From the Department of Neurobiology, Care Sciences and Society Karolinska Institutet, Stockholm, Sweden

# ENHANCED MOBILISATION AND PHYSICAL REHABILITATION AFTER ABDOMINAL CANCER SURGERY – FEASIBILITY, EFFECTS, AND EXPERIENCES

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Stockholm 2024

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Enhanced Mobilisation and Physical Rehabilitation after Abdominal Cancer Surgery – Feasibility, Effects, and Experiences Thesis for Doctoral Degree (Ph.D.)

Bу

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"The human capacity for burden is like bamboo – far more flexible than you'd ever believe at first glance." – Jodi Picoult

## Populärvetenskaplig sammanfattning

Personer som diagnostiseras med cancer i nedre buken, till exempel tjocktarm, blåsa och äggstockar behöver ofta genomgå stor bukkirurgi för att ta bort sin tumör. Efter operationen mår många dåligt, känner sig svaga, illamående och upplever smärta. Trots det är det viktigt att man rör på sig och undviker sängliggande för att minska risken för komplikationer. Dessa patienter behöver ofta omfattande stöd för att komma i gång och röra på sig efter operation då det kan vara svårt på egen hand. Det är dock oklart hur man bäst ska strukturera detta stöd för att patienterna ska röra på sig så mycket som möjligt, vara delaktiga, och må så bra som möjligt. När patienterna sedan skrivs ut från sjukhuset är det fortsatt viktigt att röra på sig och motionera för att vidare minska risken för komplikationer och för att återfå sin funktion, styrka och ork. Även när det gäller detta så är det oklart hur man bäst ska stötta patienternas rehabilitering och mer forskning har efterfrågats.

I denna avhandling har metoder för att stötta patienters rörelse på vårdavdelning efter operation utvärderats. Först genom att intervjua vårdpersonal som har använt en Träningstavla (Scandinavian Phystec AB) som verktyg för att stötta patienters aktivitet på vårdavdelning efter bukkirurgi pga. cancer. Tavlan är en whiteboard där dagliga aktiviteter och mål sätts upp, till exempel att gå 100 meter i korridoren fyra gånger en dag eller att sitta uppe i fåtölj minst 30 min två gånger osv. Vårdpersonalen som använt tavlan upplevde att dessa aktiviteter och mål motiverade patienterna som annars inte riktigt visste vad som förväntades av dem. Vårdpersonalen upplevde även att det underlättade deras arbete att kunna referera till tavlan och använda den som ett verktyg för att motivera patienterna att röra på sig efter operation. Samt att patienterna verkade mer engagerade när de använda tavlan. Men det framkom även att den kan tyckas gammeldags, klumpig och svår att rengöra.

En digital version, Pedatim, har därför tagits fram som bygger på samma principer som Träningstavlan. Pedatim är en surfplatta med en applikation som väsentligen har samma funktion som Träningstavlan men i digitalt format. Dagliga aktiviteter och mål sätts upp likt ett träningsschema för patienterna som de ska följa på vårdavdelningen efter operation. I denna avhandling utvärdera des genomförbarheten av att använda denna digitala Träningstavla, Pedatim, för att stötta aktivitet efter operation hos patienter som genomgått bukkirurgi pga. cancer. I studien fick patienter som genomgått bukkirurgi pga. cancer prova att använda Pedatim under tiden de var inlagda på sjukhus efter operation. De bar en rörelsemätare som mätte deras aktivitet och de fick besvara frågor om användbarheten av Pedatim. Även studiens design utvärderades inför en eventuell framtida studie. Resultatet av studien visade att patienterna uppfattade Pedatim som lätt att använda och att den gav stöd och vägledning i hur mycket de skulle röra på sig vilket upplevdes öka motivationen. Dock framkom ett behov av tillgänglig teknisk support. Baserat på rörelsemätarna verkade patienterna även röra på sig gradvis mer. Även studiens design bedömdes som genomförbar med behov av små modifikationer inför en eventuell framtida studie.

I denna avhandling utvärderades även effekten av ett 12 veckors träningsprogram i primärvården hos patienter som opererat bort urinblåsan pga. cancer. Patienterna som deltog i studien lottades till hemträning i 12 veckor eller träning i primärvården i 12 veckor. Patienterna som tränade hemma uppmanades att gå dagliga promenader och utföra benstärkande övningar. Patienterna som tränade i primärvården träffade en fysioterapeut 2 gånger i veckan och genomförde styrketräning och konditionsträning. Resultatet av studien visade att de som tränat i primärvården ökade sin dagliga fysiska aktivitet, skattade en högre livskvalitet och minskad trötthet jämfört med de som tränade hemma vid uppföljningen 4 månader efter operation.

Patienterna som genomgått träning i primärvården intervjuades sedan för att bättre kunna förstå hur man ska kunna stötta rehabilitering efter denna typ av kirurgi pga. cancer. Det visade sig att patienterna upplever stora svårigheter när de kommer hem från sjukhuset och behöver stöd för att starta med rehabilitering. De är motiverade till att kunna återgå till ett normalt liv men behöver anpassad träning baserat på deras förutsättningar. Faktorer som stöd av vårdpersonal, nära till träningslokal och successiv stegring av träning upplevdes som viktiga av patienterna.

Sammanfattningsvis visar denna avhandling på att patienters rörelse och aktivitet på vårdavdelningen efter bukoperation pga. cancer går att stötta genom att använda verktyg som Träningstavlan och Pedatim. Dessa ökar patienternas motivation och delaktighet, samt underlättar arbetet för vårdpersonal. Vidare visas även att träning i primärvården kan hjälpa dessa patienter att öka sin dagliga fysiska aktivitet och livskvalitet, samt minska trötthet.

## Abstract

Cancer incidence is growing worldwide and, as advances in diagnostics, treatment, and rehabilitation are made, the numbers of cancer survivors are also increasing. Therefore, there is a need to find and evaluate methods to improve the lives of cancer survivors after treatment. Following abdominal cancer surgery, postoperative mobilisation and physical rehabilitation are recommended to improve outcomes, reduce the risk of complications, and improve health-related quality of life. However, there is a lack of evidence regarding its effects or how it should be structured to improve outcomes and promote adherence. The overall aim of this thesis was to contribute to the field of rehabilitation following abdominal cancer surgery by exploring methods to enhance postoperative mobilisation and evaluate the effects of physical rehabilitation following surgery. The goal was to facilitate patient adherence and engagement in rehabilitation and improve physical functioning and healthrelated quality of life following surgery.

**Study I** explored healthcare professionals' experiences of using the Activity Board as a tool to support postoperative mobilisation after abdominal cancer surgery. Seventeen healthcare professionals were interviewed, divided into four focus groups, and qualitative content analysis was used to analyse the interviews. The results indicate that the Activity Board is a tool that facilitates daily work and promotes patient participation. It was described as easy to use, providing valuable information and enabling healthcare professionals to support patients better, as well as having a positive impact on patient motivation.

**Study II** evaluated the feasibility of using a digital version of the Activity Board, called Pedatim, to enhance mobilisation following abdominal cancer surgery. In this non-randomised feasibility trial, 20 patients were recruited and each received a Pedatim tablet to use during their stay in hospital following surgery. Based on predetermined criteria, the overall study design was deemed feasible apart from the eligibility criteria. The Pedatim tablet was also deemed scientifically feasible as a tool to enhance postoperative mobilisation.

**Study III** evaluated the effects of an exercise intervention in primary care after radical cystectomy for urinary bladder cancer. In this randomised controlled trial, 90 patients were included and randomised to either control or intervention, with the intervention group receiving a referral to a physiotherapist following hospital discharge to perform a twice-a-week, 12-week exercise programme in primary

care. The control group received encouragement to perform a simple home exercise programme. At the follow-up, four months after surgery, a positive effect could be seen in the intervention group compared to the control group in terms of physical activity in daily life, fatigue, and health-related quality of life.

**Study IV** evaluated patients' experiences of the exercise intervention in Study III. In this qualitative study, 20 patients were interviewed individually, and the interviews were analysed using thematic analysis. Four main themes were identified: 1) Having to adapt to new circumstances, describing the challenges regarding physical activity patients face after discharge; 2) Optimising conditions for rehabilitation, describing how practical conditions affect patients' ability to exercise; 3) Motivated to get back to normal, describing patients' desire to get back to normal life and the factors influencing that motivation; and 4) The importance of a supportive environment, describing the impact of social support, support from physiotherapists, and how the environment where exercise takes place influences patients' ability to exercise.

In conclusion, enhancing postoperative mobilisation following abdominal cancer surgery by using tools such as the Activity Board and the Pedatim tablet is feasible and useful for both patients and healthcare professionals. These tools increase patient motivation, participation, and adherence, as well as facilitating healthcare professionals' work in supporting patients' postoperative mobilisation. Furthermore, exercise in primary care following radical cystectomy for urinary bladder cancer improves physical activity in daily life, reduces fatigue, and has a positive impact on health-related quality of life compared to a simple home exercise programme. Patients who exercised in primary care following radical cystectomy were also positive towards exercise because they were motivated to get back to normal life. However, they did face challenges when arriving home from surgery, which affected their ability to exercise, and therefore conditions need to be optimised to facilitate patients' rehabilitation.

## List of scientific papers

- Karlsson P, Porserud A, Hagströmer M, Nygren-Bonnier M. Healthcare professionals' experiences of using the Activity Board as a tool for postoperative mobilization in patients after abdominal cancer surgery Journal of Cancer Rehabilitation 2022;5(1):90-97
- II. Karlsson P, Nygren-Bonnier M, Henningsohn L, Rydwik E, Hagströmer M.

The feasibility of using a digital tool to enhance mobilisation following abdominal cancer surgery—a non-randomised controlled trial Journal of Pilot and Feasibility Studies 2023;9(1):147

- III. Porserud A/Karlsson P, Aly M, Rydwik E, Torikka S, Henningsohn L, Nygren-Bonnier M, Hagströmer M.
   Effects of an exercise intervention in primary care after robotassisted radical cystectomy for urinary bladder cancer – a randomised controlled trial In manuscript
- IV. Karlsson P, Nygren-Bonnier M, Torikka S, Porserud A, Henningsohn L, B Olsson C, Rydwik E, Hagströmer M.
   Patients' experiences of an exercise intervention in primary care following robot-assisted radical cystectomy due to bladder cancer: A qualitative study In manuscript

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## List of abbreviations

HRQoL	Health-Related Quality of Life
MET	Metabolic Equivalent
POD	Postoperative Day
RCT	Randomised Controlled Trial
RARC	Robot-Assisted Radical Cystectomy
SUS	System Usability Scale
WHO	The World Health Organisation

## Introduction

Healthcare in Sweden is generally considered to be of a high standard, with a focus on person-centred healthcare and evidence-based practice. The Swedish Health and Medical Care Act also states that the goal of the Swedish healthcare system is to provide good health and care on an equal basis for all citizens. However, this is not always achieved, and there is progress to be made in several fields, not least within rehabilitation.

As scientific research within rehabilitation is a relatively young field, there are still aspects and areas that are largely unexplored and these need more high-quality evidence to provide the sought-after person-centred and evidence-based healthcare equally for all. For example, there are well-developed, evidencebased rehabilitation trajectories for patients who have suffered a stroke, or myocardial infarction, or have undergone elective orthopaedic surgery. However, when it comes to abdominal surgery in general, and abdominal cancer surgery specifically, there is no clear rehabilitation pathway for patients. Instead, they receive information and support based on general principles before and after surgery, and then often have to take responsibility for their rehabilitation themselves.

In this thesis, methods to structure and standardise rehabilitation for patients undergoing abdominal cancer surgery are explored, in the hope of providing a foundation for a rehabilitation pathway that might be developed in the future.

## 1 Background

## 1.1 Cancer

Cancer is one of the leading causes of death and morbidity worldwide. In 2020, the World Health Organisation (WHO) reported almost 19.3 million new cases and 10 million cancer-related deaths (1). As the population grows and increasingly ages, the burden of cancer is only expected to rise, further fuelled by risk factors associated with a growing economy and globalisation (1). By 2040, it is estimated that the global cancer burden will have increased by 47% compared to 2020, meaning that one in three, or as many as one in two, will suffer a cancer diagnosis during their lifetime (1). Risk factors for developing cancer include age and heredity, but also modifiable lifestyle factors such as smoking, alcohol intake, diet, and physical inactivity (2–5).

However, the risk of dying from cancer is slowly decreasing as advancements are made in methods for early detection and treatment (5, 6). Consequently, as both the burden of cancer and number of cancer survivors increase, there is a growing need to address issues associated with cancer survivorship (6, 7). Cancer survivorship can be defined as a continuum, beginning at a patient's first diagnosis, regardless of the current stage of their disease, until death (6). This includes all patients diagnosed with cancer, and therefore incorporates patients living with no signs of cancer or impairment, and patients with advanced cancer or major impairments following disease or treatment (6, 8). There is a need to better understand, and better address, cancer survivors' situations in order to be able to support health outcomes and improve Health-Related Quality of Life (HRQoL) (7, 8). Common issues experienced by cancer survivors are often related to treatment, or side-effects of treatment, such as postoperative complications, fatigue, pain, and anxiety (9-12). This thesis focuses on rehabilitation following treatment for cancer in the lower abdomen, mainly urinary bladder cancer, but also colorectal and ovarian cancer.

