electronic patient records, as well as automatic merging of the ambulant data in a sensible and easy-to-view-manner was required. This requirement, that is integrating monitoring data into a coherent overview which is easily accessible by the professional, has been reported in other studies evaluating symptom monitoring [41]. Also, using a single platform that integrates all functionalities is regarded advantageous for adoption and implementation [25, 42]. Therefore, high priority was given to these requirements during design of the application. However, we also found dissimilarity in needs and requirements between HCPs. The usability study clarified that the perception if data is visualized in a 'sensible' and 'easy-to-view' manner – one of the most critical requirements – is highly individualized. For example, while pulmonologists and nurses prioritized ratings of well-being and fatigue on top of the screen, surgeons on the other hand requested to remove these outcome measures from the overview due to irrelevance for treatment. This divergence in requirements demands a flexible and modular application. So that HCPs can adapt the contents of the application based on patients' needs or their own, personal preferences.

The co-creation in our study is thought to foster feelings of involvement and, consequently, will promote chances of acceptance and implementation. However, developing an application that works well does not guarantee successful implementation [43]. For successful implementation it is necessary to take into consideration the clinical purpose for which the telehealthcare application is used and the way the application is implemented into healthcare, also called service configuration. An example of such a service configuration, tailored to the clinical processes and context of the NKI, was described in Figure 3 of this article. When implementing in other health care settings, the content, clinical purpose and service configuration should be validated again with HCPs and other important stakeholders. Doing so, the application will better match the clinical purpose, the service configuration and the requirements of the HCPs working at these institutes.

Several limitations of our methods should be considered. First, the results of the

usability study might be biased by inclusion of ‘enthusiasts’ (that is early adopters), while unfamiliarity with technology might have prevented other patients or HCPs to participate. This may have resulted in a lower number of reported usability issues as well as a higher percentage of participants who report positive intention to use a telehealthcare application. However, we did not collect data of participants not willing to participate. Therefore, we cannot draw firm conclusions to what extent bias might have influenced our results. During the following steps, reasons for non-participation should be recorded, since this can be a measure to indicate the acceptability of the application [43, 44]. Second, in our usability study participants were given minimal instructions and limited time to practice with the application. This is considered a good method to evaluate the ease of use, since it reflects the experiences of a first-time user [45]. However, it does not give insight into feasibility and adoption, such as compliance. For this, a different study method is required, during which participants will use the application for longer periods of time.

Following the staged approach suitable for development and evaluating tele healthcare [43, 46], our next step will focus on evaluating feasibility of the application with the aim to evaluate the relevance, time needed and overall feasibility for healthcare professional to use (data of) this telehealthcare application as part of post-surgery lung cancer care in larger series of patients and using controlled designs.

CONCLUSIONS

The present study shows a positive attitude of both HCPs and resected lung cancer patients towards the use of telehealthcare applications to improve quality of current care, and to decrease insecurity of lung cancer patients about experienced symptoms, recovery, and healthy behavior. In close cooperation with HCPs and resected lung cancer patients a new telehealthcare application was developed, consisting of a symptom monitoring module and a web-based exercise module. Usability was rated acceptable, and majority of HCPs and patients were willing to adopt the application as part of regular care following lung resection. Future research is needed to optimize usability of the application, to evaluate feasibility of the application integrated as part of clinical care processes, and to optimize adoption and implementation of the application. In this process special attention is required for the crucial role of HCPs in patient compliance to telehealthcare interventions. This emphasizes the role of the HCP in the success of the application, and the need to actively involve professionals during design to promote acceptance, as well as inform and educate them during the implementation phase on how to use the system.

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5

AMBULANT MONITORING AND WEB-ACCESSIBLE HOME-BASED EXERCISE PROGRAM DURING OUTPATIENT FOLLOW-UP FOR RESECTED LUNG CANCER SURVIVORS: ACTUAL USE AND FEASIBILITY IN CLINICAL PRACTICE

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ABSTRACT

Purpose: The aim of this study is to evaluate the feasibility of a telehealthcare application for operable lung cancer (OLC) patients, consisting of ambulant symptom and physical activity monitoring (S&PAM) and a web-accessible home-based exercise program (WEP), and identify possible barriers for successful adoption and implementation.

Methods: A two-stage mixed methods design was used, in which 22 OLC patients and their treating healthcare professionals (HCPs) participated from pre-surgery to three (stage 1; n = 10) or six (stage 2; n = 12) months post-surgery. Actual use and acceptability (usability, usefulness, and satisfaction) were evaluated.

Results: Seventeen OLC patients (age (SD): 59 (8) years; 8 female) actively used the modules. S&PAM use varied from 1 to 11 monitoring days prior to outpatient consultations. Patients used WEP most frequently during the first 5 weeks, with an average of four logins a week. Fifty-eight percent used WEP beyond 7 weeks. No adverse situations occurred, and patients felt confident using the applications. Perceived added value included active lifestyle promotion, decreased anxiety, and accessibility to specialized HCPs. Physiotherapists used WEP as intended. Contrarily, physicians scarcely used information from S&PAM. To promote future adoption, strategies should focus on high-level patient tailoring of the technology, and formalization of including the applications in the clinical workflow.

Conclusions: Ambulant monitoring and web-accessible home exercise is clinically feasible for OLC patients. However, low level of adoption by referring physicians may hamper successful implementation.

Implications for cancer survivors: Patients perceived both ambulant monitoring and web-accessible exercise as an added value to regular care and feasible to use in the period before and after lung resection.

INTRODUCTION

Lung cancer is associated with high symptom burden and high level of unmet needs during and after treatment [1]. Although lung resection has the best treatment outcomes in terms of survival in early stage lung cancer, resected patients are faced with an additional worsening of physical fitness, lung function, quality of life, and symptoms such as pain or fatigue following surgery [2-4]. Good quality survivorship care post-surgery is essential to optimize recovery and prevent rehospitalization. Physical training and ambulant symptom monitoring might promote recovery and optimize treatment outcome [5-8]. Yet, availability and accessibility of such non-invasive interventions specifically adapted for operable lung cancer (OLC) patients remains extremely low [9].

Telehealthcare, defined as delivery of care by a healthcare professional over a distance using information and communication technologies (ICT) [10], is hypothesized to be a promising method to improve both the accessibility and quality of post-surgery cancer rehabilitation. Studies in various cancer diagnoses showed beneficial effects of telehealthcare on physical fitness, symptom management, and patient empowerment through frequent health monitoring, home-based exercise programs, and tailored information on disease and treatment [11-14]. Using the internet, smartphones, and sensors, telehealthcare services are accessible on patients' demand, wherever and whenever they need, providing timely support and promoting health-related self-management behaviors. Currently, evidence is emerging that telehealthcare applications are also acceptable for OLC patients and clinically safe [8, 13, 15].

However, showing acceptability and clinical safety is not sufficient for successful adoption and widespread use in everyday care [16, 17]. The context of use is considered important as well [17-19], which means that insight in acceptability and use within this context is of utmost importance to make the potential of telehealthcare come true.

Therefore, the primary aim of this study was to evaluate the feasibility of a telehealthcare application when used in clinical practice. Research questions to be answered were: (1) how do patients and HCPs use the application during outpatient follow-up in terms of frequency and duration; and (2) is the application acceptable for patients and HCPs as offered. A secondary aim was to identify factors for successful adoption and implementation following the staged approach of Jansen-Kosterink and Vollenbroek-Hutten [16]. By doing so, essential factors can be detected in an early phase, which enables efficient modification of the application before larger-scale implementation.

METHODS

A repeated-measures, single-arm, mixed-methods feasibility study was performed from January 2014 to January 2016. The study was approved by the Institutional Review Board Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital (NL44192.031.13/N13POR), and all participants provided informed consent prior to participation in the study. The staged approach was used to guide the evaluation [16], resulting in a stage 1 - optimization of usability for use in clinical practice - and a stage 2 - evaluation of clinical feasibility - study.

Sample and setting

Participants were recruited from the Netherlands Cancer Institute (NKI), Amsterdam, the Netherlands, between January - May 2014 (stage 1) and January - July 2015 (stage 2). Eligible participants were Dutch-speaking adults aged 18 years or older, diagnosed with primary non-small lung cancer (NSCLC) and scheduled for curative lung resection. Participants were identified during the multidisciplinary meeting at the NKI, and patients' treating oncologist validated eligibility. A study information letter was sent to eligible patients, after which patients were contacted by the first author. When interested, a first appointment was scheduled at the NKI prior to surgery.

Participants were excluded if they had no access to a computer or internet, were unable to walk independently with or without walking aid (e.g., cane), exhibited severe cognitive disorders or emotional instability, or suffered from uncontrolled comorbidities. HCPs (oncologists, surgeons, physiotherapists) involved in the care of the included patient were also recruited.

Intervention

The telehealthcare application, called the Remote Monitoring and Treatment (RMT) application, has been described previously [20]. Briefly, it consists of two modules: (1) a symptom and physical activity monitoring (S&PAM) system, and (2) a web-accessible exercise program (WEP) with remote supervision by a physiotherapist.

The S&PAM module aims to increase insight in the severity of and change in self-reported symptoms, well-being, and daily physical activity. The system consists of an android smartphone - used as input device for self-rated symptom severity (*pain, dyspnea, fatigue*; scored by moving slider between 0 ('no [symptom] at all') to 10 ('extremely/a lot of [symptom]')), mood (*valence, calmness, energetic arousal*; scored from 0 (e.g., 'tense') - 6 (e.g., 'calm') [21, 22]), weight, and pain medication use - and three on-body sensors, i.e., an accelerometer, heart rate sensor, and an oxygen saturation

sensor (Fig. 1a). The symptom scores are combined with physiological parameters from the sensors and summarized into graphs, accessible for both patients and HCPs via a web portal, which is integrated with existing electronic medical records (EMRs) at the hospital.

Figure 1 The remote monitoring and treatment (RMT) service for lung cancer patients. A) The symptom and physical activity monitoring (S&PAM) system consisting of a smartphone, heart rate sensor, pulse oximeter and accelerometer. B) Example exercise of the web-accessible home-based exercise program (WEP) including a movie and written instructions as displayed in the online portal.

The WEP module aims at improving physical fitness of the patient by means of an online, tailored exercise program, which is based on patients' fitness and goals - assessed during a face-to-face intake - and is performed at home. Each exercise is illustrated by a movie with spoken instructions, and supported by written text (Fig. 1b). Progress is monitored via patient self-report (number of exercises successfully completed, and the experienced difficulty of the exercise) and automatically logged information on use (frequency, duration of login, number of pages, and exercise views). If a patient experiences problems with exercise execution (e.g., unclear how to perform an exercise or non-acute bodily pain related to the exercise program),

the patient can click a button on the web portal reading “cannot perform exercise, report to therapist”, which results in a standardized email sent to the responsible physiotherapist with instructions to contact the patient. For acute physical problems, the patient is instructed to contact his/her GP.

The modules were accessible for patients via ‘MyAVL’, the interactive patient portal from the NKI [12] but ran on the Continuous Care and Coaching Platform hosted at the research institute [19].

Study procedures

Stage 1 study: preparation of the RMT application for clinical use

To optimize usability of the application for clinical use, the RMT application was offered to a small sample of operable NSCLC patients and their HCPs at the NKI from pre-surgery to 3 months post-surgery.

Patients, pulmonologists, and physiotherapists participated in telephone or face-to-face semi-structured interview to evaluate satisfaction 3 months post-surgery. All interviews were performed by the first author and lasted between 15 and 30 min. Participants were asked to describe how they used the application, what they thought of the ease of use, and if they had experienced any problems (e.g., technical) using the application. Their comments resulted in a list of critical requirements for adaptation of the RMT application. Results are summarized in this article and adaptations were realized before start of the stage 2 study.

Stage 2 study: evaluation of clinical feasibility of the RMT application in clinical care

Before start of the study, thoracic surgeons and pulmonologists of the NKI were given a 30-min presentation about content and possible benefits of the S&PAM module, where in the EMRs the data could be found and how these should be interpreted. Physiotherapists of the NKI were familiarized with the WEP portal during a 2-h workshop. Additionally, a paper manual was provided. Telephone and email support for the use of the modules was also available for both patients and HCPs.

Study protocol

The study protocol is summarized in Figure 2.

Pre-surgery (t₀) - At baseline, patients received the system for the S&PAM module, oral instructions, and a paper manual. Patients were asked to use the system in the period before surgery for a minimum of 3 days a week, preferably for 2 weeks. The first week

following the appointment, the investigator checked if scores were displayed in the EMR, and when necessary, encouraged the patient to complete measurements before surgery.

Figure 2 Study protocol stage 1 and stage 2 study.

Stage 1 ran from two weeks prior surgery (t0) to three months post-surgery (t2) only. S&PAM: Symptom and physical activity monitoring module; WEP: Web-accessible home exercise program; UTAUT: Unified Theory of Acceptance and Use of Technology

Post-surgery - Outpatient appointments with the physician (thoracic surgeon or pulmonologists) and the physiotherapist were scheduled at 1 month post-surgery, as per usual care. After hospital discharge, the patients were contacted by the investigator and reminded to use the S&PAM system for a minimum of 3 days a week, preferably all weeks until the 1-month physician appointment at the hospital (t1).

First month post-surgery (t1) - Two days before the outpatient visit, physicians received an email with a reminder that additional information from the S&PAM system was available in the EMRs, including instructions where and how to access this information. Patients returned the S&PAM system during their visit to the hospital.

During the physiotherapist consultation, patients received user instruction for the WEP portal, including a personal login and a paper manual. A brief and individualized assessment of the patient's fitness level was made, after clarifying individual exercise goals and preferences. A tailored exercise program was then constructed by the physiotherapist and made accessible to the patient within the first week following the appointment. The exercise program was adjusted at least once a month. If needed, the physiotherapist could adjust the program more often. No specific guidelines were given regarding the number or content of contacts between patients and

the physiotherapists. Contact between patient and therapist was possible via chat messages on the portal. More complex issues, such as problems with performing exercises or changes in health, could be discussed by telephone or email. The WEP module was offered until 6 months post-surgery.

Three and six months post-surgery (t2 and t3) - Three weeks prior to the 3 and 6 months follow-up, the S&PAM system was again sent to the patients by the investigator, including written instructions for use. Patients were asked to use the system prior to their appointment for 3 days a week during 2 weeks. Two days before the appointment, physicians received a reminder that monitoring data was available for this patient in the EMR. Again, instructions were included where and how to access this information. Patients returned the S&PAM system during their follow-up visits to the hospital.

Dropout was defined as a patient who did not attend the final measurement at t3. Every patient was contacted to determine their reason(s) for dropping out.

Data collection

Patient characteristics

At baseline, demographics such as sex, age, marital status, education level, and employment status were collected via a questionnaire. Experience with internet and computer technology was self-reported in terms of frequency and duration. Clinical information (diagnosis, cancer stage, treatment details, number of comorbidities, lung function) were obtained from the hospital medical records.

Actual use

Symptom and physical activity monitoring - To reflect use of the S&PAM module, the following measures were logged, extracted from the database, and further analyzed:

Patients:

- The number of days that patients used the monitoring system, calculated as the number of days that data were available from the system (accelerometer or symptom scores) expressed over all periods together as well as per treatment period (pre-surgery, first month following surgery, prior to 3 months consultation, and prior to 6 months consultation).
- Frequency (number) and duration (minutes) of login on the S&PAM portal expressed over all periods together.

Physicians:

- Frequency (number) and duration (minutes) of login expressed over all weeks together.

Web-accessible home-based exercise program - For the WEP module, the following use measures were evaluated:

Patients:

- Number of weeks patients used the service, measured as number of weeks from the first to the last week that a patient logged in on the portal.
- Frequency (number) of logins per week.
- Average duration (minutes) of login per session.
- Reason for ending service (provided by patients through self-report)

Physiotherapists:

- The frequency (number) and duration (minutes) of login expressed over all weeks together were logged.
- Time needed to perform the first consultation (including instruction), setting up and adapting a tailored exercise program, as recorded by the therapist per patient.

Acceptability

A combination of quantitative and qualitative measures was used to measure acceptability of the S&PAM and WEP modules in both patients and HCPs.

Patients - An online questionnaire based on the Unified Theory of Acceptance and Use of Technology (UTAUT) [23] was administered at pre- (t0) and post-intervention (t3). The modules (S&PAM and WEP) were evaluated independent from each other in the questionnaire. Scores prior to surgery give an indication about the expectations patients had about the RMT service, while the scores at study completion represent their experiences or acceptability of the RMT service. The questionnaire evaluated the components effort expectancy or usability, performance expectancy or usefulness, social influence, behavioral intention to use. Facilitation conditions were measured in terms of perceived self-efficacy. Computer availability and internet access were inclusion criteria for participation and therefore not measured as part of facilitation conditions. Attitude and satisfaction were added, as they are hypothesized to influence intention to use and actual use [18, 24, 25]. Each item was phrased as a statement, and scored on a 7-point Likert scale (from completely disagree to completely agree). Negative phrased items were transformed so that a higher score indicated higher

expectation/experience. For each component, the item scores were summed, and the average score was taken as the final outcome measure.