## 1.1.1 Urinary bladder cancer

As of 2020, more than 570 000 patients are diagnosed with urinary bladder cancer globally each year, making it the 10<sup>th</sup> most common cancer worldwide (1). Each year, over 200 000 people die due to urinary bladder cancer, currently making it the 12<sup>th</sup> most common cancer-related cause of death (1). Incidence is approximately three times higher in men than in women and the median age of

diagnosis is approximately between 70 and 73 years (1, 5, 6, 13). In Europe, the five-year relative survival for urinary bladder cancer is approximately 70% (13). When evaluating trends in Sweden, a gradual increase in incidence can be seen, but also an improved survival rate (14).

Besides age, the most prominent risk factor associated with urinary bladder cancer is tobacco smoking, but also exposure to substances such as industrial chemicals or arsenic in drinking water (13). Urinary bladder cancer is generally divided into two major categories: non-invasive, and muscle invasive. Muscle-invasive bladder cancer is a more serious and advanced stage of urinary bladder cancer, where the tumour has infiltrated the muscle layer of the urinary bladder (13). In the case of a non-invasive tumour, the treatment is usually local and can involve minor surgery, whereas muscle-invasive bladder cancer often requires major surgery (13).

#### 1.1.2 Colorectal cancer

Globally, there were more than 1.9 million new cases of colorectal cancer in 2020, and approximately 930 000 deaths, making it the 3<sup>rd</sup> most common cancer worldwide and the second leading cause of cancer-related death (15). Colorectal cancer includes cancers of the colon or rectum, or both. Several of the most prominent risk factors for colorectal cancer are highly correlated to lifestyle, such as smoking, alcohol consumption, unhealthy diet, physical inactivity, and obesity (15, 16). Thus, incidence rates of colorectal cancer are higher in countries with a high human development index (15). Approximately 60% of patients diagnosed with colorectal cancer globally are aged 50–74 years. The incidence ratio between women and men depends on age group and context, but it is generally higher among men (15, 16).

#### 1.1.3 Ovarian cancer

The global incidence of cancer in the ovary was over 300 000 in 2020 and the number of deaths attributed to ovarian cancer was over 200 000 (1). The ratio between incidence and death rate makes it one of the most common cancer-related causes of death for women (1, 17). Ovarian cancer mainly affects postmenopausal women, with age and heredity seeming to be the most prominent risk factors, but smoking has also been associated with an increased risk (18).

### 1.2 Health-Related Quality of Life

HRQoL is a concept consisting of multiple dimensions. It is often used to evaluate the impact of different health-related aspects on quality of life, and is sometimes wrongly used interchangeably with quality of life (19, 20). There is no consensus regarding the definition of the term, but it includes perceived wellbeing in the physical, mental, and social domains of health, or aspects related to, or affected by, disease (20). Measuring HRQoL was derived from the notion of wanting to assess health outcomes that extend beyond mortality and morbidity as healthcare advancements were made and life expectancy increased (20). The assessment of HRQoL is usually achieved by self-assessment, using patientreported outcome measures; incorporating different domains such as general health, physical health, mental health, and activity limitations, with the aim of providing a comprehensive assessment of health-related aspects, and the potential impact of disease on quality of life (19). Thus, HRQoL can be summarised as a measure of self-perceived health (20). Therefore, the HRQoL of a patient with cancer can be greatly influenced by such factors as the diagnosis, treatment, rehabilitation, and environmental factors.

#### 1.2.1 HRQoL and urinary bladder cancer

The HRQoL of patients with urinary bladder cancer is affected due to both the diagnosis and its symptoms, but also following treatment because both sexual and urinary functioning is affected by surgery (21, 22). There can also be an effect on HRQoL depending on the surgery method, with studies suggesting that patients receiving an orthotopic neobladder might have a slightly higher HRQoL than patients with an ileal conduit (22, 23). Patients' HRQoL is also affected by their recovery as HRQoL tends to normalise over time, except when there are persistent consequences such as impotence or incontinence (23, 24). However, there is also research suggesting that the domains of physical functioning might remain low even as long as 12 months after surgery (24). Furthermore, the type of urinary bladder cancer has a major impact on HRQoL, with patients with muscle-invasive urinary bladder cancer reporting a significantly lower HRQoL than those with non-muscle-invasive urinary bladder cancer (25).

### 1.3 Theoretical framework

This thesis uses the biopsychosocial model as its theoretical framework. This means that the foundation to understanding patients' suffering lies in understanding how disease, suffering, and illness are affected by biological,

psychological, and social dimensions (26). The model can be used as both a practical clinical guide and a philosophical framework for clinical care in order to understand that patients' subjective experiences contribute to health outcomes, and not biology alone (26). The essence of the model is that disease and symptoms do not necessarily correspond to a patient's subjective experience of illness or suffering, and vice versa: a psychological feeling of illness or suffering is not necessarily associated with biological or physical ailments (26). A cancer diagnosis and treatment for cancer are associated with an impact, both biologically and psychologically, and both aspects can play a role in the patient's wellbeing according to the biopsychosocial model (27). This can also be related to HRQoL as it includes physical, psychological, and social domains (20). Therefore, the theoretical framework for this thesis is based on the idea of supporting and improving patients' physical functioning, and thus improving their role functioning, and biological and physiological conditions for health. This will also strengthen patients' opportunities for activity and participation, and in the end improve their HRQoL. One must however consider that this model is not an explanatory framework for health, but a model for viewing health as multidimensional, affected by several aspects (28, 29).

#### 1.4 Abdominal cancer surgery

Surgery is the most common treatment for solid cancer tumours, and is often combined with chemotherapy or radiotherapy (12). Radical cystectomy is considered the gold standard for treatment of muscle-invasive bladder cancer and is often combined with neoadjuvant chemotherapy (30, 31). The surgery is often performed using robot-assisted technology, known as a Robot-Assisted Radical Cystectomy (RARC) (32). RARC involves removing the urinary bladder as well as any adjacent structures affected, or with a high risk of being affected, by metastases. The surgery also includes urinary diversion by either an orthotopic neobladder or ileal conduit with a urinary stoma (30). Urinary diversion by ileal conduit is the most common (33).

Colorectal cancer surgery is performed through both open and laparoscopic surgery, where the latter is to be recommended, when possible, to improve patient outcomes and reduce the risk of complications (34). The use of robotassisted technology has also increased recently in colorectal cancer surgery and has been proven to be both feasible and safe (34). In the early stages of ovarian cancer, the standard approach is open surgery through midline laparotomy to enable exploration of the pelvic and abdominal peritoneal area for suspicious implants and thus minimise the risk of rupture of the primary tumour (35). Minimal invasive surgery, such as that using laparoscopic techniques, can then be used for restaging (35). In advanced stages, the standard approach is also open surgery through midline laparotomy, with the goal of removing all macroscopic disease (35).

### 1.4.1 Complications following abdominal cancer surgery

Following RARC, the risk of complications is high, and 19–75% of patients need to be readmitted to the hospital following such surgery (36). Common complications include infection, and cardiac and thromboembolic complications (37). Complications also include aspects that can have an effect on HRQoL, such as sexual dysfunction, urinary incontinence, and reduced physical functioning (38, 39) In Sweden, approximately 50% of patients experience complications within 90 days of surgery, and 11% need a further operation within 90 days (33). Patients' age and the prevalence of comorbidities is thought to contribute to the high risk of complications (30, 40). Complications associated with colorectal cancer surgery are also common and include infection, nausea and vomiting, pain, and ileus (34, 41).

### 1.4.2 Enhanced recovery after surgery

To minimise the risk of complications and improve patient outcomes, surgery is often performed in alignment with so-called "fast track" programmes, also called perioperative programmes, or enhanced recovery programmes (34, 41–46). Adherence to these programmes has been shown to lead to shorter length of stay, reduction in complications, lower readmission rates, and a dose-response relationship, where better adherence to the programmes is associated with better outcomes (43, 44, 46, 47). These programmes contain guidelines regarding several aspects to be considered before, during, and after surgery, such as nutrition, bowel preparation, fluid management, pain control, surgical approach, and postoperative mobilisation (34, 43, 45–47).

#### 1.4.3 Postoperative mobilisation

Postoperative mobilisation is an umbrella term that is not clearly defined but generally incorporates all physical activity and mobilisation in hospital following surgery. Furthermore, in this thesis, mobilisation refers to patients' movements out of bed to sitting, standing, and walking following surgery in a hospital setting. The definition of early mobilisation also varies, and recommendations can range from any mobilisation within 24 hours following surgery, to strict schedules of a minimum of two hours out of bed on the day of surgery, and a minimum of six hours on postoperative day (POD) one. In addition, the quality of evidence is generally low (34, 43, 45, 47, 48).

Early mobilisation is strongly recommended following surgery and is an important part of the enhanced recovery programmes because it is thought to reduce postoperative complications and shorten length of stay (34, 43, 45–47). An association between more steps taken during the first postoperative days and faster recovery can be seen in colorectal patients (34). However, the consequences of prolonged bedrest following surgery are already known, and include muscle loss, reduced physical functioning, and an increased risk of pulmonary complications and thromboembolic disease. This is why early mobilisation remains a strong recommendation, and more intervention studies are needed with the aim of evaluating and increasing mobilisation (34, 43, 45, 47, 48). There is also a specific need for evidence regarding effective early mobilisation protocols that can increase mobilisation and improve outcomes (48). Early mobilisation has also been shown to be safe and not to have a negative impact on readmission or the severity of complications following abdominal cancer surgery (49).

Despite the knowledge that prolonged bedrest is negative, patients' physical activity and mobilisation levels tend to be low following surgery (50). Lack of education and resources have been identified as potential barriers to early mobilisation and clinical decision-making tools and education could improve compliance (51). Real-time feedback on mobilisation, a positive culture that priorities mobilisation, and wearable technology are also highlighted as potential tools to help structure early mobilisation (51). In a study that explored patients' experiences of early mobilisation following abdominal cancer surgery, patients expressed a strong motivation to achieve mobilisation because this made them feel better and helped them reach their goal, which was to get home again. But they also stated that they needed support from caregivers and required information about the process of mobilisation and what is expected of them (52).

#### 1.4.4 Enhancing postoperative mobilisation

As mentioned above, there is very little available evidence exploring and evaluating early mobilisation or models to support early mobilisation following abdominal cancer surgery. However, studies have shown that providing structure, behavioural support, and multimodal rehabilitation can lead to improvements in clinical outcomes. In this thesis, enhanced mobilisation refers to efforts to support or improve the mobilisation process following abdominal cancer surgery.

In a study by Porserud et al., the effects of using an Activity Board with goals and activities to enhance mobilisation following abdominal cancer surgery were explored. It was found that levels of mobilisation increased compared to the controls, and clinical outcomes were improved, such as a shorter time to first flatus and stool, and a shorter length of stay. It was concluded that the Activity Board could be a suitable tool to enhance mobilisation following abdominal cancer surgery (53). Patients' experiences of using the Activity Board were also explored by Porserud et al. The Activity Board was perceived by patients as a tool that enables participation and facilitates empowerment in relation to rehabilitation, further strengthening its potential as a tool to facilitate enhanced mobilisation (54). Healthcare professionals' experiences of using the Activity Board have also been explored in this thesis. The results indicate that the Activity Board is a tool that facilitates daily work and promotes patient participation. However, the Activity Board is also described as cumbersome and somewhat obsolete, and a more modern option is called for (55). Another study exploring the effects of enhanced mobilisation showed that a progressive mobilisation regime with standardised goals successfully increased mobilisation levels in patients (56).

### 1.5 Physical activity

Physical activity is defined as any bodily movement that is produced by skeletal muscles and results in energy expenditure (57). Ergo, everyone performs physical activity in order to sustain life, but there is a large variation in the amount performed between different individuals, or by an individual over time, as a result of personal choice, lifestyle, and circumstances (57). Exercise is a sub-component of physical activity that is planned, structured, and repetitive, with the objective of improving or maintaining physical fitness components (57). Levels of aerobic physical activity can be expressed as intensity, where an

absolute intensity is the required amount of energy expenditure to perform an activity. A common measure of this is the metabolic equivalent (MET), where one MET is the equivalent to rested sitting. Aerobic physical activity can then be divided into different intensity categories: sedentary behaviour at 1–1.5 METs (such as sitting, standing), light-intensity at 1.6–3 METs (slow walking), moderate-intensity at 3–6 METs (fast walking), and vigorous-intensity at 6 or more METs (running, sporting activities) (58).

#### 1.5.1 Physical activity recommendations

There is also a strong correlation between physical activity and health, and regular physical activity can prevent and/or mitigate cardiovascular disease, type-2 diabetes, and site-specific cancers, as well as improving all-cause mortality, mental health, sleep, and HRQoL (58, 59). Physical activity has also been shown to be beneficial as a primary prevention of specific cancers such as breast, colon, endometrial, bladder, kidney, oesophageal, and stomach (60). To gain these health benefits, the WHO recommendations on physical activity and sedentary behaviour state that all adults should perform 150 to 300 minutes of moderate-intensity, or 75 to 150 minutes of vigorous-intensity, aerobic physical activity per week, or a combination of these (59). It is also recommended to limit sedentary behaviour and replace it with light-intensity physical activity in order to gain increased health benefits (59). There is a non-linear dose-response relationship between physical activity and health, where going from no physical activity to just a small amount of activity brings substantial health benefits. Furthermore, increasing physical activity to the level of the recommendations brings even more health benefits. Activity levels greater than the recommended levels do not seem to bring any greater benefits. Thus, meeting the recommendations should be seen as a goal and guideline and becoming a little active is far better than not being active at all (58, 59, 61, 62). It is also recommended to perform regular muscle strengthening activities and to reduce sedentary behaviour (59). The specific recommendation regarding adults aged 65 year and older, including people with disabilities and chronic conditions, such as cancer, is that they should incorporate multicomponent activities that focus on balance and strength training at moderate or higher intensity, on three or more days a week (59).

#### 1.5.2 Measuring physical activity

When measuring physical activity or a physical activity behaviour, there are several aspects to consider, including what aspects of the physical activity it is desirable to measure, and what means or measurements to use. Physical activity can be divided into four dimensions: type, frequency, duration, and intensity of performed activity (63). When measuring physical activity or a physical activity behaviour, it is common to estimate the energy expenditure in calories or metabolic equivalent of the activity, or to summarise how much time is spent in a physical activity of a particular intensity during a specific time period (63). There are generally two common methods of measuring physical activity: subjective self-reported, and objective monitoring (63–65).

Self-reported measures of physical activity are generally questionnaires based on individuals' recall of previous activities. These measures are the most commonly used and do not require a lot of resources. However, they are also subject to recall bias and are less reliable when measuring low- to moderateintensity activities (63, 65). The evidence for the use of objective monitoring, usually by means of wearable devices, is increasing. Objective monitoring (or wearable devices) has shown a lower degree of variability and proven to be more reliable (63, 65). Accelerometers are most commonly used and are wellevaluated objective monitors for measuring physical activity in clinical and epidemiological research (66). Accelerometers can be used to assess physical activity and calculate energy expenditure, steps, and intensity levels (63, 66).

### 1.6 Cancer rehabilitation

The Swedish National Board of Health and Welfare defines rehabilitation as interventions that aim to assist individuals with acquired disabilities, based on their needs and circumstances, in regaining or maintaining the best possible functional ability, as well as in creating favourable conditions for an independent life and active participation in social life. Rehabilitation incorporates early, coordinated, and multifaceted interventions by different competencies and organisations (67). Furthermore, cancer rehabilitation is defined as efforts, based on an individual's needs and circumstances, aimed at preventing functional impairments and enabling the person to maintain or regain the best possible functional and activity abilities, quality of life, and active participation in social life, despite the consequences of cancer and cancer treatment (67). Cancer rehabilitation should be based on four core areas: physical, psychological, social,

and existential. It should also be person-centred, where the individual should be seen as an active partner and participant in the rehabilitation process (67). This thesis focuses on the physical aspects of rehabilitation, primarily aimed at supporting physical activity and improving physical functioning, which in this thesis is defined as physical rehabilitation.

#### 1.6.1 Physical rehabilitation and cancer

Physical rehabilitation should be aimed at patients regaining or maintaining their best possible level of physical functioning and activity, and maximising HRQoL through exercise (67). Cancer survivors are recommended to adhere to the general recommendations for physical activity as mentioned above, as well as incorporating exercise with the goal of reducing the burden of both diagnosis and treatment (59, 68). Exercise is generally considered safe both during and after treatment, but some contraindications do apply, such as allowing adequate time to heal following surgery. Also, individuals who experience extreme fatigue, anaemia, ataxia, or have an ongoing infection are recommended not to exercise (67, 68). Following abdominal cancer surgery, strength training must also start with low resistance and then slowly increase the resistance to avoid hernias. The objective should be to regain and improve physical functioning, body image, HRQoL, and mental health, as well as reducing long-term and late effects of cancer treatment, and potentially reduce the risk of recurrence or a secondary cancer (67, 68).

Exercise in cancer survivors has been shown to have specific positive effects on commonly experienced issues related to both diagnosis and treatment, such as anxiety, physical functioning, fatigue, depressive symptoms, and HRQoL (69). Based on the available evidence, there are specific recommendations regarding type of activity and intensity to target individual health-related outcomes in cancer survivors, as shown in Table 1 (69). However, further research is needed to determine the efficacy of exercise for specific cancers and outcomes, timing, and type of treatment (69). The available evidence and recommendations summarised in Table 1 are predominantly based on studies conducted on patients with early-stage breast or prostate cancer, and further studies in other cancer types and advanced stages are needed (69).

**Table 1.** Specific recommendations regarding physical exercise and healthrelated outcomes in cancer survivors.

Health-Related Outcome	Recommended frequency, intensity, time, and type	Evidence level
Anxiety	Moderate-intensity aerobic exercise three times per week for 12 weeks, or twice weekly combined with resistance training for 6 - 12 weeks	Strong
Depressive symptoms	Moderate-intensity aerobic exercise three times per week for 12 weeks, or twice weekly combined with resistance training for 6- 12 weeks	Strong
Fatigue	Fatigue         Moderate-intensity aerobic exercise three times a week for at least 12 weeks, or a combination of moderate-intensity aerobic exercise and resistance training 2-3 times a week, or twice weekly moderate-intensity resistance training	
HRQoL	Noderate-intensity aerobic exercise and resistance training 2-3 times a week for at least 12 weeks	
Lymphedema	Supervised resistance training with a focus on large muscle groups 2–3 times per week with the principle of starting low and progressing slowly	Strong
Bone health	e health Moderate to vigorous-intensity resistance training combined with high-impact training performed 2-3 times a week	
Sleep	ep Moderate-intensity aerobic exercise, particularly walking, 3-4 times per week for 30-40 minutes per session over 12 weeks	

#### 1.6.2 Physical rehabilitation following radical cystectomy

The available literature on exercise interventions following cystectomy in patients with urinary bladder cancer is limited, but suggests that physical activity and exercise might improve physical functioning and HRQoL, suggesting that further investigation is warranted (70, 71). A pilot study by our research group, exploring the feasibility and effects of a group exercise intervention conducted at the hospital following discharge, found that the intervention increased patients' functional capacity and physical role functioning seemed to be maintained over time. However, it was concluded that the intervention did not seem feasible for most patients, with distance to the hospital seeming to be a major barrier (72). Adherence and acceptability for exercise seem to be increased when conducted in primary care instead of at the hospital (73).

Jensen et al. evaluated the effects of a multidisciplinary pre- and post-operative rehabilitation programme involving home exercises prior to surgery, enhanced mobilisation at the hospital following surgery, and a home exercise programme after discharge (56, 74, 75). They found that postoperative mobilisation was significantly improved regarding patients' walking distance and found an improvement in patients' ability to perform the personal activities of daily living (56). The one-year follow-up also showed that the intervention group had a significant improvement in physical function and had regained nutritional status compared the control group (76). They found no significant impact of on global HRQoL, but a positive impact on HRQoL sub-domains such as bowel management and respiratory function, and concluded that physical exercises can have a positive impact on HRQoL following radical cystectomy (74). The evidence regarding physical rehabilitation's impact on global HRQoL in urinary bladder cancer patients following radical cystectomy is also inconclusive, and further research is required (77). Thus, physical rehabilitation and exercise seem to be beneficial for patients following RARC for urinary bladder cancer, but there is a need for more high-quality studies to determine its effect on physical functioning and HRQoL (70, 71).

## 2 Rationale

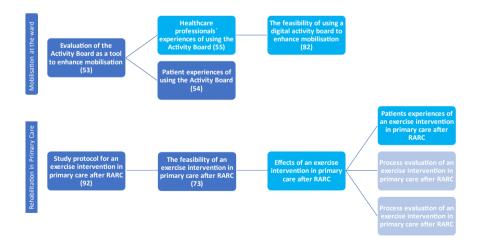
Physical rehabilitation and exercise are recommended for patients to improve physical functioning, activity, and HRQoL (67). (67). Cancer survivors are recommended to adhere to the general recommendations for physical activity and to incorporate exercise, with the goal of reducing the burden of both diagnosis and treatment (59, 68). Exercise in cancer survivors has been shown to have specific positive effects on commonly experienced issues related to both diagnosis and treatment, such as anxiety, physical functioning, fatigue, depressive symptoms, and HRQoL (69). However, cancer patients seem less likely than the general population to be physically active, or to change their physical activity behaviour following diagnosis, calling for strategies to support physical activity behaviour in cancer survivors (78). Patients with urinary bladder cancer are no exception, as a recent study showed that one third of the 936 included patients self-reported a sedentary lifestyle and poor physical health (79).

Following abdominal cancer surgery, early mobilisation is a strong recommendation because it is thought to reduce postoperative complications

and shorten length of hospital stay (34, 43, 45–47). However, evidence is lacking on how to structure early mobilisation to improve outcomes and support adherence, and more intervention studies aimed at evaluating and increasing mobilisation are needed (34, 43, 45, 47, 48). Methods to enhance mobilisation has been tested by our research group by using the Activity Board which proved successful (53). But in the process of evaluating the potential usefulness and potential implementation it is also important to gain an understanding of facilitating aspects, potential barriers, perspectives of stakeholders involved (80–82). Evidence on the effects of physical activity and exercise following RARC for urinary bladder cancer is also lacking, but there are indications that it could have a positive effect on physical functioning and HRQoL (70). Physical activity should be included in the treatment pathway of urinary bladder cancer, but there are still knowledge gaps that need to be explored regarding how it should be included, in which settings, and how to support patients (56, 70, 71, 77).

There is therefore a need to explore methods of supporting physical activity in cancer survivors, in order to enhance mobilisation and support physical rehabilitation following surgery.

This thesis is part of a larger project with the overall aim of evaluating methods for improving outcomes for patients undergoing abdominal cancer surgery. An overview of the related studies and the role of my thesis can be seen in Figure 1.



**Figure 1.** An overview of studies related to this thesis and their settings, prior studies as dark blue, studies included in the thesis as light blue, and future studies as gray.

## 3 Research aims

The overall aim of this thesis was to contribute to the field of rehabilitation following abdominal cancer surgery by exploring methods to enhance postoperative mobilisation and evaluate the effects of physical rehabilitation following surgery. The goal was to facilitate patient adherence and engagement in rehabilitation and improve physical functioning and health-related quality of life following surgery.

The individual aims of the included studies were:

- 1. To describe healthcare professionals' experiences of using the Activity Board to support patients after abdominal cancer surgery.
- 2. To evaluate the feasibility of using the Pedatim tablet as a tool to enhance mobilisation following abdominal cancer surgery.
- 3. To evaluate the effect of a physical exercise programme in primary care following robot-assisted radical cystectomy for urinary bladder cancer.
- 4. To explore patients' experiences of an exercise intervention in primary care following robot-assisted radical cystectomy.

## 4 Materials and methods

## 4.1 Overview of the included studies

This thesis consists of four studies using different methodologies. For an overview of the included studies, see Table 2. Study I is a qualitative study exploring healthcare professionals' experiences of using the Activity Board as a tool to support patients' mobilisation following abdominal cancer surgery. Study II is a feasibility study exploring the feasibility of using the Pedatim tablet to support patients' mobilisation following abdominal cancer surgery. Study III is a randomised controlled trial (RCT) evaluating the effects of an exercise intervention in primary care following RARC for urinary bladder cancer. Study IV is a qualitative study exploring patients' experiences of the exercise intervention in study III.

	Study I	Study II	Study III	Study IV
Study design	Qualitative	Feasibility	RCT	Qualitative
Participants	17 healthcare professionals	20 patients	90 patients	20 patients
Intervention	The Activity Board	The Pedatim tablet	Exercise in primary care	Exercise in primary care
Analysis	Content analysis	Descriptive statistics	Mann- Whitney U- test	Thematic analysis
Primary outcome	Experiences	Process feasibility	Physical function	Experiences

Table 2. An overview	of the included studies	. their design.	and methodologies.
		,	

## 4.2 Context

All the studies included in this thesis were conducted at the Karolinska University Hospital in Solna, Sweden. Patients scheduled for surgery at the Karolinska University Hospital for urinary bladder cancer, colorectal cancer, or ovarian cancer are admitted the day before surgery to the gastrointestinal ward, the urology ward, or the gynaecology ward, respectively. Following surgery, patients generally spend one night in a postoperative recovery unit before they return to the ward. On these wards, surgery and care is performed in accordance with the enhanced recovery protocols mentioned earlier, including goals regarding early mobilisation. By means of standard care, patients' postoperative mobilisation is encouraged and supported by healthcare professionals on the ward, mainly nurses, assistant nurses, and physiotherapists. To support this process, the wards were using a tool called the Activity Board for between six months and five years prior to the start of this thesis, depending on the ward.

The Activity Board (Scandinavian Phystec AB) is a tool designed to facilitate mobilisation in hospital settings. It is a whiteboard on which daily activities and goals can be scheduled using magnets and pictures, with a red magnet for a notyet-completed activity, and a green one for a completed activity. The board can be placed in a patient's room on the ward, in a position where it is clearly visible on the wall. A healthcare professional, usually a physiotherapist, sets daily activities and goals on the board together with the patient, based on the patient's status. These activities are related to postoperative rehabilitation and often include sitting, walking, and breathing exercises, and the goals are usually related to how frequently the activity should be performed during a given day. The board can then act as both a reminder to the patient, and a schedule. The board contains red and green magnets that represent the number of times a patient should perform an activity. A picture of the Activity Board in use is presented in Figure 2.