At the end of the study, a patient focus group was performed by the investigator. Discussion focused on usability and perceived usefulness of the application for resected lung cancer patients, patients' motivation for use, and if they thought the application should be part of standard care for resected lung cancer patients (intention to use). The first aim was to generate input for improvement of the application itself. The secondary aims were to gather information about the clinical value of the application as well as influencing factors that motivate or hamper patients to use these kinds of applications. The focus group was recorded with permission of the participants and notes were taken.

Healthcare professionals (HCPs) - Acceptability of the S&PAM module was evaluated via an online questionnaire at the end of the study (January 2016). The questionnaire was sent to 16 HCPs that are involved in the outpatient care of operable lung cancer patients (two specialized oncology nurses, four thoracic surgeons, ten pulmonologists). If an HCP indicated that he/she had not used the results of the S&PAM module, reasons for non-use were registered as well as the expected usefulness of symptom monitoring in clinical care for lung cancer patients.

A focus group with physiotherapists who used the WEP module was performed by the first author at the end of the study to evaluate acceptability of the WEP module in terms of usability, usefulness, satisfaction, and intention to keep using the module.

Data analysis

IBM's Statistical Package for the Social Sciences (SPSS, 23) was used for the statistical analyses. Demographic, patient expectation and experience (UTAUT components) were calculated as frequencies (percentage), medians, and interquartile ranges.

For evaluating the actual use of the web portals of S&PAM and WEP all logins less than 2 min in duration were excluded from analysis. Following, logins that occurred on the same day were considered a single session and duration of these sessions were summed. Means, standard deviations, and ranges were calculated for the use measures. For visualization of actual use, dot plots were generated capturing each individual use values, means, and 95% confidence intervals (95% CI). CI's were calculated using the t-distribution due to small sample size.

For qualitative insight into feasibility and acceptability, notes of the focus groups were combined with results of the questionnaire to highlight the most important aspects. Responses on the HCPs questionnaire were summarized using descriptive statistics.

RESULTS

Stage 1 study

The RMT service was offered to 10 patients (60% female; median age (IQR): 56.6 (52.8–62.8) years), of which eight patients used one or both modules of the RMT service. Seven physicians were involved in the care of these patients (three surgeons, four pulmonologists). Detailed description of patient characteristics can be found in Supplementary Material 1. In post-intervention, patients indicated good usability and usefulness, confidence in using the modules ('self-efficacy'), and a positive attitude and intention to use the modules (i.e., all components a median score of >5 out of 7). Overall, patients felt satisfied with the modules, rating the S&PAM and WEP modules with a 5.3 (4.5–6.5) and a 5.6 (4.5–6.9), respectively (out of 7). Four patients (two female) and four HCPs (two physiotherapists, two pulmonologists) participated in the semi-structured interviews. Two patients declined participation in a personal interview, but gave written comments on the questions from the interview. From the interviews and written comments, eight critical issues were extracted for the S&PAM and five critical issues for the WEP module. Critical issues and the functional requirements for adaptations have been summarized in Supplementary Material 2.

Stage 2 study

Sample

Eighteen NSCLC patients scheduled for curative lung resection were approached for participation. Twelve patients agreed to participate (33% female; median age (IQR): 59.5 (54.5–66.0) years); a consent rate of 67%. Detailed description of patient characteristics can be found in the Supplementary Material 1. Most important reasons for refusal were surgery before enrollment could take place ($n = 2$), too little experience with computers/internet ($n = 2$), or emotional burden ($n = 1$). Following enrollment, four patients dropped out of the study, three prior to intervention, and one after 2 months of participation. Reasons for drop-out were cancelation of the surgery ($n = 2$), emotional burden ($n = 1$), or complications following surgery ($n = 1$). Internet experience was high in this sample, with all patients indicating using the internet almost every day for more than 3 years. Twelve physicians were involved in the care of enrolled patients (four surgeons, eight pulmonologists).

Actual use of the modules

Ambulant symptom and physical activity monitoring (S&PAM)

Ambulant S&PAM system - All patients used the S&PAM system at least once, resulting in 179 monitoring days. On average, patients used the system between 5 to 6 days per treatment period (i.e., pre-surgery, 1, 3, and 6 months post-surgery (Fig.3a).

Figure 3 Use of the RMT application. A) S&PAM: Number of days with physical activity data (dots) and symptom scores (crosses); PS: post-surgery. WEP: B) Frequency of login on the WEP portal per training week; C) Average duration of login per session per training week. Training week 1 indicates the first week that a patient logged in on the web portal.

A patient data point is represented by a dot/cross. Data points that overlap each other are visualized with larger dots/cross; the more overlapping points the larger the dot/cross. The average (horizontal lines) and 95% CI (vertical lines; calculated with t-distribution) are given.

During the study, in three patients, heartrate and oxygen saturation monitoring was removed from the system. One patient experienced problems with attachment of the heartrate sensor because of his thorax wound post-surgery. One patient was anxious about using these sensors and for the other patient there simply was no sensor available. Technical issues were reported by six patients, but all issues could be resolved remotely. Most often reported was a loss of connection between the pulse

oximeter and the smartphone during increased physical activity ($n = 4$). Two patients indicated problems rating the symptoms on the smartphone prior to surgery (t_0). As can be seen from Figure 3c, there are in general fewer days with PA data than there are for subjective symptoms. This was caused by low quality data in terms of missing data points.

Web portal - In total, patients logged in 28 times on the portal to view the results of the symptom monitoring. Nine patients logged in at least once. Mean duration of login was 8 min (min-max: 2–35 min). On average, patients clicked on 11 different pages per session (SD = 12 page clicks). Patients looked most to the pages containing the detailed information about heart rate and oxygen saturation (40% of all page clicks), followed by the summary of symptom scores and daily activity (33% of all page clicks). Of the 12 physicians involved, only three physicians logged in on the portal (once each), with an average login time of 12 min.

Web-accessible home-based exercise program (WEP)

Eight patients (67%) used the exercise portal at least 1 week following lung resection. Patients started 4 ($n = 3$), 5 ($n = 2$), 6 ($n = 2$), or 7 ($n = 1$) weeks following resection. Use of the portal in terms frequency of use per week and average duration per session are visualized in Figure 3b/c. Patients used the exercise portal most frequently in their first 5 weeks of use. Seven patients (58%) used the portal for 7 weeks or longer. During the program, none of the patients used the shortcut button to indicate difficulty in exercise performance or reported an acute, serious problem as a result of the exercise program. Twenty percent of all sessions lasted 20 min or longer; while the majority of all sessions (66%) lasted less than 10 min.

Half of the patients reported that after some weeks practicing at home, they printed the exercise program and performed the exercises at a local fitness center ($n = 3$) or community center ($n = 1$). Reasons for exercising in these centers were availability of better equipment ($n = 1$), support from trainer ($n = 1$), and 'used to go to the fitness center prior to surgery' ($n = 2$). Reasons for ending were that patients felt that they had reached their fitness goals and were fit enough to pick up their usual exercise activities ($n = 5$), outpatient follow-up ended ($n = 1$), or that exercises were too easy ($n = 2$).

Two physiotherapists participated in the study. They logged in 46 times during the study, with a total duration of 805 min. Time investment per patient was as follows (mean $\pm$ SD): intake with the patients 60 ± 7 min (including 30 min consultation part of 'standard' care), first set-up of exercise program 35 ± 9 min, and adaptation of the training program 19 ± 7 min.

Acceptability

Eight patients completed the online questionnaire at both t0 and t3, and six of these patients participated in the patient focus group. Dot plots of the results from the online patient questionnaire can be found in Supplementary Material 3. Seven HCPs completed the online questionnaire; five pulmonologists and two specialized oncology nurses.

Ambulant symptom and physical activity monitoring (S&PAM)

Patients - At t0, patient expectations were generally high (medians >5 out of a score of 7), with the exception of usability (median (IQR): 4.3(4.0–6.0)), and all patients had a positive intention to use the S&PAM module.

Following the intervention (t3), most patients indicated that the monitoring system had good usability and all felt competent using the module (that is, score >5 on perceived self-efficacy). Patients felt satisfied with the module and had the opinion that the module should be offered by the hospital to all eligible OLC patients as part of standard care (median satisfaction score =6.0 (IQR = 5.6–6.2); median intention to use score =6.0 (IQR = 5.0–6.8), respectively). On average, scores for usefulness indicated that patients experienced benefit using the system during treatment. Nevertheless, three patients scored rather low on usefulness (score between 3 and 4). Qualitative data show that they were disappointed with the lack of feedback from their physician on the results of the S&PAM, which made the module less useful, and, as a consequence, decreased motivation to use the S&PAM system. During the focus group, this decline in motivation was confirmed by all other patients. As a result, patients felt no need to extend measurements beyond the prescribed frequency. Next to that, patients also requested tailoring of the monitoring protocol in terms of monitoring frequency and sensors employed, based on their individual pattern of recovery and needs.

Patients mentioned several points of improvements regarding usability. Connection problems between pulse oximeter sensor and smartphone during activity (n = 4), and difficulty understanding visualization of the results on the portal (n = 4) were the aspects mentioned most often.

Healthcare professionals - The majority of the HCPs (n = 5) expected added value of a symptom monitoring system in the care for lung cancer patients in that it might improve insight into the capacity, symptoms, and daily activity, and with this information, improve treatment choices. Most HCPs reported that they would use the S&PAM during chemo (n = 4). But in their opinion, also surgery (n = 3), concurrent (n

= 2), and radiation therapy (n = 2) might benefit from the use of the S&PAM module. Yet, only two pulmonologists who completed the online questionnaire indicated to be aware that their patients had used the S&PAM module. None of these HCPs actually checked the results of the monitoring in the EMRs. Reasons mentioned for not using the information from S&PAM were unawareness that a specific patient participated in the study, lack of time to check the information, and non-compatibility with the content and process of their work.

From a HCP perspective, most relevant to optimize future use was to emphasize and improve HCPs' perception of the added value of the symptom monitoring system (n = 7).

Web-accessible home-based exercise program (WEP)

Patients - Prior to intervention (t0), expectation scores were high with all UTAUT components median scores higher than 5, and all patients had the intention to use the WEP module as much as needed.

In the following use, most patients were satisfied with usability of the module, except for two (score <5) since the program was difficult to access on mobile phone, which hampered execution of the program on a different location than home. Nonetheless, all patients felt confident in their ability to use the module ('self-efficacy').

Seven patients found the WEP module useful (score >5 out of 7), but one patient scored extremely low (2 out of 7). During the focus group, this patient indicated a lack of interaction with the physiotherapist, insufficient tailoring of the exercises, and lack of insight in progression as most important reasons for dissatisfaction. The majority of patients (n = 7) had the opinion that the module should be accessible to all operable lung cancer patients (score ≥5 on intention to use).

Physiotherapists - Overall, physiotherapists indicated satisfaction and voiced a positive intention to keep using the WEP module. Therapists found it easy to provide user instruction to the patient, due to the simplicity of the patient portal. However, some suggestions for improvement were given for the therapist portal, including navigation between the summary of patient reported progress and corresponding exercises (to quickly adapt instructions based on the progress), and rearrangement of visualization of the chats (i.e., all the chats into one 'chat-roll' with a clear mark for messages that have been read).

Regarding usefulness, therapists believed that the module might contribute to improved accessibility of a cancer rehabilitation program and support of patients towards an active life-style by decreasing anxiety for physical activity. For improvement, a smartphone-supported application was considered likely to improve accessibility even more. In general, the necessary time investments were regarded acceptable to the therapists. It appeared critical to instruct the patient when and for what to use the chat function of the module as to prevent unmanageable number of messages.

To ensure successful implementation of the module, therapists advised a more blended care approach, that is, a combination of supervised and home-based training as to facilitate adequate evaluation of patients' fitness and optimize program tailoring. Also, official (organizational) agreements are needed to ensure financing of the treatment and time to use the module next to face-to-face patientcare.

DISCUSSION

This study aimed to evaluate the clinical feasibility in terms of actual use and acceptability of a telehealthcare application, the Remote Monitoring and Treatment (RMT) application, for lung cancer patients treated with lung resection when used in daily clinical practice. Our findings suggest that the use of remote monitoring and treatment is feasible to lung cancer patients when offered pre- and post-surgery. Patients actively used the modules prior and following surgery, and perceived both modules as a beneficial contribution to their care. Also, the continuous treatment and involvement of ‘experts’ from the cancer institute, who were expected to be better informed about cancer and the treatment patients had received, was seen as a big advantage of using ICT-supported rehabilitation. These results are in line with previous studies that showed willingness of lung cancer patients to exercise at home following surgery [15] or daily rate symptoms on a smartphone during radiotherapy [11].

During the study, several issues emerged that need consideration for successful patient adoption. One of the important factors observed is usability of the RMT application. Results show that participants felt confident using on-body sensors, a smartphone, and corresponding protocols. This positive attitude might have been facilitated by a perceived usefulness of the system as well as a flexible monitoring protocol (e.g., change to a different monitoring protocol that did not include heart rate and pulse oximeter sensor) and availability of (paper) manual and a ‘helpdesk’. These factors have previously been linked to the acceptance of personal health devices in patients with chronic conditions [26]. Unfortunately, the S&PAM module suffered from loss of connection between the pulse oximeter and the smartphone during performing physical activities. Patients felt annoyed by this problem and it resulted in loss of data for the HCPs. Although SpO_2 is considered clinically relevant both pre- and post-surgery for lung cancer patients [27, 28], it should only be included in the monitoring protocol when the sensor’s performance is adequate and reliable in the ambulant setting. Also, previous studies have shown the added value of S&PAM without SpO_2 measurement [8, 11]. Therefore, we recommend that only patients at risk for desaturation should be offered the pulse oximeter [28].

For the WEP, the main usability issue reported was accessibility of the program from a mobile platform such as a smartphone. Providing the program on smartphone or tablet may facilitate patient use, due to accessibility at various locations which is preferred by patients (e.g., fitness center, local therapist, or communal centers), but also accessibility by a broader (e.g., elderly) population due to increasing number of people possessing tablets rather than desktops [29].

Another factor that influences patient use is motivation. For both modules, patients explicitly reported a perceived decline in motivation towards the end of the study, caused by a lack of sufficient feedback by physicians and the system, and insufficient tailoring of the modules to the needs and capacity of the patients. In agreement, Hoaas et al. recently reported that providing patients with (objective) signs of improvements as well as treatment tailoring in terms of individual goal setting were seen as most important for COPD patients maintaining motivation to participate in a long-term telerehabilitation program [18]. Lack of motivation is not unique to the use of telehealthcare applications, but has been the object of evaluation in other, not ICT-related, interventions that focus on behavior change, such as promoting physical exercise [30]. Tailoring, or personalization, of treatment and feedback is considered beneficial for treatment compliance and long-term behavior change [31, 32]. Evidence is growing that shows the potential and unique capability of technology to provide high level of personalization through monitoring on an individual level and translate this complex gathering of information into tailored feedback and treatment [33-35]. Adding a gaming layer ('serious gaming'), a virtual coach, or social component such as online group-based exercise to the program, may further enhance motivation [35]. Given the fast technological developments, we should strive for an individual, holistic approach that takes into account the complex interaction between the patient - including his/her health, norms, beliefs, and goals - the context and changes herein. For our RMT application, this means that we should utilize information about the patient (such as age, sex, cancer stage, experience with technology), his/her treatment (including treatment phase, care processes) to tailor the intervention protocol, and adapt the protocol frequently based on newly acquired information. Next to tailoring, other motivational strategies have been reported by our patients and HCPs that might improve the use and adherence of the RMT service. The most promising improvements were providing feedback about health and recovery via a smartphone app instead of a web-based portal since it is readily available and more user-friendly; and a more blended treatment approach, that is combining face-to-face consultation with home-based treatment as to optimize continuous tuning of the treatment to the patient.

In contrast with the overall positive findings regarding feasibility and acceptability from patients, the findings from HCPs were mixed. From the HCPs' perspective, both modules were regarded beneficial and a valuable addition to care for operable lung cancer patients. However, evaluation of HCP satisfaction with the S&PAM module was unsuccessful, since physicians that completed the questionnaire all indicated non-use of the module. Since HCPs play a key role in making innovations available to patients and the influence they may have on the adoption and adherence of patients [17, 20, 36], active involvement of HCPs is regarded crucial for successful implementation of

telehealthcare and should be given more attention. In line with a recent publication of Vollenbroek et al. [17], our results also show that a process of co-creation of the telehealthcare applications and protocols that are considered useful for their patients, was clearly not enough for physicians to actually start using these modules as part of their daily practice. Interestingly, in our study, large variation was observed in HCPs using the modules. Physiotherapists that participated in the study showed high level of involvement, while physicians hardly used the information from the S&PAM module in their patients' consultation. Research suggests that ease of use, perceived usefulness, and organizational- and work-related factors play an important role in HCP adoption [19, 37]. In our current study, it is difficult to draw firm conclusions about facilitating and impeding factors due to the small sample size. However, since ease of use and perceived usefulness of symptom monitoring were rated positive in the current and our previous study by HCPs [20], the low use in clinical practice suggest a role of these work- and organization-related factors. For example, for the WEP module, the physiotherapists explicitly reserved time in their schedule for usage of the module, and they were solely responsible for the content of the exercise program and also served as the primary contact for patients regarding the WEP module. In contrast, no explicit agreements were made with physicians in terms of their role and responsibilities, and no time was reserved for learning and working with the S&PAM. Another issue might be that only few patients used the S&PAM, causing that usage of the monitoring data was not part of their daily routine. Lastly, the intervention protocol lacked clear guidelines how the modules and the results generated, should be integrated with hospital-based care. For example, specific cut-off scores for symptom levels were lacking, as was a clear protocol for handling alarming results of the S&PAM such as high pain scores.

This study provides valuable insight in how adoption and implementation of the RMT application in clinical practice can be promoted. While the technology can be further improved, we believe that integration of the RMT application with existing care processes is of paramount importance. This is in line with the work of Jansen-Kosterink, who states that it is not the technology, but the way the technology is embedded in care processes ('service configuration') that defines the service [38]. Therefore, implementation strategies should focus on formalization of the tasks and processes needed for usage of telehealthcare in practice, which should include the availability of time, funding and creating leadership [19, 37], and education of all involved personnel about the benefits of the service, as well as defining clinical protocols for the resulting information. Additionally, a stage 3 (large-scale) evaluation study is needed to evaluate effectiveness (clinical outcomes), adoption, adherence, and cost-effectiveness when used in clinical practice [16].

Strengths and limitations

This study is one of the few that evaluated feasibility of ambulant symptom monitoring and web-accessible home-based exercise in clinical practice for lung cancer patients that underwent lung resection. We used the staged approach, resulting in a two-stage study, that allows for gradual development and fine-tuning between technology and clinical context. Several limitations of our study need consideration. First, our convenience sample might have resulted in inclusion of 'enthusiasts', resulting in higher IT literacy and levels of use. Also, patients with complications or who experience high levels of stress as a result of diagnosis are less likely to participate in the study. Exclusion due to lack of experience with or access to IT is a well-known barrier for successful adoption and implementation of telehealthcare in the elderly [39]. Currently, there are no reliable data available on IT literacy for this specific subgroup of patients, but the low percentage (i.e., 11%) of patients excluded in the current study for this reason probably is a too optimistic figure for the population as a whole. On the other hand, the number of chronically ill and elderly that have access to the internet and own a smartphone or tablet is increasing fast in the Netherlands [29, 40]. For example, in 2016, 82% of chronically ill patients were estimated to have internet access [40], and 63% of people 65+ years used a smartphone [41]. These numbers suggest that a lack of IT literacy as a barrier for participation will decrease in the upcoming years for elderly and chronically ill patients.

Second, the first author performed several research activities, including recruitment, S&PAM instruction, and leading the patient focus group. Therefore, patients might have been less willing to report negative comments during the focus group. However, the questionnaires were completed anonymously and resulted in better rating of the modules than the results during the focus group, suggesting that this effect can largely be ignored. Lastly, in the present study, we did not report effect of the intervention on treatment outcome and patients' health or costs of the intervention. Although patients experienced the intervention as a beneficial addition to their treatment, additional research is needed to confirm clinical effect and cost-effectiveness objectively and in a larger sample.

CONCLUSION

Our study demonstrates that remote monitoring and treatment is feasible to lung cancer patients when offered pre- and post-surgery. Patients actively used the ambulant symptom monitoring and web-based exercise modules prior and following surgery, and perceived both the modules as a beneficial contribution to their care. However, we also showed that a low level of adoption by referring physicians may hamper successful implementation.

A stage 3 (large-scale) evaluation study is needed, with focus on both involvement of HCPs through organizational formalization and adequate education, as well as promotion of patient motivation through individual tailoring of treatment content and feedback. Following the staged approach, outcome should evaluate clinical effect (in relation to the goal of each module), costs (in time and money), and factors that determine use and effect in both HCPs and patients.

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SUPPLEMENTARY MATERIAL 1

Table A Sample characteristics

	Stage 1 (n=10)	Stage 2 (n=12)
Age, <i>Median (IQR)</i>	56.6 (52.8-62.8)	59.5 (54.5-66.0)
Sex, <i>n (%)</i>		
Female	6 (60%)	4 (33%)
BMI, <i>Median (IQR)</i>	26.6 (22.8-29.3)	24.5 (21.3-27.1)
Marital status, <i>n</i>		
Relationship, living together	7	11
Single	1	--
Divorced	2	--
Widow	--	1
Employment status, <i>n</i>		
Full-time job	4	1
Part-time job	1	3
Retired	2	3
Unemployed	3	4
Voluntary work	--	1
Comorbidities, <i>n</i>	7	10
Smoking (yes/quit/never), <i>n</i>	2 / 5 / 3	3 / 8 / 1
Pack years, <i>Median (IQR)</i>	30.0 (0.0-36.3)	27.0 (8.0-41.0)
Lung function, <i>Median (IQR)</i>		
FEV ₁ (L)	3.0 (2.3-3.6)	2.8 (2.4-3.2)
% predicted FEV ₁ ^a	98 (82-105)	93 (73-98)
FVC (L)	4.1 (3.1-5.2)	4.1 (3.5-4.8)
% predicted FVC ^a	111 (103-119)	105 (95-112)
% predicted DLCO ^a	87 (71-96)	67 (62-81)
Surgery extent, <i>n</i>		
Lobectomy	10	8
Pneumectomy	--	2
Neoadjuvant, <i>n</i>	1	2
Adjuvant, <i>n</i>	3	1

^a percentage of predicted values (from medical record); IQR = interquartile range; BMI = body mass index; FEV₁ = forced expiratory volume in 1 (first) second; FVC = forced vital capacity; DLCO = diffusion capacity of the lung for carbon monoxide.

SUPPLEMENTARY MATERIAL 2

Critical issues elicited during stage 1 study

Table A Symptom and Physical Activity Monitoring (S&PAM)

	Reported problem	Changed for stage 2 study
Content & Information	<i>“Current classification of pain medication is ambiguous and cannot be used in clinical care.”</i>	Patient reported pain medication automatically classified on portal in: paracetamol, NSAIDs, mild opioid, strong opioid, co-analgetics.
	<i>“Mood is an important indicator for recovery following lung resection, but is not included in the measurement protocol.”</i>	Addition of self-reported mood to smartphone monitoring protocol using a subsample of six questions selected from the Multidimensional Mood Questionnaire (MDMQ) to measure valence, calmness, energetic arousal [21, 22].
	Unclear when physiological data (heart rate or oxygen saturation) is actual missing or unreliable due to low quality data.	If data from the zephyr or nonin was missing or was low quality for > 1 minute, this was explicitly stated in the graph on the web portal.
Navigation & structure	Text on the portal caused ambiguity about interpretation of the results.	Text was changed and for each displayed result/graph an explanation was provided on the portal.
	One of the physicians had to log in for access to the symptom monitoring portal	Accessibility of the symptom monitoring data from the EPR without additional log in was assured.
Design & presentation	<i>“Current visualization of pain medication use does not correspond with the graph with pain scores, which makes it difficult to interpret the results quickly.”</i>	Reports of pain medication were added to/integrated with the graph that visualized pain scores.
	<i>“Colours of trendlines in graphs do not correspond with the colours indicated in the legend.”</i>	Colours of the trendlines were adapted.
	Unrealistic value for weight was entered on the smartphone.	For each variable, including weight, unrealistic values were defined, and were rejected by the system.

Table B Web-accessible home-based exercise program (WEP)

	Reported problem	Changed for stage 2 study
Content & Information	The therapist can only select exercises from an existing database; it is not possible to add an exercise to this database for a specific patient.	Blank exercises added for which therapists can define own text, instructions, and pictures.
	Due to limited contact between therapist and patients, timely adaptation of the exercise program is easily forgotten.	Therapists will receive an automatically generated reminder by email when no exercise program is available the upcoming week.
Navigation & structure	None	--
Design & presentation	Patients cannot perform the exercise session on a different day than prescribed by the therapist, which might hamper adherence.	<i>Not solved for stage 2 due to time limitation.</i> Taken as re-design input for next releases.
	Exercise progression is difficult to interpret from the current progression overview, since it summarizes weekly performance.	Summary of performance/progression can be set individually: therapist can select if a summary is needed per day or per week.
	Notifications of new messages remain active/visible on the portal, while all messages have been read by the therapist. This causes confusion whether or not all new messages have been read.	As soon as a therapist clicks on a new message, its notification will disappear from the home screen.

SUPPLEMENTARY MATERIAL 3

Figure A UTAUT component scores for the S&PAM and WEP modules prior to intervention (t0 •, n=12) and post-intervention (t3 , n=8). A patient data point is represented by a dot/cross. Data points that overlap each other are visualized with larger dots/cross; the more overlapping points the larger the dot/cross. The median (horizontal lines) and IQR (error bars) are given. Components: EE=effort expectancy; PE=performance expectancy; ATT=attitude; SI=social influence; PSE=perceived self-efficacy; BI=behavioral intention to use; Satisf=satisfaction.

6

ACCEPTANCE AND ADOPTION OF TELEHEALTHCARE SERVICES BY HEALTHCARE PROFESSIONALS: EXPLORATION OF PERCEIVED FACILITATORS AND BARRIERS OF 'USERS' AND 'NON-USERS' OF TELEHEALTHCARE

Submitted

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ABSTRACT

Background: Adoption of health technology by healthcare professionals (HCPs) is regarded a prerequisite for widespread implementation and sustainability. Unfortunately, HCPs adoption of telehealthcare in clinical practice has found to be disappointing, thereby hampering implementation and realization of potential benefits. Therefore, the aim of this study was to provide insight in and compare possible barriers and facilitators to accept and adopt telehealthcare in clinical practice between HCPs who use telehealthcare applications ('users') in clinical practice and those who don't ('non-users').

Methods: An online survey study was performed in users of telehealthcare (n=70) and non-users (n=77) to measure behavioral intention to use (BIU) telehealthcare services and factors from the individual (compatibility with workplace values and work processes), technological (perceived usefulness and perceived ease of use) and context for implementation (organizational facilitating and social influence) domains. To explore the relation between acceptance and predictive factors, BIU was categorized into positive acceptance ($BIU \geq 4$) and negative acceptance ($BIU \leq 3$). Following, scores for each factor were compared between both groups (Mann-Whitney U).

Results: Users perceived better compatibility of telehealthcare with workplace values and work processes, and also experienced better support from the social domain compared to non-users. Non-users showed a significant knowledge gap regarding the organizational domain and significantly lower acceptance than users. In non-users, 51% scored positive acceptance, which was associated with significantly better scores on factors from all three domains compared to non-users with negative acceptance. Some users (11%) indicated negative acceptance following initial adoption, which was significantly related to lower scores on several items of the individual domain compared to users with positive acceptance.

Conclusions: Barriers and facilitators for professionals' adoption of telehealthcare can exist on different domains, that is the individual, technological and context for implementation, and can be present pre-adoption until post initial adoption. Although positive acceptance and perceptions of telehealthcare are essential, they do not guarantee successful adoption. Given these findings, we conclude that successful adoption of telehealthcare in clinical practice requires a holistic approach regarding implementation by proactively and repeatedly identifying and addressing barriers and facilitators on the individual, technological and context for implementation domain, from pre- until post-adoption.

BACKGROUND

Telehealthcare is 'the provision of personalized healthcare by a healthcare professional over a distance using Information and Communication Technology (ICT)'[1]. Telehealthcare enables individual treatment, monitoring and coaching in the personal environment, flexible in time and location, promoting patient self-management. Studies in various patient populations report that telehealthcare, provided as either additional or (partly) substituting usual care, can result in equivalent health outcomes as compared to more traditional, face-to-face, treatment regimens [2-5]. Especially in chronic conditions, telehealthcare might be beneficial and even cost-effective, since it supports and promotes long-term behavioral lifestyle changes. To fulfill the promises of telehealthcare sustainable implementation in clinical practice is essential. However, only few applications make it to fully integrated health services in clinical practice.

Adoption of health technology by healthcare professionals (HCPs) is regarded a prerequisite for widespread implementation and sustainability [6-9]. In patientcare, HCPs are the so-called gatekeepers in the accessibility of treatments to patients. Also, telehealthcare services by definition need active HCP participation. Unfortunately, HCPs adoption of telehealthcare in clinical practice has found to be disappointing [6, 10], thereby hampering implementation and realization of potential benefits.

Various theories and frameworks have been developed to explain and predict technology adoption by its end users [8, 9, 11-18]. To identify and validate predictors for adoption, studies have used *intention to use* (i.e. acceptance) as an outcome measure instead of *actual use* (i.e. adoption), under the assumption that positive intention will lead to actual use [16]. However, this relation between positive acceptance and successful adoption of the technology in practice have shown to be far from straightforward [6, 10, 19, 20]. This challenge the usability of these predictors to promote adoption in clinical practice. Moreover, it is unclear if barriers and facilitators to accept and adopt telehealthcare services differ between 'users' and 'non-users', that is those who use telehealthcare applications and those who don't. Another shortcoming of previous research on predictors for telehealthcare adoption is the limited focus on predictors that are sensitive to interventions [16, 21]. Predictors that are sensitive to interventions provide the possibility to influence the rate and extent of adoption of telehealthcare in clinical practice through targeted activities, and are therefore of special interest for those involved in implementation processes.

Therefore, the aim of this study was to provide insight in and compare possible barriers and facilitators to accept and adopt telehealthcare in clinical practice between HCPs

who use telehealthcare applications and those who don't. In this study, acceptance was defined as the degree of a HCPs behavioral intention to use (BIU) telehealthcare services [18], while adoption referred to actual use of telehealthcare in patient care [9]. To provide practical guidance for future implementation planning, we included factors that are sensitive to interventions, such as beliefs and knowledge [16].

METHODS

Research design and sample

A cross-sectional survey study was performed. HCPs were recruited via various strategies to aim for diverse participator profiles. Healthcare institutions that participated previously in research activities and HCPs known personally by the authors were asked by the researchers, but also professional associations for medical and paramedical professions and posts on social media (twitter account research facility, Facebook of the authors) were used to get HCPs involved. There were no other inclusion criteria than that HCPs currently needed to be involved in patient care and Dutch speaking. In the email or social media post a short description of the aims of the study was given. Interested HCPs could click on a link in the email or social media post to access the online questionnaire. Completion of the questionnaire was regarded as consent of the HCPs to participate in the study.

No information is available about the number of HCPs reached. No sample size calculation was performed.

Outcome measures

Adoption and acceptance

Our main outcome measures were adoption and acceptance of telehealthcare services by HCPs. Adoption was measured as a dichotomous outcome, namely being an active user of telehealthcare or not. All HCPs who completed the questionnaire and answered affirmative on the question: "Do you currently use telehealthcare?" will be referred to as 'users' in this paper. Consequently, all HCPs who completed the questionnaire and answered negative on the question: "Do you currently use telehealthcare?" will be referred to as 'non-users'. Acceptance was operationalized as behavioral intention to use (BIU) telehealthcare. BIU was measured with a single item rated on a 5-point Likert scale (1-5) ranging from "totally disagree" to "totally agree" (Supplementary material 1, item 32).

Determinants of acceptance and adoption

Various theoretical models have been developed to explain and predict technology acceptance and adoption by its end users, with the Technology Acceptance Model (TAM) being one of the most influential models applied to the health sector [17]. The TAM hypothesizes that two primary predictors, perceived ease of use (PEOU) and perceived usefulness (PU), influence the intention to use (i.e. BIU) a technology, which in turn determines actual use [17, 18]. The popularity of TAM possibly relates to its simplicity, which makes it easy to apply in research of various technologies. Although the determinants of TAM have shown to be significant predictors for BIU, the parsimony of the TAM simultaneously limits its applicability [8, 15]. TAM only includes factors from the technology domain (i.e. PU and PEOU), while there is a need for a more comprehensive approach that takes into consideration the complexity of both the human behavior and the context of implementation [8, 11, 15]. Therefore, in this study factors were added that capture these characteristics of the individual and the context, next to PU and PEOU. For each domain, i.e. the individual, technological and context, the selected factors are defined below.

Individual domain

The individual domain refers to characteristics of the individual who will use the technology. In this study the individual domain encompasses the factors perceived compatibility with workplace values, perceived compatibility with work processes, and knowledge. Compatibility is the (perceived) fit between the values of the HCP, existing processes and a telehealthcare application [8, 22], and as such is mere a combined factor, i.e. capturing the interaction between two domains.