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Figure 2. A picture of the Activity Board in use at a ward.

## 4.3 Methods employed in the individual studies

### 4.3.1 Study I

A qualitative study using focus groups guided by a semi-structured interview guide was conducted during the summer and autumn of 2018.

### 4.3.1.1 Recruitment

Using a purposive sampling strategy, healthcare professionals with experience of using the Activity Board were recruited on the gastrointestinal, urology, and gynaecology wards. Leaflets were posted on the wards with information about the study, and the head nurses on the wards also informed healthcare professionals about the study at general assemblies on the wards (83).

### 4.3.1.2 Data collection

Four focus group interviews were conducted during the summer of 2018. These focus groups were led by a senior researcher assisted by a junior researcher and lasted between 45 and 61 minutes. The focus groups were divided by ward, thus each interview took place on the corresponding ward. The semi-structured interview guide addressed: the nature of postoperative mobilisation, the Activity Board's effect on patients, collaboration with the patients, practical aspects of the Activity Board, teamwork, and future implementation/developments (83).

#### 4.3.1.3 Data analysis

The data was analysed using inductive content analysis as described by Elo and Kyngäs (84). The interviews were first transcribed verbatim, then read and reread. Then, units of meaning were extracted and condensed, codes were formed and then compared, and eventually sorted into categories and sub-categories. An overarching theme was then identified based on the content of these categories and sub-categories.

### 4.3.2 Study II

A non-randomised feasibility study was conducted between January and May 2022. The primary objective was to assess the process feasibility of the study design, and a secondary objective was to assess the scientific feasibility of the Pedatim tablet in its ability to enhance mobilisation. The study design was guided by Thabane et al. 2010 (85).

#### 4.3.2.1 Recruitment

Medical records were screened to find patients scheduled for surgery due to colorectal cancer, ovarian cancer, or urinary bladder cancer on the urology or gastrointestinal ward at Karolinska University Hospital. Patients with an expected postoperative hospital stay of a minimum of three days were deemed eligible, if they were over 18 years old, understood Swedish in speech and writing, and were able to walk independently or with a walking aid. Patients were excluded if they experienced complications during surgery, or a planned surgery method that would result in restrictions on mobilisations such as sitting or walking. Patients were also excluded if they had cognitive impairments or were participating in another clinical rehabilitation study. Eligible patients received written information about the study via mail and a follow-up phone call during which they could ask questions and choose whether or not to agree to participate. Healthcare professionals working on the wards were also invited to take part in the evaluation of the usability of the Pedatim tablet. They were recruited using convenience sampling and informed that they could provide anonymous feedback by filling in a form and leaving it in a mailbox on the ward (86).

#### 4.3.2.2 Intervention

The patients taking part received a Pedatim tablet to use as a tool to support postoperative mobilisation. The Pedatim tablet is a further development of the Activity Board mentioned above, and was designed by the same company, Scandinavian Phystec AB. The tool is essentially a digital activity board following the same principles as the original Activity Board but projected onto a digital tablet. An image of the Pedatim tablet in use can be seen in Figure 3. Patients received the tablet together with user instructions upon admission to the ward, the day before surgery, or upon returning to the ward from the postoperative recovery unit. They then used the tablet throughout their hospital stay and it was collected when the patient was discharged from hospital. Both the researchers and healthcare professionals on the ward received information, training, and user instructions about the Pedatim tablet prior to the start of the study (86).



**Figure 3.** A picture of the Pedatim tablet on a patient's bedside table (left), and a zoomed view of its user interface (right).

## 4.3.2.3 Outcomes

The main objective, assessment of process feasibility, included several outcomes: recruitment measured as the percentage of available patients included in the study, sufficient eligibility criteria, number of dropouts, compliance measured by number of patients using vs not using the tablet, and acceptability measured by the System Usability Scale (SUS). SUS is a questionnaire that is widely used to assess the perceived usability of a technical system, such as an application (87). SUS has been validated both in general applications and specifically in digital health applications (88, 89). As an addition to SUS, an open question was also added: "Please describe your experience of using the Pedatim tablet, using your own words".

The secondary objective, assessment of the scientific feasibility, includes an indication of treatment effect, in this study defined as the tool's ability to promote physical activity on the ward following surgery, measured by the number of sit-to-stand transitions and steps taken per day using an activPAL (PAL technology) accelerometer (86). The activPAL is validated to measure position and acceleration, which can then be translated into steps, stepping speed, posture transitions, and body posture using PAL technology software (90, 91). Length of stay was also measured, and any technical or practical issues regarding the tablet were registered as unforeseen events. Feasibility criteria were also predetermined for each outcome of the process feasibility, a threshold that had to be met for an outcome to be determined as feasible. These criteria were based on clinical experience and previous clinical trials (86).

#### 4.3.2.4 Data collection

On POD 1, the activPAL accelerometer was applied and worn by the patient throughout their hospital stay. Before discharge from hospital, the accelerometer was returned, and the patient was asked to fill in the SUS, along with the open question. Data was also collected using medical records. Healthcare professionals were also encouraged to answer the SUS, and instructed to leave their anonymous form in a mailbox on the ward (86).

## 4.3.2.5 Data analysis

The analysis of the feasibility of the process was conducted in two steps; firstly with descriptive statistics regarding each outcome, and secondly by determining if the outcome was feasible by whether or not it reached the feasibility criteria threshold. Regarding scientific feasibility, the variables derived from the activPAL measurements, number of steps, and sit-to-stand transitions per day, were also analysed using descriptive statistics to describe patients' physical activity patterns during the first few days after surgery. As length of stay varied, the physical activity measurements from the activPAL were analysed for POD 1–4 (86). The analysis of the open question added to the SUS was conducted using tabular thematic analysis (92).

#### 4.3.3 Study III

A single-blind randomised controlled trial comparing an active control group with an intervention group was conducted between September 2019 and March 2023 (93).

#### 4.3.3.1 Recruitment

Medical records were screened to find eligible patients who were scheduled for RARC due to urinary bladder cancer between September 2019 and October 2022. Eligible patients were consecutively invited to participate in the trial if they: could understand Swedish in speech and writing, were able to walk independently or with a walking aid, and lived in Stockholm County. Patients were excluded if they were scheduled for palliative surgery or had cognitive impairments. Eligible patients were given written information about the study by a registered nurse during a pre-surgery planning session at the hospital. After 2– 3 days, patients were called via telephone by the researchers to enable them to ask questions about the study and choose whether or not to participate. Written informed consent was collected upon the patient's arrival at the hospital on the day before surgery (93).

## 4.3.3.2 Intervention

Preoperatively, all patients received information about the importance of physical activity following surgery. All patients also received enhanced mobilisation using the Activity Board during their stay on the ward (53, 54). Upon discharge from hospital, patients were randomised to either the active control group or the intervention group. The active control group received written information about the importance of physical activity following surgery and instructions on how to gradually increase their physical activity following discharge through daily walks and a leg-strengthening exercise, and examples of how to monitor their activity using, for example, applications or pedometers. The control group only received this information once, along with a folder, and did not receive any follow-up regarding progression or adherence.

The intervention group received a referral to a primary care facility of their choosing. A total of 18 primary care facilities were recruited prior to the start of the study and received information and education from the research team about the study, the study population, RARC, the exercise programme, postoperative restrictions, potential complications, and adverse events. The participating primary care facilities were scattered across Stockholm County in order to be able to offer patients primary care in relatively close proximity to their home. Once a patient had received a referral, the primary care then contacted them to schedule a first visit, planned for approximately three weeks following surgery. Once started in primary care, patients were to conduct a twice weekly, 12-week exercise intervention under the supervision of a physiotherapist. The exercise programme consisted of a progressive strength programme with exercises for large muscle groups, initially with an intensity of 2x15 repetitions, and gradually increasing intensity to 2x10 repetitions. It also contained aerobic exercises with a recommendation of moderate intensity performed, for example, on a treadmill or stationary bicycle. Patients were also encouraged to take daily walks and perform specific home-based exercises for the abdomen and pelvic floor muscles. The programme was approved by the responsible surgeons at the hospital and any postoperative restrictions were considered when planning the progression of the programme (93).

#### 4.3.3.3 Outcomes

The study had several outcomes measurements were conducted with validated instruments. The main outcome being defined as physical function was measured with the six-minute walk test (94, 95) Secondary outcomes included: maximum gait speed measured over six metres (96), leg strength measured by a 30-second chair stand test (97), grip strength measured using a JAMAR dynamometer (98), pain measured using a Numeric Rating Scale (99), self-perceived fatigue using the Piper Fatigue Scale (100, 101), psychological well-being and anxiety using the Hospital Anxiety and Depression Scale (102), HRQoL using the EORTC-QLQC30 (103), and EORTC-BML30 (104), and physical activity in daily life was also measured using activPAL accelerometers (90, 91). For an overview of the included measurement instruments and points of data collection, see Table 3.

	Preoperative (day before surgery)	Postoperative (day before discharge)	Four months after surgery
Six-minute walk test	х	x	х
Gait speed	х	х	х
30 second chair stand test	x	х	х
JAMAR grip strength	х	х	х
Pain, NRS	х	x	x
Piper Fatigue Scale	х	х	x
HADS	х	x	x
EORTC-QLQC30	х	х	х
EORTC-BLM30	х	x	x
activPAL		x	x

 Table 3. An overview of the included measurement instruments and time of data collection.

HADS = Hospital Anxiety and Depression Scale NRS = Numeric Rating Scale

## 4.3.3.4 Data collection

Data was collected by means of measurements, firstly at the time of the patient's arrival in hospital, the day before surgery. Then the patient's progress on the ward was followed through their medical records and, on the day before scheduled discharge, the measurements were conducted again. At approximately four months following surgery, patients were again called to the hospital to perform follow-up measurements. The researchers followed their exercise intervention before being called to follow-up measurements. Patients in the control group were called to follow-up strictly based on the time from discharge to the four-month timepoint.

## 4.3.3.5 Data analysis

The statistical analysis was conducted using IBM SPSS software version 28. Firstly, descriptive statistics were used to describe the sample and outcomes. As the data was non-normally distributed and missing data, the Mann-Whitney U-test non-parametric test was used to analyse the difference between the control group and the intervention group at follow-up. The paired Wilcoxon signed rank test was used to analyse the within-group differences between preoperative status and status four months after surgery for the intervention group and control group respectively. The analysis was performed using both the intention-to-treat principle and per protocol, and the significance level was set to 0.05.

## 4.3.4 Study IV

A qualitative study using individual interviews guided by a semi-structured interview guide was conducted between October 2020 and March 2023.

#### 4.3.4.1 Recruitment

Using purposive sampling, patients who had been randomised to the intervention group in study III, and had exercised in primary care, were invited to participate in this study. Together with the study information and informed consent form used in study III, patients were informed about the possibility of being contacted and asked to participate in an interview following the intervention. Patients who had completed their exercise intervention in primary care were contacted via telephone by the researchers and asked to participate in this interview study.

#### 4.3.4.2 Data collection

Patients who agreed to participate were each scheduled for an individual interview. A semi-structured interview guide was used to allow for probing questions and further exploration, depending on patients' responses. The interview guide focused on the main topics of: arriving home from hospital, getting started with exercise, the exercise intervention in primary care, the effects of exercise, their thoughts on rehabilitation following surgery, and other reflections. Because of the Covid-19 pandemic, which was ongoing at the time, interviews were primarily conducted via distance using a digital platform or telephone, with a few interviews conducted face to face. The interviews were recorded and transcribed verbatim.

#### 4.3.4.3 Data analysis

To analyse the data, reflective thematic analysis was used according to the step-by-step process described by Braun and Clarke 2006 (105). Firstly, familiarisation with the data was achieved by reading and re-reading the transcripts. The next step was generating initial codes and marking interesting aspects of the data in relation to the aim of the study. This was followed by a search for themes by organising the codes and grouping them into preliminary themes. All the data relevant to each theme was then gathered, and the themes were reviewed to evaluate where they fit in relation to the initial codes, notes, and data. Each theme was then properly named and defined, followed by the final step of the process, which was to produce the report (105).

## 4.4 Ethical considerations

The ethical principles stated in the World Medical Association's Declaration of Helsinki were followed in all the studies within this thesis (106). First and foremost, all participating patients received written and oral information about the relevant study, followed by a time for consideration (usually 1–3 days). They were then followed up by telephone and given an opportunity to ask questions and consider participation. Upon agreeing to participate, written informed consent was collected face-to-face by the researchers before surgery to allow for further questions or clarifications. Patients were informed both in writing and orally that participation was completely voluntary and that choosing not to participate would have no consequences for their scheduled care. They were also informed that they could withdraw from the study at any time without giving a reason. The well-being of all patients participating in the studies was taken into careful consideration. Conducting clinical studies always carries risks, and in this thesis, promoting physical activity in frail elderly patients with cancer could have consequences and unforeseen adverse effects that might impact negatively upon their health. However, research indicates that exercise, even among frail, elderly patients with cancer, is to be considered safe, and that the potential negative consequences of sedentary behaviour or lack of exercise are greater (59, 60, 69). Therefore, the risks were considered to be far outweighed by the benefits. However, measures were taken to enhance patient safety. Exercise was conducted in an environment with healthcare professionals present and involved healthcare professionals who had received education and information regarding each patient's status, any risk of complications, potential adverse effects, and relevant contact information if the patient seemed to be suffering from adverse effects.