Previous studies suggest that *compatibility with workplace values* of HCPs might be an important predictor of perceived usefulness [16, 22]. That is, the perceived usefulness, or value, of a telehealthcare service will differ between HCPs depending on what they find important (i.e. value) in their work, and how the specific technology is compatible with these workplace values [23]. *Compatibility with work processes* is seen as a measure of the amount of change needed in existing working practices or processes with the new technology [16, 22]. It is proposed that users rate PEOU based on previous experience with similar systems or technologies [16]. Consequently, a technology or system that is perceived as being compatible with current practice might positively influence perceived ease of use, and thereby promote acceptance and adoption.

Next to compatibility, we hypothesize that a lack of knowledge might negatively influence acceptance and adoption of telehealthcare applications. As stated by

behavioral change models, awareness or knowledge of an individual plays an important role in (changing) beliefs and behavior [24, 25]. Therefore, we also explored the (lack of) knowledge regarding the individual, technological and contextual domains.

Technological domain

The technological domain includes the components perceived usefulness (PU) and perceived ease of use (PEOU). PU, also referred to as performance expectancy, is defined as the degree to which an individual believes that using a particular technology will enhance job performance [17, 18]. Studies on acceptance and adoption of technology by HCPs show varying results regarding the role of PU as a predictor. While often PU has been found a strong predictor of acceptance and adoption of telehealthcare in HCPs [7, 18, 26-29], Schaper et al did not found a significant effect of PU on acceptance (operationalized as intention to use) in occupational therapists [8]. Also, Gagnon et al, who evaluated the effect of various factors on acceptance of electronic health records by physicians, reported no effect of PU on intention to use [30]. Despite these ambiguous findings, PU was included in this study to gain more evidence on its role regarding acceptance and adoption of technology in HCPs.

PEOU, or effort expectancy, is the degree of ease associated with the use of a technology or system [18]. In the same studies of Gagnon et al and Schaper, PEOU was found a determinant for intention to use new technologies, suggesting ease of use being of higher importance than PU in physicians [8, 30]. The importance of PEOU as a predictor of technology acceptance has been confirmed by other studies performed in healthcare sector [27, 28, 31].

Context for implementation

The context for implementation is the influence of the specific (working) environment of the HCP on technology use and includes the components social influence and organizational facilitating conditions. Social influence is the degree to which an individual believes that important others (e.g. patients, colleagues, managers) think that use of the technology is a good idea [18]. The literature reports conflicting findings regarding the role of social influence in technology acceptance and adoption of HCPs. Some researchers suggest that HCPs, especially physicians, might be less susceptible to social norms and, consequently, social influence will not influence acceptance and adoption of technology [8, 29]. Still, the majority of studies report significant effects of social influence on acceptance or intention of technology [12, 14, 18, 30, 32, 33].

Organizational facilitating conditions are defined as the degree to which an individual believes that use of the technology is supported by the organization [18], for example

availability of training, technical support and infrastructure, or communications and expectations about use in the organization. Organizational facilitating conditions have found to be an important determinant for successful technology acceptance and adoption in healthcare [7, 8, 14, 16, 18, 32-35].

Development questionnaire

Items were adapted from existing questionnaires [16, 36, 37] and translated to Dutch where needed. For each factor, additional items were composed by the authors based on experience from previous research on adoption and acceptance of telehealthcare service. For nine items, the description slightly differed between users and non-users as to align the description with the experience or the lack of it between these two groups (see Supplementary material 1). The questionnaire comprised 31 items (Supplementary materials 1) evaluating the factors PU (7 items), PEOU (2 items), compatibility with workplace values (6 items), compatibility with work processes (4 items), social influences (3 items), and organizational facilitating (9 items). Each item was phrased as a statement and rated on a 5-point Likert scale (1-5) ranging from "totally disagree" to "totally agree". To explore knowledge of HCPs on these factors the response option "I don't know" was added to the items of all factors.

Additionally, the questionnaire included items to measure demographics: age, sex, occupation, and occupational setting (e.g. hospital, rehabilitation center, private clinic). For users, open-ended questions were added to describe the telehealthcare application(s) they were currently using in patient care and their most important reason to use this application. For non-users, an open-ended question was added questioning their most important reason for not using telehealthcare applications at this moment.

Face validity of the questionnaire was evaluated by two experts in health technology adoption and two HCPs (a physiotherapist and a nurse).

Data analysis

Negative phrased items were transformed so that a higher score indicated (more) positive perceptions.

To explore difference between participants based on acceptance of telehealthcare services, we categorized the score for BIU (see paragraph 2.2.1) into two categories: positive acceptance (a score of 4 or higher) and negative acceptance (a score of 3 or lower).

The total frequency of “I don’t know” was summed per item and per participant, as to quantify (lack of) knowledge level.

The open-ended questions were coded by the first and second author using the factors included in our study (as described under paragraph 2.2.2) to identify the most important barriers and facilitators for adoption of telehealthcare applications. If an answer did not fit our predefined factors, a new code was added using the Consolidated Framework for Implementation Research (CFIR)[38].

Statistical analyses

IBM’s Statistical Package for the Social Sciences (SPSS, 23.0) was used for the statistical analyses of all data. Descriptive statistics and graphs (PP-Plots and histograms) were used to assess normality of the outcome measures. Continuous variables were expressed as mean with standard deviation (SD) or median with interquartile range (IQR), categorical variables as counts with corresponding percentages.

The questionnaire was analyzed on item level, since exploratory factor analysis did not result in satisfactory factors.

We used the Mann-Whitney U test to analyze:

- the difference between users and non-users in Likert score on each item;
- the difference between users and non-users in total frequency of “I don’t know”;
- the difference in item score between non-users with positive acceptance and those with negative acceptance;
- the difference in item score between users with high acceptance and those with low/moderate acceptance.

For each test, effect sizes were calculated following Fritz et al. [39], with effect size (r) .1, .3 and .5 representing small, medium and large effects, respectively [39].

RESULTS

A total of 189 questionnaires were completed online. Forty-two questionnaires were excluded due to missing items, resulting in 147 complete questionnaires. Table 1 summarizes characteristics of the responding HCPs. Of the participants, 48% ($n = 70$) indicated to be current users of telehealthcare, while 52% ($n = 77$) were non-users. Mean age was 39 years for both users and non-users. Majority of participants were woman (76%), but no significant differences between men and women regarding actual use or not were observed ($p = .091$). Most participants worked as a paramedic (either physiotherapist or occupational therapist), with majority of participants working in a rehabilitation center or (private) physiotherapy practice. Of the users 50% described the telehealthcare services they used in clinical practice. Of these, the two most often

used services were e-mail to communicate with patients and colleagues, and exercise programs via a web portal or apps (table 1).

Table 1 Characteristics respondents

	Users (n=70)	Non-Users (n=77)
Age (years)	39 ± 11	39 ± 12
Sex, n (%)		
Male	19 (27)	12 (16)
Female	49 (70)	62 (81)
Missing	2 (3)	3 (4)
Occupation, n (%)		
Nurse	7 (10)	18 (23)
Specialized nurse	1 (1)	1 (1)
Specialist	1 (1)	2 (3)
Physiotherapist	35 (50)	34 (44)
Occupational therapist	15 (21)	11 (14)
Other	11 (16)	11 (14)
Institution, n (%)		
Hospital	16 (23)	15 (20)
Nursing home	0 (0)	4 (5)
Rehabilitation center	20 (29)	23 (30)
Physiotherapy practice	24 (34)	18 (23)
General practitioner practice	2 (3)	1 (1)
Visiting nurse	5 (7)	11 (14)
Self-employed	1 (1)	
Other	2 (3)	5 (7)
Telehealthcare application used, n (%)		
Email	22 (31)	NA
<i>Email only</i>	14 (20)	NA
<i>Email in combination with other telehealthcare application</i>	8 (11)	NA
Online training/exercises	12 (17)	NA
E-consult	4 (6)	NA
Phone	2 (3)	NA
Online questionnaires	3 (4)	NA
Monitoring	4 (6)	NA
Missing	35 (50)	NA

Adoption users and non-users

Users scored significantly higher on BIU than non-users ($p < .001$, $r = .41$). Overall, largest difference in scores between users and non-users were observed on items of the individual domain. All item scores for users and non-users can be found in table 2.

Individual

Non-users were less positive in their beliefs that the use of telehealthcare is part of their job (Values1), that the use of telehealthcare is a good idea (Values 4), and that it

is compatible with their patient group (Values3) or current work processes (Process1). In total, non-users scored significantly more often 'I don't know' on the items than users (*Non-users*: Mdn = 6, IQR = 1-8; *users*: Mdn = 1, IQR = 0-2; $U = 4166.00$, $z = 5.82$, $p < .001$, $r = .49$). As can be seen in table 2, knowledge in both users and non-users was lowest on items of the implementation context.

Technology

Compared to the non-users, users of telehealthcare had less positive beliefs that the use of telehealthcare provides additional information about functioning of their patients (PU7) and that telehealthcare is easy to use (PEOU1).

Context

Non-users expected less support from their patients (Social1) and managers (Social2) compared to the experiences of the users. Furthermore, non-users scored significantly lower on the existence of formal agreements recorded by the management of their organization about the use of telehealthcare applications (FC6).

Self-reported critical barriers and facilitators for adoption

Of the users, 56% reported what they think was their most important facilitator for adoption. For majority of the users PU was seen as the most important facilitator to adopt telehealthcare (65%). Other factors reported were preference of the patients (13%), the wish to keep track of innovations (15%), and participating in a project group or other organizational factors (8%).

Of the non-users, 40% reported what they think was their most important barrier for adoption of telehealthcare in clinical practice. The most important barrier experienced by HCPs were organizational facilitating factors (32%). Other barriers reported included lack of experience or awareness (22%), PU (14%), perceived difficulty to learn or use (11%), lack of incentives/ reimbursements (8%), lack of compatibility with workplace values such as 'hands- on' work (8%), preferences of patients (3%) and lack of compatibility with work processes (3%). In Supplementary material 2 the original description of barriers and facilitators is provided.

Acceptance telehealthcare in non-users

Of the 77 non-users, majority (51%) indicated high intention to use telehealthcare in future (i.e. score 4 or higher on item BIU) and as such were regarded to have a positive acceptance towards telehealthcare. Non-users with positive acceptance indicated more positive beliefs in all three domains, i.e. the individual, technical and context as compared to non-users with negative acceptance (table 3, columns 'non-users').

Individual

As can be seen in table 3, non-users with positive acceptance expected better compatibility of telehealthcare with their workplace values and work processes than non-users with negative acceptance. Especially, large effect sizes were seen for the beliefs that the use of telehealthcare applications is part of the job (Values1) and that the use of telehealthcare in clinical practice is a good idea (Values4).

No significant difference was observed between non-users with positive and negative acceptance regarding the level of knowledge (median frequency "I don't know" positive vs negative acceptance = 4 vs 7; $p=.22$; $U=621.00$; $r=0.14$).

Technology

Regarding PU and PEOU, non-users with positive acceptance had higher expectations that the use of telehealthcare would result in lower healthcare costs (PU1), in more effective and efficient patient care (PU 2,3) and would be easy to learn (PEOU2) than those with negative acceptance.

Context

Non-users with positive acceptance had higher expectations that the use of telehealthcare would be approved by their patients, managers and colleagues (SI 1,2,3). They also reported less fear that the costs would outweigh the benefits (Org2), as well as positive expectations regarding availability of support from colleagues when they would need it (Org 3). Non-users with positive acceptance expected large organizational changes within the foreseeable future compared to those with negative acceptance (Org 8).

Acceptance telehealthcare in users

Of the 70 HCPs who actively used telehealthcare in clinical practice, 8 (11%) rated negative acceptance (i.e. score 3 or lower on BIU item) for continued use of telehealthcare in clinical practice. Especially beliefs of the individual domain were lower in those users with negative acceptance compared to users with positive acceptance.

Individual

Compared to users with positive acceptance, users with negative acceptance had worse perceptions regarding the ability to achieve treatment goals using telehealthcare (Values2), that use of telehealthcare is a good idea (Values4), and valuing telehealthcare being an extra service for the patient (Values 6). They also perceived telehealthcare causing unfavorable changes in their clinical practices (Process3).

No significant difference was observed between users with positive and negative acceptance regarding the level of knowledge (median frequency "I don't know" positive vs negative acceptance = 1 vs 2; $p=.18$; $U=179.50$; $r=0.16$). Still, considerable number of users indicated that they were unaware of the opinion of their managers and colleagues regarding telehealthcare (20% and 16%), as well as whether their organization recorded agreements for the use of telehealthcare in clinical practice (21%).

Technology

Regarding perceived usefulness, users with negative acceptance were less positive that telehealthcare would reduce pressure on healthcare (PU4) or would provide additional information about their patients (PU7).

Context

Perceptions of availability of adequate ICT infrastructure to support use of telehealthcare was worse in users with negative acceptance compared to those with positive acceptance (Org5).

Table 2 Item scores and differences users and non-users on individual, technological and context for implementation items

	Likert score				Frequency "I don't know"			
	Users Median [IQR]	<i>n</i>	Non-users Median [IQR]	<i>n</i>	p-value	Effect size	Users N (%)	Non-users N (%)
<i>Compatibility with workplace values</i>								
Values1	4 [4-5]	70	3 [3-4]	72	<.001	-.37	0 (0)	5 (7)
Values2	4 [4-4]	69	4 [4-4]	69	.376	-.08	1 (1)	8 (10)
Values3	4 [4-5]	70	4 [3-4]	73	<.001	-.35	0 (0)	4 (5)
Values4	4 [4-4]	69	4 [3-4]	74	<.001	-.40	1 (1)	2 (3)
Values5	4 [2-4]	70	3 [2-4]	74	.023	-.19	0 (0)	3 (4)
Values6	4 [4-4]	70	4 [4-4]	75	.005	-.23	0 (0)	2
<i>Compatibility with work processes</i>								
Process1	4 [3-4]	70	3 [2-4]	68	<.001	-.46	0 (0)	8 (10)
Process2	4 [3-4]	69	3 [2-4]	65	.003	-.26	1 (1)	12 (16)
Process3	4 [3-4]	70	3 [3-4]	64	.014	-.21	0 (0)	13 (17)
Process4	3 [2-4]	69	3 [2-4]	72	.701	-.03	1 (1)	5 (7)
<i>Perceived usefulness</i>								
PU1	4 [3-4]	68	4 [4-4]	64	.588	.05	2 (3)	13 (17)
PU2	4 [3-4]	69	4 [3-4]	65	.539	-.05	1 (1)	12 (16)
PU3	4 [3-4]	68	4 [3-4]	65	.611	-.04	2 (3)	11 (14)
PU4	3 [3-4]	70	3 [3-4]	63	.985	.002	0 (0)	14 (18)
PU5	3 [2-4]	70	4 [3-4]	63	.268	.10	0 (0)	14 (18)
PU6	4 [4-5]	70	4 [4-4]	72	.112	-.13	0 (0)	5 (7)
PU7	4 [3-4]	70	4 [4-4]	72	.005	.24	0 (0)	5 (7)
<i>Perceived ease of use</i>								
PEOU1	4 [3-4]	69	4 [4-4]	60	.019	.21	1 (1)	17 (22)
PEOU2	4 [3-4]	69	4 [3-4]	67	.386	-.07	1 (1)	10 (13)
<i>Social norms</i>								
SI1	4 [3-4]	68	3 [2-4]	57	<.001	-.46	2 (3)	20 (26)
SI2	4 [3-4]	56	3 [2-4]	49	<.001	-.37	14 (20)	28 (36)
SI3	4 [3-4]	59	3 [2-4]	35	.041	-.21	11 (16)	42 (55)
<i>Organizational facilitating conditions</i>								
Org1	3 [2-4]	68	3 [2-4]	61	.376	-.08	2 (3)	16 (21)
Org2	4 [2-4]	62	3 [2-4]	47	.144	-.14	7 (10)	30 (39)
Org3	4 [3-4]	64	4 [3-4]	60	.464	-.07	6 (9)	17 (22)
Org4	4 [3-4]	69	3 [2-4]	51	.187	-.12	1 (1)	26 (34)
Org5	4 [3-4]	69	4 [2-4]	60	.057	-.17	1 (1)	16 (21)
Org6	3 [2-4]	55	2 [2-4]	43	.038	-.21	15 (21)	34 (44)
Org7	4 [2-4]	63	3 [2-4]	48	.164	-.13	7 (10)	29 (38)
Org8	3 [2-4]	63	2 [2-4]	67	.996	-.0004	7 (10)	9 (12)
Org9	3 [2-4]	64	3 [2-4]	61	.241	-.10	6 (9)	16 (21)
<i>Behavioral intention to use</i>								
BIU	4 [4-5]	70	4 [3-4]	77	<.001	-.41	--	--

IQR Interquartile range; *Values* Compatibility with workplace values; *Process* Compatibility with work processes; *PU* Perceived usefulness; *PEOU* Perceived ease of use; *SI* Social influence; *Org* Organizational facilitating conditions; *BIU* Behavioral intention to use

Table 3 Item scores and differences users and non-users with low versus high acceptance