All the studies included in this thesis received approval from the regional ethical review board in Stockholm, and the Swedish Ethical Review Authority, case numbers: 2012/2214-31/4, 2017/2349-32, and 2021–04323.

# 5 Results

The study participants in this thesis include both healthcare professionals in Study I, and patients in Study II-IV. An overview of the participating patients of Study II-IV in this thesis can be seen in Table 4.

	Study II	Study III	Study IV
Total	N=20	N=90	N=20
Age, years			
– Mean (SD)	69 (11)	71.3 (8.5)	70 (8.6)
Sex, N (%)			
- Female	11 (55)	28 (31)	6 (30)
- Male	9 (45)	62 (69)	14 (70)
Diagnosis, N (%)			
- UBC	9 (45)	90 (100)	20 (100)
– CRC	8 (40)		
– OV	3 (15)		
Surgery method, N (%)			
- RARC	9 (45)	90 (100)	20 (100)
- Laparoscopic	3 (15)		
- Open	8 (40)		
Urinary diversion, N (%)			
- Ileal conduit	n/a	75 (83)	19 (95)
- Orthotopic	n/a	15 (17)	1(5)
Neoadjuvant therapy, N (%)	n/a	29 (32)	5 (25)
Length of stay, days (SD)	5.8 (1.4)	8.7 (5.4)	8 (2.9)

 Table 4. An overview of the participants of each study and characteristics.

UBC = Urinary Bladder Cancer

CRC = Colorectal Cancer

OV = Ovarian Cancer

# 5.1 Study I

In this study, 17 healthcare professionals participated and were interviewed in four focus groups, based on the unit or ward where they worked. In total six nurses, seven assistant nurses, and four physiotherapists participated, one male and 16 female, mean age 32 years with a mean clinical experience of 5 years. Focus group one was held on the urology ward, where two registered nurses and two assistant nurses participated. Focus group two was held on the gastrointestinal ward with two registered nurses and three assistant nurses. Focus group three was held on the gynaecology ward and involved two registered nurses and two assistant nurses. The fourth and final focus group was held in the Department of Physiotherapy, where four physiotherapists working on the above-mentioned wards participated.

## 5.1.1 Overarching theme

The result was one overarching main theme, in which the Activity Board could be seen as *A* tool that facilitates daily work and promotes patient participation. It was described by the participants as easy to use and a helpful tool with great potential. They stated that it provided valuable information and enabled them to support patients better. It was also described as having a positive impact on patients as experienced by the participants, encouraging them to take charge of their own rehabilitation. This main theme is supported by four categories: *A* source of information, Using the Activity Board to support the patient, Work procedures, and Potential and development.

## 5.1.2 A source of information

Participants described the Activity Board as a useful source of information for both healthcare professionals and patients. The information on the board helped with daily planning because the activity status, shown as red or green magnets, could indicate if a patient needed assistance regarding mobilisation. It could also convey a patient's health status, as failure to perform activities could indicate that a patient was feeling unwell. It also acted as a visual reminder to assist patients and promote mobilisation.

"You understand what to ask the patient. "I see, but why haven't you been up today, have you been tired, or have you been feeling unwell?"

## 5.1.3 Using the Activity Board to support the patient

Participants explained that supporting patients' postoperative mobilisation is an important part of their daily work. They went on to describe how the board can be used to assist this work by using goal-setting to support and guide patients. They also explained that the board allows them to provide more patient-centred support based on each individual's status and needs. The participants also described it as a tool to support patients' motivation and said that they seemed eager to achieve their goals. The board also supports patients' understanding of the importance of mobilisation and related aspects because these are clearly highlighted on the board, enabling participants to use the board as a reference when supporting patients.

"But a lot of people are asking, well, what do you expect from me now? How much of this do I need to do now? Then you can sit down with this board and, ok, let's look ahead, how much do you think you can do?"

## 5.1.4 Work procedures

The participants explained that the procedures involving the Activity Board on the ward are important to gain the full benefits. With proper routines, the board was described as facilitating teamwork, but there were also examples of situations where routines were lacking. The board was sometimes used as a reference during rounds and briefings, which was described as positive because aspects related to mobilisation could be discussed if, for example, a patient had not reached their goals. However, this was very dependent on who was working and sometimes the board was overlooked completely. A need for regular education about the Activity Board was also described, with some participants explaining that they were not comfortable with changing the activities and goals on the board.

"If a patient is starting to feel unwell on Friday afternoon and we don't have a physiotherapist on site until Monday, then I would like to get more information on how to change the board and how to think about adjustment."

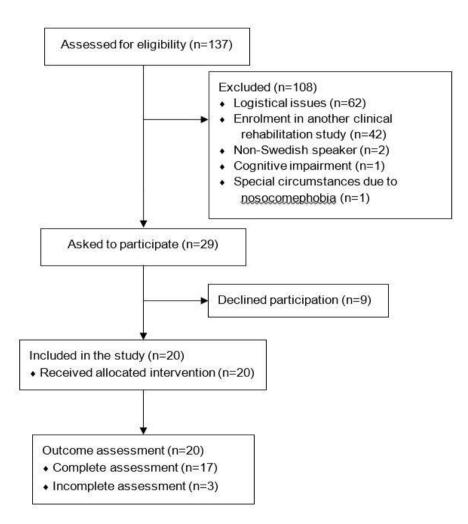
## 5.1.5 Potential and development

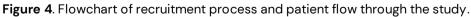
The participants described the board as a tool with great potential, even extending beyond mobilisation. They elaborated on several aspects related to enhanced recovery after surgery that could be incorporated into the board and its concept of goal-oriented behavioural support, such as urostomy training and nutrition. There were also several practical aspects in need of development according to the participants. They described the whiteboard as potentially obsolete, cumbersome, and heavy, including having several small parts that need to be cleaned between use by every patient.

"Then you could see right away, no I am not going to change your urostomy, you can do it by yourself. Then you have both urostomy training and mobilization and you're even closer to home!"

# 5.2 Study II

A total of 20 patients were recruited for this study, nine from the urology ward and 11 from the gastrointestinal ward. Surgery methods included RARC, laparoscopic surgery, and open surgery for urinary bladder cancer, colorectal cancer, and ovarian cancer. A flow chart of the inclusion and patient flow through the study can be seen in Figure 4 (86).





## 5.2.1 Process feasibility

The primary objective of this study, assessing the process feasibility, included the domains of recruitment, compliance, and acceptability. An overview of the process feasibility outcomes can be seen in Table 5. In total, 137 patients were screened. Of these, 29 patients were found to be eligible and asked to participate in the study, while 108 were excluded. Of the 29 eligible patients asked to participate, 20 agreed. Thus, of all 137 available patients screened, only 21% were eligible for inclusion. Therefore, the eligibility criteria of the study design were not deemed feasible. However, 69% of the patients asked to participate chose to do so. There was no dropout during the study and compliance with using the intervention was 95% and thus deemed feasible (86).

Regarding acceptability, 17 of the 20 patients answered the SUS form, resulting in a mean score of 77 out of 100 on SUS, indicating good usability and it was thus deemed feasible. The attached open question was answered by 14 patients and three healthcare professionals, resulting in three themes: "Easy to use and motivating", "Support from healthcare professionals", and "Technical support". The Pedatim tablet was described as intuitive and easy to use, with goal-setting and completing activities seen as motivating. However, patients did describe a need for support from healthcare professionals in terms of getting reassurance that they were using the tablet correctly and being given help to regularly revise the activities and goals. In the case of technical issues with the tablet, both patients and healthcare professionals described the need for technical support (86).

Process feasibility Feasible Result domain Recruitment Of all available patients, 21% were No eligible for inclusion Of all patients asked to participate, Yes (>50%) 69% accepted Yes (<20%) Dropouts were 0% Compliance 95% of participants used the Yes (>75%) Pedatim tablet. Acceptability Mean score of SUS 77/100 Yes (>70)

**Tabel 5.** An overview of the process feasibility outcomes and determination of feasibility.

## 5.2.2 Scientific feasibility

The secondary objective of the study, assessing the scientific feasibility of the tool, consisted of an indication of treatment effect and unforeseen events. In relation to indication of treatment effect, 17 patients wore the activPAL accelerometer from POD 1 to discharge from the hospital. Length of stay varied between four to nine days, with a mean of 5.8 days (SD=1.4). Daily steps and sit-to-stand transitions are presented for POD 1-4 (n=15). Overall, a progression can be seen each day, but there are substantial individual variations. Mean number of steps increased from 623 (SD=766) on POD 1 to 1823 (SD=1446) on POD 4, and mean sit-to-stand transitions increased from 11 (SD=8) on POD 1 to 29 (SD=12) on POD 4.

There were a few unforeseen events during the study as minor technical issues emerged with the tablets. Technical issues ranged from losing connection to the local network, glitches, and errors when entering values. All these issues could be resolved with the help of technical support from the developers of the Pedatim tablet.

## 5.3 Study III

A total of 202 patients were deemed eligible and invited to participate in the study. Of these, 100 patients agreed. However, ten of these dropped out during their hospital stay prior to randomisation, leaving a total of 90 patients included in the study. These were randomised into either an active control group or an intervention group. Mean age of the included participants was 71.3 years (SD=8.5), and 69% of participants were male. Apart from the intervention group having been treated by Bacillus Calmette–Guérin to a greater extent prior to surgery than the control group, there were no significant differences between the groups regarding demographic or clinical characteristics at baseline. There was a 19% dropout rate between baseline and follow–up in the intervention group, and 12% in the control group.

There was no statistically significant effect on the primary outcome of physical function when comparing the intergroup differences between baseline and follow-up when following the intention-to-treat principle during the analysis. However, there were positive effects for the intervention group regarding the secondary outcomes: daily physical activity, fatigue, and HRQoL (in the domains of global health, total symptoms, and bladder-cancer-specific symptoms) compared to the control group. A description of the outcomes at the timepoint

of collection can be seen in Table 6. A per-protocol analysis was also conducted to include patients who had exercised for at least one third of the scheduled sessions. The result of this analysis did not yield any differences from the intention-to-treat analysis.

Patients started their exercise intervention a mean of 39 days after discharge from hospital (SD=21), with approximately 25% starting within the planned three weeks following discharge. Patients participated in a mean of 17 exercise sessions (SD=6). No adverse events were reported during exercise.

Intervention group Control group n=47 n=43 Outcome variable Day before Discharge 4-month Day before Discharge 4-month follow-up gu-wollof (Baseline) (Baseline) surgerv surgery Physical function, m 491 (173) 376 (120) 490 (129) 492 (194) 370 (97) 515 (132) 2640 (2980) 2810 (2390) 7400 (4650) Physical activity, daily 7060 (3830) steps, n 1.51 (0.405) 1.06 (0.395) 1.60 (0.538) 1.71 (0.520) 1.12 (0.540) 1.58 (0.440) Gait speed, m/s Leg strength, n 12 (6) 8 (4.5) 13 (6.75) 12.5 (5) 9 (5) 12 (6.5) Grip strength\*, kg 36.4 (13.0) 31.6 (14.6) 34.4 (12.2) 33.0 (14.3) 30.6 (13.7) 37.1 (12.1) Pain (0-10) 0 (0.25) 1 (4) 0 (0) 0 (0) 1 (3) 0 (1) Fatigue (0-10) 0.5 (5) 6 (3) 1 (4) 4 (5) 6 (3) 4 (5.25) 5 (7) 4 (4.25) Depression 3 (3.5) 1.5 (4) 4 (4) 6 (4) (0-21) Anxiety 6 (5) 6 (6) 2,5 (5) 6 (4) 7 (5) 4 (6) (0-21)HRQoL global health 67 (33) 42 (33) 83 (33) 67 (31) 33 (33) 67 (33) (0-100) HROoL total function 80 (23.3) 47 (28) 87 (20.5) 82 (14) 51 (22) 78 (25.3) (0 - 100)HRQoL total symptoms 15 (15) 54 (28) 13 (13.5) 15 (20.3) 51 (28) 18 (13.8) (0-<u>100)</u>ª HRQoL bladder cancer 29 (20.5) 33 (22) 18 (24.5) 29 (14.5) 36 (20.5) 26 (21.8) specific symptoms (0–100)<sup>a</sup>

**Tabel 6.** Description of the outcomes and the time point of collection, presented as median (IQR).

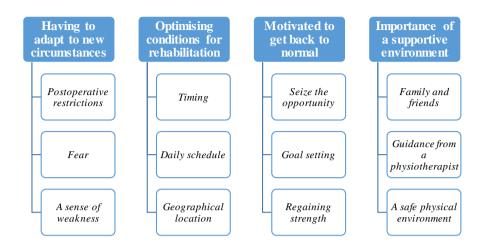
\*Mean value of right and left hand together, a higher score means more symptoms.

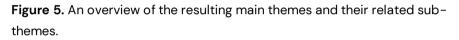
## 5.4 Studie IV

A total of 23 patients who performed the exercise intervention in study III were asked to participate in this interview study. Of these, 20 patients agreed to participate.

#### 5.4.1 Overview of the results

Four main themes were identified, and an overview of the results with main themes and their related sub-themes can be seen in Figure 4.





#### 5.4.2 Having to adapt to new circumstances

Patients described having to adapt to their new circumstances when they returned home following surgery. They said that they did not recognise their bodies and that they felt uncertainty about ever getting back to normal again. They had to adapt to having postoperative restrictions, which were described as hindering them in everyday life and limiting their ability to exercise. They also described a feeling of fear due to their situation: they feared complications if they did not adhere to the rehabilitation regime, but also if they over-exerted themselves, fearing potential ruptures of their urostomy or surgical incisions. They also described a feeling of weakness and fatigue, and being barely able to manage the tasks of daily life. They expressed a feeling of not recognising themselves and not being able to do or enjoy things as they used to.

"Of course, you were very scared that the operation would so to speak fall apart. That those ends that they cut together and made a new connection with the kidneys, of course you were scared that all that would break and create further problems. So, you had to be very careful with everything. I couldn't lift things or work in the garden that I normally do. And all the time you were scared that something would break somewhere in, in the belly, seeing that it had been stitched together."

#### 5.4.3 Optimising conditions for rehabilitation

Participants described a need for optimising the practical conditions to facilitate exercise. Getting a referral to primary care was described as one factor that made it easier to get started because it is otherwise easy to postpone exercise, or not to start at all. Timing was described as a sensitive balance between getting started early and allowing some time to recover from surgery and returning home. They said that they wanted contact with the primary care facility early so that they could plan the start of their exercise regime as soon as possible. There were also some issues with fitting the exercises into their daily schedule; due to limited energy and follow-up visits within the healthcare system and the hospital, some participants struggled to fit rigid exercise sessions in their schedule, especially if they were working and no longer on sick leave. They then expressed a need for flexibility regarding the exercise sessions, such as when during the week they were to be performed. This was not described as an issue to the same extent by retired participants who, in contrast, expressed a desire to exercise at the primary care facility more often than twice weekly.

"About this training, it was probably more about fitting it in with work, you don't get time off to do this because it wasn't on a doctor's prescription but a project."

The location of the primary care facility was described as crucial to facilitate exercise, with participants describing unnecessary travel as something to be avoided, due both to their limited physical capacity and stamina, and to their need to plan regarding toilet visits. Close proximity to primary care was also described as a facilitator because it makes it easier to motivate oneself to go when it is not difficult to get there.

"But then of course you arranged it so that I had one right here in Solna, right across from where I live? But if I had had to travel and – council transport or something like that? Then I think I would have hesitated."

#### 5.4.4 Motivated to get back to normal

Participants described a strong motivation to get back to normal, to regain their strength and energy, and be able to do and enjoy activities as they used to, such as increasing independence, getting back to work, and resuming leisure activities. They described exercise as a way to achieve this but emphasised the need for assistance and support to do so. They said that they wanted to seize the opportunity that they had been given to exercise at the primary care facility with the support of a physiotherapist and wanted to make the most of this 12– week period. Their goal was described as getting back to their previous abilities and level of functioning and participation in daily life. They explained that exercise-related goals did not feel as relevant but instead focused on the overarching goal of getting back to normal, engaging in hobbies, working, sporting activities, gardening, or playing with grandchildren. Gradually regaining strength, energy, and endurance was also described as motivating and participants said that they felt they were making progress due to the exercise they had performed.

"The training programme has been a great help for me so to speak. It meant that directly after, directly after midsummer, just coming, just coming out of hospital and getting going, then it makes it easier to walk and easier, easier to exert oneself, and easier to do all the things that you normally do, in the garden and look after it and so on."

#### 5.4.5 Importance of a supportive environment

Considering their circumstances and conditions, participants described the importance of a supportive environment to be able to get started and follow through with exercise in primary care. Getting started is a challenge, but they explained that it is easier to motivate oneself to do it with social support from friends and family. Exercising under the supervision of a healthcare professional was also described as a major facilitating aspect. Fearing complications if they did anything wrong, they expressed a feeling of safety at the primary care facility, where they could manage to challenge themselves in a safe environment. The physical environment of primary care was also described as a facilitating aspect because many participants lacked previous experience of traditional exercise establishments or fitness centres. This, together with being frail, feeling weak, and having a urostomy, led the participants to state that they felt safer and more secure in a healthcare setting with other patients.

"But I definitely think that this rehab played a big part. That you got going and moving. Otherwise, it would no doubt be easy just to do nothing. Sit there and go oh dear, oh dear. Do I have the strength for this? But because I was doing things down there at the rehab, under supervision, then of course I noticed that I am not as locked down as all that. I can – there is guite a lot that I can do."

# 6 Discussion

This thesis has sought to contribute to the field of rehabilitation following abdominal cancer surgery by exploring methods to enhance postoperative mobilisation and evaluate the effect of physical rehabilitation following surgery. The goal was to facilitate patient adherence to and engagement with rehabilitation and to improve physical functioning and HRQoL. The context of the thesis, and of the included studies, can be divided into two rehabilitation settings: postoperative rehabilitation on the ward following surgery, focusing on methods to enhance mobilisation, and rehabilitation following discharge from hospital focusing on physical rehabilitation.

# 6.1 Enhanced mobilisation

In the postoperative setting, methods to enhance postoperative mobilisation were explored in Studies I and II. To gain a more complete understanding of users' experiences of the Activity Board as a tool to support postoperative mobilisation, healthcare professionals' experiences were explored in Study I of this thesis.

The results of Study I show that healthcare professionals perceive supporting patients' postoperative mobilisation as an important part of their daily work and that the Activity Board is a useful tool that facilitates this process (55). The board was perceived as easy to use and provided the healthcare professionals with valuable information regarding patients' mobilisation status and the level of mobilisation that was expected (55). Lack of time and insufficient knowledge among healthcare professionals about early mobilisation have been identified as barriers to early mobilisation following abdominal surgery (107). By using the board, healthcare professionals gain a better understanding of adequate levels of early mobilisation and find that their daily work in supporting patients is made easier.

Furthermore, healthcare professionals share the patients' experience described in another study that the board helps patients to take charge of their rehabilitation. Moreover, the board is described as promoting motivation and improving patients' adherence to exercise programmes. The results also indicate that patients take charge of their own rehabilitation and show a growing independence from healthcare professionals, making it easier for those professionals to support patients when using the board (54, 55). This also supports the work in alignment with person-centred healthcare, where the patient should be viewed as an active member of the healthcare team, rather than a passive participant (108).

The perceived patient engagement and their perceived increased motivation has support in the literature because, according to self-determination theory, intrinsic motivation increases when autonomy and competence are increased (109). One could argue that, when using the board and seeing progression, patients might experience increased autonomy and competence, something that was confirmed when exploring patients' experiences (54). However, the board was also described by healthcare professionals as large, cumbersome, somewhat obsolete, and challenging to disinfect in accordance with the hospital's hygiene policy, thus calling for a more modern option (55). This led to an investigation of other options as alternatives to the Activity Board to enhance mobilisation following surgery.

The Pedatim tablet explored in Study II was developed by the same company as the Activity Board (Scandinavian Phystec AB). It builds on the same principles but uses a digital tablet instead of a whiteboard (86). At the time of the study, the Pedatim tablet was still at the prototype stage and had not yet been used in this clinical context. Given that it builds on the same proven principles as the Activity Board, a feasibility study was conducted to evaluate whether the Pedatim tablet might be feasible as an alternative to the Activity Board for enhancing postoperative mobilisation following abdominal cancer surgery.

Both the process feasibility of the study design and the scientific feasibility of the intervention were evaluated. Based on predetermined feasibility criteria, the overall study design was deemed feasible, apart from the eligibility criteria. Of the 20 patients who received a Pedatim tablet, only one did not use it during their postoperative mobilisation on the ward, due to technical issues with the tablet, indicating a high level of compliance. The usability of the tablet was also high, with a mean score of 77, well above the benchmark score of 68, indicating that patients did not seem to have any issues with navigating or using the tablet (88). This compliance, in combination with the high usability and patients' answers to the open question added to the SUS, shows that the Pedatim tablet seems feasible for patients to use and that they have a positive attitude towards using it. So, even though it is a different format than the original Activity Board, the results indicate that the Pedatim tablet is perceived in a similar way,

promotes motivation, and is easy to use. There were some technical difficulties, but this is unsurprising given that the Pedatim tablets were prototypes and were being tested in a clinical setting for the first time. However, these problems did highlight the importance of technical support being available and the need for "champion-users" among the healthcare professionals on the ward (86). When attempting to implement e-health measures, it has been shown that involving healthcare professionals and ensuring that they are properly educated and trained is crucial for success, and this is something that needs to be considered for future implementation of the Pedatim tablet (110).

The scientific feasibility was defined as the Pedatim tablet's ability to promote physical activity on the ward. An overall progression in physical activity could be seen during the first postoperative days that was higher than we had seen in a previous study evaluating physical activity following abdominal cancer surgery in the same context (53). There are considerable individual differences and the sample in this study is not large enough to draw definite conclusions, but this indicates that the Pedatim tablet is feasible as a tool to promote postoperative mobilisation. However, the efficacy needs to be evaluated further.

Based on the results from Studies I and II, it seems that using a visual and interactive tool such as the Activity Board or the Pedatim tablet could be suitable options to enhance mobilisation following abdominal cancer surgery. As previously mentioned, increased adherence to postoperative protocols is associated with better clinical outcomes (43, 44, 46, 47). Even though adherence per se has not been specifically evaluated regarding the Activity Board or the Pedatim tablet, increased mobilisation has been observed (53, 86), which is also associated with positive clinical outcomes (48). Furthermore, factors associated with improved adherence can also be observed in our studies and in the design of the Activity Board and Pedatim tablet.

A review assessing key factors associated with adherence to physical exercise in patients with chronic conditions in older adults, including cancer, found key factors that could be related to our studies and these tools. For example, it is important that the exercise is individualised, that patients are supported by a multidisciplinary team, receive supervision, are properly informed regarding exercise and their condition, receive feedback, progress monitoring is available, patients experience self-efficacy and competence, have an active role, and are involved in goal setting (111). Based on the results of Studies I and II, and the previous evaluation of patients' experiences as well as an objective evaluation of the Activity Board, the concept of the Activity Board and the Pedatim tablet seems to promote a large number of these adherence-increasing factors (53-55, 86). As previously mentioned, patients also expressed a need for support from healthcare professionals and more information regarding postoperative mobilisation, something else that these tools provide (52).

## 6.2 Physical rehabilitation

In Studies III and IV, the focus shifts to physical rehabilitation following discharge from hospital. In Study III, the effects of a physical exercise programme in primary care following robot-assisted radical cystectomy for urinary bladder cancer were evaluated. There was no significant intervention-effect regarding the primary outcome of physical function. However, there were significant differences in favour of the intervention group in the domains of daily steps, fatigue, and HRQoL, indicating the potential benefits of supervised exercise following RARC. Previous studies have also shown that supervised exercise is beneficial for increasing physical functioning, improving HRQoL, and decreasing fatigue, anxiety, and depression in cancer patients in general (112, 113). However, there is a lack of evidence regarding the effects of exercise following RARC for urinary bladder cancer, and exercise following soon after surgery. Study III contributes with new insights into the potential benefits of exercise following RARC, and further strengthens the notion that physical activity and exercise should be included in the treatment pathway for patients undergoing RARC for urinary bladder cancer.

One reason for the insignificant difference between groups regarding the primary outcome of physical functioning, measured using the six-minute walking test, could be that the study involved an active control group. They received instructions to be physically active and take daily walks as well as performing sit-to-stand exercises. The compliance of the control group was not measured, but it would be reasonable to assume that this might have had an effect on their physical functioning as measured by the six-minute walking test. Even though the intervention group took a significantly higher number of daily steps than the control group, both groups had a median of over 7000 steps per day. This could be compared to a recent study that evaluated a prehabilitation programme for patients undergoing radical cystectomy, where patients walked a mean of 3000 steps per day 90 days following surgery (114). A definite conclusion cannot be drawn, but this indicates that the control group in our study might have higher

physical activity and physical functioning because they were encouraged to be physically active and take daily walks, something that is not included in the usual care pathway.

Furthermore, the additional significant effects seen in the intervention group could be associated with evidence showing that moderate-intensity aerobic exercise combined with resistance training is effective in reducing fatigue and increasing HRQoL in patients with other types of cancer (69). Besides physical rehabilitation containing both aerobic and resistance training, the intervention group was also monitored and supported by a physiotherapist during their exercise sessions. This might also have an impact on the results because the patient's self-efficacy and competence is supported by a healthcare professional. In previous studies, patients with urinary bladder cancer have expressed a need for support and information from healthcare professionals in order to feel confident about exercising (115, 116).

Thus, the largest effect of the exercise intervention in primary care following RARC for urinary bladder cancer seems to be improvements on HRQoL domains and psychological wellbeing. There are only a few studies that have explored the HRQoL of bladder cancer patients following treatment, and even fewer in relation to physical activity and exercise, and they show inconclusive results (70, 74). But Study III suggests that physical rehabilitation, and in particular supervised physical rehabilitation, might be beneficial for patients' HRQoL and psychological wellbeing following RARC due to urinary bladder cancer.