	Non-users					Users					Effect size
	Negative acceptance	n	Positive acceptance	n	p-value	Effect Size	Negative acceptance	n	Positive acceptance	n	p-value
<i>Compatibility with workplace values</i>											
Values1	3 [2-3]	34	4 [3-4]	38	<.001	.62	4 [3-4]	8	4 [4-5]	62	.245
Values2	4 [3-4]	33	4 [4-4]	36	.001	.41	3 [3-4]	8	4 [4-4]	61	.008
Values3	4 [2-4]	35	4 [4-4]	38	.001	.39	4 [4-5]	8	4 [4-5]	62	.526
Values4	3 [2-4]	37	4 [4-4]	37	<.001	.52	3 [3-4]	8	4 [4-4]	61	.008
Values5	2 [2-4]	35	3 [2-4]	39	.072	.21	2 [2-4]	8	4 [3-4]	62	.063
Values6	4 [3-4]	36	4 [4-4]	39	.010	.30	4 [3-4]	8	4 [4-4]	62	.018
<i>Compatibility with work processes</i>											
Process1	3 [2-3]	34	3 [3-4]	34	.002	.38	4 [3-4]	8	4 [3-4]	62	.481
Process2	2 [2-4]	31	4 [3-4]	34	.008	.33	3 [2-4]	8	4 [3-4]	61	.093
Process3	3 [2-4]	30	4 [3-4]	34	.001	.41	3 [3-3]	8	4 [3-4]	62	.003
Process4	3 [2-4]	35	3 [2-4]	37	.293	.12	3 [2-4]	7	3 [2-4]	62	.850
<i>Perceived usefulness</i>											
PU1	4 [3-4]	30	4 [4-4]	34	.002	.38	3 [3-5]	8	4 [3-4]	60	.262
PU2	4 [3-4]	29	4 [4-4]	36	.003	.36	4 [3-4]	8	4 [3-4]	61	.098
PU3	3 [2-4]	29	4 [4-4]	36	<.001	.44	4 [2-4]	8	4 [3-4]	60	.127
PU4	3 [2-4]	30	4 [3-4]	33	.131	.19	2 [1-3]	8	4 [3-4]	62	.007
PU5	3 [3-4]	32	4 [3-4]	31	.182	.17	4 [3-4]	8	3 [2-4]	62	.687
PU6	4 [4-4]	33	4 [4-5]	39	.124	.18	3 [2-4]	8	4 [4-5]	62	.079
PU7	4 [4-4]	34	4 [4-4]	38	.224	.14	4 [2-4]	8	4 [3-4]	62	.022
<i>Perceived ease of use</i>											
PEOU1	4 [3-4]	28	4 [4-5]	32	.173	.18	4 [3-4]	8	4 [3-4]	61	.754
PEOU2	3 [3-4]	31	4 [3-4]	36	.022	.28	4 [2-4]	8	4 [3-4]	61	.240
<i>Social norms</i>											
SI1	3 [2-3]	27	4 [3-4]	30	<.001	.50	4 [3-4]	7	4 [4-4]	61	.222
SI2	3 [2-3]	25	3 [3-4]	24	.001	.47	4 [4-4]	7	4 [3-4]	49	.662
SI3	3 [2-3]	16	4 [3-4]	19	.007	.47	4 [2-4]	6	4 [3-4]	53	.516
<i>Organizational facilitating conditions</i>											
Org1	3 [2-4]	32	2 [2-4]	29	.786	-.03	2 [1-4]	8	3 [2-4]	60	.145
Org2	2 [2-3]	23	4 [3-4]	24	<.001	.58	3 [2-3]	6	4 [2-4]	56	.133
Org3	4 [3-4]	25	4 [4-4]	35	.013	.32	4 [3-4]	8	4 [3-4]	56	.821
Org4	3 [2-4]	22	3 [2-4]	29	.757	.04	3 [2-4]	8	4 [3-4]	61	.262
Org5	4 [2-4]	28	4 [3-4]	32	.499	.09	4 [2-4]	8	4 [4-4]	61	.046
Org6	2 [2-4]	20	3 [2-4]	23	.151	.22	4 [2-4]	7	3 [2-4]	48	.544
Org7	2 [2-4]	23	4 [2-4]	25	.346	.14	4 [2-4]	7	4 [2-4]	56	.957
Org8	4 [2-4]	34	2 [1-4]	33	.003	-.36	2 [1-4]	7	3 [2-4]	56	.408
Org9	2 [1-4]	31	3 [2-4]	30	.365	.12	3 [2-4]	6	3 [2-4]	58	.884

IQR Interquartile range; Values Compatibility with workplace values; Process Compatibility with work processes; PU Perceived usefulness; PEOU Perceived ease of use; SI Social influence; Org Organizational facilitating conditions; BIU Behavioral intention to use

DISCUSSION

The present study investigated the beliefs and knowledge of healthcare professionals regarding factors on the individual, technical and implementation level as well as behavioral intention to keep or start using (BIU) telehealthcare. These beliefs, knowledge and BIU were studied and compared in both HCPs who currently use telehealthcare applications in clinical practice (users) and those who don't (non-users). The knowledge gained in this study can be used to provide new insights on barriers and facilitators but also to develop sustainable implementation strategies for telehealthcare in clinical practice.

In our study, potential barriers and facilitators for adoption were identified on all three domains, that is the individual, technological and context of implementation. First, the scores of the questionnaire indicated the largest difference between users and non-users on compatibility with workplace values and processes and social influence. That is, users perceived a better fit between telehealthcare and their values and work processes and more support from their patients, colleagues and managers than the non-users. This is in line with conclusions of previous studies that good compatibility of the innovation with workplace values and processes and an encouraging social environment promote adoption [14, 16]. Examples of activities that might promote perception of compatibility are involving stakeholders early in design as to take their needs and preferences into consideration, and educating and facilitating common vision making with HCPs during which the compatibility of the application with values and processes is emphasized. The importance of social influence for successful adoption has previously been described [12, 14, 30, 32, 33]. Again, joined sessions that create a common vision between HCPs regarding telehealthcare use may positively influence HCPs' beliefs about opinions of their colleagues and managers. Especially the presence of clinical leaders that openly communicate positive beliefs regarding use of telehealthcare may drive successful adoption by other HCPs [14]. Second, in our sample users reported PU as one of the most important facilitators for adoption of telehealthcare application. This is in line with a recent review of Gagnon et al. who also conclude that PU is one of the most important factors that influences adoption, both as a facilitator and a barrier [13]. Surprisingly, item scores of the technological domain did not show large differences between users and non-users, that is, all HCPs were quite positive regarding the usefulness and ease of use of telehealthcare applications. That we did not find large differences on PU and PEOU between groups might be explained by our recruitment method. Regarding recruitment, HCPs were primarily approached via social media. It is possible that HCPs that actively use social media relatively have more positive perceptions regarding technology, resulting in high

scores on the items of the technological domain. It is highly likely that in practice more negative perceptions of PU and PEOU (but also on the other domains) will be present and need to be addressed. Activities to promote perceptions of PU and PEOU might include providing the opportunity try and get acquainted with the application [40, 41], and inform HCPs how the application improves care or solve current problems. Lastly, no large differences on item scores of the organizational facilitating factor were observed between users and non-users. However, non-users showed low knowledge regarding the context for implementation (measured as social influence and organizational facilitating factors), and non-users also reported organizational facilitating factors most often as the critical barrier for adoption. This is in line with findings from others who have concluded that creating knowledge or awareness about organizational facilitators and encouragement or support from the social environment is paramount for promoting adoption [11, 13, 14]. Creating awareness can be reached through timely and clear communication involving all levels of the organization about organizational vision statements, formal agreements and availability of support of telehealthcare use. Other examples of important contextual factors that can promote adoption are availability of incentives or reimbursements [9, 11], clinical leadership [14], and support of the technology through management, training, material and human resources [13].

The finding that barriers and facilitators for HCPs' adoption of telehealthcare can be present on all domains, is in line with previous studies and reviews that report the need of a holistic approach towards implementation of technology in clinical practice to promote adoption, instead of focusing solely on characteristics of the technology such as the frequently used TAM [7, 9, 11, 13, 42]. Arising from that, evaluation of possible barriers should also address these levels, and, based on the barriers found, targeted interventions can be planned and deployed to promote adoption. The specific importance of each factor, that is whether it might pose a barrier or even might be a facilitator, will vary based on the characteristic of the technology (or intervention), the phase of implementation as well as specific characteristics of the individual and implementation context [11, 42]. As an example, in our study, the majority of users reported the use of rather simple technologies such as email. When implementation of more complex telehealthcare applications is desired, it is likely that more barriers will be perceived for successful implementation on all domains, which even more justify identification and addressing barriers on these domains. The present study used a cross-sectional design which hampers insight in adaptation of beliefs over time and the influence of this change on acceptance, adoption and implementation. We advise for future studies to evaluate the change in beliefs, acceptance, adoption and implementation to clarify how the various factors influence the successful adoption

and implementation as to guide a targeted implementation plan.

Another interesting finding from our study is that positive acceptance of telehealthcare does not guarantee successful adoption. HCPs who adopted telehealthcare, that is the 'users' of our sample, in general had higher acceptance (measured as intention to use) than the non-users (or non-adopters). Still, more than half of the non-users indicated positive acceptance together with positive beliefs towards telehealthcare. However, these positive beliefs and intentions apparently did not result in successful adoption. This implies that successful acceptance and adoption does not 'just happen'. As advocated by various researchers, adoption can only be reached using a proactive approach [9, 11]. Various factors were reported by the non-user as barriers for successful adoption on the individual, technological and context of implementation domain. Repeated evaluation of existent barriers is needed followed by targeted activities to bridge this gap between intentions and actual behavior.

In line with previous dissemination and implementation research, our study supports that promotion of acceptance and adoption should be approached as a long-term, dynamic process. Our results show that barriers and facilitators are present from early in the process of implementation (that is, prior to adoption; as measured in the non-users) until after initial adoption has taken place (as measured in the users). Often, projects and funding end after initial adoption and a first evaluation in clinical practice, resulting in diminished attention towards sustainable implementation of the application in clinical practices [9, 11, 42]. In our study some of the HCPs who initially adopted telehealthcare, reported dissatisfaction and a low intention to keep using the application in future. The challenge therefore is to design a plan for implementation that spans over single projects funding as to maintain a continued focus on promoting acceptance, adoption and sustainability to prevent de-adoption of the application over time. This requires long term vision and commitment of management and clinical leaders, resulting in strategic partnerships and sponsorship as well as inspiring leadership in moments of disappointing results or staggering implementation.

Although our study had some limitations regarding methodology (e.g. cross-sectional design, self-constructed questionnaire) this study provides insight into beliefs of HCPs regarding factors that influence acceptance and adoption of telehealthcare applications in practice. The results support the importance of a holistic approach regarding implementation by proactively and repeatedly identifying and addressing barriers and facilitators on the individual, technological and context for implementation domain, from pre- until post-adoption. Future studies should focus on the effect of targeted implementation strategies on successful acceptance, adoption and implementation of telehealthcare applications.

CONCLUSION

Barriers and facilitators for professionals' adoption of telehealthcare can exist on different domains, that is the individual, technological and context for implementation, and can be present from prior to adoption until after initial adoption. Although positive acceptance and beliefs of telehealthcare are essential, they do not guarantee successful adoption. Given these findings, we conclude that successful adoption of telehealthcare in clinical practice requires a holistic approach regarding implementation by proactively and repeatedly identifying and addressing barriers and facilitators on the individual, technological and context for implementation domain, from pre- until post-adoption.

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SUPPLEMENTARY MATERIAL 1

Table A Items questionnaire

ITEM	Users	Non-users
Compatibility with work values [16, 36, 37]		
1	Values1 I think it is part of my job to use telemedicine	I think it is part of my job to use telemedicine
2	Values2 Telemedicine helps me to achieve my treatment goals	Telemedicine may help me to achieve my treatment goals
3	Values3 I think that telemedicine is appropriate for (part of) my patients	I think that telemedicine is appropriate for (part of) my patients
4	Values4 The use of telemedicine in the care of my patients is a good idea	The use of telemedicine in the care of my patients is a good idea
5	Values5 Telemedicine makes healthcare more impersonal.	Telemedicine makes healthcare more impersonal.
6	Values6 Telemedicine is an extra service for the patient; and I think that important in my job.	Telemedicine is an extra service for the patient; and I think that important in my job.
Compatibility with work processes [16, 37]		
7	Comp1 The use of telemedicine is compatible with my work habits	The use of telemedicine is compatible with my work habits
8	Comp2 Telemedicine is easy to apply during usual care of my patients	Telemedicine is easy to apply during usual care of my patients
9	Comp3 The use of telemedicine may imply unfavorable changes in my clinical practice	The use of telemedicine may imply unfavorable changes in my clinical practice
10	Comp4 I think that using telemedicine changed my daily work duties.	I think that using telemedicine will change my daily work duties.
Perceived Usefulness [36]		
11	PU1 Telemedicine may decrease healthcare costs	Telemedicine may decrease healthcare costs
12	PU2 The use of telemedicine improves effectiveness of the care of my patients	The use of telemedicine may improve effectiveness of the care of my patients
13	PU3 The use of telemedicine improves efficiency of the care of my patients	The use of telemedicine may improve efficiency of the care of my patients
14	PU4 Telemedicine may reduce the pressure on healthcare	Telemedicine may reduce the pressure on healthcare
15	PU5 Telemedicine improves accessibility of healthcare for patients	Telemedicine improves accessibility of healthcare for patients
16	PU6 Telemedicine enables self-management of own recovery/treatment in patients	Telemedicine enables self-management of own recovery/treatment in patients
17	PU7 The use of telemedicine provides additional information about functioning of my patient	The use of telemedicine may provide additional information about functioning of my patient

<i>Perceived ease of use [37]</i>			
18	PEOU1	I think that telemedicine is difficult to use	I think that telemedicine will be difficult to use
19	PEOU2	It was easy to learn how to use telemedicine	I think that I could easily learn how to use telemedicine
<i>Social norms [36, 37]</i>			
20	Social1	Most of my patients welcome the fact that I use telemedicine	Most of my patients will welcome the fact that I use telemedicine
21	Social2	My manager(s) believe that I should use telemedicine	My manager(s) believe that I should use telemedicine
22	Social3	Most of my colleagues welcome the fact that I use telemedicine	Most of my colleagues welcome the fact that I use telemedicine
<i>Facilitating conditions [16, 36, 37]</i>			
23	FC1	When I want to, I can make time for the use of telemedicine	When I want to, I can make time for the use of telemedicine
24	FC2	I am afraid that the costs of telemedicine outweigh the benefits for my organization.	I am afraid that the costs of telemedicine outweigh the benefits for my organization.
25	FC3	I can rely on sufficient help from my colleagues may I need it when using telemedicine	I can rely on sufficient help from my colleagues may I need it when using telemedicine
26	FC4	My organization provides sufficient materials and facilities for effective use of telemedicine	My organization provides sufficient materials and facilities for effective use of telemedicine
27	FC5	I think that my organization has the necessary ICT-infrastructure to support my use of telemedicine	I think that my organization has the necessary ICT-infrastructure to support my use of telemedicine
28	FC6	The management of my organization has formally recorded agreements regarding the use of telemedicine	The management of my organization has formally recorded agreements regarding the use of telemedicine
29	FC7	In my organization one or more persons have been appointed to coordinate the implementation of telemedicine	In my organization one or more persons have been appointed to coordinate the implementation of telemedicine
30	FC8	Large organizational changes are taking place at this moment or in the foreseeable future (reorganization, merge, downsizing, employee turnover, introduction other innovations such as electronic patient record)	Large organizational changes are taking place at this moment or in the foreseeable future (reorganization, merge, downsizing, employee turnover, introduction other innovations such as electronic patient record)
31	FC9	Telemedicine is a priority in my organization.	Telemedicine is a priority in my organization.
<i>Behavioral intention to use [37]</i>			
32	BIU	I have the intention to keep using telemedicine in the future	I have the intention to use telemedicine when I get the chance.

SUPPLEMENTARY MATERIAL 2

Table A Most important reason to use TM at this moment (users n=39).

Respons users	Facilitator
Request of patient.	Social Influence
Involved in project group to evaluate the use of TM as part of treatment	Organizational / facilities
Working process within organization.	Organizational / facilities
As an addition to standard treatment; not as a replacement. I believe TM is insufficient as replacement.	Perceived Usefulness
For 30% of the people that use it [TM], is has an added value for me and for them.	Perceived Usefulness
Intervention/monitoring in real-life setting instead of during consultation only.	Perceived Usefulness
Extra service and information for the patient.	Perceived Usefulness
I do not want to be disturbed by phone. I can answer mails at a time that is convenient to me.	Perceived Usefulness
I believe that this will be the future.	Innovation
To meet [the wishes of] the patient.	Social Influence
Because of low burden, while still keeping in touch [with patients].	Perceived Usefulness
To keep track of innovations and implement eventual.	Innovation
Participation in project group.	Organizational / facilities
Innovation.	Innovation
For the client; I also hope for time savings.	Social Influence Perceived Usefulness
To facilitate the care/treatment for patients.	Perceived Usefulness
Monitoring physical activity of patients.	Perceived Usefulness
Service to patients.	Social Influence
To keep up with time / innovations.	Innovation
Accessibility.	Perceived Usefulness
Added value for the patient.	Perceived Usefulness
Looking ahead to the future.	Innovation
Added value for the patients to practice well, [such as] the visual support.	Perceived Usefulness
Service to the patient, resulting in a motivated patient!	Perceived Usefulness
Added value for the patient.	Perceived Usefulness
As an addition to treatment in the practice.	Perceived Usefulness
Expectation of the patient.	Social Influence
Clarifies the exercises that patients have to perform at home.	Perceived Usefulness
Easily accessible for (old) patients.	Perceived Usefulness
Time savings during care moments/consultations.	Perceived Usefulness
Ease of communication and timely consultation and advise.	Perceived Usefulness
Addition to [standard] care of patients.	Perceived Usefulness
Increase of coaching and support of patients.	Perceived Usefulness
Additional support next to face to face consultations.	Perceived Usefulness
Facilitate working process.	Perceived Usefulness
Of additional and distinctive value.	Perceived Usefulness
Addition to [standard] care, no replacement.	Perceived Usefulness
As part of research and to go with nationwide innovations.	Innovation
Efficient, effective.	Perceived Usefulness

Table B Most important reason not to use TM (non-users, n=31)

Respons non-users	Barriers
Most of my patients/clients are of high age that working with a computer is not an option. Mostly there is not a computer of something like that available in the home.	Perceived Ease of Use
Lack of knowledge how it [TM] works, for which questions, and what is needed to start working with it.	Knowledge/awareness/experience
It takes time, which I won't get compensated for.	Reimbursements Organizational/facilities
Impersonal.	Values
I am a clinical nurse. At this moment, I do not see benefit of TM on a clinical ward.	Perceived Usefulness
My clients very much care about the social contact part; and not the contact via a screen or something like that.	Social Influence
I am afraid it [TM] will increase my work load and that I will be busy with it after work in my free time. TM can be easy and time saving, but there is a risk that it will expand further and further and that patient support is possible from home. For me that's the danger. It all seems quite handy, but there will definitely be drawbacks. Nevertheless, I am still open [to TM].	Perceived Usefulness Work process
Unknown makes unloved. Unloved makes unsafe.	Knowledge/awareness/experience
At this moment, it is not being used at my workplace.	Organizational / facilities
Ventilation need of the patient. I work at an ICU, obviously there is no use of TM	Perceived Usefulness
Insufficient knowledge.	Knowledge/awareness/experience
I value 'hands-on' working/treatment. In our job I value the contact with the patients, observing movement and correcting it directly. With TM I too often see mistakes occurring.	Values
No compensation, it takes more time, less able to practice your (hands-on) specialization (manual therapist), no live contact with patients.	Reimbursements Values
I do not see the added value of TM for my patients.	Perceived Usefulness
A lot of patients do not have internet or cannot work with it, this is a barrier. They also do not own an expensive smartphone with apps. It also takes additional time to communicate and administrate. There is not yet a link with software. If it will only be more, more, without sufficient compensation, the benefits will not weigh upon the costs.	Perceived Ease of Use Reimbursements
The possibility/conditions are not entirely available. I'm positive to explore the possibilities of TM.	Organizational / facilities
Wait and see. Disappointment with early implementation, disappointing results, a lot of trouble.	Knowledge/awareness/experience
No experience with the method.	Knowledge/awareness/experience
Not relevant on a nursing ward.	Perceived Usefulness
Not yet implemented in organization. Has started.	Organizational / facilities
None. I'm open for the use of TM, it seems a good solution for my patient group during night shifts. I believe that the implementation of TM should get more attention so that the organization where I work can start using this new method of healthcare supply.	Organizational / facilities

Unclear what is possible and the preferences/perceptions of patients.	Knowledge/awareness/experience Social Influence
Not yet possible. Webportal pain in development.	Organizational / facilities
At this moment, the environment is unsafe. Therefore, use is not yet possible.	Organizational / facilities
Lack of time and facilities.	Organizational / facilities Knowledge/awareness/experience
Not discussed / a topic of discussion in our organization.	Organizational / facilities Knowledge/awareness/experience
No facilities available.	Organizational / facilities
We will be using EPD.	Organizational / facilities
Primarily older clients who do not have internet or something.	Perceived Ease of Use
An important factor for our nursing home where I work is that it is a psycho-geriatric nursing home.	Perceived Ease of Use
Time pressure at tumor project team to employ new activities.	Organizational / facilities

7

GENERAL DISCUSSION

In 2011, this research project started with the overall aim to gain knowledge on how to improve the quality and accessibility of home-based cancer rehabilitation to support functional recovery following lung resection using telehealthcare. Starting from previously gained experience with telehealthcare applications in other diagnosis groups, this thesis described subsequently the design, evaluation, and adoption of a telehealthcare service for NSCLC survivors undergoing lung resection. In this last chapter, the results of the studies are integrated and their relevance for clinical practice as well as needs and possibilities for future research are discussed.

PRINCIPAL FINDINGS

Design

The design of the telehealthcare application built on existing technology that was already available for other chronic diseased populations such as COPD and chronic fatigue [1-3], as to speed up the first phase of the design process. Next to that, in project conception explicit choices were made to focus on physical activity behavior, given its potential as a therapeutic option to improve functional outcome following cancer diagnosis and treatment [4-6]. The content of this thesis can therefore best be viewed and understood in the context of these choices.

As part of the design phase we explored whether a focus on physical activity monitoring to support home-based rehabilitation is clinically relevant. Results of this thesis showed that accelerometer-based ambulant monitoring can capture a variety of physical activity behavior measures - including variability, intensity and distribution of physical activity bouts - which provide insight in and can differentiate between individual patterns of daily behaviors of survivors (chapters 2 and 3). Next to that, measures of physical activity behavior were associated with symptom burden (chapter 2) and recovery following lung resection in NSCLC patients (chapter 3). As such, we conclude that physical activity monitoring is clinically relevant. Results also showed large interindividual differences as well as intraindividual changes over time, which requires a personalized approach in the telehealthcare service (chapter 3). Using accelerometry, such a personalized approach can be realized. For instance, interventions to promote healthy physical activity behavior may vary from increasing time spent in prolonged bouts of moderate-to-vigorous physical activity in one patient, breaking up prolonged bouts of sedentary behavior in another patient, or starting with removing existing barriers for physical behavior change [7-9].

The second part of the design focused on requirements elicitation by assessing the

perceived need and value for telehealthcare to improve supportive care following lung resection of both NSCLC survivors and healthcare professionals. As can be found in chapter 4, both survivors and professionals perceived a need for supportive care post-surgery. Highest needs were reported for ambulant monitoring of health status, a web-based exercise program, and tailored information regarding disease, treatment and lifestyle. The use of technology to provide supportive care was not seen as a barrier by survivors, under the prerequisite that the technology, such as sensors, would be user-friendly for home-based use and that their use would guide healthcare professionals' treatment and actions. For healthcare professionals, integration of data from the telehealthcare service with existing electronic health records in a sensible and easy-to-view manner was rated critical for feasibility.

Evaluation

Using an iterative approach, evaluation was inextricably linked with design activities. In this thesis, we used an iterative process of design and evaluation following the staged approach [10], with frequent user involvement. As described in the staged approach, evaluation of a telehealthcare application should be tailored to the maturity of the technology, as to prevent irrelevant negative findings of a premature design [10, 11]. Following this approach, scenario evaluation (chapter 4), usability testing (chapter 4), and evaluation of acceptability and clinical feasibility (chapter 5) were performed.

First, the results of our evaluations showed that NSCLC survivors are able and feel competent to use telehealthcare applications, including ambulant sensors (chapters 4 and 5). This is in line with previous studies, which also observed the competency and willingness of chronically diseased populations to interact with health technology [12, 13]. This leads us to conclude that smartphone or web-based interventions including on-body sensors are acceptable for use in cancer rehabilitation. The use of sensors, however, does need tailoring based on clinical or personal preferences. That is, the monitoring protocol – including monitor frequency, and selection of outcomes and sensors – should be determined based on the treatment goal and survivors' characteristics and preferences (chapter 5).

Second, NSCLC survivors and healthcare providers perceived the use of telehealthcare beneficial for both the quality and accessibility of rehabilitation following lung resection (chapter 5). Healthcare professionals reported benefit of monitoring through increased insight in functional recovery, which could inform and improve treatment choices (chapter 5). Next to that, survivors indicated that insight in symptoms using ambulant monitoring resulted in decreased feelings of anxiety about recovery. Survivors also felt that the web-based exercise program supported behavioral change

towards a physically active lifestyle while having access to and support from specialized professionals. From a survivors' point of view, lung cancer and its treatment may result in a loss of autonomy and competency, due to uncertainty about outcome, loss of confidence about physical functioning, and high dependency on the specialist's knowledge and skill [14, 15]. Their comments on how telehealthcare supports their recovery, suggest that ambulant monitoring and web-based exercise might satisfy the survivors' need for autonomy and competency.

Despite this perceived value of telehealthcare to improve the quality and accessibility of post-surgery rehabilitation in NSCLC survivors, uptake of the service, especially by physicians, was low (chapter 5). Consequently, survivors reported disappointment with and, as a result, demotivation to use telehealthcare due to the lack of involvement and support of the healthcare professionals (chapter 5). Professionals' and patients' comments indicate that these unsuccessful outcomes were not necessarily caused by characteristics of the technology, but also influenced by a mismatch of the telehealthcare service with contextual factors, such as existing work processes, tasks, responsibilities and expectations.

Adoption

In chapter 6, potential barriers and facilitators for adoption of telehealthcare by healthcare professionals were further explored. To do so, factors from three domains, known for their influence on acceptance and adoption, were evaluated, being: 1) the individual domain comprising the factors compatibility with workplace values and work processes, 2) the technological domain comprising perceived usefulness and perceived ease of use, and 3) the context of implementation domain which comprised organizational facilitating and social influence factors. The results showed that barriers and facilitators for professionals' adoption exist on all three domains. This is supportive of findings and conclusions from previous studies regarding the need of a holistic approach towards implementation of technology in clinical practice [16-20].

Next to that, the results suggest the presence of (varying) barriers and facilitators throughout the entire process of acceptance, adoption and implementation. That is, barriers and facilitators were present from pre-adoption (as measured in non-users) until after initial adoption has taken place (as measured in the users) (chapter 6). This supports the notion that promotion of acceptance and adoption should be approached as a long-term, dynamic process [18].

CONCLUSIONS AND RECOMMENDATIONS FOR FUTURE

Now, at completion of the project and this thesis, we can make up the balance of our efforts to improve the quality and acceptability of home-based cancer rehabilitation using telehealthcare services. Throughout this project we increased knowledge of the clinical relevance of ambulant monitoring to improve post-surgery outcomes in cancer survivors and its potential for personalized support. Also, in-depth insight in the needs and requirements for post-surgery supportive care of NSCLC survivors and the healthcare professionals involved in this care trajectory was gained. In close cooperation with these survivors and professionals an ambulant monitoring system and a web-based exercise module were developed, which monitors and supports functional recovery at home. We also discovered that the use of these kinds of technologies, being on-body sensors and web-based portals, are acceptable for survivors. Together, this brings the promise of home-based, personalized cancer rehabilitation for NSCLC survivors within reach.

Contrary to these advances, we have to conclude that not all efforts were successful. First of all, further improvement of the technology is necessary for optimizing its applicability and effectiveness. Second, to improve the fit with users' and other stakeholders' needs, the design process might benefit from a less technology-driven and a more value-driven approach. Lastly, in the end we have not reached wide-scale, sustainable adoption and implementation of the developed modules (being symptom and physical activity monitoring and web-based exercise), thereby failing to improve quality and accessibility. In this final paragraph we want to look ahead and discuss what is needed regarding the technology, design and implementation to move telehealthcare into clinical practice, and with that, enable cancer rehabilitation at home.

Technology: the need for holistic sensing and intelligent reasoning

The technology used consisted of on-body sensors, a smartphone, and a web-based portal for exercises and visualization of monitored data. Although acceptable for survivors, they also reported lack of tailoring of the exercises and monitoring protocol, lack of feedback on progress, and lack of accessibility of data on mobile devices (chapter 5). From the perspective of the healthcare professional, an important barrier for adequate use appeared the lack of compatibility with work processes such as available time, and applicability of information for consultation and treatment. To improve uptake and effectiveness of telehealthcare in cancer rehabilitation, we should strive for a holistic, personalized approach using multimodal sensing and intelligent reasoning.

To be more specific, in the monitoring application for NSCLC survivors, sensing comprised particularly physical components, being physical activity behavior, symptoms, heart rate and oxygen saturation. However, advances in technology already enables the collection of multimodal data from subjects regarding a combination of physical activity behavior, health, fitness, cognition, emotion, and context which together provide a much more complete picture about the individual in their natural context [21-26]. To optimize use, the advanced possibilities of mobile phones should be exploited enabling continuous monitoring in an unobtrusive way [24, 26].

In addition, in both the monitoring and web-based exercise application reasoning was limited to constructing graphs or score tables from the sensor data and self-rated scores of for example symptoms and difficulty of exercise performance, which was done for each module separately (chapters 4 and 5). Reasoning is the process of multi-source data integration into meaningful information [27], and is a requisite for decision-support and personalized care. Addition of intelligent reasoning might provide clinically relevant decision support for healthcare professionals as well as personalized and comprehensive support for cancer survivors through integration of multi-modal data, such as data from the individual (for example, sensing data, performance of exercises, information from electronic health record, individual's goals and needs), treatment guidelines and professional expertise.

Reasoning remains challenging, since it requires standardization of various critical processes such as data-handling, classification of outcomes (e.g. behavior and symptoms), and clinical decision making [28]. For example, regarding physical activity behavior, for successful reasoning consensus must be reached how to clean the data before analysis, what is the (personal) behavioral pattern to strive for, and which combination of physical behavior parameters and other personal and contextual factors require action or intervention [28].

Also, reasoning requires data analyses techniques that can deal with the individual, adaptive, 'noisy' nature of data gathered in the uncontrolled setting of daily life [27]. Examples of such new analysis techniques that have become available are (multilevel) longitudinal analyses [29, 30], and machine learning based methods that can determine the existence and strength of interrelationships of various factors using neural networks [31, 32], or detect changes over time in behavioral patterns using a combination of user-characteristics, preferences and data [33]. So, instead of suffering from heterogeneity in samples and data-gathering, rather these new methods may exploit this complexity and variety between individual, behavior and context.

Value-based design approach

In this study, we revealed user needs by presenting users with various examples of telehealthcare applications (chapter 4). This provided us with relevant information how telehealthcare could support post-surgery recovery, but it did not provide in-depth insight in the underlying values, needs and motives of participants' behavior. Probably a more value-based design would have been better. Behavior change theory, such as the self-determination theory, suggest that user behaviors are shaped by the satisfaction of self-determined needs or values [34, 35]. Indeed, in our own research we found that perceived compatibility with workplace values might have affected acceptability and adoption of the telehealthcare service by healthcare professionals (chapter 6). For example, specialized nurses, often the case managers in cancer care and central to the entire care process of survivors, might value quality improvement of treatment through a holistic, comprehensive understanding of the patient. While on the other hand, surgeons might value quality improvement through higher efficiency in recognizing complications following surgery. These differences in values might lead to different requirements. Also, as value-based approach reasons from the identified (economic, social, behavior, medical) values, it enables finding solutions which may include but is not limited to technology, thereby promoting product-service design [36, 37].

Additionally, next to the end-users we involved in our user-centered design, it is advised to identify other relevant stakeholders that might influence the adoption and implementation of the telehealthcare service. Examples of possible influential stakeholders that should be considered for involvement in the process of value clarification and design are healthcare insurers, policy makers, or commercial business enterprises [17, 19].

In conclusion, a combined approach, starting with value clarification followed by design in co-creation with users and other stakeholders might provide solutions that better fit users' actual needs, and through that will promote uptake and adoption [17, 37, 38].