A recent study by Rammant et al. evaluating the relationship between physical activity and HRQoL one year following radical cystectomy confirms that a higher level of physical acidity can be correlated with an increased HRQoL (117). This can also be connected to the biopsychosocial model, because the biological, psychological, and social aspects of health can affect each other (26). By gradually increasing their physical functioning, and thus improving the biological aspects of health, patients might also perceive psychological benefits such as feeling stronger and less tired, being able to cope with everyday life, and participate in activities, and thus experience an improvement in HRQoL. They might also experience beneficial psychological effects from exercise which affects their HRQoL as the relationship between exercise and mental health is well established (118, 119).

In Study IV, patients' experiences of the physical rehabilitation programme in Study III were explored. The results yielded four themes illustrating aspects that affect patients' ability to exercise in primary care following RARC for urinary bladder cancer. Arriving home following surgery is associated with several challenges in daily life, and patients have to adapt to their new circumstances. They often express fear and uncertainty about rehabilitation and exercise. Other studies have also found that patients need time to adjust and that they struggle with their new circumstances after arriving home, which affects their ability to perform exercise (115, 116, 120). Fear of the consequences of exerting oneself or pushing too hard, such as the rupturing of surgical wounds, leakage of the urostomy, or hernia is described in Study IV and was also confirmed in these previous studies (115, 116). This indicates that patients might benefit from support and guidance from healthcare professionals when starting with rehabilitation and exercise following RARC, something that is also confirmed when exploring determinants for physical activity in patients with urinary bladder cancer (116, 120).

Patients expressed strong motivation to regain their abilities and return to a normal life. They were less interested in goals related to physical functioning or performance, but instead focused on regaining abilities in relation to their daily life, such as playing with grandchildren, returning to work, sporting activities, or gardening. This motivation to return to normal, and the goals associated with it, has been confirmed in other studies, as has the importance of patients gaining increased self-efficacy during Self-efficacy has been shown to be one of the most important predictors for physical activity behaviour in cancer survivors (121). Patients in Study IV stated that exercising under the supervision of a physiotherapist played a major role in in their confidence and building their self-efficacy regarding exercise over time. They also said that this allowed them to push their limits because they felt safe with the guidance provided by the physiotherapist. This further strengthens the notion that patients stand to gain from physical rehabilitation supervised by healthcare professionals.

Even though our interventions target patients' biological and physical aspects from the biopsychosocial model, the social aspect also needs to be taken into consideration (26). In a study exploring the need for support following radical cystectomy, patients also expressed the need for support from peers and partners (122). Social support has also been described by researchers as a facilitating aspect in promoting patients' physical activity (116). This was also found in Study IV, where friends and family played a role in supporting patients and increasing their motivation to pursue rehabilitation. Family caregivers often play a role in patients' rehabilitation process and should be incorporated by receiving targeted information that can help them to support patients more effectively (120). Another study also suggests that relatives should be considered an important resource in the rehabilitation process because they tend to have a positive impact on Considering that the social environment can have an impact on patients' perceptions of health and wellbeing according to the biopsychosocial model (26), and that the literature, including Study IV, suggests that the social environment also has a positive impact on patients' rehabilitation process, family caregivers should be incorporated into the rehabilitation pathway.

There is also a need to optimise the practical conditions to facilitate physical rehabilitation for patients following RARC. Patients said that not having to travel far for rehabilitation is both easier from a motivational standpoint, but also practical because travelling is associated with difficulties due to urinary issues, and reduced physical and mental energy. In a previous study, where rehabilitation was conducted at the hospital following cystectomy, a major limitation to patients' compliance was the distance they were required to travel (72). Patients also said that exercising in a healthcare setting such as primary care feels safer and more appropriate than at a regular fitness centre or public gym because they would rather be surrounded by peers and other patients, as well as having access to healthcare professionals.

The results from Studies III and IV suggest that physical rehabilitation in primary care following RARC for urinary bladder cancer could both increase daily physical activity and improve HRQoL. Furthermore, patients experience physical rehabilitation in primary care as beneficial because it helps them to regain their abilities and return to a normal life. Along with previous studies, the results of Studies III and IV further the notion that physical rehabilitation should be part of the treatment pathway for patients after surgery for urinary bladder cancer (70, 71). However, the need for support from healthcare professionals was emphasised by patients and should be taken into account when planning exercise interventions for these patients. Even though patients have a designated contact nurse at the hospital, they still expressed a need for more continuous support and monitoring. During the interviews in Study IV, patients explained that they felt a need for continued contact with healthcare providers

in general. Moreover, they said that participating in a study (Study III) not only provided them with the support they needed to engage in exercise and rehabilitation, but also made them feel safer and more confident because they received follow-ups from our research team. This further supports the notion that patients desire more support and contact with healthcare in general throughout their rehabilitation process.

## 6.3 Methodological considerations

#### 6.3.1 Trustworthiness

Studies I and IV were both qualitative studies using different methods. However, some methodological considerations are generic for qualitative studies, and they are therefore discussed together. When discussing the quality of qualitative studies, trustworthiness is essential (123). Trustworthiness consists of four areas that need to be considered when conducting qualitative research: credibility, transferability, dependability, and confirmability. Credibility in qualitative research can be used in preference to internal validity and represents the idea of how well the findings correspond to reality. It is therefore considered one of the key aspects of trustworthiness (123). Credibility is enhanced by applying wellestablished and suitable research methods. Transferability can be used in preference to external validity, and refers to the extent to which the findings of a study can be applied to other situations. Dependability addresses the issue of reliability, where measures should be taken to ensure that, given the same circumstances, the results would be the same if the study were to be repeated. Confirmability is used in preference to objectivity, where steps should be taken to ensure that the data is derived objectively from the informants, and is not dependent upon the researcher (123).

Another important aspect of qualitative research, which is also generic, is the sample size. The term saturation is often used in qualitative research, meaning that no further new data is forthcoming once a certain number of informants have been interviewed. Studies have been conducted to explore the concept of saturation and found that, when conducting individual interviews, most qualitative categories have been identified after six interviews, and after 12 interviews saturation has generally been achieved (124). The concept of saturation is problematic, however, because it is ill-defined and depends on several factors, including the researchers' experience with qualitative methods,

the interviewers' experience of interviewing, and the quality of the interview guide, to name just a few (124, 125).

Instead of saturation, Malterud et al. propose the concept of information power to guide sample size in qualitative research (126). Information power refers to the amount and quality of information that can be extracted from a sample; it depends on both the design of the study and the population providing the information (126). If the informants are non-specific, for example not purposefully sampled, and the aim is broad, the sample required is larger because the information power is considered low. In comparison, a narrow aim with a specific and purposive group of participants requires a smaller sample because the information power is considered high (126). There is still no specific number that can answer the question of how many informants is enough according to the concept of information power; instead, it should be used as a framework to discuss whether the sample appears to be sufficient or not (126).

There is also the question of the appropriate method for gathering data in qualitative research. In both Studies I and IV, interviews were chosen as the data-collection method. Interviews are the most widely used method in qualitative healthcare research and are appropriate when exploring views, beliefs, experiences, and motivations. Interviews are usually conducted individually or in focus groups, where group dynamics also generate data (127). When comparing individual interviews with focus groups, the total number of items generated on the same subject is similar, but on a personal basis, individual interviews can yield a broader range of items (128).

In Study I, focus groups were chosen because the group dynamic was also of interest and was thought to have the potential to generate valuable data. The ambition was to include different types of healthcare professionals in order to improve credibility and transferability (123). However, no physicians participated and, thus, their perspectives remain absent. The discussions in the focus groups were nuanced and opinions and experiences differed among the informants, strengthening credibility. Dependability is influenced by the method of using focus groups because the answers and data are dependent upon the group dynamics, something that might not be possible to reproduce. The study was conducted at a single hospital, which affects transferability negatively. Due to the purposive sampling and the specificity of the aim, together with the

similarities in the different groups' answers, the sample size was considered sufficient in accordance with the concept of information power (126).

Informants were divided into groups depending on which ward they worked on in order to create a safe environment for them and to fuel discussions regarding their work on the wards. The physiotherapists were gathered together in their own focus group to enable healthcare professionals on the wards to speak freely about any potentially negative aspects of the board, because the physiotherapists were responsible for the boards on the wards. Mixing professionals might have produced a different result. Credibility and confirmability were strengthened by using the same semi-structured interview guide for each interview, keeping the follow-up questions within similar domains, peer briefing and researcher triangulation, and prolonged engagement with the data (123).

In Study IV, individual interviews were conducted to enable a more in-depth exploration of patients' experiences. As for Study I, the information power is considered high because the sample was purposively recruited and the aim was narrow, focusing on patients' firsthand experiences (126). Thus, the 20 patients included were considered to be enough to answer the study's research question. However, a limitation is that only patients who had completed the intervention chose to participate in this study; patients who had prematurely ended their rehabilitation period did not choose to participate. This introduces selection bias and leaves potential barriers unexplored. Furthermore, in some cases, there had been a relatively long period of time between the end of the intervention and the interview, possibly introducing recall bias (129). Methods to enhance trustworthiness were taken in accordance with the suggestions made by Nowell et al. in thematic analysis (130). A prolonged engagement with the patients and the data was maintained, and researcher triangulation was used, with preliminary findings also being checked against the raw data. The study was also designed by members of the research team who had experience with qualitative methods, and a pilot interview was conducted before the main interviews began (130). The pilot interview did not result in any changes being made to the semi-structured interview guide.

#### 6.3.2 Internal and external validity

The internal validity refers to the rigor of the methodology in a study and the procedures that are taken to ensure that the findings of a study is true, and not

the result of alternative causes (131). Identifying potential threats to internal validity early in the planning of a study is crucial to minimize the risk of systematic errors and bias (131). Many aspects affect a study's internal validity. Examples of measures to enhance it include using a specific population, randomisation, blinding, intention-to-treat analysis, statistical analysis of baseline data, analysis of adherence to protocol, and using validated and standardized outcome measures, to name a few (129, 131). External validity, on the other hand, refers to the generalisability and applicability of a study's results to the population from which the study sample was drawn, or to other patients and settings (132). Generalisability concerns whether the sample is a good representation of the population and whether it is large enough to encompass all characteristics of that population (132). A threat to generalisability is selection bias, where the recruited sample is skewed or not representative of the population (129). The applicability aspect of external validity concerns whether study results can be applied in other contexts. This depends on whether the populations are comparable in terms of prognosis and outcomes, whether the treatment and method are suitable in different contexts and under various circumstances, which is something the reader must determine (132). However, there is a fine line between internal and external validity. A trial with very high internal validity is often so narrow and specific that it compromises its generalisability in terms of external validity (129). Validity is not a dichotomous concept but must be discussed and assessed based on various factors of a study's methodology (131).

A feasibility study was chosen for Study II in order to determine both the feasibility of the study process for a potential future efficacy trial, and to determine if the Pedatim tablet could be feasible as an intervention to support mobilisation following abdominal cancer surgery. The protocol for recruitment was designed on the basis of experience within the research group from previous and ongoing research studies in this context, involving this patient group. The number of patients who agreed to participate upon invitation was satisfactory. However, a recruitment issue was identified regarding the eligibility criteria. There is also a risk of selection bias in this study as the patients who accept participation in rehabilitation studies tend to be positive to physical activity, as well as the lack of randomisation (129). Ongoing clinical rehabilitation studies, logistical issues with screening, and the limited number of tablets available resulted in the vast majority of available patients being ineligible for inclusion.

The main reason for not conducting a randomised feasibility study using a control group was experience from previous and ongoing studies in this context and with these patient groups. The randomisation process itself was not something that needed to be evaluated, and we already had data on patients' physical activity levels on the wards from a previous study. But, given that the results of a clinical study are highly contextual, a control group would have enabled an objective comparison of mobilisation with and without the Pedatim tablet. It would also have allowed us to calculate effect size and future power calculations.

The feasibility criteria were named and set with inspiration from Thabane et al., where, in our study, the acceptability of the intervention was defined as usability of the tablet (85). As the intervention consisted of a novel digital tool, we wanted to assess the perceived usability among these often frail, elderly patients, and whether healthcare professionals found it easy to use from their perspective. Therefore, the aim was not to gain an objective determination of the tablet's usability, but rather to develop an understanding and identify potential needs before a future efficacy trial.

The SUS was chosen because it is one of the most widely used and validated measures for assessing usability in eHealth applications (89, 133). A limitation is that the SUS only gives an indication of usability and not a specific reason for high or low usability scores. Therefore, an open-ended question was added to the SUS form. This resulted in descriptions highlighting patients' need for support from healthcare professionals, and healthcare professionals' need for technical support. Despite numerous reminders, the response rate from healthcare professionals was low, potentially introducing sampling bias, and arguments for excluding their answers from the analysis would be valid. However, the data collected from the healthcare professionals provided a contrast to the patients' answers and highlighted important issues.

The activPAL accelerometer was used to assess patients' physical activity on the ward. Even though it is a well-validated device for measuring acceleration and position among frail elderly patients, there are some limitations, such as detecting slow walking speeds. It is not unreasonable that patients would have a low walking speed immediately following surgery, and this could lead to an underestimation of steps taken (134, 135).