Implementation

Most and for all, as we have realized throughout this project, sustainable implementation of telehealthcare services requires a whole-system approach, addressing the micro-, meso-, macro-level of the healthcare system. Telehealthcare services can best be seen as a system of care that requires effort and specific activities from various actors to make the telehealthcare service work [19, 20, 39]. Telehealthcare to support home-based rehabilitation of cancer survivors comprise different contexts (for example, the hospital, patients' home, physiotherapist practice), and multiple stakeholders with varying, often conflicting needs (for example, cancer survivors, nurses, specialists,

physiotherapists, management, health insurance companies, technology companies, researchers) [40]. Although we have employed techniques to involve users and communicate the impact of telehealthcare on the care process (for example, a user-centered design approach and the use of scenarios, see chapters 4 and 5), the evaluation was limited by the emphasis on technology characteristics and involvement of only two of the relevant stakeholders, being healthcare professionals and survivors. To deliver integrated rehabilitation services in the homes of cancer survivors a holistic approach for design and evaluation is necessary to reach alignment and consensus between all relevant stakeholders – that is, any party involved with the design, purchase, financing, provision or use of the service – regarding aims and responsibilities in the usage of telehealthcare services. Recently, systems thinking emerged in the design, evaluation and implementation of innovations for complex systems such as healthcare settings [18, 41]. Systems thinking is ‘the process of understanding how things influence one other within a whole’ [18]. Systems thinking is concerned with identifying the various attributes (people, institutes, interventions, or other ‘things’) of a system, their interrelatedness, and resulting behavior patterns over time. By acknowledging and addressing the multilevel and dynamic characteristics of healthcare systems, systems thinking approaches and methods might prove useful to optimize the fit between telehealthcare with the context of implementation.

Next to that, in our approach there was a clear lack of proactive actions to promote and evaluate the process of adoption and implementation. Adoption does not ‘just happen’ but needs attention and targeted activities to address the barriers present [18, 42]. Therefore, rather than seeing implementation as a post-design activity, implementation conditions should be considered from the beginning and be intertwined with design and evaluation [17].

AFTERTHOUGHT

Since the start of this project, approximately seven years ago, the research addressing telehealthcare services in cancer survivors has grown enormously. The potential of such technology-mediated care to improve the quality and accessibility of supportive care for survivors is still envisioned. Yet, cancer survivors can only taste the true value of telehealthcare if they have access to the most appropriate telehealthcare service at the right time. This requires more than a single project, a fancy technology and a few enthusiasts (although these certainly help). Luckily, research brought, and still brings, increased understanding of the complex and dynamic nature of the context for telehealthcare design, evaluation and implementation, as well as tools to make progress in this field. Together with enhancements in technology, increased interest in preventive and personalized care, and acknowledgement of the role and responsibility of healthcare insurance companies as crucial stakeholders, I believe that our vision of integrated, personalized supportive care for cancer survivors using telehealthcare is within reach. As Sinatra used to sing:

"The best is yet to come"

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SUMMARY
SAMENVATTING
DANKWOORD
CURRICULUM VITAE
LIST OF PUBLICATIONS
RRD PROGRESS RANGE

SUMMARY

Lung cancer is the most commonly diagnosed malignancy among adults worldwide. Curative lung resection is the preferred treatment for early-stage lung cancer, significantly improving 5-years survival rates in this population. Although being the preferred treatment, patients report persistent disability in daily functioning such as mobility, sleeping, breathing, and quality of life following lung resection.

Cancer rehabilitation comprising exercise rehabilitation or physical activity programs have shown to improve treatment- and health-related outcomes in lung cancer survivors undergoing lung resection. Increasing physical activity may especially benefit lung cancer survivors to prevent or break through a vicious circle of deterioration of physical activity levels, functional capacity and symptom burden, which is often observed following diagnosis and treatment of lung cancer .

Since its introduction, the accessibility and tailoring of rehabilitation programs for cancer survivors have been discussed. With the coming of internet and mobile technologies it is considered that rehabilitation for cancer survivors can be provided more tailored and timely using this technology, also called telehealthcare. Using the internet, smartphones and sensors, telehealthcare services are accessible on patients' demand, wherever and whenever they need, providing continuous monitoring of health and behaviors, timely support, and easy access to specialized professionals. Despite the potential of telehealthcare to improve cancer rehabilitation, the use of tailored telehealthcare services in lung cancer survivors to provide personalized rehabilitation at home has been limited.

The overall aim of this thesis was to gain knowledge on how to improve the quality and accessibility of home-based cancer rehabilitation that aims to support functional recovery following lung resection using telehealthcare. To do so, this thesis consecutively addressed the design, evaluation and adoption of a telehealthcare service for lung cancer survivors undergoing lung resection.

The first part of this thesis (chapters 2,3 and 4) described the design of the telehealthcare service for which a user-centered, iterative design approach was used to come to proper functional requirements for the telehealthcare service that fit the actual needs of the users.

Chapter 2 established the advantage of ambulatory monitoring methods and outcomes of physical activity behavior and fatigue for personalized cancer

rehabilitation in long-term cancer survivors. In this study, daily physical activity behavior was measured objectively and subjectively in cancer survivors and healthy controls using accelerometry and a Visual Analogue Scale implemented on a smartphone, respectively. Also, fatigue was assessed in the cancer survivors on a smartphone using the Visual Analogue Scale, and retrospectively using the Multidimensional Fatigue Inventory (MFI) questionnaire. Results demonstrated imbalanced physical activity patterns throughout the day in cancer survivors as captured with the accelerometer. Also, patterns of fatigue throughout the day in cancer survivors were associated with survivors' objective daytime patterns of physical activity behavior. That is, the more a survivor felt fatigued, the greater the decline in physical activity throughout the day. A low correlation between objective and subjective physical activity measures was observed, suggesting low awareness in cancer survivors about their daily physical activity performed.

In **chapter 3** the usefulness of ambulatory monitoring for post-surgery rehabilitation of lung cancer survivors was addressed by providing insight in the physical activity behavior patterns of operable lung cancer survivors from preoperative to six months postoperative, and evaluating the association between physical activity behavior early following surgery with perceived symptoms and quality of life at six months post-surgery. Using accelerometry, significant changes in physical activity behavior over time were captured in resected lung cancer survivors. Also, variability in physical activity behavior between patients in both amount as well as change over time were demonstrated, suggesting clinical relevance of the use of ambulant monitoring as well as the need for physical activity behavior 'profiling'. Regarding clinical relevance of physical activity behavior for recovery, patients who were more active in the first month following surgery reported better health outcome six months postoperative.

In **chapter 4** the perceived need and value of both operable lung cancer patients and their healthcare professionals regarding technology-supported cancer rehabilitation were captured through a user-centered design approach. Both survivors and professionals perceived a need for supportive care post-surgery. Highest needs were reported for ambulant monitoring of health status, a web-based exercise program, and tailored information regarding disease, treatment and lifestyle. The use of technology to provide supportive care was not seen as a barrier by survivors, under the prerequisite that the technology, such as sensors, would be user-friendly for home-based use and that their use informs healthcare professionals' treatment and actions. For healthcare professionals, integration of data from the telehealthcare service with existing electronic health records in a sensible and easy-to-view manner was rated critical for feasibility. These findings culminated in a list of functional requirements and

a first prototype of the telehealthcare application consisting of: 1) self-monitoring of symptoms and physical activity using on-body sensors and a smartphone, and 2) a web based physical exercise program.

The second part of this thesis (chapters 4, 5 and 6) focused on the evaluation and adoption of telehealthcare in clinical practice. As a first step, the usability of both modules of the telehealthcare application was investigated in **chapter 4**. The results showed that the majority of lung cancer survivors and healthcare professionals were willing to use the application as part of lung cancer treatment. Accessibility of the data via electronic patient records was essential for healthcare professionals. Lung cancer survivors regarded a positive attitude of the healthcare professionals towards the application vital. Overall, the usability of the modules was rated acceptable.

Chapter 5 continued with an evaluation of acceptability and feasibility of the developed telehealthcare application in clinical practice using a two-stage mixed methods design. Expectations, experiences and actual use of the service by 22 lung cancer survivors and their healthcare professionals were evaluated with the service being offered as an addition to standard post-surgery follow-up care from pre- to six months post-surgery. Expectations prior to use were high and all survivors indicated positive intention to use the modules. Seventeen lung cancer survivors actively used the modules. Use of the ambulant monitoring module varied from 1 to 11 monitoring days prior to each outpatient consultations. Survivors used the web-based exercise module most frequently during the first five weeks, with an average of four logins a week. Fifty-eight percent used the web-based exercise module beyond seven weeks. No adverse situations occurred, and patients felt confident using the modules. Perceived added value included active lifestyle promotion, decreased anxiety, and accessibility to specialized healthcare professionals. Physiotherapists used the web-based exercise module as intended. Contrarily, physicians scarcely used information from the physical activity and symptom monitoring module.

In **chapter 6**, the barriers and facilitators for successful adoption of telehealthcare services by healthcare professionals were identified, providing guidance to promote acceptance, adoption and, thereby, successful implementation of telehealthcare services in clinical practice. In this study, an online survey was conducted in users of telehealthcare (n=70) and non-users (n=77) to measure behavioral intention to use (BIU) telehealthcare services and factors from the individual (compatibility with workplace values and work processes), technological (perceived usefulness and perceived ease of use), and context for implementation (organizational facilitating and social influence) domains. The results of this study showed that barriers and facilitators

for healthcare professionals' adoption of telehealthcare can exist on different domains, that is the individual, technological and context for implementation, and can be present from pre-adoption until post initial adoption. Healthcare professionals who actively used telehealthcare in clinical practice (the users) perceived better compatibility of telehealthcare with workplace values and work processes, and also experienced better support from the social domain compared to non-users. Non-users showed a lack of knowledge regarding the organizational facilitating domain and significantly lower acceptance than users. Of the non-users, 51% scored positive acceptance, which was associated with significantly better scores on factors from all three domains compared to the non-users with negative acceptance. Some users (11%) indicated negative acceptance following initial adoption, which was significantly related to lower scores on several items of the individual domain compared to the users with positive acceptance.

In the final chapter (**chapter 7**), the results of the studies were integrated, and their relevance for clinical practice as well as needs and possibilities for future research were discussed. To summarize, throughout this project we increased knowledge of the clinical relevance of ambulant monitoring to improve post-surgery outcomes in cancer survivors and its potential for personalized support. Also, in-depth insight in the needs and requirements for post-surgery supportive care of lung cancer survivors and the healthcare professionals involved in this care trajectory was gained. In close cooperation with these survivors and professionals an ambulant monitoring system and a web-based exercise module were developed, which monitors and supports functional recovery at home. We also discovered that the use of these kinds of technologies, being on-body sensors and web-based portals, are acceptable for survivors.

Contrary to these advances, we have to conclude that not all efforts were successful. First of all, further improvement of the technology is necessary for optimizing its applicability and effectiveness. That is, to improve uptake and effectiveness of telehealthcare in cancer rehabilitation, we should strive for a holistic, personalized approach using multimodal sensing and intelligent reasoning. Second, to improve the fit with users' and other stakeholders' needs, the design process might benefit from a less technology-driven and a more value-driven approach. Lastly, in the end we have not reached wide-scale, sustainable adoption and implementation of the developed modules (being symptom and physical activity monitoring and web-based exercise), thereby failing to improve quality and accessibility of cancer rehabilitation. Sustainable implementation of telehealthcare services requires a whole-system approach, addressing the micro-, meso-, macro-level of the healthcare system. To deliver

integrated rehabilitation services in the homes of cancer survivors a holistic approach for design and evaluation is necessary to reach alignment and consensus between all relevant stakeholders – that is, any party involved with the design, purchase, financing, provision or use of the service – regarding aims and responsibilities in the usage of telehealthcare services. Next to that, adoption does not ‘just happen’ but needs attention and targeted activities to address the barriers present. Therefore, rather than seeing implementation as a post-design activity, implementation conditions should be considered from the beginning and be intertwined with design and evaluation.

Together, this will bring the promise of home-based, personalized cancer rehabilitation for lung cancer survivors within reach.

SAMENVATTING

Longkanker is de meest voorkomende vorm van kanker onder volwassenen wereldwijd. Bij patiënten met longkanker in een vroeg stadium geeft curatieve longresectie een significante verbetering van de 5-jaars overlevingskans, en is daarom in deze patiëntengroep de voorskeurbehandeling. Hoewel longresectie een verbetering geeft van de overlevingskans, heeft deze behandeling een grote negatieve impact op het dagelijks functioneren en hebben patiënten als gevolg van de longresectie vaak nog langdurig aanhoudende beperkingen en klachten waaronder verminderde mobiliteit, verslechterde kwaliteit van leven, pijn en vermoeidheid. Oncologische revalidatie wordt gezien als een effectieve interventie om de behandel- en gezondheidsgelateerde uitkomsten na longresectie te verbeteren, waarbij fysieke revalidatie of interventies om patiënten fysiek actiever te maken essentieel onderdeel zijn van de oncologische revalidatie.

Echter, vanaf het moment dat oncologische revalidatie beschikbaar kwam, staan de toegankelijkheid en de personalisering van oncologische revalidatie voor patiënten met kanker ter discussie. Telezorg (het gebruik van informatie- en communicatietechnologie om behandeling te bieden over een afstand) wordt gezien als een belangrijk middel om oncologische revalidatie beter gepersonaliseerd en tijdig toegankelijk te maken voor patiënten met kanker. Telezorg diensten maken gebruik van het internet en mobiele technologieën zoals smartphones, en geven daarmee toegang tot behandeling en gespecialiseerde zorgverleners waar en wanneer de patiënt dat wenst. Daarnaast maakt de opkomst van sensoren continue monitoring van gezondheid en gedrag mogelijk. Ondanks de potentie van telezorg om de kwaliteit en toegankelijkheid van oncologische revalidatie te verbeteren, is bij patiënten met longkanker het gebruik van telezorg diensten om gepersonaliseerde revalidatie thuis aan te bieden nog beperkt.

Het doel van deze thesis was onze kennis te vergroten over hoe de kwaliteit en toegankelijkheid van oncologische revalidatie thuis verbeterd kan worden door het gebruik van telezorg diensten, om functioneel herstel na longresectie te ondersteunen. Om dit resultaat te behalen, beschrijft deze thesis achtereenvolgens het ontwerp, evaluatie, en adoptie van een telezorg dienst voor patiënten met longkanker die een longresectie hebben ondergaan.

Het eerste deel van deze thesis (hoofdstukken 2, 3 en eerste deel van hoofdstuk 4) beschrijft het ontwerp van de telezorg dienst waarbij een gebruikers-georiënteerde, iteratief ontwerp benadering is gebruikt om te komen tot de juiste functionele eisen

voor de telegzorg dienst die aansluiten bij de behoeftes van de gebruikers.

Hoofdstuk 2 vergelijkt het dagelijks fysieke activiteitengedrag van overlevenden van kanker met die van een groep gezonde controles waarbij fysieke activiteiten gedrag zowel objectief als subjectief gemeten is met accelerometrie en een Visueel Analoge Schaal (VAS). Daarnaast werd vermoeidheid bij de overlevenden gemeten op een mobiele telefoon met de VAS en retrospectief met behulp van de Multidimensional Fatigue Inventory (MFI) vragenlijst om te zien of vermoeidheid gecorreleerd is met het fysieke activiteiten gedrag. Resultaten lieten zien dat overlevenden van kanker in vergelijking tot de controles gedurende de dag een onevenwichtig fysiek activiteiten patroon hebben. Daarnaast liet de relatie tussen vermoeidheid en fysiek activiteitenpatroon zien dat hoe vermoeider een overlevende zich voelde, hoe groter het verval van fysieke activiteit was over de dag. In de studie werd verder een lage correlatie gevonden tussen objectief en subjectief gemeten fysieke activiteit, wat zou kunnen wijzen op een vertekend beeld bij overlevenden van kanker over de hoeveelheid dagelijks fysieke activiteit die men verricht.

In **hoofdstuk 3** is de bruikbaarheid van ambulante activiteiten monitoring voor postoperatieve revalidatie van patiënten met longkanker onderzocht. Dit is gedaan door inzicht te geven in het fysiek activiteitengedrag van operabele longkankerpatiënten van preoperatief tot zes maanden postoperatief, en het evalueren van het verband tussen fysiek activiteitengedrag vroeg na operatie met ervaren symptomen en kwaliteit van leven op zes maanden na operatie. Gemiddeld genomen liet de activiteiten data significante veranderingen in fysiek activiteitengedrag zien over de tijd bij geopereerde longkankerpatiënten. Wel was er sprake van een grote variabiliteit tussen patiënten in zowel de hoeveelheid activiteit als het patroon over de tijd. Deze variabiliteit ondersteunt zowel de klinische relevantie van het gebruik van ambulante activiteiten monitoring als ook het belang van 'personalisering en profiling' met betrekking tot fysiek activiteitengedrag. Ten slotte lieten de analyses van deze studie zien dat patiënten die actiever waren in de eerste maand na operatie betere gezondheidsresultaten rapporteerden zes maanden na de operatie wat het belang van fysieke revalidatie vroeg na operatie benadrukt.

In **hoofdstuk 4** zijn de ervaren behoeftes en waardes van operabele patiënten met longkanker en hun zorgverleners ten aanzien van technologie-ondersteunde oncologische revalidatie onderzocht met een gebruikers-georiënteerde ontwerp benadering. Zowel patiënten als zorgverleners ervoeren een behoefte voor nazorg postoperatief. Resultaten lieten zien dat patiënten de meeste behoefte hadden aan ambulante monitoring van de gezondheidsstatus, een online oefenprogramma en

gepersonaliseerde informatie over de aandoening, de behandeling en leefstijl. Het gebruik van technologie om nazorg te bieden werd door patiënten niet gezien als een barrière, onder de voorwaarde dat de technologie, zoals sensoren, gebruiksvriendelijk zou zijn voor gebruik thuis en dat het gebruik ervan richting geeft aan de behandeling en acties door zorgverleners. De integratie van data van de telezorg dienst met het bestaande elektronisch patiëntendossier waarbij de resultaten praktisch en makkelijk uit te lezen zijn, werd als essentieel beschouwd voor de bruikbaarheid voor zorgverleners. Deze bevindingen resulteerden in een lijst van functionele eisen en een eerste prototype van de telezorg dienst, bestaande uit twee modules:

- 1) zelf-monitoring van symptomen en fysieke activiteiten met behulp van lichaamssensoren en een mobiele telefoon;
- 2) een online fysiek trainingsprogramma.

Het tweede deel van deze thesis (tweede deel van hoofdstuk 4, en hoofdstukken 5 en 6) beschrijft de evaluatie van de gebruiksvriendelijkheid, aanvaardbaarheid en haalbaarheid alsook de adoptie van telezorg in de klinische praktijk.

Als een eerste stap is de gebruiksvriendelijkheid van beide modules - zelf-monitoring van symptomen en fysieke activiteiten en het online trainingsprogramma - van de telezorg dienst onderzocht in **hoofdstuk 4**. De resultaten laten zien dat de meerderheid van de patiënten en zorgverleners bereid waren om de dienst te gebruiken als onderdeel van de behandeling voor longkanker. Toegankelijkheid van de data via het elektronisch patiëntendossier was essentieel voor zorgverleners. Patiënten vonden een positieve houding van de zorgverlener over de dienst essentieel. Over het geheel genomen werd gebruiksvriendelijkheid van de modules gescoord als acceptabel.

Hoofdstuk 5 vervolgt met een evaluatie van de aanvaardbaarheid en haalbaarheid van de ontwikkelde telezorg dienst in de klinische praktijk door middel van een mixed methods design. In twee, elkaar opvolgende pilots zijn de verwachtingen, ervaringen en daadwerkelijk gebruik van de dienst geëvalueerd in 22 patiënten met longkanker en betrokken zorgverleners waarbij de dienst aangeboden is als een toevoeging op de standaard zorg na longresectie van pre- tot zes maanden postoperatief. De bevindingen uit de eerste pilot zijn gebruikt om de telezorg dienst te verbeteren voor gebruik in pilot 2. Uit deze pilots bleek dat patiënten hoge verwachtingen hadden ten aanzien van de gebruiksvriendelijkheid en meerwaarde van de telezorg dienst, en alle patiënten rapporteerden een positieve intentie om de modules te gebruiken. Zeventien patiënten maakten actief gebruik van de modules. Gebruik van de ambulante monitoring module varieerde van 1 tot 11 monitordagen voorafgaand aan de poliklinische consulten (instructie: minimaal 3 monitordagen voorafgaand

aan elk consult). Patiënten gebruikten de online fysieke trainingsmodule het vaakst in de eerste vijf weken, met een gemiddelde inlogfrequentie van vier keer per week. Achtenvijftig procent gebruikte de online fysieke trainingsmodule langer dan zeven weken. Er deden zich geen ongunstige situaties voor en patiënten voelden zich vertrouwd in het gebruik van de modules. Met name promotie van een actieve leefstijl, afname van onzekerheid en toegang tot gespecialiseerde zorgverleners werden door genoemd als meerwaarde van gebruik van de modules. Fysiotherapeuten gebruikten de online fysieke trainingsmodule zoals bedoeld. Daarentegen maakten specialisten slechts zeer beperkt gebruik van de verzamelde informatie van de fysieke activiteit en symptoom monitoring module.

In **hoofdstuk 6** zijn de belemmerende en stimulerende factoren voor succesvolle adoptie van telezorg diensten door zorgverleners geïdentificeerd. In deze studie is een online vragenlijst uitgezet onder gebruikers van telezorg (n=70) en niet-gebruikers (n=77) om de intentie tot gebruik van telezorg diensten te meten en ook de factoren uit de domeinen individu (compatibiliteit met werkgerelateerde waarden en werkprocessen), technologie (ervaren meerwaarde en ervaren gebruiksvriendelijkheid), en context van implementatie (organisatorisch en sociale invloed). De resultaten van deze studie laten zien dat belemmerende en stimulerende factoren voor adoptie van telezorg door zorgverleners kunnen voorkomen in verschillende domeinen, namelijk individu, technologie en context van implementatie, en dat deze factoren aanwezig kunnen zijn vanaf het moment vóórdat de dienst daadwerkelijk gebruikt wordt (pre-adoptie) tot na de keuze om een telezorg dienst te gaan gebruiken (adoptie). Zorgverleners die actief gebruikmaken van telezorg in de klinische praktijk (de gebruikers) ervoeren betere compatibiliteit van telezorg met hun werkgerelateerde waarden en werkprocessen. Zij ervoeren ook betere ondersteuning van de sociale omgeving dan de niet-gebruikers. Niet-gebruikers lieten een groter gebrek aan kennis zien ten aanzien van de organisatorische bevorderende factoren en een significant lagere acceptatie dan de gebruikers. Van de niet-gebruikers liet 51% een positieve acceptatie zien wat gerelateerd was met significant hogere scores op de factoren in alle drie de domeinen in vergelijking met de niet-gebruikers die een negatieve acceptatie hadden. Sommige gebruikers (11%) hadden een negatieve acceptatie ondanks hun adoptie van telezorg diensten in de klinische praktijk. Deze gebruikers hadden significant lagere scores op verschillende items in het individuele domein in vergelijking met gebruikers die een positieve acceptatie hadden.

In het laatste hoofdstuk (**hoofdstuk 7**) zijn de resultaten van de studies samengevoegd en is de relevantie besproken van de bevindingen voor de klinische praktijk alsook de noodzaak tot en mogelijkheden voor vervolgonderzoek. In dit project hebben

we onze kennis vergroot over de klinische relevantie van ambulante monitoring om uitkomsten voor patiënten met kanker na chirurgie te verbeteren, en inzicht gekregen in het potentieel van ambulante monitoring voor gepersonaliseerde ondersteuning. Daarnaast is diepgaand inzicht verkregen in de behoeftes en eisen voor postoperatieve nazorg van patiënten met longkanker en de betrokken zorgverleners bij dit zorgtraject. Veel resultaten zijn positief. Zo is in nauwe samenwerking met deze patiënten en zorgverleners een ambulant monitoring systeem en een online fysieke trainingsmodule ontwikkeld die functioneel herstel in huis monitort en ondersteunt. Resultaten lieten ook zien dat het gebruik van dit soort technologieën, met onder andere lichaamssensoren en online portalen, acceptabel zijn voor patiënten. Ondanks deze belangrijke uitkomsten en bevindingen, zijn niet alle doelstellingen van het project behaald. Allereerst is verdere verbetering van de technologie noodzakelijk om de toepasbaarheid en effectiviteit te optimaliseren, waaronder het verder personaliseren van de modules door middel van multimodale intelligente systemen. Ten tweede, om de afstemming met de behoeftes van gebruikers en andere stakeholders te verbeteren, is in het designproces een meer waarde-gedreven benadering nodig en een minder technogie-gedreven benadering. Als laatste, in deze studie hebben we geen grootschalige, duurzame acceptatie en implementatie van de ontwikkelde modules (symptoom- en fysieke activiteit monitoring en online oefeningen) bereikt, waardoor de kwaliteit en toegankelijkheid van oncologische revalidatie niet zijn verbeterd. Duurzame implementatie van telezorgdiensten vereist een aanpak van het hele systeem, gericht op het micro-, meso-, en macroniveau van de gezondheidszorg. Om geïntegreerde revalidatiediensten te leveren in de huizen van patiënten en overlevenden van kanker is een holistische benadering voor ontwerp en evaluatie noodzakelijk, zodat afstemming en overeenstemming wordt bereikt tussen alle relevante belanghebbenden – elke partij die betrokken is bij het ontwerp, de aankoop, de financiering, de levering of het gebruik van de dienst – met betrekking tot doelen en verantwoordelijkheden bij het gebruik van telezorgdiensten. Daarnaast is adoptie niet iets dat vanzelf gebeurt, maar wat aandacht en gerichte activiteiten vraagt om de aanwezige barrières te slechten. Hierbij is het essentieel om deze gerichte activiteiten te plannen voordat de nieuwe telezorg dienst geïntroduceerd wordt in de klinische praktijk en het proces van adoptie en implementatie vanaf het allereerste begin te verweven met het proces van ontwerp en evaluatie. Dit alles samen brengt de belofte van gepersonaliseerde oncologische revalidatie in huis voor patiënten en overlevenden van (long)kanker binnen handbereik.

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Een borrel bij RRD; één van de eerste social events sinds mijn start als promovendus. Blij sta ik te kletsen met een paar collega's en probeer samen te vatten wat mijn onderzoek zal gaan zijn. "En wanneer wil je klaar zijn?" is de vraag. Ik weet nog dat ik ze bevreemd aankeek: hoezo, wanneer ik klaar wil zijn? Aan het eind van mijn contract natuurlijk; na 5 jaar....

Al snel leerde ik dat weinig in een promotietraject precies gaat zoals je van te voren bedacht hebt.

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Ondanks dat veel van mijn promotie zich heeft afgespeeld in Amsterdam, voelde ik mij het meest thuis in Enschede, mijn 'standplaats'. Lieve collega's van RRD en BSS,

ik wil jullie bedanken voor de gezelligheid, tijdens de kerstlunches, de afdelingsuitjes, of gewoon rondom het koffiezetapparaat. Bedankt voor de kritische blik, inspirerende discussies en opbouwende feedback; jullie inbreng hebben zeker bijgedragen aan mijn project en mijn onderzoek. Joke, Inger, Wies, en Sandra, bedankt voor al jullie hulp en ondersteuning bij het regelen van heel veel praktische zaken. Leendert, mede dankzij jou hadden we (meestal) voldoende en goedwerkende meetsystemen (als ik ze tenminste niet achterliet in de trein of de auto van een onbekende...). Boris en Dennis, zonder jullie programmeringskunsten was geen van de onderzoeken beschreven in dit boekje mogelijk geweest. Simone, bedankt voor je schrijftips, het gezellige schrijfweekend in Leeuwarden en al je info die de voorbereiding op deze 'grote dag' een stuk vergemakkelijkten. En dan kamer 10/11: Anne, Sanne, Wander, Jan-Willem, Fanny, Erik en Wiebe. Na een herindeling bij RRD kwam ik na mijn verlof ineens in een soort kantoortuin terecht, met jullie. Ondanks dat het gezelligheidsniveau een goede focus wel eens in de weg stond, kon ik me geen beter gezelschap wensen in het laatste jaar van mijn promotie. Jullie toonden altijd interesse in mij en in mijn werkzaamheden. Bedankt voor het delen van jullie persoonlijke verhalen, de gezellige borrels en etentjes, en natuurlijk al jullie snoep en chocola. Ik zie uit naar nog vele diners van het samen-eten-eten-eten groepje (mnomnmnomnmnom)! Een speciaal woord van dank aan Mirka; jij bent één van de meest gestructureerde en tegelijkertijd meest hartelijke en enthousiaste persoon die ik ken. Hoewel je geen fysieke werkplek had op kamer 10/11, kwam je heel regelmatig buurten en ben je een vast onderdeel van ons eet-groepje. Je zit nooit om een woord verlegen, maar neemt altijd de tijd om te luisteren. Je positiviteit is geweldig en ik ben erg blij dat je mijn paranymf wil zijn op deze belangrijke dag.

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Het uitvoeren van mijn promotietraject en daarnaast het draaiende houden van een jong gezin samen met een man die regelmatig weg is, was nooit mogelijk geweest zonder de onvoorwaardelijke steun en liefde van mijn familie. Lieve pa en ma, Karel en Claartje, en schoonouders Bennie en Ineke, hoewel het zo nu en dan best lastig was om uit te leggen wat ik nu precies aan het doen was, waren jullie altijd geïnteresseerd in mijn onderzoek. De momenten dat jullie de kids onder jullie hoede hebben genomen zijn inmiddels ontelbaar, maar boden zeker het afgelopen jaar de flexibiliteit, rust en ruimte om dit proefschrift af te ronden. Pa en ma, jullie hebben mij geleerd om hard te werken, kritisch te zijn en niet op te geven bij wat tegenslag. Dit heeft mij zeker geholpen om te komen waar ik nu ben. Bennie en Ineke, jullie bewijzen het tegendeel van alle vooroordelen over schoonouders. Samen met mijn ouders vormden jullie een onmisbare en stabiele basis in de (regelmatig voorkomende) momenten van hectiek. Hiervoor ben ik jullie vieren enorm dankbaar.

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CURRICULUM VITAE

Johanneke Gerdien (Josien) Timmerman was born in Almelo on October 22nd 1981. In 2000 she received her high school diploma from the Gymnasium at Het Noordik, and started the study Biomedical Sciences at the Radboud University in Nijmegen. After completing the first year, she commenced the study Occupational Therapy at the University of Applied Science Amsterdam. In 2006 she received her Bachelor's degree, and started as an ergonomic advisor at Roessingh Diensten Groep, Enschede. Being interested in human behavior and exploiting peoples' possibilities, Josien applied for the master Human Movement Sciences at the University of Groningen. In 2010 she received her Master's degree (cum laude) after a two-year research master with the specialization 'Movement, aging and health'. In her final year, she performed a study in nursing home De Hoven Delfzijl on the effects of exercise on Behavioral and Psychological Symptoms of Dementia in institutionalized elderly. Also, in the final year she mentored first-year students as a student assistant.

After graduation she started as an occupational therapist at De Posten, Enschede. In 2011 she was appointed to work on the AcaRe2Move project as a PhD researcher in a collaboration between Roessingh Research and Development (Enschede), the department of Biomedical Signals and Systems from the University of Twente (Enschede), and the Netherlands Cancer Institute - Antonie van Leeuwenhoek hospital (Amsterdam).

Since 2017 Josien works at Ziekenhuis Groep Twente (ZGT; Almelo/Hengelo) at the Academy, where she is responsible for optimizing local quality procedures regarding scientific research, providing epidemiological and statistical support, and student supervision. Next to that, she is involved as a researcher in the commencement of scientific research in the Obesity Center ZGT on predictors and treatment for (un)successful weight loss and healthy lifestyle in morbidly obese patients following bariatric surgery.

LIST OF PUBLICATIONS

Scientific journals

Timmerman, J.G., Dekker-van Weering, M.G.H., Tönis, T.M., Hermens, H.J., Vollenbroek-Hutten, M.M.R. (2015). *Relationship between patterns of daily physical activity and fatigue in cancer survivors*. European Journal of Oncology Nursing, 19(2), 162-168.

Timmerman, J.G., Tönis, T.M., Dekker-van Weering, M.G.H., Stuiver, M.M., Wouters, M.W.J.M., van Harten, W.H., Hermens, H.J., Vollenbroek-Hutten, M.M.R. (2016). *Co-creation of an ICT-supported cancer rehabilitation application for resected lung cancer survivors: design and evaluation*. BMC Health Services Research, 16 (1), 1-11.

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Timmerman, J.G., Dekker-van Weering, M.G.H., Vollenbroek-Hutten, M.M.R. *Acceptance and adoption of telehealthcare services by healthcare professionals: exploration of perceived facilitators and barriers of 'users' and 'non-users' of telehealthcare*. Submitted.

Achterkamp, R., Dekker-van Weering, M.G.H., Evering, R.M., Tabak, M., **Timmerman, J.G.**, Hermens, H.J., Vollenbroek-Hutten, M.M.R. (2018). *Strategies to improve effectiveness of physical activity coaching systems: Development of personas for providing tailored feedback*. Health Informatics Journal, 24(1): 92-102.

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Timmerman, J.G. *Telerevalidatie in de oncologie: Van ontwerp naar adoptie en acceptatie in de klinische praktijk*. Presented as an oral presentation at the 22^{ste}

Symposium voor verpleegkundigen en paramedici. Oncologie in Perspectief: Maatwerk, June 2016, Amsterdam, The Netherlands.

Timmerman, J.G., Dekker-van Weering, M.G.H., Tönis, T.M., Stuiver, M.M., Wouters, M.W.J.M., Hermens, H.J., Vollenbroek-Hutten, M.M.R. *Towards cancer rehabilitation at home. The AcaRe2Move project "Telerehabilitation"*. Presented as an oral presentation at the closing symposium of the A-CaRe2 program, April 2016, Amsterdam, The Netherlands.

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Timmerman, J.G., Dekker-van Weering, M.G.H., Tönis, T.M., Stuiver, M.M., Wouters, M.W.J.M., Hermens, H.J., Vollenbroek-Hutten, M.M.R. *Towards Cancer Rehabilitation at Home. Design of a Telerehabilitation Service for Lung Cancer Patients*. Presented as an oral presentation at the 15th World Conference on Lung Cancer, October 2013, Sydney, Australia.

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