There are several issues related to Study III that needs to be addressed, many of them a consequence of the covid-19 pandemic. Based on a prior power calculations, it was estimated that a minimum of 32 patients was needed to be able to show that the intervention would have an effect on the primary outcome physical function measured with the Six-minutes walking test (93). As patients treated for urinary bladder cancer often have a high risk of complications and readmissions, a large safety margin was taken as dropouts due to complications and comorbidities were assumed to be high (36, 37, 93). The goal was therefore to include a total of 120 patients. However, due to the covid-19 pandemic there were several practice issues that emerged which affected the study in several ways, not least regarding inclusion of patients. Despite the risk of selection bias, we believe that the sample is a good representation of the population. There were no significant differences regarding characteristics of the groups at baseline.

During periods of the pandemic, the urological ward was used as a covid–19 ward making inclusion of patients impossible as they were scattered all over the hospital. A decline in available patients was also identified, probably due to a lowered tendency to seek medical care for urinary symptoms during this time. These factors together with the recommendation to avoid unnecessary visits to the hospital resulted in a pause in the study on two occasions, resulting in a prolonged study period. Therefore, a decision to end the inclusion at 100 patients was taken due lack of time as the study had already been prolonged by 50% (one year) of the original time plan. Of these 100 included patients, 90 remained in the study to the point of baseline testing and randomization, ten patients dropped out of the study before this point.

The pandemic also had consequences for the administration of the intervention and gathering of data. In several periods during the pandemic, physiotherapists in primary care were furloughed, resulting in a shortage of primary care centers to refer patients to for the intervention. Patients who often were considered in high-risk groups were also disinclined to visit primary care or go outside during periods of the pandemic, resulting in several patients dropping out and ending the intervention prematurely. These circumstances also resulting in patients not being able to visit the hospital for follow-up testing. During periods of the pandemic, questionnaires and accelerometers were therefore sent to patients via post in order to collect data to the extent possible. Subsequently, there is missing data from several timepoints during the study, especially regarding the primary outcome of physical function. It cannot be excluded that this might have had a major impact on the findings of the study. Moreover, the limited number of participants and data also limits the possibility control for potential confounders.

The six-minute walk test was used to measure the primary outcome, physical functioning. It is a well-validated measurement to assess physical function in patients with cardiovascular and pulmonary disease, but also in cancer patients and community dwelling elderly (95, 136). There are several individual factors that can influence the result of the test. Determination when walking seems to be one factor that highly influences the result and can vairy substantially between individuals and context (137). There are also indications that it might not be suitable for serial measures as its ability to detect change might not be fully reliable (138). There have been studies evaluating the clinically relevant change of the six-minute walking test in patients with heart failure or chronic obstructive pulmonary disease, concluding that an improvement of 32–45 meters indicate a clinically relevant change (139–141). In Study III both the control group and the intervention group increased their results substantially more, 157 meters and 131 meters respectively. The six-minute walk test might therefore not have been the most optimal measure to detect differences in these two groups.

The EORTC QLQ-C30 is one of the most used measurements to assess HRQoL in cancer patients and has been validated for a wide range of cancers (142, 143). The EORTC QLQ-C30 is sensitive for change over time, the scoring of sub-scales range from 0 to 100 and a minimally important difference has previously been set to 10 points. In some sub-scales and cancers, the minimally important difference is as low as 5 points (144). In Study III, one of the analysed sub-scales of did not show a significant intervention effect, however, the change of 10 points still indicates a clinically relevant difference. The EORTC module for assessing HRQoL in patients with muscle-invasive bladder cancer, the EORTC BLM30, has not yet been properly validated. A study assessing the validity of the Dutch version found that the measure exhibited good measurement properties but that it needs to be validated further (145). Compared to other EORTC quality of life measures and modules, there is still no comprehensive scoring guide available. The measure contains six multi-item scales and one single item scale, all scored as symptom scales meaning that a higher score equals a higher symptom-burden. In a review exploring how the measure has been used in research they found that there were large variations in how the scales were used, some only used selected scales and others used all scales (146). In Study III, the results of all scales were assessed together to give an overall score but as there is no proper scoring manual, it remains uncertain whether this is a reasonable method to score the EORTC BLM30 module. However, it provided an overall score of patients perceived symptom burden related to the bladder that could be compared between the intervention group and control group, further analysis should later be made regarding differences of specific scales.

Some issues related to the intervention and referral process was also identified. Patients' status following surgery and the challenges they face when arriving home from the hospital seemed to have led patients to postpone the start of the intervention further then planed (within two weeks following discharge). The compliance to the scheduled rehabilitation sessions, and adherence to the protocol might also have fluctuated, something that can affect the results and needs further evaluation. The challenges of referring patients to rehabilitation and the adherence to rehabilitation protocols, both in chronic conditions and post-surgical is confirmed in a study by Sanches et al. (147). As with our patients, the postoperative status seems to highly influence patients willingness to attend rehabilitation were low physical activity, low self-efficacy and pain are barriers (147). Another study identifying patients who access musculoskeletal physiotherapy found that out of over 15 000 patients with a referral to the physio therapist, only 24 % accessed the physiotherapist (148). This suggests that only a referral might not be enough to support patients to start with rehabilitation and confirms issues experienced in our study. The initial plan was also to conduct a single-blinded trial where assessors conducting the testing of patients would be blinded to the patient's group allocation. However, this proved to be impossible due to logistical reasons and thus, assessors were not always blinded to the group allocation when conducing the tests, something further affecting the internal validity of the study.

# 7 Conclusions

Enhancing postoperative mobilisation following abdominal cancer surgery by using tools such as the Activity Board and the Pedatim tablet is feasible and useful for both patients and healthcare professionals. These tools increase patient motivation, participation, and adherence, as well as facilitating healthcare professionals' work in supporting patients' postoperative mobilisation. However, the effectiveness of the Pedatim tablet is yet to be objectively determined.

Exercise in primary care following radical cystectomy for urinary bladder cancer improves physical activity in daily life, reduces fatigue, and has a positive impact on health-related quality of life compared to a home exercise programme. Patients who exercised in primary care following radical cystectomy were also positive towards exercise because they were motivated to get back to normal life. However, they did face challenges when arriving home from surgery, which affected their ability to exercise, and therefore conditions need to be optimised to facilitate patients' rehabilitation. There is still a need to investigate the optimal delivery of physical rehabilitation and exercise following radical cystectomy for urinary bladder cancer, but this thesis confirms the notion that physical activity and exercise should be integrated into the treatment pathway.

#### 7.1 Conclusion of the individual studies

**Study I:** The results of the study show that the Activity Board could be a helpful tool in supporting postoperative mobilisation following abdominal cancer surgery. It facilitates daily work for healthcare professionals and promote patient participation.

**Study II:** Using the Pedatim tablet to enhance mobilisation following abdominal cancer surgery was deemed feasible. However, to determine its effectiveness, a RCT is needed. The study design was deemed feasible with changes to the eligibility criteria required before a RCT. A progression of patients' physical activity at the ward was observed and user experience was positive, indicating that it supports motivation. Involving and educating healthcare professionals, having available technical support is important for future implementation.

**Study III:** Both the intervention and control groups improved their physical function, but the patients who exercised in primary care experienced additional positive effects compared to the control group on physical activity, fatigue, and health-related quality of life. Hence, exercise in primary care after discharge

from hospital could be a promising method after radical cystectomy for urinary bladder cancer. Further research is needed to evaluate the process of this study as well as to understand the optimal delivery of physical activity following RARC for urinary bladder cancer.

**Study IV:** The study found that patients participating in Study III are positive towards physical exercise in primary care following radical RARC. They are motivated to get back to normal life but face major challenges when arriving home following surgery, which affect their ability to perform physical activity and engage in exercise. Conditions need to be optimised to support patients' ability to engage in exercise. A supportive environment is needed, including guidance from healthcare professionals enabling patients gradually to develop self-efficacy regarding exercise and focusing on goals related to patients' normal lives before surgery.

## 8 Points of perspective

Enhancing postoperative mobilisation following abdominal cancer surgery is important both to reduce the risk of complications, and to support patient recovery. This thesis showed that using tools that engage patients and increase their motivation, such as the Activity Board and the Pedatim tablet, could be beneficial as they increase patients' physical activity on the ward as well as increase their motivation and participation in the mobilisation process. These tools also facilitate healthcare professionals daily work in supporting patients which brings further benefits from an organisational standpoint. However, further research regarding the effectiveness of the Pedatim tablet is needed. Furthermore, there is still a need to continue to evaluate the effects of postoperative mobilisation and how it best should be structured.

This thesis showed that physical activity following RARC is beneficial and that an exercise intervention in primary care improves daily physical activity, reduces fatigue, and improves HRQoL. There are still knowledge gaps regarding how to best implement physical activity and exercise interventions for urinary bladder cancer patients following radical cystectomy. However, this thesis contributes to the building evidence that physical activity and exercise should be an integral part of the treatment pathway for patients with urinary bladder cancer.

There is also continued research needed based on this thesis. A process evaluation and cost-effectiveness analysis of Study III is needed to further understand how to implement physical activity and exercise interventions following RARC. The long-term effects of Study III and a potential difference in complications between the groups should also be evaluated. Patients need for support following RARC also needs to be explored further to better understand how to facilitate physical activity and exercise following surgery.

### 9 Acknowledgements

First and foremost, I would like to thank all **the patients** who participated in these studies. During the work on this thesis, I have met so many patients who saw it as their duty to contribute to research in order to help others. Their courage and sense of solidarity is an inspiration!

Also, my sincere gratitude to all **the healthcare professionals** at the Karolinska University Hospital that contributed to these studies and assisted our work at the wards.

Furthermore, a thank you to all **the primary care units** that contributed to the research by welcoming our patients for physical rehabilitation and providing invaluable feedback: Bromma Rehab, Hälsan Östertälje, Järfälla Rehab, Medfit Haninge, Norrtälje Rehab Tiohundra, Nykvarn Rehab, Praktikertjänst Rehab Flemingsberg, Praktikertjänst Rehab Huddinge, Praktikertjänst Rehab Liljeholmen, Praktikertjänst Rehab Sollentuna, Praktikertjänst Rehab Väsby, Praktikertjänst Rehab Älvsjö, Rehab City Lidingö, Solna Sundbyberg Rehab, Södermalm Rehab, Täby Rehab, Värmdö Rehab, and Åkersberga Rehab AktivaRE.

I would also like to thank **Karolinska Institutet** and the **Research School in Health Science (FiH)** for an excellent education.

I would especially like to thank the following people for their contribution and support during my doctoral education:

My main supervisor, **Maria Hagströmer**. There are few people with your patience, ability to encourage those around you, and generosity both professionally and personally. Your passion for education and pedagogy runs like a stream through your supervisorship, and as your student, I have thrived and constantly been encouraged to learn and reflect. Your flexibility is also unparalleled as you are always available for support and wisdom.

My co-supervisor, **Malin Nygren-Bonnier**. You are one of the main reasons that I started this path to begin with, as you saw potential in me already as a bachelor student. You have then continued to support me and contributed with your wide knowledge and experience throughout my journey. You always contribute with positive energy and prove that academia does not have to be synonymous with pretentiousness.

My co-supervisor, **Elisabeth Rydwik**. I have greatly appreciated your input and support during my education. You have always provided me with another point of view and a different perspective when I have struggled with issues or got stuck.

My co-supervisor, **Lars Henningsohn**. Thank you for your invaluable feedback from the medical point of view and for giving me a deeper understanding.

My mentor, **Lena Nilsson-Wikmar**. Our journey together began a long time ago, on another continent, and I feel lucky to have you as a mentor both in academia and life.

My colleagues, **Nina Brodin**, you are also one of the reasons I started my academic career and got interested in research. You showed me that research is fun and rewarding, both on a personal and a professional level. And, **Marie Halvorsen**, you are one of the most supporting persons I have met, and I have greatly valued your advice in hard times, and laughter in good times.

My close colleague and professional partner in crime during these years, **Andrea**. Thank you for all your support, problem solving, and for teaching me so much during this time. Also, thank you for questioning me when I seem confident but have no idea what I am talking about. And **Simon**, thank you for constantly being positive and flexible, always eager to solve the many problems that occur during clinical research.

A warm and special thanks to my original doctoral student colleagues who became my friends for life, **Nathalie**, and **Linn**. You are amazing people, and I am grateful for all the joy and tears that we have shared, and for the many more memorable moments to come! And to my dear **Cecilia**, thank you for your love and support during this time, for all the wonderful moments and adventures, and for giving me strength and motivation when I needed it, you are truly an inspiration.

**My research group** for providing a great learning environment, social exchange, and professional development.

To all my doctoral student colleagues who have supported and encouraged me during these years, especially **Andreas**, **Johanna**, **Charlotte**, and **Bérangère**.

To all the great clinical physiotherapists that have both assisted with the research but also provided support and great discussions, **Ulrika**, **Kitti**, **Thea**, **Michelle**, and **Isabelle**.

To all my **friends and family**, thank you for believing in me, encouraging me, and for helping me prove that no matter your circumstances, hard work and dedication makes anything possible.

A special thanks to **the funding bodies** that made this research possible: Magnus Bergvall Foundation, Regions Stockholm ALF-Medicine, Research School in Care Sciences, the Swedish Cancer Society, the Swedish Research Council, Tornspiran Foundation, Wallenius Foundation, and Åke Wiberg Foundation.

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